Treatment of Rheumatoid Arthritis.

With special reference to the Endocrine Aspect.

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Introduction

This Thesis endeavours to set out some original work on a series of cases of Rheumatoid Arthritis. The patients mostly were those seen at the Charterhouse Rheumatic Clinic, and the biochemical work has all been done in the Laboratory there by permission of the Executive Council of the Clinic. The Clinic has no bed accommodation so the work is mostly on out-patients. One case was also treated in hospital by the author, but the laboratory work was in the same hands.

There is nothing spectacular nor dramatic in the gradual return of the patients to mobility and to the happiness of taking their proper place in the home again. Standardisation of recovery is difficult in these cases, and the standard used has been the simple one of the return of the patient to full or partial ability to run her home as a housewife.

There is no question that the quick and dramatic results are obtained by the use of the newer hormones, but they are in small supply and difficult to obtain. When the author conceived the idea of using adrenalin, Cortisone had not yet appeared; at least, not to the author's knowledge. The only merit that can be claimed is that the work is entirely original.

The work on the endocrines seems in its infancy,

and from tabulated cases prepared for this thesis, there are emerging more factors, which may have significance, but this thesis must be finished. From one table drawn up, there has emerged the fact that that there is a difference in the latent period, that is the period between stress and onset, in multipara, and nullipara. This fact has just been noticed and the full significance has not been worked out, so the point is not raised in this thesis, beyond this brief mention.

Rheumatoid arthritis is not a disease in which it is possible to say that there is one definite cause, and that, given the cause, the disease process will automatically take place. It is rather the result of many failures in a hard struggle by the body against forces too great to be withstood any longer. These forces begin in heredity. Another factor in shortening the latent period between stress and onset was the War with the necessity of sleeping in cold and damp cellars. That climate affects this disease was known to the ancients. There is so much yet to learn, knowledge which can only be obtained by careful history-taking as well as by all the very modern methods, that the author is truly appalled to have chosen such a subject.

TREATMENT OF RHEUMATOID ARTHRITIS WITH SPECIAL REFERENCE TO THE ENDOCRINE ASPECT.

The Historical Survey.

With the onset of zonal belts of cold and damp climates we find the earliest evidence of arthritis. When the Earth was uniformly warm, great monsters roamed the Gobi Desert and swam in the seas. There are the fossilised remains of these monsters, with the deformities, to be seen; the University of Kansas has the remains of one in the shape of a great land lizard of thirty-nine tons This creature apparently held himself upright at times, on his tail; this inflicted a certain amount of trauma on account of the great weight and he shows the characteristic deformities of an ankylosed spine, now called Marie-Strumpel disease. From the sea, also, there are the fossilised remains of giant swimming monsters of the Dinosaur Period, which show the lipping of the inter-phalangeal joints which happened as the seas grew colder. To similar deformities in men at a very much later date, Dr. Heberden gave his name (Bach, 1947).

Dr. Rudolph Virchow (1871) gives a detailed history of the cave-bear, or Ursus Spealaeus, in Europe during the Pleistocene Period. Dr. Bach states that monsters he described were alive 110,000,000 years ago, but

Dr. Virchow merely refers to the time when the bears were robust healthy animals 500,000 B.C. By 30,000 B.C. the climate had definitely become much more cool and damp, and the bears were now subject to wasting bone diseases; these, such as rickets and arthritis, and what Dr. Virchow calls Holhengicht (Virchow, 1895) or cav -gout, ultimately killed these animals. There is a picture drawn by Dr. Virchow of cave-man with twisted joints, limping after his prey.

Pemberton and Osgood (1934) aver that from the earliest times climatic conditions have played a great part in the determination of the occurrence of chronic arthritis and that occupation plays the greater part in determining the presence of hypertrophic arthritis. In 400 B.C. the Master of Medicine, Hippocrates, emphasises this and advises his patients that a warm, equable climate is best for them. Later on Galen (1821) stressed this point in the treatment of these cases.

Before Hippocrates there were the priest-physicians of the Egyptians; thus there are the hieroglyphics of the court-physician to the Assyrian Monarch, Assurbanipal (668-628 B.C.) (Osgood, 1940). A new element begins with him; he believed that there was an associated focus of infection and he advises the Monarch that the cause of the pains in his head, sides and feet was to be found in his teeth. His advice was extraction of the teeth. The

tablet with these hieroglyphics is in the British Museum, and was found by Professor Layard in a mound near Ninewah in 1849. The examination of Egyptian mummies shows a high incidence of dental caries and bony ankylosis, the end stage of rheumatoid arthritis. So much so, that rheumatoid arthritis was considered the disease par excellence of the ancient Egyptians. Roy L. Moodie in his Paleopathology (1923) discusses the findings of others, Sir Marc A. Ruffer (1931), G. Elliot Smith and Wood Jones, as well as his own. They all confirm this view, and Pemberton and Osgood, in their book to which reference has already been made, add the fact that these Egyptians lived in the Nile Valley and frequently chilled their bodies in the waters of the Nile while bathing.

In spite of their knowledge, these priest-physicians sent their patients to the healing baths associated with the various gods and goddesses, so that the patient from the earliest times associated medicine with religion. That was, it would seem, the foundation of psychiatry. And it is curious that some patients will still go far afield to find some particular physician "who does them good". And there is undoubtedly a great deal in this, as Professor Stockman used to emphasise in his lectures, which I was fortunate enough to attend.

Hippocrates lifted medicine from what was practically the realms of witch-doctoring to our modern conception of the Ars Medica. In his Aphorisms (1849) he lays down that exact bedside examination is necessary, and on that and the experience and skill of the physician depend the well-being of the patient. There are various translations of these Aphorisms, perhaps the most useful is the Oeuvres Complètes (translated by E. Littre, Paris, and published about 1849). Hippocrates describes a typical case of acute arthritis, and calls it by that name. He notes that the disease is not fatal, the pains fleet from joint to joint, that there is an associated fever; in fact, his arthritis resembles acute rheumatism, particularly when he finds that is is apt to attack the young rather than the old. The other disease he describes in this connection he calls podagra. From the description he gives of the acute pain attacking the great toe, this corresponds to our gout. In any case his treatment was to hold for many centuries, as well as his teachings. And in fact it holds good today, rest and applied heat, local or general heat such as in baths, will help most cases.

From the time of Hippocrates until Guillaume de Baillou, writing under the latinised name of Ballonius (1642) published his Opera Omnia in the Sixteenth Century,

there was little advance in the knowledge of arthritis. Certainly there were some thinkers and writers, but they did not make great advances. One of them was Aretaeus in the First Century; he did try to effect what has hardly been achieved today, an exact nomenclature on the subject. Thus he names pain in the feet, podagra, in the hands, cheiragra; and in the hips, sciatica. Furthermore, his description of one syndrome is the first real approach that there is to rheumatoid arthritis, if we exclude the Hieroglyphics of the Egyptians. Aretaeus gives a good description of the disease, noting that the joint affection may wander through the body or remain fixed till death. "It passes through the muscles of the back and thorax, the vertebrae of the neck and back are painful, and the pain adheres to the top of the os sacrum." It is in these last two sentences that there is shown a more exact conception of rheumatoid arthritis.

From the time of Hippocrates the humoral theory of disease was the dominant theory. Galen (1821), slightly later, adhered to this hypothesis. Thus as their teachers taught them, so did the physicians, until the Seventeenth Century, believe and practise. The humor apparently might come from within to the surface of the body as a catarrh, for example the nasal secretion, or it might

go from the brain to some internal organ or joint. Some writers held the view that it need not necessarily come from the brain, but from organ to organ, but this was a later school of thought. This humoral theory coloured all medical language, thus catarrh, literally translated from the Greek means "I flow down". Thus also rheum, and these explain the "fluxions" and "defluxions" which the early writers used to explain what we now should call acute exacerbations. I cannot explain the theory so well as Professor Stockman and I beg leave to quote from his Rheumatism and Arthritis (1920). I am honoured to have an autographed copy of this work. "The point of view of humoral pathology can perhaps be most shortly explained by a quotation from van Swieten. 'I believe I have demonstrated that the ancients were not mistaken in naming the matter of a 'catarrh' that begins to descend from the head towards the lower parts, a 'defluxion'. When all the cavities of the joints are annointed with this slippery matter, if the same alteration should happen in them as happens in the mucous membrane that invests the nose, the jaws, and lungs, whilst the defluxion remains very troublesome pains may follow in the joints from the same causes. Thus, in the spring and autumn, catarrhs and runnings frequently happen, and then also diseases of the joints are frequent. The

rheumatism, therefore, belongs to these diseases that the ancients called 'fluxions, defluxions', diseases that impelled the matter to a certain part with great pain, although no blemish could be observed in the part itself.'"

The troublesome humor was supposed to be distilled drop by drop, hence the origin of the word "gout", from "gutta" later to become "goutes", then to the modern gout. The drops of a mauvais humor distilled in the head arrived in due time in the great toe, and it is true that after a Lucullian feast this was a common ailment. Dieting then became part of the physician's armoury. Later on, severe bleeding, as much as ten ounces daily was advocated by Sydenham (1734). Though it is worthy of note that as he grew older he did not advocate such severe measures. Caelius Aurelianus in the Fourth Century wrote De morbis acutis et chronicis , where he defines podagra as pains in the feet, and arthritis as pains in many joints. Delpeuch, in La Goutte et le Rheumatisme (Paris, 1900), quotes passages from Cato, Lucilus, and others to support the fact that rheumatism was distinguished from gout under the name of morbus articularis. There is yet more literature about the period of these Roman times, but it has all the same humoral theory, and has no thought to the infection theory introduced by the Egyptians; in fact, one doubts if

they knew of it. One fact emerges, and that is that till Guillaume de Baillou worked as a physician in Paris, in 1538-1616, few strides were made in knowledge. As a matter of fact, though Baillou published an Opera Omnia (1642), the full scale of his wisdom was not apparent until his nephew, Jean Thevart, in 1642, presented the full history of his uncle's achievements in his Liber de Rheumatisme.

Hippocrates began Period One, in the history of Medicine, by raising medicine from a cult of the priest-physicians, to a profession, where exact observation of the patient and the disease were of paramount importance.

Baillou then began Period Two. It was a renaissance of learning and Baillou chose among his other studies to make a special study of Rheumatism. It is clear that he was still dominated by the old theory of the humor. But now he describes a thin tenuous humor, serous fluid, trying to get to the surface of the body through channels which were not there, and on its path choosing muscles, tendons, and organs, especially affecting the tendon sheaths of the joints.

Baillou did not believe that the humor had to come from the head. He believed that it might come from some other part of the body, and gives the example of the liver unburdening itself into the uterus or intestine.

The pain he attributed to the acrimony of the humor. There is still no hint of an infectious focus. So the treatment remains basically the same, bleeding, combined with purging, to evacuate the humor. There were said to be four humors existing in the body; blood, phlegm (pituitary matter), and black and yellow bile. The proper evacuation of these humors and the re-establishment of the body to health by their elimination was attained also by the drainage of pus, by poluria, diarrhoea, or by coryza. Like Hippocrates, Baillou was a believer in sound bedside clinical examination, allied with the knowledge which the subsequent post-mortem would give. Experience thus gained helped with the treatment of the next patient.

Thomas Sydenham in 1676 gives the first more satisfactory description of acute rheumatism, but rheumatoid arthritis seems to have been considered a secondary disease to which Sydenham gives the name "scorbutical rheumatism", Nevertheless he gives an excellent description of the disease. Sydenham considered that there was a third variety of this ailment, to this syndrome he gave the name of lumbago. Sydenham, Vesalius and William Harvey were all physicians working in this period, influenced by the fine example of Baillou, and it is not far from the truth to ascribe to them the groundwork on which has been built our present knowledge and skill in the treatment of rheumatic conditions.

Sydenham was very honest; he describes how the humor seizes the viscera, then he adds a phrase which has given rise to much discussion, "where a scurvy ends, there a dropsy begins". Was Sydenham fully aware of the true implications of that statement ? I doubt that he had penetrated quite so far.

In Hermann Boerhaave (1668-1738) (see van Swieten) we find the next great teacher. By this time Medicine had advanced, and accurate, clinical, bedside examination was taken as a matter of course. A fair number of patients succumbed, post-mortems were held, and medical knowledge advanced. Boerhaave made special studies of the visceral symptoms, but his greatest claim to fame may well be that he founded on sure lines a good Clinic at Leyden. There surrounded by a group of brilliant physicians he taught and treated as became his time. There was not much change in the treatment, as the central thought was the same, an humor. Still, the Clinic was an advance in those days and from it emerged his pupil, Gerhard van Swieten (born 1700), to whom reference has already been made. He had the honour of being appointed as Physician to the Empress Marie Therese. In Vienna, where he practised, he set up another Clinic, on the lines of the Leyden Clinic. Medical study now had its centre

there, and it remained there for a long time. In fact till before the War many patients liked to go to the Vienna Clinic; maybe it was only because a prophet is not without honour, save only in his own country. In any case mention must be made of Antonius Störck (1731- or 1749-1805) and Francois Sauvages (1706-1763). Sauvages, still dominated by the humoral theory, managed to free his mind from the muddled thinking of the day, to differentiate between acute and chronic arthritis, and to classify fourteen varieties of the disease. This was a marvellous achievement for those times. His findings led him to believe that gout affected the joints and rheumatism the muscles. He realised that when the disease was far-advanced the joints also would be affected in rheumatism. His learning he embodied in his "Nosologia Methodica".

England now takes up the challenge of learning in the person of William Cullen (1712-1790). In his "Synopsis Nosologia Methodica" (1795) this brilliant physician recorded his observations. He was the first to break, though not entirely, with the humoral theory, and in that if nothing else he claims his place in the history of rheumatism. His observations led him to believe that it was possible to differentiate surely between acute and chronic rheumatism, as it was then called. He finds that

the primary cause is cold, with strain as a supporting factor, and he can find no logical reason to believe in the "peculiar acrimony" hypothesis. His pathology may not be quite so sound as that of some of his predecessors, but his reasoning is more balanced. Another grand Scot, to quote Professor Stockman, to follow on this work was David Pitcairn. He was a physician at St. Bartholomew's Hospital, and had it not been for the writing of his devoted pupil, Matthew Baillie (1797), might have escaped notice. Matthew Baillie attended Dr. Pitcairn's lectures, and "walked the wards". David Pitcairn gave much attention to the lesions of the heart, the more extraordinary, as one must remember that as yet there was no stethoscope. Still, he taught that practically all the structure of the heart could be affected. He describes pericarditis, endocarditis, and enlargement of the heart itself. London was now the centre of advanced teaching.

Another Scot, a close friend, was William Charles Wells (1812). Wells gave credit that as early as 1788 David Pitcairn had noted heart lesions, but he made an exact study clinically, and followed up his post-mortems, thereby clearly establishing the fact that in rheumatism one could expect pericarditis, endocarditis, myocarditis, involvement of the valves of the heart with subsequent enlargement of the organ. Important also, he

noticed that the liver sometimes became enlarged.

Wells left London for Philadelphia; there he founded a Clinic, and in 1810 published "Rheumatism of the Heart", in which were encompassed the observations of Pitcairn. The rapid pulse and palpitation were noted as well as the subcutaneous nodules. But it was Edward Jenner (1789) who more accurately dissected and assessed the damage done to the heart; this knowledge he imparted to the Medical Society in a series of lectures, illustrated by dissections of the heart in acute rheumatism.

John Haygarth (1740-1827) published a History of Rheumatism (1805). He did not claim that this was on the sound clinical and morbid anatomical lines of Cullen and Wells, only to mention two great names, but it is worth noting because it gives another line on treatment. Treatment had remained much the same all this time. Now Haygarth asserts his view that Peruvian bark was the treatment par excellence. Time did not substantiate that claim but it must be noted as it was a break from the routine. In 1800 Landre Beauvais first gives an accurate picture of rheumatoid arthritis, but that name was not then known and he calls this phenomena asthenic gout.

In 1802 Dr. Heberden directed attention to the enlargement of the terminal interphalangeal joints

on the hands in certain forms of rheumatism. They bear his name to this day.

In 1678 Scheele discovered uric acid; Wollaston (1797) reported that uric acid was to be found in the tophi of gout, and to this day there are preparations on the market to dispel uric acid.

Discoveries and publications flowed steadily, if in a ragged manner. In 1819 Laennec had invented the stethoscope, and so made possible more accurate study of the heart and lungs. Jean Baptiste Bouillard (1796-1881) had thus the advantage of this, but his especial study was more generalised and included the articular damage done by arthritis. He insisted that the lesions were caused by an inflammation, although there was no sign of suppuration. This was a great contribution to the knowledge of rheumatism, but Bouillard did not imply that there was never suppuration, merely that it was not an essential. In point of fact he gives histories of cases in which suppuration actually did occur; these would seem to have been of a pyogenic nature. His "revolution" was that all the tissues of the body were affected by rheumatism, not only the fibrous tendons round joints, or any one part, but that the body whole was affected, some parts more than others according to the nature and severity of the rheumatism.

Bouillard embodied his discoveries in two main treatises which he called Traitéclin. de maladies du coeur, 1835, and Traitéclin. du Rheumatisme articulaire, 1840.

In 1847 Begbie made a valuable contribution. He described and differentiated chorea. In 1848 a great scholar and physician began his work, Sir Alfred Garrod. I had the honour to serve under the son, Sir Archibald Garrod, in Malta in World War 1. Before we enter this period it is necessary to remember a country practitioner, Dr. Maclagen. Working on the theory that where a disease occurs there also is the remedy (e.g. cinchona having been found near the swamps where malaria was rife), Dr. Maclagen noted that in damp places where rheumatism flourished there was the willow. He made an infusion of the bark and called it Salicin. He found that he had good success in the treatment of his patients with this, so in 1881, he published "Rheumatism, its nature, its pathology, and its successful treatment".

Then in 1881, Hirschsprung describes most accurately the subcutaneous nodules which Wells (1812) had noticed, but now there is the exact position of them in the picture, and they are called by his name. The heart again comes in for special notice by the work of Aschoff and Tawara (1906), and Carey Coombs. These workers

maintained that in the heart there were specific nodes in the connective tissue framework springing from the region of the small blood vessels. The nodes were called the nodes of Aschoff, and were found to be present in rheumatic carditis. Poynton and Paine refer to them in their book, Researches in Rheumatism (1913). The nodes were also discussed in the British Medical Journal (1906).

There is now a clear picture emerging of the rheumatic diathesis, and Sir Archibald Garrod, with much knowledge, attempts to classify the forms the disease may take. Important to this thesis is the fact that now Sir Archibald definitely calls the chronic articular rheumatism "rheumatoid arthritis" as early as 1859. Pemberton and Osgood (1934) give a good description of this, and I will quote from the paragraph on page eleven: "His son Sir Archibald E. (Garrod) in 1890 found it necessary to differentiate the types still further, and designated our Type One (atrophic arthritis) as 'rheumatoid arthritis', adding the sub-divisions of (a) acute and (b) chronic, and including the juvenile chronic arthritis described by Still (1897) under this heading. Our Type Two (hypertrophic arthritis), the younger (Sir A. E.) calls 'osteo-arthritis', which term is synonymous also with Charcot's partial chronic articular rheumatism and

includes Heberden's nodes, morbus Coxae senilis, etc."

John Kearsley Mitchell (1798-1858), and American, studying and practising in the Clinic in Philadelphia, to which Clinic reference has already been made, advocated a theory that acute rheumatism was essentially a disease of the central nervous system. He believed that a lesion in the spinal cord gave rise to its various manifestations. The old Hippocratic theory was coming to life again, thus from the Island of Cos, to Leyden, to Vienna, to London, and now the New World of America there was study on the hypothesis laid down in 400 B.C. Constall, Hutchinson and Buzzard affirmed that the trophic centre for joints could be found in the medulla oblongata. Friedlander agreed with this, but added that it was a micro-organism having a special affinity for joints which caused the ailment. Thus there is now wedded the idea of a nervous lesion in the central nervous system with the "germ theory". Dr. S. Weir Mitchell (1903) carried on the brilliant work of his father.

Everywhere there were now contributions to the literature of rheumatism. There is Charcot, in 1881, publishing his "Clinical Lectures and Chronic Diseases". In these lectures he describes at least three types of rheumatism. First, the progressive articular

rheumatism which he calls "nodular rheumatism". This type clinically and pathologically resembles the type formerly known as atrophic arthritis. His second type he calls "partial chronic articular rheumatism"; this is identical with hypertrophic arthritis, or the nodosities of Haygarth. His third type he called "Heberden's rheumatism", and this would seem to be merely a mild variety of hypertrophic arthritis. So striking was the contribution made to the clinical and morbid joint lesions that his work must have special reference, and to this day a certain disease of the joints bears his name. In this particular disease, he describes an extreme degree of tissue destruction, with associated rapid development of a typical flail-like joint, "a Charcot joint", but we attribute this now to tabes dorsalis when it occurs in the lower limbs and syringomelia when it occurs in the upper limbs.

Classifications grew now rapidly, and for that matter are still being made, as fresh aspects of the disease come to general knowledge. Wilson in 1885 had isolated definite "germs" from the blood stream of affected patients and that is true practically to this day, as the organisms in this disease are to be found, not in the synovial fluid of the affected joints, but in the blood stream, and even in the nodes. This, of course,

is not the case in suppurative effusions, where the infecting agent usually belongs to the B. Pyogenes group. I have had the honour to serve in a Military Hospital, Imtarfa, Malta, where Sir Archibald Garrod was the Consultant Physician. (It will be understood that I am leaving the particular arthritis due to B. SHiga, and the other dysenteries alone; this Hospital had every form of infection, except leprosy.)

The Arthritides due to some specific disease are having short mention as this thesis is concerned with the entity Rheumatoid Arthritis. Poynton and Paine, in their "Researches on Rheumatism" (1913), found a diplococcus present in acute arthritis, whether in man or animals. They found that the rabbit was the ideal animal for this particular experimental work, and that before the disease had shown manifestations in the limbs there were lesions in the heart. Not the surface of the valves were affected first, but the valves were attacked from within. The clumps of the diplococcus formed beneath the endocardium, in the region of the valve ring, connective tissue proliferation ensued and a granulation thus formed and it was only when this granulation broke down that the surface of the valve exhibited the diplococcus. In Man the diplococcus is found in the deeper part of the visceral

pericardium, in the fibrino-cellular exudation, and in the parietal pericardium. These micro-organisms circulate through the blood stream during an acute exacerbation, and in a severe case may even cause a generalised septicaemia. Suppose this unhappy result to have occurred, with death as the final termination of the case, were it possible to have a post-mortem the diplococcus is to be found in all the organs; thus the case may have simulated a pneumonia, or some kidney disturbance, etc. Poynton and Paine also found this diplococcus in pure culture in the perivascular spaces of the pia mater, in the capillaries, and in some parts of the motor area of the brain, in a case of chorea, in which the heart was but little affected.

Enough has now been said to show that after the humoral period there was the germ period, but with the reservation that reasoning thinkers took into account the climatic effect and advanced thinkers were beginning to look to the central nervous system as a further causative agent.

Professor Stockman taught that when the tissues were properly massaged by deep Swedish massage, the patient had a dose of autogenous vaccine, of what quantity one could not necessarily be certain; therefore rest after massage was essential. I well remember that

he used to produce his Swedish masseur to show us how massage should be done, and I must confess that with years of experience behind me I have found few masseurs willing to put so much hard work into their massage. It therefore was a good thing for me when I read of the work of Dr. Warren Crowe, then in Harrogate. I went over to see his work and decided that I would try the more exact method of dosage which his vaccine allowed.

Dr. Warren Crowe believes that rheumatoid arthritis is caused more by the staphylococcus, and osteo-arthritis by the streptococcus. I am not taking into account at this moment autogenous vaccines. He cultured again and again until he found the more usual strains of these organisms present in ordinary types of the disease, and from them he made a stock vaccine, in varying degrees of strength. His objective was to get the maximal curative effect with the minimal discomfort to the patient, also that the patient might be enabled to live and carry on his work in his normal habitat. I quote from "Bacteriology and Surgery of Chronic Arthritis and Rheumatism" by Dr. Warren Crowe (1927), page eleven: "Finally, to complete the series of suggested specific microbes, we must mention the M. rheumaticus of Poynton and Paine, and my micrococcus deformans which I have assigned as the primary cause of rheumatoid arthritis. These

will be referred to again later on. Of the rest confirmation is lacking."

Work went on, more or less, proving or disproving these causative agents, but the treatment was the same. Few practitioners cared to venture far into the vaccine field, the conservative methods of the centuries still held good. The author remembers that some practitioners in the area where her practice was were in the habit of handing over their rheumatic cases "for some of that new vaccine stuff".

During World War II, it was rumoured that German pilots were being given adrenal extracts to increase their fighting efficiency (Cortisone and A.C.T.H. Copeman, 1953). As early as the 1930s work had begun on the chemical constituents of the adrenal cortex. Dr. Copeman gives an excellent description of the evolution of the Steroids on page two of the book to which reference has just been made.

RHEUMATISM

Acute ..... Rheumatic fever et al.

Chronic .... 1) Non articular

2) Osteo-arthritis ... Mechanical, traumatic & strain.

Endocrine degenerative.

3) Rheumatoid arthritis ... Still's

True.

Menopausal.

Senile degenerative.

4) Spondylitis ..... English

American (rheumatoid sub-group)

5) Gout ..... Alcoholic, de facto or inherited.

Metabolic.

The degenerative endocrine group needs elaborating :-

Menopausal ..... Pre- N.A.R. & O.A. Hypo-oestrinic.

Transitional.

Post- R.A. Hypo-progesteronic.

Senile ..... Osteo-arthritic type.

Rheumatoid senile type.

Clinical picture of a Rheumatoid arthritic patient.

There is a classification on page 25 to which the author has adhered. In the sub-heading 3) there is first mentioned Still's Disease. This particular form of rheumatoid arthritis is not often seen in the Clinic, merely because there are not many child patients. In practice it has been found that often these children do well on the stock vaccine of Charterhouse. As they do not come into the adrenaline picture they are not mentioned, more than to say the author has in mind a survey of the babies of rheumatoid arthritic mothers treated before pregnancy with adrenaline and those treated with other methods.

A true rheumatoid arthritic patient, properly examined and found to be only rheumatoid, both by clinical and laboratory methods, is not so easy to find. The disease follows some shock or strain; in other words, fear. There is usually a seemingly latent period before the disease manifests itself. This period varies, the temperament of the patient has some bearing on this, also the factor of heredity, but it will be shown that the period of latency was materially shortened in cases to be presented where the patient was subjected to cold and damp, such as in cellars and shelters in London during the Blitz.

The actual onset may be sudden or insiduous, with or without fever. But there is one sure factor, pain is always present. Maybe tingling of the fingers, with pain in bed at night may bring the patient to seek advice. Usually the case is more advanced before advice is sought, and there may be the heavy look of the Cushing syndrome. The elbows are probably fixed as they are soon affected, and the shoulder girdle thus follows on. The patient by this time has probably been in and out of various hospitals and had many forms of therapy.

The clinical picture of a true rheumatoid arthritic patient in the early stages is one of an anxious worried patient, with wasted flesh, and if the onset be rapid, quickly crippled hands, knees and/or feet. There is a good deal of pain, and the patient may run a temperature. This is a systemic disease, and not just the disease of one or more of the larger joints of the body. The moon-face sometimes described, does not usually appear until the case is one of the prodromal pre-menopausal pituitary type with gross fluid retention.

