A Study of the Sedimentation Rate of the Blood and its Application in General Medicine

ProQuest LLC.
789 East Eisenhower Parkway
P.O. Box 1346
Ann Arbor, MI 48106 – 1346

Table of Contents

Introduction

The tendency of modern medicine is towards an increase in laboratory metnods, which, in spite of their obvious value, cannot supplant any clinical observations. Into an already crowded field arrive new biochemical tests, some to stay, others to be forgotten rapidly. The following is an attempt to evaluate the sedimentation rate of the blood, and to find out what are its uses and limitations.

The test has been applied to over 400 cases, the rate in each case having been ascertained at least weekly. In the medical wards of a general hospital, the diseases met with are of sufficiently wide variety to render them suitable for such a study as this, and they have been chosen for this work. Reports of all the cases would serve little purpose, and in the section dealing with individual diseases, general observations and results, with illustrative cases, have been given. All the tests have been performed by the autor, and the literature has been carefully studied, references being given whenever the observations of others are quoted.

Historical Note

The sedimentation of red blood corpuscles and the phenomenon of its rapidity in certain diseases was known to the ancient physicians. Nevertheless to Robin Fahraeus must be given the credit of reviving the matter. In 1918 he published a paper in Hygeia, in which he stated that the test could be used as a diagnostic measure in pregnancy, since in this condition a rapid rate of sedimentation of the erythrocytes occurred. However, in infectious diseases and in many other maladies a rapid sedimentation rate was also found to be present, and although the test is of little significance in the diagnosis of pregnancy, its use in other fields has been greatly developed.

Bleeding is one of the oldest remedies and has been resorted to, not only for the treatment of the most varying diseases, but also as a prophylactic measure in healthy cases. From the days of Hippocrates and Galen, medical men have been interested in the gross appearances of the blood. It was observed that when the blood of a healthy person, after it has been withdrawn from a vein, coagulates, a homogeneous red mass forms; this after some time contracts and presses out a small quantity of pale yellow serum. In certain pathological and physiological states, however, the red blood cells situated at the uppermost layers of the blood, sediment rapidly before coagulation occurs, and the coagulum resulting, is not of an even red nature, but consists of an upper yellowish layer and a lower red zone.

From this, arose the ancient conception of health. The blood was thought to consist of four separate fluids, and health depended on their proper admixture (1). These four humours correspond to the four layers which can be seen when a large quantity of blood is removed from a patient by venesection and allowed to clot.

1) The lowermost layer is composed of red blood corpuscles, deprived of oxygen (melancholia)
2) A bright red layer above this is formed of aerated red cells (sanguis)
3) A greyish white layer, which is composed of leucocytes, platelets and fibrin (mucus, phlegma)
4) A yellowish layer, which is blood serum (cholera)

Disease was, according to their theory, caused by a variation in the relative amounts of these substances, but particularly by an increase of the phlegma. The cause of this latter conception arose from the fact that in many pathological conditions, the blood, withdrawn by venesection, was found to be covered by a membranous layer, which was thought to be an undue increase of the phlegma circulating in the blood. This fibrinous layer became known under numerous names, such as "crusta phlagistica," "buffy coat," "size," "crusta inflammatoria," etc. Even after the downfall of the four-fluid theory, medical men continued to interpret disease in terms of the crusta inflammatoria. The latter was supposed to be an alien substance, absent from normal blood, and in an attempt to rid the body of this

so-called noxious material, the practice of blood-letting increased.

Gram (2) performed some investigations concerning the crusta inflammatoria and concludes that there are two conditions under which a buffy coat is formed.

1. When the Sedimentation Rate is increased.

2. When the coagulation time is prolonged.

Of these two, by far the more important is the former cause, and the crusta inflammatoria coincides with increased rate of sedimentation of the erythrocytes. The crusta phlogistica is, he states, a pathological phenomenon. Hence, one can readily understand, the great appreciation given to it by the ancients, for just as an increased sedimentation rate is an expression of disease (with the exception of pregnancy), so is the crusta inflammatoria.

At a later date, the crusta inflammatoria began to be looked on as a quantitative measure of the extent of the morbid processes in the body, and it was also observed that in severe illness the buffy coat might eventually disappear on the patient's recovery.

Blood letting was practised up to the early part of the 19th century--a remarkable fact--and indeed in the 18th century the practice was so popular that almost all diseases were treated by venesection. During the 19th century a sharp reaction set in, and venesection as a therapeutic measure, almost entirely disappeared. Virchow,

at that time, was introducing cellular pathology into medicine, and the microscopic examinations of the blood diverted attention from their gross appearances. Hence the diagnostic importance of these earlier studies was gradually forgotten, until Fahraeus in 1918, accidentally noticed an increased rate of sedimentation in the blood of pregnant women, and once more the significance of the reaction was brought to the notice of the medical world. Since then, the test has become widely used in most fields of medicine.

Theories of Causation

Blood consists of solid particles floating about in a liquid medium. By virtue of their higher specific gravity the particles have a tendency to sink, when the blood is stagnant. While in the blood vessels, where the blood is in motion, this tendency is minimal, whereas in stagnant blood,--as one sees it in the sedimentation tube--the erythrocytes sink with more or less rapidity to the base. That this sedimentation is not an artefact caused by removal of the blood from the body, can be readily shown from the following experiment.

A cutaneous vein of the arm, without a lateral branch and remaining superficial, is blocked by two rubber bands, separated by about 10 cm., and applied with sufficient tightness to suspend circulation in the vein. A patient with a rapid sedimentation rate is preferably chosen. The arm is so placed that the vein is in a vertical position, and thus we have the vein in the form of a sedimentation tube, within which is a column of stagnant blood. After a time, depending on the individual's sedimentation rate, the distal part of the vein comes to contain only plasma, the erythrocytes having sedimented to the basal portion. This can be shown by the fact that the distal part loses its characteristic blue colour or by inserting a fine needle attached to a syringe into that section of the vein, whereupon the contents withdrawn are seen to consist of serum.

Were the sedimentation rate merely dependent on differences of specific gravity there would be little necessity for further discourse on its aetiological nature. However, the explanation of the various factors influencing the rate is extremely difficult, and as yet there is no generally accepted theory.

Hunt (3) demonstrated that the plasma and not the erythrocytes held the controlling factor. He took two samples of blood, one of which sedimented rapidly and the other slowly, and interchanged the plasma. The result obtained is shown below.

"Fast" plasma + "Slow" red blood cells = Fast Sedimentation Rate.

"Slow" plasma + "Fast" red blood cells = Slow Sedimentation Rate.

Some of the important theories will be reviewed here.

Fahraeus (1) considers increased sedimentation to be dependent on increased agglutination of the erythrocytes. This agglutination is identical with the rouleaux formation of the erythrocytes. The corpuscles unite in a regular manner, with their flat sides against each other. In rapidly sedimenting blood the rouleaux are large and composed of a great number of red cells, in contrast to the few forming the small agglomerates found in blood with a normal suspension stability. Moreover the rouleaux in rapidly sinking blood are of firmer consistency and re-

quire much greater pressure to break up their formation. In bloods with rapid sedimentation rates the rouleaux are often so large as to make them visible to the naked eye in the sedimentation tube. Some time is required before the agglomeration of erythrocytes takes place, but once they reach a certain size, they grow no more. In rapidly sinking bloods the rouleaux form with greater rapidity than in blood with high suspension stability.

Fahraeus considers the rate of sedimentation to vary with the size of the agglomerates: the larger, by reason of their considerably decreased surface area sink more rapidly.

Rouleaux formation is a non-specific reaction and independent of agglutinins as we understand them in bacteriology. Their presence occurs in vivo as well as in vitro. Plowman (4) by varying the intraocular tension by means of external pressure, was able to demonstrate the presence of rouleaux in the retinal arterioles.

Rouleaux formation is an exceedingly interesting phenomenon and appears to depend on the discoid shape of the erythrocytes, for if a substance be added which changes the shape of the cells to spherical, no rouleaux are formed. The erythrocytes are however still capable of agglutination on the addition of a suitable serum, and this property differentiates rouleaux formation or pseudo-agglutination from iso-agglutination seen in blood grouping (5). If a

drop of fluid from the lower part of the column of sedimented blood, be examined under the microscope, the rouleaux are clearly seen. Their form is unstable and after two or three days at room temperature, they disintegrate. Ponder (6) says, that why the red cells collect in rouleaux and not in spherical or other shapes, is that only contacts in which the cells are broadside will result in lasting cohesion.

Many authorities consider the plasma to contain a substance responsible for this rouleaux formation and are of the opinion that increased fibrinogen or a reduced albumin-globulin ratio will cause a diminution in the suspension stability of the blood. (7) (8) (9) (10) (11).

Gram (2) made a detailed survey of the fibrin content of the plasma and found it to be increased in most diseases.

On the other hand others fail to find any alteration in the plasma proteins in rapidly sedimenting blood (12) (13).

Stoke's law has been invoked in an attempt to explain the sedimentation rate on a simple physical basis (14).

$$V = \frac{2 (S_1 - S_2) \cdot r^2 \cdot g \cdot}{9 u}$$

where v = velocity of fall

s_1 = specific gravity of the aggregate

s_2 = specific gravity of the plasma

g = gravitation constant

r = radius of the particle

u = viscosity of the fluid

This formula only applies to spherical bodies and Ponder (18) has further modified it to meet the biconcave shape of the erythrocyte. All factors which increase the radius will accelerate sedimentation, and so the larger the agglomerates the faster their rate of fall. The formula however assumes that the suspended bodies exercise no influence on one another, whereas this is not the case, as the erythrocytes have a negative charge of electricity and repel one another. The equation has proved to be quite inadequate for the solution of the problem.

Reyner (16) attempted to explain the sedimentation rate on the basis of changes of surface tension. He introduced sodium oleate and formaldehyde and was able to control the surface tension by the addition of either substance in varying amounts, and with these changes could produce an accompanying change in the velocity of sinking of the red blood cells.

The electro-physical theory depends on the supposition that variations in the electrical charges of the erythrocytes influence the sedimentation rate. Anything which will reduce this charge will lessen the repelling influence of one erythrocyte against another, and so allow of rapid agglutination (17). Hoeber (18) in 1914 showed that the erythrocytes wander to the anode pole and therefore carry a negative charge. Further, if this plasma be treated with substances which are adsorbents for positive particles,

the negative burden of the corpuscles is increased and the sedimentation rate of the blood lowered. Plasma fibrinogen and to a lesser extent plasma globulin allow the red corpuscles to discharge their electricity but plasma albumin acts in an opposite manner. An increase in fibrinogen or a decrease in the albumin-globulin ratio will effect an increase in the blood sedimentation rate (19).

An additional theory, accepted by few, deals with the ratio of cholesterol to lecithin, and considers this the important controlling factor.

In spite of the numerous articles published on this part of the subject, up to date, no theory is universally accepted and it is probable that the truth lies in a combination of causal factors.

The Technique of the Sedimentation Test

The literature on this subject reveals a multiplicity of methods and modifications, which is most confusing. This is an extremely unfortunate state of affairs, making comparison of results of different observers difficult and often impossible. The sedimentation tubes vary in size, in height and in shape; moreover, their internal diameters range through a comparatively wide measure. The amounts of blood used, the anticoagulants and methods of recording the rate of sedimentation differ widely. The anticoagulants employed may be biologic products, organic compounds or simple inorganic salts, and may be in solid or liquid form. Among the methods of registration of results, one finds--to mention only a few--the time taken for the blood cells to sediment through a certain distance, the distance traversed by the erythrocytes in a certain length of time, the height of the erythrocyte column, and the expression of the result in percentage and graphic forms. Many writers introduce a new technique or a variation of an old one (20) (21) (22) (23) (24); one cannot sufficiently emphasize the necessity of a uniform technique, for, even allowing that method to have certain disadvantages, provided these do not interfere with the result in a conflicting manner, a standard expression of sedimentation values would arise for universal employment. Figures, in themselves, are insufficient to give a sedimentation value and should always be accompanied by the name of the method used.

The blood of veins, peripheral arteries and capillaries have all the same rate of sedimentation and blood may be taken from any of these sources for the purposes of the test. It is only important to take the blood quickly, in order to prevent clotting, which would render the test useless. The numerous methods employed, divide themselves into the macroscopic and microscopic forms. In the macroscopic method, blood is obtained from a vein by means of a needle and syringe. The needle should have a sharp point and preferably a short bevel. It is important to puncture the vein in the first attempt, for otherwise, the substance sucked up from the surrounding damaged tissues, may frequently cause clotting of the blood. A vein in the antecubital fossa of the arm is usually selected. Prior to the venupuncture a tourniquet is applied to the arm. A band of rubber tubing is the best type of tourniquet for the purpose and should be so applied as to allow of its ready release by the operator without causing movement of the arm, which might disturb the position of the needle in the vein. Plass and Rourke (25) point out that the use of a tourniquet might influence the velocity of sedimentation. However, in their experiments, cyanosis and even petechiae were produced in some cases. Using the sphygmomanometer, and so being able to regulate the pressure accurately, I found that, if the pressure was kept midway between systolic and diastolic levels, as much as four minutes from the

time of application of the sphygmomanometer, failed to affect the rate. Blood was taken from the other arm immediately afterwards--no tourniquet being used--and results compared. Only if very marked cyanosis or petechiae occurred was the sedimentation rate altered, and then it was in the nature of an increase. For practical purposes, rubber tubing is less likely to interfere with the test and should be used in preference to the sphygmomanometer; the radial artery should be palpable at the wrist during its application.

