

On the VISCOSITY of HUMAN BLOOD PLASMA and SERUM in
HEALTH and DISEASE

A Thesis for the Degree of Doctor of Medicine.

Submitted to the University of Glasgow

by

JOHN HARKNESS

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VOLUME

ONE

Part 1

P R E F A C E

PREFACE

The estimation of the viscosity of blood plasma has attained an accepted place among the accredited tests of clinical pathology. The original suggestion that the plasma viscosity measurement might be valuable to the clinician was made by Miller and Whittington (269) in 1942. No-one except myself followed up this suggestion.

I worked at first in conjunction with Whittington and Houston (successor to Miller) and later with other clinical colleagues. All the interest in the test shown by other workers dates from the later papers of Houston, Harkness and Whittington (1945) (119) and Harkness, Houston and Whittington (1946) (99) and even that of Cowan and Harkness (1947) (54). Thus while I have no claim to the original idea of the estimation, I may claim that but for my intervention it might have sunk into oblivion and I do claim that I was responsible for the major part of the later development which led to its present status as a valuable test.

This thesis is based on that portion of the combined researches for which I was alone responsible. It is based on eight years work.

The main thesis consists of three parts. The first part deals with the investigations into the fundamental technical aspects of the estimation of the plasma viscosity; the second part is concerned with the plasma viscosity in normal persons and the changes in response to physiological stimuli; and the final part describes the changes in the plasma viscosity in disease.

An Appendix contains the details of the technical methods, the tabulated results, and some selected case histories. Reprints of the published papers are included in a pocket of the back cover.

* * * * *

Part 2

INTRODUCTION

Part 2INTRODUCTION.

§ 1.

Life on this planet probably began, in water, when a fundamental change occurred in a small mass of protoplasm and it became a single cell. Evolutionary development led to organisms of larger and more complicated single cells and later to organisms of more than one cell. These early forms of life, if they were to survive, had to be capable of dealing with all the changes occurring in their aqueous surroundings, eg., changes in reaction, temperature, chemical constitution, etc.. As the organisms increased in size only the outer cells were coming into contact with the water, while the inner cells were protected and thereby given scope to develop special functions, such as the contraction power in muscle cells and stimulus conduction in nerve cells.

All metabolic processes take place as reactions between substances in aqueous solution and an internal system for the transport of metabolites in solution was also developed. To Claude Bernard (18, 19) is the credit of first proposing the hypothesis that the larger products of evolution, a group which includes Man, live in an outer variable medium of water or air with which only the outer cell layers (plus the lining of the alimentary and respiratory systems) are in contact,

while the inner cells live in contact with an internal aqueous system (his "milieu intérieure") of almost constant characteristics. Although the internal medium maintains a constancy of its composition and its properties, recent work has demonstrated that this constancy does not arise from a static arrangement but rather from a dynamic equilibrium in which a balance is maintained in spite of large reactions.

The fluid within the human body has been divided into (Gamble (86)), (1) the intracellular fluid forming part of the protoplasm of the cells, and (2) the extracellular fluid consisting of (a) the interstitial fluid - the fluid lying between the cells and within the lymphatics, and of (b) the intravascular fluid - the fluid contained within the cardiovascular system of heart, arteries, veins and capillaries. It is again stressed that these fluids are in equilibrium and any alteration in one part of the system will produce an effort to re-establish the equilibrium by changes either in this primarily affected part or in the other parts. Alterations in the fluid of the cells will affect the fluid of the blood.

The blood in its course through the veins comes close to the skin at several parts of the body, especially in the antecubital fossae, and is there readily available for removal. Records show that from earliest historical times blood has been removed from these veins either to be studied as an aid to

diagnosis or as part of therapy. From the appearances of blood shed from these veins and allowed to clot in a shallow receiver, the Greek medical school of Cos (B.C.400) developed the 'Humoral Pathology' which affected the principles of medicine up to the nineteenth century. Venous blood, allowed to stand and clot, shows four layers:- an upper liquid layer of serum (= yellow bile of Greeks), a layer above the cells, known later as the 'buffy coat', formed by the contracted clot of fibrin (= phlegm), the upper layer of the erythrocytes which have more oxygen and thus a redder hue of oxyhaemoglobin (= blood), and the lower layer of de-oxygenated erythrocytes with reduced haemoglobin (= black bile of Greeks). The four humours corresponded with the Greek philosophy of classification into fours - eg. the four elements of air, water, fire and earth and the four qualities of dryness, moistness, warmth and coldness. The proportions of the four layers in the clotted blood varied from person to person, and in the individual in the course of an illness. According to the relative proportions of the layers the Greeks classified their patients (eg. an excess of phlegm = phlegmatic) and their treatment was directed to restore the balance of the layers of the blood. Later, the bleeding of patients as a form of therapy had as one of its objects the removal in the shed blood of the excessively large layer and thus a restoration towards normal proportions.

In the eighteenth and nineteenth centuries several attempts were made to correlate the blood appearances with the clinical condition and the chemical constitution of the blood, but there was little success in either field. The examination of the shed blood was one of the things which was neglected when the work of Virchow focussed all attention to the cellular structures of the body and their changes in disease.

In 1918, Fahraeus (73) re-introduced a modification of this historical examination of large volumes of shed blood. He used a solution of sodium citrate to prevent the blood from clotting and studied the rate at which the erythrocytes settled out in a long narrow column of this blood held in a vertical glass tube. He found that the rate of fall was faster than normal during the later months of pregnancy and proposed the use of this measurement as a diagnostic test for this condition. In a later publication (74) he studied the rate of fall in other disease conditions and he attempted to correlate the rate of fall with changes in the chemical composition of the plasma. This test was first known as the Blood Sedimentation Rate (contracted to BSR) but when it was later realised that it was only the erythrocytes which settled, the test was renamed as the Erythrocyte Sedimentation Rate (or ESR.). (Fahraeus (74) gives an excellent bibliography of the work by earlier writers who studied the rate of erythrocyte settling,

including that of John Hunter.)

Since the original paper by Fahraeus, over 3,000 articles in the English language alone have been published on this ESR test. Nevertheless, the knowledge of the chemicals which control the rate of fall has shown but little advance on his original work and must be regarded as unsatisfactory. The variation in the chemical constituents of the plasma and the ESR have formed the basis of numerous papers. It has been shown by several authors (Fahraeus (74,75), Tiffeneau and Gysin (241), Frazer and Rennie (84), and others) that there is some relationship between the changes in the plasma proteins and the changes in the ESR, while some other workers (eg. Bendien and Snapper (15)) go so far as to give a formula by which the ESR can be calculated from the protein fractions. Unfortunately, while this correlation formula may yield calculated values with excellent agreement with experimental results, the discrepancies can be frequent and large. No-one has yet demonstrated beyond question that the ESR changes are caused by changes in the proteins themselves and not by some other factor or factors changing much in the same phase as the proteins. Gordon and Wardley's (68) recent experiments with artificial plasma built up from purified protein fractions were unable to settle this problem.

I have had a special interest in the ESR test from the occasions when it was used to investigate an illness I had while a medical student. In 1941-42 I spent a year in a study of the haematological changes which follow the exhibition of sulphonamide drugs - I was investigating the claim by Browning (34) that rheumatic subjects are more likely to react severely to sulphonamides than patients ill from other diseases. Among my battery of tests I had included the Westergren ESR and I found that in serial testing the ESR might increase when the drug was given to a normal control subject. (See Fig. 1) This research programme had to be left incomplete because of war-time staffing difficulties. I transferred my research plan to an investigation of the relationship between the ESR changes and the alterations in the chemical composition of the plasma as induced by the sulphonamides. I hoped that by replacing the study of random pathological conditions by a controlled physiological experiment I might gain a success in a field of research in which so many previous workers had failed.

§ 2.

Following Fahraeus' original publication, several different methods were suggested of expressing the rate at which the erythrocytes settled in the column of blood but

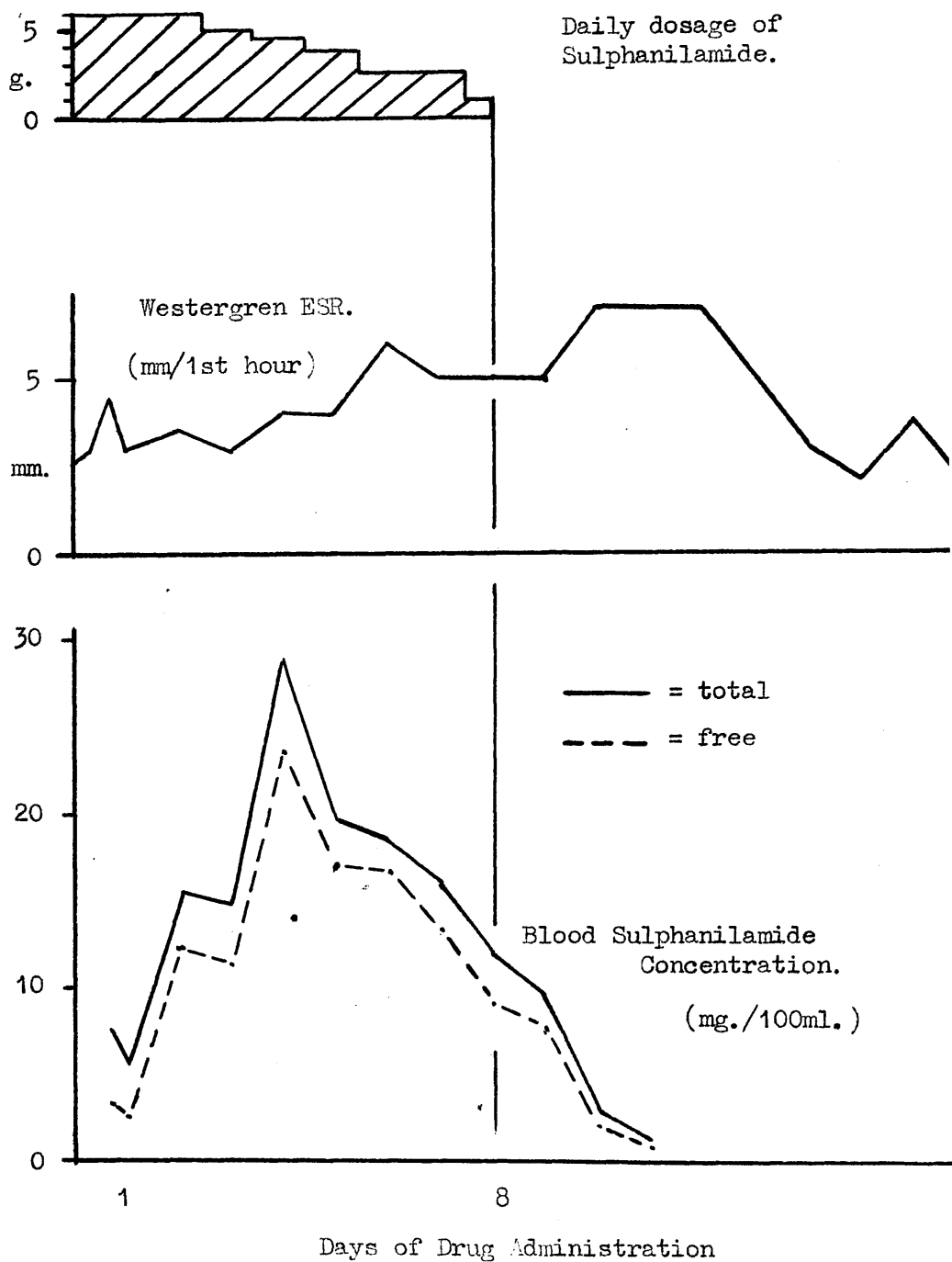


Fig. 1 The increase in the Westergren ESR. following the administration of Sulphanilamide to a normal subject in the ordinary therapeutic dosage.

there were only three basic forms, ie. (a) fall (in millimetres) in a fixed period of time (usually 1 hour); (b) time (in minutes) taken to fall a fixed distance (18 mm.); and (c) the rate of fall at that period when the velocity was maximal, the rate being expressed as a distance relative to time, such as mm./hour.

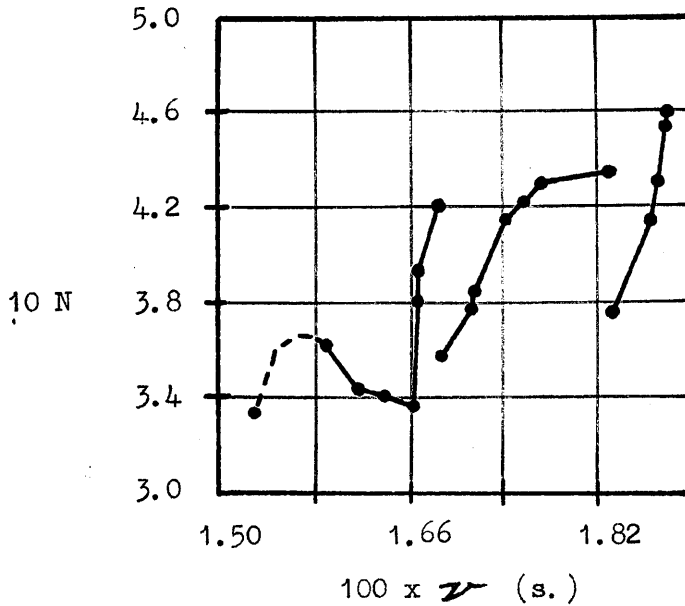
In 1940, Day (61) introduced another modification in the manner of expressing this rate of fall - his "Sedimentin Index". He measured the fall of the erythrocytes at frequent time intervals and plotted these figures on squared paper, time along one axis and distance of fall along the other; the points were joined to form a curve; a straight line was drawn along that part of the curve where the velocity of fall was maximal and from the slope of this straight line the distance (in millimetres) fallen in 100 minutes was estimated. The logarithm of this figure was his sedimentin index - it displaces the conventional units of time and distance. Day studied tuberculous patients. The novel mathematical treatment of the results rather over-awed Dr. A. K. Miller, medical superintendent of the Crossley Sanatorium, Frodsham, Cheshire, and he passed the journal on to Mr. R. B. Whittington, MSc. lecturer in hydrodynamics in the Engineering Department of Manchester University. Mr. Whittington had a special interest in hydrodynamics and a personal interest in the ESR test. He decided to carry out some investigations of the haemo-mechanics involved in the sedimentation of

erythrocytes in plasma using blood samples supplied by Dr. Miller from his sanatorium patients. The results were published in 1942 as four papers (249,250,251,252).

As the erythrocytes settle downwards they have to displace plasma and furthermore, plasma has to flow upwards into the space vacated by the cells. One of the factors which has to be considered in this process is the viscosity of the plasma as a highly-viscous plasma would resist both the displacement by the cells and the flow to the upper part of the tube more than a less viscous plasma. A plasma of low viscosity has been included among the factors producing rapid ESR values by the writers on the ESR test who dealt with this aspect only from a theoretical aspect. However, in his actual experiments, Whittington found an apparent anomaly in that the rapid ESR bloods frequently had a plasma of high viscosity. The correlation between the ESR values and those of the plasma viscosity was not linear. The 20 estimations of both values were reported by Whittington (249) and Whittington and Miller (252) and on a scatter diagram these 20 points were joined by three curved lines. (This 3-curve diagram was to affect all future work on the plasma viscosity estimations, in a manner not-foreseen at the time of the original publication.)(Fig. 2)

They next considered if there was any relationship between

Fig. 2



This figure has been traced from Whittington's (249) paper.

The citrate plasma viscosity has been multiplied by a hundred and expressed as "stokes".

"N" was the "agglutination number" and represented the size of the aggregates of the erythrocytes at the end of the first period of the sedimentation curve.

The sedimentation velocity is related to it very closely.

"N" can be calculated from viscosity measurements, but as with other non-Newtonian fluids, the value of "N" depends upon the characters of the particular viscometer in which it is measured. Whittington obtained a correlation between "N" and the sedimentation velocity (V_t) according to the equation -

$$N^{7.7} = 0.759 V_t$$

the plasma viscosity value and the clinical condition of the patient from which the blood was drawn. They found that the plasma viscosity was generally increased in tuberculosis and that there was a correlation between the degree of this increase and the severity of the clinical condition as assessed by the Ministry of Health scheme (166). The results of 63 tests were published in the Lancet (267) with the recommendation that the estimation of the plasma viscosity could aid the clinician in the management of his tuberculous patients.

At the end of 1942 Dr. Miller left the Crossley Sanatorium. Mr. Whittington knew nothing of the proposed successor and of any further work on the plasma viscosity in the Crossley Sanatorium or elsewhere.

§ 3.

During 1941 and 1942 there were several articles on the ESR test in the British Medical Journal which resulted in a lengthy correspondence. The final letter, by Hilliard (112), quoted Whittington's papers and I worked back through the whole series. I was specially interested by the relationship between the ESR and plasma viscosity results, and by one sentence (251) - "In the case of viscosity, for example, though as far as we are aware this has not yet been studied, it is inconceivable that the plasma protein fractions should

all exert the same relative influence on the plasma viscosity as on the agglutination". ("Agglutination" is the clumping of the erythrocytes into aggregates which sediment together, and the ESR has been shown to be dependent largely on the size of these aggregates and thus on the agglutination.)

I then had the idea of including the estimation of the plasma viscosity into my scheme for the investigation of the ESR test. Whittington's original 20 duplicate estimations of plasma viscosity and ESR indicated that if there was a relationship between the two values it could not be a simple one. Yet I considered the possibility of correlating the changes in the ESR with those of the plasma viscosity, the plasma viscosity changes with those in the constituents of the plasma, and thence indirectly correlating the ESR changes with the constituents of the plasma.

Therefore I travelled from Montrose to Manchester to discuss my problems with Mr. Whittington and found him, as described in the previous section, with his colleague, Dr. Miller, due to leave the Crossley Sanatorium.

§ 4.

Whittington and I found that our problems and fields of investigation overlapped and we decided that by combining our forces into a common plan we could better tackle these

problems than by continuing in our individual researches. We decided that Whittington should continue with his academic research on the viscosity of pure liquids and with such plasma as he might receive from the Crossley Sanatorium, while I attempted to find some correlation between the clinical severity of a variety of diseases, the chemical composition of the plasma (especially the protein fractions), the ESR, and the plasma viscosity. It was to add other physical properties of plasma, such as osmotic pressure, specific gravity, and surface tension, when I could obtain the appropriate apparatus. This partnership has continued since (unbroken even by the departure of Whittington to America in 1948) and a series of papers has been published on our results under our joint authorship (99,100,101,102,118,119,120).

§ 5.

Other Collaborators.

Dr. John Houston succeeded Dr. Miller at the Crossley. He became interested in the researches and assisted both by giving Whittington his laboratory facilities and by dealing with the clinical aspect in the choice of patients and the assessment of their clinical condition.

Dr. Ian C. Cowan, director of the department of physical medicine at Sunderland Royal Infirmary, assisted us in the study

of rheumatic diseases by selecting patients for study and by assessing the severity of their conditions. We were also helped by Dr Nicol and Mr Waugh, the other members of the team of doctors which controlled the Rheumatism Clinic. (See Nicol, Waugh, Cowan and Harkness (182)). Dr Cowan has obtained his M.D. degree at Aberdeen University in 1950 for a thesis based on his share of this work.

Dr. A. B. White helped at Portsmouth by selection of patients fulfilling the requirements for a special study. He was responsible for the final assessment of their clinical condition.

In addition, many other doctors assisted me in a less direct manner by sending me patients with diseases in which I might find my investigations of special interest and by making available the clinical information concerning them.

§ 6.

As many of the results have already appeared in papers of joint authorship, it is essential that the share of each author should be clearly defined.

The Crossley laboratory consists of a small room with the equipment necessary for urine and sputum testing, plus the apparatus for estimating the plasma viscosity, ESR, and haematocrit values. Whittington visited once per week or month; the other

technical assistance was supplied by convalescent patients. Drs. Houston, Cowan, and White did no laboratory work. Their share consisted in the choice and examination of patients. The papers were written mostly by myself, modified by Whittington, and approved of by these clinicians. Whittington (a) supervised the estimation of, and estimated the plasma viscosities of Houston's patients, (b) carried out experiments on the viscosity of pure liquids, (c) calibrated and correlated the early viscometers, (d) analysed the results produced in all the laboratories, and (e) produced the mathematical analysis of the protein fractions in our paper (100).

I, myself, (1) assessed the clinical condition of my Montrose patients, (2) assisted in the assessment of the Sunderland and Portsmouth patients, (3) estimated the viscosity of the plasma and serum of all these patients (3,000 + tests), (4) estimated the protein fractions and the non-protein-nitrogen content of these plasmata and sera, (5) prepared pure fractions of albumin and globulin, (6) estimated the viscosity and specific gravity of protein solutions, (7) estimated the specific gravity of plasma and serum, (8) measured the ESR, (9) conducted further experiments with sulphonamides, (10) calibrated and correlated the later viscometers, (11) also

analyzed the results produced by my laboratory, and (12) carried out the series of experiments on anticoagulants, ultrafiltrates, temperature effects, etc. (to be described in detail later) which were necessary before the technical aspect of the plasma viscosity test could be regarded as satisfactory.

There are many problems arising in the course of these researches which await solution, yet I believe that a stage has now been reached at which, from my own results alone, I can give a general picture of the present knowledge on the subject of the estimation of the plasma viscosity. From these results this thesis is derived.

§ 7.

The plasma viscosity had been measured by several earlier workers in a rather haphazard manner but it is to Whittington and Miller that the credit should go for the original use of this measurement as a clinical pathology test as a guide to the severity of the clinical condition in pulmonary tuberculosis. Nevertheless, almost identical work was being done in China by T'ang and Wang (240) at the same time as the English workers were carrying out their experiments; this Chinese paper only came to the notice of British readers in 1946.

I was the only person to give further attention to the paper of Miller and Whittington (267) and to carry out further tests

with their technique.

The plasma viscosity test is now used in many parts of the world by workers who date their interest to the papers of Houston, Whittington and Harkness (99,119) or even to the later paper by Cowan and Harkness (54).

Thus, while I have no claim to the original idea of this test, I may claim that my work has been largely responsible in advancing the test to its present state of an accepted and valued laboratory procedure.

* * * * *

Part 3DEFINITIONS

Part 3DEFINITIONS.

In deciding which terms and tests have to be defined for the reader of this thesis I have to assume that he has a knowledge of the interpretation of the values obtained in the ordinary tests of clinical pathology, even if the technical details are not so well known. I will also assume that he knows nothing whatsoever concerning the estimation of the viscosity of plasma.

(A) Viscosity and Plasma Viscosity.

Physicists are still uncertain concerning that physical property of liquids called "viscosity". The viscosity of gases is understood much better; certain equations and formulae have been derived by which this viscosity can be estimated. The earlier workers on the viscosity of liquids applied these same formulae, with modifications, to the liquids in the belief that the viscosity of a liquid was analogous to the viscosity of a gas. Unfortunately, it has been shown that such an assumption was not valid. In the past few years, many workers (including Whittington) have begun their investigations anew on this property of liquids.

A practical example will help in giving an idea of what is meant by the term "viscosity". Consider three 40-gallon casks containing water, treacle, and pitch and in each we make an

air-inlet in the lid and remove a 3" bung in the side near the bottom. The water would gush forth, the treacle would ooze out, and the pitch would take days to months to empty out. Each liquid resisted the force of gravity in its attempt to force it through the hole and it is to this property of 'resistance to change in shape' that the term viscosity is applied.

The British Standard Specification 188:1937 ("Determination of Viscosity of Liquids in Absolute (C.G.S.) Units") contains the following definitions. - "The viscosity of a fluid is that property to which is due the internal resistance offered to the motion of any portion of that fluid with a velocity different from that of a contiguous portion". It determines the resistance to shear (shear = forces in slow stirring, flow through a capillary, and the like). For quantitative expression of viscosity a distinction is made between the dynamic viscosity (also referred to as "absolute" viscosity)(symbol = μ) and the kinematic viscosity (symbol = ν). "The dynamic viscosity of a fluid is the tangential force on unit area of either of two parallel planes at unit distance apart when the space between the planes is filled with the fluid in question and one of the planes moves with unit velocity in its own plane relatively to the other". "The kinematic viscosity of a fluid is equal to the quotient of the dynamic viscosity by the density of the

fluid, thus $\nu = \frac{\eta}{\phi}$ where ϕ is the density of the fluid". The C.G.S. unit of dynamic viscosity is the "poise", that of kinematic viscosity is the "stoke". The centistoke ($=1/100$ of stoke) is a unit of more convenient dimensions for plasma studies as the kinematic viscosity of water at 20°C. is 1.008 centistoke. (Usual contraction for centistoke = cs.)(31).

There is a further complication to this subject. Fluids can be divided into "Newtonian" and "non-Newtonian". With Newtonian fluids (a group which includes such liquids as water, benzene, aqueous solutions of electrolytes) the viscosity can be measured under a variety of conditions but identical values are obtained. In contrast, the viscosity of a non-Newtonian fluid is dependent upon the conditions under which it is estimated and the viscosity is a function of each instrument. Using 'x' viscometers, calibrated with Newtonian fluids, a single non-Newtonian fluid might yield 'x' viscosity results, all differing slightly from each other. It is obvious that the term 'viscosity' cannot properly be applied to non-Newtonian fluids as the corresponding property cannot come within the limits of the first definition above - but the term of 'viscosity' is retained for lack of a better term.

Among the non-Newtonian fluids is the group of "colloidal solutions" of which plasma and serum are members.

Thus when I write of 'plasma viscosity' it will be realised that I mean - "that property which in Newtonian fluids is known as 'viscosity' " and that the physical property must be interpreted only according to the known conditions under which it is estimated.

(B) Plasma and Serum Protein Fractions.

The plasma of human blood normally contains 6-8 g. protein per 100 ml. of protein. This protein is not uniform but can be divided into a number of fractions: the number of the fractions and the nature of the fractions depend upon the technique used in the separation. The fractions separate according to their physico-chemical properties and not according to their original function within the body.

Plasma protein can be subdivided into two major fractions called Albumin and Globulin: that portion of the Globulin which has the power to form the fibrin clot is called Fibrinogen, and it has become customary to speak of three fractions, viz. Albumin, Globulin (meaning total globulin minus fibrinogen), and Fibrinogen. Thereby we have the same Albumin and Globulin values for plasma and serum, as the latter is only the plasma from which the fibrin has been removed. This convention is used throughout this thesis.

The best method available to our laboratory for the protein fractionation was the classical salting-out technique of Howe in which the total globulin was precipitated from serum by a 1.5 molar solution of sodium sulphate. The albumin of the filtrate was measured, the globulin was obtained as the difference from the total serum protein, and fibrinogen was measured as the fibrin clot obtainable from plasma.

The fractions of albumin and globulin prepared for the study of protein solutions depended on similar methods so that the results from solution experiments should be applicable to the plasma and serum. The fibrinogen was obtained from the Medical Research Council, without knowledge of its method of preparation.

(C) ESR or Erythrocyte Sedimentation Rate.

The erythrocyte is so minute (diameter = 7μ) that the surface area is very large relative to its volume and mass. In a column of blood there are groups of forces acting in opposition. The difference in the specific gravities of the cells (= 1.097 approx.) and the plasma (= 1.027 approx.) tends to make the cells fall towards the bottom of the tube: the friction between the cell surface and plasma, the mutual repulsion of the cells because of their electrical potential, etc. hinder this fall.

The resultant force is so small that the cells would take many hours to sediment, if the cells were to remain as separate units.

However, in all bloods there is another force of variable magnitude which aggregates the cells into clumps in which the surface area (increasing as the square of the radius) is now less in relation to the mass (increasing as the cube of the radius). These larger masses are subject to relatively less resistance in their fall than the single cells: they fall rapidly. There is a sharp upper border where the upper margin of the column of sedimenting cells meets the clear supernatant plasma.

The ESR test measures the rate at which this upper border to the erythrocyte column falls and is usually expressed as the depth of plasma obtained in defined time periods. If the depth of the plasma is noted at intervals of a few minutes in a tall column of blood and if these results are plotted on squared paper, graphs such as shown in Fig. 3 are obtained. The sigmoid curves can be divided into three parts as indicated in line II - first part, OX, "period of aggregation", during which the cells first fall slowly as discrete units and later a little faster as the aggregates are formed: second part, XY, "period of maximum velocity", during which the aggregates increase no more in size but fall at a uniform speed which is also the maximum

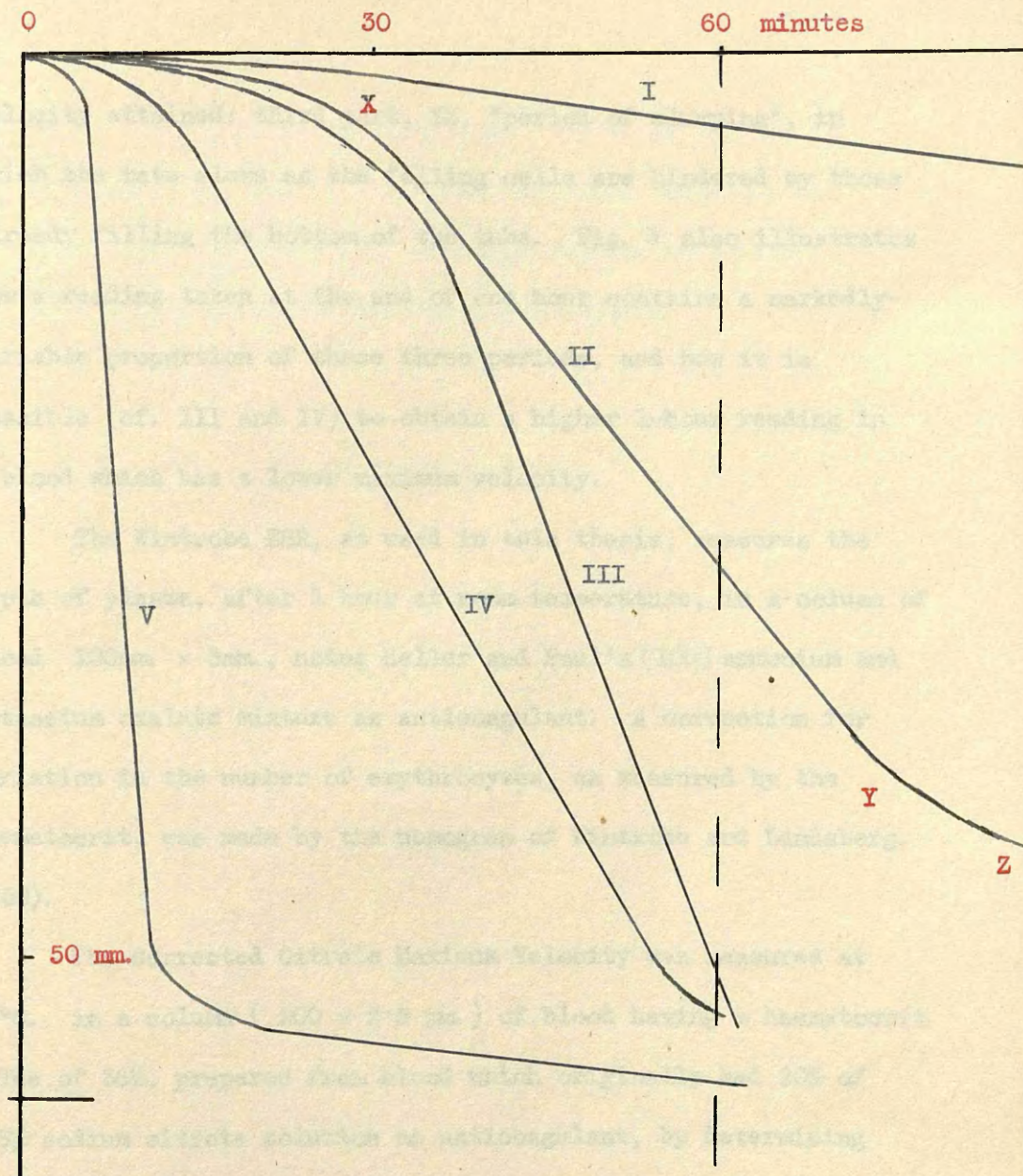


Fig. 3 The different types of sedimentation curve.

The curves are prepared by joining the frequent plots corresponding to the distance fallen (in mm.) on the vertical scale against the time (in minutes) on the horizontal scale.

The part - XY - is the period of constant and maximum sedimentation velocity.

velocity attained: third part, YZ, "period of clumping", in which the rate slows as the falling cells are hindered by those already filling the bottom of the tube. Fig. 3 also illustrates how a reading taken at the end of one hour contains a markedly-variable proportion of these three periods, and how it is possible (cf. III and IV) to obtain a higher 1-hour reading in a blood which has a lower maximum velocity.

The Wintrobe ESR, as used in this thesis, measures the depth of plasma, after 1 hour at room temperature, in a column of blood 100mm. \times 3mm., using Heller and Paul's (106) ammonium and potassium oxalate mixture as anticoagulant. A correction for variation in the number of erythrocytes, as measured by the haematocrit, was made by the nomogram of Wintrobe and Landsberg. (258).

The Corrected Citrate Maximum Velocity was measured at 20°C. in a column (200 \times 2.5 mm.) of blood having a haematocrit value of 36%, prepared from blood which originally had 20% of 3.8% sodium citrate solution as anticoagulant, by determining the maximum velocity from frequent readings and a graph such as in Fig. 3.

(D) Note on Significance of Results.

It is essential that the reader is warned that in this thesis there is a correlation of the results of many tests.

The text should leave the reader in no doubt as to what is being compared - whether it is the numerical values of the tests or the interpretations of these results as usually applied by physicians or clinical pathologists.

* * * * *

Part 4METHODS

Part 4METHODS

This section supplies the details of the estimation of the plasma viscosity only. The other techniques are described in the appendix.

The Estimation of the Viscosity of Plasma and other liquids.

<u>Apparatus:-</u> Water-bath at 20.0°C	<u>Reagents:-</u> Distilled water
Whittington viscometer	Absolute alcohol
Stop-watch	Dried ether
Water suction-pump.	3% aq. NaOH soln.

Water-bath - These baths cost £30-£200 to purchase. A satisfactory model was made from a glass accumulator tank, 10"x12"x14" deep, holding 30 pints to its working level. The temperature could be controlled manually to within 0.03°C. as measured on a N.P.L. thermometer graduated in 0.1 degrees; the heating was by a small immersion heater and cooling was by ice cubes or cold water added. A light source behind the bath tended to neutralise the heat loss from the tank and allowed a more accurate reading of fluid levels in the viscometer: see Fig. 4.

Whittington Viscometer - see Fig. 5. Whittington designed this modification of the classical Ostwald viscometer which required about 10 ml. fluid so that his instrument requires only 0.7 - 1.0 ml. The viscometer is of very simple construction. Two Westergren ESR. tubes (300 mm. long and 2.5 mm. bore, with 200 mm. graduations at one end) were joined to the ends of a U-shaped capillary of 200 mm. length and 0.35 mm. diameter, and

Fig. 4 The arrangement of the apparatus for the viscosity estimation.

The viscometer is adjusted until the limbs are vertical, as compared with the plumb-line.

The ESR. tube is also made vertical by comparison with the plumb-line.

The water is heated by the immersion heater and mixed by the electric stirrer.

A small electric bulb is placed behind the bath to illuminate the graduations of the glass-ware. It is not shown in this sketch.

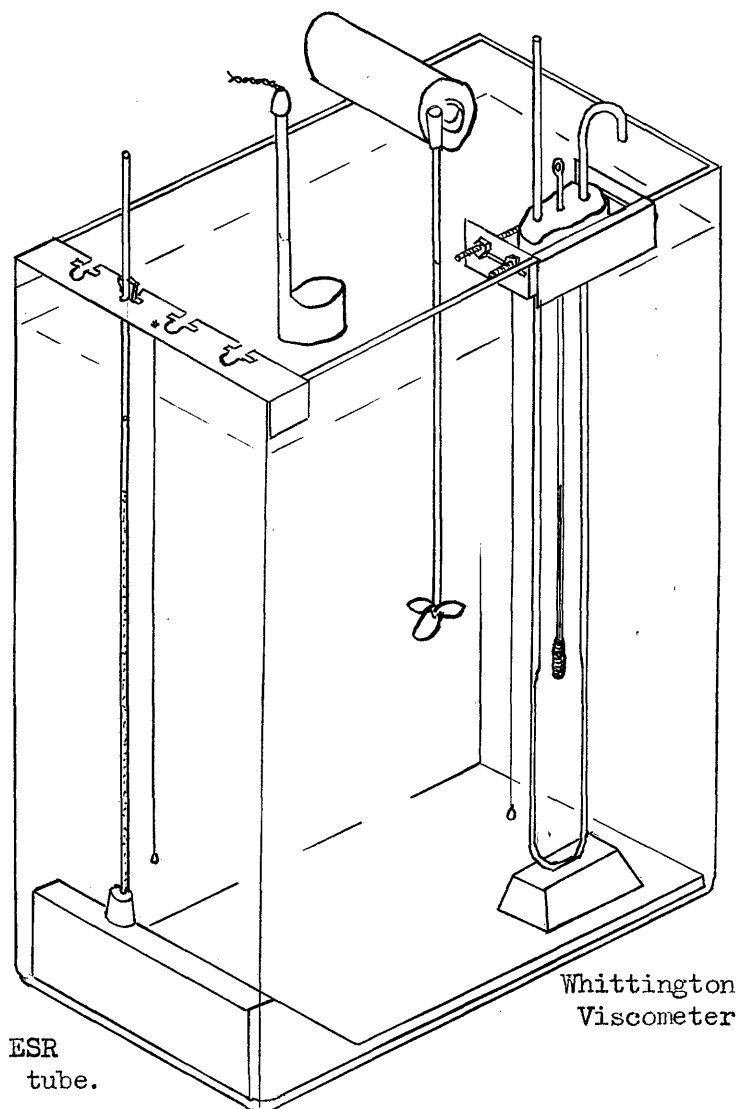
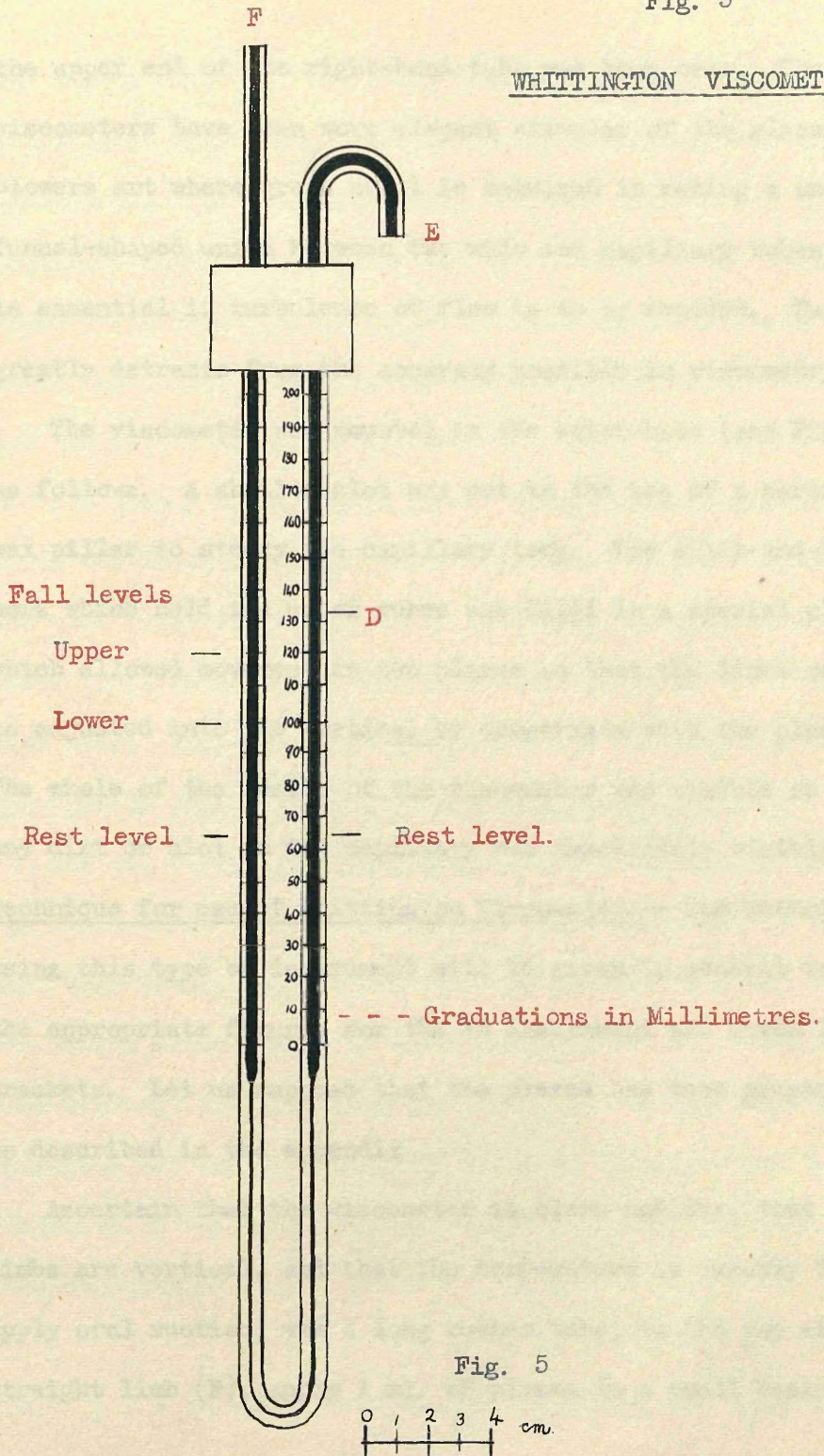


Fig. 5

WHITTINGTON VISCOMETER.



the upper end of the right-hand tube was bent over. The later viscometers have been more elegant examples of the glass-blowers art where great skill is required in making a smooth funnel-shaped union between the wide and capillary tubes which is essential if turbulence of flow is to be avoided. Turbulence greatly detracts from the accuracy possible in viscometry.

The viscometer was mounted in the water-bath (see Fig. 4) as follows. A shallow slot was cut in the top of a paraffin wax pillar to steady the capillary loop. The split-and-wired cork which held the upper tubes was fixed in a special clamp which allowed movement in two planes so that the limbs could be adjusted into the vertical by comparison with the plumb-line. The whole of the inside of the viscometer was visible so that any dirt or clot in the capillary was immediately visible.

Technique for use of Whittington Viscometer.-- The method for using this type of instrument will be given in general terms and the appropriate figures for the V5 instrument are given in brackets. Let us suppose that the plasma has been prepared as described in the appendix.

Ascertain that the viscometer is clean and dry, that the limbs are vertical, and that the temperature is exactly 20.0°C . Apply oral suction, via a long rubber tube, to the top of the straight limb (F), apply 1 ml. of plasma in a small basin below

the curved limb (E), and bring the fluid level round to 'D' (132) which experience shows as the most suitable for each instrument. The basin is rapidly removed and suction is continued until the level in the left limb is 3 mm. above the upper "fall" level (123). Allow to drain for 3 minutes. The fluid levels are made equal in both limbs by suction at 'E', and the levels noted to the nearest 1/10 th mm. Change now to suction from a water vacuum pump. Apply suction again at 'F' to bring the level above the upper fall level by 2mm. (122). Note the time taken for the level to fall from the upper (120) to the lower (100) fall level. Repeat the levelling of the fluid on both sides, and again note the time taken for level to fall.

Calculation of the Viscosity from experimental results:-

(1) The viscometer calibration is made with the fluid-level in the limbs which we call the "ideal" rest levels but it is obvious that such levels will not be attained on each filling. Also, the levels alter during an experiment because of a continual slow drainage of fluid from the upper part of the right limb which was wet in the process of filling. A correction for the variation of the experimental rest levels from the ideal is made in equation (1)

$$T' = T^o (1 - \Delta k) \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where k = a constant (0.0116); T^o = experimental time of fall;

T' = time which would have been obtained if the rest levels had been ideal; and Δ = (sum of experimental rest levels - sum of ideal rest levels (129.7)).

(2) The kinematic viscosity in centistokes is found by equation

$$\nu = AT' + B/T' + C \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where A , B , and C are constants.

For Newtonian fluids, the factors for viscometer V5 are

$$A = + 0.01055, \quad B = + 7.369, \quad C = 0$$

For Plasma, for reasons to be given later, the factors are

$$A = + 0.01254, \quad B = + 8.519, \quad C = - 0.201$$

These complicated equations can be readily solved by the use of a nomogram. Fig. 6 is a copy of that prepared for the V5 instrument except that the laboratory drawing is much larger. The viscosity value to be reported is the average of the duplicate experimental results.

Cleaning the viscometer. - The plasma is recovered by applying pressure at 'F'. The viscometer is washed and dried by suction at 'F' to draw through in succession - water, alcohol, ether, air. Time taken for the complete test, from drying to drying, is about 15 minutes. Other small laboratory duties can also be undertaken in this period when the fluid is draining or falling.

To maintain the viscometer free from protein deposit the instrument should be cleaned regularly with dilute caustic soda solution (3-10%). I usually begin the week with this treatment. A thorough washing with water is necessary to remove the last trace of alkali.

It is recommended that a similar washing with alkali should follow any plasma known to have a high globulin content, or the preliminary cleansing of the protein can be made with normal saline which will not precipitate the globulin as would distilled water.

* * * * *

Part 5M A T E R I A L

Part 5.MATERIAL.(A) Royal Asylum of Montrose. (1943 - 1946)

421 tests were made on the physically ill patients among the total population of 700, and on a few sick members of the staff. I was the medical officer in charge of the male patients and staff.

These tests included many on tuberculosis which was rife among the patients and on pyogenic infections. A series of general paralysis of the insane cases was also studied.

(B) Sunderland (1946 - 1948)

The laboratory at Sunderland Royal Infirmary carried out the pathological investigations for all the hospitals in the region from the Tyne to Tees.

The close liaison with the Rheumatism Clinic produced 1067 tests in the rheumatic diseases. Another 424 tests were made on the patients in the general medical and surgical wards, especially on the malignant diseases.

(C) Portsmouth. (1948 - 1952)

The Central Laboratory supplies the pathology service for the Portsmouth Area and the Isle of Wight.

The 1218 tests, at the time of typing, include most of the normal control series, the subjects of physiological stimuli, many tests on children, a further series of G.P.I. patients, the series of sarcoidosis subjects, the series of tests during pregnancy, and a special study of some aspects of tuberculosis.

Many of the tests reported in the Pre-clinical Part (Part 6) which deals with the technical aspects of the estimation of the plasma viscosity were made at Portsmouth and involved an additional measurement of several hundred viscosities.

* * * * *

Part 6PRECLINICALSTUDIES

Part 6.Studies on the non-clinical aspects of the estimation of the
viscosity of plasma and serum.

This part of the thesis is concerned with the study of that physical property of plasma and serum which in Newtonian fluids has been defined as "viscosity". It is the preliminary to the following part in which the variations in the plasma viscosity under physiological conditions are described, and to the later part in which the changes in the plasma viscosity as a result of disease conditions are considered.

We are here chiefly concerned with two problems - the errors possible, from a variety of causes, in the estimation of the plasma viscosity; and the relation of the plasma and serum viscosities to the chemical composition of their respective fluids. Other relevant but lesser problems are also discussed.

(A) The potential errors of my technique.

§ 1. General consideration of the technique.

If the Whittington viscometer has been filled to the proper rest levels with a representative sample of a plasma, the error arising in the actual estimation should be of the order of 0.01 cs. or less (= less than 0.5% of total viscosity value). There are five possible sources of error - (1) time of fall, (2) rest levels,

(3) temperature of water-bath, (4) dirt in viscometer, and (5) alteration in the characteristics of the viscometer. Let us consider these in turn.

(1) Error in timing the fall.

There is a period of time between the eye detecting the arrival of the meniscus to the graduation marks and the movement of the finger to stop the watch and this "reaction time" may vary slightly (eg. by 1/10th second). The process to be timed at the beginning and end of the fall period is exactly the same and the reaction time should be the same for each process. They thus tend to cancel each other out. Examples of serial tests, when the rest levels had become constant, are 164.1, 163.6, 164.0, 164.0, 164.2 seconds, and 159.4, 159.4, 159.6, 159.6, 159.6 secs..

Larger errors could be introduced by parallax by making the eye too high or too low in relation to the graduations. This source of error was almost excluded by drawing lines on the back of the water-bath at the same height as these graduations; the eye was adjusted to bring the graduation and its corresponding back level into line.

The error due to timing should not exceed 0.5 seconds and is usually of the order of 0.2 or 0.3 seconds in a total of 150 seconds (= 0.2%).

(2) Error due to variation in the rest levels.

An error of 0.1 mm. in reading a rest level introduces an error of 0.002 cs.; however, the meniscus level should be read with an accuracy which does not include so large an error as even 0.1 mm. The secret of an accurate reading lies in obtaining a satisfactory system of illumination.

During the filling of the viscometer a thin film of plasma remains on the wall of the right limb. The plasma drains down slowly to increase the volume of fluid under test; drainage is greatest in the first three minutes and negligible after twenty minutes. Similarly, a little plasma remains on the wall of the left limb when the fluid levels are made equal after each fall. From the third to fifteenth minute, a time sufficient for three falls to be timed, the sum of the rest levels is greater by 0.5 to 0.8 mm. after the fall than before it. The mean of the rest levels of before and after the fall might be used in the calculations with more accuracy than the single preceding values; the maximum error, corresponding to the 0.8 mm. difference, would be only 0.008 cs. We believe that by the calibration of the viscometers using the preceding rest levels only the possible error has been reduced to so small a figure as to be negligible.

Errors due to inefficient filling of the viscometer can be minimised by requiring that the sum of the rest levels must

not differ from the sum of the ideal rest levels by more than 4 mm. If too much fluid has been introduced, the difference between the levels in the limbs during the fall will be less than usual and the hydrostatic pressure forcing the fluid through the capillary will be correspondingly reduced, hence making the time of fall too long. The opposite results from insufficient fluid. The correction equation can be calculated from the dimensions of the viscometer: this formula was found to give excellent agreement with our experimental results in which we derived a correction equation by timing a single fluid with a wide variety of rest levels. Furthermore, our experimental results showed that the correction equations could be applied for errors in filling which resulted in the sum of the rest levels being deficient or excessive by 10 mm. The correction equation thus appears to give adequate and accurate allowance for the minor variations in the fluid volume contained in the viscometer.

Air bubbles cannot be permitted in either limb. The rest levels, the time of fall, and the hydrostatic head of pressure are all affected to an amount for which no accurate correction can be made.

(3) Errors due to variation in the temperature of the water-bath.

Experiments to be reported later will indicate that a change

in the temperature of the water-bath by 1°C alters the time of fall by an amount equivalent to 0.05 cs.. at 20°C . As the temperature can be maintained to within 0.03°C , the error from this source should not exceed 0.002 cs..

(4) Errors due to dirty tubes.

Mechanical blocking of the capillary is the potential source of large errors (eg. 25% or more). The dirt can consist of specks of fibrin, cotton fibre, etc which act as plugs in the capillary or of a general deposit of precipitated protein on all the glass wall.

Experience and vigilance are the best means of detecting a capillary blockage. One inspects the plasma as it fills the Pasteur pipette and as it flows in the viscometer. The resistance to oral suction alters with blockage; the rate of flow varies when the suction pump is applied at alternate ends of the viscometer. With a blockage, duplicate fall-times never agree well enough to yield viscosities within the necessary 0.01 cs. This is one of the reasons for running the test with duplicate readings.

A general deposit of protein, resulting from a precipitate of globulin by distilled water, can be removed by a 3% NaOH solution, applied for 10-15 minutes. A viscometer may require this treatment twice in one day if many nephritic bloods are

being examined. On one occasion, in a study of the rheumatic diseases, I tested over 200 plasmata without requiring to clean the instrument in a period of 6 weeks - this was also a special study on the question of cleanliness of viscometers and a frequent check was made with distilled water viscosity estimations within this 6-week period. Such delay in cleaning must not be regarded as a routine procedure.

(5) Errors from an alteration in the characteristics of the viscometer.

The results obtained from a viscometer would vary according to any change induced into the bore size of the capillary tube. Such a change could result from large variations in temperature (glass does not fully regain its original dimensions for periods measured in units of months) and by the solvent action of distilled water and the caustic soda cleaning solution.

My results with distilled water viscosity measurement in viscometer V5 indicate that no change has occurred within the period of 1944 to 1951. In this time over 2,000 measurements of viscosity has been made in this instrument.

§ 2. The use of nomograms.

A nomogram has been used throughout these studies wherever a result has been derived from experimental values by

a complicated formula. A nomogram reduces the time for the solution of the equations to a few seconds and it excludes the errors included by faulty arithmetic. If carefully drawn, the results produced with the assistance of the nomograms for the viscometers should be within 0.001 cs. of those produced by the detailed solution of the calibration equations by ordinary arithmetic.

Discussion.

To be considered as a suitable test for clinical pathology the technique for the estimation of the plasma viscosity must measure this value on a volume of plasma removable without distress to the patient, with a sufficiently high degree of accuracy at a cost in equipment and technician's time comparable with the value of the information obtained for the clinician from the experimental results.

The volume of plasma (2-3 ml.) which was available to Whittington from ESR blood samples was an important factor in the original design of his viscometer with a capacity of 0.7 - 1.0 ml. Reflection on the daily blood regeneration, the negligible effect of menstrual loss on blood values, and the recovery from the donation of a pint of blood will indicate that a patient could usually spare 50 ml. of blood without incurring any ill effect. The removal of such a volume, however, would lead

to considerable mental distress for several reasons. In addition to the pain arising from the large needle required, the ordinary patient has only the vaguest ideas of the total blood in the body and such an amount would be vastly greater than what is accepted as the 'usual' volume of blood required for testing. (In Portsmouth and Sunderland, the 'usual' volume is 5 ml. This probably arises from the routine procedure of these haematological departments where 5 ml. has been removed for the ESR and blood counts which form the majority of the tests requested by the clinicians.) Large blood volumes are unsuitable for serial tests as the psychological stimulus of their removal might possibly introduce significant changes in the very value which is to be studied. Macfarlane and Biggs (172) and Latner (137) have shown that fear can alter the chemical composition of the blood; similarly, Houston (120) had a patient whose temperature, ESR, and plasma viscosity increased on the mere proposal of a minor operation.

It follows therefore, that the technique chosen as suitable for the measurement of the plasma viscosity should need only the plasma obtainable from approximately 5 ml. of blood. The Whittington viscometer can use the plasma derived from the remainder from 5 ml. of blood after the other haematological investigations of ESR and blood counts have been made.

The criterion for the suitable degree of accuracy required in the estimation of the plasma viscosity as a clinical test is the smallest difference between two results which is considered to be of clinical significance. From my experience, the minimal difference of significance is about 0.015 cs.. Even if all the theoretically-possible errors occurred in the estimation in a clean Whittington viscometer these do not amount to more than 0.014 cs. - later-reported experiments will show that errors of such a magnitude (as measured by difference between duplicates) do not occur in practice. Thus the Whittington viscometer has a satisfactory degree of accuracy.

The economic aspects of the estimation of the plasma viscosity as a clinical test require that - the initial cost of equipment should be low (certainly under £50), no special services need be supplied, the bench space occupied should not be excessive, the reagents should be inexpensive, the technician must not be highly trained, the viscometer should be robust to withstand handling by such junior technicians, and the time taken for each test should be sufficiently low so that many tests can be performed daily if required. All these requirements are met by my technique. If three viscometers are used in the water-bath and the time wasted while waiting for the levels to fall and for

the plasma to drain down after filling thereby employed usefully, a student technician should cope with 20 - 30 tests in an afternoon.

Three basic principles govern the design of most viscometers in general use:- (a) measurement of the force between two concentric cylinders rotating on each other with the fluid in the space between; (b) measurement of the time taken for a more dense sphere to fall through a column of the fluid; and (c) measurement of the rate of flow of fluid through a capillary tube.

Type (a) - Rotating Cylinders.

du Nouÿ (184) has designed an elegant model which requires only 1 ml. of fluid. It is a delicate instrument, including a galvanometer-wire suspension of the inner cylinder. The surface tension effects are excluded by adding a drop of oil to the plasma surface, which must make the later cleaning more difficult. The cost of over £200 is prohibitive for most laboratories. This viscometer, however, is a useful research tool for the examination of the continuous changes in the viscosity of a fluid and it does not subject the fluid to the mechanical stresses of flow through a capillary which might be sufficient to break down fragile complex (and highly-viscous) structures.

Type (b) - Falling or Rolling Ball.

A tube, graduated at two levels, is included within a water-jacket. The tube is filled with the fluid and a sphere of selected density, the time taken for the ball to pass between the marks is noted with the tube inclined at a standard angle, and the viscosity is calculated from this time.

Standard commercial models have a capacity of 30 ml; smaller models (234) down to 1 or 2 ml. capacity have to be made specially and are thus expensive. They are not more accurate than the capillary type as they are liable to the same errors of timing, etc.; the temperature control of the small volume in the water-jacket is not exact unless a thermostatic control is incorporated. There may be a benefit in the absence of a capillary with its risk of blockage.

This particular type of viscometer may have a potential value in the fact that the viscosity is calculated from the experimental results according to Stoke's Law, in contrast to the capillary type which applies Poiseuille's Law.

Type (c) - Capillary Flow.

There are numerous viscometers which depend upon the flow of fluid through a capillary tube. The viscometers used to study the viscosity of plasma and serum can be placed in three groups.

A very simple instrument can be made from a pipette with two graduations plus a constriction to the outlet; the capacity can be very small but most designs use 0.5 to 2 ml.. T'ang and Wang (240) used the instrument originally described by Satô (123); Woodmansey and Wilson (259) and Steel (232) of Harrogate designed their own instrument but it is almost identical with Satô's; Mann, of the Mayo Clinic, (158) advocates a hypodermic needle as a replaceable constriction. Temperature regulation is difficult because the outflow at the lower end makes complete immersion impossible. All such instruments are inaccurate in that the 'viscosity' value is really a combination a fraction reflecting the true viscosity of the fluid together with a fraction depending on such non-viscosity factors as turbulence of fluid-flow and surface tension effects (in the Ostwald, Whittington and similar viscometers the surface tension effect is the same in both limbs and therefore self-cancelling). Steiner (personal communication) has informed me that in some viscometers the true viscosity fraction is responsible for only 10% of the apparent viscosity differences between two fluids. It is a pity that the apparent simplicity of this technique has encouraged so much work to be done with these instruments by medical technologists who have not had the advice on this problem by specialists in the physics of viscometry.

Moreover, with capillary-flow viscometers the 'viscosity' of colloidal solutions depends upon the 'shear' which in turn depends on the pressure exerted to force the liquid through and on the dimensions of the capillary tubing. That Mann should have recommended an instrument designed with a variable shear from needle to needle, without an appreciation of the effect upon his viscosity results, is particularly to be regretted.

The Hess viscometer (= Hellige in America) has been used by Benson in his recent study (16). It has been the instrument chosen by many investigators since 1907; many large series of figures have been published especially in Germany. Yet it is now realised that the significance to be given to these results is low because of faults inherent in the instrument itself (in spite of the extravagant claims of accuracy made by its manufacturers). The chief attraction to its use has been its need of one drop only of plasma or serum. Some of the points open to criticism are now mentioned. Only recently has a water-bath been used to maintain a constancy of temperature - previously a tiny thermometer (? accuracy) was attached and a correction was made from this air temperature, with no guarantee that the plasma and water were of equal temperature: the viscometer itself is small and graduated only to 0.1 cp. divisions, the second place of decimals being obtained by interpolation, and some authors

did not even attempt this: the tubes are graduated with water - a Newtonian fluid: the force producing fluid flow is either oral suction or rubber-ball suction and is thus variable, producing a variable shear with its associated inaccuracies.

The third group of capillary viscometers consists of the classical Ostwald viscometer and its modifications. The smallest B.S.S. Ostwald requires approximately 10 ml. of fluid. It requires a minimum of 10 minutes for the fluid contents to adjust itself to the temperature of the water-bath; the volume of the fluid has to be carefully adjusted to a standard mark at each test. The accuracy attainable is high (error about 0.2%) but not significantly better than with the Whittington type. Stewart Lawrence (138) designed a small Ostwald viscometer, with a capacity of 2.5 ml. only. He fills it from an accurate pipette and so obviates the later adjustment after filling. It has a wider-bored capillary than the Whittington and is thus less liable to blocking, but it does not offer any other advantages in use. The Whittington viscometer is also a modified Ostwald. It has been accepted for use in laboratories in all parts of the world because of its simplicity, cheapness, and high possible accuracy. In addition, these viscometers are now sent to me by the glass-blowers so that I can calibrate them with plasma and correlate

them to the V5 viscometer scale, thus correcting for any variation in the shear. Thus all reported values from a laboratory using a Whittington viscometer can be understood by everyone who also uses this scale of values. Published results from any other source can be appreciated only when some key to this scale of viscosity values can be obtained from some characteristic feature common to all workers, eg. if Woodmansey gives 1.80 as the highest normal value we can surmise that this is equivalent to the upper limit of normal on the V5 scale also (1.915) rather than that his highest normal value is really 0.035 cs. below ours. Similarly, the average serum viscosity of the last month of pregnancy of continental workers is 2.4 (quoted by Schwalm (224)) as compared to my 1.655, and this remarkable difference should be regarded only as a technical difference rather than as a clinical difference. Further examples of comparison of viscosity values estimated by different instruments are given later for citrate plasma, oxalate plasma (Wintrobe), and serum.

For the past year I have attempted to design an automatic viscometer in which the fluid is poured into one orifice and the result presents on a dial. My plans are practical but not yet economically possible. Until this type of instrument has been perfected in a cheaper model the Whittington

viscometer can be recommended as an accurate instrument and as the type filling the requirements of the instrument for the measurement of the plasma viscosity as a test in clinical pathology.

* * * * *

(B) The errors in the estimation of the plasma viscosity due to differences between samples.

In the next four paragraphs the results of duplicate experiments will be reported. These tests have two important aspects - they indicate just how small the error in the estimation of the plasma viscosity by my technique can be, and they indicate that the reported value does bear a close relation to the viscosity of venous plasma in the subject tested.

§ 3. The error of routine plasma viscosity measurement.

The description of the technique states that the reported value is the mean of two values which agree to within 0.01 cs.. Such large differences are seldom included within our results.

Ten consecutive plasma viscosity tests were chosen at random from amongst the clinical cases where special care for minute accuracy was not taken. The ten pairs of viscosity values are:-

2.550,2.548; 1.836,1.842; 1.903,1.897; 1.848,1.851; 1.920,1.920;
1.874,1.880; 2.040,2.043; 1.828,1.832; 1.925,1.923; 2.021,2.022.

The largest variation from the mean was only 0.003 cs. Other series might have been selected in which the variations from the mean were larger or even smaller; I believe that the above is a representative sample of the accuracy in my routine working.

§ 4. The sampling error of a single plasma specimen.

Ten ml. of venous blood were collected into mixed-oxalate anticoagulant and centrifuged; 4 ml. of plasma were pipetted into another tube; the viscosity was estimated on two samples drawn from this plasma specimen.

The results of 25 tests are given in Table A in the Appendix.

The differences had a range of 0.000 to 0.006 cs., with a mean difference of 0.0027 cs., and a standard deviation of 0.0020 cs. There was no consistent change in the direction of the difference between the first and second sample, ie. increase or decrease.

§ 5. The sampling error of a single blood specimen.

Dr. J. Stewart Lawrence, in a personal communication, has found large differences in the plasma viscosities from different blood samples from the single syringe of blood. My own preliminary results did not confirm this and therefore a more comprehensive investigation was made. The results of 45 tests are given in Table B of the Appendix.

A 20 ml. syringe was filled with venous blood, without the assistance of a tourniquet. Two specimens (5ml. each) were collected into mixed oxalate and the viscosity of their plasmata estimated. The sampling from the syringe was varied as much as possible - the blood was sometimes mixed within the syringe before sampling and sometimes not; the samples to be compared might be the first and last 5 ml. volume of blood, or second and third.

As might have been expected, the difference between the duplicates was greater than in the previous section, but the mean difference was still only 0.0066 cs., with a standard deviation of 0.0048 cs. There were now seven tests with a difference greater than 0.01 cs.

§ 6. The sampling error of a single subject.

For these experiments, subjects were chosen with large

veins of the arm so that a sample was taken from each arm without venous stasis and with a minimal time interval between samples.

The results, presented in Table C of the Appendix, indicate that the difference of the plasma viscosities of the two arms was similar to the difference found between two samples of blood from a single blood specimen. The mean difference was 0.0054 cs., with a standard deviation of 0.0035 cs..

Discussion on §3 - §6.

From the results presented in these four sections it may be claimed that my technique can present an accurate and reproducible measurement of the plasma viscosity of venous blood. The mean error is only 0.006 cs.

A measurement of a plasma viscosity is representative of the viscosity of all the plasma, one part of a blood specimen is representative of the whole specimen, and the blood from one arm is representative of the venous blood of both arms. The next stage in this investigation will be the comparison of the plasma viscosity of the venous blood of the arm with that of blood derived from the veins of the head and legs, from the veins of the internal organs of the body, and from the arterial systems.

A technique with a high possible accuracy is valuable in a clinical investigation as it allows a sharper distinction to be made concerning the changes in the serial results of an individual patient which may be of clinical significance. Thus I believe that in some instances a change of as little as 0.015 cs. has been important, and while such a difference could arise from experimental errors, such errors occur so infrequently that they can be dismissed as an unlikely cause. This accuracy should be contrasted with that claimed by Dawson and Salt (59) who, using a Woodmansey and Wilson viscometer, obtained an error of ± 0.08 cp.: similarly, Mann could never be certain that his results did not contain an error of 5% .

Later in this thesis there will appear complex graphs of the relationship of the plasma viscosity to the sedimentation rate, and of the serum viscosity to the serum and plasma protein fractions. These graphs could not have been drawn if the error of the estimations had not been so small; with larger errors the results which now fall on a definite single line would have appeared with a degree of scatter which could have obliterated the linear relationships.

Tables B and C show the accuracy with which the packed-cell-volume, the Wintrobe ESR, and the total plasma

protein by a specific gravity technique can be estimated in duplicate tests. It will be shown later that for the total protein, the error is much greater than appears here.

* * * * *

(C) The errors possible in the estimation of the Plasma Viscosity which do not arise in the viscometer.

The results presented in the previous sections were derived by a technique in which I had the full responsibility from the obtaining of the blood specimen by venipuncture until the final cleaning of the viscometer. It was essential, however, to investigate what errors might be introduced unwittingly by a less meticulous worker and what precautions should be taken to prevent their occurrence.

The experiments will be described according to the chronological order of the procedure of the plasma viscosity estimation.

§ 7. Errors arising from the technique of venipuncture.

A later section will indicate that the plasma viscosity value depends upon the plasma proteins. It follows, therefore, that the plasma viscosity value can be altered by any manoeuvre at the time of blood sampling which will alter the plasma protein-content. The only likely cause of error is the production of venous stasis in order to facilitate venipuncture and in order to allow dammed blood to be aspirated. In the literature there are several references (20,192,197,210) to the increase in the plasma proteins as a result of stasis, Peters claiming a 38.5% increase in one instance after 5 minutes.

I attempted one test only to confirm these reports, as it caused much distress to the subject. A light tourniquet was applied for 5 minutes, by clock timing; two venipunctures were performed. The results are:-

Normal Subject. (P.S.)	Plasma Viscosity.	Total Prot.	PCV.	Wintrobe ESR.	Haemoglobin.
	cs.	g. %	%	mm/ 1 hr	%
Before stasis	1.803	7.09	43.6	1.75	105
After stasis	1.937	7.70	45.2	2.25	108

The error introduced into the plasma viscosity was very large and emphasized the need for the prohibition of long venous stasis for blood sampling for this test.

On the other hand, I found that with a brief constriction in order that a vein became engorged sufficiently to be visible or palpable, and with the pressure released immediately the needle entered the vein, no significant error was introduced. This claim is difficult to prove by figures, but attention is drawn to the serial tests on the same subject as above, normal male P.S., where there must have been a variation in the amount of stasis incurred each day yet the plasma viscosity produced consistent values, and to the results in §6 above where the difference in the stasis of the two arms is not reflected in a significant difference in the viscosity results. (See Fig. 53, page 199)

Furthermore, with a syringe lubricated with paraffin there is no necessity to hurry the removal of the blood. The blood originally in the vein above the needle can be milked towards the heart. Similarly, if the vein tends to collapse on suction with the syringe a gentle pressure on this single vein will produce sufficient damming of flow to allow the blood to be removed as fast as it flows into the vein. The blood sample of 5 ml. should be obtained in under one minute.

§ 8. The errors possible from variation in the proportion of anticoagulant in the blood.

If air bubbles had entered a syringe and if the blood receiving vessel was ungraduated, it was often impossible to be certain that exactly 5 ml. of blood had been added to the mixed oxalate crystals prepared for that volume. Experiments were carried out in which 5 ml. samples of blood from one syringe (cf. §5 for report on the uniformity of the contents of a syringe) were added to amounts of this anticoagulant to yield concentrations equal to $\times 0.5$, $\times 2$, $\times 3$, and $\times 5$ of the normal.

See Table D of Appendix for the experimental figures.

These results indicated that an excess of blood to the anticoagulant introduced less error than a deficiency. An excess of 1 ml. over the expected 5 ml. caused an error of only 0.005 cs., while a deficiency of 0.5 ml. might produce an error of 0.01 cs., but usually nearer 0.006 cs.. I have found that by practice with syringes and 7 ml. bijou bottles I could keep my error to ± 0.25 ml., which should have introduced no significant error into my results.

The errors from less experienced workers can be eliminated by two simple devices - the receiving tube can be graduated or the receiving vessel should have a capacity so that it must be

filled completely with blood except for the air bubble needed to mix the blood.

§ 9. Effect of variation in the time taken to separate the plasma from the erythrocytes.

Any text-book of biochemistry, when dealing with such estimations as the alkali reserve, inorganic phosphate, and chloride of plasma, emphasizes the changes which might occur between the plasma and cells, and between the plasma and atmosphere. It was necessary to determine whether the plasma proteins might be affected similarly.

A 15 ml. blood specimen was collected and divided into three samples. The first and second were centrifuged at once; the viscosity of the plasma of the first was estimated as soon as possible; the second tube was stoppered and the viscosity of its plasma was measured after 24 hours; the third specimen was placed in a bijou bottle, and mixed several times during the day by gentle rotation, centrifuged after 24 hours, and the viscosity of the plasma measured within a few minutes of that of the second sample.

The results are given in Table E of the Appendix.

These experiments indicated that a significant change can

be introduced in the plasma viscosity by the prolonged contact of the plasma and cells outside the body. The change was consistently towards an increase in the viscosity but the degree of change was not sufficiently constant to allow of its correction by an empirical correction formula. The error could increase a high normal value to an abnormal value.

The errors from this source can be eliminated by centrifuging the blood without delay and by removing the plasma from the cells into another container.

§ 10. Errors which may arise during the centrifugal separation of the plasma from the erythrocytes.

The centrifuge has become such an accepted article of laboratory equipment that one has tended to use it with scant consideration of all its potential actions on the contents of the centrifuge tubes. A very early experiment focussed my attention on these actions as a possible cause of error in the plasma viscosity estimation - in an early test with a plasma in which the pipetting disturbed the cells, I believed that I had not drawn any cell into my pipette but I recentrifuged and repeated the investigation: the second value was greater than the first by an amount outwith the range of experimental error. At that time I was following the usual laboratory procedure of using the

centrifuge tubes unstoppered and I soon suspected that therein lay the cause of the increased viscosity, by evaporation.

Several sets of experiments were performed in relation to this problem. In all tests a MSE major centrifuge was used, with its 16-bucket head, running at 2,300 r.p.m. for 15 minutes by the timing device incorporated in the machine. The temperature was measured at the intervals by placing one thermometer in contact with the metal head and another into the water contained in one centrifuge tube.

Experiments (i) - see Table F in the Appendix. (page a31)

On two occasions, four 10-ml. graduated Pyrex centrifuge tubes were centrifuged unstoppered, containing distilled water, for four 15-minute periods, the centrifuge being stopped for a time sufficient only for the appropriate readings.

The loss of water after 15 minutes was about 1%, but after 60 minutes the loss could be 8.5%. The amount of the loss increased as the temperature increased. Such a large change in volume could not be explained by differences in the specific expansions of water and glass but could be explained by an evaporation of the water.

Experiments (ii) - see Table H in the Appendix. (page a33)

These tests were repeated with open and capped Wintrobe Haematocrit tubes, containing blood.

The loss of fluid, although detectable, was less than with water in tubes. The difference in the losses can be explained by the difference in the surface areas from which the fluid could evaporate. Kagan(129) has similarly found the loss in proportion to the area of the surface of the fluid.

The results stress the need for the routine use of capped haematocrit tubes. The cells were packed into a smaller volume for the whole 60 minutes, and even this value could not be taken as the minimal constant volume. An apparent constancy was noted in the open tubes in the 30 and 45 minute readings as the decrease in the total volume as a result of evaporation from the plasma surface was almost proportional to the decrease in the cell volume as a result of increased packing; in the 60 minute values, however, the evaporation loss exceeded the packing to give the anomalous result of an increase in the haematocrit value expressed as a percentage. Because of the large radius of its head the MSE major centrifuge exerts a much greater centrifugal force than the ordinary small laboratory centrifuge which may rotate at 3 - 4,000 r.p.m..

From these studies it may be concluded that the haematocrit value as ordinarily measured after centrifuging in a small centrifuge for 30 minutes, with the tube uncapped, is neither accurate nor minimal.

Experiments (iii) - see Table G in the Appendix. (page a31)

10 ml. samples of blood were centrifuged in uncapped graduated tubes for four 15 minute periods, removing about 1 ml. for tests at each interval. There was a small increase in the plasma viscosity after 15 minutes, but by the end of 60 minutes this increase might equal 10% of the original value.

In contrast, the plasma viscosity was lower after 60 minutes centrifuging in a capped tube than after 15 minutes in an open tube.

Experiments (iv) - see Table I in the Appendix. (page a37)

Two 5 ml. samples of a blood specimen were centrifuged at the same time, one capped and one open, for 15 minutes.

There was a slight loss of fluid by evaporation from the open tube which was sufficient to introduce a significant increase in the plasma viscosity (mean increase = 0.0171 , standard deviation = 0.0043).

The results of experiments (iii) and (iv) indicate that a significant increase in the plasma viscosity value can arise from the use of uncapped centrifuge tubes in the 15 minutes which is the minimum time required to ensure a clear plasma from all blood samples. The simple procedure of placing a rubber bung into each tube before centrifuging eliminates this possible error.

Experiments (v) - see Table J in the Appendix. (page a38)

These experiments were performed in order to determine (a) if centrifuging could be replaced by allowing the cells to sediment to leave a clear supernatant plasma, and (b) if centrifuging causes any alteration in the plasma.

Two 5 ml. samples of a blood specimen were obtained: one sample was centrifuged (uncapped) at once, the plasma was separated and its viscosity measured; the other was placed in a closed centrifuge tube and allowed to stand on the bench until 1 ml. of clear plasma was available and then its plasma viscosity was also measured.

In comparing the values of the parallel series of results it is necessary to take into consideration the increase of about 0.02 cs. which was incurred by centrifuging in an uncapped tube and the increase in the viscosity which may occur on prolonged contact of the plasma with the cells. Nevertheless, the differences between the results are noteworthy on account of their direction as well as their size. A plasma from the sedimented blood sample could easily have a higher viscosity than that of the centrifuged sample on account of some retained erythrocytes (a point which was unfortunately not checked at the time of the experiments) but a change in the plasma protein

must also be considered, as it only by such a protein change that a lower value in the sedimented plasma could be explained. The largest differences in the viscosity values exceed the usual range of experimental error. It is known that the β -globulin fraction can be broken down into its protein and non-protein components by mechanical stresses and it is possible that centrifuging exerts sufficient stress to cause a change of some similar kind to occur; the further investigation of the plasma proteins will form a future research now that the filter-paper technique (55, 65, 82) has brought the refinements of electrophoretic fractionation within the capacity of any laboratory.

Discussion:- These five sets of experiments have all emphasized the need for the capping of centrifuge tubes when estimating the plasma viscosity, thereby eliminating an error of appreciable size. The last set has shown that even the minimum period of centrifuging may introduce a slight change in the viscosity value, probably due to protein changes.

These tests have shown that the ordinary method of estimating the haematocrit value may not be the most accurate available. Uncapped centrifuge tubes should be prohibited from even "routine" laboratory procedures.

§ 11. Changes in the plasma viscosity with passage of time.

It is known that the ESR test (from which the plasma viscosity estimation stemmed) becomes invalid if there is a delay of more than four hours between the venipuncture and the setting up of the tubes; the osmotic pressure of plasma, another physical property, may alter within thirty minutes; du Nouy claimed that the serum viscosity did not become constant within the first two hours; hence it was essential that I should study the changes which might occur in the plasma viscosity with the passage of time.

The experiments can be divided into (a) short-term tests which extended from 30 minutes to approximately 24 hours, and (b) long-term tests extending up to 8 days. For the short-term tests, 10 to 20 ml. of blood were centrifuged, the plasma was separated into a stoppered tube, and 1 ml. samples were removed at intervals from this bulk specimen. For the long-term tests, 20 ml. of blood were centrifuged, the plasma was separated, 1.2 ml. samples were pipetted into clean but non-sterile tubes (1.5" x 0.25") which were allowed to stand stoppered on the bench without special precautions except to avoid heating, and a tube was selected at random each day for testing.

(a) Short-term tests. - see Table K in the Appendix. (p. a40)

The results presented in this table indicate that no appreciable change occurred in the plasma viscosity values in the

first 24 hours. Tests performed specifically to obtain the earliest possible viscosity (about 30 minutes from venipuncture) showed that such a value was identical with values obtained later. The results of §4 (= tests on duplicate samples of a single plasma specimen) can also be regarded as further evidence that small differences of time do not introduce a variation into the plasma viscosity values.

(b) Long-term tests. - see Table L in the Appendix. (p. a41)

These results indicate that valid viscosity measurements can be made on plasma specimens up to 5 days old; thereafter, a significant change can occur in some specimens, but not in all. In several tubes a fine flocculation became evident: on shaking the tube the flocculation became resuspended but it did not disappear, yet the viscosity was identical with that of preceding and succeeding clear plasmata.

Discussion:-

The constancy of the plasma viscosity over a period of time should not be taken to mean that no change is taking place in the chemical constituents of the plasma, but rather that any changes are of such a nature that the viscosity is not affected appreciably.

The viscosity of the plasma depends upon the protein and its subfractions. It has been shown that solutions of albumin (35)

and of globulin (36) maintain their physical characteristics unchanged for long periods; serum and plasma can withstand lyophilisation without alteration in their viscosities (2); and plasma and serum can be stored in a frozen state for months or years and still yield identical patterns on electrophoretic examination. A constant plasma viscosity on simple storage on the bench is thus not unexpected if the plasma can withstand these larger traumata.

The papers suggesting marked changes in the plasma were based on incomplete investigations. The ESR changes after 4 hours have been shown, by interchange experiments with fresh and old plasma plus fresh and old cells, to be due entirely to alterations in the cells, the power of the plasma to produce agglutination remaining unchanged for several days. du Noüy, with his rotating-cylinder viscometer, found that the viscosity of serum first increased and then fell gradually until a constant value was attained after 2 hours. Satô (218) verified this finding with a Hess capillary-type viscometer but he also showed that if a second sample of the serum was introduced into the viscometer without it being cleaned, the rise and fall in the viscosity were not seen - thus the changes in the serum viscosity are due to errors entirely produced by the viscometers. The changes in the osmotic pressure after 30 minutes if the measurement is made

by a 'dynamic' technique which requires a few minutes only rather than the usual 'static' equilibrium method which takes 24 hours or longer appeared in a paper which has not been verified by any other worker (all my notes and its reference were lost in the mail and I have never traced the paper again).

A test in clinical pathology which is based on a plasma property which is constant over a long period of time has marked practical advantages - especially if one makes a comparison with the ESR test with its 4-hour restriction. In the laboratory, provided that simple precautions are taken to prevent evaporation, the viscosity of a plasma can be measured at the convenience of the technician; an individual estimation can be interrupted and resumed again after several hours, without introducing an error. A large number of tests can be accepted at one time but the actual measurement can be spread over several days. There would be no ill-feeling if a specimen arrived about 20 minutes before the laboratory was due to close. Similarly, to the clinician, the advantages are numerous. This test is useful in just those conditions which can be treated in large-attendance out-patient sessions; the number of tests acceptable by the laboratory will be the capacity of the laboratory in the next few days and not in the next few hours. This test can also be useful at an evening clinic; the plasma can be separated by the

sedimenting of the cells or by a few minutes centrifuging, to be followed by thorough centrifuging in the laboratory in the morning, and thus the need for the patient to attend again during the day at the laboratory can be eliminated. Also, as no two laboratories are separated by more than 5 days by air, the results produced in these laboratories can be compared directly by the examination of multiple samples of plasma specimens - sealed ampoules would prevent evaporation in transit and would withstand changes in atmospheric pressure.

§ 12. The stability of the viscosity of the plasma in face of rough treatment of the blood and plasma.

Section 11 indicated that separated plasma retains its viscosity unchanged if allowed to stand undisturbed; § 9 indicated that contact of plasma with erythrocytes for hours and days caused a small but appreciable change in the plasma viscosity. The next subject of study was the effect of rough treatment of the blood and plasma on the viscosity results, especially to determine if the plasma viscosity was sufficiently stable to allow of postal transit of specimens.

Two sets of experiments were made:- (i) 15 ml. of blood were collected into mixed oxalate and heparin anticoagulants, centrifuged, and the plasma separated. 2 ml. were taken

as the control sample: 5 ml. were put into a 7 ml. bottle and shaken thoroughly for 4 hours in a Griffin and Tatlock Microid Flask Shaker. see Table M in the Appendix for results. (a42)

With the eight tests with mixed oxalate plasma the difference between the viscosities of the shaken plasmata and the controls ranged from + 0.009 to - 0.006 cs., ie. within the experimental error; with the four heparin tests, the difference was of a similar magnitude.

This mechanical shaking far exceeds in degree of violence ill-treatment any postal specimen might suffer, but the period of violence is much shorter. Within the limits of this testing technique, the plasma viscosity value has been shown to be stable.

(ii) 20 to 25 ml. of blood were collected into mixed oxalate anticoagulant. Two 5 ml. samples of blood were placed in bijou bottles: one was left untouched on the bench; one was posted from Portsmouth to Glasgow and back to Portsmouth (about 1,000 miles in 3 to 7 days); the two bloods were centrifuged and the viscosity of their plasmata measured. 10 ml. of blood were centrifuged and the plasma separated: the viscosity of one part was measured at once as the control value; 4 ml. was sent on the postal journey and its viscosity measured on its return. 5 ml. of blood was allowed to stand on the bench for 4 hours; the supernatant plasma was pipetted off and sent on the postal journey, it was

centrifuged on its return, and the viscosity of this plasma was measured. The results are in Table N in the Appendix. (a43)

The results indicate that in the eight tests of normal postal service the difference between the viscosities of postal and control plasmata did not exceed the experimental error; in the last four tests where snow-storms caused a delay and increased the time interval to 7 days, the maximum difference was only 0.036 cs., which compares well with the differences obtained with plasma samples allowed to stand undisturbed on the bench (see § 11). The supernatant plasma showed excellent correlation with the control value. Similarly, the plasma from the transported whole-blood sample did not differ from the plasma of the blood remaining in the laboratory, but both of these showed an increased plasma viscosity when compared with the control plasma. (As shown later in the clinical part, the error involved would have been of small significance in the clinical interpretation of the viscosity result.) The seven-day delay introduced gross changes because of bacterial growth in these non-sterile containers.

Discussion:- The mechanical shaking, and the delay and shaking of the postal journey, produced such negligible effects on the viscosity of the samples that a postal service for plasma specimens is possible. A properly-centrifuged plasma sample

can be sent by one laboratory to another; the clinician in his consulting room probably does not possess a centrifuge but he can allow the blood to stand on his desk for a few hours until the cells settle enough for him to pipette off a plasma sample which can be centrifuged on its arrival in the laboratory - his error will be within the experimental error of the technique. The postal transmission of the whole-blood specimen cannot be recommended if the plasma can be obtained, but the error with this whole-blood is still sufficiently small for the clinician to apply the plasma viscosity results to his patients, except that greater care will be necessary at that part of the viscosity range where normal and abnormal results meet. Although the ordinary postal specimen would be received in 2 days at the most, the earlier experiments on delayed separation of cells and plasma have shown that a small error is unavoidable with whole-blood specimens.

§ 13. The effect of temperature changes on the plasma viscosity.

Plasma exists in nature as a fluid circulating in the body at $37^{\circ}\text{C}.$, and the first choice of temperature at which the plasma viscosity should be measured would be this $37^{\circ}\text{C}.$ Any other temperature of measurement entails the possibility that

the values so obtained bear only an inconstant relationship to the original viscosities. The use of 37°C . immediately raises a practical problem. A water-bath accurate to 0.03°C . or better at 20.0°C . is easily constructed by apparatus available to any laboratory at a cost measured in shillings; to obtain the same constancy of temperature at 37°C . requires much more elaborate equipment costing many pounds. (The commercial water-baths recommended for viscometry, accurate to 0.01°C ., cost £200 approximately.) Furthermore, even if 37°C . was the temperature chosen for the measurement of the viscosity of the plasma it would still have to be shown experimentally that the cooling to room temperature after venipuncture and centrifuging did not introduce irreversible changes into the plasma, a definite possibility if one believes, as I do, that there is a protein equilibrium system in the plasma and such systems might be affected by temperature changes: if the experimental proof was not forthcoming, the only possibility remaining would be that all laboratory procedures were carried out in a thermostatically-controlled room at 37°C ..

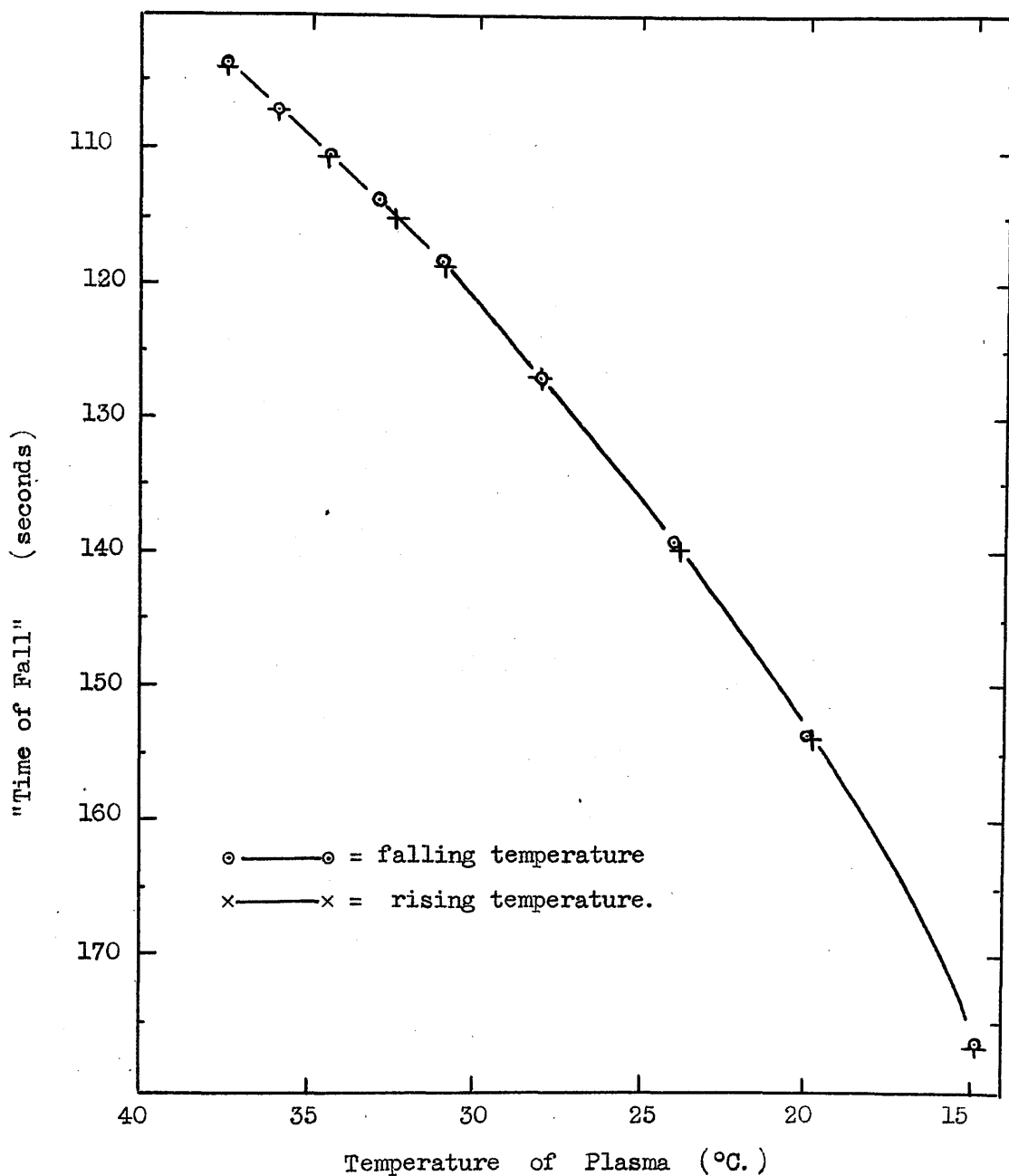
My experiments were of three types.

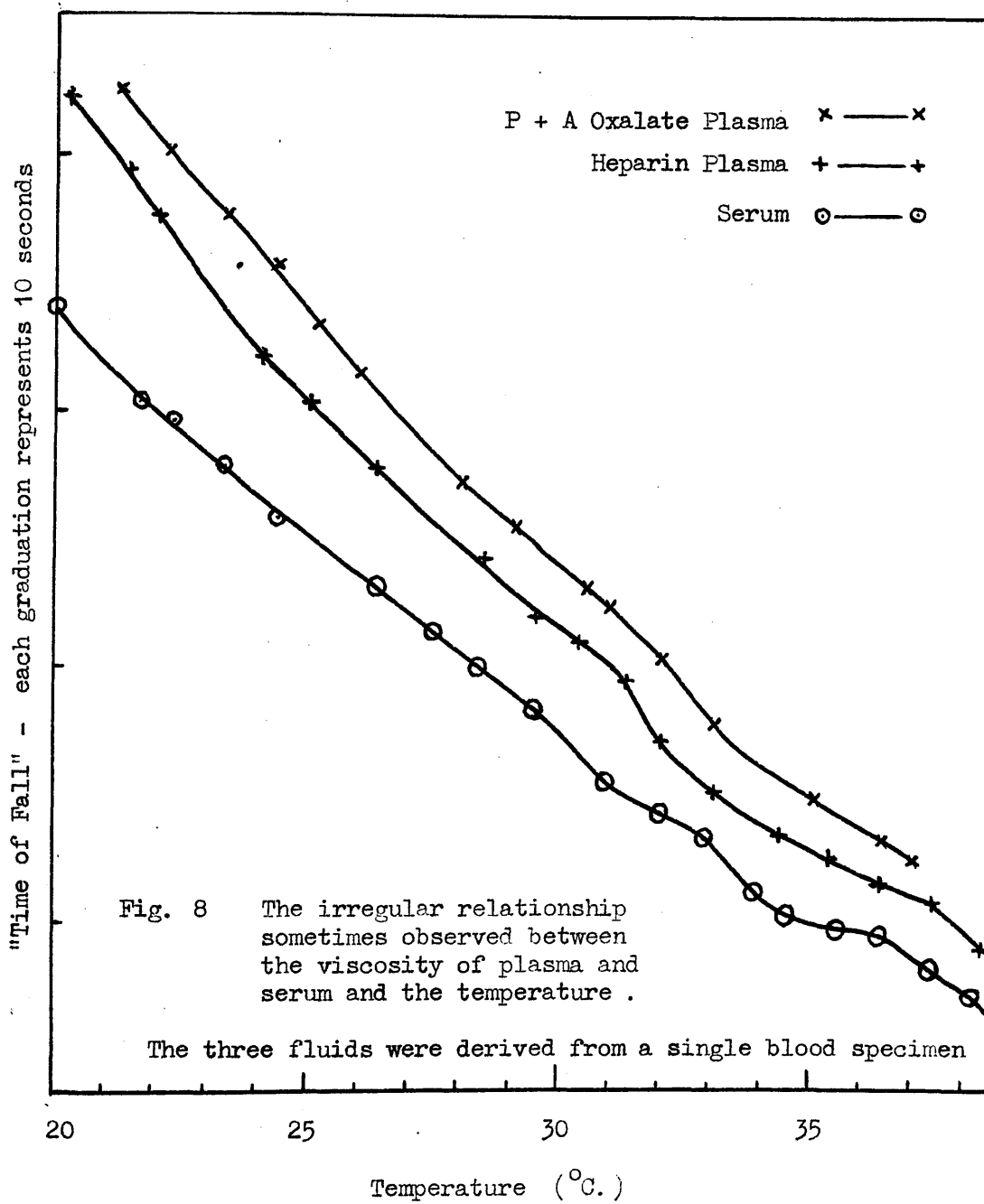
(i) For this test all the syringes, glass-ware, etc. were warmed to 37°C . in an incubator; a centrifuge was arranged in another incubator. 10 ml. of blood were collected with the

warm syringe. 5 ml. were collected into mixed-oxalate in a warm tube and centrifuged in the incubator: the plasma was separated and introduced into a viscometer already at 37°C: the 'time of fall' was measured at various temperatures down to 15°C. The other 5 ml. of blood were collected into mixed-oxalate at room temperature, centrifuged as usual, and the plasma was put into a viscometer at 15°C; the 'time of fall' was measured at various temperatures up to 37°C. The 'times of fall' were plotted against the temperatures to produce Fig. 7 ; within the limits of the accuracy of the technique, the two graphs were identical. Only one test of this type was made because of the possible damage to centrifuges by high-temperature use and Mr. Steiner, in a personal communication, had informed me that he had obtained identical results when trying out this method of comparison.

(Note:- In all tests on temperature effects, the corrected 'time of fall' ($=T'$) has been considered rather than the 'viscosity' calculated from it — for reasons given later in the discussion.)

(ii) Serial tests were made at a variety of temperatures from 15°C. up to 40°C. on mixed-oxalate plasma, heparin plasma, citrate plasma, and serum. Representative graphs of these results are given in Figs. 8,9 and 10 , in which the 'time of fall'





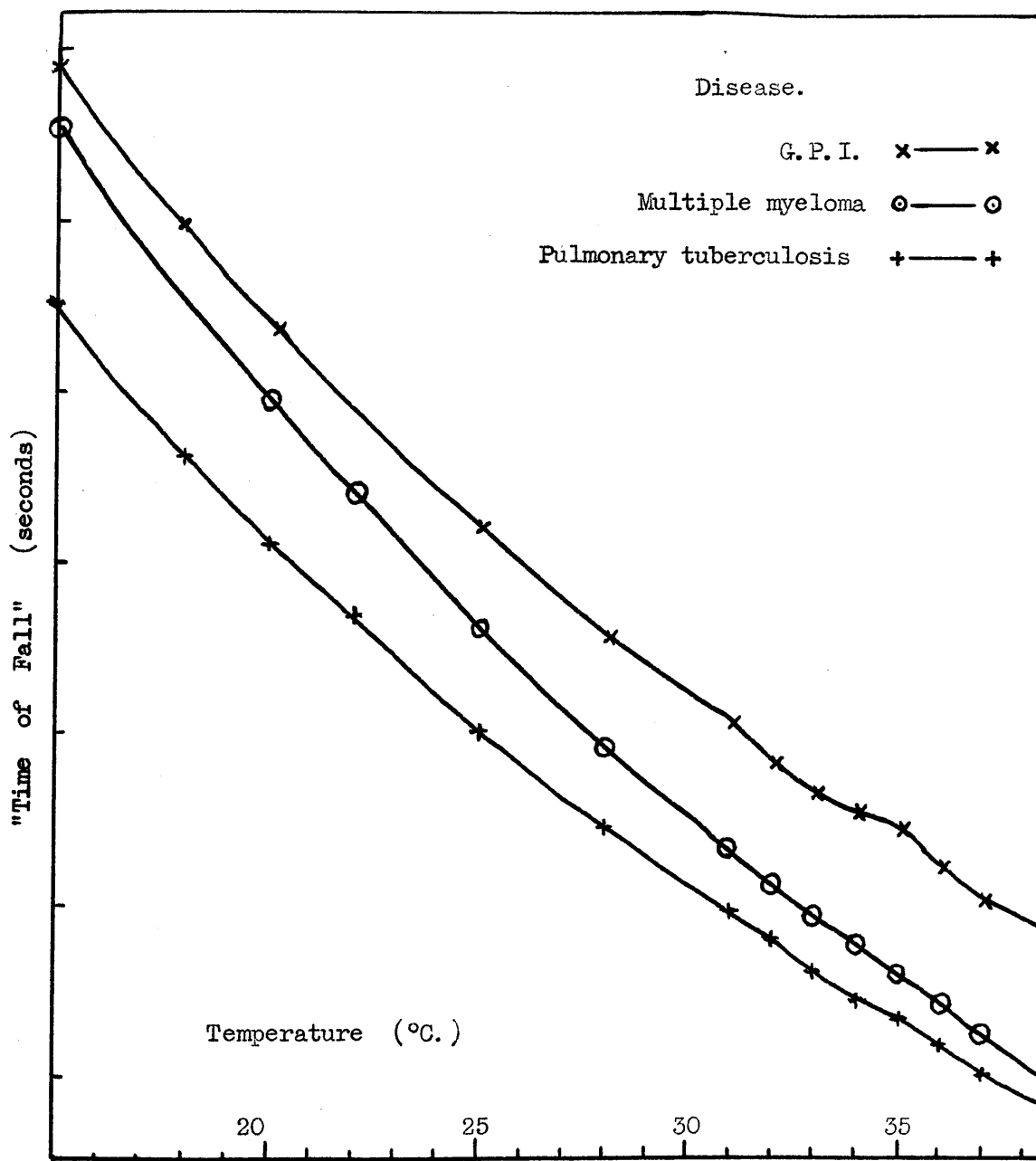


Fig. 10 This graph contains the results from three patients.

The "kink" in the temperature/viscosity curve is observed in the two patients with pulmonary tuberculosis and general paralysis of the insane, yet it is absent from that of a patient with multiple myeloma.

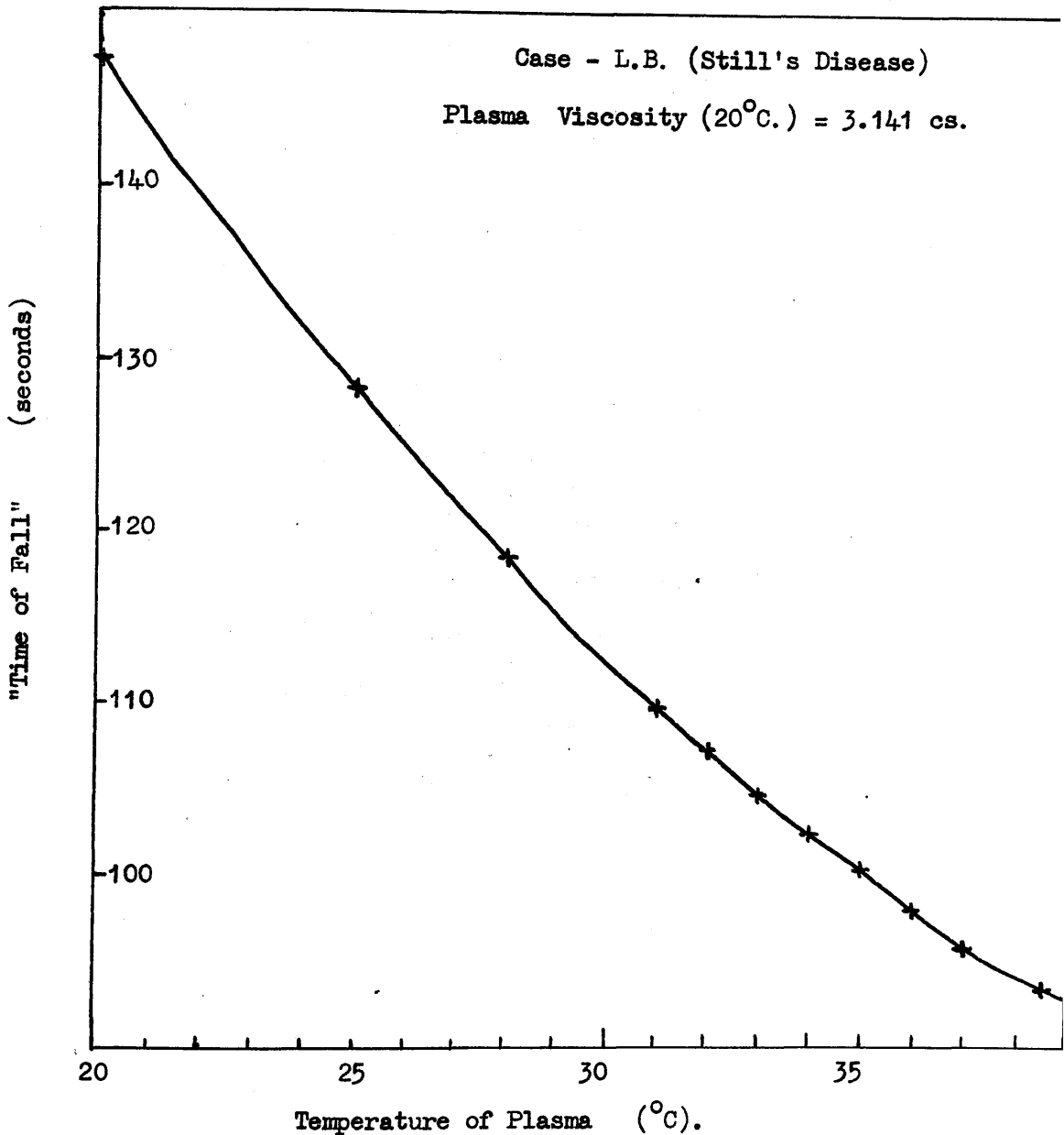


Fig. 9

This graph is included to show that the "kink" in the viscosity/temperature relationship does not depend upon the degree of the increase of the plasma viscosity above normal.

This patient (L.B.) had a plasma viscosity of 3.141 cs. (very high indeed)

(= viscosity) has been plotted against the corresponding temperatures.

The three types of plasma and the serum all yield graphs of two distinct forms. In one form, the curve is perfectly smooth and regular, as in (i) above: in the other, there appears a 'kink' about 32°C. where there is a decrease in the viscosity plus a return to the original line of the curve when there is a sudden increase again in the viscosity with a further small increase in temperature. Fig. 8 includes the curves of the serum and plasma of a single blood specimen and the kinks are almost identical. The kink was only found in the plasma and serum from subjects suffering from disease; its presence could not be foretold; its presence did not bear a close relationship to the plasma viscosity value; the few tests so far performed have not shown it to be related to any special type of illness.

(iii) The viscosities at 18, 20, 22, 25, and 37.5°C. were measured in a larger series of mixed-oxalate plasmata to determine if a consistent relationship was maintained between the viscosity and temperature variation, and if consistent, to derive formulae by which the results at different temperatures can be correlated. Two series of results at least have been published with 25°C. as the standard temperature (138, 240).

The results are given in Table O of the appendix.

The 'time of fall' for distilled water in my viscometer showed a decrease of 31.5% on increasing the temperature from 20°C to 37.5°C: the International Tables give figures which correspond to a change of 31.7%.

Under the same conditions, the 'time of fall' for plasma decreased by a mean of 32.4 % (standard deviation = 0.81)

The change for serum was of a similar magnitude (= 31.6 %)

The 'time of fall' for plasma was about 11.7% less when measured at 25°C as compared to 20°C.

Discussion:- The results presented in this section have been restricted in number. It was realized that the cooling of the plasma to room temperature under the usual method of preparing this from the blood specimen might have caused the removal of plasma constituents insoluble at room temperature; hence it was essential that the tests here reported should be repeated with plasma prepared at 37°C and tested at decreasing temperatures as in section (i). (These investigations will be undertaken soon.)

The results of all three types of tests have shown that the viscosity of the plasma as measured at 20°C. bears a consistent relationship to the viscosity at 37°C. and at intermediate temperatures. There was a variation about the mean percentage of decrease in the viscosity on increasing the temperature by 17.5°C. but this might be due to change in the plasma such as

escape of dissolved gas, etc.. The consistency of my results for change of temperature of this order compares well with the seven tests reported by Jochims (127) who increased his temperature from 19.5 to 40°C with a decrease in viscosity of 35.1 to 37.7%, as measured by an Ostwald viscometer: Schwalm (224) reported 11 tests, using a falling-ball viscometer, in which the increase in temperature from 20 to 40°C produced a decrease in the plasma viscosity of 20.3 to 38.9% - yet he was critical of the accuracy obtainable with capillary-type instruments! My value of 11.7% decrease in viscosity on raising the temperature from 20 to 25°C is almost identical with the 11.2% suggested by J. Stewart Lawrence (139).

Corrections for temperature change cannot be so accurate for plasma and other non-Newtonian fluids as for the Newtonian fluids such as water. When the viscosity of a non-Newtonian liquid is measured in two viscometers, the 'apparent viscosity' will be lower in the instrument with the higher rate of shear; other things being equal, the faster the flow through the capillary the higher is the rate of shear. It follows, therefore, that as the temperature is increased with a resulting increased velocity, the rate of shear also increases. The greater decrease in the 'time of flow' and thus of the viscosity for plasma (32.4 %) as compared with water (31.5%) can be explained by the non-

-Newtonian character of plasma; conversely, the existence of this very difference is additional evidence of the non-Newtonian nature of plasma.

The formula by which the viscosity (ν) is derived from the time of fall (T) contains the two constants A and B. Further experiments are necessary to determine whether these two factors are equally affected by temperature changes; until then the figures given for A and B can be applied only at the temperature at which they were actually estimated.

$$\nu_{20} = A_{20}T' + B_{20}/T' + C_{20}$$

The existence of a kink in the 'time of fall'/temperature curve is interesting. Speculation as to its cause leads to three theories.

The kink might arise from a cause inherent in the conditions of the experiments. This explanation is unsatisfactory in that the kink was not found consistently and it occurred only with plasma from abnormal subjects. Furthermore, Whittington was able to obtain identical kinks with some of his citrate plasmata from tuberculous patients, although it must be remembered that he was using the same type of apparatus.

The kink might arise from a temporary alteration in the protein equilibrium system between the plasma protein fractions and the complex molecule formed by a combination of the fractions.

I cannot devise an experiment, at present, by which this theory could be put to a practical test.

The kink might arise from a change in a single protein fraction. A protein of the "cryoglobulin" family could produce the effects seen in the experiments reported here but the protein would have to be one of very special characters, such as have not been noted previously. The best known protein of this type is the Bence-Jones protein of the urine which precipitates at the correct pH and salt concentration on raising the temperature to 50-55°C and which redissolves on heating further to a temperature just below that of boiling water. (Incidentally, the Bence-Jones protein is now regarded as a family of proteins of different composition, but all having in common this special reaction; similarly, it has been shown that the critical temperatures for a single Bence-Jones protein can vary with changes in the pH and electrolyte content of the urine.) Bence-Jones protein has not been identified with certainty in the blood but other cryoglobulins have been detected. Very rarely, as in the case studied by Wintrobe and Buell (257), the cryoglobulin can be present in tremendous amounts (eg.- 7.25g.%), but the two classifications for the presence of these proteins consider concentrations measured more in terms of milligrams per 100 ml. Wertheimer and Stein (248) defined their Cold Fraction as that

"protein portion of serum which precipitates when the serum stands for twenty four hours at from 7 to 11°C." (Later extended to 72 hours), while Lerner, Barnum and Watson (144) examined their sera daily for 6 days while stored in a refrigerator at 5°C. Lerner et al. were able to detect the cryoglobulins in 31 out of a total of 121 tests performed on a wide variety of disease conditions. Flembert and Lehmann (81) detected a globulin which precipitated at 33°C; Hill, Dunlop and Mulligan (111) found a protein in the plasma of their case of multiple myeloma which precipitated at 32°C and redissolved at 38°C. Jochims (127), Hill et al. (111), and Hansen and Faber (95) used viscometry in the study of these abnormal proteins. In the light of the properties of the proteins already described, it seems possible that a protein can be present in the plasma and serum with the kinks, with the appropriate behaviour towards alteration in the temperature of the fluid. This particular protein may have escaped previous notice for two reasons - the physiologists who would be studying the effect of temperature change on the plasma viscosity would probably use blood from normal volunteers (in which the kink is absent) as was done by Steiner and by myself in (i) above, and the technique of other workers may not have been so scrupulously accurate as myself (and Whittington). It will be interesting to note if the kink can be obtained on cooling the

plasmata which have been prepared at 37°C. The existence of a precipitated protein at 34°C, for example, should be detected by other types of examination such as photometry or centrifugation and thus it should be possible to subject this hypothesis of a cryoglobulin to further experimental testing independent of viscometry.

§ 14. The Effect of Different Anticoagulants on the Plasma Viscosity.

Whittington, in his original work, set out to study the results produced by Day (60) and followed the latter in using a sodium citrate solution as his blood anticoagulant. My later approach to the plasma viscosity estimation was more critical; besides a study of the plasma viscosity and ESR. as physical measurements, I wished to determine which anticoagulant was the most suitable for the further development of the plasma viscosity as a test in clinical pathology.

There were four anticoagulants in common use in the medical laboratories - sodium citrate solution, potassium oxalate alone, potassium and ammonium oxalates mixture, and heparin - and a series of tests were carried out in which specimens of blood were divided among these anticoagulants and parallel measurements made on their plasmata: to complete the study, measurements were also made on the serum.

The results are given in Table P of the appendix. (page a51)

Potassium oxalate alone, in the concentration usually employed (= 2mg./ml.), produced a diminution in the size of the erythrocytes by a passage of fluid from these cells into the plasma, as indicated by a lower haematocrit value as compared with the other anticoagulants which are claimed to leave the cell-size unaffected. The fluid from the cell appeared to have a low protein content as the specific gravity and the plasma viscosity of the resultant plasma were lower than in undiluted plasma. The decrease in the PCV. was not constant either as a percentage of the total blood volume or of the haematocrit value in heparin blood. Similarly, there was no constant relationship between the decreased plasma viscosity of potassium oxalate plasma and the plasma viscosity of either heparin or mixed-oxalate bloods. Hence, as the potassium oxalate alone had no advantages to offer in other directions over heparin or mixed oxalate, its further use for the preparation of plasma for viscosity estimation was soon abandoned. (See fig. 11 and 12)

The 3.8% aqueous sodium citrate solution also fell short of the requirements of the ideal anticoagulant. We have no proof that the citrate remains in the plasma and has a diluting effect only; the chemical methods for the estimation of the citrate are too inaccurate (error at least 2%, probably nearer 5%) .

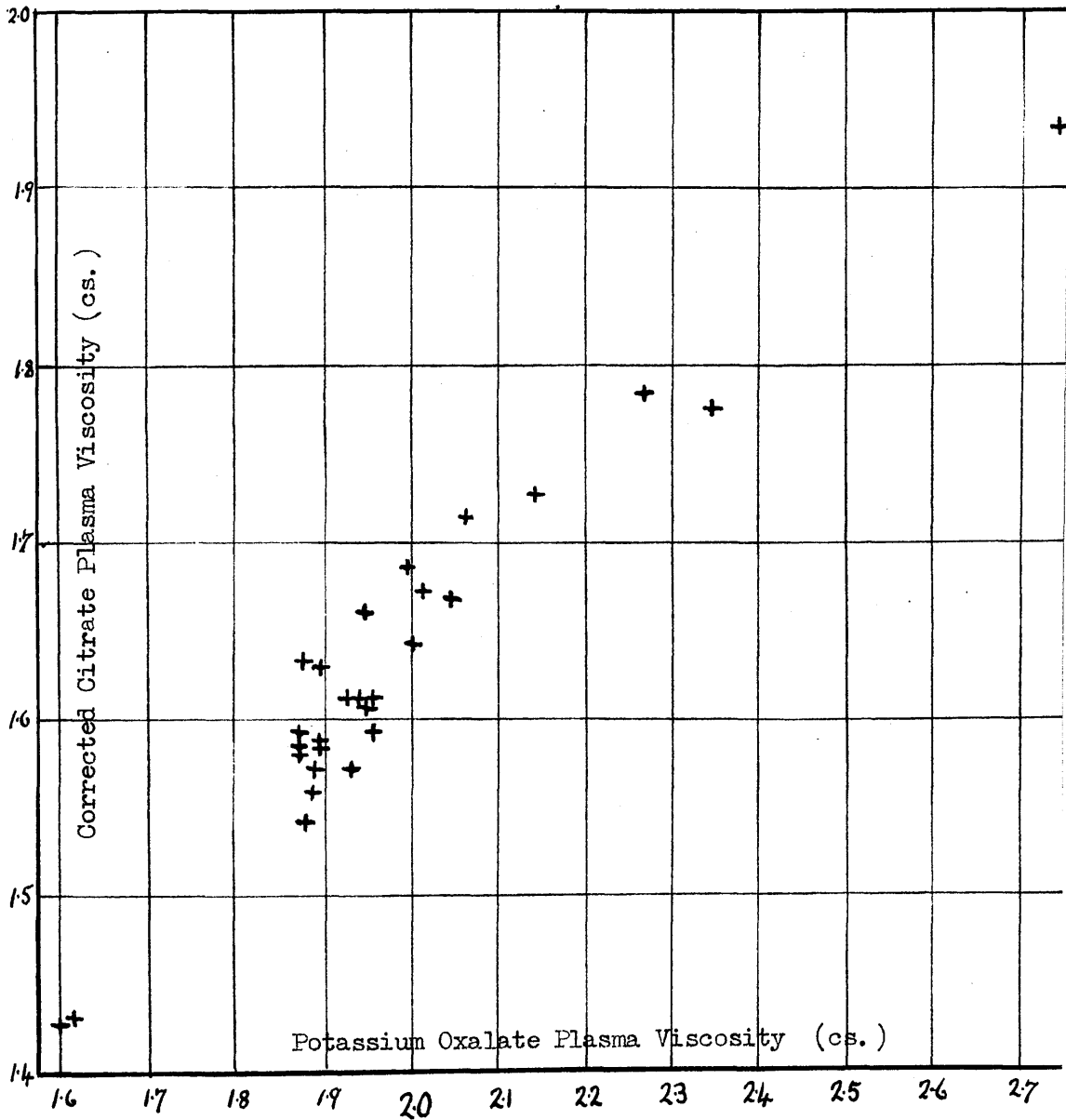


Fig. 11 The correlation between the viscosities of citrate plasma (corrected) and potassium oxalate plasma; duplicate samples were taken from the same specimens of blood.

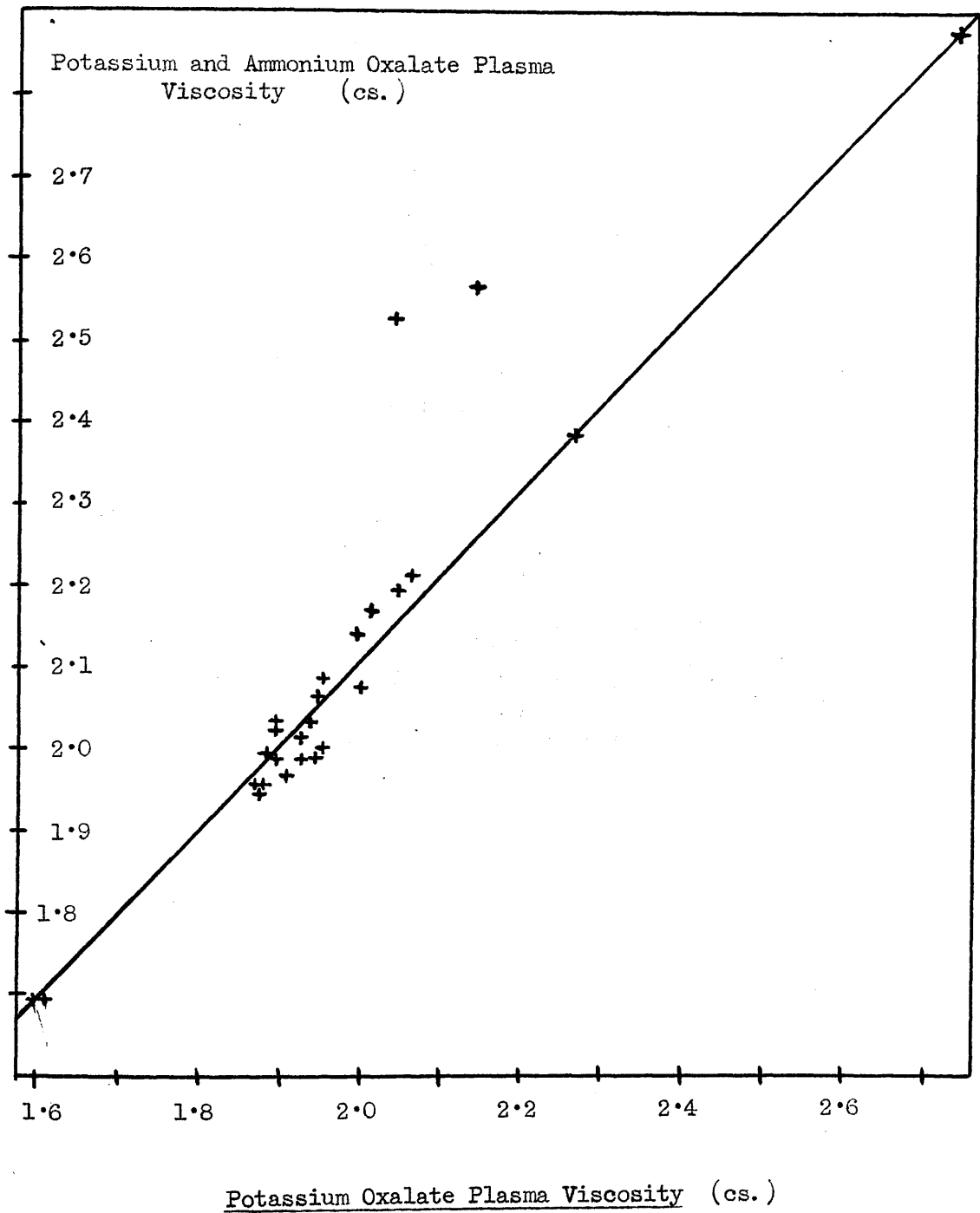


Fig. 12 The correlation between the viscosities of potassium oxalate plasma and of potassium and ammonium oxalate plasma; duplicate samples were taken from the same specimens of blood.

The sodium citrate solution has the following disadvantages which have led to its abandonment also except in a few laboratories which have always used it, following Whittington's original publications. (i) The mixture of blood and citrate must be made with accurately-measured volumes, usually 8ml. and 2 ml. This citrate-blood mixture can be used only for the viscosity and ESR estimations. (ii) To obtain this accurate mixture calibrated glass-ware must be used which is fragile and costly. Such glass-ware is not suitable for use in busy outpatient departments, etc. (iii) Each viscosity estimation requires an accurate haematocrit measurement also (preferably in duplicate) and when large numbers are being tested the strain on the centrifuges is considerable and the prolonged use of these centrifuges may interfere with the routine tests of the laboratory. (iv) An empirical correction has to be made to the experimental viscosity result to allow for variations in the proportions of cells and plasma in the blood samples. The corrected result is what we suppose would be the value if the blood had originally had the 'normal' composition of 45% cells and 55% plasma. This formula includes the possible error arising from the passage of citrate into the cells and the actual error which arises from the fact that the haematocrit reading includes an extra 5% because of the plasma retained in the interspaces between the individual packed erythrocytes.

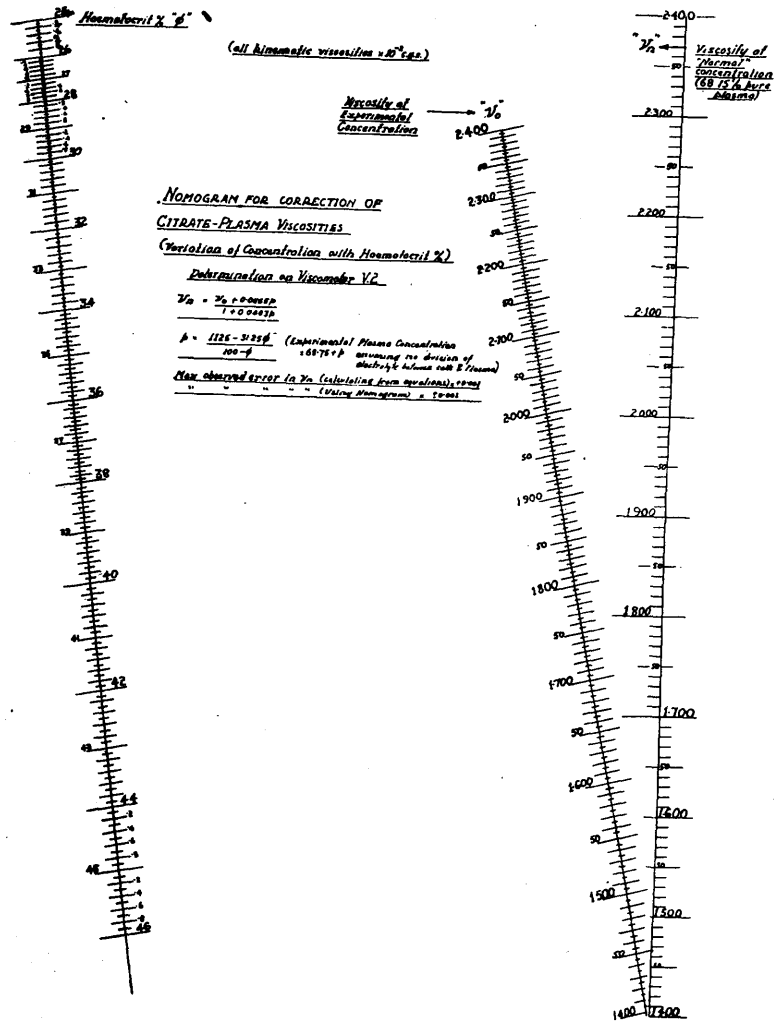


Fig. 13 The nomogram by which the experimental citrate plasma viscosity is corrected to the viscosity expected if the cells had originally amounted to 36% of the total volume (=45% in undiluted blood)

In this calculation no allowance has been made for the plasma (about 5%) which remains in the interstices of the packed erythrocytes.

Fig. 13 presents the nomogram by which the correction for the variation in the haematocrit from the ideal (36%) value could be made to the experimental citrate-plasma result. (The correction formula is included within the figure.)

An attempt was made to test the validity of applying such a correction formula by preparing a second blood sample in which the citrate content had been calculated to yield a perfect 20:44 citrate:plasma mixture. (The nomograms and the various formulae are given in Fig. 14) It was also possible to prepare a similar perfect citrate:plasma mixture from the ordinary citrate-plasma by the further addition of citrate solution, but the viscosity of this preparation was not studied.

My investigations amount to three tests only (see page 105). While the plasma viscosities in two tests agree to within the experimental error of the technique, there is a marked discrepancy in the third. Further research is essential on this point; the subjects should have both a severe anaemia and a high plasma viscosity.

The ESR results are also of interest. Two bloods were prepared to contain citrate:plasma:cells as 20:44:36 by different manipulations, yet in only 1 of the three sets of pairs was the agreement really close (see lines K and L).

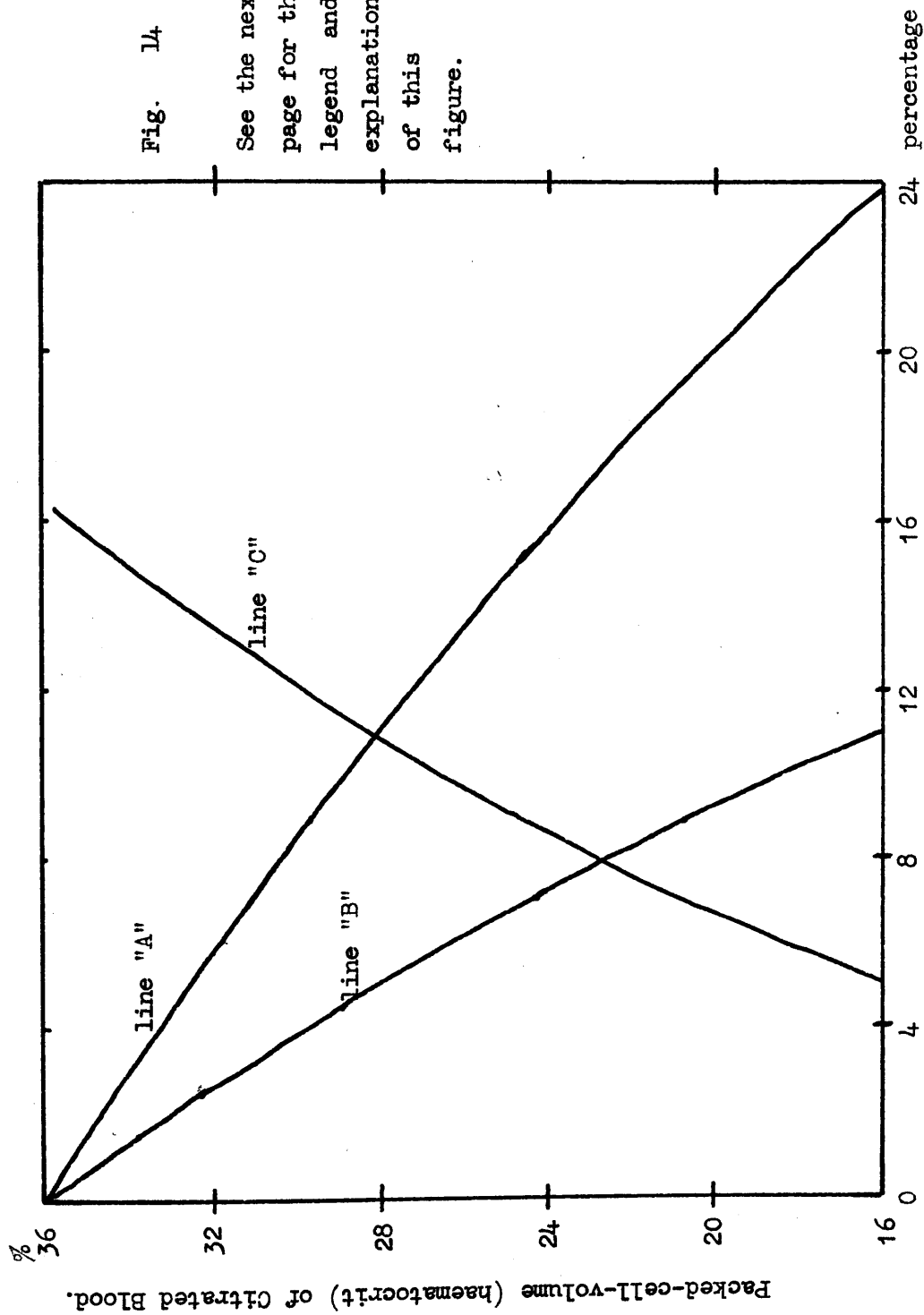


Fig. 14

Let ϕ = the haematocrit reading of a blood prepared by mixing 4 volumes of blood with 1 volume of 3.8% aqueous solution of sodium citrate.

- (1) To obtain a blood in which the cells will amount to 36% (equivalent to 45% in undiluted blood) remove or add to the blood a volume of citrate plasma equal to
- $$100 \left(1 - \frac{\phi}{36} \right) \% \text{ of total blood volume.}$$
- (2) To prepare another blood sample, with a total volume of 10 ml. in which the perfect ratios of citrate:RBC.:plasma are 20:36:44, begin by placing this volume of citrate solution into a 10 ml. volumetric flask and filling to mark with blood.

$$\frac{800 - 10\phi}{256 - \phi}$$

- (3) To obtain a citrate:plasma mixture identical with (2) but using the ordinary plasma, line "A" gives the percentage by which the ordinary mixture is deficient in citrate which can thus be added to the separated plasma -

$$100 \times \left(\frac{36 - \phi}{100 - \phi} \right) \%$$

- (4) Line "B" presents the amount by which the plasma in the ordinary citrate:plasma mixture is in excess -

$$\frac{500}{11} \left(\frac{36 - \phi}{100 - \phi} \right) \%$$

- (5) To prepare a perfect 20:36:44 mixture from the ordinary mixture, calculate how much citrate plasma must be removed according to the formula in (1) above; then calculate how much more has to be removed by the following formula and remove it; and add this same volume of citrate solution.

$$\frac{20\phi}{(80 - \phi)} \% \text{ of the volume calculated by formula (1)}$$

This formula is represented in line "C".

Experiments to prove the formula for the correction of the ordinary citrate plasma viscosity value to what it would have been if the erythrocytes had been exactly 45% of the blood volume.

From a preliminary estimation of the packed-cell-volume (line A) in a second specimen a plasma was prepared in which the citrate to plasma ratio was the ideal 20:44.

Later tests also prepared an ideal plasma from the ordinary plasma mixture.

	Number of test.	1	2	3
A	PCV. of preliminary blood test, with citrate to blood as 2ml. to 8 ml.	11.7	23.0	23.5
B	PCV. of second blood test, similarly made with citrate:blood as 2:8	11.7	23.8	24.0
C	Volume of citrate required to yield a citrate:plasma mixture of 20:44. This is calculated from the PCV. of line A. Total volume of mixture equals 10 ml.	2.79	2.45	2.43
D	PCV. of blood prepared with citrate of line C.	10.6	21.6	23.0
E	The PCV. value as calculated from the results of lines C and B.	10.44	22.1	22.3
F	Experimental plasma viscosity values of blood of line B.	1.397	1.625	1.805
G	Viscosity of line F, corrected by the formula.	1.398	1.588	1.745
H	Viscosity of citrate-plasma of blood of line C. This value should be the same as in line G.	1.392	1.583	1.715
I	Maximum sedimentation velocity in blood of line B. (cm/sec $\times 10^{-4}$)	13.0	12.22	-
J	Max. sed. vel. in this blood after the PCV. had been adjusted to 36%	0.60	4.03	9.83
K	Max. sed. vel. in this blood after the plasma had been adjusted to a citrate:plasma ratio of 20:44 and the PCV. to 36 %.	0.47	4.44	6.94
L	Max. sed. vel. in blood of line C, with PCV. adjusted to 36%. This final blood was expected to be of identical composition as line K.	0.47	3.12	7.50

The citrate anticoagulant has one advantage in that it allows of the estimation of the corrected maximum sedimentation velocity as well as the plasma viscosity, and the relation of these two values has an additive value to each other in the clinical interpretation of the results (see also § 21 later).

The mixture of potassium and ammonium oxalates was first recommended by Heller and Paul (106) because the constricting action of the potassium oxalate on the erythrocytes was balanced by the expanding action of the ammonium oxalate. Heparin also does not affect the cell size. It is probable that the plasma from either of these anticoagulants would be equally suitable for the viscosity estimation; the differences between the results of the duplicate tests in Table P are usually small. Mixed-oxalate plasma, however, has a wider potential use than heparin plasma both in biochemistry and haematology, and the mixed-oxalate plasma has been chosen as the most suitable plasma for our purposes. Other workers have come to a similar conclusion independently.

The results of Table P have been shown in Fig. 11 and 12, and are shown further in Fig. 15, 16, 17, and 18.

The correlation between the viscosities of plasmata containing different anticoagulants is not linear. Also, the

Fig. 15

The relationship of the Corrected Citrate Plasma Viscosity and the Potassium and Ammonium Oxalate Plasma Viscosity approximates to a straight line.

Discrepancies must occur as the correction equation for the citrate dilution does not take into account the plasma still present among the packed erythrocytes of the haematocrit tubes.

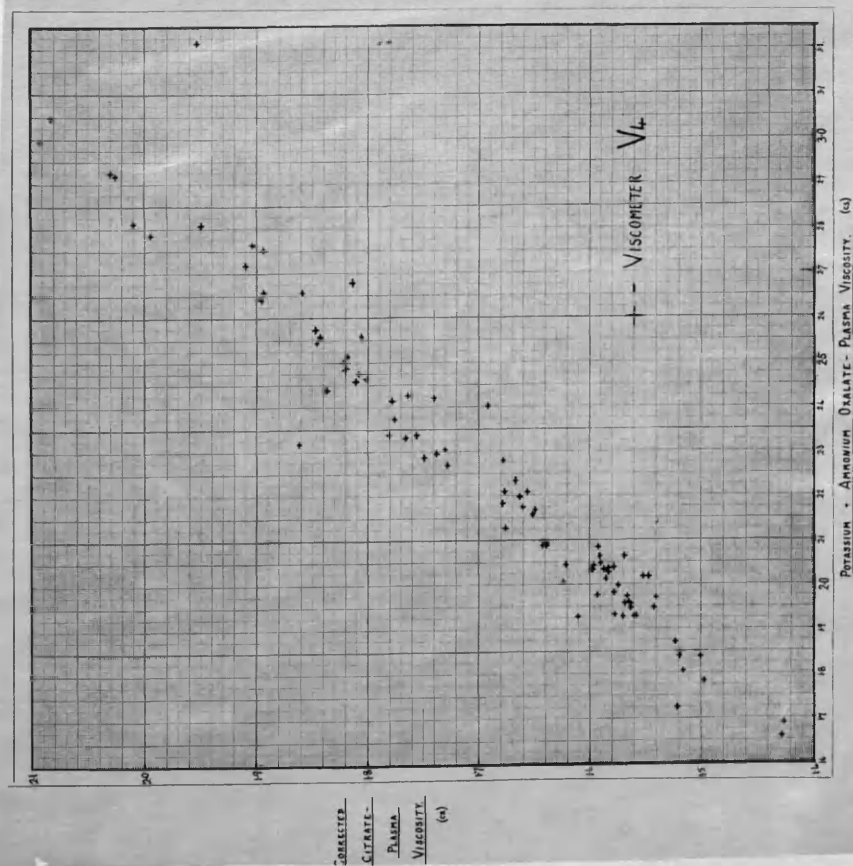
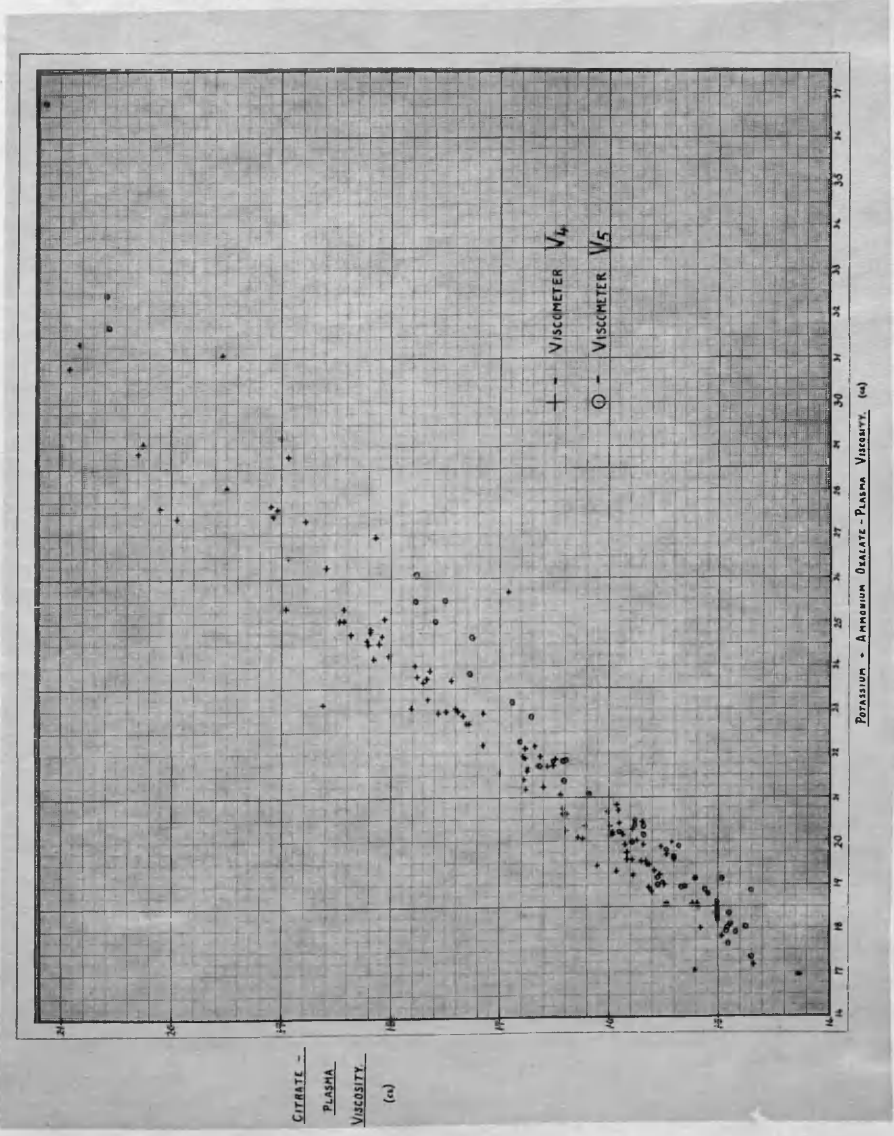


Fig. 16

The V_4 and V_5 instruments had been correlated with Citrate Plasmata to yield results which differed by less than 0.01 cs.

Note how the calibration formulae yield different values with Potassium and Ammonium Oxalate Plasmata, as there are now two lines of correlation between the oxalate and citrate plasma viscosities.

This phenomenon is caused by the non-Newtonian character of plasma.



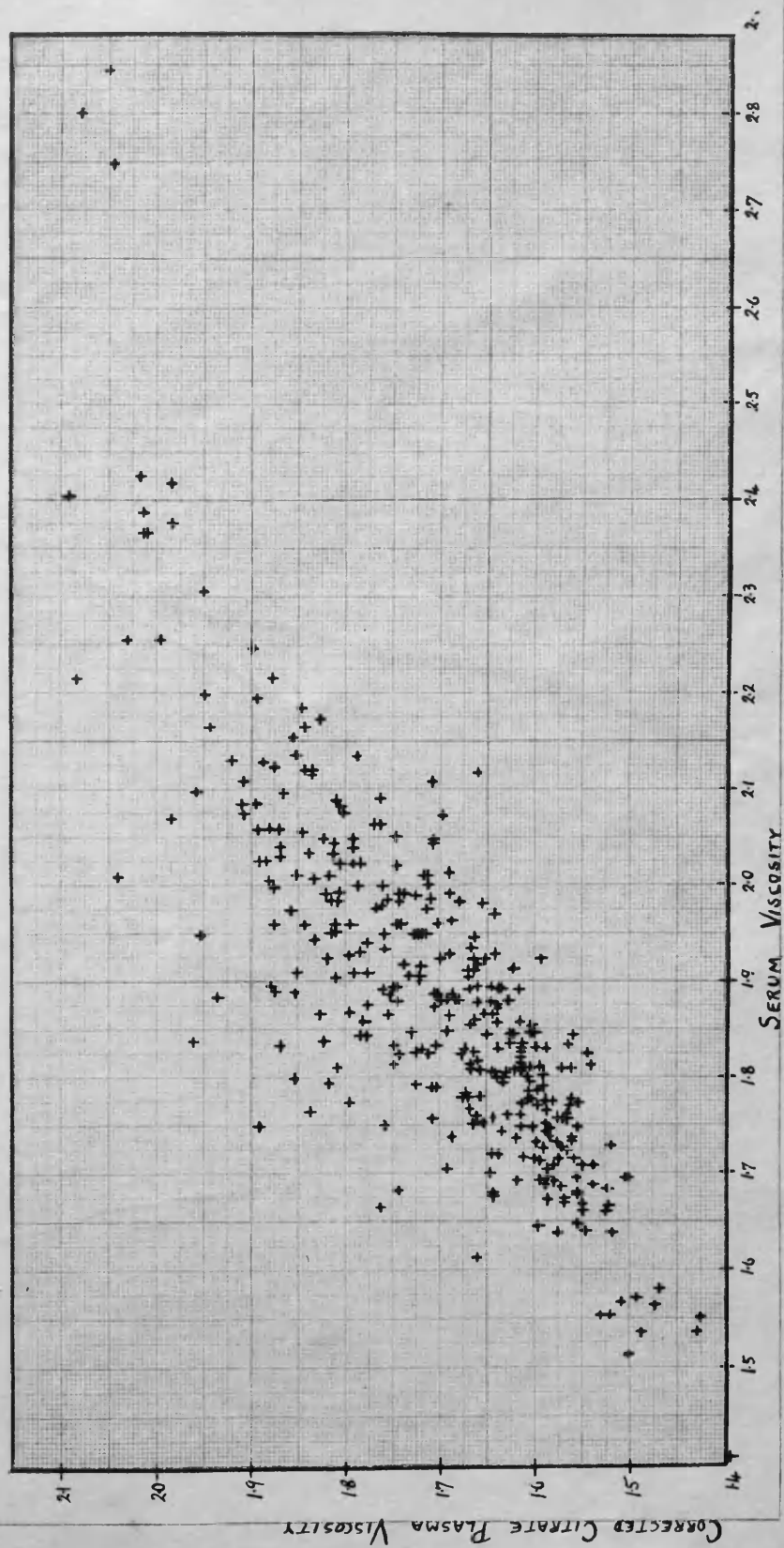


Fig. 17 The relationship between the viscosities of Serum and Citrate Plasma.

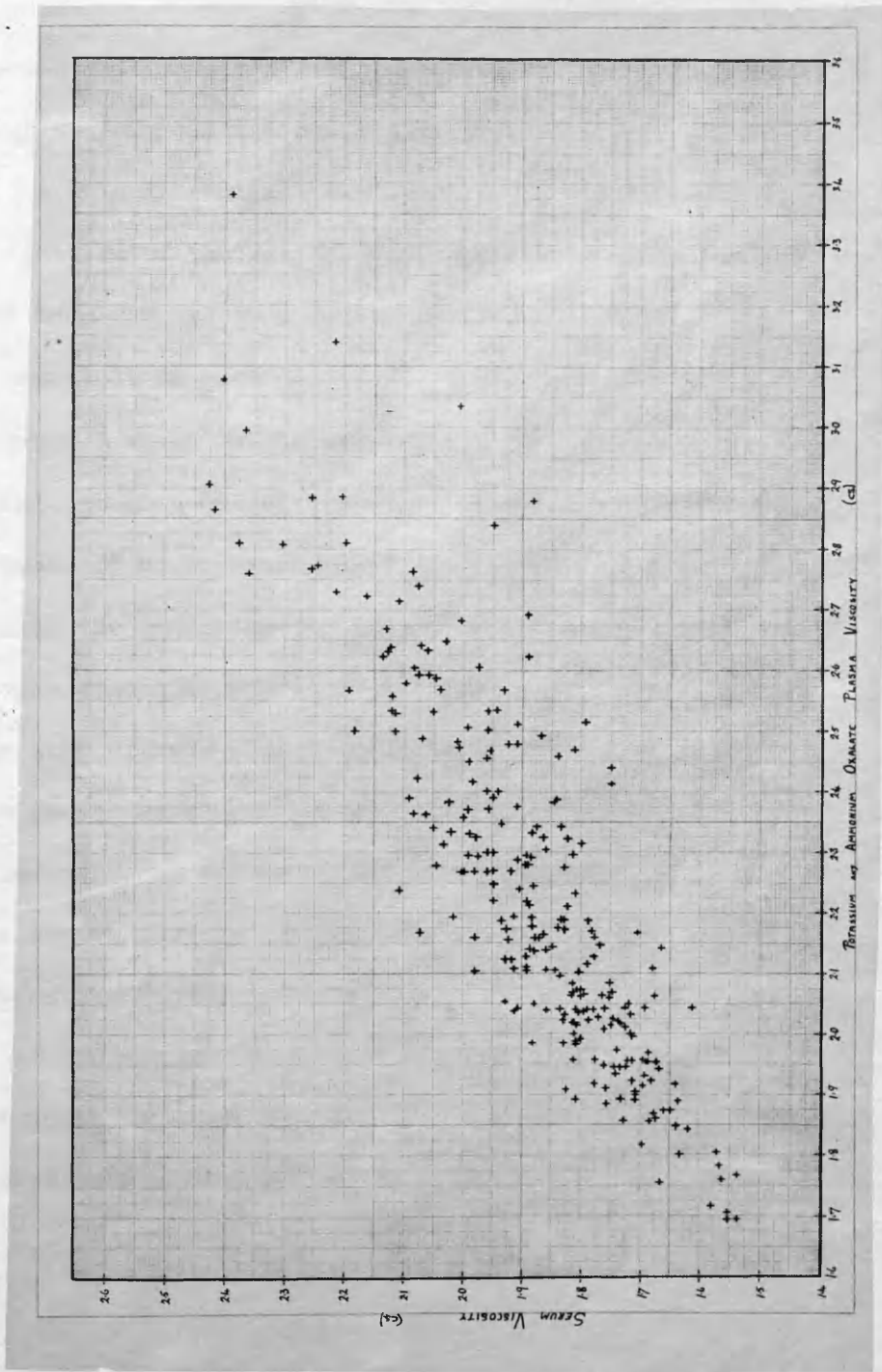


Fig. 18

There is a roughly linear relationship between the Plasma and Serum Viscosities.

Departure from this line is due to the large possible variations in the Fibrinogen concentration.

consideration of the serial results of a single subject shows that the correlation can change over a period of time (cf. Fig. 55).

This inconstant relationship has raised difficulties in the definition of the ranges of normal values because if these ranges had been derived by a series of studies with single types of plasmata it is possible that a later duplicate estimation might produce a value within one normal range and outwith the other range. Such a dilemma faced me in the interpretation of the results of normal male subject , No 47, when on 29:10:47 and 2:1:48 the mixed-oxalate viscosity was abnormal while the citrate-plasma viscosity was a low normal; a little over a year later the same citrate-plasma viscosity figures were associated with low normal mixed-oxalate plasma viscosity figures. This discrepancy serves as an indication that the anticoagulants are not relatively inert substances apart from their action in preventing fibrin formation.

Because of the variation in the fibrinogen content it was not to be expected that the plasma viscosity/serum viscosity correlation of Fig. 17 and 18 would be linear.

*** **

(D) The Correlation of the Viscosity of Plasma and Serum with the Chemical Constituents of these Fluids.

The mean viscosity of normal plasmata is about 1.850 cs. as compared with the 1.008 cs. of distilled water. In the following sections the attempt is made to discover if this difference in viscosities can be ascribed to any particular component or components of the plasma.

In a table of the concentrations of the various constituents of serum and plasma attention is drawn at once both to the high absolute concentration of the proteins and to their great concentration relative to any of the other plasma components. Also, from a knowledge of viscosity in general, it is known that the viscosity of a solution of a substance with large molecules (such as protein) is greater than a solution of equal concentration of a substance of small molecules (such as urea and glucose). It thus seemed probable that the proteins were the constituents having the greatest, if not the complete, effect in increasing the viscosity of the plasma over that of water.

The problem was tackled by three experimental approaches. The viscosity was measured of the plasma after the proteins had been removed, the viscosity was measured of the solutions of the purified protein fractions, and the viscosity of the plasma and serum was compared with the concentration of the total protein

and the protein fractions.

§ 15. The viscosity of the ultrafiltrate of plasma and serum.

By the technique described in the appendix, the viscosity of the ultrafiltrates of ¹⁰~~5~~ sera was studied. The values fell within a narrow range (1.021 - 1.035) with a mean of 1.029. Included in this series was a case of chronic nephritis who had a non-protein-nitrogen level increased to 125.3 mg/100 ml. yet his ultrafiltrate viscosity was only 1.026. Thus a three- or four-fold increase in the nitrogen-containing non-protein components has introduced no significant increase into the ultrafiltrate viscosity, confirming the hypothesis that the proteins are chiefly responsible for the plasma viscosity values. (Table Q)

My viscosity value for ultrafiltrates compares well with the 1.02 cs. already published (147,179,193).

It also compares with the 1.021 cs. result of my estimation of the viscosity of isotonic saline (0.9%).

(Note: The original crude apparatus yielded excellent ultrafiltrates but required almost 100 ml. of blood; hence the scanty results presented in Table Q of the appendix. Recently a simple apparatus was described (69) in which the pressures available by high-speed centrifuging are employed to force the ultrafiltrate from less than 10 ml. of serum through Gradocol

membranes. Further experiments will be made with this apparatus* both on serum and plasma from patients with diseases known to have gross abnormalities in the composition of these fluids. These results and their discussion will be inserted here later.)

(* not delivered in time for results to be obtained)

§ 16. The viscosity of solutions of the purified protein fractions - albumin, globulin, and fibrinogen.

(The results reported in this section have formed the basis for a publication - "On the viscosity of solutions of human albumin and globulin" by Harkness and Whittington, *Biochimica et Biophysica Acta*, 1947, 1, 487-496.)

Introduction. The viscosity of a liquid was defined as that property which is responsible for the internal resistance offered to the relative motion of different parts of the liquid. Since the work done in overcoming frictional resistance is transformed into heat, a connection must exist between the viscosity coefficient and the kinetic energy transformed into heat. Thus, there is the alternative definition of the viscosity coefficient

$$q = \mu \left(\frac{dv}{dl} \right)^2 \quad (\text{ergs per sec. per cm}^2)$$

where q = the kinetic energy transformed into heat in unit time for unit volume. The view of the viscosity coefficient as a

measure of the energy dissipated (eg. in forcing liquid through a capillary) is sometimes more fruitful than the commoner one in forming a physical picture of the processes affecting viscosity such as the increased viscosity on introducing colloidal molecules into a pure liquid (5).

In a dilute suspension of large rigid spheres, in which each sphere may be considered surrounded completely by a large volume of unaltered solvent, Einstein (68) in 1906 calculated the formula of

$$\mu/\mu_0 = \mu_r = 1 + 2.5 \phi$$

where μ = absolute viscosity of the solution,

μ_0 = absolute viscosity of the pure solvent,

$\mu/\mu_0 = \mu_r$ = relative viscosity,

ϕ = volume fraction of the disperse phase
(volume of particles / total volume).

The viscosity is not increased directly by the suspended particles but arises indirectly as a result of disturbance of the solvent flow. The relative viscosity at low concentrations is independent of the nature of the disperse phase and of the particle size.

The introduction of spherical colloidal particles into a pure solvent leads to increased viscosity mainly as a result of the extra dissipation of energy involved by flow distortion around each particle. With asymmetrical particles (eg. plasma proteins) additional causes are also involved — thus the rotation of the asymmetrical particles, enforced by the velocity

gradient, results in extra energy dissipation, a mechanism which is clearly much less important the more nearly spherical are the suspended particles; the deformation of the particles in the velocity gradient and the much greater interactions occurring in the suspension of asymmetrical particles provide further possible mechanisms.

Many colloidal materials are strongly solvated in solution. Solvation involves the strong binding of solvent molecules, usually in a layer not more than a molecule thick, the (particle + solvent layer) acting as the kinetic unit in solution - so producing an effective increase in the volume concentration of the solute. The degree of solvation of the plasma proteins is still under discussion.

Methods. From blood drawn from normal human subjects, specimens of the sodium salts of albumin and globulin were prepared, as described in detail in the appendix. Care was taken in their repurification but it cannot be guaranteed that there was not a small amount of the other protein contaminating the final products. Albumin was dissolved in distilled water to a concentration of about 15% and its viscosity was measured at this and decreasing concentrations. Similarly, the viscosity was measured on globulin dissolved in normal saline. A specimen of fibrinogen was obtained from the Medical Research Council and studied in

in aqueous solution. The concentrations were measured by analysis of the nitrogen content by micro-Kjeldahl techniques.

The viscosity results are reported both with the Newtonian-fluid calibration and in terms of the arbitrary V5 scale.

Results. The results are given in Table R of the Appendix.

From these, Fig. 19 was constructed; similarly Fig. 20.

