THE ERYTHROCYTE SEDIMENTATION RATE IN ACUTE RHEUMATISM AS AN AID TO PROGNOSIS AND TREATMENT.

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THESIS FOR THE DEGREE OF M.D.

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THE ERYTHROCYTE SEDIMENTATION RATE IN ACUTE RHEUMATISM AS AN AID TO PROGNOSIS AND TREATMENT.

I. INTRODUCTION.

In the following enquiry an attempt is made to find a method of clearly differentiating, in cases of rheumatism of various types, (A) those in which although clinically free from symptoms, an active process is still present from (B) those in which the condition is cured or at least quiescent.

The method of investigation used is the erythrocyte sedimentation rate. A review of the various methods commonly used is included, together with some experimental details and a universal expression of the sedimentation rate.

The whole subject is viewed entirely from the clinical standpoint; and the test is advanced as a definite aid to prognosis, and as a guide to the length of time treatment should be continued.

II. THE RHEUMATIC MANIFESTATIONS AND SOME OF THE PROBLEMS PRESENTED.

The manifestations of rheumatism are of daily interest to the medical profession, and each year more articles appear on the subject than on any other disease. It is with some degree of hesitation that an addition is made to the numerous forms of enquiry: but the fact that so much has been written and so many contradictory statements are to be found makes one bold enough to add some personal findings.

Rheumatism, with its resultant heart lesions, is at the root of a considerable amount of disability among the school children, the adolescent and the young adult population of this country. Some interesting figures are given in the Ministry of Health Report in 1927 (1) where it is shown that in England and Wales 25,000 fatal cases of rheumatic heart disease occur annually and that about 40% of the total deaths from heart disease are rheumatic in origin.

The crippling of the young life by the incidence of rheumatic heart disease has a very far reaching economic as well as a personal aspect. The patient becomes a chronic invalid at an early age almost before he is able to work and from the economic standpoint is a drag on his family and the community in general. Unsuited for almost any work, he draws his

weekly insurance allowance from the National Health funds, suffering as he does from chronic disability.

That is one aspect but from the personal standpoint he has the suffering of a crippled and useless life and no prospect but an early death. This surely is the more important aspect and the one which it is the duty of the Medical Profession to alleviate and eradicate as far as possible.

The etiology of rheumatism remains obscure and until this is more fully understood the cure and prevention must remain somewhat uncertain.

From all the investigations which have been made certain etiological factors appear to play a part in the causation of the disease but the real importance of any one factor is difficult to estimate.

Environmental factors appear to have some significance and it is generally found that where there is bad housing and especially damp, the incidence of rheumatism is greatest. From this aspect great reforms are taking place with new housing schemes and general improvement of the slum conditions which should lead to the lowering of the incidence of the disease. There are, however, to be found numbers of cases of rheumatism in good houses where the conditions are not in any sense adverse, and there would appear to be an environmental factor in the causation of such. In the poorer child it is probably rather a condition of/

of chronic disability from the bad surroundings causing a predisposition to any type of infection rather than to rheumatism itself.

There would also appear in a certain number of cases a hereditary factor. When the condition occurs in more than one child in a family there may also be found an evidence of rheumatism in one or other of the parents. Some writers state that they have found the hereditary factor more prevalent in the better classes, and that a predisposition on the part of either parent was able to be transmitted to the child. In opposition to this view however is the theory that the disease is spread by contagion from the parent to his child and from brother to sister. Consequently here again the importance of these factors is not as clear as it might be as regards the causation of the disease.

The etiological factor from the bacteriological side is one of great interest and in the vast research that has been done there is an amazing amount of contradictory evidence.

As far back as 1885 Wilson (2) isolated from the pericardial fluid and from the lungs, in cases of rheumatic fever a micro-organism which he declared to be the cause of the disease.

In 1891 Pierre Achalme (3) in Paris described a large anaerobic bacillus which he recovered from the blood, pericardial and cerebro-spinal fluids and the valves/

valves from a case of acute rheumatic infection.

In 1894 Von Leyden (4) disputed the specificity of this organism, as he had isolated a form of diplococcus, which was believed to be related to the streptococcus, from the blood and vegetations on the valves in cases of rheumatic infection. Westphal, Wassermann, and Malkoff (5) in confirming this work produced articular lesions in rabbits by inoculating them with the organism. Triboulet and Cyon (6) produced endocarditis in guinea-pigs by similar inoculation.

Later, in 1900 Poynton and Paine (7) described the presence of a minute gram-positive coccus in culture from the blood and effusions in the joints and also from the vegetations on the valves in 8 successive cases during life. They termed the organism the "diplococcus rheumaticus" and suggested that it was the same as described by Wassermann and his co-workers and by Triboulet.

Since these original and early bacteriological discoveries very many workers have been unsuccessful in confirming the statements made.

At the present time there is no organism known that can be claimed as the causative organism of rheumatism and at the same time fulfil Koch's postulates. There appears to be only one comparatively universal finding and that is the fact that the organism is of the streptococcal group or related to it in some way/

way. Most workers have isolated some type of streptococcus but there is great variation in the types both in their morphological and immunological characteristics.

In order to try to correlate this diversity of opinion as to the exact nature of the causal organism the theory that rheumatism is an allergic phenomenon has many adherents. In 1912 Shick (8) advanced this allergic cause in reference to arthritis and endocarditis in scarlet fever, and in 1915 Faber (9) brought forward this as a theory for the explanation of the conditions found in rheumatism. In a survey on the subject Jenkins (10) reminds us that the clinical picture of anaphylaxis and rheumatism are very similar indeed. He postulates that the allergic theory is the only one that accounts for all the phenomena presented and their reactions to the known treatment. The liability to allergy can be inherited or acquired and so also, he states, can rheumatism. Anaphylaxis is a non specific reaction and therefore rheumatism may be the reaction to a non specific organism. Another fact is that the shock depressant drugs known to be useful in anaphylaxis are of use and are used in the treatment of acute rheumatism.