The vein in the elbow is frequently made more prominent by flicking it with the finger. The anticoagulant may be placed in the syringe or in the storage tube. During the sucking up of the blood, much aspiration with the syringe should be avoided since air is forced in, and accurate measurement of the blood rendered impossible. If the anticoagulant is in the syringe, after the quantity of blood has been drawn up and the needle removed from the vein, the plunger is drawn back to introduce a little air into the barrel of the syringe, and the contents agitated to allow thorough mixing of the blood and anticoagulant. Similarly, if the anticoagulant is in the storage tube, the mixture must be well shaken at once. It is important to avoid marked forcing of the blood through the narrow bore of the needle in ejecting the contents of the syringe into the storage tube, for, if this be done, haemolysis of the red cells is apt to result. The wisest plan is to remove

the needle from the syringe and then to squirt out the contents.

In taking the blood for microscopic methods, the small quantity which suffices, can be extracted from the ball of the finger (this is preferable to taking it from the lobe of the ear). The finger may previously be held in warm water to dilate the blood vessels. After cleansing the skin, the prick is carried out by a straight cutting needle or by a small lancet. Often two pricks made one immediately after the other, give a more satisfactory result. In order to obtain the necessary quantity of blood, it is best to wait for about fifteen seconds after the puncture, since a contraction of vessels sets in immediately after the puncture. After the quarter of a minute has elapsed the spasm has generally passed off, and in response to light pressure, a sufficient quantity of blood oozes out quickly. Pressure on the finger does not appear to alter the result of sedimentation and is best carried out by exercising a gradually increasing pressure from the proximal to the distal end of the finger. The finger must be dry and the smallest amount of alcohol remaining on it will influence the rate of sedimentation.

The question of anticoagulants arises here. Coagulation may be retarded by applying such a substance as oil or vaseline to the wall of the tube. This does not prove satisfactory however, since coagulation occurs after a

time. A substance which will prevent coagulation is mixed with the blood. Solid forms of anticoagulants have been advocated because they avoid dilution of the blood. However, it is difficult to measure the small quantities used for the purpose, and variations are thus apt to creep in, rendering the proportion of anticoagulant inconstant. Examples of these solid forms are hirudin, heparin, N.A.B., sodium fluoride, potassium oxalate and ammonium oxalate. Rourke and Plass (26) are of the opinion that heparin in solid form is the ideal anticoagulant. They obtained the blood of a haemophilic patient whose clotting time was over 5 hours; the rate of sedimentation of the blood with no added anticoagulant and with the addition of 1 mg. of heparin per 5 cc. of blood were compared and no difference in the results was found. I employed heparin in some 50 tests and my results were unsatisfactory. Others (27), (28), recommend a mixture of 4 mgs. of potassium oxalate and 6 mgs. of ammonium oxalate per 5 cc. of blood. This mixture I also found to be unsatisfactory. Rees-Walton (29), similarly found solid forms of anticoagulants inferior to citrate solution.

Solutions of oxalates and citrates are the commonest types of fluid anticoagulants. Highly concentrated solutions are preferred by some but their use is attended by changes in osmotic pressure and should not be employed. Sodium citrate in isotonic solution--3.8%--is widely used

and is very satisfactory. Different percentages of citrate solution used, do not give identical results. A series of tests brought this fact out clearly. I used three strengths of citrate, 3.8%, 3%, and 5%, and into each of these introduced equal quantities of blood from the same patient. The results given below bring out the variations in results.

CASE I.	1 hr.	2 hrs.	12 hrs.	24 hrs.
3% citrate	38	68	120	122
3.8% citrate	33	65	118	122
5% citrate	30	60	110	118

CASE II.	1 hr.	2 hrs.	12 hrs.	24 hrs.
3% citrate	16	29	70	74
3.8% citrate	9	27	67	74
5% citrate	7	20	55	63

The chief objections to the use of sodium citrate are that it dilutes the blood and being an electrolyte, may interfere with the electrical burden of the erythrocytes.

Nevertheless, sodium citrate in 3.8% solution appeared to offer the best results and has been employed in all my tests. The amount of citrate solution used is of great importance. The proportions of blood and citrate must always be kept constant. Below are figures from an experiment showing the fluctuations which arise when varying quantities of citrate are used.

CASE I.	1 hr.	2 hrs.	12 hrs.	24 hrs.
2 cc. citrate	84	120	146	148
1.5 cc. citrate	70	114	138	146
1 cc. citrate	53	96	135	143

CASE II.	1 hr.	2 hrs.	12 hrs.	24 hrs.
2 cc. citrate	5	14	58	64
1.5 cc. citrate	5	12	55	62
1 cc. citrate	2	6	55	64

The quantities of citrate quoted were added to 4 cc. of blood.

It is advisable to use a sterile solution of sodium citrate, since fungoid growths are apt to occur and affect the anticoagulant. The bottle should be kept in a cool place and be stoppered. With the least suspicion of impurity, the solution must be discarded and a fresh stock made up for use.

The macroscopic are much superior to the microscopic methods and should be used wherever possible. Brief reference will be made to the methods in most common use, while a detailed account of the Westergren method, which was used in all the cases reported on, shall be given.

Macroscopic methods

The three principal methods are:

1). The distance method of Westergren (30), in which the

distance through which the erythrocytes fall in a certain time is measured.

2). The graphic method of Cutler (31) in which the distance of the sedimentation of the erythrocytes is measured at frequent intervals over an hour, for the construction of sedimentation curves.

3). The time method of Linzenmeier in which the time required for the blood cells to reach a certain distance is measured.

It has been demonstrated that the results obtained by the three methods are reasonably concordant despite the wide variations in technique (32).

The Westergren Method

Blood is withdrawn from a vein in the manner described above and the blood and 3.8% sodium citrate solution mixed in a proportion of 4 : 1, e.g. if 2 cc. of blood be used, 0.5 cc. of anticoagulant should be added. Both these quantities should be accurately measured. A smaller amount of citrate would suffice to prevent the blood clotting, but it is practical to use this surplus to make more certain that coagulation will not occur. The mixture is placed in a storage tube--an ordinary clean, dry test tube will meet the purpose. The fluid is well agitated before being sucked up into the sedimentation tube. The latter consists of a long, thin, cylindrical, transparent glass tube, with

an internal bore which is even and cylindrical, having an internal diameter of 2.5 mm. The tube is calibrated in millimetres from below upwards, the uppermost number being 0 and the lowermost 200. The mixture is sucked up several times into the tube and allowed to run back each time into the test tube, to ensure complete admixture; then in the same manner as one deals with the regulation of the height of fluid in a pipette, the level of the blood is brought to the zero mark; the tube is closed at the bottom by placing it in a rubber cork situated on a rack specially designed for the purpose. At its upper end the tube is held in position by a spring clip arrangement, and a vertical position thus attained. A number of tubes situated side by side on the rack and set up at the same time, allow readings of them all to be taken simultaneously. Readings are taken at the end of one hour, two hours, twelve hours, and twenty-four hours. More shall be said of these times at a later stage.

Several points must be considered here. Firstly, how long can one wait between the period of collection of the blood and of setting it up in the sedimentation tube?

Obviously this is of great import, since a delay of time is often unavoidable because of circumstances. However, provided the storage tube is closed with a cork, to prevent evaporation, an interval of 3 to 4 hours may be allowed to elapse without any effect on the velocity of sedimentation (33). This is readily verified by setting

up a test immediately after collection of the blood and comparing the results with a test set up from the same blood, several hours later. In many cases even 6 to 7 hours had no apparent influence on the sedimentation rate. Delay in carrying out the test for too long a period from the time of collection of the blood, leads to a decreased rate of sedimentation.

Another factor of importance is the cleanliness of the sedimentation tubes. Not only must they be clean, but they must also be absolutely dry. The tubes should be cleaned only with water, since alcohol causes plasma fragments to coagulate. The syringe need only be clean and not sterile. A small amount of citrate solution should be drawn up and allowed to run round the interior of the barrel of the syringe before being ejected. The blood or citrate solution, if that be placed in the syringe instead of the storage tube, may now be drawn up.

Alterations in the carbon dioxide and oxygen content of the blood do not apparently affect the sedimentation. Arterial and venous bloods have identical rates. Two sedimentation tubes were set up, so that the lower openings were closed by inserting them into a mass of plasticine, the upper apertures being left uncovered. The upper level of one blood column was covered with a layer of oil and the readings of both taken at the same intervals; in both the results were identical. In another experiment the two

tubes were set up as above, but the tube without the oil was surrounded by a wide tube with one end open to the air and the other end attached to an oxygen cylinder, from which the oxygen was allowed to flow. The tube was thus surrounded by an atmosphere of oxygen. The results in both tubes coincided.

The diameter of the internal bore bears a relationship to sedimentation rate. Narrow bores influence the sedimentation rate in a rather variable way, up to a diameter of about 1.5 mm. Beyond this measurement in the wider tubes, the influence decreases so rapidly as to be of practically no account. The height of the column of blood--200 mm. in a Westergren tube--is a significant factor. Below are several figures showing the changes resulting from commencing sedimentation at 0 and at 100, using the same bloods, in Westergren tubes.

	1 hr.	2 hrs.	12 hrs.	24 hrs.
I. Starting at 0	45	65	95	100
" " 100	125	132	151	151
II. " " 0	111	134	140	145
" " 100	162	166	166	168
III. " " 0	3	15	58	65
" " 100	102	110	131	146

In all these cases quoted 3.8% sodium citrate was used as an anticoagulant.

The sedimentation tubes must be in a vertical position

and the Westergren rack is so designed as to ensure this. The rack must be placed on a horizontal surface and must not be moved after commencement of the test. Velocity of sedimentation increases markedly in a sloping tube (15).

The effect of the external temperature is of extreme importance and disregard of this factor is a frequent source of error. The tubes must not be placed near any source of heat and in summer should be situated in the shade. Heat exerts the same influence on the velocity of sinking, irrespective of the diseased condition, causing an increase in sedimentation rate with an increase in environmental temperature. Cold has an opposite effect (34). The tests should be carried out at an average room temperature.

Microscopic Methods

Payne (35) points out that in children, where difficulty is often experienced in obtaining a vein suitable for venupuncture, the micromethod must be resorted to. He used a graduated pipette, into which sodium citrate is sucked up to the 0.1 cc. mark and blood, collected by puncturing a finger, to the 0.5 cc. mark. The tubes are set up in a vertical position and read at 1, 2 and 24 hours.

Jacob Cutler (36), Beaumont-Maycock (37) and McSweeney (38) describe similar methods.

General Considerations

In the sedimentation tubes the red corpuscles sediment, leaving plasma in the upper part of the tube. Normal subjects vary individually in their rate of sedimentation. In general, it may be said that, a rapid rate of sedimentation is an expression of some disease process (an exception is pregnancy). However, the converse does not hold true and a normal sedimentation rate may exist in the presence of obvious pathological changes in the body. Thus, certain diseases will cause a diminished suspension stability of the blood, while others will apparently not affect it. The degree of velocity imparted on the sedimentation of the erythrocytes, differs not only in the distinct morbid processes, but in different patients suffering from the same malady and also in different stages of that malady. The only physiological condition which influences the sedimentation rate is that of pregnancy. After the third or fourth month of pregnancy the sedimentation rate begins to rise and increases until it reaches its acme at childbirth. It remains high until involution has occurred--usually during the third or fourth week of the puerperium. The sedimentation rate is therefore, of no value in clinical diagnosis during these periods. An operation wound of sufficient degree, fractures and frequently bruising and injury to tissues will increase the rate of fall of the erythrocytes. A large haematoma may have a similar effect. The period following operations, during which the sediment-

ation rate is affected varies with the extent of the operative interference and resulting trauma of tissues involved; the appearance of complications will further influence the suspension stability. As a rule after an uncomplicated appendicectomy, sedimentation rate returns to normal limits, three to four weeks after the operation. Fractures take longer, again depending on the size of the bone broken, nature of the fracture, e.g. comminuted, compound, and on the presence or absence of sepsis.

Menstruation per se does not cause a rise in sedimentation rate. Nevertheless a certain acceleration may appear in certain pathological conditions during the menses. The explanation probably lies in the fact that other maladies may become more active during menstruation and so the latter cause an increased rate indirectly.

Normal adult females have in general a faster rate than males, whereas no difference exists between the sexes under the age of puberty (39). Apparently some change must occur at puberty--probably of an endocrine nature--which causes this variation.

Blood from the umbilical cord and from the new born infant show a low normal or retarded rate of sedimentation (40), the rate beginning to rise during the first few weeks of life. Between the second and sixth month of life, the sedimentation rate is more rapid than the adult rate, which is reached in the second half of the first year. Although no direct correlation between age and sedimentation rate

appears to exist, a few mm. above adult normal values may not be abnormal in children. Similarly in old age slight increase in the sedimentation rate need perhaps have no clinical significance since often old foci of inflammation or degeneration which are difficult to discover may be the cause.