Discussion. The viscosity of the protein solutions did not increase equally with each increment of protein concentration, the addition of further protein having an increasingly greater effect. The plotting of η against c (g./100ml.) yielded the three curves of Fig. 19, where the viscosities of 1% solutions were 1.400 cs. for fibrinogen, 1.130 cs. for globulin, and 1.065 cs. for albumin; while similarly a viscosity of 1.600 cs. corresponded to 1.3 g./100ml. of fibrinogen, 4.0 g./100ml. of globulin, and 8.0 g./100ml. of albumin.

Cohn (44) has given the dimensions of the protein molecules as (ie. length of ellipsoid \times equatorial diameter of ellipsoid) $900 \times 33^\circ\text{A}$ for fibrinogen, $320 \times 36^\circ\text{A}$ for globulin, and $150 \times 38^\circ\text{A}$ for albumin. If one could imagine the extra energy expended to rotate the long fibrinogen molecule as compared to that of albumin, one can readily understand how this difference in viscosity arises. Similarly, one can visualise the long fibrinogen molecules interfering with each other.

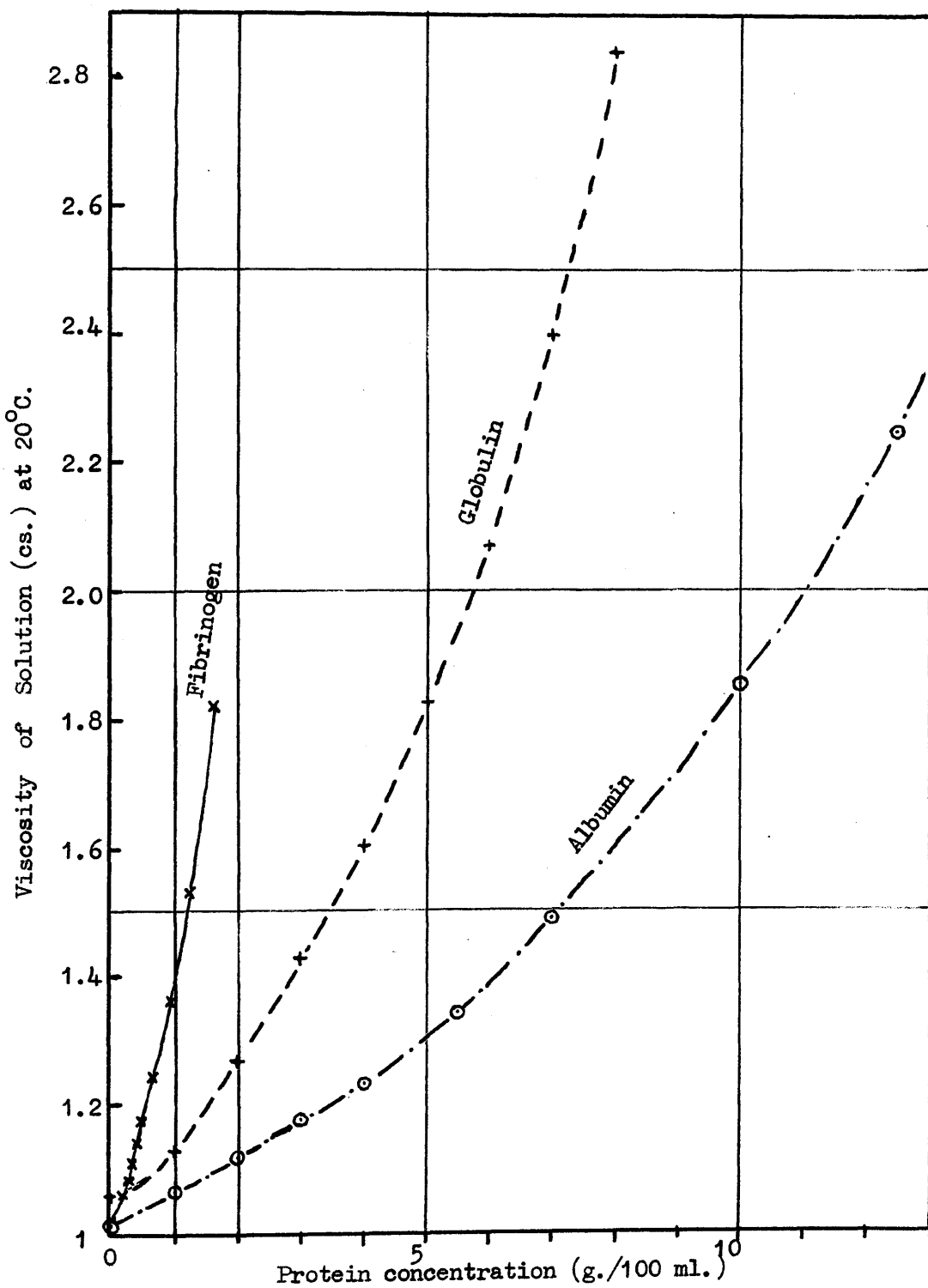


Fig. 19 The Viscosity of solutions of the purified plasma protein fractions at different concentrations.

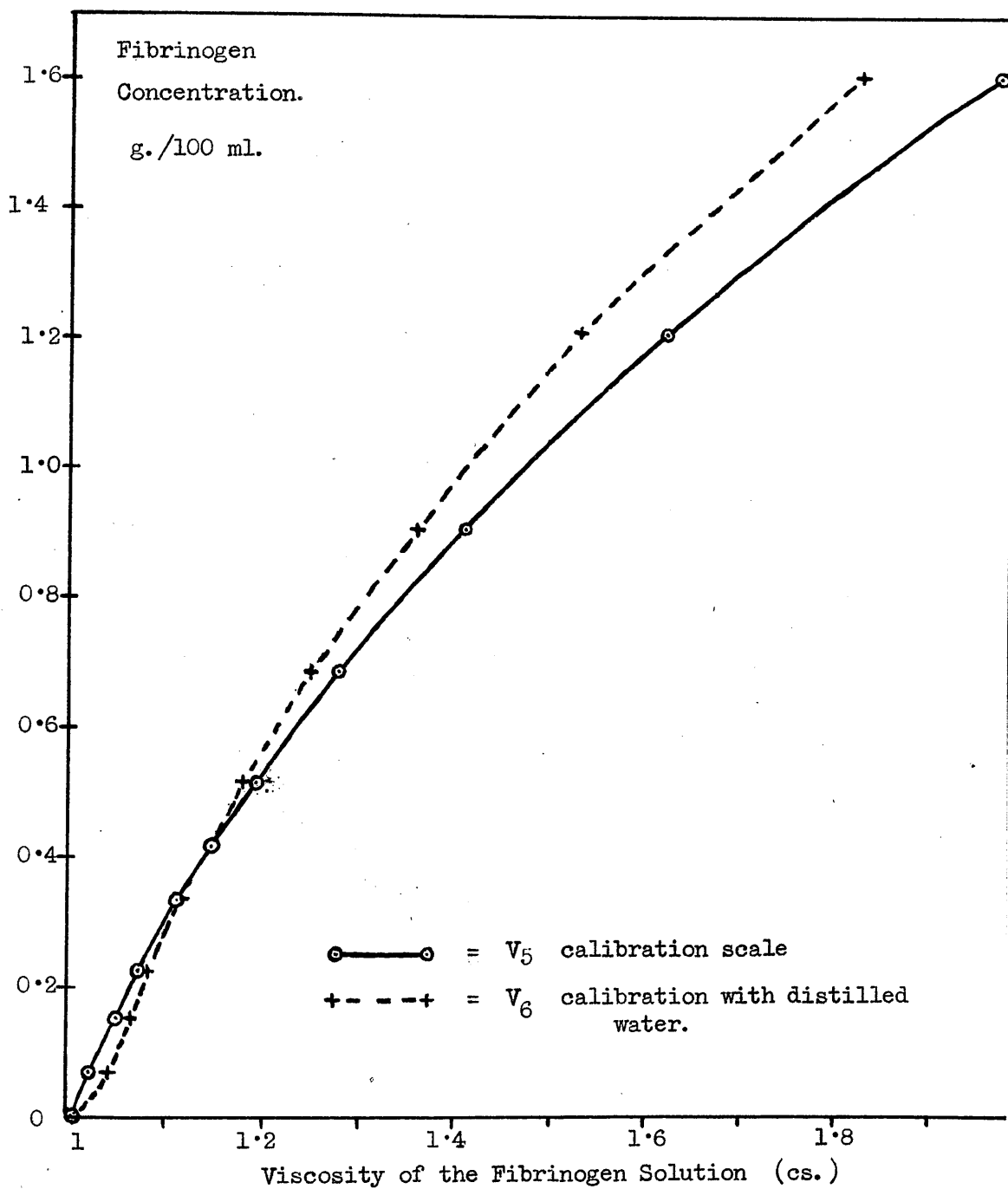


Fig. 20 The viscosity of a solution of Fibrinogen in water.
The fibrinogen was supplied by the Medical Research Council.

Taking the albumin viscosity effect as unity, the effective action of globulin was roughly 2· times, and that of fibrinogen was roughly 6· times. These figures should be remembered when we proceed to the discussion of the relative effects of the protein fractions on the plasma viscosity itself.

If $\log \mu$ were plotted (rather than ν) against the protein concentration, the graphs of Fig.21 could be drawn. It appears that each viscosity/concentration curve is now formed really from two straight-line relationships, and furthermore that the change from one slope to the other occurs at the same viscosity value ($\mu = 1.4$) for all three. This finding suggests that the explanation of the phenomenon lies in the characteristics of the viscometer rather than in the protein solutions: to the critical viscosity value at which the lines change direction we have applied the term - "shear point". It should be noticed also that the viscosities of the protein solutions at the concentrations encountered in the serum and plasma lie to the left of the "shear point" of these figures, yet the viscosities of the natural fluids lie to the right of this point; this makes it difficult to apply the findings for solutions to the plasma itself.

The viscosity of the albumin and globulin solutions has been studied many times previously (3 ,40 ,41 ,105 ,109, 179). All agree concerning the shape of the ν/c line of correlation

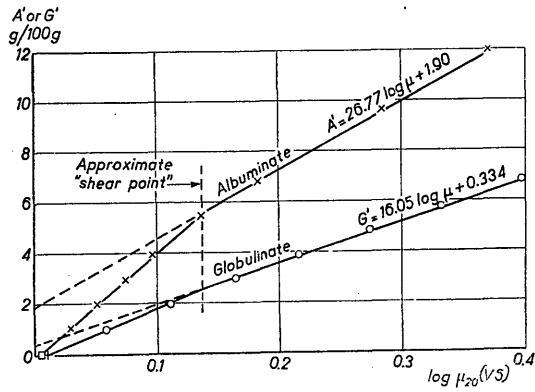


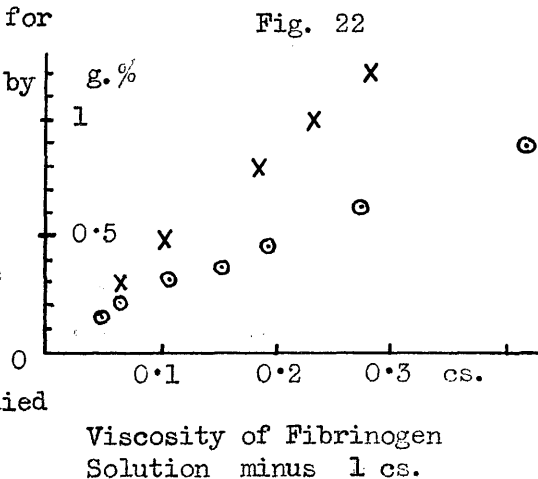
Fig. 4. Variation of $\log \mu_{20}$ with concentration:

- × sodium albuminate (V6)
- „ globulinate (V6)
- + „ chloride (0.895 %)
- water

Fig. 21 On plotting $\log \mu$ of the solutions of albumin and globulin against the protein concentration, the line for each was formed by two parts. The angle of both lines corresponded to the same viscosity value ($\mu = 1.4$).

but none would coincide exactly if the curves were superimposed. The responsibility for these differences can be divided between variation in the proteins as the techniques for their preparation differed from worker to worker and discrepancies arising from the characteristics of the viscometers. As an example of the latter cause, Fig. 22 presents the values for

the fibrinogen solution as measured by Lawrence (X) and myself (O) on fibrinogen obtained from the same source. Lawrence suggested that the viscometers could be calibrated and correlated with a commercially-supplied



albumin solution, but in view of the differences possible in the batches of protein, I do not consider that this would be the best method available - the method to be described in the following section is superior as it is independent of the protein characteristics.

It is well known that in certain homologous series of compounds (occurring in nature as liquids) the relation between the viscosity at a given temperature and the molecular weight is fairly uniform - for instance, in the aliphatic hydrocarbons, if $\log \mu_{20^\circ}$ be plotted against the molecular weights, the compounds

lie close to a straight line, from pentane to octane. In an original hypothesis Whittington and I attempted to apply this finding for pure liquids to substances in solution (for details consult the reprint of our paper).

We proposed that instead of treating a solution as consisting of solute and solvent we would treat it as if it were a single substance with an "effective molecular weight" made up from the components. If the weight of the molecule of solvent = M and that of solute = M_S , and if the concentration of the solute (g./100 g.) be S , then the relative gram moles of solute and solvent, per 100 g. of solution, are

$$S/M_S \text{ and } (100 - S)/M \text{ respectively.}$$

Taking moments, therefore, we defined the "effective molecular weight" of the solution (M') as

$$M' = \frac{100}{\frac{S}{M_S} + \frac{100 - S}{M}}$$

Evidently, as $M_S \rightarrow \infty$, as in the case of proteins, then

$$M' = \frac{100M}{100 - S}$$

For aqueous solutions

$$M' = \frac{1800}{100 - S}$$

and for saline solutions

$$M' = \frac{1810}{100 - S}$$

On testing this hypothesis with the results for sucrose solutions published by Bingham and Jackson (21), an excellent straight-line relationship was obtained between M' and $\log \mu_{20^\circ}$,

where $M' = \left(\frac{1800}{100 - S} \right) (1 + \alpha S)$ where $\alpha = - 0.00143$.

(The $(1 + \alpha S)$ factor was introduced to compensate for the omission of the S/M_S which was not negligible.) (cf. Table -R(b))

Applying the same formula to protein solutions, both the albumin and globulin solution values lie on the sucrose line (until $\mu = 1.4$) if $\alpha = + 0.025$ for globulin and $\alpha = + 0.008$ for albumin. After μ exceeds 1.4, (= approximate "shear point") the protein line diverges from the sucrose line, but still lies as a single line. When the fibrinogen solution was studied the falling-drop apparatus was not available, the specific gravity was not measured, and μ could not be calculated from γ ; but from the small concentrations used the specific gravity could not have increased by more than 1.5%. The results available indicate that the fibrinogen solution behaves exactly as the other proteins, that the fibrinogen line coincides with the other proteins' line, and that $\alpha = + 0.093$ approximately.

Further, on plotting the α values against the (Fig. 23) corresponding M_S values, a straight line is obtained if M_S for salt = 58.5, for albumin = 69,000, for globulin = 159,400

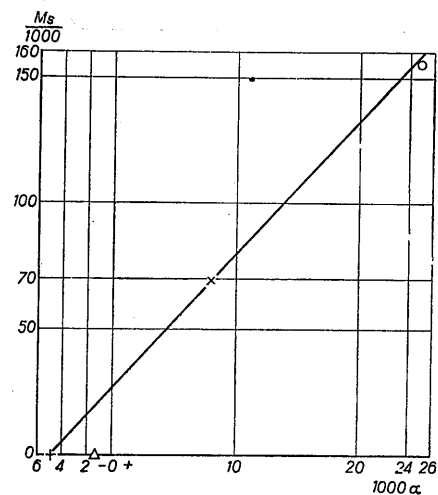


Fig. 3. Variation of α with M_s at 20°C .
Aqueous solutions of:

- + sodium chloride
- x " albuminate
- o " globulinate
- Δ sucrose

Fig. 23

See text for an explanation of this figure.

The relation between the Molecular Weight of the proteins and the factor " α " whose derivation is given in the text.

The basic hypothesis is to treat an aqueous solution as if it was a homogeneous single substance.

and for fibrinogen = 520,000. These figures are very close to those generally accepted for the molecular weights for these protein fractions. This technique, with further values derived from proteins of accepted molecular dimensions, offers another method of measuring the molecular weights of new substances somewhat analogous to the intrinsic viscosity techniques (125) used at present to study the large polysaccharide molecules.

It can be demonstrated also that the effect of temperature on viscosity is capable of expression as alterations in " α ".

The reference to the "effective molecular weight" of solutions has been included here as the idea was original; from the promising results which I have obtained with protein solutions Whittington has proceeded with further fruitful researches with other substances (unpublished results).

Yet another method for correlating and calibrating (Fig. 24) viscometers also becomes available. The sucrose line is a universal standard and readily reproducible. It should be possible to use an albumin solution (purity is not critical) to derive calibration formulae for any viscometer by which the $\log \mu$ values can be adjusted to allow the protein lines to coincide with the sucrose line. Such a scheme would eliminate the effect of the variation in the shear of individual viscometers. It would

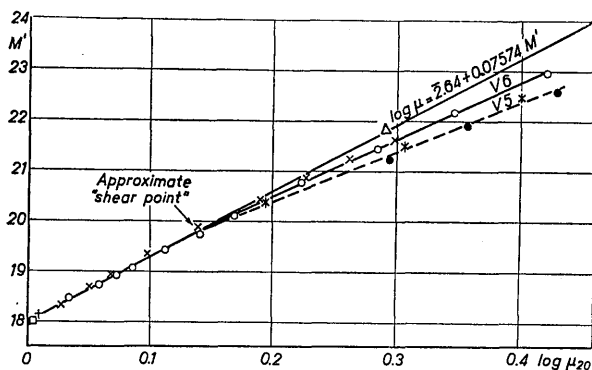


Fig. 2. Variation of $\log \mu$ with "effective" molecular weight.

$M' = \frac{100 M}{100 - S}$ ($1 + aS$) where M = mol.wt of solvent; S = g/100g concentration of solute

\triangle Sucrose 20% (BINGHAM and JACKSON) $a = -0.00143$

+ Sodium chloride 0.895% $a = -0.00496$

\square Water

\times Sodium albuminate V6

* " " V5 (calculated) $\left. \begin{array}{l} \\ \end{array} \right\} a = +0.008$

\circ " globulinate V6 $\left. \begin{array}{l} \\ \end{array} \right\} a = +0.025$

\bullet " " V5 (calculated)

Fig. 24

This figure shows how the viscosity of a protein solution can be made to coincide with the "sucrose line".

This figure contains the foundations of

- (a) a method by which the molecular weight of a solute may be calculated if the characteristics of the viscometer have been studied with solutions of substances of known molecular weight, and
- (b) correlating viscometers by a protein solution to supply results corresponding to this sucrose line which is internationally reproducible.

have been more satisfactory, in the light of our subsequent experience, if all our family of viscometers had been correlated to this sucrose line rather than to the arbitrarily-chosen V5 instrument - a consideration of Fig. 24 will show how simple such a procedure would be.

§17. The Serum Viscosity / Serum Proteins Relationship.

The first 212 tests in which I made the estimation of both the serum viscosity and the serum proteins will be considered only as these results have been analyzed previously as the basis of two papers by Whittington and myself (97,100) and further later results have added no more information to that obtainable from the originals.

Methods. The viscosity of the serum was measured at 20°C. and the values recorded in the V5 scale.

The albumin and the total globulin were estimated by a micro-Kjeldahl technique, plus fractionation by the classical sodium sulphate salting-out method of Howe (121).

Results. The results are presented in Table S* of the Appendix.

The protein concentrations were plotted against the serum viscosity to yield Fig. 25 . The distribution presents a wide scatter but there is a back-ground regular trend of pattern which

(* the results have not been collected into a single table, but can be extracted from the various other tables of parts 7 and 8.)

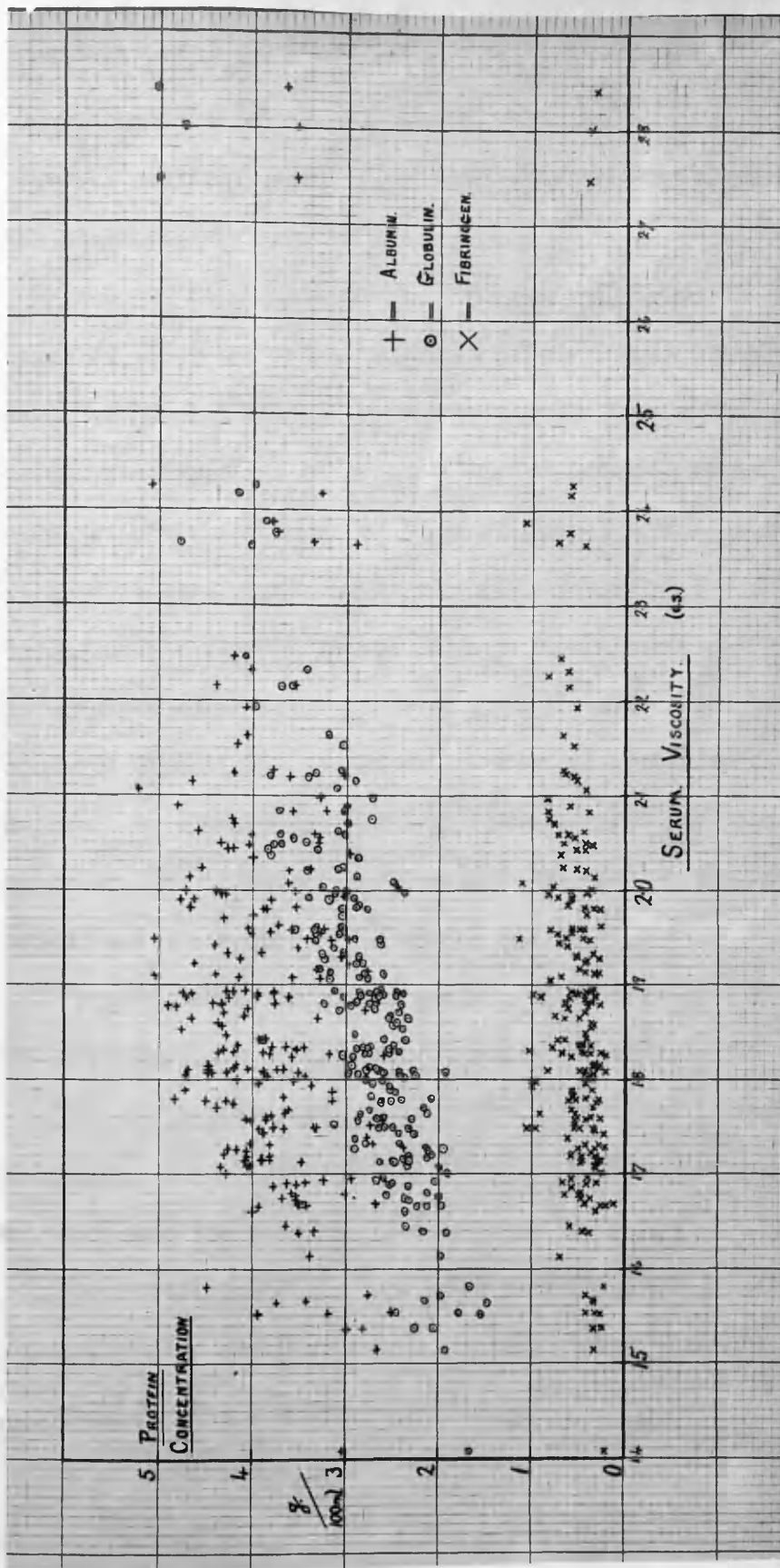


Fig. 25 The relationship of the Plasma Protein Fraction concentration to the Serum Viscosity (all cases are included here).

The underlying pattern, shown in Fig. 26, is readily detected.

prevents one from applying the adjective "random scatter" to the diagram.

Now, if from the total tests I removed those values from cases of liver and kidney disease, together with those from the cases of general disease approaching death (a condition later defined as "terminal decay") the distribution shown in Fig. 26. remains. The points can be joined by broad lines, as shown. It appears that as the serum viscosity increases the albumin values can be found arranged along periodic curves; the globulin is arranged along similar curves with the same phase but in the opposite direction. At the nodes where the periodic curves approach or even cross, the A/G (albumin/globulin) ratio may be unity or less; the A/G ratio will be highest at the intermediate stage when the curves are farthest apart.

Fig. 26 also includes a graph of the fibrinogen values as it is permissible to consider fibrinogen only as a globulin which has the special property of forming a clot under appropriate conditions. The fibrinogen curve moves in the same phase and direction as the total globulin curve.

The total protein values (not graphed) increase as the viscosity increases, without a periodic-curve distribution as obtained for the components.

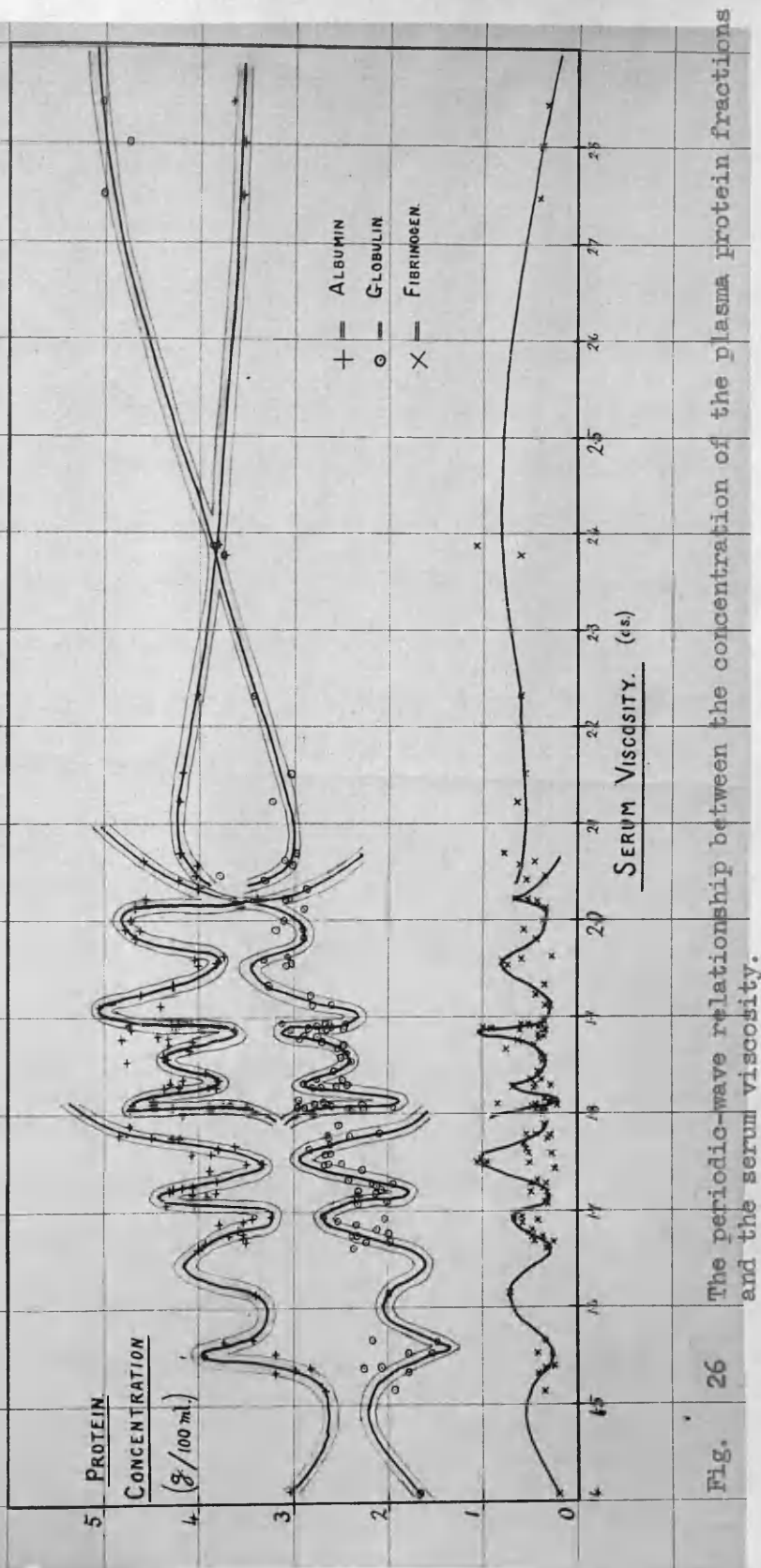


Fig. 26

The periodic-wave relationship between the concentration of the plasma protein fractions and the serum viscosity.

This figure is derived from the results of Fig. 25 by excluding those of primary disease of the liver and kidneys and of cases of "terminal decay".

Discussion. As can be confirmed by a study of a few results in Table S* it has not been possible to get an agreement between the viscosity of the serum and the sum of the viscosity of its ultrafiltrate plus the increments of (viscosity of pure protein solutions of the same concentration as occurs in serum minus the viscosity of the solvent). The kinematic viscosities (ν) and the absolute viscosities (μ) were studied according to the Newtonian fluid calibration, the V5 scale, and after calculation to the sucrose line, yet the viscosity of the serum always exceeded the sum of the viscosities of its components. (The sucrose line technique was specially useful as with it the divergence at the "shear point" can be eliminated; the results of pure solutions lie to the left of this point while the serum results lie to its right.) This discrepancy led us to postulate the existence in serum of a combined-protein formed from albumin and globulin - this large molecule would have an effective action in increasing the viscosity by an amount greater than the sum of its constituents acting as discrete molecules.

From this hypothesis Whittington analyzed my results working from an equation by which a mass-action equilibrium was proposed between free albumin and free globulin and a complex of albumin-globulin. He derived the figures -

$$A^{0.59} x G^{0.41} = K(A + G) \quad (K = 0.51 \text{ approx.})$$

(* see footnote on page 128)

Support for the method of analysis and for our hypothesis came in a personal communication from Dr. J.D. Hamilton of Canada, who had employed a different approach to end with a similar belief in a protein complex and an equation as under - (94)

$$A^{0.5} \times G^{0.5} = 0.63(A + G)$$

The agreement between these two equations is noteworthy.

(A reprint of our publication is included in the folder of the appendix.)

Unfortunately I did not study solutions of mixtures of the pure proteins. The regular relationships obtained by such workers as Rohrer (212) and Nugent and Towle (187) for solutions of the single proteins and their mixtures are rather against the existence of a combined-protein under these experimental conditions. This may be due to small but vital changes induced in the proteins in the maltreatment of their separation and purification.

A series of papers by the Heyder-Rohrer-Naegeli school in Berlin introduced a novel method for the fractionation of the serum proteins by a combination of viscosity and refractive index measurements. A series of viscosity measurements was made on various mixtures at various concentrations of albumin and globulin solutions, prepared from a single blood specimen. An elaborate chart was constructed from which, if one knew the

viscosity and the total protein content, the ratio of albumin to globulin (A/G) could be readily estimated. They proposed that the total protein content of the serum could be estimated from its refractive index, and the A/G ratio could then be calculated if the viscosity was known. This elegant plan did not take into consideration the differences in the viscosities which might be due to instrumental characteristics or the qualitative differences which may be found in the proteins in certain diseases, as no mention is made of studies with pure proteins derived from ill subjects: furthermore, the possibility of a protein-complex was not allowed for. This scheme of fractionation was used widely on the continent for 2 or 3 years (cf. Bircher (22,23,25)) until a more critical approach led to its complete discard; some papers included such impossible results as 100% albumin or even 0% albumin(122).

In the previous section we saw that the viscosity effect of globulin in solution was approximately twice that of albumin. Consideration of the results in Fig.26 might indicate that a generalisation concerning the effect of these proteins in the serum would make their ratio nearer 3:2. This again could be explained by the presence of a protein-complex.

The periodic wave relationship between the serum viscosity

and the protein fractions is quite novel. One immediately asks how it had been missed by previous workers in this field and several answers can be proposed - (a) such a periodic wave relationship would appear so unusual that some might attribute it to chance only, (b) the worker might have omitted to include it in his results as he could offer no explanation for its occurrence, (c) a large series of results is essential so that all the 'critical' values may be encountered, and (d) a high degree of accuracy in the technique of viscometry is required as it is obvious from Fig. 26 that minute errors at critical points would disturb the pattern greatly. I had had the experience of a similar periodic relationship between the plasma viscosity and the ESR, so that I was willing to accept my findings without qualms. Nevertheless, a search was made in the literature for similar investigations but that of Petschacher (193) was the only one in which the protein fractionation was by the same technique and the viscometry was similar (Ostwald at 25°C.). His 57 values were reported in the form of a table only. I plotted Fig. 27 to correspond to my own, and the similarity is indeed striking. Further, if a letter (a, b, etc.) is applied to each characteristic point in turn in both figures (ie. each peak and trough) and if the viscosities of these letters are plotted against each other, a regular sigmoid curve of correlation is obtained - Fig. 28.

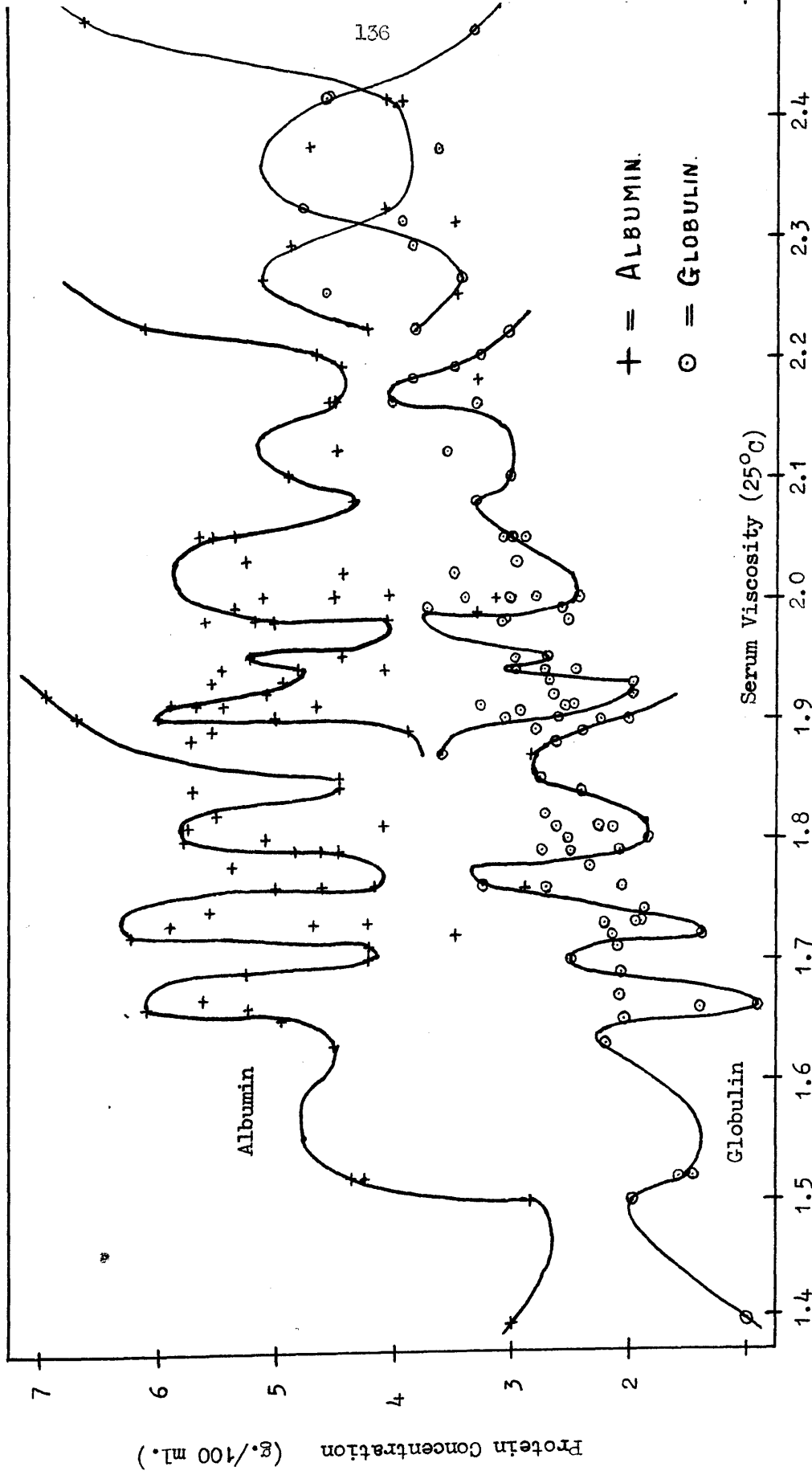


Fig 27 The periodic wave which can be drawn into Petschacher's results.

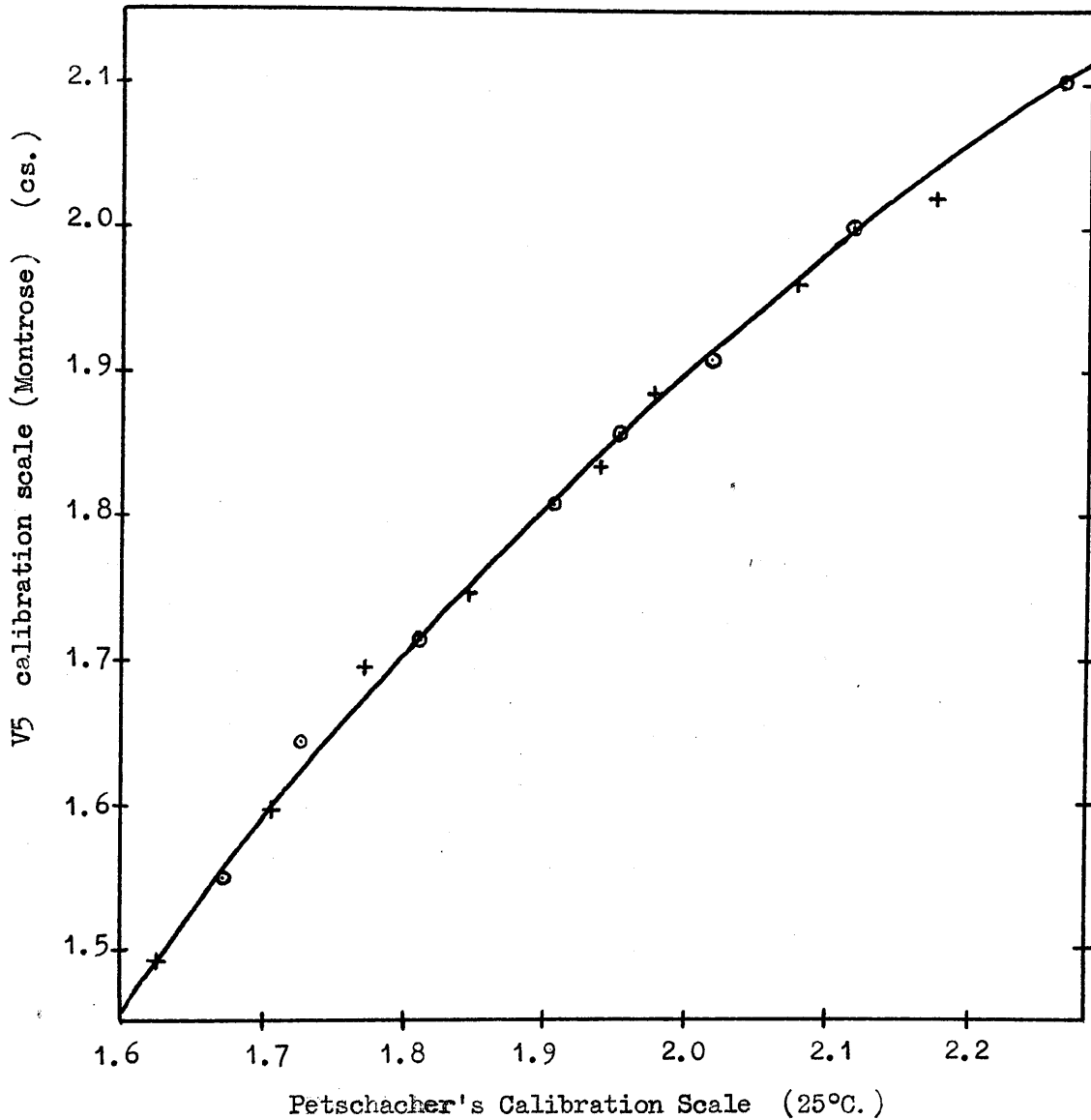


Fig. 28 The line obtained by plotting the characteristic points (ie. viscosity corresponding to a wave peak or trough) in the serum viscosity/protein fraction concentration, of my wave in Fig. 26 against the corresponding value of Petschacher's wave of Fig. 27.

Proceeding one stage further, if the correlation graph is used to convert Petschacher's viscosity results to my V5 scale, and if the serum albumin and globulin of the periodic lines corresponding to these V5 viscosities in Fig. 26 are read off, these protein values differ by less than 0.2 g. from Petschacher's originals.

I also considered that it was possible that similar periodic relationships could be discovered where the albumin and globulin fractions had different physical properties. Therefore I plotted the osmotic pressure of serum against the concentration of its proteins, as reported by Wells (246). (The fractionation technique was similar to my method.) As the albumin exerts a greater osmotic pressure than the globulin, the relationship is reversed as compared to the viscosity effect. Making this adjustment, Fig. 29 makes one consider seriously that this periodic relationship would be again encountered if some of the irregular diseases were removed.

In spite of pondering on this subject for years I have still no explanation to offer for the occurrence of the periodic curve in the serum viscosity / protein relationship.

Two other problems arise.

Later, in the clinical part of this thesis, it will be shown that in normal subjects the plasma viscosity values fall within a narrow defined range, that in illness in which there is

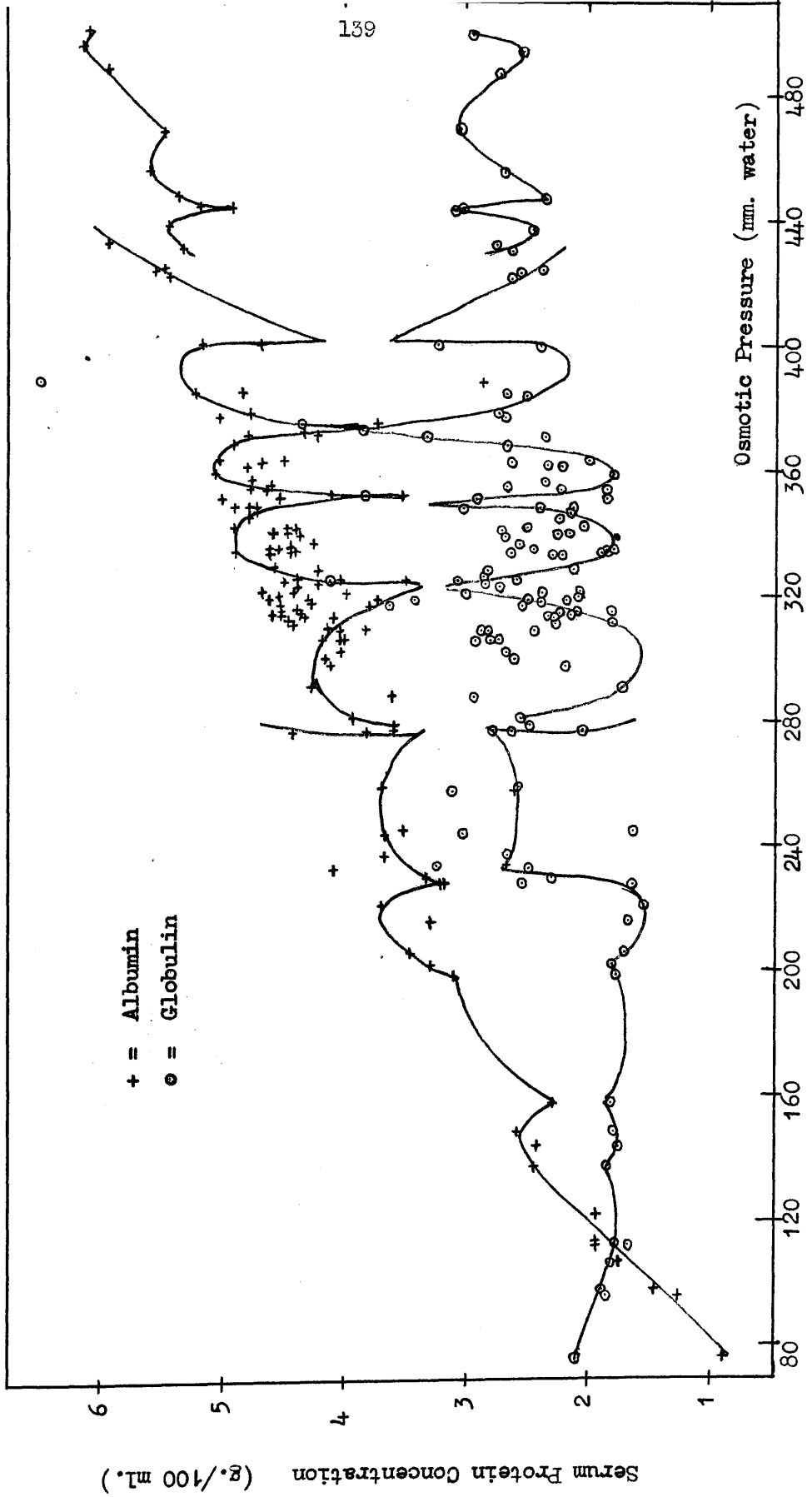


Fig. 29

The periodic wave relationship which may be drawn in the Osmotic Pressure/Protein Fractions diagram.

a generalised or systemic reaction the plasma viscosity rises, that the increase is proportional to and indicative of the degree of this systemic reaction, and that with recovery the plasma viscosity falls again to the normal range. In the rheumatic diseases where changes in the fibrinogen are moderate, Salt (217) and Coke (49) (also in personal communications) find that the serum viscosity changes much as does the plasma viscosity; my own results showed a wider variation as they included more cases of acute disease with high fibrinogen levels. The periodic curve was obtained by joining many results from individual patients. We are now faced with the problem of the behaviour of serial results of the individual patient in the course of an illness - as the viscosity increases and decreases, are the curves followed through each peak and trough? There is no answer yet because of the intensive tests necessary being beyond my capacity as long as my researches are being carried out as an addition to routine duties and not on a full-time basis. I found that it was possible for the results in one subject to move more than the distance between two critical points of the periodic curve within 24 hours. Hence it will be necessary that serial tests be made at intervals of a few hours only, which requires a staff of several technicians. In contrast, some cases of chronic disease

may have results showing no change over a period of weeks or even months. There is less difficulty in believing that such rapid and involved protein movements occur if one considers the work of Schoenheimer and other workers who showed that 50% of the protein of the liver is changed every three days, the results of Chick who found that euglobulin could change its characters in vitro to that of pseudoglobulin, and those reports where it was shown that a subject can be maintained in a positive nitrogen balance by the intravenous injection of plasma alone.

van Slyke is credited with the introduction of the estimation of the albumin/globulin ratio to clinical medicine, and it is claimed that as the severity of a disease process increases so does the A/G decrease and that an A/G ratio of 1 or less has a serious clinical significance. Now, on consideration of my curves again it is noted that the A/G ratio would be 1 or less at the several points where the albumin and globulin approach each other. This low A/G value can correspond to a serum viscosity just above or far above the normal range. Thus the A/G ratio and the serum viscosity are both claimed as guides to the same clinical states yet a comparison of them simply as physical values shows that the two tests must differ - which is the more reliable? My own opinion is that the viscosity is to be preferred. From my experience in chemical pathology I have come to discard the use

of the A/G ratio completely and rely upon the absolute values of the albumin and globulin. Salt (217) also favours the measurement of both the viscosity of the serum and the protein fractions, without the calculation of their ratio.

§ 18. The plasma viscosity / plasma protein relationships.

The viscosity of the mixed-oxalate plasma and the plasma protein fractions were studied in the same series of subjects as reported in §17 for the serum functions.

The fibrinogen was measured as the fibrin clot obtained by recalcifying plasma, the albumin and globulin were measured in the serum, and by allowing 0.75 as the specific volume of fibrinogen these two serum proteins were recalculated as plasma constituents by multiplying by $(100 - 0.75 \times F) / 100$.

Results. See Table S* of the appendix.

The plasma viscosity was plotted against the protein concentrations to yield Fig. 30. The absence of the periodic curves is noteworthy.

The fibrinogen values were plotted against the differences in viscosity between plasma and serum, and Fig. 31 was obtained. Also in this figure are the results of the solution of fibrinogen, with the original viscosity values converted to the V5 scale.

* see footnote on page 128.

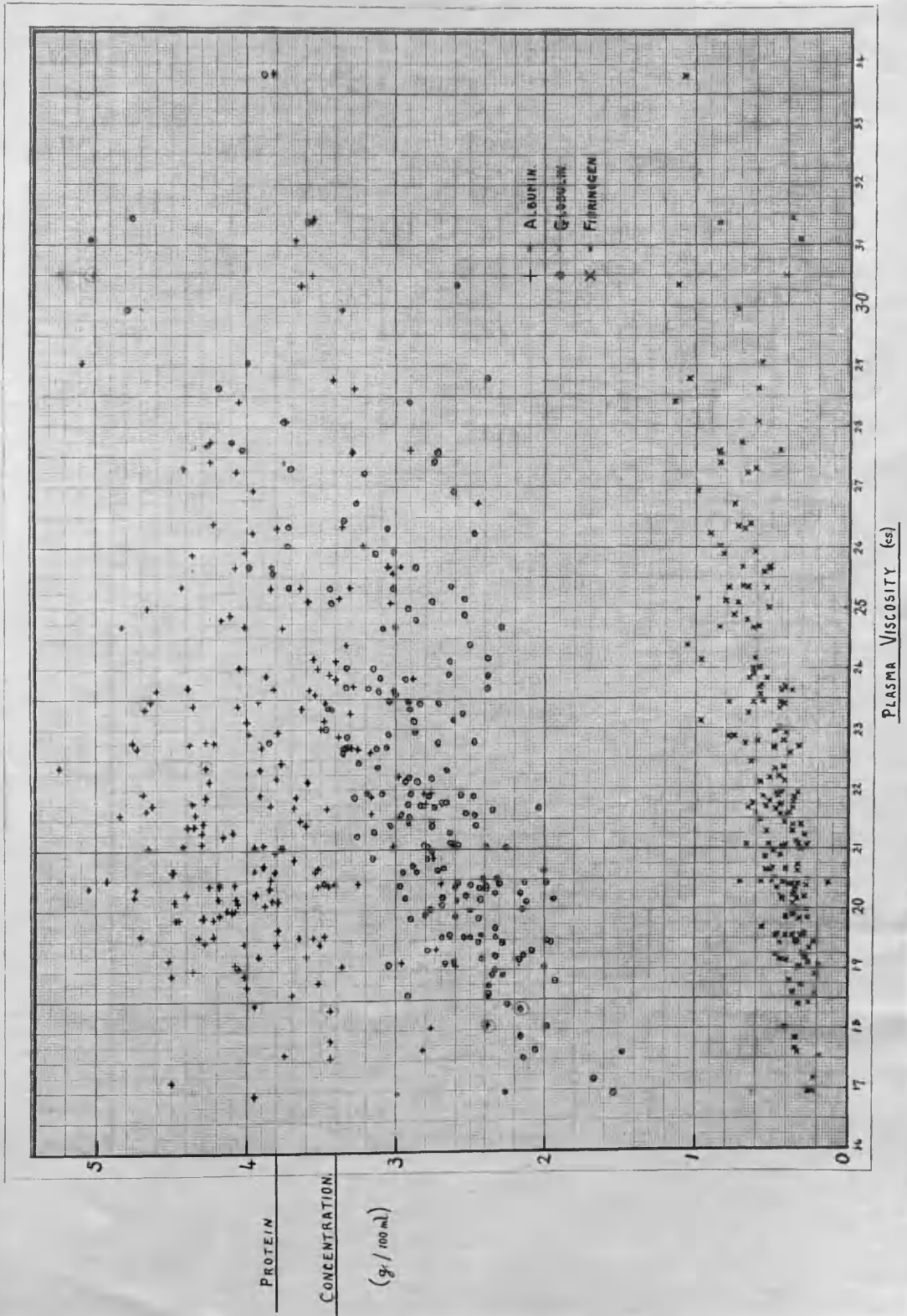


Fig. 30 The relation of the Plasma Viscosity to the concentration of the Plasma Protein Fractions.

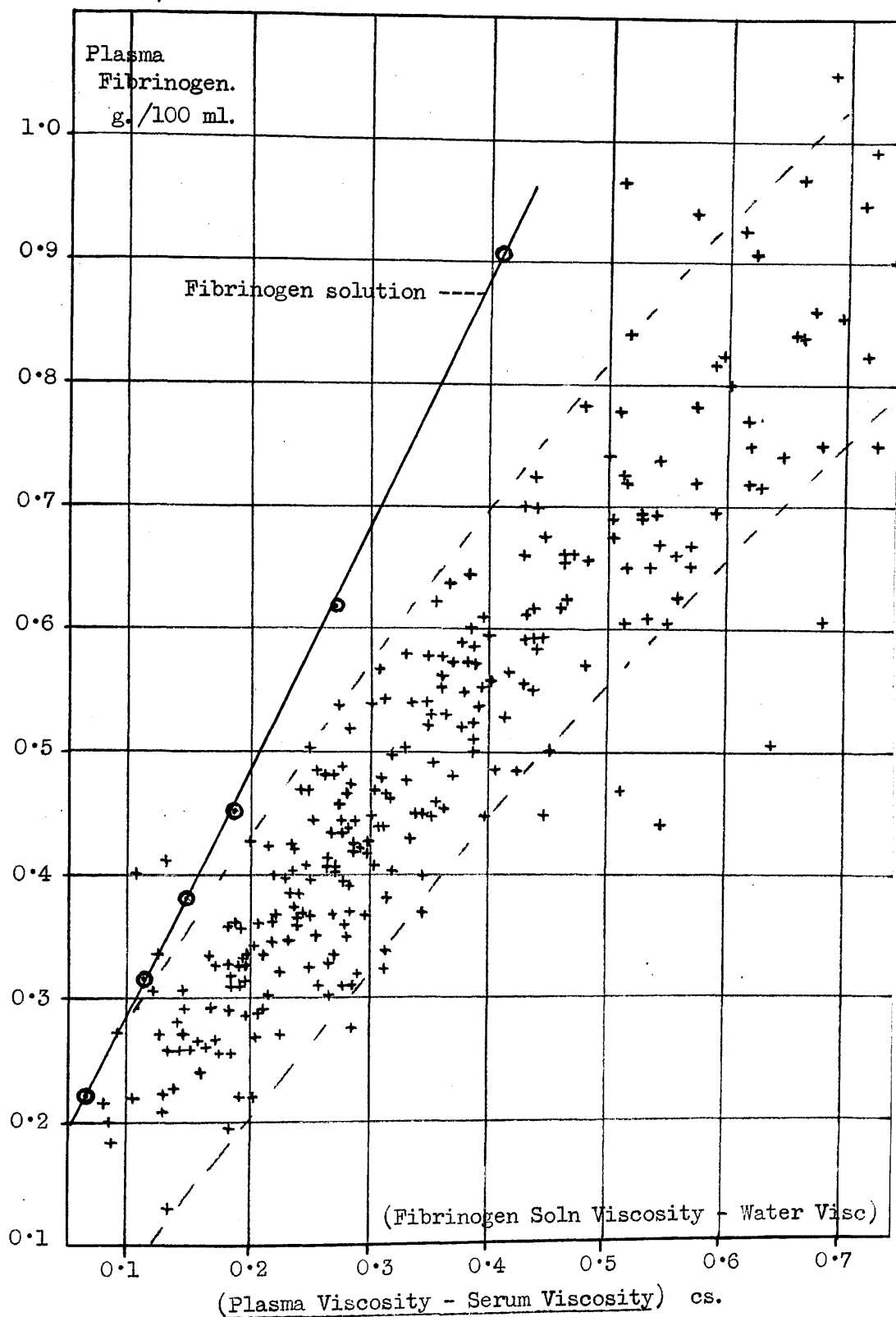


Fig. 31 The relationship between the plasma fibrinogen and the difference between the plasma viscosity and serum viscosity is only approximately linear, and this line is markedly different from the viscosity line of a fibrinogen solution.

Discussion. The absence of a periodic relationship between the viscosity of plasma and its protein constituents is due to the difference in the speed at which the protein fractions vary. The fibrinogen has a very rapid rate of change, about 100% in 24 hours being seen in cases of acute inflammation. A change of similar dimensions would not be found in the albumin or globulin in less than a week, such a slower rate lending itself to the maintenance of the periodic relationship.

An increment in the fibrinogen concentration has a greater effect in increasing the viscosity of plasma than in increasing the viscosity of a pure fibrinogen solution; we have already encountered this phenomenon for albumin and globulin. The same explanation is offered, ie. there exists in the plasma a protein-complex formed from albumin, globulin, and fibrinogen whose effect on viscosity is greater than the sum of its constituents acting singly. This discrepancy between the fibrinogen effect in plasma and solution has been verified by Lawrence (131).

Furthermore, the increment by the fibrinogen in plasma is not constant if one compares the fibrinogen values with the difference of the plasma and serum viscosities, as in Fig. 31. If one used the mean line of the plotted values together with this viscosity difference as a means of estimating the fibrinogen concentration, an error of 25% could be frequently met at low

fibrinogen levels. This error might arise if there was a variation in the size of the protein-complex or in the proportion of the fibrinogen in the complex. (The idea of a protein-complex in the plasma has been made by several other authors (eg. (171,231))).

Lawrence (131) has suggested that information regarding the chemical composition of the plasma can be obtained by his scheme for the fractionation of the proteins by serial viscosity measurements after successive protein removals. This scheme can be criticised on the grounds that it is inaccurate (eg. he uses the plasma-serum viscosity difference to estimate protein) and that information which bears a closer relation to the protein composition can be obtained more readily, eg. by filter-paper electrophoresis (55, 65, 82)..

One further point has to be made from the results. There was no instance in which the plasma viscosity was increased beyond its upper level of the normal range ($= 1.915$ cs.) by a high albumin level: an abnormally high plasma viscosity is due to an increase in the globulin and/or fibrinogen.

* * * * *

§ 19. The plasma protein equilibrium factor.

We had to postulate the existence of a protein complex in the plasma to explain the failure to correlate the viscosity with the protein fractions. Whittington continued with his mathematical analysis of my results, beginning from a mass-action equation

$$A_f^\alpha + G_f^{1-\alpha} + F_f^\beta \rightleftharpoons K(A_b + G_b + F_b)^{\alpha + \beta}$$

He also prepared Fig. 32 which I later redrew to the form shown here, by which it is possible to read off the value of \underline{K} if the values of albumin, globulin and fibrinogen are known. This chart includes the A/G ratio as one ordinate, and the A/F ratio as the other. (100)

I found that this \underline{K} value had a closer relation to the clinical condition of the patient than the simple A/G ratio from which it is partly derived; it could also possess greater clinical significance than the ESR or the plasma viscosity estimations, on occasions. It is an ingenious method for the expression of the inter-relationships of the three protein fractions as a single numerical value. (97)

(Reference is made here to this factor as its existence was derived from the results prepared in my viscosity studies. Reprints of the papers in which appear Whittington's analysis and my clinical application of the factor are included in the appendix.)

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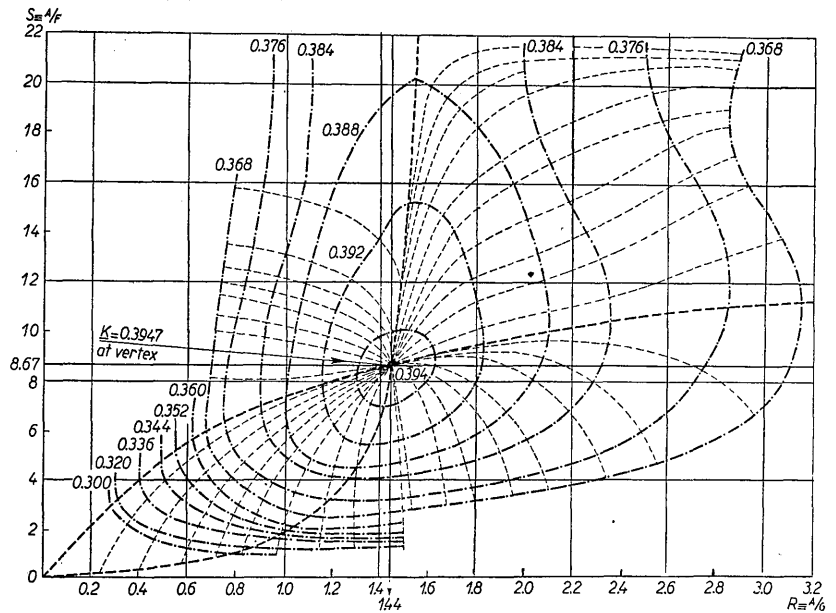


Fig. 3. Nomogram for estimation of K from $R \equiv A/G$ and $S \equiv A/F$. Contours of equal K values. Orthogonals of maximum change in K with least change in protein fractions.

Fig. 32 Taken from my paper (97)

The nomogram by which the plasma-protein-equilibrium-factor (K) may be calculated from the A/G and A/F ratios.

The consideration of the A/F ratio has led to an improvement over the single A/G ratio.

§ 20. The relation of the specific gravity of plasma and serum to the protein content.

Some of the data given here have been used as the basis of a publication by Whittington and myself - a reprint is contained in the appendix.

The Heyder-Rohrer-Naegeli scheme for the fractionation of the serum protein from the measurement of the viscosity and the refractive index, referred to in §17, failed in its practical application because (in my opinion) they attempted to apply their results from pure protein solutions to the serum without making any allowance for a possible combined-protein complex of higher effective molecular weight and specific viscosity than its components. I decided that if I had a simple method for the estimation of the total protein I might reinvestigate this problem from measurements of the serum viscosity.

It was essential that the method for the measurement of the total protein be simple and accurate, otherwise the routine chemical methods of fractionation and estimation would be less time-consuming. In the early 1940s the specific gravity methods were being advocated widely, several techniques had been devised, and the possible accuracy claimed was high. All these methods assume that the non-protein constituents affect the specific gravity to a constant amount and that the protein fractions

all affect the specific gravity equally (186). The specific gravity and the total protein were correlated by formulae; unfortunately there seemed to be a different formula in each paper. Nevertheless, I decided to give this method a trial.

Methods. The specific gravity was measured by the falling-drop methods of Barbour and Hamilton (12) and Phillips et al. (194). The total protein was measured accurately by a micro-Kjeldahl technique. The details of these methods are given in the appendix.

Results. For serum I obtained the best correlation between my specific gravity results (Barbour and Hamilton method) by the formula originally derived by Weech et al. (245) from dog experiments: for plasma, as I was using Phillips copper sulphate method, I used the formula recommended by him.

I express my results in Fig. 33 where there are three frequency curves for the differences of the protein as estimated by a specific gravity method from the protein as estimated by the micro-Kjeldahl method; one curve refers to my serum results, one to my plasma results, and one to the results of Adams and Ballou for serum tested by Phillips technique(4).

Discussion. There can be a discrepancy of 1.5 g./100ml. between the protein as estimated by these methods.

Both methods used will yield specific gravity results which in duplicate tests agree to 0.0001. The copper sulphate method

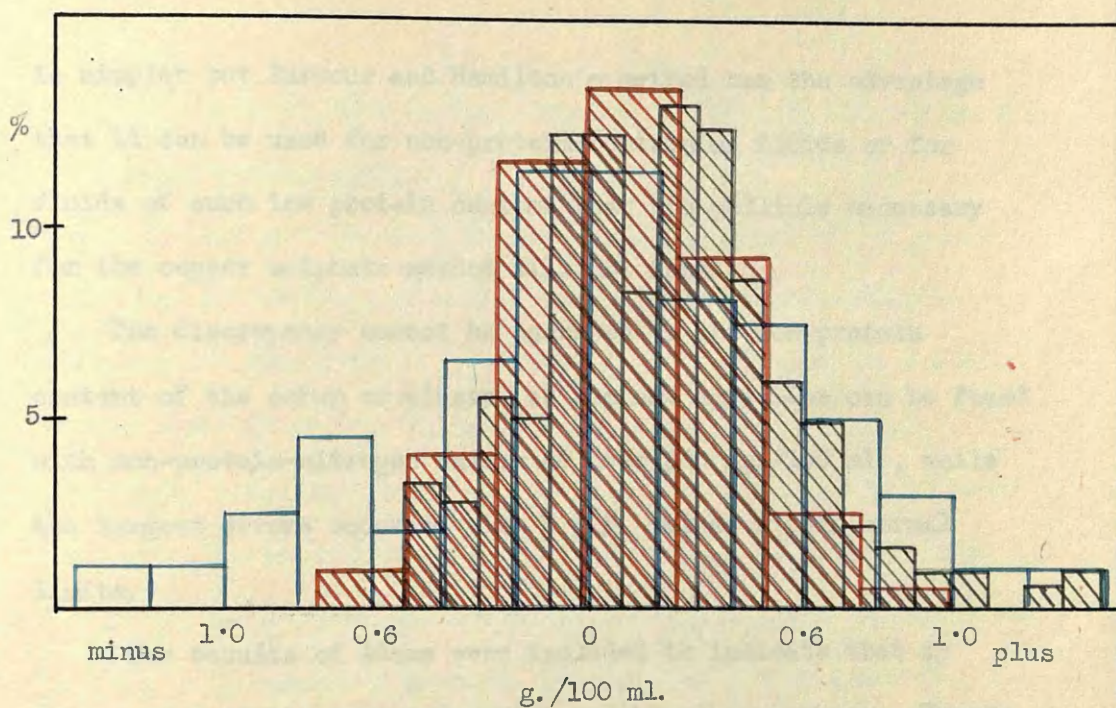


Fig. 33 The relation of the Total Protein of Plasma and Serum calculated from the specific gravity to the value obtained by a micro-Kjeldahl technique.

The black area represents my results for Serum, with Barbour and Hamilton's Falling Drop specific gravity technique

$$\text{Serum Protein} = 347.9(\text{Sp. gr.} - 1.00726) \text{ g./100 ml.}$$

The red area represents my results for Wintrobe's Oxalate Plasma, and Phillips Copper Sulphate specific gravity technique.

$$\text{Plasma protein} = 360(\text{Sp. grav.} - 1.0080) \text{ g./100 ml.}$$

The green area represents the results of Adams and Ballou (4) for Serum, using Phillips method.

is simpler but Barbour and Hamilton's method has the advantage that it can be used for non-protein-containing fluids or for fluids of such low protein content that the pellicle necessary for the copper sulphate method will not form.

The discrepancy cannot be ascribed to the non-protein content of the serum or plasma, as perfect agreement can be found with non-protein-nitrogen values of over 100 mg./100 ml., while the largest errors occurred with N.P.N. values within normal limits.

The results of Adams were included to indicate that my errors were of the same order as found by other workers. Papers still appear in which the method of specific gravity is praised, but more are critical (8,113,151,152,263,264,243)

An indirect criticism of the method can be detected in the gradual disappearance of the copper sulphate bottles from many laboratories of repute. Their departure will certainly be hastened by the simple but elegant protein fractionation by electrophoresis on filter-paper (55 , 65 , 82).

Because of these potential errors in the technique for the estimation of the total protein I did not pursue my proposed investigations for serum and plasma protein fractionation by a viscosity method.

* * * * *

(E) The relation between the plasma viscosity and the erythrocyte sedimentation rate.

Later, in the part devoted to the clinical aspect of the plasma viscosity estimation, it will be shown that the viscosity is increased in the presence of disease and can be used as a guide to the severity of the reaction to this pathological process: in that part there will be a comparison of the values of the plasma viscosity and the ESR tests to the clinician. We will confine our attention here to the comparison of two physical measurements.

Methods. The appendix includes the details of these estimations. From citrate blood, the corrected plasma viscosity and the maximum corrected erythrocyte sedimentation velocity were measured. From mixed-oxalate blood, the plasma viscosity and the 1-hour ESR, corrected for variation in the haematocrit according to the chart of Wintrobe and Landsberg (258), were measured.

Results. The results have not been collected into a single table but may be noted scattered throughout various other tables. The relevant information can be depicted in Fig. 34, 35, 36, 37, and 38, and also in Fig. 80 and 89 of the clinical part.

Discussion. The discussion can be divided for convenience according to the ESR techniques.

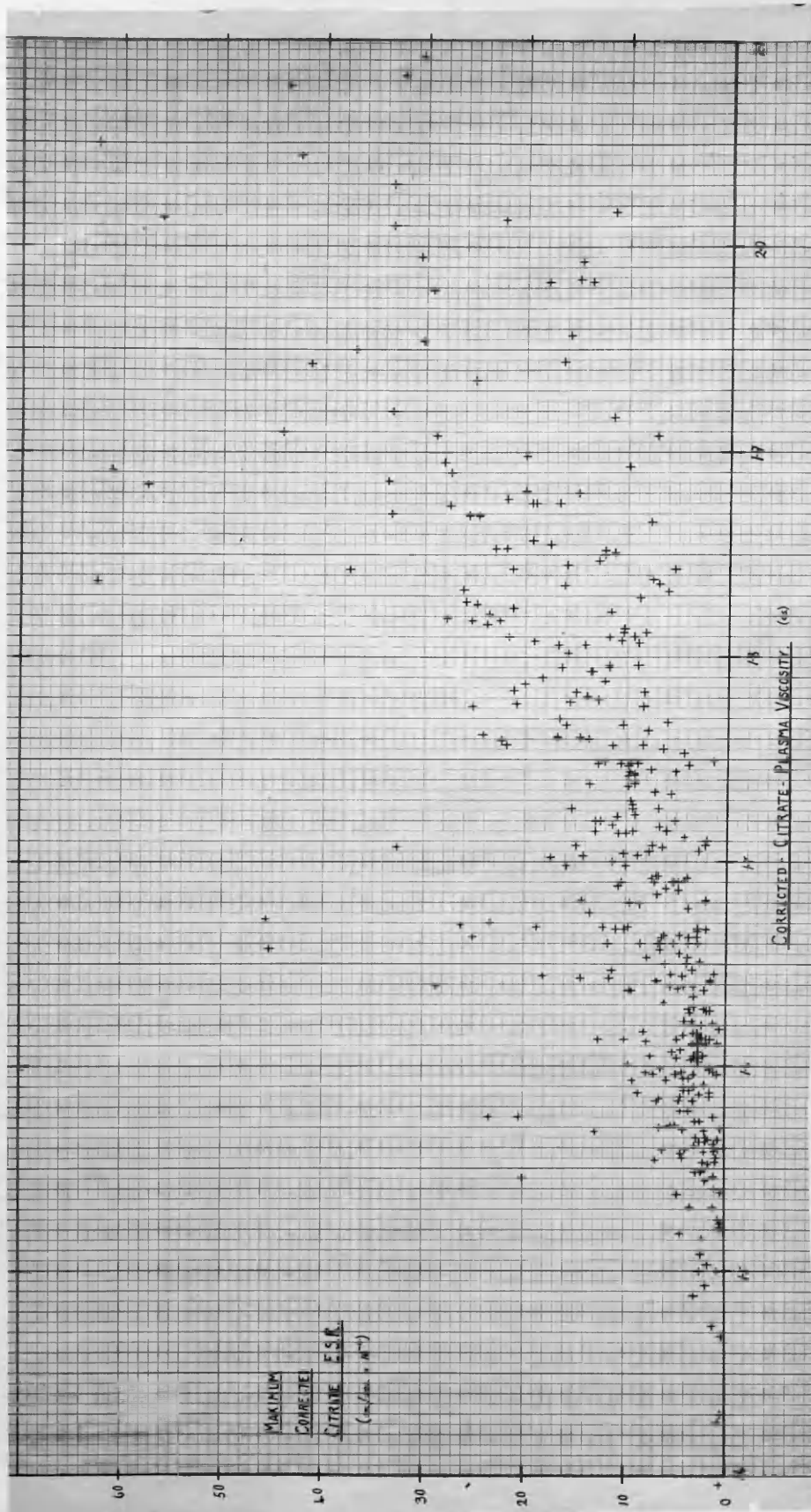


Fig. 34 The relationship between the Citrate Plasma Viscosity and the Maximum Sedimentation Velocity. All cases have been included, but the underlying pattern of Fig. 35 can be readily detected.

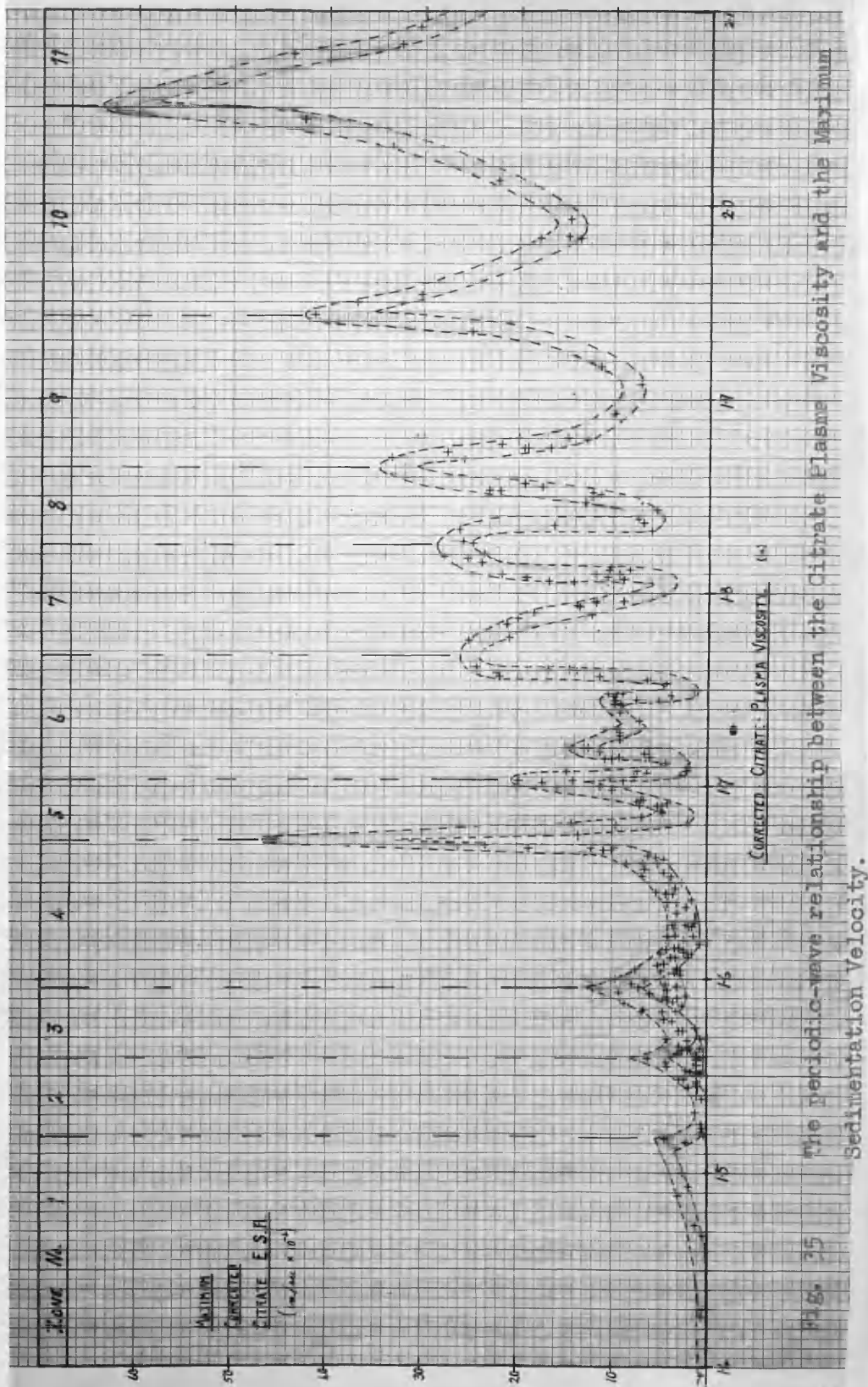
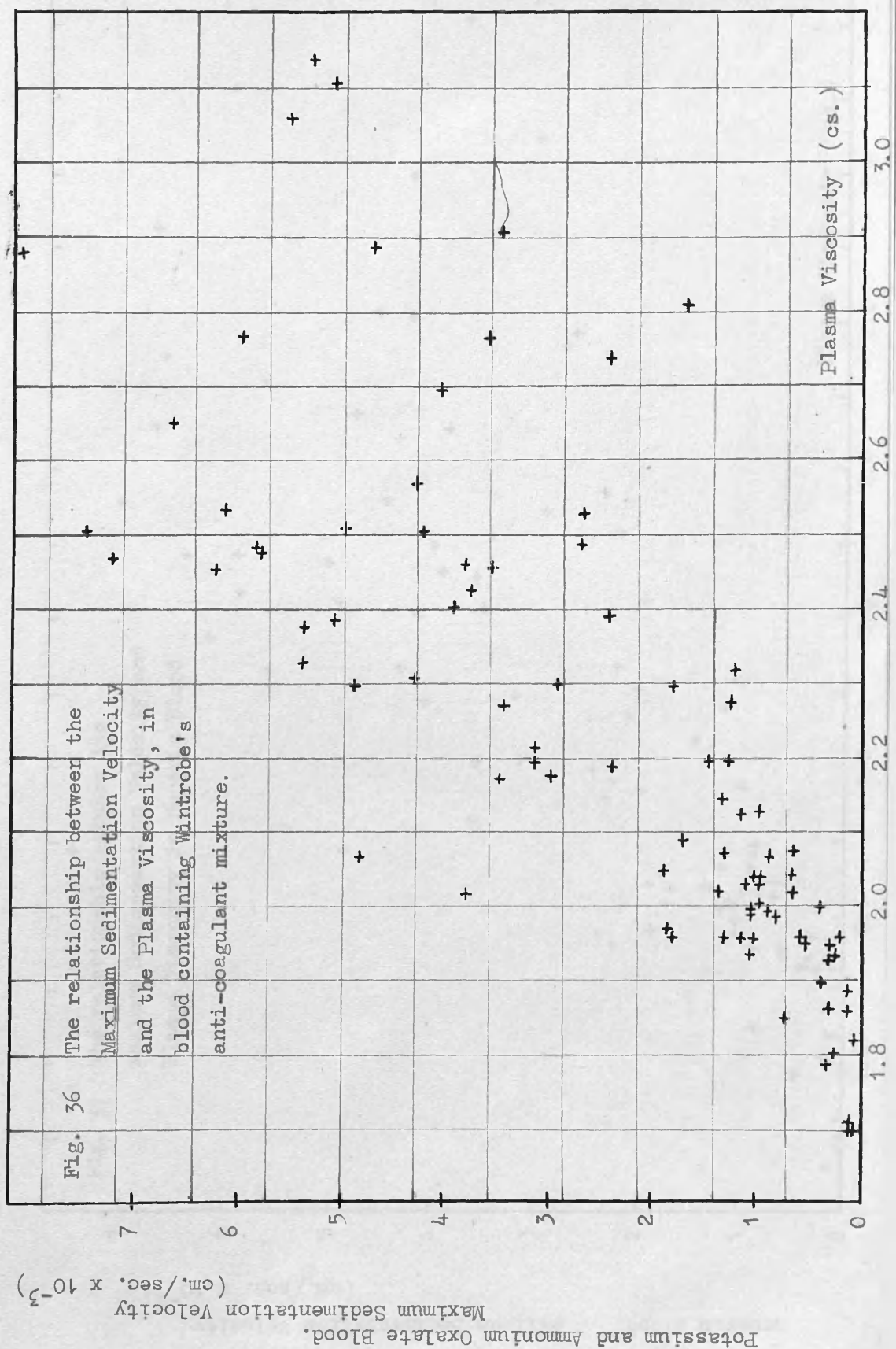
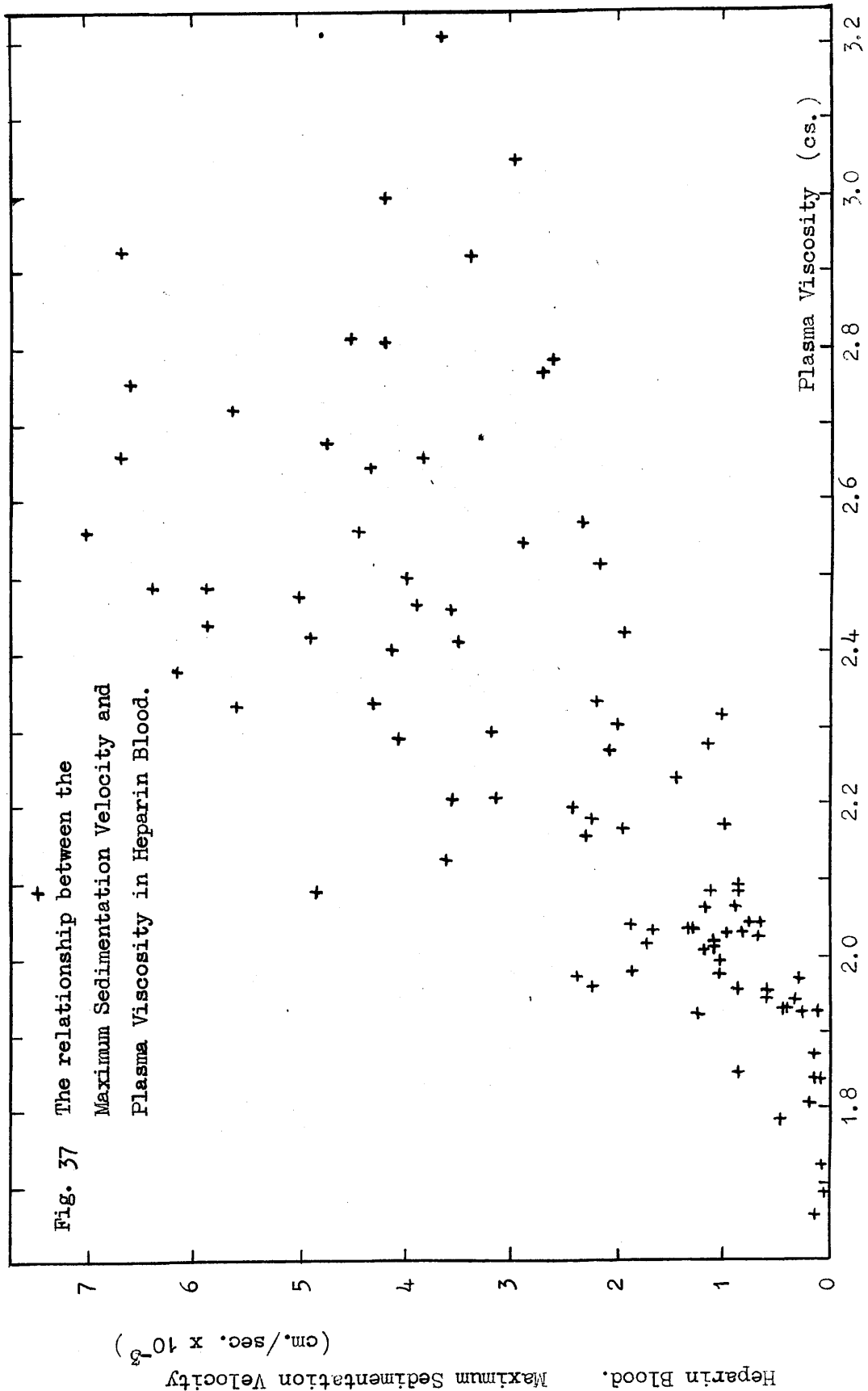


FIG. 35 The periodic-wave relationship between the Citrate Plasma Viscosity and the Maximum Sedimentation Velocity.

This figure is derived from the total results (Fig. 34) by excluding the cases of "terminal decay".





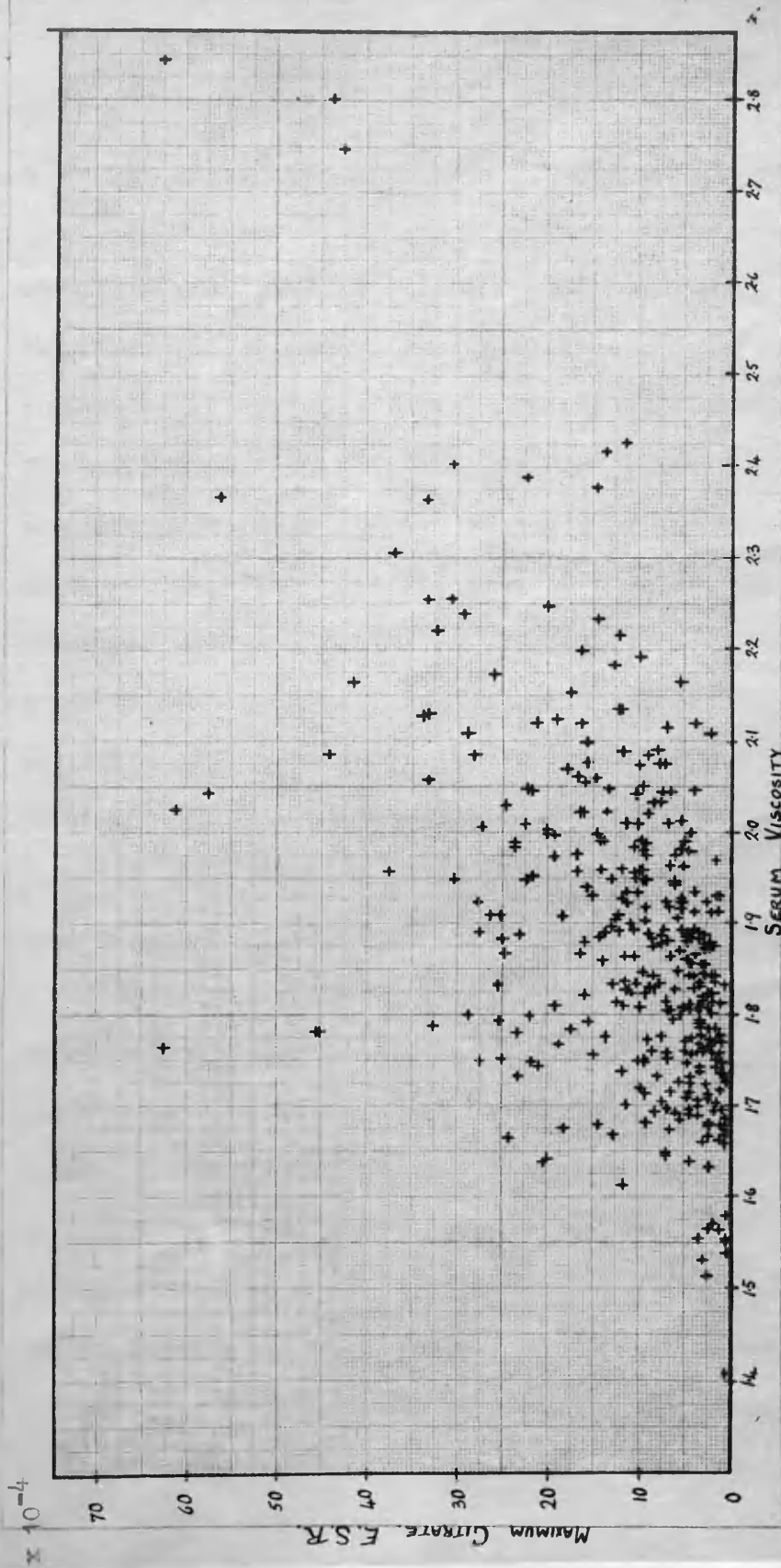


Fig. 38 The relationship between the Serum Viscosity and the Maximum Citrate Sedimentation Velocity

§ 21. Corrected maximum erythrocyte sedimentation velocity.

Whittington's original 20 tests in duplicate of the ESR and plasma viscosity had indicated that a straight-line correlation was unlikely - he joined his points by three discontinuous curves. Later, when I came to plot my ESR/viscosity relationships I found that they could be joined by a continuous periodic curve, as in Fig. 35 . Whittington was able to confirm my curve from further results of his own and his curve was identical in shape. Moreover, if each peak and trough was given a letter and our viscosity values corresponding to these points plotted against each other, a regular curve of correlation was obtained: we used this discovery as the basis of our attempts to correlate the results for non-Newtonian liquids (such as plasma) when measured in viscometers calibrated with Newtonian liquids (Fig. 39)

There is independent support for the existence of this curve in the results of Gibson (87) who studied mixed-oxalate plasma viscosity and a maximum sedimentation velocity in oxalate blood. He did not discover a curve but he did find that there were peaks in his ESR/viscosity distribution chart. Unfortunately he was using an instrument which was not correlated to the V5 scale; nevertheless, on plotting the plasma viscosity values corresponding to his peaks (oxalate blood) against my values (citrate blood) I obtained a series of points which could be

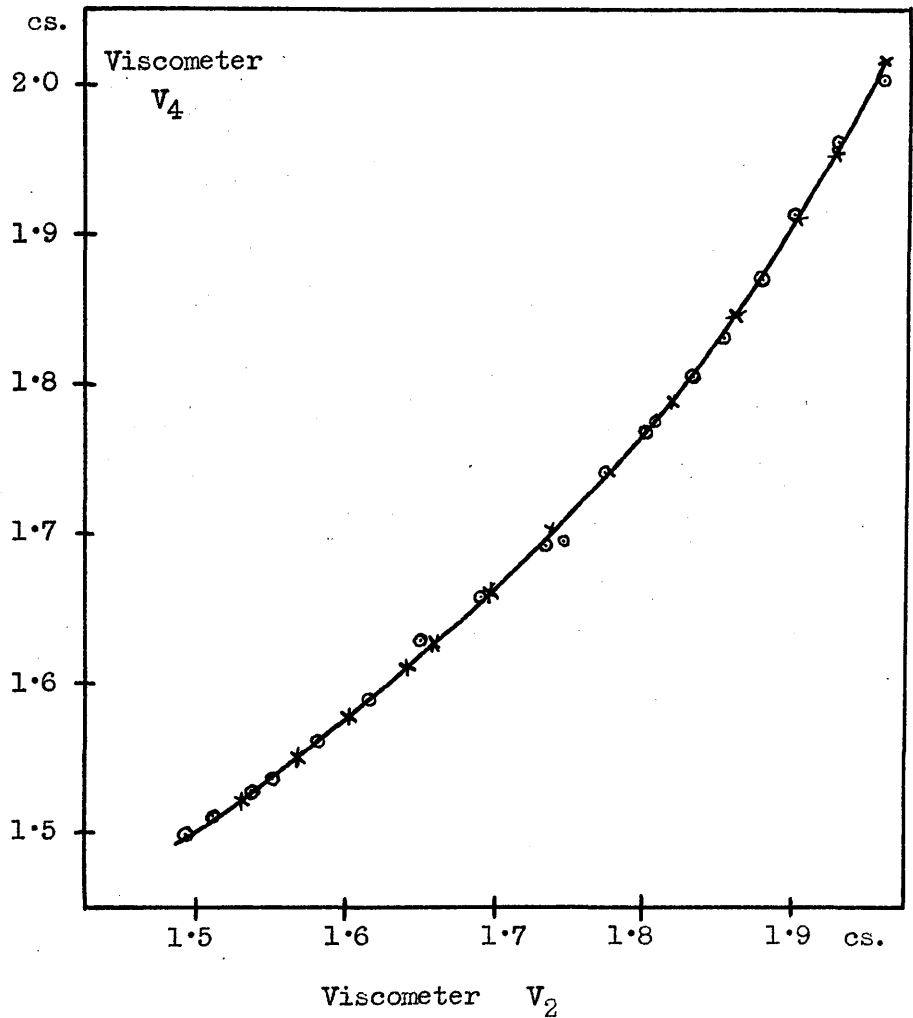
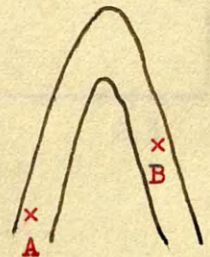


Fig. 39 The correlation of Viscometers by the comparison of the characteristic points on the plasma viscosity/ESR. (maximum velocity) periodic curve. Viscometer V_4 was used at Montrose; V_2 was used in Cheshire.

○ = experimental values.
 × = values calculated from logarithmic smooth curve.

joined by the smooth curve of Fig.40 . This curve allows me to make an approximate correlation between his results and my own.

The periodic curve was made by drawing a line through a large number of separate points representing individual tests. The behaviour of serial results of patients in disease with reference to this curve has not been tested as I found that the speed of this movement would entail that these serial tests be carried out at intervals of a few hours. I have never had a team of investigators available such as this problem required for its solution. If in two successive tests, point A is succeeded by point B, we must admit that we do not know if the curve has been followed to the peak and down again, or if there has been such a rapid jump across the gap that random testing fails to detect an intermediate value. (cf. F.M. where the citrate viscosity fell from 1.811 cs. to 1.725 cs. in 6 hours) (see Table XV).



From the shape of this periodic curve it is obvious that it is impossible for both the ESR and the plasma viscosity to be exact guides to the same thing - (in this instance, to the severity of the reaction to pathological processes). While the general trend is for the ESR and plasma viscosity to increase and decrease together, it was quite possible for a high value in one

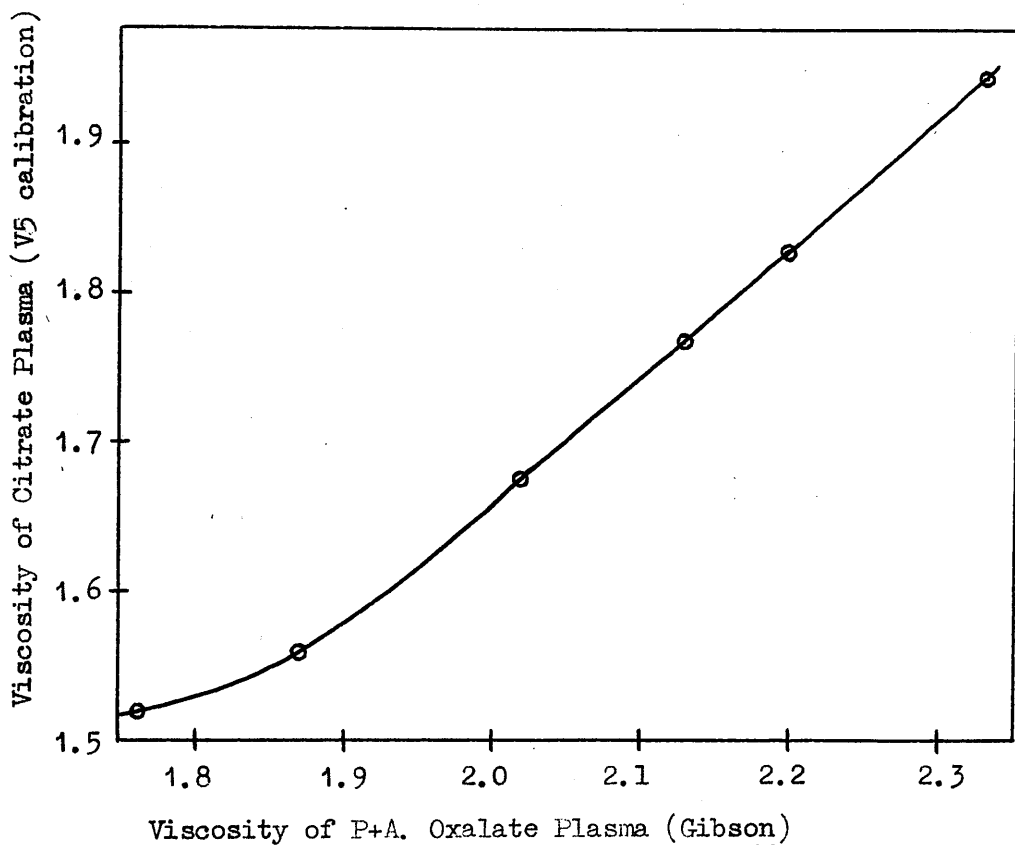


Fig. 40 The relation of characteristic points (peaks) on the V5 periodic wave of Corrected Citrate Plasma Viscosity and the Maximum Corrected Citrate Sedimentation Velocity (as shown in Fig. 35) and the viscosity at the peaks in the potassium and ammonium oxalate plasma viscosity and a maximum sedimentation velocity as derived by Gibson (87).

It is necessary to use a maximum sedimentation velocity technique to obtain the regular peak arrangement.

to be associated with a low value in the other.

No explanation can yet be given for this periodic wave formation with its complicated inter-relationships. These waves seem to be inherent in the measurements of physical properties of plasma and serum, as we have already noted in the discussion on the serum viscosity/serum protein section (§ 17).

There are many instances in which the ESR/viscosity point does not lie on this periodic curve, but the explanation of this will be delayed to the clinical part where it is discussed under the title of "terminal decay".

Also, in our treatment of our viscosity values from the clinical aspect we wished to have some large subdivisions of the total range; we divided the range into "zones", a zone being the distance between the principal peaks of this curve, and we designated each zone by a number as in Table T .

The periodic curve proved to be a sensitive guide to small errors in the ESR estimation technique. For instance, when a series of results would not conform to the curve, I traced the discrepancy back to an accelerating effect from a faulty stirrer which made the whole bench vibrate gently. One interesting case showed a slow ESR which had an apparently low maximum velocity where a fast rate was expected from the viscosity result; the test was continued until in the seventh hour the erythrocytes

fell faster and soon attained the calculated maximum velocity; the "period of aggregation" had lasted 6 hours and the constant rate of fall in that period might well have been mistaken for the true maximum velocity.

§ 22. The Wintrobe 1-hour ESR.

The peaks, troughs, and curves of the other ESR method are no longer detectable with the one-hour method in which the reading includes a variable proportion of the "period of aggregation" and the "period of maximum velocity".

Steel (232) and Arnold and Salt (7) have claimed that the relationship between the plasma viscosity and the ESR is so close that they have presented equations, prepared statistically from calculated regression lines, by which one value may be estimated if the other is known. This good correlation arises from their unfortunate restriction of their choice of cases to a single disease group. They studied cases attending their rheumatic clinics: from a knowledge of how such diseases affect the population, one can say that the majority of their groups would consist of female patients suffering from chronic rheumatoid arthritis or that they selected their subjects and they had not a random sampling. Now, if you look at my figures correlating the ESR and plasma viscosity in rheumatoid arthritis and tuberculosis,

you may note that (a) the line passing through the origin and the average of the distribution (ie. the line of regression) differs; it may differ in the same clinical condition between the sexes, and (b) if a line is drawn for the chronic conditions this line cannot be continued further for the higher viscosity values in the more severe clinical condition as there is not the corresponding increase in the ESR values. The chronic rheumatic diseases are usually associated with an increased globulin, slightly increased fibrinogen and a slightly decreased albumin; when one also considers those cases of acute inflammation in which the principal protein change is a high fibrinogen, and those cases of advanced tuberculosis and cancer where the protein characteristically has a low albumin level, the scatter around a single line of correlation becomes extremely wide. I would also cite my series of selected cases of tuberculosis in which there were more than 75% raised viscosity results as compared with only 25% raised ESR values.

My opinion concerning the ESR/plasma viscosity correlation can be stated as follows - generally, an increased ESR is associated with an increased plasma viscosity (and vice versa) but the amount of this increase in one bears only a low correlation with the increase in the other while discrepancies are frequent and sometimes large.

* * * * *

(F) The non-Newtonian character of plasma:

the V5 scale of viscosity.

In this section are gathered several topics to which reference has been made in various earlier sections.

The importance of the non-Newtonian character of plasma lies in the difficulties which it causes in the correlation of the plasma viscosity results. As long as the plasma viscosity results were to be restricted for the use of the clinicians attached to a single laboratory it does not matter very much what type of viscometer is used provided that it is capable of a sufficiently high degree of accuracy. However, if the plasma viscosity results are to be included in publications or if the results are to be included in patients' notes being sent beyond the parochial limits of the original laboratory, it is essential that the viscosity values conform to a standard to which all workers can correlate their results. (52,269).

Whittington and I had this problem always before us and we devised three methods by which viscometers can be correlated.

(i) The earliest attempts depended upon the periodic curves obtained from the plotting of the serum proteins against the serum viscosity and from plotting the maximum sedimentation velocity against the plasma viscosity. Fig. 28 shows how it

was possible to convert the Petschacher values, measured at 25°C. to the V5 scale at 20°C. This technique of correlation need not be considered further as the labour involved in making the numerous estimations necessary for a detailed periodic curve precludes its general acceptance, especially as the next two methods are much simpler. (See also Fig. 39 and 40)

(ii) It is possible to calibrate a viscometer with colloidal solutions whose viscosity has been measured in an arbitrarily-chosen standard instrument. Whittington calibrated about four viscometers with citrate plasma against the V5 instrument, and since his departure to the USA, I have calibrated a further thirty to the same scale with mixed-oxalate plasma. It is also possible to use one of these new instruments to "breed" more viscometers all on this scale. It is relatively easy to prepare calibration formulae by which the plasma viscosity results on any two viscometers differ by values within the experimental errors of the technique.

I offer this service of calibration to the V5 scale gratis to anyone interested in the plasma viscosity test to prevent the chaos which has arisen in connection with the ESR test from the multiplicity of suggested methods. Thus there are now viscometers calibrated by me in use in Australia, America, Europe and Great Britain.

(iii) In my opinion, however, the method of correlation will depend upon the discoveries regarding the relation of the viscosity of protein solutions to the viscosity of sucrose, as I have described in § 16. The sucrose standards can be prepared so that one can use the figures of Bingham and Jackson; the viscosity and specific gravity measurements, plus the protein concentration estimation, could be completed in one or two days, using a commercial albumin product as their protein standard. All viscometers already calibrated to the V5 scale can be adjusted to this sucrose line by the use of Fig. 24 as a nomogram.

The V5 scale, to which I have made so many references, is only the scale obtained originally on the fifth viscometer in a series prepared with the capillary tube bent into two vertical limbs (hence the 'V') as compared to Whittington's first design in which the capillary was a single horizontal tube ('H' type). This instrument happened to be the one in which I had made the greatest number of studies and Whittington converted his results accordingly. This V5 instrument is now preserved as a reference instrument only and is used when more viscometers arrive for calibration.

I requested the British Standards Institution to prepare a specification for the plasma viscosity estimation but the

Institution could not accept this responsibility.

The use of a V5 scale as a standard can be regarded also as the standardisation of the "rate of shear" at which the "viscosity" was being measured. Another possible field of investigation is the study of the plasma viscosity at different rates of shear. It is quite possible that two plasmata of identical (V5) high viscosity values, one due to high fibrinogen and the other to high globulin, might differ when measured at other rates of shear.

The Whittington viscometer is an instrument suited for such a study as different rates of shear can be obtained by varying the standard conditions of the estimation - it may be filled to the 100,100 levels in the limbs, and the time of fall noted from 200 to 180 mm, and then with half of the contents removed until the 50,50 levels are reached, the time of fall from 100 to 80 mm. can be recorded. However, more elaborate procedures with multiple viscometers and multiple pressures may be necessary to detect small differences in the plasma characteristics.

Dr. Scott Blair, in personal correspondence, has supported this plan of investigation as being a possible source of further useful information regarding the physical properties and characteristics of the protein constituents of plasma. (27)

* * * * *

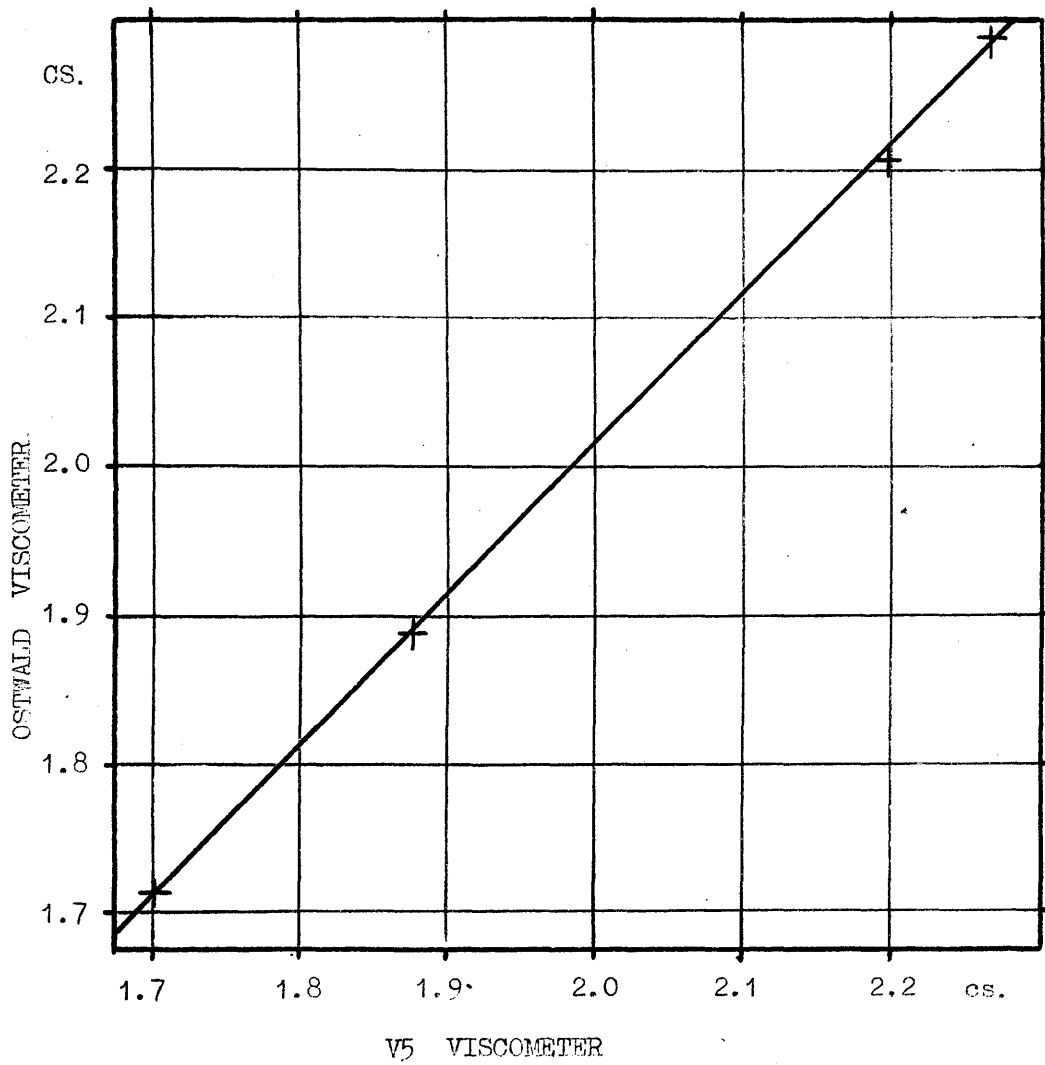


Fig. 41 This figure shows the close relationship between the viscosities of plasmata as estimated on the special V5 calibration and in a 10 ml. B.S.S. Ostwald Viscometer which had been calibrated with distilled water only.

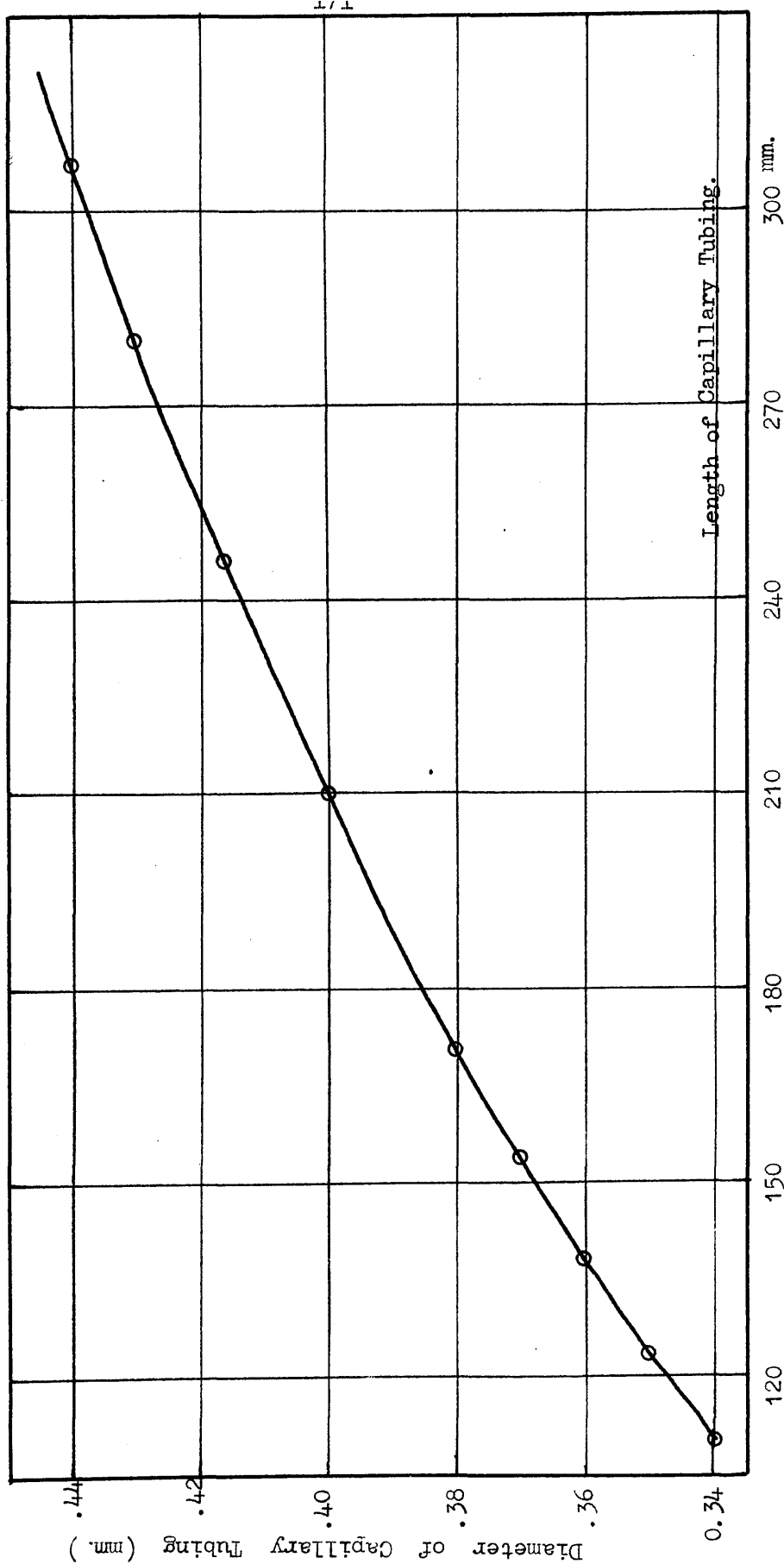


Fig. 42 Length of capillary of known diameter required to prepare a viscometer with the same "time of flow" as Viscometer V5 (approximately 60 seconds are desirable)

(G) The relation of the ESR to the constituents of the plasma.

All this research began in the desire to determine which constituent of the plasma was responsible for the changes in the ESR. The scheme proposed for the investigation of this problem indirectly, via the plasma viscosity, had been discarded in favour of an intensive study of the plasma viscosity itself; however, from the results which have become available it may be deduced that the proposed scheme had but little chance of success. I interpret my results as indicating that there is no close relationship between the ESR changes and any single plasma constituent capable of detection by the present techniques of investigation.

Method. The maximum corrected citrate sedimentation velocity and the proteins fractionated according to the method of Howe were estimated as described in the appendix.

Results. The detailed results are not collected into a single table but are scattered throughout the tables of the appendix.

No hint of a close correlation was ever noted between the ESR and any of the small-molecular constituents of the plasma, such as urea, glucose, cholesterol, etc..

The relationship of the ESR to the protein fractions is indicated in Fig. 43, 44, 45, 46, 47, 48, and 49.

Discussion. Even where an attempt has been made to reduce the comparison to between the ESR and a single fraction by considering

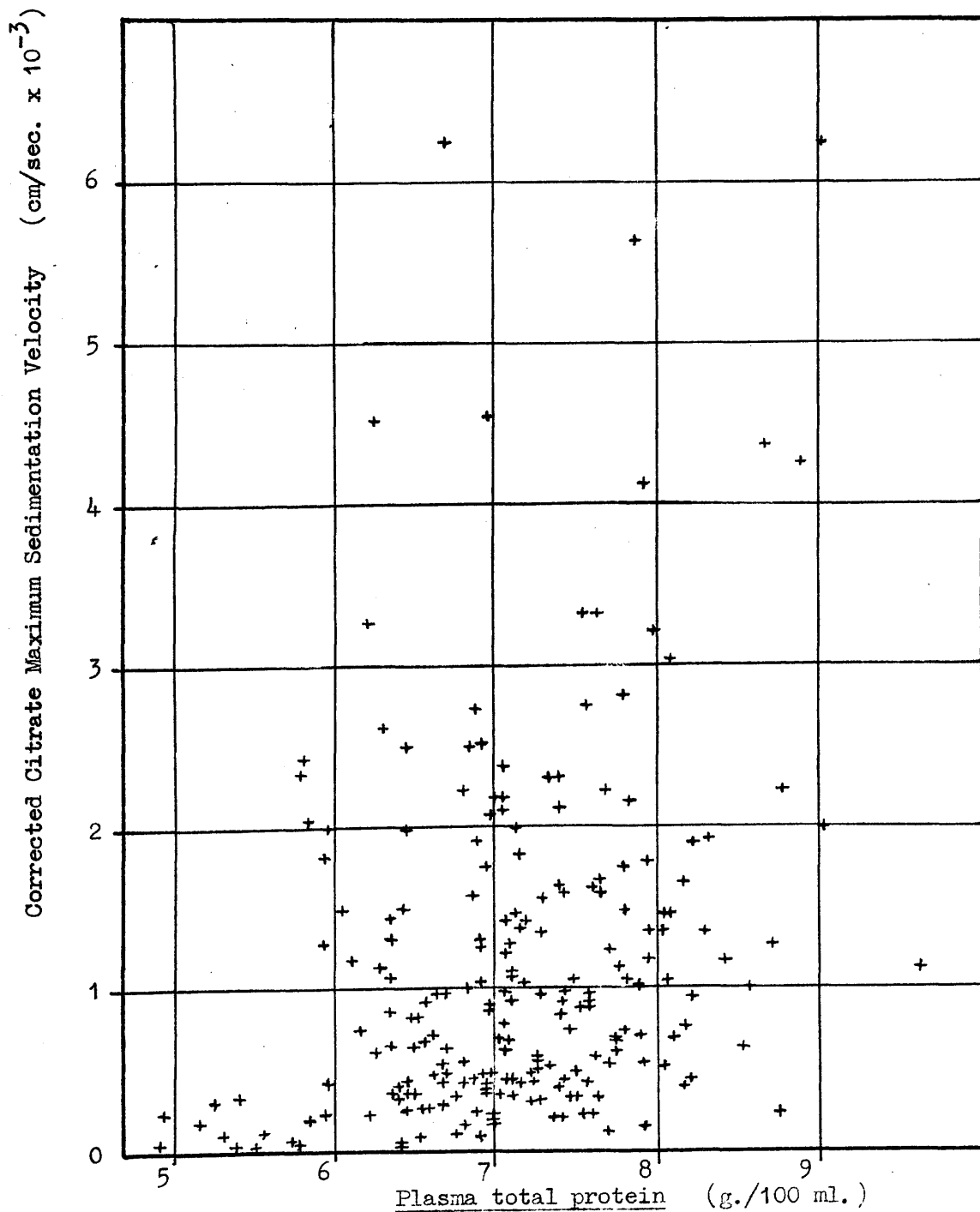


Fig. 43 The relationship between the ESR. and Plasma Total Protein.

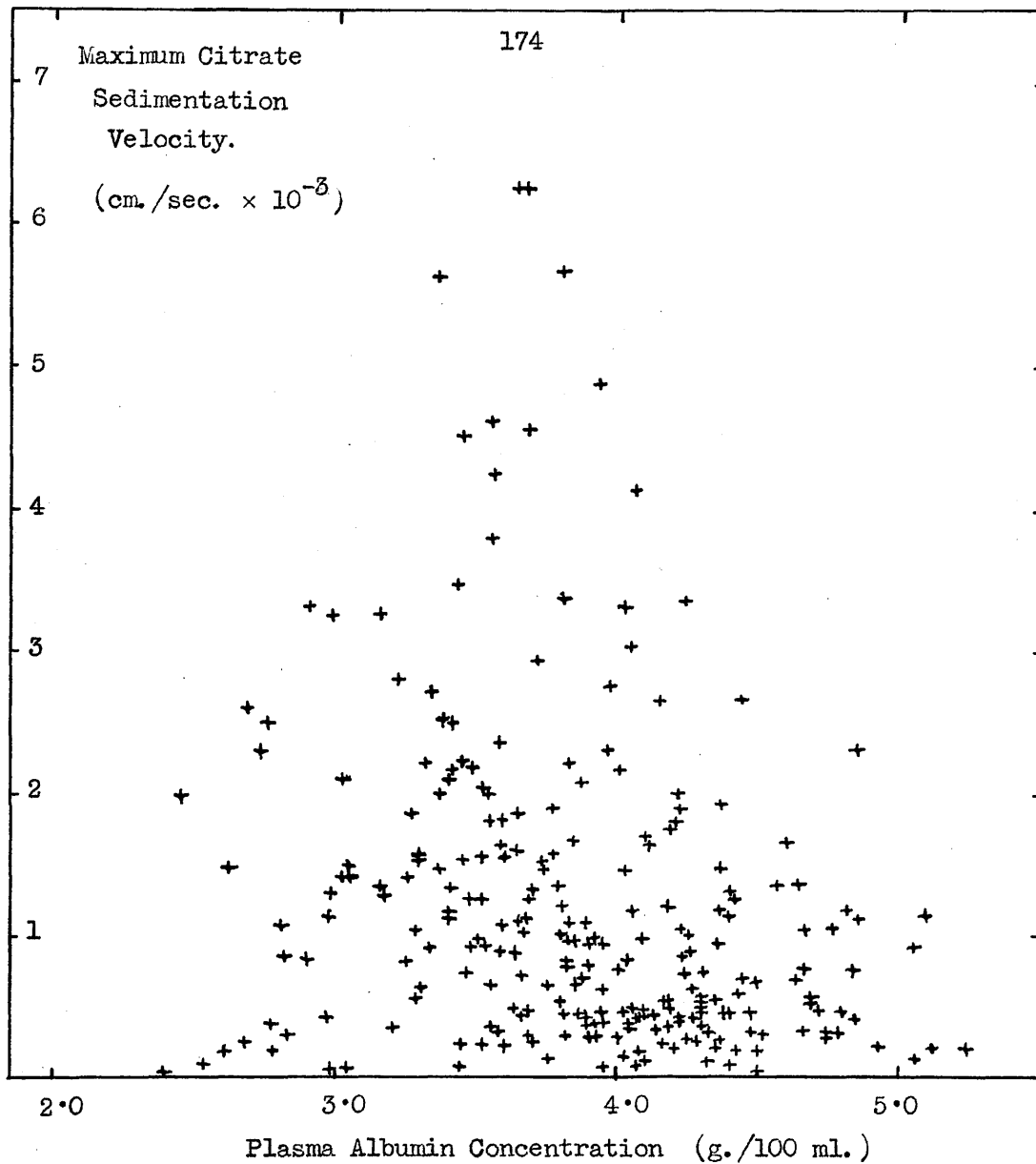


Fig. 44

There appears to be no regular relationship between the ESR. and the Plasma Albumin Concentration.

This diagram contains all the Albumin results.

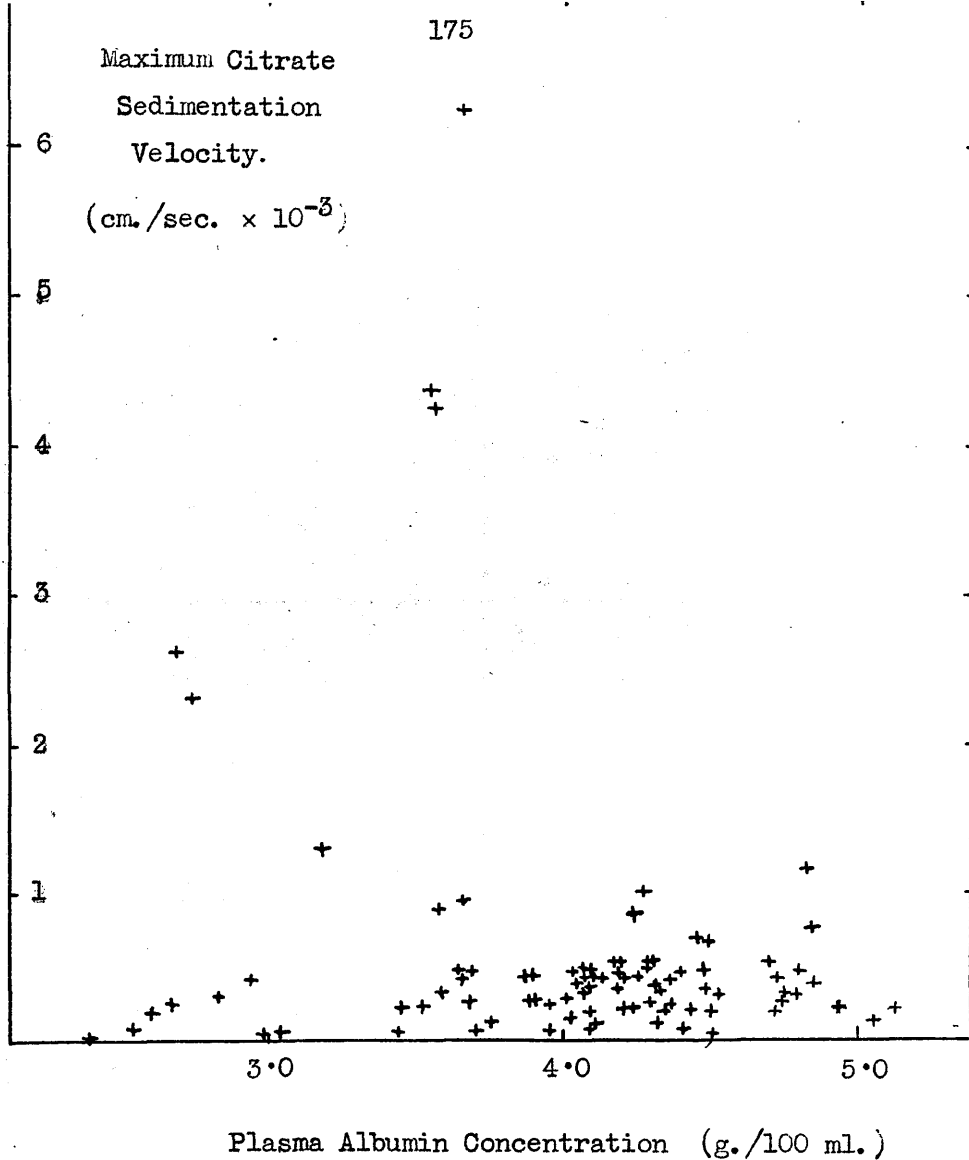


Fig. 45

The correlation between the ESR. and the Plasma Albumin Concentration, in those cases where the Fibrinogen was less than 0.4 g./100 ml.

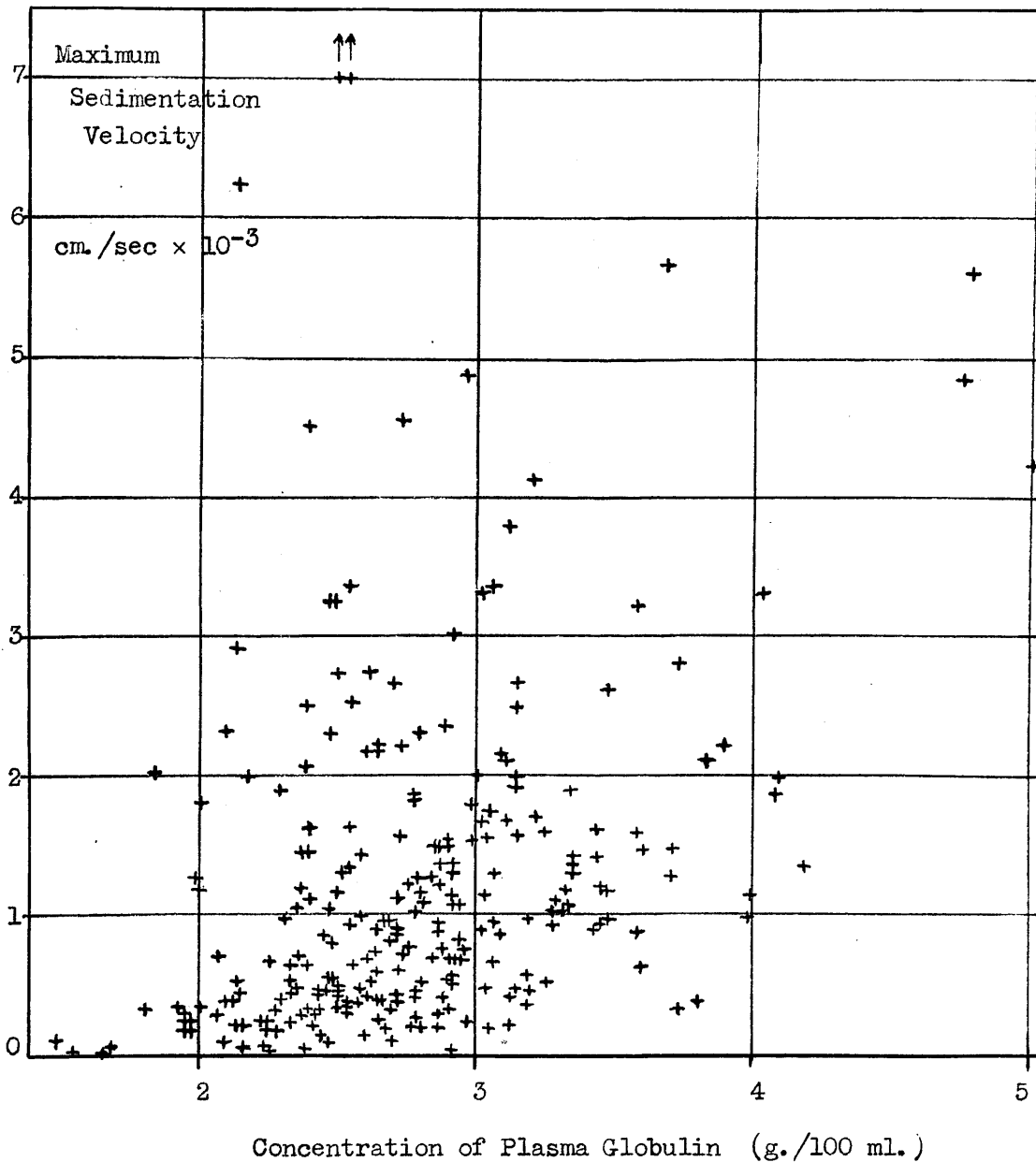


Fig. 46 The relationship between the Plasma Globulin and the Maximum Citrate Sedimentation Velocity.
All the tests are included in this figure.

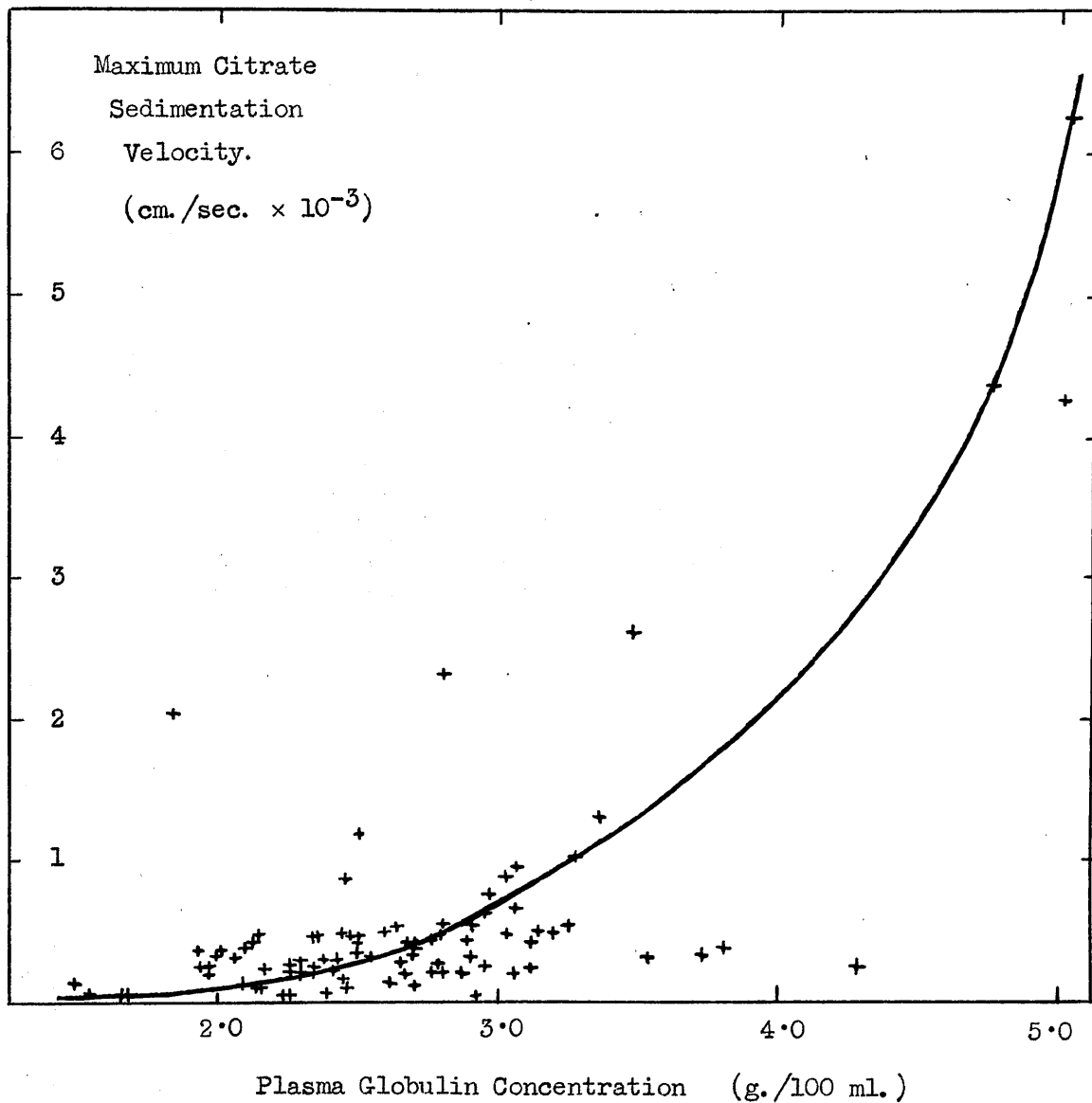
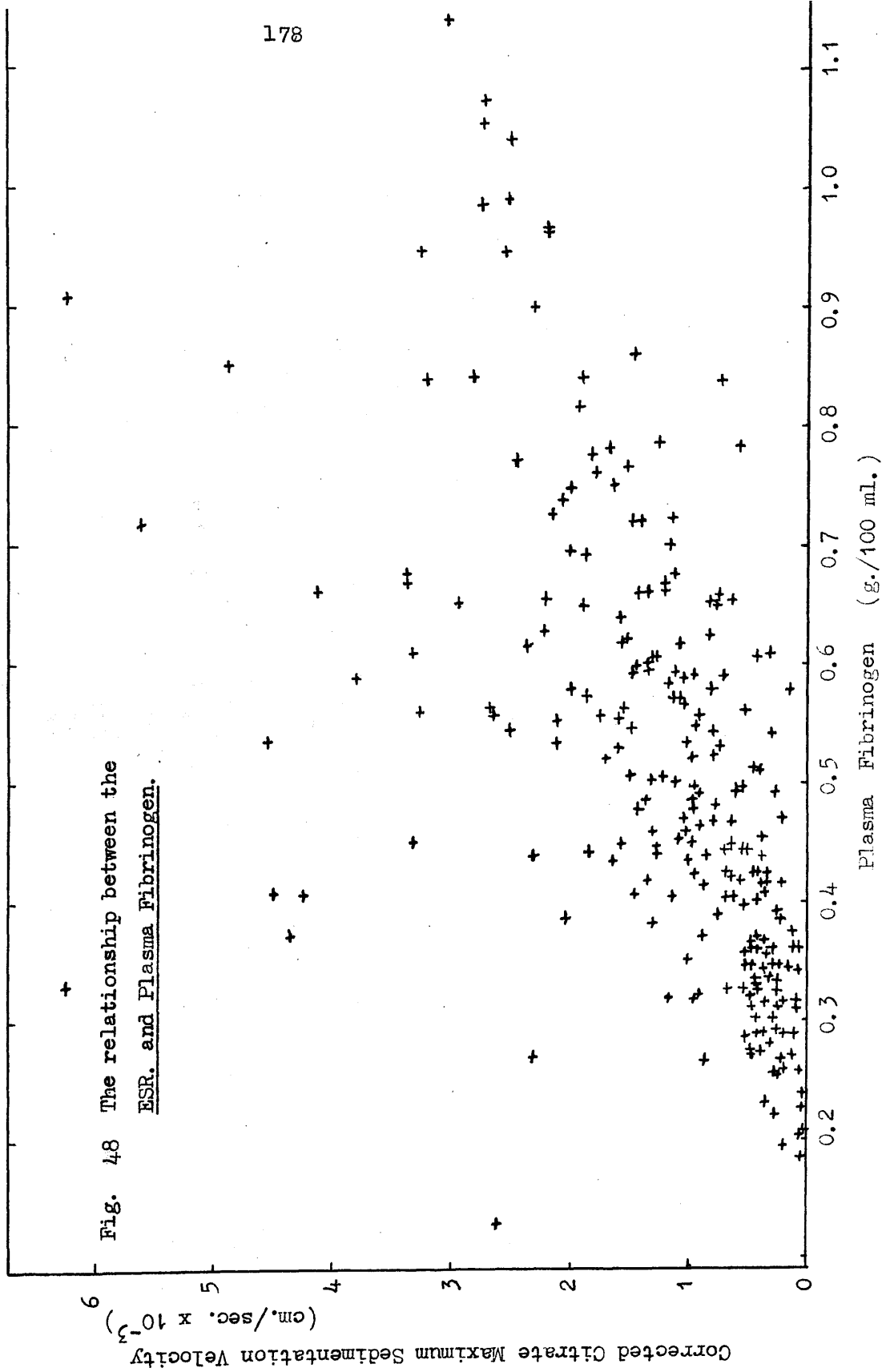


Fig. 47

The relation of the ESR. and the Plasma Globulin, in those cases where the fibrinogen was less than 0.4 g./100ml.

There is a tendency for the ESR. to be high where the globulin concentration is high, but there are many exceptions to this general statement - a high ESR. may be found in association with a low globulin, and a low ESR. with a high globulin.



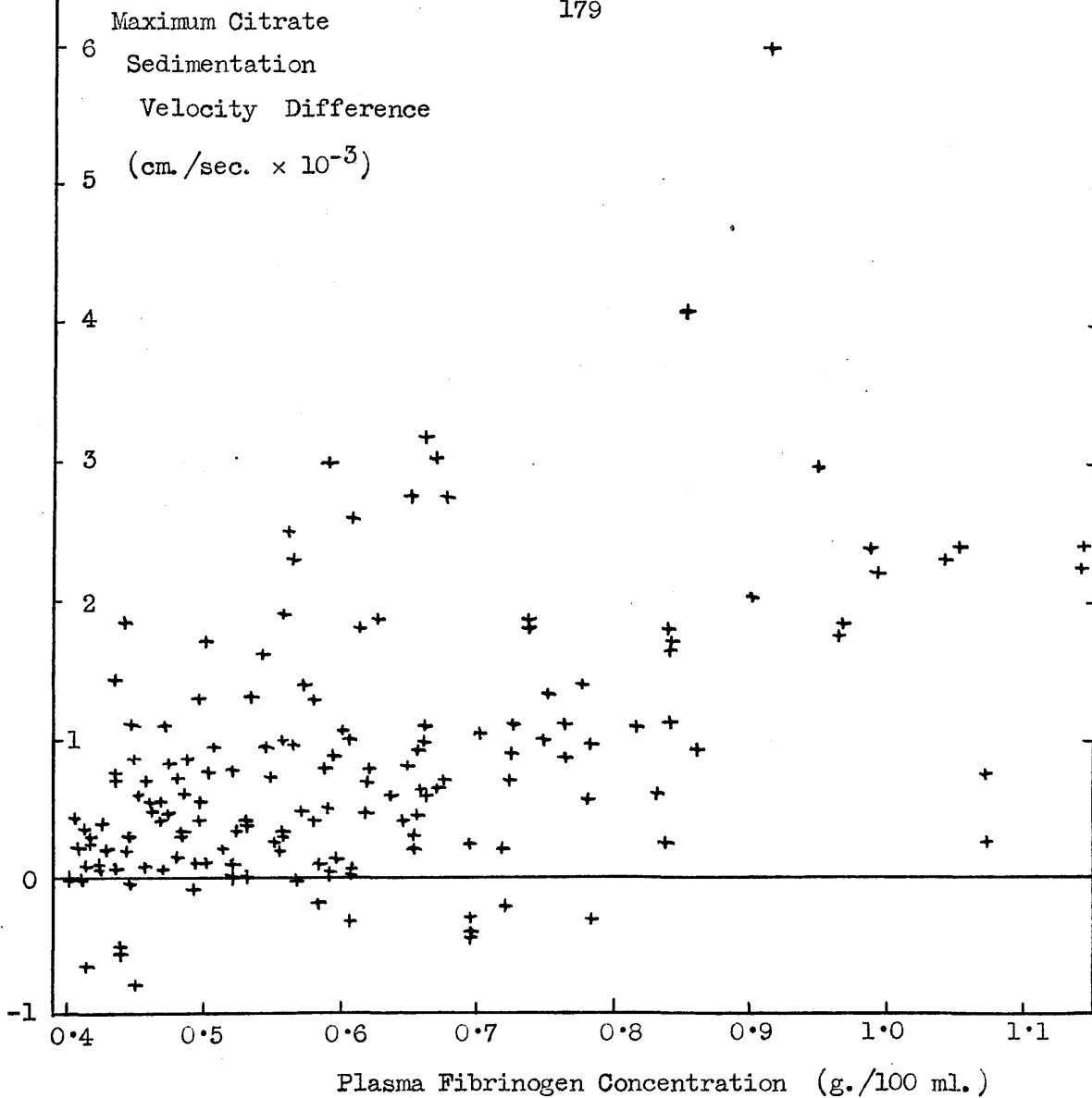


Fig. 49 The correlation of the Plasma Fibrinogen with
(the total ESR. minus the ESR. attributable to the
globulin as estimated from the line of Fig. 47)

Even after this attempt to eliminate the globulin action
there is no close relation between the level of the ESR. and
the level of the fibrinogen.

only those cases in which the other two fractions were normal, the relation cannot be regarded as close or approximating to a straight line. There is the definite tendency for a high ESR to be associated with an increased globulin and/or fibrinogen, but the relationship is not sufficiently close for one to say that it is "cause and effect".

The hypothesis that the proteins are chiefly responsible for the ESR changes fails to explain two phenomena. (i) It fails to discriminate between the effect of the protein concentrations in a normal person and the same concentrations in the early stages of disease. A normal subject may have a protein pattern of - Albumin = 4.8 g./100 ml, globulin = 2.6, and fibrinogen = 0.38 , and have a correspondingly normal low ESR: another normal subject has a pattern of A = 4.8, G = 2.2, and F = 0.25, with an identical ESR value, yet, when in response to an infection, his ESR and proteins change, the protein pattern may have the results of the first case but now associated with an increased ESR. This problem can be tackled better by a comparison of the increase in the ESR with the change in the plasma proteins from their basal normal values. The present method of making the first measurement when disease is already present is unsatisfactory. If the volunteers could be obtained there are several stimuli (such as protein-shock, TAB injections, oral sulphonamide administration)

which will produce the necessary changes in the blood. (ii) As death approaches in such cachectic diseases as tuberculosis and cancer, there is a progressive decrease in the plasma proteins, especially the albumin fraction. There may be an associated decrease in the ESR from its highest values but this decrease is less than expected from the final protein pattern. The extreme example of this in my series occurred in a senile patient with gangrene of toes, who, 9 days before death, had a protein pattern of $A = 3.55$, $G = 2.54$, $F = 1.02$, and a maximum velocity of 540 mm./hour (the correction of the PCV. excluded anaemia effects).

My investigation followed the plan used repeatedly in the past by other workers and my results were similar to those previously produced. They are equally sterile of any definite interpretation except that this approach to the problem is unlikely to yield a satisfactory solution.

It is my impression, and I speak from personal experience, that the ESR is a test which has attracted the investigations of the young doctor whose enthusiasm is greater than his powers for constructive criticism. His clinical experience with the test has been confined to a number of diseases for which the test is an "accepted" procedure and he has not encountered the apparently

anomalous results which occur in the advanced stages of disease where the outcome is so obvious that further testing has been discontinued as serving no useful purpose to the clinician. He tackles the problem by a direct attack in a search for a plasma constituent which changes in parallel with the ESR, with the intention of ascribing the change in the ESR to this constituent. Nowhere has it been stressed sufficiently that the protein changes and the ESR changes may show a degree of correlation because they are responses to a single cause or stimulus.

I believe that the technique with the greatest chance of a successful solution of this problem is a fresh attempt to isolate and identify the "sedimentin" (so-called in analogy to precipitin and agglutinin) postulated by Day (60) as being responsible for the aggregation of the erythrocytes which is the fundamental process in the ESR. Day did not attempt to define the nature of his sedimentin. It might well be protein in character, forming but a small part of the large fractions into which the standard methods divide the plasma protein, just as the various antibodies whose specificity can be identified by agglutination tests form part of the gamma globulin. If as part of the reaction to an infection or similar stimulus there should be a change in the protein fractions in general and also in the

sedimentin part, it follows both that there would be an apparent close relation between the large fractions and the ESR and that discrepancies in this relation will depend on the differences in the primary responses by the proteins and sedimentin.

The nearest attempt to such an investigation were the experiments by Gordon and Wardley (88) who prepared artificial plasmata from the pure protein fractions as separated by electrophoresis. Perhaps a greater success might be attained if less attention were paid to the plasma proteins and even to plasma itself as a source of sedimentin. Pleural exudate has a low protein content but is particularly rich in sedimentin; it can be richer in sedimentin than its corresponding plasma as its addition to the blood causes an increase in the ESR greater than can be explained by its dilution effect. With the delicate chemical fractionating techniques for protein as developed by Cohn, plus the physical techniques of electrophoresis, chromatography, and ultracentrifugation now available, it should be possible to determine the nature of sedimentin more finely than hitherto, always provided it is of protein nature.

Gray and Mitchell (89) studied the effect of protein fractions by adding them to whole blood and then noting the change in the ESR. from the original.

* * * * *

Discussion to Part 6.

Short discussions have been included at the end of each section and there only remains the necessity of a brief general survey.

The results of this part have shown that it is possible to estimate with accuracy a physical property which is truly representative of the viscosity of the venous-blood plasma. No error has been introduced by the measurement at 20°C. rather than at body temperature. The plasma can withstand any physical violence or delay that it is likely to encounter in a routine laboratory. The only real sources of error are venous stasis, delayed separation of the plasma from the cells, and concentration of the plasma in un-capped centrifuge tubes; now that these are recognized the obvious steps can be taken to prevent their occurrence.

The ultra-filtrate experiments placed the responsibility for the variations in the plasma viscosity on the proteins alone. The results of the study of the solutions of the separated protein fractions do not coincide with those of the tests where the plasma and serum viscosities and the protein fractions were estimated. This discrepancy suggests that the plasma and serum proteins do not exist in nature as simple solutions of the discrete fractions. This suggestion is in

accord with the recent trend in biochemistry to treat the plasma proteins as a single entity which is capable of subdivision by application of electrical and chemical stimuli, etc.

Our results have yielded two other tests whose potential use has not yet been fully studied. The tests are the treatment of solutions to yield the molecular weight of the solute, and the plasma protein equilibrium factor.

There is a suggestion that the correlation of a physical property of plasma and serum with the protein fractions (and the ESR.) may have the shape of a periodic wave; such waves have been noted with the plasma viscosity, serum viscosity, and perhaps the serum osmotic pressure. No explanation for this phenomenon may be risked at this stage of our experience.

The ESR. results presented a low correlation with any of the protein fractions so that it was impossible to ascribe the ESR. changes to these protein changes.

* * * * *

End of Part 6.

On the VISCOSITY of HUMAN BLOOD PLASMA and SERUM in
HEALTH and DISEASE.

A Thesis for the Degree of Doctor of Medicine.

Submitted to the University of Glasgow.

by

JOHN HARKNESS.

VOLUME

TWO

C O N T E N T S

VOLUME TWO

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Part 7

The

PLASMA VISCOSITY

in

HEALTH

Part 7.A study of the plasma viscosity in normal subjects and of the effect of physiological stimuli.

This part of the thesis will be concerned with the range of values of the plasma viscosity which can be encountered in normal subjects and the range of variation in these values which can be induced by physiological stimuli. This study is a necessary preliminary to the consideration of the changes found in the pathological conditions of part 8.

§ 1. The plasma viscosity in normal subjects.

Material. Approximately equal numbers of both sexes of healthy young adults were studied. These were obtained from three main sources - (i) volunteers from all branches of the staff of the Portsmouth laboratory service who had recently passed their medical examination (including X-ray of chest) for superannuation, (ii) emigrants who also had been medically examined and who attended the laboratory for their Wassermann examination, and (iii) a few patients who were referred to me by a cooperating clinician when his most thorough examination had failed to detect any organic disease.

The subjects walked into the laboratory and had their blood sample removed within a few minutes, while seated at a bench; no precautions were taken to standardise the time of day, amount of previous exercise, or relation of sampling to meals.

Results. See Table U in the appendix.

The results are presented graphically in Fig. 50.

In 95 tests on 53 males, the mixed-oxalate plasma viscosity values ranged from 1.663 to 1.910 cs., with a mean of 1.8148 and a standard deviation of 0.054. Fig. 50 shows that the distribution curve approximates to a "normal" curve.

In 63 tests on 51 females, the plasma viscosity values ranged from 1.665 to 1.910 cs., with a mean of 1.8024 and a standard deviation of 0.062. In Fig. 50, however, the distribution does not comply with the requirements of a "normal" curve; there are two peaks, one on either side of the mean. Thus although the range of values and the mean values are almost identical in the two sexes, the standard deviation is greater in the females because of the difference in distribution of the values towards the ends.

The third graph of Fig. 50 presents the frequency of distribution curve when the 104 subjects are treated as members of a single family; the mean is 1.810, with a standard deviation of 0.057.

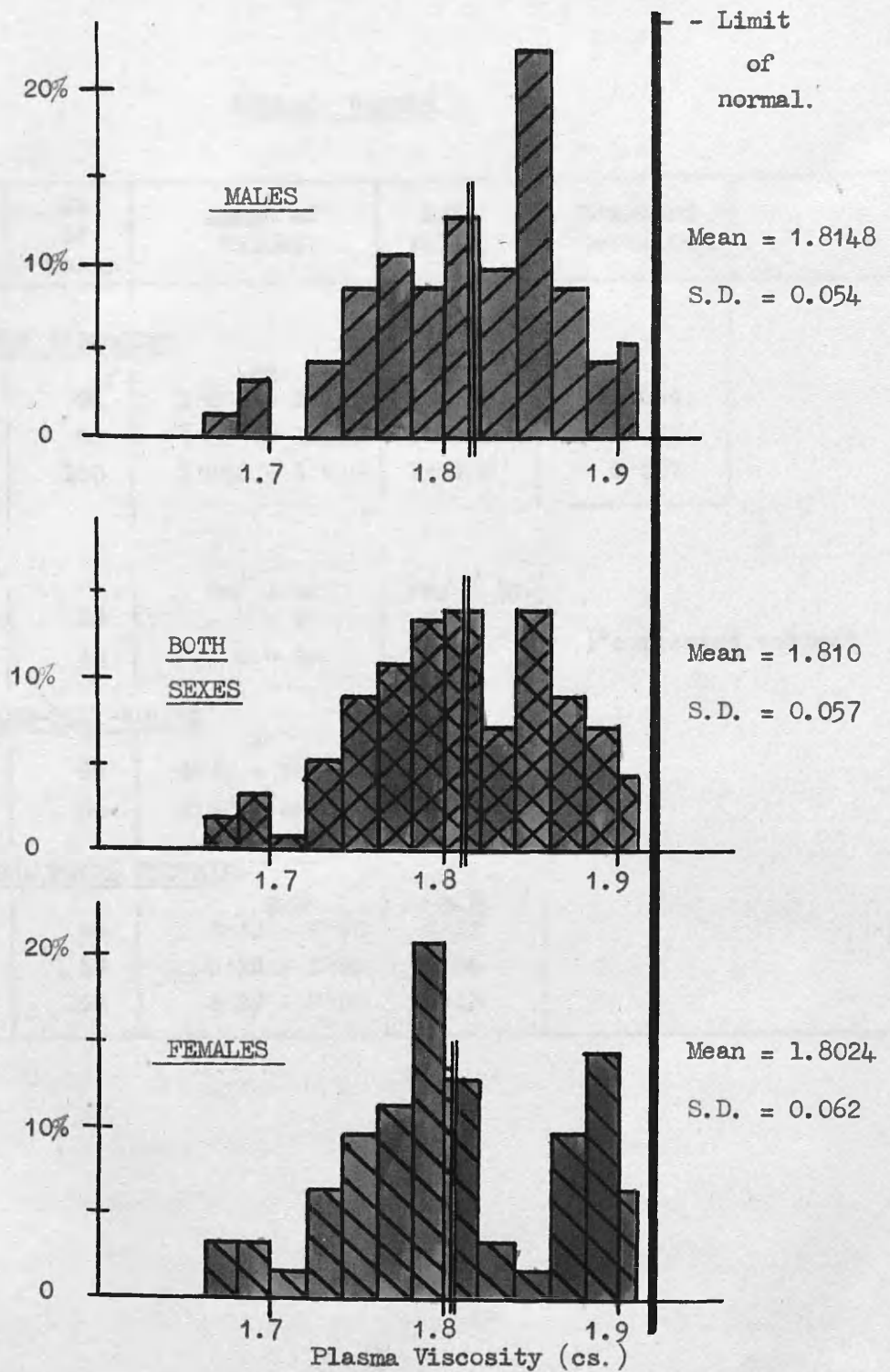


Fig. 50 The incidence of the Plasma Viscosity results in Normal Adults of both sexes.

(54³ male subjects; 51 female subjects)

NORMAL VALUES.

Sex	No. of Tests	Range of Values.	Mean Value.	Standard Deviation.	
<u>PLASMA VISCOSITY.</u>					
M	96 ⁵	cs. 1.663 - 1.910	cs. 1.8148	0.054	
F	63	1.665 - 1.910	1.8024	0.062	
M+F	158	1.663 - 1.910	1.8100	0.057	
<u>ESR.</u>					
M	50	mm/ 1 hr 0 - 8	mm/ 1 hr. 2.24)"corrected values"	
F	43	0 - 25	7.84		
<u>PACKED-CELL-VOLUME</u>					
M	89	% 40.0 - 52.9	% 45.7		
F	59	31.0 - 46.0	41.6		
<u>PLASMA TOTAL PROTEIN.</u>					
M	88	g. % 5.39 - 7.96	g. % 7.23		
F	58	6.16 - 7.85	7.06		
M+F	146	5.39 - 7.96	7.13		

Discussion. It has been a constant misfortune to our team of investigators that none of us had access to normal subjects (such as medical students) who would act as controls and volunteers for experiments with physiological stimuli. We attempted to overcome this deficiency by studying the 'apparently normal', ie. members of the nursing staff who were symptom-free and asylum inmates who showed no abnormality to my physical examination (X-ray facilities were not available). This plan was discredited when two of my normal patients showed frank evidence of pulmonary tuberculosis within months of testing and who must have been in the early stages of the disease at that particular time. Hence our original series of normals has been discarded in favour of one where an experienced clinician, with full ancillary diagnostic services, has failed to discover evidence of disease in people the majority of whom were also apparently healthy. The stricter choice of subject has caused a reduction in the published upper limit of the normal range of 1.950 cs. to our present level of 1.915 cs.