The muscles waste and thus the joints appear even larger than the disease makes them. There may be chest complications, bronchitis plagues such a patient sadly. With lack of movement constipation is

is difficult to avoid, and with the purgation the patient tends to suffer from haemorrhoids. The blood pressure is low, e.g. 90/60. The pulse tends to be quick. There are many books written about the rheumatic heart, and, as has been noted in the History Section, lectures with dissections of the heart. Clinically, there is often a soft mitral murmur; irregularities in the rhythm are common, and it is not unlikely that the Bundle of His has also been affected. There are frequently extra-systoles. But if the patient has stood up well to the disease and the physician skilful the heart tends to adjust itself to the altered conditions; here again the use of substances that may give too much power of movement to the patient is dangerous. The author has seen that the greatest care must first be given to the heart and viscera, as the old dictum is true to-day as it was when written, "rheumatism licks the joints but bites the heart".

As the age group grows older and the pre- and post-menopausal groups come into the scope of review, it is noticeable that recovery is more difficult. The resilience of youth is not there, nor the hope which youth has. Also there is now veritably an endocrine case with which to deal. These cases are often mixed with non-articular rheumatism or the beginning of osteo-arthritis

It becomes a problem, then, to know which particular division of rheumatism to treat. The rheumatoid side is obviously to the physician the more important, but to the patient it is the pain. The usual two reasons given for not seeking advice sooner are that "it was only rheumatism", and "rheumatism does not kill one and I was busy". With the public becoming more health-minded one does see early cases now, especially where there is a history of rheumatism in the family. Should the patient ignore the early signs of trouble, there may be a period of remission, during which the fears of the patient are further lulled, and the history will then be "I got better from that attack without treatment". There is even a feeling of agression that the next attack has not cleared up spontaneously.

With ideal conditions, such as a happy and secure home, the period of latency may last for some years, but even should the disease begin as a rheumatoid spondylitis, the next symptoms may manifest themselves in the hands and wrists. (The case No.5 to which reference will be made later). From there the disease strikes as it pleases. Often it is the elbows which are next affected, the knees quickly follow, and the feet. As the feet become more and more painful on movement, the

patient tends to restrict activities. If the appetite has remained the patient then has the additional trouble of the added weight, thus movement is less. The patient becomes lethargic and the face has an appearance of "moon-face", as is described in Cortisone and A.C.T.H. (Copeman). The added bulk of the patient often has an almost translucent appearance, the "ancients" believed that this was the humor flowing from the head. This tissue does not pit on pressure, but the chemistry of the body fluids has been changing, and with this water retention from whatever cause, the muscles gradually appear to lose their hard consistency and wasting sets in. The joints are affected; they become swollen and tender, the lethargic patient has had enough pain, so he or she rests the joint in the position most comfortable. By this time the patient is usually in the position of the chair in which he spends most of his time. The joint is set with pannus, ably described by Professor Stockman in his lectures, as a substance which flows like lava, and like lava sets, thus the joint is immobilised. There is erosion of cartilage, loss of joint space, and eventually ankylosis. Orthopaedic surgeons to whom the author has appealed to free such a joint are against touching such a structure as the danger of a flare-up of the rheumatoid condition would

make the patient much worse. Yet, in the future, it is obvious that once the rheumatoid condition is under control, to have a working joint some surgery will be necessary. In this connection the author was asking the help of Mr. Kennedy of Epsom recently, and he described a case which is not yet in print, it is understood. In the particular case a surgeon undertook to try and replace cartilage in the knee with nylon pads. There was a very severe reaction, so severe that it was considered justified to enter the joint again. This was accomplished and the nylon pads removed. The effusion died,down, and as the condition improved the surgeon tried to tell the patient the rationale of the operation, whereupon the patient told him, that had she been consulted first she could have said it would be a failure as she was so allergic to nylon that she could not even wear nylon stockings. That is the first time the question of allergy to nylon has been heard of by those surgeons.

The effects of rheumatoid arthritis on the cardio-vascular system have been known since the time of David Pitcairn. Now the assessment of the disease with modern instruments can be added. The pulse is more often rapid than slow; a pulse of 100 and over is often found. The blood pressure of the true

rheumatoid is low, e.g. 90/60. The heart has a soft sound which is soon recognised. Where there has been damage by fever there is often a blowing systolic murmur present. In the true rheumatoid, however, the author has not found the extensive damage to the cardio-vascular system that is occasioned in rheumatic fever. To check on this cases have been sent to the Heart Hospital for expert opinion; no patient has been admitted nor has any treatment for the heart been considered necessary.

AUTONOMIC NERVOUS SYSTEM.

The effect of the Autonomic Nervous System is described well in an article by Dr. Nathan Sussman of Harrisburg in Rheumatism, (1953).

PREVIOUS WORK ON USE OF EPINEPHRINE IN RHEUMATOID ARTHRITIS.

In the Journal of American Medical Association (1950) there is an article which has noted the effect of epinephrine. The article is by Dr. Maynard Guest and his colleagues. He points out that Long (Recent studies on the function of the Adrenal Cortex) is of the opinion that epinephrine has an indirect action on the adrenal cortex, and is dependent on the presence of the anterior pituitary gland. Dr. Guest quotes the method employed by Dr. Thorn in giving 0.5 mg. epinephrine subcutaneously every 6 hours. The eosinopenia was noted, and the conclusion drawn agrees with that of the author "There was no relationship between the eosinopenia and the therapeutic response to treatment with epinephrine". When the author began this thesis this was true, but now in the light of further research there is an elusive clue. It is rather as if the response to stimulation by adrenaline was marked at first, and then there seems to come a period of 'saturation', as if the tissues of the patient were tired and could not be pushed further. This is substantiated by the Differential Sedimentation Test. After a rest, then the tissues react once more. Furthermore Dr. Guest found that "improvement continued after the treatment was discontinued". That also is in accordance

with the findings recorded in the thesis. It is comforting to read the Summary and find that Dr. Guest states "There is reasonably plausible rationale for the use of epinephrine in Rheumatoid Arthritis". But he cautiously adds that the dosage and length of time which the patient may take in which to show improvement are not yet known. He admits that the length of time taken for the experiments recorded in his paper is short.

In both this work recorded by Dr. Guest and his colleagues and that of Professor Parr in Australia it would appear to the author that there is not sufficient time given for a response to the stimulus of the adrenaline by the tissues of the patient. In other words the patient is drowned in stimuli. Already the tissues of the patient have been damaged by the disease, and now they are being asked to carry a load of which they are not capable. Damaged kidneys to excrete more products of disease, damaged liver to deal with a yet greater 'load' almost above all damaged brain and will-power of the patient to contend with more pain, for the process of 'getting better' means using muscles which have long been in disuse and are painful to use once again. As well as using the necessary skill in administering the hormone, it is here seen where the true skill of the physician is of service. He must be able to help the patient over

this bad time, and it is in this part of the healing process that the personality of the physician counts, and only here.

CLINICAL SECTION.

GENERAL SURVEY OF CLINICAL MATERIAL.

In this Section the author means to show the work done and why adrenaline was chosen. At the time these cases were selected for treatment by adrenaline the author had not read the work of Dr. Hench and his colleagues in America. It must be explained here that the author was and is a busy general practitioner, and does not get all the time it is necessary to have to keep up with the volume of reading which it is proper to do. At first it was difficult to persuade the Laboratory Staff at Charterhouse to undertake any further work. It was obvious that laboratory tests were necessary and as the cases progressed all the help possible was given and time for reading was better as the author managed to get an assistant; but all this took time.

The author sets out to show that there are some rheumatoid arthritic cases which only need some help to allow their own resistance to regain its power, and they will get better. These cases are, it would seem, the cases which are described in text-books as having a spontaneous recovery or remission.. With help, such as adrenaline gives, the recovery or remission may be quicker, and thus cause less deformity. Secondly the author would like to show, that by the tests applied

by the American Group of workers, the patient himself makes a limited amount of Cortisone (a substance to be discussed later), and will in time make a recovery, with no evil side-effects, albeit that the recovery is much slower. This in point of fact may be no bad thing as in the Historical Section it was shown that the heart and the viscera were all affected in this disease. If the power of mobility be given to such an affected patient dramatically, and quickly, it can well be understood that there will be side effects and even death. The author would like to lay down the hypothesis that until the internal organs are considered sufficiently well and strong by the use, say of some slower method such as adrenaline, it is dangerous to use the corticotrophic hormone, now called A.C.T.H. or more so Cortisone. In any case it would save a lot of money as both these substances are difficult to obtain and expensive.

In the Classification given in this thesis, rheumatoid arthritis comes under heading three. There is no noted case of Still's Disease, as there are not many children at Charterhouse, but in time the author hopes to show the result of children born to parents, where the mother has been treated with adrenaline, and, the D.S.T (a test to be described later), considered

fit for pregnancy. The blood of some of these babies has been taken out but cannot be included in the series as the children have not any clinical signs of rheumatoid arthritis. The blood count is also being done, as some of these children, especially of mothers coming after confinement, only show clinical signs of anaemia.

Adrenaline (see Appendix) was chosen, as it seems to be a sound clinical method of assisting the syndrome. It has been shown by workers in laboratories where it is possible to use animals that a lesion occurs somewhere between the central nervous higher centres, the hypothalamic nuclei, the anterior pituitary gland, and the adrenal cortex where the healing hormone is eventually produced. That this hormone is 17-hydroxy-11-dehydrocorticosterone, more shortly called Cortisone.

Cortisone appears to be an all-sufficing hormone which is the end-product when the adrenal cortex has been stimulated. It can therefore be administered with the assurance that it will effect healing, even though no adrenal cortex be there to be stimulated, as may be the case with disease or tumour. Adrenocorticotrophic hormone requires the presence of some, at least, of the adrenal cortex. It is an excitant. At the Third International Conference on the

Standardisation of Hormones in 1938, it was decided to call this hormone the corticotrophic hormone, but in spite of this it is usually called A.C.T.H. Adrenaline was the first hormone to be discovered. As early as 1895 Oliver and Schafer found that the adrenal medulla contained a pressor substance, which constricted blood vessels and caused a rise in blood pressure. Takamine and Aldrich working independently, isolated adrenaline, but it was Aldrich who established its formula in 1901. Stolz synthesised it in 1904. There has been much work done with hormones and in the last few years it has been shown that another substance, "nor-adrenaline" can be extracted from the adrenals of some animals and from some human adrenal tumours. For the purpose of this thesis it seems only necessary to note that there is a substance "nor-adrenaline", as the necessary work to establish its exact functions in relation to adrenaline are not yet accurately known. It is known that there is a period before the adrenaline can affect the patient. That is often seen, and gives one time to get the patient out of the examination room and into some place where a nurse can attend, if necessary. The author has found this first period to be of very variable time, sometimes hardly seconds, then one expects to find a fairly severe

reaction. The pallor, shivering and faintness however soon wear off, and in twenty minutes or so, especially if a hot drink of tea be given, the patient is ready to go home.

Because of the constriction of the arterioles thus sending the blood to the large vessels, it is important that the blood pressure of the patient should be taken first. Should the blood pressure be high, small doses, as small as 2 mms. of adrenaline will have good effects. In this respect, the collagen diseases may be mentioned, as it is with these that one is treating patients with hypertension. Chronic senile eczema in an elderly man of over seventy who had had every kind of treatment, including 'ray therapy' cleared up in six months. He was in bed when treatment began, swathed in bandages, with a blood pressure of 200/100 mm., pulse 82, regular, no oedema of the ankles, and had never had any, even when walking. Two minims adrenaline administered hypodermically, every other day was all that he could tolerate. In time his blood pressure was reduced to 160/100, and he could tolerate six minims adrenaline twice weekly. Three months later he had a remission of the disease which lasted till his daughter rather late in life had a baby, and the emotional upset had disturbed

the balance of his glands; treatment was again instituted and was only required for three months He has been free now for over three years.

This digression is only to illustrate the potency of adrenaline. But a full and interesting account is given in Dr. Raymond Greene's book "The Practice of Endocrinology", enlarged (1951) edition. The author has had the good fortune to meet Dr. Greene on several cases, and knows from first hand the benefit of his advice.

The pathway by which the stimulus works, whether it be real or induced, is well illustrated in a monograph "Cortisone" J. M. Carlisle, M.D., A. Gibson, M.D., and E. Schmatolla, M.D. This monograph also gives an excellent picture of the pathway. There is also a good description of the principal groups of adrenal cortical hormones and their chemistry.

The adrenaline used for this series of cases was a preparation of Boot's, 1:1000. A clear fluid, sterilised and kept in rubber-capped bottles. The dosage varied, but in the standard tests to which reference will be made later, the dose was always exact, six minims. The latent period for which one may hope, in order that the patient may leave the consulting-room is well described in full on page 91 of Raymond Greene's

book to which reference has been made already. One sentence might well be picked out as illustrating the effect of chronic stress which in its turn causes disease, "This action of adrenaline is of short duration on account of the rapidity with which it is destroyed in the tissue, but a sustained effect on the blood pressure can be produced by repeated injections at short intervals."

The purpose of this thesis is to demonstrate that Adrenaline may be used in the treatment of rheumatoid arthritis, and that the use of the hormone is as an excitant. Thus under the strain of fear the higher nerve centres, for the safety of the body, will send out the appropriate stimuli to the Hypothalmic Nuclei, thence the stimulus travels to the anterior pituitary; the humoral pathway is followed by the adrenocorticotrophic hormone, so the adrenal cortex is stimulated to send out the necessary hormone, Cortisone. All this has been proved by the work of many research students on animals. In 1949 Dr. Hench, Kendall and Thorn with their colleagues showed some of this work, and the results. But even yet it is not clear where the break may come. As Adrenaline was in plenty, and as it was the oldest hormone isolated, and especially as the amount of the hormone could be accurately given, the

author decided to use it.

Before the author could reasonably ask the Laboratory to undertake the extra work entailed there had to be some original work done to prove the point. The author tried small doses of adrenaline on some patients with the collagen diseases in her practice. One such has been mentioned, the Job's eczema. Some tentative work was begun in the Clinic and then the Director of the Biochemical Laboratory agreed to allow the tests to be made, without which this paper would be valueless. It is a little difficult now to recapture the adventurous spirit in which this work was undertaken, as it is all now explained and so very much has been written about the pituitary-adrenal syndrome. There was at that time a momentous interview, as it seemed to the author, with Professor Smithers of the Royal Cancer Hospital, London, in which the theory of Fear producing stimuli was discussed. Certain cases were described and one, Mrs. D., Professor Smithers thought, resembled lymphosarcoma. This case is discussed later, with letters from the Royal Cancer Hospital, but it would appear that adrenaline over a prolonged period has more effect on the nodules, as an exact description of the nodules of Mrs. D. are certainly smaller than those

treated with A.C.T.H. and Cortisone and described by Dr. Copeman in his book "Cortisone and A.C.T.H." (1953).

Because this work was undertaken by an unknown person and there was much ground work to be accomplished first before real studious routine work could be attempted, it would seem that this thesis is but a feeble imitation of much good work done by masters with full research possibilities at their command. It cannot be made too clear that every step was fought for with a dogged determination, and that this work is entirely original. It is incomplete, in that much clinical work and attached laboratory work is needed to find out just where the mechanism breaks down, and why one patient under fear will develop rheumatoid arthritis, and another asthma, and yet another nodules so suspicious of lymphosarcoma.

Also the complete relief of the patient from pain and disability, this last including orthopaedic attention, must not be forgotten. How to increase a joint space, synovial fluid and to produce pads at least as efficient as those provided by Nature are problems which stir the imagination and spur one to action.

Looking back over the years since the first inception of this work was conceived it is strange to read a confirmation by Dr. Raymond Greene in

his book (to which reference has already been made, page 91) of the hypothesis "which lies at the root of the work. The most widely accepted view now is that adrenaline secretion is continuous so long as nervous impulses can reach the medulla but that it is accelerated as a result of the response of the organism to fear ...". It was on just such a thought that the author started this particular work so many years ago.

LABORATORY TESTS.

The author has not yet found any test for rheumatoid arthritis so sure as the Differential Sedimentation Test of Dr. Harry Coke.

This D.S.T. has been carried out in each case at least once, frequently many more times. In rheumatoid arthritis cases the Basal Sedimentation Test has often been taken, and it frequently is regarded as a standard test. In the D.S.T. Dr. Coke uses only the serum, because in some anaemias and diseases the shape of the red blood cells change. In any case there is the potential danger that rouleaux of these cells may affect the sedimentation. This cannot happen in the D.S.T. The D.S.T. is fully explained by Dr. Coke in "Rheumatism" (1939).

The Clinician receives from the Laboratory a graph with a red field, a green field and the sedimentation value. It is a matter of time and experience to assess these findings. The green field shows the tissue reactivity and the red field a reflection of the general state of toxicity, which may be metabolic, hormonal, or due to absorption from the presence of some closed focus of infection. With these aids, and the clinical history and picture in front of him an exact state of the patient's condition is possible, that leads further than only the

diagnosis, as it is possible to determine the type of treatment, and even the dosage required.

For the value that the adrenaline was to the patient the laboratory performed the four hour test with a measured quantity of adrenaline. For this purpose the standard quantity of six minims 1:1000 adrenaline was used. The author is assured that the method used was that described by Roche, Hills and Thorn, (1949) and the actual counting of the eosinophiles by the use of the Randolph technique. Thus the eosinopenia, or otherwise was determined. Also in many cases the white blood cell count was done, and as time went on and more experimental work was done, the serum postassium, sometimes also the serum sodium, and always if time permitted the sedimentation rate. Usually the Wintrobe method was the one employed.

It cannot be stressed too much that this work was undertaken during Clinic time mostly and that the work of the Clinic had to go on; nor that the laboratory staff had this extra work imposed upon them, when they were sufficiently busy. One last point is most important, Charterhouse is a voluntary Clinic. Therefore it is more usual to get patients there who have already had treatment for the condition at the State Hospitals. To be perfectly honest it is only now that the effect of adrenaline on the

patient, since the author first begain in 1950, is really showing good results. The return to health began soon after the first injections, but it is now that the joints are loosening. Dr. Copeman refers to the difficulty of any exact standard test to determine the return to normal, and it is difficult; but when a patient who has not knelt for years suddenly finds that she is kneeling naturally, and without thinking of the renewed action, till she finds herself putting "away my winter boots in a low drawer", as one patient told me this week, then one can be sure the joint is loosening and painlessly. This patient, Case 6, is described later on. Yet she came to the Clinic as an ambulance case. This thesis does not set out to say that adrenaline is better or as good as Cortisone or A.C.T.H., but it is effectual and obtainable. Furthermore, in Cortisone and A.C.T.H. (1953) Dr. Copeman on page 72 refers to the small supplies of these drugs in Great Britain, and the almost certain necessity of the therapy having to be continued for possibly an indefinite time. There are many patients suffering from rheumatoid arthritis and if the treatment has to be a long one in any case, here is an hormone which is obtainable and cheap. Perhaps it is no bad thing that it has taken so long before this thesis could be written for now there are results, even of joint relaxation.

The Criteria employed to assess the return to activity of the patient.

Most of the patients discussed have been ambulance cases in the first instance; from the D.S.T. it has been shown that there was almost maximal rheumatoid activity. There has been in most cases complete crippling. Many cases could not feed themselves, dress themselves, or attend to their natural requirements. In the Clinic importance has been attached to the first time the patient could walk, aided, but walk into the examination room. Then as the patient became stronger and a more erect posture was possible, the noticeable change in height. Co-incident with this, often first, the patient began to h, have a cup of tea, which she drank by herself, then to dressing. It is quite extraordinary the self-confidence it gives a patient to feel that she is regaining independence. From then on the recovery, though slow, is sure, as the patient has confidence that the disease can be overcome. In other words fear is receding and the patient will in truth heal herself. In this disease where the emotions play such a part it is indeed true to remember that the physician cannot heal, but only make the path clear for Nature to take its course.

About this time in the process of

recovery the mentality of the patient begins to quicken. The lethargy gets less as euphoria grows, and the patient will now willingly do exercises to hurry on the recovery. It now becomes necessary for the physician to act as a brake, to explain that hurry is not possible. The moon-face becomes more the normal face of the patient, and here it is noticeable that cardio-vascular changes are taking place. In the true, simple rheumatoid case the blood pressure rises to 120/100, and in older patients even higher, in the mixed arthritis with much rheumatoid affection, but where the arteries have hardened and the blood pressure has been high, the blood pressure tends to fall to a more normal level. For instance, in a mixed degenerative endocrine rheumatoid arthritis patient where the blood pressure has been 180/120, it will fall to 160/100. The degenerative endocrine case is naturally an older person.

To attempt to classify this kind of case is difficult as is pointed out by Dr. Copeman. However, some few tables have been attempted and they would agree with the findings of other workers, a) that there is a period of latency between the stress and the first onset of symptoms; b) that this period is materially affected by environment, especially cold and damp; c) that a bad physical inheritance has an adverse effect, (the author has

found that in many family histories cancer and tuberculosis are present): that sex occurrences, such as the menopause, tend to lay the patient open to rheumatoid arthritis, and that the menstrual cycle has a definite bearing on the progress towards recovery. It is also agreed that treatment must be kept up, though the author will show a case which had pigmentation, suggestive of Addison's disease, and this patient felt so well, and her test were satisfactory so treatment was relaxed since June, 1952; on coming up for clinical examination in April this year, Case 8, has lost the pigmentation on the dorsal aspects of both hands, and the fingers are gradually clearing. The staining is also gradually leaving her body, and this staining she has had since she was in her twenties, when she was told nothing could be done. She is now 58.

Frequently I have found that the clinical symptoms follow the findings of the D.S.T. This is in keeping with the idea that outward clinical symptoms are but the evidence of some inward disturbance, and with the endocrine balance it is found that the D.S.T. is of great help.


R

CASE I. Aet. 69.

This case was first seen on 13.9.50, the patient then was sixty-six years of age. She was a very severe case and came by ambulance to the Clinic.

Previous history

She had been healthy until a car accident in 1935. She sustained no major injury, but was severely shaken. Other physicians had tried the method of physiotherapy, chrysotherapy, vaccine and progesterone therapy; nothing seemed to help her.

Family history

There was nothing of note except that "mother had rheumatism". Her condition in life was quite comfortable, her husband devoted. In March 1951 he had a heart attack and died. There was one daughter, married and devoted to her mother.

Symptoms.

In 1948 the fingers began to stiffen, and gradually the whole of the body became involved with a feeling of malaise. Mrs. D. could not move without assistance, not even to feed herself.

Clinical findings

The flesh was wasted, the skin sallow, even almost yellow, the joints swollen, very little movement, and that increased the pain which was constant. The palms of the hands were moist and there were subcutaneous nodules. The right ankle was more swollen than the left, the elbows were grossly swollen, and she found it difficult to pick up even a light object. There was no cardiac abnormality; of course exercise tolerance test was impossible as the patient could not move. Blood Pressure was 140/100. The lungs showed a few crepitations at the bases.

Treatment

This patient was given six minims of 1:1000 Adrenaline subcutaneously, having had her blood taken before, and four hours after. The Randolph method was used for the estimation of the eosinophils.

	Before	After 4 hours
White blood cells	7970	7270
Eosinophils	155	0
	- 100%	

On 20.9.50. the blood pressure had fallen to 88/60, but the patient felt better and had had her first four days

free from pain for two years. She was given the same dose again. On 27.9.50. the pulse was 92, stronger, and the blood pressure 130/80. The swelling was less round the joints, she was sleeping better, had had six days free from pain and was more cheerful. The D.S.T., which had been taken on her first visit, shows she was a case of almost maximal activity; haemoglobin = 65%. The result of the D.S.T. is appended. Weekly injections of six minims of 1:1000 adrenaline were given and the patient was advised to take a preparation of cod-liver oil and iron. By 18.10.50 she was beginning to walk a few steps. This patient was ideal to treat as she has a will-power which few patients have. The blood pressure was taken weekly and varied between 118/70 and 130/90. On 3.11.50 the patient was walking a little, but with great pain, Dr. Seth-Smith was asked to see her. He agreed that deep-ray therapy might take away some of the pain, so the adrenaline was stopped and she had deep-ray therapy as follows:-

6.11.50.	Wide Field to trunk.	130 K.V., 4mm Al. 17½ F.S.D. 40-40 = 80r.		
13.11.50.	Knee joints.	170 K.V. ½ CuI Al.	ant flexed.	100r
28.11.50	" "	As above		100r
4.12.50	" "	As above	post	100r

9. 1.51.	Knee joints.	170 K.V. ½ CuI Al.	ant flexed	100r
12. 1.51.	" "	as above	post.	100r
19. 1.51.	" "	as above	ant flexed	100r
23. 1.51.	" "	as above	post.	100r
29. 1.51.	" "	as above	ant.	100r
2. 2.51.	" "	as above	post.	100r

Total one wide field · 80r

Total knee joints 900r

980r.

On 9.1.51 the patient returned to the Clinic; she had definitely retrogressed. The pain in her back was worse, her general condition was worse, and she had lost what might be described as the beginning of euphoria. The blood pressure was 158/100. She was put back on six minims adrenaline weekly, but it took longer to pick up. There was a slower response. By March the patient was dressing herself, even if slowly, and could raise her arms to attempt to do her hair, unfortunately at this time the husband had a heart attack and died. This slowed down the progress of the patient very considerably. In May progesterone, 5 mgm. was added to the treatment, but that week the patient had more pain, so it was discontinued. The adrenaline was stepped up to eight minims each week, and the patient did

did well, the blood pressure averaged 136/100, pulse 80. The knees now began to crack, and crunch and the swelling in the knees and ankles was steadily getting less. In July it was decided to try again with the added dose of 5 mgm. Progesterone, and this time the response was "really wonderful". Progress continued, and was good, but ten minims adrenaline and 10 mgm. Progesterone was too much as it caused increased pain, even though each hormone was tried out separately. In September the patient was walking slowly with a stick. This case was discussed with Professor Smithers, who suggested she might be a case of lymphosarcoma. She had to be persuaded to see Professor Smithers and the letter received from the Royal Cancer Hospital is as follows:

"Biopsy left axillary gland received 23.8.51.

Macroscopic: Mass (3.6. x 2.6 x up to 1.2 cm.) of firm white and greyish brown tissue.

Microscopic: There is marked hyperplasia of the follicles, all of which have large Fleming's centres and hyperplasia of the reticulum discharging many lymphocytes into the sinuses. The appearances are not diagnostic of lymphosarcoma and are more suggestive of a non-specific reactive hyperplasia.

I think the diagnosis of a non-specific reactive hyperplasia fits in better with the clinical appearance. She has, after all, got rheumatoid arthritis. Glands are

fairly widespread, being found in both axillae, and in the neck. Most significant of all, th re is a large epitrochlear gland on the left side, though, oddly enough, nothing on the right side. I think that is very much more like rheumatoid arthritis and quite unlike lymphosarcoma.

I suggest that you continue to treat her as you are at present doing, with this as a convinced diagnosis."

There was another four hourly test done on 26.10.51.