The readings of the sedimentation rate in all my cases were taken at the end of one, two, twelve and twenty-four hours. While the twelve hour reading is perhaps unnecessary and may be omitted without loss, I consider the other three to be important. The level of the plasma is read off at these intervals. This level is sometimes clear cut, sometimes an indistinct zone and sometimes no real boundary exists, the column of red blood cells vanishing upwards in an increasingly thinner red cloud. In this last type of case reading of the result is often impossible. In the middle type of case quoted, the reading is taken at that part of the column where the yellow of the plasma merges into the red of the column of erythrocytes--that is at the point where differences of densities appear. At the end of twenty-four hours a white layer is seen above the red level; this consists of leucocytes and platelets and in the twenty-four hour reading should be included as part of the plasma. The reddish tint of the plasma, which is sometimes seen, is not due to haemolysis of red cells in the great majority of cases but to rouleaux of corpuscles floating in the plasma. If coagulation or even a tendency

towards clotting takes place the test must be rejected.

There are three stages in the sedimentation of erythrocytes.

1). The "Preagglutination" stage.

During this period sedimentation is slow. Rouleaux are being formed and some time elapses before the aggregates have gained their definite size. The sinking, therefore, is slow, increasing steadily until a constant velocity is reached. The duration of this stage is variable, but generally speaking, is shorter the more rapid the sedimentation rate. This however, is by no means constantly so, and sedimentation during the whole of the first hour may be slow, while the second hour reading may show a definitely abnormal rate.

2). The Stage of "Agglutination."

During this stage the rouleaux are fully formed and the velocity is constant. This is the stage of true sedimentation and all are agreed that it is the ideal period for estimating the suspension stability of the blood. However, one cannot be sure of the exact time of its commencement and cessation. In some cases it would appear to start early, in others late.

3.) The Stage of "Packing."

As the red blood cells heap up at the base of the tube the uppermost rouleaux are increasingly retarded in their fall, until finally sedimentation ceases. Settlement begins in the second third of the column. At the end of

twenty-four hours, the sedimentation has not entirely ceased. In rapidly sedimenting blood there is very little drop in the red column between 24 and 48 hours; however in bloods with a 24 hour reading of about 100, a not inconsiderable difference is often observed between these periods.

There would appear to be some difficulty in determining which times are best for the taking of readings. Some recommend a reading at the end of the first half hour. However, on many occasions, I have observed a slow rate during this period, whereas, the reading at the end of the first hour has been of pathological import. Reading at the end of an hour may also be criticised from the point of view that in very rapidly sedimenting columns, packing has already taken place and so interferes with the true value; while this is so, a reading of such dimensions is of sufficient diagnostic import to render the effect of retardation of little consequence. The second hour reading is of little value in very rapid one-hour readings. In the type of case in which there is a low one hour reading due to a prolongation of the first stage, a high second hour reading may be indicative of disease and in such a case is valuable. These cases, however, are relatively uncommon.

Examples.

Case I. Diagnosis: Rheumatoid Arthritis in an active stage

1 hr.	2 hrs.	12 hrs.	24 hrs.
5	43	89	124

Case II. Diagnosis: Pulmonary tuberculosis (positive sputum examination)

1 hr.	2 hrs.	12 hrs.	24 hrs.
8	48	96	130

Case III. Diagnosis: Pyloric Carcinoma

1 hr.	2 hrs.	12 hrs.	24 hrs.
9	50	110	132

The twelve hour reading, as has been previously indicated may be left out. It has, however, been included in the cases reported. A twenty-four hour reading gives an additional indication of the suspension stability of the blood, the smaller its quantity the more stable the blood. It is not a measurement of the relative volumes of plasma and erythrocytes. Weekly variations in its value are found in normal patients, of perhaps up to 20 mm.

Normal values are difficult to lay down. Some maintain that the sedimentation rate is a constant in normal individuals (41); while others consider it to fluctuate daily. Hoverson and Peterson (42), (43), came to the conclusion that there are wide variations of the sedimentation of the erythrocytes in normal subjects, and that at times the daily variation may be as much as 100%. They are of the opinion that meteorological changes account for these differences. Greisheimer (44) obtained similar results. From my own observations, I have convinced myself of the fluctuating nature of the sedimentation rate and that one cannot confine its normal value to too narrow a

range. Rees Walton (29) in a table gives the normal values as stated by some observers.

Author	Male	Female
Krindler and Popper	3 - 6 mm.	4 - 8 mm.
Westergren	1 - 3 mm.	5 - 7 mm.
Gram	2.5 - 6 mm.	2.5 - 7.25 mm.
Fahraeus	3.3 - 10 mm.	7.4 - 13 mm.

These readings refer to the level of the plasma at the end of one hour.

All are agreed that the female rate is more rapid than the male. For males a reading up to 10 mm. and for females up to 12 mm. has been accepted as within the normal range of the one-hour reading. A two-hour reading of over 40 mm. has also been considered as indicative of pathological changes in the body, even in the presence of a normal one-hour reading. The lower the 24-hour reading, the less its significance of disease. Normal values lie as a rule between 60 and 100 mm. The 24-hour reading can only be accepted as of secondary importance, the one- and two-hour readings giving the greatest indication of the suspension stability of the blood. One frequently finds reference made to retarded rates of sedimentation. It is difficult to quote a figure for such rates. Certain conditions definitely appear to cause a high sedimentation to sink to normal levels. An example is found in cases of active rheumatic carditis, where a previously high sedimentation

rate sinks to normal ranges with the onset of cardiac failure.

Whether exercise affected the sedimentation rate was a simple matter to clarify and my results agree with those of Rourke and Plass (26). The ingestion of food had similarly apparently no effect on the velocity of sinking of the erythrocytes. There thus appears to be no reason for prescribing the test at any particular time of the day or under conditions of rest.

It was thought wise to investigate also the possibility of alterations of sedimentation rate being caused by ultra violet radiation and x-rays. The former when used as a therapeutic measure in patients who had a normal rate prior to exposure, did not in any case studied, cause a rise of sedimentation above normal values. Sedimentation tubes were directly exposed to the rays of a mercury quartz vapour lamp and again no alteration of rate, as compared with a series of tubes set up at the same time from the same patients and kept under ordinary conditions.

The effect of x-ray therapy was studied in five patients suffering from carcinoma of the lung and in one case of Hodgkin's disease. In all the cases a definite acceleration of rate was produced. Two cases are shown below. Pohle (45) obtained varying results in his series of cases of x-rays.

Case I. Male, age 68. Diagnosis: Carcinoma of right upper lobe of the lung.

Date	1 hr.	2 hrs.	12 hrs.	24 hrs.
8/10/36	42	84	133	135
24/10/36	26	40	100	110
Course of x-ray therapy commenced 24/10/36 and finished 6/11/36.				
8/11/36	111	134	140	145
13/11/36	84	120	138	140
20/11/36	90	125	140	142
23/11/36	73	106	135	135
30/11/36	57	100	128	134
6/12/36	50	88	134	135

There is a pronounced rise after the x-ray therapy, and a gradual fall after cessation of treatment.

Case II. Male, age 65. Diagnosis: Carcinoma of the eparterial bronchus

Date	1 hr.	2 hrs.	12 hrs.	24 hrs.
9/6/36	35	69	122	127
16/6/36	31	68	112	117
20/6/36	38	70	108	114
Case was treated by x-ray				
30/6/36	87	114	136	139
10/7/36	82	112	134	135
18/7/36	72	102	129	136
26/7/36	61	90	126	128
30/7/36	42	69	125	126
10/8/36	39	63	120	122

The figures show again here, what has been stated of the effect of x-ray therapy on the sedimentation rate in these cases.

Localised diathermy had no effect and in two cases of hyperpiesis treated with general diathermy no change in the sedimentation rate took place. Massage had no effect, however vigorously it was applied, but some manipulative treatment--such as breaking down joint adhesions under anaesthesia--frequently cause an increase in the rate of sedimentation. Injections of vaccines and sera will cause a rise only if general reaction occurs. Injections of peptone, milk, blood, etc., act in a similar manner.

The association and relationship of the rate of sedimentation to fever will now be reviewed. Acceleration of sedimentation and rises of temperature have usually a common cause. That pyrexia per se however, is a cause of increased sedimentation is very improbable, and a normal sedimentation rate may be found in the presence of pyrexia, e.g. pertussis. In normal individuals who are suddenly affected with pyrexia, the sedimentation rate takes some time before an increase occurs. Thus fever and leucocytosis appear before any upset of the suspension stability of the blood is evident. In acute appendicitis the sedimentation rate may be normal within the first 24 to 48 hours, while pyrexia and leucocytosis may be pronounced. Although some time elapses in such acute conditions, before increased velocity of sedimentation takes place, the increase remains

over a longer duration than the leucocytosis and pyrexia, and may be very high some days after the temperature has reached normal. The maximum rate is often reached some days after the highest temperature. The gradual fall of sedimentation with resolution of the disease is much slower than its rise. During an acute specific fever, e.g. lobar pneumonia, when the maximum sedimentation rate has been attained, this rate alters but little, although the temperature may fluctuate widely. That is, the mere degree of pyrexia, with no accompanying changes in the general and local conditions, has no direct effect on the sedimentation rate. Should however, an empyema arise, the value rises, and such a rise may be the first indication of a complication in acute specific fevers. In remittent or intermittent fever, one may find a high temperature with a low sedimentation, as the temperature is more quickly affected than the suspension stability of the blood. Hence a high temperature and low sedimentation rate may co-exist and vice versa. However, in chronic diseases, on which an acute exacerbation is imposed, the sedimentation rate responds more quickly than in cases with an acute pathological condition occurring in a previously healthy organ. That normal temperatures are often present with rapid sedimentation rate is well known, e.g. in cases of rheumatoid arthritis. It will thus be seen that pyrexia and rapid sedimentation rate do not respond in the same manner in

all diseases, and the degree of one does not reflect the degree of the other.

The question of the influence of anaemia on the sedimentation rate is one which arises in almost every paper on the subject. There is a wide divergence of opinion on the matter. Many hold that the blood picture affects the rate of sedimentation. Cherry (10) states that any marked changes in the blood above or below normal will upset the velocity. Chung (46) considers the haematocrit to be an accurate index of anaemia as well as polycythaemia; he centrifugalises the blood, and, after reading off the volumes of the red blood cells and plasma, adds or removes such quantity of the latter as will correct their proportions to normal values. Walton (29) enumerates the erythrocytes using one drop of saturated solution of potassium oxalate for 8-10 cc. of blood. By means of a graph he corrects the sedimentation rate for any anaemia present. Rourke and Plass (23) lay stress on the cell volume content of the blood and allow correction for this. H. C. Gram (57) constructed curves for adjustment of differences in haemoglobin content, which he thought to be an important influencing factor. On the other hand, Warren (47) demonstrated that anaemia had apparently no constant effect on sedimentation rate. He could not correlate the red cell counts with the sedimentation rate of the cases investigated. With very low cell counts he often obtained

normal values of sedimentation. In pernicious anaemia all his cases had rapid rates; of six cases of sprue only two had high sedimentation velocities, even although some of the cases with normal rates of sedimentation showed a more pronounced degree of anaemia than did many of the patients with pernicious anaemia, in which latter as has been said, a diminished suspension stability of the blood was always present. Zecker and Goodell (48) are of the opinion that the cell volume factor is of little importance. Newham and Martin (12) found no correlation between the size of the red blood cells and the rate of sedimentation, Lebel and Lottrup (49) in an extensive research on the relationship of haemoglobin to the blood sedimentation rate, found that on allowing correction to be made for low values in concordance with Gram's method, the sedimentation values thus obtained were often normal where the clinical evidence had made them feel sure of rapid rates.

From numerous observations I have failed to convince myself of the influence of the red cell count or haemoglobin content per se, on the sedimentation rate. As has been already shown, the plasma contains the controlling factors and variations in the qualities of the plasma will affect the rate. It seems improbable therefore that mere numerical differences in the red cell count will influence sedimentation to any great extent. Mere artificial dilution of the blood by alterations in the quantities of plasma is

not a true test of the importance of the red cell count, since, in anaemia other factors play a part, which cannot be imitated by artificial blood dilution. Anaemia is accompanied by such changes as to render recalculation by formulae or tables futile. Moreover, a great deal of the practical significance of the test lies in its simplicity of technique, and the methods of correction advised have failed to convince me of their value. Below I quote a number of cases which demonstrate the failure of anaemia to cause rapid sedimentation. For practical purposes, reduction in the red cell count or haemoglobin percentage need not be corrected.

Case I. Male, age 63. Diagnosis: Diverticulitis and haemorrhoids. Chronic bleeding per rectum.

Blood Pictures

Date	Red Cell Count	Haemoglobin	Colour Index
11/10/36	2,500,000	25%	0.5
21/10/36	3,290,000	28%	0.43
28/10/36	4,270,000	38%	0.45
4/11/36	4,930,000	62%	0.63
12/11/36	4,920,000	62%	0.63

Sedimentation Rates	1 hr.	2 hrs.	12 hrs.	24 hrs.
11/10/36	2	6	45	63
21/10/36	5	9	47	68
28/10/36	3	8	46	68
4/11/36	4	9	43	70
12/11/36	3	6	40	65

Case II. Female, age 53. Diagnosis: Gastric ulcer.