Nevertheless the problem that presents itself while the bacteriologists are still searching for a definite/

definite causal organism and while the Public Health Authorities gradually better the slum conditions, is that of treating the patient who has developed the condition, and of ensuring that as far as is within one's ability that his treatment is adequate.

The investigation in this enquiry is an attempt to differentiate, in those cases where symptoms of rheumatism have been present, whether the patient on the one hand can be safely considered to be cured, or at least the disease regarded as in a state of quiescence, or whether on the other hand the process is still active.

The beds of our general hospitals are occupied by many cases of acute rheumatism and rheumatic fever, and their sequelae. In the treatment of such cases it is often extremely difficult to decide when a patient should be given full liberties to get up and to leave the hospital.

The grave decisions are:- "When should the patient be allowed to get up?" and "When should he be allowed to return to his work?" Considering the very deleterious and far reaching results of insufficient treatment and care in the subacute or clinically cured cases, when the possibility of the development or exaggeration of carditis are very great, these questions are of vital importance.

There are also cases which are going about at their/

their work and are suffering from slight joint pains, "growing pains" and other manifestations of acute rheumatism. In such cases an attempt is made to find out to what extent the active process is present.

L. Findlay in his book on rheumatism (11) says: " It is therefore wise to assume in every case even " when there is no overt evidence that carditis does " exist and keep the patient at rest until it becomes " quiescent. To decide however when carditis is quies- " cent is a matter of greatest difficulty.

It is therefore with the idea of trying to find some test in order to aid one in the estimation of the activity of the rheumatic process that the sedimentation rate has been studied. During the last few years an increasing interest has been taken in the sedimentation rate in various conditions with, however somewhat indefinite results.

Various writers have suggested the test as a useful guide in acute rheumatism. Payne (12) and Bach and Hill (13) (14) have made use of the Sedimentation Rate in the estimation of the progress of acute rheumatism in children, and show some cases illustrating its use. Kahlmeter (15) also refers to its use in rheumatism and as an aid in differentiting the types of arthritis. Collis and Sheldon (16) have made use of the test as a guide in the treatment of cases with streptococcal vaccine. Petermann and Seegar (17) rather depreciate the/

the use of the S.R. in rheumatism but their use of the test was confined mainly to cases of chorea which it will be seen react rather differently from the other forms of rheumatism.

III. THE ERYTHROCYTE SEDIMENTATION TEST.

The various physical properties of blood that has been withdrawn was of interest to the older physicians who lived in days when blood letting was a common remedy for all maladies. It was not however until 1912 that the measurement of sedimentation of the erythrocytes was made use of as a clinical test. It was Frahaeus (18) who introduced the test, having accidentally found that there was an increase in rate in pregnancy and suggested it as a diagnostic one for that condition. Since that date many workers have made use of the test in the investigation of all types of pathological conditions.

The literature on the subject is vast and very wide in its field of application.

There have been many technical alterations and adaptations of the original methods resulting in many varying expressions of normal and abnormal rates of sedimentation.

The rationale of the test and the causation of the varying rates in different individuals and in different pathological conditions has not any very clear explanation. Many theories have been propounded and many factors stressed as important in the production of an increased sedimentation rate. All these have been well summarised by Kilduffe (19) and he gives the factors as follows:- The rate varies with

1. The electrolytes of cells and serum which in turn are influenced by

2. Variations in the amount and ratio of serum proteins.

3. Viscosity of the blood.

4. Variations in the composition of the adsorption envelope of the erythrocytes.

5. Presence and amount of certain lipoids in serum notably cholesterol and lecithin.

6. Variation in number of the erythrocytes.

7. Variation in size of the erythrocytes.

8. Technical variations.

It will be seen from this summary that there is a considerable possibility of variation from different factors.

Most workers agree that as the loss of electric charge of cell will allow of increased agglutination and massing together of the cells forming larger units, so will there be an increased rate of sedimentation.

The loss of electric charge is apparently increased by the variation of amount and ratio of the serum proteins. An increase of serum globulin and fibrinogen causes an increase in sedimentation rate; and the plasma albumin has the opposite effect.

Variations in the viscosity of blood are small in their effect and variation in composition of the adsorption/

adsorption envelope of the erythrocyte rather impossible to estimate.

Broadly it appears that the combination of variations of these factors by a pathological process causes the increase in rate of sedimentation. However the last three factors based on Kilduff's summary fall somewhat outside the variation from the pathological cause, and therefore should be standardised and corrected for.

The three factors can be suitably grouped under one heading i.e. that of variation in technique, of which there is a very diverse and hopelessly incoordinated number of methods.

Walton (20) in a very able article states that there are four main component parts to the test from a purely experimental standpoint.

These four are:-

1. The tube.
2. Number of red blood cells.
3. Temperature at which blood sediments.
4. Anticoagulant used.

The last two of these factors are of less importance and most easily standardised and consequently will be considered first:-

3. Temperature at which the blood sediments.

It has been shown that there is a definite variation in the rate of blood sedimentation with the variation in external temperature. Gordon & Cohn (21) have shown the effect on rate by varying the temperature from that of an ice box to an incubator, and they suggest as a fixed temperature 22-24°C. as being the most convenient, and that all sedimentations should be carried out at that level. The majority of writers agree that up to 25°C. there is only a small increase of rate and after that each degree of rise makes a marked difference. Walton (20) gives as his limits 19-23°C. All sedimentation stated later in this enquiry were at room temperature varying betweeen 20-25°C. and this was considered sufficiently accurate for practical purposes.

4. Anticoagulant. The anticoagulant that is universally used is Sod: Citrate; the concentration varying somewhat in different observers' technique. Frahaeus (18) originally used 2% solution. Westergren (22) used a 3.8% solution and Haskin, Trotman, Osgood and Mathieu (23) used solid citrate dried on the sides of the tube. It seems unnecessary to go to the trouble of drying off the citrate especially as certain workers have been unable to be certain that this method is as effective as an anticoagulant.