	Before	After 4 hours	
Eosinophils	0	0	= 0
Sedimentation Rate	26/100 (corrected 31/100)	45/100	
Potassium	20.0	20.4	+ 0.4
Pzcked cell volume	32%		

"much better" (Dr. Harry Coke)

In January 1952 the patient was very anaemic and was advised to take iron. She missed getting out in the air. The weather was bad, and her circumstances did not permit a visit to a sunny climate. By February the palms were dry, and the patient was doing ironing and small household duties. Progress was uneventful, and now she felt the effect of the weather, but, as with all these patients, it is emotional stress which seems to be the more

likely factor to cause a relaps. The Differential Sedimentation Test is appended and another letter from the Cancer Hospital on 28.1.53 states:-

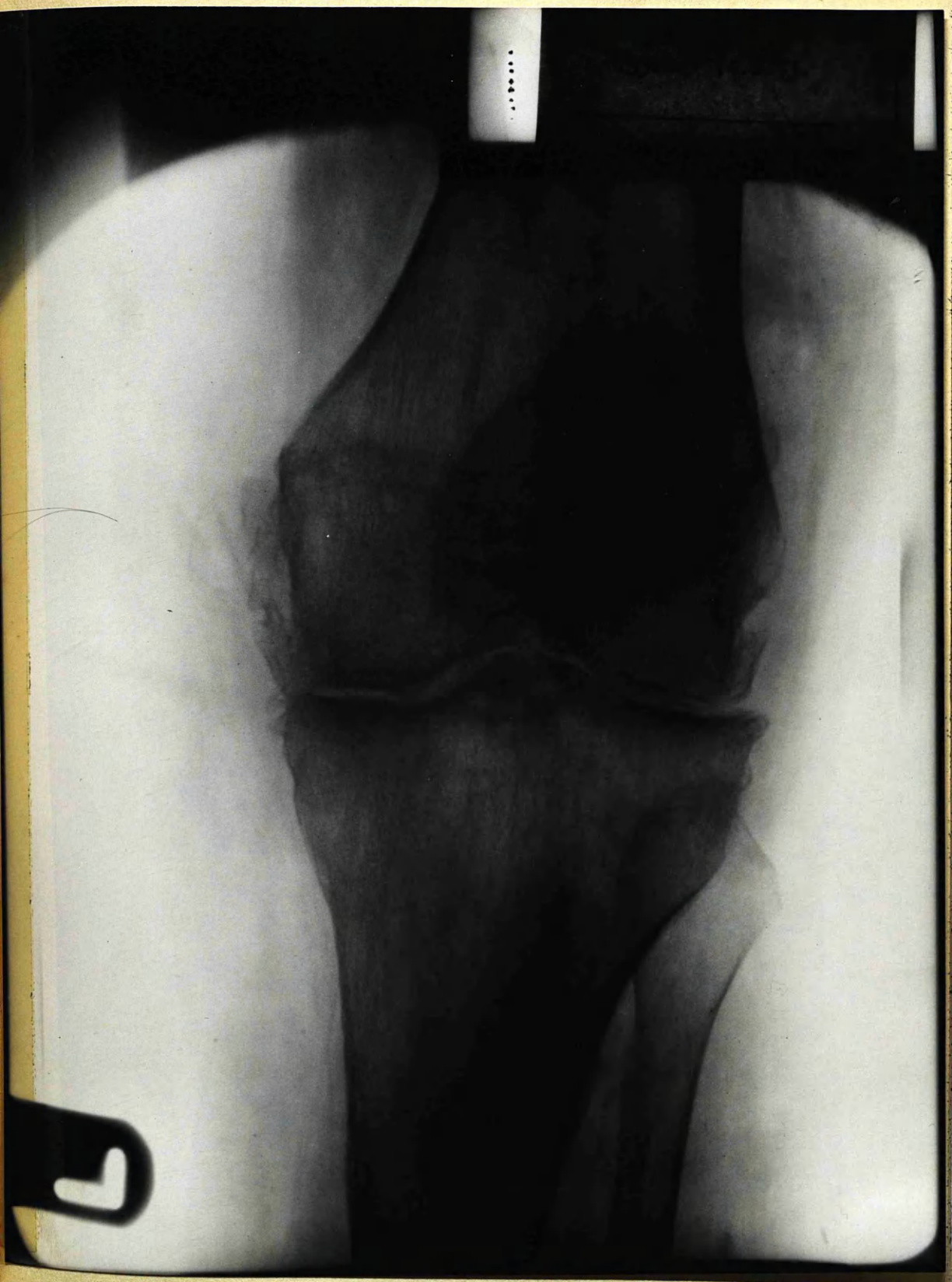
"I am so glad to hear that she has got on so well; I think there can be little doubt that she did not have any lymphosarcoma."

Case 1 still walks curiously like an ape, but she gets along anywhere, and does not use the lift, stairs do not worry her now. She is so happy that she can do all the work of the house and free her daughter to go out and earn her living, and the patient, being a skilled treadle machinist, is working at home to make a little extra money. She still comes each week for her treatment, but does not mind now if circumstances necessitate her losing her injection one week.

The nodules accurately described in the letter from the Cancer Hospital have grown less in size till now there is not one larger than a dried green pea. Her colour is steadily becoming whiter, and the flesh is losing the almost transparent look, becoming firmer and muscular. The spleen in this case was never the size described by Copeman(1948), and it must be said that a case like this seems evidence of Dr. Copeman's contention that Felty's Syndrome may only be yet another manifestation of rheumatoid arthritis and not a separate entity.

The Knees in a case of Advanced Rheumatoid Arthritis.

There is clearly shown the smooth, even erosion seen in such cases, or in Felty's Syndrome. The even erosion is also seen in cases of Degenerative Endocrine Rheumatoid Arthritis.



CASE. 1. No. C. 19500

DIFFERENTIAL SEDIMENTATION TEST.

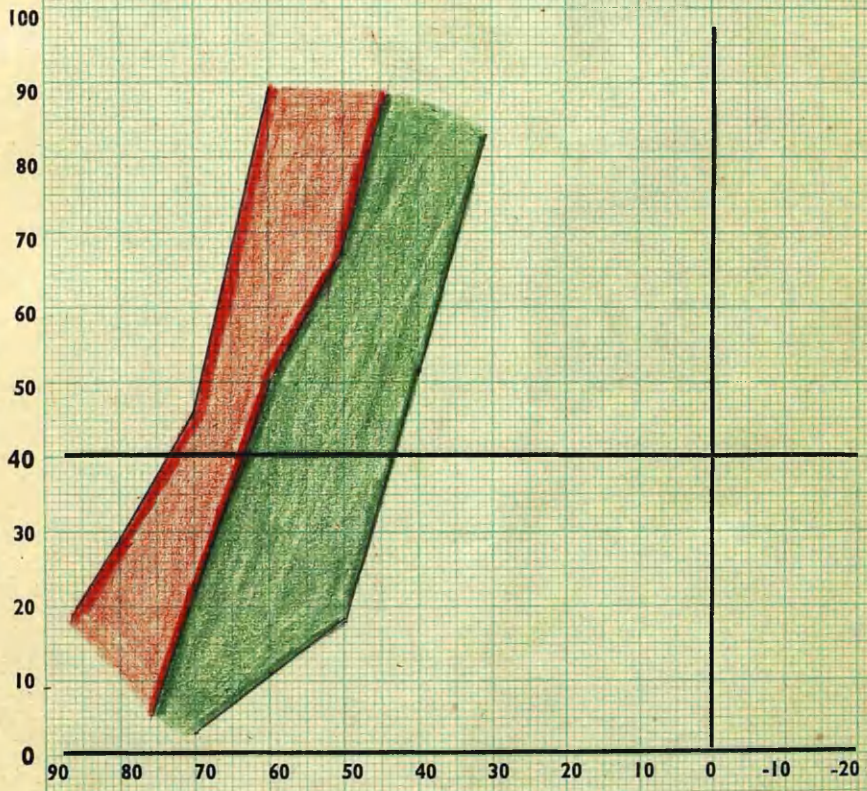
Name DONOVAN TKS Sex, M. F. Age - 66

Date 22.8.50

RESULT: 63% 35/31 = 1:1 No. in Series 1

(0-10. 15/20. 07-1.0 = approximate normal)

Clinical Diagnosis,



M. = 0

from :-

CHARTERHOUSE RHEUMATISM CLINIC,
54-60, WEYMOUTH STREET,
W.1.

CASE. 1. No. C. 23389

DIFFERENTIAL SEDIMENTATION TEST.

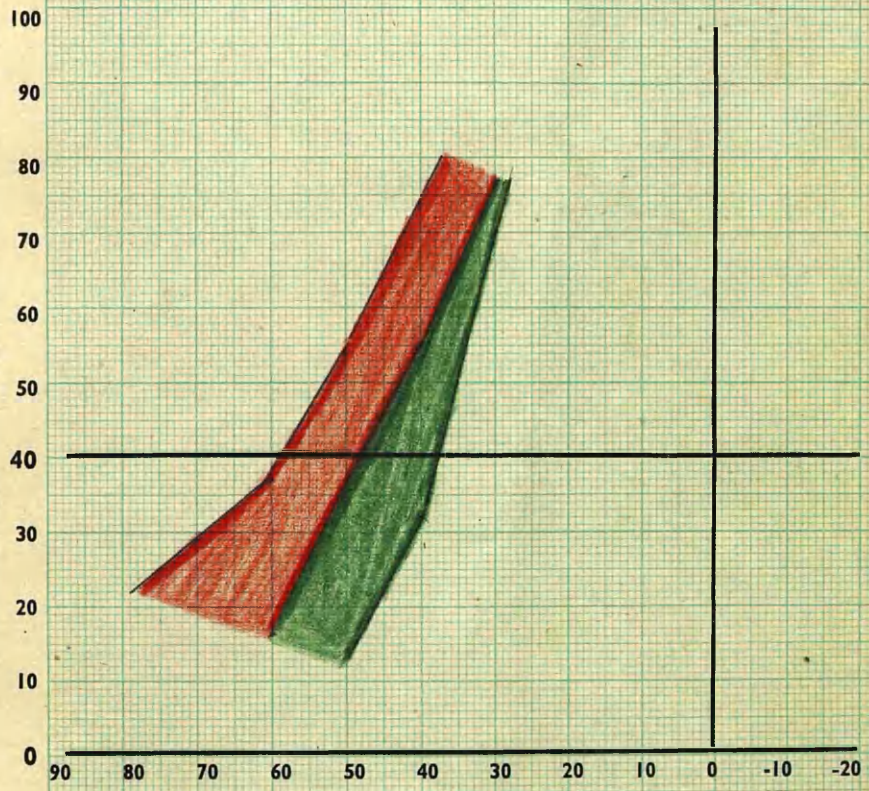
Name DONOVAN Mrs Sex, M. F. Age - 68

Date 12.9.52

RESULT: 47% 21/21 = 1·0 No. in Series 2

(0-10. 15/20. 07-1.0 = approximate normal)

Clinical Diagnosis,



M. = 24

from :-

CHARTERHOUSE RHEUMATISM CLINIC,
54-60, WEYMOUTH STREET,
W.1.

CASE. 1. No. C. 24260

DIFFERENTIAL SEDIMENTATION TEST.

Name DONOVAN TRS Sex, M. F. Age - 69

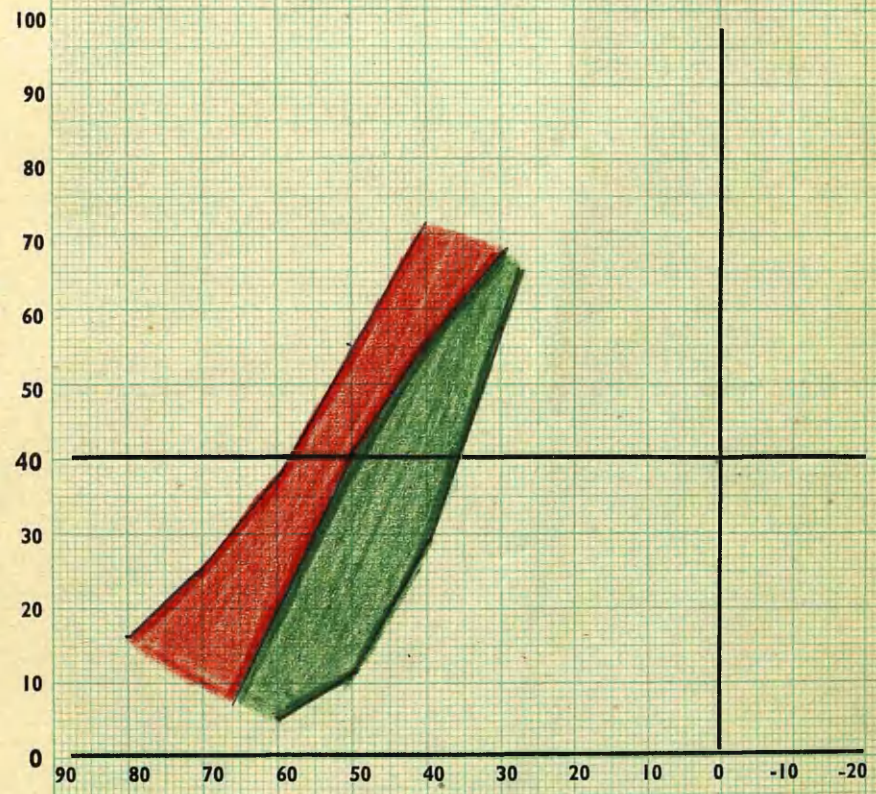
Date 27.2.53

No. in Series 3

RESULT: 50% 14/29 = 0.48

(0-10. 15/20. 07-1.0 = approximate normal)

Clinical Diagnosis,



M. = 26

from :-

CHARTERHOUSE RHEUMATISM CLINIC,
54-60, WEYMOUTH STREET,
W.1.

CASE 2. Aet. 39.

Previous history

This patient commenced menstruation aet 17, and was regular, and with very little discomfort until lately, aet 35, when she notices the menses are becoming irregular, and scanty. She has one daughter aet 8, who is a healthy child and whose D.S.T. shows no evidence of disorder, though the child complains of vague pains in her limbs at times. When the patient was two months pregnant with this child she developed a "lump" in her right hand and the hand was painful. For this she had "electrical treatment". At that time the patient also complained of "burning" and frequency of micturition. The hospital treated her for this also, and as war was on in London at that time they evacuated her to Somerset where her baby was born. The confinement was rather long, labour lasting thirty-four hours, but the actual delivery was normal. While in Somerset she had vaccine treatment with no apparent effect and the gold treatment "nearly killed me", and she was given blood transfusions after. These treatments were instigated while she was carrying the child as the rheumatoid arthritis was steadily gaining ground.

Family History

Her mother is alive and has suffered from ulcerated legs for many, number unknown, years, Her father is still working, but suffers from "rheumatism". There is no further history of serious illness, and the patient cannot go back further in her family history. The patient was the second child, her eldest sister dying of meningitis aet 9. She has five other brothers and sisters and they are all healthy.

Symptoms

The onset was slow, beginning in the hands and shoulders, but she became rapidly worse two months after her confinement. Her knees and feet were next affected and then spread became general with malaise and constitutional disturbances. She was next moved to Harrogate and there she had Spa treatment and a nodule was found and removed from the inner side of her right arm.

Clinical findings

The patient was a severe case of rheumatoid arthritis. She too had had all the usual therapies for this condition, chrysotherapy, physiotherapy, vaccine, etc. She was pallid, badly crippled with the shoulders fast, could not look after herself, had lost all interest in her appearance, damp palms, ulnar deviation,

and the look of the chronic invalid. She came to the Clinic in an ambulance, and was carried into my room. She was in constant pain, and her flesh was soft, almost transparent, but there was no pitting. Her joints were swollen and painful and she never slept through a night, even with the aid of some drug. She seemed to have had them all. The blood pressure was 112/60, the pulse 100, and any exertion made it go faster, though an exact exercise tolerance test was impossible. Her appetite was poor and her appearance that of a poorly nourished person, though her husband was in quite a good job, and the living circumstances quite comfortable. Her home life is happy and both husband and child devoted to her.

Treatment.

The patient had her first injection of adrenaline, six minims, 1:1000, on 17.5.50. There was no reaction beyond the usual immediate shivering, which lasted twenty minutes. After that the ambulance took her home and that week there was less acute pain.

	Before	After 4 hours
White blood cells	6,450	7,300
Polymorphs	59.5	68.5
Lymphocytes	33.5	26.0
Monocytes	6.0	4.5.

(Contd.)

	Before	After 4 hours.
Eosinophils	0.5	1.0 - 73 per mm.
Basophils	0;5	nil
Randolph method.	Total W.B.C. - 5,800	
	Total Eosin - 75	

As is usual the blood was first taken in the Laboratory, then the patient had six minims adrenaline and waited four hours, at the end of that time the blood was again taken for the last test.

By 16.6.50 the patient could move, and there was less pain. The blood pressure was 115/80, and her weight was nine stones, six pounds, six ounces. In spite of what seemed to be adverse, that is the eosinophils rose, the injection of six minims adrenaline was given each week. On 15.7.50 the blood pressure was 110/80, the pulse 96, and the patient could now go for little walks with the aid of a stick and the arm of her husband. The colour was a little better, and the wrists were a little less swollen. One week later, the patient told me she had gone for a little walk pushing her chair, the pain was much less, and confidence in herself was beginning to return. In other words, euphoria was beginning. By August there was the most complete co-operation of the patient. She volunteered

the statement that the day she had her injection her knees were more mobile and she always went for a walk. She felt tired, but expected that as she had been still so long, and she did not mind. By now she had complete confidence in her movements. Exercises were started, and it was startling to see what a tall girl she really was. Her flesh was losing the transparent look, and at much pain, but happiness to herself, muscular power was returning. The blood pressure remained on the average 118/80 and the pulse 90. The patient now walked much further. In September she noticed that her hands were much less swollen and that she could touch the back of her head. This meant a great deal to her as now she could do her own hair and look after herself, proper pride in her appearance appeared, and she began to try to make a frock for her little girl and even for herself. The patient was now doing the greater part of her own work, including her washing. She was no longer dependent entirely on others and that means so much to patients. It is at this stage the patients really feel improvement and they will fight through, though it means much pain as the muscles start again; by now this patient was almost upright in her gait, but her trouble was that she did so dislike the crunching of the bones in the joints as she moved.

25.8.50	Before	After	
Total W.B.C.	5980	6550	
Total eosinophils	111	22	-80%
Sedimentation rate	31/100	37/100	
B.S.R.	29/100 (Corrected)	39/100	
Packed cell volume	41%		

By the end of September the patient was able to have a bath all by herself, the first time for six years. Her hair was now glossy and cared for and she no longer looked ill. The patient explained to me more clearly than other patients that the top half of her body felt much better than the lower. She could grip very well, though there was still some swelling in the knuckles, but the palms of the hands were no longer damp, and the ulnar deviation was less noticeable. But she could not help complaining that it "felt like broken glass" in her knees. The crunching noise and sensation also bother her. Her shoulders were practically free, she could reach with a full reach in her right arm, and only a slight restriction in the left.

In December the blood pressure was 112/80 with a normal pulse of 80.

	Before	After	
W.B.C.	7,500	7,800	
Eosinophils	22	0	= -100%
Sedimentation Rate	37/100	36/100	
P.C.V.	43%		

January is a hard month and she caught influenza, losing thereby three pounds; she could not have her treatment and became very stiff. Her blood pressure fell to 100/60, but on her regular adrenaline again she soon regained the ground which had been lost. In fact in February, 14.2.51. another four hourly test showed this:

	Before	After	
W.B.C.	6,200	6,444	
Eosinophils	11	0	= 100%
Potassium	18.8	16.2	= 2.6
Sedimentation Rate	13/100	12/100	

The Director of the Laboratory reports on the D.S.T:-

"Quite a considerable improvement since September, 1947, and since the last Test in March, 1948 Better now since the inception of test observations in June, 1945. Present position is that only of a chronic O.A. Tissue reactivity factor returned to normal".

I append the original D.S.T. Blood pressure was 120/80, and the pulse was 76, of good volume and steady. In March I found that the dose of six minims did not last the week, so that was increased to eight minims. This seemed to be the right amount, as the patient "lasted" ten days, therefore the dosage was increased to ten minims. This seemed to suit the patient, and she remained comfortable. In June 1951 it was seen very clearly that the time would come when attention must be diverted, the thought of getting some sort of joint cavity with synovial fluid, and cartilage back, before these patients could be released from the permanent discomfort of these crunching joints, and with that in my mind the method of entering the joint spaces and injecting with acid potassium phosphate was tried. This has a certain amount of success, sometimes allied with manipulation. Manipulation alone did not seem to be quite sufficient, as the joint was painful and the patient held it steady, thus the object was defeated. Once more there was a stiff joint. Acid potassium phosphate cannot loosen contractures of tendons, but it can, and often has, opened up joints. (See Warren Crowe (1927)). This realm must be left to surgery at present; but, in time, the technique of making all joints moveable will come. A comfortable and workable

joint with a cartilaginous layer must be obtained.

The patient had various joints injected by this method and is still having her knee injected as necessary. It will be readily understoood that the treatment as far as is possible adheres to a set pattern, but the welfare of the patient must come first, and as Medicine is an Empirical Art, and not an Exact Science, there are discrepancies. In June, 1951, the patient noticed that her periods were excessive and tending to become rather frequent. Five milligrams Progesterone was given each fortnight intramuscularly at the same time as the adrenaline. This appeared to put the matter right as the patient has had no trouble since. In November as the weather became inclement, the patient did not seem so well. This was proved by a four hourly test:

21.11.51	Before	After.	
Eosinophils	133	22	= -84%
Potassium	19.5	17.5	= 2.0
Sedimentation Rate	23/100 no correction	37/100	
P.C.V.	42%		

The patient was questioned more closely, and she told me that about 7.11.51, she had a chill with much diarrhoea, and that after that she did not seem

to be so well. She had not told me as she did not think it had anything to do with her rheumatism and her home doctor had treated her for the condition. It was then obvious that it was not only the inclement weather, but the loss of fluid with the mineral salts which had affected her. This was adjusted and the dosage of adrenaline dropped to six minims per week and again the patient picked up. She went on steadily, but not dramatically improving but it was noticed that in the hot summer weather she was not so well, and she told me she sweated quite a lot, this loss of fluid meant the unbalance of the mineral salts with consequent discomfort to the patient. I have noted that any loss of body fluid causes trouble, especially when using adrenaline.

In October there was another four hourly test done:

1.10.52.	Before	After	
Eosinophils	110	0	
Sedimentation Rate	16/100	19/100	
Potassium	19.7	18.9	= -0.9

On 13.4.53, this patient was asked to come for a thorough overhaul, such as is hardly possible in the time of a busy clinic. The history of her confinement was investigated as she had been worse

during the carrying of a first child. The patient then told me she had been a bus-conductress during the war, and her husband had been in the Forces. She became pregnant, but had managed "to get rid of it", and further added that her husband dated her illness from that abortion. Therefore that is yet another case in which one wonders why the traditional carrying of the first child has not improved the arthritis, only to find out as one gains the confidence of the patient that it is not the first child.

On 13.4.53, the patient walked, as usual now, into the examination room, her hair glossy and elaborately coiffuered, her frock made by herself, to tell me that she is free from pain, except on especially exerting herself, for instance, on white-washing a ceiling. Her ankles are neat, and there is no sign of oedema, further she can wear ordinary shoes. Her knees are slightly flexed, the right knee being more affected than the left, the hips have good movements and she can raise both arms high above her head. The right elbow is still not free, but she has sufficient movement for all practical purposes. There was nothing abnormal found on auscultation of the lungs. The blood pressure was 140/100, pulse 80, regular and good volume. The spleen was not palpable, nor the liver but she has been referred now to a Gynaecologist, as

there is a mass in the right iliac fossa suspicious of an ovarian cyst.

The hands are now dry, and no longer swollen, and the ulnar deviation is nearly corrected, so much so that the patient easily wears gloves which she has not been able to do for several years. The patient continues to come to the Clinic for maintenance doses of adrenaline and progesterone, and so that she continues under supervision with her orthopaedic exercises. She does all her own work and even goes to dances with her husband.

CASE. 2. No. C. 14137

DIFFERENTIAL SEDIMENTATION TEST.

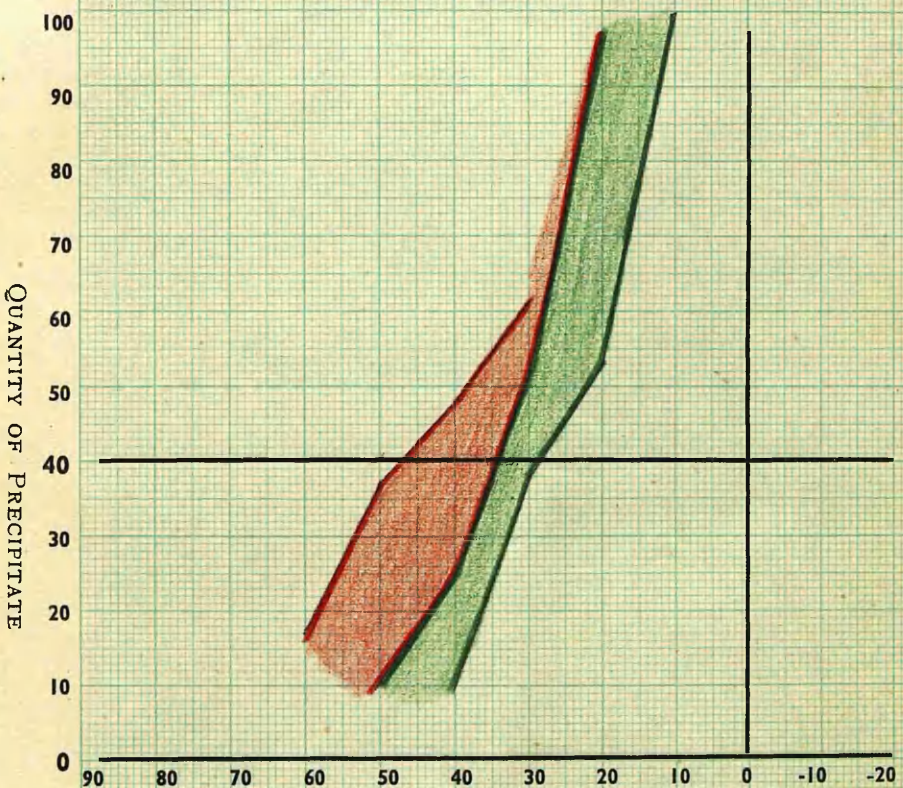
Name WITHERS TRS Sex, M. F. Age - 34

Date 11. 3. 48

RESULT: 34 % 16/13 = 1.2 No. in Series 4

(0-10. 15/20. 07-1.0 = approximate normal)

Clinical Diagnosis,



M.= 0

from :-

CHARTERHOUSE RHEUMATISM CLINIC,
54-60, WEYMOUTH STREET,
W.1.

CASE. 2. No. C. 20420

DIFFERENTIAL SEDIMENTATION TEST.