The range of values (1.665 - 1.910) was obtained from a series of normal young adults. I have no comparable figures for the normals at the extremes of youth and old age, but I believe that the same range is applicable to all ages, for the following

reasons. From the clinician's aspect, it was found that 1.915 cs served as a dividing line between normal and abnormal just as effectively in the extremes of age as in the young adults from whom it was derived. Also, in the many young and old whom I followed through their illness with serial tests, a satisfactory convalescence resulted in plasma viscosity values within this normal range.

No explanation can be offered for the two peaks in the frequency distribution of the results of female subjects; it might be hazardous to try to explain something which may be due only to chance sampling. From the statistical aspect and from the practical clinical aspect, one can treat the results of the two sex groups as if they were members of a single family of results.

A single range of values thus includes the normal plasma viscosities of all ages and both sexes. Compare this with the results of the ESR test where the ranges are different for the two sexes, where some workers apply the adult ranges to children while others apply the female range to children but do not show a uniformity of opinion as to the age at which the male child should be transferred to his adult range.

Apart from a small percentage of the total normal range at its upper limits (1.900 - 1.910), all values within the range

have the identical clinical interpretation as there is no result which can be regarded as "more normal" than another; 1.875 cs. is equivalent to 1.775 cs.. In contrast, the lower values within the normal range of the ESR test are preferred to the higher values and in a female subject an ESR of 18 is not equivalent to 8 or even 3 mm./1st hour, Wintrobe technique.

Referring again to Fig. 50 , it is seen that the upper limit to the normal values has been sharply defined. The highest recorded value in my series was 1.910 cs., but I made an arbitrary extension to 1.915 cs. for my practical test. No value over 1.915 was ever seen without some present or later evidence that an active disease process was present or a physiological stimulus of such severity that it could not be encountered in the patients who would arrive at a laboratory for investigation. On the other hand, plasma viscosity values below 1.915 cs. could be seen in the presence of obvious active disease and therefore a viscosity within the normal range is no guarantee of the absence of disease; it will arise in part 8 that the frequency of this anomalous association of disease and normal viscosity will be discussed several times. Furthermore, while the value from perfectly normal subjects, (ie. normal to all our criteria) can be as high as 1.910 cs. I prefer to regard the values in the 1.900 - 1.915 cs. range with suspicion, and I make another test after 2 or 3 weeks when

a result more characteristic of normality or abnormality should be found.

My extension of the upper limit of normal values for the plasma viscosities beyond the highest I had seen in my series is in sharp contrast to the manipulations of the ESR test. With it, the practice appears to be that a series of ESR tests is made on normal subjects and then an arbitrary choice is made for the upper limit of normal somewhere within the range of experimental results; the remaining higher values are merely disregarded. A typical example of such treatment is that of Wintrobe who, after verifying by physical examination the normality of his apparently-healthy students, discarded the upper 6% of the results in both sexes. Among his female subjects his highest value came into the 27-29 mm./hr. group; he introduced some statistical analysis, without taking into consideration that his results did not have a "normal" frequency distribution, found that his $(\text{mean} + 2 \times \text{standard deviation}) = 20.8$ which he approximated to 20 instead of 21, and thus derived what is accepted universally as the upper limit of the normal range for the ESR test in female patients ! Gibson (87) did exactly the same, choosing a lower value than his experimental maximum. He next proceeded to make a comparison of the sensitivity of the ESR and the plasma viscosity tests using his arbitrary choice as a guide to abnormality, thus favouring

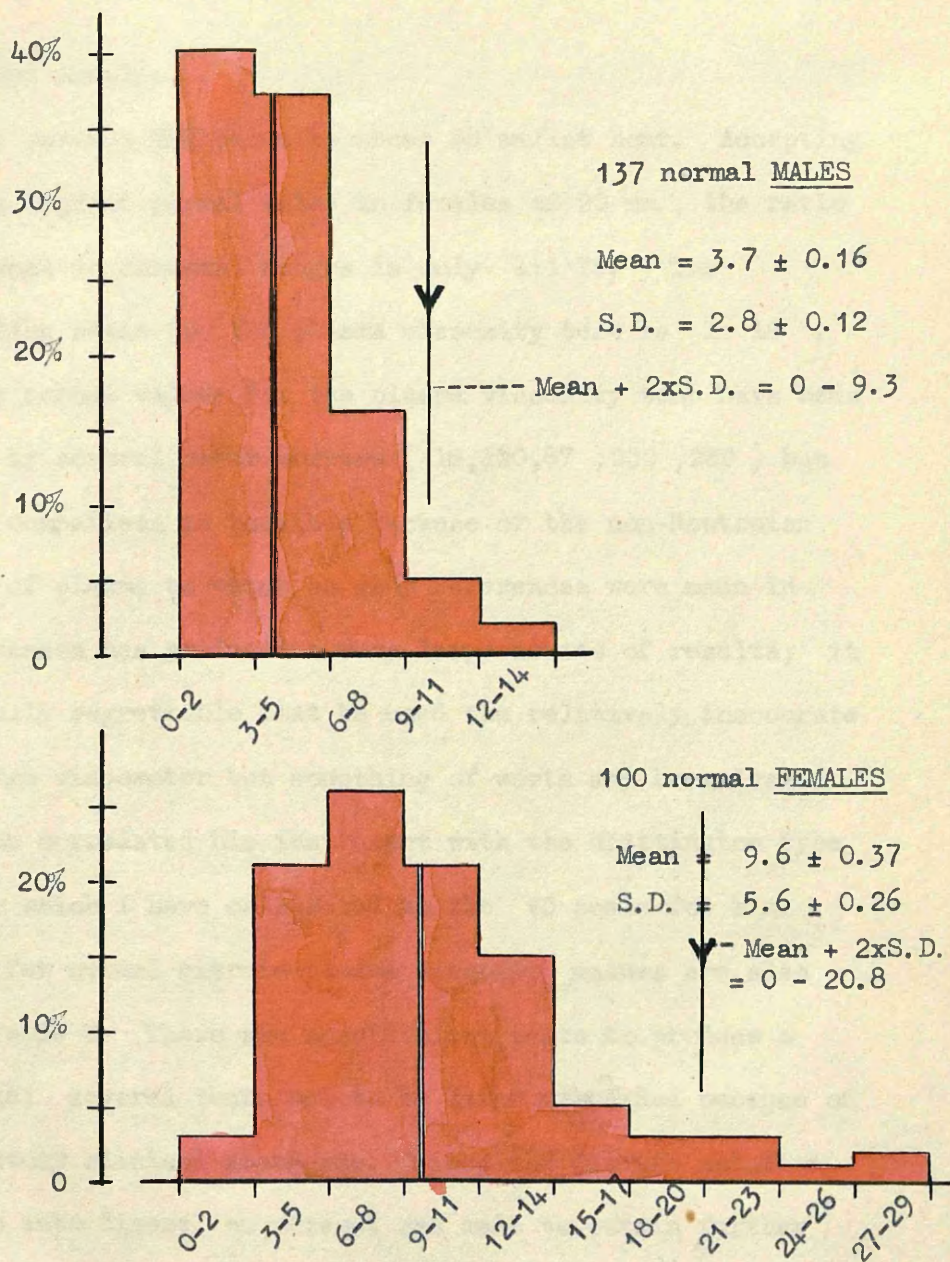


Fig. 51 The incidence of Wintrobe ESR. results in Normal Adults of Both Sexes.

(Published originally by Wintrobe & Landsberg,

J. Amer. Med. Sci., 1935, 189, p102)

the ESR test unduly.

The maximum ESR value is about 55 mm/1st hour. Accepting Wintrobe's highest normal value in females of 20 mm., the ratio of the normal to abnormal ranges is only 1:1.75. The corresponding ratio for the plasma viscosity test is 1: 18 .

The normal values for the plasma viscosity test have been published by several other workers (16,130,87 ,232 ,259) but no direct comparison is possible because of the non-Newtonian character of plasma to which so many references were made in part 6. Benson has produced a very large series of results; it is especially regrettable that he used the relatively inaccurate Hess-Hellige viscometer but something of worth may be salvaged when he has correlated his instrument with the Whittington type viscometer which I have calibrated to the V5 scale for him.

A few normal citrate-plasma viscosity values are also given in Table T. There are insufficient tests to produce a valid range; several tests had to be later discarded because of unsatisfactory clinical standards. Since the citrate solution has fallen into disuse, no attempt was made to obtain further normal values with it.

Conclusion. Of the total range of plasma viscosity values, the normal results form a narrow and well-defined zone. The normal range (1.665 - 1.915) is applicable to both sexes and all ages.

* * * * *

The Effect of Physiological Stimuli on the Plasma Viscosity.

The results in the following sections are sometimes rather meagre in numbers and this deficiency can be attributed to our lack of volunteers; no-one enjoys being the subject of repeated venipuncture so that few volunteers could be expected to take part in more than one study. However, I believe that there are sufficient tests to allow valid conclusions to be drawn.

§ 2. Variations in the plasma viscosity from day to day.

Method. Daily tests for 4 to 6 days were made on seven young adults - 5 male pathologists, 1 female technician, and 1 female cleaner. The blood samples were removed at the same hour each morning. No restriction whatsoever was made in their general mode of living and no special constancy of diet, amount of work and leisure was required in the mornings prior to the test.

Results. These are given in Table U of the appendix.

Representative results are presented graphically in Fig. 53 and 52.

Discussion. Of the four estimations - plasma viscosity, ESR, haematocrit, and total protein - the plasma viscosity shows the greatest constancy. The variation about the mean value was less than 1%.

There is no constant correlation between the changes in the

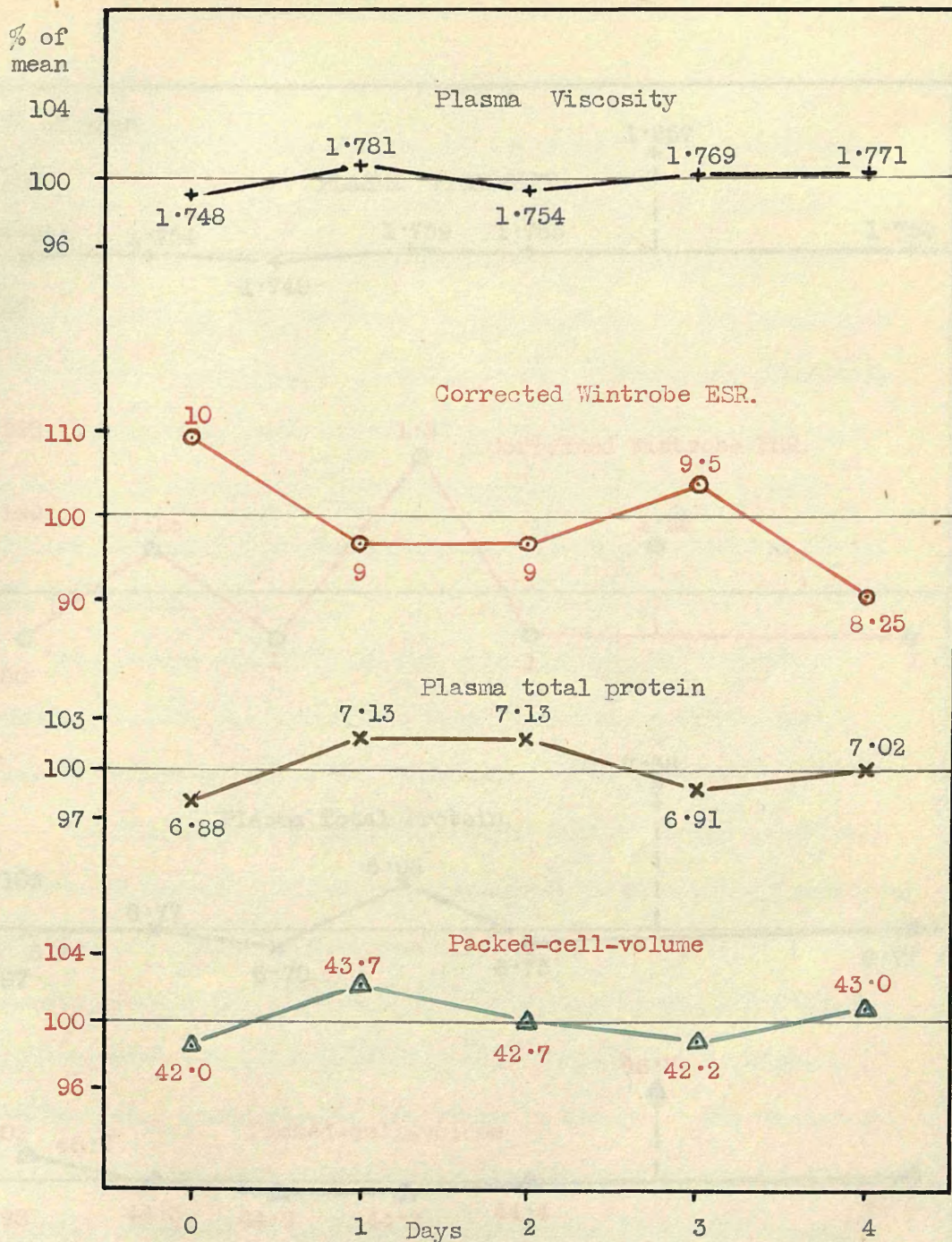


Fig. 52

The daily variations in the results of a normal adult female.

The values are expressed as percentages of the means.

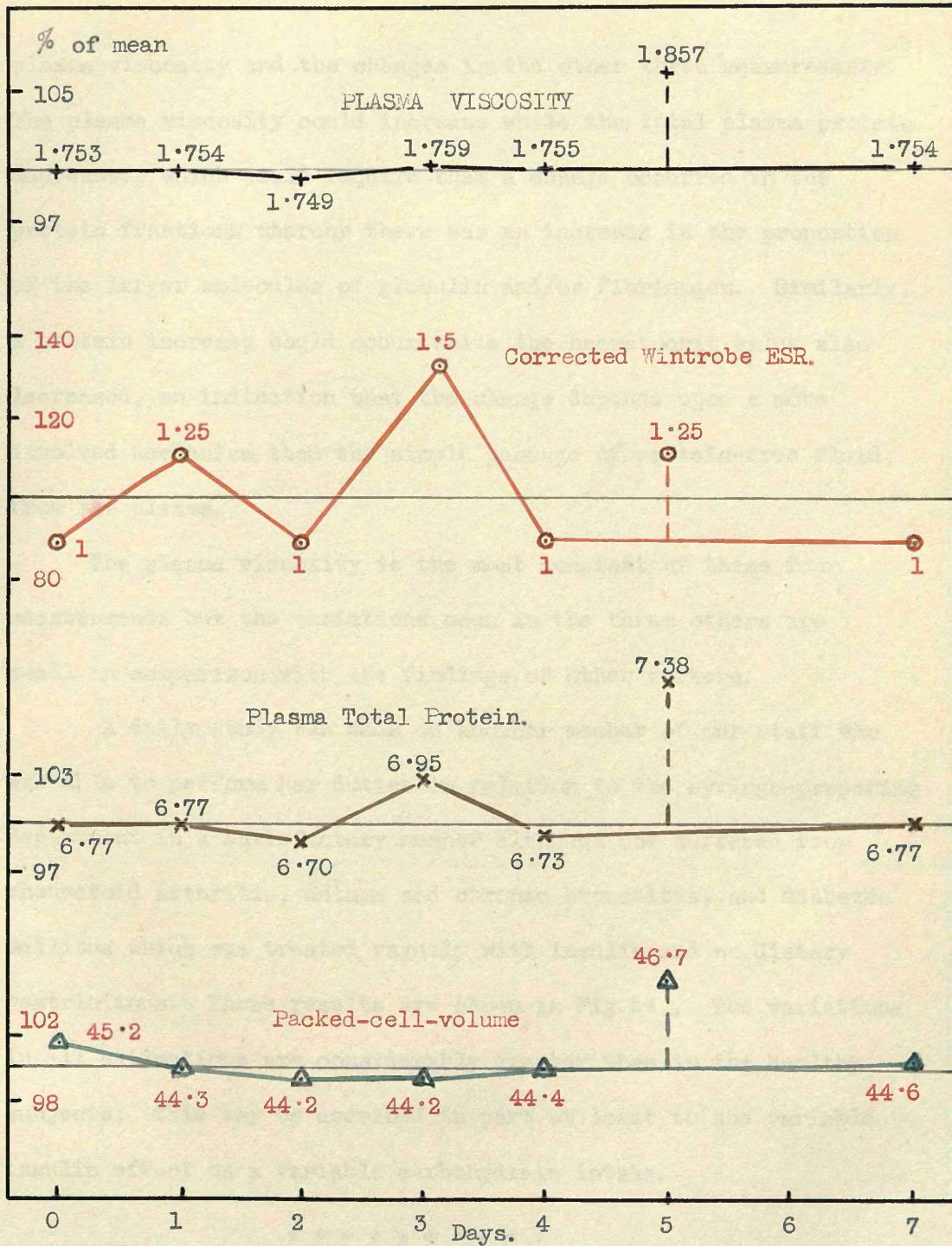


Fig. 53 The daily variation in a normal adult male.
The rise at the 6th test was due to post-alcoholic dehydration.

plasma viscosity and the changes in the other three measurements. The plasma viscosity could increase while the total plasma protein decreased, which would require that a change occurred in the protein fractions whereby there was an increase in the proportion of the larger molecules of globulin and/or fibrinogen. Similarly, a protein increase could occur while the haematocrit value also decreased, an indication that the change depends upon a more involved mechanism than the simple passage of protein-free fluid from the plasma.

The plasma viscosity is the most constant of these four measurements but the variations seen in the three others are small in comparison with the findings of other workers.

A daily study was made on another member of our staff who was able to perform her duties in relation to the syringe-preparing department in a satisfactory manner although she suffered from rheumatoid arthritis, asthma and chronic bronchitis, and diabetes mellitus which was treated vaguely with insulin and no dietary restrictions. These results are shown in Fig.54 . The variations in all estimations are considerably greater than in the healthy subjects; this may be ascribed in part at least to the variable insulin effect on a variable carbohydrate intake.

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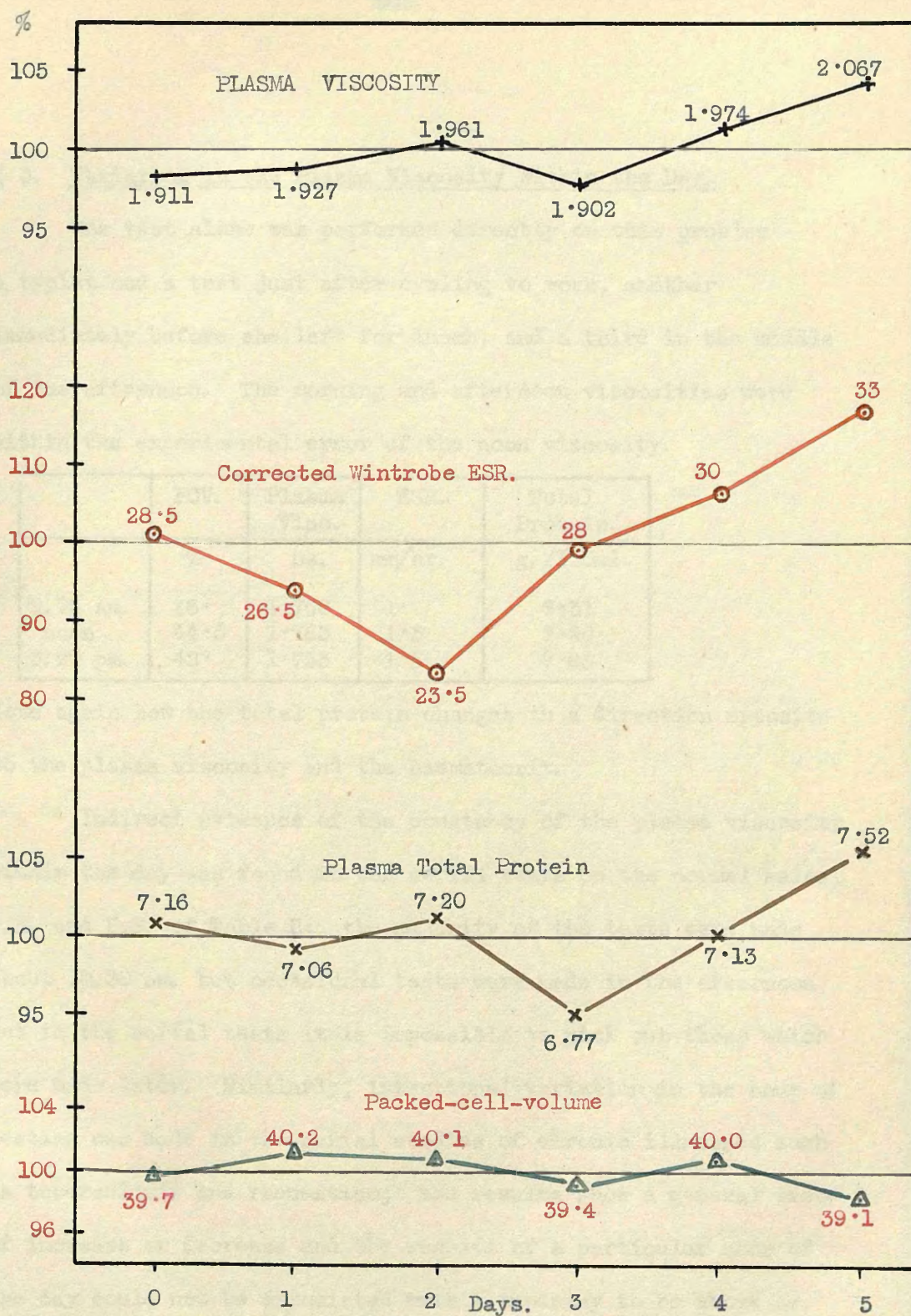


Fig. 54

The daily changes in a working woman who suffered from chronic bronchitis, rheumatoid arthritis, and diabetes mellitus.

§ 3. Variation in the Plasma Viscosity within the Day.

One test alone was performed directly on this problem - a typist had a test just after cycling to work, another immediately before she left for lunch, and a third in the middle of the afternoon. The morning and afternoon viscosities were within the experimental error of the noon viscosity.

	PCV.	Plasma Visc.	ESR.	Total Protein.
	%	cs.	mm/hr.	g./100ml.
9.15 am.	46·	1·763	1·	7·31
noon	44·5	1·763	1·3	7·20
3.20 pm.	42·	1·753	1·5	7·63

Note again how the total protein changes in a direction opposite to the plasma viscosity and the haematocrit.

Indirect evidence of the constancy of the plasma viscosity within the day was found in the serial tests on the normal males, J.H. and P.S. of Table U; the majority of the tests were made about 10.30 am. but occasional tests were made in the afternoon, yet in the serial tests it is impossible to pick out those which were made later. Similarly, intentional variation in the hour of testing was made in the serial studies of chronic illnesses such as tuberculosis and rheumatism; the results show a general trend of increase or decrease and the results of a particular hour of the day could not be associated with a tendency to be above or below the general level.

§ 4. Variation in the Plasma Viscosity with the Seasons.

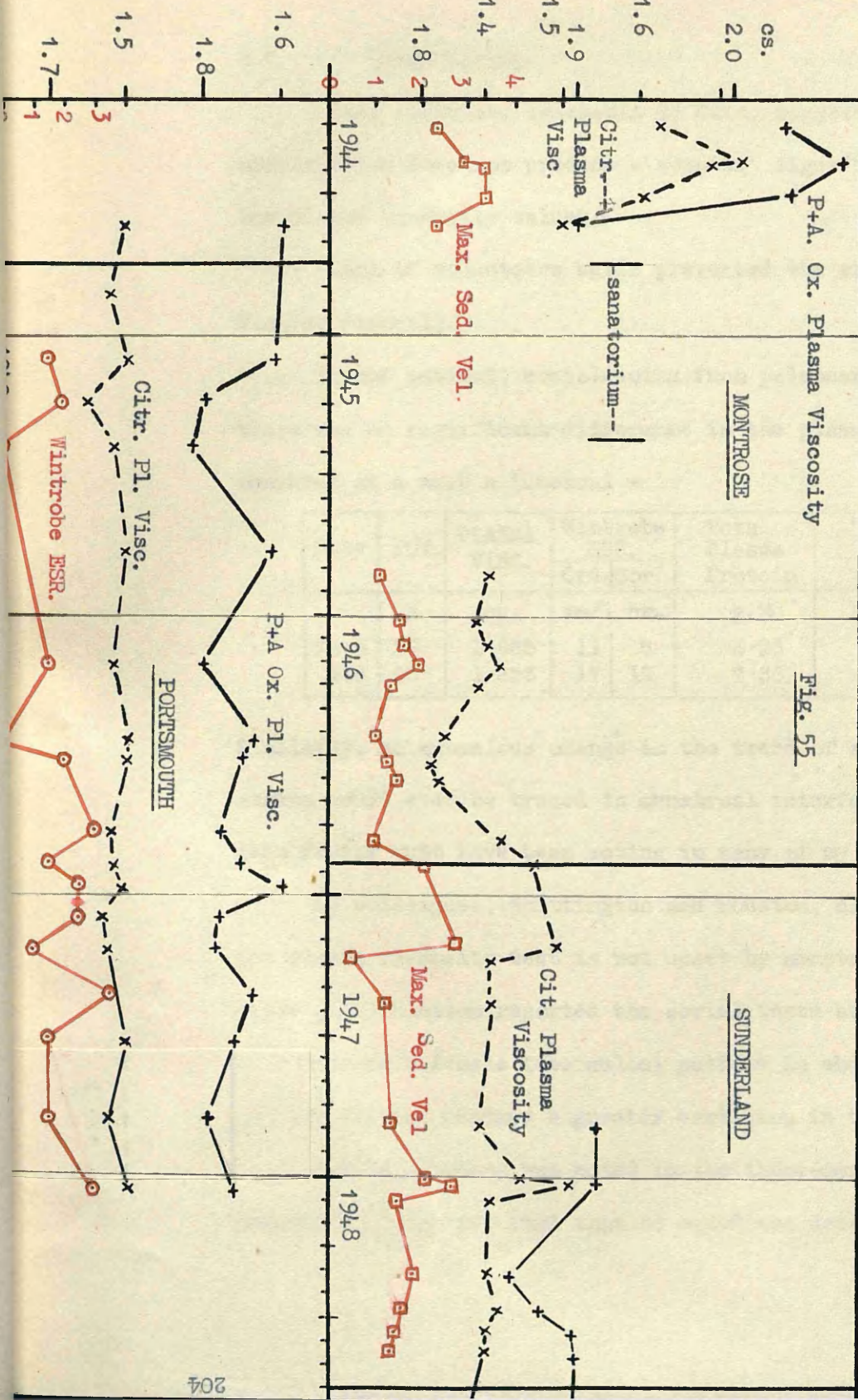
Fig. 55 presents the serial tests made on the writer over a period of 8 years. The graph is divided into three parts according to where he was living - the first part relates to Montrose, Scotland, the second to Sunderland, N.E. England, and the third to Portsmouth, S. England. (The picture is rather complicated by the period in a sanatorium which may cause the later Montrose results to be regarded as convalescent instead of normal.) The cold, damp, foggy winters of N.E. England were accompanied by catarrh of the respiratory tract and this is reflected in the graph by the winter increases in the viscosity; in the milder south the catarrh was absent and there was no longer the winter viscosity increase. This single test suggests that there is no seasonal variation in the plasma viscosity due to the seasons themselves but that if infections or other conditions which may cause a systemic reaction become associated with a season their secondary viscosity increase (see next part) may be mistakenly associated with the season.

In Table U of the appendix, other normal subjects have been studied at intervals and again there is no great difference between the results at different seasons. The same might be said of a very few chronic cases where there was no clinical change over a period of several months.

Plasma Viscosity (cs.)

○ = Corrected Wintrobe ESR. (mm./1st hour)

□ = Maximum Sedimentation Velocity (cm./sec. $\times 10^{-4}$)



§ 5. Menstruation.

Our evidence, available to date, suggests that menstruation does not produce a constant significant change in the plasma viscosity values.

Lack of volunteers again prevented the problem being tackled directly.

In one patient, convalescing from pulmonary tuberculosis, there was no significant difference in the plasma viscosity values measured at a week's interval -

Date	PCV.	PLASMA VISC.	Wintrobe ESR.		Total Plasma Protein	Remarks
			Ord.	Cor.		
	%	cs.	mm/1 hr.		g. %	
28:5	38·	1·865	11	6	6·95	
4:6	38·	1·853	17	12	7·38	

Similarly, no anomalous change in the trend of a plasma viscosity series could ever be traced to menstrual interference, although this factor must have been acting in many of my serial investigations.

My colleagues, Whittington and Houston, also believe that the plasma viscosity test is not upset by menstruation. In our paper (120) Houston reported the serial tests at 3 to 4 day intervals on a female tuberculous patient in whom the 13 menstrual periods did not produce a greater variation in the plasma viscosity values than was noted in the inter-menstrual phase. Benson (16) has reported that he could not detect an effect due to

menstruation, but the low accuracy of his technique must be remembered. Allbutt (6) found no change in the viscosity of whole blood during the menstrual phase.

I consider that the pre-menstrual disturbance of the water-balance of the body has a greater potential action in causing a variation in the plasma viscosity level than the actual menstrual phase itself; support is given to this belief by the report by Allbutt that the whole-blood viscosity is raised in the premenstrual phase. Similarly, I consider that it might be possible to detect in a subject under basal conditions of rest in bed or of a regular mode of living, the lesser water disturbance at the time of ovulation. These aspects will require further study in the event of the test being adopted by the gynaecologists.

* * * * *

§ 6 PREGNANCY.

Pregnancy was the condition in which the ESR was first measured by Fahraeus (73) and in which his preliminary tests found the ESR to be increased. Later it was shown that the ESR was raised in a variety of diseases.

Because the test was applied almost exclusively to the study of disease no thorough repetition of Fahraeus' original study was made to place the effect of pregnancy on the ESR on a satisfactory basis. It is stated in the text-books that the ESR is raised in pregnancy but no guide is given as to the amount of this increase or its differences at the various periods of gestation. The clinician has been allowed to take the attitude that -"the ESR. is increased in pregnancy" - and to abandon the test for its ordinary uses for the whole duration of pregnancy. The authority to which most writers refer is a paper by Obermer (189) who used a method of his own devising which makes it impossible to transfer his findings to any other standard ESR technique; also, his 88 tests form an inadequate number. Similarly, Walton (244) reported on 30 tests.

My opportunity of studying the plasma viscosity changes during pregnancy did not arise until 1951 when I had to remove the blood for routine ante-natal Wassermann tests. I had no proof of the normality of these pregnancies beyond the patient's

appearance, her lack of symptoms, and the absence of any indication by her clinician to the patient that any complication might be present. In any case, this was to be a pilot investigation to discover if there were any potential uses of the plasma viscosity in this condition: the results are sufficiently numerous to allow of critical consideration. (I am now engaged in a repetition of this investigation in co-operation with an obstetrician and another clinical pathologist as part of a research into the haematological changes of normal and abnormal pregnancies.)

Results. The details are included in Table V of the Appendix.

The means of the gestation periods (of 4 weeks) have been plotted in Fig. 56 to 59 , for plasma viscosity, ESR, haematocrit, and plasma protein fractions.

Discussion. (a) Plasma Viscosity.

Fig. 56 and fig. 57 indicate that for the first 31 weeks of apparently-normal pregnancy the majority of the plasma viscosity values is still still within the limits of normality for non-pregnant women. In my opinion, the instances of individual results above the normal level are remarkably few when one takes into consideration the high incidence of minor complications of pregnancy (eg., pyelitis, cystitis) which may cause no complaint and the large changes going on within the body in the uterus, placenta, and breasts.

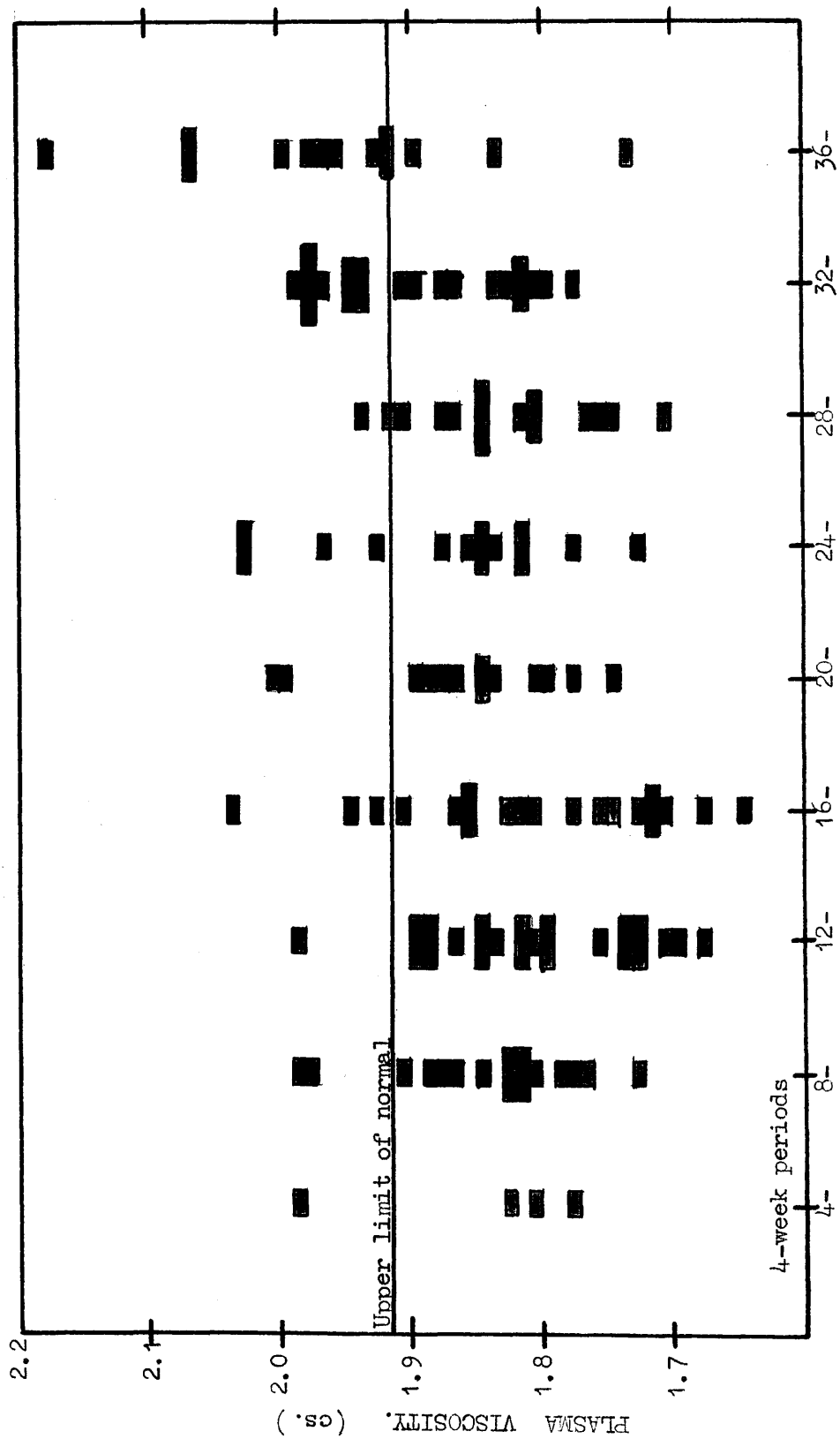


Fig. 56 The plasma viscosity values in Pregnancies which were apparently normal.

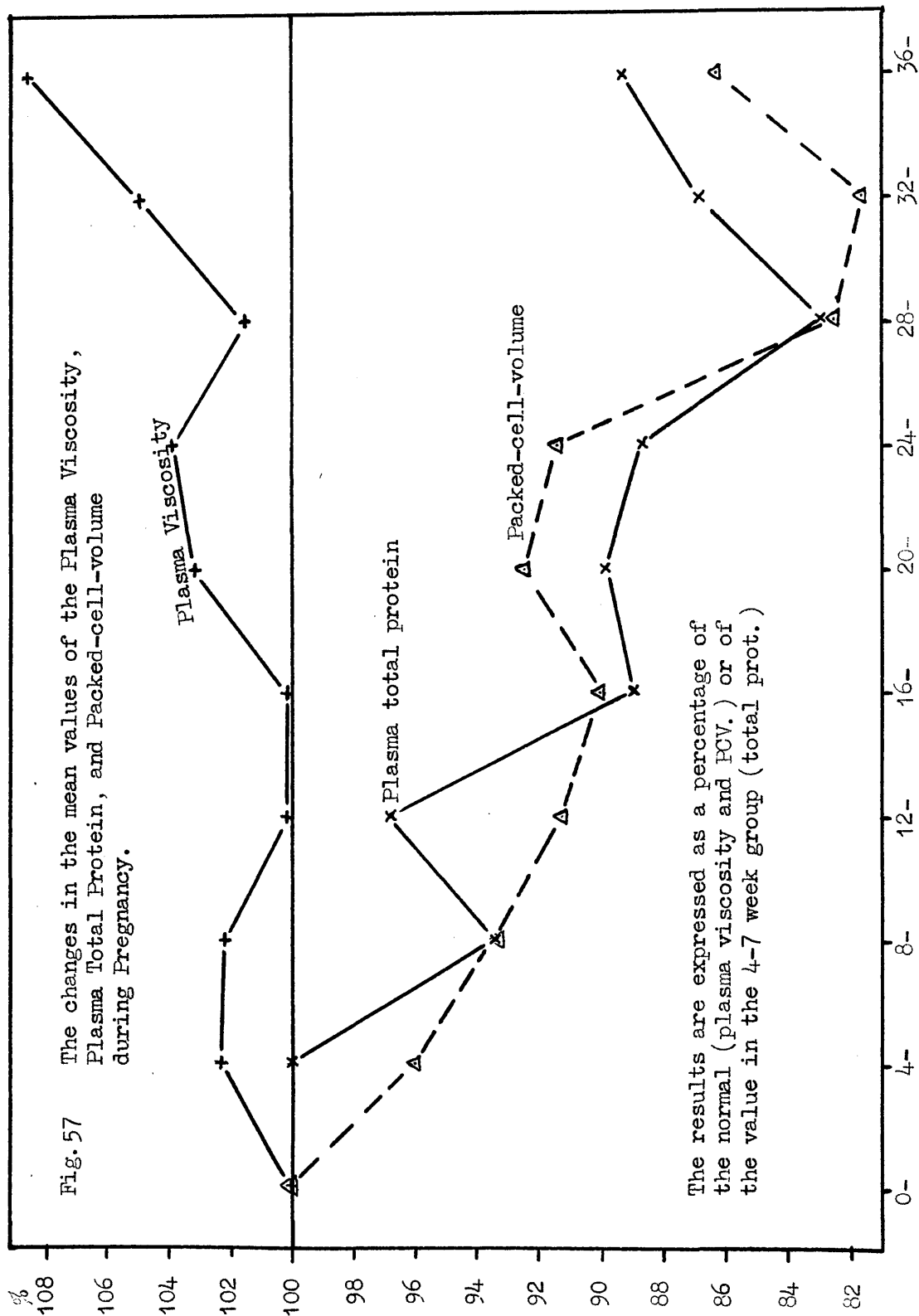
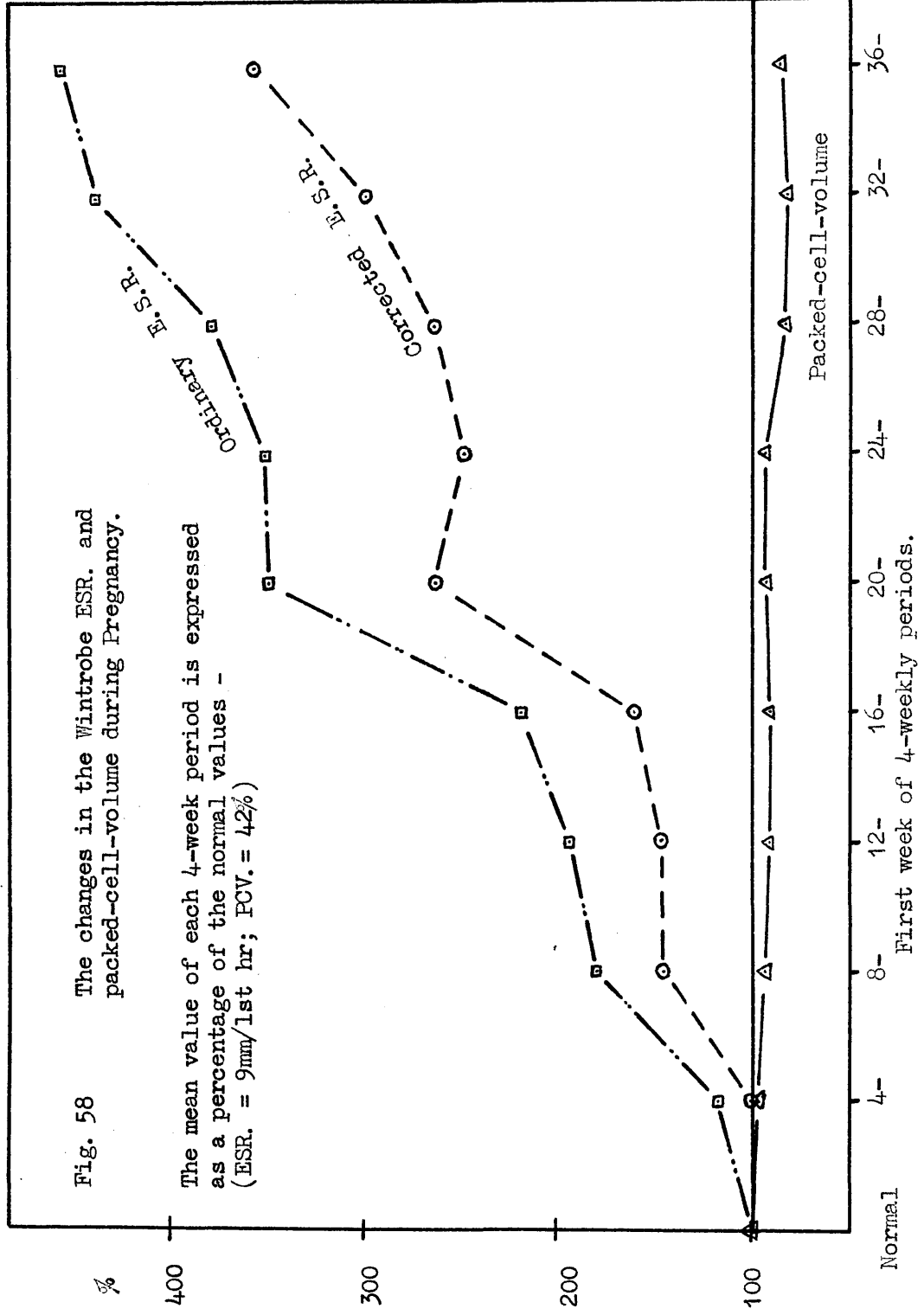
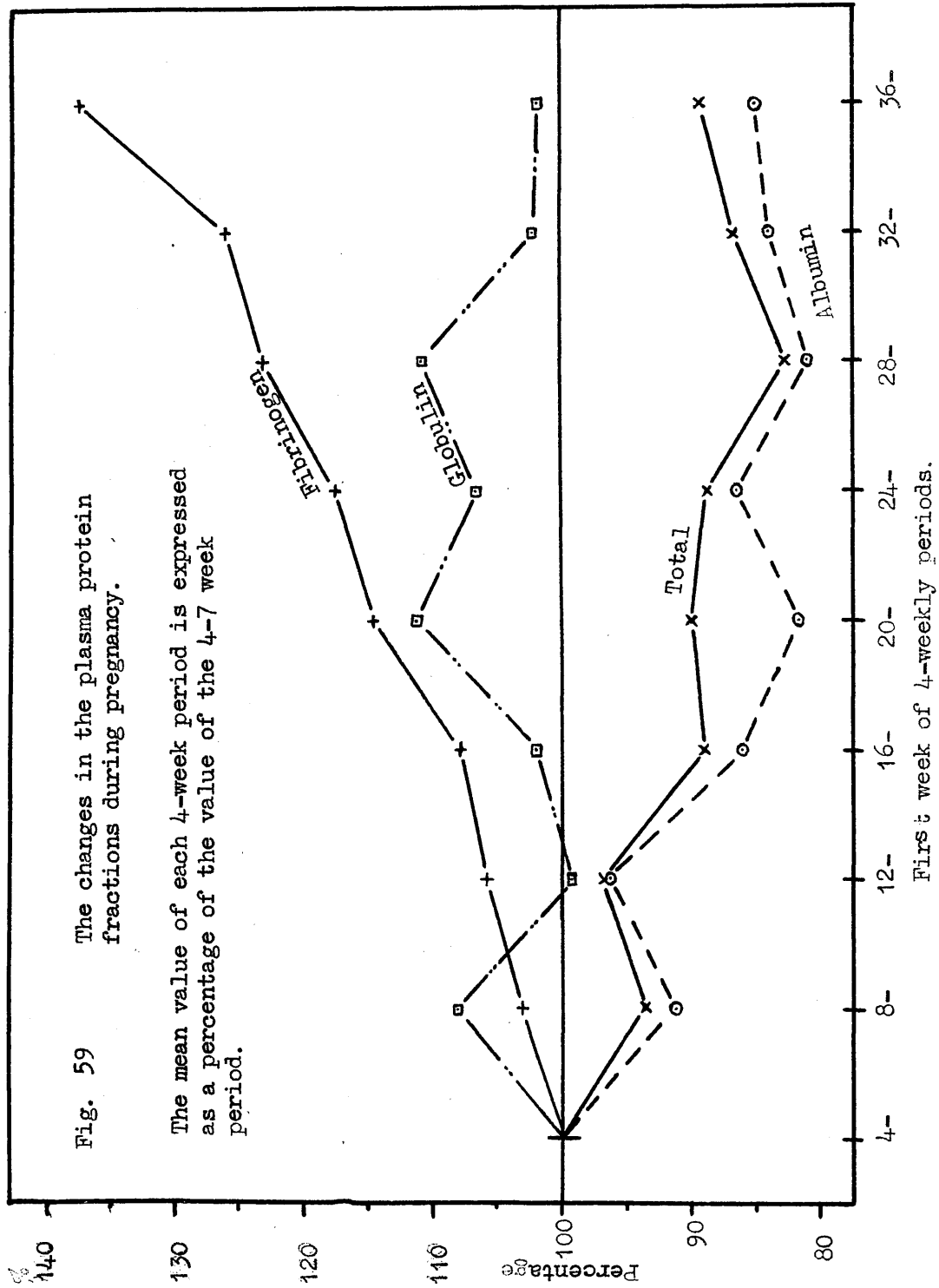


Fig. 58 The changes in the Wintrobe ESR. and packed-cell-volume during Pregnancy.

The mean value of each 4-week period is expressed as a percentage of the normal values -
(ESR. = 9mm/1st hr; PCV. = 42%)





After the 32nd week, not quite half of the results are above the usual upper normal limit; after the 36th week only 3 out of 13 tests fall within the normal limits.

However, the extent by which the values are abnormally-high is small, seven cases only exceeding 2.000 cs.

The clinical application of these results is as follows. Until the 31st week, a pregnant woman has a plasma viscosity which is usually within the same limits as her non-pregnant normal sister; values above 2.000 cs. should be interpreted as abnormal and an explanation for the increase should be sought for in a complication of pregnancy or in an additional disease process; values between 1.915 and 2.00 cs. must be accepted as normal at present, but viewed with suspicion, until our later studies which include co-operative evaluation of the clinical condition have verified the need to extend the normal range or have attributed the small increases to minor complications. After the 32nd week the upper limit is necessarily placed at 2.000 cs, and a still higher level is required for the last four weeks. With these slight reservations, the plasma viscosity test can be used by the clinician up to the 32nd week of gestation at least, just as he is accustomed to use the test in non-pregnant women and in men. The plasma viscosity serial tests will be reliable indications of reactivation of tuberculous or rheumatic disease; they will also

reflect the presence of a more acute infection. For example, in a patient who was 6-months pregnant, with a pyrexia of unknown origin, the diagnosis of a reactivation of a previous rheumatic fever was strongly supported by the plasma viscosity of 2.066 cs.; such a high value was only equalled twice and surpassed once in my series.

The literature contains references to small numbers of plasma viscosity estimations during pregnancy, but only Hamilton (93) has included enough cases to make a comparison possible. Runge (215,216) noted the average plasma viscosity of the mother was 2.4 which was 25% more than the viscosity of her child; the total protein was only 13% more, and he traced the apparent discrepancy to the lower fibrinogen concentration in the child.

Schwalm (224) found that the plasma viscosity remained ^apractically unchanged during normal pregnancy but his series consisted only of 24 tests in the last month; the serum viscosity was lower at the end of pregnancy, due to the increase in fibrinogen levels. The accuracy of his technique, using a falling-ball apparatus is open to criticism.

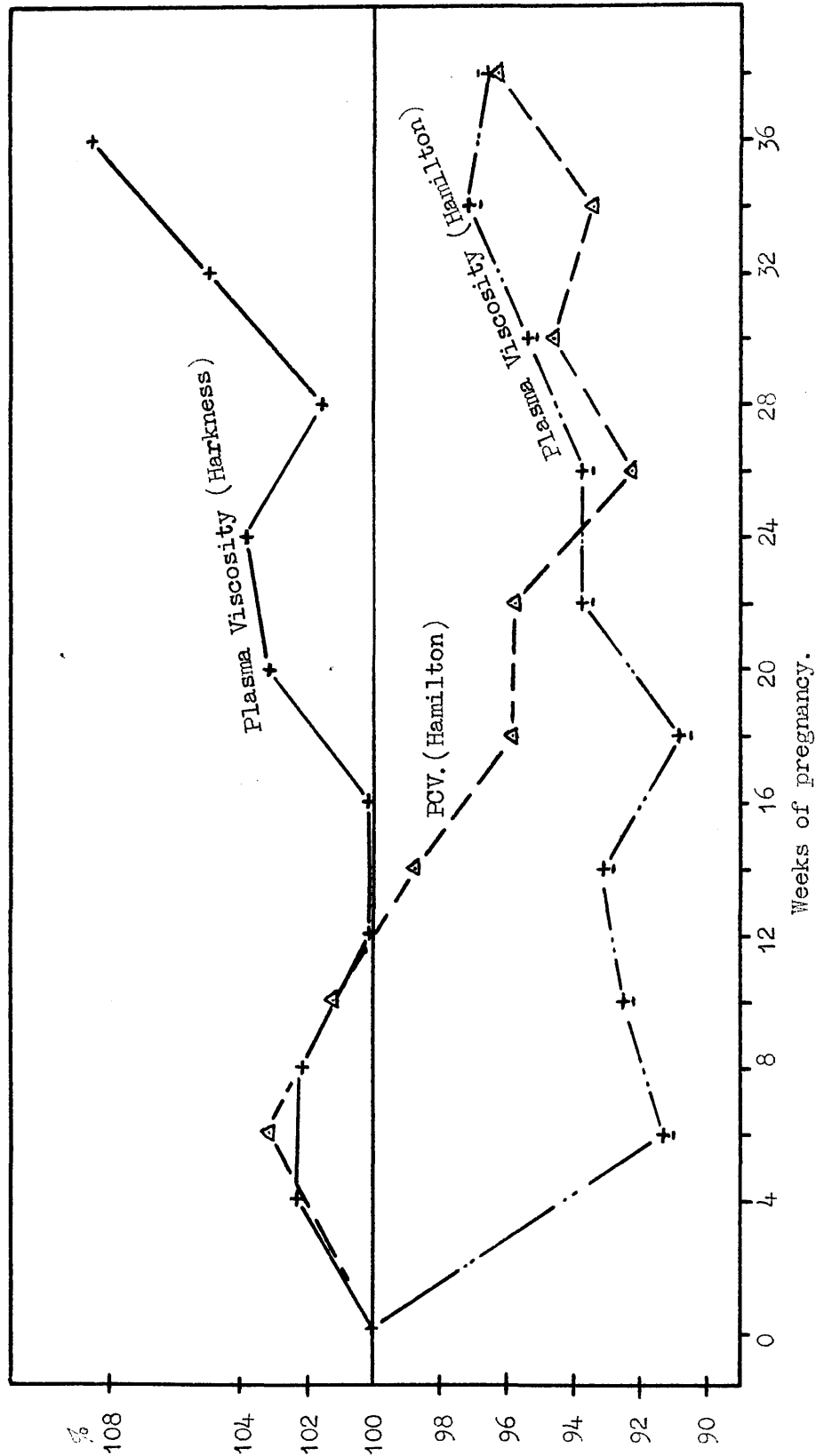
Benson (16) originally claimed that the plasma viscosity remained unchanged during pregnancy (number of tests unknown) but in a private communication (17) he has informed me that by using

the Whittington viscometer which I had calibrated for him, he had been able to verify my claim that the viscosity increased slightly in the last two months of pregnancy.

Hamilton (93) collected a series of 362 normal pregnancies, with at least 10 tests per week commencing at the 8th week. She used an Ostwald viscometer, at 20°C. The mean of her normal controls was only 1.74 cs. She was one of the few medical writers who realised the importance of the non-Newtonian nature of the liquids with which she was dealing - "It must be clearly understood that the viscosity of blood varies with the conditions under which it is measured and compatible results can be obtained only when a single viscosimeter is used and when standard conditions (temperature, pressure (if any) and completeness of mixing) are maintained. Results using a different make of viscosimeter even under similar conditions may not be identical but relative trends will be shown to the same extent". She found that the plasma viscosity in the 6-9 week group was lower than the control mean, and thereafter the variation was slight; the variation from the normal was stated as - "The fall is not significant statistically". I have copied her mean results in Fig. 60 for comparison with mine; the shape of the curves is much the same for both series as Hamilton's results also show a tendency to increase as pregnancy lengthens. A possible

Fig. 60 A comparison of the changes in the Plasma Viscosity during Pregnancy according to myself (+) and according to Hamilton (Δ), expressed in terms of the percentage changes in the mean values of 4-weekly periods.

The shapes of the curves are similar; discrepancy of levels is due to Hamilton's high normal.



and probable explanation lies in her choice of her 23 controls. "Twenty-three normal, healthy young women in the child-bearing age, comprising a group of nurses, technicians and patients about to undergo minor gynaecological operations." There is no guarantee that the nurses or technicians were truly free from minor disease; we have reported (120) how the fear of a minor operation was able to produce a significant rise in the plasma viscosity and this factor would be acting in the gynaecological subjects who might have been suffering from diseases which would have raised the plasma viscosity initially. (Although the paper was published in 1950 the author was apparently unaware of the use of the plasma viscosity as a test in clinical pathology as no reference is made to any such paper) Thus I believe that the control value is unduly high. By taking the mean of the 6th week group as the control value (=100%) it can be seen that our two curves would be almost superimposed and certainly not significantly different. Her results may also be interpreted as indicating that there is no alteration of significance in the first 29 weeks of pregnancy but thereafter there is a slight increase.

(b) Haematocrit.

During pregnancy there is an increase in the total blood volume. The change in a blood constituent is the resultant of the diluting

fluid being introduced and the increased formation of the substance which tends to maintain the original concentration. The decrease in the haematocrit values is an indication that the formation of new erythrocytes has not kept pace with the dilution, while, in actual fact, the total circulating erythrocytes has actually increased.

The fall in my series occurs earlier and to a more severe degree than that of Hamilton; her results are included in Fig. 60. She treated her patients with prophylactic doses of iron and in this may lie the explanation of our difference.

(c) Plasma proteins.

The changes in the total plasma protein are similar to those of the erythrocytes; nevertheless, as the fractions do not show the same percentage changes, positive variation action must be taking place in addition to the dilution.

The globulin changes are least; an increase is later followed by return to the normal level.

The albumin showed an almost consistent fall.

The fibrinogen increased steadily throughout pregnancy.

My figures of the 16th week period are instructive. The mean globulin is almost normal (102%): the mean plasma viscosity is also almost normal (100.1%). Therefore, the effect on the plasma

viscosity of the 7.7% increase in fibrinogen ($=0.03$ g./100 ml.) was equivalent to the effect of the 11.1% decrease in albumin ($=0.68$ g./100 ml.). These figures illustrate, even if somewhat crudely, the effect of the difference in the molecular sizes of the proteins.

Now, although the fibrinogen is increasing steadily it does not attain a level accepted as abnormal until the 20th week; the globulin level at the 12th and 16th weeks is almost normal on both occasions; yet, the associated ESR values are also increased. This finding is another slight support to my contention that the action of newly-added fibrinogen differs from the normal plasma content in its effect on the ESR - a subject whose normal plasma fibrinogen level is 0.37 g./100 ml. will have a lower ESR than a subject whose level of 0.37 consists of 0.05 g. added to his normal level of 0.32 g./100 ml. It would appear that the effect of the protein on the ESR involves something more than a simple concentration action.

(d) Erythrocyte Sedimentation Rate.

There is a steady increase in the mean ESR values throughout pregnancy, with a specially-sharp rise between the 16th and 20th weeks. The uncorrected and corrected results had risen by 457% and 345% respectively above a level of 9 mm./ 1st hour.

by the end of pregnancy, yet the mean of the corrected ESR. results was still only 13.9 mm./1st hour after 19 weeks. Only one result below 10 mm. was found after the 20th week. The incidence of values over 20 mm. before the 20th week is sufficiently low to allow the ESR. test to be used as usual up to that date. Thereafter, the upper limit of normality has to be raised to 40 mm./1st hour: there is a small region between this and the maximum of 55 mm. in which the result would be significant of super-added active disease. The curtailing action of pregnancy on the usefulness of the test is very much greater with the ESR than with the plasma viscosity.

The increase in the ESR. is not caused entirely by the decrease in the haematocrit as the application of the correction chart is able to retain the normal level in the first mean value only. The explanation is to be found in the alteration in the protein fractions, especially the fibrinogen, although the effect may be ultimately due to some substance changing in the same phase as these proteins and associated with them.

* * * * *

§ 7 Dehydration.

Three instances of post-alcoholic dehydration were encountered by chance among the physiological controls. Two tests were made on the Monday after non-excessive alcohol on the Sunday (male, K.H.; female, F.K.): one (male, P.S.) attended his annual re-union with his old students in the middle of his control period. This state of dehydration was associated with an increase in the plasma viscosity which had disappeared completely within a further 24-hours.

It is unfortunate that all these subjects had initial low plasma viscosities as we cannot tell if a normal viscosity can be raised to an abnormal level by this stimulus - a high plasma protein content might react less violently than a lower protein because the osmotic pressure action of the protein might then be effectively different.

Strauss (237) has reported on the cause of the dehydration which followed whiskey ingestion; he attributed it to a diuresis.

* * * * *

§ 8 Fluid Intake in Excess

This section on excess fluid intake should be contrasted with § 11 in which are described the changes resulting from three laboratory tests of functional capacity in the body.

I have no personal tests to report but wish to include the information available in the literature for the sake of completeness. There are no published results for the plasma viscosity itself but two papers note the changes in the protein on which the viscosity is ultimately dependent.

Kagan (129) found an average fall in 3 cases of 0.15 g.% after 600-750 ml. of water: and an average fall in 3 cases of 0.5 g.% in 1 hour after drinking 1,500 ml. of water, with a return to normal after a further hour.

Renbourn (207) could produce no significant variation in the plasma proteins or haematocrit values following the tremendous stimuli of 1 litre of water hourly from 9 am. to 6 pm., or of 5 litres of water, with 0.5 ml. of pituitrin at 10 am. and 2 pm.

Kagan found a greater effect with normal saline where in 3 cases the average fall in serum protein was 0.9 g.% two hours after ingesting 1,500 ml.; another two hours later the serum protein was still 0.1 g.% below the original level.

These results would indicate that the ingestion of large

volumes of water or more-especially of water plus salt is a potential cause of a diminution of the plasma proteins and of the plasma viscosity. The small degree of change produced in the reported experiments would indicate that the viscosity changes would probably be insignificant.

Satô (220) has studied the effects of water and saline ingestion on serum viscosity, and these results are directly transferable to plasma viscosity terms. In 4 tests with water, a fall of 0.05 cs. was noted in 3 and of 0.07-0.08 cs. in 1; the minimum value was found in 10 - 30 minutes, but it required two or three hours for the original value to be regained: the volume ingested in each test was 1 litre. With the same volume of normal saline, the minimum was not attained for 2 or 3 hours and the recovery was not complete until the 5th hour or later - 1.579→1.521→1.579 (4 hours) ; 1.621→1.550→1.592 (after 5 hours) These results would indicate that the ingestion of 3 pints of saline about 2 or 3 hours before the venipuncture for plasma viscosity measurement might reduce a low-abnormal value to within the normal range; I cannot imagine a situation in which such an action is likely to occur in the ordinary use of this estimation.

* * * * *

§ 9 Exercise.

Again I have no tests of my own to report and must refer to the publications of others.

Renbourn (207) found variations in the plasma proteins of borderline significance in troops who had marched 10 miles in 3 hours with full equipment in Northern India.

In contrast to this prolonged exercise, Satô (220) studied the effect of 1 minute of exercise on the serum viscosity. In his five reported cases the increase was small, amounting only to 0.64%, 0.85%, 0.86%, 1.36%, and 5.53%.

Satô quotes Magaria (155) as finding an increase in the serum viscosity of the order of 1% on exercising to exhaustion, and Mabuti and Miwa (153) as finding no alteration in the serum viscosity of rabbits after exercising (but they used the Hess viscometer which is accurate to the first decimal place only).

These results are reassuring. They would eliminate the exercise of the journey to the laboratory as a possible cause of a slightly-increased plasma viscosity value and they allow more significance to be attached to small variations during serial testing.

* * * * *

§ 10 Posture.

Publications by other workers are again required for results concerning this physiological stimulus.

The adoption of a horizontal posture leads to a rapid fall in the plasma proteins which is maximal in 5-6 hours. Renbourn (207) found a mean fall of 0.35 g.% in 30 minutes and a mean fall of 0.65 g.% after 48 hours in bed. Widdowson and McCance (254) had an average fall of 0.48 g.% after 2 hours in bed in 8 normal controls, and of 0.36 g.% after 3 days in bed. Perara and Berliner (191) measured the plasma proteins at 2-hourly intervals to find the maximal fall in 5-6 hours when the average fall amounted to 0.8 g.% which was equal to 10-15% of the total. This fall is important as it might reduce a low-normal ambulant level into a hypo-proteinaemic level when in bed. They also noted by tilting experiments that an increase of 0.48 g.% in the plasma protein after 5 minutes walking following 45 minutes resting was largely due to the change in posture. The return to the ambulant posture was associated with an increased plasma protein. They wrote - "The effect of the horizontal position upon the resting individual is comparable to the administration of a slow but sustained infusion".

Such large protein changes cannot but have an effect on

the plasma viscosity. They must be taken into account in the study of the patients. Two periods in an illness are especially liable to include this postural effect. At the beginning of an illness, the retiral to bed will in itself produce a fall in the plasma proteins which will be occasionally just sufficient to withdraw a slightly-raised plasma viscosity back within the normal range. Then, when a patient gets up in the convalescent stage, the postural effect may be sufficient to cause an apparent increase in the plasma viscosity which would be interpreted by the unwary as a sign of a complication, recurrence, or that the patient had not yet reached a stage at which he might be allowed up; this effect is most important in dealing with cases of pulmonary tuberculosis where the patient passes from the ambulant to the bed state several times daily and where the constancy of time of venipuncture is no criterion that the postural effect will be correspondingly constant. Similarly, if the serial tests in a disease like rheumatic fever have been carried out until a satisfactory low value has been reached with the recumbent patient, an apparently higher value is quite to be expected when he reappears as an out-patient clinic.

* * * * *

§ 11. Tests of Function, made in a Biochemistry Department.

The opportunity was taken to study the effect of the physiological stimuli afforded by the biochemical investigation of the gastric, renal, and carbohydrate metabolic functions. The results presented here are the preliminary tests; they have shown that the future studies must include that of the plasma ultra-filtrates and the proper centrifuge-type of apparatus has only recently become available.

(a) Gastric Analysis.

The gastric contents of the fasting subject were removed through a Ryle's tube, 100 ml. of 7% alcohol were given to drink, and 5-10 ml. samples of gastric fluid were removed at intervals of 15 minutes. If achlorhydria was detected in the fasting and first post-alcohol samples, a deep subcutaneous or intra-muscular injection of 0.5 mg. of histamine was administered.

A blood sample was taken at the very beginning of the test before the subject was disturbed by the passing of the Ryle's tube, and another was taken 2 hours after the alcohol solution had been drunk.

Results: These are given in Table W of the Appendix. The three subjects (out of a total of 9) who received histamine are marked in Fig. 61 by interrupted lines.

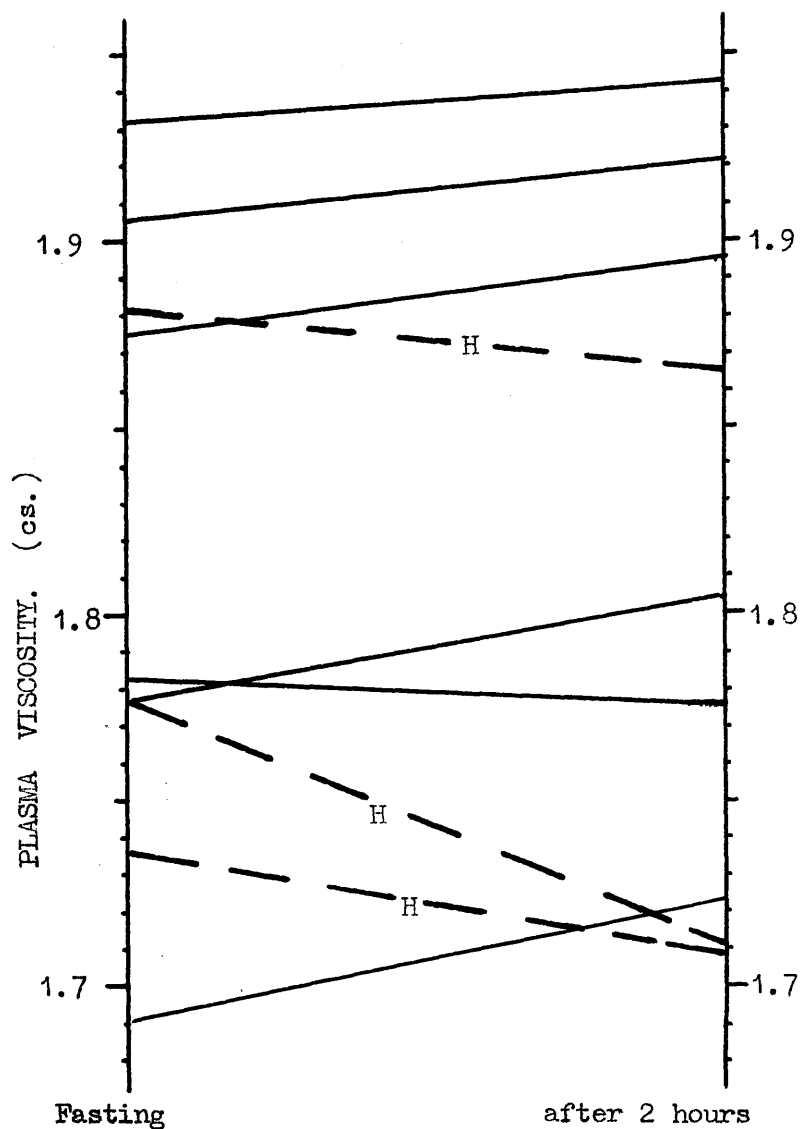


Fig. 61 The effect on the Plasma Viscosity of the ingestion of 100 ml. of 7% alcohol, after emptying the stomach.

The interrupted lines represent the three subjects who also received an injection of 0.5 mg. of histamine.

Discussion: Of the six subjects who did not receive histamine, five showed a slight increase in the plasma viscosity while the sixth had a fall which was within the experimental error of the initial value. The haematocrit values also changed but little, 4 showing an increase and 2 a decrease. In contrast, the total protein had decreased in 3, remained unchanged in 2, and increased in 1 only.

These results may be explained as follows. The stimulus of the alcohol has caused a flow of gastric juice at a rate faster than the reabsorption in the small intestine, and a slight dehydration has occurred; this is reflected in the fall in the fluid portion of the blood (ie. increased haematocrit) and in the plasma viscosity. As the total protein has not shown a parallel change, an alteration in the plasma protein pattern must have taken place in which the proportion of the large molecules of globulin and/or fibrinogen has increased.

The three subjects who received histamine all showed a haemo-dilution (fall in haematocrit, plasma viscosity and plasma total protein). Further, this change occurred in the subject who later produced free acid in excess of the average amount. Because of its recognised action on the blood capillaries and their permeability for fluid, it is readily believed that the injection of such a large amount of histamine has been followed by the

passage of fluid into the vascular system in sufficient volume to produce this significant haemo-dilution.

The increase in the plasma viscosity after this small amount of alcohol has been caused by the increased flow of gastric juice: we have already noted a similar change after alcohol (§ 7) but in that instance the acting physiological mechanism was a diuresis (Strauss (237)).

(b) Renal Function Tests.

A combination of the Urea Clearance and Urea Concentration tests was used. The urine was collected at hourly intervals for 5 hours in a fasting subject. A blood sample was collected at the end of the first and third hours; 15 g. of urea, dissolved in about 250 ml. of water, were administered at the end of the second hour.

Results: These are presented in Table W of the appendix and in the accompanying figure (Fig. 62).

Discussion: In the twelve tests, the plasma viscosity increased in four, decreased in three, and showed no significant change in five. Some of these changes were large, the greatest being a fall of 0.015 cs.

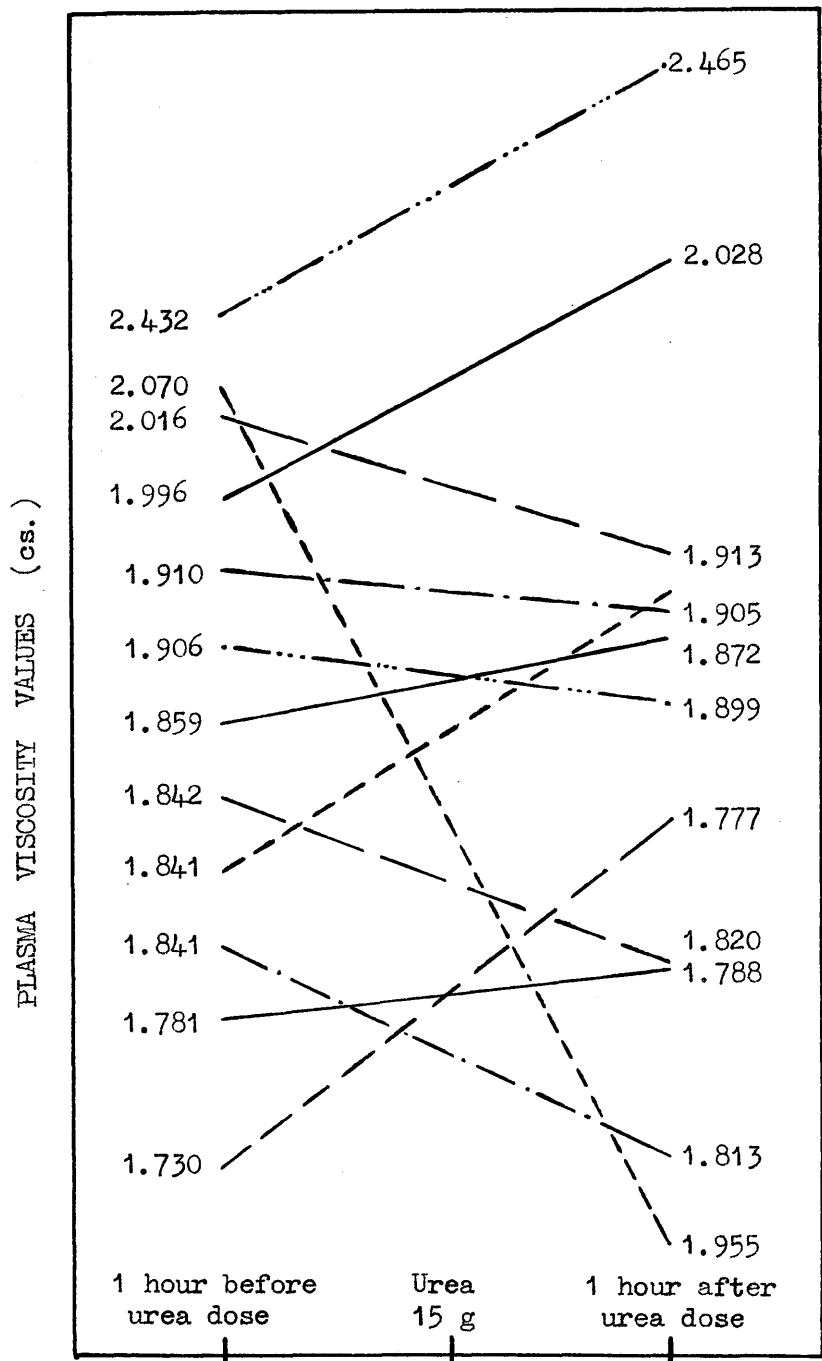


Fig. 62

The effect on the Plasma Viscosity of the ingestion of 15 g. of urea in about 250 ml. of water, on a fasting subject.

The tests were made one hour before and after the ingestion.

A clue to the cause of the different responses is available in the differences in the volumes of urine and their urea content which have been excreted between the blood samplings - the second and third urine samples in the table. The correlation is not absolute, but where a dehydration may have been caused by the excretion of a large urine volume the plasma viscosity has increased; similarly, a small urine volume tended to be associated with a decreased plasma viscosity. In all instances there is a variable factor acting whose effect is opposed to that of urine excretion, ie. the fluid absorption after the urea dose.

(c) Glucose Tolerance Test.

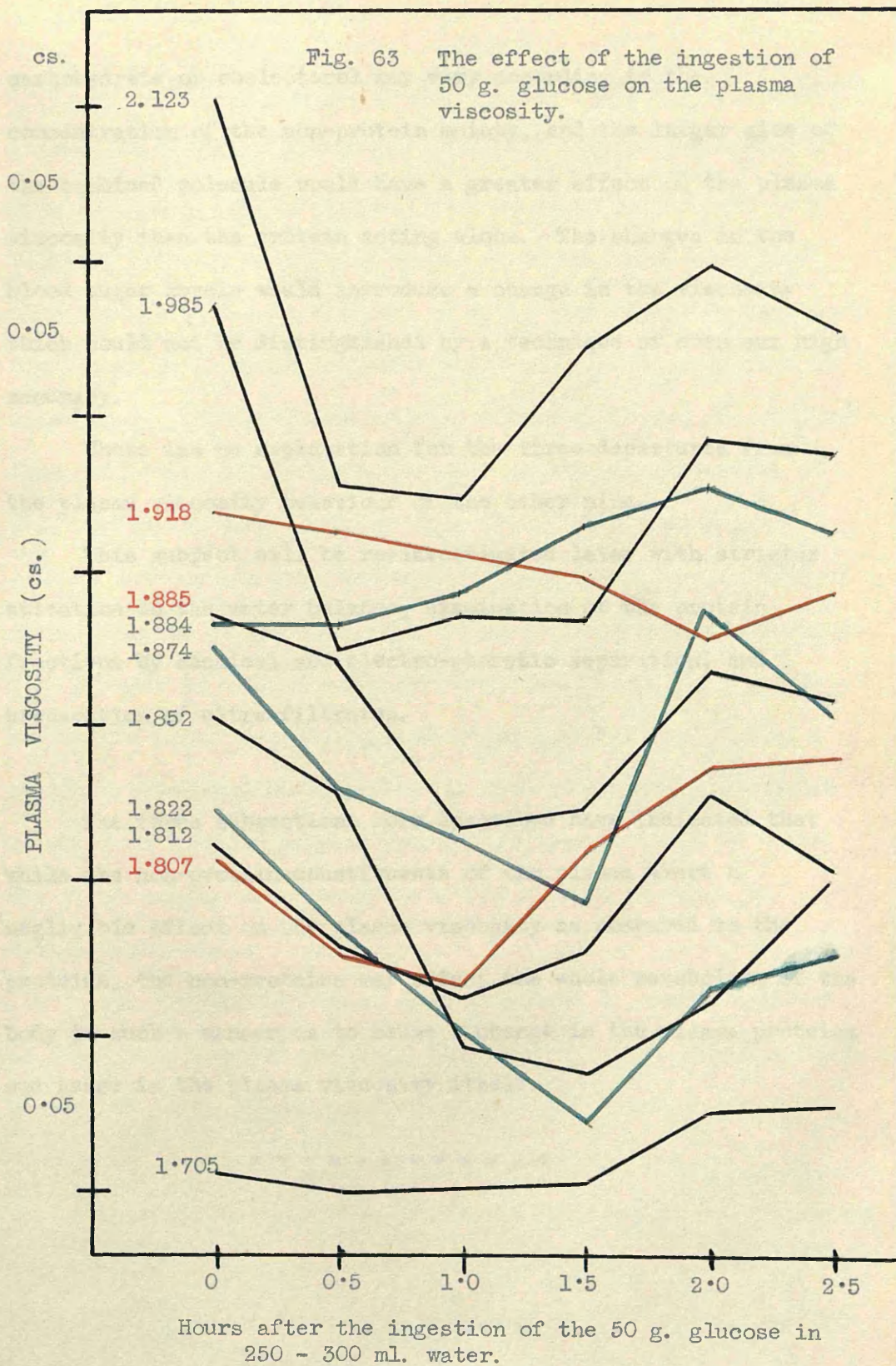
The fasting subject received 50 g. of glucose dissolved in 150 - 250 ml. of water. Blood samples were removed in the fasting state and at half-hourly intervals after the glucose ingestion for two and a half hours. The subjects spent the time seated; they were allowed to read or knit, but smoking was prohibited. They were allowed to take an additional 250 ml. of water at their own discretion; few availed themselves of the opportunity.

Results: These are given in Table W of the Appendix, and in the accompanying figure(Fig. 63).

Discussion: In nine of the twelve tests the results have a common pattern - there is a fall in the plasma viscosity for one or one and a half hours, a rise to approximately the original level, and sometimes a final slight fall. The figure resembles an inverted blood sugar curve.

No difference in the pattern could be distinguished between diabetic and non-diabetic subjects. No correlation was noted between the degree of the viscosity change and the degree of blood sugar change.

Three possible mechanisms are in action to cause the variations in the plasma viscosity level. The state of body hydration will depend upon the balance in water absorption from the administered glucose solution and in urinary water excretion. It is regretted that more careful note of these volumes was not made at the time, yet the two reported tests show that a haemo-dilution can occur in the face of large urine excretions and a haemo-concentration can occur in face of small excretions. The discrepancy between the changes in the plasma viscosity and the plasma total protein might be due to changes in the plasma protein fraction pattern. The molecules of combined protein formed from the protein and such non-protein substances as



carbohydrate or cholesterol may vary according to the concentration of the non-protein moiety, and the larger size of the combined molecule would have a greater effect on the plasma viscosity than the protein acting alone. The changes in the blood sugar levels would introduce a change in the viscosity which could not be distinguished by a technique of even our high accuracy.

There was no explanation for the three departures from the plasma viscosity behaviour of the other nine.

This subject will be re-investigated later with stricter attention to the water balance, examination of the protein fractions by chemical and electro-phoretic separation, and preparation of ultra-filtrates.

The three subsections here described have indicated that while the non-protein constituents of the plasma exert a negligible effect on the plasma viscosity as compared to the proteins, the non-proteins may affect the whole metabolism of the body in such a manner as to cause a change in the plasma proteins and hence in the plasma viscosity itself.

* * * * *

§ 12 The effect of the exhibition of sulphonamides on the plasma viscosity, serum viscosity, serum protein, haematocrit and ESR.

Material and Methods. The subjects in these experiments were all men, between the ages of 23 and 65 years. They were not physically examined at the time of testing except to exclude such conditions as pyogenic infection which were known to respond to these drugs. Two subjects later developed phthisis; one suffered from post-encephalitis. The response of the abnormal group of subjects was however identical with that of the normal group.

An attempt was made to restrict their lives to a routine of work, leisure, sleep, diet, etc. so as to reduce other physiological stimuli to a minimum and to allow the serial blood sample to be removed under almost identical conditions. The effect of a possible psychological stimulus was reduced by not allowing the subjects to know beforehand when a blood sample would be taken. The blood sample was removed by myself at 7.30 am. from the fasting subjects.

6 men were given 2 g. of sulphanilamide by mouth, followed in 4 hours by another 2 g., and thereafter by 1 g. 4-hourly until a total of 20 g. had been administered. With another 6 men the same procedure was carried out with sulphapyridine.

Sodium citrate solution (3.8%) was used as the anticoagulant; the serum protein was calculated from the specific gravity determined by the falling-drop technique of Barbour and Hamilton.

Results. The details are given in Table Y of the appendix.

The effects of sulphanilamide and sulphapyridine were identical and therefore only the sulphanilamide results are presented in graphical form. These figures have been taken from my paper in the "Lancet" on this topic. (Fig. 64) (98).

The plasma viscosity, serum viscosity, serum protein, and ESR. had all increased within 48 hours of the administration of the sulphanilamide. (The sulphapyridine tests were done at different time intervals, and the increases were evident within 24 hours of giving that drug.) That these increases are not due to haemoconcentration can be ascertained from the haematocrit (PCV) values, in which the variation is smaller and inconstant, and by making allowance for the PCV. variation in calculating the changes in these other values (such as has been done for the serum protein only in the diagram).

The increase in the plasma viscosity exceeds the variation found in serial tests when ordinary physiological stimuli alone are acting. More significant however is the fact that the increase is sufficiently great, in every instance, to raise the initially normal plasma viscosity values into the abnormal range (over 1.600 cs. for corrected citrate plasma viscosity).

Discussion. This series of 12 tests is small, but I have had no

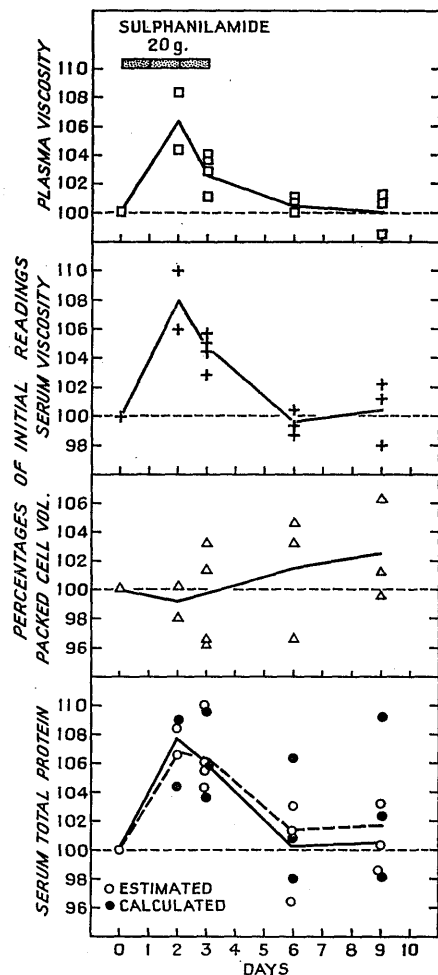


Fig. 1.—Variations in plasma viscosity, serum viscosity, packed cell volume, and serum-protein on exhibition of sulphanilamide. Results are expressed as percentages of values before administration of sulphanilamide. The lines join the means of the experimental results.

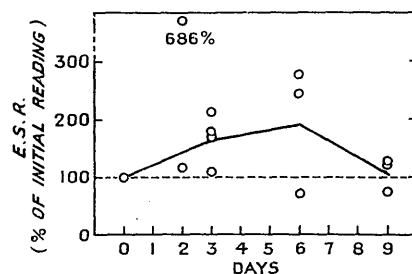


Fig. 2.—Variation in erythrocyte-sedimentation rate on exhibition of sulphanilamide. Results are expressed as percentages of value before administration of sulphanilamide. The line joins the means of the experimental results.

Fig. 64 Taken from my paper in Lancet (98).

The increase in the ESR., serum total protein, serum viscosity, and plasma viscosity on the exhibition of sulphanilamide in ordinary therapeutic doses to normal subjects.

further opportunity for experiments with these drugs on suitable volunteers under suitable basal conditions.

I published the results in order to draw attention to an effect of the sulphonamides which had not been previously reported but which seemed worthy of further investigation. The findings can be discussed from two aspects.

(i) Effects of Sulphonamides on Plasma and Serum.

The

interaction of the sulphonamides with the blood-protein has been described by Davis (57) but there has never been mention of any action by the drugs on the amount of the proteins. The increase in the serum-protein can be detected within 24 hours of giving sulphonamides and disappears within 3 days of stopping them. From the diagram it seems that the effect (ie. increase) on the second day was greater than on the third day and that the protein was already beginning to fall although the sulphanilamide was still being given. This opinion is supported by my earliest work where I found that the ESR was first slightly increased but had returned to its basic level before the completion of a 10-day course with sulphanilamide; control experiments had showed that this increase did not occur as a result of serial blood sampling alone but required the exhibition of the drug.

The effect on the protein must be regarded as the primary

change in the blood constituents, of which the plasma viscosity, serum viscosity, and ESR. are but reflections.

Further metabolic studies should show whether the protein increase is due to an increased protein formation or to a decreased utilisation.

(ii) Significance of Clinical Pathology Tests.

The

results of this section indicate that caution must be taken in the interpretation of the values derived in the tests of clinical pathology. Thus, in a case of pyrexia of unknown origin which was treated empirically with sulphonamides (admittedly bad therapeutics) following admission on an afternoon, the tests performed on the next morning would almost certainly be abnormal. If the clinician was unaware of the drug action, a diagnosis of an organic cause of the pyrexia might then be made with some confidence and a prolonged search made to discover its nature; furthermore, the fall in these values after the second or third day, whether the sulphonamides were stopped or continued, could be interpreted as an improvement in this non-existent disease.

Similarly, the action of salicylates in rheumatic diseases is still argued - whether the drug has a direct action on the disease process itself or acts by producing changes in the distribution of fluid in the body which relieves the symptoms.

(Reid - 205,206).

Bendien, Neuberg and Snapper (14) and Homburger(115) have shown that the addition of salicylate to blood, in vitro, can produce a slowing of the ESR. Homburger (116) also produced a lowering of the plasma fibrinogen and the ESR. in three cases of carcinoma by the administration of this drug; similarly Rapoport and Guest (203) found a decreased ESR. in subjects receiving salicylic acid or its acetyl derivative. The only reference to the effect on the proteins of normal persons is a paper by Dryer et al.(64) who could detect no change whatsoever in the electrophoretic pattern after 4 g. per day of acetyl-salicylic acid for seven days: unfortunately, they did not measure the ESR. In their book on the salicylates, Gross and Greenberg did not include among their 4093 quoted references any which dealt with the effect on proteins(90). This further emphasizes the trend of concentrating the studies on the response to drugs in the disease conditions without an adequate preliminary investigation of the response by normal persons.

Later, in the section on tuberculosis, I will refer to the change in the gold flocculation test which I noted after the administration of streptomycin and of streptomycin plus para-aminosalicylic acid. I could not determine whether this was due to a hepatotoxic action or to just an altered liver response.

Fearnley and Bunim (78) have recently reported on the fall in the plasma fibrinogen level and in the ESR. following the administration of A.C.T.H. to normal persons. They concluded - "But until more information is available it seems prudent to regard a normal E.S.R. as an unreliable indicator of absence of rheumatic activity in patients under the influence of A.C.T.H. and cortisone."

Doubtless, further investigations of other drugs will reveal that part of the response shown by the tests of clinical pathology is due to the action of the drug on the subject independent of its action on the disease process.

* * * * *

Discussion to part 7.

Innumerable quantitative and qualitative examinations have been made on the protein content of human blood plasma and yet our understanding of these proteins is still far from complete. These studies have given an indication of the amounts and the characters of the protein fractions normally present in the plasma without designating the functions fulfilled by the various fractions. Albumin is claimed to be important in the control of the fluid balance between the tissues and the blood stream, by virtue of its high effective osmotic pressure. Part of the globulin plays a part in the defence of the body as the immunity factors are included in the globulins; the function of the remaining (majority) globulins remains uncertain. The function of the fibrinogen in the normal body economy is also uncertain

Schoenheimer's work (223) with radio-active isotopes has emphasized the dynamic equilibrium which exists between the proteins of the plasma and the tissues, and among the plasma protein fractions themselves. He also stressed how great were the changes in the plasma proteins; he included them in the group of proteins showing the highest speed of change. Nevertheless, there is an accurate control on the plasma proteins whereby a careful balance is drawn between the anabolic and catabolic

activities. This control affects the individual fractions independently; there is no regular relationship between the changes in the total protein and the plasma viscosity. Similarly, the protein changes are more than a mere variation in concentration as a result of the passage of fluid to and from the blood, as the changes of the packed-cell-volume and the total protein do not correspond. However, the acknowledgement of an accurate control of the level of the plasma proteins has not helped to explain their functions.

The total protein of the plasma of women is slightly lower than that of men and this is enough to explain the difference in the mean plasma viscosities without having to include a difference also in the protein pattern of the two sexes. The lower plasma proteins of childhood would lead one to expect a lower plasma viscosity level also, but my experience has been such as to suggest that the diminution can be disregarded for practical purposes. These results of mine are not in agreement with Satō's (220) who found a diminution in the serum viscosity from youth to old age and in the females of the same age groups as compared with males (his results are presented on the top of the next page). Benson, in contrast, measured the plasma viscosity in 361 normal individuals yet makes no mention of any differences on account of sex.

The serum viscosity of different age groups in the two sexes, according to Satô -

No. of tests	Age range	μ
Males		
25	17 - 23	1.890 \pm 0.018
45	24 - 40	1.797 \pm 0.010
23	41 - 58	1.744 \pm 0.011
Female		
16	17 - 23	1.775 \pm 0.016
20	24 - 40	1.732 \pm 0.011

The absence of a diurnal, daily, or seasonal variation is also the finding of Benson, in periods up to six months. More indirect, but confirmatory, evidence is to be found in the reports on the plasma proteins by Renbourn (207), Kagan (129), Widdowson and McCance (254), Perara and Berliner (191), and Dyson and Platt (66) where the variations within the day amounted to 0.2 g.% approximately and where Kagan and Dyson could detect no variation due to meals.

This latter finding is most reassuring in view of the significant changes which I have shown as following the ingestion of large amounts of glucose and urea in small volumes of water.

Of the two stimuli peculiar to women, menstruation can be ignored and the pregnancy must have advanced to an obvious stage before it has an appreciable effect, for which due allowance may be made.

The reports in the literature also suggest that the effects of exercise are negligible.

Three physiological stimuli thus remain whose effect on the plasma viscosity test must always be taken into consideration when interpreting an increased plasma viscosity in clinical pathology.

Alcohol produces an immediate and prolonged increase of the plasma viscosity. Its effect need not be considered in children or hospital patients: in domiciliary and out-patient tests a morning examination will reduce the chance of the immediate effect, a search should be made for the odour of alcohol in the subject's breath, and recourse to direct questioning must be made on the slightest suggestion of its action. I believe that alcohol was responsible for major effects in one patient only (and even there I had no proof) - the case of acute rheumatoid arthritis who showed such large variations within a matter of days without corresponding changes in the clinical state.

The precautions to be observed in avoiding the potential pitfalls arising from changes in the plasma viscosity due to postural variations have been discussed already.

Drugs remain a big problem. Their use has become almost universal and forms such a common part of modern living that they may never be mentioned to the clinician. Aspirin, the drug most

frequently self-administered, is particularly important because it has the general salicylate action in causing a redistribution of the water within the body (Reid, Watson and Sproull (206)) and it may also produce a marked diuresis in susceptible subjects (my unpublished observations suggest that the latter group includes a high proportion of adults who have suffered from rheumatic fever in their youth). Aspirin is also the drug taken most frequently in the rheumatic diseases where the plasma viscosity test has been frequently employed. The action of the sulphonamide group of drugs has been described. Fearnley and Bunim (78) have administered A.C.T.H. to normal persons and observed large changes in the fibrinogen, serum protein, and the ESR. Thus all three types of drug have shown an action which will affect the plasma viscosity values, and further search will probably reveal other drugs with a similar action. A direct question is therefore essential concerning the tested subject's recent history of drug exhibition.

To summarise - if one can exclude the effects of drugs, late pregnancy, and the ingestion of alcohol or concentrated salt solutions, the changes in the plasma viscosity in response to the ordinary physiological stimuli will be small indeed and these normal values will be confined to a narrow range which is the same for all ages and sexes. In serial testing, one must make

certain that the postural position has been constant throughout or allowance made for alterations in it. Because of the meagre effect of physiological stimuli the significance of minor changes in the plasma viscosity values are thereby enhanced.

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Part 8

The

PLASMA VISCOSITY

in

DISEASE

Part 8.The Estimation of the Plasma Viscosity as a test in Clinical Pathology.§ 1. Introduction.

In the previous seven parts the estimation of the plasma viscosity has been considered from the technical aspect and the values noted in normal subjects and following physiological stimuli. We will now proceed to a consideration of the plasma viscosity in disease. It will be shown that a knowledge of his patient's plasma viscosity will assist the clinician in his diagnosis, prognosis and treatment. The extent of this assistance is sufficiently great for the estimation of the plasma viscosity to be included in the routine tests of the clinical pathology laboratories.

The behaviour of the plasma viscosity will be studied in the different kinds of disease and where there are enough results various aspects of the plasma viscosity test will be stressed. However, in the next paragraphs, the relevant conclusions of parts 1 - 7 are summarised and a general indication is given concerning the information to be obtained from the later clinical sections.

(1) In normal health the plasma viscosity values of both sexes and all ages fall within a well-defined narrow range (1.665-1.915 cs.)

(2) The physiological stimuli of ordinary life, ie. diet, sleep, moderate exercise and physical labour, may cause small changes in the plasma viscosity but not sufficient to move the value outwith the "normal" range. The ordinary physiological stimuli include menstruation, and the first thirty weeks of pregnancy.

(3) Physiological stimuli of a severer nature, such as caused by ingestion of glucose or urea with small volumes of water, etc. can cause changes in the plasma viscosity sufficient to move a normal value outwith its normal range. Such stimuli are unlikely in patients attending a laboratory for a routine test.

(4) Disease conditions may be divided into two groups:-

(a) "Local" disease is a condition which affects a small or large part of the body but which does not cause a general upset such as could be evidenced by a loss of weight, elevation of temperature, sweating, etc. Examples of a local disease are an osteo-arthritis of a joint and a fibrositis of large areas of the body.

(b) "General" or "Systemic" diseases may or may not have local lesions but they are characterised as having the signs and symptoms of weight loss, etc. which results from a reaction in the body as a whole. Examples are malaria

(without a special local lesion) and rheumatoid arthritis.

The plasma viscosity usually remains within the normal range or shows a small increase in "local" diseases; it is usually increased in "general" diseases.

(5) The plasma viscosity increase is non-specific; the increase is found with all kinds of general disease.

(6) The increase in the plasma viscosity in response to general disease may be eighteen times the extent of the normal range.

(7) However, for the common diseases of tuberculosis, rheumatism, etc. the increase is restricted to seven times the range.

(8) The amount by which the plasma viscosity increases is roughly proportional to the amount of the general reaction.

(9) Many diseases have a general reaction whose severity bears a close relation to the severity of the local lesion. Hence, it follows, that in many instances the increase in the plasma viscosity is also proportional to the severity of the local lesion.

(10) Just as both sexes have the same normal range of values, so also the same severity of clinical condition is associated with the same increase in viscosity in both sexes.

(11) With the cessation of the general reaction following an improvement in the primary local lesion the plasma viscosity value falls once more to reach the normal range.

(12) It will be shown that the plasma viscosity estimation is a sensitive test. The viscosity becomes abnormal in some hours in acute diseases and abnormal values change also in response to changes in the clinical condition.

(13) The test will also be shown to be reliable. Apparently false positive tests may occur but further intensive or prolonged studies have proved a pathological cause for the viscosity increase; especially instructive cases will be described in the section on tuberculosis and rheumatism. False negative results, ie. plasma viscosity values within the normal range, do occur in an incidence of from 0 to 25% of the tests of different types of disease studied; a normal plasma viscosity value is thus no guarantee of the absence of organic disease, but in the sections on the various diseases it will be shown how low the incidence of false negatives can be.

(14) The plasma viscosity estimation is presented as a test in clinical pathology as being a guide to the general reaction of the patient to disease. This is the same use to which the established ESR test is put. Throughout the following sections there will be a constant comparison of the value of these two tests to the clinician as it would be wrong to attempt to introduce another test unless this produced more reliable results than the original.

By a statistical comparison of the results it will be shown that the plasma viscosity has the necessary superiority to merit its inclusion in addition to the ESR. Furthermore, analysis of my ESR results might lead to the interpretation that the ESR test yields such unreliable results that it might well be discarded, as has happened in one sanatorium and rheumatism clinic at least.

(15) It was shown in part 6 how the plasma viscosity reflects the change in the globulin and/or fibrinogen; the albumin and non-protein constituents may be neglected.

The results of the various sections will indicate the nature of the protein changes. There is a general pattern in the protein change in acute disease as follows - the fibrinogen fraction first increases, and if the condition rapidly resolves, it returns to normal: if the disease lasts more than a few days and is severe, the globulin also increases, this increase being at a slower rate than that of the fibrinogen; if continued further, the globulin increase continues, the albumin falls slightly, and the fibrinogen falls from its initial high level to a value still above the upper limit of normal - this response has reached almost to the 'chronic' disease picture: with recovery, the steps are retraced and the normal protein pattern is resumed. A chronic disease, of several weeks or months

duration, is usually associated with an increased globulin, a slightly decreased albumin, and a normal or slightly increased fibrinogen.

A high plasma viscosity value can be expected in those conditions in which the globulin and/or fibrinogen are increased. (16) It will be shown also why the plasma viscosity is measured rather than the protein fractions themselves. These reasons can be summarised as - (a) the measurement of the viscosity as compared to the protein fractions is more simple, rapid and accurate; (b) the viscosity range of normal subjects is narrow and defined while the possible normal variation in the protein fractions is large: there are several instances in which the plasma viscosity has moved from its defined limits when the protein fractions could all be regarded as normal; (c) the daily variations and other changes in response to physiological stimuli are greater with the proteins than with the viscosity so than changes are of less significance as indications of an alteration in the clinical condition; (d) it is relatively simpler for the clinician to interpret the changes in the single viscosity value than the relative and absolute changes in the three protein fractions.

(17) Whittington and I have applied the name - "terminal decay" -

to an interesting phenomenon which occurs in the final stages of most diseases which are progressing towards death. A falling plasma viscosity is usually interpreted as an indication of a return of the protein pattern towards normal and an improvement in the clinical condition. However, where the outcome is to be death, at an interval of months to days before this event, the proteins begin to decrease in an irregular manner which affects all the fractions but chiefly the albumin. The plasma viscosity shows a corresponding decrease and may have reached normal limits at the time of death. Since this terminal decay can begin some months before death without any apparent alteration in the patient's condition otherwise and since we have never recorded a reversal of this decay with any treatment, the importance of its detection for assessing the prognosis is obvious.

(18) The majority of the plasma viscosity results from chronic general diseases of all types falls within a restricted part of the total possible abnormal range; this small range we have named - "The zone of chronicity".

(19) Similarly, the "zone of effusion" is a restricted range of the viscosity scale which contains the majority of plasma viscosity results from patients who were actually forming the fluid at the time of testing.

* * * * *

§ 2. The plasma viscosity test in rheumatic diseases.

The group of rheumatic diseases contains a variety of conditions whose relationship may be no closer than that they affect the same structures.

There is no classification of these diseases which is acceptable to all clinicians and pathologists who make a special study of them. The aetiology of many being vague and a cause of much dispute, the classification is reduced to one which is dependent on the clinical appearances of the conditions. I have included a brief definition for my groups of diseases, together with their synonyms, in order that the reader may adjust my results into his own scheme of classification.

The large majority of the patients attended the Rheumatic Clinic of Sunderland Royal Infirmary. The organisation of this clinic has been described (182) as we regarded it as a model of its kind. The organisers believed that the problem of the full investigation and the decision on the best treatment could be tackled only by a team of specialists who assessed the condition and planned the treatment in consultation together. With this basic principle in mind, the arthritis clinic began work with a team of four - a physician (Dr. A.A.McI. Nicol), a surgeon (Mr. W. Grant Waugh), a medical officer in charge of physical medicine (Dr. I.C. Cowan), and a clinical biochemist (myself).

According to the needs of the patient, specialists in other branches of medicine were added to the original team. This arrangement was most valuable to me in that I was investigating a patient rather than a blood specimen attached to a form, and it allowed me to take my share in the assessment of each patient. The clinical assessment was made most carefully as it was realised from the beginning that our results might be worthy of later publication. The final assessment was made by Dr. Cowan who also controlled the therapy (he obtained the degree of Doctor of Medicine at Aberdeen University in 1950 for his share of this combined investigation). This assessment was made independently and without knowledge of my laboratory results, except in those cases where the discrepancy between the laboratory and clinical opinions was so great that the patient had to be investigated fully again.

It would be impossible to give the detailed case reports of the 1,200 tests in rheumatic diseases. The numbers lend themselves to a statistical analysis; the rheumatoid arthritis cases have been selected for this treatment. The detailed results are given in the tables of the appendix, together with some illustrative case histories. The graphical presentation of these results is included in this text.

(A) Rheumatoid Arthritis.

Synonym:- Atrophic polyarthrititis

Definition:- In the classical form, this disease is found in asthenic women in the child-bearing age groups; it is a polyarthrititis generally commencing in the small joints of the fingers and toes and spreading centripetally. The aetiology is unknown, but the pathology is of an inflammatory nature.

Ankylosis is common. From this group has been excluded those cases where a focus of infection was believed to be connected in some way with the disease, but there are included those cases occurring on or about the menopause in which an endocrine factor was considered to be significant.

We divided our cases into four degrees of severity.

(i) Residual deformity; "burned-out". Into this group fall those cases which had an attack of rheumatoid arthritis several years previously, who had had no recurrence and showed no signs of present local or systemic activity, but who had varying degrees of joint deformity.

(ii) Chronic. This group includes the cases where the disease is best described as 'smouldering'. There is usually a long history of the disease; the affected joints are in various stages of inflammation, with pain on movement, synovial thickenings and

"cold" effusions; there is marked muscular wasting. In this group is observed the greatest degree of joint damage and consequent deformity; the pathological changes in the joints are irreversible.

(iii) Subacute. Here there are marked signs of toxaemia - eg. loss of weight, lassitude, anorexia, tachycardia, hot moist skin; the involved joints are painful on movement and at rest, this rest pain being a feature of this group; the affected joints are hot, swollen and tender; and there is active muscle wasting.

(iv) Acute. These cases have the symptoms and signs of the subacute group but in a greater degree; pyrexia is frequently present.

It must be stressed that this classification takes into consideration the whole patient and not just the lesions in his joints and muscles. Rheumatoid arthritis is a general disease with local manifestations in the locomotor system. There can be a variation in the relation of the severity of the local lesions to the severity of the general upset; it is possible for the local conditions to become symptomless while the general disease remains active.

The changes in the plasma viscosity in rheumatoid arthritis will be described first; thereafter a comparison will be made between the results of the plasma viscosity and of the ESR.

Results:- For details, see Table II of the appendix.

The results are summarised in the following table -

Clinical Severity.	No. of tests	Sex	PLASMA VISCOSITY		Mean PCV.	Mean ESR	Mean tot. prot.
			Usual range	Mean			
Normal	158	B	1.663-1.910	1.810	-	-	7.15
	96 [*]	M	1.663-1.910	1.815	45.7	2.2	7.23
	63	F	1.665-1.910	1.802	41.6	7.8	7.06
Residual deformity	8*	B	1.740-1.990	1.909	41.8	19.8	7.40
	23'	B	1.740-1.990	1.909	41.9	15.0	7.24
Chronic	154*	B	1.950-2.300	2.121	42.6	25.2	7.50
	387'	B	1.950-2.300	2.119	42.2	24.7	7.77
	517	B	1.880-2.380	2.123	42.0	25.5	7.75
	93	M	" "	2.147	-	17.4	-
	424	F	" "	2.118	-	25.6	-
Subacute	22*	B	2.330-2.550	2.513	40.8	36.1	8.50
	79'	B	2.300-2.550	2.506	41.1	34.6	8.56
	96	B	2.300-2.720	2.523	40.9	33.4	8.58
	14	M	" "	2.494	-	32.3	-
	82	F	" "	2.528	-	33.6	-
Acute	16*	B	2.500-3.400	2.897	38.8	38.8	9.54
	29'	B	2.500-3.600	3.002	39.9	35.9	9.50
	32	B	2.500-3.660	3.019	39.6	32.5	9.58
	13	M	" "	3.199	-	17.7	-
	19	F	" "	2.897	-	34.7	-

* = the figures of the original B.M.J. paper (54)

' = the figures of the J.Clin.Invest. paper (120)

It has been possible to apply statistical analysis to these figures. For example, the chronic group could be subdivided into

five subgroups - males, females, both sexes in B.M.J. paper, both sexes in interval until J.Clin.Invest. paper, and both sexes subsequent to that paper. There was no significant difference to be detected between any of the subgroups or between a subgroup and the total. Similarly, there is no difference between the sexes of the acute and subacute groups. However, there is a significant difference between the mean results of the chronic, subacute and acute groups.

Clinical group.	Plasma viscosity		No. of tests.
	Mean	Standard deviation.	
Chronic	2.123	0.1592	515
Subacute	2.523	0.185	96
Acute	3.019	0.346	32

The difference between the means of the chronic and subacute groups ($= 0.400$) and of the acute and subacute ($= 0.496$) is 19.6 and 7.7 times the respective standard errors of the difference of the means; it is accepted that values exceeding 2.5 are very unlikely to occur owing to chance sampling errors.

Further comparison of the plasma viscosity is made in Figs. 65 to 80. The frequency distributions are shown according to sex and clinical severity; in Fig. 65 I had to make an arbitrary assumption, when I made the distances between the lines of the clinical groups equal, that the subacute disease was of a

five subgroups - males, females, both sexes in B.M.J. paper, both sexes in interval until J.Clin.Invest. paper, and both sexes subsequent to that paper. There was no significant difference to be detected between any of the subgroups or between a subgroup and the total. Similarly, there is no difference between the sexes of the acute and subacute groups. However, there is a significant difference between the mean results of the chronic, subacute and acute groups.

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CLINICAL SEVERITY OF RHEUMATOID ARTHRITIS

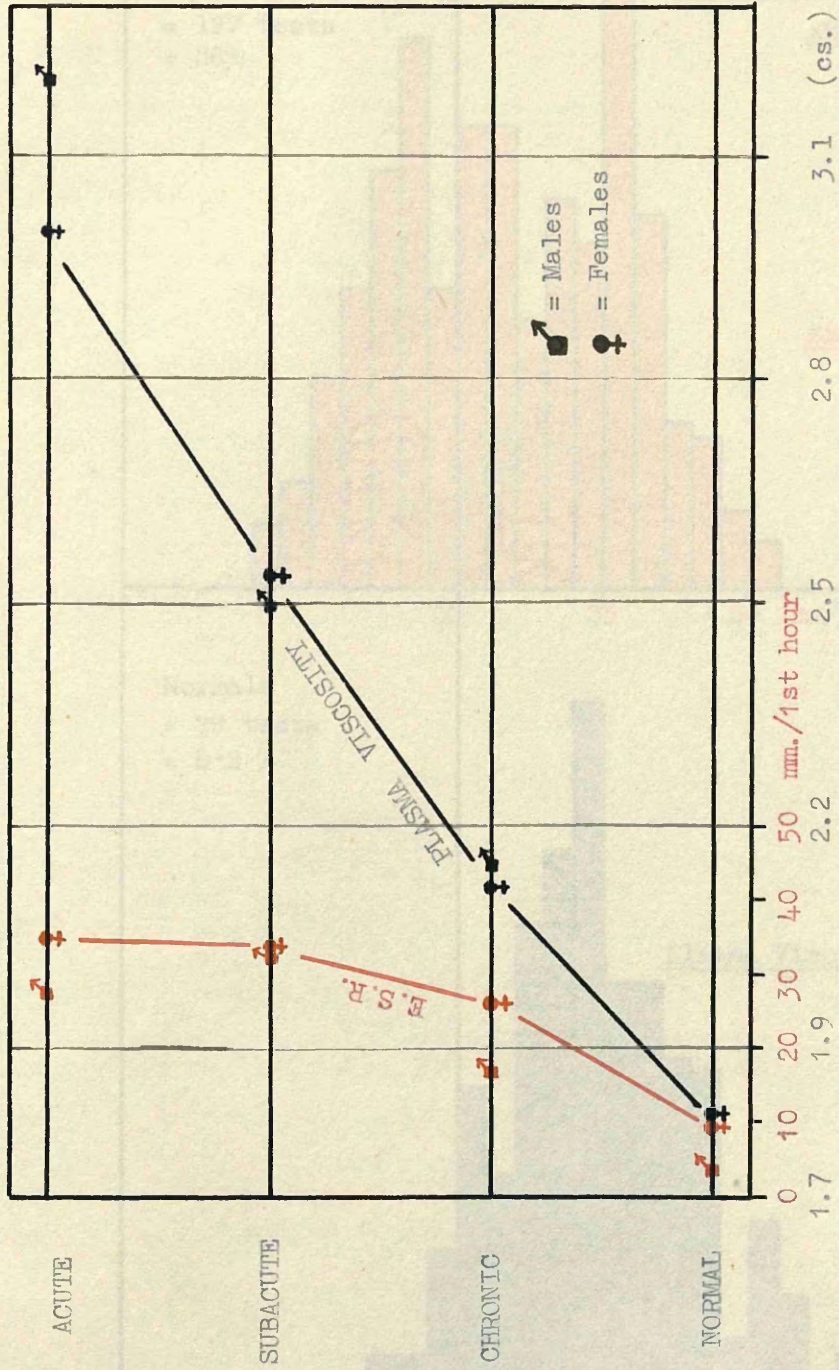


Fig. 65 The Average Values of the Plasma Viscosity and Corrected Wintrobe ESR. correlated with the Clinical Severity of Rheumatoid Arthritis. (The scales have been adjusted to make the normal ranges of both tests the same.)

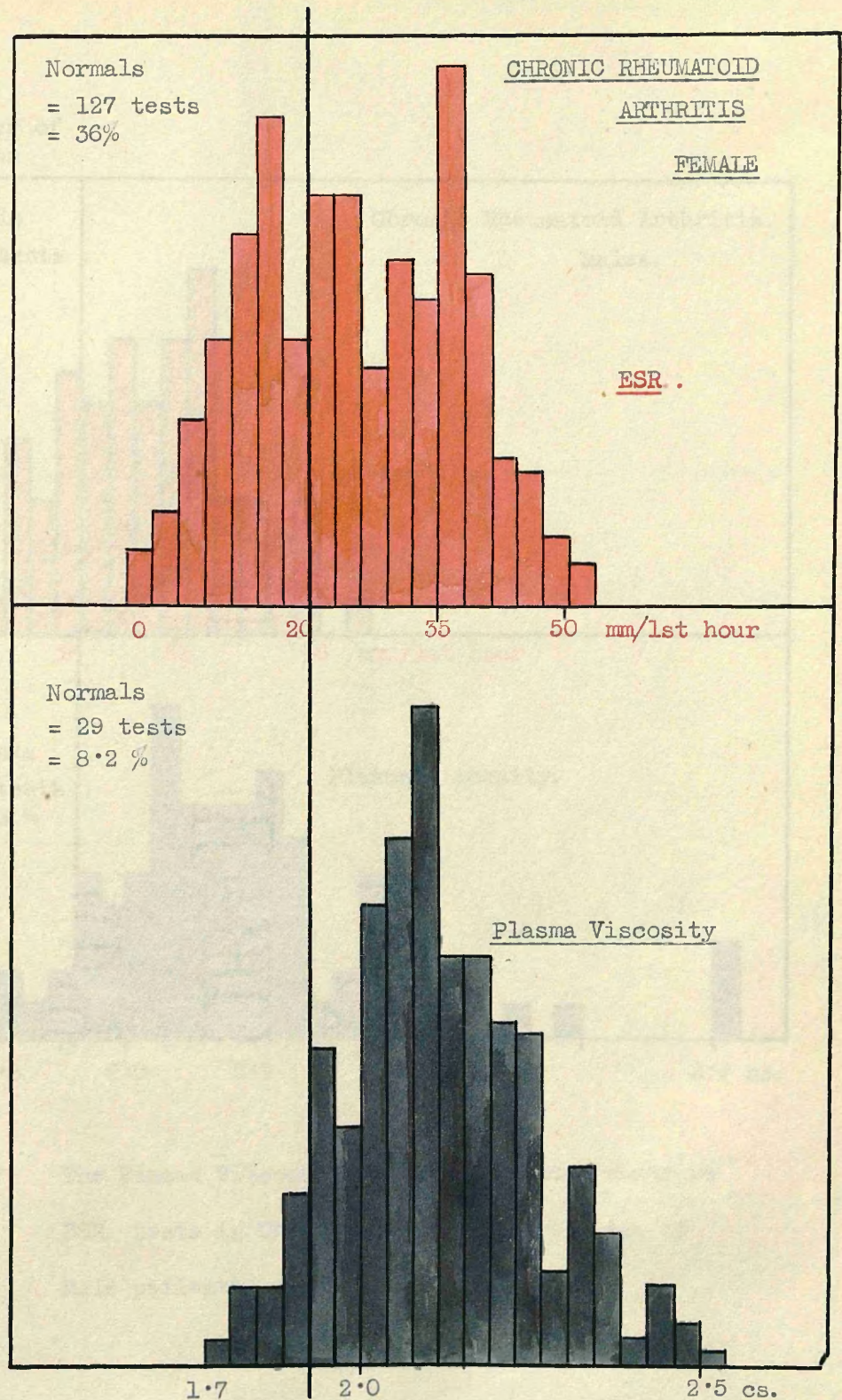


Fig. 66 The Plasma Viscosity and ESR. results in Female Chronic Rheumatoid Arthritis.

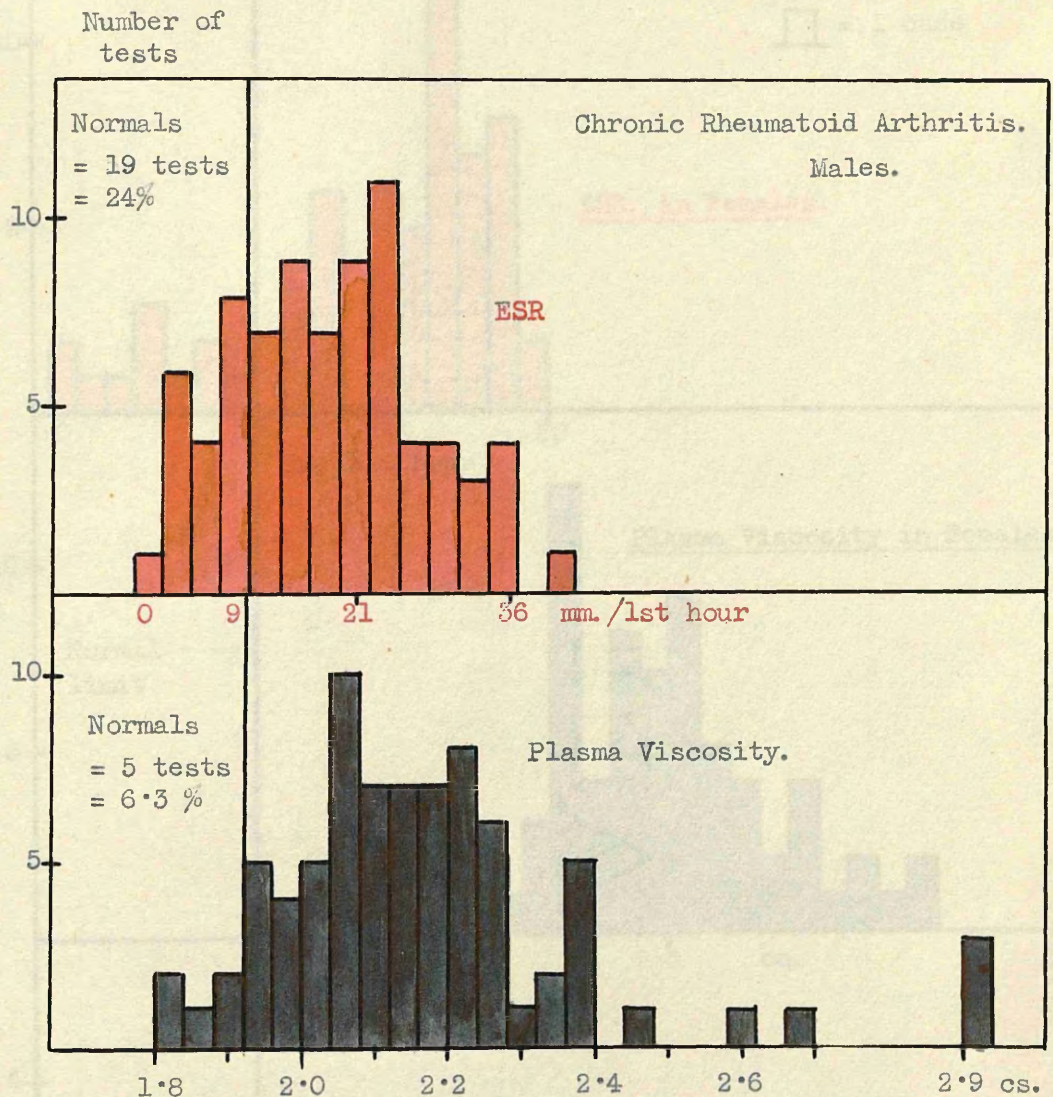


Fig. 67 The Plasma Viscosity and the Corrected Wintrobe ESR. tests in Chronic Rheumatoid Arthritis of Male patients.

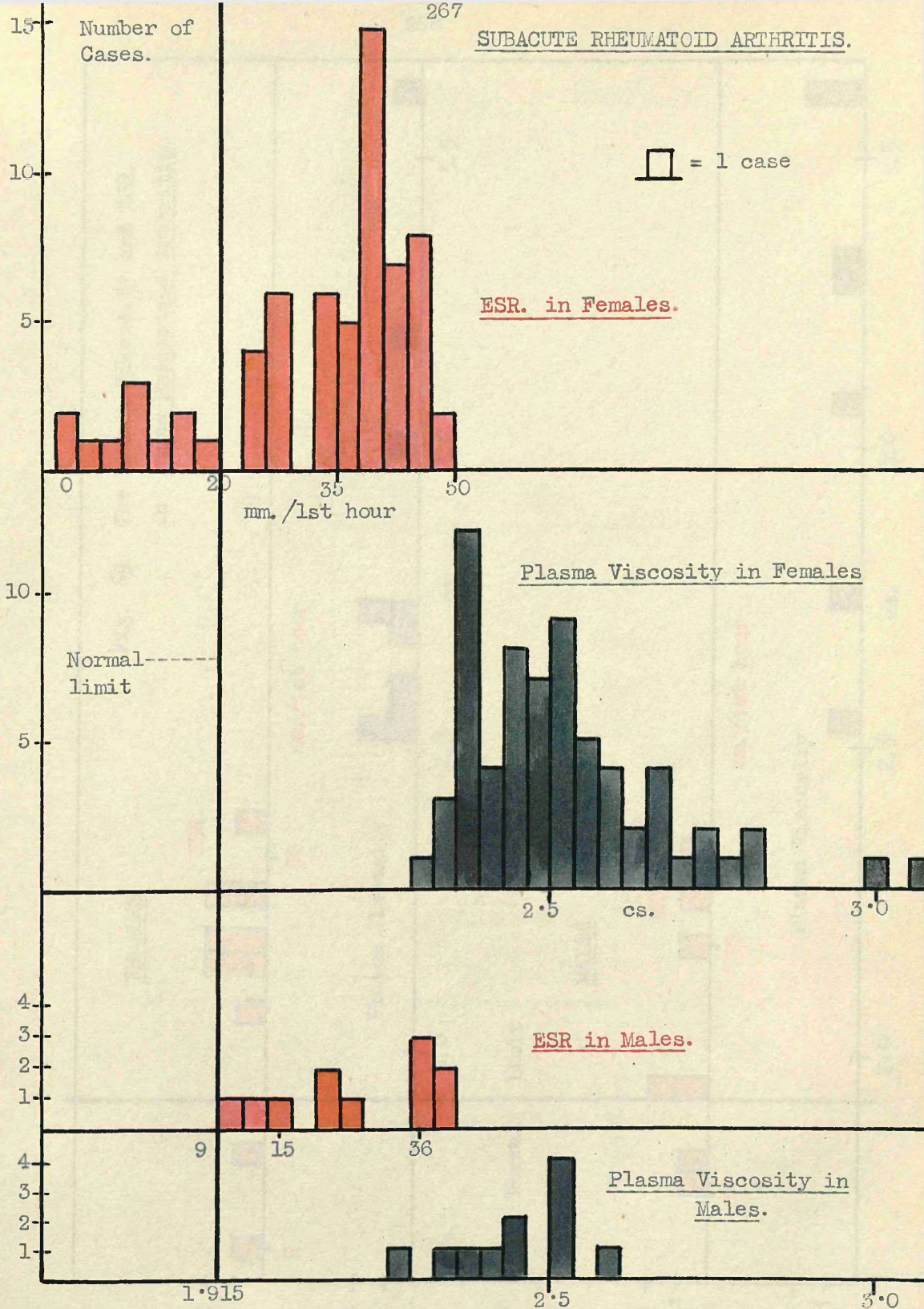
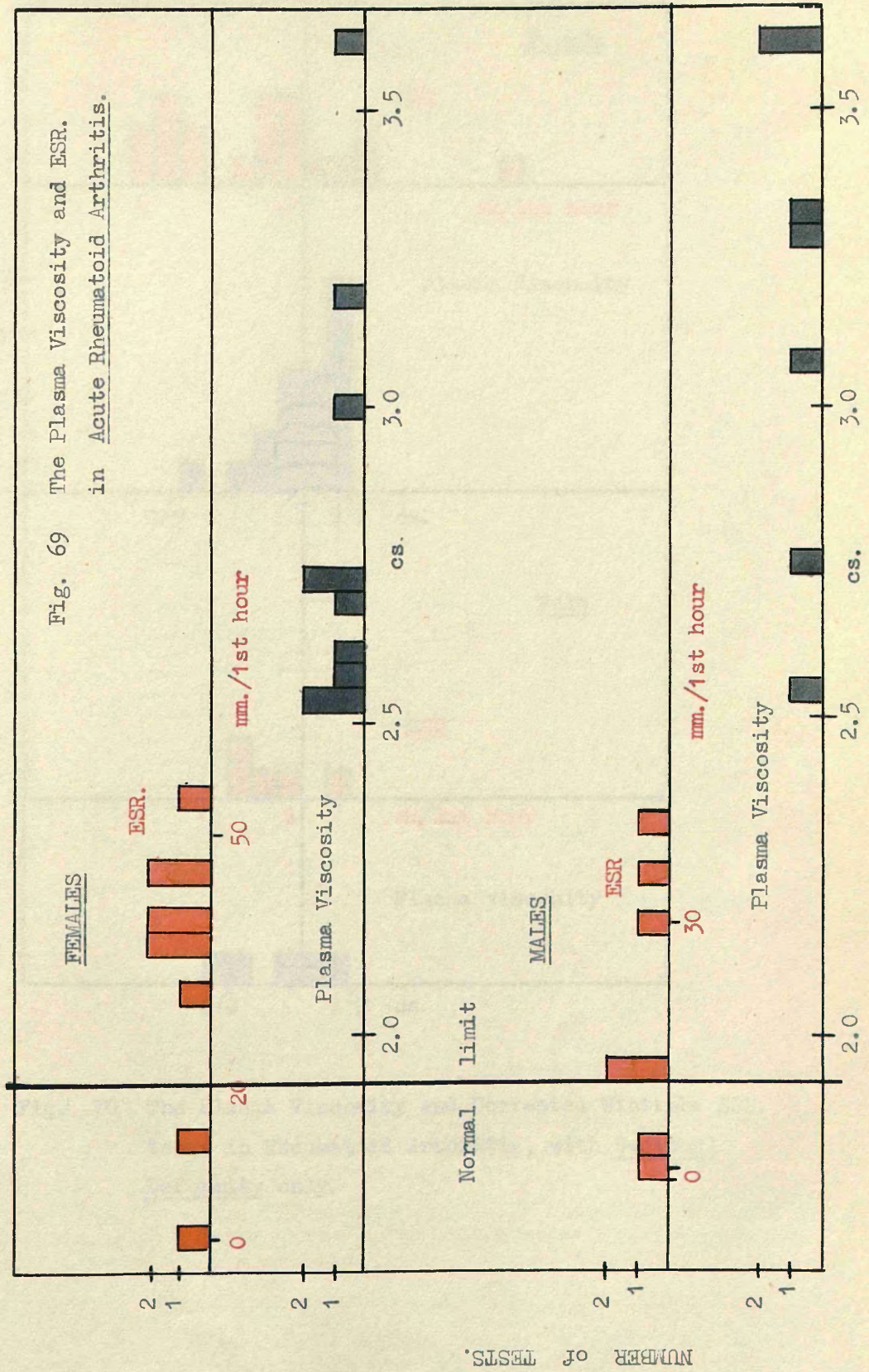


Fig. 68 The Plasma Viscosity and ESR. results in Rheumatoid Arthritis of both sexes. - SUBACUTE.

Fig. 69 The Plasma Viscosity and ESR.
in Acute Rheumatoid Arthritis.



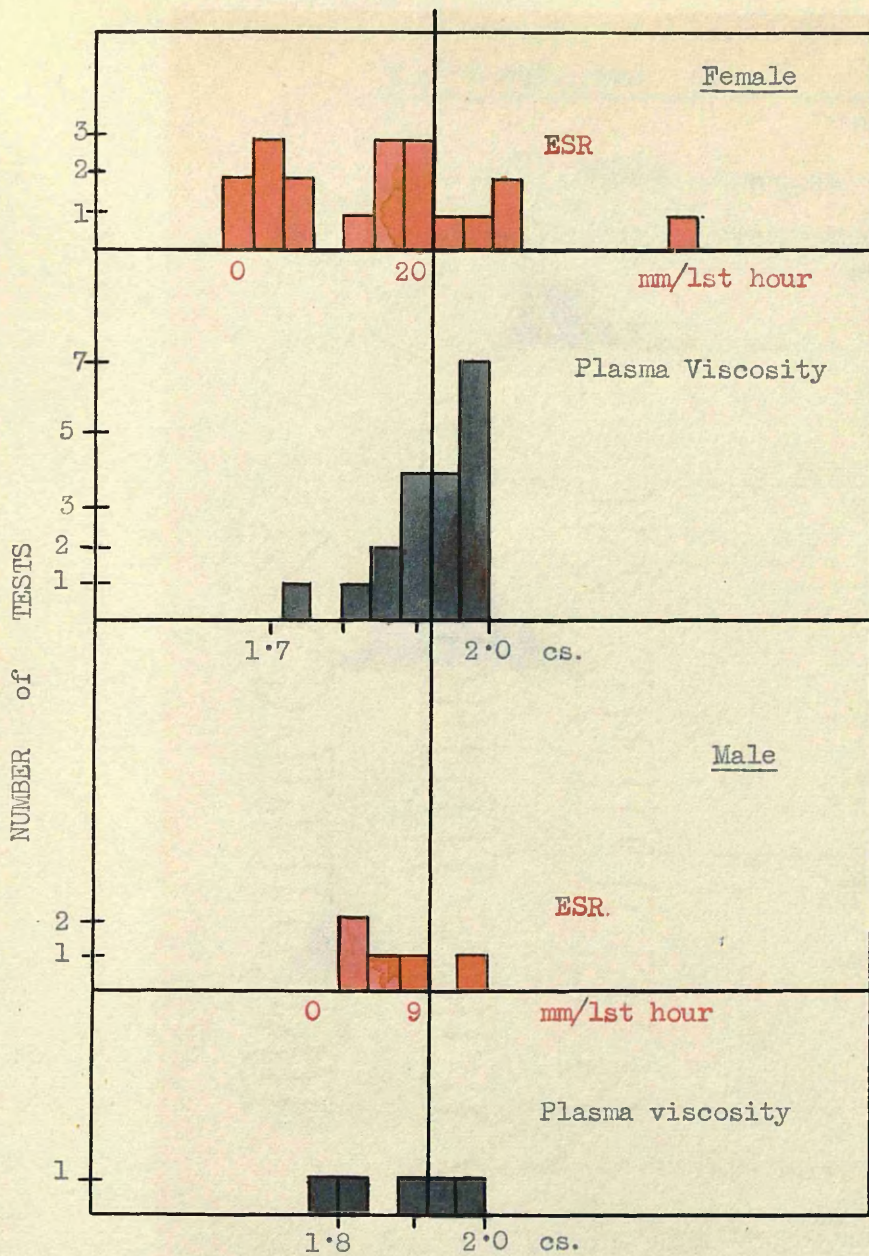


Fig. 70 The Plasma Viscosity and Corrected Wintrobe ESR. tests in Rheumatoid Arthritis, with Residual Deformity only.

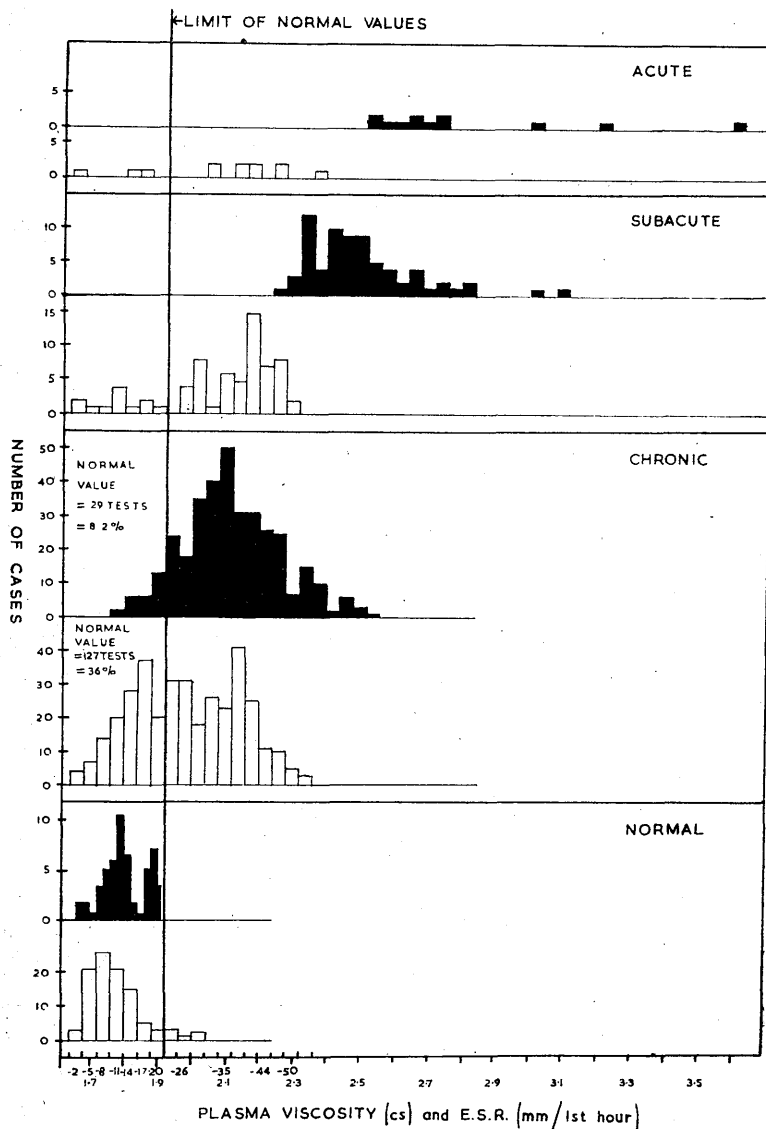


FIG. 2

The distribution of the plasma viscosity and ESR values of individual patients within the groups of female patients, clinically classified as described in the text.

The solid diagrams represent the Plasma Viscosity results.

The open diagrams represent the ESR results.

Note the high incidence of normal ESR values in the presence of activity detectable by the clinician. Note also how the ESR range is the same in each group. (The normal ESR diagram is that originally produced by Wintrobe and Landsberg, *Jl. Amer. Med. Sci.*, 189, 1935, 102.)

Fig. 71 Taken from Harkness and Cowan (103)

It shows the distribution of the Plasma Viscosity and ESR results in different grades of clinical severity in Rheumatoid Arthritis of female patients.

Note (a) the higher incidence of normal ESR values.

(b) the same range of ESR values is covered in all grades of severity of this disease.

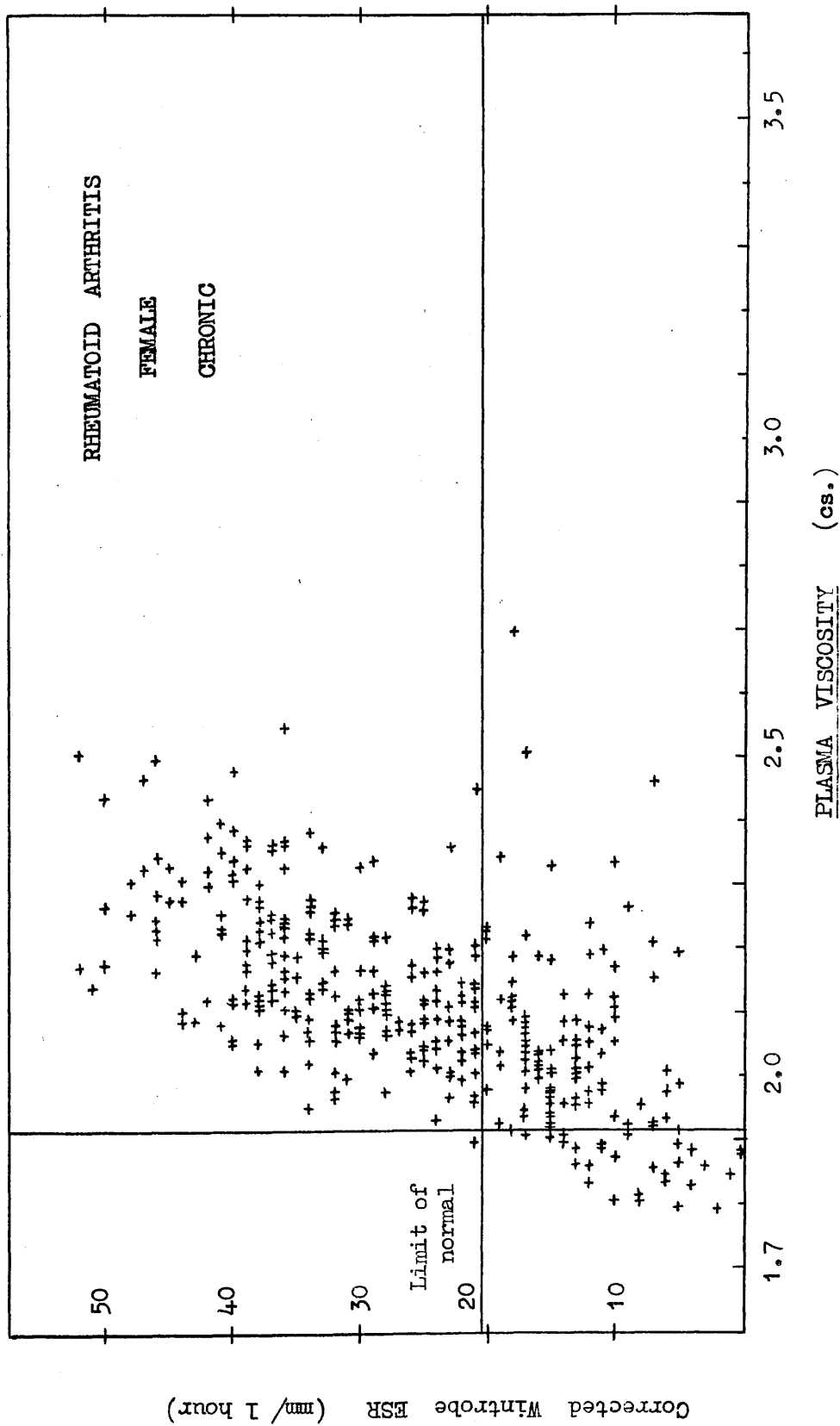


Fig. 72

The Plasma Viscosity and ESR, tests in Chronic Rheumatoid Arthritis in Female patients.

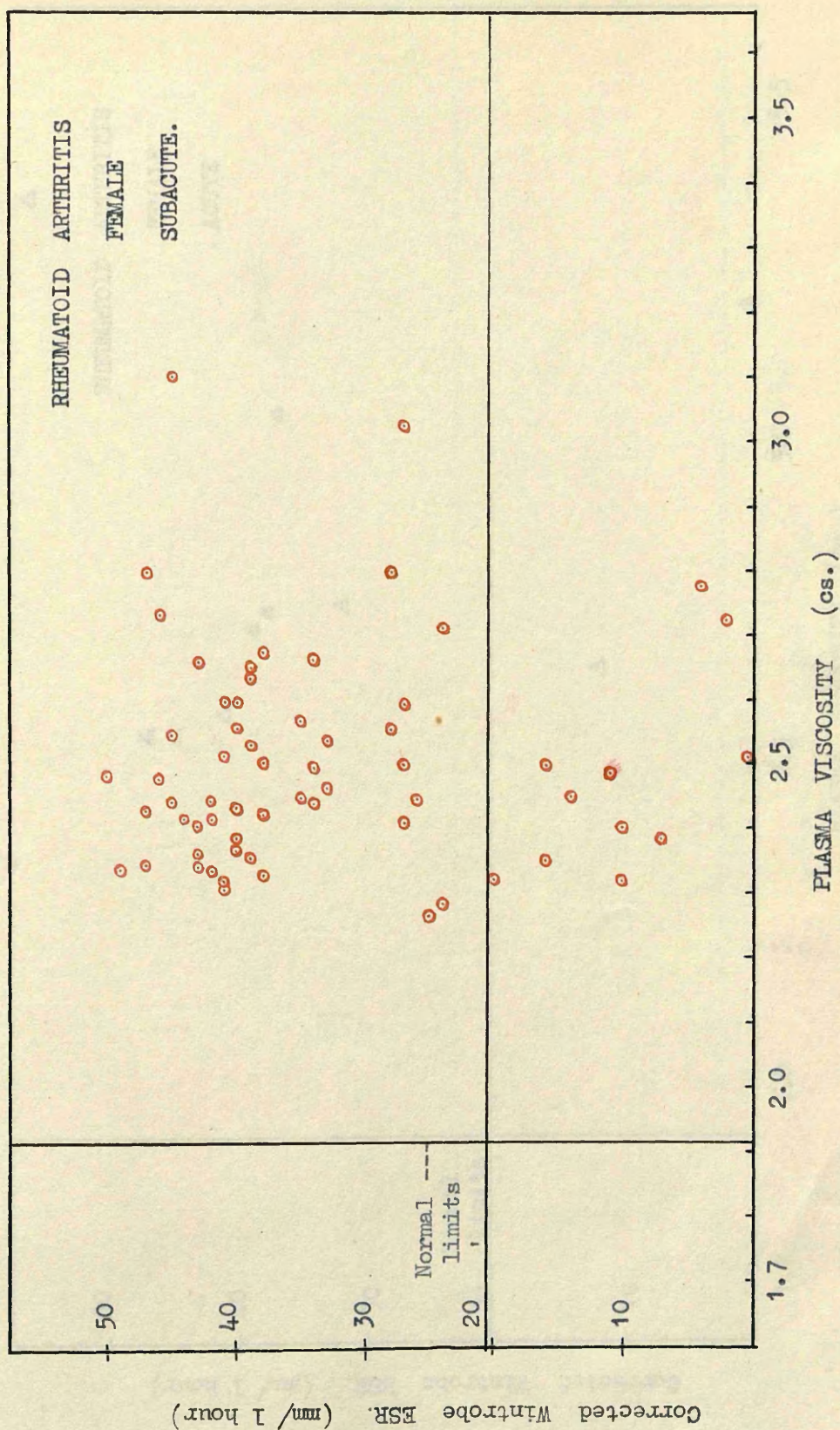


Fig. 73 The Plasma Viscosity and ESR. results in Subacute Rheumatoid Arthritis in Female patients.

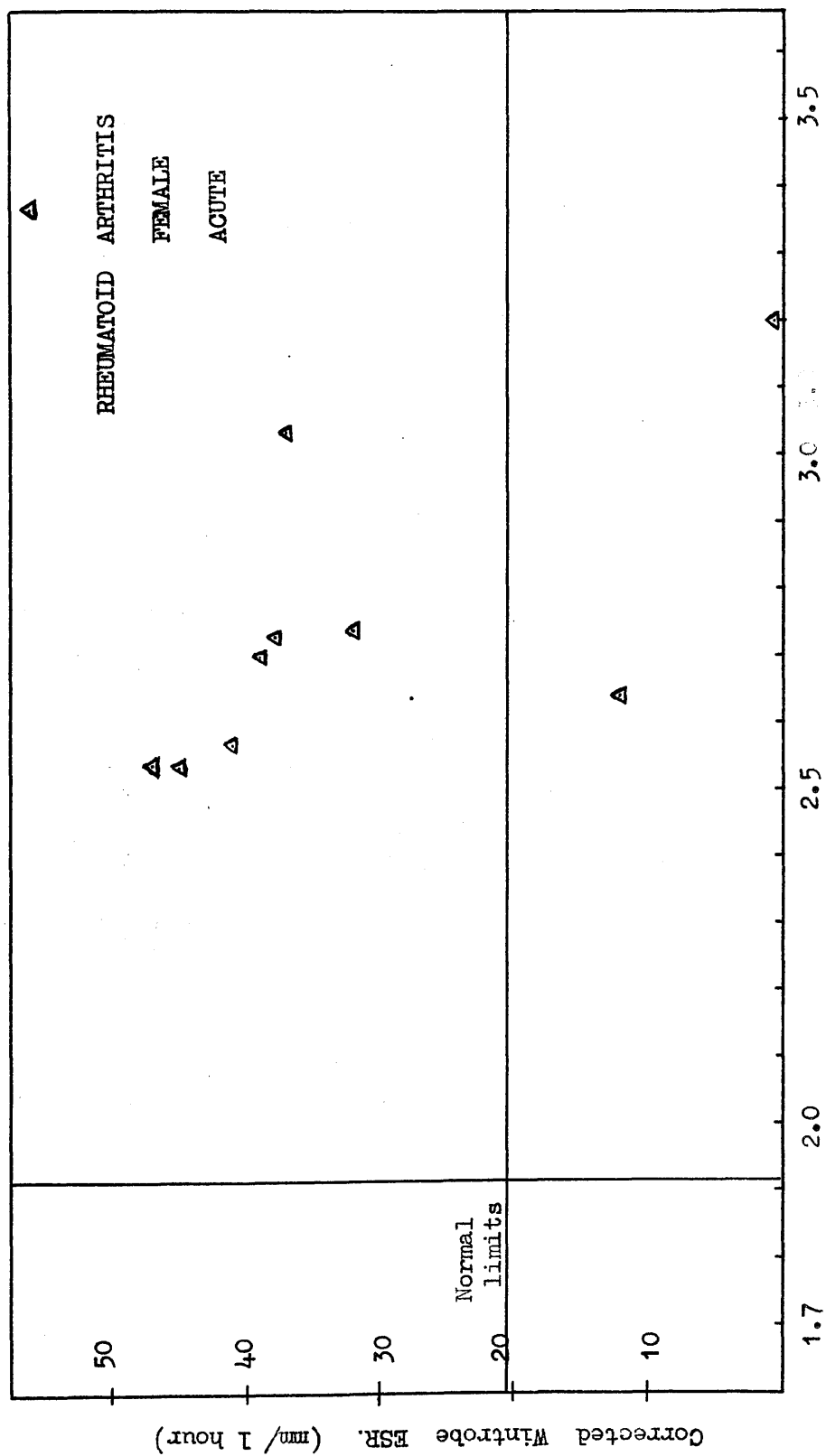


Fig. 74 The Plasma Viscosity and ESR. results in Acute Rheumatoid Arthritis in Female patients.

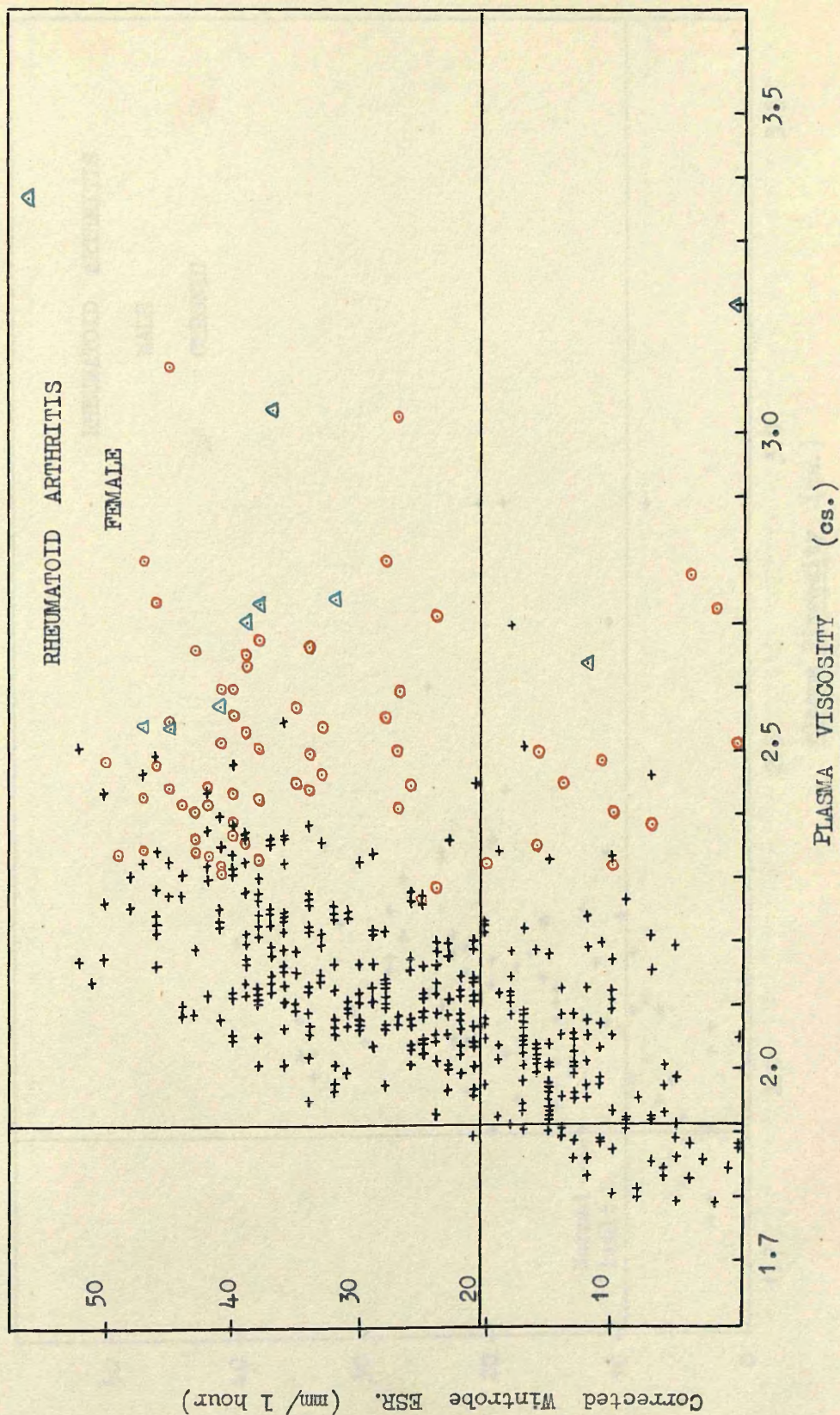


Fig. 75 The Plasma Viscosity and ESR. tests in Acute (▲), Subacute (○), and Chronic (+) Rheumatoid Arthritis. (Females)

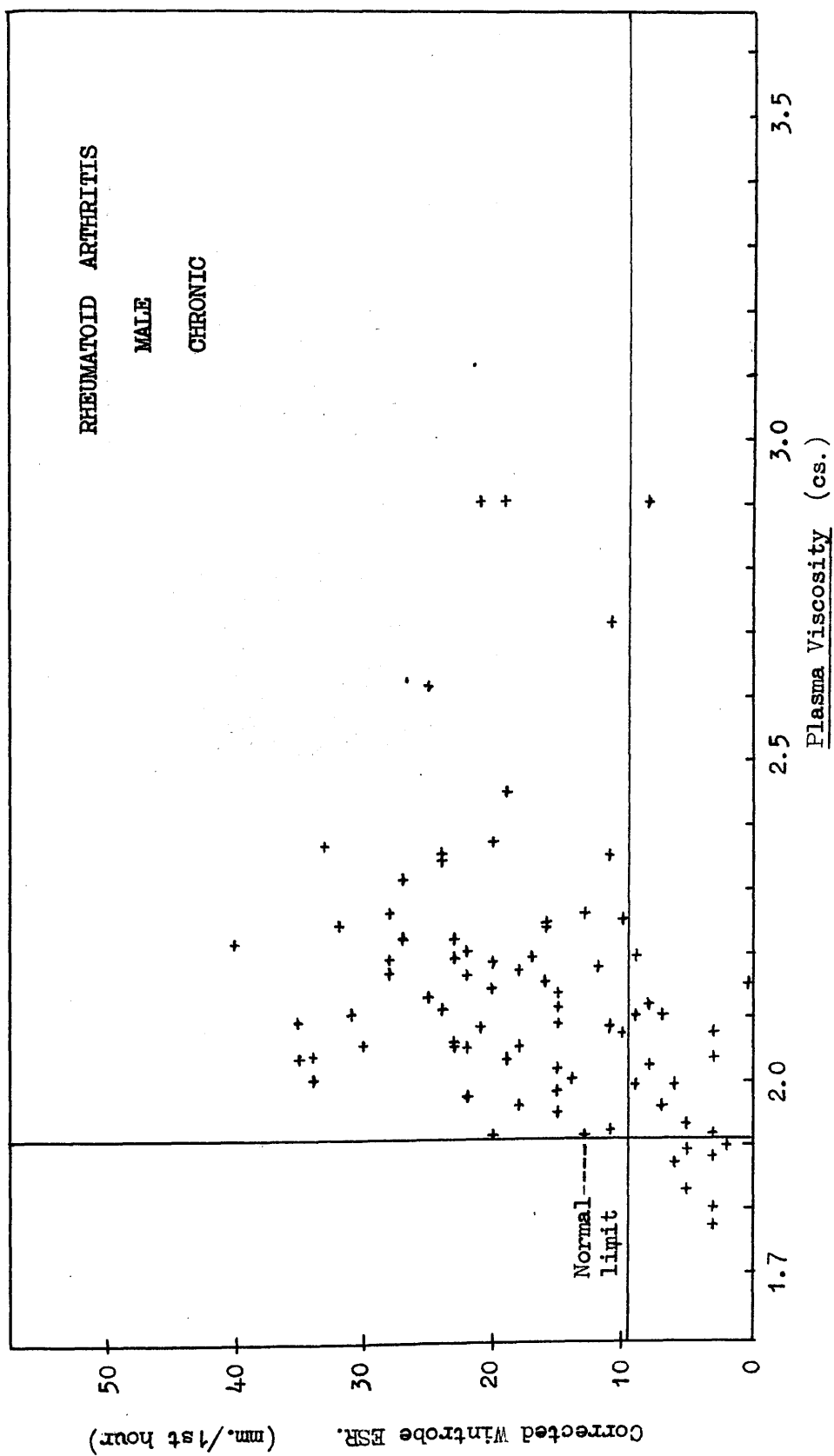


Fig. 76 The Plasma Viscosity and ESR. tests in Chronic Rheumatoid Arthritis in Male Patients.