The patient was admitted with a history of severe haematemesis on the preceding day. The drop in sedimentation rate is co-incidental with the cessation of severe activity around the ulcer and not with improvement in the blood picture.

Date	Red Cell Count	Haemoglobin	Colour Index
21/7/36	2,320,000	35%	0.76
27/7/36	3,050,000	41%	0.67
4/8/36	2,900,000	44%	0.76
11/8/36	3,140,000	52%	0.83

Sedimentation Rates	1 hr.	2 hrs.	12 hrs.	24 hrs.
21/7/36	30	70	137	146
27/7/36	11	30	79	110
4/8/36	7	21	80	112
11/8/36	5	18	63	98

Case III. Male age 36. Diagnosis: Chronic Azotaemic Nephritis

Date	Red Cell Count	Haemoglobin	Colour Index
30/9/36	1,640,000	30%	0.91
7/10/36	2,090,000	36%	0.86
14/10/36	1,740,000	31%	0.88

Sedimentation Rates	1 hr.	2 hrs.	12 hrs.	24 hrs.
2/10/36	25	40	135	146
8/10/36	11	30	136	146
13/10/36	8	19	96	109

Case IV. Female, age 45. Diagnosis: Anaemia due to chronic bleeding from peptic ulcer

Date	Red Cell Count	Haemoglobin
25/8/36	2,540,000	36%
30/8/36	3,080,000	39%
8/9/36	3,100,000	52%
16/9/36	3,400,000	58%

Sedimentation Rate	1 hr.	2 hrs.	12 hrs.	24 hrs.
25/8/36	5	16	63	85
30/8/36	7	22	74	92
8/9/36	3	15	63	66
16/9/36	8	19	68	72

The Blood Sedimentation Rate in Disease

The Rheumatic and Arthritic Group of Diseases

Under this heading will be included rheumatic fever (acute rheumatism), osteo-arthritis, rheumatoid arthritis, gout, chronic rheumatism, and sciatica.

Acute Rheumatism

It is accepted that during the acute stage of rheumatic fever the sedimentation rate is accelerated. The principle in therapeutics in this disease is that of the prevention of cardiac damage, and if that occur of minimising any subsequent impairment of the myocardium. Hence it is of the utmost importance that a patient remain in bed until all evidence of activity has ceased. From clinical signs and symptoms it is often difficult to be certain of this stage. The administration of salicylates frequently causes prompt subsidence of fever and polyarthritis, but in spite of this alleviation of symptoms, the activity may still be great and the sedimentation rate remain high, indicating, what is now generally recognised, that salicylates are not a cure for rheumatic fever. A. C. Ernstene (50) made a comparison between the leucocyte count and the sedimentation rate in estimating the presence of activity of the disease, and found the sedimentation rate to be much more reliable. Struthers and Bacal (51) in considering the various indices of activity in use, consider the sedimentation rate to be of greatest value. Among their indices are body weight, leucocyte count and the sleeping pulse rate.

Regarding the latter Schlesinger (52) demonstrated that the study of the pulse rate while the patient is awake is not sufficient in itself to establish the presence of an active carditis in afebrile children suffering from heart disease, owing to the nervous element present during the counting of the pulse rate. He further pointed out that the sleeping pulse rate is the important gauge. This is normally 10 beats per minute slower than the alert rate. A sleeping pulse rate continuously and decisively above normal is strongly indicative of active heart disease. In cases of chorea a normal sleeping pulse rate excludes active carditis. Bruce Perry (53) also states sedimentation rate to be the most delicate index of activity of infection in rheumatic carditis. He lays emphasis on the fact that single readings do not rule out the possibility of a smouldering infection but a persistently low sedimentation rate rarely occurs if the rheumatic process is active. Payne and Schlesinger (54) agree with the principles quoted above and point out that the onset of congestive cardiac failure causes the sedimentation rate to fall, and such a fall in the absence of signs of clinical improvement may be looked on as of grave prognostic import.

My own results, some of which are given below, agree with the findings of the authorities quoted. Accelerated sedimentation occurs in rheumatic fever and is usually of very rapid rate even if the case show slight or no fever

or unimportant articular signs. This increase of rate persists during the period of activity of the disease and during relapses. In the acute stage of the disease if clinical signs of activity are obvious the test is perhaps superfluous, but during the recrudescence of the illness it is of supreme value. No case of rheumatic fever should be allowed out of bed until sedimentation is normal. Repeated tests must be adopted and a single reading is insufficient. While the patient is up, the sedimentation rate should still be performed for some time afterwards, to demonstrate either total quiescence or relapse. A rise during this period is an indication for renewed rest. It is fascinating to watch the gradual drop of the sedimentation rate in cases of uncomplicated rheumatic fever. The occurrence of a drop in the velocity in congestive cardiac failure in cases of rheumatic carditis must always be borne in mind, and it is a grave sign. An interesting point brought out by Bruce Perry, is that subcutaneous nodules appear late in the disease as judged by the sedimentation rate and may persist even after the disease has become inactive (53).

Chorea uncomplicated by carditis does not affect the sedimentation rate, and no reliance can be placed on the test to indicate those cases liable to cardiac involvement. A slight rise may be seen in some cases of chorea but this increase is of slight degree.

Case I. Male, age 15.

Diagnosis: Rheumatic Fever. Case a typical one, with joint swelling and pyrexia. No carditis occurred. The sedimentation rate shows a gradual drop to normal.

Date	1 hr.	2 hrs.	12 hrs.	24 hrs.
24/6/36	45	70	123	130
29/6/36	50	82	105	110
5/7/36	71	100	131	131
7/7/36	45	73	101	103
11/7/36	37	75	110	111
16/7/36	38	80	105	107
20/7/36	27	49	78	100
23/7/36	20	48	82	98
30/7/36	15	35	78	92
5/8/36	12	28	60	70
11/8/36	7	23	68	70
15/8/36	5	21	61	65

Case II. Female, age 17. Diagnosis: Rheumatic Fever

The patient did not develop any complication

Date	1 hr.	2 hrs.	12 hrs.	24 hrs.
20/8/36	98	127	135	136
19/9/36	14	38	85	99
25/9/36	19	36	85	97
30/9/36	15	35	62	90
6/10/36	13	34	65	68
18/10/36	12	30	43	53
28/10/36	6	18	40	50

The rates between 20/8/36 and 19/9/36 have not been included. The case demonstrates the long period between 19/9/36 and 28/10/36 during which the rate was not very high but yet indicative of activity. The patient was not allowed out of bed until 28/10/36.

Case III. Male, age 10. Diagnosis: Rheumatic Fever

The case was allowed up after the sedimentation rate was normal. However, the rate was still watched and a rise coincided with a re-awakening of activity of the disease, the child being then returned to bed.

Date	1 hr.	2 hrs.	12 hrs.	24 hrs.
23/6/36	74	100	131	132
29/7/36	15	30	52	60
3/8/36	8	15	35	43
10/8/36	5	10	37	51
15/8/36	8	13	42	45
25/8/36	36	62	105	107
3/9/36	40	58	110	116
10/9/36	21	30	64	82
15/9/36	12	34	63	65
20/9/36	8	19	46	61

Case IV. Female, age 18. Diagnosis: Rheumatic Fever

The case did not resolve and carditis developed. The sedimentation rate remained up for weeks; the girl was transferred to another hospital on 23/6/36.

Date	1 hr.	2 hrs.	12 hrs.	24 hrs.
24/3/36	43	100	126	128
29/3/36	46	65	110	112
12/4/36	53	88	129	130
30/4/36	61	73	89	96
12/5/36	32	49	83	89
19/6/36	45	64	102	105

Three cases of chorea of varying severity, which all cleared up with no sequelae are given below.

	1 hr.	2 hrs.	12 hrs.	24 hrs.
Case "A"	3	12	53	60
Case "B"	9	20	64	80
Case "C"	7	18	30	47

Chronic Rheumatism

This group consists of cases of fibrositis, lumbago, "muscular rheumatism," neuralgia, sciatica, etc. In none of my cases was there any disturbance in the rate. Indeed, the importance of the test in this group of diseases lies in the normal values obtained, for, if a case of sciatica present an acceleration of sedimentation rate, it can be taken as an indication for a thorough search for some underlying pathology, e.g. carcinoma of the prostate, or some co-existing disease. A diagnosis of rheumatism should be revised if obviously rapid sedimentation is present.

Case I. Female, age 58. Diagnosis: Fibrositis affecting the abdominal muscles and fat.

1 hr.	2 hrs.	12 hrs.	24 hrs.
5	11	47	54

Case II. Male, age 34. Diagnosis; Lumbago

1 hr.	2 hrs.	12 hrs.	24 hrs.
2	4	23	33

Case III. Male, age 55. Diagnosis: Sciatica

1 hr.	2 hrs.	12 hrs.	24 hrs.
4	7	45	57

Specific Infective and Toxic Arthritic Group

Under this heading gonococcal, syphilitic, tuberculous and infective arthritis fall. Osteo- and rheumatoid arthritis are discussed under a separate heading. In all such cases sedimentation is increased if the condition is active. If the disease be quiescent normal values are registered.

Case I. Male, age 22. Diagnosis: Toxic arthritis. Septic focus thought to be an apical tooth abscess

Date	1 hr.	2 hrs.	12 hrs.	24 hrs.
27/6/36	70	85	130	132
10/7/36	74	120	132	132
21/10/36	83	115	122	127
4/11/36	80	112	120	122

Case II. Male, age 53. Diagnosis: Syphilitic arthritis and iritis

1 hr.	2 hrs.	12 hrs.	24 hrs.
88	115	143	143

The patient was discharged with this high value to a venereal disease centre.

Case III. Female, age 14. Diagnosis: Tuberculous Arthritis

Date	1 hr.	2 hrs.	12 hrs.	24 hrs.
9/7/36	134	134	135	135
15/9/36	107	130	140	140

Gout

I have been fortunate in seeing five cases of gout. One of the cases was an early one, while the others were in an advanced state. Gouty arthritis was distinguished by history of onset, periodic acute or subacute attacks with intervals of remission, gouty tophi, raised blood uric acid and x-ray findings of "punched out" areas in epiphyses of the bone. In all the cases increased rates were observed. Kahlmeter (55) also obtained rapid values in his series of cases.

Case I. Male, age 61. Diagnosis; Chronic gouty arthritis

The patient had a history of 30 years' duration. The mobility of all the affected joints--elbows, wrists, fingers, ankles, knees and toes--was very slight. Tophi were present over the right elbow and on the ears.

Date	1 hr.	2 hrs.	12 hrs.	24 hrs.
23/10/36	62	80	94	100
8/11/36	55	88	120	120
30/11/36	12	35	83	89
12/12/36	17	42	89	98

The rate of sedimentation did not appear to be influenced by the symptoms complained of by the patient. For example, a high rate was obtained when the joint pains were absent and vice versa.

Case II. Male, age 51. Diagnosis: Gouty Arthritis
The patient was admitted with an acute arthritis of the left metatarso-phalangeal joint. There had been previous attacks of the same condition, affecting both big toes and the right elbow over a period of three years.

In this case the sedimentation rate declined as the inflammation subsided.

Date	1 hr.	2 hrs.	12 hrs.	24 hrs.
3/11/36	74	114	130	132
4/12/36	16	52	100	105
13/1/37	9	27	51	62

Osteo- and Rheumatoid Arthritis

These two types of arthritis have now been clearly differentiated and separated, although osteo-arthritic changes are not infrequently superimposed on joints affected with rheumatoid arthritis. Osteo-arthritis (hypertrophic arthritis) is generally considered a degenerative lesion and its age incidence is ~~greater~~ later in life than that of rheumatoid arthritis (atrophic arthritis). The latter type tends to affect multiple joints in contrast to osteo-arthritis, and there is evidence of a generalised tissue response to the causal agent. From these facts one would expect to find an acceleration in the velocity in sedimentation in atrophic but not in hypertrophic arthritis, and this is indeed the case. The suspension

stability of the blood in active rheumatoid arthritis is nearly always decreased, while in the degenerative form, i.e. osteo-arthritis, it is normal or only slightly lowered. Similarly in spondylitis, which in this group of diseases, falls into the two divisions of ankylosing spondylitis and spondylitis osteo-arthritica, we find that the former, which corresponds to the atrophic arthritic type, usually has increased velocity of sedimentation, while the latter, which is of a degenerative or traumatic nature, possesses a sedimentation rate of within normal limits.

While the sedimentation rate seems to offer a relatively simple method of differentiating these two types of arthritis, it must be clearly recognised, that the test should not be the sole criterion in the differential diagnosis, and clinical findings must be carefully considered (56).

In my series of 36 cases of rheumatoid arthritis, I have found marked fluctuations in the sedimentation rate, which were not explainable by clinical findings. Weekly variations of as much as 30 mm. in the first hour, without any apparent reason and without any change in the patient's regime, have led me to doubt the value of the test in this type of disease as a prognostic agent or as a quantitative measure of the degree of involvement or activity of the process. Others, e.g. Kahlmeter (55) consider the

test a good prognostic index in this disease. Hunt found the test of little value in the diagnosis or prognosis of the arthritic maladies (3).

Case I. Female, age 76. Diagnosis: Osteo-arthritis of the right hip joint, in an advanced stage.