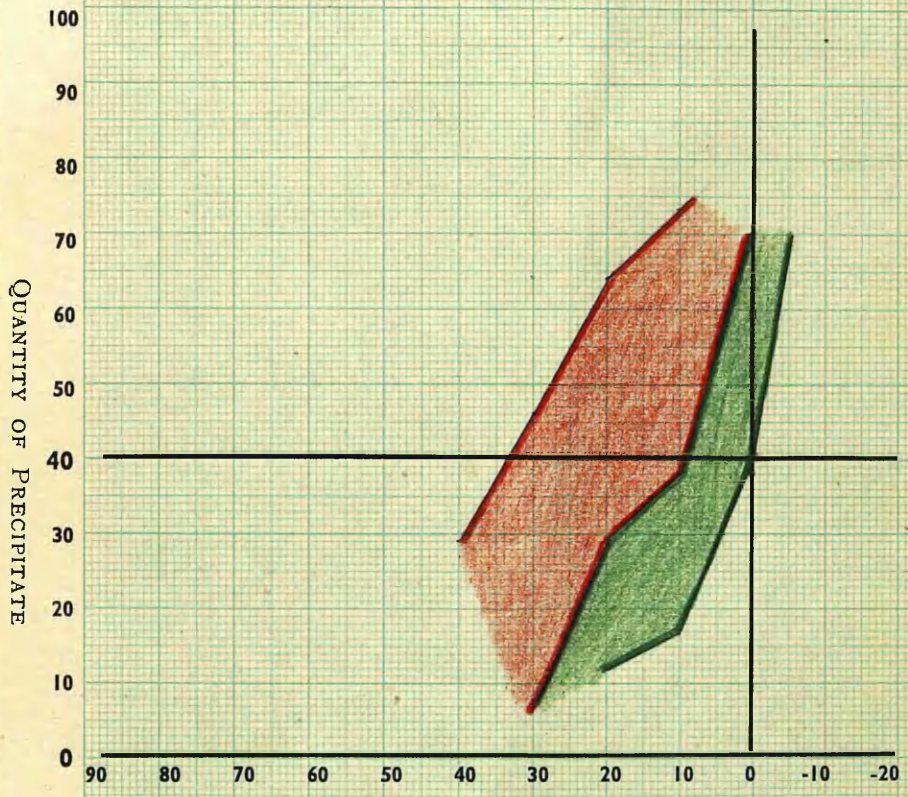
Name WITHERS TRS Sex, M. F. Age -37

Date 21. 2. 51

RESULT: 9 % 34/21 = 1·6 No. in Series 5

(0-10. 15/20. 07-1.0 = approximate normal)

Clinical Diagnosis,



M. = 0

from :-

CHARTERHOUSE RHEUMATISM CLINIC,
54-60, WEYMOUTH STREET,
W.1.

CASE. 2. No. C. 23440

DIFFERENTIAL SEDIMENTATION TEST.

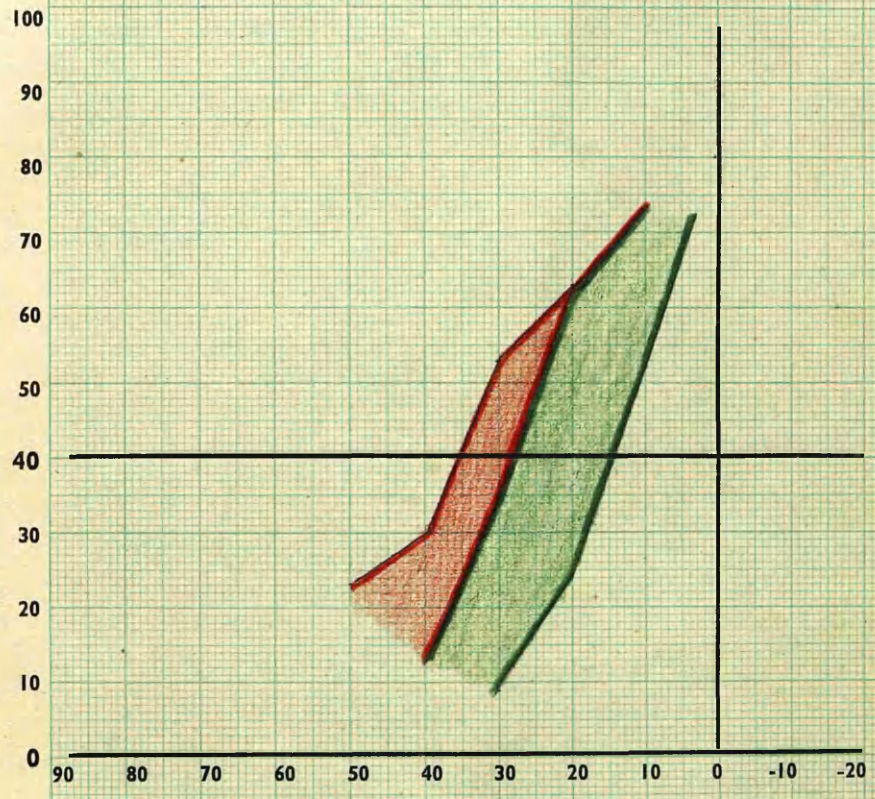
Name WITHERS Mrs Sex, M. F. Age - 38

Date 24. 9. 52

RESULT: 28 % 15/28 · 0·54 No. in Series 6

(0-10. 15/20. 07-1.0 = approximate normal)

Clinical Diagnosis,



M.=

from :-

CHARTERHOUSE RHEUMATISM CLINIC,
54-60, WEYMOUTH STREET,
W.1.

CASE 3 Aet 28.

Previous history

This patient gave a history of only childish ailments, nothing serious. Aged 6 she had her tonsils and adenoids removed. At times she had attacks of bronchitis. Her menses began age 13, and sometimes there was dysmenorrhoea. She married at 27. During this last war she became a W.R.N.S. and served in Harwich in 1941, later she was moved to Egypt, where she served for two years.

Family history

She can only give a scanty family history, her mother is alive and well, and apparently has no ailments. Her father died some years ago of cancer of the stomach. There is no history of asthma, or for that matter of anything else in the family. She was an only child, and her childhood was happy, with some degree of comfort, and enough to eat.

Her married life is happy, and she has two children, twins aged three.

Symptoms

It was in 1947 that the first signs of the disease appeared in the right wrist. The twins were born in 1950 and the pregnancy made no difference to

the disease, but one month after the confinement trouble began in the right knee. The temperament of Case 3 is a nervous one which she tries to hide behind a rather forced laugh, but she has quite a gay disposition, and is not morbid.

Clinical findings

This patient came to the Clinic complaining that her right knee had become stiff during the last three weeks.

Descriptions of her joint deformities by orthopaedic surgeons: Her extremities are always blue and cold, the feet even in summer, especially the right let, a phenomena noticed in so many advanced cases. The other reflexes are present, and some exaggerated, owing to her nervous make-up. The blood pressure was low, 102/64, pulse 98. There was nothing abnormal discovered in the lungs or abdomen. The right wrist was practically fixed, and the mid-phalangeal joints swollen. The right knee was flexed. There was much pain and the D.S.T. points out that it is of a non-articular type. A four hourly test was done, as under:-

	Before	After 4 hours
W.B.C.	8730	10,130
Eosinophils	244	167 = -32%

The test was the Randolph, and the standard six minims 1:1000 adrenaline given.

Treatment

Treatment was now begun on the set pattern , namely six minims 1:1000 adrenaline given subcutaneously once weekly. Gradually the wrist loosened and the pain became less severe, in fact the patient became used to sleeping through the night without any drug. Mr. Alexander Law saw the patient and told me that he considered the condition of the patient too good for operative interference, as the joints were loosening. The blood pressure continued to fall, in fact it was now, 27.9.50, 98/70. But as the action of the heart was adequate, and the patient continued to feel better, treatment was continued.

By 8.11.50, the condition of the patient had improved as well as the joints, in fact better. She now used the wrist in her daily work and could walk quite well, albeit with a bent knee. Another Randolph count was done.

	Before	After 4 hours
Total W.B.C.	9400	8700
Total Eosinophils	130	111 = -15%
Sedimentation Rate	38/100 (1 hr.)	45/100 (1 hr.)
P.C.V.	38%	

The patient continued uneventfully during the winter, then did not seem to be making such good progress, and another test was taken:

	Before	After 4 hours	
Eosinophils	110	110	no change
Potassium	16.6	17.4	+ 0.8
Sedimentation Rate	35/100	37/100	
P.C.V.	42%	39%	

In spite of this report treatment with the adrenaline was continued, as it was thought that she might have lost some fluid owing to an attack of influenza, combined with the effect of the infecting agent, also the end of the winter was in sight, and the resistance of the patient was at a low ebb. 2 mgm. Progesterone weekly was given additionaly, but this had an adverse effect. Alone, the adrenaline in the same dosage, gradually improved the euphoria of the patient, and her blood pressure rose again to 130/100. Then economic factors arose, and in consultation it was agreed that the patient might continue with vaccine under her own doctor, as he was unwilling to give adrenaline weekly.

The patient returned in June, 1952, much worse. Adrenaline was restarted, but there had been considerable further damage to the joints. A report is

appended from Mr. Alexander Law. In November the patient was knocked down by a car and rendered unconscious. There was no bony damage but she was considerably shocked. There was a further consultation with Mr. Law and the treatment was continued as before. In December it was decided to advise the patient to take two tablets of Butazolidine per diem. This has helped her considerably. Progress has been steady, but the patient cannot afford to miss her weekly treatment, and that, with the Butazolidin keeps her free from pain and able to do her daily work. Her circulation is still poor in the extremities, the right knee jerk is still missing, but she is cheerful, and happy with her family. The heart tends at times to be soft, and have a hissing sound, but there is no definite murmur. There is no oedema, nor panniculitis, and the muscles she has are good. The measurement round the quadriceps above the knee on the right side is one and one half inches less than on the left.

CASE 3 Reports.

Right knee and right wrist.

Nature & duration of disease or injury.

Partial ankylosis right wrist came on quite suddenly three years ago. Now has swelling of right knee.

X-ray report

Right wrist

The appearances of the right carpus appear due to an old rheumatoid variety of arthritis, (sub acute arthritis) The proximal now have become ankylosed to the radius, and all the joints are damaged.

The condition seems to be inactive now.

Right knee

The joint space is diminished and the peri-articular soft tissues are swollen, indicating a similar sub-arthritis (or peri-articular inflammation.)

S. R. Reynolds.

21st April, 1950.

History

The problem at the present time is stiffness in the right wrist and knee.

She has improved very much on her special therapy.

She has been treated at this Clinic since May 1950 by means of vaccine therapy and injections of adrenaline.

O/E

Synovial thickening of the right wrist, which is held in some 20° of flexion and 10° of ulnar deviation.

There is a little rock of movement, which is not painful.

Grip is moderately good and there is no gross involvement of the metacarpo-phalangeal or inter-phalangeal joints.

Pronation is carried through 50°

Supination through 75°

Right knee

There is also synovial thickening without any excessive joint effusion.

A little quadriceps wasting with definite weakness.

Patella is movable, though slightly tethered.

Flexion extension is from 50° to 170°.

X-rays

There are arthritic changes throughout the carpus and

wrist joint, but no gross changes in the metacarpo-phalangeal or interphalangeal joints.

With regard to the knee, although there is a narrowing of the joint space the outline is smooth and well maintained.

Opinion

Advise treatment designed to strengthen the quadriceps, particularly exercises and faradism. There is, as yet, no need for operative interference.

31st August, 1950.

On Examination

She walks with a flexed knee on the right side with a considerable limp.

There is marked synovial thickening of the right knee.

Flexion deformity of 30°

Movement from 90° to 150° with some grating.

Considerable tethering of the patella.

Increased heat of the over-lying skin.

Atrophy of the quadriceps.

There is synovial thickening of both wrists with some radial deviation on the left with extension of 30° from flexion of 30°.

Ulnar deviation of 10°.

Right wrist

Synovial thickening is more pronounced.

There is no extension

There is some flexion deformity.

A mere jog of flexion-extension movement.

Slight ulnar deviation.

There is also deformity of the metacarpo-phalangeal joint of the index and little fingers, of the proximal inter-phalangeal joints of the little finger and hyper-extension deformity of the distal interphalangeal joint of the middle finger.

OPINION

To have corrective plasters applied to the right wrist and the right knee.

These serial plasters will have to be changed every three weeks until the final ankylosed position has been reached.

5th June, 1952.

CASE. 3. No. C. 18950

DIFFERENTIAL SEDIMENTATION TEST.

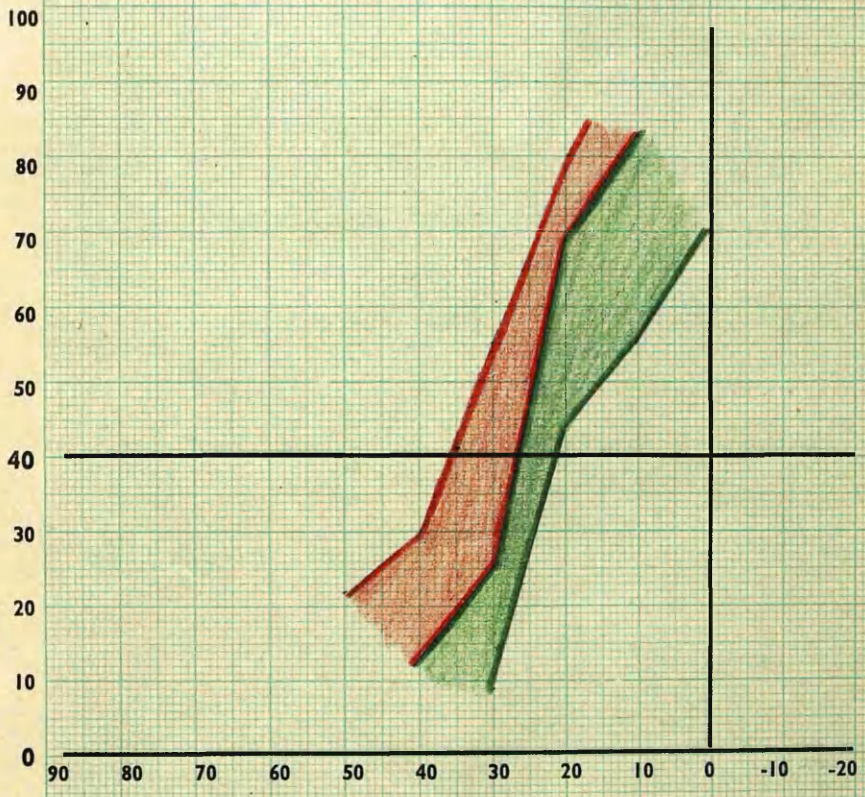
Name BAYLIS Mrs Sex, M. F. Age - 28

Date 5.5.50

RESULT: 26 % 25/17 = 1·47 No. in Series 1

(0-10. 15/20. 07-1.0 = approximate normal)

Clinical Diagnosis,



M. = 19

from :-

CHARTERHOUSE RHEUMATISM CLINIC,
54-60, WEYMOUTH STREET,
W.1.

CASE. 3. No. C. 25057

DIFFERENTIAL SEDIMENTATION TEST.

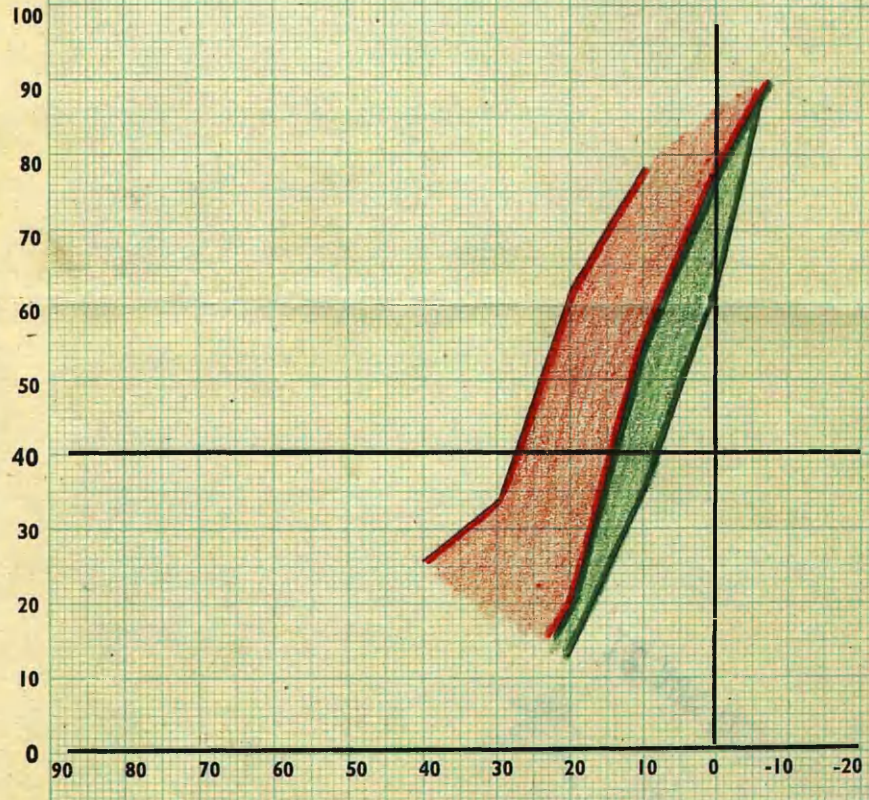
Name BAYLISS Mrs Sex, M. F. Age - 31

Date 7.8.53 No. in Series 2

RESULT: 14% 32/14 = 2·3

(0-10. 15/20. 07-1.0 = approximate normal)

Clinical Diagnosis,



Serum Sedimentation

M. = O

from :-

CHARTERHOUSE RHEUMATISM CLINIC,
54-60, WEYMOUTH STREET,
W.1.

CASE 4. Aet. 50.

Previous history

She gave a history of having had the usual childish ailments, and in her case a naevus was removed when she was three months old. She had several attacks of influenza, and aet. 15 was supposed to have had a "touch of T.B.", following congestion of the lungs. Her menses started at 13 with dysmenorrhoea, and they were scanty. She was married when she was 23, and has had two children, and no miscarriages. The first child was a boy, she carried badly, and had a hard confinement, ending with a forceps delivery. The boy is now 28 and very fit. The other child is a girl, now aged 16, also fit and well, but again she carried badly and had a difficult confinement, but it was not instrumental. Her son is in the Navy, and her daughter at school. Her husband is in regular employment and they seem quite happy.

Family history

Grandparents, paternal, grandfather died of old age, aet. over 95 years. Grandmother, not known. Maternal grandfather died aet. 54 of a "heart attack". Grandmother died aet. 60 of cancer.

The patient's own mother died aet. 66 of cancer of the liver. Her father is still alive

aged 80 and only suffers from a "little rheumatism".
Her place in the family is assfollows:-
Her eldest brother is alive and well, but has "a little stomach trouble".
Her second brother has Parkinson's Disease.
The patient is next with rheumatoid arthritis.
Her next brother died of T.B. aet. 30.
Next a sister who died of T.B. aet. 29.
Next a brother who suffers from "rheumatism".
Lastly, a brother who had T.B. "on the spine when a child". He was in an orthopaedic hospital for five years, and was passed A.1. in this war, serving with the R.A.F.

Symptoms

Six years ago patient complained of rheumatism in the right knee, three months later the left wrist was affected. She has had electrical treatment and physiotherapy with little effect.

Clinic Findings

Her D.S.T. report confirmed the clinic history "Appears to be a severe menopausal rheumatoid type. May be a relapse at the menopause of a previous true rheumatoid arthritis". The report is appended. Her general condition is quite good, but she tends to the type of cushing's syndrome. As usual the

wedding ring finger is most affected. But the mid-phalangeal joints of all the fingers are somewhat affected. There is as yet no ulnar deviation. The feet are flat and the toes are all deviated, but there is no sign of bunion. She has difficulty with the right knee which is swollen and from which, from time to time, we have removed 40 c.c. of fluid. At present there is little free fluid, and she is walking better, but the knee cannot straighten. The quadriceps of that leg is wasted just over one inch. The left wrist is fixed. But in the wrist she has no pain and the hand is quite workable. She is very sensitive to cold and her feet are extremely cold to touch, especially the right, and in this leg there is again no patellar reflex. At the beginning of the treatment in 1950 the blood pressure was always around 115/80. It is now about 140/80. The patient now feels more comfortable in the cooler weather than in really summer weather.

20.4.53. The patient is able to do all her own work, and get about on public transport, though her right knee still is enlarged. Her blood pressure is 140/90 mm. and the pulse 64 per minute. As far as possible, the abdomen was palpated and found normal, except the wall of the abdomen which was tender with [redacted] panniculitis. There is no present history of

bronchitis or other lung troubles. The hands are warm, and mobility is good, and they are working hands; there is only left the resultant deformity of the mid-phalangeal joints from the original onset of the disease. The feet are still flat, but are not painful. They have a poor circulation, but there is no present history of chilblains. In March Butazolidin tablets were added, and it was found that the patient tolerated them well, and sleep was better.

Progress

The patient was encouraged to speak frankly of how this treatment had affected her. Her considered opinion is that she has benefited greatly; hope has come back as the patient has been able gradually to move more freely, and she now takes no aspirins or other similar drugs. In her case, the adrenaline has worked, though there is still much to be done clinically to rehabilitate the patient, as well as to help her with the panniculitis, but it is found that it is not always advisable to diet patients who cannot afford to buy the correct food, especially in winter time. The usual advice now is to diet in summer for these patients, as nourishment is so hard to get.

CASE. 4. No. C. 20103

DIFFERENTIAL SEDIMENTATION TEST.

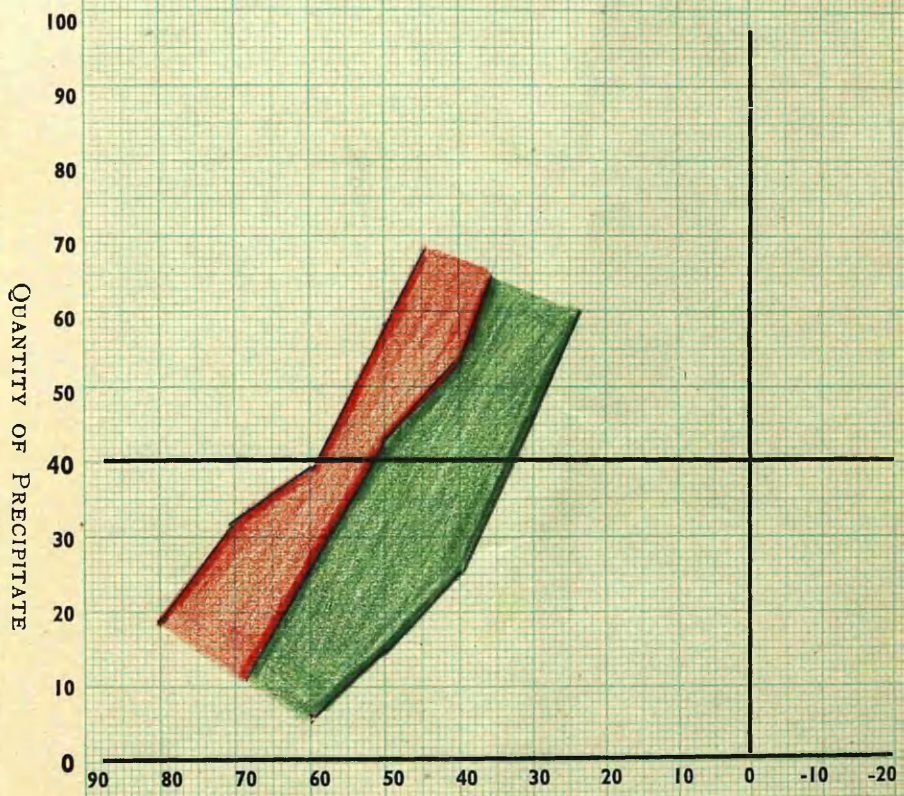
Name LITTLE MRS E Sex, M. F. Age - 50

Date 8.12.50

RESULT: 51% 17/26 - 0.65 No. in Series 1

(0-10. 15/20. 07-1.0 = approximate normal)

Clinical Diagnosis,



M. = 16

from :-

CHARTERHOUSE RHEUMATISM CLINIC,
54-60, WEYMOUTH STREET,
W.1.

CASE. 4. No. C. 23204

DIFFERENTIAL SEDIMENTATION TEST.

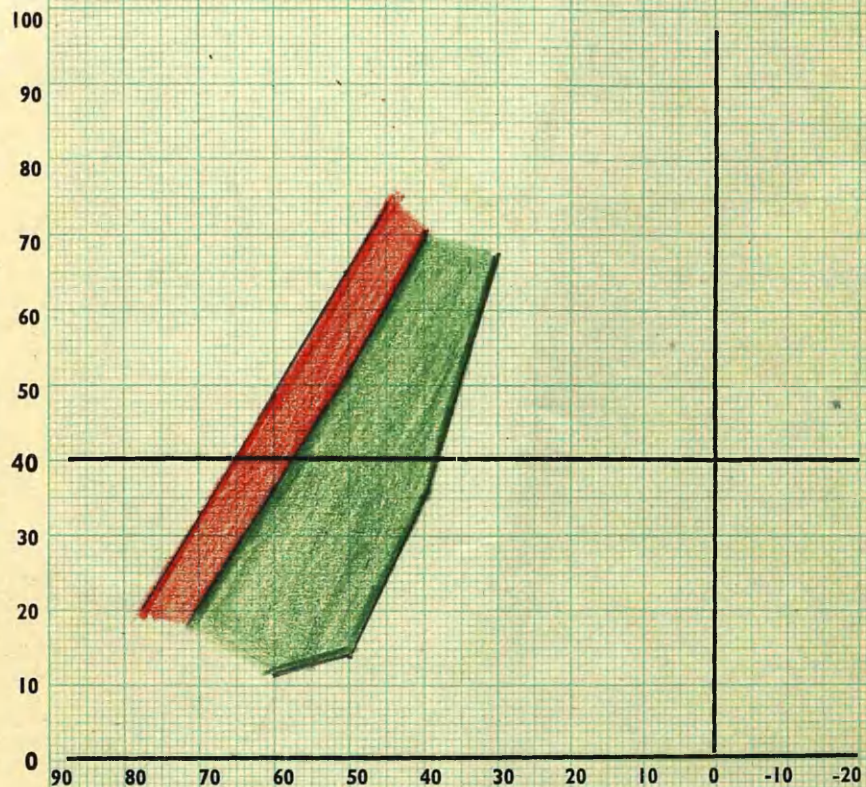
Name LITTLE Mrs Sex, M. F. Age - 52

Date 8.8.52

RESULT: 57% 14/28 · 0·5 No. in Series 2

(0-10. 15/20. 07-1.0 = approximate normal)

Clinical Diagnosis,



QUANTITY OF PRECIPITATE

Serum Sedimentation

M.= 15

from :-

CHARTERHOUSE RHEUMATISM CLINIC,
54-60, WEYMOUTH STREET,
W.1.

CASE. 4. No. C. 24648

DIFFERENTIAL SEDIMENTATION TEST.