In/

In the Westergren (22) and other methods one-fifth part of citrate is used. If one-tenth of the amount will suffice there is a definite advantage in that the total red cell count is not reduced so greatly and a truer reading given and there is a more easily defined differentiation of the upper limit of red cells. It was in order not to dilute the blood that Haskins (23) and his co-workers introduced the solid citrate but as stated this is not in practice the most effective method.

Again following Walton's (20) method a 3.8% solution of Sod. Citrate was used throughout all the experiments and one-tenth of the final volume of blood being used in all cases. This amount was found to be sufficient to prevent clotting.

The amount of citrate was always accurately measured and so also was the blood. On one or two occasions clotting did occur but this was due to insufficient mixing of citrate and blood in the barrel of syringe. If the plunger is withdrawn after the needle is out of the vein and the barrel rocked back and forward several times no clotting was found to take place.

In the micro methods described, where blood is collected from a prick of the pulp of the finger into a small test tube as described by Cutler (24), the anticoagulant is not measured in any way but merely poured/

poured into the tube and then emptied out.

The anticoagulant should therefore be standardised in two ways, one a standard solution of citrate should be used and freshly prepared as evaporation soon will concentrate it. Secondly the amount of anticoagulant to the amount of blood should also be standard.

1. The Tube.

In the type of tube and of its size and width there have been many variations.

Frahaeus (25) original tube was 17 cm. long and had an internal bore of 9 mm. and contained about 10 cc.

Westergren (26) tube is 200 mm. long with an internal bore of 2.5 mm. and contains 2 cc.

Cutler (27) original tube is one containing 5 cc. and marked off in mm., the column being 50 mm. in height. He deprecates the use of fine capillary tubes as he suggests that there is capillary attraction and the cells tend to stick to the sides. He also reads off the length of plasma every 5 minutes for one hour and plots the result as a graph describing the various results by shape of curve.

Linzenmeier (28) tube is of rather a different type being 6.5 mm. in internal bore, and a capacity of 1 cc. There are two marks on the tube 18 mm. apart and time is recorded how long it takes for the level of/

of the sedimenting blood to pass those two marks.

There are also some fine capillary types of tubes known as the Linzenmeier-Raurert (29) tubes. They are fine capillary pipettes and incorporate a mixing chamber for mixing the blood and citrate.

Payne (12) makes use of short length of glass tubing with internal bore of 1.6 - 1.9 mm. and a column of blood 10 cm. in height having a volume about 0.3 cc.

Zechwer and Goodell (30) use a graduated centrifuged tube containing 10 cc. of blood.

Walton tubes (20) are stated to be 6 mm., of an internal bore and 32.5 mm. in height and contain 1 cc. of blood. Theoretically such a tube only contains 0.918 cc. consequently the tubes must have been actually a very small degree more than 6 mm. in internal diameter.

Cutler (31) describes a tube modified from the original 5 cc. as described by Cutler in 1926 (25). These tubes are 50 mm. in height and contain 1 cc. of blood. The tubes are measured off in mm.

It will therefore be seen that there is very great technical variation and this has led to a very great diversity in the expression of the results obtained.

Fischel/

Fischel (32) suggests expression of the sedimentation rate as a percentage, and I have carried out some experiments in various tubes with an idea of using such an expression.

If it were feasible an expression of the amount of supernatant plasma, as a percentage of total volume of blood, seemed to be a rational one and one that would be universal to all tubes.

The following experiments were performed along the line of verifying this method of expression.

1. First a series of tubes of varying bore were filled to same level and the sedimentation was found to be the same in all the tubes.

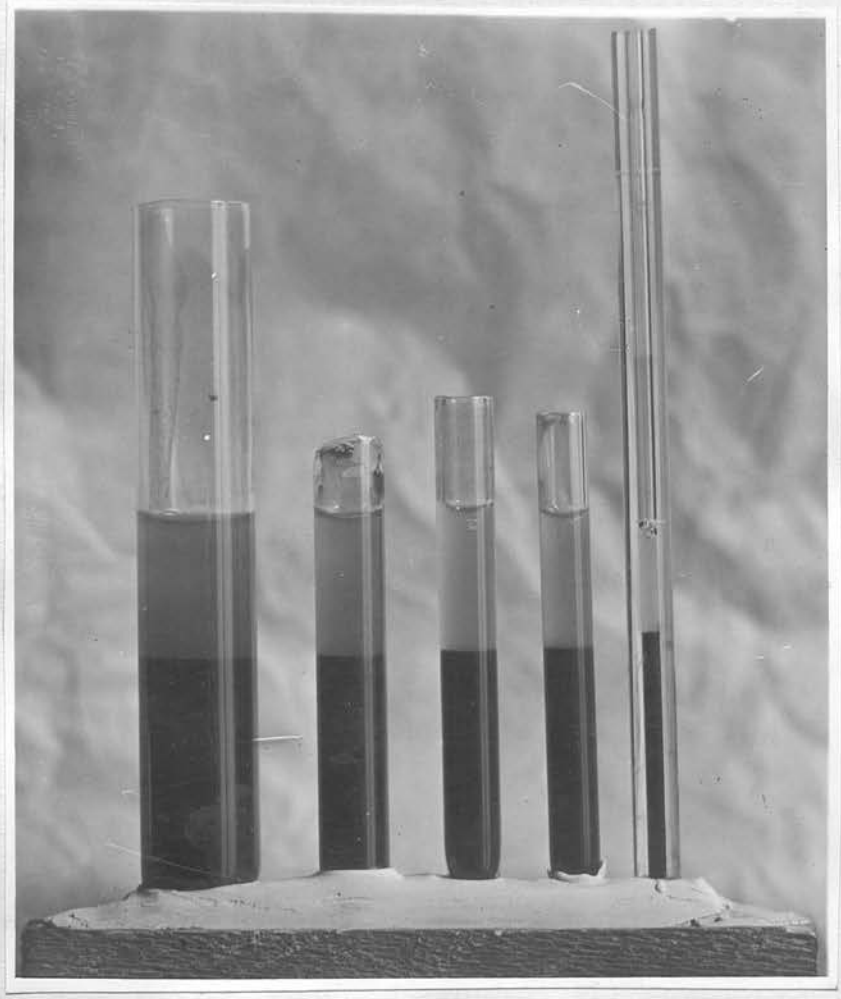
2. Tubes of varying bore were filled to varying heights and the percentage sedimentation calculated.