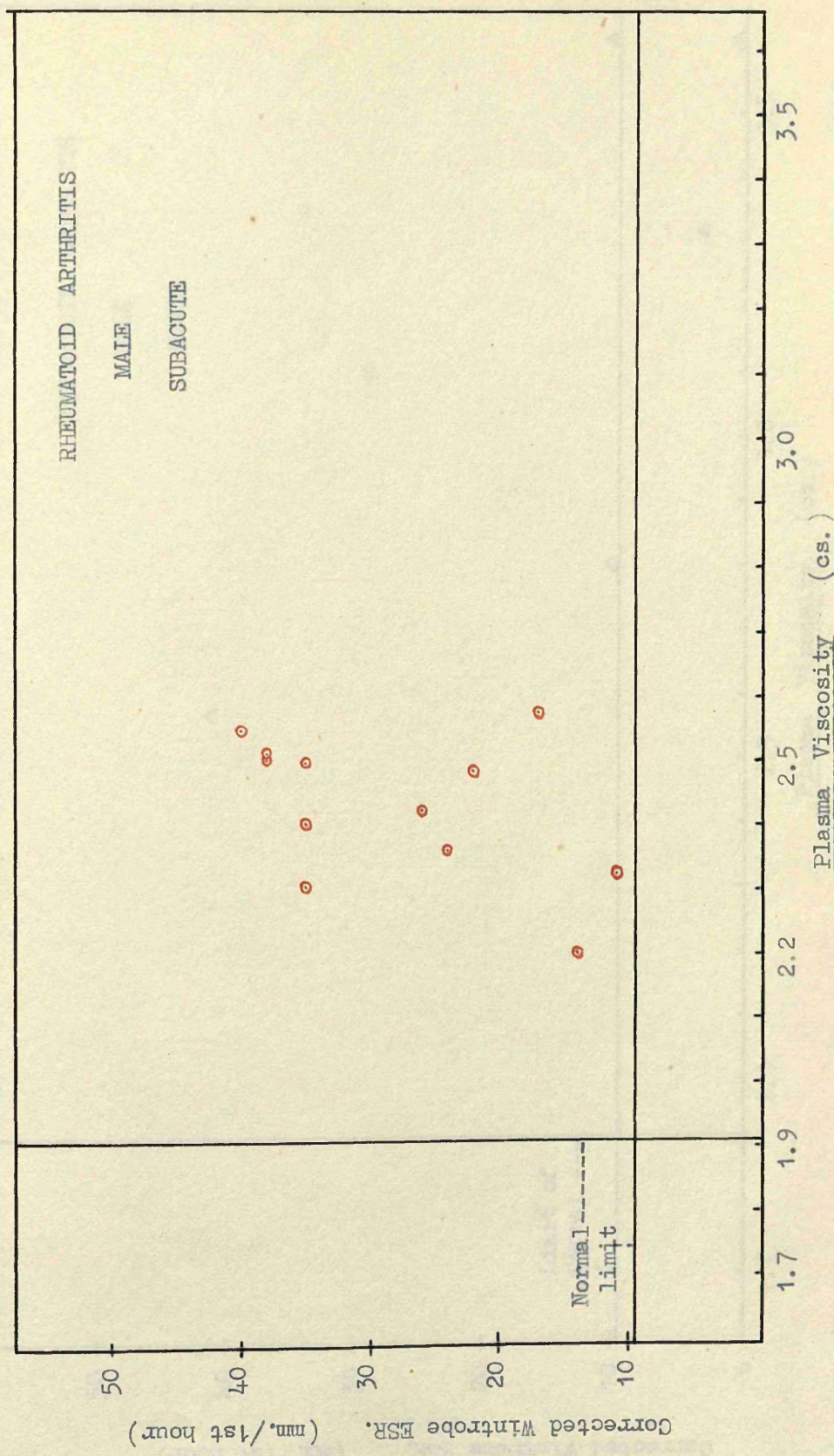


Fig. 77 The Plasma Viscosity and ESR. tests in Subacute Rheumatoid Arthritis in Male patients.

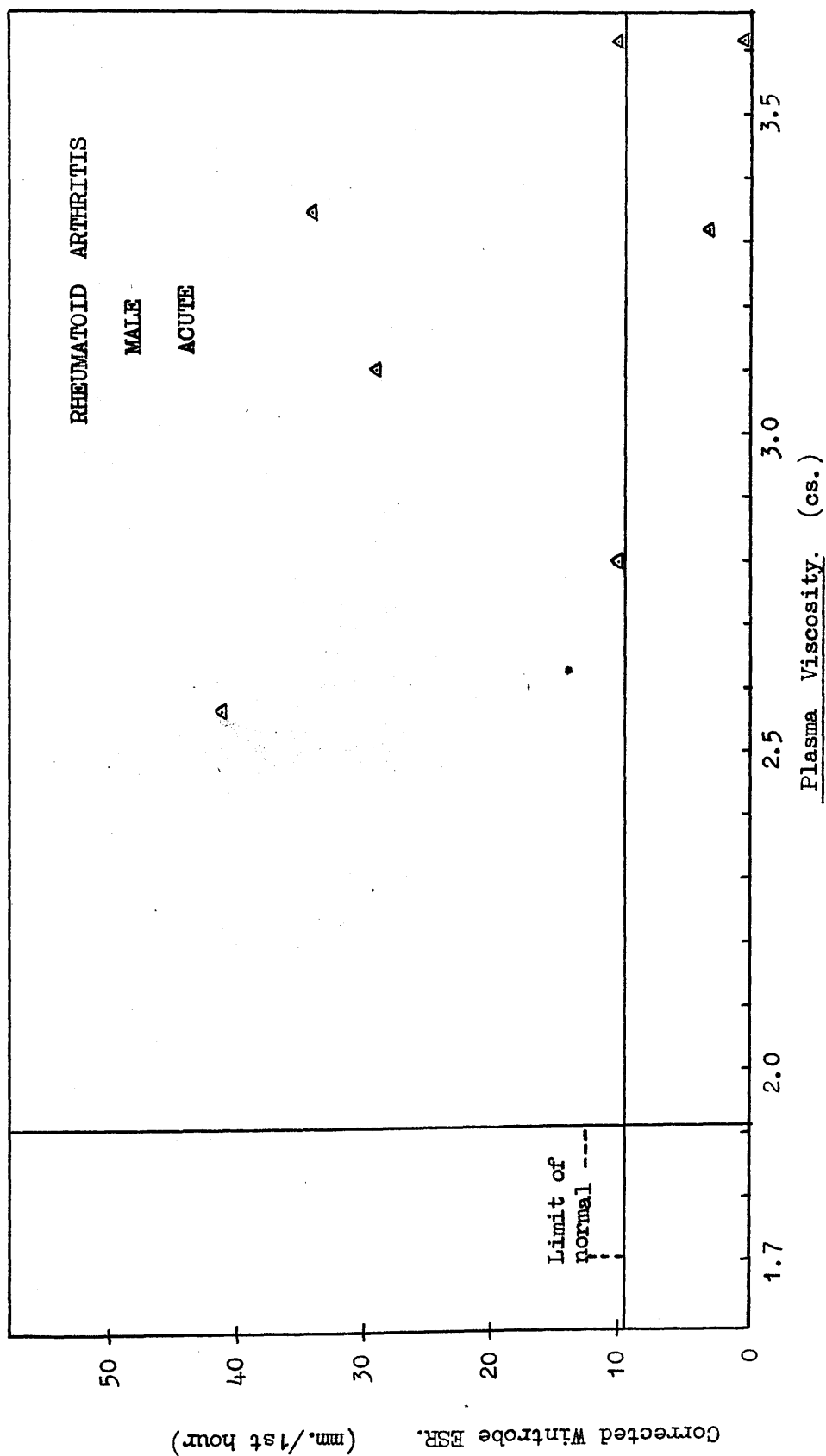


Fig. 78 The Plasma Viscosity and ESR. tests in Acute Rheumatoid Arthritis in Male patients.

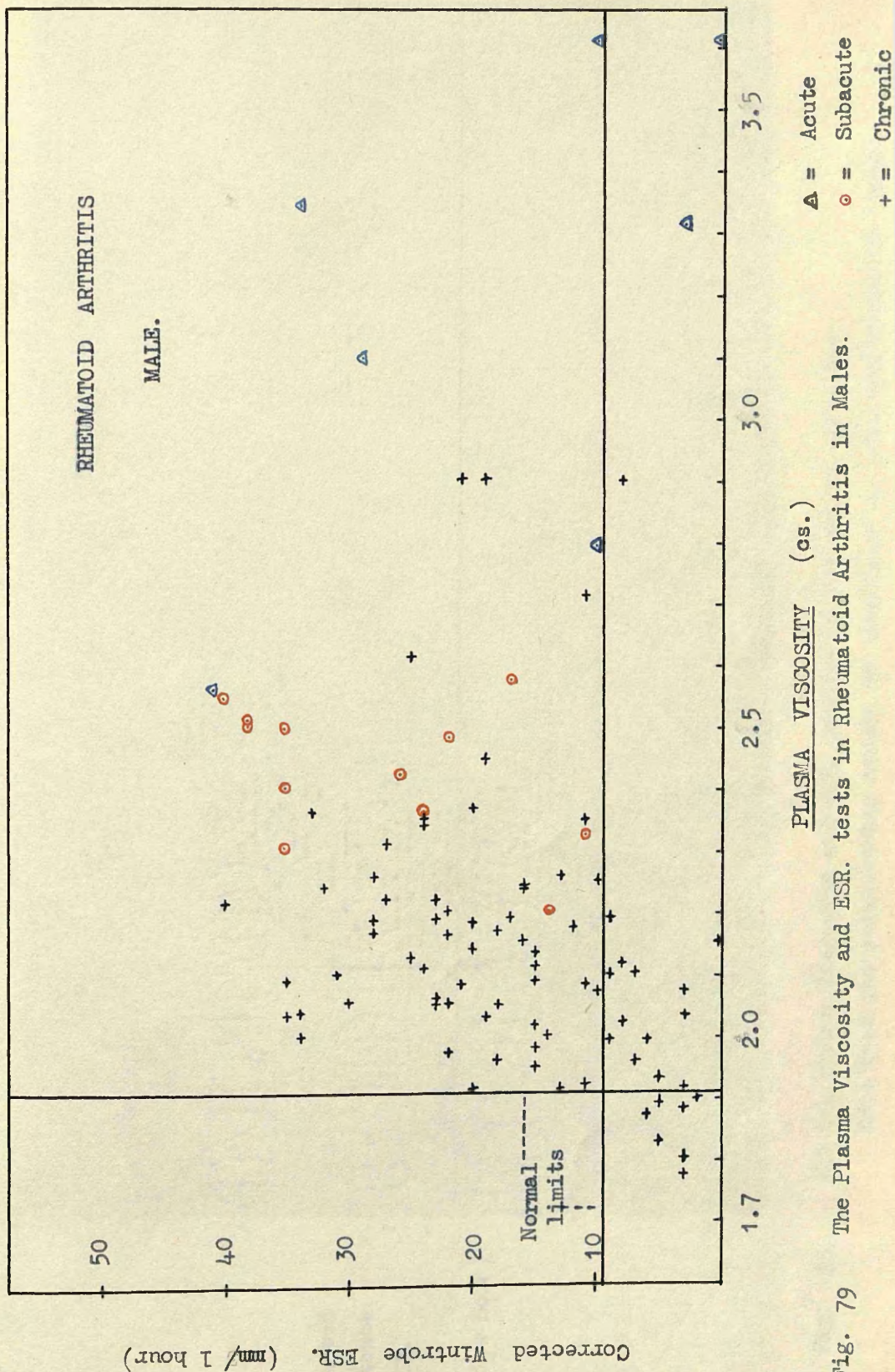
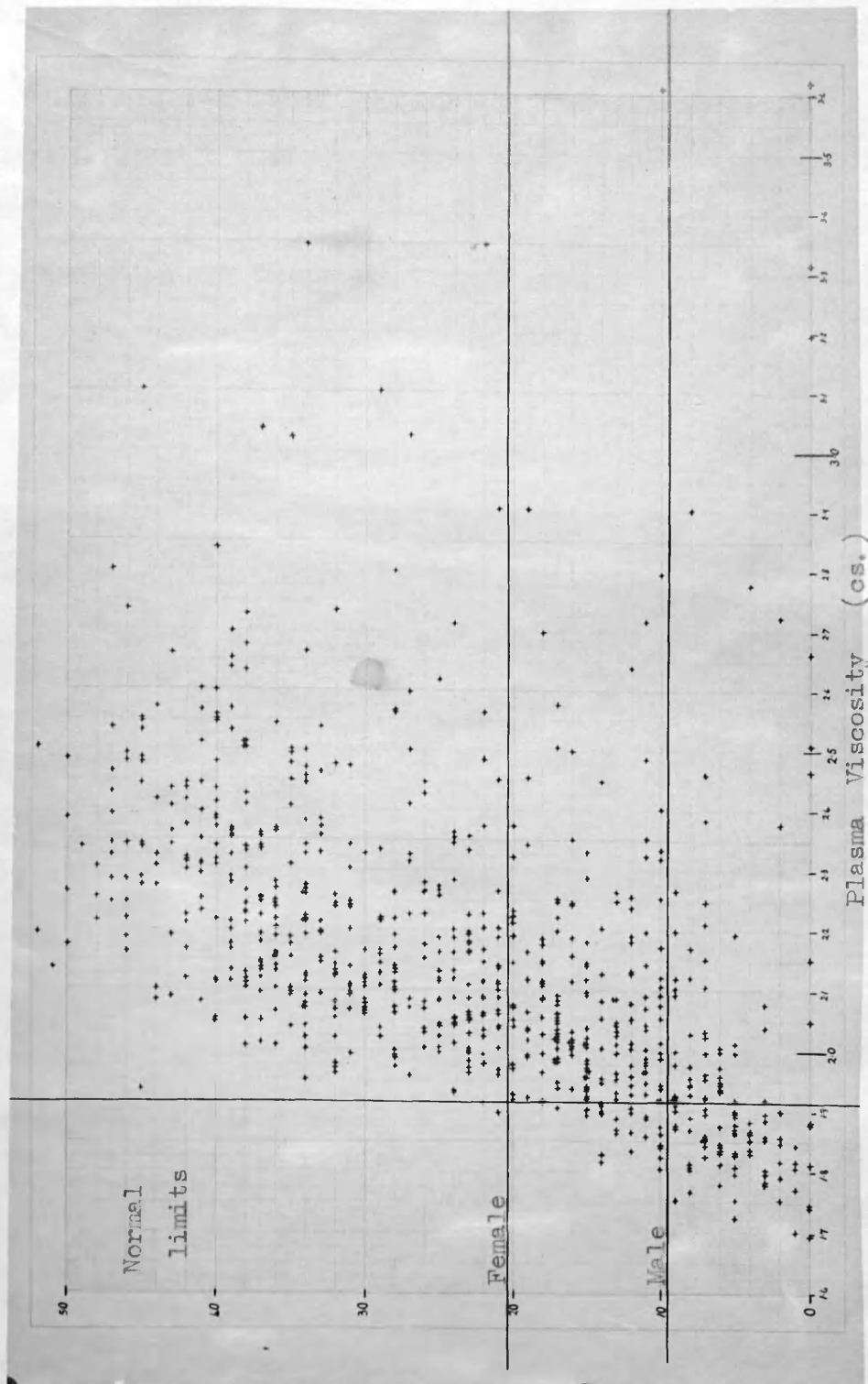


Fig. 79 The Plasma Viscosity and ESR. tests in Rheumatoid Arthritis in Males.



Corrected
Wintrobe
ESR.

(mm./1st hour)

Fig. 80

All the Plasma Viscosity and ESR. results in Rheumatoid Arthritis.

Note that the relationship cannot be considered as even approximately linear.

severity greater than the chronic as the acute was greater than the subacute.

Excluding the 'Residual' group for the present, my results for the plasma viscosity test in rheumatoid arthritis might be stated as follows.

Clinically active rheumatoid arthritis was usually associated with an increase in the plasma viscosity which raised the value to beyond the 'normal' range; indeed, with the acute and subacute patients there was no instance of a normal value.

The amount by which the plasma viscosity was increased was proportional to the severity by the clinical assessment. The plasma viscosity measured the general reaction to the disease: inasmuch as the severity of the locomotor lesions frequently were parallel to the severity of the clinical assessment of the whole patient, the plasma viscosity usually increased in proportion to the severity of the local lesions also. Discrepancies were more common between the viscosity value and the local condition than with the general condition.

In the individual case, as the severity of the general reaction increased so did the plasma viscosity rise: as the general condition improved, either spontaneously or in response to treatment, so also was there a corresponding fall in the viscosity.

The changes in the plasma viscosity bore a close time relationship to the changes in the clinical condition.

The extent of the viscosity change was the same in both sexes for the same degree of clinical change.

The mean viscosities of the clinical groups were well separated from each other; the scatter about the mean, within each group, was restricted but there was a slight overlapping of the groups which prevented the viscosity being used as an absolute guide to the clinical assessment of any individual patient.

The apparent errors of the plasma viscosity test in showing normal results in chronic rheumatoid arthritis were in excess of their true proportion as several cases were here included which had responded well and had made an apparent 'recovery' - the word 'recovery' is so designated as there is a widely- and strongly-held opinion among clinicians that a complete recovery in rheumatoid arthritis is so exceptional as to be ignored. Their motto might be - "once a rheumatoid, always a rheumatoid"; the spaces between the acuter episodes are regarded only as quiescent periods; patients in these quiescent periods following shortly after definite evidence of clinical activity were still classed with the chronic active cases.

Discussion. The plasma viscosity will be discussed again in comparison with the ESR, but it is discussed here on its own merits. The results can be described conveniently under the headings of diagnosis, prognosis, and treatment.

Diagnosis - The plasma viscosity is a useful guide to the presence of active rheumatoid arthritis. If other causes of an increased plasma viscosity (such as an infective focus) can be eliminated, the finding of an increased viscosity in a patient in whom the vague symptoms of lassitude, loss in weight, vague joint symptoms and very few joint signs makes the clinician suspect arthritis, allows a diagnosis to be made with some confidence and the appropriate treatment begun without delay. The plasma viscosity test is a sensitive and reliable index of the presence of a general reaction in rheumatoid arthritis and of the degree of this reaction.

The test is also a sensitive and reliable guide to changes in the condition of the individual patient. A decrease indicates an amelioration; an increase reflects a worsening.

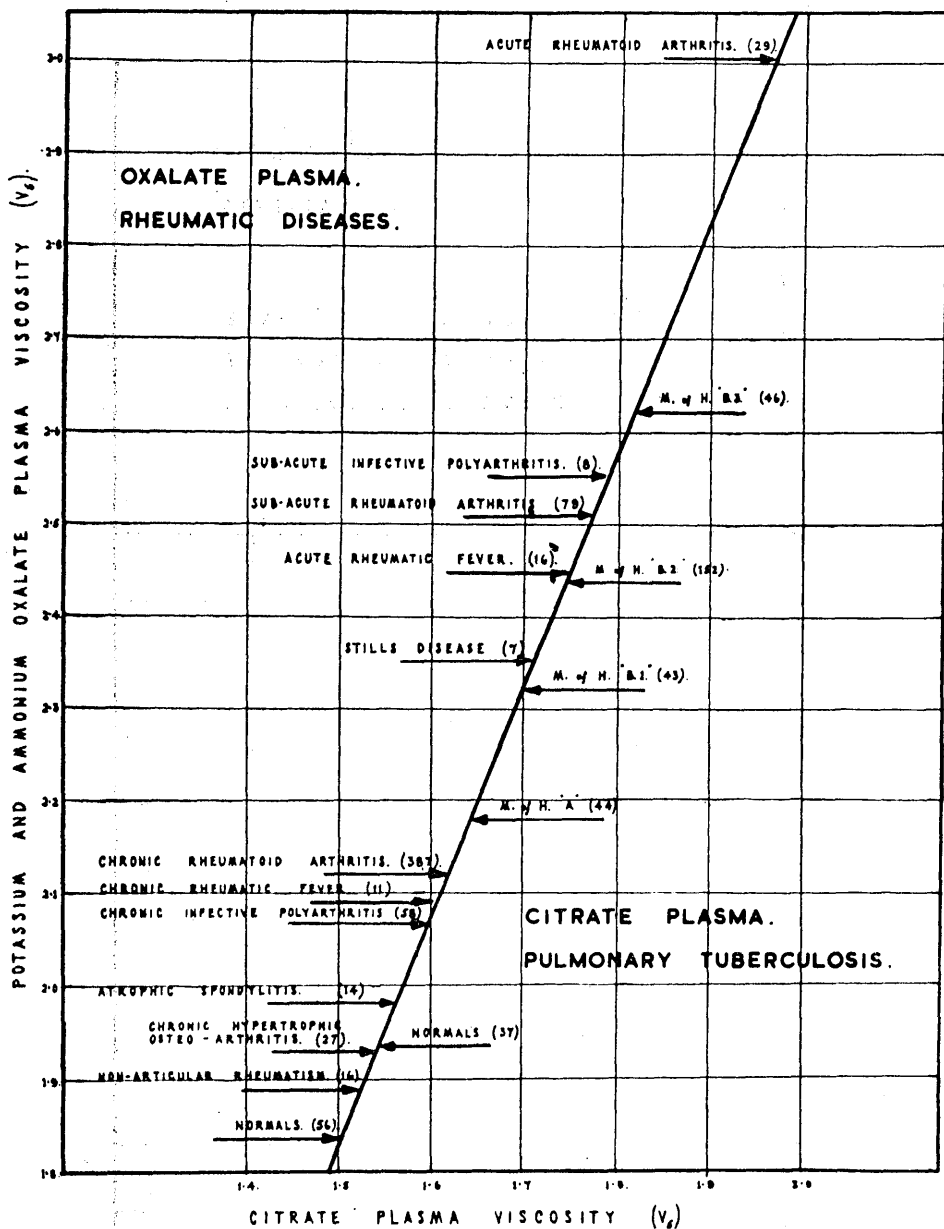
Prognosis - The plasma viscosity test has several special values to the clinician in deciding the prognosis of the cases.

A high plasma viscosity result carries a worse prognosis than a lower value, since recovery from a condition producing a severe general reaction would be expected to take longer than

from one producing a lesser reaction. Nevertheless, it has been possible to produce such improvement that the higher viscosity values have fallen until the normal range is reached and such patients can be regarded as much "cured" as a rheumatoid arthritis case can be.

"Zone of Chronicity." There is a restricted range of values (1.95 - 2.25 cs.) within the total range of plasma viscosity values into which falls the majority of the results from the patients with a wide variety of diseases with a chronic general reaction - eg. rheumatoid arthritis, rheumatic fever, tuberculosis, syphilis, pyogenic infection, etc. Reference will be made to this zone again when these other diseases are discussed. Cowan and I gave a great deal of attention to this subject because, before Cortisone and A.C.T.H. altered the treatment so fundamentally, we believed that we were making some progress in guiding treatment into something besides the exhibition of gold or bismuth.

(a) A patient who first presented herself with a result in this zone usually proved very irresponsive to therapy. The effect of gold was not so dramatic as in patients with higher viscosity values; this finding corresponds to the belief that patients with high ESR values respond better to gold than those with low ESRs. It is possible, however, that a satisfactory



DISTRIBUTION OF AVERAGE VISCOSITIES

DIFFERENT ANTICOAGULANTS IN THE TWO DISEASE GROUPS
NUMBER IN BRACKETS INDICATES NUMBER OF TESTS IN EACH GROUP

Fig. 80 (b) Taken from our paper (120)

This figure shows the relative distribution of the means of various types of disease and of the different clinical severities of single diseases.

outcome may be achieved even in these chronic cases.

(b) With gold therapy, local heat and massage, etc. considerable improvement might be effected in the local conditions of the patients with values in this zone; some even became symptom-free. The plasma viscosity made a sharp division into two groups. Where repeated estimations of the plasma viscosity had revealed a failure to return to the normal range the condition was to be regarded only as quiescent or dormant, with a relapse in the future as the inevitable outcome; this relapse might be associated with a recognisable trigger stimulus such as exposure to cold, sore throat, influenza, etc. but there were other cases in which a definite stimulus to set off the relapse could not be recognised. In contrast, where the plasma viscosity had attained the normal range a definite stimulus was always to be detected (cf. case 2, 5) and necessary.

(c) The zone of chronicity lay as a hazard between the high plasma viscosities of the more severe cases and the low normal values. A subacute or acute case of rheumatoid arthritis might respond initially to treatment, with a corresponding reduction in the viscosity towards normal and its corresponding hopeful prognosis: however, the decline may halt in this zone of chronicity, as an indication that the nature of the disease has altered and the prognosis is correspondingly much worse, with the dismal

prospect of the long-drawn-out struggle of the chronic case. No other test in clinical pathology is able to indicate this alteration in character of the disease process. (A similar zone will be described for pleural effusions in tuberculosis, which also acts as a possible bar to a straightforward recovery.)

(d) The foregoing results caused Cowan and myself to try an empirical type of treatment. If a patient would not show a reduction of her plasma viscosity in response to therapy then we attempted a preliminary increase in the plasma viscosity by producing an increased general reaction with vaccines, etc., and then a further course of treatment with gold was instituted - the hope was that the patient would now respond so well that she would traverse the chronic zone to the normal range without halt. Unfortunately I left Sunderland before any results of this scheme became available. I learned later from Coke (47) that he had employed the same gambit when his special ~~V~~SR test also failed to show a decrease, and he believed that it was a successful mode of treatment in some of these difficult patients.

The subjects who had residual deformities only showed an abnormally high plasma viscosity in many instances. I interpret this as indicating that in the latter the disease is not completely cured and a relapse is possible at any moment. It strongly supports the claim that rheumatoid arthritis is never cured and

justifies the clinics which never remove the name of a patient from their list of sufferers.

Treatment - The treatment of resistant patients within the zone of chronicity has been described above.

The test also assists the clinician in deciding the response of the individual patient to a particular type of treatment; a falling viscosity reflects a favourable response.

A raised viscosity after a course of treatment indicates that a cure has not been produced and that further treatment will be necessary.

Cowan has informed me that the decrease in the plasma viscosity with cortisone treatment has always been most dramatic. I have seen one case only and while the initial decrease was obtained the viscosity soon returned to its original level in spite of the continued use of the drug.

(Further discussion appears later, in respect to the proteins, liver functions, etc.)

The ESR test in rheumatoid arthritis.

My experiences with the Wintrobe ESR test have been most unsatisfactory and disappointing.

Results. These have been included in detail in Table II of the appendix. They have been shown in graphical form in Fig.65 to 80 .

Clinical Assessment	Sex	No. of tests	Corrected Wintrobe ESR.	
			Mean	Standard deviation
Chronic	F	354	25.6	11.46
	M	78	17.4	11.60
	B	432	24.1	9.85
Subacute	F	64	33.3	12.60
	M	10	26.2	16.86
	B	74	32.3	13.4
Acute	F	10	34.6	16.23
	M	7	17.8	16.08
	B	17	27.6	17.79

The number of tests differs from the viscosity table as the ESR was not measured in every instance.

(a) The range of ESR values was the same for all the grades of clinical severity; the highest value in the chronic group was above the highest of the subacute group.

(b) A statistical comparison was made of the six groups formed by the two sexes in three clinical assessments. Taking as the criterion that two groups were significantly different (ie. not drawn by chance from a single varied family of results) if the difference of their means was more than 2.5 times the standard error of this difference, it can be shown that female chronic and subacute groups differ, as does the chronic male and chronic female. There is no difference in the three male groups, or in the subacute-acute female groups, or in the chronic-acute female groups.

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(c) In Fig. 65 , where the length of the base-line equivalent to the plasma viscosity normal range was made equal to that for the female ESR normal range, the relationships of the means of the ESR groups to themselves and to the corresponding means for the plasma viscosity results have been again presented. It stresses again how little difference there may be between the groups and makes obvious the anomalous decrease in the male acute mean from the subacute mean.

(d) The frequency of distribution graphs indicate how the ESR results cover the same range in all groups; they also indicate the frequency with which apparently normal ESR values may be found, from 0% in subacute males to 36% in chronic females.

(e) Study of the serial tests in individual patients has shown that wide fluctuations are possible in the ESR results which frequently could not be correlated with any change in the clinical condition, as assessed by the clinician.

A comparison of the Plasma Viscosity and ESR tests in Rheumatoid Arthritis.

In part 6, in that section where I described the periodic relationship between the plasma viscosity and the maximum ESR, it was indicated that it was impossible for both measurements to be accurate guides to the same thing, ie. the systemic reaction to disease.

As a corollary, the better is one measurement as a guide to this systemic reaction by so much is the other less accurate.

Furthermore, I believe that the uncritical opinion is unduly biassed in favour of the ESR by those instances in which each change in the clinical state has been mirrored by an equivalent change in the ESR; when such a case is seen it is remembered while the others with smaller or larger discrepancies between the ESR interpretation and the clinician's findings are rapidly forgotten. The ESR has much latent criticism facing it among clinicians and pathologists.

The ESR has a much higher incidence of false negative tests - amounting to no less than 36% in chronic females. In contrast, the false negatives in the plasma viscosity amounted to 8.2% only. In the 433 tests which I analysed (103) , 28 were normal in both the ESR and plasma viscosity, 118 had normal ESRs associated with abnormal viscosities, but in one instance only was an abnormal ESR associated with a normal plasma viscosity. Thus, the extra effort in measuring these 433 ESRs has produced an improvement by less than 0.25% on the information yielded by the viscosity estimation alone. I believe that this is a satisfactory refutation to the proposal that both measurements should be made.

The abnormal range for the female ESR values is 1.75 times the length of the normal range; for males it is about 5 times. The abnormal range for the plasma viscosity for both

sexes for ordinary illnesses is about 7 times the normal range but on rare occasions the abnormal range can extend to 18 times. The effect of the small possible increase in an ESR value is well demonstrated in the insignificant increase in the mean ESR figures for the female subacute to acute groups; the ESR had reached its maximum in the subacute group and no further increase was possible with the increase in clinical severity. The plasma viscosity does not suffer from these restrictions. This difference between the two tests can be noted in Fig. 65 where the plasma viscosity line stretches far to the right, and in Fig. 71 where the ESR values appear above each other while the viscosity groups tend to move towards the upper levels with increasing clinical severity.

The scatter diagrams of Fig. 72 to 80 are important from two aspects. They show that the highest plasma viscosity can be associated with the lowest ESR value, but not vice versa. They also show that different groups of results would yield different lines and equations of correlation between the ESR and the plasma viscosity.

My experience with the two tests in individual patients emphasized the superiority of the plasma viscosity test. In the end the only significant result in the ESR test was an increased value: a normal value does not rule out the possibility of an

active disease as the ESR error in that aspect can be 36% ; the degree of activity is not indicated closely by the degree of abnormality in the ESR value (from statistics above); we were never discomfited by discarding the ESR result when there was a discrepancy between the clinical assessment and this value, but we learned that such a discrepancy with the plasma viscosity test could not be ignored with impunity.

There is nothing in the ESR test to correspond to the zone of chronicity whose importance we have discussed.

There is one type of case in which the ESR might be superior on occasion, and that is the early case - this aspect is covered however by the statement above that an abnormal result alone has significance.

I am of the opinion that the ESR is so unreliable and its results of such doubtful value that it could well be discarded in favour of the plasma viscosity test where this is available. I would go further and suggest that a critical consideration of the evidence here presented would lead to the conclusion that the ESR as measured by the Wintrobe technique yields so little real information that it is not worthy of retention even if the alternative plasma viscosity test were not available. Cowan, at Sunderland, on the basis of these results has discarded the ESR completely; I am attempting to do this also at Portsmouth.

While not so emphatic in his condemnation of the ESR test, Stone (236) writes concerning it - "Throughout the course of the disease widely different figures may be found, rises and falls occurring over the months, having no clear relation to the clinical condition.

Under the influence of gold therapy the general tendency is to a lower level and an ultimate fall to normal. But the rate does not necessarily decrease with clinical improvement: quite often much the same figure is found although unmistakable amelioration in symptoms and signs has occurred. All that can be said of an increased sedimentation rate, whatever be the actual figure, is that it shows the infective agent to be at least latent, if not still active.

When the earliest manifestations of rheumatoid arthritis are appearing, and especially in the "pre-rheumatoid" stage, a normal figure may be found, and may be most misleading. It should not be allowed to disturb one's clinical judgment".

In contrast, the literature contains many papers which stress the value of the ESR test in rheumatic disease.

Gibson (87), in his paper comparing the plasma viscosity and ESR tests writes - "I have refrained from quoting individual cases. Any such selection may easily be misleading. The apparent unreliability of either test could have been shown by a

suitable selection of cases". Therefore, I must ask the reader to accept that the individual cases reported fully in the appendix were not specially selected to favour the plasma viscosity test and are representative of the general results.

The original publications on the plasma viscosity of Whittington and Miller had aroused my interest alone among clinicians and laboratory workers; however, the later publications of Houston, Whittington and myself showed that the plasma viscosity test was of value in the investigation of many diseases among which rheumatic fever was specially named and the test was adopted by several laboratories. Their results have now been published and these have to be discussed.

The reports have not been uniformly in favour of either the ESR or the plasma viscosity tests. Where a good ESR technique was used, especially one which measured a maximum sedimentation velocity, the value of the ESR to the clinician was correspondingly higher; where an inferior viscosity technique was used, so was this test correspondingly decreased in significance. The problem can be summarised approximately to the ratios obtainable of the abnormal range to the normal range of values; eg. Race (202) reduced my 7:1 ratio for plasma viscosity to 1:1, and thus found

that test less informative.

It is also more than a coincidence that those workers who had had previous wide experience of the ESR test (and some had even carried out the fundamental experiments required to develop their own special technique) reported more favourably on their ESR results than those who approached the problem initially unbiassed in favour of either test: the gross discrepancies in the percentage of ESR values in the abnormal range should be noted from report to report.

A suitable order for the discussion of these publications is according to spas and rheumatic centres.

(i) Buxton. Race employed the "Spa" ESR method which measures the fall in a wide tube in one hour, making a correction by formula for variation in the haematocrit result. "Previous experience with the Wintrobe technique has shown that it may be grossly inaccurate when the cell volume approximates to the normal level and that normal results may be obtained when the wide-tube method indicates a definite abnormality (Collins and others, 1939)". He had the benefit of one of my Whittington-type viscometers, correlated to the V5 scale by Whittington, but he introduced a modification of our technique which invalidated his use of my values for the normal range (especially when the older high 1.950 cs. upper level was used). Race had as his anticoagulant

an indefinite volume of potassium oxalate solution: this would cause a reduction in the plasma viscosity by dilution and by the cell-constricting-action already described in §14 of part 6. It is most important to realise also that he was dealing with chronic rheumatic diseases only which could explain why in his series of 71 tests his highest figure was 2.23. Because his upper limit of normal viscosity was unduly high, the ESR was favoured and this may be part of the reason why he concluded that "Contrary to the results of Harkness and others, who found the plasma viscosity test to be a more reliable index of activity in chronic rheumatic diseases than the erythrocyte sedimentation rate as performed by the Wintrobe method, the results obtained with the wide-bore method recommended by Collins and others showed a greater sensitivity and in several cases gave an abnormal value when the viscosity was within normal limits". However, he did find that the plasma viscosity was a better guide to the extent of the disease because it was not restricted, as was the ESR, by an upper limiting value - "-but it is quite obvious that the viscosity shows the extent of the abnormality better than is indicated by the C.S.S. figures." "It is clear, however, that the viscosity, being quite independent of the cell-packing factor, will give a somewhat better indication of the degree of abnormality."

As Race complains of the upper limit to the possible ESR values interfering with a proper reflection of the extent of the disease in these chronic conditions, it would have been interesting to hear how much greater was the complaint when dealing with diseases of still greater severity such as in the acute and subacute groupings.

(ii) Harrogate. Woodmansey and Wilson introduced a viscometer of their own design (similar to that designed by Satô (123)) which has a simple construction and which is more simple and rapid to use than the Whittington model. Their "viscosity" value, however, includes a variable fraction which is dependent on non-viscosity factors such as surface tension and this fraction is neither constant nor negligible as they have assumed. They also depart from standard viscosity units and report their results as a ratio ($= 100 \times \text{time of flow of plasma} / \text{time of flow of distilled water}$). The experimental errors are large: the specific gravity effect on the ratio is disregarded; the timing errors are equivalent to 1.5% of the final value; the water-bath controls the temperature of the fluid but not of the glass of the viscometer and a variation of 1°C. causes an error of 2.5%.

They approached the problem in a critical mood (259) - "It is generally agreed, however, that the erythrocyte sedimentation

rate is not always a reliable index even if a correction is made for anaemia." From their study of 200 consecutive cases, they concluded - "We believe that the plasma viscosity gives a more accurate figure than the erythrocyte sedimentation rate for estimating the activity of rheumatoid arthritis".

Their technician, Steel, has written two short articles on the relation of the plasma viscosity results to the ESR results, treated from the aspect of physical measurements rather than from the clinical aspect (232,233).

(iii) Worcester and Droitwich. Arnold and Salt repeated the mathematical analysis of Steel, and in a series of 182 tests (7) obtained a correlation coefficient of 0.750. They also derived a series of equations by which one value might be calculated if the other was known. They found that the plasma viscosity did not suffer from the handicap of an upper limit and thus concluded - "Plasma viscosity determinations are valuable for further defining colloidal abnormalities in blood samples in which the corrected sedimentation rate is maximal."

Dawson and Salt (59) investigated a series of patients with the ESR and plasma viscosity tests at weekly intervals while they were undergoing a three-week course of treatment. They found - "In general, it appears that either the C.S.R. or the

P.V. value is dependable as an initial index of activity in chronic rheumatic disease, the C.S.R. being rather more sensitive for the detection of slight degrees of activity and the P.V. value being more reliable for demonstration of extreme severity of the disease process." "These findings suggest that, in rheumatic disease of short duration, C.S.R. values may occasionally yield more marked evidence of abnormality than do P.V. values. In contrast, when the disease is severe and of long duration, P.V. determinations may sometimes yield more pronounced evidence of the gravity of the condition than do C.S.R. determinations." "It is concluded from the foregoing observations that the C.S.R. test is reliable for diagnostic purposes and is sufficiently sensitive to reveal slight changes in a patient's condition, sometimes but not always associated with small degrees of clinical change. The P.V. test is likewise reliable for diagnostic purposes but is less sensitive as an indicator of slight changes in a patient's condition, seldom varying within short periods of time even when there is clinical improvement. For diagnostic purposes the greatest amount of information is elicited by performing both the C.S.R. and P.V. tests. In most cases the results will be in agreement, but occasionally the values will show a lack of correlation. When this occurs, the C.S.R. results are likely to be more reliable in mild early cases of rheumatic disease; the

P.V. results are likely to be more dependable in severe cases of long duration."

These workers divided their ranges into five - a normal range and 4 abnormal subdivisions - for both the ESR and plasma viscosity. As a larger percentage of the ESR values were in the higher groups as compared with the viscosity tests, they interpreted this as showing that the ESR values are more markedly differentiated from normal than are the abnormal plasma viscosity results. I will have to deal with this point again with Gibson's paper and will leave it until then.

Salt assisted in the preparation of the "Spa" technique for the ESR measurement and it is not surprising therefore that in his introductory remarks his attitude to the test is shown - "The well-established erythrocyte sedimentation test (E.S.R.) is generally accepted as satisfactory in these respects, occasional anomalies serving to maintain the interest of rheumatologists rather than to discredit the test".

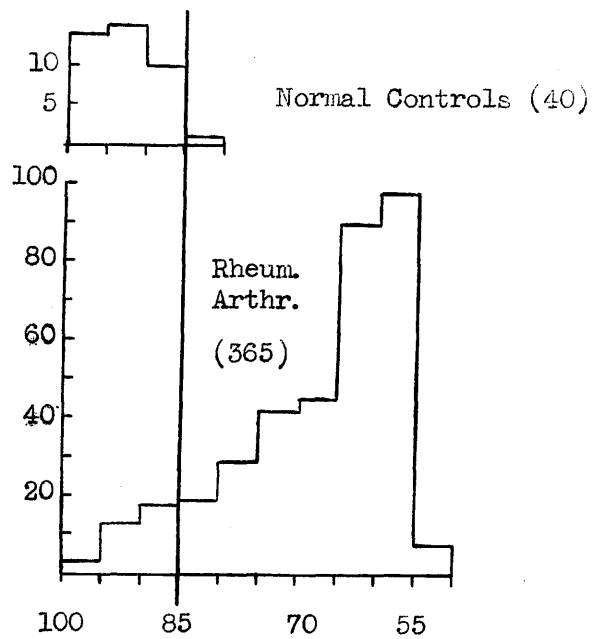
(iv) Bath. Gibson (87) has presented the best exposition of the correlation of the ESR and plasma viscosity by other workers. He used a Harrogate viscometer and a variety of ESR techniques. I will quote his findings rather fully and include some of his diagrams and results.

(The C.S.S. is a one-hour ESR by the Spa tube, corrected by formula for PCV. variation: the C.S.I. is a maximum velocity technique, corrected later by a chart for PCV. variation.)

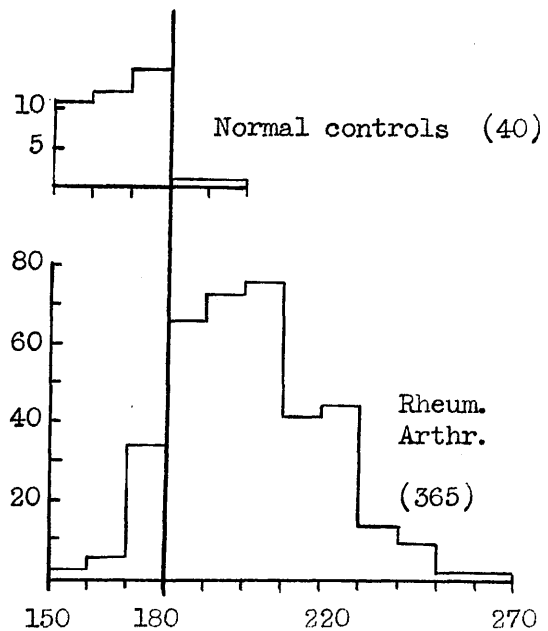
The results of 365 tests on 286 consecutive cases of rheumatoid arthritis are presented in Fig. 81, copied from his paper. Gibson stressed how the higher incidence of abnormal ESR results came at the upper values in contrast to the plasma viscosity where the greatest came just above the upper limit of normality (Dawson and Salt found this similarly and drew the same conclusion) "It will be seen that the peaks of the curve are in groups far removed from the normal, in this respect contrasting with the viscosity distribution in the same series. In empirical tests of this kind in which an estimate is made of some ill-defined abnormality, their value both in diagnosis and in assessment of improvement or deterioration depends mainly on the extent of abnormality indicated and the differentiation which this estimate affords between diseased and normal persons. On this criterion the B.S.R. appears to be more informative than viscosity."

This conclusion is not invalidated by the occurrence of early packing when the B.S.R. is estimated by the short tube of the Spa Hospitals Method. The writer agrees with Race (1948) that differentiation within the most rapid B.S.R. groups (C.S.S. 55-65%) is not clearly made by the tube in question. This is seen

Number of
cases



Frequency distribution of BSR. (C.S.S.) in normal controls and rheumatoid arthritis.



Frequency distribution of Plasma Viscosity (Relative) in normal controls and rheumatoid arthritis.

in the graph by the accumulation of large numbers of cases in these groups. This is not, however, a very serious disadvantage and it is far out-weighted by the sensitiveness of the method to small deviations from normal and by the consistency of its results which other methods lack." I consider that these results may be interpreted in a manner more favourable to the viscosity test; the viscosity pattern is similar to my own findings.

From their derivation from consecutive cases it is probable that the majority of the tests were made on female patients with chronic disease. As chronic disease of all types occupy a restricted zone just above normal, Gibson's values conform to this pattern; the fact that a result falls in this zone is more important than the distance by which it departs from the normal range. Furthermore, if the numbers of acute and subacute cases had been increased to equal the chronic, the plasma viscosity results would have shown a corresponding increase in the intermediate abnormal values and in the high abnormal values, while the ESR values would merely have piled high in the ranges where the highest incidence appears at present. It is not valuable to claim a relatively greater tendency to high values in mild disease if in severe disease the same relative positions cannot be maintained.

In these 365 tests, the ESR was normal in 34 (9.3%), the viscosity was normal in 41 (11.2%): 13 of the 34 normal ESR.

tests had associated abnormal viscosities, while 20 of the normal viscosity tests had abnormal ESRs. Using both tests no less than 344 (=94.2%) would have had abnormal tests.

"The disagreement in some cases was very great and both tests in certain cases disagreed with the short-term assessments of the patients' clinical condition. Cases could be quoted in which the B.S.R. agreed better with the clinical state and an equally good case could be made out for the viscosity as showing better agreement."

"The conclusion seems to be warranted that B.S.R. and viscosity are measuring two different aspects of plasma abnormality. The B.S.R. is mainly influenced by fibrinogen, the viscosity by the total protein picture with globulins predominant. I cannot agree with the statement that because the tests do not agree then one of them must be inaccurate. Both may be perfectly accurate indices of different facets of abnormality in the same plasma". I am in full agreement with this last sentence of Gibson but I must insist that if it is true then the indices cannot be equally applied to measure the same thing (in this instance the general reaction to the disease): one or other must be superior unless the errors of both are equally large.

Gibson concluded - "Viscosity estimation has an important

place as an aid to the clinical assessment of activity in rheumatic disease. It supplements, but does not replace, the B.S.R.. In any case or series in which a close watch is required on progress, both tests taken together give results which are more complete than either separately. The combination of tests should be of especial value in therapeutic trials in which for statistical purposes two independent indices would be available."

Ratio of abnormal to normal ranges for ESR and plasma viscosity.

(a) ESR. The C.S.S. technique as used by the previous authors has a normal range of 100-85%, an intermediate or borderline range from 85-80% which was included with the definitely abnormal range for statistics, and an abnormal range of 80-50%. Thus the ratio is 7:3.

With Gibson's C.S.I. technique the ratio was 8:1 which is closer to the viscosity ratio by my methods.

(b) Plasma Viscosity. Race studied only chronic cases and had a ratio of 1:1 (it would have been higher if he had produced his own normal range).

Woodmansey and Wilson had a ratio of 7:2,

Dawson and Salt had a ratio of 7:2, and

Gibson had a ratio of 9:3.

While the extent or range of their normal zone was similar to my

series (0.2, 0.3, 0.3 respectively as compared to 0.25) yet their absolute values differed; Woodmansey and Wilson = 1.60 -1.80 although Steel gives 1.60-1.82 with a border zone up to 1.86; Dawson and Salt = 1.50-1.79; Gibson = 1.50-1.80 cs. Their highest value was only 2.9 as compared with my values frequently over 3 and up to a maximum of 3.7 .

(v) Walkden Clinic, Manchester. Lawrence has elaborated on the single plasma viscosity measurement by which he measures the viscosities in the fluids remaining after the fibrinogen has been removed as a clot and the globulins by salting-out methods. There is no doubt that this new method yields more information than obtainable by our original measurement. However, this method will not be widely adopted as 4 viscosity measurements are needed for each plasma plus manipulations of centrifuging, filtration, etc. The filter-paper electrophoresis technique is easier and yields the same information as Lawrence's method but in terms which have a standard interpretation. (138,139,140)

I quote his results for 245 cases of clinically active disease - not all rheumatic. "ESR abnormal in 43 per cent; plasma viscosity abnormal in 59 per cent; fractional viscosity abnormal in 86 per cent; ESR or fractional viscosity abnormal in 94 per cent."

"Comparison of the differential plasma viscosity with the E.S.R. and the simple plasma viscosity indicates that the first is a more sensitive indicator of pathological plasma protein changes than either of the other two and that the E.S.R. is the least reliable."

(vi) Charterhouse Rheumatism Clinic, London. Coke uses a Whittington viscometer to the V5 scale. He has not published the details of his tests and the summary is taken from his part in the discussion on Gibson's paper to the Royal Society of Medicine (49) - "My experience can be summarized by saying that the serum viscosity appears to be a useful addition to the assessment of the rheumatic patient, but there is little evidence that it should or indeed will ever replace the erythrocyte sedimentation rate."

Coke studies serum rather than plasma as his scheme for the laboratory investigation of patients had been founded on serum and he was not prepared to upset these plans until he had found that serum viscosity would not yield as much information as the plasma viscosity. Salt (217) has also suggested more recently that serum viscosity might repay further investigation. As I informed Coke earlier in a private communication (47) I do not consider it important which fluid is studied in chronic states where the fibrinogen is either normal or but slightly increased.

However, if the test is to be used more widely and include such acute conditions as rheumatic fever the plasma is the more suitable fluid; the earliest changes are in the fibrinogen and its detection requires the use of plasma. It would be possible for the laboratories whose work is confined to tuberculosis or rheumatism to obtain satisfaction with the serum viscosity estimation but I know from my own experience in a general hospital laboratory where I had the tests in duplicate that the plasma viscosity results are more valuable than the serum viscosity.

I am against the introduction of variations of the viscosity test except for techniques, such as Lawrence's, which produce significantly better information. Consider the chaos which has arisen in the ESR test because of the multiplicity of methods.

Also, as plasma is the fluid present in the circulating blood, I think we should attempt to study this whenever possible rather than only a fraction of it.

The relation of the plasma proteins to the plasma viscosity and to the clinical condition in rheumatoid arthritis.

On many occasions when I have described my plasma viscosity test and explained how it was ultimately dependent on protein changes I have been asked if the same information was not

obtainable by the simpler specific-gravity technique of protein estimation. The duplicate results in the rheumatoid arthritis can serve to answer this question.

The total plasma proteins were measured by the copper sulphate method of Phillips et al. (194). The upper limit for the plasma total protein is given in many books and papers as 8.0 g. per 100 ml.

The individual results in Table II show that a large majority of the chronic cases have total proteins still within the normal range. The majority of the subacute and acute cases have total proteins outwith the range, but each exception to this general statement weakens the possible value of the protein estimation relative to the viscosity estimation (100% abnormality in these two groups). There is relatively less difference between the means of the three groups for the total protein than for the viscosity results.

It has been shown that the protein fractions have equal effects on the specific gravity (186). Therefore, as the albumin decreases in disease it will cancel out the same amount of increase in globulin or fibrinogen and the resultant increase in the total protein may be small. The difference in the effect of the protein fractions on the viscosity has been described in detail earlier,

in §16 of part 6. A small increase in the fibrinogen or globulin would be able to compensate for even a large decrease in albumin and abnormal fibrinogen or globulin will almost always be associated with abnormal viscosity.

Nevertheless, I have found it worth while to estimate both the viscosity and the specific gravity when attempting to make an estimate of the acuteness or otherwise of a disease process. A very high viscosity result associated with a normal or low abnormal total protein must be due to fibrinogen increase chiefly and therefore with an acute clinical condition; a moderate rise in the viscosity and a moderate rise in total protein probably results from an increase in the globulin fraction which is more characteristic of a chronic lesion.

The explanation of the viscosity increases in rheumatoid arthritis is found in the changes in the plasma protein fractions. Gutman (91) has reviewed the work of many investigators and shows that the changes in the serum proteins in rheumatoid arthritis characteristically lead to a decrease in albumin and an increase in globulin; there is also an increase in the plasma fibrinogen. The increase in globulin is due chiefly to increments in the alpha- and gamma-fractions, of an extent and proportion referable to the stage of the disease, although the bulk of the increase

cannot be accounted for by the development of specific antibodies. Wallis (268) has concluded that the hyperglobulinaemia is the result of the combined effects of inflammation, tissue destruction, and immunization, the last being the principal contributor in all but the early stages of the disease.

Salt (217) found that the "differences in plasma globulin (including fibrinogen) concentrations determined chemically, are seen to be closely paralleled by the values for plasma viscosity and for corrected sedimentation rate. A significant diminution in the albumin content of the plasma also accompanies the augmented globulin and fibrinogen levels, whereas the fibrinogen content differs only slightly in the two sub-groups." " - the hyperglobulinaemia demonstrable in patients with chronic rheumatic disease is due chiefly to increments in the euglobulin and pseudoglobulin I fractions, - " "Serum total protein concentrations may also be increased because of the hyperglobulinaemia, but the increment may be partially off-set by a depletion in the albumin component."

I did not have many tests in which I fractionated the proteins by Howe's salting-out technique, but these results have been in full accord with Salt's later findings.

The relation of the gold and thymol flocculation tests to the plasma viscosity and the clinical condition in rheumatoid arthritis

The serum colloidal gold reaction and the thymol turbidity tests were introduced by MacLagan in 1944 (174,175) and the thymol turbidity was later improved by its extension to a flocculation technique (176). While MacLagan intended that these tests should be used for the investigation of liver disease and liver function, he realised that they could yield abnormal results in diseases which did not primarily affect the liver. It was shown (163,177) that abnormal results were due chiefly to qualitative and quantitative changes in the gamma globulin but that the other globulins and the albumin played an active role in modifying the gamma globulin action.

It is generally accepted that the fibrinogen is formed in the liver only: the site of formation of the albumin and globulin is not known definitely but the liver again plays a large part in their formation. The plasma viscosity is a measure of the abnormal fibrinogen and globulin and is thereby an indirect measure of an alteration in the protein-forming function of the liver. (An abnormally low catabolism of the proteins must also be considered.)

I thought that some useful information might be derived if a

comparison was made between the plasma viscosity and these other empirical tests for liver function. Therefore nearly a thousand tests were made in parallel between the gold flocculation and the plasma viscosity; the thymol turbidity and flocculation tests were discontinued early when the degree of correlation was absolutely low and relatively low as compared with the gold flocculation results.

Results. - These are given for the individual cases in table II, and these are shown graphically in Fig. 82.

They can be summarised as follows:- In a total of 401 tests in rheumatoid arthritis 317 abnormal gold flocculation results were obtained ($=79.05\%$). There was a relation between the severity of the disease and the incidence of abnormal results - 100% in 13 female and 4 male acute tests, and in 7 male sub-acute tests; 87.5% in 40 female subacute tests; 78.3% in 267 chronic female tests and 70% in 70 chronic male.

From Fig. 82 also it is noted that the degree of abnormality tended to be higher with the more severe clinical states, yet a normal result could be associated with moderately high viscosity values.

An abnormal result could be found in those patients in whom the disease was apparently burned-out and quiescent.

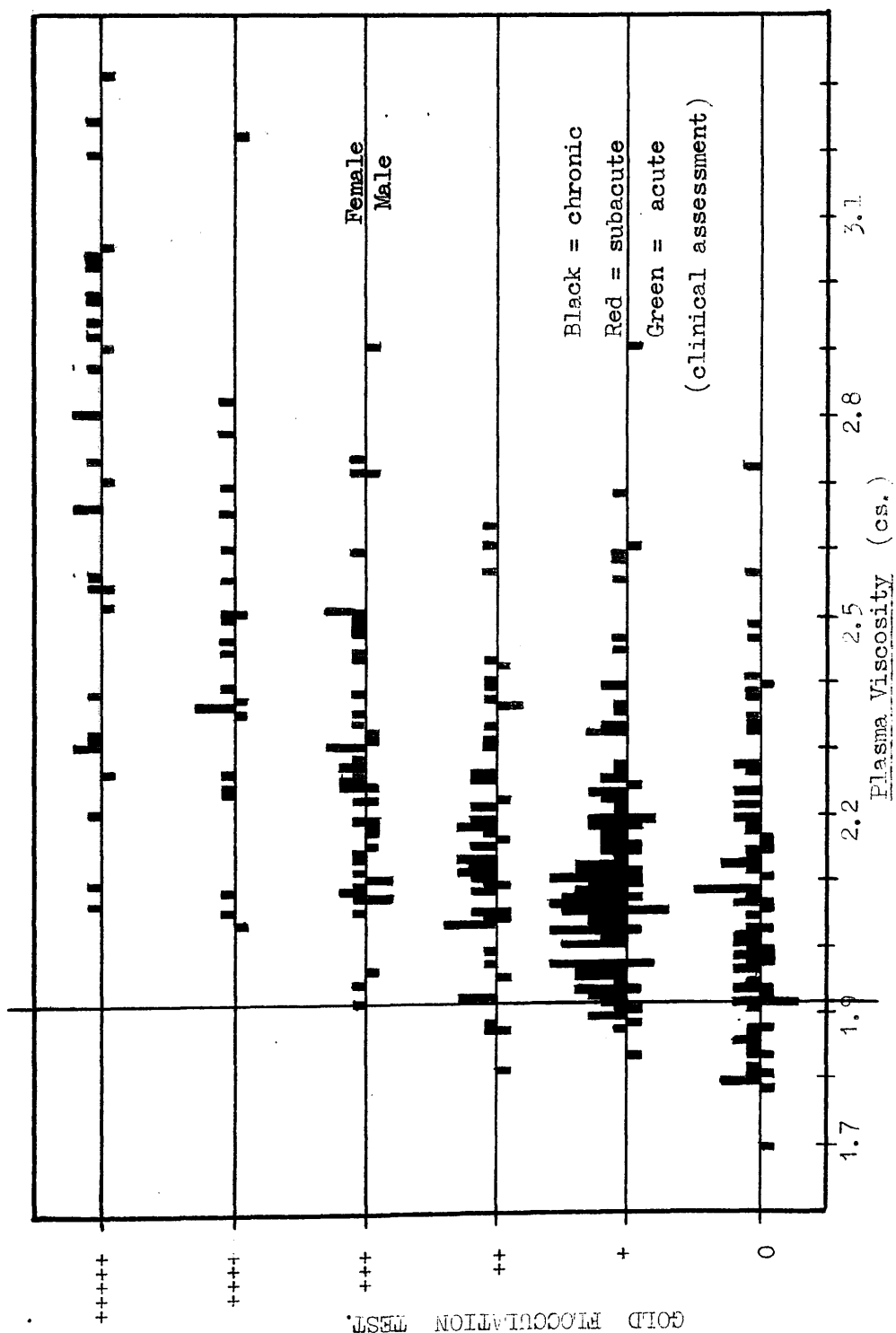


Fig. 82 The relationship between the Plasma Viscosity and the Gold Flocculation Test in Rheumatoid Arthritis.

Discussion. The high correlation between the gold flocculation test and the plasma viscosity and clinical severity is found only in rheumatoid arthritis and the related diseases of rheumatic fever and Still's disease. In the later similar series of duplicate tests with tuberculosis abnormally high viscosity values are almost constantly associated with normal gold tests.

§ B of this part is concerned with Infective Arthritis which is similar to rheumatoid arthritis except that a focus of infection is believed to have a large part in the production of the locomotor lesions. The results for the chronic cases of this disease in the plasma viscosity test are not distinguishable statistically from those of chronic rheumatoid arthritis, but the incidence of abnormal gold tests was much lower. Cowan and I applied this finding empirically to our investigation of cases which might be rheumatoid or infective arthritis - a patient with a normal gold flocculation test had a specially thorough search for a possible focus of infection.

The discovery of an abnormal gold flocculation test in a patient with vague signs and symptoms was an additional guide to a confident diagnosis of rheumatoid arthritis.

I had made a preliminary draft of a paper on the uses of the gold flocculation test in arthritis when Fraser (83)

published his results from a smaller similar series of tests. He also studied the cephalin-cholesterol flocculation test but found 19% only abnormal in rheumatoid arthritis and 15% in rheumatic fever. "A relationship was observed between the results of the serum colloidal gold test and the erythrocyte sedimentation rate. It is concluded that the former is a useful test in rheumatoid arthritis, although a little less sensitive than the latter." "There was a moderate degree of relationship between the results of the serum colloidal gold reaction and the plasma albumin and globulin fractions, inverse in the former and direct in the latter. There was no apparent relation to the total protein or fibrinogen fraction." He found 61% abnormal gold results in his 133 tests in rheumatoid arthritis and 40% in 20 tests in rheumatic fever. Incidentally, he had 30 normal ESR results in his 133 tests.

Carter and MacLagan (38) had 76% incidence of abnormal gold flocculation tests in a series of 34 patients with rheumatoid arthritis: "there was a rough though definite correlation between the gold test and the sedimentation rate": all tests of 3+ and over had ESR results over 25 mm. in 1 hr. (Westergren) and the negative reactions had ESRs below 20 mm. The thymol turbidity test was abnormal in 38% only of these cases.

The plasma alkaline phosphatase in rheumatoid arthritis.

My technician at Sunderland, Mr. L. Haugh, A.I.M.L.T., was specially interested in the phosphatase enzymes. He estimated the alkaline phosphatase content on the plasmata after I had completed the viscosity test. His results will be presented as a thesis for his Fellowship in the I.M.L.T..

In rheumatoid arthritis the alkaline phosphatase results tended towards two groups - a low group of about 4 - 6 K.A. units, and a high group of 12 - 17 K.A. units per 100 ml.. No correlation was obtained between these groupings and the clinical severity of the individual cases, the plasma viscosity or the gold flocculation tests. The only consistent finding was that in response to a satisfactory treatment the phosphatase of both groups tended to an intermediate value about 10 K.A. units.

In spite of the abnormal protein fractions, alkaline phosphatase, and flocculation tests which are so frequently associated with abnormal liver function that they are used in the diagnosis of liver disease, it is noteworthy that the incidence of liver disease at the post mortem examinations of patients with rheumatoid arthritis has been remarkably low (9).

The packed-cell-volume (haematocrit) in rheumatoid arthritis.

When I was a student my textbook of medicine (Price, 4th edition, 1933) taught that in rheumatoid arthritis - "anaemia is usual". I refer to this matter here for the sake of completeness as my results indicate the beneficial effects of the exhibition of iron in large doses. All patients attending the Rheumatism Clinic at Sunderland received Pil. Fersolate prophylactically and this procedure had been copied by the medical colleagues in general practice.

Consideration of my results in Table II and in the table on page 262, will show how seldom a severe anaemia was ever seen by us.

A scheme for the laboratory investigation of arthritic patients.

My routine investigation of an arthritic patient included the tests described above - plasma viscosity, total plasma protein, gold flocculation, haematocrit, and ESR - together with a total and differential leucocyte count and a simple urine examination. To this I frequently added the serum uric acid, protein fractionation originally by a chemical salting-out method but now by filter-paper microelectrophoresis, and urinary 17-ketosteroid excretion. The clinicians associated with my laboratories have

found this scheme most informative and satisfactory: it can be recommended for the use by other laboratories (? minus the ESR).

It is interesting to compare my scheme with the tests proposed by Wuhrmann and Wunderly (260) in their book devoted to the protein changes in disease - their choice for routine testing is - ESR, solubility curve of the plasma, Takata-Ara reaction, Cadmium opacity reaction, nephelogram (= modified Weltmann reaction), and electrophoretic analysis of the proteins. The Takata-Ara, cadmium opacity, and nephelogram are reactions which depend on abnormal proteins, qualitative or quantitative, and are thus akin to the gold flocculation test.

* * * * *

The plasma viscosity test in other rheumatic diseases will now be described, but in less detail than in the case of rheumatoid arthritis. Only the outstanding points will be stressed.

(B) Infective Arthritis.

This disease presents a clinical picture identical with that of rheumatoid arthritis except that there is a focus of infection which is held to be one of the causes of the locomotor lesions. Many clinicians, especially American, do not differentiate between this type and the classical rheumatoid arthritis, treating them as a single entity.

Results. See table III of the appendix for details.

In 44 tests on chronic female patients, the mean plasma viscosity was 2.053, with 81.8% abnormal results; 50% only of the ESR tests were abnormal and 41% of the gold flocculation tests.

In 21 tests on chronic male patients, the mean plasma viscosity was 2.065, with 85.7% abnormal; 70.6% of the ESR tests and 33% of the gold flocculation tests were abnormal.

In 10 tests on sub-acute female patients, the mean plasma viscosity was 2.479, with 100% abnormal; 87% of the ESR tests and 43% of the gold flocculation tests were abnormal.

Discussion. The similarity of the means of the plasma viscosities of the two sex groups of chronic infective arthritis should be noted: this is further support to the claim that the behaviour of the plasma viscosity test can be regarded as from a single family of subjects composed of all ages and sexes.

These results for the chronic cases of this disease are not significantly different on statistical analysis from the results of the chronic cases of rheumatoid arthritis: the majority falls within the limits (1.95-2.25) of the 'Zone of Chronicity', as one would expect if the existence of such a zone was to be credited. The subacute results are similar to the subacute results of rheumatoid arthritis. (see Fig. 80 b.)

The use of the gold flocculation test in the differential diagnosis of this disease and as an indication for a thorough search for a focus of infection have been discussed in the previous section.

The superiority of the plasma viscosity test as compared to the ESR can be discovered in the percentage figures for the incidence of abnormal results.

* * * * *

(C) Still's Disease.

Synonym - juvenile rheumatoid arthritis.

The spleen and lymphatic glands should be enlarged to fit the classical description; the joint lesions are similar to those of an atrophic arthritis of the adult.

Results. These are given in Table IV of the appendix.

Discussion. In this series of tests on eleven patients it is noteworthy that no plasma viscosity value came within the normal range; the ESR. results include a few high-normal figures.

The severity of the general reaction in this disease is indicated by the degree by which the plasma viscosity had increased. The increase was greater than one would have expected from a consideration of the lesions in the locomotor system alone. An example of this discrepancy was the case of a young man who was crippled by long-standing deformity of his joints but who complained little of present pain in the joints; he had suffered from the disease for 9 years; his plasma viscosity value was no less than 3.100 cs. (An adult with a similar history would almost certainly have had a plasma viscosity value within the zone of chronicity, about 2.1 cs.)

The details of the case-history of L.B. are included in the appendix because they illustrate several points. Local treatment to the affected joints was able to produce an improvement

in them but it did not make a significant change in the plasma viscosity. There appears to be a considerable variation in the plasma viscosity values yet almost every one of these changes can be correlated with a change in the total clinical state. On two occasions, major joints were affected for the first time when she was under observation and the plasma viscosity increased at the time of the fresh involvement.

The dramatic response to Cortisone therapy is shown in the diagram which accompanies her case notes. A fall of 1.25 cs. occurred within 6 days. The relapse on stopping the treatment was just as dramatic in her laboratory tests but the improvement in her locomotor system persisted with but little diminution until treatment with a further supply was resumed after a few weeks. I have ventured to criticise this particular dosage in that it was never sufficient to cause a return of the plasma viscosity to within the normal zone; I argued on the analogy of gold treatment to adult rheumatoid arthritis where a persisting abnormal plasma viscosity, even in the absence of symptoms, is synonymous with an ultimate relapse.

The return of the plasma protein fractions to a pattern approximately normal was also worthy of notice.

The high incidence of positive gold flocculation tests is similar to the findings in the adult type of this disease.

* * * * *

(D) Rheumatic Fever. (including Chorea and Erythema Nodosum)

Rheumatic fever can be defined as an acute, specific disease, characterised by fever, arthritis and a special tendency to endocarditis or carditis. (Acute rheumatic fever will be considered first; chorea and erythema nodosum come later in subsections.)

Results. See table V in the appendix, and the case histories given there in some detail.

Discussion. The majority of these tests were carried out on hospital in-patients. The rheumatic condition might have been so severe that hospital nursing was necessary or it might have been of such long duration that intensive treatment in hospital was being tried as a means of cutting short its course. Thus these results are not representative of all types of the disease. Therein also lies the explanation why I have so few early cases so that the complete cycle of the disease is incomplete. These results can also be discussed conveniently from the aspect of diagnosis, prognosis and treatment.

Diagnosis. The plasma viscosity occasionally fails to become abnormal in the early stages of the disease until a few days or a week or so after the obvious clinical onset; therefore the clinician must rely on his clinical acumen and he must not be put off his diagnosis of an active disease by a normal viscosity.

This is one of the few occasions in which I admit that the ESR test can yield more information; the ESR may become abnormal before the plasma viscosity (although the opposite most certainly occurs also) and an abnormal ESR supports the diagnosis of an acute disease.

If the disease runs its usual course of a few weeks, the plasma viscosity serial results can be plotted as a smooth curve, with an eventual return to normal values. The ESR appears to be more labile: although the mean of the serial results produces a curve similar to that of the plasma viscosity yet the variation of the individual tests from this mean curve can be relatively large without any corresponding change detectable by the clinician. A departure from the plasma viscosity curve is significant either as an increase indicates a relapse or complication or a decrease indicates an effective response to therapy.

The refusal to admit of the occurrence of false positive results in the plasma viscosity test has two important applications in rheumatic fever.

Firstly, in the children who are off-colour, underweight, and complaining of "growing-pains", an abnormal viscosity value leads to the diagnosis of an active lesion which must be treated accordingly with rest in bed, salicylates, etc., even if the ESR is normal; similarly, an abnormal ESR must take precedence

over a normal viscosity. An abnormal gold flocculation test is further support to the diagnosis of an active process.

Secondly, the plasma viscosity is the best guide to the time at which the disease is sufficiently convalescent to permit the passage from complete rest towards active movements. The ESR test has long been used for this purpose. Some clinicians, such as Reid et al. (206), regard this aspect of the ESR test so highly that they are prepared to use it as the criterion of cure in their consideration of the mode of action of salicylates. One of the fluctuations in the ESR curve might take it into the normal range and then return to the abnormal again without there ever arising the question of a relapse from cure; such would be the general interpretation of such a sequence in the plasma viscosity test. As long as the patient has a raised plasma viscosity, then so long must the patient be kept at rest in bed.

Prognosis. The case which is progressing in a satisfactory manner has serial plasma viscosity results which show a corresponding decrease. A relapse or complication will be indicated by an increased viscosity. The individual case, B.R., is an excellent example of this correlation between clinical change and laboratory test result.

The 'Zone of Chronicity' is also found in rheumatic fever.

The mean value of the 13 tests in the table is 2.052 , which is very close to the means of infective and rheumatoid arthritis. These cases were more than an acute attack lasting several weeks: they were cases in which the arthritic signs and symptoms were often negligible and the general malaise being important. Some of these patients could even work in spite of the evening rise of temperature, tachycardia, etc. The finding of the characteristic viscosity level was the most significant single piece of information in the examination of such patients. (see Fig. 80 b)

Treatment. The plasma viscosity serves as a useful guide to the effectiveness of treatment. A satisfactory regime is associated with a decreasing viscosity which should reach the normal range of values; an unsuitable mode of treatment or an inadequate dosage of a suitable drug will be accompanied by a slower fall in the viscosity or even by an increase. Such an example is the case, B.R. , already cited.

The plasma viscosity results were not increased beyond the level the clinician might expect from the severity of the general upset in the patient. This point is important in that it is rather against the theory that the rheumatic fever is due to an allergic state with a hyper-sensitivity to a streptococcal infection; in an allergic reaction, one would have expected an

unusually high viscosity value, such as we find occasionally in cases of erythema nodosum. Wilson and Lubschez (255) have found that the protein pattern changes by electrophoresis are the same as in other acute infections: they wrote -"No evidence was obtained in these studies that the immune responses of rheumatic subjects to infections presumably streptococcal in origin differed from that of non-rheumatic individuals".

The high incidence of positive gold flocculation tests is to be noted. The percentage of positive reactions, however, does not compare well with those of the Weltmann Serocoagulation Reaction test which, in the hands of Nelson and Seal (180), had a correlation with the clinical assessment of from 93 to 99 %. They showed that this correlation was better than that for the Cutler ESR. It will be of interest to compare the Weltmann test with the plasma viscosity test. Even if the Weltmann proves to be the superior in rheumatic fever it is very unlikely that it will be applicable with the same accuracy to all diseases producing a systemic reaction in the same way as the plasma viscosity test can be applied.

* * * * *

CHOREA.

The plasma viscosity test was applied to a small series of cases of chorea; there were few opportunities for investigating this condition as these patients seldom required other biochemical tests.

Results. These are given in Table VI of the appendix.

The results can be divided into two groups - (i) where no other evidence of rheumatic activity was found, the plasma viscosity was within the normal range even when the involuntary movements were so severe that it required the assistance of two nurses to keep the patient's arm sufficiently steady for the blood sample to be taken, and (ii) where there was evidence of rheumatic activity by joint pains or carditis, the plasma viscosity was usually increased.

Discussion. A recent annotation in the British Medical Journal (Jan., 6, 1951) on chorea quotes* the study by Lewis-Jonsson on 704 choreic patients in Scandinavia. 467 of these showed other evidence of rheumatic activity (polyarthrititis, carditis, erythema annulare or nodules); 22 followed non-rheumatic disease such as encephalitis, hemiplegia, etc.; there remained 215 cases of cryptogenetic chorea which because of the similarity in age, sex, and seasonal incidence to that of frank rheumatic chorea he has

(* = all these references have now been checked by author)

concluded to be monosymptomatic rheumatism. This is further supported by the quoted work of Sutton and Dodge (239) who found that in 91 cases of initially uncomplicated chorea while only 10% had heart disease after 3 years, no less than 40% had it after 10 years. Kagan is also quoted as claiming (265) that from the ESR he could detect which cases would eventually develop rheumatism, because in their 165 patients a normal ESR during the first attack indicated that rheumatism was not the cause: this conclusion is at variance with that of Lewis-Jonsson (145) who found a normal ESR in nearly half of 150 cases of rheumatic chorea. The experience of most clinicians is that if the ESR is raised in chorea then some other rheumatic sign, such as carditis, is usually present, but that in uncomplicated chorea, even if the patient later develops rheumatism, the ESR is usually normal. Evidently the factor in rheumatic infection which causes a raised ESR is not the same as that which gives rise to choreic symptoms.

My results would indicate that the last two sentences of the previous paragraph could be written with "plasma viscosity" in place of "ESR". The uncomplicated cases, in which no other sign of rheumatic activity was detected, had normal plasma viscosity values. Not all the cases with carditis or other signs of activity showed a raised value but several of them did so.

The normal values associated with carditis, etc. cannot be taken as evidence of failure by the plasma viscosity test; these choreic patients were all hospital in-patients where they had been sent because of the severity of their involuntary movements or because they had not responded to treatment at home. If the patient had been admitted after salicylate therapy, the 'activity' in the joints might have been controlled although the symptoms of chorea persisted. Such a case was D.V. in whom the first plasma viscosity test was made early in the disease condition and in whom salicylate therapy had been begun prior to the testing.

The case of M.F. is particularly interesting. The persistent high plasma viscosity and ESR tests caused repeated searches for other signs of rheumatic activity but without success... Her symptoms cleared, she felt very well, and her physician allowed her to resume her normal mode of life. As she was menstruating twice per month there may be a gynaecological cause for these high values, but I am most interested in her future history as her present values are definitely abnormal and almost within the zone of chronicity.

The normal gold flocculation results in all but one patient are also remarkable. This incidence of abnormal values is much lower than is found in rheumatic fever itself or in erythema nodosum of rheumatic origin. This is additional support to the

hypothesis that in chorea the rheumatic mechanism is not acting exactly as it does in rheumatic fever.

If a normal plasma viscosity value is found early in chorea, if there is no other sign of rheumatism in the heart, joints or skin, and if salicylates have not been administered, the clinician may treat his patient as a case of uncomplicated chorea; we do not yet know how this normal value is related to later evidence of carditis. If an abnormal plasma viscosity is found, the patient should be treated as a case of rheumatic fever until there is very strong evidence that this activity has ceased.

Further researches on the lines of the long-term studies of Lewis-Jonsson and of Sutton and Dodge may yield valuable information regarding the significance of the plasma viscosity results from a prognostic aspect. Similarly, further researches are required into the response of the gold flocculation test and other tests which depend upon abnormal protein fractions.

* * * * *

Erythema Nodosum.

This is a suitable point at which to discuss Erythema Nodosum as this syndrome of skin lesions and other symptoms has been claimed to be related to rheumatic fever. More recently a tuberculous primary cause has been favoured more.

Results. These are presented in Table VII of the appendix.

The plasma viscosity was increased when the disease began, and the return to normal values took weeks or months.

The gold flocculation test was abnormal where the primary stimulus was a sore throat.

Discussion. In an authoritative paper based on a study of 155 patients, Favour and Sosman (77) concluded that erythema nodosum is a hypersensitivity disease; there is an individual predisposition but a variety of infections and chemical agents and local trauma contribute to its occurrence. They found an associated respiratory infection in 80% of attacks, in half of which a beta haemolytic streptococcus was isolated from the throat. They were against the commonly-held idea of a tuberculous or rheumatic causation as, in their experience, tuberculosis was a rare antecedent infection and rheumatic heart disease was a rare sequela.

The increase in the plasma viscosity would be in agreement with the hypothesis of a hypersensitivity reaction in some

instances. The values for M.W., A.E., and M.C. were surprisingly high because there was no other sign of a severe general reaction and the patients did not feel severely ill. Moreover, the severity of the upset in the protein metabolism was shown by the plasma viscosity values persisting at abnormal levels long after the primary condition had cured and the patient had resumed the normal mode of living.

My series contains an unduly large proportion of cases of tuberculous origin but this arose from an inadvertent selection of cases; for a period I collected all the blood samples from the tuberculosis wards and if this condition was mentioned I added enough blood to allow me to estimate the plasma viscosity also.

The results of the gold flocculation test were particularly interesting. Their number is too few to permit of confident assertions but I consider that they suggest a possible correlation between the abnormal positive values and sore throat (probably streptococcal) and between normal negative values and other types of primary stimulus. An intensive study of the gold flocculation test in relation to the nature of the primary stimulus in erythema nodosum was planned in collaboration with Dr. Inman, specialist in skin diseases at Sunderland, but was one of the researches which I had to abandon when I left that town; there has been no later opportunity of resuming this investigation.

(E) Osteo-arthritis.

Synonyms:- Osteoarthrosis; hypertrophic, or degenerative, or non-ankylosing arthritis.

Results. These are given in the TableVIII of the appendix.

They are also presented graphically in Fig. 84 , which includes a tracing of Gibson's results (87) for the same condition.

Of the 36 tests on 32 patients exactly half were still within the normal plasma viscosity range, and the abnormal values fell into the lowest part of the abnormal range.

Discussion. I will quote from Gibson's paper (87) - "My experience has always been that in true osteo-arthritis, as found for example in the hip or knee, the B.S.R. is typically in a zone just outside the normal range. This is illustrated in fig. 8, in which the distribution of results in 42 cases is compared with 40 controls. The shift to the right is apparent.

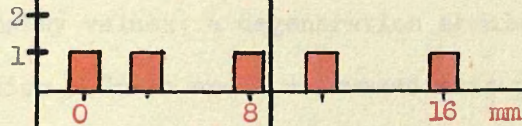
The viscosity in the same series shows the same shift to the more abnormal groups. The highest number in the controls is in the 170-179 range while in osteo-arthritis it is from 180-189. As in the case of R.A. the graphs again show the spread of B.S.R. results is further from the normal line than that of viscosity, indicating a rather greater sensitivity in the former."

My ESR. results were not nearly as abnormal as Gibson's, as I found 5 abnormal tests in a total of 23; they do confirm that

OSTEO-ARTHRITIS.

Males

ESR.

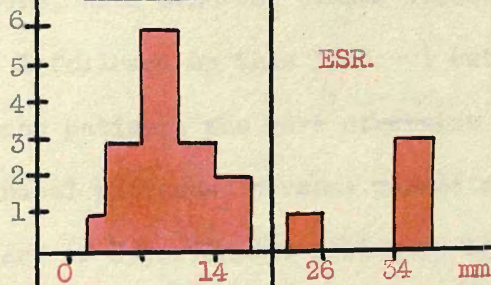


Plasma Viscosity

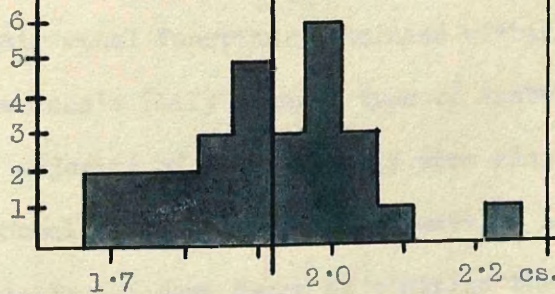
Number of Cases.

Females

ESR.



Plasma Viscosity



Pl. Viscosity

Normals

O. A.

ESR.

Normals

O. A.

Gibson's Results.

Fig. 84 The Plasma Viscosity and Corrected Wintrobe ESR. tests in Osteo-arthritis. The inset figure is a tracing of Gibson's diagram of his results in this condition.

the abnormal ESR. values are in the zone just outside the normal range.

As the disease is of a degenerative rather than inflammatory nature I was rather surprised to find so many abnormal plasma viscosity values; a degeneration should not produce a systemic reaction. Cowan and I discussed this point on several occasions. He eventually correlated the viscosity values with the general condition rather than the local lesions and was thereby enabled to divide his osteo-arthritic patients into two groups - (1) an elderly group, of spare build, with normal plasma viscosities, and (2) a middle-aged group, with obesity and/or high blood pressure, with abnormal plasma viscosities.

I followed up this lead. I estimated the plasma viscosity of obese patients who were otherwise apparently normal, eg. ante-natal patients, persons passed as satisfactory for emigration, etc. and of hypertensive patients, eg. ante-natal or essential hypertension patients who were referred to me for the estimation of their renal function: included within these groups were several of Lawrence's (141) younger type of diabetes mellitus. The large majority of these results were also found to lie just above the normal zone, between approximately 1.935 and 2.065 cs. This is exactly the same range as contains the highest incidence of the osteo-arthritis results.

I therefore have ascribed the increased plasma viscosity results not to a systemic reaction to the local joint lesion but to a systemic reaction to general obesity or hypertension.

A clinician who encounters an osteo-arthritic patient with an increased plasma viscosity must realise that the general condition also requires treatment in addition to the damaged joint. The plasma viscosity test might be used to distinguish between the obese, who are in need of reducing, and those who, by heredity, tend to be robustly built.

Gibson's plasma viscosity results are similar to my own.

In contrast to rheumatoid arthritis, the gold flocculation test in this disease is usually negative.

Kellgren and Moore (133) have recently distinguished a clinical entity within the osteo-arthritis group of patients, for which they have suggested the name of "primary generalized osteo-arthritis". It was found most frequently in middle-aged women. These authors stressed that it was a constitutional disorder. The ESR. was frequently slightly increased. It would appear, therefore, that the plasma viscosity was probably making the same separation but that we had lacked the clinical acumen to follow it to the full potential possible.

* * * * *

(F) Fibrositis.

Fibrositis is a disease of doubtful aetiology, doubtful pathology, and even doubtful existence - some writers have denied that there is such a disease as fibrositis and have suggested that this diagnosis covers a failure to recognise its true nature. I have applied this diagnosis to the cases of painful and tender induration of the subcutaneous connective tissue (panniculitis) and of the fibrous tissue of the muscles (myositis).

Results. The details of the 32 tests are given in Table IX of the appendix. They are also presented graphically in Fig. 85. which includes a tracing of Gibson's results.

Discussion. Although the local pain may be very severe and although large areas may be involved, there is no indication of a general upset in the body - there is no elevation of temperature, anaemia, loss of weight, etc. The absence of a systemic reaction explains why the majority of the plasma viscosity values have remained within the normal range. Until we have learned more about the pathology of the disease we cannot be certain why it does not cause a systemic reaction.

The gold flocculation tests were normal except for two instances.

Gibson confirms our findings in all respects.

* * * * *

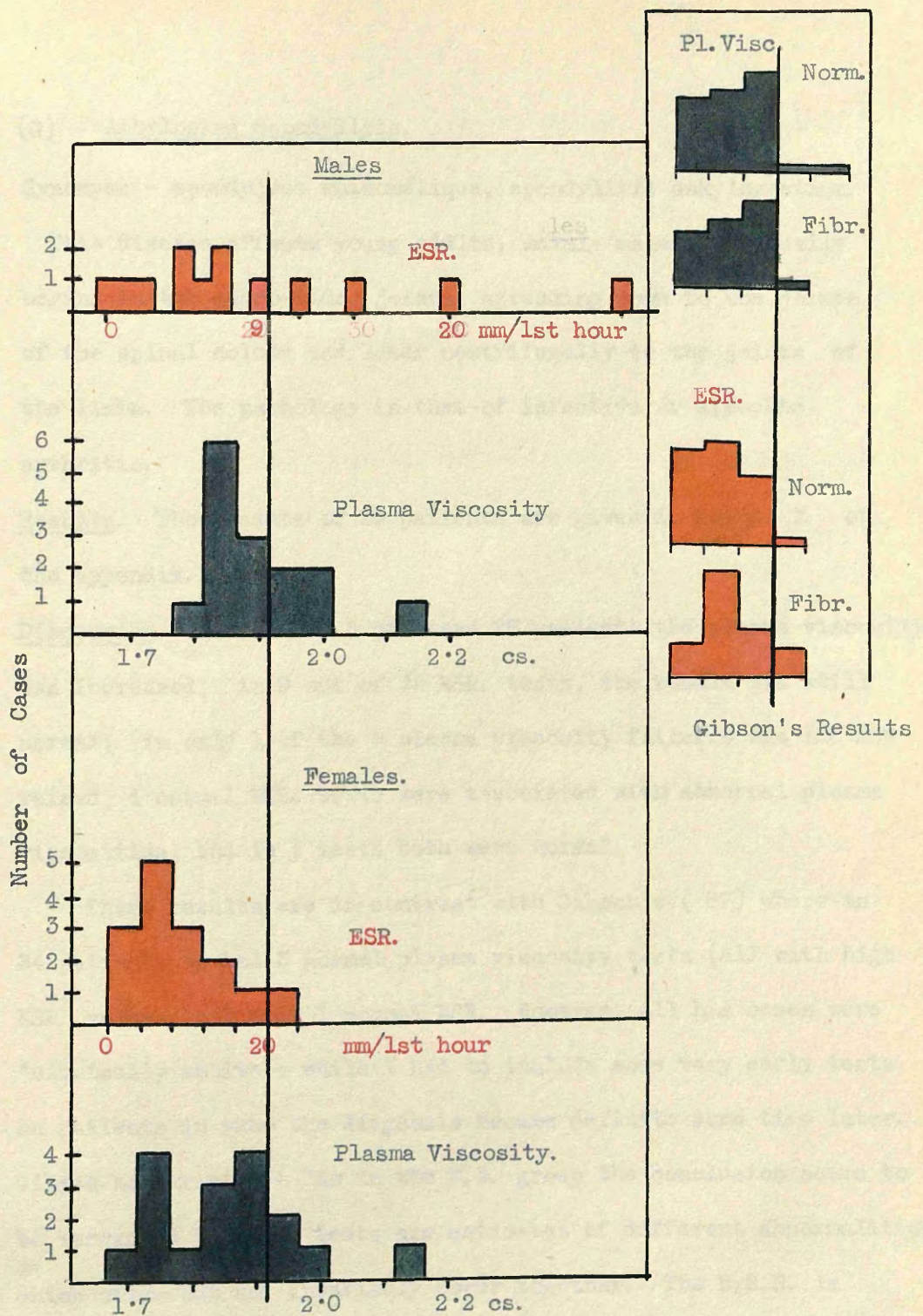


Fig. 85 The Plasma Viscosity and ESR. results in Fibrositis.

The inset figure represents a tracing of Gibson's results for this condition.

(G) Ankylosing Spondylitis.

Synonyms - spondylose rhizomélique, spondylitis ankylopoetica.

This disease affects young adults, mainly males; it usually begins in the sacro-iliac joints, spreading soon to the joints of the spinal column and later centrifugally to the joints of the limbs. The pathology is that of infective or atrophic arthritis.

Results. The results of 26 patients are given in Table X of the appendix.

Discussion. In all but 5 of these 26 patients the plasma viscosity was increased; in 9 out of 22 ESR. tests, the result was still normal; in only 1 of the 5 plasma viscosity failures was the ESR raised, 4 normal ESR. tests were associated with abnormal plasma viscosities, and in 4 tests both were normal.

These results are in contrast with Gibson's (87) where in 34 patients he had 3 normal plasma viscosity tests (all with high ESR. values) and only 1 normal ESR. However, all his cases were "clinically active", while I had to include some very early tests on patients in whom the diagnosis became definite some time later. Gibson has written - "As in the R.A. group the conclusion seems to be warranted that the tests are estimates of different abnormalities which often but not invariably occur together. The B.S.R. is rather more sensitive but in order to secure the maximum of

information both should be applied." My ESR. results do not support his contention regarding the greater sensitivity of that test, but this may be due partially to his better ESR. technique. Even allowing for that, I cannot see how his method could increase my results of 2 or 4 mm./1st hour to abnormal levels.

The proof of the plasma viscosity superiority is being shown by the Portsmouth clinicians who apply the plasma viscosity test to all the patients with vague pains of the sacro-iliac region because they now believe that an abnormal viscosity is a strong indication of an active disease which may be later definitely diagnosed as ankylosing spondylitis; the ESR. has been discarded. (These results have not been included as in many of the recent tests the clinician is unable to state a diagnosis.)

The results also indicate how the disease activity has persisted for 7 or 8 years, with the typical "chronic" viscosity values.

One patient was treated with great benefit with A.C.T.H. and his case notes have been included.

The low incidence of abnormal gold flocculation tests (confirmed by Gibson) is in support of the hypothesis that the general character of this disease is different from that of rheumatoid arthritis, in spite of the similarity of the pathology of the local disease in the joints. (See also Mowbray (270))

(H) Gout.

The series of cases includes an unusually large proportion of female patients; gout was found to be much commoner in the female population around Sunderland than one would have expected from reading about the disease in medical text-books.

Results. The results from 16 patients appear in Table XI of the appendix.

Discussion. In the acute attack, the plasma viscosity is increased just as in any other type of acute inflammation of an important structure.

The diagnosis in many patients was made with difficulty from rheumatoid arthritis; the gold flocculation test was positive sufficiently often in the cases of gout as to be of little assistance.

One case in which the chronic activity persisted for 18 months had several plasma viscosity tests during this period; the values came within and just above the usual zone of chronicity.

The ESR. test has produced a series of results here which coincides completely in the interpretation with that of the associated plasma viscosity tests.

* * * * *

§ 3. The plasma viscosity in tuberculosis.

As the plasma viscosity estimation is recommended for use in those clinical conditions in which the ESR has hitherto been the accredited test, it was natural that I studied the viscosity test in the different types of tuberculous disease.

(A) Pulmonary Tuberculosis.

Statistical analysis of my results for pulmonary tuberculosis has not been possible, as for the rheumatoid arthritis. My early Montrose results were derived from the patients of an asylum. No X-ray facilities were available. The patients usually swallowed their sputum and gastric lavage was not considered a possible procedure as it would have involved the use of restraint. Thus the clinical assessment, and even the diagnosis, would have been based on evidence too weak to warrant inclusion in a thesis which attempts to assess the correlation between the clinical condition and the plasma viscosity results. My later Portsmouth results came chiefly from a selected series of patients chosen specially because this correlation was expected to be low. The intermediate Sunderland results were satisfactory but too few in number.

Methods. The plasma viscosity has been studied with sodium citrate solution and mixed oxalates as anticoagulants; the ESR was correspondingly measured as a maximum sedimentation velocity and as the Wintrobe 1-hour value, corrected by graph for variation

in haematocrit values. The plasma proteins were fractionated by the salting-out technique of Howe.

Material. No special choice of subject was made at Montrose or Sunderland. At Portsmouth a special study was made of the cases picked-up by the Mass X-ray unit, the cases on streptomycin therapy, and a series of 59 consecutive cases in whom there was a positive sputum accompanied by a low ESR value (ie. Westergren less than 10 mm./1st hour).

Results. These are given in detail in Table XII of the appendix.

These have been summarised into tables within the text and in the figures.

The cases were classified according to the Ministry of Health scheme (166) which can be briefly summarised as follows:-

- A - category: in whom tubercle bacilli have never been discovered,
 - B - category: in whom tubercle bacilli have been found at some time.
- Each category is subdivided as follows:-

- Group 1. Slight or no constitutional disturbance; physical signs and radiological findings of very limited extent; no complications (tuberculous or other) of prognostic gravity.
- Group 3. Profound systemic disturbance of constitutional deterioration, and marked impairment of function, either local or general; all cases with grave tuberculous or non-tuberculous complications are placed in this group.
- Group 2. All cases which cannot be placed in Group 1 or Group 3.

A patient once classified in category-B can never enter category-A;

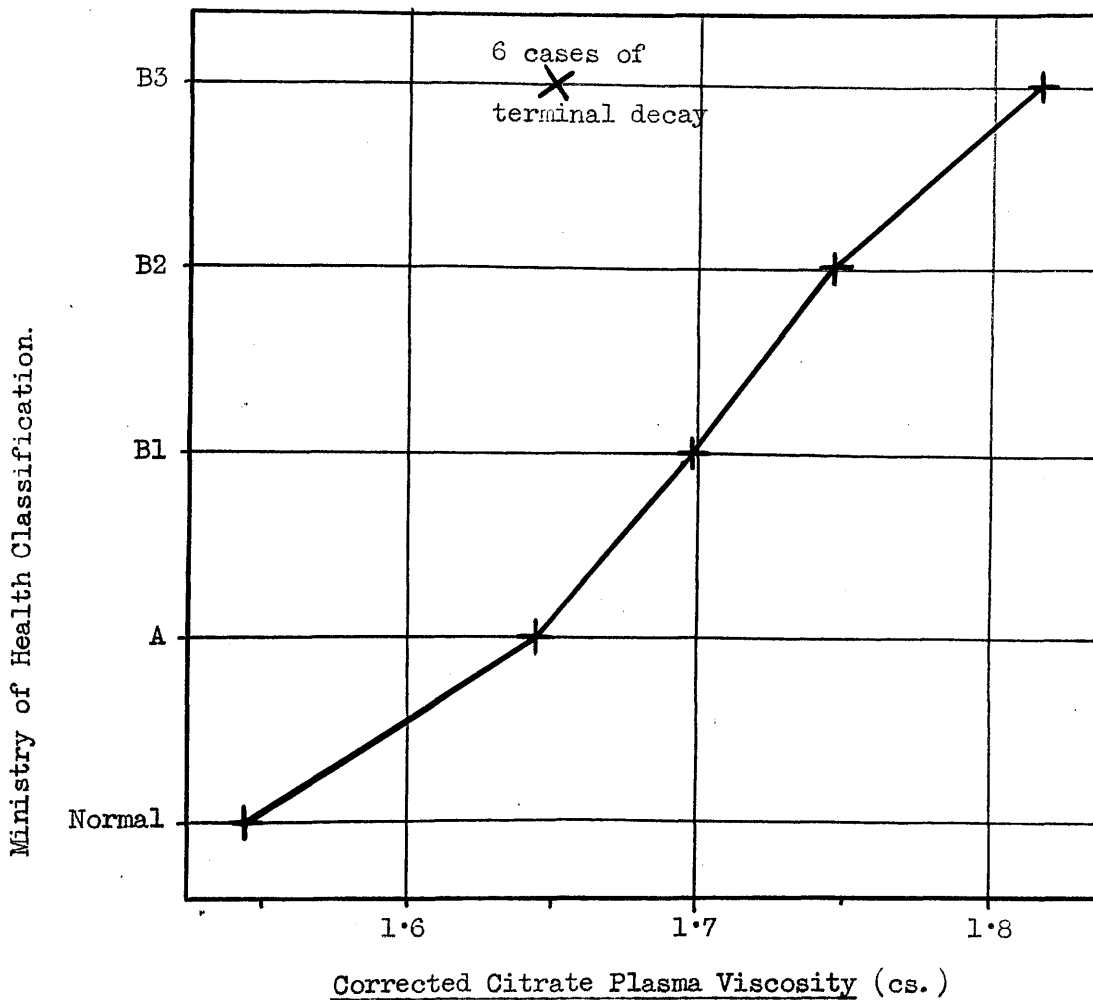


Fig. 85 (Taken from our paper - Houston et al. (120))

The distribution of the mean plasma viscosities in the groups of patients classified according to the Ministry of Health (166) scheme.

330 tests were made on 289 individuals.

37	normals,	with mean of	1.544 cs.
44	in group A,	" "	1.644
43	" " B1,	" "	1.698
152	" " B2,	" "	1.746
46	" " B3,	" "	1.817
6	" " B3,	" "	1.650 cs., who were in
	the state of terminal decay.		

a category-A may have to be changed to category-B should the sputum become positive at a later stage of the disease.

Dr. A. B. White, chest-physician to Portsmouth, was responsible for the clinical assessment of his cases. He was interested in the correlation of the physical signs, the X-ray appearances, the laboratory investigations, and the symptoms in order to determine which were the most reliable indications of "activity" in this disease. He made his clinical assessment without the knowledge of my laboratory results, except in those cases where the discrepancy was so great that the patient had to be reinvestigated (eg. patient J.F.) (178).

Discussion. The discussion can be made under four main headings.

(i) the correlation of the plasma viscosity with the clinical condition, (ii) the comparison of the plasma viscosity and the ESR tests, (iii) pleural effusion, and (iv) "terminal decay".

(i) The correlation of the Plasma Viscosity and the Clinical Condition in Pulmonary Tuberculosis.

From the tables of results, graphs, and individual case reports the following claims may be made.

(a) The presence of active tuberculosis was accompanied by an abnormal viscosity in 91% of the tests, although there were included convalescent patients in whom it might be argued that the disease

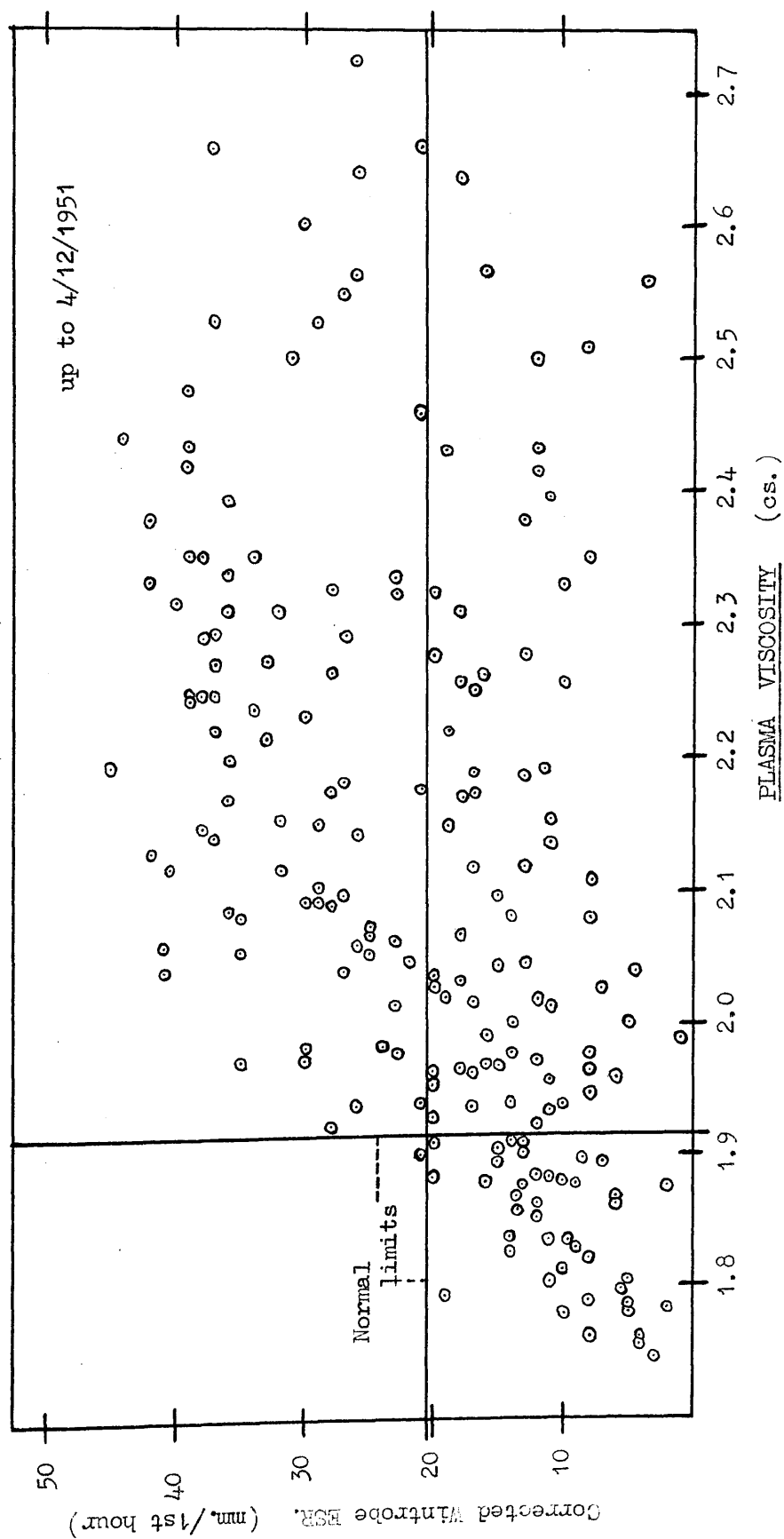


Fig. 87 The results of tests on all female tuberculous patients (active and quiescent) in Portsmouth series

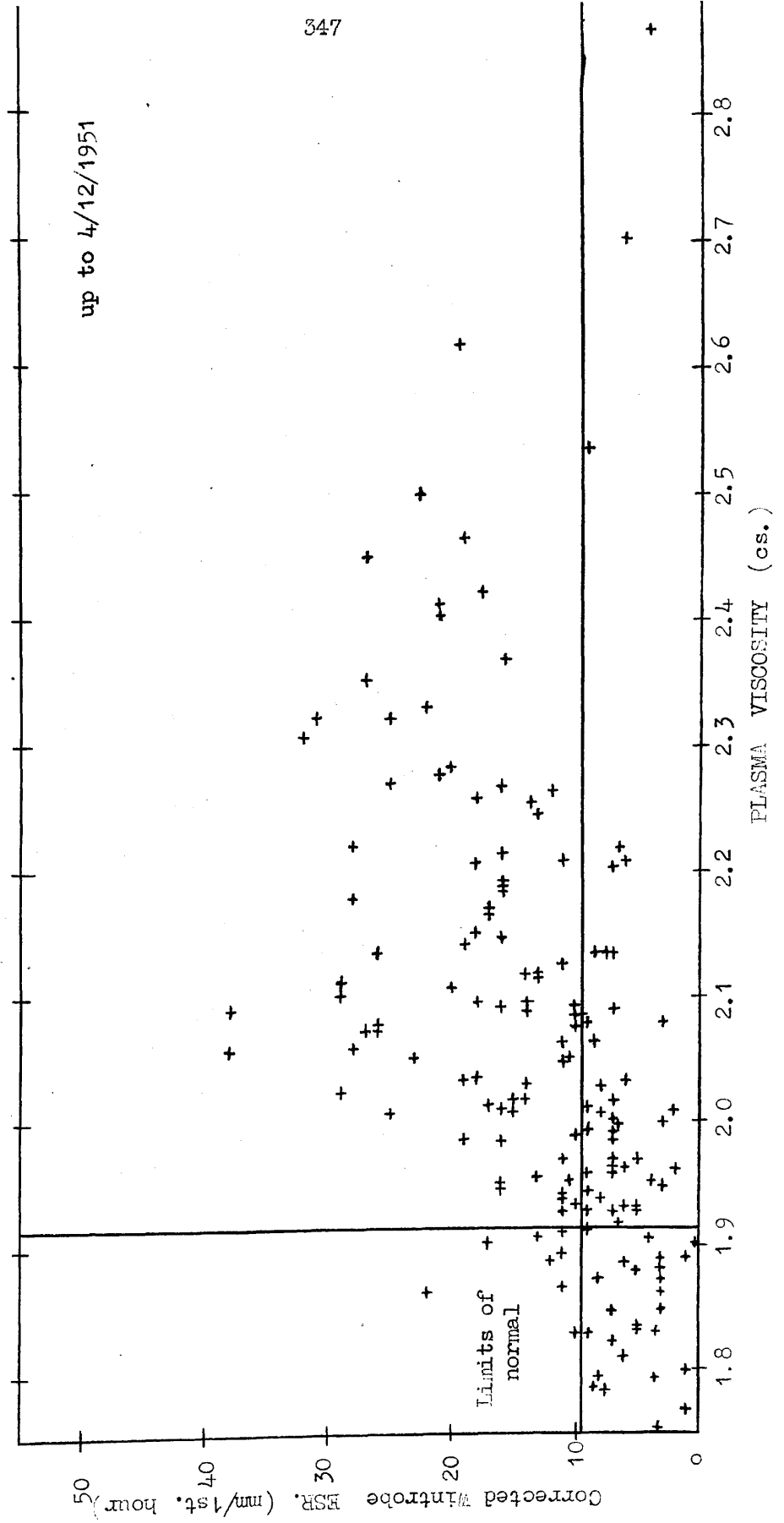


Fig. 88 The results of tests on all male tuberculous patients (active and quiescent) in Portsmouth series.

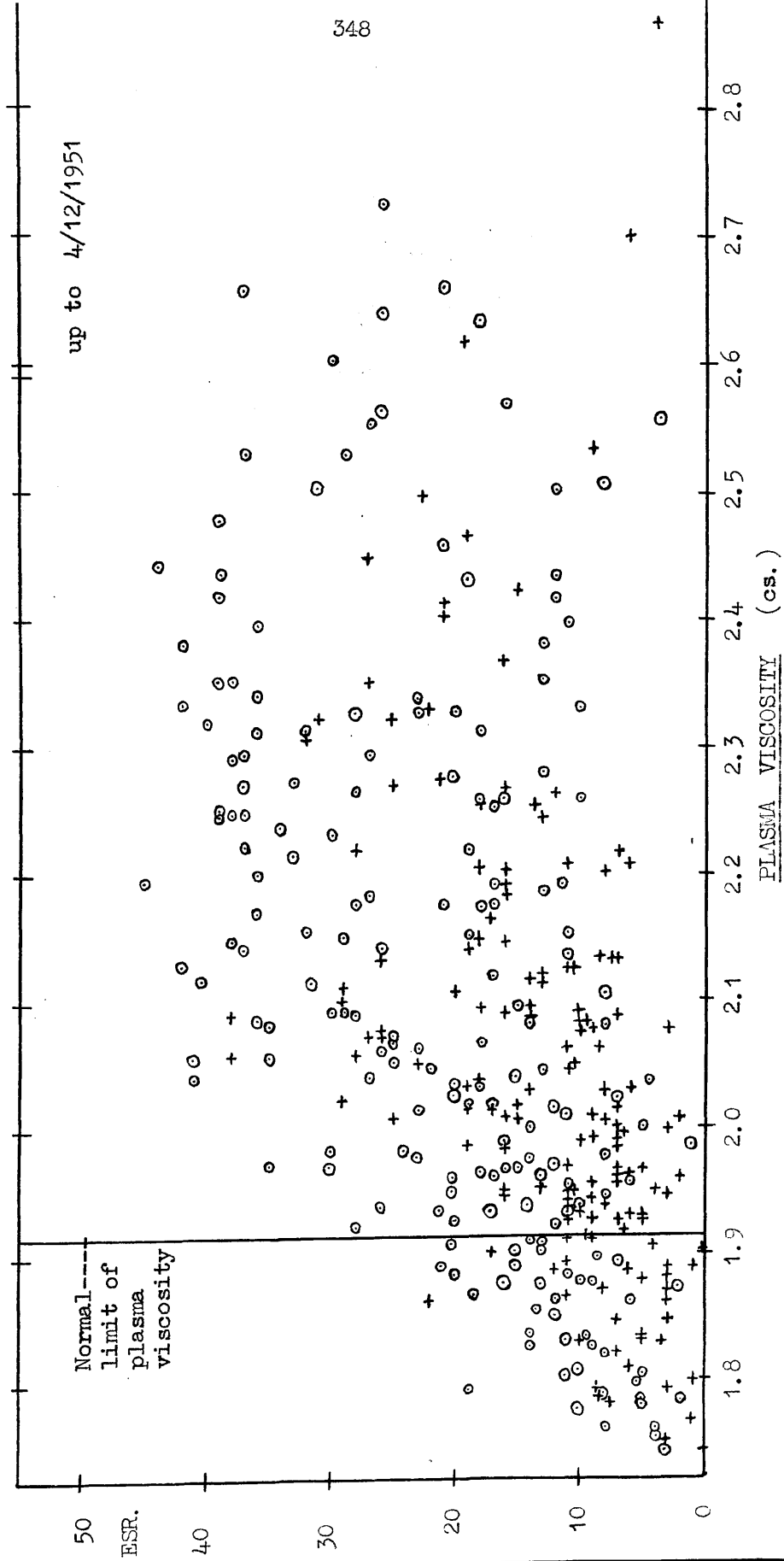


Fig. 89 The combined results of all the tests on tuberculous subjects at Portsmouth.

As many were tested who were quiescent, all results within the normal zone were not failures.

was becoming quiescent.

(b) Where the clinical condition is assessed on a quantitative basis, there is a good correlation between the degree of clinical severity and the amount by which the mean viscosity is increased above normal levels.

I include the results from the Frodsham sanatorium which were included in our combined paper (120); the decision to place the lines at equal distances apart was purely arbitrary as there is no criterion by which one can judge exactly how much B.3 exceeds B.2 as compared to how B.2 exceeds B.1 . (Fig. 86)

(c) The scatter of the results about the mean in each group is so great that there is an overlapping of adjacent groups. The plasma viscosity test cannot therefore be used as an absolute guide to the clinical assessment.

(d) The plasma viscosity reflects the general reaction to the disease. As the reaction called forth is increased on account of greater clinical severity because of the involvement of more tissue, by the spread to other lobes, or by complications the plasma viscosity increases; as there is clinical improvement as a response to therapy the plasma viscosity decreases until, in a satisfactory case, the value may again fall within the normal range.

(e) In serial tests on individual patients, the plotted results

lie on fairly smooth curves. These curves are parallel to the general trend of the clinical condition.

A worsening or complication is reflected in the laboratory results as a definite peak occurring in the course of the curve; the time interval between the stimulus, such as the induction of a pneumoperitoneum, and the appearance of the peak is short; this indicates that the plasma viscosity estimation is a sensitive index of the concurrent clinical state.

Examples of these curves are given with the case histories, in the appendix.

As in other diseases, the plasma viscosity changes in pulmonary tuberculosis reflect the changes in the plasma protein fractions. My salting-out technique shows that the initial change is an increase in fibrinogen, followed by an increase in globulin; the albumin decreases and in very severe cases may reach 3g./100ml. or less. With improvement, these changes are reversed, the albumin being the last to regain the normal range. These results have been confirmed by the papers of other workers (67, 73, 126, 164). Seibert et al. (225, 226, 227), with electrophoretic studies, show that in the early stage of human pulmonary tuberculosis the first serum globulin to change is the gamma fraction - "it is reasonable to suspect that the rise in this component in the early stage of

the disease process may represent an antibody reaction of the organism". As the disease progresses, the next change is in the α_2 globulin. Finally there is an increase in all the globulins, especially the α_2 fraction: the increase in globulin is balanced by a fall in albumin so that the total protein does not rise. This last claim regarding the normal levels of the total protein has been confirmed in my tests where the measurement was made by a specific gravity technique.

The estimation of the protein fractions is used as a test of liver function. There is additional evidence of altered function in tuberculosis in the bromsulphalein results of Hurst et al. (124) and Kruger and Gerber (136), and in the prothrombin index results of Savacol and Chodoff (221) who write -"in fact, the plasma prothrombin level appears to be a fairly sensitive index of the activity of pulmonary tuberculosis". Hurst could find no significant histological alterations in the liver to account for the modified function, except in those cases complicated by amyloid disease.

It should be noted how infrequently a positive gold flocculation test is encountered among my results, even in the presence of a high plasma viscosity - this may be explained by the smaller changes in the gamma-globulin as compared to rheumatoid arthritis and similar diseases.

(ii) A comparison of the Plasma Viscosity and ESR tests in
Pulmonary Tuberculosis.

There is still no agreement on the relationship of the plasma viscosity to the ESR in pulmonary tuberculosis except that the plasma viscosity is the more informative test.

When I had found a normal ESR associated with a very high plasma viscosity in E.B., one of my earliest Portsmouth tuberculous patients, Dr White and I decided that a suitable comparison of the tests could be made in just those cases where the ESR was so obviously at fault. We collected a consecutive series of 59 patients in whom the clinical "activity" was guaranteed by the detection of tubercle bacilli in the sputum within a month of the laboratory tests and in whom the preliminary Westergren ESR was 10 mm. or less. The state of the patients varied widely from sanatorium patients on full bed rest to convalescent patients who were doing a complete day's work and attending the out-patient department or chest clinic. Dr. White used this series also to determine the relative value of the different criteria of "activity" available to himself - eg. X-ray, physical examination, weight loss, temperature fluctuation, etc. - and it is hoped that we will publish our combined results.

Method. I collected the blood from all of these patients. From

a single sample a Wintrobe ESR was measured and the viscosity of the plasma. The usual correction in the ESR for haematocrit variation was made because in several instances the ESR was low as a result of excess of erythrocytes.

Results. These are given in detail in Table XII of the appendix.

They can be summarised in the following table:-

		WINTROBE ESR.			
		Normal	Abnormal		
PLASMA VISCOSITY	Normal	9	4	13	22.0%
	Abnormal	35	11	46	78.0%
		44	15	total	
		74.6%	25.4%		

In addition to this special series, the reader should consider the total tuberculosis results as presented in Fig. 87, 88, 89, and some of the case histories.

Discussion. By statistical analysis (110) the results in the table of this page are significantly different. The duplicate tests have yielded information in 4 instances only (all males) more than obtainable by the plasma viscosity alone. These results support my contention that the plasma viscosity is the more

reliable test. They also emphasise, however, that the plasma viscosity test itself is not infallible, as some of the cases with normal values had advanced to definite cavitation.

The three figures were constructed from every test made in Portsmouth on tuberculous subjects; they therefore contain the tests made several years after the acute episode when the possibility of a relapse was under consideration and they include the tests performed well into the convalescent stages of the disease: thus, a value within the "normal" range is not always equivalent to a failure to diagnose an active lesion. The plasma viscosity may show "normal" values occasionally in the presence of disease but it never shows abnormal values in the absence of disease; hence every result in the lower right segment of the figures is equivalent to a failure of the ESR test: compare these large numbers with the few instances indeed where the opposite has occurred, in the upper left segment. These diagrams also show how the ESR test suffers by having an upper maximum limit as compared to the virtual limitless scale of the viscosity.

The reliability of the ESR test in pulmonary tuberculosis has varied tremendously from worker to worker. I cannot refer to every paper on this subject and will confine myself to a few representative examples. Wintrobe (256) reviewed the ESR test

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and quotes^{*} Baryai and Anderson as finding only 7.35% normal ESR values in tuberculosis (2,000 patients), Cutler as having 5 normal tests in 5,000 patients, and Friedman and Kaminsky as finding not a single discrepancy (11,56,131,85). These reports are difficult to correlate with the report of Noehren (165) who found that slightly more than one third of his patients (U.S. naval personnel) never had an abnormal ESR throughout the whole course of the disease. Sinton found the agreement between the ESR value and the clinical assessment held good in 54% of his tests only (271). McIntosh and Keay (132,173) are particularly critical of the ESR, concluding with the sentences - "Since in the female subject the test carries an error of anything from 12 to 30% its employment is, for practical purposes, valueless. No other test having an error of this magnitude would be tolerated in practice. Those seeking guidance on the E.S.R. should follow the advice of Hilliard (1942), who "abandoned the use of blood sedimentation tests long ago." ". They also include an informative table concerning the number of abnormal ESR tests which were obtained by other workers in the cases picked up in Mass X-ray units and classified as "active" tuberculosis - this table is given at the top of the next page.

(* = these references have now been checked by the writer,

	No. of subjects examined with active tuberculosis	No. of abnormal E.S.R.s
Stiehm (1933) (238)	69	33
Braeuning (1938) (32)	75	33
Clive (1943) (43)	102	84
Kahan and Close (1944) (130)	138	27
Robinson (1944) (209)	45	35
Abeles and Pinner (1944) (1)	91	54

The literature concerning the plasma viscosity in tuberculosis is short, only two independent papers having to be considered. T'ang and Wang (240) have the credit of first suggesting the use of the estimation of the plasma viscosity as a test in clinical pathology, although there had been previous reports of changes in the plasma viscosity in disease. Their paper appeared in 1940 but it did not come to the attention of British readers until 1946 by which time Whittington and myself had got our independent work published. They studied blood preserved with a 1 in 10 dilution with 3.8% sodium citrate solution, so that their results are not directly comparable with any of mine: this difference is shown in their 'normal' range of 1.500-1.714, with a mean of 1.627. They also used a temperature of 25°C. Their results for 176 cases of pulmonary tuberculosis are given in the table on the next page. Discussing the relative sensitivity of the plasma viscosity and the ESR as indications of the activity of tuberculosis they wrote -

Clinical Assessment	Average Viscosity	Average E.S.R.
50 normal subjects	1.627	4.9
52 arrested tuberculosis	1.623	4.7
69 moderately active	1.744	13.5
55 active	1.920	20.6

"Although our data are not sufficient to allow us to draw a definite conclusion with regard to the relative sensitivity of viscosity and sedimentation test in tuberculosis, from Table 3 it can be seen that there are more cases of active tuberculosis (pulmonary and otherwise) with increased viscosity than with increased sedimentation rate, and this is particularly true in cases of pulmonary tuberculosis of mild activity and tuberculous meningitis. The authors are, therefore, inclined to think that plasma viscosity determination is perhaps a more sensitive test for activity of tuberculosis than the sedimentation rate". "In general, the viscosity of the plasma is parallel with the activity of the disease". They also found that generally there was a parallelism between the plasma viscosity and the ESR.

Benson (16) has studied the two tests in 294 adults who suffered from pulmonary tuberculosis: there were 92% abnormal viscosity results as compared to the 73% abnormal ESR results. "Patients ill with pulmonary tuberculosis generally showed plasma viscosity values which were proportional to the degree of clinical

evidence of activity. As the tuberculous process regressed or attained stability the plasma viscosity values approached normal limits (Table VI). On the other hand, as the disease progressed and became worse the viscosity values remained within abnormal limits (Table VII)." "But whereas the plasma viscosity values appear almost constantly high in a disease such as tuberculosis, the total plasma proteins are very frequently found within the normal range of 6 to 8 g. per cent." "It is concluded that plasma viscosity offers valuable evidence in clinical medicine as a screening method for the determination of organic disease which may cause physiochemical plasma alterations."

(Lawrence (139) has studied the fractional plasma viscosity changes in tuberculosis. Bircher (24) measured the serum viscosity and concluded - "In tuberculosis the refractoviscosimetric quotient of the serum has a definite relation to the stage of the disease".)

My colleague Houston, as a result of his comparison of the tests performed in parallel, has concluded that the ESR test was not worth estimating when the plasma viscosity was available; he has now gone further and discarded the ESR test completely even when the plasma viscosity is not available, as he believes, like McIntosh and Keay, that the test should be abandoned as unreliable. However he is in the position of having to deal only with

patients of a sanatorium in whom the tuberculosis has been diagnosed. In December 1951, Benson informed me that he also had discarded the ESR test completely following his experience with the plasma viscosity test. (17).

From my own results and from a consideration of the work published by others I take up a position almost, but not quite so extreme, like Houston. I retain the ESR for one purpose only - to assist in the diagnosis of doubtful activity. There have been instances when the ESR could yield information not available by the plasma viscosity alone on that problem: the only significant finding is an abnormally high ESR. I consider that the clinician can obtain the information supposedly supplied by the ESR in the course of the disease by other more reliable methods.

(iii) Pleural Effusion : the "Zone of Effusion".

The "Zone of Chronicity" was described in the section on rheumatic disease as a restricted range into which falls the majority of the results from all types of chronic disease. Similarly we have found that in those cases in which there is evidence (X-ray, physical examination, etc.) that the pleural effusion is being formed at the very time of testing, the plasma citrate viscosity comes within Nos. 6 to 8 of the citrate-plasma subdivisions, and to this range we have applied the term - "Zone

of Effusion".

The combined results of Frodsham, Montrose, and Sunderland are presented in Fig. 90 , which is reproduced from our combined paper (120).

The Zone of Effusion applies only when effusions are actually forming, as a static effusion can be associated with almost any plasma viscosity value. We also noted that on tapping an effusion while the patient's plasma viscosity was in this zone, the fluid rapidly reformed. As a corollary, we found that the reabsorption of pleural effusions occurred when the viscosity was above or below this zone.

Three individual cases deserve special mention.

Dr. Houston induced an artificial pneumothorax on a patient while his viscosity was within this zone, and a large effusion rapidly formed.

As the zone of effusion is fairly low in the total viscosity range, it follows that nearly all cases with pulmonary tuberculosis will have a value within this critical range at some time or other yet only a minority have pleural effusions. Dr. Houston had a patient who produced an effusion as she rose into this zone and reabsorbed it when her plasma viscosity was higher: on the later downward passage as her condition improved she had a recurrence of the effusion, which was reabsorbed when her viscosity again

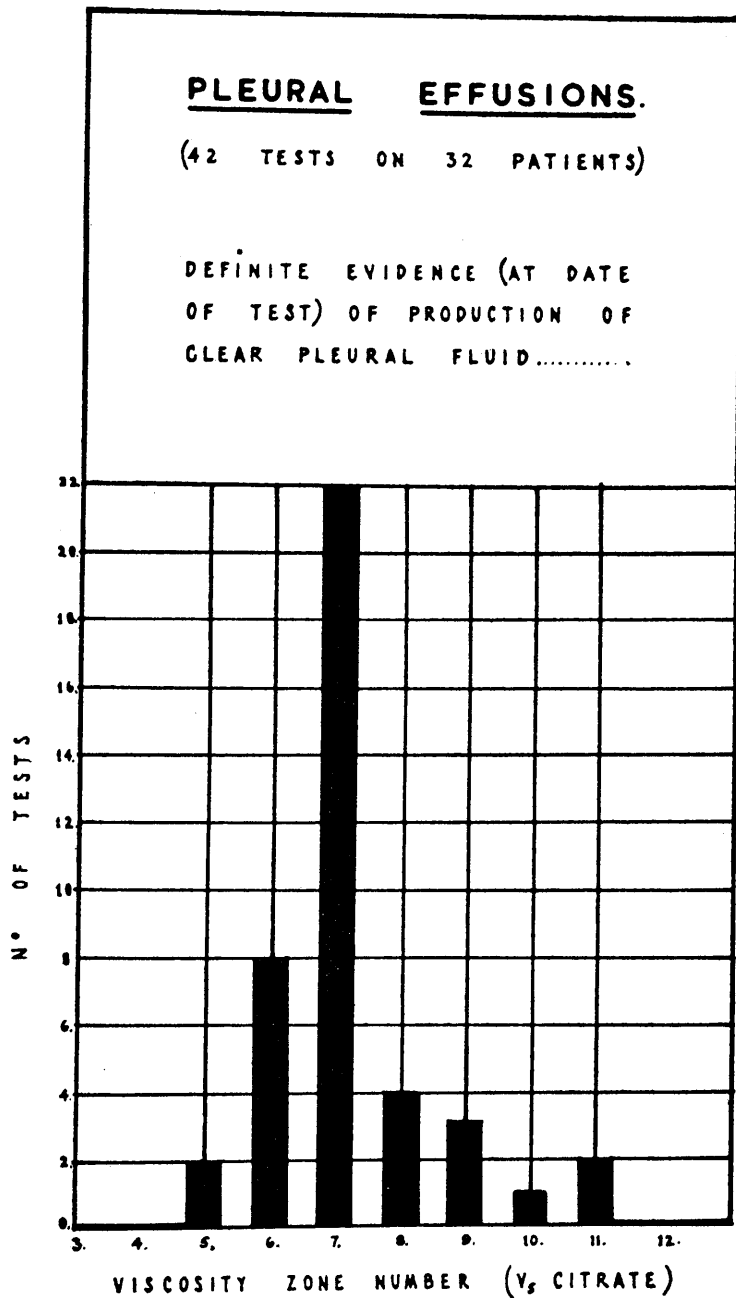


Fig. 90 Taken from our paper (120).

When there was definite evidence that the pleural effusion was actually forming at the time of the test, most of the plasma viscosity values came within zones 6-8. ("Zone of effusion")

rose: on her next downward movement of her viscosity the effusion was again formed and it was again reabsorbed with increase in her viscosity: on her next attempt the plasma viscosity returned to the normal range without complications.

At Sunderland, I was lucky enough to see a child while forming a pericardial effusion (tuberculous) and the plasma viscosity fell within the zone of effusion.

I often discussed this phenomenon with Whittington but we could reach no conclusions which we could subject to experimental study, at that time. One hypothesis is that the formation of a pleural (or pericardial) effusion requires the simultaneous presence of two factors - (1) a pleural endothelial lining in a critical state ready to excrete or secrete the fluid, and (2) a condition in the hydrodynamics of the plasma. If the second factor is a critical osmotic pressure, as it well might be, it is ultimately a question of the condition of the plasma proteins which would explain why the plasma viscosity also becomes involved. The osmotic pressure of plasma and pleural fluids have been studied already without the detection of any characteristic values, but this I ascribe to a failure to make a clear distinction between static and forming effusions; also, the osmometers used in earlier works have all been of the classical "static" type which take days to come to an equilibrium, as contrasted to more

recent "dynamic" types where equilibrium is reached in 20-30 minutes. In a reference which I cannot now trace, I read that by the dynamic instruments it was possible to detect differences in the osmotic pressure in diseases of liver and kidney which were not detectible by static instruments. Therefore, I have now obtained a Simms Osmometer (229) to study this problem but have had no suitable cases to date. In this connection, I have been informed very indirectly that Dr. A. McFadzean found that, in Egypt during the recent war, the formation of a pleural effusion was associated with a specific gravity (and hence with a plasma total protein) of a characteristic narrow range of values. It should be noted that he also was measuring the physical value of the plasma at the time of fluid formation. I understand that he has not published this finding.

Reference to this zone is made later in the discussion on the use of the plasma viscosity in prognosis and treatment.

(iv) "Terminal Decay."

I have referred to the condition for which we have made this title on earlier occasions but this appears to be the most appropriate part of the thesis in which to discuss it fully. We apply the title - "terminal decay" - to the interval between the

time when the disease gains the upper-hand over its host and the time of death. The human body marshalls its defence mechanisms to combat an infection by the tubercle bacilli or other organisms and the protein changes in the plasma are an indication of the extent of the body's reaction. Somewhere between the initial infection and the fatal termination there must be a point at which the resistance is overcome and the invading power gains mastery. This point of transition will vary from patient to patient, depending partly on the virulence of the organism (=the seed) but more on the individual's constitutional capacity of resistance (=the soil). The previous sections have shown that the plasma viscosity is a fair measure of the general reaction of the body; terminal decay can set in when the plasma viscosity is moderately or very high, thus indicating numerically how the powers of resistance can vary. However, as high viscosities are associated with severe disease conditions which naturally have a poorer prognosis, the terminal decay was found most frequently subsequent to such high values.

The behaviour of the plasma protein fractions, plasma viscosity, and ESR. during terminal decay is quite characteristic. The plasma proteins decrease in amount: the decrease affects the albumin firstly and later the globulin and fibrinogen and these changes are detectible in the total and fraction values, in the

albumin/globulin ratio, and in the plasma protein equilibrium factor. The plasma viscosity also falls, the values plotted against time intervals forming a smooth curve which eventually reaches the normal range of values about the time of death. Thus the apparently 'normal' plasma viscosity results occasionally seen in very ill patients are associated with markedly abnormal protein patterns. The relationship of the plasma proteins to the ESR is different from that to the plasma viscosity, and while the ESR may also decrease, the return to normal ranges is seen more rarely; at the onset of terminal decay the ESR may even continue to increase for a short period. Because of the changes in the ESR and the plasma viscosity, the point for the duplicate estimation will no longer fall on the periodic curve described in §21 of part 6, or will do so only by chance.

Some graphs are included here from representative cases (not all tuberculous) which show how the plasma viscosity falls as death approaches. The phenomenon is found in acute as well as chronic diseases. (Fig. 91, 92, and 93)

In a disease of such long duration as pulmonary tuberculosis, it may happen that the decrease in the plasma protein, as indicated by the decrease in the plasma viscosity, occurs without any other change in the clinical picture. It may even be difficult to tell whether this decrease reflects the first sign of decay or an

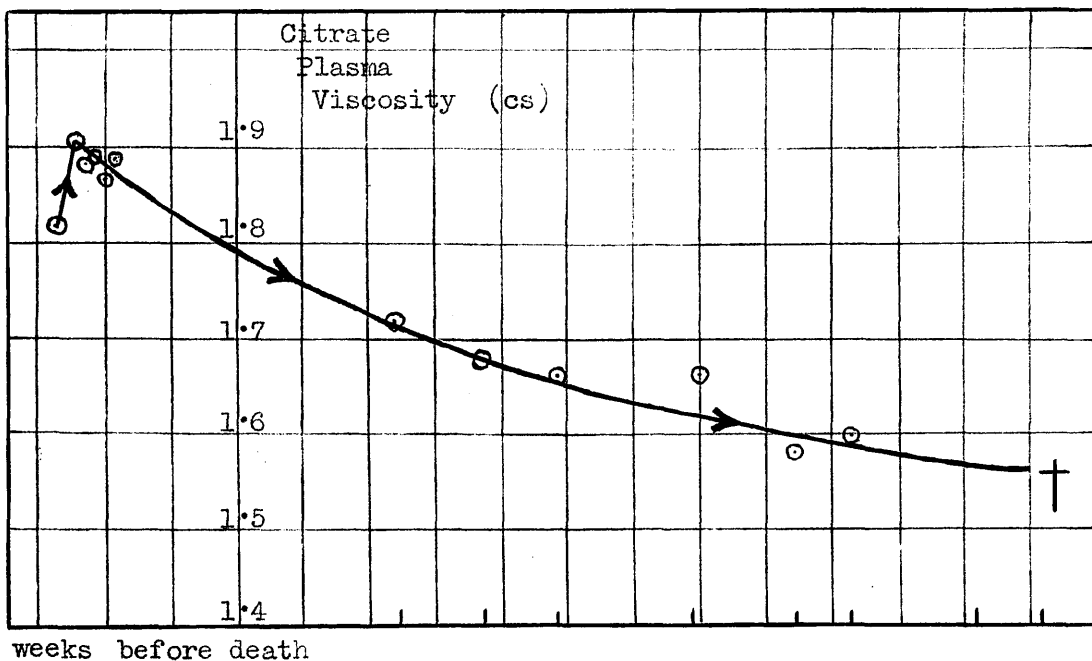


Fig. 91 "Terminal Decay" in a case of pulmonary tuberculosis.

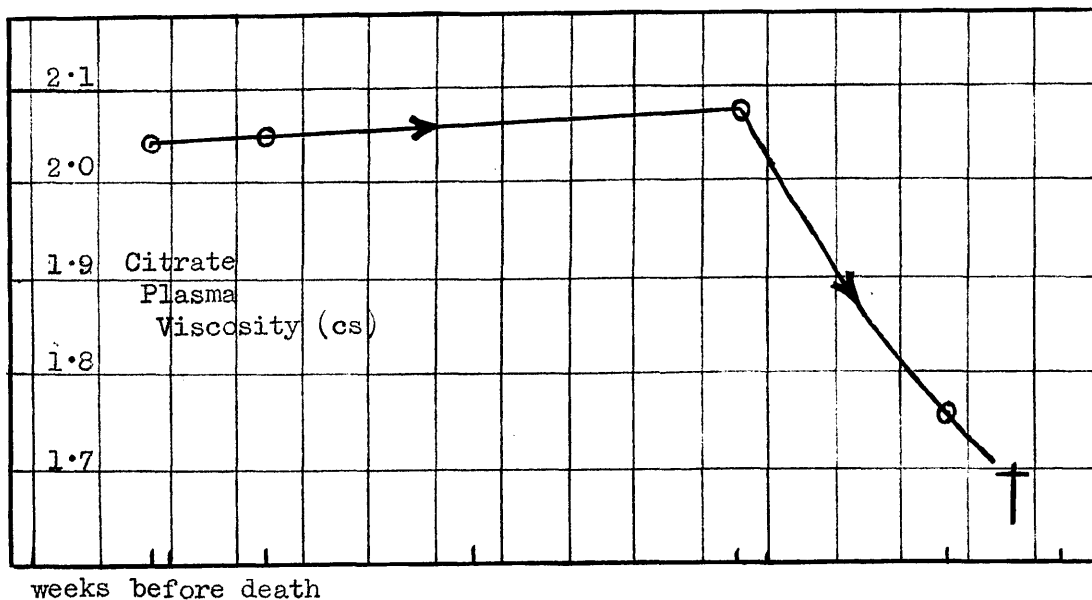


Fig. 92 "Terminal Decay" in Pulmonary Tuberculosis in a Mongolian Idiot.

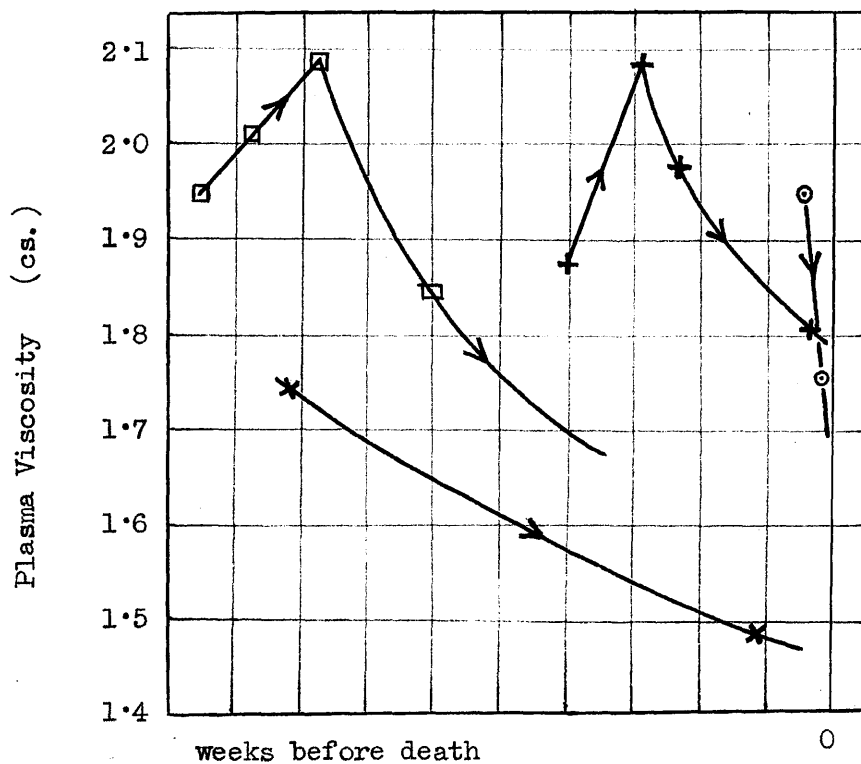


Fig. 93 These graphs show how the Plasma Viscosity falls as death approaches.

It is therefore possible to find a normal or low abnormal viscosity value in association with severe diseases in their terminal phase.

x — x = pulmonary tuberculosis.

□ — □ = pulmonary tuberculosis, plus pyaemic abscesses.

○ — ○ = intestinal obstruction

+ — + = cancer of ovary, plus septic knee.

improvement, and to settle this point recourse may be made to the plasma protein fractionation or to the correlation of the plasma viscosity with a maximum sedimentation velocity and its relation to the periodic curve.

The duration of terminal decay may be as long as 6 months. Once terminal decay was established I was never able to interrupt its course by any therapy available in 1943-1948. Similarly, even with the better facilities of his sanatorium, Dr. Houston failed to halt even one case. I have had no opportunity to study the response of patients in terminal decay to the latest treatment of tuberculosis with streptomycin and para-aminosalicylic acid.

The low viscosity and protein results as a terminal phenomenon has been noted by other workers. Bircher (24) reports normal serum viscosity values in his severest disease group; Benson (17) writes -"The patients ill with pulmonary tuberculosis who died during the period of observation had high plasma viscosity values which occasionally approached normal levels a few days to three months before death"- but he already knew of this special finding from reading our publications; Herwig found that a low albumin had a very bad prognosis (108); and Ham and Curtis (92) noted a low fibrinogen in the terminal stages of tuberculosis.

- - - - -

Discussion (continued)

It is my confident belief and claim that the plasma viscosity test can yield very valuable assistance to the clinician in his study of the individual patients. It helps him in reaching the correct diagnosis, prognosis and treatment.

Diagnosis - The detection of an abnormal plasma viscosity can be interpreted as an indication of a systemic reaction in the patient, but it cannot indicate the exact nature of the primary stimulus. However, if other causes of increased viscosity values can be excluded, the detection of a raised plasma viscosity in a patient in whom tuberculosis is suspected is very strong evidence of the presence of a lesion which is "active". Two examples can be given of the sensitivity of the test from this aspect. A female technician in our laboratory had been under the supervision of the chest clinic for many years as her father had been in a sanatorium. She volunteered to act as a normal control for my plasma viscosity series on 31st May when her result was 2.012, and it was only then that I obtained her family history. In view of this finding I asked that the chest clinic should re-examine her, which was done with nothing abnormal detected. She continued at work, was examined at 3 month intervals, but following her test in January when a satisfactory report was again issued she asked that her viscosity be examined again. Her viscosity was now 2.103.

I now insisted on a further specialist opinion and an active lesion was verified by more intensive investigations and by her sputum becoming positive. The clinician then agreed that this lesion was probably present and active at the first testing, some eight months previously. The author detected his own plasma viscosity had become abnormal in April yet the clinicians and radiologists had great difficulty in detecting the small focus of infection by August, but in this instance the treatment begun so early led to a speedy and satisfactory outcome.

Dr. White found the test very reliable in diagnosing the activity of patients after courses of treatment, of patients in whom a possible relapse was suspected, and of pick-ups by the Mass X-ray unit.

A plasma viscosity within the normal range is no guarantee that active tuberculosis is not present, but the error is likely to be small as the incidence of normal values in my total series was only 9%. This compares well with Benson's 8%.

Prognosis - I have found that the higher is the plasma viscosity so is the prognosis worse. This is to be expected from the correlation between the clinical assessment by the Ministry of Health scheme and the mean plasma viscosity results: a high viscosity usually corresponds to more extensive disease.

I reproduce a table from our first publications (119) in which the incidence of a fatal outcome was shown for the higher citrate plasma viscosity zones: these results were derived by me from a wide variety of diseases, and not from tuberculosis alone.

Viscosity Zone	No. of cases.	Deaths	
		No.	%
6	25	5	20
7	19	7	37
8	9	4	44
9	17	11	65
10	5	3	60
11	4	4	100

At that time I had a plasma viscosity level above which every result was associated with early death; further experience has shown, however, that recovery is possible with even extremely high viscosity values.

A low plasma viscosity is no guarantee of a satisfactory clinical course; we can only presume that the chance of this occurring is greater.

A very grave prognosis must follow the detection of terminal decay, with its consistently fatal ending.

There may arise occasionally a social problem in which the guidance to the time of death by the falling plasma viscosity/time chart may prove useful.

Serial tests will indicate the general trend of the disease, the viscosity falling with improvement and rising with worsening.

An unexpected peak in the curve of serial tests may be the first indication of a complication.

A satisfactory response to therapy is shown by a return of the plasma viscosity to the normal range and its maintenance there.

Treatment - The treatment of pleural effusions can be assisted by the knowledge of the patient's plasma viscosity relative to the "zone of effusion". We have found that the removal of fluid while in this zone leads to it reforming; whenever possible, tapping should be delayed until the plasma viscosity has moved upwards or downwards.

After his mishap, Dr. Houston now hesitates to induce an artificial pneumothorax when the plasma viscosity is in this zone.

A programme of treatment which leads to a decrease in the plasma viscosity can be accepted as satisfactory; if the viscosity is increasing, the therapy needs to be reconsidered.

If the plasma viscosity remains high after such collapsing procedures as artificial pneumothorax, pneumoperitoneum, or phrenic crush, it may be interpreted as a sign of continued toxin absorption and of the need for more drastic treatment to produce complete rest in the affected part of the lungs.

* * * * *

A (ii) Epituberculosis : primary tuberculous complex.

When a primary tuberculous complex is being formed there is a general upset in the body which is shown by the elevation of temperature and tachycardia, and in the malaise. The severity of this reaction is indicated by the elevation of the plasma viscosity.

Nine out of the fourteen patients examined and whose results are presented in Table XII, page a185, showed such an increase in the plasma viscosity: the serial tests had a decrease in the viscosity in response to treatment. The five normal viscosity values must not be regarded as failures of the test as some of these patients were not examined until just before discharge from hospital when the clinician wished the test to be carried out as a confirmation that the general reaction had ceased.

* * * * *

(B) Non-pulmonary Tuberculosis.

This section is concerned with tuberculosis of the bones and joints, meninges, and skin and soft tissues, and with miliary tuberculosis. The results might have been divided into pre- and post-streptomycin groups as this drug has changed the outlook so greatly.

Generally, as with the tuberculosis of the lungs, this infection of the other tissues produces a systemic reaction, with its complementary increase in the plasma viscosity.

(i) Bones and Joints.

The incidence of abnormal values is shown in Table XIII of the appendix.

My orthopaedic-surgeon colleagues now acknowledge two problems in which they are glad to acknowledge the assistance which they are obtaining from the plasma viscosity test.

In an early stage of an infection of a bone (eg. spine) or a joint (eg. ankle) a marked increase in the plasma viscosity could be observed when the signs and symptoms were otherwise meagre and the diagnosis uncertain. Nevertheless, it is accepted that there were occasions when the surgeon detected a disease which was active by other criteria and yet associated with a normal plasma viscosity; but such events were rare and certainly

less frequent than with the ESR test.

They also find the viscosity test a valuable guide to prognosis and treatment. Rest to the affected part could be achieved by a plaster cast, etc. with the result that the local symptoms and the signs of general toxaemia disappeared. The surgeons now accept that a persisting abnormal plasma viscosity is a guarantee of a general reaction to a persisting local activity which requires appropriate treatment. In view of the known false-negatives, a normal viscosity cannot guarantee the absence of activity but only makes the probability of a quiescent state so much more likely. A fall to the normal range of an originally increased plasma viscosity is an indication that the treatment is causing a lessened toxin absorption.

(ii) Meninges.

T'ang and Wang had five cases in their series with tuberculous meningitis. Each case had a normal ESR but an abnormal plasma viscosity; it was partly because of these results that they concluded that the plasma viscosity test might be a more sensitive index than the ESR. Since their paper in 1940, the introduction of streptomycin has altered the outlook for these patients completely. Refinements have been made in the methods

of diagnosis so that it is reached at an earlier stage and active treatment begun without delay. Hence there are fewer chances of studying the untreated advanced cases such as those available to the Chinese workers.

My results are presented in Table XIII of the appendix, and in the individual case notes. Several normal plasma viscosity values are included. In contrast to T'ang, I did find some high ESR values but their incidence was less than that of abnormal plasma viscosity values.

The diagnosis of a tuberculous meningitis will depend upon the examination of the cerebro-spinal fluid; the plasma viscosity increase is an interesting phenomenon which has no practical use to the clinician.

The viscosity test becomes of real significance after the streptomycin treatment has been given. The C.S.F., in a case which will eventually clear completely, does not return to a composition which is within the normal range for protein, cells, chloride, and sugar, for a period measured in weeks or months. The criterion of improvement is that the progress towards the normal range is not interrupted, which requires frequent serial lumbar punctures. Now, if in such a convalescent patient a high plasma viscosity result is found, two explanations are possible -

(a) there is an active tuberculous lesion somewhere else in the

body (probably the site from which the infection spread to the meninges originally), or (β) the tuberculous infection of the meninges is causing a systemic reaction although it is producing no localising signs or symptoms; a relapse is therefore inevitable. (This reasoning has assumed that the plasma viscosity increase has not been the result of some non-tuberculous stimulus). If the plasma viscosity has ever attained the normal range and later becomes raised, the certainty of a relapse is still greater. The notes of a relapsing meningitis have been included; the viscosity was increasing and a relapse had been forecast to the clinician before her C.S.F. culture again showed tubercle bacilli. (Her results are not in the table as they became available after its completion.)

The clinicians are going to follow up their other cases now and it may be possible to devise a scheme of examination where the use of the plasma viscosity test will obviate the need for so frequent lumbar punctures.

(iii) Skin, soft tissues, organs, etc.

The plasma viscosity was found to be abnormally high in the majority of patients with active tuberculosis affecting the skin, lymph glands, kidneys, etc. (see table XIII)

The weakness of the plasma viscosity test, on account of its non-specific character, was particularly noticeable in this group of diseases. While the raised viscosity value was an indication of a systemic reaction to an organic change, it remained for the clinician to decide the nature of the primary stimulus. For example, I have included two case-notes concerning two girls with identical plasma viscosity results: one had enlarged cervical lymph glands because of a tuberculous infection there, and the other had cervical lymph glands enlarged because of a chronic inflammation of the tonsils.

The value of the test to the clinician lies in its detection of an organic cause of the signs and symptoms, and in the return to normal with satisfactory treatment.

(iv) Miliary Tuberculosis.

The plasma viscosity was elevated in most of these cases until the disease was brought under control by streptomycin. The viscosity was raised because of the systemic reaction both to the miliary foci and to the primary focus from which the spread had taken place. (see Table XIII)

This is a point at which it is appropriate to report on

the change in the gold flocculation test following streptomycin therapy. A positive gold flocculation response is not a frequent finding in any type of tuberculosis, but it was seen on many occasions when streptomycin was administered to patients with different types of tuberculosis. As para-aminosalicylic acid was exhibited in association with the streptomycin as a standard procedure and as this P.A.S. had caused liver dysfunction in a few instances, it was thought at first that the P.A.S. was responsible for the gold flocculation response. However, in the rare occasions in which the streptomycin was given alone, the positive gold flocculation results were encountered. I have had no opportunity of studying the effect of P.A.S. alone. There is no means of telling whether the altered plasma protein which is ultimately responsible for the gold flocculation test has been produced as a result of liver dysfunction or as a direct action by the liver now capable of more efficient protein formation. This is a further example of the need to distinguish between a change in a laboratory test due to a variation in the disease process and a change due to the treatment of that disease (cf. the section in part 7 concerning the effect of sulphonamides).

* * * * *

§ 4 VENEREAL DISEASE.

Although the number of tests made in this group of diseases is small the significance of the findings is high. The paucity of tests arose from two causes. Very soon after our paper had been published in the British Medical Journal I had some correspondence with Dr. K.E. Hughes of the Venereal Diseases Department of St. Mary's Hospital, London concerning the possible use of the plasma viscosity test in the investigation of these diseases; it was my impression that he intended to employ the test thoroughly and I left this field of research to him. In 1950, however, I learned that he had made no tests whatsoever. Also, my Sunderland colleague who specialised in these diseases planned a study on certain aspects of tertiary syphilis but accepted another post soon after; Portsmouth did not have a civilian specialist in V.D. until autumn 1951.

(A) Syphilis.

I have no results available for the primary and secondary stages.

A little over thirty patients were studied in the tertiary stage.

General Paralysis of the Insane (G.P.I.)

The results are given in Table XIV of the appendix and presented

graphically in Fig. 94.

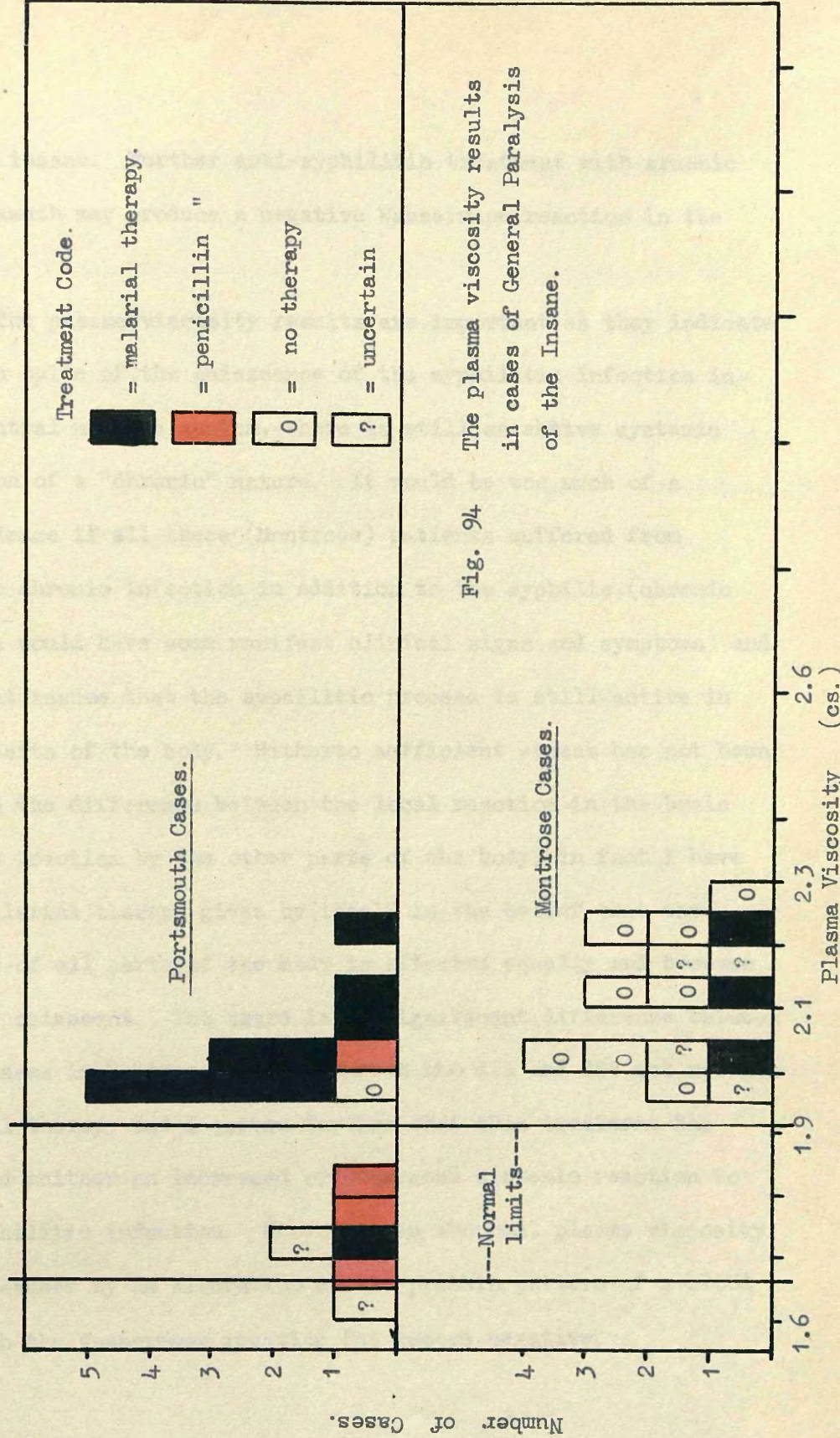
The tests were made on all the known cases of G.P.I. in Montrose Asylum in 1943-44 and in St. James' Hospital, Portsmouth in 1951. Each group of patients was tested within a few weeks so that the environmental factors would be constant.

The ordinary population of Montrose Asylum is drawn from the rural areas of The Mearns, Caithness, and Shetland where the incidence of syphilis is low: during the war patients from Larbert Asylum (urban) were evacuated to Montrose and several G.P.I. cases were included. Unfortunately no record* of previous treatment accompanied them. Thus my 15 Montrose patients included only 3 in whom I was certain that malarial therapy had been given; 8 had received no malaria; and 4 patients may or may not have been treated with malaria. I gave malarial therapy to some of these 8 with the intention of including results of before and after treatment but these patients were all removed back to Larbert before the second tests could be made.

The Portsmouth group of 16 patients included 1 definitely without treatment, 2 with no recorded treatment, 4 with penicillin therapy, and 9 with malarial therapy.

Discussion. It is generally accepted that hyperpyrexia (induced either by a hypertherm apparatus or therapeutic malaria) can cause a halt in the mental deterioration of general paralysis

(* a request to Larbert for this information has been ignored.)



of the insane. Further anti-syphilitic treatment with arsenic and bismuth may produce a negative Wassermann reaction in the blood.