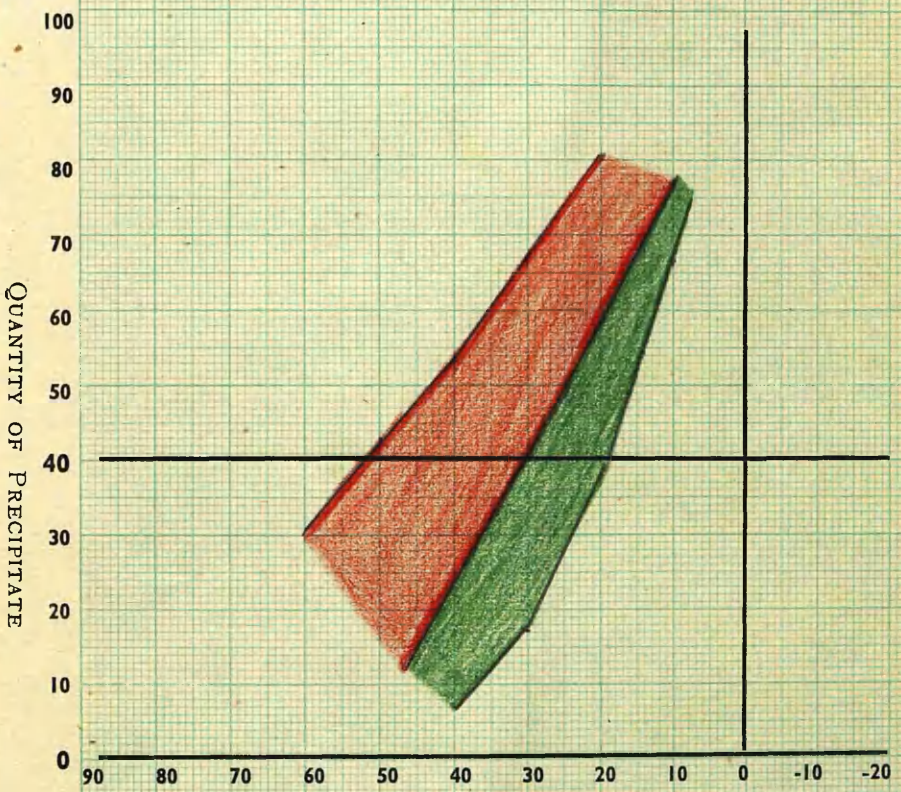
Name LITTLE Mrs E Sex, M. F. Age - 53

Date 8.5.53 No. in Series 3

RESULT: 30 % 27/23 - 1·17

(0-10. 15/20. 07-1.0 = approximate normal)

Clinical Diagnosis,



M. = O

from :-

CHARTERHOUSE RHEUMATISM CLINIC,
54-60, WEYMOUTH STREET,
W.1.

CASE 5 Aet. 27

Previous history.

As a child this patient had tonsillitis every winter. Aet. 7, she had Scarlet Fever. She had the usual childish ailments. Tonsillectomy aet.23.

Family history.

Maternal grandfather died of lock-jaw aet. 80.

Paternal grandfather died aet. 80 'in his sleep'. He had no particular ailments, except that as he grew older he suffered from rheumatism.

Patient knows little more of her family history, but thinks there is no cancer nor tuberculosis in the family. Her mother is alive and well, she had three children (1) the patient, (2) a still-birth, (3) a boy, aet. 15, alive and well.

Symptoms.

The patient gave a very candid and clear history of what in her opinion was the cause of her rheumatoid arthritis, "lack of sleep, too much drink, late hours, and men". Apparently when she was 14 years of age she looked 18. There was a war on and she frankly told me she was "a good time girl". Her mother warned her but she

"lasted exactly 4 years, and one morning I woke up and could not move, my joints were swollen and painful, and I felt awful". That was her exact story. She was eventually sent for hospital attention, after the usual remedies at home had been tried. Chrysotherapy, physiotherapy and all the remedies were tried, without avail, she remained crippled, with slight movement, so tonsillectomy was advised. That had apparently no effect on the course of the disease, so the patient eventually came to the Clinic. From her Record Card there it is seen that she was very sensitive to vaccine, and that the D.S.T. show a steady deterioration, the red field getting big, the sedimentation value high, 46%, for a young girl. Gold sulphide had little effect. In May, 1951, treatment on the lines of this thesis was instituted.

Clinical Findings.

The patient was badly crippled and could not look after herself properly. There were the usual damp palms and fusiform swellings of the mid-phalangeal joints of the fingers, but no definite ulnar deviation. The elbows were set at right angles, and the shoulder-girdle fixed. The knees were swollenaand movement was painful. The feet were swollen and quite flat. The gait was shuffling when the patient was taken from her

wheel-chair. The spleen was not palpable nore the liver, blood pressure 130/100, pulse 100, regular; there was no murmur. After the first 6 mm. of adrenalin the blood pressure came to 118/80, pulse 84, and the patient, after the initial shock, began to feel better.

	Before	After	
Eosin.	44	0	-100%
Potassium	15.0	17.2	+2.2
Sedimentation Rate	42/100	46/100	
P.C.V.	35%		

The treatment of 6 mm. adrenalin administered subcutaneously once weekly was continued, and the patient began to walk, but found taking her coat off still an impossibility, still she began to take an interest in her appearance and her dresses. On 11.10.51 another test by the Randolph four hourly method was carried out.

	Before	After	
Eosin.	156	44	-72%
Potassium	20.6	21.4	+0.8
Sedimentation Rate	42/100 corrected 23/100	45/100	
P.C.V.	31%		

The patient was now walking well, and taking a grip on her life again. 5mgm. Progesterone intramuscularly were also administered each week, and

during the cold weather Priscoll (Ciba) 25 mgms. tablet was advised before the journey by ambulance, and helped the patient considerably. In fact she grew to know when to take a tablet, as she found she could move better when the weather was bitterly cold. The knees were still puffy, but they too could bend and move better, and the swelling of the feet had gone down. The blood pressure was 120/100, and the pulse regular, and of good volume.

Her menses commenced when she was 11-12 years of age, and she suffered with dysmenorrhoea. She had married about three years ago, from the time the special treatment was inaugurated. Her progress was rapid for a case treated with adrenalin so she added to the complications by becoming pregnant. Adrenalin was stopped as soon as she told of her condition and a D.S.T. was taken. The patient "carried" badly, this is contrary to the school of thought which says that the patient "carries" the first child well, and experiences a feeling of well-being. Some members of the Clinic staff remember that it could be possible that this is not the first child, but in view of the patient's frankness to me I hardly cared to ask such a very delicate question.

The Prothrombin time is noted on the chart, and that had been upset so Vitamin K was advised.

The patient volunteered the statement that she 'carried badly until the last six weeks when I never felt better'. I would like to record here that the patient was put on stock vaccine during her pregnancy, and tolerated that well, but when the inevitable relapse occured one month after her confinement, the patient returned to the Clinic and asked for 'the special injection'. She was very certain on that point. The D.S.T. graphs with the Kunkel Test are appended. Her blood pressure remained fairly steady, never rising above 130/100. But it is worthy to note that though the patient feels easier again the D.S.T. shows that the patient is back to the bio-chemical position in which she was before the pregnancy. There are two D.S.T's taken during the pregnancy. One of 9.7.58 and one of 17.11.58. It is interesting to note that in the second D.S.T. the tissue reactivity was showing a probable relapse, even though the patient was feeling better, and this relapse duly occurred.

This case is specially interesting because of the pregnancy, and the effect on the rheumatoid arthritis. This case, and another case (Case 18) later in the series, demonstrate how the gonadotrophic hormones affect rheumatoid arthritis.

CASE. 5. No. C. 18235

DIFFERENTIAL SEDIMENTATION TEST.

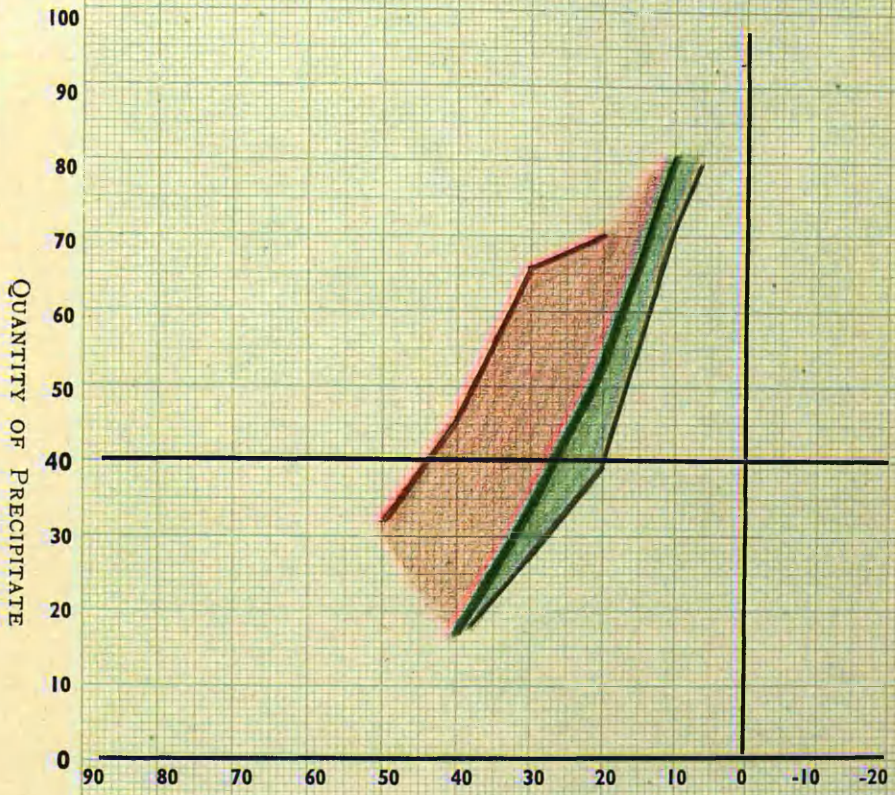
Name NORRIS TIRS V Sex, M. F. Age - 24

Date 18.1.50

RESULT: 27% 27/9 = 3.0 No. in Series 4

(0-10. 15/20. 07-1.0 = approximate normal)

Clinical Diagnosis,



Serum Sedimentation

M. = 6

from :-

CHARTERHOUSE RHEUMATISM CLINIC,
54-60, WEYMOUTH STREET,
W.1.

CASE. 5. No. C. 18663

DIFFERENTIAL SEDIMENTATION TEST.

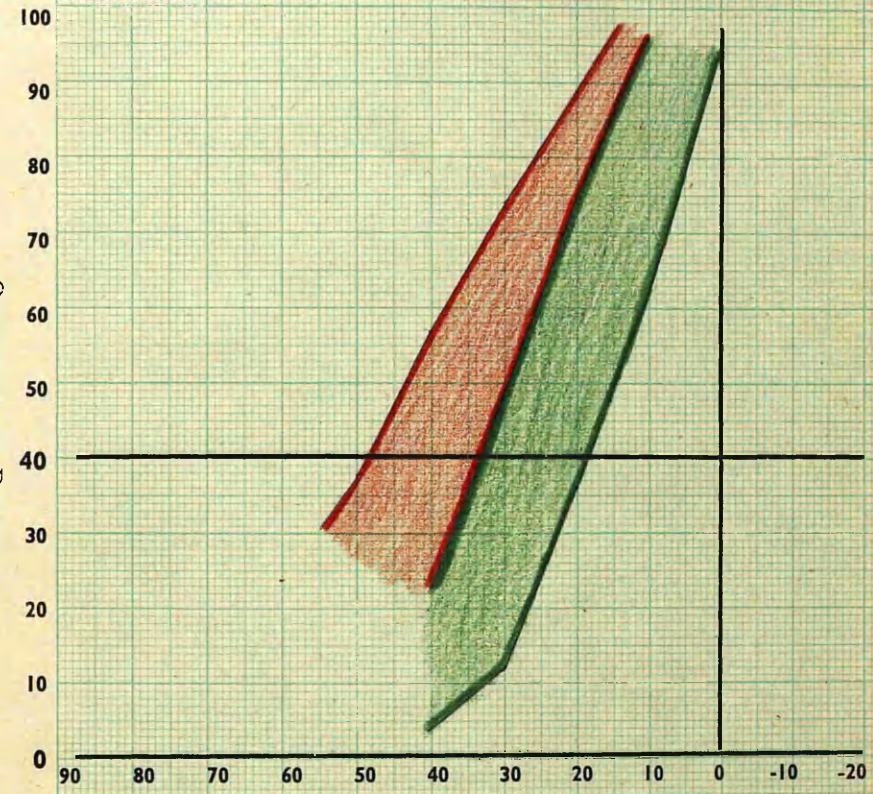
Name NORRIS Mrs V Sex, M. F. Age - 24

Date 22. 3. 50 No. in Series 5

RESULT: 33 % 29/30 = 0.97

(0-10. 15/20. 07-1.0 = approximate normal)

Clinical Diagnosis,



M. = 7

from :-

CHARTERHOUSE RHEUMATISM CLINIC,
54-60, WEYMOUTH STREET,
W.1.

CASE. 5. No. C. 22308

DIFFERENTIAL SEDIMENTATION TEST.

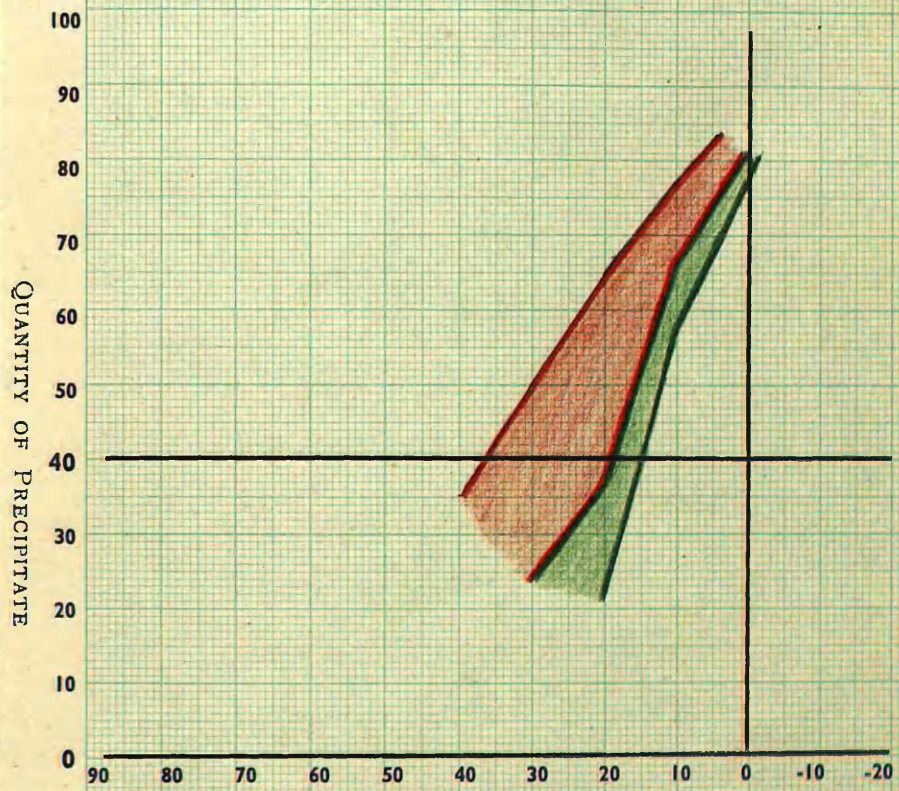
Name NORRIS TRS V Sex, M. F. Age - 26

Date 21.2.52

RESULT: 19% 27/15 = 1·8 No. in Series 6

(0-10. 15/20. 07-1.0 = approximate normal)

Clinical Diagnosis,



M.= //

from :-
CHARTERHOUSE RHEUMATISM CLINIC,
54-60, WEYMOUTH STREET,
W.1.

CASE. 5. No. C. 23073

DIFFERENTIAL SEDIMENTATION TEST.

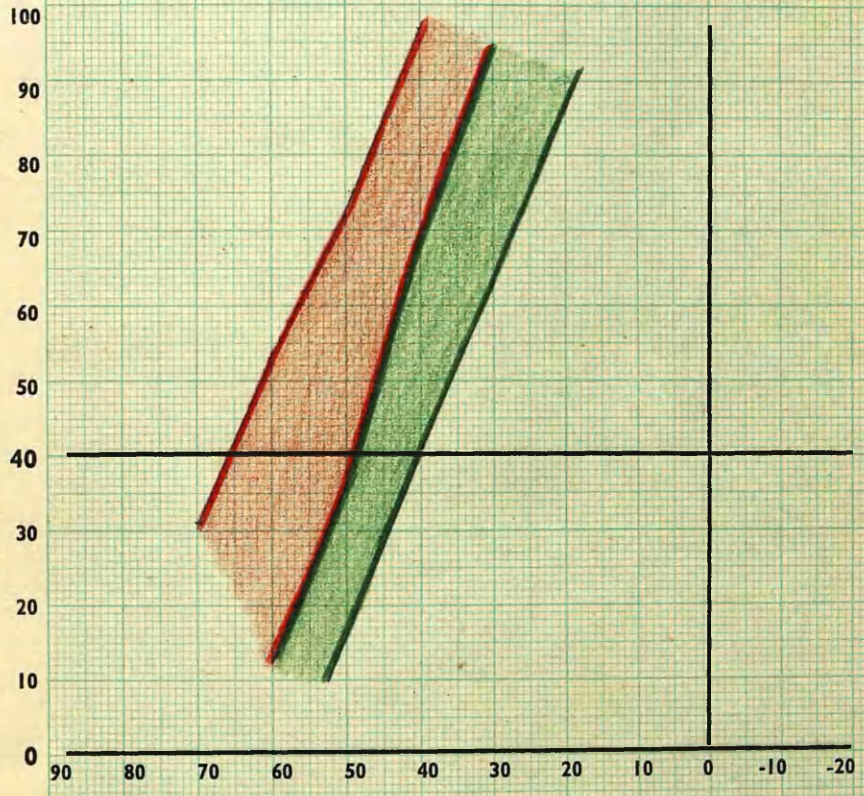
Name NORRIS Mrs V Sex, M. F. Age - 26

Date 9. 7. 52

RESULT: 49 % 35/21 = 1·67 No. in Series 7

(0-10. 15/20. 07-1.0 = approximate normal)

Clinical Diagnosis,



M. = 22

from :-

CHARTERHOUSE RHEUMATISM CLINIC,
54-60, WEYMOUTH STREET,
W.1.

CASE. 5. No. C. 23770

DIFFERENTIAL SEDIMENTATION TEST.

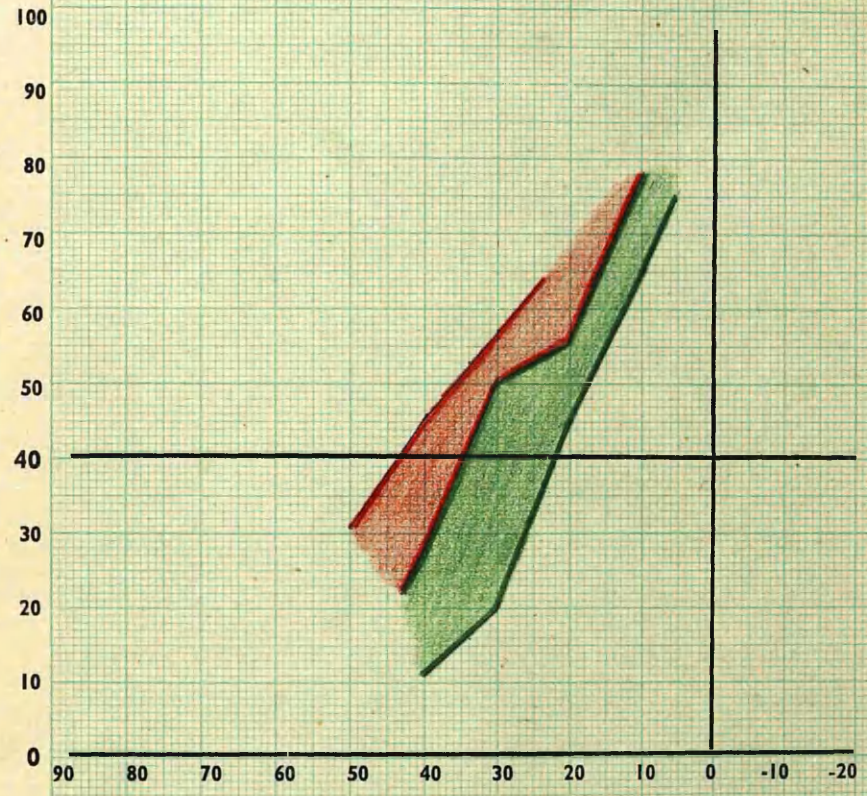
Name NORRIS TRS V Sex, M. F. Age - 26

Date 17. 11. 53

RESULT: 34 % 13/24 - 0·54 No. in Series 8

(0-10. 15/20. 07-1.0 = approximate normal)

Clinical Diagnosis,



M. = 10

from :-

CHARTERHOUSE RHEUMATISM CLINIC,
54-60, WEYMOUTH STREET,
W.1.

CASE. 5. No. C. 24357

DIFFERENTIAL SEDIMENTATION TEST.

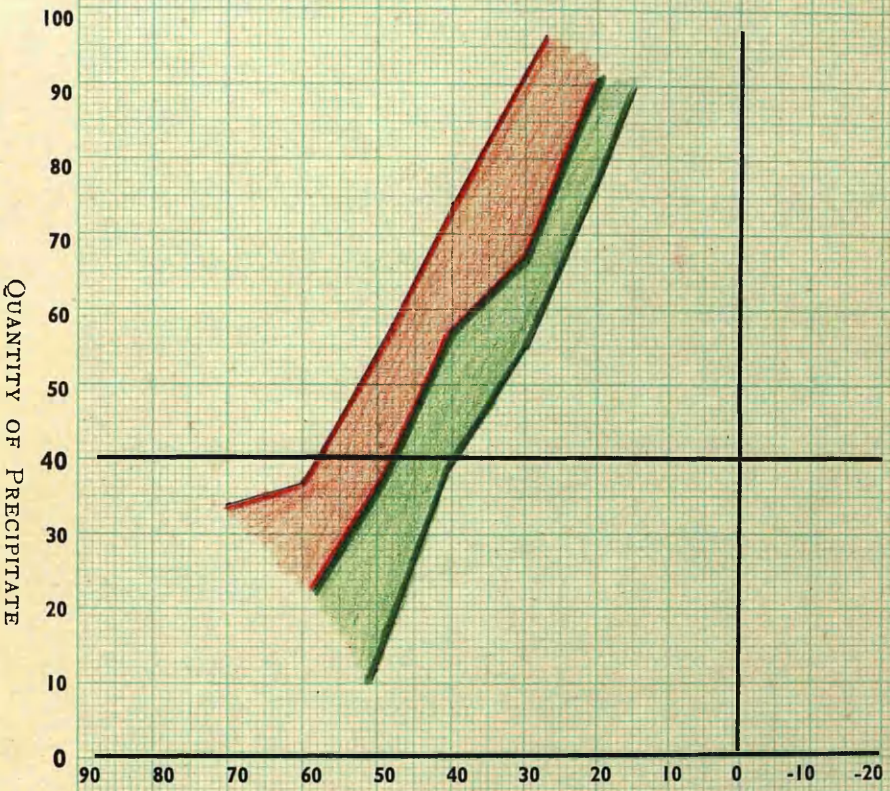
Name NORRIS Mrs V Sex, M. F. Age - 27

Date 13. 3. 53

RESULT: 48% 18/22 = 0·82 No. in Series 9

(0-10. 15/20. 07-1.0 = approximate normal)

Clinical Diagnosis,



M.= 11

from :-

CHARTERHOUSE RHEUMATISM CLINIC,
54-60, WEYMOUTH STREET,
W.1.

CASE 6. Aet. 60.

A female patient, unmarried, who had been a patient of the Clinic for some time.

Previous history.

There was no history of childish ailments, in fact she had been a very healthy little girl. The menses commenced aet. 13, and in her late 'teens the time between menses became three weeks, previously that had been the normal four weeks. The menses lasted 7-10 days, leaving only about 15 days clear, this lasted until the menopause set in. She suffered from dysmenorrhoea, and later on, from approximately 18-30 years the menses were accompanied by bilious attacks. When the bilious attacks finished she noticed that she suffered from boils and carbuncles, that worry made these worse and that they coincided with the menstrual cycle.

Family history.

The patient was adopted by an aunt and knows very little of her family history. Of her father there is little known, except that his mother lived till she was 84 years. She thinks that her father died of 'smoker's heart' aet. 63. Her mother suffered from asthma. This patient was a secretary stenographer, and parries questions most adroitly. All she will allow is

that she has suffered from "great mental strain" from time to time

Symptoms

The menopause was aet. 55, and classical rheumatoid arthritis set in then. Three months before the war, i.e. in 1939, she had had a stiff neck, this she attributed to working in a draughty office, and for this she received electrical treatment at St. George's Hospital, London. This crepitus has never really left her. The patient was in London during the Blitz, but only had one night in a shelter. She is a quiet reserved type. In 1948, pain in the shoulder really began, followed by pains in the hands, and the right leg. Again electrical treatment was tried. This time with no good result. Within in six months the left leg was affected as was all the body, but the boils had stopped.

The rheumatoid arthritis was really at the worst peak about 2-3 years after the menopause, and during that time the patient admits to many worries in business and at home. Previous to the special treatment being instituted the patient had had treatment at Hospital, and in the Clinic. Vaccines had been tried, also chrysotherapy, in its many forms but there had been little success.

The patient carried the anxious worried facies of the rheumatoid arthritic patient, her gait was slow and shuffling, she could not walk properly. Blood pressure was 140/90, pulse regular but soft. There was a soft blowing systolic murmur, the apex beat was on the nipple line. The abdomen was rather tender, and the liver was one finger's breadth below the costal margin. As she was so tender and could not relax properly exact palpation was difficult but the spleen was palpable, and tender. There was tenderness in both iliac fossae, the right one more than the left. The shoulders were fairly fixed and the patient could not do her own hair nor take off her own coat. There was restriction of the head towards the left and much crepitus. Ulnar deviation was slight, but the hands were swollen and damp and painful. The lungs were clear and there was no history of cough. The back was stiff, and the patient was beginning to attain the 'sitting-chair' position.

On 20.10.50 a Randolph count was taken as well as a D.S.T.

	Before	After	
Total W.B.C.	7300	9300	
Eosin.	110	44	-60%
Sedimentation Rate	19/100	25/100	

D. S. T. result appended. In the ensuing weeks the blood pressure did not very much, perhaps 138/100, the pulse rate about 90-84. But the swelling of the wrists began to get less, and the pain in the hands was definitely less. Sometimes this patient had as little as 3 mins. 1-1000 adrenaline weekly, but improvement continued. The smaller dosage was very occasionally given to see the effect. Otherwise the dosage is the standard dosage of 6 mins. 1-1000 adrenalin. Thus she has been left on the standard dose of 6 mins. 1-1000.

On 31.8.51 the patient told me she was walking in the Park and doing her small washing, and was completely independent. Confidence, and with confidence, euphoria was a happy symptom. It was decided to have another four hourly test taken.

	Before	After	
Eosin.	44	0	-100%
Sed. Rate	28/100 corrected 24/100	27./100	
Potassium	20.0	19.2	-0.8
P.C.V.	40%		

5 mgm. of Progesterone was again tried intramuscularly and now the patient did well with this and her adrenaline subcutaneously once weekly. Progress was steady and another recount was taken on 8.1.52.

	Before	After	
Eosin.	44	0	-100%
Sed. Rate	14/100	29/100 corrected 87/100	
Potassium	22.4	20.4	-2
P.C.V.	41%		

"ought to be a good deal better" (Dr. Coke)

A D.S.T. was taken at the same time and is appended.