From the photograph of experiment 1 and table of results of 2 it will be seen that as far as the tubes of a bore above about 3-4 mm. the results are very uniform.

Another experiment was performed using a Zeckwer and Goodell (30) tube with a bore about 20 mm. and haemoglobinometer tube with bore of 6 mm.; the one containing 10 cc. and the other 2 cc., and it was found that there was a very uniform reading even every 5 mm. during the hour.

The/

A PHOTOGRAPH OF THE SEDIMENTATION IN TUBES OF INCREASING INTERNAL BORE FILLED WITH THE SAME BLOOD AND TO THE SAME HEIGHT IN EACH.



This photograph shows tubes of widely differing bore which were filled to the same height with the same patient's blood and allowed to sediment for an hour. The internal bore of the tubes reading from left to right is as follows.- (1) 15 mm. (2) 9 mm. (3) 6 mm. (4) 5 mm. (5) 2 mm. It will be seen that they are all at the same level at the end of one hour except the smallest which shows the effect of capillary attraction and the consequent unreliability of the small bore tubes.

Experiments on cases of varying Erythrocyte Sedimentation Rate in different tubes showing correction to percentage.

Case	Type of tube.	Length of Column.	Internal Bore.	S.R.	As %.
C.B.	Zeckwer & Goodell	100%	15 mm.	63%	63%
	Walton	29 mm.	6 mm.	18 mm	62%
	Haemoglobinometer	100%	5 mm.	62%	62%
	-	55 mm.	5 mm.	34	61.9%
J.G.	-	50 mm.	5 mm.	24 mm.	48%
	Walton	32.5 mm.	6 mm.	15.5 mm.	48%
	-	38 mm.	5.5 mm.	18.5 mm.	48%
	-	64 mm.	5 mm.	31 mm.	48%
	Haemoglobinometer	100%	5 mm.	48%	48%
G.S.	Walton	50 mm.	5 mm.	20.5	41%
	Capillary	100 mm.	3 mm.	40	40%
	Zeckwer & Goodell	100%	15 mm.	41%	41%
J.G.	Haemoglobinometer	100%	5 mm.	23%	23%
	-	50 mm.	5 mm.	11.5 mm.	23%
	Walton	32.5 mm.	6 mm.	7.5 mm.	23%
T.C.	Walton	31 mm.	6 mm.	17.5 mm.	56.4%
	-	82 mm.	4 mm.	36 mm.	56.1%

E.J./

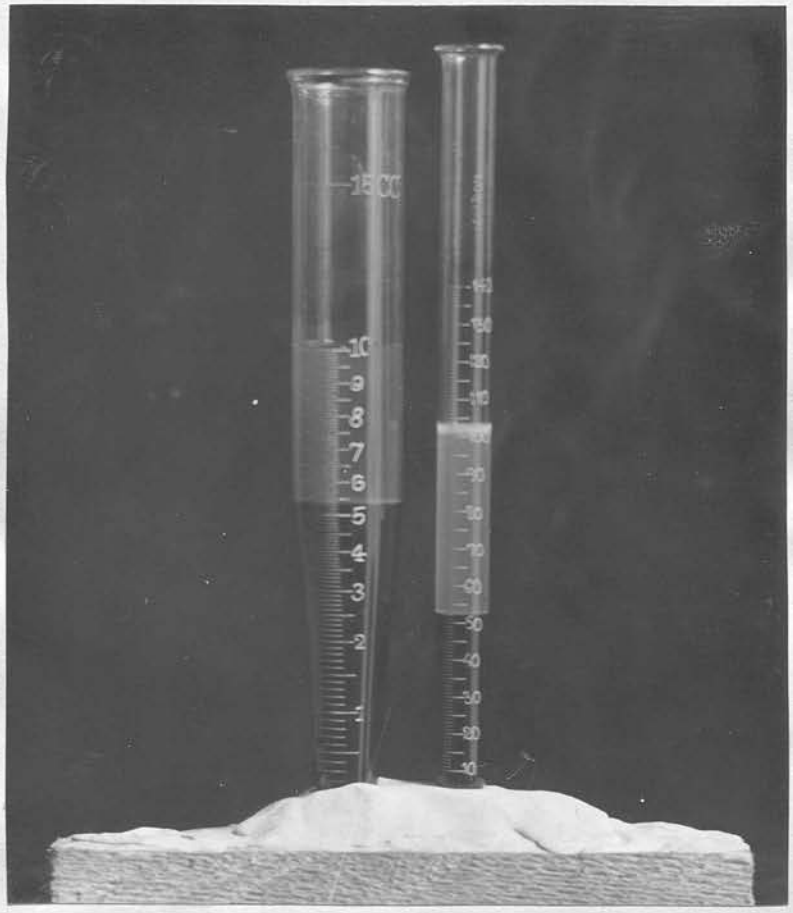
Case	Type of tube.	Length of Column.	Internal Bore.	S.R.	As %.
E.J.	Walton	32.5 mm.	6 mm.	15.5	47%
	Capillary	100 mm.	3 mm.	46	46%
	Zeckwer & Goodell	100%	15 mm.	44%	44%
	Haemoglobinometer	100%	5 mm.	44%	44%
	-	50 mm.	5 mm.	22.5 mm.	45%
	-	26 mm.	5 mm.	11.5	44%
	Haemoglobinometer	100%	5 mm.	25%	25%
	-	50 mm.	5 mm.	12.5 mm.	25%
M.L.	-	50 mm.	5 mm.	25 mm.	50%
	-	36 mm.	5 mm.	18 mm.	50%
	Haemoglobinometer	100%	5 mm.	50%	50%
J.B.	-	50 mm.	5 mm.	30 mm.	60%
	-	23 mm.	5 mm.	14 mm.	60%
W.D.	-	50 mm.	5 mm.	23 mm.	46%
	-	25 mm.	5 mm.	12 mm.	48%

The following are readings in cases showing readings in Haemoglobin tube and Zeckwer and Goodell tube at same times.