1 hr.	2 hrs.	12 hrs.	24 hrs.
8	s0	76	88

Case II. Male, age 65. Diagnosis: Osteo-arthritis of right hip joint.

1 hr.	2 hrs.	12 hrs.	24 hrs.
8	22	102	110

Case III. Male, age 67. Diagnosis: Rheumatoid arthritis.

The case was a very severe one, involving most joints of the body. Treatment had no effect.

Date.	1 hr.	2 hrs.	12 hrs.	24 hrs.
1/11/36	60	104	124	124
12/11/36	40	71	117	120
16/11/36	52	91	122	125
23/11/36	48	80	120	124
30/11/36	48	88	120	123
6/12/36	42	84	125	128
14/12/36	48	82	126	127
21/12/36	55	85	124	127
30/12/36	61	100	124	127
15/1/37	72	108	124	128

Case IV. Female, age 50. Diagnosis: Rheumatoid arthritis

The case was an advanced one and numerous joints were affected. Treatment by allochrysine lumiere had a very beneficial effect which was not reflected in the sedimentation rate.

1 hr.	2 hrs.	12 hrs.	24 hrs.
45	79	126	128
26	40	82	90
54	100	111	112
31	75	125	133
65	112	120	121
27	57	80	90
35	80	127	128

The above figures represent fortnightly readings and show the marked fluctuations often found in this disease.

Case V. Male, age 57. Diagnosis; Rheumatoid arthritis

1 hr.	2 hrs.	12 hrs.	24 hrs.
8	30	84	93
20	45	88	98
18	43	86	99
17	38	85	100
5	43	92	102
16	44	84	93
20	45	92	106
22	49	90	107
17	45	97	101

1 hr.	2 hrs.	12 hrs.	24 hrs.
13	35	75	92
15	35	75	77

The case was one in which the knee, ankles, wrists, fingers and shoulder joints were markedly affected. The severity of the condition is not reflected in the degree of sedimentation, which would lead one to expect a mild degree of joint involvement or an inactive stage.

Case VI. Female, age 42. Diagnosis: Rheumatoid arthritis

The figures below were taken before and after manipulation of the joints, and show such a decided acceleration of rate as to make the physical therapy the probable cause of the increase.

	1 hr.	2 hrs.	12 hrs.	24 hrs.
Before manipulation	18	38	79	103
After manipulation	53	89	124	129

Case VII. Male, age 63. Diagnosis: Spondylitis Osteoarthritica.

1 hr.	2 hrs.	12 hrs.	24 hrs.
8	23	70	92

Case VIII. Male, age 48. Diagnosis: Ankylosing Spondylitis

1 hr.	2 hrs.	12 hrs.	24 hrs.
73	110	135	135

Case IX. Female, age 6. Diagnosis: Still's disease.

Knees and ankles affected. The rates given below have a six months' interval between them. The case showed but little improvement at the end of that period.

1 hr.	2 hrs.	12 hrs.	24 hrs.
12	33	79	94
10	35	75	101

Diseases of the Lungs and Respiratory Tract

Pneumonia shows markedly accelerated rates both in the lobar and lobular forms. The increase in sedimentation appears to commence soon after the onset of the disease, as seen in two cases admitted within thirty-six hours of the initial shivering attack. This acceleration increases until it reaches its zenith. This, in uncomplicated lobar pneumonia occurs about the 5th to 6th day; thereafter it begins to fall, reaching normal values in about 3 to 4 weeks after the pyrexia has ceased. In unresolved pneumonic conditions the rate may remain high for several months after the conclusion of the fever. If the sedimentation rate retains its high level after the 10th day in lobar pneumonia, complications must be searched for. In an illustrative case shown below, the sedimentation rate gave a clear indication of the presence of a complication, in this instance, empyema.

Empyema, lung abscess, arthritis, spread of the inflammatory process (pneumonia migrans), are attended with a very high sedimentation rate. Emphysema, in itself, does not influence the rate of sedimentation. In cardiac oedema of the lungs the rate is within normal limits. Pneumokoniosis, if uncomplicated, shows no decrease of the suspension stability of the blood. In bronchitis, variable results are obtained. If the inflammatory process has not penetrated deeply, sedimentation rate is unaltered. An increased rate is usually evidence of penetration of the inflammatory process. The amount of sputum passed bears no relation to the sedimentation rate, and cases of profuse expectoration were seen without increase in sedimentation. In bronchiectasis the sedimentation rate may or may not attain abnormal levels. This also depends on the degree and extent of local inflammation and of a generalised toxaemia.

Dry pleurisy causes a very rapid sedimentation rate, which slowly sinks to normal with resolution of the case.

Acute and chronic rhinitis, pharyngitis and tracheitis as a rule do not influence the sedimentation rate, but severe acute tonsillitis does in some cases cause a definite rise in rate. Chronic tonsillitis does not affect velocity of sedimentation.

Case I. Male, age 48. Diagnosis: Lobar pneumonia. The right base was affected.

Date	1 hr.	2 hrs.	12 hrs.	24 hrs.
11/8/36	118	121	125	126
18/8/36	60	90	110	118
20/8/36	33	70	101	108
27/8/36	14	35	73	85
8/9/36	9	27	54	59
14/9/36	7	15	56	62

The crisis occurred on 16/8/36. From that time there was no pyrexia. The increased sedimentation rate will be noted and its gradual descent to normal values.

Case II. Female, age 64. Diagnosis: Bronchopneumonia.

Date	1 hr.	2 hrs.	12 hrs.	24 hrs.
3/10/36	105	110	120	125
10/10/36	83	94	113	118
17/10/36	95	109	121	123
24/10/36	65	83	100	105
30/10/36	46	65	93	99
4/11/36	32	58	95	97
10/11/36	21	45	82	87
16/11/36	22	38	79	88
25/11/36	10	18	63	70
3/12/36	9	14	52	60

The cases resolved by lysis on 16/10/36.

Case III. Male, age 38. Diagnosis: Lobar pneumonia, followed by empyema

Date	1 hr.	2 hrs.	12 hrs.	24 hrs.
11/12/36	96	113	120	125
14/12/36	110	122	128	130
20/12/36	56	84	124	128
27/12/36	108	128	135	137

The marked fluctuations in rate are evident here. The case had been ill for one week prior to admission on 10/12/36. A needle was inserted into the pleural cavity on 15/12/36 and pus obtained. A rib was resected on 27/12/36, making sedimentation rate of no direct value after that date.

Case IV. Female, age 23. Diagnosis: Diaphragmatic pleurisy.

Date	1 hr.	2 hrs.	12 hrs.	24 hrs.
9/6/36	68	106	116	128
15/6/36	33	61	84	115
28/6/36	8	24	58	61

Case V. Male, age 27. Diagnosis: Spontaneous pneumothorax

Condition occurred when patient was attempting to start a car by winding the handle. No evidence of tuberculosis.

1 hr.	2 hrs.	12 hrs.	24 hrs.
5	14	36	42

The rate remained normal during the whole of the illness.

Case VI. Male, age 63. Diagnosis: Carcinoma of lung.

1 hr.	2 hrs.	12 hrs.	24 hrs.
61	90	126	128

Case VII. Female, age 40. Diagnosis: Bronchiectasis.

Pyrexia and very purulent and offensive sputum were present. The rates are at intervals of one month.

1 hr.	2 hrs.	12 hrs.	24 hrs.
50	92	109	111
16	54	83	95
8	24	69	73

The patient was musch improved at the time of the last reading.

Case VIII. Male, age 48. Diagnosis: Dry Bronchiectasis

1 hr.	2 hrs.	12 hrs.	24 hrs.
0	5	55	90

Case IX. Male, age 19. Diagnosis: Lung abscess.

This condition followed aspiration of pus during an operation on the maxillary antrum. The case ended fatally.

1 hr.	2 hrs.	12 hrs.	24 hrs.
120	134	140	140

Case X. Male, age 55. Diagnosis: Pneumokoniosis

No complications were present. The patient had been employed in unpacking woollen goods over a period of 15 years, in a badly ventilated room.

1 hr.	2 hrs.	12 hrs.	24 hrs.
3	11	46	62

Case XI. Female, age 32. Diagnosis: Acute follicular tonsillitis

1 hr.	2 hrs.	12 hrs.	24 hrs.
20	32	68	79

Case XII. Male, age 56. Diagnosis: Acute laryngitis and pharyngitis

1 hr.	2 hrs.	12 hrs.	24 hrs.
7	21	66	80

Case XIII. Female, age 47. Diagnosis: Acute bronchitis, superimposed on chronic bronchitis.

Date	1 hr.	2 hrs.	12 hrs.	24 hrs.
3/10/36	32	66	111	114
10/10/36	20	35	58	71
18/10/36	8	16	59	62
25/10/36	9	14	44	63

The condition resolved and the rate is seen to follow the improvement in the condition.

Case XIV. Female, age 26. Diagnosis: Acute bronchitis

1 hr.	2 hrs.	12 hrs.	24 hrs.
5	11	35	48

Case XV. Male, age 63. Diagnosis: Chronic bronchitis

1 hr.	2 hrs.	12 hrs.	24 hrs.
33	66	89	95

Case XVI. Female, age 33. Diagnosis: Chronic bronchitis

1 hr.	2 hrs.	12 hrs.	24 hrs.
5	12	45	62

This case, unlike that of the preceding one, had a normal sedimentation rate throughout the illness.

Case XVII. Female, age 53. Diagnosis: Congenital Syphilis of the lung.

Patient had suffered from attacks of haemoptysis for 10 years. Deafness and almost total blindness since the age of 20. Optic fundi: disseminated choroiditis. W.R. ++++. Fibrosis of the right lung base.

1 hr.	2 hrs.	12 hrs.	24 hrs.
32	66	120	129

Pulmonary Tuberculosis

These cases are not common in the medical wards of a general hospital and hence I cannot give extensive details of the value of the sedimentation rate in this disease. The cases which were admitted were soon transferred to a suitable institution.

In 5 cases of pleurisy with effusion, a very rapid velocity was obtained in all.

Case I. Male, age 17. Diagnosis: Right sided pleural effusion.

The treatment adopted was aspiration of the fluid, but although the quantity present decreased, at the end of

three months no subsidence of the sedimentation rate was noted.

1 hr.	2 hrs.	12 hrs.	24 hrs.
42	78	126	131
37	60	112	118
44	99	112	130
62	107	132	133
65	104	132	135

The above rates were taken at intervals of two weeks.

Case II. Male, age 52. Diagnosis: Pleural effusion

1 hr.	2 hrs.	12 hrs.	24 hrs.
75	104	114	116

Case III. Female, age 25. Diagnosis: Pleural effusion.

1 hr.	2 hrs.	12 hrs.	24 hrs.
50	95	120	122

The test has been widely used in the diagnosis and prognosis of tuberculosis. For the former purpose it is undoubtedly useful. In any case of chest disease, in which the clinical findings point to a pathological process which does not as a rule cause any marked degree of alteration of the sedimentation rate, a suspicion of tuberculosis should be aroused and the case thoroughly investigated from that point of view. In three cases quoted below the radiographical and clinical evidence was

against a diagnosis of tuberculosis, but the sedimentation rate was high and after numerous and repeated sputum examinations, tubercle bacilli were discovered.

Westergren (58) found in his investigations that no single value of the sedimentation rate was even approximately normal in active cases of tuberculosis of the lungs. Banyai and Anderson (59) found only 7.35% of patients with active tuberculous lesions in the lung, to possess a normal rate, and consider the test of the greatest value in estimating the activity of the disease and in controlling the amount of physical activity allowed to individual patients. Dr. Cutler (60) (61) uses the test in the management of cases treated by artificial pneumothorax and in the routine examination of cases in a tuberculosis dispensary. Early stages of tuberculosis show alterations of sedimentation rate according to Ringer and Roach (62). In utilising the test in the evaluation of the activity of the lesion, it must be remembered that secondary infections on a tuberculous lung by organisms other than the tubercle bacillus, will cause an accelerated sedimentation rate (63). The test is very valuable in cases of haemoptysis especially in suspected malingering. If the sedimentation rate is high, the indication is that the blood has come from the lung.

Case I. Male, age 55. Diagnosis: Pulmonary tuberculosis.

The original diagnosis was not that of tuberculosis,

but in view of the rapidity of sedimentation the sputum was persistently examined, until on the nineteenth occasion, tubercle bacilli were found.

1 hr.	2 hrs.	12 hrs.	24 hrs.
41	71	115	119

Case II. Female, age 32. Diagnosis: Tuberculosis of the lungs.

1 hr.	2 hrs.	12 hrs.	24 hrs.
50	75	118	121

Case III. Female, age 48. Diagnosis: Inactive tuberculosis and gastric ulcer.

1 hr.	2 hrs.	12 hrs.	24 hrs.
8	20	66	76

Case IV. Female, age 48. Diagnosis: Pulmonary tuberculosis.

1 hr.	2 hrs.	12 hrs.	24 hrs.
40	65	102	110

Diseases of the Heart

The rate in the study of cases of rheumatic carditis has already been dealt with.

Congestive cardiac failure is nearly always accompanied by a slow rate of sedimentation. The greater the degree of congestion, the slower the rate. With the subsidence of cyanosis and oedema the rate inclines to rise but does not reach abnormal figures unless some other disease sets in.