The patient was now so much better that it was felt safe to leave off the Progesterone which the patient had had from 27.4.51, and progress has been steady to this day, the patient walks unaided, and without a stick, loves new clothes and takes pride that she can stand upright and 'look nice, like any one else'. In other words she is no longer an invalid. She can kneel on her knees to do her packing, and within her own limitations leads an ordinary life. She still needs her adrenalin and when she has been on holiday is quick to return to the Clinic for her 'dose'. She has lost weight and can wear the clothes she wore before her illness. The abdomen is not so tender, nor the pains on palpation in the iliac fossae. The liver is not palpable, the spleen is doubtful. There never was any glycosuria, nor albumen. As there was some panniculitis present the

the fluids were restricted, also the use of salt, except in the actual cooking, carbo-hydrates were cut down.

Progress and some clinical findings.

Progress was as usual fairly rapid at first, and then the period of 'stale-mate' was reached. By 3.11.50, the periods of sleep were longer, and she was not so sleepy in the day-time. The patient could now take 6 mins. 1-1000 adrenalin once weekly quite well, the blood pressure remained 140/100, pulse 84. It is in common with all the patients treated, with Cortisone, A.C.T.H. or adrenalin that she said 'the top half' of her body was getting better first. By 19.1.51, the patient was complaining that she only lasted 2 days in comfort. The blood pressure was 138/100 and the pulse 78. Clinically it was decided to give her Potassium, so she had Pot. Bicarbonate gr.5, tablets thrice daily. This appeared to help her and a further four hourly test by the Randolph method was taken, because it was thought the potassium balance was wrong and biochemically the last test had proved it.

9.2.51.	Before	After	
W.B.C.	6288	7066	
Eosin.	22	0	-100%
Sed. Rate	a.13/100 b.17/100	19/100	
Serum Potassium	17.7 mgm.	17.8 mgm%	↑0.8
Serum Sodium	325 mgm.%		

That the patient had needed potassium was proved by this test.

The patient was now taking 10 mins. 1-1000 adrenalin once weekly. The progress was tedious and local remedies were now applied to the painful joints, such as local injections into the joint cavity itself. The patient now found she could walk up stairs by herself, cut up her food, and do her own hair. All these small things helped her to regain confidence in herself. The reaction to the adrenalin began to manifest itself in headaches lasting for days after the injection so the dose was dropped to 6 mins. These unpleasant symptoms disappeared. This patient did not do well on progesterone. There were always unpleasant symptoms when this was tried,

CASE. 6. No. C. 19875

DIFFERENTIAL SEDIMENTATION TEST.

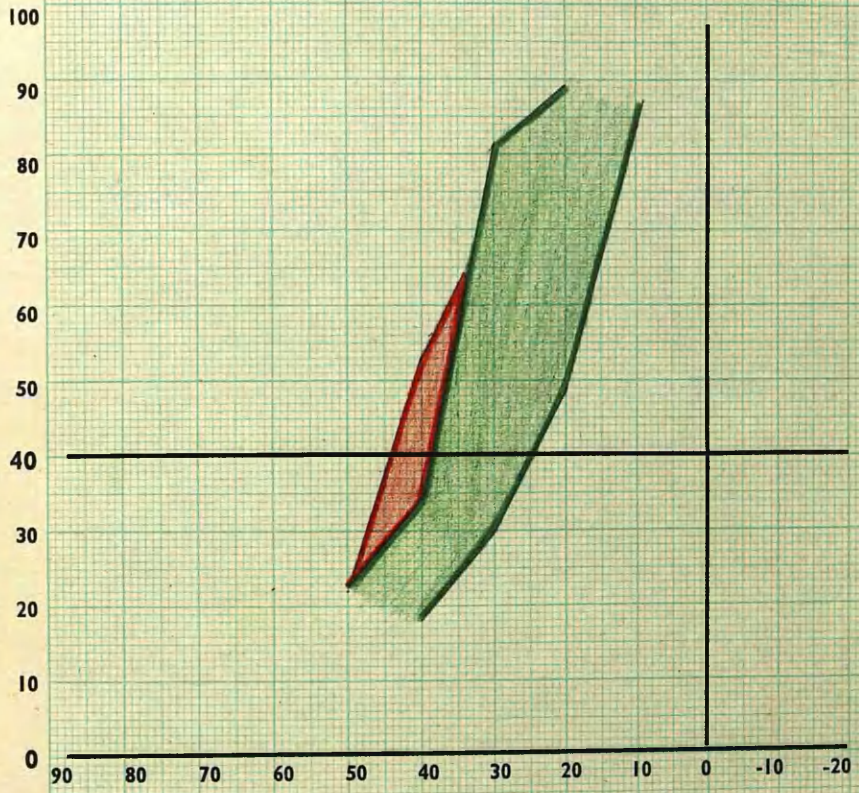
Name ELLIS Miss Sex, M. F. Age - 60

Date 27.10.50

RESULT: 39 % 16/21 .076 No. in Series 1

(0-10. 15/20. 07-1.0 = approximate normal)

Clinical Diagnosis,



M. = 16

from :-

CHARTERHOUSE RHEUMATISM CLINIC,
54-60, WEYMOUTH STREET,
W.1.

CASE. 6. No. C. 22192

DIFFERENTIAL SEDIMENTATION TEST.

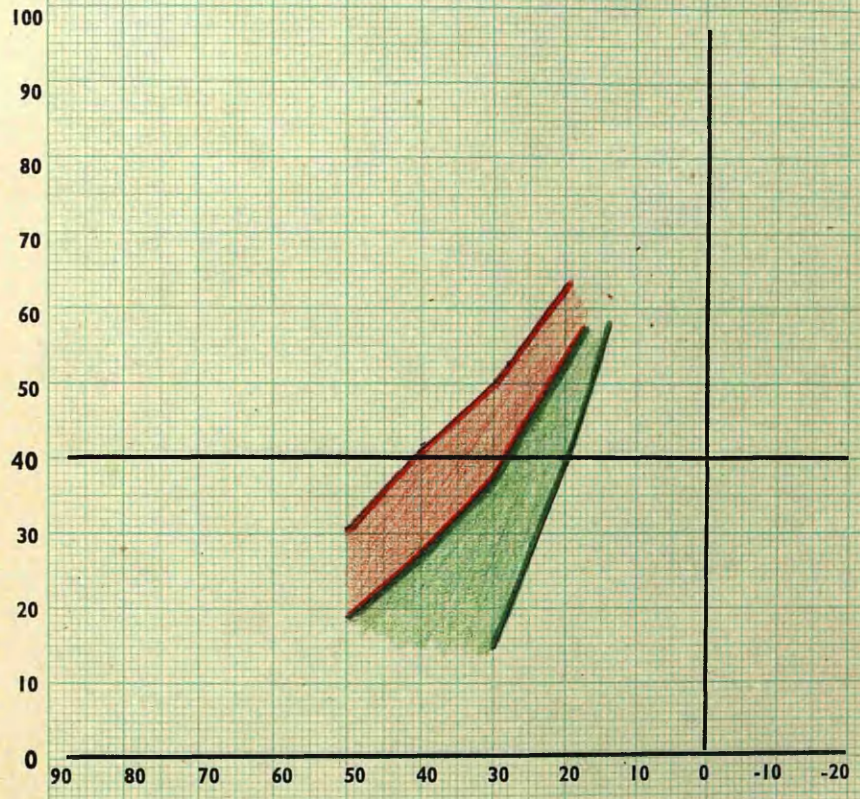
Name ELLIS Miss Sex, M. F. Age - 62

Date 25. 1. 52

RESULT: 28% 13/21 · 0·6 No. in Series 2

(0–10. 15/20. 07–1.0 = approximate normal)

Clinical Diagnosis,



Serum Sedimentation

M. = 40

from :-

CHARTERHOUSE RHEUMATISM CLINIC,
54-60, WEYMOUTH STREET,
W.1.

CASE. 6. No. C. 23346

DIFFERENTIAL SEDIMENTATION TEST.

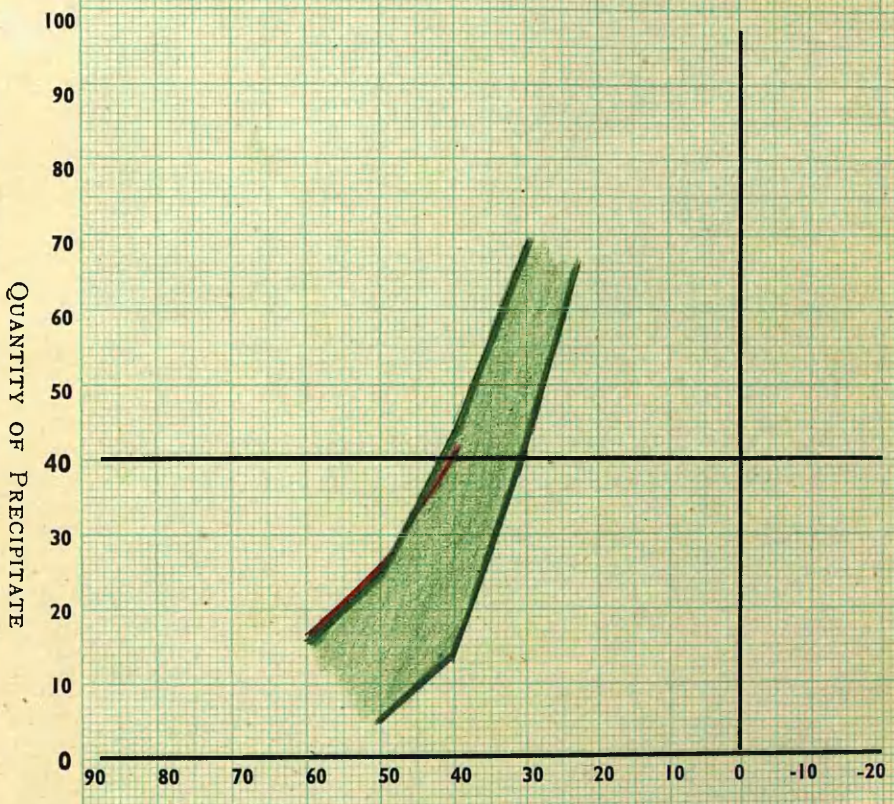
Name ELLIS Miss Sex, M. F. Age - 62

Date 5.9.52 No. in Series 3

RESULT: 42% -2/28

(0-10. 15/20. 07-1.0 = approximate normal)

Clinical Diagnosis,



M. = 23

from :-

CHARTERHOUSE RHEUMATISM CLINIC,
54-60, WEYMOUTH STREET,
W.1.

CASE. 6. No. C. 2435

DIFFERENTIAL SEDIMENTATION TEST.

Name ELLIS Miss Sex, M. F. Age - 63

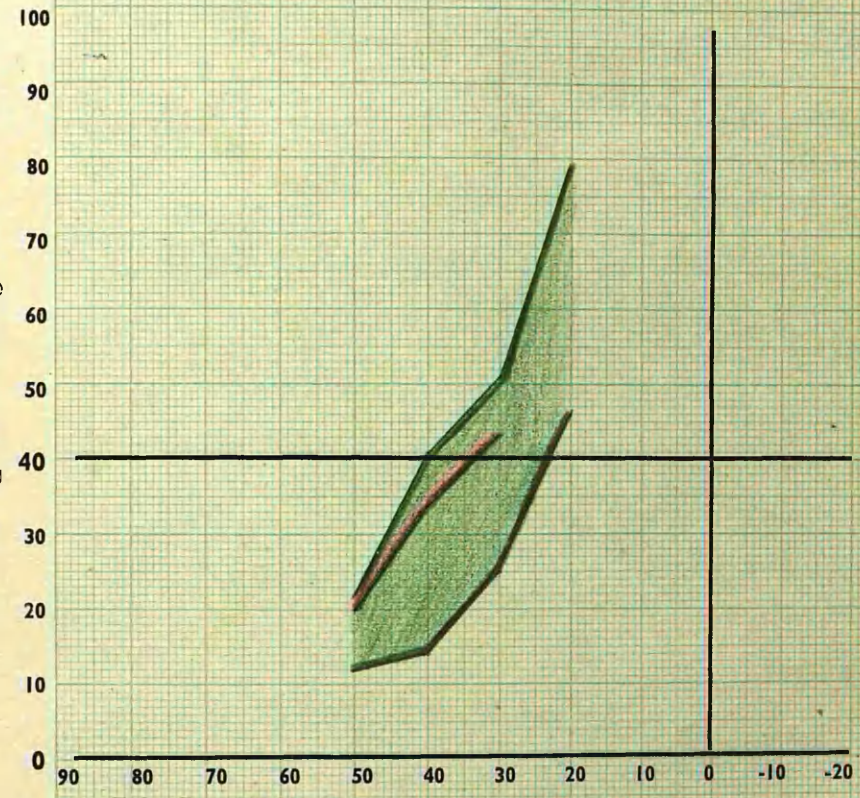
Date 6.3.53

No. in Series 4

RESULT: 41% -7/26

(0-10. 15/20. 07-1.0 = approximate normal)

Clinical Diagnosis,



QUANTITY OF PRECIPITATE

Serum Sedimentation

M. = 23

from :-

CHARTERHOUSE RHEUMATISM CLINIC,
54-60, WEYMOUTH STREET,
W.1.

CASE 7. Aet. 22.

Female patient.

Previous history.

This patient had the usual childish ailments, also a septic gland in her neck which had to be excised aet 2. Her menses commenced aet 12-13, with dysmenorrhoea. The patient got married aet 18.

Family history.

Her mother's father died early, and nothing is known of him. His wife is still alive but 'very old'. There is no history of ill-health. The patient's father is alive but suffers from malaria and catarrh contracted in World War 1. Her mother is also alive, but had an abscess when the patient was born, and 8 years ago had another abscess. No further family history can be elicited.

Symptoms and progress of the disease.

The patient was well until 6 months after her confinement. She had the baby aet. 20, as 'they had decided to wait'. The confinement was normal, and she fed the baby for 5 months. One month later the index finger of her right hand began to swell,

and be painful. From there it fairly rapidly spread all over her body. She was sent to hospital, and admitted, there she received 'heat' treatment, and other forms of apparently physiotherapy, but all to no effect.

On her arrival at the Clinic two years after the beginning of the disease the wrists were fixed. The mid-phalangeal joints had the typical fusiform swelling, and the gait was painful and shuffling. The feet were so swollen that the patient could not wear proper shoes, but had some home-made sandals on, in which she shuffled along. The hips were free, and she could move her knees, but with difficulty, especially if she had been sitting still for any length of time. There was the anxious look on her face, there was no panniculitis, rather emaciation, and she gave a history of loss of appetite. The blood pressure was low, 100/90, no oedema of the ankles, the pulse regular, 88. This patient had a systolic murmur. Exercise tolerance tests were satisfactory, it was only on continued exertion, such as a long day with the baby that she experienced breathlessness. In this case adrenalin was marvellous, as after the second week, that is after two injections of 6mins 1-1000 adrenalin she experienced a sense of euphoria, and could actually clench her fists.

The D.S.T. is appended. This patient could not wait for the four hourly test.

By 5.9.52 this patient was so recovered that she told me she was going to Scotland with her husband and baby for a holiday. She did well but in November, with the bad weather there was a slight relapse with chest pains. There were no clinical sounds, and a further D.S.T. was taken, and is appended. Gold Sulphide (Crookes Collosal) 0.025 strength, 0.2cc was given each week intramuscularly, the patient did well and Butazolidine, two tablets daily was advised. The patient now wears her ordinary shoes, and is learning to pick up her feet and walk properly again. She is in no pain, and sleeps and eats well. The wrists are still fixed but she adapts herself to that condition and as the disease grows less it is hoped to loosen them for her, by local injection. She has full use of her hands and there is no ulnar deviation, though the fusiform swellings remain. She is in full charge of her household, and baby, living her ordinary life and she will soon be on the discharge sheet, it is to be hoped. But she is young, and there is the question of another baby, hence the change of treatment.

CASE. 7. No. C. 23045

DIFFERENTIAL SEDIMENTATION TEST.

Name TUCKEY Mrs J Sex, M. F. Age - 22

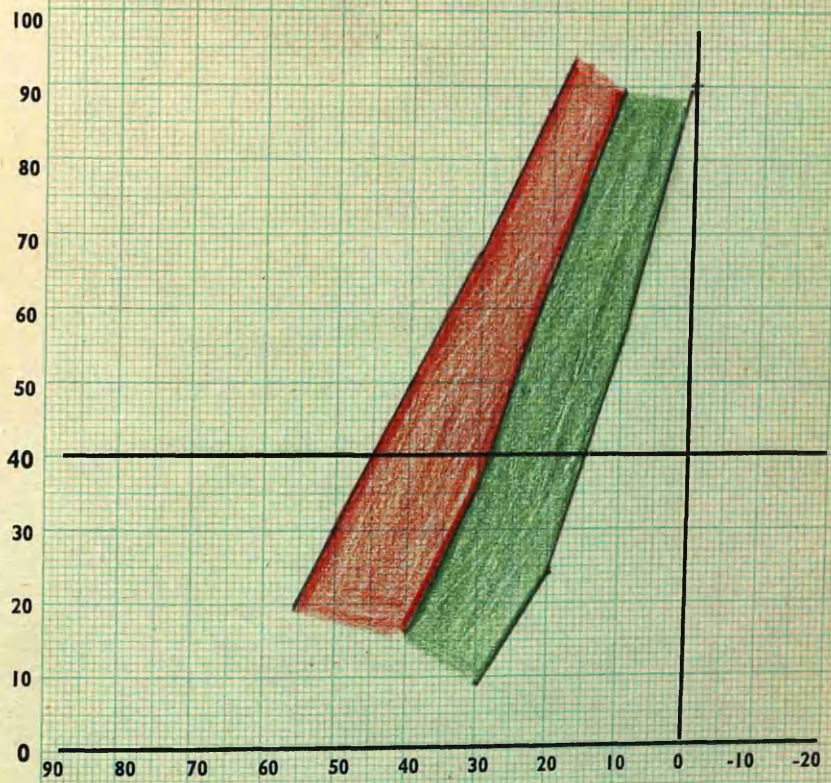
Date 4.7.52

No. in Series 1

RESULT: 28 % 32/28 = 1·14

(0-10. 15/20. 07-1.0 = approximate normal)

Clinical Diagnosis,



M.= 8

from :-

CHARTERHOUSE RHEUMATISM CLINIC,
54-60, WEYMOUTH STREET,
W.1.

CASE 8. Aet 50.

Female patient.

Previous history.

This patient had the usual childish ailments, nothing serious, and no operations, in fact she was a very healthy child. She did have one attack of tonsillitis, but it was not considered sufficiently serious to warrant tonsillectomy. She has never been in hospital in her life. Her menses commenced aet. 15, with some pain at times hardly sufficient to call it dysmenorrhoea. She had a perfectly normal menopause aet. about 42.

Family history.

Little is known of this, her mother died aet. 68 of heart failure, and had been ailing for some time before after a fall in which she hurt her back. Her father died of cancer of the throat.

Mother's family.

Patient's eldest sister died "mental" in her fifties.

Second sister died of cancer of the stomach in her fifties.

Then patient

Third sister died of meningitis aet. 6

Brother had operation for duodenal ulcer, suffers from heart trouble.

Sister died of T.B. aet 29.

Sister died of T.B. aet 30.

Brother suffers with his heart, ? due to the War.

Progress and symptoms.

The patient attributes her disease to the deaths of her two sisters within one year. She found that very hard to endure. Also that brought a feeling of unrest into her home, and what she vaguely describes as "trouble". The patient herself had one son aet. 34, he is married and has two healthy children, But he suffers from "a slipped disc".

The patient was in London during the Blitz, but never went into cellars, she admits that one night it was so bad she stood at the top of the cellar steps, and wondered. Then in 1945 she had a pain in her knee. The fingers followed, and then the rest of the body.

This patient is especially interesting in that she was said to have developed the

typical Addison staining of the body and hands when she was twenty. She was taken to a Specialist in Harley Street who told her that nothing could be done, but that it would not hurt her. It remained the same till after treatment with adrenalin had been discontinued for some time and is now clearing up. This is by the way.

Before treatment with adrenalin was instituted the patient had been to many hospitals and there had had all the usual forms of therapy. At the Clinic the patient had been treated with vaccine and of course gold in all the various forms had been employed. She had the typical anxious look, no appetite, loss of sleep, and there was the fusiform swelling of the fingers. The knees were stiff, the feet swollen, though not oedematous. Blood pressure 128/90, pulse 88, regular. The heart sounds were soft, and there was nothing abnormal to be found in the abdomen. The lungs were clear.

A four hourly randolph test was taken.

21.6.50.	Before.	After.	
W.B.C.	6450	7840	
Eosin	133	69	-52%

The giving of 6mins. of 1-1000 adrenalin was continued weekly, and in view of her poor colour a further blood count was taken on 2.8.50. R.B.C. 5,030,000. Hb. 96% B.S.U. Colour index 0.96

The treatment was continued regularly. The blood pressure varied little, and in October there was very little generalised pain, the headaches were much less and the pain did not stay so long, the fingers were much improved and she could use them. There was the beginning of euphoria.

4.10.50.	Before.	After.	
W.B.C.	5800	6900	
Eosin	100	33	-67%

It is noted that by 25.10.50. the blood pressure had fallen to 118/100, and the pulse to 78. But the heart was adequate, the pulse was regular, there was no murmur, and no oedema of the feet or ankles.

7.3.51.	Before.	After.	
W.B.C.	6355	6488	
Eosin.	89	22	-75%
Potassium	18.5	17.2	-1.3
Sed. Rate	18/100	20/100	
P.C.V.	41%		

The blood pressure went to 102/80 but the treatment was continued. Gradually from here the patient picked up and in May there is a note that the patient is helping with the spring-cleaning. It was noticed on 15.8.51 that the staining on the hands was changing. It was not so marked. The patient noticed that if she had to miss a week she suffered for it. It would appear that this treatment can help even when the typical staining of Addison's Disease is present. Progress was uneventful, and a further recount was taken on 30.1.52.

	Before	After	
Eosin.	22	156	-30%
Sed. Rate	33/100 corrected 27/100	20/100	
Potassium	20.6	18.5	2.1
P.C.V.	39%		

The D.S.T.s are appended.

The patient stopped coming to the Clinic in June 1952 as she felt so well. When she was asked to return for a check on 27.4.53. no one recognised her. The anxious look had gone, she looked a sonsy happy grandmother. She has had no treatment

since leaving the Clinic and had not even had an aspirin. She ate and slept well and has put on weight. Strangest of all the staining was going. The blood pressure was 158/80, there was nothing abnormal discovered in the abdomen, and the cardiac condition was satisfactory. The lungs were clear, and there were no nodules anywhere. All the reflexes were present. Dr. Coke was asked to see this patient and seemed satisfied. Of course the question of leucodermia cannot be ruled out, but the patient has been asked to wear sleeveless dresses and report in October, for a further check. Otherwise the case is closed, at least till some trouble may upset the glandular balance once more. It may never happen.

CASE. 8. No. C. 18659

DIFFERENTIAL SEDIMENTATION TEST.

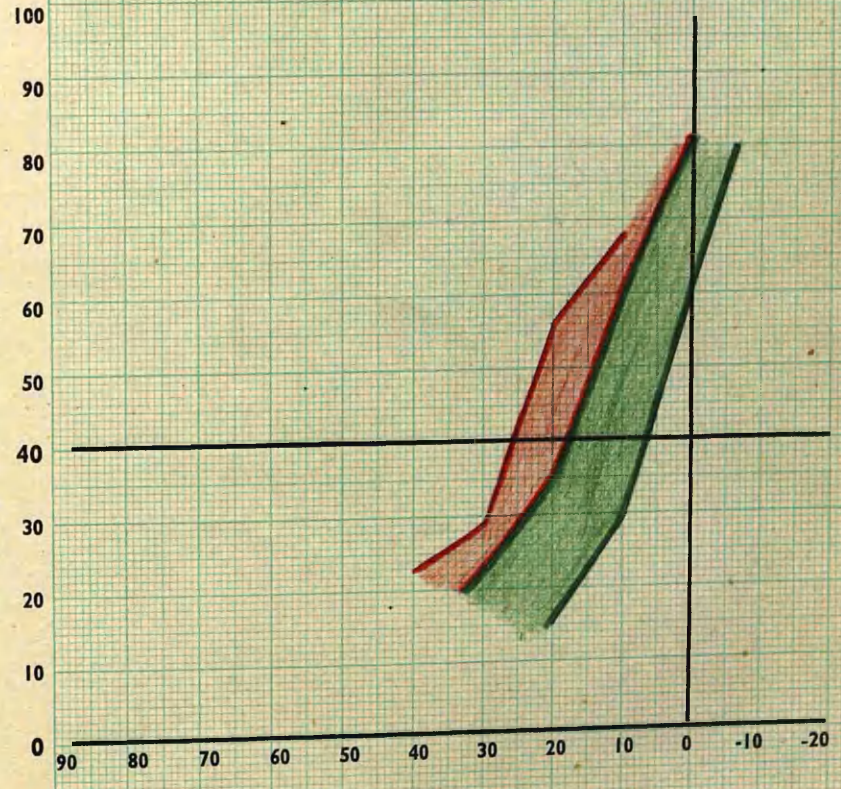
Name WARE TRS Sex, M. F. Age - 55

Date 27. 3. 50

RESULT: 18 % 19/22 = 0·87 No. in Series 1

(0-10. 15/20. 07-1.0 = approximate normal)

Clinical Diagnosis,



M.= 23

from :-

CHARTERHOUSE RHEUMATISM CLINIC,
54-60, WEYMOUTH STREET,
W.1.

CASE. 8. No. C. 24575

DIFFERENTIAL SEDIMENTATION TEST.

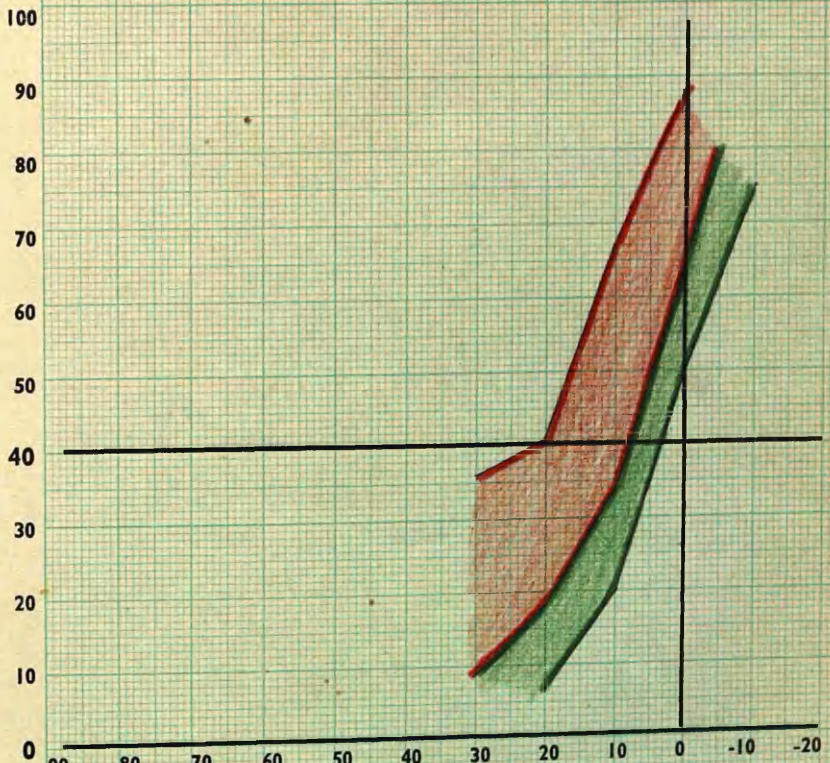
Name WARE Mrs Sex, M. F. Age - 58

Date 27. 4. 53 No. in Series 2

RESULT: 8 % 32/14 • 2·3

(0-10. 15/20. 07-1.0 = approximate normal)

Clinical Diagnosis,



M. = 11

from :-

CHARTERHOUSE RHEUMATISM CLINIC,
54-60, WEYMOUTH STREET,
W.1.