C.B.

Min:	0	5	10	15	20	25	30	35	40	45	50	55	60	Min.
Zeckwer & Goodell	100	94	68	56	49	46	43.5	41	40	39	38.3	37.5	37	
Haemoglobin.	100	93	68	55	49	45	43	41.5	40	39	38.5	38	38	
E.J.														
Min:	0		10		20		30		40		50		60	
Zeckwer & Goodell	100		95		82		71		64		58		56	
Haemoglobin.	100		95		83		71		64		59		57	
J.G.														
Min:	0		10		20		30		40		50		60	
Zeckwer & Goodell	100		94		71		61		58		55		52	
Haemoglobin.	100		95		71		62		58		56		53	
M.G.														
Min:	0		10		20		30		40		50		60	
Zeckwer & Goodell	100		98		96		92		87		79		77	
Haemoglobin	100		99		96		93		88		79		77	

A PHOTOGRAPH OF THE SEDIMENTATION OF THE SAME BLOOD AT SAME TIME IN TWO DIFFERENT TYPES OF TUBES.



The left hand tube is a 10 cc. graduated centifuge tube as recommended by Zeckwer and Goodell and the other is an ordinary Haemoglobinometer tube containing 2 ccs. The haemoglobinometer tube which was filled first will be seen to read about 52% and the other tube about 53%. The correlation between two such tubes during the hour is found to be very near and that they read almost exactly the same every five minutes.

The results were not found to hold good in the narrow bore tubes. A tube of 2.5 mm. as used in the Westergren method did not sediment so quickly as compared with the wider tube.

Also there was not found to be the same correlation if half the amount of blood was used in the narrow tubes. The sedimentation rate of 1 cc. in a narrow tube was found to be relatively faster than in 2 cc.

Schackle (33) has doubted the expression as a percentage and gives figures for correction when small amounts of blood are used, but the tube he uses is of the Westergren type, and in such capillary attraction becomes an added factor.

Walton rather avoids the use of fine bore tubes and states that capillary attraction becomes a factor in tubes under 2 mm.

Cutler (27) also deprecates the use of fine bore tubes from the same reason.

And it would appear that provided tubes of an internal bore of about 3-4 mm. and over, a universal expression of the sedimentation rate as amount of plasma, as percentage of total blood was feasible and correct.

One/

One confidently states therefore that as far as the bore of tube is concerned it should be at least 3-4 mm. As regards length of the column of blood and total amount there is no need for any definite amount provided there is sufficient to make the reading convenient and practical.

If a tube was devised theoretically with the idea of containing as little blood as was convenient with an accurate reading, then it might be something as follows. It was calculated that if a tube of an internal bore of 5.04 mm. were filled to the 50 mm. mark then the volume contained would be 1 cc. This has many very suitable points about it.

1. The amount of blood is small.

2. The reading can be immediately expressed as a percentage by doubling the result obtained.

3. The bore of tube is well outside the minimum found convenient.

The tubes should be made with flat bottoms in order to make the measurement of the column as accurate as possible. The tubes in practice need only be near to 5 mm. in diameter provided they are not any wider for that would entail the use of more than 1 cc. of blood. The expression as percentage does not require them to be as accurate as if such an expression were not used.

Taking these facts into consideration it will be seen that the tube that is almost identical to the one theoretically/

theoretically designed, is Cutler's (31) modified 1 cc. tube and ones very similar were used without the graduation into mm. A steel rule was used as a measure instead. A mark at 50 mm. was made on the glass for convenience of filling them.

2. The blood count.

The blood count as a factor in altering the blood sedimentation rate is pointed out by Walton (20) as a factor which has been neglected. The need for correction and importance of the red count as a factor was pointed out by Gram (34) in 1929, and also Rourke and Ernstein (35) in 1920, but such a practice is not in general use. Walton lays a very special stress on this point and shows that if a series of tubes are set up with a verying blood count that the S.R. varies proportionately. He shows that in a series of tubes where R.B.C. is 1, 2, 3, 4, 5 million the S.R. varies as a straight line graph in fast sedimenting bloods but in slow normals the curve is one convex downwards. The illustration on the following page demonstrates the type of graphs found.

He gives as normal figures for sedimentation at various counts as follows:-

Millions		5.	4.	3.	2.	1.
S.R. in mm.	M.	2	8	14.5	21	27.5
	F.	3.5	9.5	15.5	21.5	27.5

Expressed in percentage.

Millions R.B.C.s	5.	4.	3.	2.	1.
Males	6%	24%	44.5%	64.5%	84.6%
Females	11%	29%	47%	66%	84.6%

And over a large number of experiments in which he set up a series of tubes with such dilutions, he shows that at all rates of sedimentation, that is in cases where it is fast and in cases where it is normal, the S.R. at the end of one hour at 1 million was always the same and the figure was 27.5 mm. Therefore expressing 27.5 mm. as a percentage of 32.5 mm.: 84.6%.

Some experiments were performed in confirmation of this work and the results are shown here. The photograph shows very graphically in a case of moderately fast S.R. the very definite effect the red blood count has on S.R.