Case I. Male, age 50. Diagnosis: Hyperpietic cardiac failure.

Markedly dyspnoeic, cyanosis and oedema present. Blood pressure 190/130. Urea clearance test normal.

1 hr.	2 hrs.	12 hrs.	24 hrs.
4	10	47	62
9	26	80	92
5	15	57	64
3	6	46	60
4	10	55	70
7	19	60	78
5	14	54	68

These notes represent intervals of one week.

Case II. Male, age 67. Diagnosis: Hyperpietic cardiac failure.

The case presents similar features to the one described above. Blood pressure 190/110. The sedimentation rates at weekly intervals are given.

1 hr.	2 hrs.	12 hrs.	24 hrs.
5	11	58	64
9	34	68	80
18	25	78	88
12	29	77	92
8	20	69	85
8	17	64	80
7	17	64	78
5	12	55	71
4	7	46	64

Case III. Female, age 35. Diagnosis: Cardiac failure. Mitral stenosis and regurgitation.

1 hr.	2 hrs.	12 hrs.	24 hrs.
2	4	21	40
2	5	23	30
0	2	21	40
0	2	30	40
3	6	30	45
8	14	45	53
8	20	45	60
8	19	43	61

In this case a gradual rise can be seen in the latter part of the weekly series and it coincided with disappearance of the oedema and marked improvement of breathlessness.

Infective Endocarditis

This was accompanied by an accelerated sedimentation in the two cases seen. The series is very small but the test may prove of value in differentiating malignant from benign endocarditis, in which latter the rate is normal, during the quiescent stage.

CaseI. Male, age 26. Diagnosis: Malignant Endocarditis.

The patient had a history of rheumatic fever with cardiac damage. He was admitted with a high temperature and during the period of his stay--about three months--the pyrexia persisted. Blood cultures remained negative. Marked endocarditis was present. Clubbing of the fingers

commenced and a few petechiae were seen. No splenomegaly.

1 hr.	2 hrs.	12 hrs.	24 hrs.
34	68	119	128
30	66	100	120
76	110	120	122
70	104	123	123
40	76	123	124
32	64	115	117

The figures shown are divided by intervals of two weeks.

Case II. Male, age 28. Diagnosis: Mitral regurgitation, due to old rheumatic endocarditis.

1 hr.	2 hrs.	12 hrs.	24 hrs.
5	15	68	79

Arterio-sclerosis and Simple Hypertension with Cardiac Hypertrophy

In all such cases the rate was normal.

Case I. Female, age 68. Diagnosis: Marked arterio-sclerosis and high blood pressure.

The urea clearance test was normal. B.P. 210/160.

1 hr.	2 hrs.	12 hrs.	24 hrs.
7	20	105	114

Case II. Male, age 65. Diagnosis: Essential Hyperpiesis.

1 hr.	2 hrs.	12 hrs.	24 hrs.
2	10	45	65

Cardiac asthma, paroxysmal tachycardia, extra-systoles, and auricular fibrillation in themselves have no effect on the rate of sinking.

Case I. Male, age 29. Diagnosis: Paroxysmal tachycardia.

1 hr.	2 hrs.	12 hrs.	24 hrs.
4	10	35	43

Case II. Female, age 35. Diagnosis: Auricular fibrillation. No cardiac failure present.

1 hr.	2 hrs.	12 hrs.	24 hrs.
7	14	33	64

Coronary thrombosis shows an increased velocity of fall of the erythrocytes. Rabinowitz et alia (64) found that the increased rate appeared later in the disease than leucocytosis and fever, and persisted for some time after these had returned to normal. Hirsch (65) in his cases noted an acceleration within a few hours of the onset. Paul Wood (66) found rapid rates in those cases in which the thrombosis was extensive, whereas mild degrees of thrombosis influenced the rate but little. The chief value of the test in the condition of coronary thrombosis lies in its use as an index of the period during which the patient must remain in bed. This period must at least be as long as the sedimentation rate remains abnormal. Two cases are described.

Case I. Male, age 64. Diagnosis: Coronary thrombosis.

Patient was admitted on 3.10.36, two days from the onset of the attack.

Date	1 hr.	2 hrs.	12 hrs.	24 hrs.
3.10.36	43	65	109	116
10.10.36	35	61	96	111
17.10.36	27	45	80	97
24.10.36	20	41	76	89
30.10.36	14	39	71	78
5.11.36	10	30	50	63
12.11.36	7	24	36	59
19.11.36	7	22	33	58
25.11.36	8	21	35	53

Case II. Female, age 70. Diagnosis: Coronary thrombosis.

Admitted on day after the onset of the attack.

Date	1 hr.	2 hrs.	12 hrs.	24 hrs.
13.6.36	26	44	62	83
26.6.36	24	49	61	89
27.6.36	14	36	55	82
3.7.36	16	30	50	79
10.7.36	8	20	42	58
20.7.36	5	14	46	55

Luetic Aortitis. Only two cases were studied and each showed abnormal rates. Danger (67) talks of a diagnostic triad in the diagnosis of the condition. These are:

1. Angina pectoris
2. A negative carotid sinus reflex
3. A rapid sedimentation rate.

A positive Wassermann reaction occurred in two-thirds of his cases. The angina or carotid sinus signs may be absent, but in all his patients the sedimentation rate was increased. Wood (66) found fifteen out of seventeen cases of syphilitic aortitis to have accelerated rates.

Case I. Male, age 63. Diagnosis: Aneurism of the ascending aorta due to syphilitic infection.

1 hr.	2 hrs.	12 hrs.	24 hrs.
45	68	110	120

Case II. Male, age 59. Diagnosis: Aneurism of the ascending aorta.

Wassermann reaction of blood positive.

1 hr.	2 hrs.	12 hrs.	24 hrs.
33	60	96	105

Diseases of the Alimentary System

Several cases of pyorrhea alveolaris were studied to ascertain their influence on the test. Evidence of other disease was absent in them all. In no case was an increased velocity obtained.

In inflammatory processes involving the stomach, little alteration is seen in the suspension stability of

the blood. Thus in three cases of acute gastritis and eleven cases of chronic gastritis, the values were within normal range. Duodenal and gastric ulcers in a series of forty cases gave normal values with the exception of two cases. In the latter, there had just occurred a haematemesis of rather severe degree. That the increased rate was due to the activity of the local process and not to the anaemia is shown by the fact that after a few days' treatment normal figures were obtained, while the blood picture had altered very little. Indeed, many of the cases of the series were accompanied by anaemia, and sedimentation velocity was normal. That activity of the ulcer does not necessarily cause alteration of the rate, is shown by the normal figures seen in cases with gross melaena.

Case I. Male, age 45. Diagnosis: Acute gastritis

The condition resulted from an excess of alcohol taken in undiluted form.

1 hr.	2 hrs.	12 hrs.	24 hrs.
5	10	35	45

Case II. Female, age 48. Diagnosis: Chronic gastritis

1 hr.	2 hrs.	12 hrs.	24 hrs.
2	8	73	83

Case III. Male, age 27. Diagnosis: Gastric ulcer.

1 hr.	2 hrs.	12 hrs.	24 hrs.
3	4	35	49

Case IV. Male, age 35. Diagnosis: Duodenal ulcer

1 hr.	2 hrs.	12 hrs.	24 hrs.
7	12	46	66

While carcinoma of the stomach shows a rapid rate as a rule, Witts (68) published an account of a case with normal sedimentation rate. In five cases seen there was in all of them an accelerated velocity.

Case I. Male, age 69. Diagnosis: Pyloric carcinoma.

1 hr.	2 hrs.	12 hrs.	24 hrs.
50	88	132	140

Case II. Male, age 61. Diagnosis: Carcinoma of stomach

1 hr.	2 hrs.	12 hrs.	24 hrs.
28	62	104	117

Pyloric stenosis with no evidence of malignancy in three cases showed elevated values. It would seem from this, that no great reliance must be placed in the test for the purposes of distinguishing the simple from the malignant type of the disease.

Case I. Female, age 59. Diagnosis: Pyloric stenosis not due to carcinoma.

1 hr.	2 hrs.	12 hrs.	24 hrs.
25	52	105	117

Case II. Male, age 67. Diagnosis: Pyloric stenosis due to cicatricial contraction of pyloric ulcer

1 hr.	2 hrs.	12 hrs.	24 hrs.
15	23	93	106

Case III. Male, age 45. Diagnosis: Pyloric stenosis, resulting from contraction of peptic ulcer.

1 hr.	2 hrs.	12 hrs.	24 hrs.
38	69	120	124

The numerous varieties of dyspepsias met with, due to such causes as faulty mastication, irregular meals, excess of tobacco, etc., do not interfere with sedimentation. Similarly, constipation and simple diarrhoea have no effect.

Three cases of ulcerative colitis seen gave rapid values. One case of chronic dysenteric colitis showed an accelerated rate. In two cases of chronic colitis of unknown aetiology the rate was high.

Case I. Female, age 26. Diagnosis: Ulcerative Colitis.

1 hr.	2 hrs.	12 hrs.	24 hrs.
33	49	82	95

Case II. Female, age 50. Diagnosis: Chronic dysenteric colitis

1 hr.	2 hrs.	12 hrs.	24 hrs.
60	90	136	137

Case III. Male, age 35. Diagnosis: Chronic colitis of unknown aetiology.

1 hr.	2 hrs.	12 hrs.	24 hrs.
21	28	79	92

Case IV. Male, age 13. Diagnosis: Chronic colitis of unknown origin.

1 hr.	2 hrs.	12 hrs.	24 hrs.
22	45	100	110

Case V. Female, age 33. Diagnosis: Visceroptosis

1 hr.	2 hrs.	12 hrs.	24 hrs.
8	18	74	87

Case VI. Female, age 46. Diagnosis: Intestinal adhesions following abdominal operation.

1 hr.	2 hrs.	12 hrs.	24 hrs.
4	8	64	82

Case VII. Female, age 32. Diagnosis: Anorexia nervosa.

1 hr.	2 hrs.	12 hrs.	24 hrs.
4	8	64	82

Six cases of chronic appendicitis all had normal ranges. Carcinoma of the colon is usually accompanied by rapid values, but a case is quoted below with normal figures.

Case I. Female, age 28. Diagnosis: Chronic appendicitis

1 hr.	2 hrs.	12 hrs.	24 hrs.
3	17	32	34

Case II. Female, age 76. Diagnosis: Carcinoma of the ascending colon.

1 hr.	2 hrs.	12 hrs.	24 hrs.
62	67	130	175

Case III. Male, age 63. Diagnosis: Carcinoma of the Colon.

1 hr.	2 hrs.	12 hrs.	24 hrs.
5	9	47	68

This case is worthy of particular attention.

The Liver and Gall Bladder

In diseases of the liver variations in results are obtained and the rate may fluctuate in the same disease. Many believe the liver to be the seat of formation of fibrinogen, while others maintain that the liver is merely a storage place for that substance. If sodium glycocholate be added to citrated blood the rate of sedimentation is retarded. This takes place in bloods with normal and abnormal values. The blood of patients suffering from severe icterus contains an excess of bile salts which, as has been shown in vitro, will slow the rate of sedimentation. In the milder type of jaundice the bile salt effect is often absent. Rourke and Plass (9) experimenting on animals, explained the retardation caused by toxic jaundice, by diminution of the circulating fibrinogen. Walton (29) explains the variations in cases of jaundice in terms of retention of bile salts. In the first phase, he says, bile salts are not sufficiently increased to effect a retardation of the sedimentation of the sedimentation rate, whereas this occurs in the second phase, so sedimentation rate is slowed. In the third phase the reactionary powers

of the body are sufficient to counteract the bile salts and the rate will be influenced by the pathological process. Rosenthal and Blowstein (69) state that bilirubin does not affect the sedimentation rate, bile salts and cholesterol inhibit the rate, while lecithin, fibrinogen and globulin increase it. They consider increase in blood cholesterol to be an important factor; but conclude that the value of the reaction is doubtful in cases of jaundice.

Obstructive jaundice usually gives rapid rates. Cholelithiases showed varying results and seemed to depend on the presence or absence of local inflammatory activity. Malignant liver disease and cholangitis gave rapid rates in two cases.

Case I. Male, age 17. Diagnosis: Catarrhal Jaundice.

1 hr.	2 hrs.	12 hrs.	24 hrs.
3	14	52	65

Case II. Male, age 55. Diagnosis: Multilobular cirrhosis of the liver.

Cause not ascertained. Patient was a non-alcoholic. Post-mortem did not reveal the aetiology.

1 hr.	2 hrs.	12 hrs.	24 hrs.
22	41	91	100

Case III. Male, age 69. Diagnosis: Primary carcinoma of the liver.

The case died two weeks after admission.

1 hr.	2 hrs.	12 hrs.	24 hrs.
35	63	110	115

Case IV. Female, age 65. Diagnosis: Obstructive jaundice due to calculus.

1 hr.	2 hrs.	12 hrs.	24 hrs.
45	85	125	127

Case V. Male, age 69. Diagnosis: Solitary gallstone.

No symptoms were present.