The plasma viscosity results are important as they indicate that in spite of the quiescence of the syphilitic infection in the central nervous system, there is still an active systemic reaction of a "chronic" nature. It would be too much of a coincidence if all these (Montrose) patients suffered from another chronic infection in addition to the syphilis (chronic malaria would have some manifest clinical signs and symptoms) and one must assume that the syphilitic process is still active in other parts of the body. Hitherto sufficient stress has not been laid on the difference between the local reaction in the brain and the reaction by the other parts of the body; in fact I have seen malarial therapy given by itself in the belief that the disease of all parts of the body is affected equally and becomes equally quiescent. Yet there is no significant difference between those cases in Montrose and Portsmouth who did and did not receive malarial therapy and I assume further that this treatment has produced neither an increased or decreased systemic reaction to the syphilitic infection. Moreover, an abnormal plasma viscosity may be caused by an alteration in the protein pattern of a blood in which the Wassermann reaction has become negative.

Malarial therapy must be followed by thorough anti-syphilitic treatment.

Four Portsmouth cases were treated with Penicillin and in no less than three (=75%) did the plasma viscosity return to within the normal range. These figures are too few to permit definite assertions but it does appear as if penicillin therapy has acted against the total syphilitic infection to cause such an amelioration (if not complete cure) that the systemic reaction cannot be detected by the plasma viscosity test. This is a fundamental improvement over the hyperpyrexial forms of treatment. Even with penicillin, however, the blood Wassermann reaction remained positive (++) in one of the three patients in whom the plasma viscosity had become normal; the persisting abnormal plasma viscosity was associated with a negative Wassermann reaction.

Penicillin therapy is now the standard method of treating cases of G.P.I. With the passage of time there will arise more results from this treatment and enough will be obtained for a statistical analysis. I intend to study the cases at other local mental institutions in the near future.

Tabes Dorsalis.

A patient may present himself at a V.D. department suffering from tabes dorsalis yet with a record of what was considered as

adequate treatment, both in duration and intensity, in the primary and secondary stages. If further treatment with arsenic and bismuth is given, the Wassermann of the cerebro-spinal fluid can remain positive for years. The venereologist is constantly faced with the problem of deciding when the disease may be considered sufficiently inactive that treatment can be discontinued. Dr. Henry Bell in the Sunderland V. D. department had seen my Montrose G.P.I. figures and knew of the rheumatic disease tests, and he decided to co-operate in a study of this problem with the application of the plasma viscosity test.

The initial tests revealed that the plasma viscosity of cases of active tabes dorsalis was indeed increased into the "zone of chronicity". The results are similar to those from cases of G.P.I.

Both Dr. Bell and myself left Sunderland soon after these tests were made and I have had no further opportunity to resume this study.

This disease is also being treated with penicillin and it is possible that, as with the G.P.I. cases, the plasma viscosity will return to normal values.

Pachymeningitis (Syphilitic) or Cerebral Syphilis.

Of this third type of tertiary syphilis two cases only were seen. The results were again abnormally high and within the "zone of chronicity". These values had persisted in spite of anti-syphilitic treatment at the early stages of the infection and again, prior to the tests, during the tertiary stage when the symptoms of the disease were again becoming manifest.

Discussion.

These preliminary results of the plasma viscosity test in the tertiary stage of syphilis, although few in number, are still sufficient to indicate that the application of the test to this disease is potentially valuable.

The exact relationship between the plasma viscosity test on the one hand and the Wassermann, Kahn, and similar tests on the other should be investigated further. However valuable the latter tests may be, it is acknowledged that they are not infallible so that an additional test would be welcomed. It is acknowledged also that a positive Wassermann in the later stages is no guarantee of activity of the disease process; the problem of the persisting positive Wassermann reaction in tabes under treatment has been mentioned above.

A problem somewhat akin to the ESR./plasma viscosity relationship is now presenting itself - which of the two tests, plasma viscosity or Wassermann reaction, is to be believed when the duplicate results on an individual patient are to be interpreted in direct opposition ? I have sufficient experience with the plasma viscosity test now to accept its abnormal values as a certain indication of activity, even if the Wassermann reaction is negative; on the other hand, false negatives do occur and therefore a normal plasma viscosity should be interpreted with great caution when associated with a positive Wassermann reaction. The collection of more individual values and preferably serial individual studies, together with a most careful assessment by the clinician, are essential to settle the latter point; such was the object of the research proposed by Dr. Bell and myself.

We also require some long-term investigations on individuals from the primary to the secondary and even to the tertiary stage; the response to penicillin treatment has been excellent but the failures form a percentage sufficiently high to yield enough cases to make their study worth while.

It has been claimed that, just as with invasion by other organisms, the infection by the spirochaete produces an increase in the plasma globulin and fibrinogen. An increase in the plasma viscosity could therefore be expected in the primary and secondary

stages also. It is a definite possibility that the plasma viscosity test may act as a guide to a satisfactory response to treatment on a shorter time basis than the Wassermann reaction. A course of treatment which is to have an ultimate cure may be reflected in an early return of the plasma viscosity to normal before the Wassermann has changed: failure to produce a normal viscosity, even if the Wassermann may change temporarily, might be an indication of future trouble. This is reasoning in analogy with the position in rheumatoid arthritis where we have noted repeatedly that a normal plasma viscosity is the highest criterion for quiescence; even if a patient becomes symptom-free with gold therapy, unless the plasma viscosity has become normal, an ultimate relapse is assured. I am certain that the renewed or long-continued activity of syphilis which appears clinically as the tertiary stage could be detected as an increase in the plasma viscosity before the signs and symptoms become manifest.

I do not think that it is too fantastic to foresee a time when the estimation of the patient's plasma or serum viscosity will be as routine a procedure in syphilis as the measurement of his Wassermann reaction; the viscosity of the serum could be estimated prior to the preparation of the serum for the Wassermann test; an automatic viscometer would reduce the time required for each test sufficiently to make this a practical procedure for a

laboratory handling hundreds of sera per week. Although the fibrinogen is increased in the tertiary stages, the globulin increase would be reflected in the serum viscosity.

Bircher and McFarland (25), using Naegeli's combination of refractimetry and viscometry, noted that the changes were indistinguishable for primary, secondary, tertiary, and central nervous system syphilis. The total serum protein remained unchanged, as measured by the refractometer. The protein fractions, however, had an altered ratio in favour of an increased globulin; this change was detected as an increased viscosity. They also noted that arsphenamine treatment caused a fall in the viscosity, but in 31 only out of 40 cases; the fall was greatest in those cases where the serum viscosity was originally highest.

Similarly, Holker (114) found that the serum of untreated syphilitics tended to be more viscous than that of normal persons. The increase was more marked in secondary than in primary, and more in tertiary than in secondary; the increase was less marked in parasyphilitics. His numbers were rather low for cases tested.

Subject	No. of tests.	Serum viscosity.	
		Mean	Range
Normal	8	1.75 cs.	1.69 - 1.85 cs.
Primary	7	1.83	1.71 - 1.98
Secondary	6	1.89	1.72 - 2.26
Tertiary	9	1.94	1.74 - 2.12
Parasyphilis	4	1.75	1.71 - 1.87

Chopra and Choudhury (42) noted that the serum viscosity range in syphilitics (25 cases; stages not specified) was 1.60 - 1.95 cs. as compared to their normal range of 1.40 - 1.64.

Kopp (135) has reported that the plasma proteins regained their pre-treatment level within 14 - 24 days of stopping malaria therapy, no matter the number or severity of the rigors.

These earlier papers all support my claim that further studies with the plasma viscosity test in syphilis may yield very valuable information to the clinician.

(B) Gonorrhoea.

No ordinary cases were examined.

Two cases of gonococcal arthritis had increased plasma viscosity values, just as would be found with any other type of infection (acute) of such a vital structure as a joint.

(C) Lympho-granuloma Inguinale.

A single patient with this infection was studied.

His plasma viscosity was abnormally high.

* * * * *

§ 5 SEPSIS.

This group includes a variety of clinical conditions produced by the invasion of tissues by pyogenic organisms.

Results. These appear in Table XV of the appendix.

By the time that a septic condition has advanced sufficiently for the doctor's advice to be sought, the plasma viscosity has become increased to abnormal levels; the increase is approximately proportional to the severity of the toxæmia caused by the sepsis; and the viscosity returns to the normal range when the original sepsis has cleared.

Discussion. The invasion of the tissues by the pyogenic organisms is followed by the absorption of the toxins and products of tissue destruction, which calls forth a reaction of the body as a whole. Antibodies against the organisms and their products are formed and circulate in the blood as part of the plasma gamma globulin. In addition, there is an initial increase in fibrinogen and a later increase in the other globulin fractions - how these increases benefit the body has not yet been determined. These protein increases are reflected in the increase in the plasma viscosity.

Acute Sepsis. As the fibrinogen can increase by 100% in 24 hours and as the plasma viscosity is almost invariably abnormally high when the fibrinogen exceeds 0.4 g.%, the test becomes abnormal by the time the patient first presents himself for examination.

The sensitivity of the test was shown by the abnormal result in an apparently normal subject being traced to an axillary abscess which he considered so trivial as not worthy of mention.

The highest values in this group occurred in those patients in whom the septic condition (eg. bed sores, gangrene) would be the cause of their death.

Chronic Sepsis. This group includes the conditions of indolent sepsis - the child with enlarged cervical lymph glands and tonsils from which beads of pus might be expressed, the unfortunate youth with boils on his neck at all stages of development and healing, and the patient with a brown-blue indurated skin of the axilla, with subcutaneous abscesses which do not "point", etc. These patients had their plasma viscosity within the "Zone of Chronicity" which has been described already.

The plasma viscosity test does not assist the clinician greatly in the management of his patients; it usually merely expresses in numerals what is clinically obvious.

I have had no opportunity to study the use of the test in gynaecology but I think that it might, on occasions, indicate a deep-seated septic focus such as salpingitis. It might help in the differentiation between the acute appendicitis and the more chronic salpingitis.

SARCOIDOSIS.

It has been difficult to decide where, in the thesis, this disease should be inserted because its exact nature has not yet been elucidated. Robinson and Pound (211), on the basis of a thorough survey of 30 cases, conclude that the disease could be interpreted as a chronic infective process of unknown aetiology. Hence I have included my series as a special section after pyogenic infection.

Dr. Lendrum, medical director of the Mass Radiography Unit in Portsmouth, has a special interest in this condition and has a series of patients on whom he makes 6- or 12-monthly checks - he hopes to show that without treatment his end results will not be significantly inferior to those with Vitamin D, etc. Therefore, although some of these patients have been under observation for many years and have been showing a regression in the enlargement of the hilar glands and other sarcoid lesions, no positive steps have been taken to stop the activity of the disease.

Results: These are presented in Table XVI of the appendix, and representative case notes are included.

Discussion: Only one patient had the plasma viscosity within the normal range of values; the test was made about a fortnight after the diagnosis of sarcoidosis had been reached by the histological examination of an excised parotid tumour; a thorough

investigation has failed completely to detect any other evidence of this disease. Tests to be performed at a later date will prove most interesting. No explanation could be obtained for the fall in the plasma viscosity of patient, D.A., within a month; his future tests are also awaited with interest.

The results of A.C. indicate that pregnancy has not affected the patient's reaction to the disease; the fall in the ESR. might be attributed to the passing from the gravid to non-gravid state and this case is an example of the limitations placed upon the ESR. test by its changes during pregnancy.

The majority of the remaining plasma viscosity values falls within the zone of chronicity and thereby support is given to the hypothesis that the disease is of a chronic inflammatory nature. The plasma viscosity can be just as high in the cases of several years duration as in those more recently diagnosed. Now, although these patients feel quite well and their lesions are regressing, I must interpret the raised viscosity as a definite indication that the activity persists with no abatement in its reaction by the patient. Instead of waiting many more years until the clinicians can make their decision on the merits of different types of treatment we can make a statistical analysis of two series of plasma viscosity values. The Portsmouth tests have been made within the last few months only and Dr. Lendrum's complete

series has not yet been examined. It is my intention to approach the Brompton chest hospital which employs calciferol with enthusiasm in this disease for its co-operation in repeating the test on a series of cases where they believe this treatment has caused a clinical improvement. A significantly larger number of normal plasma viscosity results would indeed support the claims in favour of vitamin D therapy. (This investigation is similar to that proposed for penicillin in tertiary syphilis) The benefits arising from obtaining a definite decision regarding the proper treatment need no further stressing.

A problem in diagnosis frequently presents itself in differentiating between the hilar gland enlargement of sarcoidosis and tuberculosis. The plasma viscosity test, by itself, has been of no assistance. However, our present battery of tests has given two leads in this connection. The gold flocculation test has been found to be positive in a large number of cases of sarcoidosis, (4 out of the last 5 tested), which is a less-common finding in tuberculosis. Also, in these same five tests, the β_1 globulin was increased in all. The chemical protein fractionation methods can show only a tendency for the globulin to be increased in both of these diseases.

In addition to its possible assistance in the differential diagnosis, the abnormal gold flocculation test gives a hint about

the aetiology of the disease. It suggests that the infecting organism is more akin to the cause of rheumatic fever or rheumatoid arthritis than to the tubercle bacillus.

* * * * *

§ 5 SPECIFIC FEVERS.

Very few cases of the specific fevers were studied because I had no colleague in charge of these diseases who would take an interest in the plasma viscosity test.

By their very name, in which the general reaction is indicated by an elevation of body temperature, it might be forecast that the plasma viscosity would be increased.

My 14 patients of Table XV (D) in the appendix had 13 raised plasma viscosities and one value of 1.913cs.

The extremely high result in the case of amoebic hepatitis was in agreement with the profound systemic reaction; the very high result in the case of paratyphoid was unexpected as he was neither dehydrated or severely ill.

As with septic conditions, the value of the plasma viscosity test in specific fevers is not great: the number of occasions on which the clinician need call on its assistance is low. Perhaps it may find a use the diagnosis of delayed response to the new antibiotics and sulphonamides where a continued high viscosity will indicate that the speedy resolution has not been forth-coming as usual. Case W.B. was an example where the resolution with sulphonamides was delayed and the viscosity test showed this.

* * * * *

§ 6 TUMOURS.

(a) Simple Tumours.

Results. These are given in Table XVII(a), of the appendix.

Discussion. A simple tumour which produces no hormonal secretion and which exerts no pressure on vital structures is usually associated with a plasma viscosity value which lies within the normal range. In the event of a degeneration in a tumour (eg. in a fibroid) the absorption of material from the tumour can cause a general reaction which will include an alteration in the plasma proteins and an increase in the plasma viscosity. Similarly, it might be possible for a reaction and plasma viscosity increase to follow on the absorption of tissue in face of tumour pressure, but such a case has not occurred in my experience.

Simple tumours which produce hormonal secretions (eg. thyroid, parathyroid, pancreas and pituitary) can cause such an upset in the working of the body that the plasma proteins and viscosity become abnormal. Case M.M. was a parathyroid adenoma and her viscosity was slightly raised. Her case history is given in some detail as the diagnosis of non-malignancy which I maintained on the basis of these non-specific tests was against the consensus of the opinion of several clinicians, yet at operation I was proved to be correct.

(b) Malignant Tumours.

Results. These are given in Table XVII(b) of the Appendix.

In the majority of the tests the plasma viscosity was high. Nevertheless, viscosity values within the normal range could be found early in the disease (yet inoperable) and again later, as a result of "terminal decay".

Discussion. The plasma viscosity values in malignant tumours depend upon the stage to which the tumour has progressed, as in almost every instance the plasma viscosity will be abnormal at some time between the growth beginning and death.

(1) In the early stages of the clinical history the plasma viscosity may be normal. This stage may include cases in which there is a palpable mass (eg. in breast or stomach) detectable by the clinician. It may include cases with early local spread and involvement of the nearest lymph glands. The protein pattern remains normal also so that we know that we are not yet dealing with "terminal decay".

(2) Later, the presence of a malignant tumour in the patient is almost always associated with an increased plasma viscosity. The increase is usually moderate - under 2.4 cs., but when the secondary deposits become widespread (especially if the bone-marrow is involved) much higher values may be noted.

The plasma viscosity increases when -

- (i) the tumour (or its metastases) is increasing and producing the absorption of other tissues by pressure or by invasion;
 - (ii) the tumour produces toxins which are absorbed to produce a systemic reaction as shown by an elevation of temperature, loss of weight, loss of appetite, lassitude, etc.: in contrast to the stage (1) above, while the laboratory tests are now abnormal the clinician may be unable to determine the exact location of the primary growth; at this stage the plasma viscosity/ESR point may still lie on the periodic curve of correlation;
 - (iii) the tumour undergoes definite degeneration with a consequent absorption of these products; and
 - (iv) the tumour becomes infected with pyogenic organisms.
- (3) Later still, the plasma viscosity falls as part of the phenomenon of terminal decay. A normal plasma viscosity value is thus consistent with an advanced malignant tumour.

The clinical group of 'tumours' has yielded me some of my greatest successes in diagnosis by the plasma viscosity and some of my most dismal errors. However, I still think that a lot of useful information can be obtained from the test if it is used with caution; more information can be obtained if it is used as part of a battery of tests.

When a clinician is searching for a tumour, simple or malignant, as an explanation of his patient's signs and symptoms, a plasma viscosity value within the normal range is of little help. From my experience it is known that a malignant tumour may still be present in spite of this normal result, although such an event is rare. However, a normal value might help in the differential diagnosis, as a normal value would be most unusual if a palpable mass was an inflammatory lesion.

The detection of an abnormal viscosity assists the clinician in confirming that there is a general reaction to some kind of primary stimulus which might well be neoplastic in nature. Furthermore, if the changes which can occur in a simple tumour to cause a reaction can be excluded, an increased viscosity plus a tumour strongly indicates its malignant nature.

Much more information can be obtained by the study of serial tests with the plasma viscosity; other non-specific tests can be added to produce a battery of investigations. My particular choice consists of the corrected citrate plasma viscosity, the corrected citrate maximum sedimentation velocity, haematocrit, plasma protein fractionation with a consideration of these results both as absolute values and in terms of my plasma protein equilibrium factor, and the serum viscosity. A diagnosis of a

malignant tumour could be supported if in serial tests at a few weeks interval there were noted any of the following; the certainty of the diagnosis increases with the total number of tests showing abnormal results.

- (i) A decreased haematocrit which continues to fall.
- (ii) An increased plasma viscosity.
- (iii) A changing plasma viscosity: ie. an increase in the early clinical stage or a decrease in a late stage .
- (iv) An increased ESR.
- (v) A plasma viscosity/ESR correlation point which falls outwith the periodic curve. As a 'decayed' value might fall on a lower curve (ie. to the left of the diagram) by chance only, serial tests reduces the possibility of finding false negative results.
- (vi) A low plasma albumin, which continues to fall.
- (vii) A protein equilibrium factor which is numerically low, which lies towards the lower left corner of the diagram, and which gets progressively smaller.
- (viii) A serum viscosity/serum protein fraction correlation, which does not conform to the pattern shown in § 17 of part 6.

The plasma proteins change at first as in any other type of general reaction and later they change as in any other type of terminal decay. These changes have been described in detail in other sections.

(c) Multiple Myelomatosis.

This disease has a characteristic excessive growth of the plasma cells of the bone marrow. Because Willis (253) believes that the spread can be by metastasis or by multifocal origin he classifies the condition among the malignant tumours.

Results. These are given in detail in Table XVII(c) in the appendix. Individual case histories are also included there.

Discussion. The plasma viscosity results for this disease had a very high average value and included the highest ($=6.660$ cs.) in my series of tests: as far as I am aware, the only value which surpasses this was found by Mann (private communication) in a case of congenital hyperfibrinogenaemia. ^($\eta = 20$ cs.) Hill et al. (111) describe a case in which the cryoglobulin present in the plasma produced a viscosity approaching infinity at 32°C ., although its relative viscosity at 43°C was approximately 2.6 .

Such high viscosity values may be diagnostic as in no other disease of my own experience could I find these results in association with such mild signs and symptoms. For instance, case R.W. was referred to the laboratory for a plasma viscosity test as ordinary physical examination revealed no explanation for her pains in the back. The laboratory report included the diagnosis.

It is possible to have a lower and perhaps a normal plasma viscosity in a case of multiple myeloma as the extreme changes in the plasma protein fractions are not constant features of this disease, being present in about 70% of cases only. Rundles et al. (214) have recently detected abnormal proteins present in 25 of a series of 30 cases (=83.3%) but the amount varied from a few mg. up to 7-9 g. per 100 ml.: they examined their sera by an electrophoretic fractionation technique. The increase in the amount of protein is due to abnormal proteins rather than to the normally-present fractions; the abnormal fractions vary in their molecular size from case to case. Qualitative differences can be distinguished between normal fractions and the myeloma fractions of apparently identical molecular size, such as the low incidence of positive flocculation tests reported by Martin (177) in spite of high serum 'gamma' globulin values. My own series does not agree with Martin's as I have a high incidence of these abnormal flocculation tests. Maher and Mann report only 1 positive thymol turbidity test in a series of 4 tests (156).

Case H.D. is of especial interest as it shows how a small change in the total protein, at these extremely high levels, can cause very large variations in the plasma viscosity; a decrease of 0.77 g.% produced a fall of 0.978 cs. overnight. However, the

first blood specimen was collected by another member of our staff who would have taken few precautions to avoid stasis: I retrieved the plasma sample after I had detected the abnormal protein fractions by chemical fractionation: therefore such a large variation from day to day may have included a large part due to technical errors. I went specially to the patient myself on the second occasion.

A search was made in the plasma of a patient (M.G.) for a cryoglobulin but no "kink" was detected in the temperature/viscosity curve. As this curve was derived by warming a plasma from room temperature to body temperature it is possible that a cryoglobulin precipitated during the time the blood was allowed to stand on the bench and that this precipitate was removed with the erythrocytes during the centrifuging. I intend to study the next plasma from an ambulant patient at the laboratory from 37°C. downwards.

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§ 7 LIVER DISEASE.

The plasma viscosity test was applied to 73 patients who were suffering from a variety of diseases of the liver and the gall-bladder.

Results. These are given in Table XVIII of the appendix.

Discussion. The plasma viscosity was found to be increased in the majority of the diseases affecting the liver parenchyma, yet this finding has added very little to the clinician's knowledge of his patient. As has been shown by publications too numerous to quote, the diseases of the liver comprise the group in which a great deal of information can be obtained by a consideration of the absolute values of the plasma protein fractions, whether these fractions have been determined by salting-out, electrophoresis, or ultra-centrifuge techniques. Furthermore, the study of the qualitative as well as the quantitative changes in the protein fractions by the flocculation tests of MacLagan (174, 175), together with the measurement of the excretory powers of the liver as indicated by the serum bilirubin and alkaline phosphatase levels, will often supply sufficient information for a diagnosis to be made.

The plasma protein changes are reflected in the plasma viscosity. In disease of the liver parenchyma, even in the early

acute phase, the protein fraction which is most affected is the globulin. Where the globulin is increased at any stage of the disease, the viscosity is usually also increased; where the globulin participates in the general protein decrease, such as occurs in the final stages of cirrhosis, the plasma viscosity will be normal or even abnormally low.

In acute cholecystitis the plasma viscosity is increased just as in inflammatory conditions of any organ or tissue of the body.

Except for two instances which might have been cases with "terminal decay", the plasma viscosity was increased in jaundice due to obstruction in the bile-ducts. This may be the response to the lesion producing the obstruction (eg. cancer of pancreas) rather than to liver changes arising from the obstruction; even a stone in the duct produces an inflammation around it which in turn will call forth a general reaction.

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§ 8 RENAL DISEASE.

In this section we are concerned with nephritis or Bright's disease, rather than with pyelitis or abscess of the kidney which may be expected to produce the same plasma viscosity changes as caused by sepsis in any other tissue or organ.

My classification was into three stages of nephritis and nephrosis, according to Price (201) and to Muir (170).

A. Nephritis.

- (i) Acute glomerulo-nephritis.
- (ii) Subacute nephritis (= large white kidney)
- (iii) Chronic nephritis (= small white kidney)

B. Nephrosis.

Results. These are presented in Table XIX of the appendix, and in the individual case histories.

Discussion. The results are composed of a series of single tests performed at a time when the diagnosis was fairly certain, but it must be recognised that there are intermediate stages between the nephritis groups. My tests do not attempt to indicate the total possible responses of the plasma viscosity in these conditions but are intended merely as a pilot investigation in order to discover whether there is another fruitful field for a more thorough research programme.

In acute glomerulo-nephritis, the plasma proteins show

the changes common to all types of inflammation - viz. an increase in the fibrinogen fraction - which in turn causes the plasma viscosity to rise into the abnormal range. The plasma viscosity did not become markedly abnormal except in two instances.

Subacute nephritis was associated with a protein pattern in which the globulin and the albumin were low while the fibrinogen was slightly increased or normal; the corresponding plasma viscosity values were mostly within the normal range.

Chronic nephritis cases had normal or slightly raised plasma viscosity results because of the low albumin partly compensating for the increased fibrinogen, as the globulin was again within its usual range.

The characteristic change in nephrosis was a marked rise in the fibrinogen, yet, such was the decrease in the albumin and globulin, the plasma viscosity was only moderately abnormal.

(It was shown in part 6 that the non-protein constituents did not affect the plasma viscosity even when grossly deranged.)

At present I can see no stage or condition of nephritis in which the plasma viscosity test can assist the clinician by supplying information concerning the patient not otherwise available, except perhaps in determining when the inflammatory phase of the acute stage has passed by a return of the raised viscosity into its normal range. Even there, however, the test

cannot differentiate between a low viscosity due to a "cure" and one where the condition is going to progress into the subacute stage.

There is a close relationship in this series between the viscosity and the ESR results.

The clinician would gain a satisfactory picture of his patient's condition, from the laboratory aspect, by estimating the haematocrit, protein fractions considered as absolute values and relative to each other, blood urea, and cholesterol.

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§ 9 Disorders of Carbohydrate Metabolism.

These tests were made on the fasting blood specimens taken at the beginning of Glucose Tolerance Tests in order to teach my technicians how to use the viscometer. In many instances the patient had been referred by a general practitioner who was later unable to supply the clinical details of blood pressure, etc. We must therefore not attempt to read too much significance into the results.

Results: These are given in Table XX of the appendix.

Discussion: The nine tests made in cases of low renal threshold and lag curve types of disorder fell within the normal plasma viscosity range.

The incidence of high normal and low abnormal values is unusually large in cases of diabetes mellitus; the viscosity value bore little relation to the shape or maximum height of the glucose tolerance curve.

It is not possible from these few results to ascribe the raised plasma viscosity to the dehydration which occurs in diabetes (the haematocrits were not abnormally high), to the increase in the plasma proteins which follows the administration of insulin (37), or to a true systemic reaction to a general degeneration. The high incidence of hypertension and obesity (10) within the diabetic group would lead one to expect a high

incidence of abnormal plasma viscosities.

Emphasis has been recently laid on the two chief types of diabetes mellitus by Lawrence (141) and by Lister et al. (272). It is possible that a significant correlation could be obtained between the plasma viscosity values and the clinical group, but to arrive at a definite opinion on this the whole problem must be re-investigated with a more adequate clinical control.

Case No 18 should be noted where an obese diabetic, with a moderately increased blood pressure, still had a normal plasma viscosity, thus indicating that the association of these changes with an abnormal viscosity is not absolutely consistent.

Harris and McLoughlin (96) found that the viscosity of the whole blood was increased in 35 out of 40 cases with increased blood pressure.

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§ 10 Miscellaneous Diseases.

During the collection of the blood specimens from patients for the biochemical investigations requested by the clinician-in-charge I have taken this opportunity of removing an additional sample for the plasma viscosity estimation in the rarer diseases. The numbers now available in the different diseases are still not sufficiently large to allow of any definite opinion and I do not intend to include them in this thesis.

Instead of making a full-scale and intensive research into a large group of diseases as we have done previously with tuberculosis and rheumatoid arthritis, I now make a few tests in selected diseases. In this manner I hope to detect a tendency to abnormal plasma viscosity results in some diseases and I can consider if such a finding would be of significant value to the clinician before I study that disease more intensively. For example, I am making plasma viscosity tests in the skin disease patients who are occasionally referred to me, in order to discover if there are certain types of skin disease (excluding septic lesions) in which the abnormal plasma viscosity results have a high incidence: the high viscosity would be an indication of an upset of the general metabolism as contrasted to an upset confined to the skin.

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Discussion to Part 8.

Each different disease has had its own discussion but it is necessary to have a general discussion concerning the plasma viscosity test in disease.

Each infective disease is the inter-action of the infecting organism (the seed) and the host (the ground). To obtain a complete picture of the disease process it is essential that the clinician receives information on both facets. The character of the organism can be investigated by the detection of the actual bacillus (eg. tubercle bacillus in sputum), the reaction of a bacillus to drugs in vitro, its toxicity to animals, and the host's formation of specific anti-bodies (Widal reaction). The assessment of the part played by the host does not lend itself to its expression in numerical or other form which allows the comparison of two individual patients or the comparison of the serial stages in any one patient. There is no scale in which so many marks are allocated to each sign and symptom and in which the sum would be a guide to total reaction. Therefore, the clinician and the clinical pathologist have become accustomed to employ a variety of tests which measure the extent of the change in function of one organ of the body and to use this aberration of a part as an index of the derangement of the whole.

Many of these tests are non-specific in as much as the same reaction can be produced by a variety of diseases.

Some of the non-specific tests are important because the incidence of the reacting diseases is uneven and the significance of the detection of an abnormal result is high from the aspect of diagnosis - eg. Paul-Bunnell test in infective mononucleosis, blood cold agglutinins in atypical pneumonia.

There are other tests in which their value to the clinician lies in the large number of diseases in which they are liable to show changes. Into this group come the plasma viscosity and the ESR. tests.

These non-specific tests usually have their origin in the discovery (chance or purposeful) of a high positive correlation between the findings in some laboratory procedure and a certain type of disease. My introductory part included a brief sketch of the development of the ESR. test and how from the study of this ESR., Whittington chanced on the plasma viscosity changes which Whittington and Miller rendered into the plasma viscosity test. The earlier literature contains many references to the measurement of the plasma viscosity in disease (160,195,242) and even to a comparison of the plasma viscosity and ESR. values (148,161,200) yet it remained for Whittington and Miller (and T'ang and Wang) to have just that extra power of observation and ingenuity to

carry the correlation between the plasma viscosity and the clinical condition the step further and to advocate its estimation as a test in clinical pathology. The later developments of the test, in which I played the major part, have been more of the nature of persistent hard work.

Furthermore, in the original investigations , one worker notes in a particular disease (type or group) a particular reaction which differs from his normal controls; his picture is an abnormal black in contrast with a normal white. His publication leads to the use of the test by other workers for (a) the same disease as was studied and (b) other diseases. These workers may discover exceptions in (a) in which the test fails to respond, and other diseases in (b) which yield the same reaction; and in both (a) and (b), with the larger number of tests, it frequently happens that a few abnormal values are encountered among the controls. With the extension of the canvas the original results form but a small portion and the original crude black-on-white has been modified either to a smudge of greys or the delineations of an etching. (cf. the ESR was originally noted to be abnormal in pregnancy, and later work directed its use to general diseases) If a test can survive this stage of independent investigation and still yield a positive impression, it will be retained in use and attain an accepted place in clinical pathology until it is

superceded by a later test in which the etching is of a higher standard. This is the present state regarding the ESR. test which I now claim as due to be replaced by the superior plasma viscosity test.

Before a reaction should be introduced as a test in clinical pathology it is essential that the sponsor should have made certain that it fulfils the following requirements:-

- (A) it yields information that the clinician will find valuable in the management of his patients;
- (B) the information supplied has a value related to the cost in equipment, reagents, and man-power required to produce it;
- (C) the same information is not already available by an established test, if the latter is as simple to perform;
- (D) the same information could not be obtained by the direct measurement of the constituent on which the reaction ultimately depends; and
- (E) the scope, sensitivity, and reliability of the new test should have been investigated thoroughly so that it can hope to withstand the independent investigation by others.

I believe that in the evidence reported in this thesis I have shown that the plasma viscosity test has satisfied all these criteria.

(A) The value of the plasma viscosity test to the clinician.

It is claimed that the plasma viscosity is increased by the reaction by the body as a whole against a disease and that the amount of this increase in viscosity is in proportion to the severity of this reaction. It is further claimed that the degree of this reaction is thereby summarised into a single numerical value which can be compared with other similarly-produced figures.

I have made repeated references to the importance of the plasma viscosity estimation as a guide to diagnosis, prognosis, and treatment but I will recapitulate briefly.

Diagnosis - The plasma viscosity can be abnormal in the early stages of disease when the signs, symptoms, and results of other laboratory tests are inadequate to allow a definite diagnosis (eg. pulmonary tuberculosis, ankylosing spondylitis); it can be the determining factor for a decision on "activity" in the presence of vague symptoms (eg. rheumatic fever); and it can assist in the differential diagnosis in which the conditions are known to have significantly different responses (simple and malignant tumours, for example).

Prognosis - The prognosis of a disease is related to the severity of the host's reaction which the test indicates; the changes in the reaction in response (or lack of response) to treatment are also shown; the termination of an active reaction to disease

can be determined with a reliability greater than in any other tests, on occasion. The phenomenon of terminal decay requires special mention.

Treatment - The changes in the plasma viscosity test indicate the satisfactory nature (or otherwise) of treatment. The potential uses of the test as a guide to the duration and type of treatment especially in syphilis and sarcoidosis have been discussed earlier.

(B) The cost of producing the plasma viscosity result relative to its value to the clinician.

This is a problem which vexes all laboratories which use the plasma viscosity test. It has not been possible to combine accuracy with numerous testing.

There has been no worker with the plasma viscosity test who has not reported on it favourably. The initial tests are regarded as in the nature of a research problem where the economics involved receive scanty consideration; however, having introduced the test to the clinicians, the laboratory is frequently faced with their request that the new test should be used in addition to, if not in place of, the ESR. test in their routine investigations. Mann, at the Mayo clinic, has managed to measure scores of plasma viscosities per day by employing his own type of viscometer

which has a potential error of 5% due to blockage, in addition to being subjected to the criticisms of all single-tube viscometers such as used by Gibson, Woodmansey and Wilson, Satô, Arnold, etc.

I have been designing automatic viscometers which Whittington condemned until January 1952. With the model now planned, in which the only error is a fraction of the error in the calibration of a 1 ml. pipette, at least 20 tests per hour will be possible with any intelligent technician.

At the present stage where four tests per hour is a fair output per technician, I cannot recommend the plasma viscosity test for use at the clinician's every whim but retain it for definite problems of the individual patients - eg. ? activity in a mass-radiography pick-up, ? quiescence in rheumatic fever.

(C) Is the same information supplied by any other test ?

The ESR. test is the only one with which the plasma viscosity needs comparison, as it is the only one which claims to indicate the same thing.

If in the comparison, the plasma viscosity test cannot show a superiority (equality is insufficient reason for the discarding of an established test) then it must be forgotten and its

recommendation with-held.

In the course of this thesis I have shown by statistical analysis of groups of cases in rheumatoid arthritis and pulmonary tuberculosis, and by a more general consideration of other types of disease and of individual case histories that the plasma viscosity test is definitely superior to the ESR. test. The same evidence also supports the contention (which is the corollary to the question posed above) that the ESR. test is so frequently in error, unreliable and insensitive that it might well be discarded. As a result of their own experiences, the ESR. test has already been discarded by Benson, Cowan, and Houston. I favour its retention for a single use - the detection of activity in the early stages of a disease - as I believe that there are rare occasions in which the ESR. becomes abnormal before the plasma viscosity test. To ask that such a long-established test as the ESR. should be abandoned now is not a matter to be suggested lightly but I am convinced that it is the proper procedure. I would have been happier in this suggestion if my automatic viscometer was in commercial production yet I can quote Houston as being quite content without his ESR. and having only an occasional plasma viscosity test available with convalescent patients as his technicians.

(D) Could the same information be obtained from an investigation of the plasma constituents (ie. proteins) on which the viscosity depends ?

The estimation of the plasma protein fractions has always been a technical headache because it has been impossible to combine speed with accuracy - the accurate Kjeldahl method is not convenient for the routine laboratory.

This thesis has shown that significant changes in the total protein occur only in association with marked clinical changes. Although it can be measured rapidly but inaccurately with a specific gravity technique, the total protein estimation has few uses as a clinical test as compared with the plasma viscosity.

Even employing the simplest colorimetric techniques, combined with a chemical fractionation, it would be impossible to meet the demands of the clinicians if this method was to replace the plasma viscosity and ESR. The recently-introduced filter-paper electro-phoresis technique has many potential uses but it is still too time-consuming for universal adoption. If later modifications render it an acceptable technique, the protein fractionation may not necessarily displace the plasma viscosity test completely as two major difficulties will restrict its use.

(a) The limits of the normal range for each protein fraction are

so wide apart - eg. 1.3 - 3.0 g./100 ml. of globulin - that relatively large changes may be necessary in initially-low normal values before they become recognized as abnormal. The fractions which are primarily affected have the greatest effect on the viscosity and it is therefore possible (as I found on several occasions) for the plasma viscosity to be definitely abnormal before the protein pattern is accepted as abnormal.

(β) The interpretation and comparison of 4 or more fractions (according to the technique in use) is much more difficult than the single numeral of the plasma viscosity. It is harder to reach a final assessment of the relative and absolute variations in the multiple fractions in the serial tests of the individual patients unless a complicated system such as Whittington and I developed for the combined-protein molecule reduces the fractions to a single numeral also. It would be equally awkward to compare the results of two patients.

It must be stressed that nothing written above is intended to discredit the measurement of the plasma protein fractions in disease of the liver, kidney, tumours, and other diseases where experience is proving it valuable. The criticism is directed only against the routine use of protein fractionation as the index of the severity of the general reaction.

- (E) Can the test hope to withstand independent criticism, comparison with similar tests and their developments, and comparison with suggested modifications in itself ?

The original work by Whittington and Miller (and T'ang and Wang) dealt solely with the plasma viscosity test in tuberculosis. My later work at Montrose, Sunderland and Portsmouth showed that the test could be applied to a wide range of diseases indeed; this extension of our knowledge of the test did not give us cause to modify our claims concerning its use which is now based on over 4,000 tests.

Furthermore, the independent work by Arnold, Benson, Dawson, Gibson, Lawrence, Race, Salt, Steel, Wilson, and Woodmansey has introduced no major controversial opinions concerning the plasma viscosity test itself, while the variety of opinions expressed by them on the relative merits of the plasma viscosity and ESR tests arises really from the differences of the ESR test only. Their reports have been discussed earlier and need not be mentioned again except to point out the dangers of studying restricted disease groups such as done by Race, by Steel, and by Arnold and Salt.

We may therefore conclude that the plasma viscosity test has passed the preliminary independent investigations in a satisfactory manner.

The plasma viscosity test has a fairly low percentage of "failures" where an abnormal viscosity is not detected in the presence of activity by clinical assessment in a type of disease which usually produces a systemic reaction. It is quite possible that further experience will explain why this minority of individuals behaves differently and this very variation from the majority reaction may add further significance to the test. However, until this knowledge has been gained, it is possible that other tests or modifications of the plasma viscosity test may be proposed as its superior because of a lower percentage of failures. It is therefore proper for us to consider the position of our sponsored test relative to these other tests and their future developments.

In a way these other tests (Takata-Ara (177), Cadmium sulphate of Wuhrmann and Wunderly (260), Thymol test of MacLagan (174), Gold flocculation of MacLagan (175), Weltmann's test (53), etc.) support the validity of our own plasma viscosity test in that most of them are based on a measurement of the general upset of the body as indicated by a change of the liver function as indicated by an alteration in the plasma protein. Tests of this nature have usually been introduced to measure the primary liver dysfunction of infective hepatitis, cirrhosis, etc. and then

applied to the liver dysfunction secondary to disease of other parts of the body. There is justification in this procedure in the high incidence of abnormal results with a variety of liver function tests in such diseases as pneumonia (262), malaria (157), tuberculosis (136), rheumatic fever (180), rheumatoid arthritis (83), amoebiasis (228), and others, and by the lesions of the liver at post-mortem in such diseases (eg. 9). Some writers have shown that a better correlation can be obtained between the clinical assessment of a disease and some of these tests than obtained with the ESR. (eg. Weiger's paper (247) reports a better correlation with Hayem's solution reaction as compared with the ESR. in tuberculosis) and it is only a matter of time before a similar comparison is made with the plasma viscosity test.

My own comparison between the plasma viscosity and gold flocculation tests has had instances in rheumatoid arthritis (see Fig. 83) where the gold test was abnormal in the presence of a normal plasma viscosity, yet the reverse was much more frequent. Similarly, the very difference of the behaviour of the two tests in Infective and Rheumatoid Arthritis was made a significant diagnostic point. The gold flocculation test was usually normal in tuberculosis.

I believe that there are four aspects of the plasma viscosity

test which will maintain its superiority over the other tests and any likely development in the near future.

(i) Provided we can reach an agreement on a standard viscosity scale (eg. to the Sucrose line) the plasma viscosity test will have an internationally acceptable standard which will be independent of modifications of only parochial importance.

The results are in the form of simple numerals of which the clinician need only remember the upper limit of the normal range.

A variation of clinical significance need be only 1-2 % of the total possible range of change.

Contrast this with the tests (cephalin-cholesterol flocculation, for example) where the total responses are restricted to six (0 to +++++), where the result is subject to the idiosyncracies of personal interpretation, and where the crude division does not lend itself to close correlation with the clinical condition.

(ii) While it is possible that a flocculation test might give a closer correlation with the clinical state than the plasma viscosity test in some particular disease, it is most probable that this same test will be normal in the presence of other diseases causing a systemic reaction. It follows, therefore, that where such a test is more specific in character it may be used

only in the appropriate disease which requires that the clinician be certain of his diagnosis. The plasma viscosity test reacts more or less equally for the same clinical severity of a wide variety of diseases; what it may lose by lack of sensitivity, it gains by the capacity for a more general application.

(iii) The flocculation and similar tests seem to depend upon one fraction only of the plasma proteins, which is usually a globulin. (The principal globulin may be modified in its action by the albumin and other globulin fractions.) Thus, a test of this type will have little application in the more acute diseases where the main protein change is in the fibrinogen and where the total course may be so brief that the globulins never have time to change at all.

(iv) To have equal application in acute and chronic diseases, a test reflecting protein change must be based on a reaction in which the small absolute fibrinogen change of the acute disease has an effect equal to the larger absolute globulin changes of the chronic disease, somewhat in the proportion of their molecular dimensions.

The reactions likely to comply with this requirement are those measuring the physical rather than the chemical properties of the protein fractions. The specific gravity effect has been

shown to be the same for Albumin and Globulin, and probably for Fibrinogen. The surface tension of serum was shown by du Noüy to have a range of variation which amounted to only 3% of the values. The osmotic pressure of serum and plasma is not readily measured and the physical characters are the opposite of those demanded - the fibrinogen effect is negligible, and the globulin less than albumin. The viscosity fulfils the specifications excellently, as shown both by the experiments with solutions of the purified proteins and by the correlation of the serum and plasma viscosity with the protein components.

The only other test at present in use in clinical pathology which attempts this differential reaction to fibrinogen and globulin is the ESR in which the sedimentation velocity has been shown to be affected by the molecular size (88, 89) (cf dextran experiments (107)), but I have already demonstrated the inferiority of the ESR.

We can conclude, therefore, that although there may be superior tests with an application restricted to certain diseases, provided the diagnosis is certain, there is no prospect of a test which can be so widely applied as the plasma viscosity and which will retain as good a correlation to the clinically assessed severity.

Two modifications of the plasma viscosity test require consideration.

Coke has used a Serum Viscosity Test to his own satisfaction. Salt has recently suggested that the serum viscosity should be studied further. Because of its absence of change in acute disease and because the abnormal range of values relative to the total range appears to be relatively smaller than the corresponding figures for the plasma viscosity (see Fig. 18), I cannot see any immediate benefit arising from the use of this modification. From my own experience with duplicate estimations in several hundreds of tests in a variety of disease conditions I am certain that the Plasma Viscosity is definitely superior.

Lawrence has introduced the Fractional Plasma Viscosity test in an attempt to combine plasma protein fractionation with the plasma viscosity estimation. He has supplied statistics which are convincing evidence that more information is made available by his technique than the simple plasma viscosity test in his hands. (However, his abnormal results in only 59% of his plasma viscosity tests are very much lower than the figures of Benson, Gibson, or myself, who obtained results more of the order of the 86% of his fractional technique). However, his figures are not convincing proof that the extra information

is worth the extra cost in technician's time required by the various manipulations and the three additional viscosity estimations. There exists already a plethora of protein fractionation techniques with their corresponding normal ranges of figures (salting-out with various salts; electrophoresis by various buffers; ultracentrifuge; etc.) and to add yet another which, because it involves the measurement of the viscosity of non-Newtonian fluids, is not reproducible exactly by independent workers would be permissible only if the value of the results really introduced something fundamentally better. I cannot concede that Lawrence has done so. The reader will remember that I could not justify the expenditure for replacing the routine ESR. tests with the plasma viscosity estimation until the automatic viscometer became available commercially, and the additional information produced by Lawrence's method does not merit the quadrupling of the cost. Doubtless there will be individuals who will be able to adopt Lawrence's technique and who will obtain much information from it, but I do not imagine that it will be used generally in pathology departments.

We may conclude, therefore, that the modifications so far suggested in the plasma viscosity test itself are either inferior or too complicated to become generally accepted by clinical pathologists.

The plasma viscosity test remains one of the very best among the non-specific laboratory indications of the systemic reaction by the patient to his disease process.

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Part 9S U M M A R Y

Part 9SUMMARY

- (1) The history of the development of the Plasma Viscosity Test from the Erythrocyte Sedimentation Rate Test by Whittington and Miller, in tuberculosis, has been described.
- (2) The events leading up to my own interest in this test have also been related and how I have become the principal worker in the later developments of the test.
- (3) The physical property of ordinary liquids named "Viscosity" has been defined.
- (4) Fluids have been divided into "Newtonian" and "non-Newtonian"; the non-Newtonian liquids have only "apparent viscosities" as the corresponding physical property varies according to the conditions under which it is measured.
- (5) Plasma and serum are non-Newtonian liquids.
- (6) A technique for the accurate estimation of the viscosity of small volumes of plasmata has been given in detail.

(A) Preclinical Part.
- (7) The potential errors of the technique have been discussed and have been shown to be less than 1 % theoretically and still less practically.

- (8) Venous stasis must be avoided during the venipuncture.
- (9) Significant errors can be introduced into the plasma viscosity estimation by centrifuging with un-capped tubes. Evidence is given for a marked degree of concentration of the plasma by such treatment; most measurements of the constituents of the plasma must be similarly affected.
- (10) A significant change can be caused in the plasma viscosity by a delay in the separation of the plasma from the erythrocytes, either before or after centrifuging.
- (11) The viscosity of a plasma is not affected by mechanical violence.
- (12) Neither is it affected by standing on a bench for five days with precautions taken only against loss by evaporation.
- (13) The viscosity of plasma decreases by approximately 2.35 % for each rise in temperature by one degree centigrade.
- (14) The viscosity of a plasma estimated at 20°C is representative of the viscosity at body-temperature (37°C).
- (15) In some ill subjects, however, the viscosity/temperature curve contained a kink between 32 and 36°C. approximately, whose cause was tentatively suggested as being due to a cryoglobulin.
- (16) Of the anti-coagulants in common use in the laboratories of clinical pathology, the mixture of potassium and ammonium

oxalates of Heller and Paul has been shown to be the most convenient for general use.

- (17) The viscosity of a plasma is representative of the whole plasma sample from which the 1 ml. was taken, of the total blood specimen from which the plasma was prepared, and of the venous blood of both arms.
- (18) The viscosity of the ultra-filtrate of serum (and therefore probably of plasma also) can be regarded as constant in spite of large changes in the non-protein constituents.
- (19) The viscosity of plasma is ultimately a measure of the viscosity of the plasma proteins.
- (20) The viscosity of solutions of the separated protein fractions, in equal concentration, is greatest with fibrinogen and least with albumin; in 1% concentrations the effect of fibrinogen, globulin, and albumin is in the proportion of 6:2:1 approximately.
- (21) An original hypothesis by which a solution is treated as if it were a single homogeneous compound has been derived from a study of these results, whereby the molecular weight of the solute may be calculated by viscosity measurements.
- (22) The viscosity of serum and its component protein fractions were studied in a large series of cases. The viscosity of the

the serum was found to be greater than the value calculated from the viscosities of its proteins.

The globulin:albumin action now seemed to be nearer a ratio of 3:2 .

- (23) A combined-protein molecule, formed by the union of albumin and globulin molecules, was suggested as a possible explanation for the unexpected viscosity results.
- (24) A similar combined-protein was suggested for the proteins of plasma.
- (25) Brief mention has been made to the plasma protein equilibrium factor which Whittington derived by a mathematical analysis of my results, on the hypothesis that there exists in the plasma a dynamic equilibrium between the free protein fractions and a combined-protein molecule.

A brief mention is also made to the possible use of this plasma protein equilibrium factor in clinical medicine; I have suggested that it is more valuable than the simple albumin/globulin ratio.

(Reprints of the two papers are included in the appendix.)

- (26) A periodic wave relationship is demonstrated between the serum viscosity and the protein fractions; confirmation of the wave-pattern was obtained in the published results of Petschacher.

It is possible that a somewhat similar wave-pattern may be obtained between the osmotic pressure and the proteins.

- (27) Large discrepancies (up to 1.5 g./100 ml.) were found between the duplicate estimations of the serum and plasma total proteins by a micro-Kjeldahl and a specific gravity technique.
- (28) The plotting of the points of the duplicate estimation of the corrected citrate plasma viscosity and the maximum corrected citrate sedimentation velocity produced another periodic curve relationship.
- This curve can be reproduced by independent workers.
- (29) The point may fall off this curve in patients suffering from primary liver disease, protein loss via the kidneys, and the clinical state called "terminal decay".
- (30) Gibson obtained a somewhat similar pattern with blood containing the oxalate mixture as anti-coagulant.
- (31) The pattern is seen only where the ESR. technique measures a maximum sedimentation velocity as contrasted to the more common - distance fallen in 1 hour - techniques.
- (32) The Wintrobe ESR./plasma viscosity relationship has a very wide scatter which cannot be correlated to a straight line nor to a periodic curve.

The linear correlations which appear in other papers are based on studies of restricted types of disease.

- (33) The correlation between the ESR. and the plasma proteins have not been sufficiently strict to ascribe a "cause and effect" relationship. In general, a high ESR. was associated with an increased fibrinogen and/or globulin.

It is suggested that a closer correlation might be found between the change in the ESR. and the change in the plasma proteins from the normal basic levels.

- (34) The need for an international standard to which all viscometers may be correlated is emphasized.
- (35) Three techniques have been described by which viscometers can be correlated:-
- (i) by the correlation of the viscosities of the characteristic points of the ESR/viscosity periodic wave;
 - (ii) by a correlation of the viscosities of the characteristic points of the serum viscosity/protein periodic wave;
 - (iii) or by deriving the equation by which the viscosity values of a protein solution are made to coincide with the sucrose line.

(B) Physiology

- (36) The plasma viscosity results in health have a restricted range of values which is the same for both sexes and all ages.
- (37) The variation within the day, from day to day, and from season to season is small.
- (38) Moderate exercise and ordinary food and fluid intake cause no significant changes in the plasma viscosity.
- (39) The viscosity, however, can be varied significantly by the post-alcoholic dehydration and by the ingestion of concentrated solutions of urea and glucose in the fasting state.
- (40) The reported changes in the plasma proteins with variation in posture for any length of time are such as to produce a lowered plasma viscosity in the recumbent position and an increase on again becoming vertical. It is most important that the effects of posture and exercise be separated in such experiments.
- (41) Menstruation does not cause a consistent change in the plasma viscosity.
- (42) During pregnancy there is no significant change until the last two months during which the viscosity rises slightly.
- (43) The effects of the sulphonamides upon the subject himself, as contrasted with the effect upon the disease process, has

been studied in subjects free from any disease known to be influenced by these drugs. There was an increase in the serum proteins, serum and plasma viscosity, and ESR.

The significance to be attached to changes in the tests of clinical pathology during therapy has been discussed.

(C) Disease

(44) Diseases have been classified into two groups:-

(a) Localised and degenerative, in which there is little or no upset of the body as a whole, and

(b) Diseases, with or without a main focus, in which the working of the whole body is upset.

(45) In diseases of type (b), with a systemic or general reaction, the plasma viscosity is usually increased above the normal range of values.

(46) The amount of the increase is proportional to the severity of this systemic reaction.

(47) In those diseases where the degree of general upset is proportional to the severity of the local lesion, there is some relation between the increase in viscosity and the severity of the local lesion also.

- (48) The change in the viscosity is quite non-specific. It is much the same for the same degree of systemic reaction no matter the nature of the primary stimulus.
- (49) The plasma viscosity alters during the course of a disease and these alterations bear a close time relationship with the changes in the clinical state which are their ultimate cause.
- (50) A further rise in the viscosity is an indication of a worsening of the original condition or of a complication; a decrease usually indicates an improvement.
- (51) Such changes in the plasma viscosity allows it to be used as a test in clinical pathology.
- (52) The value of the test to the clinician has been discussed in detail under the headings of:-
- (i) Diagnosis.
 - (a) An abnormal viscosity guarantees the presence of a disease, but a normal viscosity, although suggestive, cannot guarantee its absence.
 - (b) The severity and (c) nature of the disease can be indicated.
 - (ii) Prognosis.
 - (a) The higher values carried a worse prognosis.
 - (b) The test may indicate a disease of chronic character

with its corresponding prognosis.

(c) The test denotes the response to treatment.

(d) It is frequently a very good criterion of cure.

(iii) Treatment.

(a) The treatment may be guided by the response of the viscosity.

(b) A treatment based on an attempt to increase the viscosity prior to lowering it was considered possible in chronic disease.

(c) The potential uses of the test as the criterion of cure in cerebro-spinal syphilis and sarcoidosis, and the design for further researches in this aspect, have been discussed specially.

(53) The high incidence of plasma viscosities from all types of active chronic disease within a restricted part of the total viscosity range led to it being named the "Zone of Chronicity". This zone has a special significance to the clinician.

(54) A similar high incidence of viscosities in patients actually forming a pleural effusion at the time of testing to a restricted range of values led to the range being named the "zone of effusion".

(55) We have also produced the name - "Terminal Decay"- for the

phenomenon of the fall in the plasma viscosity as death approaches. This "terminal decay" is very important to diagnosis, prognosis, and treatment.

(56) The results of the plasma viscosity and Wintrobe ESR. tests have been compared by statistics in rheumatoid arthritis and tuberculosis, and the plasma viscosity has been shown to be definitely superior; this conclusion was supported by a general consideration of other groups of results and of individual case records.

(57) It is even suggested that the ESR. test should now be discarded as unreliable.

(58) The plasma viscosity has been applied to sufficient cases of the following diseases to permit of a special discussion of each.

Rheumatic Disease: Rheumatic fever; rheumatoid arthritis;

Still's disease; infective arthritis; osteo-arthritis;

ankylosing spondylitis; fibrositis; gout.

Tuberculosis: pulmonary and non-pulmonary.

Venereal disease.

Pyogenic infection, plus sarcoidosis.

Tumours: simple and malignant.

Renal and Hepatic disease.

- (59) The behaviour of the Gold Flocculation Test has also been studied in these diseases and valuable information thereby gained.
- (60) In a discussion on the relative merits of other non-specific tests, reasons were given why I cannot foresee any of them replacing the plasma viscosity test in the near future.
- (61) Similarly, the two proposed modifications in the plasma viscosity test itself are unlikely to receive a general acceptance.
- (62) The evidence supports the claim that the plasma viscosity test is one of the very best guides to the general upset in the body as a result of disease.

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APPENDIX

to

On the VISCOSITY of HUMAN BLOOD PLASMA and SERUM in
HEALTH and DISEASE.

A Thesis for the Degree of Doctor of Medicine.

Submitted to the University of Glasgow

by

JOHN HARKNESS.

C O N T E N T S

APPENDIX.

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* * * * *

Part 1METHODS

APPENDIX - Part 1.METHODS.

The full details of the methods will be given only for those procedures which are not included in the system of tests of a large clinical pathology laboratory.

The technique for estimating the plasma viscosity has been given in part 4. of the general thesis.

(A) Collection of Blood Specimens.

From a critical study of the methods of blood removal in many laboratories and out-patient departments I am certain that these ordinary techniques would introduce appreciable errors in the plasma viscosity values. A scrupulous attention to our technique has been maintained throughout and I will not examine a plasma removed by any person who has not had the following details emphasized to him.

Apparatus:- "Vim" syringes, 10 or 20 ml. capacity, sterile and lightly lubricated with paraffin. These have glass pistons and metal nozzles.

"Vim" hypodermic needles - 22, 20, 19 gauge.

Collecting Bottles - Bijou, 1 oz. screw-capped, or centrifuge tube.

"Plain" - containing no anticoagulant.

"Potassium Oxalate" - dried salt, allowing 2 mg. per ml. blood.

"Mixed Oxalate" - containing crystals derived by drying off from the solution at 37°C., allowing 6 mg. ammonium oxalate and 4 mg. potassium oxalate per 5 ml. of blood.

"Heparin" - containing 10 units per ml. blood.

"Citrate" - these containers were 10 ml. graduated flasks or centrifuge tubes, or a 10 ml. tube which I had made to a design of my own, with the intention that the passage of the blood through the constriction during shaking



would ensure a thorough mixing of the blood and citrate solution. All these tubes contained 2 ml. of 3.8% sod. citrate solution.

Preparation of the apparatus:- Our experiments showed that the plasma viscosity could be affected by psychological stimuli and it is obviously essential that the psychological trauma of serial venipuncture should be reduced to the minimum. Hence, each needle was sharpened by myself after each use. Also, the smallest needle was used which would allow a rapid removal of an adequate blood volume - 22 gauge for 5 and 10 ml, 20 gauge for 20 ml, and 19 gauge for larger volumes.

Preparation of the patient:- The patient was arranged sitting comfortably in bed or at a table. Both antecubital fossae were examined by inspection and palpation in search of a large medial or lateral vein (the central veins were preserved wherever possible in case of later requirements for blood transfusion or intravenous therapy). The selected arm was rested on a pillow. The needle and syringe were selected and patency of the needle tested.

Removal of the blood:- A rubber tourniquet must not be used. For crippled patients I have an assistant but in all other instances I make the patient act as his own tourniquet as his attention is thereby detracted from the venipuncture. He grasped his upper arm firmly while the skin was being swabbed, the position of the vein was confirmed by palpation, and the needle introduced rapidly and smoothly. The constricting hand was removed, the dammed blood was milked towards heart by the swab, and gentle

steady traction applied to the plunger of the syringe. When enough blood was in the syringe, the needle was withdrawn. A swab was applied firmly over the puncture and the patient was made to continue this pressure with his arm held straight, not flexed as is the usual method. These few seconds will reduce the incidence of haematomata formation to the minimum and thus please the patient (while preserving a vein for immediate future use). The needle was removed from the syringe and the appropriate amount of blood injected smoothly into each container. Solution of the anticoagulants was obtained by gentle rocking; shaking was avoided as it was liable to produce frothing which, in turn, might produce haemolysis. These samples were transferred to the laboratory without delay.

On a few occasions, because of small veins or defective circulation, the antecubital veins only became detectable after the arm was warmed in hot water: rarely, the blood was removed from the veins of the wrist.

(B) Preparation of Plasma and Serum.

The contents of the blood containers were transferred to 15 ml. centrifuge tubes. These were centrifuged for 15 minutes, by a timing device, at 3,000 r.p.m.. (As the diameters of the centrifuge heads varied from laboratory to laboratory, the r.c.f. values were not constant.) It is essential that the centrifuge tubes are stoppered during the centrifuging.

(C) Estimation of the Plasma and Serum Protein Fractions.

Principle:- The protein was digested with sulphuric acid to form ammonium sulphate from which strong alkali liberated the ammonia which was distilled into a known volume of standard acid. Fibrinogen was estimated from the fibrin clot of recalcified plasma; the fractions in serum were separated by the salting-out technique of Howe (121,) using solutions of sodium sulphate.

Apparatus:- Digestion tubes and heating racks for micro-Kjeldahl tubes.
2 Markham stills (161).
Various burettes, pipettes, flasks, etc.

Reagents:- Pumice powder; normal saline, 5% calcium chloride solution, digestion mixture composed of 3 vols. of MAR sulphuric acid and 1 vol. of phosphoric acid AR, potassium persulphate AR, N/100 HCl, N/100 baryta, 0.1% methyl red and 0.03% p-nitrophenol in 50% alcohol as indicator, 1.6M, 1.33M, 1.06M sod. sulphate solns. 10% sodium tungstate soln, 2/3N sulphuric acid.

Method:- The quantities chosen of protein-containing material yielded about sufficient ammonia to neutralise 10 ml. of N/100 acid. Duplicate results agreed to better than 1%.

a) Total serum protein. With a re-calibrated pipette, 1.0 ml. of serum was added to normal saline in a 10 ml. volumetric flask and saline added to graduation: 1.0 ml of diluted serum was transferred, in duplicate, to Pyrex digestion tubes.

b) Fibrinogen. 1 ml. of Wintrobe-blood plasma was added to 30 ml. normal saline, 2 ml. of CaCl_2 soln. added, and incubation

carried out at 37°C for about an hour. The white fibrin clot was removed by whipping it onto a glass rod from which it was pulled by filter-paper and squeezed dry. The tiny clot was then washed for an hour in two changes of distilled water, again squeezed dry, and added to 1 ml. of water in a digestion tube. Duplicate tests were run when there was sufficient plasma.

c) Serum protein fractions. 1.0 ml. of serum was added to 15 ml. of each concentration of sodium sulphate soln. (to give 1.5M, 1.25M, and 1.0M finally) in stoppered flasks kept in the incubator overnight. Still in the incubator, filtration through No50 Whatman filter-papers was made with the full precautions of Robinson (208) whereby preliminary saturation of the paper with protein prevents a loss of albumin by adsorption. 2 ml. of the fluid was filtered, refiltered, and discarded; this was repeated with another 2 ml. sample. The remainder of the fluid was then filtered. 3 ml. of filtrate, in duplicate, were pipetted into digestion tubes.

d) Non-protein-nitrogen (NPN). 1 or 2 ml. of serum was added to 15 ml. of distilled water, and the protein was precipitated by 2 ml. of tungstate soln. followed by 2 ml. of 2/3N acid. A No42 Whatman paper was used for the filtration. 5 ml. of the filtrate, in duplicate, were transferred to digestion tubes.

e) To each tube was added 1 ml. of digestion mixture and a

pinch of pumice (to minimise bumping).

f) Digestion was continued on a gas micro-burner until the contents were well-charred and heavy white fumes were rising, heating was continued for another 5 minutes, and the tube allowed to cool.

g) 1 g. of pot. persulphate and 1 ml. of water were added and the digestion resumed until the contents were clear and the dense white fumes were again rising, and heating was continued for a further 3-5 minutes.

h) The contents of the tubes were transferred in turn to a Markham still, the ammonia was liberated by 40% NaOH soln. and received into 10 ml. N/100 acid, and the excess acid was titrated with standard baryta.

The 2 Markham stills allowed eight distillations per hour and revolutionised the number of Kjeldahl estimations possible by a single worker.

i) The classical protein/nitrogen factor of 6.25 was used throughout. There is not yet any agreed factor for the fractions although it has been realised that the factor probably differs slightly from 6.25 and from each other for the individual fractions.

j) To obtain the plasma values corresponding to the serum

results a correction was introduced to allow for the space in the plasma occupied by the fibrinogen (specific volume = 0.75).

k) Calculations:-

Fibrinogen = $6.25 \times$ nitrogen of Fibrin clot

Total serum protein = $6.25 \times$ (Total serum nitrogen - NPN)

Total plasma protein = Serum protein \times (100 - $0.75 \times$ fibrinogen)
+ fibrinogen.

Serum Albumin = protein in filtrate from 1.5M sod. sulph. soln.

Serum Globulin = total serum protein - albumin.

Pseudoglobulin II = filtrate protein from 1.25M sod. sulph -
albumin.

Pseudoglobulin I = filtrate protein from 1.0M sod. sulph. -
(albumin + pseudoglobulin II).

Euglobulin = total globulin - pseudoglobulins II and I.

(D) Preparation of Pure Albumin and Globulin Fractions.

Principle:- I devised a method from the papers of Hopkins (117), Young (261), and Adair and Robinson (3).

Globulin was salted-out and filtered off; the albumin was precipitated from the filtrate by adjustment of the pH. Both proteins were purified further.

All the technique required full aseptic precautions of sterile apparatus and solutions.

Method:- 1. A pint of blood was collected from each of 10

normal subjects. The clots were separated from the bottle wall by a wire and the bottles placed in the refrigerator overnight.

2. The serum was pipetted into centrifuge tubes, spun, and the clear serum was bulked and preserved in the refrigerator till next day.

A. Albumin.

a) To 1 volume of serum was added an equal volume of saturated ammonium sulphate solution, and this mixture was stored at 0°C for 1 day.

b) The precipitated globulin was removed by centrifugation.

c) To the supernatant, 10% acetic acid was added, with constant stirring, to the point of definite faint turbidity which corresponded to a pH of 6.0. The red colour of the fluid changed to yellow just before this end-point.

d) This mixture was allowed to stand for 2 hours at room temperature.

e) The same volume of acetic acid as was added in stage (c) was now added to bring the pH to between 4.9 and 5.1. The yield could be increased by a further slow addition of saturated ammonium sulphate solution to a total of 1 ml. per 100 ml. of fluid.

f) Crystallisation of the albumin took place overnight at room temperature.

- g) These crystals of albumin were separated by centrifugation.
- h) Washing; the crystals were mixed with an equal volume of a solution composed of 60 ml. of molar sodium acetate, 40 ml. of molar acetic acid, 100 ml. of saturated ammonium sulphate soln. and then recentrifuged.

The crystals were again washed and recentrifuged.

- i) Purification: 2 g. of crystals were dissolved in 50 ml. of distilled water, and the solution filtered to remove insoluble residue such as lipoids. To the filtrate were added 8 ml. of molar sodium or ammonium acetate and then saturated ammonium sulphate equal in volume to (filtrate + acetate solution). Over a period of 15 minutes, with stirring, was added a mixture of equal volumes of molar acetic acid and saturated ammonium sulphate solution; 1.33 ml of this mixture for each ml. of sodium acetate solution added in stage three above, - usually about 10.6 ml.. Crystallisation took place in the next 2 hours, during which the fluid was stirred frequently: the yield was increased on standing overnight at room temperature. The crystals were removed by centrifugation.
- j) The crystals were purified again as above.

The yield of albumin was 1 g. per 100 ml. of serum in 3-4 days.

- k) Dialysis: the crystals were redissolved in distilled water

and dialyzed at 0°C against 0.8/15 molar Na_2HPO_4 and 0.2/15 molar KH_2PO_4 per litre (pH = 7.41 at 0°C). Cellophane sausage skins were used. Dialysis continued until the levels remained constant.

1) These cellophane skins were hung in a current of warm air and after many days a dried protein product (sodium albuminate) was obtained.

B. Globulin.

a) The globulin prepared at stage (b) above was redissolved in water.

b) It was reprecipitated by an equal volume of saturated ammonium sulphate solution, and again separated by centrifugation.

c) This solution and reprecipitation was repeated for a further four times.

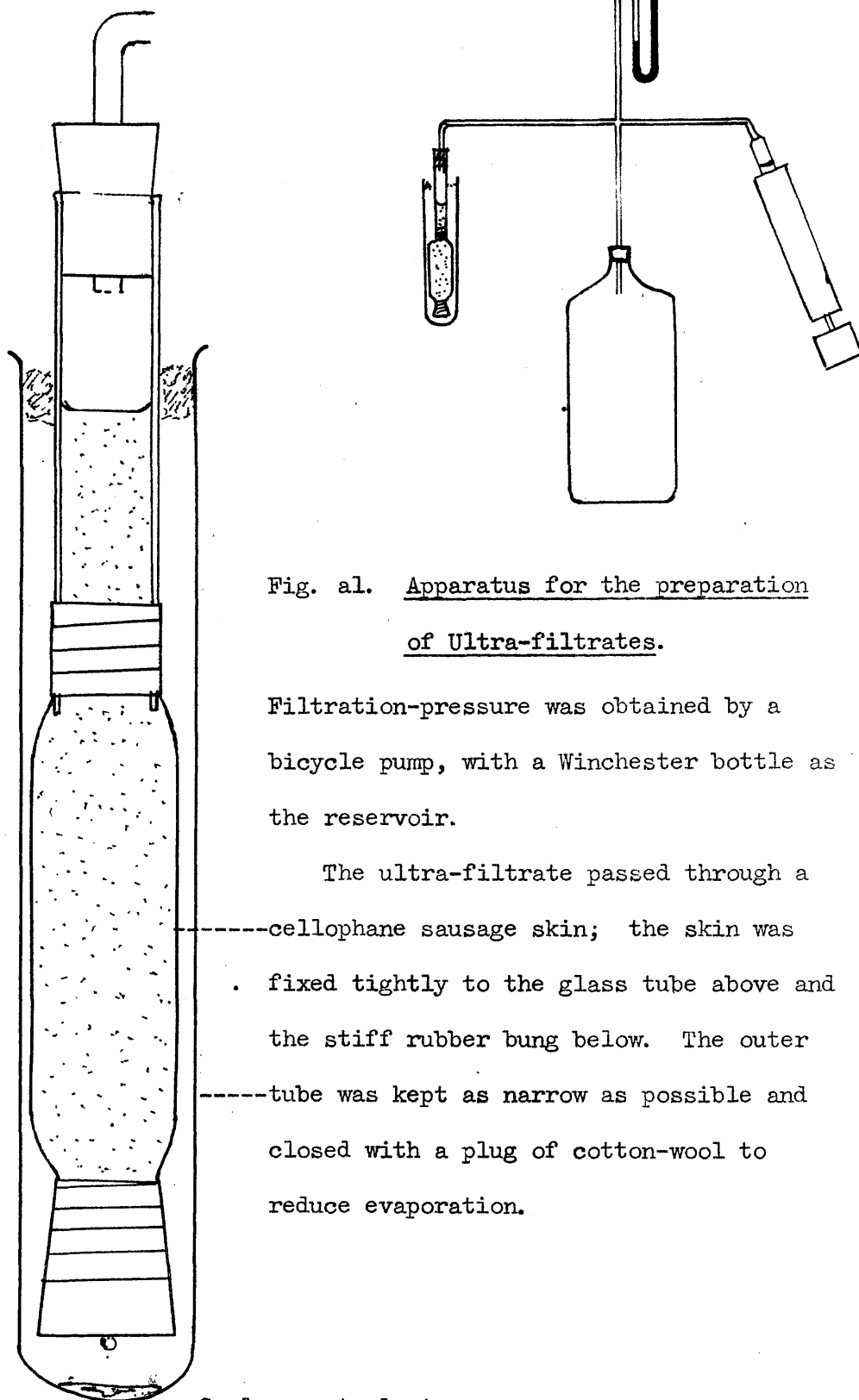
d) The globulin was dissolved in water and dialyzed at 0°C against the same buffer as used for albumin.

e) The protein was dried in a stream of air.

(E) Preparation of Ultrafiltrates from Serum.

The ultrafiltrates were prepared from sera by filtration, under pressure, through cellophane sausage skins. Figure I indicates the arrangement of the apparatus.

One end of the casing was eased onto a firm rubber bung and



sealed with cellophane tape. The other end was eased onto the end of a 4" length of glass tubing of about $3/4$ " diameter which had been selected because of the tight fit between tube and casing; seal was again made with cellophane tape. About 3" of casing lay between the bung and tube, to give a capacity of about 30 - 40 ml. when allowance was made for the expansion of the casing under pressure and loss of fluid in the filtrate. This filtrate was collected in a large test-tube, closed lightly with cotton-wool. A pressure of 3" of mercury was obtained by a bicycle pump and winchester-bottle-reservoir. The overnight yield was only about 2 ml.

All the ultrafiltrates (10) were tested for protein and no sample had to be discarded.

(Elek and Hilson (69) have recently described an apparatus by which a large yield is obtained from a smaller volume of serum than I required. The pressure head is obtained by centrifugation. This apparatus will be obtained for my further experiments.)

(F) Measurement of the Specific Gravity.

Three techniques were employed.

(i) Density Bottle Method.

In my first experiments I used a density bottle of 2 ml. capacity. As the number of estimations per day increased, this

technique became so inconvenient that it was discarded in favour of the following method.

(ii) Falling-Drop Method of Barbour and Hamilton (18).

Their original technique was followed in detail. A new nomogram was constructed to allow of rapid calculation of the results.

This method has the advantage over the third technique in that it can be used with non-protein-containing liquids as well as for plasma and serum.

Principle:- A drop of defined volume of the fluid fell through a less dense liquid with which it was immiscible and the time taken by this drop to travel a defined distance was noted; similar measurements were made with identical drops from liquids of known specific gravity; the specific gravity of the test fluid can be calculated by a comparison of the times of fall.

Apparatus:- see Figure II and III.

Water-bath; NPL thermometer, stop-watch; pipette-holder; tubes of 50cm. length and 7 mm. bore, with graduations 30 cm. apart and 10cm. from the ends.; pipettes to deliver 0.01 ml., between two graduations.

Reagents: Aqueous solutions of potassium sulphate of known specific gravity; various mixtures of zylol and bromobenzene.

Method:- a) The temperature of the water-bath was adjusted to within a degree of 20°C and the temperature noted to the nearest 0.1° on the thermometer.

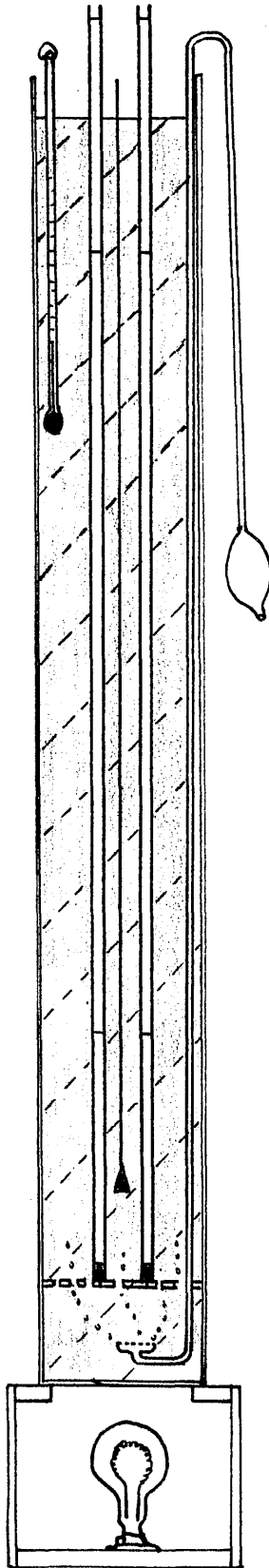


Fig. aII. Barbour and Hamilton's
Falling-drop Specific Gravity Apparatus.

A tall glass tube of 60 cm. length acts as a water-bath: a small electric bulb compensates for heat loss to the air: the water is mixed by air bubbles introduced below the perforated plate.

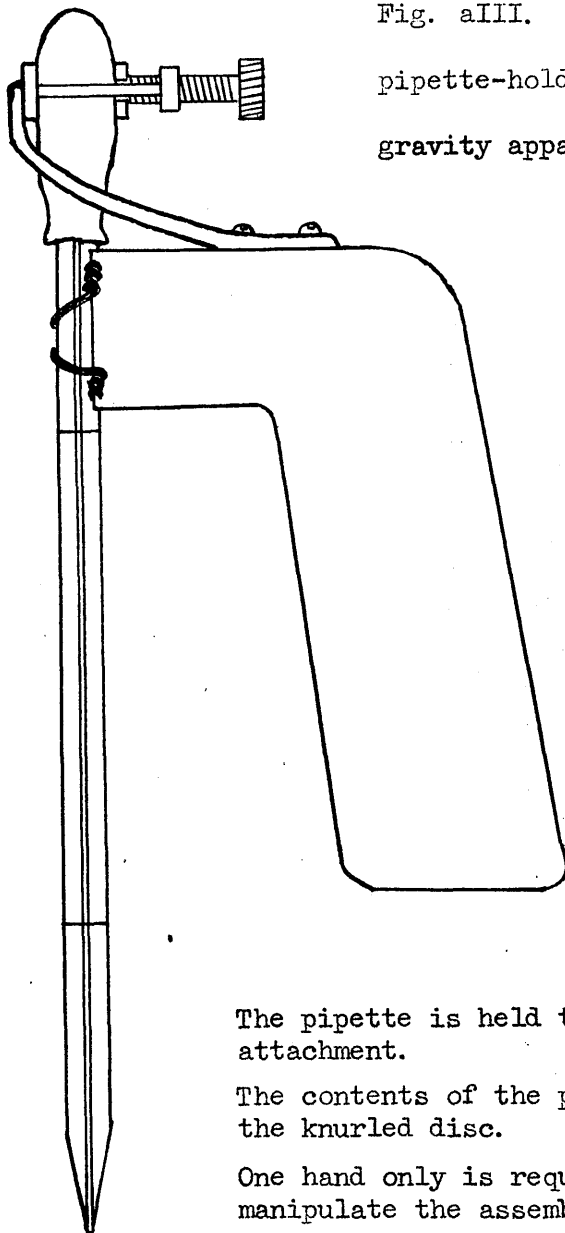
The upper surface of the plate is covered with perforated plasticine which anchors the lower end of the graduated tubes but permits easy removal.

The tubes are 7 mm. in diameter and 50 cm. in length; the graduations are 30 cm. apart and 10 cm. from the ends.

The tubes are filled to within a millimetre or so of the end. In practice the water would be higher in the outer jacket and the inner tubes would not project so far.

The graduated tubes must be maintained vertical.

Fig. aIII. The pipette and pipette-holder of the specific gravity apparatus.



The pipette is held tightly by the spring attachment.

The contents of the pipette are controlled by the knurled disc.

One hand only is required to hold and manipulate the assembled apparatus.

b) The tubes containing the bromobenzene-zylol mixtures were arranged vertically by comparison with a plumbline, in two planes.

c) The special pipette, with teat attached, was inserted into the holder (designed by myself; made by an asylum inmate).

- d) The pipette was filled to the upper graduation, the tip was wiped dry, and the tip was inserted just below the surface of the bromobenzene-*zylol*. Compression on the teat until the fluid fell to the lower graduation, a sharp upward movement to detach the protruding drop, and exactly 0.01 ml. of fluid was falling.
- e) By stop-watch, the time taken for the drop to pass between the graduations 30 cm. apart on the tubes was noted.
- f. A duplicate test usually agreed to within 0.2 seconds.
- g. The technique was repeated with solutions of known specific gravity.
- h) By means of a nomogram, the specific gravity was calculated from the times of fall, a correction for temperature variation being included.

This method is accurate to about 0.0001.

Three standard solutions of potassium sulphate, and five bromobenzene-*zylol* mixtures were sufficient to cover the range of the specific gravities from the ultrafiltrate to the heaviest plasma.

(iii) Copper Sulphate Method of Phillips et al. (194)

Principle: Solutions of copper sulphate were prepared of known specific gravity, at 0.0005 intervals. If a drop of a protein-containing fluid was introduced the protein was precipitated to form a coating to the remainder of the fluid;

the drop then adjusted its level according to the relation of its specific gravity to that of the copper sulphate solution, rising if lighter, falling if denser, remaining at constant level if identical.

Further fluid was abstracted from the drop in 30 seconds or so, and the drop fell to the bottom, leaving the bottle ready for the next test.

Apparatus:- Pasteur pipettes and teats.

Copper sulphate solutions, in 150 ml. bottles, in a series from sp. gr. 1.0100 to 1.0380.

Method:- A drop of plasma or serum was dropped from a pipette from 1 cm. above the copper sulphate solution surface. The behaviour of the drop was noted. By interpolation, the specific gravity was read to the nearest 0.0001.

(G) Erythrocyte Sedimentation Rate or ESR.

Three techniques were used in the course of my work.

(i) Wintrobe ESR.

a) 5 ml. of venous blood was added to the appropriate amount of Heller and Paul's oxalate mixture (this is often wrongly called "Wintrobe's mixture", but he acknowledges the previous work by the other two authors). The salts were dissolved by gentle rocking.

b) Immediately before the further stages of the test, the blood

was mixed thoroughly by shaking by hand or in a machine - this was essential in order to break down the aggregates of cells which had already formed during the period of standing.

c) With a long dry Pasteur pipette the blood was introduced into a Wintrobe tube to the zero level (this tube is 3 mm. in diameter and 120 mm in length, of which the graduations are from 0 to 100 in mm, the closed end being the 100 mark).

d) The tube was arranged vertically in a special stand.

e) The depth of the plasma was read after 1 hour exactly.

f) The tube was then spun in a centrifuge as a haematocrit,

g) and by the correction chart of Wintrobe and Landsberg (258) the 'Corrected ESR' was estimated. This chart correction gave the value of the ESR which would have been obtained with the average packed-cell-volumes (= 42% for females; =47% for males).

(ii) Westergren ESR.

a) 4 volumes of blood were added to 1 volume of an aqueous solution of tribasic sodium citrate, 3.8 g. per 100 ml..

b) Thorough mixing before further testing was made as in Wintrobe method.

c) A Westergren tube was filled to the upper graduation and the tube arranged vertically in the special stand. (The Westergren tube is 300 mm. long, bore is 2.5 mm, the lower 200 mm. length is graduated in millimetres, and both ends are

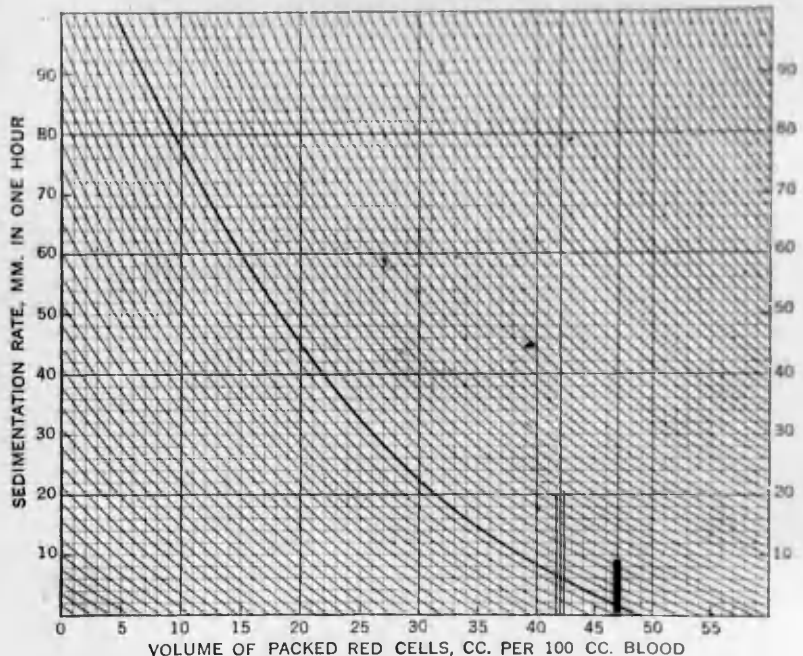


FIG. 42.—Chart for correction of sedimentation rate according to volume of packed red cells. The logarithmic curve on which this chart is based is heavily outlined. The mean normal volume of packed red cells for men (47 cc.) and for women (42 cc.) are also heavily outlined and the range of normal sedimentation is represented by solid and open columns for each sex, respectively.

To "correct" sedimentation rate, find on the chart the horizontal line corresponding to the sedimentation rate for the patient; find also the vertical line corresponding to the volume of the packed red cells in the patient's blood. Select the curve lying nearest to the point of junction of the horizontal and the vertical line and follow this to the normal line for the sex of the patient. The horizontal line corresponding to this last point of juncture gives the corrected sedimentation rate. Since the difference between the normal sedimentation rates in men and women is largely due to the difference in volume of packed red cells, all sedimentation rates may be corrected to a volume of 47 cc. and a single standard of normal (0 to 6 mm.)

Fig. aIV

The chart prepared by Wintrobe and Landsberg (258) for the correction of an experimental Wintrobe ESR. value for variation in the haematocrit from the normal 42% in females and 47% in males.

open.

d) The depth of the clear plasma was measured after 1 hour, 2 hours and 24 hours.

No correction was made for variation in the haematocrit values.

(iii) Corrected Maximum Sedimentation Velocity.

The corrected maximum sedimentation velocity was measured with blood containing citrate solution, mixed oxalates, or heparin as anticoagulant. The normal average haematocrit value was assumed to be 45% in both sexes. The technique for the citrate blood is given here; the other two methods are closely analogous.

- a) An accurate 4:1 blood: citrate solution was made in a graduated centrifuge tube, volumetric flask, or special tube as already described.
- b) The blood was mixed by shaking. Two haematocrit samples were removed and the remainder of the blood was divided equally between two graduated centrifuge tubes.
- c) The haematocrits were spun for 30 minutes; the centrifuge tubes for 15 minutes.
- d) The erythrocytes in one tube were adjusted to 36% by removing plasma or adding plasma from the other tube - $36\% = 45\%$ in the original blood when allowance was made for the dilution with

citrate solution.

The equation is given in Figure IV, but the nomogram removed the need for detailed calculations on each test values.

- e) The adjusted blood was thoroughly remixed by a long stirring rod or by a syringe and lumbar-puncture needle - repeated filling and emptying never produced haemolysis.
- f) A Westergren tube was filled, the lower end was closed by plasticine contained in a one-holed bung, and the tube was arranged vertically on the shelf at the end of the 20°C water-bath, as illustrated in Fig. 4 of the general text.
- g) The depth of clear plasma was noted at frequent time intervals. These values were plotted on graph paper until the line joining the points had become straight and steepest. The test was then discontinued. Thus a test might require from a half to seven hours.

From the slope of the straight line, the maximum velocity was calculated in terms of mm./hour or cm./second.

(H) Estimation of Packed-Cell-Volume (P.C.V.)

Two techniques were used.

(i) Wintrobe Haematocrit Tube.

The dimensions of the tube have been given in the section on the estimation of the Wintrobe ESR. Their capacity is slightly

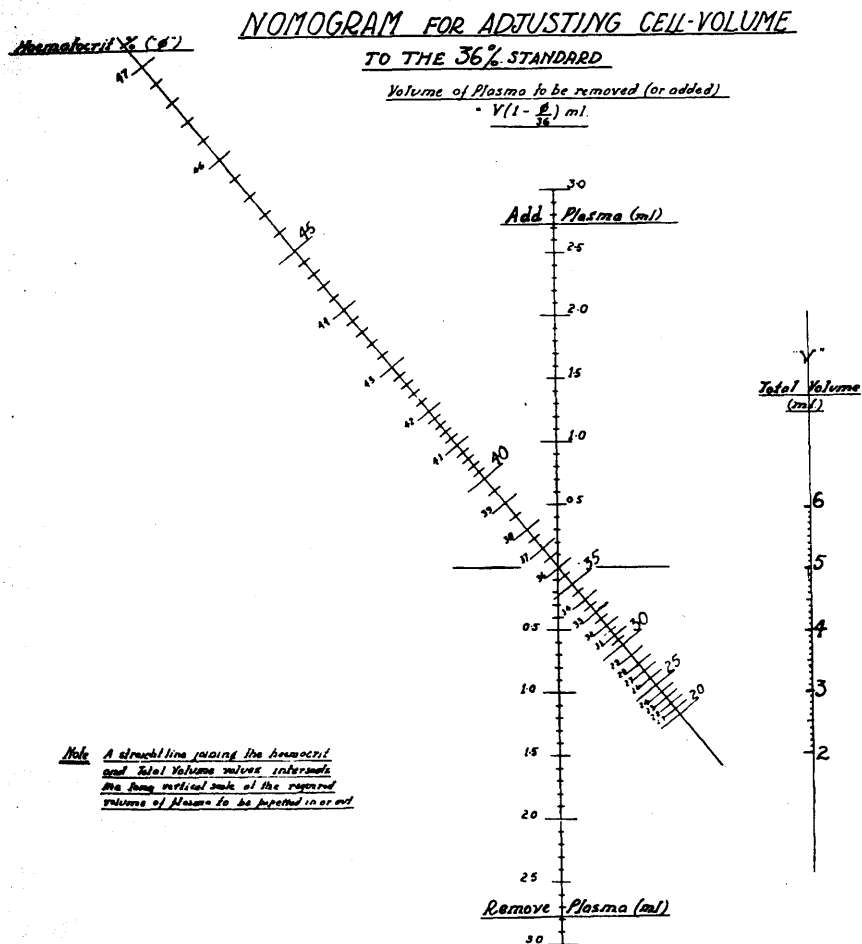


Fig. V The nomogram for the adjustment of a citrate blood so that the cells will be 36% of the total volume.

An accurate haematocrit value (ϕ) is measured; a blood sample is centrifuged in a graduated tube; a line joining the total blood volume and the haematocrit will cross the central vertical line at a point which will indicate how much of the plasma has to be removed or added. A second small volume of blood is centrifuged to supply this extra plasma if required.

less than 1 ml.

The tubes were centrifuged for 30 minutes at the maximum speed of which the MSE Minor centrifuge was capable (3,000 rpm.).

The percentage of the erythrocytes was estimated to 1/10th division, and a correction was made for any inaccuracy in the original filling-volume.

(ii) Capillary Haematocrit Tube.

These tubes are of 6 cm. length and under 1 mm. bore. They are graduated into 100 divisions. To stand the stress of centrifugation, they are held within a metal sheath.

The tubes were filled with blood as in filling a counting pipette and closed within the sheath by screwing up the rubber washers of the ends. The centrifugation was carried out as for the Wintrobe technique.

* * * * *

This concludes the methods for which the details are required. The results from these techniques have been discussed in the general text and the accuracy and value of some of the methods have also been criticised.

The estimations included in the following list are in general use by all physicians and clinical pathologists. The reference for the detailed technique is given after each test.

- (I) Gold flocculation test. (175)
- (J) Thymol turbidity test. (174)
- (K) Thymol flocculation test. (176)
- (L) Alkaline phosphatase of plasma and serum. (134)
- (M) Acid phosphatase of serum. (134)
- (N) Urea of blood and urine. (104)
- (O) Blood sugar. (134)
- (P) Cholesterol of whole blood, serum and plasma. (134)
- (Q) Uric acid of whole blood, serum and plasma. (33)
- (R) Serum calcium. (104)
- (S) Serum inorganic phosphate. (80)
- (T) Sodium of serum. (63 and 104)
- (U) Potassium of serum. (63 and 134)
- (V) Chloride of serum and plasma. (222)
- (W) Alkali reserve of serum and plasma. (104)

* * * * *

- (X) Plasma Proteins were measured colorimetrically
by a method based on a combination of
Gornall et al.,- J.Biol. Chem.,1949,177, 751
and
Woolfson et al.-Amer.J.clin.Path.,1948,18,723.
-

Part 2

TABLES of RESULTS

for

PRE-CLINICAL SECTION

The estimation of the viscosity of duplicate samples taken from single specimens of mixed oxalate plasmata.

Test 1.	Test 2.	Difference
1.653	1.652	0.001
1.660	1.662	0.002
1.661	1.661	0
1.661	1.666	0.005
1.661	1.666	0.005
1.747	1.751	0.004
1.785	1.786	0.001
1.785	1.782	0.003
1.797	1.795	0.002
1.805	1.804	0.001
1.835	1.833	0.002
1.860	1.866	0.006
1.903	1.898	0.005
1.915	1.914	0.001
1.983	1.982	0.001
1.987	1.984	0.003
2.003	2.001	0.002
2.031	2.036	0.005
2.166	2.167	0.001
2.263	2.262	0.001
2.398	2.392	0.006
2.459	2.460	0.001
2.499	2.499	0
2.524	2.529	0.005
Maximum		0.006
Minimum		0
Mean		0.0027
Standard deviation		0.0020

Duplicate estimations made on two separate blood samples drawn from single blood specimens.

No precautions were taken to mix the blood in the syringe before filling the collecting bottles.

No.	PLASMA VISCOSITY			PCV.		Wintrobe E. S. R.		Plasma Protein	
	A	B	Diff.	A	B	A	B	A	B
		cs.		%		mm/ 1 hr.		g/100ml.	
1	1.895	1.886	0.009	46.5	46.3	11	11	6.95	6.98
2	2.178	2.176	0.002	39.3	40.0	40	39	7.63	7.85
3	2.381	2.388	0.007	39.6	39.7	47	36	7.67	7.78
4	2.114	2.111	0.003	41.1	41.6	18	18	7.85	7.88
5	2.056	2.051	0.005	41.3	41.3	35	37	7.31	7.34
6	2.052	2.047	0.005	40.2	40.4	27	21	7.45	7.49
7	2.059	2.062	0.003	46.3	45.9	20	19	7.31	7.31
8	1.883	1.900	0.017	39.8	40.0	12	10	7.31	7.20
9	2.066	2.051	0.015	37.7	37.7	31	29	7.99	7.96
10	1.838	1.843	0.005	42.5	42.4	13	13	6.98	7.02
11	2.441	2.435	0.006	47.1	47.6	13	5	8.39	8.35
12	2.356	2.351	0.005	42.6	43.4	20	29	8.06	8.06
13	2.178	2.183	0.005	44.4	44.6	24	39	7.56	7.52
14	2.170	2.175	0.005	42.7	42.5	36	36	7.67	7.70
15	2.141	2.134	0.007	40.3	40.3	39	38	7.74	7.74
16	2.258	2.244	0.014	45.3	45.3	19	20	8.03	8.03
17	1.863	1.864	0.001	43.8	43.4	10	10	6.98	7.09
18	1.901	1.905	0.004	45.2	44.4	20	19	7.13	7.06
19	1.799	1.808	0.009	40.8	40.4	7	6	7.09	7.09
20	2.013	2.008	0.005	40.0	40.3	25	27	7.52	7.63
21	1.972	1.974	0.002	40.0	39.9	40	38	7.31	7.45
22	2.010	2.032	0.022	47.4	47.4	9	12	7.70	7.96
23	1.903	1.911	0.008	40.3	40.2	14	15	7.34	7.31
24	1.863	1.856	0.007	41.8	42.1	5	4	7.31	7.45
25	1.762	1.769	0.007	40.5	40.1	5	5	6.44	6.52
26	1.876	1.884	0.008	41.8	42.4	12	12	7.56	7.56
27	1.798	1.797	0.001	37.6	37.6	11	11	6.88	6.80
28	1.927	1.926	0.001	49.9	49.0	2	2	7.34	7.38
29	2.313	2.314	0.001	45.0	45.3	28	30	7.63	7.81
30	2.078	2.081	0.003	45.5	45.8	11	11	7.63	7.66
31	2.100	2.095	0.005	47.4	46.4	28	28	7.52	7.52
32	1.997	1.983	0.014	39.6	39.1	-	-	7.49	7.45
33	1.952	1.944	0.008	44.1	44.4	14	14	7.16	7.24
34	2.114	2.118	0.004	47.6	47.6	15	14	8.03	8.06
35	2.098	2.089	0.009	44.7	45.6	12	14	7.49	7.70
36	1.989	1.996	0.007	48.3	47.9	6	7	7.63	7.67
37	1.890	1.885	0.005	49.3	49.1	1	2	7.13	7.09
38	2.331	2.342	0.011	45.0	44.7	7	11	7.52	7.56
39	2.206	2.204	0.002	49.5	49.2	4	5	7.74	7.70
40	2.026	2.043	0.017	52.8	53.0	3	3	7.31	7.31
41	1.938	1.928	0.010	48.0	48.8	11	10	6.59	6.62
42	2.201	2.203	0.002	46.6	46.3	10	8	8.10	8.17
43	2.108	2.107	0.001	43.1	42.7	30	27	7.38	7.45
44	1.898	1.901	0.003	43.9	43.1	6	7	6.91	6.95
45	1.871	1.865	0.006	48.5	49.0	2	2	7.16	7.27

Duplicate tests by taking blood samples from both arms with as short a time-interval between the venipunctures as possible.

The arm mentioned first in the table is the arm from which the first blood sample was taken.

Arm	PCV.	PLASMA VISC.	Wintrobe ESR.	Plasma Total Protein	Plasma Spec. Gravity
	%	cs.	mm/l hr	g. %	
Left	49.6	1.660	0.5	6.44	1.0259
Right	49.3	1.661	1.	6.41	1.0258
Right	48.1	1.759	1	6.88	1.0269
Left	48.0	1.761	1	6.88	1.0269
Right	34.9	2.171	55	7.42	1.0286
Left	34.2	2.163	55	7.42	1.0286
Left	38.2	2.262	39	7.31	1.0283
Right	38.4	2.255	52	7.27	1.0282
Left	40.	1.845	32	6.41	1.0258
Right	40.	1.840	32	6.48	1.0260
Left	40.7	2.088	46	6.98	1.0274
Right	39.7	2.077	49	6.88	1.0271
Right	35.8	1.830	11	6.84	1.0268
Left	36.3	1.826	10	6.95	1.0270
Mean difference = 0.0054 cs.					
Standard deviation = 0.0035					

Table - D The effect of variations in the concentration of Potassium & Ammonium Oxalate Anti-coagulant.

Conc.	PLASMA VISCOSITY					E. S. R.					P. C. V.					Specific Gravity.					
	x $\frac{1}{2}$	Normal	x2	x3	x5	x $\frac{1}{2}$	Nor.	x2	x3	x5	x $\frac{1}{2}$	Norm.	x2	x3	x5	x $\frac{1}{2}$	Normal	x2	x3	x5	
1.932	1.937	1.923	-	-	-	36	35	34	-	-	35.	35.	35.	35.	-	-	1.0279	1.0286	1.0294	-	-
1.903	1.920	-	-	-	-	59	58	56	-	-	31.1	31.6	31.0	-	-	-	1.0250	1.0257	1.0262	-	-
1.715	1.711	1.711	-	-	-	2	2	2	-	-	30.0	29.2	29.7	-	-	-	1.0261	1.0268	1.0274	-	-
1.919	1.897	1.867	1.851	-	-	10	10	10	11	-	41.2	40.9	40.0	39.7	-	-	1.0283	1.0285	1.0296	1.0303	-
1.862	1.839	-	1.810	-	-	9	8	9	11	-	40.9	40.9	40.4	39.1	-	-	1.0273	1.0278	1.0282	1.0280	-
1.883	1.863	1.838	1.841	-	-	42	40	38	35	-	36.9	36.1	35.4	35.0	-	-	1.0250	1.0253	1.0264	1.0274	-
-	2.154	2.105	2.082	-	-	-	30	30	26	-	-	45.0	44.0	43.0	-	-	-	1.0291	1.0304	1.0312	-
-	2.244	-	2.205	-	-	-	-	-	-	-	-	35.7	35.4	-	-	-	-	-	-	-	-
-	1.914	-	1.885	1.846	-	-	28	-	33	39	-	44.5	-	42.0	41.0	-	-	1.0263	1.0263	1.0298	-
-	2.104	-	2.028	2.001	-	-	17	-	14	13	-	43.9	-	41.8	40.0	-	-	1.0277	1.0288	1.0303	-
-	3.115	-	3.047	2.947	-	-	15	-	26	36	-	37.8	-	35.9	34.0	-	-	1.0320	1.0336	1.0353	-
-	1.949	-	1.903	1.871	-	-	24	-	24	22	-	40.5	-	38.7	36.8	-	-	1.0268	1.0283	1.0304	-
-	1.955	-	1.867	1.834	-	-	9	-	11	9	-	48.3	-	45.4	43.3	-	-	1.0280	1.0288	1.0305	-
-	2.042	-	2.022	1.953	-	-	-	-	-	-	-	37.4	-	36.1	34.5	-	-	1.0312	1.0327	1.0342	-
-	2.355	-	-	2.306	-	-	-	-	-	-	-	33.3	-	-	32.5	-	-	1.0315	-	1.0347	-
-	2.066	-	-	2.028	-	-	-	-	-	-	-	46.3	-	-	42.5	-	-	1.0297	-	1.0330	-
-	1.885	-	-	1.872	-	-	-	-	-	-	-	41.2	-	-	37.6	-	-	1.0284	-	1.0324	-
-	2.106	-	-	2.014	-	-	-	-	-	-	-	43.6	-	-	40.2	-	-	1.0300	-	1.0322	-

Comparison of the Plasmata derived from three samples of a single blood specimen:-

'A' = supernatant plasma from 5 ml. of blood which was centrifuged as soon as possible.

'B' = supernatant plasma from 5 ml. of blood which was put into a centrifuge tube, stoppered, allowed to remain undisturbed on the bench, and centrifuged after 24-hours at same time as 'C';

'C' = supernatant plasma from 5 ml. of blood which was kept in a Bijou bottle, with several gentle mixings, for 24-hours and then centrifuged.

'B' represents plasma with minimal but continual contact with erythrocytes.

'C' represents plasma with considerable contact with erythrocytes.

Centrifugation was standardized for all samples - 15 minutes, at 2,300 r.p.m., in a MSE Major centrifuge.

PLASMA VISCOSITY					TOTAL PROTEIN.		
A	B	C	Differences.		A	B	C
			A-B	A-C			
1.637	1.667	1.678	+0.030	+0.041	6.12	6.23	6.23
1.688	1.693	1.695	+0.005	+0.007	6.26	6.34	6.41
1.710	1.732	1.723	+0.022	+0.013	6.59	6.66	6.62
1.731	1.742	1.743	+0.011	+0.012	6.48	6.30	6.30
1.806	1.820	1.808	+0.016	+0.002	6.91	7.06	6.98
1.813	1.818	1.845	+0.005	+0.042	7.27	6.95	7.02
1.817	1.821	1.842	+0.004	+0.025	6.95	6.88	6.95
1.860	1.865	1.889	+0.005	+0.029	7.24	7.09	7.09
1.863	1.868	1.882	+0.005	+0.019	7.27	7.13	7.63
1.919	1.928	1.948	+0.009	+0.029	7.56	7.13	7.45
1.972	2.011	2.024	+0.039	+0.052	6.80	6.95	6.98
1.978	2.029	2.029	+0.051	+0.051	7.49	7.56	7.67
1.981	2.005	2.002	+0.024	+0.021	6.98	7.09	7.09
1.995	1.999	2.012	+0.004	+0.017	7.45	7.45	7.49
2.022	2.038	2.040	+0.016	+0.018	6.62	6.98	6.91
2.027	2.028	2.046	+0.001	+0.019	6.84	6.77	6.95
2.042	2.038	2.068	-0.004	+0.026	7.31	7.31	7.31
2.103	2.137	2.143	+0.034	+0.040	7.45	7.49	7.49
2.207	2.215	2.217	+0.008	+0.010	7.34	7.31	7.45
2.480	2.480	2.491	0	+0.011	8.03	8.17	8.03
Range			-0.004	+0.002			
			+0.051	+0.052			
Mean			+0.0143	+0.0237			
Standard deviation			0.0146	0.0136			

The loss which may be produced by using centrifuge tubes without closures.

(F) Pyrex centrifuge tubes, calibrated in 0.1 ml marks, were filled to the 10 ml. mark with distilled water; they were spun, without caps, for 4 successive periods of 15 minutes, with the smallest possible interval between. The temperature recorded is that of an accompanying tube of water so that the thermometer did not remove any of the contents of a graduated tube.

Original		after 15.		after 30.		after 45.		after 60		Loss
Vol.	Temp.	Vol.	Temp.	Vol.	Temp.	Vol.	Temp.	Vol.	Temp.	
ml.	°C.	ml.	°C.	ml.	°C.	ml.	°C.	ml.	°C.	%
10.00	-	9.95	-	-	-	-	-	9.20	-	8.0
10.00	-	10.05	-	-	-	-	-	9.25	-	7.5
10.00	-	9.90	-	-	-	-	-	9.17	-	8.3
10.00	-	9.90	-	-	-	-	-	9.15	-	8.5
10.00	18	9.90	25	9.79	25	9.61	30	9.47	33	5.3
10.00	"	9.92	"	9.83	"	9.69	"	9.53	"	4.7
10.00	"	9.90	"	9.82	"	9.67	"	9.53	"	4.7
10.00	"	9.92	"	9.80	"	9.68	"	9.50	"	5.0

(G) 10 ml. of blood were introduced into a graduated pyrex centrifuge tube and spun without a cap for 4 periods of 15 minutes; about 1 ml. was removed at each interval for the plasma viscosity estimation. Another specimen of the blood was centrifuged for the complete hour in a stoppered tube.

Note the small amount of concentration which has occurred within the first 15 minutes, and the later larger changes.

Specimen	PLASMA VISC.	Sp. Grav.	Plasma Total Prot.	PCV / Tot.	Vol. after removing plasma	Loss	% of total	% of plasma
	cs.		g. %		ml.	ml.		
15 min.	1.937	1.0241	5.80	391:989	8.60	0.11	1.1	1.6
30 min.	1.963	1.0255	6.30	385:857	7.43	0.03	0.35	0.63
45 min.	1.982	1.0262	6.55	379:789	5.70	0.04	0.55	1.1
60 min.	2.057	1.0272	6.91	377:567	-	0.03	0.53	1.6
Capped	1.919	1.0242	5.83					
15 min.	2.233	1.0217	4.94	402:978	8.67	0.22	2.2	3.8
30 min.	2.282	1.0224	5.18	403:860	7.39	0.07	0.81	1.6
45 min.	2.325	1.0231	5.44	402:731	5.91	0.08	1.1	2.4
60 min.	2.443	1.0238	5.69	400:587	-	0.04	0.7	2.1
Capped	2.216	1.0219	5.00					

Note the increase in the plasma viscosity and the total protein as a result of centrifuging without closures to the tubes. The figures are also included for the plasma prepared by allowing the cells to sediment.

The haematocrits of four of these bloods have their results presented in Table (H).

Specimen	PLASMA VISC.	Increase		Sp.Grav.	Plas. Total Prot.	Increase		Test No. (H)	Temp. °C.
		Visc.	%			Prot.	%		
	cs.	cs.			g.%	g.%			
15 min.	1.881	-	-	1.0286	7.42	-	-	14	32
30 min.	1.897	0.016	0.9	1.0292	7.63	0.19	2.6		
45 min.	1.928	0.047	2.5	1.0297	7.81	0.39	5.3		
60 min.	2.009	0.128	6.8	1.0305	8.10	0.68	9.2		
Sediment	1.880			1.0284	7.54				
15 min.	1.743	-	-	1.0271	6.88	-	-	15	32
30 min.	1.759	0.016	0.9	1.0273	6.95	0.07	1.0		
45 min.	1.796	0.053	3.0	1.0287	7.45	0.57	8.3		
60 min.	1.914	0.171	9.8	1.0309	8.24	1.36	19.8		
Sediment	1.760	0.017		1.0271	6.88	0			
15 min.	2.102	-	-	1.0290	7.56	-	-	13	32
30 min.	2.142	0.040	1.9	1.0296	7.78	0.22	2.9		
45 min.	2.222	0.120	5.7	1.0304	8.03	0.47	6.2		
60 min.	2.382	0.280	13.3	1.0328	8.93	1.37	18.1		
Sediment	2.087			1.0285	7.38				
15 min.	1.813	-	-	1.0283	7.31	-	-	16	32
30 min.	1.837	0.024	1.3	1.0288	7.49	0.18	2.5		
45 min.	1.883	0.070	3.9	1.0295	7.74	0.41	5.6		
60 min.	2.020	0.207	11.4	1.0322	8.71	1.40	19.2		
Sediment	1.809			1.0277	7.09				
15 min.	1.919	-	-	1.0289	7.52	-	-	-	
30 min.	1.940	0.021	1.1	1.0294	7.70	0.18	2.4		
45 min.	1.994	0.075	3.9	1.0300	7.92	0.40	5.3		
60 min.	2.081	0.162	8.4	1.0318	8.57	1.05	13.7		
15 min.	1.924	-	-	1.0283	7.31	-	-	-	
30 min.	1.972	0.048	2.5	1.0286	7.42	0.11	1.5		
Sediment	1.948	0.024	1.2	1.0279	7.16				

The effect of centrifugation on un-capped haematocrit blood volumes.

The haematocrit (Wintrobe) tubes were filled to the 10 cm. graduation, then allowed to stand for about 15 min. to allow the cells to sediment and so permit of an accurate reading of the meniscus level.

The centrifuge was stopped between each 15 minute period only sufficiently to read the various levels and to measure the temperature of the centrifuge head.

The ratio in the table is the volume of the packed erythrocytes to the total blood volume.

No.	Original Volume	after 15 minutes				after 30 minutes				after 45 minutes				after 60 minutes			
		RBC/ total	Loss %	PCV, %	oC.	RBC/ total	Loss %	PCV, %	oC.	RBC/ total	Loss %	PCV, %	oC.	RBC/ total	Loss %	PCV, %	oC.
1	1008	459:1006	0.2	45.7	25	449: 999	0.9	45.0	27	446: 992	1.6	44.9	33	446: 989	1.9	45.1	32
2	1012	456:1008	0.4	45.2	"	447:1003	0.9	44.5	"	448: 997	1.5	44.4	"	444: 992	2.0	44.7	"
3	1000	450: 997	0.5	45.2	"	439: 994	0.6	44.2	"	437: 988	1.2	44.2	"	436: 986	1.4	44.2	"
4	1003	329:1000	0.3	32.9	"	320: 996	0.7	32.1	"	317: 990	1.3	32.0	"	315: 987	1.6	31.7	"
5	1008	474:1007	0.1	47.1	"	462:1000	0.8	46.2	"	458: 992	1.6	46.2	"	458: 988	2.0	46.3	"
6	1008	429:1004	0.4	42.7	"	422: 999	0.9	42.2	"	420: 994	1.4	42.2	"	416: 988	2.0	42.1	"
7	1011	434:1008	0.3	43.1	"	422:1006	0.5	42.0	"	421:1000	1.1	42.1	"	418: 997	1.4	41.9	"
8	1006	510:1004	0.2	50.7	"	500:1000	0.6	50.0	"	496: 993	1.3	49.9	"	496: 989	1.7	50.2	"
9	1002	323:1000	0.2	32.3	"	315: 995	0.7	31.7	"	314: 990	1.2	31.7	"	314: 987	1.5	31.6	"
10	1000	424: 998	0.2	42.5	"	413: 993	0.7	41.6	"	412: 989	1.1	41.7	"	410: 984	1.6	41.7	"
11	1002	444: 999	0.3	44.4	-	441: 991	1.1	44.5	-	438: 936	1.6	44.4	-	438: 977	2.5	44.8	36
12	1003	264:1003	0.0	26.3		262: 997	0.6	26.3		258: 991	1.2	26.0		257: 984	1.9	26.1	"
13	1012	343:1007	0.5	34.1		337:1000	1.2	33.7		335: 993	1.9	33.7		335: 936	2.6	33.9	"
14	1021	268:1015	0.6	26.4		261:1008	1.3	25.9		255:1003	1.8	25.4		254: 992	2.9	25.6	"
15	1013	440:1009	0.4	43.6		432:1003	1.0	43.1		429: 997	1.6	43.1		423: 988	2.5	43.3	"
16	1007	397:1006	0.1	39.4		391: 999	0.8	39.2		383: 990	1.7	39.2		337: 982	2.5	39.4	"
17	1010	413:1008	0.2	41.0		404:1004	0.6	40.2		404: 996	1.4	40.6		402: 987	2.3	40.8	"
18	1020	263:1013	0.2	25.8		259:1009	1.1	25.7		258:1000	2.0	25.8		256: 989	3.1	25.9	"
19	1017	330:1010	0.7	37.6		376:1006	1.1	37.4		374: 998	1.9	37.5		374: 990	2.7	37.8	"
20	1017	429:1010	0.7	42.6		426:1005	1.2	42.3		421: 997	2.0	42.2		420: 986	2.9	42.7	"

Table - H continued. The effect of centrifugation on haematocrit values; open and capped tubes.

Duplicate tests were made on 20 bloods, with open (O) and capped (C) tubes. The method was otherwise the same as with the previous twenty tests.

No.	Original		after 15 minutes				after 30 minutes				after 45 minutes				after 60 minutes			
	Volume	Temp	RBC/ total	Loss %	PCV. %	°C.	RBC/ total	Loss %	PCV. %	°C.	RBC/ total	Loss %	PCV. %	°C.	RBC/ total	Loss %	PCV. %	°C.
21 O	1005	19	489:1003	-0.2	48.7	26	482:999	-0.6	48.2	31	479:994	-1.1	48.2	36	478:987	-1.8	48.4	37.8
C	1009	"	489:1010	+0.1	48.4	"	483:1012	+0.3	47.7	"	483:1012	+0.3	47.7	"	482:1013	+0.4	47.6	"
22 O	1009	"	277:1007	-0.2	27.5	"	273:1006	-0.3	27.1	"	271:1000	-0.9	27.1	"	271:994	-1.5	27.3	"
C	1010	"	271:1008	-0.2	26.9	"	266:1010	0	26.4	"	266:1012	+0.2	26.3	"	263:1013	+0.3	26.3	"
23 O	1011	"	462:1010	-0.1	45.7	"	453:1007	-0.4	45.1	"	453:1003	-0.8	45.2	"	452:997	-1.4	45.4	"
C	1015	"	464:1016	+0.1	45.7	"	458:1016	+0.1	45.1	"	455:1018	+0.3	44.7	"	454:1019	+0.4	44.6	"
24 O	1004	"	346:1003	-0.1	34.5	"	341:997	-0.7	34.2	"	339:994	-1.0	34.1	"	337:987	-1.7	34.1	"
C	1002	"	344:1003	+0.1	34.3	"	340:1004	+0.2	33.9	"	338:1006	+0.4	33.6	"	336:1007	+0.5	33.4	"
25 O	1009	"	209:1007	-0.2	20.7	"	206:1004	-0.5	20.5	"	205:1001	-0.8	20.5	"	205:993	-1.6	20.6	"
C	1010	"	207:1012	+0.2	20.4	"	203:1013	+0.3	20.0	"	203:1014	+0.4	20.0	"	202:1014	+0.4	19.9	"
26 O	1006	"	312:1006	0	31.1	"	307:1004	-0.2	30.5	"	307:1000	-0.6	30.7	"	306:993	-1.3	30.8	"
C	1010	"	320:1011	+0.1	31.6	"	317:1013	+0.3	31.3	"	315:1013	+0.3	31.1	"	315:1014	+0.4	31.1	"
27 O	1002	"	350:1000	-0.2	35.0	"	347:999	-0.3	34.7	"	343:994	-0.8	34.5	"	343:987	-1.5	34.7	"
C	1008	"	351:1010	+0.2	34.7	"	344:1012	+0.4	33.9	"	343:1013	+0.5	33.8	"	341:1013	+0.5	33.6	"
28 O	1003	"	379:1002	-0.1	37.8	"	370:1000	-0.3	37.0	"	367:995	-0.8	36.9	"	366:989	-1.4	37.0	"
C	1003	"	374:1004	+0.1	37.2	"	367:1007	+0.4	36.5	"	366:1007	+0.4	36.4	"	364:1007	+0.4	36.2	"

Table - H continued.

No.	Original		after 15 minutes				after 30 minutes				after 45 minutes				after 60 minutes			
	Volume	Temp °C.	RBC/ total	Loss %	PCV. %	°C.	RBC/ total	Loss %	PCV. %	°C.	RBC/ total	Loss %	PCV. %	°C.	RBC/ total	Loss %	PCV. %	°C.
29 O	1007	26	314:1006	-0.1	31.2	33	309:1002	-0.5	30.8	38	308: 997	-1.0	30.9	39	308: 989	-1.8	31.1	40.7
C	1005	"	314:1007	+0.2	31.2	"	312:1007	+0.2	31.0	"	309:1008	+0.3	30.7	"	307:1008	+0.3	30.5	"
30 O	1010	"	403:1008	-0.2	40.0	"	397:1003	-0.7	39.6	"	392: 994	-1.6	39.5	"	392: 987	-2.3	39.7	"
C	1007	"	395:1007	0	39.2	"	390:1007	0	38.7	"	388:1008	+0.1	38.5	"	386:1009	+0.2	38.2	"
31 O	1001	"	431: 999	-0.2	43.1	"	426: 994	-0.7	42.8	"	424: 988	-1.3	42.9	"	424: 988	-1.3	42.9	"
C	1003	"	432:1006	+0.3	42.9	"	426:1006	+0.3	42.3	"	424:1007	+0.4	42.1	"	424:1007	+0.4	42.1	"
32 O	1010	"	441:1009	-0.1	43.7	"	437:1003	-0.7	43.5	"	436: 997	-1.3	43.8	"	434: 989	-2.1	43.9	"
C	1009	"	439:1010	+0.1	43.5	"	436:1012	+0.3	43.1	"	434:1013	+0.4	43.1	"	434:1013	+0.4	43.1	"
33 O	1009	"	430:1007	-0.2	42.7	"	428: 999	-1.0	42.8	"	423: 993	-1.6	42.6	"	422: 987	-2.2	42.5	"
C	1000	"	428:1003	+0.3	42.6	"	424:1003	+0.3	42.2	"	423:1004	+0.4	42.1	"	420:1004	+0.4	41.8	"
34 O	1013	"	363:1011	-0.2	35.9	"	354:1005	-0.8	35.2	"	352:1001	-1.2	35.2	"	349: 993	-2.0	35.1	"
C	1006	"	360:1007	+0.1	35.7	"	351:1008	+0.2	34.8	"	348:1009	+0.3	34.5	"	346:1009	+0.3	34.3	"
35 O	1008	"	398:1006	-0.2	39.5	"	392: 998	-1.0	39.3	"	388: 994	-1.4	39.1	"	388: 984	-2.4	38.5	"
C	1010	"	394:1010	0	39.0	"	397:1011	+0.1	39.3	"	394:1012	+0.2	39.0	"	393:1012	+0.2	38.9	"
36 O	1002	"	435: 999	-0.3	43.5	"	428: 992	-1.0	43.1	"	426: 988	-1.4	43.1	"	426: 983	-1.9	43.3	"
C	1011	"	431:1013	+0.2	42.5	"	423:1014	+0.3	41.7	"	423:1013	+0.2	41.7	"	423:1014	+0.3	41.7	"

Table - H continued.

No.	after 15 minutes			after 30 minutes			after 45 minutes			after 60 minutes		
	RBC/ total	PCV.	°C.	RBC/ total	PCV.	°C.	RBC/ total	PCV.	°C.	RBC/ total	PCV.	°C.
37 O	381:1009	37.7	25	374:1008	37.1	28	372:1007	37.0	30	370:1002	36.9	33.5
C	385:1016	37.9	"	377:1017	37.1	"	377:1017	37.1	"	373:1017	36.6	"
38 O	386:1011	38.2	"	378:1008	37.5	"	375:1007	37.3	"	373:1002	37.2	"
C	380:1009	37.7	"	373:1009	37.0	"	371:1009	36.8	"	369:1009	36.6	"
39 O	402:1010	39.8	"	397:1007	39.5	"	396:1003	39.4	"	394: 998	39.5	"
C	394:1007	39.2	"	391:1007	38.9	"	389:1007	38.7	"	389:1007	38.7	"
40 O	412:1019	40.4	"	406:1018	39.9	"	404:1011	39.9	"	404:1004	40.3	"
C	398:1006	39.6	"	394:1006	39.2	"	392:1006	39.0	"	393:1006	39.1	"

The effect of centrifuging upon the plasma viscosity values - the difference caused by failure to stopper the centrifuge tubes.

The first twenty tests were centrifuged for 15 minutes; the capped tubes only in the last two tests were centrifuged for 60 minutes.

Test No.	Plasma Viscosity			Specific Gravity		Total Protein	
	Open tube	Closed	Differ.	Open	Closed	Open	Closed
1	1.643	1.627	-0.016	1.0237	1.0234	5.65	5.54
2	1.718	1.703	-0.015	1.0263	1.0258	6.59	6.41
3	1.722	1.706	-0.016	1.0248	1.0247	6.05	6.01
4	1.770	1.748	-0.022	1.0272	1.0268	6.91	6.77
5	1.770	1.753	-0.017	1.0268	1.0265	6.77	6.66
6	1.771	1.761	-0.010	1.0237	1.0233	5.65	5.51
7	1.788	1.767	-0.021	1.0263	1.0259	6.59	6.44
8	1.804	1.780	-0.024	1.0266	1.0265	6.70	6.65
9	1.820	1.807	-0.014	1.0265	1.0263	6.66	6.59
10	1.825	1.811	-0.014	1.0265	1.0263	6.66	6.59
11	1.842	1.826	-0.016	1.0288	1.0282	7.49	7.27
12	1.872	1.845	-0.027	1.0287	1.0282	7.45	7.27
13	1.872	1.849	-0.023	1.0286	1.0284	7.42	7.34
14	1.892	1.882	-0.010	1.0248	1.0242	6.05	5.83
15	1.889	1.883	-0.016	1.0289	1.0283	7.52	7.31
16	1.903	1.888	-0.015	1.0279	1.0276	7.16	7.06
17	1.906	1.892	-0.014	1.0289	1.0287	7.52	7.45
18	1.919	1.905	-0.014	1.0278	1.0274	7.13	6.98
19	1.965	1.948	-0.017	1.0264	1.0262	6.62	6.55
20	2.180	2.159	-0.021	1.0287	1.0287	7.45	7.45
Range			-0.010 -0.027				
Mean			-0.0171				
Standard deviation			0.0043				
21	1.937	1.919	-0.018	1.0241	1.0242	5.80	5.83
22	2.233	2.216	-0.017	1.0217	1.0219	4.94	5.00

Comparison of the Plasmata derived from two samples of one blood specimen:-

'A' = supernatant plasma from a 4 or 5 ml. blood sample which stood in a stoppered centrifuge tube on the bench at room temperature until the cells had sedimented enough to yield at least 1 ml. of plasma.

'B' = supernatant plasma derived by centrifuging 4 or 5 ml. of blood in a Major MSE centrifuge at 2,300 rpm. for 15 minutes.

These results should be compared with those of the following table.

PLASMA VISCOSITY.			SPEC. GRAV.		TOTAL PROTEIN.		
A	B	difference	A	B	A	B	difference
1.637	1.681	+0.044	1.0250	1.0248	6.12	6.05	-0.07
1.710	1.742	+0.032	1.0263	1.0263	6.59	6.59	-
1.731	1.757	+0.026	1.0260	1.0258	6.48	6.41	-0.07
1.760	1.743	-0.017	1.0271	1.0271	6.88	6.88	-
1.760	1.711	-0.049	1.0274	1.0268	6.98	6.77	-0.22
1.809	1.813	+0.004	1.0277	1.0283	7.09	7.31	+0.22
1.813	1.841	+0.028	1.0282	1.0272	7.27	6.91	-0.36
1.869	1.863	-0.006	1.0278	1.0282	7.13	7.27	+0.14
1.880	1.881	+0.001	1.0284	1.0286	7.34	7.42	+0.08
1.916	1.920	+0.004	1.0257	1.0257	6.37	6.37	-
1.930	1.919	-0.011	1.0279	1.0280	7.16	7.20	+0.04
1.944	1.937	-0.007	1.0279	1.0286	7.16	7.42	+0.26
1.945	1.936	-0.009	1.0280	1.0284	7.20	7.34	+0.14
1.948	1.924	-0.024	1.0279	1.0283	7.16	7.31	+0.15
1.972	2.005	+0.029	1.0269	1.0269	6.80	6.80	-
1.978	1.996	+0.018	1.0288	1.0288	7.49	7.49	-
1.981	1.955	-0.026	1.0274	1.0273	6.98	6.95	-0.03
2.042	2.041	-0.001	1.0283	1.0283	7.31	7.31	-
2.087	2.102	+0.015	1.0288	1.0290	7.49	7.56	+0.07
2.207	2.200	-0.007	1.0284	1.0282	7.34	7.27	-0.07
Range of differences		+0.044 -0.049	+0.0007 -0.0010		+0.26 -0.36		
Mean of differences		+0.002	+0.000035		+0.014		

Comparison of the Plasmata derived from a single blood sample:-

'A' = supernatant plasma taken from the upper layer of plasma formed by the sedimentation of the cells of 8-10 ml. of blood, standing in a stoppered centrifuge tube on the bench at room temperature; about 1 ml. of plasma formed this sample.

'B' = the remaining plasma and cells were centrifuged at 2,300 rpm. in a Major MSE centrifuge for 15 minutes; 1 ml. of this plasma was removed to form this sample.

These results should be compared with those of the preceding table.

PLASMA VISCOSITY.			SPEC. GRAV.		TOTAL PROTEIN.		
A	B	difference	A	B	A	B	difference
1.681	1.675	-0.006	1.0248	1.0257	6.05	6.37	+0.32
1.742	1.733	-0.009	1.0263	1.0263	6.59	6.59	- -
1.757	1.743	-0.014	1.0258	1.0258	6.41	6.41	- -
1.760	1.708	-0.052	1.0274	1.0271	6.98	6.88	-0.10
1.777	1.767	-0.010	1.0258	1.0260	6.41	6.48	+0.07
1.841	1.818	-0.023	1.0272	1.0275	6.91	7.02	+0.11
1.869	1.863	-0.006	1.0278	1.0280	7.13	7.20	+0.07
1.916	1.917	+0.001	1.0257	1.0254	6.37	6.26	-0.11
1.930	1.914	-0.016	1.0279	1.0278	7.16	7.13	-0.03
1.944	1.954	+0.010	1.0279	1.0283	7.16	7.31	+0.15
1.955	1.989	+0.034	1.0273	1.0282	6.95	7.27	+0.32
1.996	2.041	+0.045	1.0288	1.0291	7.49	7.60	+0.11
2.005	2.010	+0.005	1.0269	1.0273	6.80	6.95	+0.15
2.017	1.998	-0.019	1.0284	1.0282	7.34	7.27	-0.07
2.041	2.065	+0.024	1.0283	1.0283	7.31	7.31	- -
2.070	2.045	-0.025	1.0285	1.0281	7.38	7.24	-0.14
2.185	2.160	-0.025	1.0303	1.0302	8.03	7.99	-0.04
2.096	2.066	-0.030	1.0297	1.0295	7.81	7.74	-0.07
2.200	2.204	+0.004	1.0282	1.0288	7.27	7.49	+0.22
2.603	2.640	+0.037	1.0298	1.0298	7.85	7.85	- -
Range of differences		+0.045 -0.052	+0.0009 -0.0004		+0.32 -0.14		
Mean of differences		-0.0038	+0.00013		+0.057		

The effect of Delay in the Estimation on the viscosity values of citrate plasma, oxalate plasma, and serum.

These fluids were separated from the cells and kept in a stoppered tube on the bench at room temperature, without an attempt to obtain sterility.

The first test was made as soon as possible.

Initial Viscosity	Delayed Viscosity	Time Interval
cs.	cs.	hours
<u>Citrate Plasma</u>		
1.707	1.698	4
1.707	1.707	28
1.540	1.553	5
1.895	1.885	5
1.895	1.876	26
1.667	1.644	24
1.657	1.653	25
2.017	2.041	25
<u>Oxalate Plasma</u>		
1.763	1.760	2
1.888	1.887	3
1.763	1.764	4
1.797	1.795	4
2.012	2.012	4
1.885	1.895	19
2.066	2.085	19
1.923	1.915	22
2.355	2.369	23
1.763	1.766	24
<u>Serum</u>		
1.893	1.898	1/2
2.046	2.050	3
2.084	2.063	4
2.044	2.041	4
1.878	1.888	4
1.694	1.693	18
2.083	2.082	24
1.566	1.574	23
2.426	2.422	24
1.878	1.888	27
2.044	2.021	27

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These fluids were separated from the cells and kept on the bench, at room temperature and without precautions for sterility, as 1 ml. samples in small stoppered tubes. Each day a tube was chosen at random.

Days.									Mean
0	1	2	3	4	5	6	7	8	
<u>Oxalate plasma.</u>									
2.466	2.490	2.472	2.468	2.470	-	2.484	2.483	2.481	2.477
1.880	1.882	1.881	1.879	1.877	-	1.888	1.882	-	1.881
1.743	1.742	1.748	1.742	-	1.754	1.746	1.745	-	1.746
1.982	1.987	1.984	1.977	-	2.002	2.003	2.005	2.020	1.995
2.012	2.013	2.003	2.008	-	2.020	2.021	-	-	2.013
1.936	1.934	1.941	1.927	1.950	-	1.948	1.952	1.957	1.943
1.874	1.875	-	1.875	1.846	1.861	1.858	1.861	1.863	1.864
1.929	1.914	1.917	1.920	1.924	1.919	-	-	-	1.921
2.220	2.226	2.245	-	2.237	-	-	-	-	2.232
2.059	2.052	2.072	2.072	-	-	-	-	-	2.064
1.777	-	-	1.785						
1.802	-	-	1.802						
2.338	-	-	2.334						
2.017	-	-	2.013						
2.421	-	-	2.425						
2.055	-	-	2.054						
1.907	-	-	1.905						
1.955	-	-	1.950						
2.800	-	-	2.765						
2.902	-	-	2.907						
3.228	-	3.240	-	3.225					
<u>Citrate plasma.</u>									
1.495	1.508	-	1.519	1.495	1.524				
<u>Serum.</u>									
1.792	-	-	1.798						
1.624	-	-	-	1.616					
<p>Maximum differences from mean 0 = + 0.025 and - 0.013</p> <p>Minimum differences from mean = + 0.007 and - 0.004</p>									

The effect of violent shaking for four hours in a Griffin and Tatlock Microid Flask Shaker on the viscosity of mixed oxalate and of heparin plasmata. In addition to the effect of ill-treatment, the effect of the four-hour delay must be considered.

Test No.	Plasma Viscosity			Specific Gravity		Total Protein	
	Before Shaking	After	Differ.	Before	After	Before	After
(A) <u>Mixed Oxalate Plasma.</u>							
1	1.730	1.739	+0.009	1.0258	1.0262	6.41	6.55
2	1.779	1.779	0	1.0278	1.0278	7.13	7.13
3	1.722	1.726	+0.004	1.0272	1.0273	6.91	6.95
4	1.692	1.689	-0.003	1.0268	1.0268	6.77	6.77
5	2.031	2.025	-0.006	1.0273	1.0273	6.95	6.95
6	1.796	1.790	-0.006	1.0267	1.0268	6.73	6.77
7	2.415	2.411	-0.004	1.0262	1.0266	6.55	6.70
8	2.076	2.075	-0.001	1.0297	1.0300	7.81	7.92
Range			+0.009 -0.006				
(B) <u>Heparin Plasma.</u>							
1	1.735	1.748	+0.011	1.0241	1.0238	6.16	6.05
2	1.777	1.768	-0.009	1.0237	1.0237	6.01	6.01
3	1.732	1.739	+0.007	1.0245	1.0245	6.30	6.30
4	1.610	1.608	-0.002	1.0218	1.0218	5.33	5.33
Range			+0.011 -0.009				

Experiments carried out to measure the effect of rough treatment and delay of postal specimen transport on the plasma viscosity. The specimens were sent 1,000 miles (Portsmouth-Glasgow-Portsmouth). The first eight specimens were received back in 3 days, the last four specimens took 7 days. The non-transported blood was centrifuged and its plasma viscosity measured after 3 days in every instance.

20 ml. of blood were collected into mixed oxalate. 10 ml. were centrifuged: the plasma viscosity, etc. was measured at once on the plasma; another sample of the plasma was sent off by post and the same measurements made on its return. 5 ml. of blood was similarly sent by post, centrifuged on its return, and the usual measurements made.

'P' = plasma specimen; 'B' = blood specimen.

Non-transported						Transported			
No.		PCV.	Spec. Grav.	Tot. Prot	Plasma Visc.	Plasma Visc.	Tot. Prot	Spec. Grav.	PCV.
		%		g. %	cs.	cs.	g. %		%
1	P	41.1	1.0307	8.17	2.421	2.425	8.42	1.0304	-
	B	44.5	1.0310	8.28	2.547	2.501	8.14	1.0306	42.5
2	P	45.1	1.0305	8.10	2.055	2.054	8.03	1.0303	-
	B	48.0	1.0305	8.10	2.086	2.092	8.03	1.0303	45.5
3	P	45.1	1.0289	7.52	1.905	1.907	7.45	1.0257	-
	B	47.5	1.0289	7.49	1.908	1.910	7.38	1.0255	45.9
4	P	41.3	1.0269	6.80	1.955	1.950	6.73	1.0267	-
	B	45.2	1.0270	6.84	1.999	1.992	6.84	1.0270	43.0
5	P	46.3	1.0284	7.34	2.017	2.013	7.45	1.0287	-
	B	-	-	-	-	2.068	7.63	1.0292	-
6	P	45.3	1.0302	7.99	2.338	2.334	7.99	1.0302	-
	B	-	-	-	-	2.363	7.99	1.0302	-
7	P	49.7	1.0275	7.02	1.802	1.802	7.02	1.0275	-
	B	-	-	-	-	1.861	7.13	1.0278	-
8	P	49.0	1.0270	6.84	1.777	1.785	6.84	1.0270	-
	B	-	-	-	-	1.887	7.38	1.0285	-

continued over -

In addition to the plasma prepared by centrifuging blood, for these last four tests a supernatant plasma after sedimentation of the cells was prepared. The blood was allowed to stand on the bench undisturbed for 3 - 4 hours, about 1 or 1.5 ml. of clear plasma was pipetted off and sent off with the other postal specimens, and this plasma was centrifuged on its return.

'P' = plasma specimen, as prepared by centrifuging,
 'S' = supernatant plasma specimen,
 'B' = blood samples.

Non-transported						Transported			
No.		PCV.	Spec. Grav.	Tot. Prot	Plasma Visc.	Plasma Visc.	Tot. Prot	Spec. Grav.	PCV.
		%		g. %	cs.	cs.	g. %		%
9	P	35.6	1.0264	6.62	1.944	1.957	6.59	1.0263	-
	S	-	-	-	-	1.942	6.55	1.0262	-
	B	37.1	1.0263	6.59	1.975	2.265	7.45	1.0287	36.5
10	P	33.9	1.0269	6.80	1.864	1.878	6.80	1.0269	-
	S	-	-	-	-	1.882	6.59	1.0263	-
	B	35.8	1.0271	6.88	1.904	2.018	7.24	1.0281	35.6
11	P	43.7	1.0285	7.38	2.129	2.155	7.52	1.0289	-
	S	-	-	-	-	2.129	7.31	1.0283	-
	B	46.9	1.0272	6.91	2.185	2.503	8.28	1.0310	49.2
12	P	37.6	1.0282	7.27	2.034	2.070	7.16	1.0279	-
	S	-	-	-	-	2.041	7.16	1.0279	-
	B	40.1	1.0279	7.16	2.066	2.187	7.81	1.0297	43.0

The effect of temperature upon the viscosity of water, plasma, and serum.

The recorded figures are the "Times of Fall", corrected for variation in the rest levels from the ideal.

There are seven tests where the test was repeated with the specimen after 24 hours on the laboratory bench; there has been no alteration in the response to temperature changes.

Fluid.		T _{20°}	T _{37.5°}	Difference as a % of T _{20°}	T _{20°}	T _{37.5°}	Difference as a % of T _{20°}
		sec.	sec.		sec.	sec.	
Water		49.0	33.6	31.5			
P+A		95.6	65.5	31.4	89.4	58.8	34.2
Plasma		97.2	65.0	33.1	89.3	59.8	33.1
		85.1	57.9	31.9	104.3	68.9	33.8
		109.4	73.8	32.6	84.7	56.7	33.1
		92.2	62.6	32.1	121.9	81.6	33.1
		86.1	58.2	32.4	87.4	59.6	31.9
		109.8	72.7	31.7	90.7	60.6	33.2
	1. A	88.8	60.9	31.4	86.9	59.2	31.8
	B	90.1	61.8	31.4	84.2	57.7	31.5
	2. A	96.2	65.3	32.1	90.5	61.1	32.5
	B	96.8	67.4	30.3	89.4	60.1	32.7
	3. A	88.0	60.9	30.8	95.4	65.1	31.5
	B	88.7	60.9	31.3	90.3	61.4	31.4
Serum	4. A	81.3	56.7	30.3	81.3	56.4	31.6
	B	81.5	56.9	30.2	76.8	51.9	32.4
	5. A	86.9	58.5	32.7	78.5	53.8	31.5
	B	87.8	59.5	32.2	75.2	53.1	29.4
	6. A	86.4	57.6	33.3	80.2	56.2	30.0
	B	86.6	57.6	33.4	79.8	53.8	32.6
					82.0	55.5	32.4
Citrate	A.	73.9	50.5	31.7			
Plasma	B.	73.8	50.7	31.3			

The effect of temperature change on the viscosity of plasma.

In this experiment it was intended to discover if the plasma had undergone any fundamental change by being cooled to room temperature.

The subject was a healthy woman and her temperature/viscosity curve did not contain the "kink" noted in some patients. It is essential that this test be repeated in a plasma from a patient with such a kink.

A specimen of blood was collected into a syringe heated to 37.5°C in an incubator, transferred to a warm tube and centrifuged in the incubator; the plasma was transferred to a viscometer already at 37.5°C. and the "time of fall" noted as the temperature was lowered to 15°C. Another portion of the blood specimen was treated at room temperature as usual; the plasma was introduced into a viscometer at 15°C and the "time of fall" measured as the temperature was gradually increased.

Specimen with temperature being reduced.		Specimen with temperature being increased	
°C	Time	Time	°C
15.0	176.7	177.1	15.0
20.0	153.7	153.9	20.0
24.1	139.3	139.7	24.0
28.1	127.1	127.0	28.0
31.1	118.4	118.8	31.0
33.0	113.7	115.2	32.5
34.5	110.4	110.7	34.5
36.0	107.1	107.3	36.0
37.5	103.8	104.0	37.5

These results are presented in graphical form as

Fig. 7, page 86 of Volume 1.

The Effect of Temperature Changes on the Plasma Viscosity.

In this table the "Time of Fall" (T), to which the viscosity is closely related, is given instead of the viscosity values. It is not certain that the calibration formula can be applied at any other temperature than 20°C. Tests were made with Citrate, Heparin and Wintrobe Plasmata, and with Serum.

Test 201 a		Test 204		Test 207		A. P. G. P. I.		M. F.		M. G. Myeloma	
Citrate		Citrate		Serum		P+A.	Ox. P.	P+A.	Plas.	P+A.	Plasma
°C	T	°C	T	°C.	T	°C.	T	°C.	T	°C.	T
15	88.0					15	120.2	15	109.4	15	128.4
16	86.8										
17	84.4										
18	82.4					18	110.7	18	100.7		
19	80.6										
20	78.4	20	93.8	20	86.1	20	105.2	20	95.4	20	111.9
21	76.5	21	91.8	21	85.4						
22	74.8	22	89.5	22	83.0			22	91.0	22	107.1
23	73.4	23	86.8	23	81.6						
24	71.6	24	84.5	24	80.3						
25	69.5	25	83.2	25	78.8	25	92.6	25	84.0	25	99.5
26	68.5	26	82.1	26	76.5						
27	67.2	27	79.8	27	75.2						
28	66.2	28	77.7	28	72.8	28	85.8	28	79.3	28	92.4
29	63.6	29	76.6	29	71.3						
30	62.3	30	73.4	30	70.4						
31	60.6	31	72.2	31	68.8	31	80.6	31	74.2	31	86.6
32	59.2	32	71.0	32	66.9	32	78.4	32	72.8	32	84.3
33	59.2	33	68.9	33	66.1	33	76.6	33	70.7	33	82.4
34	57.8	34	68.2	34	64.5	34	75.5	34	69.3	34	80.8
35	66.6	35	66.6	35	61.7	35	74.5	35	68.0	35	79.1
36	55.4	36	65.1	36.6	59.9	36	72.3	36	66.7	36	77.3
		37	64.1	37.1	59.4	37	70.8	37	64.8	37	75.5
		38	62.5	38.5	58.2						
		39	62.4			38.5	68.5	38.5	63.1	38.5	72.8
		40	61.3	40.4	56.2						

The effect of temperature changes on the viscosities of different types of plasma and of the serum of a single subject, who was suffering from chronic sepsis and possibly phthisis.

Citrate Plasma		Citrate Plasma		Heparin Plasma		Wintrobe Plasma		Serum	
24: 3:44		25: 3:44		20: 3:44		18: 3:44		23: 3:44	
°C.	T	°C.	T	°C.	T	°C.	T	°C.	T
						17.9	109.8		
						18.7	108.4		
20.0	88.7	20.0	85.1	20.0	101.5	20.0	104.3	20.0	89.8
21.4	86.7	21.7	82.3	21.5	99.3	21.3	103.2	21.7	86.0
22.6	83.5	22.6	80.1	22.2	97.6	22.2	100.8	22.4	85.5
23.6	82.1	23.5	79.0	23.1	95.3	23.4	98.1	23.5	83.5
24.8	79.3	24.5	77.4	24.2	93.0	24.4	96.4	24.3	81.4
25.6	78.2	25.6	74.2	25.1	90.5	25.2	93.9	25.3	79.7
26.0	77.8	26.6	73.4	26.3	87.7	26.0	92.2	26.4	78.6
27.2	75.1	27.3	71.2	27.4	86.3	26.9	89.3	27.5	77.1
28.0	74.6	28.4	70.0	28.5	84.3	27.9	87.8	28.3	75.6
29.1	72.6	29.7	68.3	29.5	81.9	29.1	86.0	29.5	74.0
30.3	70.8			30.4	81.0	30.5	83.7	30.9	71.1
31.1	69.4	31.1	66.7	31.3	79.4	31.0	82.9	32.1	69.9
32.5	67.7	32.0	63.9	32.1	77.1	32.1	80.7	32.9	68.9
33.7	66.6	32.8	63.5	33.2	74.9	33.1	78.3	33.9	66.8
34.8	65.5	34.2	62.8	34.3	73.2	34.0	77.6	34.5	65.9
35.5	64.6	34.9	61.3	35.2	72.6	35.1	75.3	35.5	65.6
36.4	62.7	36.2	60.3	36.4	71.4	36.3	73.6	36.3	65.1
36.9	61.6	37.3	57.9	37.4	70.5	36.8	72.9	37.3	63.7
38.0	60.5	38.4	57.3	38.3	68.6	-	-	38.2	62.7
38.8	60.1	39.7	56.4	39.8	67.0			38.9	60.8
40.1	58.2	-	-	-	-			40.0	57.9

The effect of temperature change on the viscosity of plasma.

All three bloods contained the potassium and ammonium oxalate mixture as anticoagulant.

Lipoma		G. P. I.		Still's disease.	
°C.	T	°C.	T	°C.	T
20	88.2	20.0	87.6	20.0	146.8
23	82.2	23.0	81.6		
26	76.6	26.0	75.7	26.0	128.1
29	72.3	29.0	70.6	28.0	118.4
32	67.8	32.0	66.2	31.0	109.7
-	-	33.5	64.0	32.0	107.3
				33.0	104.7
				34.0	102.4
		35.0	62.0	35.0	100.4
		36.0	60.9	36.0	98.1
		37.0	59.6	37.0	95.7
		38.0	58.2	38.5	93.2
		39.5	56.8	-	-

The effect of temperature change on the viscosity of plasma.

The anticoagulant in all the following tests was the mixture of potassium and ammonium oxalates.

The "time of fall" (T) has been studied rather than the viscosity itself.

No.	Time of Fall				Effect of 1°C. change		
	Temperature - °C.				$T_{20}-T_{18}$ as % of T_{18}	$T_{22}-T_{20}$ as % of T_{20}	$T_{20}-T_{25}$ as % of T_{20} $\times 5$
	18	20	22	25			
1	96.8	91.85	87.3	82.2	2.55	2.48	11.3
2	86.3	82.3	78.35	73.1	2.31	2.39	11.2
3	91.1	86.65	82.6	77.0	2.98	2.33	11.17
4	118.1	110.6	105.2	97.4	3.17	2.44	11.93
5	100.7	95.4	91.0	84.0	2.56	2.31	11.94
6	110.65	105.2	-	92.6	2.46	-	11.96
7	-	87.9	-	77.6	-	-	11.5
8	-	89.44	-	79.2	-	-	11.4
9	-	146.8	-	128.1	-	-	12.7
10	-	112.4	107.2	99.5	-	2.31	11.77
11	-	90.2	-	80.2	-	-	11.7
Means					2.67	2.38	11.69 = 2.34 per °C.

The effect of a variety of anticoagulants on fractions of the same blood sample.

Cit. = 1 vol. of 3.8% Sod. Citrate solution to 4 vol. blood.

P+A. = Heller and Paul's mixture of oxalates (1.2 mg. of Ammonium oxalate and 0.8 mg. of Potassium oxalate per ml. of blood)

Hep. = Heparin, 10 units per ml. of blood.

Oxa. = Potassium oxalate alone, 2mg. per ml. of blood.

PCV.			PLASMA VISCOSITY				MAX. ESR.			SPEC. GRAV.	
Cit.	P+A.	Hep.	Citr.	P+A.	Hep.	Oxal.	Cit.	P+A.	Hep.	P+A.	Oxalate
	(%)			(cs.)			cm./sec. x 10 ⁻⁴				
32.4	-	40.9	1.642	2.062	2.087	1.944	6.8	8.7	8.3	-	1.0286
29.7	-	36.8	1.610	1.944	1.926	1.873	3.2	2.6	4.2	1.0284	1.0281
34.8	-	44.6	1.678	2.140	2.280	1.996	4.8	13.5	11.4	1.0281	1.0270
29.3	-	39.0	1.692	2.568	2.401	2.141	15.0	43.0	41.3	1.0262	1.0268
29.9	-	38.0	1.592	2.084	2.081	1.955	12.6	17.2	47.2	1.0269	1.0263
35.7	-	45.8	1.642	2.073	2.097	2.000	4.3	6.6	8.1	1.0284	1.0283
34.3	42.6	-	1.621	2.035	2.044	1.897	3.2	10.2	6.5	1.0301	1.0283
31.0	-	40.0	1.542	1.997	1.948	1.885	4.3	3.8	6.0	1.0270	1.0274
29.0	37.9	-	1.587	2.015	2.032	1.939	3.3	6.4	8.0	1.0273	1.0274
35.0	46.3	-	1.578	2.026	2.037	1.896	4.6	11.0	13.3	1.0269	1.0275
36.8	47.3	-	1.426	1.694	1.688	1.600	0.6	0.5	0.4	1.0242	1.0240
33.0	44.4	-	1.656	2.170	2.208	2.012	45.6	35.0	35.6	1.0282	1.0281
31.7	41.0	-	1.578	1.956	1.980	1.868	9.2	18.5	18.6	1.0256	1.0264
31.4	40.4	-	1.596	2.014	2.041	1.925	10.0	38.3	18.8	1.0269	1.0261
28.1	37.4	-	1.677	2.211	2.208	2.061	10.8	31.4	31.5	1.0281	1.0273
28.7	38.2	-	1.740	2.383	2.420	2.267	21.1	50.9	49.0	1.0266	1.0273
32.4	42.0	-	1.649	2.186	2.168	2.043	10.1	24.3	19.7	1.0296	1.0301
25.2	33.6	-	1.547	1.968	2.016	1.908	5.3	18.6	17.1	1.0255	1.0257
38.5	49.7	-	1.896	2.532	2.646	2.043	16.7	61.8	43.1	1.0296	1.0292
34.4	46.3	-	1.428	1.695	1.659	1.614	0.4	0.7	1.4	1.0236	1.0238
29.7	38.8	-	1.568	1.990	1.956	1.897	4.1	8.8	8.4	1.0285	1.0280
29.7	40.0	-	1.574	2.000	1.996	1.954	4.2	9.6	10.6	1.0285	1.0274
29.9	39.4	-	1.585	1.991	2.012	1.943	5.3	10.4	10.9	1.0271	1.0269
29.3	39.2	-	1.552	1.988	2.018	1.927	4.9	10.5	10.8	1.0275	1.0276
34.0	44.7	-	1.570	1.954	1.927	1.869	4.4	10.1	12.3	-	1.0273
31.5	41.0	-	1.894	2.878	2.751	2.740	25.0	81.3	65.8	1.0307	1.0309
30.0	39.4	-	1.566	1.954	1.972	1.867	6.5	11.4	22.3	1.0255	1.0255
36.0	47.0	-	1.540	1.957	1.970	1.878	1.0	1.9	2.8	1.0288	1.0281
31.0	-	39.8	1.676	2.118	2.126	-	17.5	11.5	36.1	-	-
30.3	-	39.1	1.904	2.758	2.763	-	15.7	-	26.9	-	-
39.0	-	48.5	1.862	2.312	2.317	-	7.5	11.9	10.2	-	-
34.8	-	45.0	1.577	1.922	1.930	-	2.5	3.0	4.3	-	-
31.2	-	41.5	1.730	2.267	2.304	-	14.6	34.8	20.0	-	-
38.9	50.0	-	1.894	2.648	2.656	-	-	66.7	66.7	-	-
36.0	45.4	-	1.569	2.042	2.062	-	4.1	7.9	11.6	-	-
24.3	32.9	-	1.954	3.107	3.206	-	62.5	51.0	37.8	-	-
38.5	50.5	-	1.624	2.005	2.005	-	3.4	-	13.3	-	-
36.8	47.0	-	2.026	2.905	2.919	-	11.4	34.7	33.7	-	-
33.0	44.0	-	1.651	2.172	2.159	-	11.0	29.9	23.0	-	-
30.4	40.3	-	1.497	1.782	1.782	-	2.3	3.3	4.8	-	-

PCV.			PLASMA VISCOSITY			MAX. ESR.			SPEC. GRAV.		
Cit.	P+A.	Hep.	Citr.	P+A.	Hep.	Cit.	P+A.	Hep.	Citr.	P+A.	Hep.
33.1	-	46.1	1.764	2.389	2.425	7.9	24.6	19.4	1.0249	1.0274	1.0265
34.2	-	48.0	1.531	2.070	2.063	2.0	13.2	8.9	1.0254	1.0283	1.0279
29.0	-	39.5	1.821	2.450	2.484	23.6	62.5	63.8	1.0268	1.0300	1.0297
30.0	-	41.0	1.516	1.800	1.803	2.2	2.3	1.9	1.0240	1.0265	1.0249
31.2	-	43.8	1.590	2.040	2.046	3.1	6.8	7.5	1.0257	1.0291	1.0281
36.0	-	51.6	1.639	2.024	2.089	3.2	9.5	11.1	1.0251	1.0288	1.0272
24.0	-	31.1	1.950	2.807	2.806	37.0	16.9	42.2	1.0298	1.0331	1.0321
22.6	-	29.5	2.010	2.760	2.811	33.3	35.8	45.0	1.0294	1.0322	1.0305
27.3	36.3	-	1.518	1.847	1.847	4.4	7.1	7.0	1.0232	1.0247	1.0236
25.2	33.6	-	1.843	2.502	2.556	37.5	75.0	70.0	1.0263	1.0288	1.0278
35.1	47.8	-	1.811	2.455	2.457	95.8	35.8	34.4	1.0270	1.0302	1.0289
25.6	34.2	-	2.030	2.885	2.925	33.3	47.5	66.7	1.0293	1.0328	1.0316
24.3	31.6	-	1.995	2.737	2.785	30.6	24.2	26.0	1.0285	1.0320	1.0302
26.3	35.0	-	1.766	2.325	2.329	16.8	54.2	55.8	1.0260	1.0284	1.0273
31.6	42.2	-	1.639	2.062	2.091	28.6	48.9	74.4	1.0252	1.0278	1.0268
14.4	19.6	-	1.521	1.705	1.723	0.5	1.0	0.8	1.0211	1.0220	1.0208
31.8	42.5	-	1.802	2.422	2.463	15.8	37.9	38.9	1.0280	1.0318	1.0304
36.8	50.2	-	1.565	1.948	1.960	2.8	5.2	22.2	1.0248	1.0268	1.0267
32.7	44.5	-	1.660	2.122	2.173	6.7	9.6	9.8	1.0268	1.0300	1.0289
29.5	39.7	-	1.738	2.297	2.295	6.9	29.3	31.7	1.0260	1.0288	1.0278
37.3	50.3	-	1.583	1.973	2.026	3.2	8.2	6.7	1.0256	1.0282	1.0276
32.3	43.6	-	1.523	1.855	1.870	0.4	1.2	1.4	1.0254	1.0278	1.0266
30.0	40.2	-	1.822	2.459	2.500	11.7	38.9	40.0	1.0261	1.0287	1.0275
30.0	39.8	-	1.597	2.018	2.033	7.8	13.8	16.6	1.0251	1.0274	1.0266
20.2	27.3	-	2.092	3.078	2.995	30.5	55.3	42.0	1.0297	1.0327	1.0322
34.3	46.6	-	1.558	1.931	1.928	1.0	2.3	2.4	1.0253	1.0283	1.0273
35.1	45.0	-	1.560	1.883	1.928	1.0	1.3	1.0	1.0248	1.0275	1.0268
32.0	43.4	-	1.756	2.293	2.337	-	18.3	22.0	1.0264	1.0302	1.0291
34.6	-	47.1	1.843	2.530	2.543	5.4	26.8	28.6	1.0277	1.0325	1.0311
26.0	-	36.0	1.776	2.375	2.373	25.2	53.9	61.3	1.0244	1.0267	1.0256
26.5	-	36.0	1.819	2.479	2.488	27.8	58.3	58.6	1.0251	1.0275	1.0265
28.4	38.5	-	1.910	2.765	2.717	44.2	59.2	56.1	1.0257	1.0281	1.0273
32.2	-	43.3	1.859	2.624	2.655	12.2	104.	38.3	1.0268	1.0319	1.0309
21.4	-	28.1	1.818	2.483	2.514	22.5	27.1	21.7	1.0266	1.0287	1.0282
30.0	-	40.0	1.806	2.508	2.557	14.1	50.0	44.4	1.0248	1.0284	1.0272
25.3	-	34.7	1.599	2.033	2.030	6.4	9.5	9.5	1.0257	1.0280	1.0275
27.0	-	35.7	1.778	2.400	2.412	15.6	39.3	35.0	1.0256	1.0281	1.0269
26.4	-	36.1	1.663	2.193	2.197	3.7	12.7	24.3	1.0235	1.0252	1.0238
24.1	-	32.5	1.677	2.190	2.234	3.8	14.5	14.3	1.0260	1.0283	1.0273
24.7	-	34.0	1.510	1.856	1.837	0.2	2.8	1.4	1.0216	1.0226	1.0215
28.2	-	37.7	1.814	2.693	2.677	27.5	40.7	47.1	1.0259	1.0276	1.0267
31.3	-	41.2	1.563	1.891	1.947	1.9	3.6	3.1	1.0256	1.0274	1.0266
27.0	-	37.2	1.808	2.468	2.474	19.1	72.4	50.0	1.0256	1.0271	1.0264
26.5	-	36.0	2.083	3.138	3.047	32.2	53.3	29.4	1.0273	1.0308	1.0295
29.7	40.7	-	1.583	1.958	2.036	6.7	13.5	13.1	1.0248	1.0270	1.0262
26.0	35.0	-	1.837	2.472	2.438	27.2	58.1	58.6	1.0264	1.0288	1.0279
34.5	45.5	-	1.500	1.817	1.836	0.7	0.5	0.8	1.0248	1.0273	1.0258
26.5	36.3	-	1.781	2.303	2.336	13.9	43.3	43.3	1.0244	1.0266	1.0253
25.2	34.5	-	1.749	2.296	2.288	12.1	49.3	40.6	1.0236	1.0264	1.0249

PCV.		PLASMA VISC.			PCV.		PLASMA VISC.	
Cit.	P+A.	Citr.	P+A.		Cit.	P+A.	Citr.	P+A.
18.0	24.0	1.847	2.501		29.7	39.8	1.728	2.270
23.0	31.0	1.593	1.930		23.7	35.4	1.679	2.193
32.0	43.0	1.563	1.946		32.0	-	1.549	1.900
48.0	-	1.908	2.741		32.8	45.3	1.645	1.955
25.7	-	1.776	2.342		32.0	-	1.836	2.500
32.4	-	1.767	2.371		23.0	-	1.700	2.155
30.0	-	1.770	2.362		35.4	-	1.668	2.218
27.5	-	1.715	2.292		27.7	-	1.628	2.008
24.8	-	1.816	2.416		30.0	41.0	1.468	1.716
28.6	-	1.553	1.923		21.0	-	1.715	2.220
29.4	-	1.642	2.106		23.8	-	1.675	2.160
31.9	-	1.601	2.068		31.0	-	1.878	2.730
30.4	-	1.744	2.366		24.4	-	1.597	2.016
33.0	-	1.733	2.287					
Viscometer V4 results above.					Viscometer V5 results below.			
28.8	36.3	1.664	2.174		28.6	-	1.639	2.186
33.9	-	1.576	2.035		26.7	38.5	1.682	2.228
27.9	39.0	1.651	2.183		30.0	41.4	1.618	2.107
33.1	46.0	1.568	2.013		20.3	29.7	1.759	2.500
30.0	41.3	1.575	1.997		35.3	49.0	1.727	2.382
20.0	29.3	1.547	1.855		27.6	39.2	1.576	2.047
31.2	42.3	1.540	1.962		33.2	45.8	1.497	1.914
28.1	40.3	1.590	2.021		27.7	38.1	1.777	2.547
27.2	38.7	1.725	2.464		32.7	45.7	1.750	2.549
33.7	-	1.490	1.833		31.4	43.1	1.671	2.284
27.8	39.0	1.689	2.318		30.4	41.5	1.536	1.987
33.6	46.4	1.521	1.913		36.1	47.2	1.530	1.895
30.6	43.5	1.900	2.920		32.1	44.6	1.547	1.979
33.2	46.8	1.470	1.886		34.0	-	1.512	1.888
33.8	-	1.533	1.894		28.4	38.0	1.555	1.902
29.5	39.0	1.484	1.792		33.1	44.6	1.501	1.859
31.2	43.9	1.777	2.609		34.7	46.3	1.509	1.878
27.5	37.7	1.641	2.139		33.1	44.2	1.568	2.035
33.6	45.1	1.501	1.849		33.4	44.4	1.500	1.852
31.4	41.2	1.491	1.765		32.8	45.2	1.505	1.848
33.2	44.8	1.475	1.802		35.9	46.9	1.493	1.794
33.0	43.4	1.642	2.184		33.2	44.1	1.500	1.844
33.7	43.5	1.492	1.800		26.0	35.0	1.470	1.734
33.9	44.5	1.502	1.835		33.4	46.0	1.500	1.826
-	46.0	1.489	1.810		34.0	45.6	1.491	1.823
32.0	-	1.496	1.851		32.2	45.3	1.484	1.800
32.4	44.5	1.663	2.206		31.6	44.0	1.487	1.796
30.2	-	1.542	1.899		29.2	-	1.525	1.916
24.8	34.0	2.057	3.171		26.9	42.4	2.058	3.245
26.0	38.5	2.113	3.677					

The viscosity of serum ULTRA-FILTRATES.