Over a number of experiments when the blood was diluted to 1 million the S.R. was found to be 85% and this corresponds moderately well with Walton's figures of 84.6%.

Walton shows that if there is a fixed figure for all S.R. at 1 million and one experimentally finds the S.R. at any other blood count the S.R. of any dilution can be estimated by drawing a straight line graph through these two points provided the rate is comparatively fast.

For/

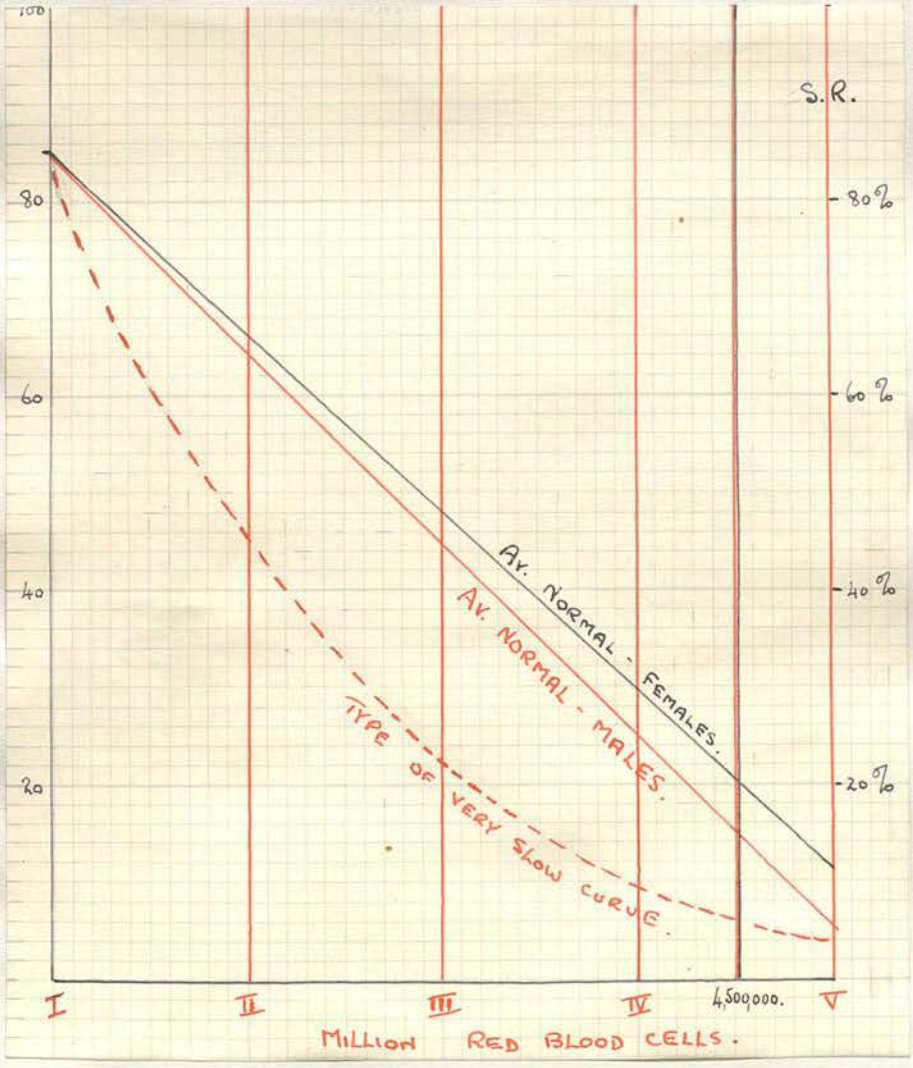
For example if the S.R. at 3,000,000 red cells is 50% and at 1,000,000 known to be 85% then a line drawn through these two points extended onwards will cross the 4 and 5 million lines at corresponding S.R. for that dilution or concentration of red cells.

The photograph shows a graph drawn for quick and easy calculation of S.R. at any figure. It will be seen to consist of a piece of graph paper marked in percentage of S.R. and in millions of red blood count. A piece of thread is fixed at 85% and 1 million red blood count with a drawing pin. The thread can be held taut to cross a fixed point found by experimentation and any point along the line is immediately demonstrated.

Walton expresses his results corrected to 5,000,000 R.B.C.s as an arbitrary figure which is reckoned as the average normal blood count. This is satisfactory enough but it must be remembered that the patient's blood has been diluted with citrate up to one-tenth of its volume and we beg to suggest that a better figure would be 4,500,000 when the dilution is taken into consideration. This gives a result of 5,000,000 R.B.C.s in the original blood.

GRAPH TO DEMONSTRATE THE EFFECT OF THE BLOOD COUNT ON THE SEDIMENTATION RATE.