1 hr.	2 hrs.	12 hrs.	24 hrs.
3	8	44	62

Case VI. Female, age 71. Diagnosis: Gall-stones and cholecystitis

Date	1 hr.	2 hrs.	12 hrs.	24 hrs.
3.7.36	22	55	138	144
10.7.36	23	58	135	140
17.7.36	28	59	116	126
24.7.36	55	102	129	132
30.7.36	45	85	125	127
8.8.36	40	72	123	127
18.8.36	35	70	127	130

The onset of an attack of biliary colic coincided with the reading of 24.7.36. The patient was operated upon on 20.8.36.

Allergic Diseases

Asthma, migraine, hay fever and urticaria are reviewed here. The allergic basis of them all is by no means universally accepted.

Twenty cases of asthma studied gave normal rates in seventeen instances. The rate depends on the accompanying bronchitis, which, if of sufficient severity, will accelerate the velocity. As the bronchitic element subsides, the rate falls to normal. The severity of the asthma was of all degrees. Neither the injection of adrenalin nor the actual attack itself had any effect on the rate of sedimentation.

Case I. Female, age 36. Diagnosis: Bronchial asthma.

1 hr.	2 hrs.	12 hrs.	24 hrs.
8	22	80	92

Case II. Male, age 18. Diagnosis: Bronchial asthma.

1 hr.	2 hrs.	12 hrs.	24 hrs.
4	16	64	72

Case III. Female, age 68. Diagnosis: Bronchial asthma and severe bronchitis.

1 hr.	2 hrs.	12 hrs.	24 hrs.
48	75	134	136
38	75	120	124
36	61	126	130
39	60	115	118

1 hr.	2 hrs.	12 hrs.	24 hrs.
34	62	110	118
28	58	120	122
37	70	129	135
40	75	120	124
14	39	93	107
9	31	79	92
7	18	78	87
6	13	53	69

The above were taken at weekly intervals and show the decrease in rate of sedimentation with improvement of the bronchitic element.

Westcott (70) found normal values in asthma, hay fever and allergic non-seasonal coryza. Schullof (71) concluded that a pathologically slow sedimentation rate is almost constantly found in allergic conditions and that a rapid or even normal sedimentation rate is indicative of a more or less severe complication. Gelfand and Victor (72) found that in hay fever, between and during the hay season, and in the presence or absence of symptoms, the suspension stability of the blood was normal. Injections of pollen extracts produced no alterations of the rate.

In all my cases of migraine, urticaria, and hay fever, the sedimentation rate was normal. It seems improbable that a normal rate is pathological as Schullof suggests.

Case I. Female, age 35. Diagnosis: Urticaria.

1 hr.	2 hrs.	12 hrs.	24 hrs.
1	4	41	57

Case II. Female, age 48. Diagnosis: Migraine.

1 hr.	2 hrs.	12 hrs.	24 hrs.
3	5	20	38

Case III. Female, age 25. Diagnosis: Angio-neurotic oedema.

1 hr.	2 hrs.	12 hrs.	24 hrs.
2	10	38	48

Case IV. Male, age 36. Diagnosis: Hay fever.

1 hr.	2 hrs.	12 hrs.	24 hrs.
3	14	38	53

Diseases of the Urinary System

Acute generalised glomerular nephritis is always accompanied by a high velocity of sedimentation. If the nephritis resolve, the curve of sedimentation gradually drops and may be used in assessing prognosis. On the other hand, if urea retention occurs the rate rises and rapid values are obtained in uraemia. In the subacute type of the disease, which is interrupted by relapses, the rate varies, being accelerated during the exacerbations. Focal nephritis may or may not be associated with a diminution of the suspension stability of the blood, according to the

extent of renal involvement. Chronic interstitial nephritis will influence the sedimentation rate as a rule only if nitrogen retention is present, the latter giving high figures. In nephrosis the rates are usually high.

Case I. Female, age 14. Diagnosis: Focal nephritis.

1 hr.	2 hrs.	12 hrs.	24 hrs.
8	16	63	89

Case II. Male, age 25. Diagnosis: Acute generalised glomerular nephritis

1 hr.	2 hrs.	12 hrs.	24 hrs.
87	108	135	138
76	100	128	130
40	74	122	124
17	38	93	108
9	30	80	92
6	12	72	75

The values are spaced by intervals of two weeks. The case shows the fall of the rate with resolution of the case.

Case III. Male, age 38. Diagnosis: Chronic interstitial nephritis.

The urea clearance test was 30% of the normal value.

1 hr.	2 hrs.	12 hrs.	24 hrs.
30	64	110	121

Case IV. Female, age 42. Diagnosis: Chronic uraemia.

Blood urea: 123 mgms. per 100 cc.

1 hr.	2 hrs.	12 hrs.	24 hrs.
29	66	108	113

Case V. Male, age 20. Diagnosis: Orthostatic Albuminuria.

1 hr.	2 hrs.	12 hrs.	24 hrs.
2	14	48	60

Case VI. Male, age 36. Diagnosis: Chronic uraemia.

Urea clearance test 25% of normal. Blood urea 153 mgms. per 100 cc.

Date	1 hr.	2 hrs.	12 hrs.	24 hrs.
2.10.36	25	40	135	146
8.10.36	11	30	136	146

The patient died very suddenly.

Renal tuberculosis is accompanied by high levels only when the process has attained a certain degree.

Case I. Female, age 23. Diagnosis: Renal Tuberculosis

The diagnosis was made by injecting the urine into a guinea-pig.

1 hr.	2 hrs.	12 hrs.	24 hrs.
10	20	65	85

Case II. Male, age 36. Diagnosis: Renal Tuberculosis.

1 hr.	2 hrs.	12 hrs.	24 hrs.
44	63	110	115

Acute pyelitis and cystitis cause an increase in sedimentation velocity. This is irrespective of the presence of pyrexia. As the process decreases in intensity the rate decreases and becomes normal with resolution. However, chronic bacilluria, which may persist as a sequela of an acute attack, may show a normal rate; and in chronic pyelitis and cystitis the rate is frequently normal. If an exacerbation occur in a chronic case, the sedimentation value becomes elevated.

Case I. Female, age 35. Diagnosis: Acute Pyelitis

The downward trend of sedimentation occurred as the case gradually improved. The intervals are of one week.

1 hr.	2 hrs.	12 hrs.	24 hrs.
89	100	130	133
78	96	128	128
56	73	130	132
44	65	86	93
42	54	69	72
31	52	63	82
25	45	59	83
16	30	55	79
10	23	62	65
8	21	53	57

Case II. Female, age 75. Diagnosis: Chronic bacilluria due to B. coli.

1 hr.	2 hrs.	12 hrs.	24 hrs.
5	45	88	94

Note the pathological second hour reading.

Case III. Male, age 58. Diagnosis: Chronic bacilluria due to B. coli.

1 hr.	2 hrs.	12 hrs.	24 hrs.
3	14	63	84

Renal calculus is unaccompanied by rapid rates, unless inflammatory changes are proceeding around the stone. Prostatic hypertrophy per se does not influence sedimentation, but if infection be superadded the rate becomes high.

Case I. Male, age 34. Diagnosis: Renal calculus.

1 hr.	2 hrs.	12 hrs.	24 hrs.
3	6	23	24

Case II. Male, age 56. Diagnosis: Renal calculus and pyonephritis.

1 hr.	2 hrs.	12 hrs.	24 hrs.
96	110	136	136

Diseases of the Blood

The influence of anaemia secondary to existing disease has already been discussed.

Pernicious Anaemia. In untreated cases the sedimentation rate is high, but with treatment, rapidly reaches low figures and this usually occurs before the blood picture is normal.

Case I. Female, age 46. Diagnosis: Pernicious Anaemia.

Date	1 hr.	2 hrs.	12 hrs.	24 hrs.
5.8.36	18	39	102	123
16.8.36	9	25	84	93

Date	Red Cell Count	Haemoglobin
5.8.36	2,950,000	65%
16.8.36	3,490,000	68%

Case II. Male, age 43. Diagnosis: Pernicious anaemia

Date	1 hr.	2 hrs.	12 hrs.	24 hrs.
3.10.36	21	45	103	110
5.11.36	7	18	53	65

Date	Red Cell Count	Haemoglobin
3.10.36	3,100,000	69%
5.11.36	3,950,000	75%

The hypochromic anaemias did not appear to affect the rate of sedimentation.

Case III. Female, age 55. Diagnosis: Hypochromic anaemia

Red cell count: 4,500,000 per cu. mm.

Haemoglobin: 32%

1 hr.	2 hrs.	12 hrs.	24 hrs.
9	25	93	109

The anaemia due to prolonged, slight losses of blood caused no upset in the rate. However, if bleeding occurs in a situation from which the blood is absorbed parenterally, rapid values may be registered, e.g. a large haematoma from injury, purpuric bleedings into joints. No case of polycythaemia was seen. In two cases of leukaemia the rate was very high. Two cases of Hodgkin's disease were seen and an abnormal level of sedimentation was present in each.

Case IV. Female, age 40. Diagnosis: Myeloid Leukaemia.

1 hr.	2 hrs.	12 hrs.	24 hrs.
38	63	110	112

Case V. Female, age 34. Diagnosis: Lymphadenoma

1 hr.	2 hrs.	12 hrs.	24 hrs.
45	80	121	128

Diseases of the Thyroid Gland

Simple adenomata and non-toxic goitre present normal ranges. Similarly myxoedema had no effect on the sedimentation rate in 3 cases.

Case I. Female, age 55. Diagnosis: Simple adenoma of the thyroid gland

1 hr.	2 hrs.	12 hrs.	24 hrs.
6	14	55	70

Case II. Female, age 76. Diagnosis: Myxoedema

1 hr.	2 hrs.	12 hrs.	24 hrs.
5	12	49	63

In thyrotoxicosis, three cases showed variable results. One case was operated on and following operation the increased rate showed signs of returning to normal levels with improvement. Mora and Gualt (73) found rapid values in all their 30 cases. J.L. de Courcey (74) also found many cases of toxic goitre with increased sedimentation rate.

Case I. Female, age 27. Diagnosis: Hyperthyroidism

Date	1 hr.	2 hrs.	12 hrs.	24 hrs.
22.9.36	56	98	140	143
29.9.36	30	57	125	130
Operation performed on 30.9.36.				
21.11.36	21	50	120	128
28.11.36	18	39	100	110

Case II. Female, age 40. Diagnosis: Exophthalmic goitre.

1 hr.	2 hrs.	12 hrs.	24 hrs.
16	38	127	130

Case III. Female, age 18. Diagnosis: Exophthalmic goitre.

The exophthalmos and goitre were very pronounced. Tremor and tachycardia also were marked. The basal metabolic rate was 55% above normal. The sedimentation rate repeated several times remained within normal range.

1 hr.	2 hrs.	12 hrs.	24 hrs.
10	20	78	82

Diabetes Mellitus

No abnormal values were obtained in any uncomplicated case and diabetes per se does not appear to influence the rate. The level of the blood sugar bore no relationship to the suspension stability of the blood, and injections of insulin did not affect it. Kramer (75) noted a large number of abnormal rates in his cases of diabetes, but many minor infections accompanied the disease. In one of my cases an abnormal value was found to be due to an infection of the urinary tract. Neuritis in three cases did not accelerate sedimentation. The same applied to four cases of cataract. No case in which gangrene was present as a complication was investigated.

Case I. Female, age 62. Diagnosis: Diabetes mellitus

1 hr.	2 hrs.	12 hrs.	24 hrs.
7	25	84	100

Case II. Female, age 48. Diagnosis: Diabetes mellitus and neuritis.

1 hr.	2 hrs.	12 hrs.	24 hrs.
5	15	73	89

Case III. Female, age 53. Diagnosis: Diabetes mellitus with a B. coli infection of the urine.

1 hr.	2 hrs.	12 hrs.	24 hrs.
25	45	80	84

The rate gradually returned to normal values with mandelic acid treatment.

Malignant Tumours

The value of the sedimentation rate in this condition is not as great as one could wish it to be. Normal rates may be obtained in the presence of neoplasms, the rate being affected more by the accompanying infection or ulceration (76).

Adams-Ray (77) found no less than 25% of cases with metastases in other organs, in which the first hour reading was below 15. Schmitz and Schmitz (78) find the test of little value in differentiating benign from malignant pelvic tumours. I have already quoted a case of carcinoma

of the colon, which was in an advanced state, and in which the sedimentation rate was normal. It must therefore be emphatically stressed that a normal velocity does not exclude carcinoma.

Diseases of the Nervous System

The series is so small that no definite inferences can be taken from it. The cases investigated are described here. All cases of neurosis and neurasthenia were normal.

Case I. Male, age 36. Diagnosis: Disseminated sclerosis.

1 hr.	2 hrs.	12 hrs.	24 hrs.
8	28	60	76

Case II. Male, age 52. Diagnosis: Disseminated sclerosis

1 hr.	2 hrs.	12 hrs.	24 hrs.
30	64	110	111

Case III. Female, age 11. Diagnosis: Cerebral tumour

1 hr.	2 hrs.	12 hrs.	24 hrs.
6	20	71	85

Case IV. Female, age 40. Diagnosis: Post-encephalitic Parkinsonian syndrome.

1 hr.	2 hrs.	12 hrs.	24 hrs.
5	19	68	80

Case V. Female, age 36. Diagnosis: Subacute combined degeneration of the spinal cord.