There is no correlation between the viscosity of the ultra-filtrate and its nitrogen content.

No.	ULTRA-FILTRATE		Ser. NPN.	Serum protein			Serum Visc.
	VISC.	Nitrogen.		Total	Alb.	Glob	
	cs.	mg. %	mg. %	g./100 ml.			cs.
1	1.026	140.0	125.0	7.14	4.59	2.55	1.782
2	1.021	28.0	28.7	6.47	4.29	2.18	1.637
3	1.024	26.9	27.7	6.66	4.37	2.29	1.644
4	1.023	22.1	24.5	6.74	4.43	2.31	1.726
5	1.034	19.3	20.7	5.97	4.31	1.66	1.602
6	1.030	26.6	26.1	6.73	4.15	2.58	1.722
7	1.035	26.3	29.5	6.58	4.41	2.17	1.720
8	1.034	22.3	21.0	6.06	4.13	1.93	1.654
9	1.034	27.6	25.5	6.16	4.20	1.96	1.627
10	1.024	31.7	26.1	6.35	4.55	1.80	1.654

Table - R

The experimental kinematic viscosity and specific gravity of an aqueous solution of albumin and of a saline solution of globulin; the absolute viscosity has been calculated from these two experimental values.

$$\text{Abs. Visc.} = \text{Kin. Visc.} \times \text{Spec. Gravity}$$

HUMAN SERUM ALBUMIN DISSOLVED IN DISTILLED WATER

Experimental		Interpolated					
A g/100 ml	ν_{V6}	A g/100 ml	ν_{V6}	ϱ^*	μ_{V6}	$\log \mu_{V6}$	A' g/100 g
15.21	2.795	15	2.745	1.0553	2.897	0.4620	14.22
10.54	1.934	12.5	2.250	1.0438	2.349	0.3709	11.98
8.79	1.691	10	1.857	1.0362	1.924	0.2842	9.654
7.33	1.523	7	1.488	1.0247	1.525	0.1832	6.829
6.28	1.409	5.5	1.342	1.0190	1.367	0.1358	5.400
5.33	1.310	4	1.232	1.0133	1.246	0.0955	3.950
4.10	1.235	3	1.174	1.0095	1.185	0.0738	2.970
3.18	1.177	2	1.119	1.0056	1.125	0.0511	1.988
2.29	1.133	1	1.065	1.0018	1.067	0.0282	0.9982
0.71	1.056	0	1.010	0.9980	1.008	0.0033	0
0.36	1.030						
0	1.010						

* $\varrho_A = 0.9980 + 0.00382 A$
All determinations at 20.0° C

HUMAN SERUM GLOBULIN DISSOLVED IN NORMAL SALINE

Experimental		Interpolated					
G g/100 ml	ν_{V6}	G g/100 ml	ν_{V6}	ϱ^*	μ_{V6}	$\log \mu_{V6}$	G' g/100 g
8.41	3.041	8	2.845	1.0461	2.955	0.4705	7.649
6.28	2.152	7	2.404	1.0410	2.503	0.3984	6.725
4.06	1.621	6	2.072	1.0359	2.146	0.3316	5.793
2.02	1.274	5	1.825	1.0308	1.881	0.2744	4.852
1.01	1.130	4	1.605	1.0257	1.646	0.2164	3.899
0	1.016	3	1.430	1.0206	1.459	0.1641	2.939
(saline)		2	1.270	1.0155	1.290	0.1106	1.971
		1	1.130	1.0104	1.142	0.0577	0.9902
		0	1.016	1.0053	1.021	0.0090	0
		(saline)					

* $\varrho_G = 1.0053 + 0.00510 G$
All determinations at 20.0° C

Table - R (b)

The values calculated from the hypothesis that a solution can be treated as if it was a uniform single substance with a molecular weight derived from the solute and solvent.

S g/100 g	μ_{20}	$\log \mu_{20}$	$\frac{1800}{100-S}$	$M' = \left(\frac{1800}{100-S} \right) (1 + a S)$
SUCROSE (BINGHAM & JACKSON)				$a = - 0.00143$
20	1.960	0.2923	22.50	21.86
40	6.200	0.7924	30.00	28.71
60	56.5	1.7520	45.00	41.14
ALBUMIN (Interpolated from Table I)				$a = + 0.008$
1		0.028		18.32
2		0.051		18.67
2.73		0.068		18.91
4		0.097		19.34
5.5		0.139		19.89
7		0.189		20.40
8		0.225		20.84
9		0.261		21.21
10		0.297		21.60
GLOBULIN (Interpolated from Table II)				$M' = \left(\frac{1810}{100-S} \right) (1 + a S)$ $a = + 0.025$
0.5		0.034		18.46
1.0		0.058		18.74
1.25		0.072		18.91
1.5		0.085		19.05
2.0		0.112		19.40
2.5		0.140		19.73
3		0.168		20.08
4		0.223		20.77
5		0.284		21.43
6		0.346		22.18
7		0.420		22.90

Sucrose viscosity is expressed in terms of BINGHAM & JACKSON's viscometer;

Albumin and Globulin in terms of V6

M' is calculated on a 30 cm slide-rule for Albumin and Globulin

Table - T.

The total range of the Corrected Citrate Plasma Viscosity can be subdivided into Zones according to the periodic curve of the Maximum corrected sedimentation velocity/plasma viscosity correlation.

Number of Zone	Limit value of Citrate Plasma Viscosity.
	cs.
1	- 1.515
2	- 1.558
3	- 1.585
4	- 1.671
5	- 1.698
6	- 1.762
7	- 1.832
8	- 1.865
9	- 1.963
10	- 2.050
11	2.050 -

Part 3

TABLES of RESULTS

for

PHYSIOLOGY SECTION

Results from Normal Adult Males.

This table also shows the daily variations in the plasma viscosity, E.S.R., P.C.V., and plasma protein.

Name	Sex	Date	PCV.	PLASMA VISCOSITY	Wintrobe E. S. R.		Total Plasma Protein	Remarks.
					Ord.	Cor.		
			%	cs.	mm/	1 hr.	g/100ml	
P. S.	M	4: 3:49	-	1.763	1	-	-	Post-alcohol
		2: 9:49	43.6	1.803	2	0	7.09	
		20: 2:50	44.8	1.753	1	0	6.77	
		21: 2:50	43.2	1.754	1	0	6.77	
		22: 2:50	44.2	1.749	1	0	6.70	
		23: 2:50	43.0	1.751	1	0	6.95	
		24: 2:50	44.4	1.755	1	0	6.73	
		25: 2:50	45.9	1.857	1	0	7.38	
		27: 2:50	44.5	1.754	1	0	6.77	
		28: 4:50	44.6	1.830	2	0	7.06	
E. D.	M	25: 4:49	45.8	1.904	-	-	7.60	
		1: 5:50	45.0	1.870	8	6	7.16	
		2: 5:50	45.0	1.902	7	5	7.20	
		3: 5:50	45.7	1.893	9	8	7.06	
		4: 5:50	44.3	1.874	3	0	7.27	
K. H.	M	15: 5:50	43.0	1.840	9	5	7.27	Post-alcohol
		16: 5:50	41.7	1.758	-	-	6.77	
		17: 5:50	43.3	1.804	6	3	6.95	
		18: 5:50	43.6	1.806	6	3	6.95	
		19: 5:50	42.6	1.772	6	2	6.80	
R. C.	M	1: 5:50	46.9	1.779	2	2	6.88	
		2: 5:50	47.9	1.797	2	3	6.84	
		3: 5:50	47.8	1.802	2	3	6.91	
		4: 5:50	47.5	1.787	2	2	6.84	
R. J.	M	15: 5:50	46.1	1.781	1	0	7.16	
		16: 5:50	46.1	1.778	-	-	6.98	
		17: 5:50	45.6	1.697	1	0	6.73	
		19: 5:50	47.2	1.762	1	1	7.20	
L. H.	M	2: 1:48	46.9	1.852	-	-	7.45	
		13: 4:48	46.0	1.825	-	-	7.45	
		13: 9:48	45.6	1.798	-	-	7.56	
J. D.	M	26: 9:50	49.2	1.880	1	3	7.74	
		24: 2:51	-	1.860	-	-	7.67	
H. D.	M	1: 3:51	43.	1.778	2	0	7.31	
M. T.	M	28: 2:51	42.5	1.866	5	1	6.98	

Name	N°	PCV.	PLASMA VISCOSITY	Wintrobe E. S. R.		Total Plasma Protein	Remarks
				Ord.	Cor.		
		%	cs.	mm/	1 hr.	g/100ml	
G. R.	10	48.9	1.899	-	-	7.34	
M. G.	11	44.8	1.858	-	-	7.31	
A. G.	12	41.6	1.851	-	-	7.09	
J. B.	13	47.4	1.844	-	-	7.02	
G. D.	14	-	1.798	-	-	6.84	
S. M.	15	48.1	1.776	-	-	6.95	
A. C.	16	42.8	1.739	-	-	6.84	
J. W.	17	47.5	1.846	-	-	7.42	
M. B.	18	46.9	1.839	-	-	7.70	
A. S.	19	46.6	1.840	-	-	7.16	
J. H.	20	51.3	1.903	-	-	7.88	
M. O.	21	47.8	1.900	-	-	7.96	
J. S.	22	43.8	1.877	-	-	7.67	
A. M.	23	51.8	1.812	-	-	7.45	
R. H.	24	40.9	1.849	-	-	7.45	
M. G.	25	-	1.729	-	-	6.41	
F. A.	26	45.3	1.849	-	-	7.70	
R. A.	27	52.9	1.892	-	-	7.20	
J. L.	28	47.8	1.850	-	-	7.16	
S. C.	29	49.0	1.770	1	3	7.27	
J. S.	30	51.3	1.910	-	-	7.67	
A. W.	31	41.9	1.734	-	-	-	
J. P.	32	43.8	1.728	-	-	7.09	
D. N.	33	45.8	1.847	3	2	7.20	
M. C.	34	46.7	1.853	-	-	7.09	
W. A.	35	-	1.807	-	-	-	
P. F.	36	47.5	1.820	3	3	-	
M. G.	37	46.4	1.848	8	7	7.16	
B. W.	38	51.0	1.743	1	4	7.06	
M. T.	39	49.0	1.777	1	3	6.84	
M. D.	40	49.7	1.802	2	4	7.02	
M. Q.	41	49.6	1.663	1	3	6.44	
G. D.	42	52.	1.801	2	7	6.95	
A. R.	43	40.	1.805	3	0	7.60	
S. E.	44	47.3	1.860	3	3	7.31	
J. H.	45	47.2	1.829	3	3	7.02	
E. E.	46	46.3	1.869	-	-	7.63	

Normal Adult Males

Name	No	Date	PCV.		PLASMA VISC.		E. S. R.			Total
			Cit.	P+A.	Cor.	P+A	Max.	Wintrobe		Plasma
					Citr.	Oxal.	Cit.	Ord.	Cor.	Protein
			%		cs.		cm/sec. $\times 10^{-4}$	mm/ 1 hr		g/100ml
J. H.	47	7: 8:44	32.0	-	1.549	1.900	2.3	-	-	7.30
		13:11:45	32.0	-	1.503	-	1.1	-	-	-
		8: 1:46	34.7	-	1.504	-	0.5	-	-	-
		10: 1:46	34.3	-	1.500	-	-	-	-	-
		11: 1:46	35.0	-	1.496	-	1.5	-	-	-
		8: 2:46	34.2	-	1.502	-	1.6	-	-	-
		4: 3:46	34.4	-	1.510	-	1.9	-	-	-
		1: 4:46	34.6	-	1.497	-	1.4	-	-	-
		6: 6:46	31.9	-	1.475	-	1.0	-	-	-
		11: 7:46	34.0	-	1.467	-	1.3	-	-	-
		2: 8:46	34.7	-	1.472	-	1.5	-	-	-
		21:10:46	33.3	-	1.510	-	1.3	-	-	-
		27:11:46	34.7	-	1.532	-	2.1	-	-	-
		3: 3:47	35.4	-	1.547	-	2.7	-	-	-
		24: 3:47	33.2	-	1.504	-	0.5	-	-	-
		19: 5:47	33.7	-	1.504	-	1.2	-	-	-
		29:10:47	33.2	45.8	1.497	1.914	1.3	-	-	7.70
		2: 1:48	33.6	46.4	1.521	1.913	2.1	-	-	7.39
		17: 1:48	34.8	-	1.555	-	2.6	-	-	-
		3: 2:48	33.2	-	1.505	-	1.5	-	-	6.76s
		6: 5:48	33.1	44.6	1.501	1.859	1.8	-	-	7.34
		21: 6:48	34.7	46.3	1.509	1.878	1.6	-	-	7.45
		17: 7:48	33.6	45.1	1.501	1.849	1.4	-	-	7.31
		12: 8:48	33.4	44.4	1.500	1.852	1.3	-	-	7.38
		12:11:48	31.3	41.2	1.491	-	-	-	-	-
		3: 2:49	32.9	45.2	1.505	1.848	-	3	1.5	-
		28: 3:49	33.2	44.8	1.475	1.802	-	3	1	-
		26: 5:49	33.0	43.3	1.493	1.794	-	2	0	6.95
		11:10:49	33.2	44.1	1.500	1.844	-	-	-	7.24
		3: 3:50	33.7	43.5	1.492	1.800	-	4	1	6.95
		13: 6:50	33.9	44.5	1.502	1.835	-	2	0	7.20
		4: 7:50	33.4	46.	1.500	1.826	-	3	2	7.02
		10:10:50	33.4	46.	1.489	1.810	-	4	3	6.88
		24:11:50	34.0	45.4	1.491	1.823	-	3	1.5	7.24
		21:12:50	32.0	45.3	1.496	1.851	-	4	2.5	7.13
		2: 2:51	32.2	45.3	1.484	1.800	-	4	2.5	7.06
		13: 3:51	32.2	44.	1.487	1.796	-	3	1	6.98
		10: 5:51	-	45.4	-	1.831	-	5	3.5	7.20
		12: 7:51	34.8	45.0	1.494	1.819	-	3	1.5	7.27
		21: 1:52	35.0	46.6	1.503	1.820	-	3	3	7.31

Normal Adult Males.

Name	No	PCV.		PLASMA VISC.		MAX. ESR.		Total Plasma Protein
		Cit.	P+A.	Cor. Citr.	P+A Oxal.	Cit.	P+A	
		%		cs.		$\times 10^{-4}$ cm/sec.		g/100ml
G.S.	48	36.8	47.3	1.426	1.694	0.57	0.49	5.65
H.D.	49	35.0	46.3	1.430	1.695	0.35	0.68	5.39
J.M.	50	30.4	40.3	1.508	1.782	2.31	3.27	5.60
C.P.	51	32.3	43.6	1.523	1.855	0.44	1.43	6.47
R.M.	52	34.5	45.5	1.500	1.817	0.68	0.50	6.34
J.U.	53	33.7	-	1.490	1.833	-	-	7.09
R.L.	54	32.8	-	1.564	-	1.67	-	6.81s
A.C.	55	38.0	-	1.538	-	0.41	-	6.71s
J.B.	56	34.2	-	1.552	-	1.63	-	6.67s
A.C.	57	32.2	-	1.525	-	0.65	-	6.41s
C.B.	58	34.2	-	1.442	-	0.34	-	-
W.D.	59	35.1	-	1.437	-	1.12	-	-

Results from Normal Adult Females.

This table also includes two subjects in whom the daily variations in the plasma viscosity, E.S.R., P.C.V., and plasma proteins were studied.

Name	No.	Date	PCV.	PLASMA VISCOSITY	Wintrobe E. S. R.		Total Plasma Protein	Remarks
					Ord.	Cor.		
			%	cs.	mm/	1 hr.	g/100ml	
L. C.	1	12:12:49	38.7	1.782	10	6	6.84	
		13:12:49	37.2	1.758	16	10	6.66	
		14:12:49	37.2	1.758	15	9	6.66	
		15:12:49	39.0	1.779	14	10	6.84	
		16:12:49	37.4	1.788	14	8	6.88	
		9:10:50	-	1.783	-	-	6.44	
F. K.	2	12:12:49	45.6	1.885	3	6	7.74	Post-alcohol
		13:12:49	42.0	1.748	10	10	6.88	
		14:12:49	43.7	1.781	9	11	7.13	
		15:12:49	42.7	1.754	9	10	7.13	
		16:12:49	42.2	1.769	9	9	6.91	
		17:12:49	43.0	1.771	8	9	7.02	
E. S.	3	-	-	1.892	-	-	-	
A. B.	4	-	42.2	1.795	-	-	7.52	
M. G.	5	-	47.1	1.897	-	-	6.95	
M. T.	6	-	41.2	1.805	-	-	7.02	
M. S.	7	-	35.2	1.828	-	-	7.13	
V. W.	8	-	46.0	1.665	-	-	6.23	
D. B.	9	-	42.7	1.750	-	-	7.02	
L. M.	10	-	42.5	1.821	-	-	7.70	
C. P.	11	-	39.9	1.807	-	-	-	
M. W.	12	-	42.2	1.850	-	-	7.67	
E. E.	13	18: 7:47	42.8	1.808	5	6	6.91	
		4: 9:47	45.0	1.799	-	-	6.80	
M. D.	14	-	44.4	1.864	-	-	7.13	
E. M.	15	-	40.0	1.773	6	4	-	
G. S.	16	-	45.2	1.749	3	6	7.34	
J. C.	17	2: 2:48	41.5	1.798	2	2	7.34	
		23: 2:48	41.7	1.788	3	3	7.45	
H. C.	18	-	40.4	1.901	27	24	7.42	
A. Q.	19	-	31.0	1.869	16	3	6.95	
M. P.	20	-	39.2	1.801	11	8	6.88	
D. S.	21	-	-	1.860	3	-	-	
A. B.	22	-	42.8	1.806	-	-	7.20	
S. S.	23	-	44.7	1.893	-	-	7.63	
R. F.	24	-	41.7	1.886	-	-	6.98	
J. P.	25	-	41.9	1.803	4	4	7.52	
N. C.	26	-	39.0	1.713	10	6	6.16	
M. D.	27	-	42.2	1.791	-	-	-	

Normal Adult Females.

Name	No.	Date	PCV.	PLASMA VISCOSITY	Wintrobe E. S. R.		Total Plasma Protein	Remarks
					Ord.	Cor.		
			%	cs.	mm/ 1 hr.		g/100ml	
M. B.	28	-	42.7	1.876	12	13	7.56	
P. V.	29	-	37.1	1.798	11	5	6.88	
M. D.	30	-	41.4	1.896	9	8	7.85	
M. R.	31	-	44.4	1.865	13	16	6.59	
M. M.	32	-	38.5	1.732	3	0	7.06	
M. S.	33	-	41.6	1.722	5	5	6.84	
M. R.	34	-	46.	1.768	1	5	7.31	
C. B.	35	-	40.9	1.888	9	8	7.45	
J. A.	36	-	42.8	1.874	7	8	7.38	
A. R.	37	-	45.	1.810	6	9	7.02	
M. D.	38	-	43.	1.885	8	9	7.34	
M. B.	39	-	38.6	1.677	9	5	6.44	
M. T.	40	-	46.	1.794	10	14	6.98	
M. B.	41	-	35.3	1.789	22	13	7.27	
P. L.	42	30: 1:51	46.	1.724	10	15	6.66	
		16: 5:51	-	1.761	-	-	6.91	
A. B.	43	-	41.9	1.728	5	5	6.55	
S. J.	44	-	43.8	1.787	5	7	6.80	
M. J.	45	-	43.3	1.690	5	6	7.02	
M. G.	46	-	39.5	1.769	13	9	6.80	
M. P.	47	-	40.	1.765	25	21	6.77	
M. M.	48	-	43.5	1.880	13	15	7.13	
B. J.	49	-	43.7	1.692	2	4	6.48	
M. H.	50	-	-	1.910	-	-	7.01	
M. H.	51	-	41.0	1.800	-	-	6.66	
<u>CITRATE</u>								
<u>PLASMA</u>								
M. H.	50	-	38.4	1.565				
M. H.	51	-	30.	1.516				
E. R.	52	-	21.	1.560				
B. M.	53	-	32.4	1.559				
M. M.	54	-	30.3	1.531				
S. H.	55	-	30.4	1.532				

PREGNANCY.

These tests were made on a consecutive series of patients who attended the Central Laboratory at Portsmouth for their routine ante-natal Wassermann examination.

There is no guarantee that the pregnancy was normal nor that the patient was free from all other disease. She appeared to be in good health, she claimed to be in good general health, she was free of the symptoms of the usual complications of pregnancy as far as I could determine by direct questioning, and her doctor had given her no hint of any such complications being present.

Another larger series is being investigated now with the co-operation of an obstetrician.

No.	PCV.	PLASMA VISC.	Wintrobe ESR.		Plasma Total Prot.	Plasma Proteins			Serum		No. of Preg.
			Ord.	Cor.		Alb.	Glob	Fib.	Urea	Chol.	
	%	cs.	mm/	1 hr	g. %	g./100 ml.			mg. %	mg. %	
<u>4 - 7th Week period.</u>											
1	42.3	1.807	5	5	6.77	4.4	1.9	0.34	28	333	1
2	36.6	1.980	20	13	7.63	5.9	2.6	0.4	24	430	2
3	41.	1.770	9	8	6.91	4.5	2.5	0.39	27	258	1
4	41.1	1.821	10	9	7.31	4.9	1.52	0.28	-	-	1
mean	40.3	1.844	11	9	7.17	4.93	2.13	0.35	26	340	
<u>8 - 11th Week period.</u>											
1	40.	1.988	15	13	6.95	4.2	2.6	0.36	22	288	2
2	39.1	1.867	16	13	6.62	4.6	2.01	0.39	29	205	1
3	42.	1.881	8	8	6.66	4.5	1.8	0.32	28	252	2
4	40.5	1.972	23	21	6.98	4.9	2.3	0.43	28	247	1
5	39.5	1.900	20	17	6.91	5.2	1.8	0.45	13	243	1
6	40.5	1.873	17	15	6.77	4.9	2.1	0.42	17	252	2
7	37.	1.810	14	8	6.93	4.8	2.1	0.35	27	-	2
8	38.4	1.843	17	13	6.91	3.8	3.04	0.36	23	-	4
9	33.	1.825	34	20	6.66	3.8	2.6	0.30	36	204	7
10	37.7	1.781	-	-	6.16	4.2	1.8	0.31	-	250	1
11	36.8	1.812	11	5	6.84	4.7	2.23	0.37	16	400	3
12	37.5	1.774	20	14	6.84	4.7	2.69	0.31	28	240	1
13	42.3	1.762	6	6	6.73	4.9	2.7	0.40	28	318	3
14	39.5	1.807	19	15	6.55	4.3	2.43	0.27	26	228	3
15	41.7	1.722	6	6	6.26	4.5	2.1	0.30	20	303	2
16	42.4	1.827	14	14	6.52	4.0	2.46	0.34	22	246	2
mean	39.2	1.840	16	13	6.71	4.50	2.30	0.36	24	263	

No.	PCV.	PLASMA VISC.	Wintrobe E. S. R.		Total Plas. Prot.	Alb.	Glob	Fibr	Urea	Chol.	No. of Pregn.
			Ord.	Cor.							
	%	cs.	mm/	1 hr	g. %				mg. /100ml.		
12 - 15th Week period.											
1	38.3	1.980	17	12	7.02	4.6	2.2	0.4	43	278	10
2	34.	1.752	4	0	5.87	4.52	1.9	0.31	20	251	1
3	36.7	1.799	17	11	6.44	4.9	1.7	0.32	32	249	1
4	40.3	1.818	21	19	6.55	4.5	2.1	0.32	16	244	2
5	37.	1.836	22	17	6.26	4.2	2.2	0.41	15	297	2
6	41.	1.699	9	8	6.59	4.6	1.8	0.3	29	199	1
7	40.	1.671	3	1	6.37	4.6	1.8	0.31	26	-	3
8	38.	1.896	23	17	6.70	4.5	2.3	0.4	20	308	1
9	37.	1.729	13	7	6.61	4.7	1.46	0.44	17	216	1
10	36.	1.868	25	17	6.98	4.9	2.58	0.32	-	359	1
11	42.	1.882	11	11	6.55	5.0	2.58	0.42	-	-	1
12	36.6	1.720	12	6	6.08	4.5	1.8	0.35	20	404	2
13	31.5	1.842	49	28	6.48	3.8	2.6	0.39	27	-	1
14	45.	1.891	6	9	6.95	4.6	1.96	0.44	16	242	1
15	39.	1.804	25	20	6.70	4.3	2.2	0.35	22	263	1
16	37.	1.812	20	13	6.73	4.7	2.3	0.37	33	517	1
17	37.1	1.706	17	10	6.05	4.1	1.8	0.45	-	294	2
18	38.7	1.790	22	17	6.34	4.0	2.75	0.35	20	330	1
19	39.0	1.841	18	14	6.37	-	-	-	-	-	2
20	-	1.735	-	-	6.37	-	-	-	-	-	2
21	-	1.732	-	-	6.30	-	-	-	-	-	1
22	41.1	1.884	-	-	6.77	-	-	-	-	-	2
Mean	38.3	1.804	18	13	6.95	4.75	2.11	0.37	24	297	
16 - 19th Week period.											
1	39.	1.721	10	7	6.08	4.2	1.92	0.3	41	279	1
2	36.	1.717	21	13	6.19	4.8	2.1	0.38	17	345	2
3	40.	1.742	20	17	6.30	4.5	2.0	0.4	25	235	2
4	35.2	1.717	18	11	6.12	4.2	1.89	0.41	-	-	4
5	43.	1.943	12	13	7.02	4.53	1.98	0.41	34	349	1
6	38.	1.902	28	22	6.05	3.5	2.3	0.3	21	365	1
7	35.0	2.030	15	6	7.31	4.2	2.7	0.36	35	357	1
8	38.	1.929	20	15	6.73	4.68	2.09	0.42	25	345	1
9	34.8	1.855	24	13	6.70	4.3	2.3	0.34	29	-	1
10	33.	1.643	23	11	5.65	3.8	2.1	0.33	-	267	5
11	38.4	1.705	14	9	5.94	4.4	2.03	0.37	20	280	1
12	40.3	1.676	10	7	6.05	4.2	2.09	0.31	21	260	2
13	40.6	1.814	13	12	6.19	4.0	2.45	0.35	29	341	1
14	39.2	1.759	28	24	5.90	3.9	2.1	0.46	19	376	4
15	39.2	1.854	24	20	6.37	4.3	2.0	0.46	22	348	2
16	40.	1.862	20	18	6.95	4.6	2.09	0.41	18	300	1
17	37.	1.777	21	15	6.95	4.9	1.84	0.36	19	290	2
18	33.8	1.826	31	17	6.33	3.93	2.51	0.38	17	-	3
19	36.9	1.805	23	15	6.41	3.76	2.76	0.38	20	-	2
Mean	37.8	1.804	20	14	6.38	4.25	2.17	0.38	24	316	

No.	PCV.	PLASMA VISC.	Wintrobe ESR.		Total Plas. Prot.	Alb.	Glob	Fibr	Urea	Chol.	No. of Preg.
			Ord.	Cor.							
	%	cs.	mm/ 1 hr		g. %				mg./100 ml		
<u>20 -23rd Week period.</u>											
1	29·	1·876	43	29	6·26	3·9	2·2	0·48	24	331	1
2	37·8	1·832	32	25	6·55	4·2	2·44	0·46	-	-	1
3	32·0	1·868	43	25	6·23	3·6	2·41	0·39	-	390	3
4	40·2	1·890	18	16	6·66	-	-	-	-	-	1
5	-	1·777	-	-	6·02	-	-	-	-	-	1
6	33·4	1·807	27	14	6·05	4·0	2·1	0·36	21	280	5
7	36·6	1·990	44	34	6·98	4·2	3·2	0·38	25	440	3
8	43·6	1·840	20	22	6·59	4·2	2·5	0·38	28	440	1
9	40·6	1·741	13	13	5·94	3·9	1·76	0·34	20	-	3
10	41·0	1·888	29	28	6·48	2·94	2·36	0·45	-	-	1
11	34·8	1·840	36	24	6·41	4·0	2·54	0·42	18	280	2
12	39·3	2·006	41	36	7·24	4·5	2·5	0·44	18	300	1
13	37·2	1·791	28	20	6·30	4·4	2·06	0·34	18	300	1
Mean	38·8	1·857	31	23	6·44	4·08	2·37	0·40	22	345	
<u>24 - 27th Week period.</u>											
1	37·	1·850	22	15	6·30	4·1	2·1	0·4	22	337	3
2	38·	1·926	27	21	6·59	4·1	2·3	0·41	20	411	1
3	38·	1·878	24	20	6·95	4·2	2·08	0·32	-	302	1
4	37·	1·777	27	20	6·08	4·4	1·46	0·54	-	262	1
5	34·	1·814	32	20	6·37	4·1	1·87	0·43	-	403	1
6	33·5	1·843	34	20	6·05	4·9	2·7	0·4	28	318	4
7	39·7	2·027	33	29	6·66	4·9	2·67	0·43	20	430	3
8	32·2	2·024	56	35	6·55	4·1	2·5	0·41	29	-	2
9	37·0	1·841	29	21	6·55	4·5	2·0	0·34	27	-	1
10	34·2	1·722	24	13	6·05	3·6	2·2	0·35	18	-	1
11	30·	1·965	59	31	6·62	4·4	2·35	0·55	-	-	2
12	40·2	1·839	17	15	5·90	4·2	2·52	0·38	26	391	2
13	37·2	1·816	26	19	6·01	4·0	2·72	0·38	25	290	1
Mean	38·4	1·871	32	22	6·36	4·27	2·27	0·41	24	349	

No.	PCV.	PLASMA VISC.	Wintrobe ESR.		Total Plas· Prot.	Alb.	Glob	Fibr	Urea	Chol.	No. of Preg.
			Ord.	Cor.							
	%	cs.	mm/ 1 hr		g. %				mg./100 ml		
28 - 31st Week period.											
1	37·	1·806	47	37	5·94	4·1	2·0	0·45	16	273	2
2	38·	1·917	35	28	5·90	3·8	1·7	0·43	28	494	1
3	29·	1·939	47	23	6·30	3·8	2·7	0·48	23	234	2
4	33·	1·840	39	23	5·76	3·9	2·1	0·44	25	447	1
5	31·8	1·808	48	28	5·94	3·9	2·55	0·45	-	-	3
6	34·3	1·753	32	20	5·76	3·82	2·03	0·45	-	-	2
7	36·0	1·746	27	18	5·76	3·8	2·01	0·39	-	400	2
8	30·2	1·867	44	23	6·26	3·8	3·18	0·42	-	400	3
9	36·	1·871	35	25	6·11	3·8	2·95	0·43	17	301	3
10	33·6	1·848	23	12	6·05	-	-	-	-	-	5
11	34·1	1·906	35	22	6·26	4·8	2·55	0·35	25	410	2
12	39·	1·817	35	30	5·76	4·45	2·26	0·54	24	380	1
13	32·5	1·707	27	13	5·47	3·8	2·12	0·38	29	290	2
14	40·0	1·769	20	17	5·69	4·3	2·57	0·33	19	370	4
15	36·6	1·841	32	23	6·12	-	-	-	-	-	2
Mean	34·7	1·829	35	23	5·94	4·01	2·36	0·43	23	363	
32 - 35th Week period.											
1	34·3	1·810	45	30	5·72	3·9	2·0	0·42	24	372	2
2	34·8	1·894	26	15	6·26	4·3	2·1	0·36	26	296	2
3	33·	1·803	25	13	5·40	3·97	1·60	0·41	21	382	1
4	34·3	1·948	33	21	6·44	4·2	1·9	0·41	20	438	3
5	34·9	1·977	32	21	6·73	4·1	2·2	0·49	26	375	3
6	36·8	1·932	31	22	6·55	4·3	2·08	0·42	21	285	4
7	29·6	1·972	58	32	6·41	4·0	1·92	0·48	23	322	2
8	34·	1·942	53	37	6·44	3·9	2·5	0·45	16	301	2
9	35·0	1·794	43	30	6·34	3·9	2·0	0·39	21	343	2
10	32·	1·961	59	37	6·84	3·9	2·3	0·49	33	378	2
11	36·7	1·983	50	39	6·59	4·2	2·42	0·48	-	-	2
12	33·8	1·871	46	30	5·98	4·0	2·47	0·43	-	-	1
13	35·5	1·827	29	19	6·23	3·89	1·89	0·52	-	-	4
14	36·2	1·837	34	24	6·26	4·55	1·9	0·45	-	-	2
15	29·6	1·811	47	24	5·72	4·5	2·18	0·42	-	242	3
16	37·0	1·868	23	17	6·16	4·7	2·47	0·43	20	280	7
17	27·5	1·975	36	12	6·48	4·8	2·48	0·42	21	520	6
18	36·	1·771	36	26	5·65	3·7	2·1	0·47	22	348	1
19	34·2	1·907	48	34	6·01	3·9	2·62	0·38	19	365	3
20	41·1	1·937	35	34	6·59	4·0	2·48	0·42	18	300	1
Mean	34·3	1·891	40	26	6·24	4·14	2·18	0·44	22	347	

No.	PCV.	PLASMA VISC.	Wintrobe ESR.		Total Plas.	Alb.	Glob	Fibr	Urea	Chol.	No. of Preg.
	%	cs.	mm/	1 hr	g. %				mg./	100 ml	
<u>36 - 40th Week period.</u>											
1	35·	2·067	56	40	6·84	4·2	1·84	0·56	27	582	2
2	39·8	1·966	45	40	6·59	4·54	1·8	0·56	28	430	1
3	35·	1·957	40	28	5·72	3·8	2·0	0·42	19	395	1
4	37·8	2·170	42	34	6·95	4·8	2·5	0·4	27	493	2
5	35·	2·069	48	34	6·55	4·2	2·4	0·5	31	407	2
6	35·8	1·973	53	40	6·77	4·2	2·53	0·47	-	-	1
7	35·	1·892	35	23	6·19	4·0	2·54	0·36	19	377	1
8	39·	1·920	35	30	6·59	4·2	2·06	0·54	-	431	1
9	34·	1·913	39	25	6·19	3·9	1·81	0·59	-	468	1
10	38·5	1·992	49	41	6·30	4·0	2·3	0·56	26	425	3
11	37·5	1·918	47	38	6·48	3·7	2·4	0·47	-	336	2
12	35·2	1·838	38	26	6·12	4·9	2·38	0·42	18	280	1
13	40·8	1·734	7	5	5·34	4·2	1·73	0·37	17	260	1
Mean	36·8	1·955	41	31	6·40	4·20	2·17	0·48	22	407	

The changes in the plasma viscosity during an alcohol test meal for Gastric function.

The first blood sample was removed from the fasting subject just before the administration of 100 ml. of 7% alcohol; the second sample was removed 2 hours later. 5-10 ml. of gastric huice were removed at 15-minute intervals.

Subjects with initial achlorhydria were given, in addition, a subcutaneous injection of histamine (0.5 mg.).

No.	S	PCV.	PLASMA VISC.	Wintrobe ESR.		Plasma Total Prot.	Remarks
				Ord.	Cor.		
		%	cs.	mm/1 hr.		g. %	
1	M	48.8	1.691	-	-	6.91	Slightly high curve
		49.5	1.723	-	-	6.91	
2	F	37.9	1.736	8	3	6.91	Achlorhydria, persisting after histamine.
		35.0	1.709	9	1	6.84	
3	F	36.0	1.875	24	15	6.62	Low acid curve
		38.0	1.895	26	20	6.73	
4	M	51.7	1.783	1	6	7.02	Normal acid curve
		51.3	1.776	1	5	6.95	
5	M	30.8	1.932	35	11	7.27	Normal acid curve
		30.9	1.943	37	13	7.27	
6	M	40.7	1.882	16	9	7.42	Free acid appeared in normal amount after histamine.
		40.1	1.866	15	7	7.24	
7	M	32.1	1.777	27	7	7.09	Achlorhydria after histamine; pernicious anaemia.
		29.1	1.712	30	4	6.77	
8	M	46.3	1.777	7	6	7.02	Normal acid curve.
		46.8	1.806	8	8	6.98	
9	M	47.0	1.906	13	13	7.38	Normal acid curve.
		46.9	1.921	14	14	7.34	

The changes in the plasma viscosity during a Urea Concentration and Clearance Test of Renal function.

Urine specimens are collected from the fasting subject and then at hourly intervals for 5 hours. A blood specimen is taken after 1 hour; 15 g. of urea in about 200 ml. of water is given after another hour; and another blood specimen is taken after yet another hour. The clearance values presented are the average of the first two hourly urine samples calculated relative to the first blood urea level and of the third and fourth urine specimens relative to the second blood urea level.

Thus the second blood indicates the effect of one further hour of fasting and one hour after 15 g. urea.

S	PCV.	PLASMA VISC.	Plasma Total Prot.	Blood Urea	Urine			Clearance
					Volume	Urea	Alb.	
	%	cs.	g. %	mg. %	ml.	g. %		% of average normal
F	41.3	2.016	7.31	20	38	1.73	o	
	40.3	1.993	7.27	53	31	2.05	o	132
					68	3.47	o	
					66	4.14	o	141
					50	4.5	o	
F	36.6	1.841	6.12	18	88	1.38	++++	
	36.8	1.877	6.41	45	62	1.22	++++	142
					142	1.15	++	
					60	3.84	++++	120
					44	4.70	++++	
F	51.2	1.730	6.41	24	24	2.2	o	
	51.4	1.777	6.88	44	33	2.44	o	123
					142	1.46	o	
					72	2.46	o	109
					72	2.78	o	
M	50.6	1.841	7.13	35	134	0.53	o	
	50.3	1.813	6.70	50	90	0.76	o	61
					90	0.77	o	
					126	1.04	o	39
					108	1.11	o	
M	46.5	1.996	7.27	37	32	1.56	o	
	46.7	2.028	7.38	64	49	1.7	o	67
					120	2.18	o	
					45	1.97	o	70
					46	2.5	o	

S	PCV.	PLASMA VISC.	Plasma Total Prot.	Blood Urea	Urine			Clearance
					Volume	Urea	Prot.	
	%	cs.	g. %	mg. %	ml.	g. %		% of average normal
F	47.0	1.910	7.63	19	25	1.45	s. tr.	
	45.1	1.905	7.52	42	30	2.06	s. tr.	116
					84	2.66	s. tr.	
					76	2.20	s. tr.	124
					52	2.90	s. tr.	
F	41.3	2.070	7.56	26	52	0.94	s. tr.	
	41.3	1.955	6.80	48	53	1.27	s. tr.	74
					76	1.91	s. tr.	
					88	2.38	s. tr.	79
					70	2.35	s. tr.	
F	41.5	2.432	8.53	55	38	0.84	tr.	
	41.5	2.465	8.64	68	48	0.96	tr.	26
					54	1.00	tr.	
					70	1.32	tr.	32
					98	1.26	tr.	
F	-	1.906	7.52	40	170	0.72	o	
	-	1.899	7.52	71	47	1.81	o	70
					210	1.04	o	
					74	2.84	o	75
					45	3.83	o	
M	-	1.842	7.49	19	56	1.40	tr.	
	-	1.820	7.34	34	44	1.58	tr.	132
					54	2.08	o	
					54	2.98	tr.	130
					26	4.30	+	
F	37.7	1.781	6.16	22	42	1.38	o	
	36.7	1.788	6.59	55	50	1.50	o	106
					140	2.24	o	
					64	3.55	o	134
					44	4.15	o	
F	43.2	1.859	7.27	22	79	0.55	o	
	42.4	1.872	7.42	55	115	0.62	o	62
					288	0.61	o	
					150	1.48	o	80
					49	3.10	o	

The changes in the plasma viscosity during a Glucose Tolerance Test for carbohydrate metabolism control.

The first blood sample was removed from the fasting subject just before the administration of 50 g. of glucose in 150-250 ml. of water. The later blood samples were removed at 30-minute intervals.

No.	S	PCV.	PLASMA VISC.	Wintrobe ESR.		Plasma Total Prot.	Blood Sugar	Urine		
				Ord.	Cor.			Sugar	Acetone	
		%	cs.	mm/	1 hr	g. %	mg. %			
F	F	44.8	1.874	8	9	6.55	180	++++	++++	
1		43.7	1.829	6	8	6.95	257	++++	++++	
2		42.0	1.812	7	7	7.06	286	++++	++++	
3		42.3	1.792	7	7	6.59	312	++++	++++	
4		43.5	1.885	7	8	7.02	272	++++	++++	
5		43.6	1.852	9	10	7.02	242	++++	++++	
F	M	49.0	1.854	1	3	7.13	59	o	o	
1		50.0	1.839	1	3	6.95	102	o	o	
2		49.2	1.837	2	4	6.95	80	o	o	
3		47.2	1.797	2	2	6.95	76	o	o	
4		47.1	1.791	1	1	6.41	66	o	o	
5		47.2	1.764	1	1	6.70	49	o	o	
F	M	45.9	1.812	2	1	7.02	62	o	o	
1		46.3	1.779	2	1	6.98	110	o	o	
2		45.0	1.762	2	0	6.95	110	o	o	
3		45.8	1.776	1	0	7.13	97	o	o	
4		46.4	1.827	2	1	7.16	55	o	o	
5		45.9	1.802	3	2	7.09	33	o	o	
F	M	47.7	2.123	13	14	7.24	55	+	±	
1		47.2	1.999	13	13	7.06	124	++	±	
2		46.9	1.995	15	15	6.88	132	+++	o	
3		47.1	2.043	13	13	6.98	113	+++	o	
4		47.2	2.069	15	15	6.98	89	++	o	
5		46.7	2.048	16	16	7.13	57	+	o	
F	M	48.8	1.885	5	7	6.73	75	+	o	Post- gastrectomy syndrome
1		48.7	1.872	6	8	6.91	171	++	o	
2		47.9	1.816	4	5	6.77	176	+++	o	
3		47.9	1.823	5	6	6.66	135	++	o	
4		47.4	1.866	6	6	6.70	94	+	o	
5		47.8	1.857	5	6	6.91	66	+	o	

No.	S	PCV.	PLASMA VISC.	Wintrobe ESR.		Plasma Total Prot.	Blood Sugar	Urine		
				Ord.	Cor.			Sugar	Acetone	
		%	cs.	mm/	1 hr	g. %	mg. %			
F	F	44.9	1.852	6	9	6.98	118	o	o	
1		44.4	1.827	5	7	6.98	188	/	/	
2		42.7	1.746	5	6	6.62	232	/	/	
3		41.9	1.737	6	6	6.70	204	++++	+	
4		41.3	1.760	7	6	6.59	174	++++	+	
5		43.4	1.800	6	8	6.84	174	++++	+	
F	F	43.5	1.822	-	-	7.09	128	tr	o	
1		41.8	1.784	4	4	7.02	198	tr	o	131 ml.
2		41.7	1.750	6	6	6.91	236	+	o	142 ml.
3		41.6	1.722	4	4	6.70	240	++++	o	163 ml.
4		41.7	1.764	5	5	6.70	214	++++	o	74 ml.
5		41.6	1.775	5	5	6.91	190	+	o	36 ml.
F	M	47.1	1.807	5	5	7.02	76	o	o	
1		47.1	1.776	4	4	6.84	126	o	o	
2		45.9	1.765	5	4	6.77	94	+	o	
3		47.4	1.808	6	6	6.84	40	tr	o	
4		48.7	1.835	5	6	6.95	35	o	o	
5		47.5	1.838	6	6	6.98	42	o	o	
F	F	41.2	1.884	9	8	7.42	84	o	o	321 ml.
1		40.9	1.882	8	7	7.52	108	o	o	36 ml.
2		41.8	1.892	8	8	7.45	91	+	o	28 ml.
3		41.6	1.914	9	9	7.38	78	o	o	36 ml.
4		42.2	1.926	9	9	7.74	78	o	o	35 ml.
5		42.1	1.913	10	10	7.49	85	o	o	24 ml.
F	F	37.5	1.918	47	38	6.48	34	tr	o	
1		37.8	1.912	48	39	6.55	66	tr	o	
2		-	-	-	-	-	104	tr	o	
3		36.9	1.897	50	40	6.30	113	/	/	
4		36.1	1.877	50	39	6.30	107	++	o	
5		35.9	1.892	48	37	6.05	116	++	o	
F	M	43.6	1.705	3	0	6.62	79	o	o	
1		44.0	1.699	1	0	6.80	32	o	o	
2		45.1	-	2	0	6.91	64	o	o	
3		42.2	1.683	3	0	6.55	55	o	o	
4		43.6	1.725	3	0	6.95	66	o	o	
5		42.6	1.727	4	0	6.77	58	o	o	
6		43.6	1.722	5	1	6.95	83	o	o	
7		43.4	1.756	4	0	6.77	82	o	o	
8		43.2	1.737	5	1	7.24	90	o	o	

No.	S	PCV.	PLASMA VISC.	Wintrobe ESR.		Plasma Total Prot.	Blood Sugar	Urine	
				Ord.	Cor.			Sugar	Acetone
		%	cs.	mm/1 hr		g. %	mg. %		
F	F	46.5	1.985	4	8	7.52	231	++++	-
1		44.4	1.874	6	8	7.16	280	++++	-
2		43.7	1.885	8	10	7.13	303	++++	-
3		44.3	1.883	8	10	7.09	300	++++	-
4		46.1	1.941	7	11	7.27	278	++++	-
5		45.1	1.936	8	11	7.24	262	++++	-

The effect of Sulphanilamide and Sulphapyridine on the Serum Protein, Plasma Viscosity, and Erythrocyte Sedimentation Rate.

(A) Sulphanilamide:-

In all subjects the sulphanilamide was given in the dosage of 2g., then 2g. after 4 hours, and then 1g. 4-hourly to a total of 20g. in three days.

The subjects were normal or suffering from conditions such as phthisis, post-encephalitis, etc., which do not respond to this treatment.

The figures in red express the result above as a percentage of the initial value; the third row of figures under serum protein expresses the value as a percentage of the initial protein, after correction for variation in the plasma proportions as shown by the packed-cell-volume.

Citrate								
Pl. Visc.	1.564		1.637				1.575	
			104.3				100.8	
Ser. Visc.	1.770		1.875				1.757	
			106.0				99.3	
P.C.V.	32.8		32.5				30.6	
			99.1				94.4	
Max. ESR.	1.67		2.01				1.17	
			120.4				70.3	
Ser. Prot.	6.81		7.38				7.01	
			108.3				102.9	
			108.9				106.3	
Days of Test	0	1	2	3	4	5	6	
Pl. Visc.	1.538		1.667				1.547	
			108.3				100.8	
Ser. Visc.	1.687		1.855				1.663	
			110.0				98.7	
P.C.V.	38.0		39.2				35.0	
			103.1				92.0	
Max. ESR.	0.41		2.81				1.01	
			686.				246.	
Ser. Prot.	6.71		7.13				6.47	
			106.4				96.4	
			104.4				100.8	
Pl. Visc.	1.705			1.768			1.705	
				103.6			100.0	
Ser. Visc.	1.872			1.976			1.888	
				105.6			100.4	
P.C.V.	28.6			31.3			31.0	
				109.4			108.4	
Max. ESR.	2.78			5.96			7.67	
				214.0			276.0	
Ser. Prot.	6.95			7.64			7.04	
				110.0			101.3	
				105.8			98.0	

(A) Sulphanilamide (contd.)

Days.	0	1	2	3		9
Citrate						
Pl. Visc.	1.605			1.653 103.0		1.616 100.7
Ser. Visc.	1.785			1.866 104.4		1.821 102.1
P.C.V.	36.7			34.6 94.2		32.7 89.0
Max. ESR.	2.19			3.79 173.		2.80 128.
Ser. Prot.	6.84			7.25 106.0 109.6		7.03 103.0 109.2
Citrate						
Pl. Visc.	1.657			1.722 104.0		1.674 101.1
Ser. Visc.	1.806	1.840 101.9		1.900 105.1		1.829 101.2
P.C.V.	34.8			33.9 97.4		34.0 97.7
Max. ESR.	6.51			10.93 168.0		8.22 126.3
Ser. Prot.	6.69			6.97 104.2 105.7		6.72 100.5 101.7
Citrate						
Pl. Visc.	1.645			1.664 101.2		1.615 98.2
Ser. Visc.	1.893			1.945 102.7		1.857 98.0
P.C.V.	32.5			33.7 103.7		32.8 100.9
Max. ESR.	5.44			6.19 113.8		4.22 77.6
Ser. Prot.	7.15			7.53 105.4 103.7		7.03 98.3 98.1

(B) Sulphapyridine.

Dosage was exactly the same as for sulphanilamide - 20g. in three days. The subjects were taken from similar clinical material.

Days.	0	1	2	3	4	5	6	7	8
Citrate									
Pl. Visc.	1.562		1.613 103.4	1.627 104.1			1.555 99.5		
Ser. Visc.	1.777		1.836 103.3	1.845 103.9			1.748 98.4		
P.C.V.	35.4		35.4 100.0	35.6 100.6			35.0 98.8		
Max. ESR.	1.04		1.50 144.4	1.54 148.0			0.86 82.5		
Ser. Prot.	7.14		7.21 100.9	7.23 101.3			6.54 91.6		
			100.9	101.1			92.1		
Citrate									
Pl. Visc.	1.614	1.598 99.0		1.660 102.8			1.602 99.3		
Ser. Visc.	1.822	1.832 100.6	102.9	1.878 102.9			1.848 101.4		
P.C.V.	33.8	32.4 95.7		33.6 99.5			33.4 98.8		
Max. ESR.	2.41	1.50 62.3		2.76 114.4			2.64 109.5		
Ser. Prot.	7.02	6.89 98.1		7.17 102.2			6.89 98.1		
		100.0		102.5			98.9		
Citrate									
Pl. Visc.	1.568	1.604 102.3	1.573 100.3						1.586 101.2
Ser. Visc.	1.757	1.845 105.0	1.760 101.1						1.766 100.4
P.C.V.	33.0	34.2 103.6	33.0 100.0						32.3 98.1
Max. ESR.	1.97	2.83 143.6	2.89 146.8						2.47 125.4
Ser. Prot.	6.77	7.24 106.9	6.85 101.1						7.09 104.77
		105.0	101.1						105.2

(B) Sulphapyridine (contd.)

Days.	0	1	2	3	4	5	6	7	8
Citrate									
Pl. Visc.	1.810	1.812 100.1		1.853 102.3			1.808 99.9		1.814 100.2
Ser. Visc.	1.903	2.033 106.8		2.011 105.6			1.983 104.2		1.950 102.5
P.C.V.	35.5	34.0 95.8		36.4 102.6			36.8 103.7		36.2 101.9
Max. ESR.	9.26	8.24 90.0		11.27 121.8			10.56 114.0		10.26 110.8
Ser. Prot.	6.95	7.62 109.7 112.1		7.63 109.8 108.2			7.00 100.8 98.6		7.44 107.1 106.0
Citrate									
Pl. Visc.	1.552		1.611 103.9	1.651 106.4					1.710 110.1
Ser. Visc.	1.772		1.773 100.1	1.924 108.5					1.985 111.4
P.C.V.	34.2		34.4 100.4	36.5 106.8					38.2 112.7
Max. ESR.	1.63		1.96 120.2	2.47 151.6					2.00 122.5
Ser. Prot.	6.67		6.75 101.2 101.0	7.27 109.1 105.2					7.89 118.3 111.2
Citrate									
Pl. Visc.	1.663	1.726 103.6	1.719 103.3				1.687 101.4		1.719 103.3
Ser. Visc.	1.923	1.946 101.1	2.010 104.4				1.963 102.1		1.956 101.6
P.C.V.	34.0	37.6 110.7	34.5 101.5				34.0 100.0		34.8 102.3
Max. ESR.	5.43	6.75 124.2	6.67 122.8				5.00 92.2		5.98 110.0
Ser. Prot.	6.95	7.56 108.8 102.8	7.38 106.3 105.7				7.09 102.0 102.0		7.47 107.5 105.3

Part 4

TABLES of RESULTS

and

CASE HISTORIES

of

DISEASE SECTION

(A) Chronic Rheumatoid Arthritis - Female.

Name	No.	Date	PLASMA VISC.	Wintrobe E. S. R.		Total Plas. Prot.	Gold Floc	PCV.	Remarks
				Ord.	Cor.				
			cs.	mm/	1 hr.	%		%	
H. C.	1	12: 5	2·200	20	24	7·88	-	45·2	
		13:10	2·051	32	38	7·16	+	45·6	Gold-21/10/47 to
		13: 9	2·105	27	31	7·74	+	44·6	13/1/48
M. C.	2	7:7	2·096	23	31	7·52	-	45·3	Gold - 7/8/47 to
		18: 9	1·981	20	-	7·13	-	-	25/10/47
		7:11	2·025	10	13	7·45	0	44·2	
R. D.	3	27:10	2·263	-	-	8·21	+	42·6	Gold 9/9 to 25/11/47
		29:12	2·088	44	43	7·31	+	41·5	Much improved.
H. F.	4	13: 1	1·949	-	-	8·44	-	47·5	
		25: 9	2·227	29	38	7·96	-	47·9	Gold 27/9 to 29/11/47
		7:11	2·252	-	-	8·46	+	48·0	
E. H.	5	24: 1	2·094	-	-	-	-	40·2	Gold begun 27/1/47
		2: 5	1·935	40	43	7·74	-	43·8	
		17:11	2·255	20	12	7·99	3+	36·1	
L. B.	6	24: 3	2·095	30	36	7·83	-	46·2	
		30: 6	2·003	21	21	7·52	-	42·2	
		7:5	2·129	14	19	7·74	-	45·8	
		23: 4	2·101	26	28	7·63	+	43·3	Gold begun 27/2/48
		10: 9	2·085	10	14	7·52	+	45·3	
A. C.	7	14: 4	2·045	2	1	7·81	-	45·7	Gold 3/4 to 26/8/47
		28: 8	2·068	-	-	7·70	-	40·8	Locally improved
		14:11	2·127	9	12	8·10	+	44·5	Much improved
I. C.	8	9: 4	2·334	24	29	8·28	-	45·4	Gold 15/4 to 15/7/47
		30: 5	2·341	46	46	8·14	-	41·9	
		17: 7	2·207	-	-	8·21	-	41·8	
		31:12	2·190	11	12	7·99	-	42·6	
		20: 2	2·061	27	28	7·60	+	42·4	
		21: 4	2·064	38	36	7·60	+	40·3	
		6: 9	2·054	33	32	7·74	+	41·4	
D. B.	9	16: 1	2·211	25	20	8·24	-	38·3	Gold 17/1 to 28/2/48
		27: 2	2·088	33	24	7·81	2+	36·3	
		28: 4	2·037	28	19	7·67	2+	36·2	
M. A.	10	3: 3	2·118	25	19	7·92	+	36·0	Gold begun 23/4/48
		7: 5	2·114	29	18	7·63	2+	35·0	after 7 injections
E. A.	11	10: 1	1·920	7	7	-	-	42·	Gold begun 18/12/46
		24: 2	1·887	-	-	-	-	39·4	Improving
A. M.	12	13:10	2·236	29	32	8·03	0	43·9	Gold 28/10 to 17/1/48
		10:12	2·180	16	15	7·81	+	41·2	Much improved

Name	No.	Date	PCV.	PLASMA VISC.	Wintrobe E. S. R.		Total Plas. Prot.	Gold Floc	Remarks.
					Ord.	Cor.			
			%	cs.	mm/	1 hr.	%		
A. B.	13	27: 8	40.3	1.977	34	32	7.27	-	Gold begun 23/9/47
		31:10	41.8	2.080	26	26	7.81	0	
		14: 4	41.2	2.024	26	25	7.49	-	Gold 13/1 to 6/4/48
		15: 9	41.2	2.072	29	28	7.31	+	
M. B.	14	7: 8	40.2	2.071	-	-	7.63	-	Gold 1/7 to 10/9/47
		25: 9	41.3	2.146	35	33	7.74	-	
		28:11	38.7	2.153	31	26	7.85	+	
		16: 1	38.5	2.193	9	5	7.78	-	Gold 12/12 to 17/2/48
		20: 2	40.7	2.274	36	34	7.92	+	
H. G.	15	24:11	43.	2.109	21	23	-	-	Gold ended 20/1/47
		21: 3	47.1	2.114	15	21	-	-	
		12:11	43.3	2.308	39	40	8.35	3+	Gold begun 12/12/47
		19: 3	39.0	1.930	29	24	7.16	0	
		13: 9	43.8	2.257	29	32	7.99	2+	
A. B.	16	29: 9	45.8	2.242	30	36	7.92	-	
		5:11	43.9	2.218	33	36	7.99	0	Gold begun 13/10/47
		24: 4	46.6	2.214	27	34	7.78	+	
A. B.	17	21: 4	38.4	2.158	-	-	7.74	-	
		28: 5	40.3	2.216	48	46	7.92	-	
		7:11	38.4	2.279	32	26	8.21	0	Gold 15/11 to 28/2/48
		12:12	40.9	2.251	39	37	7.70	2+	
		9: 2	42.4	2.061	21	22	7.88	+	improving
		8: 9	41.0	2.187	22	21	7.99	+	
A. H.	18	27:10	38.6	2.093	41	35	7.74	2+	Gold 4/11 to 27/1/48
		19:12	37.9	2.036	28	21	7.42	2+	
		3: 2	39.7	2.115	22	18	7.81	-	
E. H.	19	2: 2	39.4	2.090	39	34	7.92	+	Gold 10/2 to 27/4/48
		2: 4	39.8	2.054	38	34	7.92	+	
V. F.	20	12: 5	39.1	1.830	7	4	6.98	-	Gold 23/3 to 28/6/47
		25: 7	41.8	1.892	15	15	7.42	-	
		6:10	43.3	2.024	16	17	7.60	-	
E. C.	21	21: 7	35.5	2.126	23	14	7.74	-	Gold 29/7 to 25/11/47
		4: 9	43.1	2.206	-	-	8.03	-	
		3:11	43.8	2.112	19	22	8.24	+	much improved
G. M.	22	28: 5	40.9	2.165	31	29	7.81	-	Gold begun 6/6/47
		17: 7	41.3	2.085	-	-	7.56	-	
C. J.	23	6:12	44.	1.993	20	22	-	-	
		10:10	40.4	2.049	42	40	7.38	2+	Gold 14/10 to 20/1/48
		5:12	38.9	2.076	35	30	7.63	3+	much improved
		28: 1	40.9	2.114	42	40	7.81	3+	

Name	No.	Date	PCV.	PLASMA VISC.	Wintrobe E. S. R.		Total Plas. Prot.	Gold Floc	Remarks
					Ord.	Cor.			
			%	cs.	mm/	1 hr.	%		
I.P.	24	6: 2	-	1.959	-	-	-	-	Gold 12/2 to 2/4/47
		22: 9	40.7	2.052	25	23	7.56	-	
		13:11	37.0	2.050	5	0	7.78	2+	
		28: 1	41.4	2.004	24	23	7.56	-	
		15: 3	39.0	2.106	22	18	7.34	+	
		15: 9	41.7	2.120	37	37	7.85	2+	
E.P.	25	29: 7	35.8	2.114	53	39	7.49	-	Gold 9/9 to 20/11/47
		20:10	40.3	2.136	40	37	7.85	2+	
		10:11	42.7	2.258	24	25	8.78	3+	
		17:12	41.3	2.082	26	25	8.24	3+	
		21: 4	38.3	2.129	45	38	7.67	+	
		15: 9	40.3	2.190	46	43	7.92	+	
D.S.	26	24: 7	39.1	2.109	-	-	7.38	-	Gold 29/7 to 21/10/47
		11: 9	38.7	1.959	25	21	7.02	-	
		27:10	40.9	1.972	7	6	7.78	+	
		12: 5	36.9	1.888	20	13	6.80	-	
M.S.	27	30: 7	44.3	2.056	-	-	7.42	-	Gold 12/8 to 28/10/47 Clinically ISQ. Gold begun 6/3/48
		17: 9	43.3	1.955	13	15	7.38	-	
		10:12	44.3	1.969	18	21	7.70	+	
		10: 3	41.8	1.913	18	18	7.16	0	
		7: 5	42.3	1.911	14	14	7.06	0	
M.T.	28	10: 7	41.4	2.172	-	-	7.20	-	Gold 16/7 to 1/10/47) clinically worse Vaccine begun "Subacute"
		(10: 9	41.2	2.364	44	43	7.92	-	
		15:10	40.1	2.316	43	40	8.03	5+	
		7: 1	41.5	2.242	39	38	7.67	4+	
		18: 2	41.7	2.320	42	42	8.03	5+	
		(5: 5	40.0	2.306	45	41	7.70	5+	
M.T.	29	15: 9	42.0	2.306	40	40	8.06	-	Gold 23/9 to 16/12/47 Improved.
		5:11	45.7	2.231	15	20	8.60	+	
		20:12	41.1	1.922	16	15	7.27	2+	
M.S.	30	10: 1	40.	1.802	10	8	-	-	Gold course ending Gold begun 31/3/47 but discontinued. Gold 4/11 to 9/12/47
		10: 3	39.4	1.831	8	5	-	-	
		28: 3	38.0	1.936	20	15	7.34	-	
		31:10	36.8	2.086	30	22	7.99	+	
		19:12	34.3	1.918	19	9	7.24	3+	
E.S.	31	9:12	42.	2.167	39	39	-	-	Gold 17/1 to 25/4/47
		22: 1	40.8	2.210	40	38	-	-	
		30: 4	41.4	2.254	49	48	7.99	-	
		11: 8	43.1	2.230	39	41	8.17	-	
		25: 9	40.7	2.104	32	30	8.06	-	
		30: 4	41.6	2.041	26	25	7.92	+	
M.J.	32	28: 5	44.2	2.046	10	13	8.06	-	Gold 26/5 to 27/8/47
		28: 8	44.5	1.958	9	12	7.56	-	

Name	No.	Date	PCV.	PLASMA VISC.	Wintrobe E. S. R.		Total Plas. Prot.	Gold Floc	Remarks
					Ord.	Cor.			
			%	cs.	mm/	1 hr	%		
S. K.	33	30: 5	37.6	2.219	37	29	8.53	-	Gold 1/6 to 26/8/47
		17: 7	41.4	2.194	-	-	8.57	-	
		28: 8	42.9	2.147	21	22	8.24	-	Much improved Now "Subacute"
		(16: 1	41.5	2.321	20	20	8.96	-	
		1: 3	39.7	2.164	40	36	7.92	+	Gold 20/1 to 13/4/48
		28: 4	39.3	2.196	38	33	8.32	2+	
A. H.	34	6:12	43.	1.886	10	11	-	-	Gold begun 11/12/46
		7: 5	41.4	1.877	23	22	7.38	-	
		19:11	42.5	2.194	32	33	7.85	3+	Gold begun 2/12/47
		15: 1	39.9	2.176	43	39	7.63	2+	
		10: 3	38.5	1.961	38	32	7.02	+	
L. H.	35	27: 3	45.9	2.126	26	32	7.92	-	Gold begun 12/4/47
		21: 5	43.8	2.330	13	15	7.88	-	
A. P.	36	27: 3	44.9	1.960	-	-	7.71	-	Gold begun 24/3/47
		21: 5	41.5	1.909	10	9	7.52	-	
M. O.	37	20:10	39.8	2.393	-	-	8.46	+	Gold 28/10 to 2/12/47
		22:12	41.2	2.251	42	41	8.14	+	
		3: 3	39.2	2.125	39	34	7.81	0	Gold begun 9/3/48
		5: 5	40.2	2.339	44	40	8.42	+	
M. M.	38	3: 3	38.7	2.278	46	39	8.39	3+	Gold begun 9/3/48
		30: 4	41.4	2.300	39	38	8.10	3+	
E. S.	40	13: 8	43.0	2.339	43	44	8.68	-	Gold 13/1 to 16/3/48
		3:12	42.2	2.176	23	23	8.25	+	
		6: 2	40.2	2.072	22	20	7.74	+	
		23: 3	42.3	2.115	24	25	8.03	+	
		16: 4	39.5	2.000	27	23	7.52	0	
J. R.	41	10: 3	37.8	1.970	23	16	7.60	+	Gold begun 5/4/48
		12: 3	36.7	1.993	25	17	7.60	0	
		24: 5	38.4	1.964	20	15	7.85	0	
M. T.	42	6: 8	43.1	2.041	-	-	7.34	-	Gold begun 24/11/47 after 6 injections
		24:11	45.6	1.908	10	14	6.70	+	
		9: 1	44.8	1.928	16	19	7.20	+	
M. H.	43	25: 7	33.1	2.259	52	34	7.89	-	1947
		23: 3	33.1	2.272	41	25	7.70	3+	1948
		14: 6	30.4	2.080	56	32	6.47	3+	Gold begun 24/4/48
I. B.	44	18: 2	38.1	2.397	50	41	8.75	4+	Gold begun 5/3/48
		30: 4	36.2	2.368	48	36	9.11	4+	
		12: 5	37.7	2.360	45	37	8.17	4+	
K. H.	45	14: 4	42.6	2.462	46	47	8.17	0	Gold begun 23/4/48
		26: 5	38.3	2.324	44	36	7.63	0	
A. T.	46	26:11	42.1	2.011	12	12	7.78	0	Gold begun 6/12/47
		12: 3	39.0	1.804	13	10	6.84	0	Gold resumed 28/2/48

Name	No.	Date	PCV. %	PLASMA VISC. cs.	Wintrobe E. S. R.		Total Plas. Prot. %	Gold Floc	Remarks
					Ord. mm/	Cor. 1 hr			
S.B.	47	5:11	41.1	1.936	11	10	7.70	+	Gold 7/11 to 5/1/48 improving
		22:12	41.6	1.862	5	5	7.24	0	
		9: 2	41.1	1.830	7	6	6.84	0	
		7: 4	42.5	1.797	6	6	6.52	0	
A.B.	48	19: 3	41.5	2.245	47	46	7.90	-	Now subacute Gold 9/8 to 25/10/47)
		(7: 5	39.7	2.331	-	-	8.28	-	
		24: 7	41.2	2.478	-	-	8.60	-	
		18: 9	42.8	2.429	46	47	8.39	-	
E.S.	49	29:10	41.7	2.075	17	17	7.92	0	Gold 20/9 to 6/12/47
		17:12	43.4	2.031	14	16	7.88	+	
M.S.	50	28: 4	41.3	2.246	37	36	8.03	-	Gold 25/4 to 19/8/47 improving
		2: 7	40.3	2.355	-	-	7.92	-	
		14: 8	38.5	2.152	42	36	7.88	-	
E.S.	51	3: 9	32.4	2.261	-	-	7.63	-	Gold 16/9 to 25/11/47 now subacute improved
		(28:11	30.7	2.384	22	7	8.64	5+	
		20:12	-	2.257	23	-	7.88	-	
E.R.	52	7: 7	44.6	2.169	47	52	8.14	-	Gold begun
		11: 2	43.6	2.088	16	19	7.99	0	
		17: 3	44.6	2.034	18	22	7.92	+	
E.H.	53	18: 4	43.4	2.024	-	-	7.49	-	Improving Gold begun 12/12/47 Improved
		13:10	46.1	2.091	13	17	7.81	+	
		17:12	43.6	1.991	-	-	7.49	-	
		(2: 4	42.9	1.898	13	14	7.02	+	
M.H.	54	9: 2	43.4	1.971	13	14	7.60	2+	Gold 7/10 to 31/12/47
		30: 5	36.5	2.102	49	38	7.85	-	
		24: 9	38.0	2.112	46	38	7.56	-	
L.H.	55	14:11	34.3	2.052	34	21	7.88	+	Gold 3/3 to 20/5/47 improving Gold 4/10 to 20/12/47
		21: 2	40.0	1.916	6	5	-	-	
		23: 5	42.7	1.965	-	-	7.42	-	
		2:10	43.9	2.008	14	16	7.31	-	
		19:11	43.1	1.993	14	10	7.49	2+	
		31:12	43.3	1.970	18	20	7.31	-	
E.W.	56	10: 9	42.6	2.020	33	34	7.13	+	1946 Gold begun 3/2/48
		23:12	37.	1.963	33	23	-	-	
		28: 1	39.8	2.029	30	26	7.70	+	
D.W.	57	19: 3	45.3	2.222	29	24	7.92	+	Gold 28/10 to 6/1/48 now subacute
		17: 9	38.7	2.116	44	38	7.34	-	
J.J.	58	(29:12	39.7	2.266	29	25	8.46	3+	subacute Gold 3/6 to 20/8/47
		23: 5	45.0	2.402	7	10	8.86	-	
		28: 8	43.1	2.042	22	24	7.67	-	
		11:11	46.3	2.066	16	21	7.81	0	

Name	No.	Date	PCV.	PLASMA VISC.	Wintrobe E. S. R.		Total Plas. Prot.	Gold Floc	Remarks
					Ord.	Cor.			
			%	cs.	mm/	1 hr	%		
W. C.	59	9:12	40.	2.082	19	17	-	-	
		21: 7	39.2	2.073	-	-	7.92	-	
		2:10	37.5	2.330	47	38	8.24	-	
		21:11	35.5	2.247	50	37	8.10	3+	
		7: 4	36.0	2.191	45	34	7.96	2+	
		8: 9	36.0	2.383	51	40	8.64	3+	
M. F.	60	13:12	42.5	2.011	24	24	-	-	
M. D.	61	23:12	-	2.044	-	-	-	-	
S. G.	62	23:12	44.	2.151	5	7	-	-	
		9: 5	43.7	2.341	17	19	8.32	-	
I. S.	63	17: 1	44.	1.882	2	4	8.06	-	
J. I.	64	8: 1	43.	1.995	29	31	-	-	
M. L.	65	17: 1	48.	1.996	-	-	-	-	
E. N.	66	22: 1	44.2	1.899	12	14	-	-	
M. C.	67	23: 1	44.5	1.862	10	13	-	-	1947
		5: 2	41.6	2.021	-	-	7.85	+	1948
E. B.	68	24: 1	40.9	1.864	14	12	-	-	
		31: 3	45.1	1.930	20	24	7.31	-	
		2: 4	-	1.916	-	-	7.31	-	
		29:12	47.6	2.091	4	10	7.81	3+	
		28: 5	42.9	2.066	29	30	7.67	+	
H. B.	69	28: 1	45.5	2.016	-	-	-	-	
		(11: 8	44.7	2.425	33	36	8.39	-	now subacute
		18: 9	-	2.287	16	-	8.17	-	"
		10:10	42.5	2.284	23	24	8.03	3+)	"
		24:12	40.4	2.068	28	26	7.34	5+	
		15: 3	43.6	2.136	19	21	7.70	2+	
		7: 5	40.5	2.148	20	18	7.81	3+	
		10: 9	42.0	2.460	7	7	8.71	4+	
		15: 9	38.8	2.231	-	-	7.81	4+	
E. J.	70	31: 1	45.1	1.907	-	-	-	-	
S. H.	71	8: 2	46.9	2.290	-	-	-	-	
F. D.	72	14: 2	47.1	2.170	-	-	-	-	
H. L.	73	24: 2	45.0	2.043	-	-	-	-	
		23: 4	44.7	2.017	16	19	7.60	-	
		15:10	42.9	2.009	14	15	7.74	+	
		3:12	41.6	1.924	7	7	7.34	2+	
E. C.	74	24: 2	42.5	2.054	-	-	-	-	
E. P.	75	3: 3	41.2	1.993	29	28	7.46	-	

Name	No.	Date	PCV.	PLASMA VISC.	Wintrobe E.S.R.		Total Plas. Prot.	Gold Floc	Remarks
					Ord.	Cor.			
			%	cs.	mm/	1 hr.	%		
I. H.	76	17: 3	47.9	1.954	3	8	7.37	-	
		11: 8	44.9	1.987	14	17	7.60	-	
E. L.	77	31: 3	43.6	2.021	30	32	7.20	-	
M. W.	78	31: 3	44.1	2.011	12	15	7.13	-	
		2: 4	-	1.899	-	-	7.02	-	
		25: 7	39.6	1.997	29	35	6.99	-	
		20:10	38.9	1.976	15	11	7.06	+	
		2: 2	43.6	2.238	10	12	8.21	o	
E. W.	79	2: 4	44.9	2.361	34	39	8.96	-	
		27:11	43.5	2.505	14	17	9.14	3+	
E. J.	80	9:4	40.0	2.220	19	17	7.84	-	
		21: 5	39.7	2.175	30	26	7.88	-	
K. P.	81	14: 4	43.2	2.100	13	14	7.81	-	
M. A.	82	16: 4	45.4	2.121	6	10	8.06	-	
		9:10	47.1	2.036	15	21	7.67	-	
		10: 3	41.2	1.943	-	-	6.88	3+	
S. A.	83	3:11	35.1	1.932	14	6	7.60	+	
M. R.	84	17: 4	41.3	2.010	14	13	7.49	-	
M. S.	85	18:4	44.3	2.210	5	7	8.06	-	
E. K.	86	21: 4	46.3	2.034	6	11	7.85	-	
		17: 9	46.7	2.087	12	18	7.60	-	
D. S.	87	21: 4	41.8	2.206	-	-	7.70	-	
		30: 5	39.6	2.273	49	45	7.99	-	
		5: 9	39.1	2.255	-	-	7.99	-	
		21:10	38.7	2.154	-	-	7.67	+	
V. J.	88	28:4	39.9	2.381	38	34	8.35	-	
E. C.	89	28: 4	42.0	2.197	-	-	7.45	-	
E. S.	90	2: 5	37.0	2.038	38	29	7.52	-	
M. G.	91	5: 5	46.7	1.874	5	10	7.38	-	early case
E. D.	92	7: 5	43.6	2.106	27	29	7.60	-	early case
E. H.	93	9: 5	40.7	2.084	29	27	7.45	-	
		18: 7	43.8	2.282	43	46	8.14	-	
O. S.	94	12: 5	42.2	2.050	20	20	7.88	-	
D. B.	95	9: 5	47.7	2.005	8	15	7.38	-	
E. R.	96	12: 5	41.0	2.118	25	24	8.14	-	
		28: 5	43.5	2.007	34	36	7.74	-	
		31: 7	41.5	1.918	19	18	7.20	-	
		29: 9	45.2	2.247	26	31	8.17	-	

Name	No.	Date	PCV.	PLASMA VISC.	Wintrobe E. S. R.		Total Plas. Prot.	Gold Floc	Remarks
					Ord.	Cor.			
			%	cs.	mm/	1 hr	%		
E. R.	97	14: 5	37.7	2.147	45	37	7.34	-	
E. S.	98	14: 5	43.8	2.137	-	-	7.34	-	
A. F.	99	16: 5	42.1	1.835	6	6	7.42	-	
E. H.	100	21: 5	42.9	2.350	39	41	8.96	-	
M. W.	101	28: 5	41.8	1.889	11	11	7.45	-	
M. S.	102	28: 5	41.8	2.299	42	42	8.32	-	
J. S.	103	30: 5	41.2	2.071	28	27	7.67	-	
M. P.	104	30: 5	40.6	2.087	25	23	7.96	-	
J. T.	105	5: 6	35.8	2.049	-	-	7.52	-	
E. T.	106	5: 6	36.3	2.441	-	-	7.92	-	
H. G.	107	6: 6	43.8	2.103	-	-	7.45	-	
		4: 7	45.2	2.140	24	28	7.67	-	
G. W.	108	2: 7	44.3	2.162	22	25	7.92	-	
O. G.	109	2: 7	41.2	2.117	-	-	7.67	-	
		9: 9	39.6	2.038	-	-	7.45	-	
		30: 9	40.4	1.974	-	-	7.16	-	
		22: 12	43.4	2.326	28	30	8.46	+	
		9: 3	39.3	2.103	40	36	7.70	+	
		1: 7	42.9	2.213	32	33	8.35	2+	
		15: 9	42.4	2.101	34	35	7.70	+	
M. M.	110	2: 7	39.6	2.121	39	34	7.54	-	
		18: 9	43.8	2.071	18	20	7.42	-	
		5: 11	40.8	2.120	27	25	7.96	o	
		8: 3	38.3	2.200	37	30	7.70	+	
		7: 5	37.6	2.125	40	32	7.42	o	
K. B.	111	10: 7	43.0	2.018	-	-	7.38	-	
M. W.	112	18: 7	42.8	2.283	-	-	8.42	-	
		6: 8	40.0	2.099	31	28	7.52	-	
		30: 12	42.1	2.262	-	-	8.71	-	
		16: 2	41.9	2.331	-	-	8.82	-	
		18: 5	43.1	2.275	-	-	8.17	o	
M. S.	113	7: 7	42.6	1.791	1	1	7.24	-	? early
M. K.	114	24: 7	38.	2.122	-	-	7.92	-	
		18: 9	36.1	2.110	30	21	7.49	-	
M. O.	115	24: 7	32.9	2.230	-	-	7.74	-	
J. F.	116	24: 7	42.1	2.175	-	-	7.88	-	
A. B.	117	25: 7	45.9	2.161	26	32	8.57	-	

Name	No.	Date	PCV.	PLASMA VISC.	Wintrobe E. S. R.		Total Plas. Prot.	Gold Floc	Remarks
					Ord.	Cor.			
			%	cs.	mm/	1 hr	%		
M. J.	118	25: 7	42.9	2.305	46	48	8.18	-	
M. B.	119	28: 7	41.8	2.014	16	16	7.31	-	
		8: 9	42.6	1.938	16	17	7.13	-	
S. O.	120	6: 8	40.8	2.153	38	36	7.56	-	
B. L.	121	7: 8	38.7	2.227	-	-	8.03	-	
		24:10	40.0	2.117	46	42	7.88	2+	
		10:12	38.7	2.240	37	31	8.06	3+	
I. P.	122	11: 8	37.6	2.224	45	37	8.17	-	
E. B.	123	13: 8	39.1	2.187	40	35	7.63	-	
G. R.	124	19: 8	43.8	2.173	47	50	8.10	-	
M. C.	125	28: 8	42.9	1.834	11	12	6.77	-	
A. S.	126	2: 9	35.3	2.353	51	37	8.34	-	
		5: 9	37.4	2.373	51	42	8.35	-	
M. B.	127	2:9	23.1	1.883	27	0	6.66	-	
P. M.	128	3: 9	40.3	2.273	47	44	7.96	-	
		14: 4	41.7	2.212	39	39	8.10	-	
D. J.	129	3: 9	44.7	2.263	44	50	8.28	-	
M. S.	113	8: 9	41.5	1.844	1	1	7.49	-	
M. S.	130	12: 9	39.2	2.322	53	47	7.74	-	
		23: 4	37.0	2.478	51	40	7.92	3+	
E. S.	131	12: 9	41.0	2.053	42	40	7.38	-	
M. H.	132	15: 9	40.9	2.236	38	36	7.56	-	
		10:11	38.9	2.138	58	51	7.78	2+	
		20:12	39.5	2.224	24	20	7.99	+	
		17: 3	40.0	2.113	31	28	7.45	2+	
M. M.	133	17: 9	43.8	1.988	3	4	7.85	-	
F. M.	134	17: 9	37.0	1.995	19	13	7.24	-	
F. A.	135	17: 9	45.9	2.055	13	17	7.45	-	
M. S.	27	25: 9	43.6	2.023	20	22	7.67	-	
J. B.	136	6:10	44.3	1.902	13	15	7.38	-	
L. C.	137	6:10	43.5	1.913	20	22	7.49	-	
		9: 9	40.3	1.877	10	8	6.95	+	
M. P.	138	6:10	38.8	1.973	34	28	7.27	o	
I. D.	139	10:10	43.3	2.014	15	16	7.49	o	
		20:11	38.9	2.035	21	17	7.78	+	
		27: 2	39.7	1.963	16	13	7.13	o	
		12: 5	38.3	1.951	17	13	7.34	+	

Name	No.	Date	Pcv.	PLASMA VISC.	Wintrobe E. S. R.		Total Plas. Prot.	Gold Floc	Remarks
					Ord.	Cor.			
			%	cs.	mm/	1 hr	%		
A. W.	140	16:10	40.8	2.198	25	23	8.06	+	
M. G.	141	16:10	43.3	2.484	47	50	7.49	o	early case
I. N.	142	16:10	43.0	1.799	2	3	7.49	o	early case
		13: 2	42.8	2.004	16	17	7.67	+	
		27:10	44.6	1.915	13	16	6.91	+	
		31: 3	45.0	2.049	13	17	7.88	+	
M. P.	143	17:10	44.8	2.162	20	24	7.78	+	
		13: 2	43.0	2.187	14	16	7.78	2+	
M. O.	144	20:10	39.8	2.393	-	-	8.46	+	
M. P.	145	22:10	44.7	1.847	3	6	7.88	o	
E. S.	146	24:10	38.6	2.223	48	41	8.17	3+	
E. W.	147	29:10	38.2	2.264	45	38	7.63	2+	
		9: 2	39.3	2.492	51	46	8.96	4+	
M. R.	148	3:11	39.4	2.095	-	-	6.95	5+	
		5:12	45.8	2.202	16	21	7.45	5+	
E. E.	149	5:11	44.2	2.369	35	39	8.86	+	
		29:12	45.7	2.319	6	12	7.88	2+	
M. W.	150	13:11	42.9	2.008	37	38	7.60	+	
S. C.	151	24:11	44.1	2.106	7	10	7.38	+	
L. J.	152	24:11	42.2	2.073	-	-	7.34	+	
		17: 3	42.9	2.082	24	25	7.96	+	
M. C.	153	26:11	43.3	1.960	-	-	7.06	+	
		16: 2	39.9	1.896	24	21	7.42	+	
M. G.	154	27:11	41.2	1.935	10	9	7.85	+	early case
M. S.	155	1:12	40.2	1.977	22	20	7.52	+	
		(29: 1	43.0	2.405	43	45	8.32	o)	now subacute
		22: 3	41.1	2.086	23	22	7.75	o	again chronic
M. H.	156	5:12	43.4	2.358	21	23	8.89	3+	
J. A.	157	8: 8	45.0	1.908	-	-	7.45	-	early case
		29: 9	43.5	2.019	14	16	7.85	-	
		3:11	43.3	2.015	15	17	7.99	+	
		10:12	43.9	1.975	10	12	7.96	+	
M. C.	158	(29:10	42.1	2.569	39	39	8.93	2+)	subacute here
		12:12	41.8	2.323	39	39	7.81	+	now chronic
		28: 1	42.2	2.336	45	45	8.57	+	
G. B.	159	(31:10	40.6	2.344	50	47	8.06	o)	subacute
		19:12	39.7	2.199	44	39	7.63	o	
		3: 2	41.0	2.145	20	18	7.52	+	
		5: 4	42.2	2.119	30	30	7.42	+	
		6: 9	42.7	2.068	30	31	7.20	+	

Name	No.	Date	PCV.	PLASMA VISC.	Wintrobe E. S. R.		Total plas. Prot.	Gold Floc	Remarks
					Ord.	Cor.			
			%	cs.	mm/	1 hr	%		
E. B.	160	19:12	39.6	2.120	-	-	8.14	+	Subacute here
		3: 2	38.0	1.928	13	8	7.45	+	
		16: 4	41.4	1.966	16	15	7.52	+	
		3: 9	40.4	2.027	-	-	7.96	+	
N. R.	161	22:12	40.3	2.038	17	15	7.92	2+	
E. M.	162	29:12	43.8	2.053	8	10	7.34	2+	
H. P.	163	12:11	46.6	3.027	21	28	9.79	5+	
		31:12	46.9	2.450	13	21	8.53	-	
		9: 4	43.5	2.267	32	34	7.70	4+	
K. P.	81	14: 4	43.2	2.100	13	14	7.81	-	
		31:12	44.1	2.162	42	46	8.24	-	
		28: 4	39.0	1.978	19	15	7.63	+	
H. T.	164	5: 1	41.1	2.333	11	10	8.64	2+	
		30: 3	37.0	2.171	16	10	7.70	+	
E. J.	165	7: 1	43.4	2.135	26	28	7.92	o	
		14: 4	43.1	2.152	33	35	7.78	-	
M. T.	166	7: 1	41.6	1.935	12	12	7.49	o	
M. M.	167	15: 1	40.1	2.185	21	18	8.21	2+	
		24: 3	41.8	2.218	29	29	8.06	2+	
S. C.	151	15: 1	43.1	2.051	11	12	7.74	+	
N. B.	168	16: 1	31.9	2.265	23	9	8.06	2+	
M. L.	169	16: 1	45.0	2.239	28	32	8.10	+	
C. H.	170	16: 1	39.7	2.131	40	36	7.88	+	Burned out
		26: 5	39.4	2.261	39	34	7.92	o	
D. T.	171	19: 1	47.6	2.235	-	-	8.32	+	
		7: 2	44.3	2.001	-	-	7.31	o	
M. R.	172	19: 1	40.7	1.879	6	5	7.20	2+	
L. L.	173	28: 1	39.8	2.193	41	37	8.21	o	
		12: 3	41.8	2.217	28	28	8.39	o	
E. W.	174	3: 2	39.4	2.029	37	32	6.84	+	
W. G.	175	6: 2	37.0	1.893	11	5	7.45	+	
		22: 3	38.5	1.946	10	6	7.52	o	
M. P.	176	6: 2	43.5	1.916	7	9	7.16	+	
B. S.	177	6: 2	44.0	2.085	11	13	8.06	o	
H. H.	178	6: 2	39.7	2.052	16	13	7.67	4+	
L. W.	179	7: 1	43.2	1.980	15	16	7.87	o	
M. W.	180	25: 2	45.8	2.081	46	53	7.16	4+	
		21: 4	42.5	2.133	38	39	7.56	3+	

Name	No.	Date	PCV.	PLASMA VISC.	Wintrobe E.S.R.		Total Plas. Prot.	Gold Floc	Remarks
					Ord.	Cor.			
			%	cs.	mm/	1 hr	%		
L.B.	6	25: 2	44.2	1.950	30	34	6.95	+	See earlier note
E.B.	181	27: 2	36.5	2.052	33	24	6.98	3+	
M.A.	182	1: 3	42.9	1.812	7	8	7.02	o	
		23: 4	41.4	1.904	18	17	6.95	o	
L.H.	183	3: 3	39.0	2.070	39	34	7.49	+	
E.O.	184	8: 3	42.2	2.080	41	41	7.52	2+	
		12: 5	44.7	2.132	32	37	7.52	2+	
M.W.	185	10: 3	41.0	1.947	18	17	7.34	+	
C.C.	186	18: 3	43.3	2.082	-	-	7.99	o	
A.T.	187	18: 3	-	2.049	-	-	7.63	-	
M.T.	188	20: 3	31.5	2.543	58	36	8.39	5+	Gold begun 6/4/48
F.H.	189	22: 3	43.2	2.005	5	6	7.49	+	
E.W.	190	23: 3	36.9	2.356	42	33	8.06	+	
		28: 5	42.0	2.435	50	50	8.03	2+	
E.C.	191	6: 2	41.8	2.013	10	10	7.52	+	
		24: 3	40.0	2.066	19	17	7.63	+	
V.M.	192	31: 3	42.3	1.921	15	15	7.09	2+	
H.W.	193	2: 4	48.8	2.261	17	26	8.39	o	
C.H.	194	7: 4	40.7	2.093	33	31	7.78	+	
E.M.	195	7: 4	42.5	2.043	24	25	7.63	o	
		26: 5	40.5	1.922	21	19	7.13	+	
A.B.	196	7: 4	45.0	2.004	22	26	7.24	+	
M.S.	197	9: 4	42.3	2.189	36	36	7.52	2+	
E.B.	198	9: 4	32.7	1.880	7	0	7.27	2+	
G.T.	199	14: 4	41.8	1.859	3	3	7.49	o	
E.B.	200	14: 4	44.0	2.197	8	11	7.88	+	
M.B.	201	14: 4	44.0	2.165	27	30	7.81	-	
E.W.	202	16: 4	37.7	2.435	51	42	8.35	3+	
E.S.	203	19: 4	38.3	2.392	-	-	8.24	2+	
S.P.	204	5:12	40.5	2.100	24	22	7.60	2+	
		11: 2	47.1	2.372	16	22	8.89	o	
		23: 4	38.2	1.938	20	15	7.16	+	
M.F.	205	30: 4	43.4	1.795	4	5	7.27	o	
H.K.	206	3: 5	46.2	2.179	30	37	7.34	o	
G.H.	207	5: 5	41.0	1.987	12	11	6.98	o	

Name	No.	Date	PCV.	PLASMA VISC.	Wintrobe E. S. R.		Total Plas. Prot.	Gold Floc	Remarks
					Ord.	Cor.			
			%	cs.	mm/	1 hr	%		
J.C.	208	6: 5	35.8	2.043	34	24	7.34	+) now subacute
M.M.	209	7: 5	43.2	2.362	34	36	8.64	4+	
		(6: 9	42.9	2.440	34	34	8.86	4+	
S.B.	210	21: 5	45.0	2.112	35	40	7.63	o	
H.E.	211	22: 5	35.9	2.078	19	12	7.85	+	
M.W.	212	22: 5	34.8	2.153	50	36	7.56	2+	
E.W.	213	24: 5	40.0	2.697	21	18	9.29	4+	
M.C.	214	26: 5	44.7	2.131	21	24	7.88	o	
A.M.	215	7: 4	43.2	2.021	15	17	7.70	+	
		26: 5	41.3	2.036	27	26	7.52	2+	
R.W.	216	26: 5	45.0	2.188	-	-	8.24	o	
M.W.	217	26: 5	40.0	1.855	9	7	7.16	o	
M.T.	218	26: 5	42.2	2.400	16	16	8.75	2+	
H.B.	219	28: 5	45.4	2.250	31	37	7.99	2+	
E.T.	220	28: 5	43.2	2.068	30	32	7.52	o	
M.M.	221	2: 6	42.0	2.305	44	44	8.14	2+	
F.N.	222	18: 6	43.9	2.128	26	29	8.14	+	
B.G.	223	29: 7	-	2.085	-	-	7.13	-	
M.T.	224	4: 8	44.2	1.954	12	14	7.38	+	
C.O.	225	19: 8	40.7	2.145	39	37	7.34	o	
W.P.	226	26: 8	36.3	1.958	29	19	7.70	+	
S.G.	227	2: 9	45.7	2.140	16	21	8.14	+	
J.C.	228	3: 9	35.0	2.379	-	-	8.46	2+	
D.F.	229	8: 9	37.6	2.187	31	24	8.46	+	

(B) Chronic Rheumatoid Arthritis - Male

Name	No.	Date	PCV. %	PLASMA VISC. cs.	Wintrobe E. S. R. Ord. Cor.		Total Plas. Prot. %	Gold Floc	Remarks
					mm/	1 hr			
J.B.	1	23: 9	46.0	2.170	29	28	7.74	-	Gold begun 27/9/47
		4:11	41.2	2.041	44	34	7.38	2+	
T.B.	2	11:11	41.2	1.885	9	3	7.36	+	Gold 13/11 to 3/2/48
		30:12	41.8	2.039	8	3	8.10	-	
		12: 2	41.8	1.838	5	0	7.20	+	
A.R.	3	4: 2	44.8	2.119	18	16	-	-	Gold 6/2 to 29/4/47
		16: 9	41.7	2.096	44	35	7.56	-	
		28:10	47.2	2.373	20	20	8.60	4+	Gold begun 4/11/47
		18:11	47.0	2.353	11	11	8.32	4+	
		15: 1	48.1	2.180	11	12	7.68	3+	
		13: 2	47.4	2.156	15	15	7.70	3+	
		29: 4	46.9	2.198	17	17	7.85	3+	
		7: 9	44.9	2.314	30	27	7.85	3+	
D.R.	4	27: 2	46.3	2.154	-	-	7.62	-	Gold 14/10 to 13/1/48
		25: 9	46.2	2.140	18	15	7.60	-	
		4:12	44.5	2.102	12	9	7.38	3+	
		18:12	46.2	2.242	17	16	7.88	3+	
		29: 1	48.4	2.175	16	18	7.96	3+	
W.W.	5	4:12	37.0	2.105	18	7	7.88	+	Gold 24/10 to 13/1/48
		29: 1	43.3	2.193	28	23	8.10	+	
		11: 5	39.7	2.021	25	15	7.56	+	Gold dermatitis
F.H.	6	4: 2	49.5	2.005	-	-	-	-	Gold begun
		8: 5	47.7	2.072	-	-	7.63	-	
		4:11	49.5	2.159	-	-	8.39	0	
		22:12	44.7	1.933	8	5	7.16	+	
		5: 2	46.7	1.976	9	9	7.45	+	
		14: 9	47.8	1.983	14	15	7.31	0	
S.L.	7	18: 8	44.9	2.345	27	24	8.42	-	Gold 16/9 to 9/12/47
		11: 9	45.3	2.054	25	23	7.42	-	
		28:10	48.8	2.241	14	16	8.60	+	Clinically improved
J.P.	8	8: 7	48.6	2.353	22	24	8.28	-	Gold begun 15/7/47
		28: 8	45.2	2.243	35	32	8.21	-	
		2:10	44.7	2.203	25	22	8.03	-	Much improved
F.D.	9	26: 7	43.8	2.131	30	25	7.92	-	Gold 16/8 to 8/11/47
		11: 9	45.8	2.003	15	14	7.63	-	
		11:11	46.9	2.075	10	10	8.28	+	
		28: 2	44.0	1.875	9	6	7.45	0	
A.C.	10	29: 4	46.0	2.031	8	7	7.78	-	1947
		9: 3	41.7	1.955	22	15	7.16	2+	Gold begun 12/3/48
		12: 5	41.9	2.077	8	3	7.45	3+	

Name	No.	Date	PCV.	PLASMA VISC.	Wintrobe E. S. R.		Total Plas. Prot.	Gold Floc	Remarks
					Ord.	Cor.			
			%	cs.	mm/	1 hr	%		
T.P.	11	24: 2	35.7	2.214	-	-	-	-	
		1: 3	38.7	2.065	-	-	7.10	-	
C.G.	12	18: 3	45.6	2.184	-	-	8.0	-	
		(20: 5	43.9	2.309	40	34	8.28	-	subacute here again chronic again subacute again chronic
		16: 9	44.3	2.218	45	40	7.92	-	
		(30:10	44.4	2.502	44	39	8.86	-	
		11:12	45.0	2.225	30	27	8.10	3+	
		21: 9	45.0	2.059	33	30	7.56	o	
J.M.	13	10: 4	47.4	2.263	13	13	8.28	-	
		22: 5	46.1	2.121	9	8	8.32	-	
		24: 7	46.7	1.975	-	-	7.56	-	
		30:12	45.5	2.252	11	10	7.88	-	
J.A.	14	29: 4	45.4	2.036	21	19	7.38	-	
		9: 9	47.2	1.896	5	5	7.20	-	
		16:10	43.1	2.225	29	23	8.28	2+	
		9: 3	44.3	1.817	4	2	6.84	2+	
		7: 9	46.9	1.874	6	6	7.31	2+	
J.H.	15	1: 5	45.3	2.191	30	28	8.03	-	
J.B.	16	1: 5	47.0	2.001	34	34	7.45	-	
J.K.	17	15: 5	45.4	2.088	22	21	7.72	-	
M.C.	18	21: 5	49.4	1.918	17	20	7.38	-	
M.H.	19	21: 5	45.4	1.963	20	18	7.99	-	
J.G.	20	22: 5	50.3	1.971	-	-	7.78	-	
M.C.	21	5: 6	41.2	2.461	-	-	7.45	-	
G.C.	22	4: 7	44.1	2.115	-	-	8.06	-	
A.S.	23	16: 7	48.6	2.453	17	24	7.38	-	
R.H.	24	5: 8	45.2	1.999	11	9	7.38	-	
		22:12	44.4	2.153	1	0	7.92	+	
		14: 9	46.1	2.055	19	18	7.27	o	
T.W.	25	13: 8	36.8	2.131	-	-	7.81	-	
R.K.	26	23: 7	41.1	2.039	45	35	6.30	-	
H.D.	27	18: 8	46.2	1.965	14	13	7.09	-	
G.L.	28	25: 9	47.5	1.779	2	2	6.98	-	no clinical activity
R.F.	29	2:10	45.4	1.976	24	22	7.06	o	
W.C.	30	2:10	47.7	1.919	12	13	6.26	o	
R.G.	31	10:10	47.1	2.168	22	22	7.74	o	
R.H.	32	16:10	48.1	2.028	7	8	7.70	o	
		18:12	46.3	2.091	16	15	7.70	+	
		1: 4	46.3	1.900	3	2	7.13	2+	

Name	No.	Date	PCV	PLASMA VISC.	Wintrobe E. S. R.		Total Plas. Prot.	Gold Floc	Remarks
					Ord.	Cor.			
			%	cs.	mm/	1 hr	%		
S.B.	33	17:10	46.0	1.997	7	6	8.06	o	
J.H.	34	4:11	36.6	2.397	-	-	8.10	o	
R.W.	35	4:11	47.6	2.070	5	5	7.70	3+	
J.M.	36	12:11	42.7	2.902	24	19	9.00	3+	
R.K.	37	20:11	47.1	1.928	11	11	7.56	o	
W.G.	38	2:12	36.0	2.902	22	8	9.79	+	
K.B.	39	15:12	42.6	2.148	-	-	7.92	o	early case
		7: 2	46.5	1.918	2	2	7.70	o	
A.M.	40	15: 1	58.3	2.090	1	11	7.78	2+	
P.S.	41	16: 2	42.5	2.105	38	31	7.42	o	
G.C.	42	28:11	46.1	1.831	5	5	7.02	o	
W.M.	43	24:12	47.7	1.803	2	3	6.95	o	
M.A.	44	25: 2	44.7	2.505	46	44	8.68	4+	
H.M.	45	26: 2	49.4	2.618	22	25	8.46	+	
		22: 4	48.9	2.198	7	9	7.31	+	
B.W.	46	26: 2	49.3	1.930	10	13	7.16	o	
B.T.	47	28: 2	38.3	2.716	22	11	9.32	3+	
H.J.	48	30: 3	46.8	2.189	20	20	7.85	+	
A.T.	49	1: 4	46.2	1.961	8	7	7.13	3+	
G.F.	50	6: 5	40.4	2.056	32	22	7.52	+	
J.R.	51	22: 5	46.4	2.064	24	23	7.56	2+	
		31: 8	45.4	1.788	7	5	7.16	o	
T.S.	52	27: 5	43.0	2.113	30	24	7.63	+	
W.E.	53	3: 6	-	1.983	11	-	7.63	+	
T.B.	54	3: 7	-	2.092	-	-	7.16	-	
F.H.	55	16: 8	46.1	2.145	21	20	7.60	+	
C.T.	56	16: 8	-	2.325	-	-	7.78	-	
R.H.	57	6: 9	41.3	1.918	20	13	7.27	o	
W.G.	58	14: 9	49.0	2.367	30	33	8.17	2+	
L.H.	59	14: 9	41.7	2.261	36	28	7.45	5+	
W.R.	60	31: 8	34.7	2.105	49	28	7.16	3+	
		15: 9	37.9	2.031	34	17	6.84	4+	
		28: 9	39.2	2.055	36	24	7.92	2+	
		6:10	40.0	2.056	28	18	7.06	+	
		14:10	39.1	2.050	34	22	7.13	+	
		9:11	37.5	1.974	25	12	7.20	+	
		12: 1	40.7	1.696	9	3	5.58	o	

(C) Subacute Rheumatoid Arthritis - Female

Name	No.	Date	PCV.	PLASMA VISC.	Wintrobe E. S. R.		Total Plas. Prot.	Gold Floc	Remarks
					Ord.	Cor.			
			%	cs.	mm/	1 hr	%		
A. B.	1	7: 5	39.7	2.331	-	-	8.28	-	Gold 9/8 to 13/11/47
		24: 7	41.2	2.478	-	-	8.60	-	
		18: 9	42.8	2.429	46	47	8.39	-	
M. H.	2	11: 7	45.9	2.448	9	14	9.04	-	Gold 7/10 to 3/1/48 reduced to chronic
		16: 9	41.4	2.734	-	-	9.25	-	
		(5:12	43.4	2.358	21	22	8.89	3+)	
J. C.	3	1: 8	36.9	2.341	54	43	8.28	-	Gold 1/8 to 16/9/47
		24: 9	38.8	2.433	47	40	8.78	-	
		15:12	40.9	2.558	42	40	9.40	4+	Gold begun 16/12/47
		27: 2	37.5	2.370	50	40	8.53	3+	
		(23: 3	38.1	2.070	37	30	7.78	0)	improved to chronic
M. T.	4	10: 3	37.7	2.486	16	11	-	-	Gold begun 17/3/47 clinically worse improving
		5: 5	36.9	2.538	45	33	8.60	-	
		16: 9	37.7	2.367	-	-	7.99	-	
		23: 9	39.7	2.442	50	45	8.50	-	
M. K.	5	8: 9	41.4	2.434	-	-	8.60	-	Gold 23/9 to 9/12/47
		31:10	39.5	2.724	4	2	9.07	0	
		24:12	42.7	2.600	40	41	9.14	2+	Slightly improved
S. S.	6	22: 9	41.7	2.645	-	-	8.82	-	Gold 21/10 to 2/3/48
		30:12	41.3	2.510	1	1	8.46	-	
		12: 3	39.7	2.550	45	40	8.48	+	
K. S.	7	10:11	42.0	2.500	27	27	9.00	3+	Gold 23/9 to 9/12/47
		24:12	39.7	2.449	39	35	8.35	+	
M. C.	8	18: 9	-	2.465	38	-	8.68	-	Gold 9/8 to 25/10/47
		10: 3	40.8	2.463	35	33	8.42	+	
A. S.	9	(1: 5	40.0	2.727	42	38	8.71	-)	Acute stage Gold begun
		20: 5	37.7	2.325	-	-	7.78	-	
		17: 7	39.6	2.759	-	-	9.00	-	Gold ended 26/8/47
		28: 8	38.7	2.514	48	41	8.42	-	
		9: 4	41.9	2.651	39	39	8.75	4+	
		28: 5	40.2	2.480	50	46	8.03	3+	
		14: 7	39.2	2.446	30	26	8.32	3+	
A. S.	10	4: 7	36.3	2.675	50	38	9.14	-	Gold begun 12/11/47
		17:11	42.7	2.665	33	34	9.14	5+	
		16: 4	34.8	2.503	53	38	8.96	4+	
M. H.	11	21: 4	41.7	2.498	40	34	8.32	-	
M. S.	12	30: 4	38.8	2.546	52	45	7.88	-	
M. S.	13	5: 5	42.8	2.410	26	27	8.14	-	
		11: 9	42.0	2.405	43	43	8.21	-	
M. T.	14	19: 5	41.1	2.351	17	16	8.39	-	

Name	No.	Date	PCV.	PLASMA VISC.	Wintrobe E. S. R.		Total Plas. Prot.	Gold Floc	Remarks
					Ord.	Cor.			
			%	cs.	mm/	1 hr.	%		
P.M.	15	16: 5	40.8	2.339	52	49	7.92	-	
		26: 9	39.8	2.418	49	44	8.32	-	
J. J.	16	23: 5	45.0	2.402	7	10	8.86	-	
M. S.	17	29: 7	37.8	3.102	53	45	9.22	-	
		3: 9	37.1	2.793	-	-	8.93	-	
		3:10	-	2.686	56	-	8.78	+	
		3: 5	36.9	2.637	49	39	8.57	2+	
H. B.	17	11: 8	44.7	2.425	33	38	8.39	-	
		18: 9	-	2.287	16	-	8.17	-	
		10:10	42.5	2.284	23	24	8.03	3+	
E. P.	18	11: 8	42.7	2.447	-	-	8.42	-	
G. H.	19	1: 9	39.1	2.415	47	42	8.86	-	
J. H.	20	1: 9	41.6	2.660	46	45	9.32	-	
M. T.	21	10: 9	41.2	2.364	44	43	7.92	-	
M. S.	22	20: 9	43.5	2.479	-	-	7.99	-	
A. T.	23	23: 9	39.7	2.442	50	45	8.50	-	
M. C.	24	29:10	42.1	2.569	39	39	8.93	2+	
G. B.	25	31:10	40.6	2.344	50	47	8.06	o	
M. H.	26	3:11	40.2	2.338	42	38	8.21	3+	
H. C.	27	12:11	43.3	2.308	39	40	8.35	3+	
N. C.	28	12:11	45.9	2.800	21	28	9.07	5+	
H. P.	29	12:11	46.6	3.027	21	27	9.79	5+	
C. E.	30	17:11	42.7	2.778	3	4	9.18	4+	
M. M.	31	24:11	38.8	2.599	46	40	8.10	+	
S. N.	32	24:11	42.4	2.597	26	26	8.06	3+	
E. W.	33	27:11	43.5	2.505	14	16	9.14	3+	
E. S.	34	28:11	30.7	2.384	22	7	8.64	5+	
D. W.	35	29:12	39.7	2.266	29	25	8.46	3+	
S. K.	36	16: 1	41.5	2.321	20	20	8.96	+	
E. S.	37	19: 1	36.1	2.386	51	40	8.14	o	
M. S.	38	2: 2	43.0	2.405	43	44	8.32	o	
M. P.	39	17: 3	46.7	2.564	22	28	8.93	o	
E. T.	40	7: 4	38.2	2.978	-	-	9.07	5+	
		28: 5	41.0	2.800	48	47	8.57	5+	
		25: 6	40.6	2.735	48	46	8.60	5+	
E. B.	41	18: 4	35.5	2.531	53	39	8.50	-	

Name	No.	Date	PCV.	PLASMA VISC.	Wintrobe E. S. R.		Total Plas. Prot.	Gold Floc	Remarks
					Ord.	Cor.			
			%	cs.	mm/ 1 hr.		%		
D.F.	42	22: 4	31.8	2.712	42	24	8.71	3+	
M.T.	21	5: 5	40.0	2.306	45	41	7.70	5+	
G.B.	43	3: 6	-	2.732	-	-	9.07	3+	
L.S.	44	2: 9	39.2	2.499	19	16	9.00	3+	
M.M.	45	6: 9	42.0	2.440	34	34	8.86	4+	

(D) Subacute Rheumatoid Arthritis - Male

Name	No.	Date	PCV. %	PLASMA VISC. cs.	Wintrobe E. S. R.		Total Plas. Prot. %	Gold Floc	Remarks
					Ord.	Cor.			
L. H.	1	14: 1	44.0	2.485	26	22	-	-	Gold 2/1 to 5/5/47 here acute again subacute now only chronic
		8: 5	40.1	2.500	47	35	8.24	-	
		(24: 9	45.1	2.750	-	-	8.75	-	
		24:10	42.1	2.513	47	38	7.92	5+	
		9:12	45.0	2.543	26	23	8.68	5+	
		8: 1	45.1	2.324	13	11	7.85	3+	
		(14: 9	41.7	2.261	36	28	7.45	5+	
C. G.	2	20: 5	43.9	2.309	40	35	8.28	-	
		30:10	44.4	2.502	44	38	8.86	-	
J. S.	3	24: 4	43.6	2.576	21	17	8.46	-	
		6:11	43.0	2.738	-	-	-	-	
J. M.	4	12: 2	-	2.703	8	-	9.14	5+	
W. G.	5	19: 2	48.5	2.426	24	26	8.10	2+	
		29: 4	46.6	2.363	24	24	7.99	2+	
W. G.	6	9: 3	35.3	2.903	40	21	9.50	5+	
J. D.	7	9: 8	-	2.870	-	-	9.76	-	

(E) Acute Rheumatoid Arthritis - Female

Name	No.	Date	PCV.	PLASMA VISC.	Wintrobe E. S. R.		Total Plas. Prot.	Gold Floc	Remarks
					Ord.	Cor.			
			%	cs.	mm/	1 hr	%		
M.M.	1	20: 1	42.5	2.734	31	32	-	-	1947) now subacute
		(6:9:48	42.0	2.440	34	34	8.86	4+	
M.S.	2	24: 2	41.5	2.523	-	-	-	-) now subacute
		(30: 4	39.8	2.546	52	46	7.88	-	
E.T.	3	3: 3	40.9	2.691	-	-	8.5	-	agranulocytosis now subacute " " " "
		14: 7	39.8	2.983	-	-	9.14	-	
		15: 9	41.3	3.027	-	-	8.86	-	
		17:10	37.9	2.565	50	41	8.03	5+	
		21:10	41.9	3.049	-	-	9.25	5+	
		8:11	36.5	2.306	-	-	7.67	5+	
		17:12	40.8	3.032	40	37	9.11	5+	
		10: 1	41.6	2.878	-	-	9.18	5+	
		(7: 4	38.2	2.978	-	-	9.07	5+	
		28: 5	41.0	2.800	48	46	8.57	5+	
		25: 6	40.6	2.735	48	46	8.60	5+	
A.S.	4	11: 4	38.3	2.531	52	45	8.78	-	
E.M.	5	12: 4	40.3	2.698	42	39	8.82	-	
A.S.	6	1: 5	40.0	2.727	42	39	8.71	-	
E.H.	7	9: 5	43.8	2.638	10	12	9.32	-	
A.S.	6	21: 5	35.5	2.798	-	-	9.22	-	
M.C.	8	30: 5	41.4	2.536	48	47	8.96	-	
I.B	9	21: 7	43.7	3.364	52	56	10.40	-	
		24: 7	36.7	3.442	-	-	10.98	-	
		9: 9	35.6	3.147	-	-	10.04	-	
		2:10	-	3.245	-	-	-	5+	
		4:10	36.3	3.269	-	-	9.61	-	
		21:10	36.3	2.948	-	-	9.43	5+	
		13: 9	37.0	3.197	3	0	10.51	5+	
M.B.	10	1:12	43.	2.989	14	15	8.78	5+	On Cortisone " " " "
		5:12	43.5	2.890	7	8	8.64	-	
		11:12	44.	2.929	4	6	8.96	5+	
		18:12	43.	2.668	23	24	8.60	5+	
		24: 1	43.	2.608	22	23	8.03	4+	
		4: 4	42.6	2.822			8.68	4+	

(F) Acute Rheumatoid Arthritis - Male

Name	No.	Date	PCV.	PLASMA VISC.	Wintrobe E. S. R.		Total Plas. Prot.	Gold Floc	Remarks
					Ord.	Cor.			
			%	cs.	mm/	1 hr	%		
A. S.	1	22: 5	49.8	2.797	7	10	9.00	-	
W. D.	2	27: 5	41.9	2.565	51	41	8.60	-	
W. G.	3	30: 5	35.9	3.346	57	34	10.51	-	
		26: 7	37.7	3.619	3	0	11.05	-	
		30: 7	37.0	3.341	-	-	10.66	-	
		6: 9	37.9	3.611	22	10	11.38	-	
		15: 9	34.0	3.171	-	-	9.90	-	
		13:11	38.5	3.677	-	-	11.09	-	
		22:11	35.7	3.228	-	-	9.43	4+	
		(2:12	36.0	2.902	22	8	9.79	+	subacute
		9: 3	35.3	2.903	40	21	9.50	5+	"
		21: 8	38.5	3.315	12	3	10.55	5+	acute again
		14: 9	36.3	3.059	-	-	9.90	5+	
K. W.	4	1: 9	45.5	3.100	31	29	8.10	-	
L. H.	5	24: 9	45.1	2.750	-	-	8.75		
J. F.	6	17: 1	38.5	2.581	-	-	8.10	+	

Case No. 1 Chronic Rheumatoid Arthritis.

This male patient was aged 63 years when he first attended the rheumatism clinic on 15: 3:47. His relevant history was that in 1943 there was a gradual onset of fusiform swelling of the proximal inter-phalangeal joints of both hands, and of pain and swelling of both wrists. His only treatment had been a course of gold therapy in 1944 from which he derived no benefit.

He was a tall, well-built man in fairly good condition. Both hands showed fusiform tender swelling at the proximal inter-phalangeal joints, but with full range of movement at these joints. There was wasting of the interossei muscles, without ulnar deviation. The right wrist had a marked thickening of the joint with carpal cysts present; there was an increased local heat; all movements were painful; and dorsiflexion was limited by 5°. In the left wrist there was thickening around the joint and free but painful movements. All other joints appeared to be normal. X-ray examination showed a generalised osteoporosis of the carpal bones and phalanges, and diminished joint spaces at the inter-phalangeal joints. The changes were typical of rheumatoid arthritis.

There was also evidence of emphysema. A maxillary sinus was opaque to X-rays: the ear, nose and throat specialist washed it out and reported the sinuses clear after 2-3 weeks treatment. After the eradication of this possible focus of infection, a course of

Date	PCV.	PLASMA VISC.	Wintrobe ESR.		Total Plasma Prot.
			Ord.	Cor	
	%	cs.	mm/1 hr.		g.%
18: 3:47	45.6	2.184	30	28	8.0
20: 5:47	43.9	2.309	40	34	8.28
16: 9:47	44.3	2.218	45	40	7.92
30:10:47	44.4	2.502	44	39	8.86
11:12:47	45.0	2.225	30	27	8.10
21: 9:48	45.0	2.059	33	30	7.56

myocrisin was begun: the dose was 0.01 g. weekly for 12 doses.

On reviewing his condition after 6 weeks of treatment, on 20:5:47, there was no increase in the number of joints involved, but those originally affected were still swollen and tender. In view of the rise in the plasma viscosity to 2.309 cs., together with the increase in total protein and ESR., and the decrease in the haematocrit, the patient was admitted to hospital for rest in bed and further gold treatment.

By the end of treatment on 28:6:47, there was an improvement in the general condition as shown by an increase in weight and a slight local improvement as the wrists were not so swollen or painful. He was discharged to a convalescent home.

16:9:47 - he reported for review. There had been no involvement of other joints. The wrists were much improved - the periarticular thickening and the synovitis had subsided; the movements were almost free and nearly painless; the fingers were still painful. The general condition was also improved. The clinical impression of an improvement was not fully supported by the laboratory tests

where the plasma viscosity and ESR were in agreement that a considerable degree of general reaction persisted. Hence a further course of 12×0.01 g. of Myocrisin was begun.

After 6 injections there was again an increase in the plasma viscosity; after 12 injections the plasma viscosity had reached a level which was not significantly different from that at the beginning of treatment. By 11:12:47 the wrists had become almost normal while the interphalangeal joints were still swollen and painful. The right knee had developed pain, all movements were painful, and there was increased local heat and synovitis. An X-ray had the appearance of an atrophic arthritis. The fact that a further joint had become involved in spite of treatment showed that the disease was still very active and this was truly reflected in the increased plasma viscosity. We cannot tell what would have happened if the second course of gold had not been given, but one might venture the suggestion that the original high viscosity value was a better guide to the activity than the clinician's own impressions.

He received another course of spa treatment at Harrogate. The final viscosity at 9 months later showed a diminution in the level but it still remained within the zone of chronicity, in accord with the chronic clinical state.

Case No. 2

Rheumatoid Arthritis.

After 3 years of service in the WRAF in medical category A.1, this patient married in 1945 and in July 1946 gave birth to a normal healthy baby. Three months later she began to complain of pain and stiffness of the small joints of the fingers, and then of a tendency towards ulnar deviation of the fingers at the metacarpo-phalangeal joints. Gradually pain and swelling developed in both knees, and there was swelling of the right ankle.

On examination, she was underweight and had a moist skin. There was fusiform swelling of the proximal inter-phalangeal joints of both hands, ulnar deviation at the metacarpo-phalangeal joints, wasting of the interossei, periarticular thickening of both wrists with limitation of dorsiflexion of the right wrist; both knees were hot and swollen, and there was a limitation of flexion of the right knee by 20°; the right ankle was "puffy" and painful, although there was a full range of movement; the right tarsal joints were painful and limited in movement. The X-ray appearances of the affected joints were typical of atrophic arthritis. No other pathology of other parts of the body was detected.

She had been confined to bed at home for 8 months prior to her admission to hospital on 2:7:47. She was then treated by iron and vitamins, plaster splints to knees and wrists, active

Date	PCV.	PLASMA VISC.	Wintrobe ESR. Ord. Cor.		Total Plasma Prot.	Blood Urea	
	%	cs.	mm/	1 hr	g%	mg.%	
2: 7:47	41.2	2.117	9	8	7.67	57	Urea clearance =110%
9: 9:47	39.6	2.038	-	-	7.45	-	
30: 9:47	40.4	1.974	-	-	7.16	44	
22:12:47	43.4	2.326	28	30	8.46	-	
9: 3:48	39.3	2.103	40	36	7.70	-	
1: 7:48	42.9	2.213	32	33	8.35	-	
15: 9:48	42.4	2.101	34	35	7.70	-	

non-weight-bearing movements, and general rest in bed.

By the 20th August she had improved to be standing alone and walking with assistance. By the 9th September she was sleeping well, the temperature and pulse rate were normal, and the joints were more free from pain. The right knee was regaining movement but the ankle joints were still painful on all movements. The treatment was continued, plus the Guthrie Smith apparatus for assisted movements.

On 30:9:47 it was noted that the ankle joints were settling down and that a full flexion in the right knee could be obtained. Her weight was increasing. She was beginning to walk without assistance. The plasma viscosity results had shown a corresponding improvement but had not quite reached the normal range when she was discharged to continue her convalescence in her own home, on 14:10:47.

She reported on 15:11:47, when she was able to show further improvement. She was able to walk and do a little housework.

At the beginning of December she had an attack of influenza. This was followed by a flare-up of all the joints previously affected. She looked pale, lethargic and ill. Both knee joints were swollen and had increased local heat. The shoulders were painful and the right arm could not be abducted above 80°. This flare-up in the condition was reflected in the increase in the plasma viscosity. The patient was rested in bed, physical therapy was resumed, and a course of 12 x 0.0lg. Myocrisin was begun. The fluid was aspirated from the knees.

By 9:3:48 there was clinical improvement. Her weight had increased. The knees had settled; the movement of the shoulders was painless and increasing in range. The plasma viscosity had decreased but the ESR had increased.

The gold treatment was discontinued on 13:4:48 while the local therapy continued. The improvement continued steadily.

Unfortunately, on 28th June she reported pain in the right hip which had not been affected previously; a skiagram showed the osteoporosis of the head of the femur and diminution of the joint space which is typical of an atrophic arthritis. There was a further increase in the plasma viscosity as a true reflection of the increase in the activity of the disease which caused the involvement of a new major joint, yet the ESR had decreased.

With more treatment, the plasma viscosity had fallen by 15:9:48 to a level almost identical to that in the initial test. It should be noted how all values but one have fallen within the zone of chronicity and yet the variation has been sufficiently large to indicate changes in the activity of this chronic disease.

Case No. 3 Rheumatoid Arthritis -(satisfactory response to gold therapy by an early case.)

Eleven weeks prior to his admission to hospital on 19: 8:49 this man had attended his own doctor, complaining of bronchitis. Three weeks later he had pains in hands, arms and shoulders and in the ankles and knees. These pains had persisted since; they were dull aching and got less on exercising; they kept him awake at night.

On examination, there was spindle deformity of the joints of the digits. The wrists, elbows, ankles and knees had pain on movement; these joints showed periarticular thickening, especially the knees which also contained a little fluid. The lymph glands of the groin and axilla were enlarged. No pathology was detected in other structures of the body. An X-ray of the chest was normal in appearance.

The diagnosis was - an early severe multiple arthritis of Rheumatoid type.

At first the treatment was of a general sustaining nature, including splinting of the wrists at night, quadriceps drill and other remedial exercises,. 1 pint of blood was given on 23: 9:47 to assist his definite anaemia. By the 26th Sept. he was so improved as to be considered as a possible remission - there was remarkably little pain in the joints and they were no longer painful on movement.

Date	PCV.	PLASMA VISC.	Wintrobe ESR.		Total Plasma Prot.	Gold Floc	
			Ord.	Cor			
	%	cs.	mm/	1 hr	g.%		
30: 8:49	34.9	2.105	48	26	7.16	+++	Serum uric acid = 6.4 mg./100 ml
13: 9:49	36.5	2.031	34	17	6.84	++++	
28: 9:49	39.2	2.055	36	25	7.06	++	
6:10:49	40.0	2.056	28	18	7.06	+	G.C.F.T. = neg.
14:10:49	39.1	2.050	34	24	7.13	+++	
9:11:49	37.5	1.974	25	12	7.20	+	
12: 1:50	40.7	1.696	9	3	5.58	o	

However, because of the persistently abnormal laboratory results, and especially because of the plasma viscosity stationary within the zone of chronicity, the clinician decided on more intensive treatment which would include gold. Beginning on 6:10:49, 0.01 g. of Myocrisin was given and the weekly dose was gradually raised to 0.08 g. and a total of 0.51 g. had been administered by 14:12:49 when the gold was stopped.

There was a temporary recurrence of the effusion into the right knee noted on 9:11:49, but the fluid was rapidly reabsorbed. By the end of December, all the joints had shown continued improvement and by the middle of January he was so well that he was allowed to resume work as a boiler-maker.

He had had no recurrence of his arthritis at the end of 1951.

The plasma viscosity decreased in this patient in response to the general improvement following rest in bed, etc. Nevertheless, the viscosity then remained at a constant level as an indication

that in spite of the amelioration in the locomotor system there was continued activity in other parts of the body. When this was acknowledged and a further attack was made on the disease with gold a satisfactory response in the total organism was obtained and the plasma viscosity became almost subnormal (the total protein is certainly below the lowest normal value). The gold flocculation test also reflects the cessation of the rheumatoid activity; so also does the ESR.

This is one of the cases in which a recurrence of the rheumatoid arthritis is unlikely unless there is a frank primary trigger-stimulus such as bronchitis or influenza.

Case No. 4

Rheumatoid Arthritis.

This miner, aged 29 years, started to have pains in all his joints, particularly the small joints of the fingers, about a year before his attendance at the rheumatism clinic. These small joints had become swollen in the past few weeks; he had felt weak and stiff on waking; and he had been unable to work at the coal face for the last fortnight. He had suffered from rheumatic fever when 4 years old, and again when he was twenty.

On examination, he was a tall, round-shouldered, asthenic man. The skin was moist; there was acne of the face. A slight presystolic murmur was present at the apex, without a cardiac enlargement. No abnormality was discovered in any other system except the locomotor.

The hands had bilaterally symmetrical fusiform swelling of the proximal inter-phalangeal joints of the fingers and slight swelling of the first metacarpo-phalangeal joint; there was wasting of the interossei muscles; there was no ulnar deviation of the fingers. The spine showed a dorsal kyphosis, flexion of the lumbar spine limited by 20%, and spasm of the sacrospinalis muscles. All the other joints had full function and were free from pain.

Skiagrams showed osteoporosis of the phalanges of both hands and diminution of the joint space between the first and second

.Date	PCV.	PLASMA VISC.	Wintrobe ESR.		Plasma Total Protein	Gold Floc.
			Ord.	Cor.		
	%	cs.	mm/	1 hr	g. %	
26: 7:47	43.8	2.131	30	25	7.92	-
11: 9:47	45.8	2.003	15	14	7.63	-
11:11:47	46.9	2.075	10	10	8.28	+
28: 2:48	44.0	1.875	9	6	7.45	o

phalanges, and some generalised osteoporosis of the lumbar spine with dorsal kyphosis. The appearances of the lungs and head sinuses were normal. Urine was normal. The Wassermann and the gonococcal complement fixation tests were negative.

The treatment consisted of ferrous sulphate (9 grains per day), wax baths and heat to the hands, occupational therapy, and myocrysin in weekly doses of 0.01 g. for 12 weeks, beginning on 16:8:47.

The initial plasma viscosity was in accord with the clinical assessment of a disease of rather short duration and of moderate severity. By the time of the second test there was an improvement in the joints and a considerable improvement in his general condition. The third test was made a few days after he had a slight clinical relapse - he did not feel so well, his pain in the fingers and the back had increased, the knees were painful but examination could detect no abnormality there apart from a painful movement. The plasma viscosity had risen in accord with this worsening, but the decrease in the ESR. had continued.

A course of brine and aerated baths rendered the patient free from these pains in three weeks. He was discharged from the clinic on 1:12:47.

He left the mines to obtain sedentary work.

Three months later he reported back to the clinic for a review. He had kept free from pain completely, his general condition had been satisfactory, and he had been able to carry out his work in an efficient manner. There was a residual painless fusiform swelling of the proximal inter-phalangeal joints but a full range of movement was possible in them. The quiescent state of the disease was supported by the normal laboratory tests at this date.

Case No. 5

Rheumatoid Arthritis.

This woman of 33 years gave a history of 15 years duration - pain had started in the small joints of the fingers, it spread later to the elbows and knees, and the patient became bedfast. She remained so for the following 2 years during which the treatment administered by her own doctor had no effect; during this period she had a low-grade temperature increase. Treatment at a Spa by "the waters", general physiotherapy, and myocrysin did cause an improvement sufficient to let her walk again. Four years later both hips became painful and stiff; she was confined to bed for 18 months. Since that time her hips have been so stiff that she had great difficulty in walking; she complained little of the other involved joints. She had suffered from rheumatic fever when 16 years old but had otherwise been free from illness.

When she attended the rheumatism clinic in December 1947, she was a pale under-weight woman who could walk only with the assistance of two sticks. No abnormality could be detected except in the locomotor system.

The hands had fusiform swelling at the proximal interphalangeal joints with a tendency towards subluxation at these joints. Flexion was limited at all these joints. All joints were painful. The tendency to ulnar deviation at the metacarpo-phalangeal joints was greater in the left hand. The right wrist was ankylosed in good

position and painless: the left wrist had restricted painful movement and increased local heat. The right shoulder and elbow were ankylosed; the movements in the left were painful and markedly limited. The maximum movement in any direction of the right hip was 10° ; the left hip could flex to 30° , but no other movement would reach 20° - movements in both joints were painful. The right knee flexion was limited to 95° , there was gross quadriceps wasting, there was synovial thickening without an effusion; the left knee moved through a full range of movements, the quadriceps was wasted, there was synovial thickening plus an effusion, and there was increased local heat. The feet and spine were apparently free from the disease. The tone of the muscles was generally low and the wasting was most marked in the muscles controlling the severely damaged joints; the interossei of both hands were very wasted.

The skiagrams of the joints had appearances typical of an atrophic polyarthrititis; the ankylosis of the right wrist, elbow and shoulder were confirmed; there was marked diminution of the joint space of both hips.

The clinical impression was that this was a patient in whom the distress was caused by advanced joint changes in which the activity of the disease was no longer high: the general reaction was of correspondingly low severity. The plasma viscosity of this

Date	PCV.	PLASMA VISC.	Wintrobe ESR.		Plasma Total Protein	Gold Floc.
			Ord.	Cor.		
	%	cs.	mm/	1 hr	g.%	
19:12:47	39.6	2.120	39	35	8.14	+
3:2 :48	38.0	1.928	13	8	7.45	+
16: 4:48	41.4	1.966	16	15	7.52	+
3: 9:48	40.4	2.027	13	12	7.96	+

date was in accord with the clinical impression.

Treatment consisted of cod liver oil and malt extract, ferrous sulphate (6 grains per day), myocrysin in 12 weekly doses of 0.01 g., remedial exercises on the Guthrie Smith apparatus, re-education in walking, and splints to correct the ulnar deviation of the fingers.

By February 1948, at the end of the gold course, she had put on weight, she walked in a modified manner with an increased range of hip movements, the joints were less painful generally and some were considered to be quiescent. Treatment was stopped for a period of two months.

By April, her hands had improved markedly, the pain had decreased further, and she could still get about with the aid of her sticks although the hip movement range had not increased further. The disease condition was assessed clinically as being quiescent: the laboratory results remained abnormal although much decreased from the original test. Further local treatment was given in an attempt to improve the function of the joints.

Her condition remained satisfactory until August when she had an attack of influenza. A relapse in the rheumatoid arthritis followed, with a flare-up in both knee-joints and in the small joints of the hands. The plasma viscosity at the beginning of September had increased as a result, yet the ESR value remained low.

Case No. 6

Rheumatoid Arthritis.

This grocer, aged 60 years, had suffered for many years from pain and swelling in the wrists, elbows, and inter-phalangeal joints of the fingers and from pain in the feet but had received no treatment. He had been unable to work for 4 months. He had always been a healthy man apart from pneumonia in 1929 and 1942 and chronic bronchitis from 1940 onwards.

On examination at the rheumatism clinic he showed signs of a chronic bronchitis and the rheumatoid arthritis lesions only. The hands had gross fusiform swelling of the inter-phalangeal joints of the fingers, swelling of the 1st and 2nd metacarpo-phalangeal joints, ulnar deviation, wasting of the interossei. Both wrists had marked periarticular thickening and carpal cysts, with limitation of movements. Both elbows were painful on movement; the right had synovitis, local heat and an ulnar bursitis. The feet showed bilateral pes planus and marked limitation of movement of the toes.

Skiagrams of the chest had the appearance of chronic bronchitis. The inter-phalangeal joints showed diminished joint space and marginal erosion, plus osteoporosis of the phalanges. The carpal bones were very osteoporotic, and the right bones showed signs of ankylosis. The joint space in the wrists appeared diminished. The elbow joints also appeared to be normal.

Date	PCV.	PLASMA VISC.	Wintrobe ESR.		Plasma Total Protein	Gold Floc.
			Ord.	Cor.		
	%	cs.	mm/ 1 hr		g. %	
4: 2:47	44.8	2.119	18	16	-	-
5: 3:47	38.9	2.281	22	12	8.0	-
16: 9:47	41.7	2.096	44	35	7.56	-
28:10:47	47.2	2.373	20	20	8.60	++++
18:11:47	47.0	2.353	11	11	8.32	++++
15: 1:48	48.1	2.180	11	12	7.68	+++
13: 2:48	47.4	2.156	15	15	7.70	+++
29: 4:48	46.9	2.198	17	17	7.85	+++
7: 9:48	44.9	2.314	30	27	7.85	+++

The plasma viscosity and ESR results of that date were rather low for the activity by clinical assessment.

Treatment with myocrysin was begun at once in weekly doses of 0.01 g. The pain in the fingers increased markedly and the wrists became more painful and swollen. Wax baths and heat to the small joints of the fingers. The plasma viscosity had risen appreciably.

The patient was admitted to the Royal Baths Hospital at Harrogate where the intensive physiotherapy and the completion of the gold course produced a marked general and local improvement. He was an in-patient for 3 months.

He remained well for a little more than 2 months - all the small joints and the right ankle became swollen and painful some 3 weeks before the blood test was made on 16:9:47, in which the raised plasma viscosity indicated a continued activity. Gold therapy was resumed only to be followed by a worsening generally with

a right ankle so swollen and painful that walking was impossible and sleep was disturbed. The plasma viscosity increased in parallel.

He was admitted to hospital for complete rest in bed, splints to hands and ankle, and iron tonic. The gold was stopped. In December an intensive non-weight-bearing physiotherapy course began. By 15:1:48 he was just getting up again. He felt better generally. The feet were less painful and the toes were beginning to move; the elbows were settling down; but the wrists and fingers remained painful.

Procaine and lactic acid injections to the wrists at fortnightly intervals caused some improvement in the joints.

A flare-up of the chronic bronchitis in April 1948 failed to cause an activation of the joint symptoms and the laboratory tests also showed no significant change.

He stopped attending the clinic at this time and did not attend again until 8:9:48. He reported that he had returned to his work but recently the joints had become more painful. Both knees were painful and swollen, with increased local heat: the wrists, hands and feet which had given so little trouble were again painful. The clinical assessment was that of a relapse; the plasma viscosity result was in agreement with this diagnosis. It was arranged that he should be re-admitted for further treatment.

Case No. 7

Rheumatoid Arthritis (Residual deformity only)

This housewife, aged 25 years, had an attack of pain and swelling of the wrists, knees and small joints of the fingers three years prior to her attendance at the rheumatism clinic. She had been treated as an in-patient of St. Thomas' Hospital, London with gold. The improvement was marked.

She attended the clinic complaining of deformity of her hands, vague pains in the hands, and limitation of the movement of her right knee. (The only relevant illness in her past history was chorea in 1932)

She was a thin, pale woman who walked apparently normally in spite of her complaint regarding the knee. The knee had some thickening of the synovial membrane, a full range of movements, no synovitis, and associated quadriceps wasting. The wrists showed periarticular thickening with slight synovitis, and a full range of movements. The second metacarpo-phalangeal joint of both hands was swollen and thickened; the inter-phalangeal joints had symmetrical fusiform swelling; and the interossei were wasted. No abnormality in the other systems could be detected.

Skiagrams of the chest showed normal lungs and heart. There was osteoporosis of the carpus, metacarpals and phalanges, with diminished inter-phalangeal joint spaces. The right knee showed

Date	PCV.	PLASMA VISC.	Wintrobe ESR. Ord. Cor.		Plasma Total Protein	Gold Floc.
	%	cs.	mm/1 hr		g. %	
5:11:47	41.1	1.936	11	10	7.70	+
22:12:47	41.6	1.862	5	5	7.24	o
9: 2:48	41.1	1.830	7	6	6.84	o
7: 4:48	42.5	1.797	6	6	6.52	o

osteoporosis plus a reduced joint space. The antral sinuses of the head appeared opaque (this examination was made as a routine in every patient and there was nothing clinically in this patient to make the clinician suspect a septic focus).

The specialist on diseases of the nose reported that there was a bilateral antrum suppuration; this was treated within days by a bilateral Caldwell-Luc operation. The operation was followed by three weeks complete rest in bed, but no other active therapy.

The case presented a diagnostic problem. The clinician's assessment was that the rheumatoid arthritis was no longer active and could not be held responsible for the raised plasma viscosity. The blame for this was placed on the latent septic focus. The laboratory test after the operation showed a markedly reduced plasma viscosity: as there had been no change in the joints, the correctness of the original diagnosis was supported.

A course of myocrysin was begun at the end of December to stimulate metabolism and improve the general condition. Iron was administered empirically as the patient was not anaemic.

By February an improvement in the general condition was

noted and this improvement was even more obvious by April. The weight had increased; the complaints concerning the vague pains had ceased. On 8:5:48 she reported that she felt very well and that she was two-months pregnant.

The laboratory results of this case assisted the clinician by attributing the reaction to a latent infection when this had been eradicated. The results are also interesting in that they show that treatment can so relieve a rheumatoid arthritis case that the laboratory results all fall within their normal ranges.

Case No. 8

Subacute Rheumatoid Arthritis.

This housewife gave a history of arthritis of 7 months duration only. She complained of pain in the shoulders, knees and small joints of the fingers. Both knees became swollen when she stood for any length of time. During the weeks immediately prior to her attendance at the clinic she had had very severe pain in her fingers so that her sleep was disturbed. She noticed that she had lost weight and that her hands and feet perspired readily.

On examination, no pathology was detected except in the locomotor system. In both hands there was enlargement of the first metacarpo-phalangeal joint, painful fusiform swelling of all the proximal inter-phalangeal joints which still had a full range of movement, and wasting of the interossei muscles without ulnar deviation of the fingers. Both knees had increased local heat, synovial thickening, effusion, painful movement without restriction of range. The other joints appeared to be unaffected. The osteoporosis and diminution of the joint spaces as revealed by the skiagrams were typical of an early rheumatoid arthritis.

Because of the pain in the joints, the hot swollen knees, and the painful tender fusiform swelling of the inter-phalangeal joints, the disease process was considered to be very active. This was supported by the high plasma viscosity value (2.425 cs.)

Myocrisin in weekly doses of 0.01 g. doses and bed rest were

Date	PCV.	PLASMA VISC.	Wintrobe ESR.		Total Plasma Prot.	Gold Floc.
			Ord.	Cor.		
	%	cs.	mm/ 1 hr		g.%	
11:8:47	44.7	2.425	33	36	8.39	-
18: 9:47	-	2.287	16	-	8.17	-
10:10:47	42.5	2.284	23	24	8.03	+++
24:12:47	40.4	2.068	28	26	7.34	+++++
15: 3:48	43.6	2.136	19	21	7.70	++
7: 5:48	40.5	2.148	20	18	7.81	+++

begun at the patient' own home.

By 19:9:47, after 5 weeks of this treatment, there was an improvement in her general condition. The knees had also settled down but she still complained of considerable pain in the small joints of the fingers.

There was no appreciable difference on 10:10:47. Local treatment to the fingers was then begun, while the gold was still exhibited.

Slow improvement was detected on 24:12:47. The hands were much less painful, the knees still had some synovial thickening but the effusion had gone, and there was some pain in the shoulders. Treatment was discontinued for three months.

On 15:3:48, she still complained of considerable pain in the small joints of the fingers and in the shoulders, although the knees were still satisfactory. She had suffered from bronchitis during the three weeks previously and as there was no definite

deterioration in the arthritic state the increase in the plasma viscosity was ascribed to this infection. Nevertheless, when the tests were repeated 8 weeks later when the bronchitis had cleared completely, almost identical values were found. As it was believed that the systemic part of the disease had entered the chronic smouldering stage (as supported by a viscosity within the zone of chronicity) it was proposed that another attack should be made on it with Myocrisin.

This case is an example of an incomplete response by a subacute disease which eventually assumes the characters of the chronic type. The plasma viscosity has been a reliable guide to these changes in the disease process.

Case No. 9

Acute Rheumatoid Arthritis.

This male patient, aged 57 years, had a sudden onset of pain and swelling in both knees, followed by a rapid development of fusiform swelling of the inter-phalangeal joints of the fingers and painful swelling of the wrists.

He first attended the rheumatism clinic on 4:1:47. No abnormality could be detected except in the locomotor system. There was gross effusion of both knees, plus thickening of a "doughy" consistency and marked limitation of movement. There was a symmetrical and very marked swelling of the inter-phalangeal joints of both hands; there was no ulnar deviation of the fingers. The right temporomandibular joint was painful on movement and marked crepitus was detected in it. The clinical assessment was that the knee lesions were acutely active.

Skiagrams of the lungs revealed healed and calcified apical lesions on both sides. The joint appearances were typical of an atrophic arthritis.

The Wassermann and gonococcal complement fixation tests were negative. The serum uric acid amounted to 3 mg. per 100 ml.

130 ml. of straw-coloured fluid was aspirated from the right knee and 90 ml. from the left. Plaster gaiters were applied to both knees. A full course (12 weekly injections of 0.01 g.) of Myocrysin caused little amelioration except for slightly reduced

Date	PCV.	PLASMA VISC.	Wintrobe ESR.		Plasma Total Protein	Gold Floc.	Day of Week.
			Ord.	Cor.			
	%	cs.	mm/	1 hr	g.%		
30: 5:47	35.9	3.346	57	34	10.51	-	Fri.
26: 7:47	37.7	3.619	3	0	11.05	-	Sat.
30: 7:47	37.0	3.341	-	-	10.66	-	Wed.
6: 9:47	37.9	3.611	22	10	11.38	-	Sat.
15: 9:47	34.0	3.171	-	-	9.90	-	Mon.
13:11:47	38.5	3.677	-	-	11.09	++++	Thur.
22:11:47	35.7	3.228	-	-	9.43	++++	Sat.
2:12:47	36.0	2.902	22	8	9.79	+	Tues.
9: 3:48	35.3	2.903	40	21	9.50	+++++	Tues.
21: 8:48	38.5	3.315	12	3	10.55	+++++	Sat.
14: 9:48	36.3	3.059	-	-	9.90	+++++	Tues.

activity in the knees. He was admitted to hospital.

An intensive course of physiotherapy followed. He was at complete rest in bed; iodine ionisation was applied to the knees; re-education of the quadriceps muscle was practiced; and the joint movements were entirely passive. By the end of May, 1947, at the time of the first plasma viscosity measurement, very little improvement could be recorded.

A second course of Myocrysin was begun. On account of a general and local deterioration the treatment had to be stopped after six injections. The knees again required aspiration. This change was reflected in the increased plasma viscosity value. The test after a week free from treatment showed a dramatic fall in the plasma viscosity, without any obvious change in the clinical assessment.

Treatment was resumed. He was rested in bed; the knees were

aspirated frequently; and the myocrisin was resumed, combined with mixed vaccine. Sodium salicylate was given to relieve the pain, and iron to combat the persistent anaemia. After 6 weeks the plasma viscosity had increased to its originally high value and an even greater fall ensued when treatment was discontinued for a week. The joint condition had not improved in these 6 latest weeks of treatment.

Physiotherapy was continued through the autumn in a less intense programme. Quite suddenly, for no obvious reason, an improvement in the local and general condition began about the middle of November, just after another viscosity peak. Myocrysin was again given. Active exercises were resumed. He was sent home, to continue his treatment as an out-patient, in March 1948.

He failed to attend and it was learned that he was doing light work. However, in August he had a relapse which forced him to seek further treatment. The plasma viscosity had again risen to a value almost identical with that in the initial test.

This case was of particular interest because of the rapid changes in the plasma viscosity values. These changes resembled the fluctuations possible in acute pyogenic infections, rather than those of a very severe chronic condition. No similar changes were noted until the cortisone and A.C.T.H. drugs were introduced for the treatment of rheumatoid arthritis - the decrease at the

beginning of treatment could be just as great as in the 9 days here between the 6th and 9th September (cf. Case No. 10); unfortunately, the increase on cessation of drug treatment can be just as rapid as the decrease.