CASE 9. Aet. 47.

A female patient.

Previous history.

Patient states she had childish ailments, the worst being tonsillitis, but she never had the tonsils removed. As a child she was taken to Tite Street Hospital for Children regularly for headaches, and commenced to wear glasses aet. 6 and has worn them ever since. They appear to be a mixed astigmatism and hypermetropia. Her menses began at the age of fourteen and a half years. She lost heavily till she was twenty-eight, and since then the flow has steadily diminished, though the periods were regular till lately they now vary 3-5 / 21-35 . The loss is now scanty and she has no pain.

The rheumatiod arthritis began while she was in Ashtead in Surrey. The Blitz was at its height in 1941 when she was called up to work in a factory. This she was forced to give up as the work was noisy, and her head "began to have sensations". 5-6 years later the tingling began, mostly in her fingers at night associated with pain.

Family history.

Patient knows little or nothing of her ancestry. Her mother had an operation for prolapse of "some lower part", and one for removal of her

breast: one for a growth on the womb, and two more of which nothing is known. This lady is now 71 and is in hospital with a fractured femur. Her father had fits before marriage, but that seems to have cured them and he developed neurasthenia. Her mother's mother had "some children die with rickets". The patient herself had rickets "in the head", and her sister in the legs. The maternal grandmother died of cancer of the womb aet 66. She again afferred there was no more history.

The patient is one of a family of three. Her eldest sister, now aged 50 had arthritis and rheumatism, then comes the patient, and last another sister, alive and well, aet 38.

The patient has no children herself as she saw so much suffering in her mother's house with poverty and bad temper due to this neurasthenia of her father. Her mother's sister died of pernicious anaemia aet 63. The son of this sister was in St. Thomas's Hospital as a baby aged three months for three years, with a "lack of marrow in his bones". He is alive and well now. The child of another aunt, cousin of the patient, a girl, died aet 21 of pernicious anaemia.

Clinical findings.

The patient came to see me at my surgery, complaining of these symptoms, and now also pains in the breasts. There were no nodules, but the patient was much over-weight, 15 stones 15 lbs. The blood pressure was low 90/60, pulse 78. There was no crippling, nor ulnar deviation of the fingers. In November I took a specimen of her blood for examination at the Clinic.

The result was as follows:

Blood Cytology.

Red Blood Corpuscles	4,710,000 p.c.mm.
Haemoglobin	73% Brit. Stan. Units. Haldane.
Colour Index	0.78

Randolph Eosinophile-Adrenalin Reaction

	Before	4 hours after.
Total Leucocytes	7,200	9920
Total Eosinophils	99	0
Sedimentation Rate	10/100 mms.	13/100 mms. 1st. hour.

RESULT. Reduction of -100% eosin

Differential Sedimentation Test.

Report:

The changes seen in this blood are typical of those associated with the pituitary dysfunction in the pre-menopausal era, and with a clinical

condition of water-retention. The sedimentation value remains normal at 9/100, but the configuration of the curves is that of the endocrine type. The relationship of the two fields is that associated with non-articular manifestations and with the water retentional state. The condition of hypo-oestrinaemia is probably not severe at the present time. There is no evidence of the actual development of any of the active arthritis of the menopause as yet.

Treatment.

It was decided that here might be an early case of rheumatoid arthritis, associated with panniculitis. She was put on an anti-water retention diet, her fluids cut to 1 pint per day and restricted salt. She loved salt, and heaped it on to most of her food, so this was a great deprivation. Also she was given 6mins. 1-1000 adrenaline weekly. The record of her blood pressure steadily shows improvement her general condition improved, so did her sleep. The tingling left her hands and she lost weight. Eventually on 30.8.51. it was decided that she could stop treatment as there were no symptoms, but that the diet must be strict.

She remained well till 22.11.52 when she returned feeling nervy and with some tingling. During the winter she had not been strict with her diet and her husband had been ill, and finally her mother fractured her femur. The patient had been put back on 6mins. adrenaline in November, but the weather had often prevented her attendance at the Surgery, and also the illness of her husband. However, she has been regular for the past eight weeks, and is now feeling better. Her weight is 12 stone 4 lbs, the blood pressure is 152/90, pulse 82.

The patient is once more feeling that she can face life, in fact almost cheerfully. Palpation of the abdomen is still difficult, but there is no tenderness, nor rigidity anywhere, no mastitis, no nodules. Her colour is good and she goes to her office, as well as being a housewife. The patient is again having a course of 6mins. adrenaline, as the upset of her mother has upset her, also the illness of her husband, but this time her attendance at the Surgery will be less, and it is reasonable to suppose that if she follows the usual pattern, she will finish treatment by mid-summer.

CASE. 9. No. C. 19895

DIFFERENTIAL SEDIMENTATION TEST.

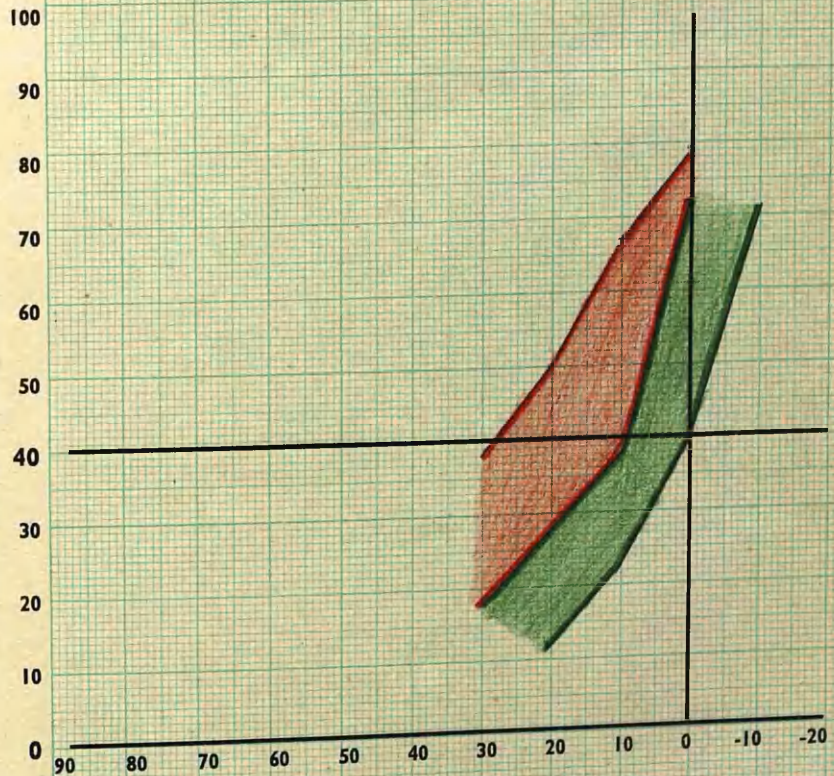
Name SEWELL Mrs Sex, M. F. Age - 44

Date 1.11.50 No. in Series 1

RESULT: 9% 27/15 = 1.8

(0-10. 15/20. 07-1.0 = approximate normal)

Clinical Diagnosis,



M. = 0

from :-
CHARTERHOUSE RHEUMATISM CLINIC,
54-60, WEYMOUTH STREET,
W.1.

CASE.9. No. C. 24460

DIFFERENTIAL SEDIMENTATION TEST.

Name SEWELL TRS Sex, M. F. Age - 47

Date 8.4.53 No. in Series 2

RESULT: 4% 33/24 = 1·37

(0-10. 15/20. 07-1.0 = approximate normal)

Clinical Diagnosis,

QUANTITY OF PRECIPITATE

Serum Sedimentation

M. = 0

from :-

CHARTERHOUSE RHEUMATISM CLINIC,
54-60, WEYMOUTH STREET,
W.1.

CASE 10. Aet 66.

A female patient.

Previous history.

The patient said she had had no childish ailments but tonsillitis, and tonsillectomy was performed. She had not since been attended by a doctor except for the birth of her children. Her menses commenced aet 13 quite normally, no special pain, and the menopause was about 50. That too was quite normal.

During the War the patient was in London during the Blitz and slept regularly in a cellar. One morning on trying to go upstairs she found she had to hobble as "the right knee was gone and I could hardly walk". The pains spread rapidly to the hands, "and everywhere"; the patient had a nervous breakdown and was evacuated to the country. At a local hospital there, treatment was at once commenced, and for nine months she was in plaster and/or "having heat". Nothing seemed to be of any avail, and before the War finished, her nerves being better, she came home.

The patient had three children, the eldest, a boy, died of meningitis aet. 10 months. The next child, also a boy, now aet. 49 is alive and well. The last was a girl, now aet 39, married, with three children. All those children are healthy.

Family history.

Her maternal grandfather was very

healthy and died aet 78 of old age. The patient does not know more of her family history. Her mother died of pneumonia when she was over 70. Her father died also over 70 of an "unattended rupture". She explains that they lived in the country, and medical aid was difficult to obtain. Her mother had six children. The eldest was a girl who died as a baby, reason unknown. The second sister died aet 20 of tuberculosis. The next, a girl, died aet 17 of tuberculosis, and the fourth, also a girl, died of tuberculosis aet 4. Her only brother came next and fell out of a window and was killed aet 18. The last child is the patient.

Clinical findings.

The patient came to the Clinic in 1946. The notes give a history of primary pain in the right hand on the ulnar side. The left knee was extremely tender and the patient found walking difficult. She had local injections of procain into the knee, and vaccine treatment was instituted - the stock vaccine 0.05 mill. aa. being used. From the notes she appears to have become sensitive to the vaccine, and the dosage was decreased. In January 1950 it was noted that there was still good movement in the hip joint. By July 1950 the patient had been seen by an orthopaedic surgeon, and he agreed to take her into hospital and arthrodese the right knee. The patient did go into hospital and the right leg was put in plaster.

On 1.3.51 the patient was found to be an advanced typical rheumatoid arthritic case. She was crippled and could not walk. When taken out of her chair and held up by attendants she was the shape of the chair and could not straighten herself nor put one foot before the other. The escort said that her food was cut up and she was practically fed. She could not dress herself, nor do her hair. In other words, she was dependent on others for the necessities of life. Both elbows were fixed, the hands had marked ulnar deviation, and the palms were crumpled and damp. Muscle tone was practically nil, and one could almost see through the globinous flesh. There was no grip. The blood pressure of the patient on 1.3.51 was 120/100. There were râles in the chest, and the patient complained of a cough. The pulse was 82. There was no power in the fingers and the elbows and shoulders were fixed. She could not stand and seemed over-weight. It must be remembered that the work of the Clinic had to go on, so as much time as could be desired could not be found for necessary examination.

The result of a Differential Sedimentation Test taken is as follows, and this confirmed the clinical diagnosis.

A four hourly test was done with the following results.

	Before	After 4 hours.	
W.B.C.	5688	5311	
Eosin.	33	11	= -62%
Potassium	19.8	16.2	= -2.0
Sed. Rate	43/100	44/100	
P.C.V.	42%		

It was sometimes very difficult to obtain blood from this patient. Her condition was so bad, the flesh globinous, the veins thin, and the elbows fixed. There are thus not so many tests, as the staff of the Laboratory had to distress the patient so much to get a specimen.

Treatment.

Treatment with adrenaline was decided upon. Each week the blood pressure was taken and the achievements of the patient listened to very carefully. Hence it was found that with only 6mins. 1-1000 adrenaline given once weekly, by 11.4.51 the patient managed with aid to stand, and though still in the posture of the chair in which she had sat for so long, stood alone - the first time for seven months. She also began to put on her own stockings and some underclothes. On May 9th the patient walked with aid. The blood pressure was 130/100. The pulse was 100, The patient was now

beginning to get hopeful, though one cannot say there was a state of euphoria yet. She felt that the injection did not last the whole week. The dosage was stepped up to 10mins. per week. There was a certain degree of panniculitis, and to clear the water from the tissues the appropriate salt-free diet was advised, and fluid intake cut down. To obviate any distress caused by the alteration of the fluid content in the body, Potassium Bicarbonate tablets, gr.5, one tablet t.d.s. were advised. On 6.6.51 the patient had already had sufficient stimulation and the original 6mins. dose was resumed. She had some bad weeks, until the body recovered from the extra stimulation. Blood pressure fell again to 112/100.

On 25.7.51 the patient walked into the examination room with aid, but with no chair. The skin was beginning to "crinkle" as the flesh hardened. Progesterone was added now, 5 mgm. intramuscularly, and the improvement became more rapid. The patient noticed that there was cracking in the joints. At this point there is often much work to be done to reassure the patient that all is well. For one thing there is often more pain as the muscles begin to regain tone, and is especially noticeable with the knee joint; the joints loosen, and sometimes it is necessary to put the patient into a hinged splint to give confidence. These patients

have been fast so long that they are truly frightened to fall down, especially the older ones as the joints become free.

This is an important point in so far that the patient has not got sufficient mobility of movement until the viscera have also had time to recover, or adjust themselves to the new conditions, hence there are no grave side-effects, nor the dramatic deaths that one can read about with treatment with Cortisone. The procedure is slower, it is ventured to think, safer. Of course, once the patient has gained a certain amount of strength the treatment of choice would be Cortisone, in selected cases. From the tests quoted it would seem that with the excitant adrenaline the patient makes a small amount of Cortisone herself. This would seem to be adequate in bad cases, at least for a time. Even with this small dosage, in a less degree, one can see what would happen with the use of the more potent hormone as one case had a fit, and she had not had fits since puberty.

By March the patient only needed adrenaline and felt better without Progesterone. The progress was slow but uneventful. In April 1952 the patient was walking unaided, although she has not straightened up yet. She could then raise her arms above her head, and do her own hair. The ulnar deviation was disappearing from the right hand though the left hand

had marked ulnar deviation. Euphoria was now marked, and a feeling of hope of ultimate recovery to a normal life. The patient was warned that she would not be as she had been before, but by now she accepted this philosophically, and only wanted to be independent of the help of others and do her own housework and cooking.

In October 1952 she complained of pain in the kidneys. A catheter specimen was taken and pus cells were obtained from the deposit. On culture a few colonies were grown of coliform A type of B. Coli. Under treatment this soon cleared up.

The patient was not encouraged to use a stick but to try and walk alone. She did.

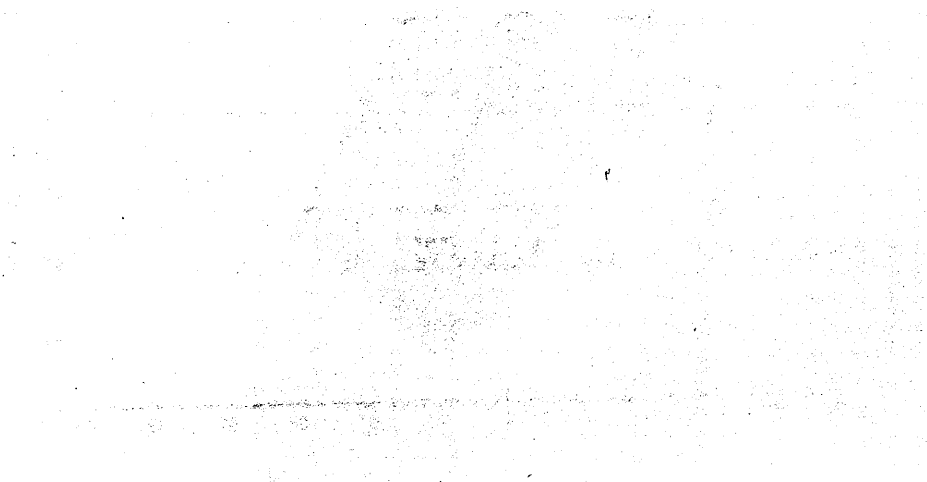
In November another four hourly test was taken:

	Before	After 4 hours.
Eosin	0	0 = 0
Sed. Rate	32/100	34/100 corrected 32/100
Potassium	18.4	16.4 = -2
P.C.V.	41%	

In January I considered that she might try Butazolidine. She had two tablets one day and three the next. She did extremely well, and lost almost the last of her pain. At the time of writing, 30.4.53, the patient can cook, even pastry, and more as she wants. She has not yet become straight, her grip

is fair, and she is quite content with her growing strength and ability.

There is one point which exact examination of these cases has shown me. While the disease process is active the reflexes are absent or faint, and when the disease process has subsided the more affected knee, to take an instance, has no jerk, even though it may have the power to move. This has come to light many times. The eye reflexes I have not noticed affected, only the knees and the elbows.



CASE. 10. No. C. 20498

DIFFERENTIAL SEDIMENTATION TEST.

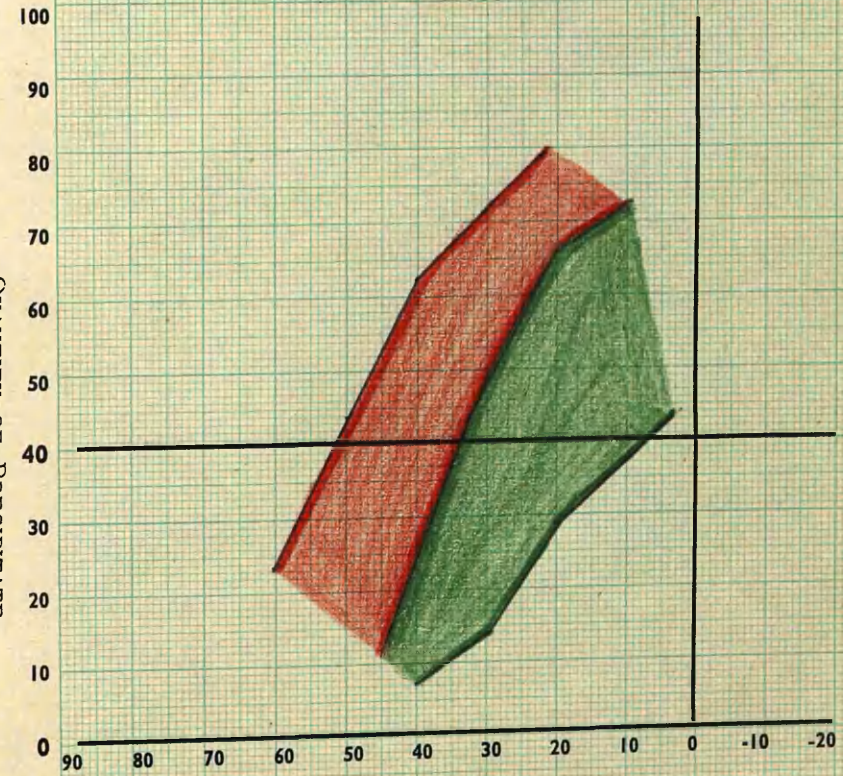
Name HUDSON TRS Sex, M. F. Age - 70

Date 7.3.51 No. in Series 1

RESULT: 33 % 29/29 = 1·0

(0-10. 15/20. 07-1.0 = approximate normal)

Clinical Diagnosis,



M. = 0

from :-

CHARTERHOUSE RHEUMATISM CLINIC,
54-60, WEYMOUTH STREET,
W.1.

CASE. 10. No. C. 23524

DIFFERENTIAL SEDIMENTATION TEST.

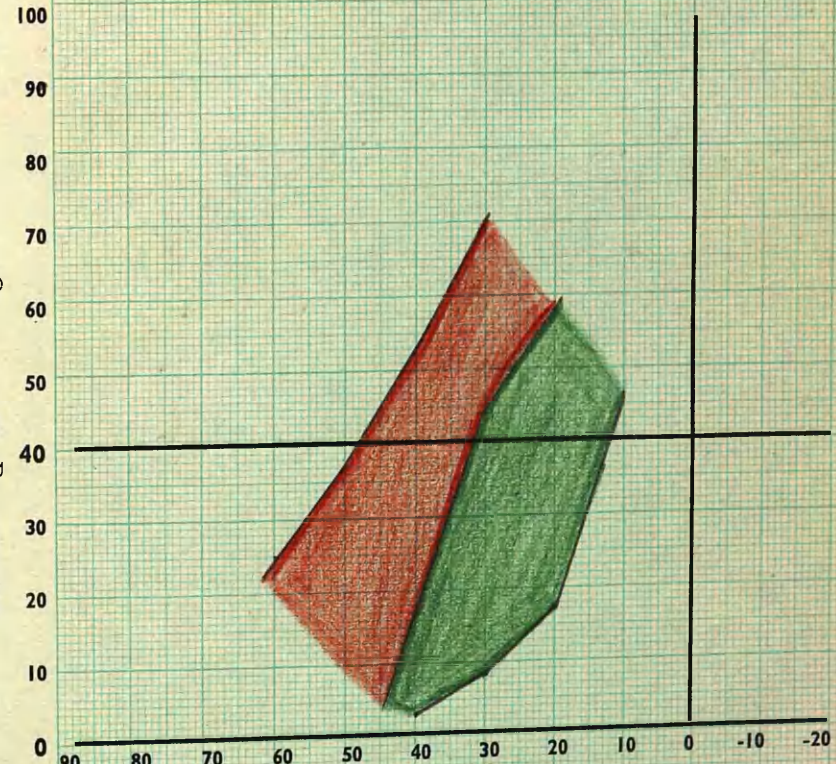
Name HUDSON Mrs Sex, M. F. Age - 71

Date 8.10.52 No. in Series 2

RESULT: 31% 28/33 = 0·84

(0-10. 15/20. 07-1.0 = approximate normal)

Clinical Diagnosis,



M.= 0

from :-
CHARTERHOUSE RHEUMATISM CLINIC,
54-60, WEYMOUTH STREET,
W.1.

CASE 11. Aet 58.

A female patient.

Previous history.

This patient is a most charming, educated woman, very sensitive, and has taken the gold medal at the London School of Music.

She had the usual childish ailments, also pneumonia aet 12. Her menses started aet 15. She suffered from "a lot of pain always". She had mucous colitis in her twenties, and married aet. 32. Her husband was 19 years older than herself but they were very happy, except that he always had hypertension, and when the "doodles" came his brain became affected, and the patient had a great deal of mental distress. She developed bad blood pressure herself, and could not bear to be alone in the house, etc. Her Husband then had diabetes and a thrombus eventually killed him.

Family history.

Her maternal grandfather died "quite young" of cancer, he also suffered from rheumatism. Her maternal grandmother had all her faculties till she had a cerebral haemorrhage and died aet. 81. Of her father's side there is nothing known. Her own father died of cancer in the left lung aet 68. Her mother is alive and quite well aet 77. There is one sister

alive and well.

Clinical findings

This patient first came to the Clinic on 18.8.49 complaining of hands, right elbow and right foot. Onset was sudden after a bomb dropped two houses away in a suburb where she lived in London. She was in London during the Blitz staying in shelters during the night, which were damp until they dried out. Her right elbow soon locked. She had always been a little "light-headed" and this got worse with the change.

Gold therapy at first helped her and then seemed to lose its effect. She had this for three months, then being able to walk about. After that the condition became stationary, with the elbow locked and the wrists swollen and painful. As time went on they became stiffer and when the patient was seen in 1949 she could not lift a cup of tea to her lips. The right elbow was swollen and impeded movement. She was in a very nervous condition and either her mother or her sister always came with her to the Clinic. Her blood pressure was 148/90.

The eosin. test was taken (Randolph method).

	Before	After 4 hours.
W.B.C.	9490	9150
Eosin	73	22 = -70%

Treatment.

It was decided to go on with the adrenaline 6mins. weekly. The blood pressure did not vary much, e.g. 23.8.50. 140/90, and the pulse always remained the same. But there was definite improvement, she could now raise a cup of tea to her lips by herself, and she was feeling better.

	Before	After 4 hours.	
W.B.C.	7150	5710	
Eosin.	22	44	= +100%

As the patient continued to improve it was decided to continue the same treatment and in October 1950 the patient was coming to the Clinic by herself and regaining confidence in herself. She was doing little jobs in the house and gradually getting used to the idea that she would not always be an invalid, and the fear of becoming a burden on someone was receding.

	Before	After 4 hours	
W.B.C.	8580	10,100	
Eosin.	155	0	= -100%
Sed. rate	26/100	31/100 mm.	1 hour
P.C.V.	39%		

In November the patient felt steadier but she was undergoing much mental distress. The blood pressure was 142/100 and Tablet Phenobarbitone grain ½ thrice daily during the period of stress were prescribed. The treatment with weekly adrenaline was strictly adhered to, and by December the phenobarbitone were discarded and the patient was once more improving, she had weathered that storm better than anticipated.

Improvement was steady and the patient was encouraged to take up her music, this was a sad blow to her at first, as she fell so far below her standards, but she is now playing Chopin and enjoying her music once more.

Another recount was taken of 19.4.51 by the four hourly method.

	Before	After 4 hours.	
Eosin	220	44	-80%
Potassium	18.8	16.8	-3.0
Sed. Rate	24/100	30/100	
P.C.V.	40%		

At this time the patient noticed that swellings round her elbows and other joints which she had thought "bone" were "getting soft". This was a great encouragement for her and she practised harder than ever with the result that the fingers regained

their strength, the elbows began to open out, and even the wrists have now some movement. Improvement continued, the giddiness grew less, the blood pressure was now 132/100. The swelling of the hands was much less, and there was very little ulnar deviation, the palms were dry.

23.7.51.	Before	After	
Eosin	67	22	-67%
Sed. Rate	35/100 corrected	32/100	43/100
Potassium	17.8	18.0	+0.2
P.C.V.	39 %		

Special report. All tests point to being not so well as on April before, and yet clinically the patient was much better.

The patient had continued with her music and was now beginning to feel that one day she might really play as she once did, and it was only by close questioning that the bitter disappointment of not being able to play as before was elicited. This had occassioned the patient much distress, and many tears. The emotional upset had thoroughly upset her, hence the blood picture.

5.12.51 the D.S.T. is again reassuring "some definite improvement since the last test". The patient now had started singing as well, and the test taken 9.4.52. shows she is recovering once again.

	Before	After	
Eosin	44	44	0
Sed. Rate	15/100	20/100	
Potassium	22.0 (haemolysed)	17.5	4.15

This patient now leads a normal life, enjoys her garden, her music, does her own housework, and is quite independent. Within limits she is a "normal". She has strong fingers and manages her wrists wonderfully. Her next joy is looking forward to a holiday, this may safely be taken as she only attends the Clinic every three or four weeks, as she feels the need.

CASE. II. No. C. 18991

DIFFERENTIAL SEDIMENTATION TEST.