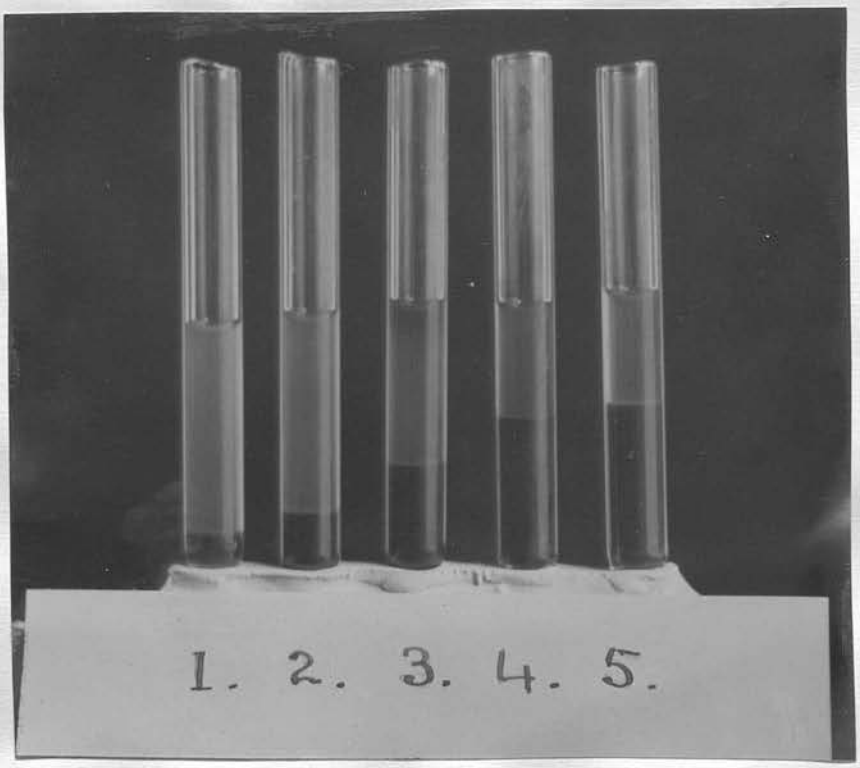
This is a small replica of the graph used to calculate the rate of sedimentation at different concentration of red blood cells. It shows the average graph for both males and females and also the convex type of curve found in slow sedimenting bloods as pointed out by Walton (20).



The vertical lines show the blood count in millions and the vertical the S.R. in percentage.

PHOTOGRAPH OF A SERIES OF TUBES OF DIFFERENT RED BLOOD CELL CONTENTS.

Beneath is a photograph of a series of tubes which were filled with the same patient's blood but plasma was either withdrawn or added to make a series of dilutions of red blood cells varying between 1 and 5 million. They show the result of sedimentation after one hour and clearly demonstrate that the blood count has a very definite effect on the reading at the end of the hour. It shows in a photographic way the same points as the graph on the preceding page.



1. Tube containing blood at 1 million r.b.c.s S.R. is 85%.
2. Tube containing blood at 2 million r.b.c.s. S.R. is 73%.
3. Tube containing blood at 3 million r.b.c.s. S.R. is 62%.
4. Tube containing blood at 4,500,000 r.b.c.s. S.R. is 43%.
5. Tube containing blood at 5 million r.b.c.s. S.R. is 39%.

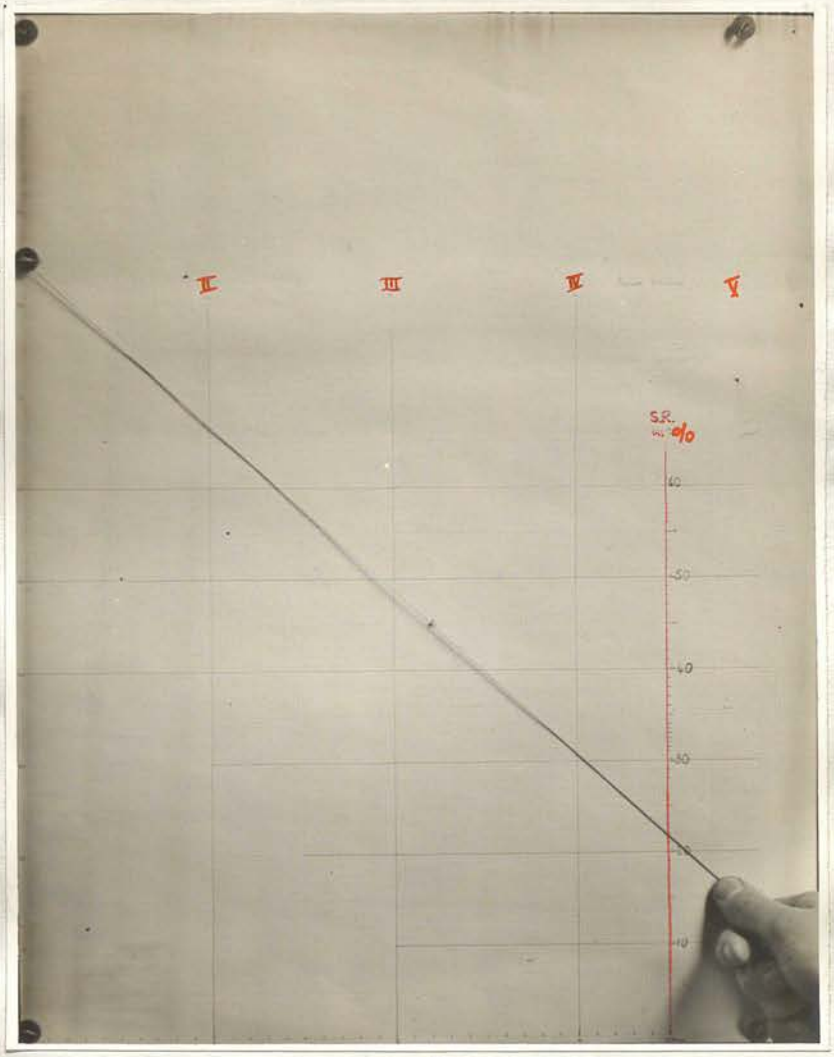
There are also two other minor points in the experimental detail which are of some importance. The first is the need for the tubes to be kept absolutely vertical and this was pointed out by Ponder (36) as a very definite source of error if not observed. The tubes in the following experiments were either held in racks or the lens inserted into plasticene which was found to be a very satisfactory method of holding the small tubes.

The question of the inadvisability, especially in children, of vein puncture is one brought forward in advocating the micro-methods used by Payne (12). In practice it was found very difficult to get sufficient blood by a stab puncture of the finger and unless the child is very young no difficulty was experienced in performing vein puncture provided care is taken. Some workers state that a tourniquet should not be used as it causes venous stasis and some intravenous sedimentation. However if, as was always done in these experiments, the tourniquet is tightened immediately before the puncture is performed, it is on for only a matter of a few seconds and seems rather too small a fallacy to be of any regard.