INFECTIVE POLYARTHRITIS

Name	No.	Date	PCV.	PLASMA VISC.	Wintrobe E. S. R.		Total Plas. Prot.	Gold Floc	Remarks
					Ord.	Cor.			
			%	cs.	mm/	1 hr	%		
A. <u>Chronic - Female</u>									
E.H.	1	3: 1	41.	1.989	20	19	-	-	early case
F.T.	2	13: 1	46.	1.911	-	-	-	-	
M.S.	3	27: 1	50.	1.985	8	17	-	-	
M.M.	4	4: 3	44.1	2.188	-	-	8.0	-	
M.W.	5	24: 3	48.8	1.948	7	14	7.47	-	
F.R.	6	2: 5	44.0	1.869	11	14	6.70	-	
J.P.	7	19: 5	42.9	1.894	-	-	7.52	-	
D.W.	8	11: 4	43.6	2.214	45	48	7.85	-	
E.W.	9	8: 8	36.8	2.245	59	47	7.38	-	
		29: 9	39.6	2.315	47	42	7.45	-	
		19:12	40.1	2.140	39	36	7.34	4+	
G.C.	10	11: 8	39.3	2.076	39	34	7.92	-	
D.A.	11	20:10	38.3	2.175	42	35	7.56	+	
		13:11	39.2	2.165	27	22	7.63	+	
		16:14	39.1	2.288	45	39	8.04	+	
M.A.	12	28:11	36.1	1.898	19	11	7.85	+	
I.H.	13	5:11	40.3	1.854	9	7	7.24	+	
V.T.	14	5: 1	41.5	1.978	12	12	7.85	o	
		24: 3	40.1	1.989	31	28	7.45	o	
P.B.	15	5: 1	49.4	2.251	8	16	8.14	o	
A.H.	16	7: 1	39.3	2.040	24	20	7.45	o	
M.D.	17	28:11	42.7	2.248	16	17	8.46	3+	
M.W.	18	12: 1	45.6	2.005	20	25	7.27	o	
M.C.	19	15: 1	42.1	2.325	27	27	7.99	o	
M.S.	20	11: 2	36.1	2.068	-	-	7.49	o	
M.C.	21	16: 2	47.8	1.995	11	18	7.38	3+	
W.M.	22	26: 2	41.7	2.050	22	22	7.63	o	
		2: 4	41.7	1.900	9	9	7.13	+	
C.W.	23	10: 3	42.0	1.916	10	10	7.34	0	
J.B.	24	3: 3	44.0	2.013	13	15	7.60	o	
		30: 4	48.4	2.096	3	9	8.60	o	
		12: 5	47.5	1.948	5	10	7.52	o	
A.W.	25	17: 3	45.1	2.142	29	34	7.67	o	

Name	No.	Date	PCV.	PLASMA VISC.	Wintrobe E. S. R.		Total Plas. Prot.	Gold Floc	Remarks
					Ord.	Cor.			
			%	cs.	mm/	1 hr	%		
<u>Chronic infective polyarthrititis (contd.)</u>									
E.M.	26	19: 3	45.5	2.092	28	34	7.70	o	
		5: 5	45.5	2.114	29	35	7.67	o	
H.T.	27	24: 3	45.8	1.973	18	22	7.20	o	
C.B.	28	24: 3	39.7	1.984	27	24	7.09	2+	
H.H.	29	31: 3	42.7	1.895	6	7	7.38	o	
E.T.	30	31: 3	41.2	2.216	35	34	8.06	2+	
M.C.	31	7: 4	37.2	1.920	15	11	7.06	o	
A.L.	32	7: 4	35.3	1.812	8	1	6.98	o	
F.H.	33	14: 4	39.1	1.942	15	12	7.56	-	
M.C.	34	10: 5	42.8	2.084	29	30	7.63	2+	
M.K.	35	9: 9	40.7	2.168	45	42	7.88	+	
<u>Subacute infective polyarthrititis - female</u>									
E.H.	36	23:12	40.	2.571	24	27	-	-	
M.S.	37	17: 2	43.5	2.441	-	-	-	-	
H.J.	38	18: 4	31.7	2.584	-	-	8.28	-	
L.G.	39	7:11	44.5	2.468	37	41	8.46	o	
M.G.	40	5: 1	43.0	2.474	30	31	9.40	o	
E.M.	41	17:11	45.4	2.518	32	38	8.86	3+	
F.M.	42	16: 1	31.1	2.663	6	0	8.32	o	
		12: 3	29.0	2.475	60	32	7.96	o	
I.B.	43	24: 3	39.6	2.384	37	33	8.21	4+	
M.H.	44	14: 4	41.0	2.210	44	42	7.34	-	

Name	No.	Date	PCV.	PLASMA VISC.	Wintrobe E. S. R.		Total Plas. Prot.	Gold Floc	Remarks
					Ord.	Cor.			
			%	cs.	mm/	1 hr	%		
<u>Chronic infective polyarthrititis - male.</u>									
W.C.	1	9: 1	49·	1·940	12	14	-	-	
T.R.	2	9: 1	49·	2·074	-	-	-	-	
J.A.	3	18: 3	48·1	2·043	10	11	7·30	-	
		23:10	47·6	1·949	5	5	7·74	3+	
W.P.	4	8: 4	45·0	2·026	20	18	7·38	-	
W.M.	5	15: 4	55·7	2·128	2	11	7·85	-	
T.J.	6	18: 4	42·2	1·978	-	-	7·16	-	
W.M.	7	24: 4	43·7	2·227	27	22	7·42	-	
H.S.	8	11:12	45·9	1·996	11	10	7·02	o	
J.H.	9	11:12	44·2	2·115	19	16	8·06	+	
		30: 3	46·3	2·120	10	9	8·17	o	
J.T.	10	18:12	43·0	2·178	30	25	8·28	o	
R.W.	11	5: 2	45·7	1·991	20	18	6·95	3+	
P.T.	12	15: 3	45·1	1·809	-	-	6·80	o	
W.T.	13	1: 4	46·8	1·816	1	1	7·09	o	
M.M.	14	13: 4	44·8	1·695	1	0	6·44	+	
A.B.	15	15: 4	44·3	2·213	38	34	7·49	o	
R.G.	16	22: 4	47·3	2·212	30	30	7·56	+	
F.K.	17	4: 5	44·2	2·377	4	1	8·24	+	
T.W.	18	6: 5	40·9	2·329	44	38	8·23	o	
R.H.	19	16: 9	48·3	2·161	-	-	8·35	o	
<u>Subacute infective polyarthrititis - male</u>									
T.R.	20	11: 9	39·0	2·646	-	-	7·99	-	
M.L.	21	9: 4	39·7	2·346	46	33	7·52	o	
A.H.	22	20: 5	43·8	2·408	44	38	7·92	4+	

STILL'S DISEASE

Name	S	No.	Date	PCV.	PLASMA VISC.	Wintrobe E. S. R.		Total Plas. Prot.	Gold Floc	Remarks
						Ord.	Cor.			
				%	cs.	mm/	1 hr	%		
L.D.	F	1	23: 4	28.8	2.081	35	14	7.60	-	
A.D.	F	2	28: 5	39.2	2.285	-	-	8.24	-	
L.S.	F	3	28: 5	38.4	2.473	-	-	8.78	-	
J.T.	M	4	24: 7	41.2	2.424	-	-	7.85	-	
			9:10	38.0	2.311	50	42	7.85	o	
J.B.	F	5	30: 7	16.8	2.052	-	-	6.80	-	
A.H.	M	6	19: 2	37.4	2.836	50	40	8.96	+	
S.G.	M	7	15: 6	39.2	2.477	50	45	8.60	+	
			2: 9	40.8	2.085	-	-	7.45	o	
L.B.	F	8	12: 4	32.	2.961	57	36	8.71	+	
			21: 4	34.	3.144	19	8	9.11	+	
			30: 4	47.	3.266	3	7	9.72	o	after transfusion
			16: 5	41.	3.021	12	11	9.09	++	
			28: 5	36.	3.052	35	25	8.94	+	
			5: 6	-	2.935	-	-	8.93	-	
			6: 7	29.5	2.687	63	35	8.57	+	
			23: 8	34.	3.337	42	28	9.20	+	
			13: 9	30.	3.005	63	36	8.75	-	
			17: 9	33.	3.353	41	25	9.29	-	
			9:10	33.3	3.141	57	30	8.93	-	
			24:10	32.	3.266	59	36	9.72	-	
			13:11	36.	3.218	36	26	9.50	+++	
			20:11	36.	3.516	49	37	9.86	-	Cortisone begins
			26:11	37.0	2.273	44	34	7.70	-	
			29:11	38.9	2.165	38	32	7.80	+	
			3:12	41.3	2.003	16	15	6.80	-	
			10:12	44.6	2.000	13	16	7.60	-	
			15:12	44.5	1.992	14	17	7.78	-	
			19:12	47.2	2.177	19	26	8.42	-	
			24:12	45.	2.155	27	31	7.57	-	Cortisone ends
			3: 1	37.	2.560	53	42	-	-	
G.H.	F	9	1: 9	39.1	2.415	47	42	8.86	+	10 yr. history
J.H.	F	10	1: 9	41.6	2.660	44	44	9.32	+	2.5 yr. history.
K.W.	M	11	1: 9	45.5	3.100	31	29	8.10	+	9 yr. history

Case No. 10

Still's Disease (treated with Cortisone)

This girl was aged eight and a half when she was admitted to hospital on 11:4:51.

Four years previously she had suffered from rheumatic fever for which she was nursed in bed for 6 months; she had apparently escaped without cardiac damage. She had remained well since then until 4 months prior to admission.

A history of a sore-throat was obtainable. A typical polyarthrititis began in December for which she received salicylate and penicillin treatment; she was allowed to sit up but more active movements were prohibited. The swellings around the joints varied in size, but never disappeared; the swellings were painless.

On admission, she was a pale thin child. Both tonsils were enlarged, but not inflamed. All systems were normal, apart from the locomotor. The liver and spleen were not palpable.

The spine, elbows, shoulders, hips, toes, and fingers were not involved. The wrists had marked peri-articular swelling and limited movement. There was also peri-articular swelling of the knees, with effusion into the right knee. The ankles also showed swelling. None of the affected joints were painful.

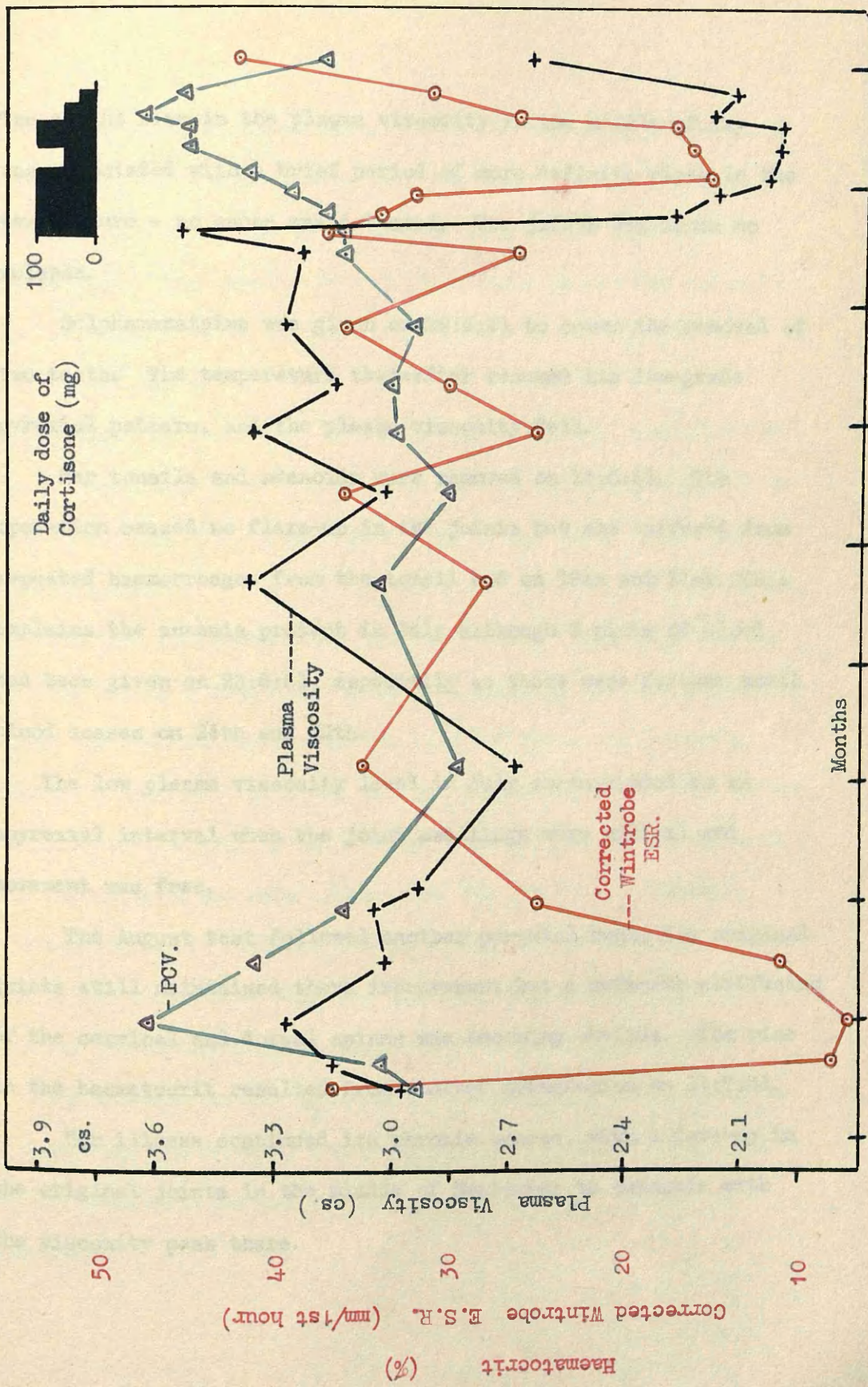
The laboratory tests corresponded to a severe general reaction.

Her treatment consisted of rest in bed and rest to the arms

Date	PCV.	PLASMA VISC.	Wintrobe ESR.		Plasma protein				Gold Floc.
			Ord.	Cor.	Total	Alb.	Glob	Fib.	
	%	cs.	mm/ 1 hr		g./100 ml.				
12: 4:51	32.	2.961	57	36	8.50	3.80	3.97	0.73	+
21: 4:51	34.	3.144	19	8	8.74	4.55	3.50	0.69	+
30: 4:51	47.	3.266	3	7	9.72	-	-	-	o
16: 5:51	41.	3.021	12	11	9.09	4.33	4.00	0.76	++
28: 5:51	36.	3.052	35	25	8.94	4.35	3.85	0.74	+
5: 6:51	-	2.935	-	-	8.93	-	-	-	
6: 7:51	29.5	2.687	63	35	8.57	4.2	3.7	0.67	+
23: 8:51	34.	3.337	42	28	9.20	4.0	4.41	0.79	+
13: 9:51	30.	3.005	63	36	8.75	-	-	-	
17: 9:51	33.	3.353	41	25	9.29	-	-	-	
9:10:51	33.3	3.141	57	30	8.93	-	-	-	
24:10:51	32.	3.266	59	36	9.72	-	-	-	
13:11:51	36.	3.218	36	26	9.50	4.0	4.76	0.74	+++
20:11:51	36.	3.516	49	37	9.86	-	-	-	
26:11:51	37.0	2.273	44	34	7.70	4.2	3.06	0.44	
29:11:51	38.9	2.165	38	32	7.80	4.5	2.98	0.32	+
3:12:51	41.3	2.003	16	15	6.80	4.1	2.36	0.34	
10:12:51	44.6	2.000	13	16					
15:12:51	44.5	1.992	14	17					
19:12:51	47.2	2.177	19	26					
24:12:51	45.	2.155	27	31	7.57	4.8	2.3	0.47	
3: 1:52	37.	2.560	53	42					

and legs by splints. Her pulse rate fluctuated markedly throughout her illness and she had a swinging low-grade pyrexia also.

On 23:4:51 she received 800 ml. of blood intravenously. There was an immediate rise in the haematocrit, plus a slight increase in the plasma viscosity while the ESR fell to 3 mm./hour. By the end of April an improvement in the movements of the right wrist and ankle could be detected and the effusion in the right knee had lessened. She was feeding herself early in May.



The slight rise in the plasma viscosity in the middle of May was associated with a brief period of more definite rises in the temperature - no cause was detected. The joints had shown no relapse.

Sulphamezathine was given on 29:5:51 to cover the removal of two teeth. The temperature thereafter resumed its low-grade pyrexial pattern, and the plasma viscosity fell.

Her tonsils and adenoids were removed on 13:6:51. The operation caused no flare-up in the joints but she suffered from repeated haemorrhages from the tonsil bed on 19th and 21st. This explains the anaemia present in July although 2 pints of blood had been given on 23:6:51, especially as there were further small blood losses on 24th and 25th.

The low plasma viscosity level in July corresponded to an apyrexial interval when the joint swellings were minimal and movement was free.

The August test followed another pyrexial bout; the original joints still maintained there improvement but a definite stiffening of the cervical and dorsal spines was becoming obvious. The rise in the haematocrit resulted from another transfusion on 11:7:51.

Her illness continued its chronic course, with a fare-up in the original joints in the middle of September to coincide with the viscosity peak there.

Another pint of blood was given at the beginning of November to prepare her for her Cortisone; the haematocrit increased. On the 19th November, she complained of pain in her hips for the first time; the involvement of these major joints was indicated by the rapid rise in the plasma viscosity to the highest value in her serial tests.

Cortisone:- She received, by mouth, 100 mg. daily from 19th Nov. to 6th Dec., and from 11th to 16th Dec; 50 mg. daily from 7th to 10th Dec., and 17th to 20th Dec.; and 25 mg. daily from 21st to 23rd. December.

Clinical improvement was obvious in three days when she was sitting easily straight up in bed; in six days she was scrambling about the bed and could move her arms and hands sufficiently freely to play ball with the patient in her next bed. She showed an increased feeling of well-being. Her weight increased steadily. The improvement was maintained until the supply was finished. The relapse which followed was not nearly so marked as was feared and it was considered that the treatment had been justified.

The laboratory results showed some noteworthy changes.

The increase in the haematocrit values must have been due to a haemo-concentration by a passage of fluid from the blood stream as the cell increase was beyond any recorded rate of cell formation.

In spite of the fluid loss from the blood, the plasma proteins decreased in amount and rapidly approached to a normal fraction pattern. This protein alteration had additive actions leading to a plasma viscosity decrease.

The changes in the plasma viscosity and ESR were roughly parallel but the time-phase of the changes were different.

In as much as this treatment never caused the plasma viscosity to attain a normal value and thus indicate a possible cessation in the "activity" of the disease process, it is open to criticism. I have ventured to suggest that a higher dosage would have had a greater chance of an ultimate quiescence if thereby a normal viscosity had been attained.

Case No. 11

Still's Disease.

This case has been included to show how extremely high plasma viscosity results can be found in this disease even after many years duration. The high values are characteristic of this disease in that the results are frequently much higher than one would forecast from the clinical assessment of the disease activity.

This man was 22 years old when his plasma viscosity was first estimated. He had suffered from rheumatoid arthritis since the age of 13. On examination, he could walk only with difficulty. Both feet were fixed at the mid-tarsal joints; the ankle movements were free. The right knee had a flexion deformity of 35°; the left was of 30°; flexion of both knees was limited to 90°; effusions form in the knees when he attempted to walk. The right hip had a restricted external rotation but otherwise it and the left hip had free movements. The muscles of the thigh and calf showed gross wasting on both sides. The elbows had deflexion deformities of 30°, and the movements of pronation and supination were accompanied by considerable crepitus. The shoulders and the spine were free.

He had received six courses of gold injections without a halt in the disease progress. More recently the treatment had been restricted to injections of procaine and lactic acid into

the affected major joints but very little relief was being obtained.

The laboratory results of 1:9:47 were:-

Plasma viscosity	=	3.100 cs.
Blood haematocrit	=	45.5 %
Wintrobe ESR.	=	31 mm. in 1st hour
Corrected Wintrobe ESR.	=	29 mm. in 1st hour
Plasma total protein	=	8.10 g./100 ml.

Case No. 12

Still's Disease.

This girl of 14 years had suffered from arthritis of hands, feet and knees for two and a half years. Gold injections and physiotherapy produced but little impression on the progress of the disease.

At the time of the plasma viscosity estimation her chief complaint was of the pain and deformity of the hands and wrists. The wrists were almost fixed; the fingers were locked at the proximal interphalangeal joints. The left elbow movement was limited. The right knee was swollen and hot; flexion deformity affected both knees. The feet and ankles were free.

Skiagrams of the wrists were suggestive of bony ankylosis and decalcification of all the bones of the wrists; the elbows were similarly affected.

Date	PCV.	PLASMA VISC.	Wintrobe ESR.		Plasma Total Protein	Gold Floc.
			Ord.	Cor.		
	%	cs.	mm/ 1 hr		g. %	
1: 9:47	41.6	2.660	44	44	9.32	++

The plasma viscosity value is typical of the higher result than one would have expected from the clinical assessment of the disease activity.

RHEUMATIC FEVER.

Name	S	NO.	Date	PCV. %	PLASMA VISC. cs.	Wintrobe E. S. R.		Total Plas. Prot. %	Gold Floc	Remarks
						Ord. mm/	Cor. 1 hr			
A. Cases which were clinically active, in that the tests were carried out early in the disease and usually before salicylate therapy had been started.										
S.L.	M	1	9:12	38.9	2.359	-	-	8.02	+	
N.K.	F	2	18:12	44.2	1.952	5	7	8.06	o	
H.K.	M	3	28: 1	39.9	2.493	48	35	7.88	2+	
R.F.	M	4	4: 3	37.9	2.123	46	30	7.78	o	
J.W.	M	5	4: 3	44.0	2.271	-	-	7.85	o	
I.M.	F	6	23: 3	35.0	2.411	55	40	7.85	+	
			30: 3	30.6	2.476	60	35	7.49	+	
			5: 4	31.9	2.455	58	34	7.99	+	
R.N.	F	7	24: 3	35.0	2.548	55	40	7.34	2+	
			30: 3	36.2	2.202	48	36	6.59	+	
			5: 4	38.8	1.970	37	32	6.95	+	
L.L.	F	8	1: 4	39.8	2.544	32	28	7.92	2+	
			5: 4	33.3	2.632	57	38	7.38	+	
M.D.	F	9	1: 4	44.0	2.249	11	13	8.21	2+	
L.C.	M	10	8: 4	39.0	2.228	-	-	7.16	o	
M.H.	F	11	16: 4	33.9	2.143	21	11	8.03	+	
H.M.	F	12	16: 4	40.2	2.323	47	44	8.03	2+	
F.S.	F	13	8: 5	27.7	2.151	65	33	7.02	+	
G.V.	M	14	13: 5	41.4	2.042	20	13	7.74	o	
A.S.	M	15	20: 5	40.9	2.470	45	34	7.45	o	
			27: 5	41.9	2.139	39	31	7.09	o	
M.S.	F	16	24: 5	41.3	2.334	38	37	7.74	+	
A.S.	F	17	27: 5	36.9	2.269	45	36	8.14	o	
W.H.	M	18	22: 6	41.2	2.341	40	31	8.42	+	
			3: 8	43.9	1.957	10	6	7.67	o	
J.C.	F	19	28: 6	31.4	1.957	47	27	6.37	o	
A.F.	F	20	28: 6	36.6	2.279	46	36	8.32	o	
			6: 7	40.6	2.064	21	19	7.96	2+	
			13: 8	41.9	1.986	10	10	8.10	+	
R.B.	M	21	24: 8	23.8	2.385	-	-	7.99	0	
			9: 8	25.9	2.562	65	22	8.14	+	
			15: 9	28.2	2.333	60	23	8.60	+	
W.R.	M	22	4:10	38.0	2.861	-	-	7.95	-	
			25:10	43.7	2.026	-	-	6.97	-	

Name	S	NO.	Date	PCV.	PLASMA VISC.	Wintrobe E. S. R.		Total Plas. Prot.	Gold Floc	Remarks
						Ord.	Cor.			
				%	cs.	mm/	1 hr	%		
A. Clinically active Rheumatic Fever (contd.)										
S.C.	F	23	15: 6	36.8	2.468	3	0	8.14	3+	
B.R.	M	24	12: 8	41.2	2.186	-	-	7.34	-	
			18: 8	38.5	2.228	-	-	7.13	-	
			25: 8	39.0	2.183	-	-	7.42	-	
			4: 9	41.3	2.107	-	-	7.24	-	
			11: 9	41.3	1.997	-	-	6.91	-	see also conval-
E.F.	F	25	26: 6	36.6	2.044	40	30	7.52	o	-escent section.
S.P.	F	26	19: 6	44.0	2.039	23	26	7.49	o	
			29:11	44.	1.957	17	19	7.45	o	
B.D.	M	27	4: 7	39.	2.203	19	9	8.68	o	
G.F.	M	28	23: 2	35.	2.078	44	25	6.98	o	
A.P.	M	29	14: 3	36.	1.931	28	13	7.30	o	
S.H.	F	30	15: 3	39.	2.121	47	41	7.78	o	
B. Clinically active rheumatic fever, in which activity has continued for months in spite of treatment.										
K.C.	F	31	30:10	40.3	2.021	31	29	7.81	-	after 7 months.
			11:12	39.4	2.032	16	13	7.96	2+	
S.P.	F	26	29:11	44.	1.957	17	19	7.45	o	after 5 months.
J.H.	F	32	17: 4	42.	1.914	20	20	7.31	o	after 8 months.
F.G.	M	33	23: 1	45.7	2.027	25	23	7.17	o	1 month after acute phase "cured"
E.S.	F	34	6: 8	28.4	2.027	40	17	7.70	2+	after 14 months
F.M.	F	35	3: 5	40.6	1.942	10	8	7.45	o	
M.R.	F	36	13: 5	35.3	2.070	45	34	7.45	+	
M.R.	F	37	18: 2	-	2.117	-	-	7.27	+	
D.W.	F	38	27: 2	42.0	2.286	15	15	8.68	+	At work, several
			20: 5	42.2	2.001	11	11	7.70	+	months after acute
			6: 8	45.4	2.024	4	7	8.17	+	phase.
			7: 9	45.2	2.264	17	21	8.28	2+	
R.V.	M	39	14: 2	45.	2.000	4	2	7.52	o	ambulant; 8 months of vague symptoms.
S.G.	F	40	1: 1	39.	1.957	21	17	-	-	after 4 months.
			15: 1	40.4	2.244	38	35	8.06	-	
			24: 1	40.4	1.998	29	25	7.42	-	
			15: 2	57.	2.145	50	40	7.67	-	

Name	S	No.	Date	PCV.	PLASMA VISC.	Wintrobe E. S. R.		Total Plas. Prot.	Gold Floc	Remarks
						Ord.	Cor			
				%	cs.	mm/	1 hr	%		
C. Convalescent rheumatic fever - cases which were once definitely clinically active.										
D.N.	F	39	14: 2	-	1.846	18	-	-	-	
G.H.	F	40	19: 3	38.6	1.917	14	10	7.70	o	
P.M.	F	41	9: 4	41.4	1.848	3	2	7.52	o	
N.W.	F	42	29: 4	38.4	1.851	8	4	7.34	o	
			2: 7	38.3	1.865	8	4	7.38	o	
L.C.	M	10	27: 5	43.3	1.942	14	10	7.52	o	cf. acute section
B.R.	M	24	9: 1	47.2	1.895	3	3	7.05	+	" " "
R.F.	M	4	15: 6	44.2	1.844	9	6	7.24	o	" " "
G.F.	M	28	19: 3	36.5	1.795	16	5	6.98	o	" " "
			3: 4	36.	1.710	8	0	6.80	o	
			16: 4	38.	1.698	7	0	6.73	o	
			30: 4	39.	1.795	8	0	6.80	o	
J.H.	F	32	30: 4	41.	1.857	14	13	7.20	o	
G.D.	M	43	11:11	41.8	1.846	10	5	7.09	-	
			30:11	39.	1.708	8	0	6.48	o	
M.E.	F	44	7:12	35.	1.701	11	3	6.30	o	
			3: 2	40.	1.772	14	12	6.80	o	
			12: 2	42.1	1.740	6	6	6.73	o	
P.D.	F	45	29: 1	38.2	1.819	25	20	7.13	0	
			12: 2	40.0	1.774	10	8	6.98	o	
			16: 4	40.	1.738	7	5	6.80	o	
			30: 4	44.	1.868	6	8	7.45	o	
R.W.	M	46	12: 2	39.3	1.749	7	0	6.95	+	
D. Cases which clinically might have been rheumatic fever - children with vague joint pains, pyrexia of unknown origin, or valvular disease of the heart.										
These cases were sent to the laboratory for tests to help in the decision concerning the "activity".										
P.T.	F	47	27: 2	37.9	1.869	14	8	7.02	o	
R.N.	F	48	3: 4	38.9	1.873	19	15	7.13	o	
			26: 4	37.4	1.815	20	14	7.16	o	
A.B.	M	49	16:11	41.	1.892	13	7	6.98	+	
			11:12	40.5	1.787	5	0	7.27	+	
A.H.	M	50	7: 2	42.	1.798	7	3	6.95	o	

Case No. 15

Acute Rheumatic Fever.

Three weeks prior to his admission to hospital on 22:7:47, this man, aged 42 years, had a sore throat which was treated by sulphonamides. He improved for 4 days but bilateral quinzy next developed and burst after a further 4 days. At the same time (ie. 8 days from start of illness) he had a pain in his right ankle; later he had pains in the ankles, knees, elbows and shoulders - the joints were painful to move, but without any marked swelling or redness. Five days prior to admission he was treated with sodium salicylate in doses sufficient to produce buzzing in the ears yet the pain in the joints was not reduced.

There was a history of previous sore throats; there was no history of previous attacks of rheumatic fever.

On admission, the throat appeared to be normal again. The joints chiefly affected were the knees, left wrist and left shoulder - the wrist was tender but not swollen, the shoulder was swollen and held rigid. The patient would not move these joints over their full range. There were no rheumatic nodules. The heart sounds were pure and its size, to percussion, was within normal limits. The spleen was enlarged to percussion but it was not palpable.

He was treated by sodium salicylate internally, methyl

Date	PCV.	PLASMA VISC.	Max. Citr. ESR.	Plasma protein				<u>K</u>	Serum NPN.
				Total	Alb.	Glob	Fibr		
	%	cs.	mm/hr.	g./100 ml.					mg. %
12:8:47	41.2	2.186	55.71	7.08	3.62	2.90	0.56	0.393	28.2
18:8:47	38.5	2.228	41.2	6.91	3.39	2.80	0.72	0.3887	26.7
25:8:47	39.0	2.183	43.5	6.68	3.65	2.37	0.66	0.3905	33.8
4:9:47	41.4	2.107	35.1	7.03	3.94	2.54	0.55	0.3938	38.0
11:9:47	41.3	1.997	28.8	6.76	3.81	2.48	0.47	0.3943	48.5
9:1:48	47.2	1.895	7.4	7.09	4.72	1.96	0.37	0.382	28.7

salicylate locally to the joints, and with potassium bromide + chloral for the pain.

A few days after admission, the apex of the heart began to move out to the left and a systolic murmur appeared. Improvement in the joints was very slow.

The plasma viscosity was first estimated on 12:8:47 when the value corresponded to that of a moderate reaction. At this time the patient was rather drowsy and his speech was indistinct - these were attributed to the salicylates, and these were replaced on 13:8:47 by calcium aspirin.

This alteration in treatment was followed immediately by an acute recurrence of the joint pains, elevation of temperature, sweating, etc. and on 15:8:47 there was a pericardial rub in the third interspace which disappeared within the day. The pyrexia continued to increase until the 17:8:47 when the sodium and methyl salicylates were resumed; there was an immediate response in a reduction of joint pains, lowered temperature and decreased sweating.

The relapse was reflected in the increased plasma viscosity (and in the fibrinogen) of the 18:8:47, yet the ESR. showed an appreciable reduction.

On 23:8:47, while he was receiving large prophylactic doses of penicillin, some decayed teeth were removed. This operation caused no apparent upset to the patient but it might be the explanation for the slight rise in the ESR. although there was no interference with the steady decrease in the plasma viscosity results.

When his temperature had remained normal for a week and he had had only occasional joint pains, he was discharged on 11:9:47 to continue his convalescence at home.

When the patient reported to the out-patient department three months later his laboratory results had returned to within the normal ranges: there was now no clinical indication of activity and there was no evidence of cardiac involvement.

The plasma viscosity test appears to have been a useful index to the pathological processes occurring in this patient.

(The behaviour of the plasma protein equilibrium factor (K) in this patient has been discussed in my paper.)

Case No. 14

Acute Rheumatic Fever.

This case is of importance as it shows how high the plasma viscosity may be at the first occurrence of pain. This finding supports the hypothesis that the disease is a hyper-reaction and that it has been active for several days at least before the symptoms appear.

This young man of 24 years had been apparently normal to physical examination when admitted to the asylum a few months prior to the present illness. He complained of pain and swelling of both knees and ankles, which pain had appeared since he went to bed on the previous night. The plasma viscosity was measured on the same day. The high plasma viscosity, increased globulin and fibrinogen, and high ESR. were changed to an extent greater than would have been possible in any disease condition of only 24-hours duration.

He responded well to salicylate therapy; he was convalescent within a month; and his heart escaped obvious damage.

Date	PCV.		PLASMA VISC.		Max. Citr.	Plasma Protein				Serum
	Cit.	P+A.	Citr.	P+A.	ESR.	Total	Alb.	Glob	Fibr.	NFN.
	%		cs.		mm/hr	g./100 ml.				mg. %
3:10:43	29.1	38.0	1.983	2.861	64.4	7.95	4.21	2.98	0.76	32.3
23:10:43	34.0	-	1.607	-	9.7	-	4.73	2.65	-	30.1

Case No. 15

Acute Rheumatic Fever.

This patient gave the classical history of a sore throat which was followed in two weeks by a polyarthrititis.

On 4:5:48 he developed a tonsillitis which kept him from work for 4 days. On 14:5:48 he had pain and swelling in both feet and ankles which were relieved by rest in bed sufficiently to let him work again on the 15th. By the 16th, however, his feet were painful again and the knees had become swollen; the wrists were affected on 17th.

On examination on admission to hospital on 18:5:48, he was complaining chiefly of pain in the wrists, left shoulder and right knee; these joints were slightly swollen and tender. His pulse rate was 100 per minute and his temperature was elevated. The apex beat was in the 5th interspace, outside the midclavicular line. There was a systolic murmur at the apex. The liver was just palpable. The throat and tonsils were apparently normal. No abnormality was detected in any other system.

Date	PCV.	PLASMA VISC.	Wintrobe ESR.		Plasma Total Prot.	Gold Floc.
			Ord.	Cor.		
	%	cs.	mm/ 1 hr		g. %	
20: 5:48	40.9	2.470	45	36	7.45	+
28: 5:48	41.9	2.139	39	31	7.09	o

His temperature fell with salicylate treatment. He was sent home on 31:5:48 to convalesce there. His heart size later diminished but the systolic murmur persisted.

Case No. 16

Acute Rheumatism, becoming chronic.

This girl of 11 years had had a previous attack of rheumatic fever; the course had been of insidious onset and mild symptoms so that her treatment but been scanty, which might have been the reason that she developed a carditis.

About the seventh of October, 1951, she began to complain of mild pains in the back, foot, shoulders, and fingers; her temperature was not elevated. There was no history of a sore throat. As these symptoms had not cleared in a fortnight her mother called in the doctor. He put the girl to bed for a week, without drug treatment, but the pain persisted. There was still no elevation of temperature but a tachycardia of 108 beats per minute was noted. There was no appreciable alteration in the heart sounds and in the presystolic murmur which was left after the original attack.

The plasma viscosity was requested in order to ascertain if any active disease was present, and the value of 2.707 cs. was a surprise to myself and the patient's own doctor.

She was treated with salicylates from 28:10:51 until 1:1:52. The pains had gone in four days and the pulse rate had fallen to 84 per minute in the same period. The pulse rate remained steady thereafter apart from an increase from 10th to 13th January, 1952.

Date	PCV.	PLASMA VISC.	Wintrobe ESR. Ord. Cor.		Plasma Total Protein
	%	cs.	mm/	1 hr	g. %
26:10:51	36·	2·707	54	41	8·75
12:11:51	37·	2·140	51	40	8·03
28:11:51	37·	1·980	37	28	7·60
17:12:51	38·0	2·160	45	37	8·14
1: 1:52	39·	1·937	21	17	-
15: 1:52	40·4	2·244	38	35	8·06
24: 1:52	40·4	1·998	29	25	7·42

This case is a good example of the manner in which the plasma viscosity test can assist the physician.

The only evidence of an active disease were some slight pains and a tachycardia, in an apyrexial patient. The rapid clinical improvement with salicylate therapy was reflected in the rapid fall in the plasma viscosity (The ESR remained unaltered).

The rate of fall suggested a return to normal levels by the middle of December, but an actual increase was detected - this change I interpret as the alteration from the acute phase of the rheumatic disease to a more subacute or chronic phase. There was absolutely no clinical evidence of this change in the clinical picture.

By the beginning of January, 1952, the ESR had reached a normal value, but the plasma viscosity persisted high. After the salicylate was stopped the pulse rate was again increased for a few days and the plasma viscosity had increased significantly.

The pulse rate increase amounted only to a rise to about 90-94 per minute from its usual 80-84.

Nine days later, the pulse had remained steady except for the evening previous to the test when it again reached 90, but the plasma viscosity and ESR. remained abnormally high.

Her physician intends to keep her at rest in bed until these two tests attain and maintain normal levels.

A test on 15:2:52 showed that another increase had occurred in the plasma viscosity to 2.145 cs.

Case No. 17

Chronic Rheumatic Fever.

This girl, aged 16 years, had been confined to bed at home for 7 months because of rheumatic fever, with severe cardiac involvement. She was free from joint pains. Her Wintrobe ESR. remained between 23 and 26 mm./1st. hour.

Her own doctor was of the opinion that her disease was not quiescent and sought the assistance of the laboratory to obtain additional abnormal tests to strengthen his position in keeping his patient in bed in face of parental criticism.

The plasma viscosity values were typical of a chronic disease process. The gold flocculation was also abnormal in the second test.

Date	PCV.	Plasma Visc.	Wintrobe ESR.		Total Plasma Prot.	Gold Floc.
			Ord.	Cor.		
	%	cs.	mm/ 1 hr		g. %	
30:10:47	40.3	2.021	31	28	7.81	o
11:12:47	39.4	2.032	14	11	7.96	++

Case No. 18

Chronic Rheumatic Fever.

This case illustrates how the plasma viscosity remains persistently elevated into the "zone of chronicity" in the presence of continued clinical activity; the ESR, in contrast, had returned to normal limits.

In April 1945, when 22 years old, this girl had an attack of rheumatic fever for which she was treated in hospital for 6 weeks. Thereafter she remained well and free from pain.

In November 1947 she had a recurrence of the rheumatic fever. She was treated at home, with 6 weeks confinement to bed followed by a slow return to full activity.

On 28:2:48 she attended the medical out-patient department for a specialist's opinion regarding her fitness to resume work. She felt well apart from occasional pain in her left shoulder and elbow. She had no dyspnoea. On examination, the apex beat was in the 5th interspace in the mid-clavicular line, there were systolic and diastolic bruits at the apex, there was a marked tachycardia, and no other abnormality. In view of these findings, together with the abnormal laboratory results, the clinician considered that the rheumatic fever was still active: she was sent home to have further complete rest.

She reported on 20:5:48. She felt very well and was keen to

Date	PCV.	PLASMA VISC.	Wintrobe ESR.		Total Plasma Prot.	Gold Floc.
			Ord.	Cor.		
	%	cs.	mm/ 1 hr		g. %	
28:2:48	42.0	2.286	15	15	8.68	+
20:5:48	42.2	2.001	11	11	7.70	+
6:8:48	45.4	2.024	4	7	8.17	+
7:9:48	45.2	2.264	17	21	8.28	++

resume work. There was no alteration in the heart to physical examination: the tachycardia was 120 per minute. Although there was some improvement in her laboratory results, the plasma viscosity and gold flocculation remained abnormal. The clinician again assessed that the disease was not quiescent and a further period of rest was ordered.

On 6:8:48 she again claimed to be very well and to be managing a little light work. Her tachycardia persisted at 120 and she had now developed an aortic diastolic murmur. The ESR. was only 7 mm. per hour. The clinician preferred the plasma viscosity abnormal value and considered that her rheumatic carditis was still active. Further rest was prescribed.

A month later, even when she still made no complaint, all the laboratory tests had become more abnormal. The clinician again assessed her rheumatic condition as active.

CHOREA

Name	S	No.	Date	PCV.	PLASMA VISC.	Wintrobe E. S. R.		Total Plas. Prot.	Gold Floc	Remarks
						Ord.	Cor.			
				%	cs.	mm/	1 hr	%		
A.G.	M	1	20: 5	40.9	1.744	5	0	6.62	o	
P.W.	F	2	24: 6	39.6	1.850	14	11	7.42	o	
E.O.	M	3	22:12	42.8	1.849	9	5	7.13	o	
D.V.	F	4	23: 2	43.	1.888	13	14	6.88	o	
			12: 4	42.	1.754	6	6	6.62	-	
			5: 5	42.2	1.815	6	6	6.91	o	
			17: 5	41.9	1.779	7	7	6.77	o	
			28: 5	41.4	1.754	4	3	6.41	o	
			4: 6	40.5	1.745	7	5	6.84	o	
			12: 6	40.2	1.789	5	4	6.44	o	
			5: 7	-	1.767	-	-	6.70	-	
R.D.	M	5	4: 4	41.	1.934	17	10	7.67	o	with carditis.
			21: 4	40.	1.934	17	9	7.24	o	
			5: 5	40.7	1.905	12	5	7.16	o	
			17: 5	38.4	1.757	13	4	6.48	o	
			28: 5	38.	1.796	9	0	6.62	o	
M.F.	F	6	23: 6	38.	1.829	7	0	6.98	o	
			21: 4	42.	1.941	17	17	7.34	o	hemi-chorea
			30: 4	43.	2.003	15	16	7.49	o	
			28: 5	42.	1.960	14	14	7.49	o	
J.P.	F	7	13: 6	41.	1.948	16	15	7.16	o	
			16: 5	38.	1.857	15	11	7.49	o	cardiac murmur
A.B.	F	8	30: 6	45.	1.943	9	13	7.20	2+	also joint pains
			28: 8	38.	1.837	16	11	6.84	-	
R.D.	M	9	19:10	40.	1.764	8	2	7.20	-	
R.N.	M	10	16:11	43.		2	0	6.48	-	
M.A.	F	11	19: 1	41.9	1.729	1	1	6.66	o	
R.O.	M	12	19: 3	37.8	1.793	11	3	6.80	o	
D.J.	F	13	17:12	44.6	1.827	12	15	7.27	o	
			31:12	39.	1.758	15	12	-	-	
			7: 1	42.0	1.833	13	13	7.02	-	

Case No. 19

Chorea.

This child was aged 13 years when she was admitted to hospital on 17:1:48. She gave a history of involuntary movements and of dropping articles for about three weeks.

In 1941 she had had an attack of chorea for which she recieved treatment in the Childrens' Hospital for seven weeks. She had not suffered from rheumatic fever or sore throats.

On examination, she was a bright intelligent child. Her hands kept moving over each other or plucking at the bed-clothes; her face kept frowning, grimacing and making other involuntary expressions; her legs made persistent gentle movements below the bed clothes. She was apyrexial. No abnormality could be detected in any other system.

Her treatment consisted of luminal and calcium aspirin.

Two days later her laboratory tests were apparently normal.

PCV.	PLASMA VISC.	Wintrobe ESR.		Plasma Total Protein.	Gold Floc.	Date
		Ord.	Cor.			
%	cs.	mm/	1 hr.	g. %		
41.9	1.729	1	1	6.66	0	19:1:48

Case No. 20

Chorea and Carditis.

The illness began in this girl of 14 years as a twitching of the arms and repeated purposeless movements. These had increased in intensity when grimacing, frowning and jerking of the head began. A week later she was unsteady on her feet and unable to walk straight; her speech was slurred. No improvement resulted from 2 weeks rest in bed at home and she was admitted to hospital at the end of the fourth week of her illness.

She had had no previous illness; there was no family history of rheumatic fever.

On admission, she was extremely restless and jumpy. All her limbs and shoulders moved in continual purposeless actions; she grimaced and frowned continually. Abnormalities were detected only in the cardiovascular and nervous systems.

There was tachycardia; the heart size appeared within normal limits; there was a systolic murmur at the apex and along the left side of the sternum.

The outstretched hands attained a slight choreiform posture. She had an "ant-eater" tongue movement. The tone of the arm muscles was low, with a general diminution of power in the arms and legs; the grip could not be sustained. The speech was slightly slurred.

Her treatment consisted of sedation with phenobarbitone.

Improvement in her choreiform movements resulted and the pulse

Date	PCV.	PLASMA VISC.	Wintrobe ESR.		Plasma Total Protein.	Gold Floc.
			Ord.	Cor.		
	%	cs.	mm/ 1 hr		g. %	
30: 6:51	45.	1.943	9	13	7.20	++
28: 8:51	38.	1.837	16	11	6.84	o

was settling. The plasma viscosity of this date was increased and this was attributed to the stage of the disease which led to the carditis; note also the positive gold flocculation test which also favours an active rheumatic fever.

An inflammation of the tonsils and fauces on 12:7:51 was treated successfully with sulphonamides and penicillin. No flare-up followed either in heart or chorea.

Later in July she could feed herself. At the middle of August she was allowed up slowly. Another sore throat interrupted the illness so that the tonsils were removed in September.

The laboratory tests at the end of August supported the clinicians in their assessment that the disease processes had become quiescent.

She was discharged at the end of September, free from any chorea but with an unchanged systolic mitral murmur and an accentuated second pulmonic heart sound.

Case No. 21

Chorea, with carditis.

This girl of 13 years was admitted to hospital on 22:2:51. Three weeks earlier she had a laryngitis and head cold; one week prior to admission she began to fidget and to have involuntary movements, which rapidly became more energetic. When she was seen in hospital these involuntary movements frequently threatened to throw her out of bed and I had to have the assistance of three nurses to restrain her movements so that her arm remained sufficiently steady to obtain a blood sample.

In February 1946 she had an attack of fidgets and grimacing which cleared only after six months treatment by sedation; a similar attack began in February 1947, lasting four months, and another in July 1950, lasting three months. During these attacks she did not feel ill and she was never confined to bed; between the attacks she also felt very well. She had never suffered from rheumatic fever. Her family history was free from rheumatic fever and nervous diseases.

On admission, she was very restless, with continuous purposeless movements of the face, arms and legs. She was very noisy and extremely dysarthric. The tone of the muscles on both sides was reduced, the right being the more flaccid. The power was reduced in all limbs; she could not sustain her arms outstretched; there was hyperextension of the fingers, and flexion of the wrists; her grip waxed and waned. The tongue movements were typically of the

Date	PCV.	PLASMA VISC.	Wintrobe ESR.		Plasma Total Protein	Gold Floc.
			Ord.	Cor.		
	%	cs.	mm/ 1 hr		g.%	
23: 2:51	43·	1·888	13	14	6·88	o
12: 4:51	42·	1·754	6	6	6·62	-
5: 5:51	42·2	1·815	6	6	6·91	o
17: 5:51	41·9	1·779	7	7	6·77	o
28: 5:51	41·4	1·754	4	3	6·41	o
4: 6:51	40·5	1·745	7	5	6·84	o
12: 6:51	40·2	1·789	5	4	6·44	o
5: 7:51	-	1·767	-	-	6·70	-
8: 1:52	-	1·729	6	-	6·77	-

"ant-eater" type. The throat was slightly inflamed. Some scattered rhonchi were detected in both lungs. She was afebrile.

The heart apex beat was in the 5th interspace, just outside the nipple line. The rhythm was regular. The first sound was soft, but no murmurs were noted. The blood pressure equalled 116/70 mm. mercury.

Her treatment consisted in phenobarbitone in doses of 1·5 grains 6-hourly, 20 grains of "disprin" 6-hourly, and rest in bed.

She made rapid progress so that there were no further choreic movements after the beginning of March.

On 2:4:51 she complained of pain in the shoulder and calf; on re-examination a blowing systolic murmur was then present at the apex. Sodium salicylate therapy was therefore begun, but the amount actually administered was doubtful as on 12:4:51 I could detect no salicylate in the blood and her medicine was proved to be lacking

any salicylate; however, her pains had disappeared by date but a few choreic movements had returned.

A further attack of sore throat and tonsillitis, with pyrexia, began on 23:4:51 and this may have been responsible for the rise in the third plasma viscosity value although the viscosity had shown no increase in response to the joint pain: treatment consisted of sulphamezathine. By 25:4:51 she was again afebrile. The phenobarbitone dosage was reduced and she again became more jumpy and her out-stretched hands attained a choreiform posture.

On 5:5:51 she was still afebrile, her choreiform movements had almost ceased, and no changes could be detected in the heart signs. The barbiturate was stopped on 21:5:51.

She began to get up on 24:5:51. There was now a coarse, diffuse systolic murmur at the heart apex.

She had another bout of pyrexia and joint pain on 2:6:51 but this passed in two days without causing any change in the laboratory tests. Thereafter her progress was uneventful and she was discharged on 16:7:51.

Her last test was made when she reported to the out-patient department after six months during which she had remained well.

ERYTHEMA NODOSUM

In addition to the results of the Plasma Viscosity and E.S.R. tests, the difference in the Gold Flocculation results should be noted; a positive result is found in a 'Rheumatic' primary stimulus, and a negative result in a 'Tuberculous' primary stimulus.

Name	S	No.	Date	PCV.	PLASMA VISC.	Wintrobe E. S. R.		Total Plas. Prot.	Gold Floc	Remarks.
						Ord.	Cor.			
				%	cs.	mm/	1 hr	%		
M.H.	F	1	11: 2	30.3	2.226	-	-	7.53	o	+ phthisis
J.S.	F	2	8: 4	38.4	1.916	14	10	7.34	o	+ phthisis
W.L.	F	3	13: 7	43.7	1.952	4	6	7.63	o	Mantoux positive
A.P.	F	4	31: 3	40.9	2.104	23	21	7.70	o	? primary stimulus
L.S.	F	5	19: 3	43.2	1.891	8	9	7.34	o	test done after skin cleared.
E.G.	F	6	18: 4	39.1	1.858	14	11	7.02	-	
M.B.	F	7	13: 2	42.	2.165	32	32	8.06	o	? primary stimulus
M.W.	F	8	11: 1	41.	2.524	5	4	8.64	4+	follows tonsillitis
			30: 1	43.7	2.310	4	6	8.82	3+	
			30: 3	41.5	1.856	4	4	7.38	2+	
R.F.	M	9	17: 4	30.	2.233	60	27	7.38	o	tuberculous stim.
			17: 5	35.4	1.748	10	3	6.44	o	
A.E.	F	10	2: 5	40.	2.577	27	24	8.57	+	follows sore throat
			23: 5	39.	1.928	26	22	7.02	o	
			6: 6	40.	2.001	17	15	7.78	o	
			27: 6	39.	2.053	34	29	7.49	o	
			18: 7	42.	1.962	30	30	7.27	o	
			19: 9	44.	1.812	8	10	6.77	o	
V.J.	F	11	15: 6	42.	2.183	36	36	7.45	o	? primary stimulus
M.C.	F	12	21:11	39.8	2.758	40	36	8.35	-	after sore throat
A.D.	M	13	10:12	36.3	2.099	48	28	7.60	o	? primary stimulus

Case No. 22

Erythema nodosum.

This patient, M.W., developed erythema nodosum following tonsillitis and quinsy - probably streptococcal, but this was not proved by bacteriological investigation. The points to be noted in the laboratory findings are (1) the positive gold flocculation tests, (2) the high plasma viscosity values which had not returned to normal by the time the patient felt quite well, and (3) the low ESR values.

This lady was aged 31 years. There was no evidence of pulmonary tuberculosis. On 22:12:50 she had a moderate attack of tonsillitis which had apparently cleared by the 24th with oral penicillin; she went on a short holiday over Christmas as she felt perfectly well; on the 27th, however, she complained again of her throat and a quinsy was found. Intramuscular penicillin was administered over the next five days during which the quinsy resolved.

A typical erythema nodosum rash appeared on both legs on 3:1:51 and it lasted about 5 days. As she was apparently anaemic her doctor kept her in bed for a further fortnight when she got up to look after her home. The patient herself felt quite well while the rash was present and afterwards; she was carrying out her normal domestic duties at the end of January with a plasma viscosity still raised to 2.310 cs.

Date	PCV.	PLASMA VISC.	Wintrobe ESR.		Total Plasma Prot.	Gold Floc.
			Ord.	Cor.		
	%	cs.	mm/	1 hr	g.%	
11:1:51	41·	2·524	5	4	8·64	++++
30:1:51	43·7	2·310	4	6	8·82	+++
30:3:51	41·5	1·856	4	4	7·38	++

This initial high plasma viscosity value of 2·524 cs. was much higher than would have been expected from the patient's own expressed opinion concerning the degree of her general upset and from the severity of the local lesions in the throat. It lends support to the hypothesis that the erythema nodosum is part of a excessively great reaction to a primary stimulus. This hypothesis would also explain why the viscosity remained high long after the primary stimulus had ceased. The degree of the reaction is also shown by an abnormal gold flocculation test persisting for three months after the skin lesion had cleared.

OSTEO-ARTHRITIS.

Name	No.	PCV.	PLASMA VISC.	Wintrobe E.S.R		Total Plas. Prot.	Gold Floc	Remarks
				Ord.	Cor.			
		%	cs.	mm/	1 hr.	g. %		
(A) <u>Females.</u>								
G.W.	1	47.7	1.867	-	-	-	-	
R.T.	2	42.0	2.071	-	-	-	-	3/2/47
		44.4	1.979	-	-	6.66	-	28/2/47
M.M.	3	46.8	2.003	-	-	-	-	
E.K.	4	47.4	1.890	-	-	7.20	-	
E.L.	5	42.2	1.984	-	-	7.41	-	
I.S.	6	47.7	1.965	5	11	7.52	-	
M.S.	7	41.4	2.056	24	23	7.78	-	
F.S.	8	42.2	1.980	17	17	7.81	-	
A.F.	9	43.6	1.922	-	-	7.02	-	
K.M.	10	37.9	1.871	10	5	7.45	-	
C.S.	11	43.8	1.753	3	5	6.66	-	4/7/47
		48.0	1.755	1	7	-	-	6/1/47
I.M.	12	43.1	1.779	5	6	6.88	-	
E.T.	13	41.1	1.928	13	12	6.88	-	
M.A.	14	42.9	1.867	5	6	7.60	0	
V.M.	15	45.6	2.011	2	5	7.67	+	
M.J.	16	39.3	2.049	42	37	7.06	0	13/2/48
		40.6	2.041	-	-	7.13	0	20/5/48
D.B.	17	-	1.688	13	-	6.37	0	
E.H.	18	33.7	2.012	55	37	7.52	2+	
M.T.	19	43.8	1.862	8	9	7.06	0	
A.G.	20	41.4	1.767	9	9	7.16	0	
D.W.	21	39.2	1.704	20	16	-	-	
I.P.	22	37.6	2.224	45	37	8.17	-	
E.S.	23	39.2	1.853	5	3	7.31	0	
E.B.	24	43.1	1.844	8	10	7.27	0	
G.L.	25	40.0	1.866	10	8	7.49	0	
(B) <u>Males.</u>								
A.S.	1	48.0	1.781	-	-	-	-	
T.R.	2	-	1.931	3	-	-	-	
H.F.	3	46.6	1.889	8	8	7.45	-	
J.M.	4	43.4	1.938	20	16	7.02	0	10/2/48
		39.3	2.001	-	-	6.95	0	14/4/48
W.C.	5	48.6	1.908	9	11	7.31	0	
E.D.	6	50.	1.923	-	-	-	-	
T.D.	7	39.3	1.672	6	0	6.30	0	

Case No. 23

Chronic hypertrophic osteo-arthritis.

This patient had injured his elbow at work several years before he attended the rheumatism clinic, complaining of pain in his right elbow and limitation of all its movements.

There was marked periarticular thickening of the joint, and some crepitus. All movements were limited, especially pronation and supination. Skiagrams of the joint showed the changes of an advanced stage of chronic hypertrophic osteo-arthritis. No other abnormality was detected by a general examination.

His laboratory results were:-

Plasma viscosity	=	1.889 cs.
Blood haematocrit	=	46.6 %
Corrected Wintrobe ESR.	=	8 mm. in 1st. hour
Total Plasma Protein	=	7.45 g./100 ml.

Case No. 24

Chronic Hypertrophic Osteo-arthritis.

This female patient, aged 50 years, had had no illnesses in her life and would not admit to any injury. She complained of pain and stiffness in both knees, of 6 weeks duration.

On examination, there was marked periarticular thickening of both knees, with considerable quadriceps wasting. There was no increased local heat and no synovitis. Her fingers showed Heberden's nodes. Skiagrams of the knees showed the appearances typical of chronic hypertrophic osteo-arthritis.

No other abnormality could be detected.

Her laboratory results were:-

Plasma viscosity	=	1.871 cs.
Blood haematocrit	=	37.9 %
Wintrobe ESR.	=	10 mm. in 1st hour
Corrected Wintrobe ESR.	=	5 " " " "
Total plasma protein	=	7.45 g./100 ml.

Case No. 25

Osteo-arthritis (with high blood pressure)

This man, aged 64 years, had complained of pains in his back for 3 years and this pain had been slowly increasing; for 1 year he had pains in his legs, present only after walking. His right shoulder and wrist were stiff.

On examination, apart from the locomotor system, the only abnormality detected was a blood pressure of 160/100. The left hip appeared to be stiff; the right shoulder and wrist were stiff and swollen; there was marked kyphosis of the spine; the hands were normal.

Skiagrams:- Osteo-arthritic changes were present in both wrists. There was gross abnormality of the head of the left femur either due to old injury or Perthes' disease. There were gross arthritic changes in the lumbar and dorsal spine.

PCV.	PLASMA VISC.	Wintrobe ESR.		Plasma protein				Gold Floc.	Serum Alkaline Phosphatase
		Ord.	Cor.	Total	Alb.	Glob	Fibr		
%	cs.	mm/ 1 hr		g./100 ml.					un./100 ml
45.8	2.052	7.5	6	6.1	3.5	2.21	0.39	o	7.5

This case is an example of the association of an increased plasma viscosity value with osteo-arthritis plus hypertension. The hypertension appears to be the factor determining this rise as similar plasma viscosity results were seen in other subjects in whom the hypertension was the only pathology.

FIBROSITIS and MYOSITIS.

Name	No.	PCV.	PLASMA VISC.	Wintrobe E. S. R.		Total Plas. Prot.	Gold Floc	
				Ord.	Cor.			
		%	cs.	mm/	1 hr.	%		
(A) <u>Females.</u>								
S.F.	1	37.8	1.701	6	1	6.44	0	
G.J.	2	38.7	1.717	6	3	6.59	0	
M.P.	3	44.3	1.723	3	5	-	-	
J.M.	4	42.8	1.730	2	3	6.91	-	
C.S.	5	47.8	1.755	-	-	-	-	
M.H.	6	46.5	1.772	1	5	6.55	0	
L.C.	7	44.4	1.825	5	7	6.98	0	
F.M.	8	38.5	1.840	14	10	6.77	0	
S.S.	9	45.2	1.843	4	7	7.10	-	
S.M.	10	41.9	1.875	9	9	7.24	0	
S.P.	11	37.8	1.895	18	13	6.77	+	
F.H.	12	-	1.897	-	-	7.24	0	
L.S.	13	42.2	1.904	12	12	7.52	0	
V.T.	14	39.9	1.925	11	9	7.45	-	
M.R.	15	45.6	1.965	12	16	-	-	
M.W.	16	48.8	1.974	1	7	7.50	-	
C.S.	17	40.9	2.139	24	22	8.28	+	
(B) <u>Males.</u>								
R.M.	1	47.4	1.796	3	3	6.44	0	
A.W.	2	47.6	1.827	1	1	6.95	0	
W.D.	3	43.1	1.828	18	14	7.06	-	
J.D.	4	47.8	1.839	1	2	7.49	0	
J.H.	5	45.2	1.849	-	-	7.31	0	
W.H.	6	52.7	1.853	1	7	7.34	-	
G.P.	7	44.4	1.864	8	5	7.20	-	
R.M.	8	43.3	1.871	13	9	7.31	-	
R.B.	9	43.3	1.898	10	6	7.56	0	
R.C.	10	49.5	1.899	2	5	7.67	0	
W.B.	11	48.3	1.953	-	-	7.07	-	
F.W.	12	48.3	1.965	9	11	7.70	-	
G.A.	13	46.2	1.996	8	7	7.49	0	
J.T.	14	42.6	2.000	35	28	7.24	0	
R.C.	15	45.4	2.163	21	19	7.88	0	

Case No. 26 Non-articular Rheumatism - Acute Fibrositis.

At the age of 17 years this male patient had had a mild attack of acute rheumatic fever and four years later he had a severe recurrence which incapacitated him for two years. Since then he had suffered from fibrositis of the neck and shoulders of varying intensity. The subcutaneous tissue over these areas was indurated. Deeper, in the muscles, there were exquisitely tender nodules, especially along the insertion of the neck muscles into the skull.

Three days before the blood test he had an acute exacerbation of the fibrositis which caused the head to be held rigidly on the spine and any rotatory movement had to be confined to levels below the shoulders. Fortunately there were earlier and later blood tests for comparison, and it is obvious that the acute fibrositis has not caused a significant alteration in his plasma viscosity result.

Date	PCV.	PLASMA VISC.	Total Plasma Prot.	
	%	cs.	g. %	
21: 6:48	46.3	1.878	7.45	3 days after acute fibrositis begun.
17: 7:48	45.1	1.849	7.31	
12: 8:48	44.4	1.852	7.38	

Case No. 27

Acute Fibrositis.

One of my male laboratory technicians had suffered from severe fibrositis of the right neck and shoulder for 3 days when his plasma viscosity was estimated on 22:5:51. He had never suffered from this condition before.

Not only was the plasma viscosity value within the normal range but it was actually less than the results of two previous tests when he was in apparently good health and acted as a control subject for my series of normals.

Date	PCV.	PLASMA VISC.	Wintrobe ESR.		Total Plasma Protein	Gold Floc.
			Ord.	Cor.		
	%	cs.	mm/ 1 hr		g. %	
26: 9:50	49.2	1.880	1	3	7.74	o
24: 2:51	-	1.860	-	-	7.67	-
22: 5:51	47.8	1.839	1	1	7.49	o

ANKYLOSING SPONDYLITIS.

Name	No.	PCV.	PLASMA VISC.	Wintrobe E. S. R.		Total Plasma Prot.	Gold Floc	Remarks
				Ord.	Cor.			
		%	cs.	mm/	1 hr	g. %		
(a) <u>Male</u>								
F.B.	1	51.8	2.246	3	7	8.0	o	Early case
R.H.	2	33.9	2.164	10	0	7.34	+++	Early case
W.G.	3	45.7	2.225	28	26	8.21	+	
J.A.	4	43.6	2.106	-	-	7.92	+	
W.W.	5	40.3	1.990	-	-	6.84	-	
P.T.	6	43.0	1.811	10	6	6.62	o	7 yr. history
G.P.	7	45.1	1.896	10	8	7.20	o	4 yr. history
C.P.	8	39.	2.204	45	31	7.60	-	7 yr.; no treatment
C.H.	9	45.7	1.953	17	16	7.13	-	8 yr.; X-ray 3 yr. ago
A.W.	10	45.3	2.610	3	2	8.64	o	1 yr.; bamboo spine.
J.B.	11	39.5	2.115	36	23	7.81	o	
G.S.	12	44.	1.983	12	9	7.67	o	
J.H.	13	-	2.175	3	-	8.28	o	
I.T.	14	46.3	1.942	5	4	7.38	o	
T.C.	15	45.1	2.034	23	20	7.49	-	
F.D.	16	-	2.543	-	-	8.70	-	
W.B.	17	34.	2.512	54	30	8.86	-	
G.W.	18	34.3	2.163	55	31	7.42	-	10: 9
		34.	1.910	54	30	6.29	-	19: 9 On A.C.T.H.
		36.	1.857	42	23	7.3	-	17:10 " "
(b) <u>Female</u>								
M.C.	19	42.	2.345	36	36	7.85	o	
M.B.	20	30.	2.357	59	33	7.52	o	
K.E.	21	42.	1.851	4	4	7.13	o	?? very early case
T.H.	22	37.9	1.857	6	2	7.16	o	very early case
M.H.	23	-	2.052	20	-	7.99	o	
M.B.	24	36.	2.092	31	21	7.52	-	
E.L.	25	17.5	1.754	77	21	5.83	o	
O.W.	26	-	1.922	27	-	7.67	o	

Case No. 28 Ankylosing Spondylitis (with A.C.T.H. therapy)

This male patient was aged 21 years. He had had no previous illness and his family history was free from rheumatic disease.

He had an attack of ankylosing spondylitis of very rapid onset. It began three years before he came under the present observation. An ache and swelling in the lumbar region rapidly increased to an intensity which made work impossible; within 6 months his hips were stiffened and he was unable to walk. Deep X-ray treatment to the back and hips caused the pain to disappear and the joint stiffness to lessen. In March 1951, he began to complain of pain in the hips; this pain was only occasionally present at first but by June it was invariably produced by any movement; pains shooting down the thighs were frequently troublesome when he was dropping off to sleep. Finally he was unable to move his legs and thus became confined to bed.

He was admitted to hospital on 21:6:51 to receive another course of deep X-ray therapy. On examination, he was a pale young man who lay rigidly in bed. His lumbar and dorsal spines were fixed rigidly, but the cervical spine moved freely. Both hips were almost fixed, no movement being greater than 10° ; the left knee could flex through 22° and the right through 15° . Skiagrams showed an obliteration of the sacro-iliac joints; the hips had rarefaction of the bones, with diminution of the joint space;

Date	PCV.	PLASMA VISC.	Wintrobe ESR.		Plasma protein				Serum Urea
			Ord.	Cor.	Total	Alb.	Glob	Fibr	
	%	cs.	mm/ 1 hr		g./100 ml.				mg. %
10: 9:51	34.3	2.163	55	31	7.42	-	-	-	-
19: 9:51	34.	1.910	54	31	7.29	3.5	2.40	0.39	24
17:10:51	36.	1.857	42	23	7.3	4.4	2.5	0.4	18

the lumbar and dorsal spines showed changes in the bones, the intervertebral joints and the costo-vertebral joints, but no bambooing. The muscles of the legs and hips showed gross wasting.

The deep X-ray treatment was given from 25:6:51 to 15:8:51. There was no significant change and the patient remained confined to bed.

A.C.T.H. treatment was begun on 12:9:51. The drug was given in doses of 20 mg. per day in the form of a slow drip which took about 12-17 hours to introduce the pint of liquid intravenously. In this manner a total of 640 mg. only had been given by 29:10:51. (7 x 20 mg. to 18:9:51, when dose was halved; 10 x 10 mg. to 30:9:51 ; 15 x 20 mg. to 17:10:51 ; 10 x 10 mg. to 29:10:51) The course was completed by 27 intramuscular injections of 10 mg. to 27:11:51 .

The response to this treatment was slow but this might have been expected from the severity of the joint fixation and the poor muscular condition. Within a week it was noted that he was moving about in his bed, markedly freed from pain. The plasma viscosity had fallen significantly in nine days, to within the

normal range, while the ESR persisted unchanged. Increased flexion of the dorsal spine was present by 2:10:51. He took his first assisted steps on 5:10:51 and walked unaided on 10:10:51.

Further improvement followed when the ground gained was consolidated by physiotherapy. When he went home on 12:12:51, he was walking with the aid of sticks; he was completely independent for the toilet, shaving, etc. He was far from cured, however. The adjective "slow" applied to this progress was used only when comparison was made with the dramatic response of the cases of rheumatoid arthritis.

Case No. 29

Ankylosing Spondylitis.

This young man had a rotation strain of his right knee, with considerable effusion in 1939; a right external meniscectomy was performed six months later. He then required treatment for an effusion of the left knee. The hips, shoulders, and later the spine* became stiff; the spine had been stiff for 3 to 4 years at the time when the plasma viscosity was measured.

On examination, on 3:4:47 the locomotor system alone was found to be abnormal. The knees showed a flexion deformity of 20° , which he could straighten on standing; there was gross wasting of the thigh muscles and gross effusion of both knees. The ankle movements were normal. Both hips had a 50% loss of flexion, no external rotation, and 20° internal rotation. The left elbow and shoulder movements were considerably restricted; the right joints were less affected. The spine had some loss of the lumbar curve and a slight prominence of the thoracic curve; it was rigid up to the second dorsal vertebra.

Skiagrams showed an ankylosing spondylitis of the sacro-iliac joints plus a general decalcification of the spine; there was decreased joint space in the hips and knees.

Treatment had consisted recently of injections of lactic acid to the hips and knees, but with no obvious benefit.

Date	PCV.	PLASMA VISC.	Wintrobe ESR.		Plasma Total Protein	Gold Floc.
			Ord. Cor.			
	%	cs.	mm/1 hr		g. %	
1: 9:47	40.1	3.021	47	35	10.12	++

This viscosity value was unusually high for this disease. The differential diagnosis from rheumatoid arthritis was assisted by the relative low gold flocculation result; in rheumatoid arthritis a plasma viscosity of this extreme height would almost certainly be associated with a 4+ or 5+ result.

GOUT

Name	S	No.	Date	PCV.	PLASMA VISC.	Wintrobe E. S. R.		Total Plas. Prot.	Gold Floc	Remarks
						Ord.	Cor.			
				%	cs.	mm/	1 hr	%		
M. W.	F	1	7: 7	41.0	2.392	49	47	8.22	-	
			11: 7	42.4	2.469	-	-	8.39	-	
			28: 7	41.8	2.302	31	31	7.60	-	
			1: 9	40.4	2.186	49	46	7.56	-	
			6:10	38.8	2.443	48	41	8.38	o	
			10:11	40.0	2.356	43	39	8.10	+	
			7: 4	40.8	2.485	47	45	8.10	o	Uric acid=3.6 mg%
			28: 1	41.1	2.286	47	45	8.14	o	
A. L.	F	2	12: 3	47.5	2.096	9	15	7.8	-	
J. P.	M	3	27: 3	43.4	2.058	-	-	7.64	-	
A. F.	F	4	2: 7	43.8	1.903	5	7	7.88	-	
E. J.	F	5	9: 7	42.2	1.898	-	-	6.98	-	
J. K.	M	6	17: 7	48.8	1.775	-	-	7.13	-	Uric acid = 3.6 mg.
P. C.	F	7	1: 8	43.7	1.965	-	-	7.49	-	
M. C.	F	8	15:10	40.3	2.137	-	-	7.67	o	Uric acid = 4.4 mg.
R. O.	M	9	11:12	45.1	2.122	36	33	7.45	o	
B. S.	F	10	15:12	43.3	2.164	21	23	8.06	o	Uric acid = 3.8 mg.
E. R.	F	11	20:12	45.1	2.159	25	29	7.88	+	
J. W.	F	12	15: 4	40.4	2.325	-	-	8.06	o	Uric acid = 7.3 mg.
			22: 4	36.9	2.092	-	-	7.34	o	
E. R.	M	13	16: 4	-	1.929	10	-	7.34	-	Uric acid = 5.6 mg.
A. D.	M	14	1: 7	45.2	1.936	15	13	6.62	5+	Uric acid = 6.4 mg.
A. P.	F	15	14: 3	42.0	2.147	-	-	-	-	Uric acid = 2.8 mg.
M. A.	F	16			2.245			7.60	2+	Uric acid = 7.8 mg.

EPITUBERCULOSIS : PRIMARY TUBERCULOUS COMPLEX.

Name	No	S	Date	PCV.	PLASMA VISC.	Wintrobe ESR.		Plasma Total Protein	Gold Floc.	
						Ord.	Cor.			
				%	cs.	mm/	1 hr	g. %		
R. L.	1	M	19: 3	38.5	2.150	30	18	7.96	+	
			17: 5	38.6	2.066	25	14	7.74	o	
			13: 6	38.	2.094	21	10	7.69	o	
			30: 6	41.	2.122	20	13	7.96	+	
			13: 7	38.7	1.955	24	13	7.56	o	
			27: 8	37.0	1.897	24	13	-	-	
			26: 9	37.0	1.796	14	3	6.73	-	
			28:11	40.	1.791	11	5	6.70	-	
R. G.	2	M	25: 4	35.	2.073	48	26	6.62	o	
			5: 5	34.4	2.133	49	26	7.27	o	
			21: 5	40.	2.214	25	16	8.21	+	
			4: 6	38.	2.737	21	10	7.67	+	
			18: 6	38.	2.035	31	18	7.67	+	
			9: 7	39.	1.966	16	7	7.27	+	
J. W.	3	F	14: 6	39.	2.432	23	19	7.85	-	
			28: 6	39.	1.972	15	12	7.63	o	
			26: 7	42.	1.963	13	13	7.78	o	
D. D.	4	M	12: 7	42.0	1.912	7	3	7.49	-	
B. H.	5	M	21: 8	-	2.119	-	-	7.74	-	
			26: 9	42.2	2.081	15	10	7.49	-	
P. C.	6	M	6: 9	40.0	1.919	41	29	7.13	-	
			11:10	35.0	1.689	6	0	6.41	-	
L. S.	7	F	26: 9	39.2	2.011	15	11	7.52	-	
			16:10	39.	1.884	15	11	6.95	-	
			31:10	40.	2.025	9	7	7.67	-	
			28:11	40.	1.915	15	13	7.27	-	
B. P.	8	M	13:10	38.	1.887	8	0	6.98	-	
			4:12	40.0	1.867	8	2	7.31	-	
N. D.	9	M	5:11	38.	1.678	5	0	6.08	-	
T. F.	10	M	7:11	39.	1.963	15	6	7.52	-	
T. D.	11	M	29:10	38.0	1.888	23	12	7.13	-	
			22:11	37.0	1.828	19	7	6.80	-	
C. T.	12	F	4:12	36.1	1.940	22	14	7.49	-	
R. B.	13	F	4:12	41.0	2.016	21	20	7.38	-	
E. L.	14	F	7: 1	44.	2.120	30	34	7.81	-	
J. G.	15	F	6:11	37.6	2.097	35	27	7.31	-	
			4:12	37.4	1.893	20	15	7.38	-	

PULMONARY TUBERCULOSIS

Name	No	S	Date	P. C. V.		PLASMA VISC.		Max.	Total	Remarks
				Cit.	P+A.	Cor.	P+A	Cit.		
				%		cs.		ESR.	%	
								$\frac{\text{cm}}{\text{sec}} \times 10^{-4}$		
H. A.	1	M	18:11	30.0	39.0	1.663	2.063	2.9	7.21	p
			6: 5	29.5	39.7	1.738	2.297	6.9	6.71	s
			25: 7	29.9	40.5	1.866	2.476	7.8	7.18	s
			4: 8	28.2	-	1.681	-	14.3	6.34	s
			17: 8	30.4	-	1.744	2.236	9.7	7.59	p
J. B.	2	M	9:11	35.3	45.5	1.707	2.279	6.4	8.54	p
			4: 8	34.6	-	1.788	-	12.2	7.03	s
A. C.	3	M	3: 7	29.0	40.0	1.743	2.324	9.2	5.58	s
			11: 7	30.0	40.0	1.806	2.508	14.1	7.19	p
			18: 7	33.0	-	1.733	2.287	5.7	7.24	p
R. C.	4	M	21:12	20.0	-	1.553	1.868	0.9	5.30	p
W. E.	5	M	2:12	37.0	-	1.692	-	3.8	8.22	p
			4: 7	40.0	52.0	1.642	2.159	1.5	7.84	s
A. E.	6	F	29:12	29.0	-	1.748	2.340	9.6	8.23	p
			31:12	28.6	-	1.742	-	9.8	7.32	s
			5: 8	32.0	-	1.836	2.500	6.9	8.10	p
			9: 8	30.0	-	1.770	2.362	16.7	8.16	p
A. G.	7	F	5: 8	31.8	-	1.708	-	7.4	7.46	s
J. G.	8	F	5: 8	29.6	-	1.714	-	10.0	7.44	s
F. H.	9	M	8: 8	32.4	-	1.767	2.371	10.4	7.18	p
J. L.	10	M	13: 9	31.0	39.8	1.702	2.118	17.5	-	pleural effusion
			23: 9	29.2	39.0	1.783	2.568	15.0	6.44	2 pts. aspir.
			12:10	28.7	38.2	1.784	2.383	21.1	7.03	1 pt. aspirated.
			4:11	28.0	35.9	1.759	2.390	22.3	6.82	1 pt. aspirated
			5: 1	29.2	-	1.870	-	33.3	7.64	p
			1: 2	29.0	-	1.886	2.631	33.7	7.54	p
			27: 3	29.0	-	1.943	2.723	41.4	7.94	p
			27: 3	26.9	-	1.920	2.669	33.3	-	
			17: 4	25.2	33.7	1.843	2.502	37.5	6.62	s
			19: 5	25.7	35.0	1.837	2.472	27.2	6.83	s
			4: 7	26.3	35.6	1.908	2.715	28.9	7.36	s
			14: 8	24.8	-	1.816	2.416	23.8	7.04	p
										fluid still present in pleura
L. J.	11	M	23:12	32.4	-	1.875	2.639	19.0	8.22	p
			12: 1	34.2	-	1.690	2.193	5.3	7.92	p
			24: 7	31.3	41.2	1.563	1.893	1.9	6.99	p
M. R.	12	F	4:12	26.0	34.3	1.663	2.085	25.0	6.44	p
			31: 1	25.7	-	1.720	2.260	13.0	6.90	p
			22: 2	23.8	-	1.738	2.269	9.2	7.11	p
			11: 8	27.5	-	1.715	2.292	9.3	7.44	p

died 19/5/45

pleurisy

(Decay-died 23/12)

Chronic case, who worked on farm.

Chronic disease
(in two sisters, ambulant.pleural effusion
2 pts. aspir.
1 pt. aspirated.
1 pt. aspiratedfluid still
present in pleura

Name	No	S	Date	P. C. V.		PLASMA VISC.		Max.	Total	Remarks
				Cit.	P+A.	Cor.	P+A	Cit.		
				%		Citr.	Oxal.	ESR.	%	
						cs.		cm./sec. $\times 10^{-4}$		
J. H.	13	M	7: 4	35.7	46.7	1.614	2.032	2.3	7.79 s	X-ray negative.
			25: 5	34.9	46.0	1.666	2.070	2.9	7.11 s	
			31: 5	33.5	-	1.647	-	3.3	7.29 s	
			3: 7	33.4	44.7	1.603	2.037	3.3	6.87 s	still working. X-ray abnormal. 15 months later.
			7: 8	32.0	-	1.549	1.900	2.3	7.30 p	
			13:11	32.0	-	1.503	-	1.1	-	
D. W.	14	M	27: 5	26.5	36.0	1.819	2.479	27.8	6.14 s	Test done 5 hrs. after spontan. pneumothorax.
			29: 5	28.4	38.5	1.910	2.765	44.2	6.66 s	
			30: 5	27.3	-	1.884	-	57.5	6.45 s	
			31: 5	27.6	-	1.891	-	61.1	6.64 s	decay begun
			1: 6	25.3	-	1.869	-	88.9	6.62 s	
			2: 6	25.5	-	1.893	-	74.4	6.55 s	
			1: 7	25.5	34.0	1.720	2.239	12.5	5.93 s	died 8/9/44
			10: 7	25.7	35.4	1.679	2.193	8.6	6.33 p	
			18: 7	26.4	36.1	1.663	2.193	3.7	6.30 p	
			2: 8	26.5	-	1.660	-	3.7	5.68 s	died 8/9/44
			12: 8	25.4	-	1.580	-	4.4	4.90 s	
			18: 8	26.5	-	1.599	-	1.6	5.16 s	
M. S.	15	F	21: 2	28.6	-	1.650	2.105	3.9	6.95 p	1944
			8: 1	24.3	-	1.745	-	9.8	-	1946 Decay
			25: 2	15.8	-	1.488	-	3.8	-	died 25/2/46
J. P.	16	M	15: 9	39.0	48.5	1.838	2.312	7.5	6.89 s	rapid decay
			28: 9	35.7	45.8	1.644	2.073	4.3	7.10 p	
			3:11	36.9	-	1.558	-	2.0	6.97 s	
N. R.	17	M	30:10	24.1	33.4	2.044	3.050	42.5	8.91 p	Rapid course in mongol, with decay. died 29/1/44
			10:11	24.3	32.9	2.050	3.107	62.5	9.03 p	
			29:12	23.5	-	2.078	3.144	43.8	8.67 p	
			20: 1	22.7	-	1.755	2.325	6.4	6.50 p	
W. L.	18	M	30: 5	23.0	31.0	1.593	1.930	5.8	4.99 s	died 13/1/45
			20: 7	24.7	34.0	1.519	1.856	0.2	5.51 p	
			2: 8	23.8	-	1.564	-	0.6	5.25 s	
			12: 8	24.2	-	1.627	-	1.9	5.52 s	
			18: 8	24.3	-	1.597	-	1.3	-	
G. J.	19	M	13: 3	32.5	-	1.835	2.533	16.2	7.61 p	One lobe only affected
			16: 3	30.2	-	1.747	2.300	9.8	7.42 p	
			3: 5	31.8	42.5	1.802	2.422	15.8	7.76 s	
			5: 7	30.4	41.2	1.858	2.605	19.3	7.08 s	recovered later.
			22: 7	27.5	-	1.877	-	21.9	6.35 s	
E. S.	20	F	8: 3	26.3	-	1.783	2.383	8.3	7.48 p	died 24/3
			21: 3	24.8	-	1.881	2.682	20.0	6.47 p	
A. S.	21	M	23: 8	19.1	-	1.572	-	6.3	-	
R. K.	22	M	39: 3	31.5	-	1.660	2.110	5.3	7.28 p	died after 2 yrs.
			5: 5	32.7	44.5	1.660	2.122	6.7	7.30 s	

Name	No	S	Date	PCV.		PLASMA VISC.		Max.	Total	Remarks.
				Cit.	P+A.	Cor.	P+A	Cit.		
						Citr.	Oxal.	ESR.	Prot.	
				%		cs.		$\frac{cm}{hr} \times 10^{-4}$	%	
A.N.	23	F	6: 7	31.6	41.8	1.559	1.892	0.6	6.62 s	not active
J.S.	24	M	15: 1	35.0	-	1.810	2.469	11.8	8.41 p	
			17: 1	32.2	-	1.875	2.589	19.4	8.32 p	
			20: 1	30.0	-	1.810	2.467	21.7	7.83 p	
			17: 2	31.1	-	1.587	1.984	8.6	6.94 p	
			14: 4	31.2	43.9	1.590	2.040	3.1	6.80 s	
			25: 7	32.0	-	1.608	-	4.4	-	still active
J.S.	25	M	29:12	31.5	-	1.812	-	10.4	8.08 p	
			31:12	31.1	-	1.793	-	13.5	7.74 s	
			7: 2	32.2	43.3	1.859	2.624	12.2	7.77 s	
			4: 8	31.5	-	1.827	-	25.9	7.49 s	died 2 yrs. later
E.T.	26	F	24: 4	25.6	34.2	2.030	2.885	33.3	7.97 s	
			25: 4	24.3	31.6	1.995	2.737	30.6	7.84 s	
			27: 4	24.0	31.1	1.950	2.807	37.0	8.32 s	
			4: 5	21.6	29.5	2.010	2.760	33.3	7.38 p	
			12: 5	20.2	27.3	2.092	3.078	30.5	8.07 s	decay begins.
			24: 5	18.0	24.0	1.847	2.501	12.8	7.31 s	died 5/7/44
M.U.	27	F	3: 2	27.4	-	1.790	2.511	18.3	7.15 p	
			14: 2	22.4	-	1.707	2.188	32.7	6.20 p	
			25: 2	24.7	-	1.787	2.357	20.0	7.18 p	
			7: 8	25.7	-	1.776	2.342	8.3	6.77 p	
			21: 8	30.6	-	1.720	-	5.2	6.45 s	
D.W.	28	M	9: 8	23.0	-	1.700	2.135	11.3	6.28 p	
			15: 8	21.0	-	1.715	2.220	13.0	6.35 p	died 6/9/44
E.M.	29	M	1: 6	34.8	-	1.796	-	11.9	7.08 s	died 18 mnths.
J.H.	30	M	6:11	27.7	38.1	1.777	2.547	14.9	8.12 p	later.
K.J.	31	F	23:10	31.2	42.3	1.540	1.962	1.4	7.78 p	Pleural effusion
R.P.	32	M	27:10	24.7	-	1.708	-	15.3	7.01 p	" "
C.H.	33	M	13:11	27.2	38.7	1.725	2.414	13.1	7.52 p	" "
G.A.	34	M	17:11	32.7	45.7	1.750	2.549	15.2	7.48 p	" "
D.S.	35	M	9:12	27.8	39.0	1.689	2.318	11.1	7.64 p	" "
K.S.	36	M	27:12	27.9	-	1.675	-	9.5	-	" "
E.Y.	37	F	30: 1	30.7	-	1.685	-	18.6	-	" "
J.S.	38	F	3: 7	27.5	37.7	1.643	2.139	6.4	7.06 p	" "
			12: 7	-	38.3	-	2.163	-	8.03 p	
L.R.	39	M	10: 8	-	43.0	-	1.889	-	7.99 p	3 mnth effusion
D.B.	40	F	13: 8	-	39.7	-	1.824	-	7.34 p	(effusion present in May, now gone.

Name	No	S	Date	PCV.		PLASMA VISC.		Max.	Total	Remarks.
				Cit.	P+A.	Cor.	P+A	Cit.		
				%			cs.	cm/sec $\times 10^{-4}$	%	
D.W.	41	M	6: 6	34.0	-	1.445	-	4.0	-	inactive.
G.G.	42	M	4: 6	32.7	-	1.440	-	2.2	-	doubtful activity
A.B.	43	M	4:10	32.3	-	1.632	-	6.7	-	artif. A.P.
M.A.	44	F	10: 2	25.7	-	1.553	-	0.6	-	inactive.
D.B.	45	M	14: 4	-	29.2	1.789	-	17.7	-	
M.B.	46	F	8: 7	21.4	28.1	1.818	2.483	22.5	6.92 s	
N.O.	47	F	12: 7	33.1	44.2	1.568	2.035	2.7	7.99 p	
G.A.	48	F	3: 3	34.3	-	1.550	-	10.2	-	? asthma ? tb.
			9: 3	33.8	-	1.533	1.894	6.2	6.91 p	
J.D.	49	F	5: 4	29.5	39.0	1.484	1.792	1.6	7.02 p	? activity
L.B.	50	M	13: 5	31.2	43.9	1.777	2.609	18.8	8.03 p	
D.M.	51	M	31:10	31.4	43.1	1.671	2.284	11.0	7.85 p	
J.I.	52	M	4: 8	22.0	-	1.637	-	9.4	4.80 s	
			16: 8	23.8	-	1.675	2.160	13.5	6.29 p	
G.C.	53	M	6:12	31.3	-	1.596	-	7.1	6.61 p	
E.G.	54	F	2: 9	-	39.8	-	2.048	-	7.78 p	
			29: 9	-	39.1	-	2.097	-	7.86 p	
			16:10	27.6	39.2	1.576	2.047	4.2	7.88 p	
			5:12	-	41.4	-	2.132	-	8.60 p	

Name	S	No.	Date	PCV.	PLASMA VISC.	Wintrobe E. S. R.		Total Plas. Prot.	Gold Floc	Remarks.
						Ord.	Cor.			
				%	cs.	mm/	1 hr	%		
L.V.	F	55	21: 8	44.7	1.925	10	12	7.56	o	early case
M.M.	F	56	17: 6	41.7	1.969	17	17	7.70	o	recent effusion
W.M.	M	57	15: 7	-	2.333	35	-	8.57	o	
A.M.	F	58	3: 9	34.6	2.001	8	0	7.88	o	
M.H.	M	59	15: 9	42.2	1.946	19	13	7.49	-	early case
W.M.	M	60	24: 4	43.7	2.227	27	23	7.42	-	
J.A.	M	61	3: 9	48.4	1.959	10	11	7.49	o	
J.M.	M	62	12: 2	49.1	2.703	8	10	9.14	5+	koni-phthisis + rheumatoid arthritis
J.M.	M	63	10: 4	47.4	2.263	13	13	8.28	-	
			22: 5	46.1	2.121	9	8	8.32	-	
			24: 7	46.7	1.975	-	-	7.56	-	
			30:12	45.5	2.252	11	10	7.88	-	
C.C.	F	63	13: 4	38.3	2.320	48	40	7.92	o	B2, on R.P. in sanatorium.
			10: 5	38.1	2.398	43	36	8.35	o	
			22: 6	38.9	2.222	43	37	7.88	+	+streptomycin
			29: 7	42.3	2.173	36	36	7.68	+	+ PAS.
			26: 8	43.2	2.090	24	26	7.74	o	
			29: 9	41.1	1.977	25	24	7.34	+	
			2:11	38.2	2.139	32	26	7.78	o	
			1:12	42.2	2.177	24	24	7.99	2+	
			4: 1	40.8	2.040	36	34	7.74	2+	
			15: 2	42.4	2.119	40	40	7.52	2+	
			21: 3	40.7	1.965	20	19	7.38	+	discharged.
M.B.	F	64	30:11	40.9	2.143	28	26	7.99	o	A2, in sanatorium
			30:12	42.1	1.961	16	16	7.60	o	
			23: 1	40.7	1.868	20	18	7.16	0	quiescent now.
M.B.	F	65	6: 9	40.0	1.973	40	36	7.31	+	B2, in sanatorium
			4:10	40.3	2.047	-	-	7.34	-	
			2:11	40.5	2.092	32	28	7.67	o	
			30:11	39.2	1.883	24	20	7.06	2+	
			5: 1	40.6	1.793	20	18	6.66	+	discharged.
W.J.	M	66	18: 3	43.	2.075	14	10	-	o	in snatorium
			12: 4	44.5	2.059	29	25	7.70	o	
			16: 5	43.2	1.999	7	3	7.49	o	
			21: 6	43.2	1.913	16	11	7.13	o	
			25: 7	47.5	2.024	29	29	7.78	o	
			26: 8	46.4	2.146	20	19	8.03	+	
			29: 9	44.7	2.012	17	14	7.56	+	
			2:11	44.6	2.000	9	6	7.67	o	
			2:12	46.2	2.009	15	14	7.81	o	
			5: 1	45.6	1.915	-	-	7.02	+	
			12: 2	46.2	1.997	7	6	7.81	o	discharged.

Name	S	No.	Date	PCV.	PLASMA VISC.	Wintrobe E. S. R.		Total Plas. Prot.	Gold Floc	Remarks.
						Ord.	Cor.			
				%	cs.	mm/	1 hr	%		
S.F.	F	67	19:11	31.5	2.529	60	37	-	o	B2, in sanatorium
			22:12	35.0	2.312	50	36	-	o	
			11: 1	36.5	2.246	50	39	-	o	
			31: 1	41.0	2.341	38	36	-	o	
			15: 2	41.0	2.093	31	29	-	o	
			18: 3	41.5	2.045	16	13	-	o	
			12: 4	43.0	2.087	34	36	7.70	o	
			9: 5	38.1	2.354	44	36	8.14	o	
			8: 6	38.7	2.266	33	27	8.28	o	
			13: 7	37.7	2.059	30	23	7.98	o	
			26: 8	41.0	1.910	14	13	7.63	o	
			21: 9	41.3	1.968	16	15	7.85	o	
			20:10	40.3	1.907	15	13	7.33	o	
										discharged.
P.F.	F	68	8:12	36.3	2.725	36	26	-	-	B2, in sanatorium
			11: 1	39.5	2.437	43	38	-	+	
			31: 1	41.5	2.554	28	27	-	o	
			15: 2	39.8	2.247	43	39	-	o	
			18: 3	37.	2.259	16	10	-	o	
			13: 4	40.4	2.274	36	34	8.14	o	
W.H.	M	69	26: 8	44.	2.072	31	26	7.70	+	B2, in sanatorium
			29: 9	43.8	2.033	21	17	7.81	o	
			2:11	44.3	2.087	16	13	8.39	o	
			2:12	45.2	1.950	14	12	7.52	0	
			5: 1	47.3	1.927	6	6	7.02	+	
J.H.	F	70	7: 9	44.6	1.894	-	-	7.67	o	? activity, in a suspect. admitted to san.
			29: 9	40.6	1.783	4	2	6.98	o	
			1:12	42.5	1.911	8	9	7.78	+	
			7:12	41.9	1.835	10	10	6.84	-	
M.M.	F	71	18: 3	37.0	1.762	14	8	-	o	B2, in sanatorium
			4: 4	38.6	2.151	35	29	7.16	+	
			12: 4	35.5	2.249	46	34	7.09	+	
			9: 5	35.7	2.295	50	27	7.38	+	
			7: 6	39.1	2.280	17	14	7.88	o	
			5: 7	40.3	2.050	24	21	7.47	+	
			24: 8	42.3	1.864	10	10	7.04	o	
			22: 9	43.5	1.826	12	14	6.77	o	
			21:10	40.3	1.766	5	4	6.48	+	
			30:11	41.0	1.782	6	5	6.77	+	
D.M.	F	72	19:11	37.9	2.569	22	16	-	o	in sanatorium. discharged.
			22:12	38.5	2.417	16	12	-	o	
			28: 3	44.3	2.176	14	17	7.81	+	
			16: 5	43.5	2.038	3	5	7.81	+	
			21: 6	43.3	2.019	17	19	7.45	o	

Name	S	No.	Date	PCV.	PLASMA VISC.	Wintrobe E.S.R.		Total Plas. Prot.	Gold Floc	Remarks
						Ord.	Cor.			
				%	cs.	mm/	1 hr	%		
D.O.	M	73	12: 5	36.5	2.413	38	21	7.81	o	B2, in sanatorium
			8: 6	40.4	2.264	20	12	8.10	o	
			5: 7	41.4	2.113	18	12	7.86	o	
			24: 8	45.3	2.258	19	17	8.03	o	
			22: 9	45.1	1.989	12	10	7.45	o	
M.P.	F	74	18: 3	43.	2.224	18	19	-	+	B2, in sanatorium
			12: 4	45.	2.130	37	42	7.67	o	
			10: 5	42.1	2.355	34	34	7.88	+	
			7: 6	43.1	2.201	34	36	7.81	o	
			5: 7	41.3	2.053	36	35	7.33	o	
			25: 8	42.1	1.922	27	27	7.02	+	
			21: 9	41.6	1.983	29	29	7.20	3+	
J.S.	F	75	13: 4	40.0	2.155	35	32	7.60	o	B2, in sanatorium
			10: 5	41.2	2.035	21	20	8.06	o	
			8: 6	43.1	1.827	8	9	7.16	o	
			13: 7	42.5	1.841	13	13	7.00	o	
			26: 8	43.2	1.861	10	11	7.27	o	
			21: 9	42.9	1.821	7	8	7.20	0	
P.Y.	F	76	27: 6	39.7	2.385	45	40	7.73	o	A2, in sanatorium
			22: 7	41.1	2.196	44	42	7.87	o	
			26: 8	42.3	2.152	19	19	7.63	o	
			29: 9	41.5	1.968	15	14	7.74	o	
			3:11	40.4	1.879	10	8	7.52	+	
			1:12	42.4	1.965	15	15	7.63	+	
			4: 1	43.4	1.977	9	10	7.74	+	
			15: 2	43.2	2.000	4	5	7.92	+	
			23: 3	39.0	1.955	15	12	7.38	o	
			5: 5	40.2	1.977	9	7	-	o	
M.B.	F	77	6: 9	40.0	1.973	40	36	7.31	+	B2, in sanatorium
			4:10	40.3	2.047	-	-	7.34	-	
			2:11	40.5	2.092	32	28	7.67	o	
			30:11	39.2	1.883	24	20	7.06	2+	
			5: 1	40.4	1.793	20	18	6.66	+	
J.C.	M	78	25: 8	44.8	1.903	19	16	7.10	o	B2, in sanatorium
			21: 9	46.3	2.017	19	18	7.70	o	
			20:10	47.3	2.021	11	11	7.83	o	
W.J.	M	79	16: 5	38.2	2.095	30	18	7.85	+	B2, in sanatorium
			21: 6	40.6	2.006	34	25	7.42	-	
			25: 7	41.7	2.141	25	18	8.03	o	
W.K.	M	80	28: 5	44.3	1.880	8	6	7.02	o	B1, in sanatorium
			22: 6	43.7	1.866	14	10	6.73	o	
			22: 7	46.4	2.090	36	35	7.60	o	

Name	S	No.	Date	PCV.	PLASMA VISC.	Wintrobe E. S. R.		Total Plas. Prot.	Gold Floc	Remarks.
						Ord.	Cor.			
				%	cs.	mm/	1 hr	%		
N. L.	F	81	10: 5	40.4	2.328	22	20	8.42	o	B2, in sanatorium discharged.
			22: 6	42.2	2.192	12	12	8.28	o	
			29: 7	40.3	2.138	38	35	7.74	o	
			25: 8	40.2	2.011	26	23	7.58	o	
P. M.	F	82	12: 5	40.3	2.149	41	38	7.02	o	died
			7: 6	39.3	2.529	34	29	8.32	+	
			6: 7	39.7	2.468	48	43	8.10	2+	
D. R.	F	83	18: 1	41.8	2.063	23	23	-	o	pleural effusion A1
J. B.	F	84	20: 1	45.5	1.946	5	8	-	o	pleural effusion A2
A. T.	M	85	2: 4	41.3	2.617	27	20	7.56	o	on PAS therapy. B3
J. H.	M	86	4: 4	45.4	2.050	12	10	7.56	+	Ambulant, B2
G. L.	M	87	8: 6	46.9	2.184	16	16	8.21	o	forming effusion B2
S. H.	M	88	21: 6	46.4	1.786	9	8	6.84	o	on PAS therapy B2
A. H.	M	89	2: 7	44.6	1.907	15	13	7.13	-	pleural effusion A1
B. O.	M	90	27: 6	40.0	2.178	39	28	7.63	o	B2
T. O.	M	91	6: 7	37.1	1.902	6	0	7.20	o	
M. H.	M	92	13: 7	44.5	2.056	40	38	7.45	o	B1
L. M.	M	93	22: 7	48.	2.090	14	15	7.85	o	
P. W.	F	94	4: 1	34.6	2.081	50	35	-	+	
D. S.	M	95	21: 4	45.9	1.944	10	9	7.60	-	
D. E.	M	96	15: 7	44.0	2.351	20	17	8.06	0	B2, prior to strept- omycin.
J. T.	M	97	22: 7	43.1	2.108	30	24	7.38	2+	
J. F.	F	160	31: 5	42.0	2.012	26	26	7.85	-	admitted to san. B2
			30: 1	46.	2.103	25	32	7.85	0	
N. A.	F	161	28: 7	33.5	1.956	25	12	7.52	0	
			31: 8	34.	1.902	24	13	7.34	0	
F. S.	M	162	17: 8	44.6	1.967	9	7	7.20	o	
N. M.	F	163	3: 4	40.	1.833	13	11	7.34	o	A1, in sanatorium
			11: 5	41.	1.904	16	15	7.42	o	
			28: 5	38.	1.865	11	6	6.95	o	
			4: 6	38.	1.853	17	12	7.38	-	
B. F.	M	163	5: 4	41.	1.976	23	16	7.45	o	very early case
S. D.	F	164	29: 5	38.	2.638	24	18	7.88	o	

Name	S	No.	Date	PCV.	PLASMA VISC.	Wintrobe E. S. R.		Total Plas. Prot.	Gold Floc	Remarks.
						Ord.	Cor.			
				%	cs.	mm/	1 hr	%		
A. S.	M	98	26: 8	42.7	2.323	35	28	7.74	o	B1, in sanatorium on streptomycin
			29: 9	43.2	2.219	28	23	7.85	o	
			2:11	42.6	2.306	42	37	7.78	o	
			2:12	46.2	2.465	18	17	8.57	2+	
			5: 1	47.2	2.270	24	24	7.74	o	
			13: 2	47.0	2.402	14	14	8.24	o	
			15: 3	44.8	2.244	14	12	7.99	o	
			4: 5	45.3	2.126	12	11	7.60	+	PAS for 6 weeks
			6: 6	47.4	2.097	28	29	7.52	o	
			5: 7	49.4	2.205	4	7	7.72	o	
			18: 8	48.9	2.208	10	11	7.85	+	
			12:10	47.	2.050	23	23	7.49	-	
			20:11	46.3	2.017	16	15	7.34	o	
			21:12	47.0	1.983	16	16	7.16	+	
			31: 1	50.3	2.166	13	17	8.10	+	discharged to a convalescent home.
			12: 3	47.2	2.064	11	11	7.85	o	
E. B.	F	99	26: 1	45.2	2.502	8	12	-	o	B2, in sanatorium, on streptomycin. until 30:4
			10: 2	44.8	2.187	11	13	-	+	
			18: 3	48.	2.194	10	17	-	+	
			12: 4	45.6	2.174	12	16	7.34	o	
			9: 5	46.4	2.232	24	30	7.92	o	
			8: 6	45.5	2.047	18	22	7.56	o	
			5: 7	46.1	2.061	20	25	7.31	o	
			24: 8	44.5	2.181	36	40	7.54	o	
			22: 9	41.9	2.333	42	42	7.63	o	
			21:10	42.3	2.381	7	7	8.06	2+	
			30:11	46.0	2.292	33	40	8.03	o	
			30:12	45.3	2.295	22	27	7.96	2+	
			31: 1	42.8	2.249	36	37	7.67	+	
			1: 3	44.1	2.313	16	17	7.67	+	
			1: 5	45.8	2.353	4	8	8.10	o	
			1: 6	44.5	2.313	30	34	7.63	o	
			5: 7	45.0	2.331	7	10	7.54	o	
			18: 8	45.4	2.260	20	25	7.81	+	
			11:10	47.	2.326	17	23	7.92	o	
			20:11	45.3	2.338	19	23	7.99	+	
			21:12	48.7	2.398	4	11	7.99	+	
			31: 1	47.6	2.460	15	21	8.03	+	
			12: 3	43.8	2.510	6	8	7.81	o	
			5: 4	42.	2.558	4	4	7.67	o	
			10: 5	40.8	2.640	28	26	7.85	o	
			19: 6	35.	2.420	54	39	7.55	o	died on 5:9
			20: 8	29.1	2.328	60	32	7.56	-	

PULMONARY TUBERCULOSIS; a selected series of patients in whom the Westergren E.S.R. was low (under 10 mm/ 1st hour) yet with a clinical activity shown by tubercle bacilli being detected in the sputum within a fortnight of these tests.

The Wintrobe E.S.R. technique, with a correction for alteration in the packed-cell-volume from normal, allows for those instances where the E.S.R. was low because of a large PCV.

Name	S	No.	Date	PCV.	Plasma Visc.	Wintrobe E.S.R.		Total Plas. Prot.	Gold Floc	Remarks.
						Ord.	Cor.			
				%	cs.	mm/	1 hr	%		
J.M.	M	100	20:11	43.3	1.888	17	12	-	o	not included in statistics
			(3: 3	45.0	1.928	13	11	-	o)	
K.D.	M	101	24: 3	48.5	2.218	5	7	-	+	
B.B.	M	102	25: 3	43.7	1.833	8	5	-	o	
V.F.	M	103	25: 3	48.1	2.030	5	6	-	o	
J.H.	M	104	4: 4	45.4	2.050	12	10	7.56	+	
F.S.	M	105	8: 4	40.9	2.534	16	9	8.57	o	
A.B.	M	106	11: 4	51.0	1.991	5	9	7.52	o	
I.C.	M	107	21: 4	40.7	1.939	15	8	7.02	o	
C.P.	M	108	29: 4	46.4	1.830	11	10	6.77	o	
N.C.	M	109	29: 4	46.7	2.005	8	8	7.99	o	
R.K.	M	110	25: 5	48.6	1.968	3	5	7.24	o	not included in statistics.
			(27: 6	47.2	1.895	11	11	6.95	o	
			25: 7	48.7	1.915	8	10	7.52	o)	
W.K.	M	111	28: 5	44.3	1.880	8	5	7.02	o	not included in statistics.
			(22: 6	43.7	1.866	14	11	6.73	o	
			22: 7	48.	2.090	36	38	7.60	o)	
J.T.	M	112	9: 6	47.4	1.834	5	5	7.45	o	
D.H.	M	113	21: 6	43.3	1.933	14	10	7.31	o	
J.W.	M	114	22: 7	47.6	2.111	28	29	7.81	o	
J.C.	M	115	25: 8	44.8	1.905	19	19	7.06	o	not included in statistics.
			(21: 9	47.	2.017	19	19	7.70	o	
			20:10	47.	2.032	12	12	7.96	o)	
F.M.	M	116	2:11	47.1	1.990	3	3	7.81	o	
A.L.	M	117	11:11	45.	1.970	14	11	7.78	o	
A.M.	M	118	30:12	42.8	1.800	3	0	7.20	+	
J.P.	M	119	31: 1	47.4	1.951	3	4	7.31	o	
R.P.	M	120	31: 1	47.5	1.919	6	7	6.80	+	
G.B.	M	121	11: 2	46.2	1.830	6	5	7.02	o	
A.B.	M	123	10: 3	47.1	1.848	3	3	6.66	o	
C.A.	M	124	28: 4	48.	2.090	15	16	7.78	o	

Name	S	No.	Date	PCV. %	PLASMA VISC. cs.	Wintrobe E. S. R.		Total Plas. Prot. %	Gold Floc	Remarks.
						Ord.	Cor.			
						mm/	1 hr			
E. P.	M	125	16: 5	49.4	2.083	9	10	7.56	+	
R. A.	M	126	30: 5	56.3	1.957	1 1/2	9	7.13	+	
D. T.	M	127	2: 6	44.9	1.931	8	6	7.34	o	
D. E.	M	128	2: 6	46.3	1.947	4	3	7.67	o	
H. H.	M	129	30: 5	49.0	1.927	2	5	7.34	o	
S. H.	M	130	30: 5	45.5	2.078	10	9	7.63	o	
V. C.	M	131	8: 6	44.1	1.952	14	11	7.16	o	
J. B.	M	132	8: 6	47.6	2.114	14	15	8.03	o	
H. L.	M	133	8: 6	47.9	1.996	6	7	7.63	o	
R. H.	M	134	20: 6	49.1	1.890	1	3	7.13	o	
F. G.	M	135	6: 7	48.3	2.077	2	3	7.92	o	
F. W.	M	136	6: 7	50.1	2.062	5	8	7.63	o	
E. D.	M	137	7: 7	-	2.868	4	-	8.60	o	
S. M.	M	138	14: 7	52.8	2.026	3	8	7.31	o	
V. B.	M	139	14: 7	48.0	1.938	10	11	6.59	o	
W. W.	M	140	19: 7	46.3	2.203	8	7	8.10	o	
J. H.	M	141	25: 7	48.5	1.871	2	4	7.16	+	
C. G.	M	142	28: 7	45.1	2.029	17	13	7.13	o	
D. R.	M	143	28: 7	50.8	2.133	5	8	7.42	o	
P. S.	M	144	15: 8	50.0	1.984	4	7	7.45	o	
A. N.	M	145	16: 8	45.5	1.930	6	5	6.98	o	
D. G.	M	146	16: 8	42.8	2.088	12	7	7.45	o	
F. S.	M	147	17: 8	44.6	1.967	9	7	7.20	o	
A. B.	M	148	16: 8	48.8	2.134	5	7	7.42	o	
A. B.	M	149	17: 8	54.0	2.015	1 1/4	7	8.03	o	
G. C.	M	150	18: 8	45.4	2.260	20	19	7.81	+	
B. S.	M	151	2: 5	50.	2.007	5	8	7.24	o	
J. D.	F	152	15: 7	48.3	2.441	5	12	8.39	o	
E. B.	F	153	26: 1	45.2	2.502	8	12	-	o	
J. R.	F	154	18: 1	36.0	2.080	16	8	7.49	+	
B. O.	F	155	8: 6	44.7	2.098	12	15	7.49	o	
Q. M.	F	156	6: 7	43.1	2.154	9	11	8.03	3+	
A. J.	F	157	22: 7	43.1	1.898	6	8	6.91	o	
G. S.	F	158	28: 7	41.4	1.780	5	4	6.44	o	
A. M.	F	159	22: 8	42.7	2.120	16	17	7.92	+	

Case No. 30

Pulmonary Tuberculosis.

This female patient, aged 61 years, had complained of a pleural effusion in 1923, from which she made a good recovery with only scanty treatment. She remained well until 1944 when her cough returned; a skiagram of the chest at that time was considered to be of normal appearance. The cough persisted, she lost much weight during 1945-46, but managed a trip to America in 1947.

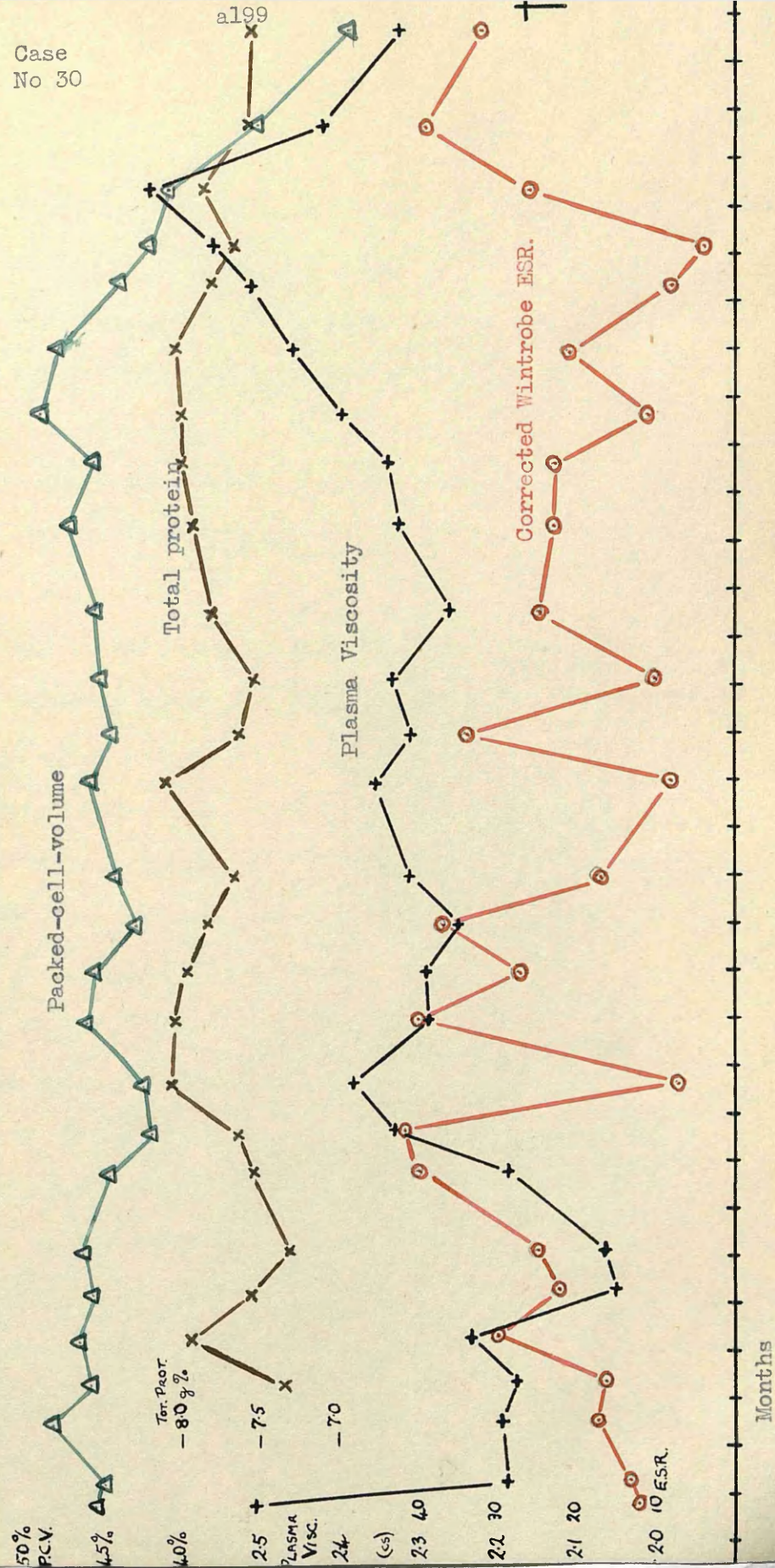
At the end of 1948 she became definitely ill. A skiagram in January 1949 revealed tuberculosis of both lungs, involving the right upper lobe and the left midzone; cavities were present in both affected parts. There were signs of toxæmia in the raised temperature, pulse rate, and loss of weight. The sputum contained tubercle bacilli in large numbers. At this time the plasma viscosity was markedly elevated, yet the ESR was within normal limits. (It was this particular finding which led to the special investigation of the plasma viscosity test in those patients who had a normal ESR in association with activity guaranteed by a positive sputum.)

Streptomycin was given in doses of 2 g. per day from 25:1:49 until 17:3:49, and then 1 g. per day until 30:4:49, to reach a total of 140 g. The clinical improvement was most dramatic - the temperature fell rapidly to normal, she felt much better, her appetite returned, and she put on a little weight. The cavity of

Date	PCV.	PLASMA VISC.	Wintrobe ESR. Ord. Cor.		Total Plasma Prot.	Gold Floc
	%	cs.	mm/ 1 hr		g. %	
26: 1:49	45.2	2.502	8	12	-	o
10: 2:49	44.8	2.187	11	13	-	+
18: 3:49	48.	2.194	10	17	-	+
12: 4:49	45.6	2.174	12	16	7.34	o
9: 5:49	46.4	2.232	24	30	7.92	o
8: 6:49	45.5	2.047	18	22	7.56	o
5: 7:49	46.1	2.061	20	25	7.31	o
24: 8:49	44.5	2.181	36	40	7.54	o
22: 9:49	41.9	2.333	42	42	7.63	o
21:10:49	42.3	2.381	7	7	8.06	++
30:11:49	46.0	2.292	33	40	8.03	o
30:12:49	45.3	2.295	22	27	7.96	**
31: 1:50	42.8	2.249	36	37	7.67	+
1: 3:50	44.1	2.313	16	17	7.67	+
1: 5:50	45.8	2.353	4	8	8.10	o
1: 6:50	44.5	2.313	30	34	7.63	o
5: 7:50	45.0	2.331	7	10	7.54	o
18: 8:50	45.4	2.260	20	25	7.81	+
11:10:50	47.	2.326	17	23	7.92	o
20:11:50	45.3	2.338	19	23	7.99	+
21:12:50	48.7	2.398	4	11	7.99	+
31: 1:51	47.6	2.460	15	21	8.03	+
12: 3:51	43.8	2.510	6	8	7.81	o
5: 4:51	42.	2.558	4	4	7.67	o
10: 5:51	40.8	2.640	28	26	7.85	o
19: 6:51	35.	2.420	54	39	7.55	o
20: 8:51	29.1	2.328	60	32	7.56	-
						died 5:9:51

of the left midzone was almost closed and that of the right apex had reduced to half its original size. This improvement in the lung and general conditions was accompanied by a decrease in the plasma viscosity; the ESR, in contrast, increased just as steadily. In June she was allowed up for an hour daily and this was increased to 2 hours in July 1949.

Case
No 30



On the 6th September 1949 she suddenly produced a temperature of 102.6°F; the evening temperatures persisted in this region until the end of the month and then gradually declined to the 99°F level. On the 4:8:49 the skiagram had shown the cavity at the right apex to have become blown up. It should be noted from the accompanying chart how the plasma viscosity (and ESR) had risen before the clinical worsening had become obvious by the increased temperature, etc.

There was little clinical or radiographic change noted throughout the next 12 months. The plasma viscosity maintained a plateau in which a central hump was associated with another temporary temperature rise. In this same period the ESR had large inexplicable fluctuations; to exclude the possibility of experimental error I made these ESR measurements in duplicate or triplicate on duplicate blood samples.

In the winter of 1950 she began to lose ground and the lung lesions began to spread. The skiagram of 21:3:51 noted gross cavitation of the upper and mid zones on the right side, with a fibrotic infiltration of the lower zone; there was infiltration of all zones on the left side. The plasma viscosity continued to rise as a result of the increasing reaction to this increasing toxin formation and absorption until the peak in May 1951; the inevitable fall of "terminal decay" set in and two more tests were

possible only before death ensued on 5th September 1951

The plasma viscosity test has been a reliable index of the pathological changes in this patient - the initial toxæmia, the improvement in response to streptomycin, the early reduction to a lower level which was maintained until there occurred the final spread which led to death. The ESR, on the other hand, had a most erratic course in which the changes were frequently directly opposed to that expected if the ESR was reflecting the alterations in the disease condition.

The positive gold flocculation tests following the administration of streptomycin should be noted. This association was not infrequent but in this case no P.A.S. was being given and the effect can be attributed solely to the streptomycin.

The results of this case also demonstrate the difference between the viscosity and total protein results. The protein changed approximately in parallel with the viscosity changes yet the protein changes were so small that seldom could any significance be attached to them.

Case No. 31

Pulmonary Tuberculosis.

This young woman was a Mass Radiography Unit pickup in Nov. 1948; an acute bronchopneumonic tuberculosis involved the whole of the left upper lobe and part of the left lower lobe. Her evening temperature was 102°F.

She was transferred to a Portsmouth hospital on 16:1:49, when the degree of toxicity attracted attention on admission. The evening temperature and pulse rate were 100°F and 110 per minute. Her sputum contained tubercle bacilli. Skiagrams showed continued active disease in the left lung where there had now appeared an upper left lobe cavity.

A pneumoperitoneum had been induced in her first hospital and this was continued with at Portsmouth. A left phrenic crush was made on 16:1:49.

Because there was no radiological or other improvement by April, streptomycin was given in 2 g. doses per day from 8:4:49 until 2:6:49 ; para-aminosalicylic acid was given in 18 g. doses per day from 14:6:49 until 25:10:49. By the end of 1949 the sputum was free from tubercle bacilli and there was some radiological evidence of clearing in the lungs. Thereafter her progress was slow and steady. She was discharged in April 1950. Her latest skiagram showed a slow absorption and hardening of the

Date	PCV.	PLASMA VISC.	Wintrobe ESR.		Plasma Total Prot.	Gold Floc.
			Ord.	Cor.		
	%	cs.	mm/	1 hr	g. %	
13: 4:49	38.3	2.320	48	40	7.92	o
10: 5:49	38.1	2.398	43	36	8.35	o
22: 6:49	38.9	2.222	43	37	7.88	+
29: 7:49	42.3	2.173	36	36	7.68	+
26: 8:49	43.2	2.090	24	26	7.74	o
29: 9:49	41.1	1.977	25	24	7.34	+
2:11:49	38.2	2.139	32	26	7.78	o
1:12:49	42.2	2.177	24	24	7.99	++
4: 1:50	40.8	2.040	36	34	7.74	++
15: 2:50	42.4	2.119	40	40	7.52	++
21: 3:50	40.7	1.965	20	19	7.38	+

of the lung infiltration, and an absence of the lung cavity. Her weight had increased by 20 lb.

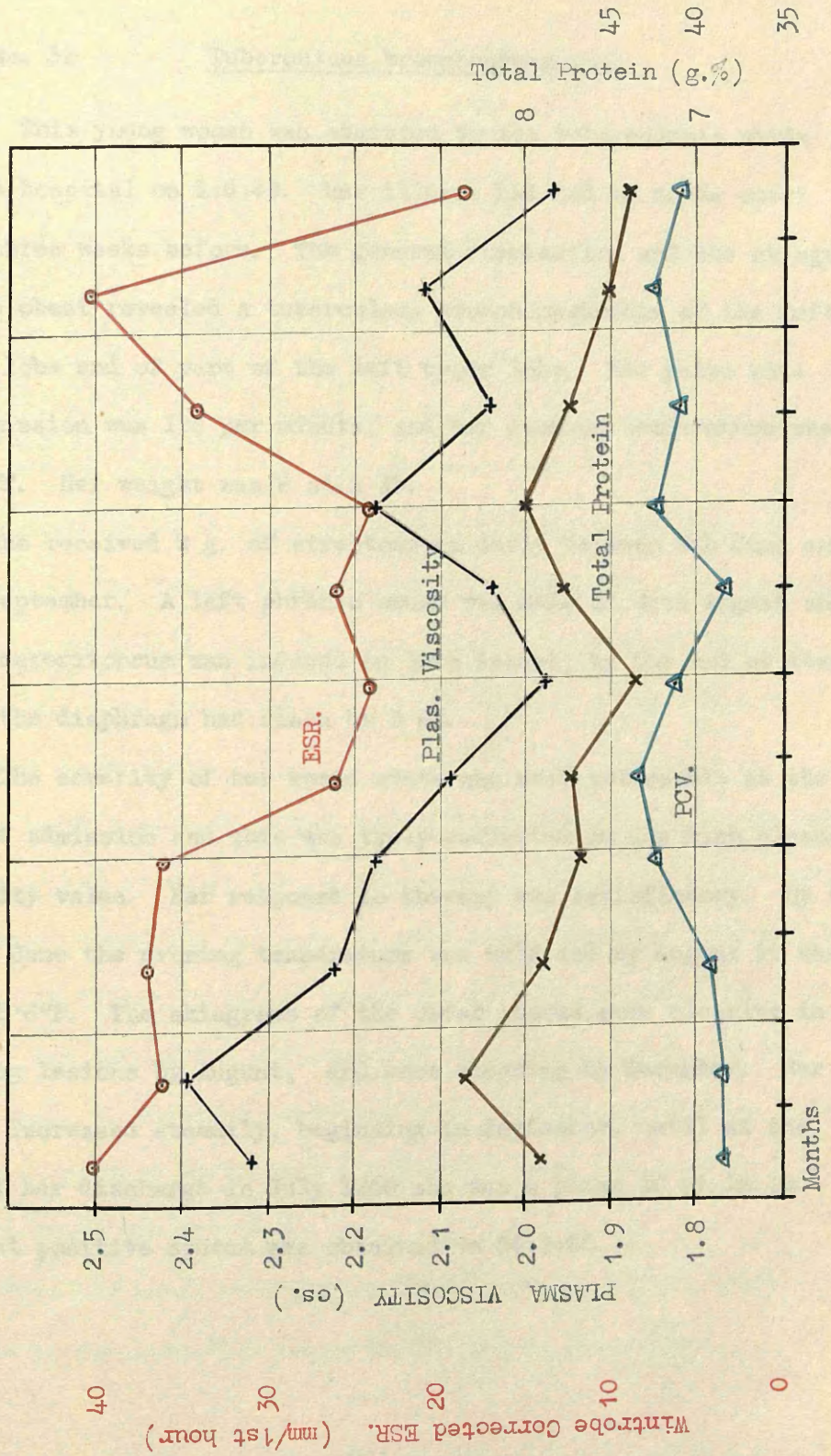
The rise in the plasma viscosity value in November 1949 followed closely on the stopping the PAS. and this rise may be related to a flare-up in a lesion which was being held in check by this drug. The later decrease was again in parallel with the clinical improvement. At the time of her discharge, the lung lesion had shown a remarkable improvement but it was still regarded as active; this clinical assessment had the support of the persisting high plasma viscosity and ESR values.

The positive gold flocculation tests should be noted.

Such findings were frequent during and following streptomycin therapy. In this instance the effect may be due to the P.A.S. also.

Case No. 31

Packed-cell-volume (%)



Case No. 32

Tuberculous bronchopneumonia.

This young woman was admitted to the tuberculosis wards of the hospital on 1:6:49. Her illness had had an acute onset only three weeks before. The general examination and the skiagrams of the chest revealed a tuberculous bronchopneumonia of the left lower lobe and of part of the left upper lobe. Her pulse rate at admission was 128 per minute, and her evening temperature was 100.8°F. Her weight was 8 st.2 lb.

She received 2 g. of streptomycin daily between 9th June and 20th September. A left phrenic crush was made on 4th August and a pneumoperitoneum was induced on 16th August; by the end of that month the diaphragm had risen by 5 cm.

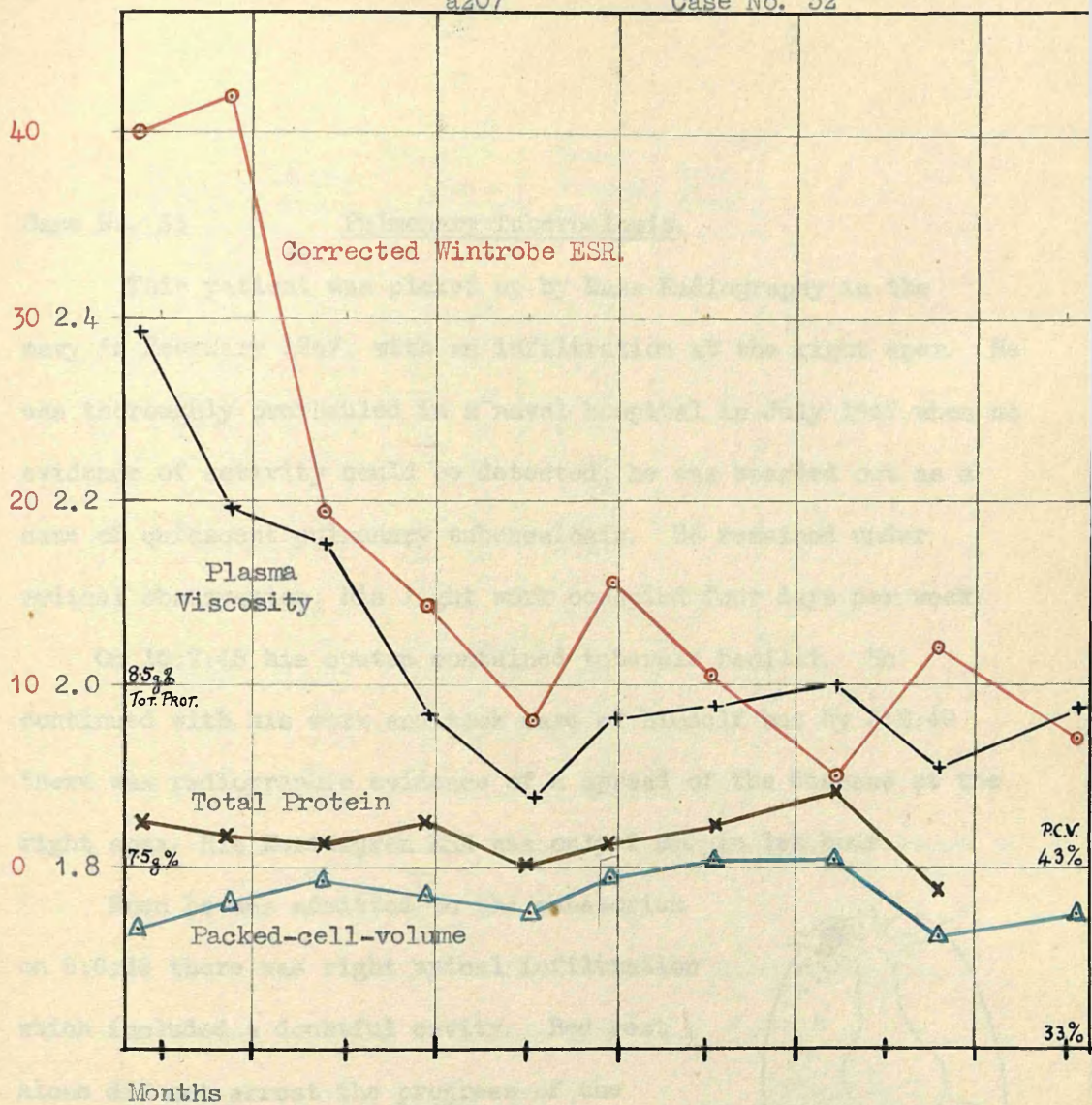
The severity of her toxic state was most noticeable at the time of admission and this was truly reflected in the high plasma viscosity value. Her response to therapy was satisfactory. By the end of June the evening temperature was 99°F and by August it was only 98.6°F. The skiagrams of the chest showed some clearing in the lung lesions by August, and more clearing by December. Her weight increased steadily, beginning in September, until at the time of her discharge in July 1950 she was a plump 10 st.12 lb. Her last positive sputum was obtained on 24:1:50.

Date	PCV.	PLASMA VISC.	Wintrobe ESR.		Total Plasma Prot.	Gold Floc
			Ord.	Cor.		
	%	cs.	mm/ 1 hr		g. %	
29: 6:49	39.7	2.385	45	40	7.75	o
22: 7:49	41.1	2.196	44	42	7.67	o
26: 8:49	42.3	2.152	19	19	7.63	o
29: 9:49	41.5	1.968	15	14	7.74	o
3:11:49	40.4	1.879	10	8	7.52	+
1:12:49	42.4	1.965	15	15	7.63	+
4: 1:50	43.4	1.977	9	10	7.74	+
15: 2:50	43.2	2.000	4	5	7.92	+
23: 3:50	39.0	1.955	15	12	7.38	o
5: 5:50	40.2	1.977	9	7	-	o

No explanation was ever reached definitely to explain the increase in the plasma viscosity again in December; the patient had had a head cold for a few days towards the end of November which might have been part of a small flare-up which was not otherwise detectable.

Plasma viscosity values raised to just above the upper limit of the normal zone has been a phenomenon encountered sufficiently frequently among the patients to make us hesitant to interpret the finding as certain proof of continued activity in the lung lesion; the air may act on the peritoneum as a minor irritant. On the other hand, it might be concluded that the pneumoperitoneum was unable to produce sufficient immobilization of the lungs to prevent toxin absorption.

Note how small were the variations in the plasma total protein as compared with those in the plasma viscosity.



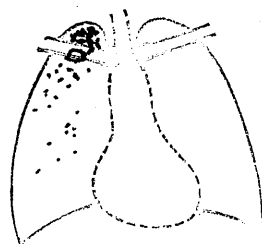
Case No. 33

Pulmonary Tuberculosis.

This patient was picked up by Mass Radiography in the navy in February 1947, with an infiltration at the right apex. He was thoroughly overhauled in a naval hospital in July 1947 when no evidence of activity could be detected; he was boarded out as a case of quiescent pulmonary tuberculosis. He remained under medical observation; his light work occupied four days per week.

On 15:7:48 his sputum contained tubercle bacilli. He continued with his work and took care of himself but by 3:2:49 there was radiographic evidence of a spread of the disease at the right apex. His Westergren ESR was only 2 mm. in 1st hour.

When he was admitted to the sanatorium on 8:6:49 there was right apical infiltration which included a doubtful cavity. Bed rest alone did not arrest the progress of the disease. A skiagram of 16:8:49 showed an invasion of the left mid zone and a cavity at the right apex of 3 cm. diameter.

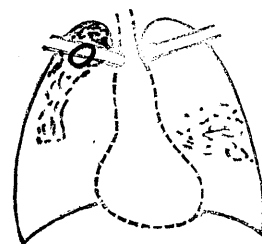


At this time, when the first plasma viscosity was soon to be made, the degree of toxæmia was estimated as of moderate severity. Streptomycin therapy was begun on 20:8:49 in doses of 1 g. daily for 42 days. The temperature returned to the normal

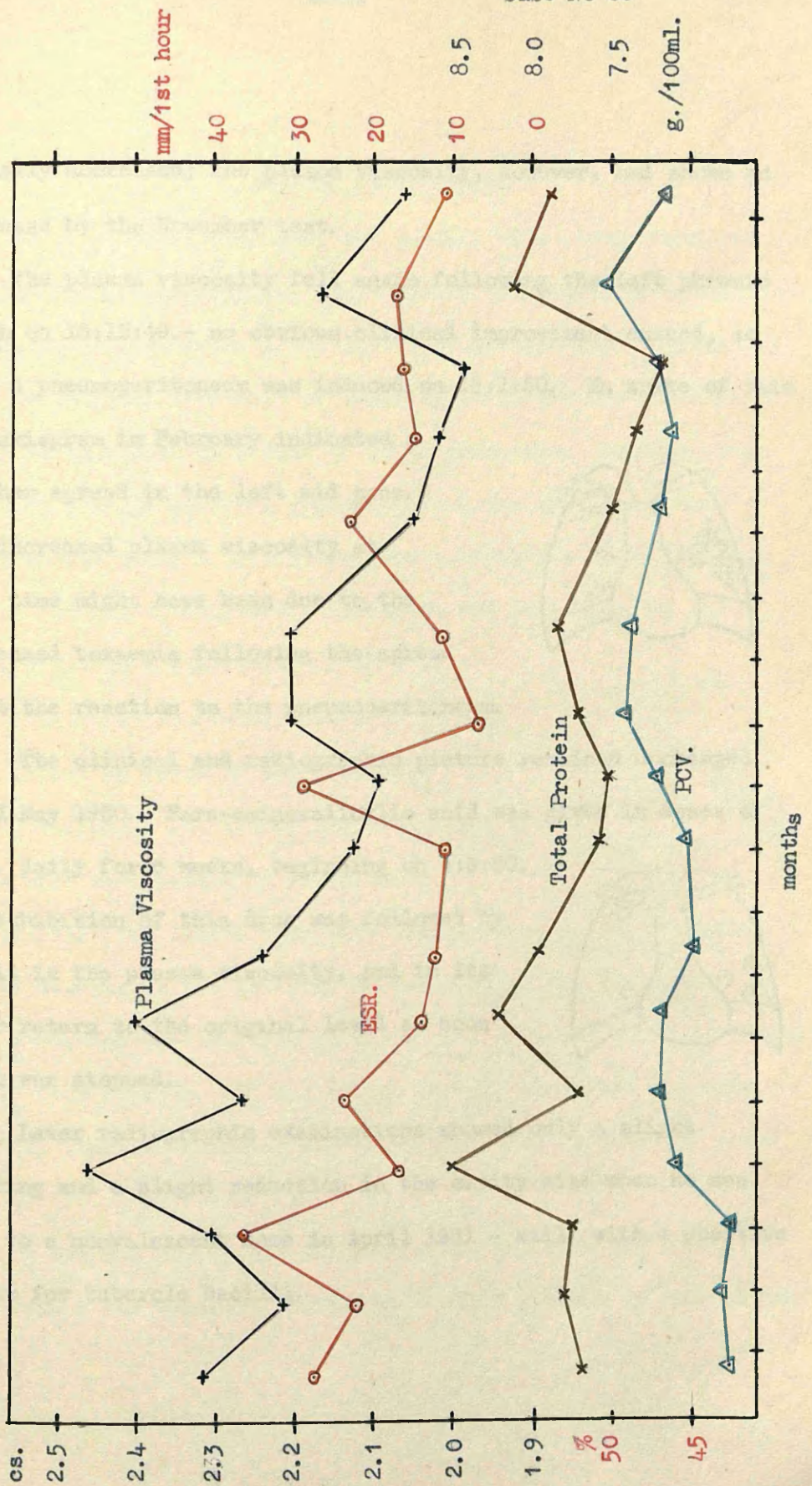
Date	PCV.	PLASMA VISC.	Wintrobe ESR.		Total Plasma Prot.	Gold Floc
			Ord.	Cor.		
	%	cs.	mm/1 hr		g %	
26: 8:49	42.7	2.323	35	28	7.74	o
29: 9:49	43.2	2.219	28	23	7.85	o
2:11:49	42.6	2.306	42	37	7.78	o
2:12:49	46.2	2.465	18	17	8.57	++
5: 1:50	47.2	2.270	24	24	7.74	o
13: 2:50	47.0	2.402	14	14	8.24	o
15: 3:50	44.8	2.244	14	12	7.99	o
4: 5:50	45.3	2.126	12	11	7.60	+
6: 6:50	47.4	2.097	28	29	7.52	o
5: 7:50	49.4	2.205	4	7	7.72	o
18: 8:50	48.9	2.208	10	11	7.85	+
12:10:50	47.	2.050	23	23	7.49	-
20:11:50	46.3	2.017	16	15	7.34	o
21:12:50	47.0	1.983	16	16	7.16	+
31: 1:51	50.3	2.166	13	17	8.10	+
12: 3:51	47.2	2.064	11	11	7.85	o

range. This initial improvement was associated with a decrease in the plasma viscosity values.

The skiagram of 7:10:49 showed that the spread into the left midzone was settling and while the infiltration at the right apex was less the cavity maintained its 3 cm. diameter. The skiagram of 7:11:49 had little change to show except that the left lung lesion suggested an early possible break-down.



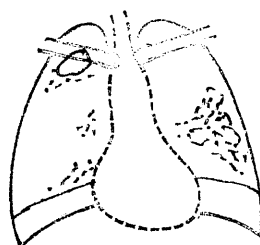
By 5:12:49 there had been a further spread at the right upper zone and at left middle and lower zone. The weight had actually increased in the past months and no change in the temperature or pulse had occurred to mark this deterioration; the ESR had



actually decreased; the plasma viscosity, however, had shown an increase by the November test.

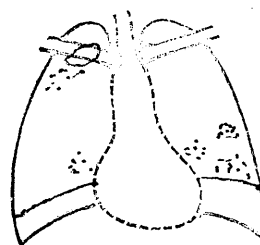
The plasma viscosity fell again following the left phrenic crush on 15:12:49.- no obvious clinical improvement ensued, so that a pneumoperitoneum was induced on 16:1:50. In spite of this the skiagram in February indicated a further spread in the left mid zone.

The increased plasma viscosity at that time might have been due to the increased toxæmia following the spread or to the reaction to the pneumoperitoneum.



The clinical and radiographic picture remained unchanged until May 1950. Para-aminosalicylic acid was given in doses of 12 g. daily for 6 weeks, beginning on 4:5:50.

The exhibition of this drug was followed by a fall in the plasma viscosity, and in its later return to the original level as soon as it was stopped.



Later radiographic examinations showed only a slight clearing and a slight reduction in the cavity size when he was sent to a convalescent home in April 1951 - still with a positive sputum for tubercle bacilli.

Case No. 34

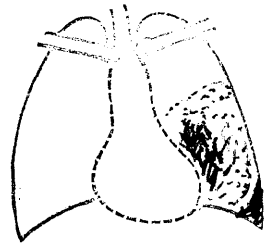
Pulmonary Tuberculosis.

After a normal pregnancy and labour, this young woman was complaining of haemoptysis, night sweats, shortness of breath, and cough, about five weeks after the birth of her baby. Because of the acuteness of the onset of these symptoms she was admitted to hospital on 7:3:49 as a case of lobar pneumonia. However, when tubercle bacilli had been recovered from the sputum and the skiagram had shown a left lower lobe tuberculous pneumonia plus a small amount of scattered disease at the left apex she was transferred to a sanatorium on 15:3:49.

The first laboratory tests of 18:3:49 were normal in spite of the obviously active disease. The second and subsequent tests were in accord with the clinical assessment. The plasma viscosity changes were closely parallel to the changes in the activity as assessed by the clinician.

Streptomycin was given in doses of 1 g. twice daily for three months from 18:3:49. By 1:4:49 the general condition was only slightly improved although the temperature had returned to normal levels.

By the end of May, the skiagram could not show any improvement and tubercle bacilli were still present in the sputum.



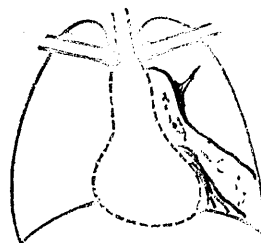
Date	PCV.	PLASMA VISC.	Wintrobe ESR.		Total Plasma Protein
			Ord.	Cor.	
	%	cs.	mm/	1 hr	g. %
18: 3:49	37.0	1.762	14	8	-
4: 4:49	38.6	2.151	35	29	7.16
12: 4:49	35.5	2.249	46	34	7.09
9: 5:49	35.7	2.295	50	37	7.38
7: 6:49	39.1	2.280	17	14	7.88
5:7 :49	40.3	2.050	24	21	7.47
24: 8:49	42.3	1.864	10	10	7.04
22: 9:49	43.6	1.826	12	14	6.77
21:10:49	40.3	1.766	5	4	6.48
30:11:49	41.0	1.782	6	5	6.77

The plasma viscosity had remained at a constant increased level during April, May, and June.

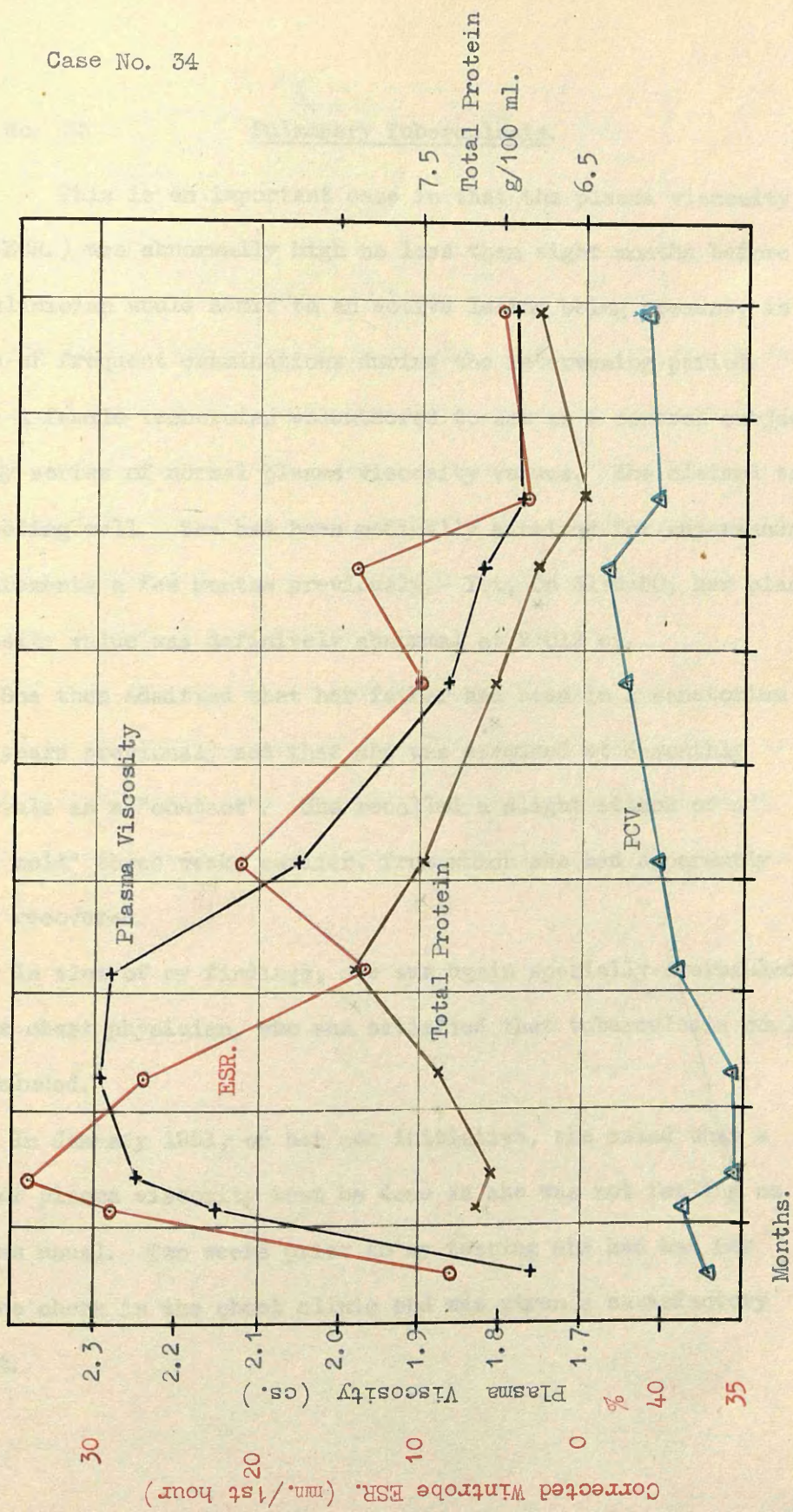
A left artificial pneumothorax was induced on 24th June and the reduced absorption of toxins was reflected in the rapid fall in the plasma viscosity and ESR values.

The skiagram on 10:8:49 showed that the left lung had collapsed completely except for a part of the lower lobe kept expanded by a single adhesion. No attempt was made to cause a re-expansion of the lung because of the long delay in surgical treatment. She was discharged in December 1949.

When she was weighed in Jan. 1950 she had increased 3.5 stones since the beginning of her illness. The lung collapse was still present in April 1950.



Case No. 34



Case No. 35

Pulmonary Tuberculosis.

This is an important case in that the plasma viscosity (and ESR.) was abnormally high no less than eight months before the clinician would admit to an active lesion being present, in spite of frequent examinations during the intervening period.

A female technician volunteered to act as a control subject for my series of normal plasma viscosity values. She claimed to be feeling well. She had been medically examined for superannuation requirements a few months previously. Yet, on 31:5:50, her plasma viscosity value was definitely abnormal at 2.012 cs.

She then admitted that her father had been in a sanatorium some years previously and that she was examined at 6-monthly intervals as a "contact". She recalled a slight attack of a "head cold" three weeks earlier, from which she had apparently fully recovered.

In view of my findings, she was again specially overhauled by the chest physician, who was satisfied that tuberculosis could be excluded.

In January 1951, on her own initiative, she asked that a further plasma viscosity test be done as she was not feeling as well as usual. Two weeks prior to my testing she had had her routine check in the chest clinic and was given a satisfactory report.

Date	PCV.	PLASMA VISC.	Wintrobe ESR. Ord. Cor.		Total Plasma Prot.	Gold Floc.
	%	cs.	mm/ 1 hr		g. %	
31: 5:50	42.0	2.012	26	26	7.85	-
30: 1:51	46.	2.103	25	32	7.85	o

The plasma viscosity had increased slightly over the first result. I took my results to the chest physician who agreed that something was being missed. Another thorough overhaul and intensive radiology revealed a lesion of the middles lobe of the right lung whose tuberculous character was indicated by the tubercle bacilli in the sputum.

The lung was eventually treated by lobectomy.

It is on examples such as this that I state my claim on the reliability of the plasma viscosity test in which an increased result is tantamount to an abnormal condition somewhere within the body.

Case No. 36

Pulmonary Tuberculosis.

This case should be considered in conjunction with Case No. 35 . In the present instance, the plasma viscosity failed to detect activity which was demonstrated by serial radiology.

At the routine examination for superannuation purposes, the skiagram of the chest revealed a calcified area at the left lung apex of one of our female student technicians. The problem of the activity of the lesion could not be settled at that time by a clinical examination or by a laboratory investigation. Later skiagrams, after two months interval, showed a spread of the apical lesion and yet the plasma viscosity had increased to 1.911 cs. only and had fallen to 1.835 after another 6 days.

Thus, it must be emphasised that a normal plasma viscosity result cannot guarantee the absence of an active tuberculous lesion.

Date	PCV.	PLASMA VISC.	Wintrobe ESR.		Total Plasma Prot.	
			Ord.	Cor.		
7: 9:49	44.6	1.896	-	-	7.67	ESR = 8 mm in 1.5 hr Active by X-ray
29: 9:49	40.6	1.783	4	2	6.98	
1:12:49	42.5	1.911	8	9	7.78	
7:12:49	41.9	1.835	10	10	6.84	

She was admitted to a sanatorium and was able to resume work after 15 months. No surgical treatment was necessary.

Case No. 37

Pulmonary Tuberculosis.

This case is another example of the plasma viscosity becoming abnormal several months before an active lesion may be detected by radiology or by physical examination.

The author had been grossly overworking during 1943; there were war-time staff depletions, holiday periods had been halved, and a research programme had had to be terminated because of such difficulties. The research into the plasma viscosity changes began in August 1943. The acid digestion of the proteins was carried out in a defective fume-chamber so that a morning sputum which appeared in the Spring of 1944 was blamed on the irritation of the acid fumes. However, the weight had decreased by 7 lb. in as many months. (See Fig. 55, page 204)

In April, a skiagram of the lungs and a general examination by a chest physician were normal.

At this time the plasma viscosity results were abnormally high. This observation was made early in the research programme and we could not then ascribe to it the significance which later experience has taught us.

Further testing produced viscosity values which slowly fell to normal, although the same high rate of work had continued and the same sputum (tubercle-free) was formed; there was no further loss in weight.

Date	PCV.		PLASMA VISC.		Max. Citr. ESR.	Total Protein	
	Cit.	P+A.	Cor. Citr.	P+A.		Serum	Plasma
	%		cs.		mm/hr	g. %	
7: 4:44	35.7	46.7	1.614	2.063	8.1	7.79	-
25: 5:44	34.9	46.0	1.666	2.070	10.5	7.11	-
31: 5:44	33.5	-	1.647	-	12.0	7.29	-
3: 7:44	33.4	44.7	1.603	2.037	12.0	6.87	-
7: 8:44	32.0	-	1.549	1.900	8.4	-	7.30
13:11:45	32.0	-	1.503	-	4.0	-	-

In August, when the viscosity was at the upper limit of the normal range, a small opaque area was detected at the right apex. Three months rest in bed in a sanatorium caused the lesion to regress and full normal duties were resumed in May 1945.

Repeated discussions have never yet settled the problem of what would have happened if the search for a lung lesion had not been persisted in - would the disease have progressed to such a stage that more active treatment would have been necessary or would it have regressed to the quiescent scar which is present in the majority of an adult population ?

Case No. 38

Tuberculous Pleural Effusion.

This male asylum inmate, aged 65 years, had been noted to be failing in his general condition prior to his complaint of a pain in his left chest on 2:9:43. The whole of the left side of the chest was dull to percussion because of the large pleural effusion. On the same day, two pints of clear straw-coloured fluid ~~were~~ aspirated. It was hoped that a partial aspiration might lead to a further ~~absorption~~ by the patient.

However, the fluid reformed. The plasma viscosity was measured on four occasions at two or three weeks interval, with an aspiration of 1 or 2 pints between, and the fluid reappeared on each occasion. The plasma viscosity values were within the "zone of effusion". From the experience acquired by myself and Houston, I now realise that when the fluid reformed after the first aspiration the chances of further formation after repeated aspiration, as long as the plasma viscosity values persisted in this particular zone, were so great as to stop such interference; aspiration should have been delayed until the plasma viscosity had increased or decreased significantly.

The asylum had no facilities for radiography. The fluid persisted in that pleural cavity for the next three years during which the patient was confined to bed. Thus the nature of the tuberculous lesion of the lung, if any, was never identified.

Date	PCV.		PLASMA VISC.		Max. Cit. ESR.	Plas.	Serum.	Aspiration
	Cit.	P+A.	Citr.	P+A.		Total	Prot.	
	%		cs.		mm/ sec.	g. %		
13: 9:43	31.0	39.8	1.702	2.118	17.5	-	-	2 pints.
23: 9:43	29.2	39.0	1.783	2.568	15.0	6.44	-	1 pint.
12:10:43	28.7	38.2	1.784	2.383	21.1	7.03	-	1 pint.
4:11:43	28.0	35.9	1.759	2.390	22.3	6.82	-	
5: 1:44	29.2	-	1.870	-	33.3	7.64	-	
1: 2:44	29.0	-	1.886	2.631	33.7	7.54	-	
27: 3:44	29.0	-	1.943	2.723	41.4	7.94	-	
27: 3:44	26.9	-	1.920	2.669	33.3	-	-	
17: 4:44	25.2	33.7	1.843	2.502	37.5	-	6.62	
19: 5:44	25.7	35.0	1.837	2.472	27.2	-	6.83	
4: 7:44	26.3	35.6	1.908	2.715	28.9	-	7.36	
14: 8:44	24.8	-	1.816	2.416	23.8	7.04	-	

Case No. 39

Terminal Decay in Pulmonary Tuberculosis.

The patient was an in-mate of the asylum in 1940-41 and was then suspected to be suffering from pulmonary tuberculosis without a definite diagnosis being made. (See Fig. 93, p367.)

She was re-admitted on 15:4:44 as a case of Recurrent Mania in the 14th day of the puerperium.* The doctor who examined her at that time noted that her general condition was very weak and that adventitial sounds were heard all over the chest. A mastitis of the right breast began on 17:4:44 and discharged on the 19th. Her mental state got worse so that she interfered continually with the dressings to the wound, yet on sulphathiazole therapy the abscess had healed by 4:5:44.

The plasma viscosity tests on 24, 25, and 26:4:44 showed the falling values expected from a healing abscess.

At the beginning of May, however, she began to bring up foul sputum and the diagnosis of pulmonary tuberculosis was made definitely. The plasma viscosity showed another increase for two tests and then another decrease, without any corresponding improvement in her general condition. The plasma protein pattern of 4:5:44, especially its low albumin content, was an early guide to the poor prognosis. She later developed a mastitis on the other side, and further abscesses. She died on 5:7:44. Permission for a post-mortem was refused.

Date	PCV.		PLASMA VISC.		Max. Cit.	Plasma protein				Serum NPN.
	Cit.	P+A.	Citr.	P+A	ESR	Total	Alb.	Glob	Fibr.	
	%		cs.		mm/h	g./100 ml.				mg. %
24: 4	25.6	34.2	2.030	2.885	120.	-	-	-	-	-
25: 4	24.3	31.6	1.995	2.737	110.	-	-	-	-	-
27: 4	24.0	31.1	1.950	2.807	133.3	-	-	-	-	-
4: 5	22.6	29.5	2.010	2.760	120.	7.38	2.90	4.03	0.45	72.4
12: 5	20.2	27.3	2.092	3.078	109.8	-	-	-	-	-
24: 5	18.0	24.0	1.847	2.501	46.1	-	-	-	-	-

Case No. 40

Terminal Decay in Pulmonary Tuberculosis.

This female asylum patient had a history of cough and loss of weight of some six months duration before she was found to have advanced pulmonary tuberculosis on 5:1:46. Her treatment consisted in bed-rest only. The disease progressed very rapidly and death ensued on 4:3:46. Permission for a post-mortem examination was refused.

This case is included to show to what low values the plasma viscosity may fall towards the end of terminal decay.

Date	Citr. PCV.	Citrate PLASMA VISC.	Max. Cit. ESR.
	%	cs.	mm/hr.
8: 1:46	24.3	1.745	35.4
25: 2:46	15.8	1.488	13.7

Case No. 41

Terminal Decay in a Tuberculous Mongol.

When he was admitted to an asylum on 30:3:43 this mongol had attained the age of 34 years which is unusually old for subjects with this condition. I examined him particularly for any evidence of pulmonary tuberculosis at that time but failed to find any by ordinary physical examination.

At the beginning of September he was confined to bed for about a week with severe enteritis for which no pathological organism could be detected.

On 11:10:43 he had a bronchitis which was really the presenting symptom of pulmonary tuberculosis. The disease progressed rapidly to produce death on 27:1:44. The admission of such a patient to an asylum where tuberculosis was so rife that no possible isolation from the infection could be made, had been the equivalent of a death sentence. (See Fig. 92, p366.)

In view of the known susceptibility of mongols to this disease, the extent of the reaction produced by this patient is worthy of note. Although the reaction was of great height, its duration was short; perhaps the susceptibility lies in this failure to maintain the fight in chronic diseases while the reaction is sufficient to combat the ordinary short-duration pyogenic infections.

Date	PCV.		PLASMA VISCOS.		Max. Cit.	Plasma protein				Serum
	Cit.	P+A.	Citr.	P+A.	ESR.	Total	Alb.	Glob	Fib.	NFN.
	%		cs.		mm/h.	g./100 ml.				mg. %
30:10:43	24.1	33.4	2.044	3.050	153	8.98	3.56	5.01	0.41	25.3
10:11:43	24.3	32.9	2.050	3.107	225	9.03	3.67	5.03	0.33	26.0
29:12:43	23.5	-	2.078	3.144	158	8.68	3.55	4.76	0.37	30.6
20: 1:44	22.7	-	1.755	2.325	23	6.50	3.30	2.55	0.65	17.8

Case No. 42

Terminal Decay in Pulmonary Tuberculosis.

This male patient had been admitted to the asylum in 1929 at the age of 28 years as suffering from secondary dementia. His general health was only moderate; he would do no work but lay on a couch all day, taking no interest in his general surroundings.

On 22:5:44 the attendant noted an extremely rapid respiration rate; the patient was too demented to complain. His pulse rate and temperature were also elevated. His physical signs were of a left spontaneous pneumothorax. On tapping the chest a mixture of air and fluid was obtained. The fluid contained cells of the monocyte and lymphocyte series, and tubercle bacilli were identified. There was also evidence of infection of the right lung.