Name WYETH Mrs Sex, M. F. Age - 52

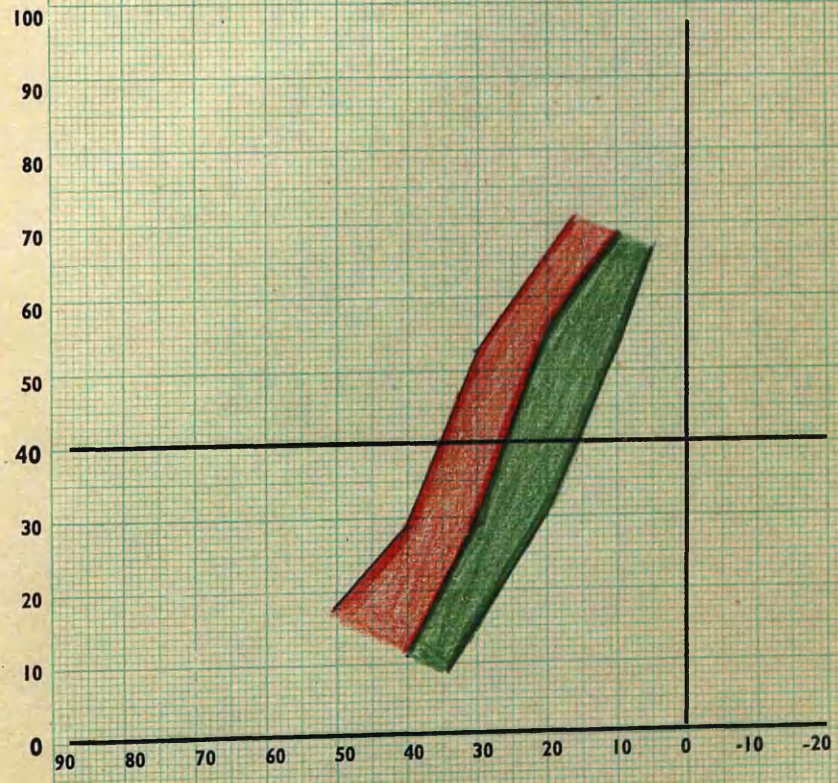
Date 12.5.50

No. in Series 1

RESULT: 26% 18/8 = 1·0

(0-10. 15/20. 07-1.0 = approximate normal)

Clinical Diagnosis,



M. = 14

from :-

CHARTERHOUSE RHEUMATISM CLINIC,
54-60, WEYMOUTH STREET,
W.1.

CASE 12 Aet 22.

A female patient.

Previous history.

There were the usual childish ailments, but in addition the patient had had many boils and abscesses. There were no operations. The patient is a natural blonde, with a very sensitive nature. Her menses commenced aet 13 years, and she suffered with dysmenorrhoea.

She gave a history of a febrile onset eighteen months before, more like a "bad" influenza than a rheumatic fever. This fever lasted, though she was not always in bed, for nearly three months, and as the fever began to leave her she noticed that her hands were painful and swollen. During this period her doctor had given her many kinds of "tablets"; they seemed to ease her pain but she grew more and more depressed. She was then sent to out-patients at various hospitals where she had electrical treatment, wax baths, and the usual routine treatments. She does not know the name of them all. Her condition remained the same, if not a little worse.

Family history.

Paternal grandmother had rheumatoid arthritis and died aet 65, bedridden. Paternal grandfather died aet 60 with cancer of the throat.

Maternal grandfather died aet 70, with cancer ? in rectum. Maternal grandmother died "soon after with bronchitis". Mother alive and well suffers from "ordinary rheumatism". Father is "crippled with rheumatism". Mother's family:-

miscarriage.
girl aet 27 alive and well
boy aet 24 alive and well
patient aet 21, rheumatoid arthritis.

Clinical findings.

This patient first came to the Clinic in July 1951. She was ambulant, but had a shuffling gait as her feet were affected and the knees swollen. She was a very pretty, unmarried girl, unusually intelligent. She had noticed that her rheumatic pains were always worse just before her menstrual periods, that during the menses she was comparatively free, and after the period the pains came on again. This was all told without any questioning.

On arrival at the Clinic, the patient could shuffle into the examination room. She was in a very upset state, and tears were always near. The hands were painful and swollen, the mid-phalangeal

joints showing the typical fusiform swellings. She could not close her fingers. The knees were swollen, but not to a great extent. It was the pain on movement that caused her disturbance. The feet were swollen and very tender so that she could not wear her proper shoes but had on some kind of loose sandals. There were no nodules, and the rest of the body seemed to have escaped further injury. The blood pressure was 120/80, the pulse 88, and there was no murmur heard. She was considered a suitable case for adrenaline, but a Differential Sedimentation Test was taken first, and a four hourly eosinophil test arranged for the following week. The results were as follows:

	Before	After 4 hours.
Eosin.	222	0 = - 100%
Sed. Rate.	39/100 corrected 35/100	32/100
Potassium.	19.0	20.2 = + 1.2
P.C.V.	40%	

Treatment.

6mins. adrenaline were administered each week, the blood pressure fell to 110/80, the pulse remained 82. By the 22.8.51. the hands were much less swollen and there was little pain. Progesterone 5 mgm was tried also on 26.9.51. This was not tolerated, and caused the patient much pain that week. It was stopped. The pain left and only adrenaline was given.

Progress.

Progress was continuing steadily when a chance remark elicited the fact that the patient was worrying because relatives wanted her to give up her fiancé - she had not worn his ring as it would not fit her finger. In less than one month she wore the ring and the date of the wedding was fixed. Progress was so rapid now that it hardly seemed possible. The patient was warned that with marriage there might be a flare-up of the condition and the fiancé was warned also. They took the risk, and she was actually married in a snow storm. That did not seem to affect her condition, but one month later she was worse. The period of exacerbation lasted for two months, during that time treatment was never relaxed, and gradually she became acclimatised to the new conditions and improvement set in. Her progress has been steady, except for the set-back of a hordeolum. This soon

cleared up. But the autogenous vaccine used did not seem to suit her so well, and the Differential Sedimentation Test shows a relapse. Adrenaline was begun once more, and she is now so well that the almost inevitable has happened and she is pregnant. Adrenaline was therefore stopped at once, four weeks ago, and the patient feels well on Charterhouse stock vaccine. A further report of this case will be made at a later date, and the blood of the baby taken. It is especially interesting to note here the part that the gonadtrophic hormones have played. It is in keeping that a balance of the pituitary-adrenal syndrome should be the deciding factor between health and illness for the patient. It is said that the pituitary gland is the leader of the endocrine orchestra.

CASE. 12. No. C. 21278

DIFFERENTIAL SEDIMENTATION TEST.

Name WILSON, Mrs R Sex, M. F. Age - 21

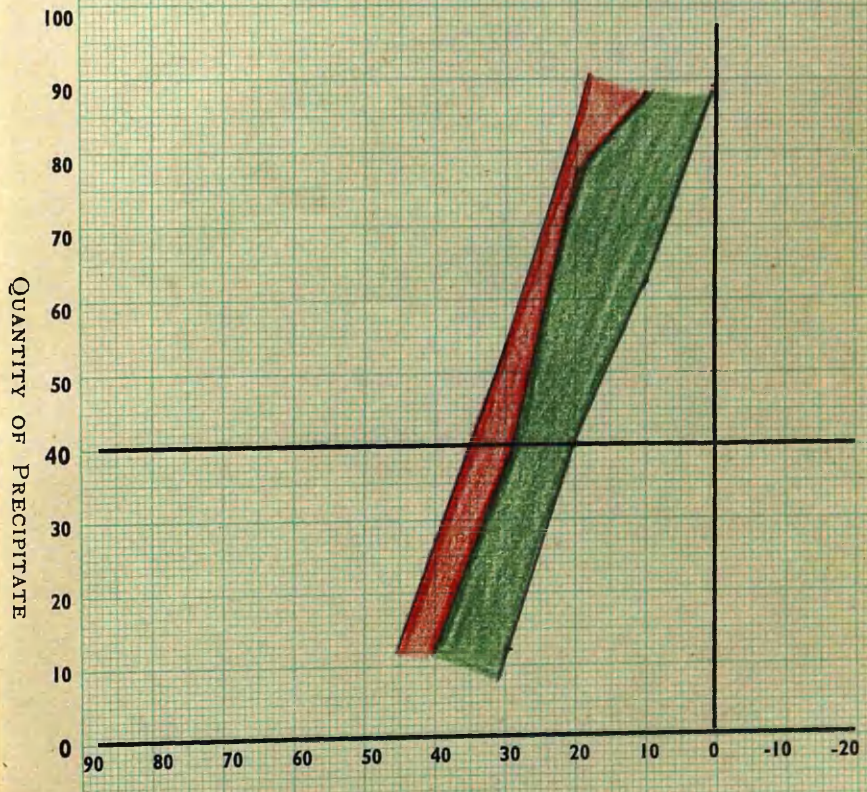
Date 24.7.51

No. in Series 1

RESULT: 29% 17/25 · 0·68

(0-10. 15/20. 07-1.0=approximate normal)

Clinical Diagnosis,



M.= 40

from :-

CHARTERHOUSE RHEUMATISM CLINIC,
54-60, WEYMOUTH STREET,
W.1.

CASE. 12. No. C. 22831

DIFFERENTIAL SEDIMENTATION TEST.

Name WILSON Thos R Sex, M. F. Age - 22

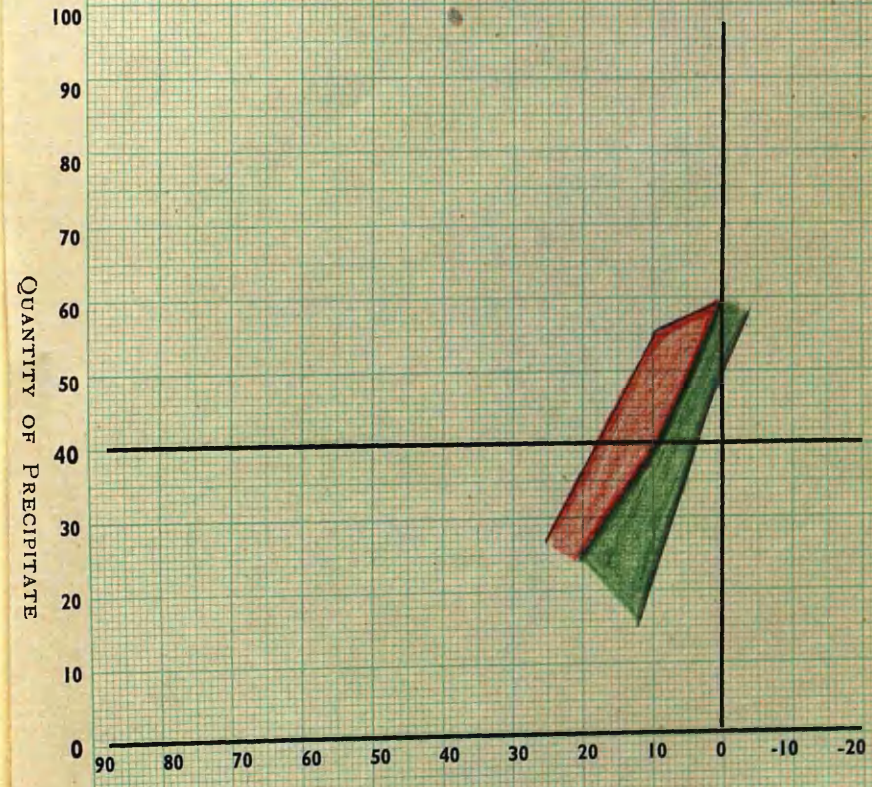
Date 21.5.52

No. in Series 2

RESULT: 9% 15/15 · 1.0

(0-10. 15/20. 07-1.0 = approximate normal)

Clinical Diagnosis,



M. = 33

from :-

CHARTERHOUSE RHEUMATISM CLINIC,
54-60, WEYMOUTH STREET,
W.1.

CASE. 12. No. C. 23528

DIFFERENTIAL SEDIMENTATION TEST.

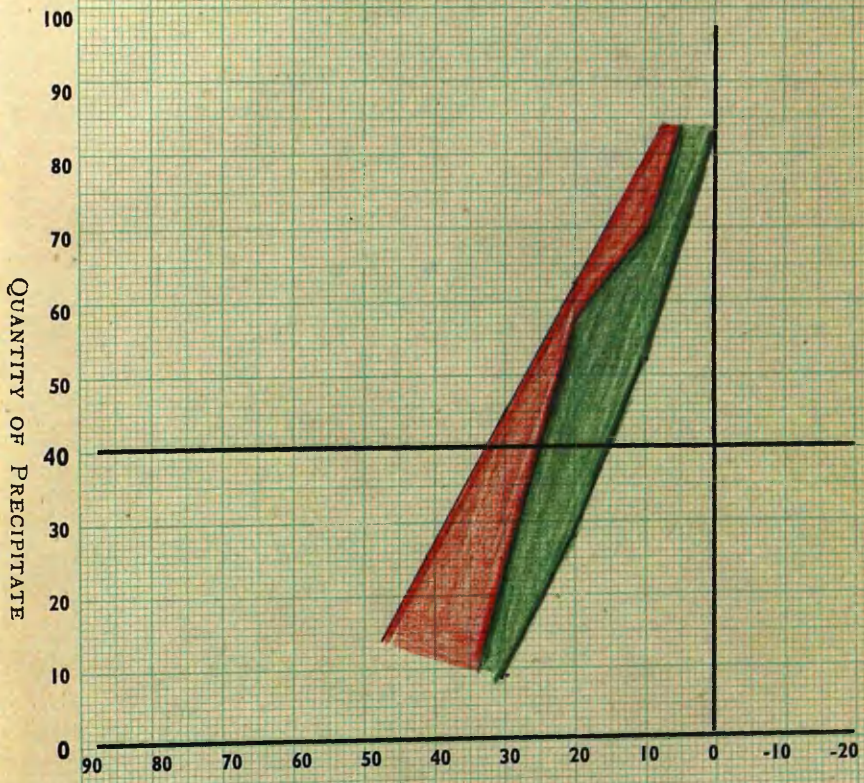
Name WILSON Mrs R Sex, M. F. Age - 22

Date 8.10.52

RESULT: 25% 14/22 = 0.63 No. in Series 3

(0-10. 15/20. 07-1.0 = approximate normal)

Clinical Diagnosis,



M. = 29

from :-

CHARTERHOUSE RHEUMATISM CLINIC,
54-60, WEYMOUTH STREET,
W.1.

AETIOLOGICAL SIGNIFICANCE OF ENDOCRINE AND PSYCHOLOGICAL FACTORS

Series of 75 cases of Rheumatoid Arthritis.

Although the main object of this thesis is to assess the value of Adrenaline in the treatment of Rheumatoid Arthritis, certain facts of interest were noted as the result of careful analysis of the patients' medical histories. These are summarised briefly below.

From the series of cases investigated the following figures may be derived :-

The series consisted of 75 cases, of which 2 were males and 73 were females, ranging in age from 24 to 75 years. Of the females, 14 were spinsters and 59 were married. Of these married women it was known that 16 had had no children; and 42 had had from 1 to 7 children each. Of the females, 43 had passed the menopause and 29 were still experiencing menstruation.

The mean age of the occurence of the menopause was 48.9 years with a standard deviation of 2.9 and a standard error of the mean of $\pm$ 1.415 years. The menopausal era may be derived from this series as occuring between 46.1 and 51.7 years. The coefficient of variation is only 5.9 per cent.

The mean age of onset, according to the definition of onset as being taken on a history of pain and swelling of the joints with subsequent crippling, was 41.55 years.

The thesis stresses both the problems of a psychological trigger factor as a causative feature of the onset of rheumatoid arthritis, as well as a latent period between a major stress factor and the actual onset.

The mean"latent period" in this series of 74 cases was 47.1 months. However the standard deviation of this figure was 48.9 and the coefficient of variation very large. The frequency distribution around the mean is therefore so diverse or scattered as to make the suggestion that the apparent latent period before onset is of no significance in relation, as it has been estimated, to the psychological stress thus pointing out that the onset cannot be ascribed to psychological stress as the only important causative factor, there being no time relationship.

Applying fourfold tables as under to the chi-square test:

a) Number of Married Females with rheumatoid arthritis in whom the latent period of onset is :-

	greater than	less than the mean
who have had children	23	18
who have had no children	4	13

b) Number of all females including spinsters who have rheumatoid arthritis in whom the latent period of onset is :-

	greater than	less than	the mean
who have had children	23	18	
who have had no children	7	23	

the X2 value for a) = 3.897 - with n = 1, the P = 0.05

the X2 value for b) = 6.354 - with n = 1, the P = 0.02

Both these figures having a value of P less than 0.05 are significant and lead to the suggestion that the psychological trigger stress factor leads to a more rapid onset of rheumatoid arthritis after the stress in those females who have not had children. It has been seen above that the latent period before onset has no significance itself in relation to the psychological stress, and these figures suggest that there may be somehormonal or endocrine disturbance associated with sterility in which the psychological stress may play a more active part. There would appear, therefore, to be evidence of two factors: stress and blood soil.

DISCUSSION.

The Ministry of Health in the latest Report published, 1951, urge the need for more and more research into the aetiology and pathology of Rheumatic Diseases. It is evident on reading the Report that there is still much shrouded in darkness. The use of the new hormones is not entirely advocated. From page 94, Part 111, 1951, "In the meantime the use of corticotrophin (A. C. T. H.), and Cortisone in the treatment of rheumatoid arthritis require the utmost caution from the physician and forbearance on the part of the patient."

Adrenaline is not quite such a powerful hormone as these later products. It is safer though it can give some swift reactions to the patient. In practice with this hormone it is always advisable to take the blood pressure and pulse rate first. Where possible it has been found advisable to try the effect of a small dose first, so small as two mins. 1-1000 adrenaline. In an article in the Lancet, June 24, 1950, page 1149, there is a comparison made in the treatment of rheumatoid arthritis with A.C.T.H., adrenaline and deoxycortone and ascorbic acid. Drs. Dresner, Pugh and Wild only leave a comparatively short time between

each treatment, and in practice it has been proved in this thesis that once healing has begun there are results to be seen as long as nine months after the last injection. Furthermore it is not argued that adrenaline is as dramatic as the later hormones, it is a long term policy. From the author's point of view, that may have something in its favour as the tissues have time to recover, and there is not too great a strain imposed on the already diseased excretory organs.

Professor Parr, from Australia, in a visit to the Clinic was kind enough to speak of his work with adrenaline. Apparently daily doses are given of as much as 1cc 1-1000 adrenaline. He appeared at the time somewhat disappointed by the results. On analysis it would seem that that was over-stimulation of the adrenal cortex, and so of the patient. Even with the small excitant dose of 6mins. once weekly there comes a time in the course of the treatment when it appears that the patient can be pushed no further. That is classed as 'saturation point', and some less stimulating treatment given. Here the D.S.T. is a valuable guide in deciding on the use of small doses of gold sulphide, vaccine, or pyridoxine. There are many other lines of treatment open while waiting, but inevitably the patient will

ask if they may not have the 'brown bottle' again. That is the clinical time to re-start the adrenaline, and from thence the way to recovery is usually fairly smooth.

In two cases of rheumatoid spondylitis in young women which are in the series of cases reviewed there has been a good response to this line of treatment; one is under treatment at present, and the other, after treatment from 2.5.51. till 7.12.52, is declared clear both by the x-ray and the D.S.T., so much so that she is having a baby. This patient was by all standards a rheumatoid spondylitis, and noticed even that the menstrual cycle had a definite bearing on the pain and discomfort suffered. She had had backache for four years before this line of treatment was adopted. No treatment anywhere, even an attempt with deep-ray, seemed effective. Her age when she began treatment was 22.

There emerges crystal clear from this work that much patience is needed on the part of the physician and forbearance on the part of the patient. Except for the immediate reaction of the patient to the adrenaline, which has sometimes been rather severe, there have been no evil side-effects observed. There has been

no glycosuria. Only in one case was there any evidence of disturbance; in this case she had a fit in the ambulance going home. As a girl she had had fits, the last one at the age of 14. Her present age is 39. However she has had only that one to date and is just beginning to do well.

In the case No.1 there were all the symptoms required for a case of Felty's syndrome, the enlarged glands and the enlarged spleen, to such a degree that Professor Smithers thought she might be a case of lymphosarcoma. This case is fully discussed in the previous section, it needs only to add that steady improvement is maintained.

With Cortisone and A.C.T.H. as scarce as they are, and with their potentialities still rather unknown it seems sound clinical sense to screen a case with adrenaline. If the case be in the early stages and there be no deterrent symptoms, then a course of either hormone may be given to avoid orthopaedic deformities, and possibly effect a cure. If the case be a late stage one then preparation of the patient with the slower adrenaline is advocated; when clinically, and by laboratory tests the patient is ready then a course of the more powerful hormone is advocated; whichever is used must depend on the skill and

knowledge of the physician. The position should be made clear to the patient first, that this is only a course, and that when it be ended perhaps full recovery may not yet be achieved.

Every week in the Medical journals there are descriptions of how the various doctors use Cortisone and A.C.T.H. The author will mention one case of mixed arthritis of long standing where only a holiday from pain was promised. That is what happened as long as the Cortisone lasted, but the crippling and the pain were back again when the moderate supply of the drug finished. That coincides with the work of the investigators to date. Whatever the aetiology will be found to be of rheumatoid arthritis in the future, at present there is hope of a cure in the early stages, and of keeping it in check in the later ones.

From the work here presented it seems clear that more than one factor plays a part in the aetiology of this disease. Both nervous systems seem affected, this seems the first step towards the disease, cold and damp are adjuvants, when, when the pituitary-adrenal syndrome is exhausted, some, perhaps small, trigger point sets rheumatoid arthritis in full

swing. The method of Hippocrates is still best, exact bedside notes; for one thing, this gains the confidence of the patient, and that is a great point. In these days of hurry these patients get little sympathy as in the beginning they may only have a great feeling of 'tiredness', and everyone is tired. These patients require great confidence in the doctor, as the treatment is necessarily long and tedious.

When that confidence is gained, the histories become truthful, one very pretty girl, case No.5, saying quite frankly at such a period, that she had brought on the disease herself, with a very gay life aet 14, as 'I looked a good 18 when I made myself up, and as there was a War on I had a good time. It took exactly four years to wear me out'. Previously her rheumatoid arthritis had been blamed on the fact that she was frightened by the Blitz. Quite frankly she blamed working all day, and drinking and having a good time nearly all night, with no sleep for her present condition. Such honest patients are few and far between.

Whatever the cause it seems depletion of the resources of the body to meet the continued demands plus some trigger point causes rheumatoid arthritis.

That would seem to be the true rheumatoid arthritis, and does not include the long-standing cases of, say non-articular rheumatism, which transmute to rheumatoid arthritis. It is agreed that in these cases there is also depletion of response possible, due perhaps to the constant pain or disease process, but the true rheumatoid case will always be able to tell the cause of the disease. It remains for the physician to gain the confidence of the patient and find out, that the exact nature of the disease may be known. This is important as these potent hormones could aggravate an already over-stimulated nervous system.

There has recently been a conference in Washington, the results are not yet published, but the age incidence is almost exactly as the table shown here. The Scandinavian School produced figures of over a thousand patients. There is a peak when Still's disease takes its toll, that is not on this table as there are few children at the Clinic, for the rest, the table nearly coincides with this Scandinavian School of work.

SUMMARY OF CONCLUSIONS.

1. This work with these special cases was originated as a result of work with adrenaline on hopeless eczema cases and others. It is entirely original, and was begun before the author heard of Dr. Hench and his colleagues.

2. It is not claimed that adrenaline can take the place of the valuable hormones discovered by these workers. Adrenaline is useful in early cases, and in later cases to screen with and save the more potent hormones, which are in such short supply.

3. Adrenaline is best given in small doses, with a period between; this period may be a week or shorter, as the patient will say when the pains return.

4. Treatment with adrenaline is not spectacular. It is hard work, both for the patient and the doctor; it is a long-term policy. Patience and care are needed for success.

5. The latent period between stress and onset varies. Cold and damp, such as the cellars during the Blitz materially shortened the period.

6. Not only the pituitary-adrenal syndrome affects rheumatoid arthritis; the gonadotrophic syndrome does also.

This thesis was made possible by permission of the Executive Council of Charterhouse Rheumatic Clinic. The cases were mostly cases from there, and the laboratory work was done there. I would like to take this opportunity to thank the Executive Council, and the Director of the Laboratories, Dr. Coke.

STANDARD DEVIATION 4088 = 63.94 X = 64.4

STANDARD ERROR OF MEAN = 7.64

TWICE (SIGNIFICANCE) S.E. MEAN = 15.28

∴ Latent period of onset after stress is: 55 months ± 16 months = 39 to 71 months. Such cases therefore outside the limits may be reviewed for additional stress within the period and a more accurate figure become thus obtainable.———

"3 years 3 months to 6 years -"

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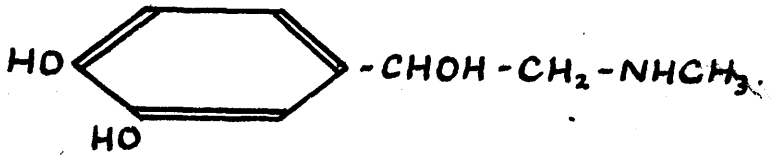
APPENDIX.

Adrenalina
(Adrenal)
Adrenaline

$C_9 H_{13} O_3 N. = 183.2.$



Synonyms: Adrenalinum; Adrenalin; Epinephrine.

This substance must comply with the requirements of the British Pharmacopoeia, and in any part of the British Empire in which adrenaline is controlled by law care must be taken that the provisions of such law are duly complied with.

Adrenaline, *l*-α-3:4-dihydroxyphenyl - β methylaminoethanol, is an active principle of the suprarenal gland, and may be prepared from an acid extract of the glands of certain mammals, or synthetically. The synthetic base may be prepared from catechol by interaction with chloracetyl chloride, and treatment of the resulting chloracetylcatechol with methylamine, followed by reduction. The product so obtained is the racemic form, and resolution and removal of the less active dextro-base can be effected by crystallisation of the *d*-tartrates, the *l*-adrenaline *d*-tartrate being the more sparingly soluble.

Adrenaline occurs as a white or pale buff-coloured, sphaero-crystalline, odourless powder; it has a slightly bitter taste which is followed by local numbness. It has a melting-point of 205-212 degrees, with decomposition, when determined at a rate of rise of temperature of 10 degrees per minute. The aqueous solution is alkaline to litmus solution. Neutral or alkaline solutions are unstable and rapidly become red on exposure to the air.

Solubility.

Sparingly soluble in water; insoluble in alcohol, ether, chloroform, liquid paraffin and many other organic solvents; slightly soluble in oleic acid, solutions being coloured owing to the presence of iron in the acid; readily soluble in aqueous solutions of mineral acids, sodium hydroxide and potassium hydroxide, but not in solutions of ammonia or alkali carbonates.

Adrenaline is inactive when taken by the mouth.

The action of adrenaline is comparable with the effects of stimulating the sympathetic nervous system. When injected intravenously

is causes a rapid rise of blood pressure, largely due to constriction of all blood vessels innervated by the sympathetic, together with the acceleration of the heart-beat, dilation of the pupil, inhibition of the movements of the stomach, intestine, and bladder, and the liberation of sugar from the liver. The immediate effects may be followed by a fall of blood pressure accompanied by a slowing and strengthening of the heart-beat, which is a reflex response due to the action of the raised blood pressure on the carotid sinus. This reflex may cause temporary apnoea. Adrenaline rapidly disappears from the circulating blood and its effects do not last more than a few minutes, unless it is given by continuous infusion or is slowly absorbed from a subcutaneous depot.

The British Pharmaceutical Codex 1949.

Excerpts taken from a monograph " Cortisone",

J.M.Carlisle, M.D., A.Gibson, M.D., and E.Schmatolla,M.D.

Reprinted from POSTGRADUATE MEDICINE, Volume 8,

Number 2, August, 1950.