1 hr.	2 hrs.	12 hrs.	24 hrs.
11	22	87	100
22	44	99	108
5	20	95	114
13	27	96	105
18	40	99	112

The red cell count was above four million per cu. mm. in all these weekly readings. The variation in rate is very pronounced.

Case VI. Male, age 58. Diagnosis: Motor aphasia, due to arterial spasm.

1 hr.	2 hrs.	12 hrs.	24 hrs.
10	29	79	88

Case VII. Male, age 35. Diagnosis: Cerebral abscess. Patient died.

1 hr.	2 hrs.	12 hrs.	24 hrs.
22	43	100	108

Case VIII. Female, age 42. Diagnosis: Polyneuritis of unknown origin.

1 hr.	2 hrs.	12 hrs.	24 hrs.
18	42	102	113

Case IX. Male, age 65. Diagnosis: General paralysis of the insane.

1 hr.	2 hrs.	12 hrs.	24 hrs.
50	74	108	116

Case X. Female, age 62. Diagnosis: Meningo-vascular syphilis

1 hr.	2 hrs.	12 hrs.	24 hrs.
11	35	84	104
18	33	82	96
10	32	85	102
12	32	81	90
15	42	84	100

Case XI. Male, age 46. Diagnosis: General paralysis of the insane.

The case was treated by injection of 10 cc. of malarial blood.

Date	1 hr.	2 hrs.	12 hrs.	24 hrs.
10.10.36	10	32	83	92
1.11.36	Malarial blood was injected. Twelve rigors were allowed before control with quinine.			
8.11.36	89	96	116	116
11.11.36	92	105	116	121
17.11.36	120	126	130	136
20.11.36	60	105	130	138
23.11.36	65	108	130	135
27.11.36	84	93	116	120
2.12.36	80	93	110	103

Cases XII, XIII, and XIV. Diagnosis: Idiopathic Epilepsy

Sex	Age	1 hr.	2 hrs.	12 hrs.	24 hrs.
Male	23	3	16	55	63
Female	44	5	18	89	94
Male	52	4	19	60	62

Miscellaneous

Uncomplicated influenza in six cases gave normal values. Cellulitis and abscesses if of sufficient extent give very rapid rates which descend with resolution of the condition. Chronic leucorrhoea has no effect on the sedimentation rate.

Syphilitis lesions will affect the rate if in an active stage (41). Phlebitis accelerates sedimentation of the erythrocytes.

C O N C L U S I O N S

The Sedimentation Rate of the erythrocytes is not a substitute for any existing test or any clinical method. It does not take the place of any diagnostic or prognostic procedure already in use, but is complementary to them all. The reaction is one which can be used in all types of disease. Its application in general medicine is twofold: in individual disease, and as a general guide to the presence of pathological changes in the body. The former has been dealt with already and indications of its utility in prognosis and diagnosis have been given. The general application of the test to disease is of the utmost importance and herein, perhaps, it serves its greatest use. Rapid sedimentation means disease (except in pregnancy), and if physical examination has proved negative, the increased rate demands a more detailed investigation, with perhaps x-ray, Wassermann reaction, blood urea, etc. Often one is confronted with the problem of how much reliance one can place on the patient's story, and if physical findings are absent the problem becomes more acute. Is the patient suffering from organic disease or are the symptoms functional? This question can by no means always be answered by the sedimentation rate. A rapid sedimentation rate is definite proof of organic disease; a normal sedimentation rate may occur both in organic disease and in the healthy. Hence, if the sedimentation rate be rapid,

the patient cannot be labelled neurotic. Unremitting care must be taken to ascertain the cause of acceleration of velocity, and this must be explained in terms of pathological changes.

The test will have fulfilled its value if it will have served as a warning and as a lead in diagnosis to the physician of the presence of noteworthy disease, the latter being often well established before it becomes manifest clinically.

The test is absolutely non-specific. Leucocytosis and pyrexia are in the same category, yet no one will deny their value. Tissue destruction, if of sufficient extent and degree will occasion a decreased suspension stability of the blood. In acute inflammatory outbreaks some time elapses from the onset of the disease, before altered sedimentation rate makes its appearance. This limits the use of the test, e.g. in acute appendicitis. In acute medical diseases, characterised by a more or less specific cause, e.g. pneumonia, the value of the test is greatest. The course of the disease can be followed in a more accurate manner than by any other existing method. The sedimentation rate serves as a delicate index fluctuating with the pathological changes present.

In chronic disease, the variations met with lead one to cast doubt on its absolute prognostic value, e.g. rheumatoid arthritis.

The test is simple and requires no elaborate apparatus or training. The interpretation is easy and the test can be carried out under any available conditions. The applicability of the reaction to disease of all natures has already been referred to.

To sum up, the test may be used in diagnosis and prognosis. In the latter case, one has to consider the value of the phenomenon in the individual disease. It does not give the diagnosis of a specific disease, but will give indication of morbid processes and will be of help in differential diagnosis.

No patient must be diagnosed as neurasthenic in the presence of abnormal sedimentation rate. Normal sedimentation does not exclude disease and in addition the test is not infallible, a low rate being obtained in a small percentage of cases in which advanced destruction of tissues exists. The rate serves as an index of that activity. In conjunction with temperature, pulse rate, history, physical findings and clinical judgment, the test will often throw light on a complicated case and give the physician increased confidence in handling the disease.

The test will give reliable results only to those who have given the reaction thoughtful study.

Bibliography

1. Robin Fahraeus, Physiological Reviews, 1929, IX, p. 241

2. H.C.Gram, Archives of Internal Medicine, 1921, XXVIII, p. 312

3. H.F.Hunt, The Journal of Laboratory and Clinical Medicine, 1929, XIV, p. 1061

4. K.G.Ploman, Annales d'Oculistique, 1920, clvii, p. 569

5. Joseph Race, Reports on Chronic Rheumatic Diseases, Number 1, p. 55, Lewis, London, 1935.

6. Eric Ponder, Quarterly Journal of Experimental Physiology, 1926, XVI, p. 173

7. I. Snapper, Proceedings of the Royal Society of Medicine, 1931, XXIV, p. 1371

8. D.R.Gilligan and A.C.Ernstene, American Journal of Medical Sciences, 1934, clxxxvii, p. 552

9. M.D.Rourke and E.D.Plass, American Journal of Physiology, 1928, lxxxiv, p. 42

10. T.H.Cherry, The Journal of Laboratory and Clinical Medicine, 1934, p. 257, XX

11. E.M.Greisheimer, C.V.Winkle and O.H.Johnson, American Review of Tuberculosis, 1929, XIX, p. 559

12. H.B.Newham and P.H.Martin, Quarterly Journal of Medicine, 1929, XXII, p. 145

13. G.R.P.Aldred-Brown and J.M.H.Munro, The Lancet, 1934, I, p. 1333

14. R. Lundgren, Acta Medica Scandinavica, 1927, lxvii, p. 63

15. Eric Ponder, Quarterly Journal of Experimental Physiology, 1925, XV, p. 236

16. C.E.Reyner, The Journal of Laboratory and Clinical Medicine, 1928-9, XIV, p. 630

17. W.W.Payne, The Lancet, 1932, I, p. 74

18. Hoeber, quoted by T.R.Waugh, Canadian Medical Association Journal, 1923, XIII, p. 604

19. D.O.Meaker, The Clifton Medical Bulletin, 1925, XI, p. 72

20. H.P.Macheal, The Journal of Laboratory and Clinical Medicine, 1934, XIX, p. 1010

21. L.D.VanAntwerp, American Review of Tuberculosis, 1934, XXIX, p. 214

22. J.W.Cutler, American Journal of the Medical Sciences, 1932, clxxxiii, p. 643

23. M.D.Rourke and E.D.Plass, Journal of Clinical Investigation, 1929, VII, p. 365

24. M.M.Wintrobe and J.H.Landsberg, American Journal of the Medical Sciences, 1935, clxxxix, p.102

25. E.D.Plass and M.D.Rourke, Journal of Laboratory and Clinical Medicine, 1927, XII, p. 735

26. M.D.Rourke and E.D.Plass, Journal of Laboratory and Clinical Investigation, 1929, VII, p. 365

27. V.G.Heller and H. Paul, Journal of Laboratory and Clinical Medicine, 1934, XIX, p. 777

28. M.M.Wintrobe and J.W.Landsberg, American Journal of the Medical Sciences, 1935, clxxxix, p. 102

29. A.C.Rees-Walton, Quarterly Journal of Medicine, 1933, II, p. 79

30. A.Westergren, American Review of Tuberculosis, 1926, XIV, p. 94

31. J. Cutler, American Review of Tuberculosis, 1929, XIX, p. 544

32. E.M.Greisheimer and A.E.Treloar,
American Journal of the Medical Sciences, 1934, clxxxvii, p. 213

33. F. Boerner and A.F.Flippin,
Journal of Laboratory and Clinical Medicine, 1935, lxxxix, p. 583

34. M.B.Gordon and D.J.Cohn,
American Journal of the Medical Sciences, 1928, clxxvi, p. 211

35. W.W.Payne, The Lancet, 1932, I, p. 74

36. J.Cutler, American Journal of the Medical Sciences, 1927, clxxiii, p. 687

37. G.E.Beaumont and J.W.Maycock, The Lancet, 1935, II, p. 19

38. C.J.McSweeney, The Lancet, 1934, II, p. 756

39. E.M.Greisheimer, et alia,
American Journal of Diseases of Children, 1928, xxxvii, p. 953

40. S.L.Ellenberg, Journal of Laboratory and Clinical Medicine, 1934, XIX, p. 944

41. H.J.Schattenberg, Archives of Internal Medicine, 1932, 1, p. 569

42. E.T.Hoverson and W.F.Peterson
American Journal of the Medical Sciences, 1930, clxxxviii, p. 455

43. E.T.Hoverson, Transactions of the Chicago Pathological Society, 1934, XIV, p. 185

44. E.M.Greisheimer, American Journal of the Medical Sciences, 1927, clxxiv, p. 338

45. E.A.Pohle, Radiology, 1925, V, p. 206

46. Huei-lang Chung, Journal of Laboratory and Clinical Medicine, 1935, XX, p. 633

47. C.W.Warren, The Clifton Medical Bulletin, 1925, XII, p. 102

48. I.Y.Zecker and Goodell,
American Journal of the Medical Sciences, 1925, clxix, p. 209

49. H. Lebel and M.C.Lottrup,
Acta Medica Scandinavica, 1933, lxxx, p. 550

50. A.C.Ernstene, American Journal of the Medical Sciences, 1930, clxxx, p. 12

51. R.R.Struthers and H.L.Bacal,
Canadian Medical Association Journal, 1933, XXIX, p. 470

52. B.Schlesinger, Quarterly Journal of Medicine, 1932, I, p. 67

53. C. Bruce Perry, Archives of Diseases of Children, 1934, IX, p. 285

54. W.W.Payne and B.Schlesinger,
Archives of Diseases of Children, 1935, X, p. 403

55. Gunnar Kahlmeter, Rheumatic Diseases (The Bath Conference) 1928

56. M.H.Dawson, R.H.P.Sica, R.H.Boots,
The Journal of Laboratory and Clinical Medicine, 1930, XV, p. 1065

57. H.C.Gram, Acta Medica Scandinavica, 1929, lxx p. 241

58. Alf Westergren, Acta Medica Scandinavica, 1921, liv p. 246

59. A.L.Banyai and S.V.Anderson,
Archives of Internal Medicine, 1930, xxxxvi, p. 787

60. J.Cutler, American Review of Tuberculosis, 1932, XXVI, p. 134

61. J.Cutler and L.Cohen,
American Review of Tuberculosis, 1930, XXI, p. 347

62. P.H.Ringer and M.Roach,
Annals of Internal Medicine, 1934, VIII, p. 258

63. W.J.Stainsby, Medical Clinics of North America, November, 1934, p. 911

64. M.A.Rabinowitz, C.Shookoff, A.H.Douglas, American Heart Journal, 1931, VII, p. 52

65. J.E.Hirsch, Annals of Internal Medicine, 1936, X, p. 495

66. Paul Wood Quarterly Journal of Medicine, 1936, I, p. 1

67. C.S.Danzer, Archives of Internal Medicine, 1931, V, p. 29

68. L.J.Witts, The Lancet, I, 1935, p. 1329

69. N.Rosenthal and M.I.Blowstein, Journal of Laboratory and Clinical Medicine, 1929, XIV, p. 467

70. F.A.Westcott and W.C.Spain, Journal of Allergy, 1932-3, IV, p.370

71. K. Schullof, Journal of the American Medical Association, 1933, c, p. 318

72. H.H.Gelfand and G.Victor Journal of Allergy, 1934, V, p. 583

73. J.M.Mora and J.I.Gault, Journal of Laboratory and Clinical Medicine, 1929-30, XV, p. 590

74. J.L.deCourcey, American Journal of Surgery, 1925, XXXIX, p. 129

75. D.W.Kramer, Journal of Laboratory and Clinical Medicine, 1935, XXI, p. 37

76. D.M.Vickers and R.Duryle, Journal of Laboratory and Clinical Medicine, 1932, p. 260

77. J.Adams-Ray, Acta Chirugica Scandinavica, 1930-31, lxvi, p. 263

78. H.Schmitz and H.Schmitz, American Journal of Obstetrics and Gynecology, 1926, II, p. 353