The first plasma viscosity test was made within 5 hours of the onset of the pneumothorax. The viscosity increased for one week and then fell; the initial fall was slow and irregular, but after a month it was more rapid and regular. (See Fig. 91, p366.)

The clinical picture showed a corresponding deterioration. The pneumothorax persisted unchanged. The temperature increased each evening. There was a progressive loss of weight. Oedema appeared at the beginning of August. He died on 8:9:44.

Treatment had consisted only of rest in bed; no surgical intervention had been attempted.

Date	PCV.		Plasma Viscos.		Max. Cit. ESR.	Plasma or Serum Protein	
	Cit.	P+A.	Citr.	P+A.			
	%		cs.		mm/h.	g. %	
22: 5:44	26.5	36.3	1.781	2.303	50	5.89 s	
23: 5:44	25.2	34.5	1.749	2.296	43.7	5.58 s	
26: 5:44	26.0	36.0	1.776	2.375	90.6	5.83 s	
27: 5:44	26.5	36.0	1.819	2.479	100.	6.14 s	
29: 5:44	28.4	38.5	1.910	2.765	159.	6.66 s	
30: 5:44	27.3	-	1.884	-	207.	6.45 s	
31: 5:44	27.6	-	1.891	-	220.	6.64 s	
1: 6:44	25.3	-	1.869	-	320.	6.62 s	
2: 6:44	25.5	-	1.893	-	268.	6.55 s	
1: 7:44	25.5	34.0	1.720	2.239	45.0	5.93 s	
10: 7:44	25.7	35.4	1.679	2.193	31.0	5.60 s	
18: 7:44	26.4	36.1	1.663	2.193	13.4	5.63 s	A=2.77, G=3.19
2: 8:44	26.5	-	1.660	-	13.4	5.68 s	
12: 8:44	25.4	-	1.580	-	16.0	4.90 s	oedema present
18: 8:44	26.5	-	1.599	-	5.7	5.16 s	
8: 9:44	died.						

This patient has important daily results which show the difference in the time phase of the plasma viscosity and the ESR. changes. The terminal decrease in the ESR. is also well demonstrated. The failure of the anaemia to increase in severity is an unusual finding.

At post mortem, 5 pints of clear yellow-green fluid were found in the left pleural cavity; the lung was compressed against the mediastinum; caseous masses to the size of a plum were found in both lobes. Large tuberculous areas were present also in the right lung. There was also a tuberculous peritonitis; 2 pints of free fluid were present and the lower abdomen had a fine fibrin membrane all over the peritoneum.

Case No. 43

Epituberculosis : primary tuberculous complex.

This patient was a boy of 7 years. His parents were free from tuberculosis when they were examined as contacts: an elderly lodger of 67 years was found to be suffering from pulmonary tuberculosis and it was thought that he might be the probable source of infection.

The illness began as a cold-in-the-head in the first week of December 1950; he was off school for a fortnight. On 17th and 18th January 1951, he had a cough and fever which were diagnosed as influenza; this was repeated after a week. On 25:1:51 he had pain in the scrotum on coughing; on 26:1:51 the scrotum was swollen. He was admitted to hospital on 31:1:51.

On examination, he was a well-developed boy who had signs of recent loss of weight. The right apex of the lung was dull to percussion; there were no adventitial sounds and air entry appeared to be equal and good. The scrotum was normal but the right spermatic cord showed marked thickening. The other systems were normal. The mantoux test was strongly positive. Tubercle bacilli were identified in the stomach washings. Skiagrams revealed an opacity occupying most of the upper right zone, and some fine mottlings throughout the left lung.

Treatment consisted of rest in bed, plus an abundant diet.

The spermatic cord was settling by 10:2:51 and normal by 19:2 .

Date	PCV.	PLASMA VISC.	Wintrobe ESR.		Plasma Total Protein	Gold Floc.
			Ord.	Cor.		
	%	cs.	mm/ 1 hr		g.%	
19: 3:51	38.5	2.150	30	18	7.96	+
17: 5:51	38.6	2.066	25	14	7.74	o
13: 6:51	38.	2.094	21	10	7.69	o
30: 6:51	41.	2.122	20	13	7.96	+
13: 7:51	38.7	1.955	24	13	7.56	o
27: 8:51	37.0	1.897	-	-	-	-
26: 9:51	37.0	1.796	14	3	6.73	-
28:11:51	40.	1.791	11	5	6.70	-

His response to this regime was satisfactory. In the summer he was nursed in the garden. He got up for brief periods in August and the time increased gradually until by October he was up most of the day. The skiagrams showed a definite improvement in the apical lesion and a gradual enlargement of the hilar glands. If it had not been for the continued presence of the lodger he could have completed his convalescence at home; on 28:11:51 he was discharged to a cottage hospital to await admission to a sanatorium.

The plasma viscosity results show a steady decrease to within the normal range; the small elevation on 30:6:51 was associated with a pyrexia due to pharyngitis and tonsillitis.

NON-PULMONARY TUBERCULOSIS.

Name	S	No.	Date	PCV.	PLASMA VISC.	Wintrobe E. S. R.		Total Plas. Prot.	Gold Floc	Remarks.
						Ord.	Cor.			
				%	cs.	mm/	1 hr	%		
<u>Meningitis.</u>										
M.M.	M	1	11: 4	48.0	2.070	-	-	6.87s	-	died on 19/4
			15: 4	51.6	2.024	-	-	6.67s	-	
Q.S.	M	2	16: 2	40.0	1.755	13	6	-	o	
J.A.	M	3	22: 7	45.	1.986	21	19	7.52	o	
Q.H.	F	4	1: 5	43.4	2.081	13	14	7.16	-	also pulmonary on streptomycin
			5: 6	38.6	2.031	30	18	7.38	o	
F.A.	M	5	2: 5	39.7	1.852	25	15	6.70	o	
			5: 6	34.6	1.946	44	16	7.27	o	
R.G.	M	6	2: 5	41.2	1.860	25	17	6.48	+	also miliary
			5: 6	42.9	1.848	15	7	6.48	o	
L.M.	M	7	3: 5	42.4	1.793	8	3	6.73	o	
S.H.	M	8	3: 5	44.8	1.780	14	11	6.05	+	also pulmonary
			5: 6	48.0	1.842	14	15	6.48	o	
M.M.	F	9	5: 6	38.6	1.938	32	26	7.24	o	also miliary
			8: 5	-	1.795	10	-	7.30	-	
B.H.	M	10	27: 6	36.4	2.133	15	8	7.63	+	
R.J.	M	11	13: 7	42.6	1.912	14	9	7.13	o	also pulmonary
V.H.	F	12	13: 7	41.8	2.074	25	25	7.20	o	
M.T.	F	13	31: 1	47.3	2.263	10	16	7.56	o	recurrence
R.S.	M	14	7: 2	41.5	1.874	14	8	6.70	o	+ pleural effusion
B.W.	F	15	5: 4	40.	2.658	50	37	8.10	o	
<u>Peritoneal Cavity</u>										
M.R.	F	16	20:11	43.7	2.017	-	-	7.88	o	ascites
			9:12	41.5	1.987	-	-	7.54	+	
J.A.	F	17	14: 7	38.5	2.603	36	30	9.11	3+	
M.H.	F	18	3: 4	41.	1.875	3	2	7.38	o	after 6 mnth treat.
<u>Pericardial Cavity</u>										
Citrate plasma										
R.S.	M	19	11: 9	22.	1.701	62	-	-	-	
			24: 9	25.6	1.706	-	-	7.47	-	
			21:10	29.1	1.830	-	-	8.39	-	
			13:11	32.1	1.618	-	-	7.61	5+	

Name	S	No.	Date	PCV.	PLASMA VISC.	Wintrobe ESR.		Plasma Total Prot.	Gold Floc	Remarks
						Ord.	Cor.			
						%	cs.	mm/ 1 hr	g. %	
<u>Bone and Joints.</u>										
H. J.	F	20	6: 7	40.1	2.810	-	-	7.57s	-	Spine, + sinuses
			13: 7	35.7	2.400	-	-	7.29	-	
			17: 8	34.4	2.730	-	-	8.74	-	
W. M.	M	21	10: 1	----	2.994	-	-	8.87	-	Ribs
H. R.	M	22	6: 4	44.0	2.149	-	-	8.24	-	Hip
M. O.	F	23	3: 6	----	2.163	26	-	8.28	+	Knee
M. F.	F	24	2: 6	----	2.227	-	-	8.42	+	Hip
W. N.	M	25	11: 3	34.2	2.147	-	-	7.99	o	Carpus
L. S.	F	26	16: 2	35.	1.892	32	21	6.81	+	Hip, at end of a long period of treatment.
			2: 4	39.	1.811	14	10	6.91	o	
			21: 4	41.	1.861	13	12	6.88	o	
			30:10	36.0	1.779	18	10	6.91	-	
			26:11	38.	1.898	29	24	7.16	-	
			7: 1	42.1	1.978	28	28	7.52	-	
M. W.	F	27	13:11	42.9	2.008	37	38	7.60	+	Femur
J. G.	M	28	14: 3	48.5	1.985	5	6	7.49	o	Foot
B. G.	M	29	31: 1	43.	2.369	21	16	8.53	-	Sacro-iliac joint
K. P.	M	30	23: 2	40.	2.330	32	22	8.68	+	Ankle
			5: 3	39.	2.499	35	23	6.75	+	
			17: 4	40.	2.321	35	25	8.68	o	
			8: 5	40.0	2.160	26	16	7.99	o	
D. H.	M	31	5:12	41.1	2.431	22	15	8.17	o	Spine
M. M.	M	32	1: 2	38.	1.784	18	8	6.55	o	Spine
			13: 3	38.	1.708	9	0	6.70	o	
			24: 4	40.	1.832	17	9	6.77	o	
			5: 5	38.4	1.747	8	0	6.48	o	
			17: 5	38.4	1.754	12	3	6.62	o	
			28: 5	36.	1.770	13	1	6.41	o	
			5: 6	-	1.909	-	-	6.91	-	
			18: 6	36.	1.703	12	0	6.55	o	
			30: 6	38.	1.811	16	6	6.55	o	
			13: 7	39.2	1.700	7	0	6.66	o	
J. D.	F	33	21: 2	46.	2.015	12	17	7.34	+	Spine
P. M.	M	34	15: 5	38.2	2.276	35	21	7.74	-	Spine, + sinuses
A. M.	F	35	3: 9	34.6	2.001	8	0	7.88	o	Knee + lung lesion

Name	S	No.	Date	PCV.	PLASMA VISC.	Wintrobe ESR.		Plasma Total Prot.	Gold Floc.	Remarks
						Ord.	Cor.			
				%	cs.	mm/	1 hr	g. %		
<u>Bone and Joints (continued)</u>										
G. H.	M	36	13: 2	40.0	2.116	35	32	7.31	o	Spine
			9: 3	40.0	1.938	25	21	6.77	o	
			2: 4	41.	1.912	21	20	6.91	o	
			21: 4	40.	1.877	18	16	6.88	o	
			22: 5	44.	1.877	11	13	7.02	o	
W. H.	F	37	6: 2	46.9	2.106	13	18	8.06	o	Spine
			31: 2	44.	2.026	17	20	7.52	o	
			18: 4	44.	1.935	15	17	7.38	-	
M. S.	F	38	5: 6	45.	2.105	25	29	6.95	o	Spine + hip
A. S.	M	39	25: 7	-	2.293	-	-	7.09	-	Spine
			1:11	35.	2.330	-	-	7.31	-	
			26:11	36.3	2.178	49	28	7.31	-	
M. W.	M	39	30: 7	47.	1.928	9	9	7.20	-	Spine
F. C.	F	40	14: 8	44.	2.278	18	20	-	-	Spine
E. P.	F	41	22: 9	39.2	2.056	27	23	7.09	-	Hip
			11:10	39.	1.951	25	20	6.95	-	
			1:11	37.	1.926	-	-	6.95	-	
			26:11	44.	2.119	11	13	7.31	-	
D. F.	F	42	26: 9	43.0	2.076	25	26	7.81	-	Spine
			11:10	40.0	2.041	18	15	7.56	-	
			1:11	38.	1.979	-	-	7.49	-	
			26:11	40.	1.971	34	30	7.31	-	
			7: 1	39.7	1.987	22	19	7.85	-	
M. A.	F	43	16:10	39.	1.884	15	12	6.95	-	Spine
			1:11	40.0	1.941	-	-	7.13	-	
			26:11	44.	1.987	20	22	7.49	-	
			7: 1	46.0	1.893	8	12	7.27	-	
J. E.	M	44	28:12	-	2.155	-	-	6.50	-	
<u>Lymph Glands.</u>										
E. L.	F	45	18: 8	40.2	1.922	15	13	7.27	o	Tabes mesenterica
M. S.	F	46	25: 4	38.	2.477	47	39	8.06	o	Glands of neck
			5: 5	43.	2.107	7	8	7.88	+	
E. F.	M	47	26: 1	41.8	2.046	18	11	-	o	Glands of groin, + sinuses, on streptomycin
			15: 2	41.9	1.823	12	7	-	o	
N. S.	F	48	17: 7	44.4	1.978	12	15	7.74	-	Glands of neck
J. G.	F	49	6:11	37.6	2.097	35	27	7.31	-	" " "

Name	S	No.	Date	PCV.	PLASMA	Wintrobe		Total	Gold	Remarks.
					VISC.	E. S. R.	Plas.			
				%	cs.	Ord.	Cor.	Prot.		
						mm/	1 hr	%		
<u>Organs and soft tissues.</u>										
W. J.	M	49	19: 7	32.5	2.190	-	-	6.93	-	Testis, bladder, etc.
			18: 8	-	2.016	-	-	6.68	-	
K. D.	M	50	15: 3	42.	2.121	35	27	7.52	o	testis, etc.
			4: 4	44.	2.255	17	14	7.45	o	
E. D.	M	51	7: 7	-	2.868	4	-	8.60	o	Addison's + lung.
J. H.	M	52	2: 4	50.	2.125	3	6	7.34	o	kidney.
A. J.	M	53	16: 4	44.	2.061	44	38	7.45	o	after nephrectomy
			24: 4	37.	2.017	25	18	7.56	o	of one of two
			5: 5	36.9	1.884	14	8	7.34	o	affected kidneys.
F. C.	M	54	7: 2	39.4	2.266	-	-	7.96	-	sinus of arm, of
			14: 8	-	2.008	-	-	6.94	-	several years
										duration.
E. F.	M	63	24: 1	41.8	2.046	18	11	-	o	sinuses of abdomen,
			15: 2	41.9	1.823	12	7	-	o	on streptomycin
E. H.	F	64	3: 9	35.	2.058	57	41	7.20	-	abscess of soft
										tissues of back
M. W.	M	65	7: 8	45.	2.450	29	26	-	-	pyelitis
F. N.	M	66	7: 9	35.	2.072	46	26	7.31	o	pyelonephritis
			18: 5	28.	2.187	48	16	7.27	-	
<u>Lupus.</u>										
J. W.	F	67	12: 3	45.5	1.834	-	-	7.25	-	
T. R.	F	68	21: 3	-	1.960	-	-	7.78	-	

Name	S	No.	Date	PCV.	PLASMA VISC.	Wintrobe E. S. R.		Total Plas. Prot.	Gold Floc	Remarks.
						Ord.	Cor.			
				%	cs.	mm/	1 hr	%		
<u>Organs and soft tissues.</u>										
W. J.	M	49	19: 7	32.5	2.190	-	-	6.93	-	Testis, bladder, etc.
			18: 8	-	2.016	-	-	6.68	-	
K. D.	M	50	15: 3	42.	2.121	35	27	7.52	o	testis, etc.
			4: 4	44.	2.255	17	14	7.45	o	
E. D.	M	51	7: 7	-	2.868	4	-	8.60	o	Addison's + lung.
J. H.	M	52	2: 4	50.	2.125	3	6	7.34	o	kidney.
A. J.	M	53	16: 4	44.	2.061	44	38	7.45	o	after nephrectomy
			24: 4	37.	2.017	25	18	7.56	o	of one of two
			5: 5	36.9	1.884	14	8	7.34	o	affected kidneys.
F. C.	M	54	7: 2	39.4	2.266	-	-	7.96	-	sinus of arm, of
			14: 8	-	2.008	-	-	6.94	-	several years duration.
E. F.	M	63	24: 1	41.8	2.046	18	11	-	o	sinuses of abdomen,
			15: 2	41.9	1.823	12	7	-	o	on streptomycin
E. H.	F	64	3: 9	35.	2.058	57	41	7.20	-	abscess of soft tissues of back
M. W.	M	65	7: 8	45.	2.450	29	26	-	-	pyelitis
F. N.	M	66	7: 9	35.	2.072	46	26	7.31	o	pyelonephritis
			18: 5	28.	2.187	48	16	7.27	-	
<u>Lupus.</u>										
J. W.	F	67	12: 3	45.5	1.834	-	-	7.25	-	
T. R.	F	68	21: 3	-	1.960	-	-	7.78	-	

Name	S	No.	Date	PCV.	PLASMA VISC.	Wintrobe ESR.		Plasma Total Prot.	Gold Floc	Remarks
						Ord.	Cor.			
				%	cs.	mm/	1 hr	g. %		
<u>Miliary Tuberculosis.</u>										
I.D.	F	56	10: 5	39.1	2.342	-	-	8.06	o	on streptomycin
			24: 5	35.6	2.235	-	-	7.24	o	
			7: 6	39.4	2.176	38	34	7.74	o	
			28: 6	41.5	2.357	33	32	8.17	o	
			2: 7	39.3	2.185	-	-	7.60	o	
			29: 7	38.7	2.204	48	41	7.62	o	
			12: 8	41.8	2.360	37	37	8.26	o	
			15: 9	40.0	2.076	25	22	7.12	-	
R.D.	F	57	18: 3	46.	2.253	12	17	-	++	on streptomycin
			13: 4	42.2	2.067	18	18	7.78	+	
			9: 5	41.4	2.136	12	11	8.17	+	stopped on 9:7
			7: 6	39.5	2.000	17	14	8.03	+	
			6: 7	39.9	1.892	11	9	7.26	+	
			25: 8	40.6	1.804	6	5	7.09	o	
			21: 9	41.7	1.805	5	5	7.24	o	
			20:10	42.0	1.860	5	5	7.38	+++	
			1:12	49.0	1.755	7	5	6.80	+	discharged
			4: 1	42.2	1.879	6	6	7.60	+	
15: 2	42.6	1.895	6	7	8.03	+				
J.S.	F	58	13: 4	40.0	2.155	35	32	7.60	o	on streptomycin
			10: 5	41.2	2.035	21	20	8.06	o	
			8: 6	43.1	1.827	8	9	7.16	o	
			13: 7	42.5	1.841	13	13	7.00	o	
			26: 8	43.2	1.861	10	11	7.27	o	
			21: 9	42.9	1.821	7	8	7.20	o	
M.M.	F	59	5: 6	38.6	1.938	32	26	7.24	o	
			8: 5	-	1.795	10	-	7.30	-	
R.G.	M	60	2: 5	41.2	1.860	25	17	6.48	+	
			5: 6	42.9	1.848	15	7	6.48	o	
D.B.	F	61	10: 5	41.	2.273	38	37	7.78	-	on streptomycin
			24: 5	42.	2.565	26	26	8.39	o	
			4: 6	39.8	2.662	27	24	8.46	-	
			25: 6	42.	2.503	31	31	7.97	-	
			30: 7	38.	2.353	47	39	-	-	
			22: 8	40.	2.239	38	34	7.92	-	
			17: 9	42.	2.216	33	33	-	-	
<u>Intestine</u>										
F.H.	M	62	13:10	36.9	1.863	40	22	6.41	-	enteritis + lung lesion

Case No. 44

Acute Tuberculous Meningitis (Pre-streptomycin)

This man of 32 years was admitted to an asylum because he had been showing evidence of mental derangement in the previous few days. When I came to examine him physically I found signs of meningeal irritation in nuchal rigidity and a positive Kernig test. There was an elevation of the temperature and the pulse and respiration rates. The optic fundi appeared to be normal. No abnormality could be detected in any other system.

A history of headaches in the two weeks prior to his admission on 10:4:44 was later elicited.

The laboratory tests on his cerebro-spinal fluid taken a few hours after admission strongly suggested the diagnosis of a tuberculous meningitis. However, in case a meningococcal or other pyogenic organism cause was being overlooked, a full course of sulphonamides was given; this drug had no effect on the T.P.R., which further supports the tuberculous nature of the disease.

The plasma viscosity was estimated on two occasions and the value was abnormally high on both; the ESR at the first testing was within its normal range.

Date	PCV.		PLASMA VISCOSITY		Max. Citr. ESR.	Serum Total Protein
	Citr.	Hep.	Cor.Citr.	Heparin		
	%		cs.		mm/hr	g.%
11: 4:44	34.2	48.0	1.591	2.063	7.2	6.67
15: 4:44	36.0	51.6	1.639	2.089	11.4	6.67

10:4:44 - The CSF. removed on this day was under slightly increased pressure; it was slightly turbid; it contained 800 cells per cmm. which were mostly small lymphocytes; Pandy's test was strongly positive. No organisms could be found in direct films; there were no facilities for culture or animal inoculation. Protein content was 800 mg. per 100 ml.

13:4:44 - The CSF. was of similar composition. The cells had risen to 900 per cmm. and the protein to 900 mg. per 100 ml.

17:4:44 - The CSF. was under such high pressure that it spurted from the needle. It had become quite turbid and the proportion of polymorphs had risen.

Following his admission, he rapidly grew weaker. On the 15th, he had become unconscious at times. He became mentally clearer after the lumbar puncture on the 17th. By the next day he was again unconscious; death took place on 19th April. The illness had lasted for about 23 days in all.

Case No. 45

Relapsing Tuberculous Meningitis.

This girl of 19 years was picked up by the Mass Radiology Unit on 4:4:50 when all the employees were having a yearly check. She was not complaining but did admit to having been tired for the previous 2 months during which she had worked overtime; to having a reduced appetite recently; and to having a sharp stabbing pain at the right costal margin associated with coughing. She denied having excess sputum, dyspnoea, night sweats or headaches. The skiagram showed an apical lesion plus miliary invasion of both lungs.

She was admitted to admitted to hospital for observation. Physical examination could detect no abnormality in the chest. There was a low-grade pyrexia and her sputum contained tubercle bacilli. Her treatment consisted of 12g. of para-aminosalicylic acid and 1 g. of streptomycin daily.

In spite of this treatment, she showed signs of meningitis in the middle of May; with continued treatment this phase of the disease also yielded so that she was discharged on 23:9:50

A skiagram on 27:1:51 could show no evidence of tuberculous activity in either lung.

On 7:3:51, she was readmitted to hospital in a comatose condition, showing the signs of a recurrence of her meningitis. Tubercle bacilli were recovered from the CSF. Treatment with PAS.

Date	PCV.	PLASMA VISC.	Wintrobe ESR.		Plasma protein.			
			Ord.	Cor.	Total	Alb.	Glob.	Fibr.
	%	cs.	mm/ 1 hr		g./100 ml			
21:11:51	46.3	1.961	14	20	7.80	5.4	1.98	0.42
12:12:51	46.	1.932	14	19	7.14	4.90	1.90	0.34
2: 1:52	43.	2.011	20	21	7.24	4.35	2.45	0.44

and Streptomycin was resumed at once and continued until 8:10:51. Her meningitis appeared to respond once again as the last positive culture of the CSF. was obtained on 7:5:51: nevertheless, the CSF. did not return to a normal chemical constitution as even by 1:1:52 the cells numbered 8 per cmm. and the protein amounted to 60 mg. per 100 ml. in a fluid which was under a pressure of 100 mm. From October 1951 she lived a normal quiet life in a convalescent annexe to the hospital and made no complaints. A skiagram of 19:11:51 was completely satisfactory, with clear lung apices on both sides.

The persistently elevated plasma viscosity values, the increased ESR and fibrinogen results, and the progressing anaemia all point to the grave prognosis that some organic disease is still active. In view of the satisfactory reports on the lungs and the abnormal composition of the CSF. I believe that the meningitic condition is only quiescent and that another flare-up is inevitable (typed 11:1:52).

On 16:1:52 the C.S.F. again contained tubercle bacilli.

Case No. 46

Tuberculous Meningitis, with Epituberculosis.

This child was born on 2:4:48 and had suffered no illness. There was no history of tuberculosis in the family and none was discovered when his parents and sister were examined as contacts.

The present illness began on 15:6:50 as a palsy of the right face, arm and leg; it lasted only 3-4 minutes and had left no trace after 20 minutes. On 18th he vomited his tea. By the 19th the child was obviously unwell; he began to ask to be put to bed. This progressed until the 23rd when he refused to get up, but objected to being handled. The doctor found dullness at the left lung base, on 24:6:50.

He was admitted to hospital on 26:6:50. He was a pale silent ill child. The lung base on the left side was very dull and the cause was revealed in a skiagram as epituberculosis with a good deal of collapse of the left lung; there was a mediastinal shift to the left. A tender mass palpable in the left epigastrium may have been the spleen; the liver was enlarged to a finger-breadth below the costal margin. The right pupil was larger than the left and it reacted sluggishly to light; the eye fundi were normal. The other systems showed no marked abnormality.

A lumbar puncture on this date produced an opalescent CSF. under a pressure exceeding 300 mm. The protein amounted to 70 mg. per 100 ml; the cells numbered 670 per cmm, nearly all lymphocytes;

the chloride was 620 mg. per 100 ml., and the sugar 25 mg./100 ml.

In spite of the severity of the general upset the temperature was 98.4°F. only, pulse was 86 per minute, and the respiration rate was 36 per minute.

The plasma viscosity was measured on the day following his admission. The value was elevated in contrast to the low ESR. level.

The child was transferred to a sanatorium where he died on 19:10:50.

Date	PCV.	PLASMA VISC.	Wintrobe ESR.		Plasma Total Protein	Gold Floc.
			Ord.	Cor.		
	%	cs.	mm/ 1 hr		g. %	
27: 6:50	36.4	2.133	14	3	7.63	+

Case No. 47

Tuberculous Pericardial Effusion.

This case is noteworthy in that the plasma viscosity value measured at the time when the effusion was forming was similar to the viscosity values characteristic of pleural effusion formation.

This boy , aged 6 years, had been healthy until 6 months before admission to hospital: he had been complaining of pain in the region of the umbilicus and of vomiting after food, both symptoms becoming worse in the last 2 weeks.

On examination at admission on 1:9:47, he was a pale restless child, with a purpuric rash over the lower abdomen. His liver was enlarged by three finger-breadths; no other abnormality could be detected in the abdomen. Cardiovascular system was normal apart from a tachycardia (130 per minute). He had a cough; there were scattered ronchi in both lungs; the percussion note and breath sounds were reduced at the left lung base; respiration rate = 26. Temperature = 102.4°F.

He was diagnosed as a case of pneumonia. He was treated with 25,000 units of Penicillin 3-hourly and sulphamezathine in 0.75 g. doses 4-hourly (total =26.25 g.) until the 7:9:47.

A skiagram of the chest on 3:9:47 suggested a pericarditis and the clinical signs were obvious by 5:9:47. There was strong pericardial friction over the whole praecordium and the cardiac

Date	Cit. PCV.	CITR. PLASMA VISC.	Max. Citr. ESR.	Plasma protein.			
				Total	Alb.	Glob	Fibr
	%	cs.	mm/hr	g./100 ml.			
11: 9:47	22.0	1.701	46.4	-	-	-	-
24: 9:47	25.6	1.706	48.4	7.47	3.70	3.35	0.42
21:10:47	28.1	1.830	31.5	8.39	4.26	3.69	0.44
13:11:47	32.1	1.618	11.7	7.61	3.58	3.74	0.29

dullness area had increased to the left. The diagnosis was made of a pericardial effusion, probably tuberculous in nature. The liver enlargement was attributed to cardiac failure.

On 6:9:47, 30 ml. of cloudy straw-coloured fluid was aspirated from the pericardium, and tubercle bacilli were identified in this fluid. The first plasma viscosity estimation was done on 11:9:47. By 13:9:47 the fluid had reformed so that 115 ml. could be removed.

Calcoiferol treatment was begun on 21:9:47. The pericardial fluid did not reform (as might have been expected because of the plasma viscosity value persisting in the "zone of effusion"). Tuberculosis of the lungs became obvious on radiological examination so that he was admitted to a sanatorium on 20:11:47.

The serial skiagrams were reported as follows:-

3:9:47 "Possible pericarditis" (No mention was made of an abnormal lung or leural condition.)

18:9:47 Pneumonia of left lung.

25:9:47 Possible bilateral bronchopneumonia.

1:10:47 Bilateral bronchopneumonia, some collapse of left lower lobe, and probable effusion at left base.

8:10:47 Pericardial effusion; no present evidence of broncho-pneumonia; resolution of previous pleural effusion, but with exudative pleurisy in left costophrenic angle; enlargement of left hilar glands, but no present evidence of tuberculous infection.

31:10:47 Resolution of pericardial effusion and heart image reduced in size; some extension from left hilum - suggestive of pulmonary tuberculous infection; resolution of the resultant pleurisy in left costophrenic angle.

10:11:47 Some haematogenous and lymphatic invasion of the right and left lungs.

Case No. 48

Tuberculosis of Spine.

Since the birth of her baby five months prior to her attendance at the rheumatism clinic, this patient had complained of severe pain in the lower part of the back. The pain was constantly present and it was worse at night. Otherwise she felt very well. She fed her baby herself for three months. Menstruation had not been resumed.

On examination, full movements of the spine could be obtained; full flexion was accompanied by some increased pain. The hip and the sacro-iliac joints appeared to be normal: there was no muscle tenderness.

Skiagrams taken on this day showed a collapse of the bodies of the 9th and 10th dorsal vertebrae, with a paravertebral abscess in the region of the 9th, 10th and 11th vertebrae. The pelvic and lumbar bones were normal. The lungs were normal.

The laboratory results on the same day were:-

Plasma viscosity	=	2.314 cs.
Blood haematocrit	=	38.0 %
Wintrobe ESR.	=	43 mm. in 1st hour
Corrected Wintrobe ESR.	=	36 mm. in 1st hour
Total plasma protein	=	8.06 g./100 ml.
Gold flocculation	=	0
Plasma alkaline phosphatase	=	6.8 K.A. units /100 ml.

Case No. 49

Tuberculosis of the Spine.

From 1936 until 1939 this female patient was treated in a sanatorium for tuberculosis of the 1st and 2nd lumbar vertebrae; she was discharged well. In December 1941 her back was again painful but she refused to be examined until July 1942 when she was again admitted for treatment. Because of mental symptoms of paraphrenia she had to be transferred to the asylum in August 1943 (aged 42 years); she then had an angulation of the spine at the region of the 1st and 2nd lumbar vertebrae, with a healed sinus in the left groin and a discharging sinus in the right groin and in the left lower flank. The discharge from the sinuses was intermittent. There was never any evidence of a tuberculous infection of the lungs.

It was found that her mental state was greatly improved when she was not confined to bed. She was allowed to move around within the asylum grounds provided she rested at other parts of the day. This procedure kept the condition active as indicated by the evening temperature increase, low body weight, and undiminished discharge from the sinuses. She died about a year after these tests were made when her intestine became infected by the tuberculosis.

Date	PCV.		PLASMA VISCOSITY		ESR.	Plasma protein				Serum NPN.
	Cit.	P+A.	Cit.	P+A.		Total	Alb.	Glob	Fib.	
	%		cs.			g./100 ml.				mg. %
13:7:44	27.0	35.7	1.778	2.412	56.2	7.29	3.52	3.15	0.62	30.1

ESR = maximum corrected citrate sedimentation velocity (mm/hr.)

Case No. 50

Tuberculous Glands of Neck.

This case was selected to show how the results from different kinds of chronic disease may be almost identical. This emphasises the non-specific nature of the plasma viscosity test.

The laboratory results of a nurse who was suffering from tuberculous enlargement of her cervical lymphatic glands were:-

Plasma viscosity = 1.978 cs.
Plasma total protein = 7.74 g./100 ml.
Blood haematocrit = 44.4 %
Wintrobe ESR. = 12 mm. in 1st. hour
Corrected Wintrobe ESR. = 15 mm. in 1st. hour

These results should be compared with those of Case No. 66.

where the girl was suffering from an enlargement of the glands secondary to a pyogenic infection of the tonsils.

Case No. 51

Multiple tuberculous lesions.

The patient was a man of 52 years. In 1924 he had suffered from tuberculosis of the upper dorsal vertebrae, for which he spent 2 years resting in a plaster cast; the recovery was so good that he could continue with the heavy labour involved in working a croft which included the carriage of heavy loads of peat. In 1935 his left kidney was removed on account of a tuberculous infection.

He was admitted to Montrose Asylum on 18:7:44 after a war-time journey from Shetland. His general condition was fair. His lungs were normal. His heart size and the blood pressure were within normal limits so that there was no indication that the loss of a kidney had led to a hypertension.

He complained of a frequency of micturition (every 20-30 minutes) which had troubled him for 7 weeks. The urine contained erythrocytes, leukocytes, epithelial cells, and 0.16 g. per 100ml. of protein. Tubercle bacilli could not be identified in a direct film of the urine: there were no facilities for culture or animal inoculation. The maximum urea concentration after 15 g. of urea was 1.1 %

The right epididymis was enlarged to twice the normal size; from it a narrow sinus passed to the surface of the scrotum; tubercle bacilli were identified in the discharge. The left

testis and epididymis were swollen to a mass of 3" diameter, due partly to a hydrocele and partly to a tuberculous epididymitis.

Date	PCV.		Plasma Viscos.		Max. Cit. ESR.	Plasma protein				Serum NPN.
	Cit.	P+A.	Cit.	P+A.		Total	Alb.	Glob	Fib.	
	%		cs.		mm/h.	g./100 ml				mg. %
19:7	24.1	32.5	1.677	2.190	13.8	6.47	3.91	2.56	0.46	63.8
18:8	24.4	-	1.597	2.016	15.6	6.26	3.83	2.43	0.42	46.8

The first plasma viscosity test was made on the day following admission: the second test was made after a month during which he was given a generous diet and adequate rest, while his sleep was relieved from disturbance by the wearing of a rubber urine receiver. He had shown an improvement by an increase in weight.

The reduction in the apparent toxæmia was reflected in the fall in the plasma viscosity. The ESR. increased; the plasma protein fractions showed no significant alteration.

The plasma viscosity results fell within that part of the total range which has become associated with chronic infections of many kinds.

Case No. 52

Tuberculous sinus of arm.

This patient was admitted to an asylum in 1926 at the age of 22 years. At that time it was noted that the left lung was dull to percussion; the diagnosis of tuberculosis was never applied, however, and he was never treated as suffering from pulmonary tuberculosis.

In May 1941 a large swelling appeared in the soft tissues on the lateral side of the left arm, just above the elbow joint; the bone was not involved. Pus was later discharged in which no ordinary pyogenic organisms could be detected by film or culture: tubercle bacilli were never identified either, but the appearance of the lesion and its later clinical course made the diagnosis of a tuberculous abscess fairly certain. The abscess never healed completely. A sinus persisted. Treatment consisted only in packing with B.I.P.P.

The plasma viscosity was first estimated in February 1944 when there was a more acute inflammatory reaction around the sinus; the second test was made in August when this reaction had subsided and the value typical of a reaction to a chronic infection was obtained.

Date	PCV.		Plasma viscos.		Max. Cit. ESR. mm/h	Plasma protein				Serum NPN. mg. %
	Cit.	P+A.	Cit.	P+A.		Total	Alb.	Glob	Fib.	
	%		cs.			g./100		ml.		
7:2:44	29.0	39.4	1.795	2.401	42.3	7.93	4.05	3.30	0.58	21.5
14:8:44	27.7	-	1.628	2.008	13.2	6.94	3.88	2.69	0.37	27.7

Case No. 53

Miliary Tuberculosis.

In October 1950 this girl of 19 years had her chest examined by the Mass Radiography Unit and the lungs appeared to be normal; the examination was made when her staff was being surveyed and she felt quite well.

In February 1951 she had pneumonia which ran an uncomplicated course. At the beginning of April she was complaining of a slight cough; when this persisted in spite of treatment for 2 weeks another radiographic examination was made and a typical miliary tuberculosis skiagram was found.

She was admitted to hospital on 23:4:51. Streptomycin in doses of 0.5 g. twice daily and para-aminosalicylic acid in 12 g. dosage daily was begun on this same day. She was not very toxic and this moderate reaction was reflected properly in the first plasma viscosity result of 10:5:51.

At the end of May she became much more ill. Her temperature had been normal since the second day of admission; it rose to 99.5° on 25:5 and reached 101.6° by 5:6:51, and thereafter fell slowly again to the normal range which was attained by the end of July. The clinician's could not explain the pyrexia but suspected the formation of a new focus. The plasma viscosity increased correspondingly and fell more slowly so that it was not until August that the level of May was regained.

Date	PCV.	PLASMA VISC.	Wintrobe ESR.		Plasma Total Protein	Gold Floc.
			Ord.	Cor.		
	%	cs.	mm/ 1 hr		g. %	
10: 5:51	41.	2.273	38	37	7.78	-
24: 5:51	42.	2.565	26	26	8.39	o
4: 6:51	39.8	2.662	27	24	8.46	-
25: 6:51	42.	2.503	31	31	7.99	-
30: 7:51	38.	2.353	47	39	-	-
22: 8:51	40.	2.239	38	34	7.92	-
17: 9:51	42.	2.216	33	33	-	-

The streptomycin dosage was doubled on 10:6:51 and stopped on 26:7:51 after 14 weeks of treatment. It was given again in doses of 0.5 g. twice daily, with PAS (12 g. daily), on 3:9:51 and continued 25:11:51. She was allowed to get up gradually from the beginning of October and had attained 7 hours per day at the time of her discharge on 2:12:51. At the time of discharge her Corrected Wintrobe ESR. was still 30 mm. in 1st hour. Her latest skiagram had been satisfactory, she felt very well, there was no evidence of toxæmia, and her convalescence at home would be under the supervision of the Chest Clinic.

Case No. 54

Miliary Tuberculosis.

This girl of 16 years was picked up in the Mass Radiography Unit on 4:3:49 when small fluffy shadows were detected at both apices. When she returned for a large skiagram on 14:3:49 she had the "snow-storm" appearance typical of early miliary tuberculosis. She was admitted to hospital immediately.

She had no signs or symptoms of an active disease process. She was afebrile throughout her illness. No abnormality could be detected by ordinary physical examination. Gastric lavage failed to reveal any tubercle bacilli on three tests. Lumbar punctures of 5:4:49 and 20:4:49 produced normal cerebro-spinal fluids.

Streptomycin treatment was begun on 17:3:49 in doses of 0.5 g. twice daily; on 21:4:49 this dose was doubled as the skiagram now was unchanged and the blood streptomycin level was only 1 unit. There was no evidence of toxic effects at the high dose and it was continued until 9:7:49: total dose = 198 g. Radiologically she was then almost clear except for small opacities at both apices and in the 2nd. left interspace. Her weight had increased by 4 lb.

Tubercle bacilli were cultured from the sputum of 25:8:49, the only occasion when a positive test was ever obtained.

By 20:11:49 her weight had increased a further 13 lb. and she was able to be up for 4 hours daily.

Date	PCV.	PLASMA VISC.	Wintrobe ESR.		Total Plasma Prot.	Gold Floc.
			Ord.	Cor.		
	%	cs.	mm/ 1 hr		g. %	
18: 3:49	46·	2·253	12	17	-	++
13: 4:49	42·2	2·067	18	18	7·78	+
9: 5:49	41·4	2·136	12	11	8·17	+
7: 6:49	39·5	2·000	17	14	8·03	+
26: 7:49	39·9	1·892	11	9	7·26	+
25: 8:49	40·6	1·804	6	5	7·09	o
21: 9:49	41·7	1·805	5	5	7·24	o
20:10:49	42·0	1·860	5	5	7·38	+++
1:12:49	39·0	1·755	7	5	6·80	+
4: 1:50	42·2	1·879	6	6	7·60	+
15: 2:50	42·6	1·895	6	7	8·03	+

She was discharged in February 1950. Her skiagram of the lungs was normal except for a small scar in the upper left zone. She remained well subsequent to her discharge.

The positive gold flocculation tests did not correspond to the usual results in tuberculosis and must be attributed to liver dysfunction because of miliary involvement.

The ESR. test never became abnormal although the disease was obviously active.

The plasma viscosity values showed a significant decrease even before there was radiological evidence of improvement. The second slight increase was not explicable by a change in the clinical assessment. On the whole, the plasma viscosity test gives a reliable indication of the pathological processes in this patient.

SYPHILIS

Sex	PCV.	PLASMA VISC.	Wintrobe ESR.		Plasma protein				Serum		Treatment
			Ord.	Cor.	Total	Alb.	Glob	Fib.	WR	Kahn	
	%	cs.	mm/l	hr.	g./100 ml.						
(a) <u>Portsmouth patients</u> <u>GENERAL PARALYSIS of the INSANE.</u>											
M	49·	1·754	-	-	6·63	4·16	2·09	0·38	++	/	Penicillin
M	51·	1·813	-	-	7·27	4·90	1·60	0·42	-	-	" "
F	41·2	1·688	1	1	6·18	4·52	1·38	0·28	-	/	" "
F	37·	2·042	17	11	6·20	3·97	1·81	0·42	-	-	" "
M	47·	1·981	-	-	6·98	4·30	2·10	0·55	++	+	Malaria
M	43·	2·207	-	-	7·30	4·30	2·33	0·67	-	-	"
M	47·	1·998	14	14	6·04	3·68	1·82	0·54	-	-	"
M	43·	2·045	20	15	7·24	3·68	2·32	0·54	-	?	"
F	40·	2·082	39	36	7·92	5·22	2·28	0·42	-	-	"
F	49·5	1·978	9	17	7·23	4·52	2·26	0·45	++	+	"
F	40·3	1·995	21	19	7·64	4·8	2·45	0·39	++	+	"
F	45·5	2·103	27	30	7·40	4·53	2·37	0·50	-	/	"
F	42·	1·731	5	5	6·48	3·98	1·67	0·43	-	-	"
F	48·	1·639	1	6	7·69	4·00	1·57	0·33	-	-	unknown. ??
F	42·1	1·710	4	4	6·23	4·00	2·00	0·23	-	-	unknown. ??
F	45·8	1·972	34	40	6·29	4·00	1·77	0·52	++	+	none
(b) <u>Montrose patients.</u>											
M	37·4	2·211	-	-	6·53	3·59	2·94	0·57			Malaria
	30·	2·106	-	-	5·69	3·01	2·58	0·66			after 2·5 months
M	41·5	2·123	-	-	7·42	4·16	3·26	0·29			Malaria
M	45·3	2·023	-	-	7·28	4·75	2·53	0·36			Malaria
M	45·0	2·138	-	-	6·85	4·39	2·46	0·32			None 15:2
	39·0	2·019	-	-	6·76	4·07	2·69	0·35			29:2
M	38·8	2·232	-	-	6·57	3·91	2·66	0·49			None
M	45·	2·212	-	-	7·11	4·25	2·86	0·41			None
M	42·5	2·107	-	-	7·23	4·42	2·81	0·32			None
M	46·	2·040	-	-	6·67	4·18	2·49	0·36			None

Sex	Date	PCV. %	PLASMA	Plasma proteins				Treatment, etc.
			VISC. cs.	Total	Alb.	Glob	Fib.	
g./100 ml.								
(b) <u>Montrose patients</u> . (contd.) <u>General paralysis.</u>								
M	7:10	41.5	2.267	6.77	4.39	2.39	0.41	Just infected with malaria. Rigors begun " "
	13:10	42.0	2.186	7.54	4.27	3.27	0.35	
	29:11	31.4	2.040	5.84	3.45	2.39	0.41	
	6:12	-	2.364	6.60	3.58	3.02	0.37	
M	7:10	44.3	2.170	6.42	3.68	2.74	0.53	No records
	8:10	41.	1.956	6.11	3.48	2.63	0.45	
	9:10	40.4	2.014	6.38	3.79	2.59	0.44	
	26:10	44.7	1.954	6.15	3.65	2.50	0.30	
	26: 1	41.6	1.891	6.37	4.02	2.35	0.32	
M	19:10	38.8	1.956	6.86	4.22	2.64	0.29	No records
	20:10	40.0	2.000	6.90	4.13	2.77	0.33	
	21:10	39.4	1.991	6.98	4.18	2.80	0.36	
	22:10	39.2	1.988	6.89	4.29	2.60	0.36	
	25:10	38.1	2.011	-	4.06	2.12	-	
M	2:11	45.4	2.042	6.38	4.08	2.30	0.43	No treatment.
	23:11	43.3	1.953	6.09	3.55	2.54	0.41	Malaria infection 6:11
	29:11	35.5	1.934	5.52	2.73	2.79	0.27	Rigors began 22:11 died 4:12
M	6:11	39.4	1.954	5.88	3.55	2.33	0.47	No records
	22: 1	35.0	1.879	5.45	3.52	1.93	0.38	
	26: 1	38.7	1.942	5.49	3.51	1.98	0.45	
	31: 1	37.5	1.916	5.53	3.36	2.17	0.44	
	9: 2	34.0	2.062	5.54	3.54	2.00	0.50	
M	13:11	43.6	2.159	7.80	4.84	2.96	0.39	No records
	22:11	43.5	2.144	7.20	4.29	2.91	0.42	
M	22:11	47.0	1.957	7.40	4.71	2.69	0.29	No treatment
	26:11	50.0	2.037	7.65	5.05	2.60	0.27	Malaria infection 30:11
	22:12	33.0	2.042	6.17	2.69	3.48	0.13	Rigors began 5:12

N.B. - The Montrose proteins were measured by an accurate micro-Kjeldahl technique, as contrasted with a Biuret method at Portsmouth. In the latter the globulin values are significantly lower and they should be viewed with suspicion. The increased globulin levels of the Montrose results are more in accord with other published values and they are accepted as accurate and used in the discussion.

Sex	Date	PCV.	PLASMA VISC.	Plasma protein				Remarks
				Total	Alb.	Glob	Fibr.	
		%	cs.	g./100 ml.				
<u>TABES DORSALIS.</u>								
M	25: 1	50·	2·030	-	-	-	-	? activity
	8: 2	49·	1·930	-	-	-	-	
	21: 3	49·	1·958	-	-	-	-	
	11: 5	44·0	2·037	-	-	-	-	
F	29:12	23·7	2·494	7·38	-	-	-	Charcot' joint + fractured femur
F	15:12	44·6	1·801	6·84	-	-	-	Aged 40; congenital; assessed as "burned out" by clinician.
F	5: 5	43·0	2·384	8·68	-	-	-	? activity
M	10: 6	-	2·182	6·98	-	-	-	? activity
M	17: 7	45·8	1·949	7·31	-	-	-	Charcot' joint
M	27:10	41·0	1·955	7·63	-	-	-	? activity, after treatment with penicillin.
F	20:10	40·2	2·040	7·38	-	-	-	Tests during treatment with penicillin.
	23:10	38·6	1·992	7·02	-	-	-	
	25:10	39·5	2·040	7·20	-	-	-	
<u>CEREBRAL SYPHILIS.</u>								
M	29: 7	-	2·080	6·80	-	-	-	
M	23: 2	47·	1·945	6·81	4·02	2·45	0·34	
<u>TERTIARY SYPHILIS, not affecting the C.N.S. specially.</u>								
F	10: 4	36·4	1·935	7·31	-	-	-	Lues, negative W.R. for 3 yr., which relapsed repeatedly in spite of courses of treatment.

Case No. 55

General Paralysis of the Insane.

This male patient was admitted to the asylum with the mental symptoms of grandeur etc. which are typical of G.P.I. He was then 42 years old, he had been mentally changed for about a year, but there was no information available regarding the date of the primary infection or any subsequent treatment.

No physical disease was detected apart from the syphilitic infection.

The plasma viscosity was measured before malarial therapy was begun.

Date	PCV.	PLASMA VISC.	ESR.	Plasma protein				Serum NPN.
				Total	Alb.	Glob	Fibr.	
	%	cs.		g./100 ml.				mg. %
26:11:43	50.0	2.037	-	7.92	5.05	2.60	0.27	26.9

These results are noteworthy in that the plasma viscosity value comes within the "zone of chronicity" and the abnormal viscosity is associated with plasma protein fractions which all come within the limits of normal values for these substances; yet the plasma viscosity is ultimately dependent on these protein fractions.

Case No. 56

G.P.I. plus von Recklinghausen's Disease.

This man had suffered from von Recklinghausen's disease (general neurofibromatosis) since birth. He was infected with syphilis at the age of 17 years and he then received some treatment which seems to have been half-heartedly applied. He again was treated with bismuth and arsenic when he was 46 years old but two years later he was admitted to an asylum with the symptoms typical of general paralysis of the insane. A general examination revealed no active organic disease apart from his cerebral condition, but he was not considered strong enough to undergo malarial therapy.

His tests, made within a few weeks of admission, show the plasma viscosity values within the "zone of chronicity" and the the individual plasma protein fractions within their normal ranges. As these results are similar to the others found in cases of tertiary syphilis, it is probable that the widespread but simple tumour has not affected the proteins or the viscosity.

Date	PCV.	PLASMA VISC.	ESR.	Plasma protein				Serum NPN.
				Total	Alb.	Glob	Fibr	
	%	cs.		g./100 ml.				mg. %
15:2:44	36.0	2.138	-	7.21	4.39	2.46	0.36	27.7
28:2:44	31.5	2.019	-	7.11	4.07	2.69	0.35	23.4

Case No. 57

Tabes Dorsalis.

This female patient was referred to a V.D. clinic when her 22 year-old daughter was found to be suffering from congenital interstitial keratitis. Her mother had not known of her infection and had received no treatment.

The patient had no symptoms but signs of tabes dorsalis were discovered. The pupils were small, not quite circular, and they reacted slowly to light (direct and consensual) and rather slowly to accommodation. The fundi were normal. The ankle and knee jerks were absent on both sides. No other abnormality to physical examination could be elicited, and a skiagram of the chest was normal in appearance.

Blood:- Wassermann = + ; Kahn = weak +ve .

C.S.F.:- Cells = 1 per cmm. ; protein = 25 mg./100 ml. ; Pandy test = negative ; Wassermann = ++ ; Lange curve = normal.

Date	PCV.	PLASMA VISC.	ESR.	Total Plasma Protein
	%	cs.		g. %
5:5:48	43.0	2.384	-	8.68

A plasma viscosity result which came within the "zone of chronicity" would have been expected, and no explanation of this higher value was ever discovered in any disease additional to the syphilitic infection.

Case No. 58 Tabes Dorsalis, plus Charcot's joint.

This male patient was infected with syphilis in 1939 but did not attend a clinic until November 1942. During the next five years he received regular courses of Bismuth and Tryparsamide injections.

By chance, in January 1947, he received a general examination and a well-advanced Charcot's joint of the left knee was found - he had never complained of any trouble with this knee. The quadriceps muscle was wasted; the tibia was displaced laterally; the knee was not "flail" but all the ligaments were stretched. The knee was supported in a leather splint which allowed him to get around quite comfortably. Bismuth and arsenic treatment was resumed. A course had just finished on 10:7:48, with the Kahn = \pm and the Wassermann still positive (+).

	PCV.	PLASMA VISC.	Wintrobe ESR.		Plasma Total Protein
			Ord.	Cor.	
	%	cs.	mm/ 1 hr		g. %
17:7:48	45.8	1.949	20	19	7.31

The clinician in charge of the patient agreed that this abnormal plasma viscosity value could be interpreted as indicating a continued activity of the syphilitic condition and the need for further anti-syphilitic therapy.

Case No. 59 Cerebral Syphilis (Parachymeningitis syphilitica)

This man, aged 59 years, had had no anti-syphilitic treatment prior to his attendance at a V.D. clinic in the spring of 1948. He was treated for 4 months.

He was admitted to hospital on 24:7:48 on account of weakness of both legs, more marked in right, of 3 weeks' duration. The weakness was well-marked after 2 days from onset.

On examination, no abnormality was found in any system apart from the legs. Both legs were weak. The deep reflexes were brisk except for the left ankle jerk which was diminished. There was impairment of the pain and touch sensations below the right knee.

Cerebro-spinal fluid:- Cells = 4 per cmm. (lymphocytes); Lange - normal; Wassermann - negative; chlorides = 740 mg./100 ml.; and protein = 20 mg./100 ml.

29:7:48 Plasma viscosity = 2.080 cs.

Total plasma protein = 6.80 g./100 ml.

The date of the primary infection could not be obtained.

Case No. 60

Cerebral Syphilis.

This man was aged 63 years at the date of estimation of his plasma viscosity.

He was admitted to Montrose asylum on 29:7:42 because of his mental symptoms. No details could be obtained regarding any previous anti-syphilitic treatment.

On admission, he was a rather weak old man but he was able to be up in the ward and carry out a few minor tasks to assist the nurses. No definite disease condition was ever detected, apart from his cerebral syphilis.

On 26:8:42, treatment was begun with 3 g. of Tryparsamide, which was discontinued on 10:11:42, after eight injections, because of failing eyesight. By the beginning of 1943 he had gone completely blind, and thereafter, for his own safety, he had to be confined entirely to bed. There had been no further deterioration in his mental and general health when his plasma viscosity estimation was made on 23:2:44

PCV.	Plasma Visc.	ESR.	Plasma protein				Serum NPN.
			Total	Alb.	Glob	Fibr	
%	cs.		g./100 ml.				mg. %
-	1.945	-	6.81	4.02	2.45	0.34	27.1

Note how the plasma viscosity is abnormally high and just below the usual range of the "zone of chronicity".

Note also how the plasma viscosity is abnormally high while the plasma protein fractions, on which the viscosity ultimately depends, are all within the ranges of "normal" values.

Case No. 61

Acute gonorrhoea, with arthritis.

This male patient was admitted to hospital on 14:12:47 with acute gonorrhoea plus an acute swelling of the right ankle and foot - diagnosed as gonococcal arthritis.

Treatment consisted of magnesium sulphate and glycerine dressings to the foot and ankle and of 640,000 units of penicillin given over 4 days beginning on 16:12:47. He was discharged on 31:12:47 to attend the Rheumatism Clinic where he received short-wave diathermy because of restricted ankle movements, and later in February he had wax baths and exercises. All treatment was stopped on 15:2:48 and he remained free from complaints.

The plasma viscosity value was initially increased and its decrease corresponded with the amelioration of the affected joint.

Date	PCV.	PLASMA VISC.	Maximum Sed. Velocity
	%	cs.	mm. / hour
17:12:47	45.2	2.016	135.7
4: 1:48	47.8	1.847	38.0
15: 2:48	48.5	1.765	10.5

Case No. 62

Lymphogranuloma inguinale.

Four weeks prior to admission to hospital, this sailor was infected in Spain. He had a history of typical swollen and matted inguinal lymphatic glands, of 10 days duration. He had no primary sore or urethral discharge; the Wassermann and Kahn tests were later proved to be negative.

On 26:2:48, on admission, he looked ill. His pulse, temperature, and respiration rate were elevated. The inguinal lymphatic glands were swollen, matted, tender, and painful. No other active organic disease was detected.

Treatment was begun at once with sulphathiazole (5g. and then 3 g. daily to a total of 24 g.) and with ichthyol and glycerine applied locally.

On the second day the laboratory tests were:-

Date	PCV.	PLASMA VISC.	ESR.	Plasma protein				Serum NPN.	Gold Floc.
				Total	Alb.	Glob	Fibr.		
	%	cs.		g./100 ml.				mg. %	
27:2:48	47.4	2.258	-	8.41	5.12	2.81	0.48	21.3	o

On 27th also, he received 15 million TAB. intravenously.

His recovery was rapid, so that he was discharged on 6:3:48.

These results correspond to the findings in a reaction to an infective process of moderate severity and show no feature characteristic to this disease.

SEPSIS and SPECIFIC FEVER

Name	S	No.	Date	PCV.	PLASMA VISC.	E. S. R.		Total Plas. Prot.	
						Max.	Wintrobe Ord. Cor.		
				%	cs.	mm/ 1 hr		%	
(A) <u>Skin.</u> + <u>Soft Tissues.</u>									
A.B.	M	1	9: 9	37.5	2.330	24.1	- -	-	septic toe.
M.H.	F	2	1:11	42.3	2.624	49.1	- -	7.33	bed sore, moribund
W.B.	M	3	9:11	39.5	2.603	47.8	- -	7.79	bed sores.
D.E.	M	4	1:12	44.0	2.172	29.8	- -	7.10	multiple septic spots
G.L.	M	5	6:12	-	2.515	-	- -	6.91	" " "
W.H.	M	6	7: 1	-	2.174	-	- -	7.92	Legs and hands, 1 mnt
D.L.	M	7	11: 1	-	2.634	-	- -	7.80	septic knee- severe
J.M.	M	8	8: 2	-	2.313	-	- -	7.05	abscess of thigh
W.R.	M	9	11: 2	-	2.535	-	- -	7.75	severe abscesses of ankle and groin.
			14: 2	-	2.480	-	- -	7.71	
			19: 2	41.7	2.278	18.7	- -	7.39	
			24: 2	-	2.236	-	- -	8.77	
			6: 3	-	2.268	-	- -	8.21	
C.F.	M	10	2: 2	-	2.487	-	- -	7.40	sepsis of face
E.S.	F	11	22: 2	-	2.248	-	- -	-	hands and leg.
H.F.	M	12	7: 3	-	2.177	-	- -	7.42	nose and scalp
			9: 3	-	2.137	-	- -	7.46	
			10: 4	21.3	2.021	2.5	- -	-	
J.C.	F	13	10: 4	-	2.167	-	- -	6.16	abscess of buttock
A.B.	M	14	21: 3	-	3.034	-	- -	7.24	gangrene of foot
I.R.	F	15	12: 4	39.5	2.450	62.5	- -	7.13	gangrene of foot
			27: 4	35.0	2.325	54.2	- -	6.64	
F.D.	M	16	19: 4	47.8	2.455	35.8	7.25 am	7.16	sepsis of elbow
			19: 4	44.4	2.306	11.5	1.30 pm	6.87	
			20: 4	44.8	2.280	23.0	1.55 pm	6.69	
			28: 4	42.2	2.062	48.9		6.59	
S.C.	F	17	10: 5	40.2	2.459	38.9	- -	6.48s	
K.W.	F	18	21: 7	37.7	2.693	40.7	- -	7.56	sepsis of knee
			29: 7	36.0	3.138	53.3	- -	7.99	
J.C.	F	19	27: 7	37.2	2.468	72.4	- -	6.89	sepsis of leg
W.R.	M	20	16: 8	-	2.068	-	- -	6.70	abscess of shoulder
I.R.	F	21	1: 5	43.9	2.171	-	- -	7.92	axillary abscesses
E.F.	M	22	10: 4	47.	1.960	-	9 9	7.78	chronic sepsis of arms.

Name	S	No.	Date	PCV.	PLASMA VISC.	E. S. R.			Total Plas. Prot.	Remarks
						Max.	Wintrobe			
							Ord.	Cor.		
				%	cs.		mm/ 1 hr	%		
(a) Skin and Soft Tissues. (contd.)										
J.C.	M	23	19: 2	-	1.978	-	-	-	7.81	abscess of shoulder
S.M.	M	24	13:12	43.	1.903	-	11	9	7.27	skin sepsis.
M.T.	F	25	24: 4	34.2	2.885	47.5	-	-	7.97s	mastitis
			25: 4	31.6	2.737	24.2	-	-	7.84s	
			27: 4	31.1	2.807	16.9	-	-	8.32s	
			4: 5	29.5	2.760	35.8	-	-	7.38	
			12: 5	27.3	3.078	55.3	-	-	8.07s	died of toxaemia on 5/7.
			24: 5	24.0	2.501	21.7	-	-	7.31s	
T.T.	M	26	23: 5	43.4	2.293	18.3	-	-	7.22s	chronic sepsis of skin + more acute abscesses.
			24: 5	47.1	2.530	26.8	-	-	8.04s	
			29: 5	39.8	2.270	12.6	-	-	7.11s	
(B) <u>Lungs.</u>										
G.L.	M	27	6:12	-	2.515	-	-	-	6.91	pulm. congestion
J.M.	M	28	23:12	-	2.175	-	-	-	6.34	pulm. congestion + fract. femur.
G.M.	M	29	25:12	-	2.007	-	-	-	6.46s	acute bronchitis.
C.H.	M	30	6: 1	41.7	2.244	37.5	-	-	7.64	pulm. congestion
J.M.	F	31	22: 1	-	2.332	-	-	-	8.04	acute bronchitis.
C.H.	M	30	25: 1	-	2.773	-	-	-	9.04	pulm. congestion.
M.H.	F	32	27: 1	-	2.533	-	-	-	7.69	pulm. congestion.
			3: 2	-	2.557	-	-	-	7.40	
C.C.	M	33	7: 2	45.0	2.267	46.3	-	-	7.08	pulm. congestion.
			21: 2	-	2.269	-	-	-	7.28	
			11: 8	-	2.218	-	-	-	7.06	
I.R.	F	34	27: 3	-	2.167	-	-	-	6.62	bronchitis.
A.L.	M	35	13: 5	42.4	2.061	17.8	-	-	7.31	bronchitis.
W.P.	M	36	18:12	46.1	2.125	-	19	18	7.15	bronchitis, chronic
M.S.	F	37	25:11	41.	2.029	-	21	20	7.99	cold in head.
P.V.	F	38	17:11	40.5	1.915	-	18	16	7.20	common cold.
M.B.	F	39	4: 1	-	2.064	-	-	-	6.10	dry pleurisy
			18: 2	-	2.101	-	-	-	6.56	
M.D.	F	40	25:11	42.8	1.925	-	6	7	7.81	pleural pain, ? cause
			16:12	43.7	1.863	-	6	8	7.27	
M.H.	F	41	9: 5	40.	1.965	-	45	41	6.48	recovering from atypical pneumonia

Name	S	No.	Date	PCV.	PLASMA VISC.	E. S. R.			Total Plas. Prot.	Remarks.
						Max.	Wintrobe Ord.	Cor.		
				%	cs.		mm/	1 hr	%	
(C) <u>Miscellaneous infection.</u>										
J.B.	M	42	9:11	45.5	2.279	-	-	-	8.54	septic teeth
H.W.	F	43	1:11	42.3	2.624	49.1	-	-	7.33	cholecystitis
M.W.	F	44	16: 2	-	2.165	-	-	-	7.49	pyelonephritis.
J.G.	F	45	10: 7	49.2	2.057	-	-	-	7.49	choroiditis, with chronic sinusitis.
M.K.	F	46	17:11	44.7	2.045	-	-	-	8.35	cystitis.
P.D.	M	47	22:11	-	1.996	-	-	-	7.31	cystitis.
P.S.	F	48	13:12	42.0	1.998	-	14	14	8.06	tonsillitis, with gland enlargement
S.L.	F	49	17: 3	-	2.238	-	54	-	7.45	salpingitis.
G.H.	M	50	14: 4	40.1	2.063	-	-	-	6.42	appendix abscess
J.B.	F	51	12: 4	32.7	2.197	-	-	-	7.75	bilateral otitis media + purpura.
(D) <u>Specific Fevers.</u>										
J.S.	M	52	17: 9	41.5	2.267	34.8	-	-	7.18	malaria
			13:10	42.0	2.186	24.3	-	-	7.89	
			29:11	31.4	2.040	8.2	-	-	6.25	
			6:12	-	2.364	-	-	-	6.97	
J.C.	M	53	23:11	43.3	1.953	-	-	-	6.50	malaria
			29:11	35.5	1.934	-	-	-	5.79	
W.P.	M	54	22:12	-	2.042	-	-	-	6.30	malaria
T.S.	M	55	14: 9	39.1	2.758	-	-	-	6.85	paratyphoid B
			27: 9	41.3	2.808	35.0	-	-	8.07	
M.F.	F	56	24: 9	38.0	2.084	17.2	-	-	6.91	dysentery
M.H.	F	57	29: 1	-	2.104	-	-	-	6.93	dysentery
C.P.	F	58	2: 2	-	1.913	-	-	-	5.97	dysentery
K.A.	M	59	15: 1	43.2	2.920	-	24	19	8.53	amoebic hepatitis
			21: 1	43.0	3.103	-	39	32	9.43	
R.T.	M	60	25: 2	-	2.158	-	-	-	7.26	erysipelas
S.S.	F	61	29:10	41.0	2.878	81.3	-	-	6.94	lobar pneumonia
M.B.	F	62	13: 3	39.	2.142	-	44	38	7.31	" "
E.C.	F	63	2:12	-	2.043	-	-	-	6.52	" "
G.H.	F	64	25:12	-	2.438	-	-	-	6.88	" "
W.B.	M	65	9:12	-	2.300	-	-	-	7.57	" "
			3: 1	-	1.985	-	-	-	7.75	

Case No. 63

Acute Sepsis.Acute cholecystitis + cholangitis.

This elderly man of 75 years had begun to complain of epigastric pain. Thereafter he had a fairly rapid onset of jaundice, a dark-coloured urine, and clay-coloured stools. He was not admitted to hospital until 8 weeks after the onset of his first symptoms.

The laboratory results were obtained on the day after admission. They supported a diagnosis of an "obstructive" type of jaundice and an inflammatory primary cause (high fibrinogen and albumin) rather than malignant. At operation, six days later, pus was found in the peritoneum, sealed off by adhesions, surrounding an empyema of the gall-bladder. Death ensued and at the post-mortem it was found that the infection had passed up into the liver without the actual formation of abscesses.

PCV.	PLASMA VISC.	Plasma protein				Ser. Npn.	Serum Bilirubin	Thymol Turbidity
		Total	Alb.	Glob	Fibr.			
%	cs.	g. / 100 ml				mg. %	mg. %	unit
39.6	2.401	7.76	3.94	2.97	0.85	36.3	19.2	1

Serum alkaline phosphatase = 30.6 K.A. units/100 ml.

Case No. 64

Sepsis of Knee, + Terminal Decay.

This female asylum patient was complaining continually of aches and pains for which no cause could be detected so that when she did eventually develop a sepsis of the knee joint the disease had progressed far before it received attention. She was 63 years old but did good work in the kitchen.

On 14:7:44 the knee was first seen and treated with heat applied to the part, eusol dressings, and rest. No improvement was obtained. On 19:7:44 the knee abscess was incised; sulpha-thiazole treatment was also begun. The knee continued to discharge until the first few days of August when a satisfactory healing ensued and the drug was stopped.

While she was in bed her doctor took the opportunity of over-hauling her thoroughly. He found that her rotundity was due in part to a large cystic growth of the ovary which he considered to be malignant in character. She was allowed to remain in bed.

Hypostatic pneumonia was detected on 14:8:44. She died on 17:8:44.

The first three plasma viscosity results show the normal rise with a severe pyogenic infection and fall as the infection healed. The fourth value is lower than the third at a time when a rise would have been expected because of the intercurrent additional infection by the hypostatic pneumonia and this further

Date	PCV.		PLASMA VISC		Max.	Plasma protein				Serum
	Cit.	P+A.	Citr.	P+A.	Cit.	Total	Alb.	Glob	Fibr	NPN.
	%		cs.		mm/h	g./100 ml				mg. %
21:7	28.2	37.7	1.874	2.693	99.	7.56	3.96	2.61	0.99	27.4
29:7	26.5	36.0	2.083	3.138	116.	7.99	3.56	3.59	0.84	71.6
1:8	27.6	-	1.978	-	106.	-	-	-	-	-
15:8	21.1	-	1.806	-	60.	-	-	-	-	-

decrease had to be interpreted as a terminal decay.

There is no guarantee in dealing with serial tests at such long intervals that the plasma viscosity had not actually fallen to a low abnormal or even to a normal value by about the 10th of August and that the final value did not, in fact, present a true increase in response to the pneumonia. Further criticism to the assumption that the 4 plasma viscosity points were to be joined into a smooth decay curve can be found in the fact that this would indicate a plasma viscosity value (at death) of approximately 1.77 cs. which is a high abnormal figure; the criticism might be countered by the claim that the hypostatic pneumonia interfered so suddenly with the gradual terminal decay due to the sepsis and malignant tumour that the curve was never given its true length. Caution must be exercised against trying to derive more information from the laboratory tests than one is truly justified.

(See fig. 93, page 367.)

Case No. 64 (b)

Terminal Decay in Acute Intestinal Obstruction.

This case is included to illustrate the speed of the terminal decay and protein changes in an acute abdominal catastrophe.

In August 1943 this female patient of 56 years had a colostomy operation because of an intestinal obstruction due to a volvulus (part of bowel affected is not known). She took a long time to recover from her operation and the surgeon did not undertake to close the colostomy.

On 20:1:44 she complained of a cold in the head and of general malaise. On 27:1:44 her abdomen began to become tense with a recurrence of an intestinal obstruction; the surgeon thought she was too weak to stand against surgical interference. She died on 30:1:44. There was no post-mortem.

The laboratory tests were made on 27th and 29th. The high fibrinogen and low globulin were indications of an acute reaction as contrasted to the expected findings in a chronic infection or malignant tumour.

Date	Cit. PCV.	PLASMA VISC.		Max. Cit. ESR.	Plasma Protein				Serum NPN.
		Citr.	P+A.		Total	Alb.	Glob	Fibr.	
	%	cs.		mm/h	g./100 ml.				mg. %
27:1:44	37.0	1.954	2.840	109.0	8.10	4.05	2.91	1.14	118.4
29:1:44	34.2	1.757	2.413	78.8	7.01	3.40	2.64	0.97	148.4

Case No. 65

Subacute Bacterial Endocarditis.

This girl was 17 years old at the time of the present illness. Seven years previously, she had been in hospital for 6 months because of acute rheumatic fever which involved the mitral valve; a recurrence, four years later, did not cause any more cardiac damage but she again required hospital care for 3 months.

This illness began as a sorethroat, about 10 weeks prior to admission; treatment consisted in penicillin tablets to suck. Two weeks later pain developed in the left shoulder; she was confined to bed for 2 weeks and received no specific treatment. When she resumed work she found that the fingers of both hands were painful, and that her ankles were swollen at night if she had been standing all day. Three weeks later she had a return of the pain to the left shoulder; one week later she was admitted.

On admission, she was in a dirty untidy condition; she was a poor witness. There were no clubbing, no cyanosis, no splinter haemorrhages, and no purpuric spots. The pulse rate was 160 per minute. Blood pressure equalled 90/60. The heart size was within normal limits; the apex beat was 3.5" from the midline in the 5th interspace, with no palpable thrill; an apical blowing pre-systolic murmur was conducted into the axilla. The liver edge was tender where it just projected below the costal margin; the palpation of the spleen produced pain without detecting the organ with certainty.

Date	PCV.	PLASMA VISC.	Wintrobe ESR. Ord. Cor.		Plasma Total Protein
	%	cs.	mm/ 1 hr		g. %
17:12:51	38.2	2.131	40	33	7.78
31:12:51	41.	2.000	24	23	-
7: 1:52	41.	1.905	15	13	7.34
15: 1:52	40.	1.783	15	13	7.06

Nothing could be detected abnormal in the shoulder joint apart from the slight tenderness.

When she was admitted on 21:11:51 the diagnosis was that of a recurrence of the rheumatic fever and she received sodium salicylate in doses of 30 grains three times per day; vitamins and iron were also administered. The initial temperature of 102°F. fell only to 100.6.

The blood culture examination detected a streptococcus viridans infection; the organism was sensitive to penicillin, streptomycin, aureomycin, and chloromycetin to a normal degree. The salicylate was stopped on 25:11:51. On the same day intramuscular injections of penicillin were begun in doses of 1 million units 6-hourly. The evening temperature still rose to 100.6°F. until 4:12:51 and to 99°F. until 11:12:51. Increasing the dose to 1.5 million units 4-hourly, on that date, caused the temperature to remain below 98.4°F.

The penicillin was stopped on 17:12:51 in favour of aureomycin in doses of 1 g. four times per day. The plasma viscosity on that day showed a low abnormal value.

The temperature rose to 100.4°F. on the 18th; penicillin was promptly resumed. After another peak to 100.6°F. on 19:12:51 the temperature was never again abnormal. The combined treatment with penicillin and aureomycin produced a satisfactory clinical response as judged by the patient's condition; the blood culture became negative; and the laboratory tests were normal by 15:1:52.

Case No. 66

Chronic Sepsis.

This girl of 11 years suffered from chronically infected and enlarged tonsils, with secondary enlargement of the lymphatic glands in the neck. There was no other abnormality.

Date	PCV.	PLASMA VISC.	Wintrobe ESR.		Total Plasma Prot.
			Ord.	Cor.	
	%	cs.	mm/ 1 hr		g. %
13:12:47	42.	1.998	14	14	8.06

These results show the slightly raised plasma viscosity associated with a relatively greater rise in the plasma total protein which is characteristic of a chronic disease process.

It should be noted also that these results for a pyogenic infection cannot be distinguished from those of a tuberculous infection, such as in Case No. 50.

Case No. 67

Chronic Skin Sepsis.

This woman had suffered from skin sepsis for 10 years. At first it affected the face, chest, shoulders, arms, and legs. Three years ago it had affected the axillae and these regions were the chief cause for her complaints. During these ten years it was seldom that her skin was completely free from an abscess somewhere.

Her own doctor began a course of injections but discontinued this because of abscess formation at the sites of injection. Penicillin cream, applied locally, was at last producing some improvement. Her Wassermann was negative.

On general examination, no abnormality could be found apart from the skin. Scars from healed abscesses were seen on all parts. The skin in both axillae was moist, darkened and indurated. In the left axilla there were several small indurated discharging abscesses. The axillary glands related to the axillary drainage were enlarged.

Plasma viscosity = 2.171 cs.

~~Blood~~ haematocrit = 43.9%

Plasma total protein = 7.92 g./100 ml.

SARCOIDOSIS.

Name	S	No.	PCV.	PLASMA VISC.	Wintrobe ESR. Ord. Cor.		Plasma protein				Gold Floc.	
			%	cs.	mm/1 hr		g./100 ml.					
F.H.	F	1	40.4	1.998	-	-	7.70	-	-	-	o	
A.C.	F	2	39.	2.468	44	38	8.17	4.0	4.0	0.38	+++	26:2 preg.
			43.8	2.354	18	20	7.00	4.6	2.08	0.32	+++	11:12
M.L.	F	3	41.5	1.877	10	10	6.91	4.5	2.6	0.35	+	parotid
M.W.	F	4	42.0	2.137	27	27	7.35	4.50	2.45	0.58	o	only
L.L.	F	5	40.5	1.987	15	15	7.67	4.90	2.54	0.36	o	
M.C.	F	6	46.3	2.518	16	20	8.96	4.9	2.97	0.53	+	
M.H.	F	7	43.5	2.055	12	14	8.15	4.6	3.2	0.35	++++	
M.T.	F	8	42.0	2.207	34	34	8.37	4.7	3.30	0.37	+++	
M.K.	F	9	43.3	1.919	31	35	7.12	4.60	2.10	0.42	+	
P.C.	F	10	45.	1.923	13	19	7.20	-	-	-	-	
O.H.	F	11	43.	1.995	35	37	-	-	-	-	o	
D.A.	M	1	-	1.922	6	-	7.60	5.0	2.36	0.34	o	24:10
			50.5	1.893	1	6	-	-	-	0.31	+	24:11
F.L.	M	2	47.	2.180	15	15	8.90	5.0	3.53	0.37	o	
M.G.	M	3	49.8	2.001	7	10	7.70	4.9	2.45	0.35	o	
F.B.	M	4	41.1	2.103	32	23	7.70	5.00	2.35	0.35	+	

Case No. 68

Sarcoidosis.

This man had had an irido-cyclitis of the left eye in 1945; his right eye became affected three months later. He had lost some weight; his Mantoux test was negative. With prolonged treatment, his eyesight had returned to normal by 1948. The eye lesions were diagnosed as tuberculous.

A skiagram of his chest showed some enlargement of the superior mediastinum for which the radiologist thought the most probable diagnosis was lympho-sarcoma.

This diagnosis was discounted when he remained well and no change had occurred in the skiagrams by 1948. In March, 1949, he had a flare-up in some lymphatic glands of the neck - probably due to a septic tooth; the skiagram of the chest had still not altered. A gland was removed from the neck for histological examination: the histological features were those of sarcoidosis. Since that date the size of the mediastinum has gradually reduced so that by the summer of 1951 the skiagram was virtually normal in appearance.

Nevertheless, the plasma viscosity in January 1952 persisted in the "zone of chronicity".

Date	PCV.	PLASMA VISC.	Wintrobe ESR.		Plasma protein				Gold Floc.
			Ord.	Cor.	Total	Alb.	Glob	Fibr	
	%	cs.	mm/ 1 hr		g./100 ml.				
14: 1:52	49.8	2.001	7	10	7.70	4.9	2.45	0.35	o

Case No. 69

Sarcoidosis.

The disease had been present in this female patient for at least eight years when the plasma viscosity was estimated; the viscosity gave a result typical of chronic infection.

In 1944 she complained of bronchitis and pain in the chest but the chest physician obtained no evidence of tuberculosis. She also suffered from irido-cyclitis of the right eye. The left eye was affected similarly in 1945; both eyes had yielded to treatment by August 1945. Also, in 1945, she was admitted to hospital for a fuller examination when her chest skiagram showed considerable hilar enlargement suggestive of lymphadenoma; no definite evidence was obtained and she was discharged.

In 1948 she attended the Mass Radiography Unit where the skiagram indicated an old left basal pleurisy, a diffuse shadowing in both lung fields, suggestive of some interstitial fibrosis, and some enlargement of the hilum on each side. She remained under observation. Subsequent skiagrams have shown the parenchymatous shadowing to have almost wholly disappeared and some persisting hilar enlargement.

The medical director of the M.R.U. is quite confident that this is a true case of sarcoidosis although the diagnosis has not been verified by biopsy.

Date	PCV.	PLASMA VISC.	Wintrobe ESR.		Plasma Protein				Ser. Urea	Gold Floc.
			Ord.	Cor.	Total	Alb.	Glob	Fib.		
	%	cs.	mm/	1 hr	g./100 ml.				mg. %	
14: 1:52	43.5	2.055	12	14	8.15	4.6	3.2	0.35	28	++++

Case No. 70

Sarcoidosis.

This female patient was picked up in the Mass Radiography Unit in 1949 when her film showed hilar and mediastinal enlargement due to enlargement of the lymphatic glands in these sites. At that time (November, 1949) she had no symptoms, her blood count was normal, and a tuberculin-jelly skin test was a doubtful positive. Subsequent skiagrams have shown a slight reduction in the hilar enlargement. To exclude lymphadenoma, a lymphatic gland biopsy was made in a groin; the histological appearance was typical of sarcoidosis.

The was still free from symptoms when the laboratory tests were made on 14:1:52.

PCV.	PLASMA VISC.	Wintrobe ESR.		Plasma protein				Blood Urea
		Ord.	Cor.	Total	Alb.	Glob	Fibr.	
%	cs.	mm/ 1 hr		g./100 ml.				mg. %
46.3	2.518	15.5	20	8.40	4.9	2.97	0.53	20

Filter-paper electro-phoresis indicated that the globulin increase was mainly in the β_1 fraction.

Table - XVII a

SIMPLE TUMOURS.

Name	S No.	Date	PCV.		PLASMA VISC.		ESR.			Plasma Protein			Alk. Phos.	Remarks.	
			Cit.	P+A.	Citr.	P+A.	Max.	Wintrobe Ord.	Cor.	Total Alb.	Glob	Fibr.			
			%		cs.			mm/1st h.		g./100 ml.			un. %		
M.M.	F 1	20: 1	26.2	36.1	1.695	2.192	13.4	-	-	7.25	3.99	2.66	0.60	19.5	Parathyroid adenoma
		3: 2	26.0	36.3	1.664	2.174	26.7	-	-	7.69	4.43	2.70	0.57	22.8	+ fractured femur
D.H.	M 2	-	-	47.4	-	1.879	-	1	1	7.92	-	-	-	-	Adenoma of bronchus
N.S.	F 3	-	30.0	41.0	1.468	1.716	0.3	-	-	6.17	4.50	1.67	0.23	-	Uterine fibroids.

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Parathyroid adenoma

Table - XVII b

MALIGNANT TUMOURS.

Name	S No.	Date	PCV.	PLASMA VISC.	E. S. R.		Plasma Proteins			A/G	A/F	K	NPN.	Remarks		
					Max.	Wintrobe	Total	Alb.	Glob						Fib.	
			%	cs.	mm / 10 ⁻⁴	mm / 1 hr.	g. / 100 ml.						mg%			
(A) Stomach																
E.K.	F	1	27: 2	18.5	1.927	2.61	-	7.09	4.37	2.23	0.49	1.96	8.86	0.390	34.4	Secondaries at oper.
E.T.	F	2	4: 3	37.2	1.655	3.89	-	6.42	4.05	2.10	0.27	1.93	14.9	0.389	39.8	
J.B.	M	3	21: 3	46.1	1.932	26.5	-	7.86	4.15	3.15	0.56	1.32	7.47	0.3941	41.8	
N.M.	M	4	25: 3	32.0	1.982	4.61	-	7.27	4.30	2.46	0.51	1.75	8.42	0.3925	46.9	
F.H.	M	5	25: 3	50.0	2.055	3.22	-	7.15	4.14	2.40	0.61	1.73	6.82	0.3920	53.1	
G.H.	M	6	21: 5	46.8	2.312	25:0	-	8.41	4.32	3.56	0.53	1.22	8.19	0.393	49.4	Secondaries in liver
J.M.	M	7	29: 5	44.4	1.781	4.78	-	6.69	4.19	2.14	0.36	1.96	11.8	0.390	48.4	
R.G.	M	8	25:11	44.0	1.969	-	-	6.34	-	-	-	-	-	-	-	
G.T.	F	9	5:12 8:12	- 36.9	1.983 2.188	-	-	7.02 7.32	- 3.74	- 2.26	- 0.33	- 1.66	- 11.5	- 0.393	- 41.8	
E.R.	F	10	6:12 16:12	35.1 32.0	1.961 1.902	-	39	7.34 6.71	- 4.35	- 1.96	- 0.40	- 2.22	- 11.0	- 0.386	- 27.3	
A.U.	F	11	11:12	47.1	2.142	-	38	6.80	-	-	-	-	-	-	-	Secondary in spine and liver.
E.H.	F	12	29: 1	39.9	2.024	-	-	6.98	-	-	-	-	-	-	-	
H.B.	F	13	2: 3	-	1.986	-	-	7.38	4.66	2.32	0.40	2.01	11.8	0.3895	20.1	
N.J.	F	14	21: 4	19.1	1.661	-	-	5.37	-	-	-	-	-	-	-	
M.D.	F	15	2: 9	45.4	2.000	-	22	6.59	-	-	-	-	-	-	-	

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Table - XVII continued Malignant Tumours.

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Name	S No.	Date	PCV.	PLASMA VISC.	E. S. R.		Plasma proteins				A/G	A/F	K	NPN.	Remarks	
					Max.	mm/hr. $\times 10^4$	Wintrobe Ord. Cor.	Total	Alb.	Glob						Fib.
(A) Stomach (Contd.)																
M.M.	M 16	12: 7	26.6	1.871	-	-	-	6.08	-	-	-	-	-	-	Obstruct. jaundice	
E.B.	F 17	16: 7	40.0	2.160	-	48	44	6.91	3.53	2.73	0.67	1.29	0.3920	36.3		
D.F.	F 18	28: 4	19.6	1.705	1.00	-	-	5.04	-	-	-	-	-	-		
(B) Colon.																
C.F.	M 19	15: 4	50.0	2.077	-	-	-	6.95	-	-	-	-	-	-	On HIL therapy	
E.S.	M 20	12: 3	48.4	1.917	29.2	-	-	6.49	3.71	2.13	0.65	1.74	5.71	0.3883		47.4
(C) Rectum.																
M.S.	M 21	14:10	39.5	2.306	-	-	-	7.43	4.02	2.66	0.75	1.51	5.39	0.391	33.6	
		8:12	42.1	2.166	-	-	-	7.03	3.94	2.77	0.32	1.42	12.5	0.3928	42.0	
		3: 2	40.9	2.190	-	-	-	6.92	3.82	2.40	0.70	1.59	5.45	0.390	35.3	
		31: 3	38.0	1.902	-	33	11	6.25	3.67	2.07	0.51	1.77	7.27	0.391	33.3	
		25: 5	39.1	1.876	-	-	-	6.24	3.67	2.08	0.49	1.76	7.57	0.392	26.2	
		23: 7	43.2	1.941	-	17	12	6.72	3.92	2.35	0.45	1.67	8.73	0.3925	30.7	
		20: 9	43.5	1.905	-	-	-	6.66	4.08	2.19	0.39	1.87	9.61	0.391	-	
E.R.	F 22	25:11	36.2	2.048	-	-	-	6.70	-	-	-	-	-	-	terminal decay also pernicious anaemia	
A.S.	M 23	17: 5	25.0	1.644	28.3	Citrate Plasma			-	-	-	-	-	-		
		4: 6	21.3	1.538	5.0	"			-	-	-	-	-	-		
		4: 7	24.3	1.452	2.9	"			-	-	-	-	-	-		
R.W.	M 24	9:12	-	1.962	-	-	-	7.27	-	-	-	-	-	-		

Table - XVII continued

Malignant tumours.

Name	S No.	Date	PCV.	PLASMA VISC.	E. S. R.			Plasma proteins.			A/G	A/F	K	NPN.	Remarks		
					Max.	Wintrobe		Total	Alb.	Glob						Fib.	
						Ord.	Cor.										
g./ 100 ml.																	
mg. %																	
(D) Pancreas.																	
J. E.	M 25	21: 5	45.2	2.156	33.6	-	-	7.42	4.22	2.53	0.67	1.67	6.33	0.3915	48.9	Jaundiced jaundiced jaundiced	
C. B.	F 26	1:10	33.0	1.694	-	-	-	5.00	-	-	-	-	-	-	-		
R. S.	M 27	10: 2	44.5	2.081	-	-	-	7.13	-	-	-	-	-	-	-		
A. C.	M 28	19: 3	41.3	1.934	-	-	-	6.48	-	-	-	-	-	-	-		
		10: 4	41.7	2.041	-	-	-	7.27	-	-	-	-	-	-	-		
S. F.	M 29	4: 8	44.0	2.341	-	-	-	5.78	3.05	2.24	0.49	1.36	6.22	0.3930	39.3	jaundiced	
W. B.	M 30	12:12	47.5	2.553	-	-	-	7.45	-	-	-	-	-	-	-	jaundiced	
R. O.	F 31	19: 6	28.7	2.476	-	-	-	6.44	-	-	-	-	-	-	-	jaundiced	
(E) Prostate.																	
T. H.	M 32	27:11	51.1	1.976	-	-	-	7.45	-	-	-	-	-	-	-	Acid phos. = 0.9 unit	
J. S.	M 33	12:12	37.1	2.675	-	-	-	7.92	-	-	-	-	-	-	-		
C. T.	M 34	28: 1	35.4	2.009	-	-	-	7.06	-	-	-	-	-	-	-		" = 2.0 unit.
W. J.	M 35	24: 2	32.8	2.166	-	-	-	6.66	-	-	-	-	-	-	-		" = 1.0 unit
C. D.	M 36	14: 6	43.9	2.090	-	-	-	7.16	-	-	-	-	-	-	-		" = 7.3 unit
		23: 7	34.3	2.703	-	52	28	7.91	3.36	3.69	0.86	0.953	3.93	0.376	28.1	secondary in lung.	
W. M.	M 37	16: 8	41.4	2.007	-	-	-	6.84	-	-	-	-	-	-	-	acid phos. = 1.4 unit	
J. A.	M 38	6: 9	40.4	2.171	-	-	-	7.27	-	-	-	-	-	-	-	" = 3.7 unit	
F. O.	M 39	10:11	40.8	1.923	-	-	-	6.23	-	-	-	-	-	-	-	" = 0.7 unit	

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Acid phos. = 0.9 unit

" " = 2.0 unit.

" " = 1.0 unit

" " = 7.3 unit
secondary in lung.

acid phos. = 1.4 unit

" " = 3.7 unit

" " = 0.7 unit

Table - XVII continued

Malignant tumours.

Name	S No.	Date	PCV.	PLASMA VISC.	E. S. R. Wintrobe Ord. Cor.	Plasma protein					A/G	A/F	K	NEN.	Remarks
						g./ 100 ml.									
						mm/ 1 hr	Total	Alb.	Glob	Fib.					
(C) Miscellaneous tumours (contd.)															
E. S.	F 54	27:10 3:11	33.7 33.1	2.471 2.549	- -	- -	6.76 6.79	3.50 3.44	2.44 2.60	0.82 0.75	1.43 1.32	4.26 4.58	0.386 0.388	25.2 23.2	sarcoma of femur
B. C.	M 55	2: 8	36.5	1.897	38	21	6.30	-	-	-	-	-	-	-	sarcoma of pelvis.
M. B.	F 56	27: 1 24: 3 17: 4	35.4 13.6 15.9	1.808 1.683 1.770	- 70 -	9	5.08 5.18	- 3.23	- 1.41	- 0.54	- 2.29	- 6.80	- 0.380	- 21.2	reticulum cell sarcoma
R. B.	F 57	15: 3	43.1	2.197	-	-	8.24	-	-	-	-	-	-	-	cancer of breast
E. W.	F 58	7: 4	28.7	2.242	-	-	7.06	-	-	-	-	-	-	-	cancer of breast.
I. C.	F 59	27: 1	39.6	2.065	19	13	7.81	-	-	-	-	-	-	-	malignancy, not diagnosed
A. S.	M 60	27: 2	46.8	1.886	14	14	6.21	3.49	2.39	0.33	1.46	10.5	0.3936	21.8	definitely.
G. H.	M 61	31: 3	42.4	2.410	35	28	7.03	3.76	2.34	0.93	1.61	4.06	0.383	36.8	"
H. S.	F 62	21: 4	25.8	1.793	-	-	6.55	-	-	-	-	-	-	-	"
A. L.	M 63	1: 6 15: 6 22: 6	- 23.8 25.7	1.766 1.783 1.774	- - -	- - -	5.72 5.76 6.01	- - -	- - -	- - -	- - -	- - -	- - -	- - -	"
P. D.	M 64	22:11	-	1.996	-	-	7.31	-	-	-	-	-	-	-	"
O. C.	F 65	28: 9	29.3	1.855	-	-	5.90	3.68	1.97	0.25	1.87	14.5	0.390	29.2	"
L. H.	T 66	12: 4	40.7	2.297	-	-	8.35	-	-	-	-	-	-	-	"
F. C.	M 67	20:12	47.	2.207	12	12	7.99	4.03	3.34	0.62	1.21	6.50	0.3922	-	"

Table - XVII continued

Malignant tumours.

Name	S No.	Date	PCV. %	PLASMA VISC. cs.	E.S.R. Wintrobe			Plasma protein.			A/G	A/F	K	NPN. mg. %	Remarks	
					mm/ 1 hr.	Ord.	Cor.	Total	Alb.	Glob						Fib.

(G) Miscellaneous tumours (contd.)															
A.S.	M 68	13: 2	23.5	1.912	61	17	6.18	4.1	2.4	0.38	-	-	-	-	cancer of prostate.
C.F.	F 69	13: 4	-	1.944	-	-	7.92	-	-	-	-	-	-	-	tumour of brain
M.E.	F 70	18: 5	50.	2.280	3	11	7.94	4.20	3.26	0.48	-	-	-	-	tumour of brain
I.G.	M 71	28: 5	24.0	1.845	27	0	6.85	4.6	2.0	0.25	2.3	-	-	-	prostatic cancer
D.E.	M 72	6: 6	44.	2.235	28	24	7.05	4.2	2.3	0.55	1.82	-	-	-	cancer of bronchus.
C.H.	M 73	27: 1	14.	1.745	67	5	5.3	3.1	1.8	0.4	1.72	-	-	-	recurrent prostatic ca.
C.M.	M 74	10: 9	-	1.716	-	-	5.77	3.73	1.68	0.36	2.21	-	-	-	multiple 2ndary deposits
B.H.	M 75	19: 9	-	1.822	3	-	6.95	-	-	-	-	-	-	-	early prostatic cancer
A.C.	M 76	19:10	-	1.926	-	-	7.24	-	-	-	-	-	-	-	cancer of rectum
H.L.	M 77	3:11	-	1.685	-	-	5.47	-	-	-	-	-	-	-	cancer or rectum
S.G.	F 78	21:11	40.	2.190	41	38	7.40	5.3	2.46	0.64	2.16	-	-	-	sarcoma of femur
R.T.	F 79	21: 1	44.2	1.781	5	7	7.20	5.1	1.73	0.37	2.95	-	-	-	sarcoma of fibula
L.M.	F 80	15:11	-	1.925	-	-	5.94	-	-	-	-	-	-	-	suprarenal tumour
J.G.	M 81	26:11	42.0	2.204	40	32	6.40	3.0	2.58	0.82	1.16	-	-	-	cancer of bronchus
G.S.	M 82	28:11	36.1	2.693	50	29	7.1	2.6	3.78	0.72	0.69	-	-	-	cancer of lung

Case No. 71 Parathyroid Adenoma.

This case presents some problems in differential diagnosis.

She was admitted to hospital to have gold therapy for her arthritis on 12:12:46. Three years prior to admission her knees became stiff, but painless; a few months later her neck was painful on turning her head. Early in 1946 her condition became suddenly worse and the severe pain in her knee confined her to a chair. Two months later she was treated at Harrogate with sulphur baths, etc. During treatment she fell and tore the right patellar tendon which was sutured; later progress to walking was slow. Since the accident in the summer of 1946 she became more helpless and could walk only with assistance

On admission, she was a small thin weak patient with no other definite pathology apart from a limited flexion of left ankle and a swollen right knee due to synovitis. In addition to the gold therapy, local treatment to the right knee consisted of radiant heat and quadriceps drill for a weakened muscle.

15: 1:47 While using the bed-pan she had a spontaneous fracture at junction of middle and lower third of the right femur. This fracture was treated in a Thomas splint and later in a plaster splint. An X-ray of the femur showed the fracture plus another rarified area higher in the shaft: her left femur showed areas of sclerosis. At this time it was noted that the patient had become

sufficiently hirsute as to need shaving. It was also noted that she had been having repeated bouts of sickness. An X-ray of her skull had yielded a picture which the radiologist then and later diagnosed as that of secondary malignant deposits.

20: 1:47 the laboratory results of this date were:-

Urine - No Bence-Jones protein; 17-ketosteroid excretion within normal limits for her sex and age (= 56 years)
 Blood - Wassermann and Kahn, negative.

Serum calcium = 16.3 mg./100 ml.

Serum inorganic phosphate = 3.9 mg./100 ml.

Plasma alkaline phosphatase = 19.5 K.A. units/100 ml.

Plasma acid phosphatase = 2.4 K.A. units per 100 ml.

Plasma total protein = 7.25 g./100 ml.

albumin = 3.99 " "

globulin = 2.66 " " NPN = 52.9 mg. %

fibrinogen = 0.60 " "

Haematocrit: Citrate = 26.2% , P + A Oxalate = 36.1%

Plasma Viscosity: Corrected citrate = 1.695

P + A Oxalate = 2.192

Maximum citrate sedimentation velocity = 13.4 cm./sec $\times 10^{-4}$

The clinicians in charge of the patient considered four main possible diagnoses - Cushing's syndrome, Paget's disease, Parathyroid adenoma or carcinoma, Malignancy elsewhere. A mass was palpated in the stomach with the patient relaxed under a general anaesthetic, and this finding, together with the report by the radiologist and the history of vomiting, led to the diagnosis of carcinoma of the stomach with secondary deposits in the bones. It was admitted that the blood biochemistry was also in agreement with a diagnosis of parathyroid overactivity.

I obtained permission for a further blood test, which was made on 3: 2:47. Her general condition was too weak to permit a barium meal or a gastric test meal being applied.

Blood - Serum calcium = 18.5 mg./100 ml.
 Serum inorganic phosphate = 4.4 mg./100 ml.
 Plasma alkaline phosphatase = 22.8 K.A. units/100 ml.
 Plasma acid phosphatase = 7.2 K.A. units per 100 ml.
 Plasma total protein = 7.69 g./100 ml.
 albumin = 4.43 " "
 globulin = 2.70 " "
 fibrinogen = 0.57 " "
 Non-protein-nitrogen = 67 mg./100 ml.
 Haematocrit: Citrate = 26% ; P + A Oxalate = 36.3%
 Plasma Viscosity: Corrected citrate = 1.664
 P + A Oxalate = 2.174
 Maximum citrate sedimentation velocity = 26.7 cm./sec. $\times 10^{-4}$

On reviewing the information then available I decided that all the signs and symptoms could be explained on the basis of a Simple Parathyroid Adenoma, except for the palpable mass in the stomach. The biochemical tests on the calcium, phosphate and phosphatase would fit in with this diagnosis; the hypercalcaemia would explain the vomiting; the changes in the skull in parathyroid disease are acknowledged to resemble that of secondary deposits. In addition, the non-specific tests supported a simple tumour as (1) the plasma proteins, and especially the albumin fraction had actually increased at a time when the fall of "terminal decay" would have been expected, and (2) the citrate plasma viscosity/maximum sedimentation velocity had remained on the periodic curve

in spite of a decrease in the viscosity and a rise in the ESR.

I pleaded that an exploratory operation on her parathyroid glands would be justified even in her weak state in view of her hopeless prognosis. This suggestion was refused; further investigations were also forbidden.

She fractured her other femur spontaneously on 30: 3:47.

She was sent home on 15: 4:47, with a very short expectancy of life.

A surgeon in another hospital successfully removed a tumour of her parathyroids which was histologically verified as a simple adenoma.

Case No. 72 Adenoma of Bronchus.

A physician colleague, aged 33 years, was sitting quietly at his fire-side when he brought up about a cup-ful of bright red blood via his larynx. Because of staff shortage he had been over-working in the wards; he was attempting some laboratory investigations for an M.D. thesis; he travelled nearly 40 miles daily; he had many domestic worries; and he had been slimming successfully during the previous six weeks with the aid of 'dexedrine' tablets. Naturally he was afraid that he might be suffering from pulmonary tuberculosis. His X-ray of the chest revealed no pathology.

The laboratory results of a blood test on the day following the haemoptysis were completely normal also.

Plasma viscosity = 1.879 cs.

Haematocrit = 47.4%

Wintrobe ESR. = 1 mm. in first hour.

Total plasma protein = 7.92 g./100 ml.

Further investigation by the bronchoscope showed an adenoma of a bronchus. The tumour was removed by an approach through the chest wall. The simple nature of the tumour was confirmed by histological examination.

Case No. 73

Fibroids of Uterus.

This patient was a nurse aged about 35 years. She was admitted to her sick quarters because of her complaint of severe abdominal pain. Menstruation was regular and not excessive in amount or duration; there had been no change recently in its character.

On rectal examination the cavity was found to be almost closed by a very firm mass in the anterior wall; the finger tip could just feel the upper border of this mass. A carcinoma of the rectum was feared but the laboratory results were all in favour of a tumour of a simple nature.

Laparotomy revealed multiple fibromata of the uterus; hysterectomy was performed.

Laboratory results on a blood investigation:-

Plasma Viscosity: Corrected citrate = 1.468 cs.
P + A Oxalate = 1.716 cs.

Haematocrit: Citrate = 30.0% ; P + A Oxalate = 41.0%

Maximum citrate sedimentation velocity = $0.31 \text{ cm./sec.} \times 10^{-4}$

Plasma total protein = 6.17 g./100 ml.
albumin = 4.50 " "
globulin = 1.67 " "
fibrinogen = 0.23 " "

Non-protein-nitrogen = 30.6 mg./100 ml.

Case No. 74 Teratoma testis, with metastasis.

My cousin, aged 21 years, had received his inoculations and his medical examination in preparation for going overseas when he came to spend part of his embarkation leave with me, in August 1946. He had had a severe bronchitis three weeks previously from which his recovery was not complete; he also complained of lassitude, lack of appetite, and vague pains in the shoulders and the praecordium.

Because of my recent attack of tuberculosis his mother was rather worried. I volunteered to estimate his plasma viscosity to reassure her.

Corrected citrate plasma viscosity	=	1.557 cs.
Maximum citrate sedimentation rate	=	24.0 mm./hour
	=	6.67 mm./sec. $\times 10^{-4}$
Citrate blood haematocrit	=	36.0%

The plasma viscosity value was at the upper part of the normal range. This satisfactory result was offset by an abnormally high ESR. which removed the combined point from the viscosity/ESR curve of correlation. Thus I was dealing with a probable case of "terminal decay".

In the asylum I lacked facilities for a thorough investigation. I made certain that he reported sick on his return to the army and thus miss his draft. A radiographic examination readily detected a secondary tumour invasion of the

lungs but the discovery of the primary growth in a teratoma of a testis (verified histologically) proved more difficult.

The earlier diagnosis made possible by the plasma viscosity test allowed of his discharge from the army and of his care in the comfort of his own home until his death only four months later.

Case No. 75 Amelioration of Cancer of Rectum by H₁₁ .

This man suffered from a carcinoma of the rectum which had ulcerated into the bladder when a colostomy was performed in the autumn of 1947. The abdominal wound broke down and granulation tissue grew out from the wound. For the later claims for the effect of this drug (H₁₁) it should be noted that the diagnosis of malignancy was confirmed by histological examination of a piece of tissue removed at the operation.

In desperation, H₁₁ was given and I first came in contact with the patient when I carried out the biochemical investigations demanded by the SUSAL laboratories in order to control its therapy. He had to be brought to the laboratory by taxi and he needed help to mount the stairs. There was a dreadful stench from his colostomy, from the foul dressings of his broken-down and granulating wound, and from the clothes soiled with septic urine. The first results show the increased plasma viscosity in accord with his horrid conditions; the albumin is notably high.

The therapy continued and the patient improved steadily. The sinus between the bladder and rectum healed; hexamine treatment ultimately produced a sterile urine. The abdominal wound slowly healed until only a few granulomatous spots remained. He learned to control his colostomy properly. His interest in life increased.

Date	PCV.	PLASMA VISC.	Wintr. ESR.	Plasma Protein				Gold Floc
				Total	Alb.	Glob	Fibr	
	%	cs.	mm/hr	g./100 ml.				
14:10:47	39.5	2.306	-	7.43	4.02	2.66	0.75	o
8:12:47	42.3	2.166	-	7.03	3.94	2.77	0.32	o
3: 2:48	40.9	2.190	-	6.92	3.82	2.40	0.70	o
31: 3:48	38.0	1.902	33	6.25	3.67	2.07	0.51	o
25: 5:48	39.1	1.876	-	6.24	3.67	2.08	0.49	o
23: 7:48	43.2	1.941	17	6.72	3.92	2.55	0.47	o
20: 9:48	43.5	1.905	-	6.66	4.08	2.19	0.38	o

He was able to resume his occupation as a dentist where the close contact with the patient demands a fastidious standard of personal hygiene.

The fall in the plasma viscosity and the plasma proteins in the first five tests might be attributed to a terminal decay and no indication is given by them that the usual progress to death will not ensue. The maintenance of the high haematocrit values, however, is quite contrary to the usual experience in such a severe case. The later increase in albumin is also contrary to the usual behaviour of this protein fraction in malignancy in its later stages, and I believe that the H_{11} must be given some credit for this extraordinary progress of disease. The high plasma viscosity values which persist at the end of the series of results are an indication that there has been no complete "cure". (No further knowledge of the case is available since I left Sunderland.)

Case No. 76 Hypernephroma.

The extremely high plasma viscosity, ESR., and protein values are noteworthy - they far exceed any values found in my series of malignant cases with other types of disease.

This patient was admitted to hospital at Sunderland in October 1946. He was complaining of marked loss of weight and of a hard cough of several months duration. He was obviously anaemic. His age was 51.

A malignant cause for his symptoms was suspected and he had a thorough investigation, including pyelograms; no indication was obtained of the site of a possible lesion. The pile-bearing area of the rectum was removed because it might have been the cause of repeated blood loss leading to the anaemia.

In January, 1947 he was readmitted and another full examination was made, but again nothing definite could be detected. He had an irregular evening elevation of temperature which lead to a further search for a septic focus - again without success. Blood culture, Widal, and Paul Bunnell tests were consistently negative. Penicillin therapy had no effect on the elevation of temperature.

Date	PCV.	PLASMA VISC.	Wintrobe ESR.		Plasma Protein				NPN.	Max. ESR.
			Ord.	Cor	Total	Alb.	Glob	Fibr		
	%	cs.	mm/ 1 hr		g./100 ml.				mg.%	mm/hr.
27: 1:47	28.1	3.278	60	26	-	-	-	-	-	184
7: 2:47	32.4	3.689	-	-	9.00	3.80	3.69	1.51	48.4	204

He next went to Manchester for the investigation of his anaemia by the haematologists of that city. The diagnosis was Aleukaemic leukaemia, but it was applied reluctantly and with hesitation.

However, two weeks before his death in May 1947 he developed haematuria and a swelling in the loin, so that a confident diagnosis of Hypernephroma was finally reached.

The high plasma viscosity values were due to unusually high fibrinogen levels. There is no known reason why the fibrinogen should be so elevated but the explanation may be found ultimately in the same mechanism by which an elevation of temperature is a characteristic phenomenon of tumours related to the kidney. This high fibrinogen produced a very low figure for the plasma protein equilibrium factor and it was well below the maximum of the group in which a 100% mortality rate had been noted; the ordinary albumin/globulin ratio was still above unity.

Case No. 77 Carcinoma of Stomach

This lady, E.R., had a year's history of epigastric pain which lasted for 1 - 2 hours, was not related to food or exertion, but was relieved by alkali. She vomited on several occasions. There had been no loss of weight. She was aged 58.

No abnormality of the abdominal contents was detected by physical examination.

A barium meal did not show evidence of a gastric ulcer or neoplasm. An alcohol test meal had an initial achlorhydria, with free hydrochloric acid after histamine injection; there was no lactic acid in the fasting juice. The tests for occult blood in the faeces were positive on 10 occasions.

Date	PCV.	PLASMA VISC.	Wintr. ESR.	Plasma Protein				NPN.	Gold Floc
				Total	Alb.	Glob	Fibr.		
	%	cs.	mm/hr	g./100 ml				mg. %	
6:12:47	35.1	1.961	39	7.34	-	-	-	-	o
16:12:47	32.0	1.902	-	6.71	4.35	1.96	0.40	37.3	o

The plasma viscosity test did not assist much in the differential diagnosis between an ulcer and a carcinoma. The most definite indication of malignancy was in the falling haematocrit values yet this might have followed the bleeding of a simple ulcer (cf. positive occult blood tests).

At operation on the 31:12:47, a large indurated malignant ulcer

was present in the stomach wall, a short distance from the pylorus. There was already secondary involvement of the associated lymph glands, but there were no obvious deposits in the liver or elsewhere.

Case No. 78

Multiple Myeloma.

This man, aged 52 years, was admitted to hospital on 6:6:50, with a history of loss of weight (24 lbs. in 1 year), anorexia plus nausea after coughing for 6 months, and a constant feeling of constriction around the lower chest, not related to food, for one month. Otherwise he had been a very healthy man except for a little sputum as a result of gas in the 1914 war.

On examination, he was a thin wasted and obviously anaemic man. There was a single enlarged lymphatic gland in left supraclavicular region. No other abnormality was detected.

His temperature was elevated: this did not respond to the empirical exhibition of salicylate, penicillin, or aureomycin.

The diagnosis made at this stage was of a Neoplasm, probably of stomach or lung.

Further special investigations did not help much. Barium meals revealed no pathology in stomach or duodenum; tests for occult blood in faeces were always negative; and free HCl was found in a test meal analysis. Skiagrams of chest showed no abnormality of lungs or ribs; no tubercle bacilli or malignant cells were ever detected in the sputum. Blood agglutination tests for B. abortus, typhoid and paratyphoid were negative. The enlarged lymphatic gland was removed and examined histologically but there was no evidence of neoplastic invasion or any other

Date	PCV.	PLASMA VISC.	Wintrobe ESR.		Plasma protein				Gold Floc	Serum Alk. Phos-ase
			Ord.	Cor.	Total	Alb.	Glob	Fibr		
	%	cs.	mm/ 1 hr		g./100 ml					units %
26: 7	28·	6·123	19	0	11·27	2·3	8·3	0·67	o	24·
27: 7	26·5	5·155	36	6	10·5	1·9	7·9	0·71	o	26·
16: 8	26·5	6·660	16	0	10·72	2·3	7·7	0·72	o	29·
17:10	22·	5·585	-	-	11·8	1·1	10·0	0·66	o	37·8

abnormality. Bone marrow biopsies on 31:7 and 4:8 showed an excess of cells of the plasmocyte and reticulum series - not sufficient to allow a definite diagnosis. Serum acid phosphatase was low (= 1·0 K.A. units per 100 ml.). Bronchoscopy did not detect a tumour when performed later in September.

The diagnosis was given with some confidence when the plasma proteins were first investigated some 7 weeks after admission. The first plasma sample was prepared by blood drawn in another laboratory and there was no check on the withdrawal being free from stasis and the history of the plasma sample until it reached me for viscosity estimation could not be guaranteed as shielded from evaporation losses, etc. Hence there may be a large part of the difference between the viscosities at 24-hours interval due to laboratory errors but it has also to be accepted that such a large difference may be due entirely to changes within the patient. He was most uncooperative so that I was unable to make further tests at short intervals on him to study this point.

The results of this patient also demonstrate how small changes in the protein fractions, when their total amount is high, can be associated with large changes in the plasma viscosity values - this is to be expected from a consideration of the graphs of the relation between the concentration and the viscosity of solutions of the purified fractions.

The gold flocculation and thymol turbidity and flocculation tests were consistently normal in spite of the increased globulin.

Case No. 79

Multiple Myeloma.

This case presents the diagnostic problems which this disease can raise. The biochemical results from my laboratory gave a lead towards the correct diagnosis.

This lady, aged 38 years, was treated in April 1948 with penicillin and sulphonamides for a septic thumb. She was in bed for two weeks, and on getting up she felt very weak, especially in the legs. She then recalled that she had had 'rheumatism' in her legs prior to the episode of the septic thumb and her rate of walking had been slowed. After a further 3 weeks of convalescence she still felt tired, she had a sharp pain in the right submammary region, she had lost a little weight, and she felt generally shaky. Her own doctor detected exaggerated reflexes, tremors of hands, no tachycardia but frequent extrasystoles, but no excess sweating. He referred her to hospital as a possible case of hyperthyroidism.

7:7:48 Her B.M.R. on this day was +8 . A skiagram of the chest was normal. She now reported a very severe pain across her back which had appeared 2 weeks previously; she was never free from pain and at its worst she had to retire to bed for relief. She had become so weak that she could not do her housework. Yet on physical examination nothing abnormal could be detected. The diagnosis of rheumatoid arthritis was now raised and she was again referred to me for her plasma viscosity to be estimated.

Date	PCV.	PLASMA VISC.	Wintrobe ESR.		Plasma protein				Plas. Alk. Phos.	Thymol		Gold Floc.
			Ord.	Cor.	Total	Alb.	Glob	Fibr		Tur.	Fl.	
1948	%	cs.	mm/ 1 hr		g./100 ml.				un.%	un.		
12:7	29.3	2.793	59	32	9.90	-	-	-	4.7	16	4+	5+
28:7	30.3	3.090	59	33	10.33	4.13	5.76	0.44	4.0	18	5+	5+
9:8	30.0	3.264	60	34	10.84	4.26	6.11	0.47	4.5	15	4+	5+
24:8	29.0	3.656	-	-	11.19	4.16	6.42	0.61	5.2	12	3+	5+
14:9	24.6	3.495	64	26	11.24	3.92	6.96	0.36	4.3	15	4+	5+
20:9	23.2	3.346	-	-	11.04	4.08	6.57	0.39	4.2	18	5+	5+

12:7:48 The laboratory tests of this date are given in the table above. In view of this indication of a severe disease condition she was admitted to the ward for a thorough investigation. She then had her severest pain in the spine and pelvic bones so that she had skiagrams taken to determine if any signs of ankylosing spondylitis. The radiologist reported that there was no evidence of ankylosing spondylitis but a generalised hypocalcification of the lumbar spine and pelvis required the exclusion of generalised osteitis fibrosa. The femora also showed a decreased calcification but the humeri appeared normal.

24:7:48 The laboratory findings of this date, especially the low phosphatase, made a parathyroid disease unlikely -

Blood urea = 24 mg./100 ml.

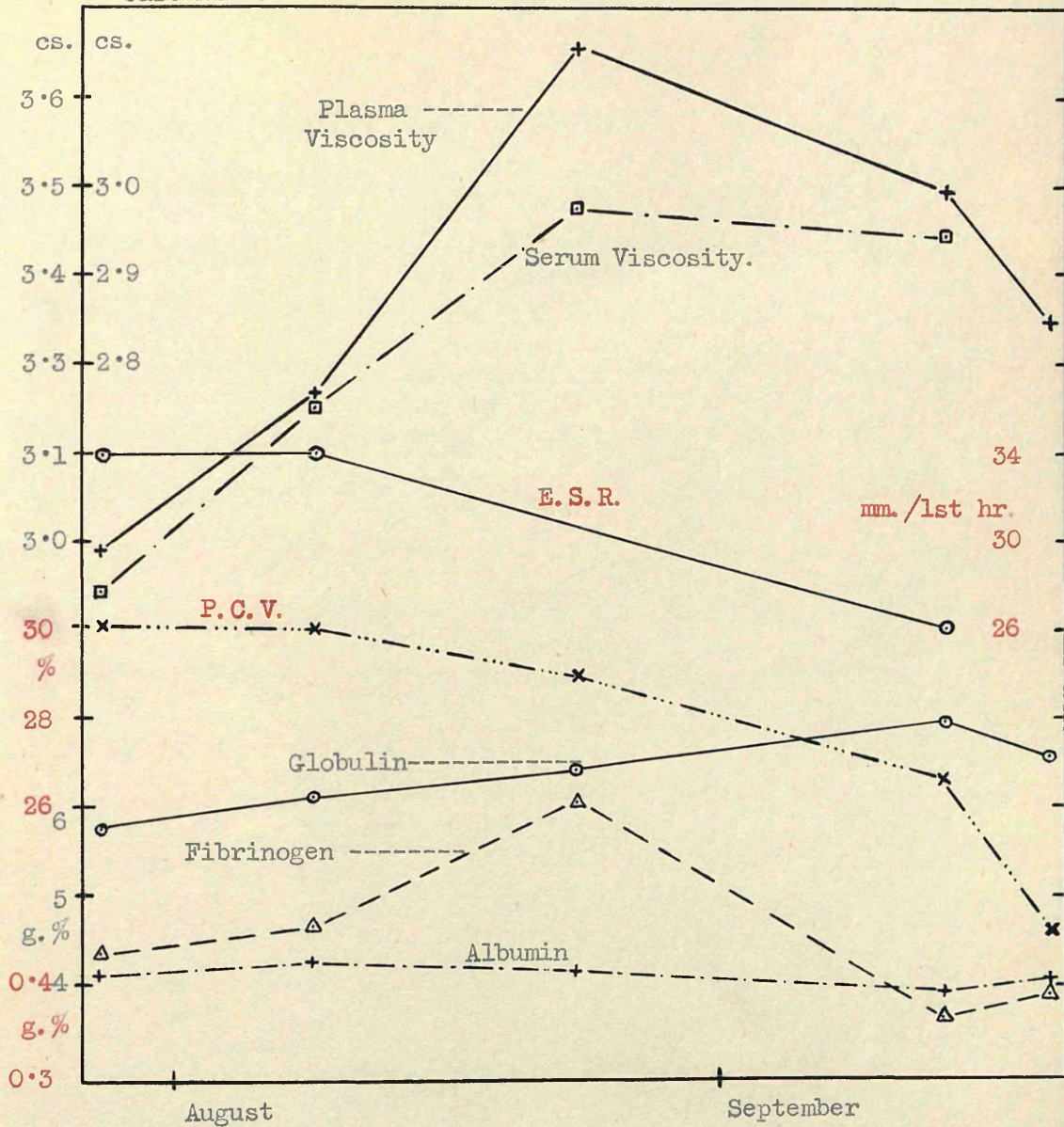
Serum calcium = 10 mg./100 ml.

Serum inorganic phosphate = 4.4 mg./100 ml.

Serum alkaline phosphatase = 4.7 K.A. units per 100 ml.

28:7:48 The repeated biochemical tests of this date, plus the other tests and clinical information, now strongly suggested the diagnosis of multiple myeloma. Bence-Jones protein could not be

Case No. 79



The plasma and serum viscosities, the corrected Wintrobe ESR., the haematocrit, and the plasma protein fractions - studied in a case of Multiple Myeloma over a period of just less than two months.

detected in the urine on repeated testing. In view of our other very high results in the case of hypernephroma (see section of cases of malignant disease) an attempt to exclude this condition was made by an intravenous pyelogram for kidney positions.

7:8:48 The diagnosis was verified by the discovery of myeloma cells in a sternal marrow puncture.

Treatment with Urethane caused little change in her condition. She was weaker and entering her terminal decay when the last test of my series was measured: she then was so light that a single ambulance attendant was able to carry her like a large infant.

Case No. 80

Multiple myeloma.

This man was admitted to hospital in a semi-comatose condition on 9:3:50 and died on 13:3:50. Because of slow cerebation a vague history only was obtained - he had had a fall at work 2 years ago; for 1 year he had pains in the back and chest and these pains had been getting so severe that he required sedatives to sleep; chief pain was in lower chest.

On examination, he was a wasted elderly man. Bony tenderness was found only over the right lower ribs. The liver was enlarged. No other definite abnormality was detected.

11:3:50 Laboratory results:-

Plasma viscosity	=	3.182 cs.	
Wintrobe ESR.	=	52 mm.	/ 1st hour
Corrected " "	=	26 " "	
Haematocrit	=	33.4 %	Gold flocculation = +++++
Plasma total protein	=	11.9 g./100 ml.	
albumin	=	4.2 " "	
globulin	=	7.3 " "	
fibrinogen	=	0.41 " "	
Blood urea	=	95 mg./100 ml.	
Serum calcium	=	15.8 " "	
Plasma alkaline phosphatase	=	9.0 K.A. units per 100ml.	
Serum acid phosphatase	=	2.5 " "	
Formalin-fast acid phosphatase	=	1.0 " "	

The post-mortem on the 14:3:50 confirmed the diagnosis. The 3rd and 5th lumbar vertebrae had collapsed. Myelomatous tissue was detected in the vertebra, ribs, calvarium, and sternum.

Table - XVIII

Diseases of the Liver.

In this table, Bil. = bilirubin in mg. per 100ml. serum; Alk.phos. = alkaline phosphatase in KingArmstrong units per 100 ml. of serum or plasma; TT = thymol turbidity in units; TF = thymol flocculation, GF = gold flocculation; Chol. = cholesterol in mg. per 100 ml. of serum or plasma.

Name	S No	Date	PCV.	PLASMA VISC.		E. S. R.		Plasma Proteins			A/G	K	Bil.	TT	TF	GF	Alk. Phos	Bl. Urea	Chol	Remarks	
				cs.	mm/1 hr	Ord.	Cor.	Tot.	Alb.	Glob											Fib.
(A) Infective Hepatitis - Acute																					
A. R.	M	1	29: 6	38.	2.265	31	18	8.70	4.2	4.09	0.31	1.03	0.384	3.0	14	4+	5+	-	-	1 mon. after relapse from previous mild attack	
			12: 7	34.3	2.355	48	26	7.62	4.2	3.2	0.22	1.31	0.387	0.8	8	2+	5+	-	-		
			26: 7	-	-	-	-	8.05	4.4	3.3	0.35	1.33	0.3922	0.6	8	2+	4+	-	-		
			16: 9	-	-	-	-	8.2	4.9	3.0	0.3	1.63	0.390	0.2	5	2+	4+	-	-		
			14:12	41.	1.987	15	9	8.90	5.0	3.61	0.29	1.38	0.3883	0.2	4	+	4+	38	205	becoming chronic	
		26: 3	43.	2.000	18	13	9.15	4.5	4.2	0.45	1.07	0.3883	0.2	4	+	2+	36	-	-		
M. D.	F	2	9: 7	39.0	1.816	-	-	6.77	-	-	-	-	-	3.8	4	0	4+	21.9	-	2 wk. history	
			24: 7	39.2	1.802	13	10	6.80	-	-	-	-	-	2.2	2	0	0	17.5	-	-	
R. M.	M	3	14:10	46.3	1.993	-	-	7.80	4.22	3.20	0.38	1.32	0.3933	4.2	1	0	0	10.2	-	2 wk. history	
E. S.	F	4	15: 6	45.2	1.845	-	-	6.08	-	-	-	-	-	8.0	4	0	2+	21.3	-	1 wk. history	
I. N.	F	5	7: 6	40.1	1.992	-	-	7.38	-	-	-	-	-	-	2	+	2+	12.7	-	10 day history after fat-free diet.	
			13: 7	39.9	1.877	12	10	6.95	-	-	-	-	-	-	1	0	+	6.4	-	-	
A. B.	F	6	7: 5	44.1	2.329	-	-	7.99	-	-	-	-	-	1.1	7	2+	3+	33.8	-	2 wk. history	
			26: 5	39.8	2.090	-	-	8.10	-	-	-	-	-	0.4	4	+	+	16.6	-	-	
			6: 7	41.3	1.983	12	11	7.74	-	-	-	-	-	-	0	0	0	16.6	-	-	
K. H.	F	7	10: 4	38.6	1.873	-	-	6.91	-	-	-	-	-	5.2	1	+	+	27.4	-	4 wk. history	
			23: 4	33.7	1.830	-	-	6.95	-	-	-	-	-	1.1	2	+	3+	10.6	-	-	
A. R.	M	8	16: 1	53.4	2.014	-	-	7.27	-	-	-	-	-	23.2	5	2+	2+	15.2	-	3 wk. history	

Table - XVIII continued

Diseases of the Liver.

Name	S No	Date	PCV. %	PLASMA VISC. cs.	E. S. R. Wintrobe Ord. Cor. mm/ 1 hr	Plasma Proteins.		A/G	K	Bil. mg %	TT TF GF	Alk. Phos um. %	Bl. Urea mg. %	Chol mg.	Remarks	
						Tot.	Alb. Glob									
						g. / 100 ml										
(A) Infective Hepatitis - Acute (contd.)																
M.F.	F 22	28: 2	39.5	1.887	20	17	7.38	3.3	0.28	1.15	0.3885	13	10	3+ 5+	230	4 wk. history
		28: 3	37.	1.910	27	20	7.91	4.5	0.31	1.45	0.392	12	7	2+ 5+	319	
		21: 4	40.	1.871	12	10	7.08	4.35	0.30	1.79	0.390	9	3	3 + 2+	-	
J.M.	M 23	8: 3	42.	1.969	15	9	7.42	4.15	0.35	1.66	0.3927	39	6	2+ 2+	291	2 wk. history
(B) Infective Hepatitis - patient convalescent when first tested.																
N.J.	F 24	9: 7	45.2	1.810	6	9	7.31	-	-	-	-	0.8	0	0	0	-
B.O.	F 25	28: 6	42.2	1.939	10	10	7.60	-	-	-	-	0.5	1	0	+	-
S.K.	F 26	30: 10	42.0	1.929	13	8	7.70	5.9	1.75	0.35	3.38	-	3	+	+	265
(C) Cirrhosis of the Liver.																
J.O.	M 27	5: 1	52.6	2.320	-	-	8.17	4.79	2.95	0.43	1.60	0.393	-	3	0 3+	-
G.V.	M 28	5: 2	25.4	2.150	-	-	8.24	-	-	-	-	-	0.2	3	+	11.0
E.C.	F 29	3: 5	38.9	1.855	-	-	7.66	5.00	0.22	2.08	0.384	-	0.5	5	2+ 5+	5.4
J.L.	M 30	6: 5	41.3	2.061	-	-	7.35	4.24	2.63	0.48	1.61	0.3941	1.1	0	0	6.7
A.B.	M 31	15: 3	38.7	2.392	-	-	7.96	-	-	-	-	-	-	0	0	25.7
J.A.	M 32	25: 5	25.5	1.576	-	-	5.33	-	-	-	-	-	-	0	0	3.3
L.W.	F 33	1: 6	-	1.831	-	-	7.09	-	-	-	-	-	-	1	0	6.1

4 wk. history
2 wk. history

Table - XVIII continued.

Diseases of the Liver.

Name	S No	Date	PCV.	PLASMA VISC.	E. S. R. Winrobe Ord. Cor.	Plasma proteins			A/G	K	Bil.	TT TF		Alk. Phos	Bl. Urea	Cho.	remarks
						Ord.	mm/1 hr	os.									
											mg %			ur. %	mg. %	mg %	
(C) Cirrhosis of Liver (contd.)																	
H. B.	M	34	25: 6	21.5	1.643	-	-	5.40	-	-	-	0	0	0	3.3	-	-
D. B.	M	35	15: 7	44.3	1.971	21	18	7.13	3.57	3.29	0.27	1.09	0.387	-	29.0	33	-
R. C.	M	36	3: 9	-	2.457	-	-	8.35	-	-	-	24	5+	5+	35.9	-	-
A. D.	M	37	27: 2	36.0	1.812	-	-	6.41	-	-	-	2	0	0	7.1	-	-
M. W.	F	38	18: 5	39.2	2.241	48	43	6.84	3.65	2.85	0.54	1.28	0.393	0.3	9.	31	221
(D) Miscellaneous conditions affecting the Liver Parenchyma chiefly.																	
J. H.	M	39	22: 9	47.2	1.869	-	-	7.02	4.22	2.58	0.22	1.58	0.3883	-	7.4	-	subacute necrosis of liver
		31:10	51.3	1.903	-	-	-	7.88	4.97	2.64	0.27	1.88	0.386	-	4.9	-	
H. T.	M	40	5: 4	46.0	2.118	-	-	7.52	-	-	-	4	+	-	7.4	-	
		27: 4	40.0	1.909	-	-	-	6.33	2.18	3.89	0.26	0.56	0.352	1.6	12	3+	5+
		10: 5	38.9	1.999	-	-	-	6.12	1.86	3.90	0.36	0.48	0.344	5.2	7	2+	5+
														4.4	5	2+	5+
F. B.	F	41	14: 5	43.8	1.806	-	-	6.62	-	-	-	20.8	5	2+	5+	20.0	-
																	acute yellow atrophy
E. M.	F	42	10: 6	-	1.913	-	-	7.45	-	-	-	0.9	0	0	+	9.1	-
		23: 7	37.4	1.995	-	-	-	7.96	-	-	-	0.4	2	0	0	7.1	-
A. D.	M	43	9: 5	27.5	1.982	62	23	6.55	-	-	-	3.2	-	-	-	-	subacute yellow atrophy, with recovery.
A. H.	M	44	18:10	49.6	1.994	-	-	-	-	-	-	17.7	0	0	0	27.7	portal thrombosis.
K. A.	M	45	15: 1	43.2	2.920	24	19	8.53	-	-	-	-	-	-	-	-	"
		21: 1	43.0	3.103	-	39	28	9.43	-	-	-	-	-	-	-	-	amebic hepatitis.

Table - XVIII continued.

Diseases of the Liver.

Name	S No	Date	FCV.	PLASMA VISC.	E. S. R. Wintrobe Ord. Cor.	Plasma Proteins.			A/G	K	Bil.	TT	TF	GF	Alk. Phos	Bl. Urea	Chol.	Remarks			
						Tot.	Alb.	Glob											Fib.		
(D) Miscellaneous conditions (contd.)																					
				cs.	mm/ 1 hr	g./100 ml															
A. H. M	46	6:11	37.4	2.042	-	-	8.35	-	-	-	-	0	0	+	5.2	-		acholuric jaundice			
		15:12	42.8	1.904	-	-	7.78	-	-	-	2.4	0	0	+	8.0	-					
		11:2	47.0	1.950	-	-	7.16	-	-	-	1.4	0	0	+	7.6	-					
N. L. M	47	9:7	26.5	1.445	citrate plasma			-	-	-	-	-	-	-	-	-		acholuric jaundice			
W. E. M	48	15:6	34.0	2.106	-	-	6.73	-	-	-	0.7	3	+	3+	38.6	-		chronic hepatitis			
J. B. M	49	24:6	39.0	2.214	-	-	7.99	2.99	0.26	0.63	2.2	8	2+	5+	20.3	-		chronic hepatitis			
W. C. M	50	7:7	45.5	2.176	-	-	8.22	4.90	0.48	1.73	0.7	0	0	0	11.3	-		subacute hepatitis			
E. P. M	51	28:3	45.0	2.827	-	-	9.29	-	-	-	9.1	20	5+	5+	15.0	-		subacute hepatitis			
(E) Disease of the Gall-bladder																					
F. W. F	52	21:6	40.0	2.134	-	-	7.45	-	-	-	-	0	0	0	18.5	-		chronic cholecystitis			
J. J. F	53	5:8	28.1	1.584	citrate plasma			-	-	-	-	-	-	-	-	-		acute cholecystitis			
A. D. F	54	20:5	44.8	2.111	-	-	7.88	-	-	-	-	-	-	-	-	-		acute cholecystitis			
L. R. M	55	23:5	39.6	2.401	-	-	7.76	3.94	0.85	1.33	-	-	-	-	-	-		acute cholecystitis			
M. S. F	56	2:4	45.5	1.992	6	10	7.92	5.5	0.35	2.66	2.2	2	+	0	15.	18		302 ac. cholecystitis			
H. W. F	57	1:11	42.3	2.460	-	-	6.43	3.96	0.90	1.60	-	-	-	-	-	-		acute cholecystitis			

Table - XVIII continued

Diseases of the Liver.

Name	S No	Date	PCV.	PLASMA VISC.	E.S.R. Winrobe Ord.	Plasma proteins			A/G	K	Bil.	TT	TF	GF	Alk. Phos.	Remarks
						Tot.	Alb.	Glob								
			%	cs.	mm/	1 hr	g./100 ml.									
											mg %				un. %	
(F) Obstructive Jaundice.																
R.O.	T 58	19: 6	28.7	2.476	-	-	6.44	-	-	-	-	0	0	0	85.	cancer of pancreas
R.S.	M 59	10: 2	44.5	2.081	-	-	7.13	-	-	-	20.4	0	0	0	18.3	cancer of pancreas
A.C.	M 60	19: 3	41.3	1.934	-	-	6.48	-	-	-	-	0	0	0	30.8	cancer of pancreas
		10: 4	41.7	2.041	-	-	7.27	-	-	-	12.0	0	0	0	38.2	
W.B.	M 61	12:12	47.5	2.553	-	-	7.45	-	-	-	16.8	0	0	0	67.4	cancer of pancreas
C.B.	F 62	1:10	33.0	1.694	-	-	5.00	-	-	-	1.0	0	0	0	31.1	cancer of pancreas
S.F.	M 63	4: 8	44.0	2.341	-	-	5.78	3.05	2.24	0.49	1.36	0	0	0	42.5	cancer of pancreas
M.P.	F 64	26:11	41.9	1.984	-	-	6.98	-	-	-	2.3	0	0	0	19.3	cancer of gall-bladder
T.B.	M 65	4: 5	49.2	2.501	-	-	7.57	4.01	2.55	0.91	1.57	0	0	0	48.2	tumour of liver
C.F.	M 66	15: 4	50.0	2.077	-	-	6.95	-	-	-	6.4	0	0	0	42.5	cancer of colon
C.B.	F 67	25: 9	35.8	2.410	-	-	7.45	-	-	-	9.8	0	0	0	18.3	due to gall-stone
T.S.	F 68	22: 6	45.6	2.134	-	-	7.31	-	-	-	9.5	0	0	+	33.7	due to gall-stone
W.L.	M 69	9: 9	46.8	2.273	-	-	7.70	-	-	-	2.1	0	0	-	22.2	probably gall-stone, but
		15: 9	46.6	2.089	-	-	7.06	-	-	-	3.5	1	0	-	10.9	not certain.
W.J.	M 70	30: 8	48.8	2.105	-	-	7.31	-	-	-	1.3	1	0	0	85	cause uncertain
E.P.	F 71	18: 3	45.0	2.271	-	-	7.52	-	-	-	9.9	0	0	0	48.4	"
T.S.	F 72	21: 5	46.	2.480	16	21	7.90	4.0	3.24	0.66	2.4	0	0	0	44.	"
C.B.	F 73	17: 2	45.8	1.671	-	-	5.76	-	-	-	1.2	1	0	0	12.7	"

Case No. 81

Acute Infective Hepatitis.

This youth had what appeared to be a mild attack of infective hepatitis beginning on 3:4:50 - anorexia, malaise, headache, diarrhoea with pale stools, dark urine for 2 days, and yellow conjunctivae for 3 days. He became quite well again until he had a relapse in May to produce the illness now to be described.

On 28:5:50 the yellow colour returned to the conjunctivae; the stools became pale in colour, the urine became dark. He felt quite well. His liver was enlarged to 2 finger-breadths below the costal margin, and it soon reached 4 finger-breadths. No other abnormality was detected on examination. There was no recent injection. He was treated at home with rest in bed and a high protein diet. No apparent improvement followed so that he was admitted to hospital on 16:6:50.

On examination on that date his liver was still enlarged, but soft and not tender; the spleen was palpable. The same treatment was continued. By the time of the first blood test (i.e. plasma viscosity) the jaundice had decreased somewhat although the liver and spleen were still enlarged - 29:6:50. By 12:7:50 the liver was slightly smaller and the spleen was just palpable; similar findings were noted on 26:7:50. He was discharged on 7:8:50 to continue his convalescence at home. He went back to boarding-school

Date	PCV.	PLASMA VISC.	Wintrobe ESR.		Plasma protein				Gold Floc	Alk. Phos	Bili- rubin
			Ord.	Cor.	Total	Alb.	Glob	Fibr			
	%	cs.	mm/	1 hr	g./100 ml.					un. %	mg. %
12: 6:50	-	-	26	-	8.5	4.4	3.77	0.33	5+	25	11.0
29: 6:50	38.	2.265	31	18	8.70	4.2	4.09	0.31	5+	22	3.0
12: 7:50	34.3	2.355	48	26	7.62	4.2	3.2	0.22	5+	22	0.8
26: 7:50	-	-	-	-	8.05	4.4	3.3	0.35	4+	30	0.6
16: 9:50	-	-	-	-	8.2	4.9	3.0	0.30	4+	44	0.2
14:12:50	41.	1.987	15	9	8.90	5.0	3.61	0.29	4+	44	0.2
26: 3:51	43.	2.000	18	13	9.15	4.5	4.2	0.45	2+	36	0.2
3: 9:51	41.6	1.796	5	0	7.50	5.6	1.58	0.32	0	38	0.2

but took no part in games.

The diagnosis at this stage was that an acute hepatitis was passing into the chronic phase, with a 50% chance only of recovery. He continued on a high protein diet and a general regime which protected him from stress. This diagnosis was further supported by the results of September, December and March. For some reason, not detectable by the clinical observers, he suddenly changed for the better. Apart from a rather high serum alkaline phosphatase and a low haematocrit, the laboratory tests had all returned to within their normal ranges by the following September; the whole illness had lasted about fifteen months.

It is noteworthy that the plasma viscosity falls within the "zone of chronicity" during that period of the illness when the clinicians regarded it as being in a chronic phase.

Table - XIX

Renal Disease.

Name	S No	Date	PCV.	PLASMA VISC.	E. S. R.		Plasma proteins.			A/G	K	NPN.	Bl. Urea	Chol.	TT	TF	GF	Alk. Phos.	Remarks	
					Wintrobe	Ord. Cor	Tot.	Alb.	Glob											Fib.
					mm/ 1 hr	cs.	g./100 ml.													
(A) Acute Glomerular Nephritis.																				
A.R.	M	1 1: 3	34.2	2.167	56	30	7.90	3.10	3.19	0.61	0.97	0.387	34	282	2	0	0	6		
A.H.	M	2 20: 3	40.	2.018	11	2	7.79	5.0	2.3	0.49	2.17	0.387	20	-	1	0	0	-		
J.W.	M	3 28: 5	38.	1.926	24	11	6.80	-	-	-	-	-	45	-	2	0	0	-		
P.T.	F	4 28: 5	35.	2.027	42	29	6.98	-	-	-	-	-	31	-	-	-	-	-		
H.R.	F	5 28: 5	40.	2.336	30	26	7.81	4.4	2.8	0.61	1.57	0.3933	29	205	1	0	0	-		
W.D.	M	6 8: 4	38.1	2.628	45	29	8.55	3.86	4.02	0.67	0.96	0.386	47	-	-	-	0	7.8		
J.W.	F	7 31: 1	46.5	2.112	-	-	7.99	-	-	-	-	-	22	-	-	-	-	-		
D.C.	F	8 15: 6	38.6	2.102	37	31	7.85	-	-	-	-	-	22	-	-	-	+	-		
J.L.	M	9 21: 5	38.9	1.948	-	-	7.23	4.01	2.86	0.36	1.40	0.393	32	320	1	0	0	8.4		
T.H.	M	10 16: 6	39.7	1.843	38	26	5.69	-	-	-	-	-	38	-	-	-	0	-		
		23: 6	44.8	2.087	38	34	6.48	-	-	-	-	-	25	-	-	-	0	4.7		
F.S.	F	11 19: 5	33.7	2.154	46	30	7.72	4.06	2.96	0.50	1.37	0.3945	44	-	0	0	+	4.4		
T.T.	F	12 28: 6	28.8	1.861	31	11	6.66	-	-	-	-	-	15	-	2	0	2+	6.1		
		6: 7	30.9	1.842	22	7	7.09	-	-	-	-	-	-	-	0	0	0	5.2		
T.S.	M	13 23: 7	32.3	1.457	-	-	3.82	2.26	1.25	0.31	1.81	0.390	33	-	0	0	0	7.1		

Table - XIX continued

Renal Disease

a320

died 3/3

(D) Subacute Nephritis.

Name	S No	Date	PCV.	PLASMA VISC.	E.S.R.		Plasma proteins			A/G	K	NPN. mg %	Bl. Urea mg. %	Chol mg %	TT	TF	GF	Alk. Phos.	Remarks
					Winthrobe Ord.	Cor	Tot.	Alb.	Glob										
L.F.	M 14	17: 8	44.2	1.808	-	-	4.83	2.76	1.50	0.57	1.34	0.384	12.1	42	-	0	0	0	5.0
G.I.	M 15	13:10	38.5	1.662	-	-	4.98	3.01	1.54	0.43	1.96	0.388	59.5	-	-	0	0	0	-
D.W.	M 16	15: 1	43.5	1.879	-	-	5.63	3.29	1.80	0.54	1.83	0.388	24.2	33	-	-	+	8.8	
J.R.	M 17	23: 2	29.6	1.584	-	-	4.40	2.10	1.99	0.31	1.06	0.3893	51.4	-	-	-	0	12.9	
		9: 3	27.6	1.825	-	-	5.31	2.75	2.19	0.37	1.27	0.3933	40.3	37	-	-	0	9.3	
		23: 3	30.8	1.779	-	-	5.38	3.21	2.34	0.33	1.37	0.3942	46.4	-	-	-	0	8.1	
		7: 4	34.0	1.920	-	-	6.43	3.89	2.20	0.34	1.77	0.392	25.6	-	-	-	0	6.0	
		20: 5	39.6	1.815	-	-	6.47	3.92	2.26	0.29	1.74	0.392	29.2	-	-	-	0	7.8	

(C) Nephrosis

J.R.	F 18	5:12	-	1.723	-	-	6.57	3.8	2.3	0.47	1.65	0.393	-	23	195	1	+	+	-
M.J.	F 19	16: 5	34.0	2.484	60	42	5.15	2.12	1.88	1.15	1.13	0.352	-	127	578	1	0	0	-
J.M.	M 20	9: 2	49.5	2.369	-	-	4.39	1.40	1.88	1.11	0.75	0.318	94.2	-	764	0	0	0	7.6
C.M.	F 21	11: 2	28.3	2.075	-	-	4.28	1.93	1.41	0.94	1.37	0.360	50.4	257	257	-	-	0	8.8
A.M.	M 22	30: 6	30.3	2.121	-	-	4.07	-	-	-	-	-	-	-	-	0	0	0	6.6
E.P.	M 23	20:8	38.5	2.107	52	38	5.45	2.7	1.8	0.95	1.67	-	-	83	368	0	0	0	34.
E.R.	F 24	7:11	38.	1.904	54	38	4.8	1.9	2.1	0.8	0.90	-	-	35	730	-	-	-	-

died 3/3

Table - XIX continued

Renal Disease

Name	S No	Date	PCV.	PLASMA VISC.	E. S. R.		Plasma proteins			A/G	K	NPN.	Bl. Urea.	Chol	TT	TF	GF	Alk. Phos	Remarks
					Wintrobe	Ord.	Tot.	Alb.	Glob										
			%	cs.	mm/ 1 hr							mg. %						un. %	
(D) Chronic nephritis.																			
T. T.	F 23	23:10	42.0	2.022	-	-	7.62	4.46	2.83	0.33	1.58	0.3925	31.2	-	3	+	4+	-	
C. L.	M 24	28: 7	23.8	1.873	70	21	5.39	2.49	2.41	0.49	1.03	0.386	81.7	140	0	0	0	3.7	
		19: 8	18.2	1.879	-	-	5.32	2.41	2.46	0.45	0.98	0.385	133.	212	1	0	0	11.4	died 14/9
B. T.	F 25	14: 2	43.	2.145	44	46	5.37	2.0	2.5	0.87	0.80	0.344	-	27	0	0	0	-	
R. M.	M 26	16: 2	29.	1.881	48	12	6.29	3.1	2.6	0.59	1.19	0.390	-	143	1	0	0	-	
J. A.	M 27	10: 5	25.9	1.774	67	24	5.65	2.23	2.29	0.45	0.98	0.384	-	94	2	0	0	-	
M. S.	F 28	17: 5	41.3	2.045	23	22	7.93	4.70	2.91	0.32	1.61	0.3922	-	36	5	2+	2+	-	
W. B.	M 29	18: 5	-	2.050	-	-	5.58	-	-	-	-	-	-	146	-	-	-	-	died 4/6
M. H.	F 30	5: 5	33.	1.617	27	14	4.85	2.8	1.7	0.35	1.65	-	-	56	-	-	-	-	
		14:11	32.	1.514	29	14	4.90	2.8	1.53	0.37	1.83	-	-	44	-	-	-	-	
M. J.	F 31	6: 6	31.5	2.165	63	39	5.46	1.7	2.0	0.76	0.85	-	-	66	1	0	0	-	
M. G.	F 32	12: 6	17.8	1.846	48	0	6.02	4.5	1.0	0.52	4.5	-	-	419	-	-	-	-	
J. A.	M 27	19: 6	28.	1.685	57	21	4.46	2.1	1.9	0.46	1.10	-	-	43	2	0	0	-	
E. L.	M 33	30: 6	44.	2.196	42	37	5.67	2.5	2.3	0.87	1.09	-	-	63	2	0	0	-	

died 14/9

a321

died 4/6

Case No. 82

Acute Nephritis.

The plasma viscosity is usually increased in cases of acute nephritis just as in any other kind of acute inflammation; the increase reflects an increase in the plasma fibrinogen.

This man was aged 65 years when he had his first attack of acute nephritis. He had led a healthy life; the only relevant illness was scarlet fever at the age of 12 years, which was free from complications.

The present illness began a little over 2 weeks prior to admission to hospital, as a sore throat, tonsillitis, headache, pains in legs, and increased temperature. These signs and symptoms cleared in a week but were followed in another few days by a swelling of the ankles, of the legs and later of the face. He was breathless. His urine diminished in volume but darkened in colour.

On examination, on admission (27:2:50) he had much oedema of the legs and sacrum and his face was puffy. The heart size was within normal limits; the vessels of the optic fundus were markedly arteriosclerotic; the blood pressure was 280/140. The urine contained a heavy cloud of albumen, large numbers of erythrocytes, occasional leukocytes, occasional epithelial casts and a fair number of hyaline and granular casts.

Treatment consisted of rest in bed, sedation, iron, low-salt

Date	PCV.	PLASMA VISC.	Wintrobe ESR.		Plasma protein				Serum NPN
			Ord.	Cor.	Total	Alb.	Glob	Fibr	
	%	cs.	mm/	1 hr	g./100 ml.				mg.%
1: 3:50	34.2	2.167	56	30	7.90	3.10	3.19	0.61	34

diet and restricted fluid intake, and penicillin.

He showed an excellent response to this treatment so that he was discharged on 4:5:50.

The diagnosis was of an acute nephritis in an arterio-sclerotic subject rather than a flare-up in a chronic nephritic.

Case No. 84

Chronic Nephritis.

In 1949, when 16 years old, this girl had a sore throat or tonsillitis which was followed by an albuminuria; her general practitioner sent her to hospital as a case of Nephritis but the diagnosis of the hospital was meningitis (it was a cottage hospital only and acute uraemia might have been missed). She had never suffered from rheumatic or scarlet fever.

Early in January 1951 she had an attack of influenza. Two weeks later she noted a swelling in her ankles and in her face and eyelids; the urine was redder than usual for a week. The blood pressure was 160/100 mm. mercury; there was gross albuminuria. She went to bed at the beginning of March and the blood pressure had fallen to 142/90 when she was admitted to hospital on 7:4:51. On examination, apart from this slightly increased blood pressure and pale mucous membranes no abnormality could be detected. The urine contained 320 mg. per 100 ml. of protein, large numbers of epithelial cells and leucocytes, and scanty staphylococci. The blood biochemistry was as is shown in the table.

She made very slow progress indeed and was not discharged until 16:11:51. A fortnight later she had another head cold which was followed by a recurrence of haematuria, oedema, increased blood pressure so that she is still a patient in January 1952.

Date	PCV.	PLASMA VISC.	Wintrobe ESR.		Plasma protein				Serum	
			Ord.	Cor.	Total	Alb.	Glob	Fib.	Urea	Cholesterol
	%	cs.	mm/ 1 hr		g./100 ml.				mg. %	mg. %
7: 4:51	31.	-	27	11	5.36	3.15	1.75	0.46	39	370
21: 4:51	-	-	-	-	4.87	2.87	1.62	0.38	40	346
5: 5:51	33.	1.617	27	14	4.85	2.8	1.7	0.35	56	321
4: 9:51	-	-	-	-	4.9	2.7	1.8	0.4	47	330
14:11:51	32.	1.514	29	14	4.7	2.8	1.53	0.37	44	320

This case illustrates how the low plasma proteins which may be found in chronic nephritis can be associated with normal or sub-normal plasma viscosity values.

Errors of Carbohydrate Metabolism.

Name	S	No.	PCV.	PLASMA VISC.	Plasma Total Protein	Remarks
			%	cs.	g. %	
<u>Low Renal Threshold</u>						
S.P.	M	1	48.1	1.776	6.95	
T.U.	M	2	42.1	1.833	7.09	
F.A.	M	3	52.9	1.892	7.20	
R.A.	M	4	45.3	1.849	7.70	
B.B.	M	5	49.1	1.761	7.09	
R.F.	F	6	41.7	1.886	6.98	
M.C.	F	7	46.7	1.853	7.09	
M.G.	M	8	-	1.729	6.41	
<u>"Lag Curve"</u>						
A.B.	F	1	42.2	1.795	7.52	
<u>Diabetes Mellitus.</u>						
M.G.	F	1	47.1	1.897	6.95	Requires insulin
G.R.	M	2	48.9	1.899	7.34	Mild; controlled by diet
G.B.	M	3	47.4	1.997	7.85	Arteriosclerosis; gangrene
M.W.	F	4	43.4	2.020	8.03	Arteriosclerotic; slightly obese
D.B.	F	5	42.7	1.750	7.02	Young girl; insulin given later
A.R.	M	6	50.0	2.047	8.14	
M.S.	M	7	46.6	1.840	7.16	Controlled with insulin
H.H.	M	8	41.0	1.839	6.37	Oedema due to Vit. B deficiency
M.D.	M	9	49.4	1.991	7.02	
I.W.	F	10	30.0	2.132	8.14	Essential hypertension.
M.C.	F	11	43.0	2.005	7.56	On insulin
M.B.	F	12	45.5	1.973	7.49	
J.T.	M	13	44.2	1.974	-	On insulin; neuritis
J.C.	M	14	-	1.978	7.81	Small abscess of shoulder; retinitis
W.T.	M	15	49.1	1.794	6.80	Blood press. = 170/110 mm. Hg.
R.A.	F	16	41.9	2.070	7.34	
M.R.	M	17	50.0	1.905	7.45	
M.A.	F	18	42.8	1.862	6.84	Obese; B.P. = 160/100 mm. Hg.

Case No. 85

Osteitis deformans (Paget's disease)

This man had been treated successfully with Pepsac for his pernicious anaemia from 1943 until 1946, but thereafter he lost his appetite, his tongue became sore, his ankles swelled, and the picture was that of pernicious anaemia in relapse. After a period of 8 months in this state liver therapy was tried for 4 months without producing any improvement.

In July 1947 he was admitted to hospital and his anaemia responded to folic acid, large doses of liver extract, and large doses of iron by mouth.

No other abnormality was found on general examination. A routine skiagram of the chest, however, revealed osteitis deformans in the dorsal spine, and the disease was later shown to be affecting the lumbar spine, skull, femora and tibiae.

In September 1947, laboratory tests indicated that the anaemia was under control.

22:9:47 Plasma viscosity = 2.221 cs.
 Haematocrit = 40.2%
 Haemoglobin = 82 %
 Erythrocytes = 4,250,000 per cmm.
 Colour index = 0.98
 Film = cells appear normal.

Plasma alkaline phosphatase = 119 K.A. units/100 ml.

Case No. 86 Osteitis deformans (Paget's disease).

This old man, aged 72 years, was admitted to hospital in December 1947 with a history that he had collapsed at Easter of that year and had been confined to bed since. He had lost 20 lb. in the 9 months; his knees had become fixed in flexure; he was incontinent of urine and faeces.

On general examination, he was a frail old man with no apparent definite abnormality apart from the flexed knees. A skiagram of the spine, however, showed gross patchy dense areas in all the bones of the spine and pelvis, with deformity at the 2nd. lumbar intervertebral joint.

The diagnosis lay between Osteitis deformans and secondary carcinomatous deposits from a primary growth in the prostate; the latter possibility was discarded because of the low serum acid phosphatase level and the very high alkaline phosphatase value.

PCV.	PLASMA VISC.	ESR.	Plasma total prot.	Gold floc.	Serum Acid Alk. phosphatase	
%	cs.		g. %		unit/100ml.	
33.3	2.139	-	6.66	o	1.5	88.2

Table - XXI

Oedema of Feet.

Name	S No.	Date	PCV. %	PLASMA VISC. cs.	Max. ESR.	Plasma protein.			A/G	A/F	K	NPN. mg. %	Remarks
						Total	Alb.	Glob					
						g. / 100 ml.							
M.C.	F	14: 3	-	2.000	-	6.54	4.08	2.15	0.31	1.90	13.2	0.390	anaemia also
J.F.	M	12: 7	34.7	2.033	9.5	6.71	3.85	2.39	0.47	1.61	8.25	0.394	115.
W.B.	M	8: 7	11.0	1.363	0.57	citrate plasma			-	-	-	-	pernicious anaemia
V.A.	F	23:10	39.6	1.972	-	7.38	4.81	2.25	0.32	2.14	9.70	0.3913	41.8
H.H.	M	4:11	41.0	1.839	-	6.37	4.36	1.60	0.41	2.72	10.7	0.377	13.1
M.M.	F	9: 2	42.0	1.931	-	7.29	4.85	2.08	0.36	2.35	13.5	0.3835	32.8
M.H.	F	11: 2	30.3	2.226	-	7.53	4.31	2.62	0.60	1.64	7.25	0.393	8.8
J.B.	M	7: 4	40.9	1.940	-	6.22	3.54	2.10	0.58	1.69	6.10	0.3912	22.0
D.L.	F	20: 8	44.7	1.782	-	7.22	4.86	2.15	0.22	2.26	22.2	0.380	9.1
A.W.	M	20:10	40.0	2.000	9.6	7.23	4.13	2.77	0.33	1.49	12.7	0.393	33.2

These cases of oedema of the feet were taken to be caused by non-renal conditions.