No ill effects or injury was found in any case following vein puncture.

Experiments were also performed in ascertaining if there was any difference in allowing the blood to sediment/

PHOTOGRAPH OF THE GRAPH USED FOR THE QUICK DETERMINATION OF THE SEDIMENTATION RATE AT ANY GIVEN CONCENTRATION OF RED BLOOD CELLS.



1. Vertical lines show the red blood count in millions.
2. Horizontal lines show the S.R. in percentage.
3. Hand holding the cord taut.
4. The point at which the cord is fixed being at 85% and 1 million r.b.c.s.
5. Shows the experimental point found in this case to be at 45% and 3,200,000 red cells.
6. The point at which the cord crosses the 4,500,000 line giving a reading of 22%.

sediment immediately or if it could be carried and sedimented later.

No difference was found and if the blood had to be carried it was carefully corked with a rubber cork in the tube and after being shaken up was set up in the stand to sediment for an hour.

But this was always carried out within 3-4 hours of withdrawing the blood and the results appeared to be uniform within that length of time.

Actual Technique used given in Detail.

1. A syringe of 2 cc. or 1½ cc. capacity was used and dried by means of washing out with alcohol and ether. The needle to be used for vein puncture was attached to the syringe while the ether was being drawn in and expelled from it.
   These needles were stored in spirit and constantly sharpened.

2. A large bore needle was now affixed to replace the one to be used for vein puncture and a solution of 3.8% sodium citrate drawn up to the required amount, and the first needle replaced. The reason of changing the needles was in order that the sterile one was not used to draw up the non-sterilized solution of citrate.
   As a general rule it was found preferable to fill the/

the syringe at the bedside as it caused less likelihood of blood clotting.

The amount of citrate was in all cases very accurately measured, either 0.2 cc. or 0.15 cc. depending on how much blood was required - 2 cc. or 1½ cc.

3. The skin of anticubital region was cleaned with ether especially over any visible veins.

4. A tourniquet of thin rubber tubing was laid in position behind the patient's arm and tightened just as the needle was introduced.

5. The needle was introduced at the side of a suitable vein and carefully insinuated into it. The correct amount of blood was now withdrawn and tourniquet released and needle withdrawn.

6. The barrel of the syringe was rotated in order to get proper mixing of the citrate solution and blood.

7. The needle was removed, as forcing blood through it might cause some haemolysis, and the tube filled up to the 50 mm. mark.

8. A Haemocytometer pipette was now introduced into the blood and the amount drawn up to the mark and diluted in the usual manner.

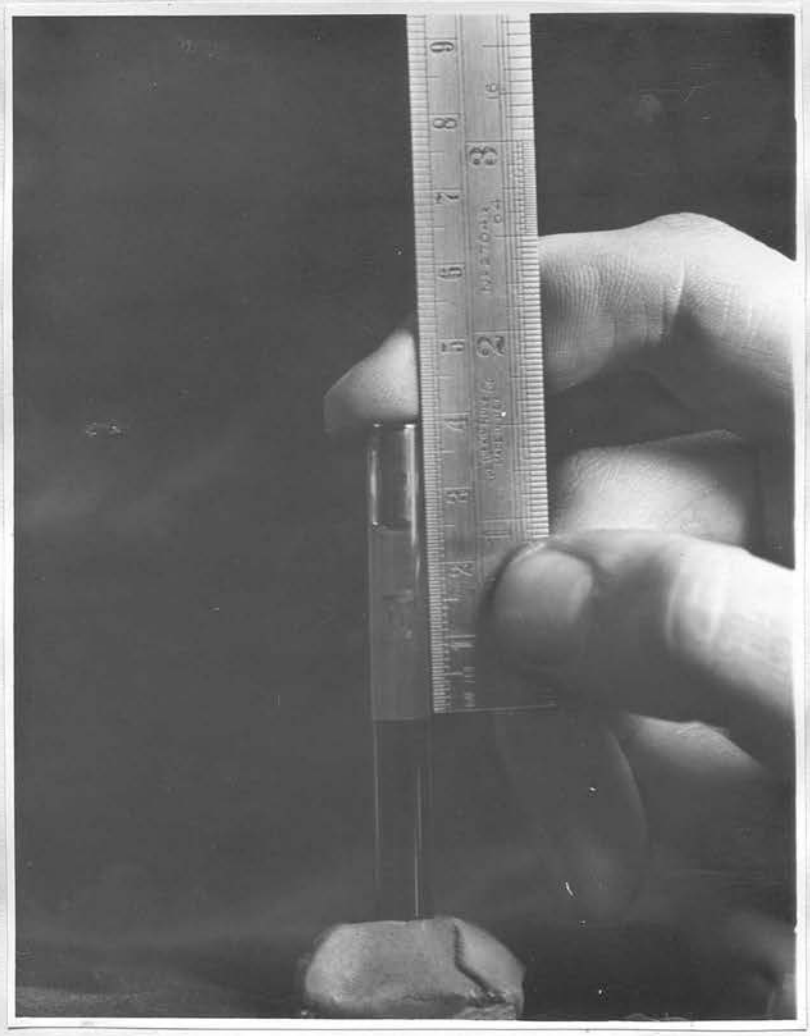
9./

9. The supernatant plasma was measured one hour after by means of a steel rule and during this time the erythrocyte count was estimated.

10. The sedimentation rate in mm. was then doubled and consequently the final expression was in percentage of sedimentation in one hour at a certain number of red blood cells per cmm.

11. The final correction was made to express the S.R. at 4,500,000 red cells per ccm. by means of the chart illustrated.

PHOTOGRAPH SHOWING THE METHOD OF MEASURING THE SEDIMENTATION RATE WITH A STEEL RULER MARKED IN CENTIMETRES.



In the photograph it will be seen that the reading is 24 mm. of supernatant plasma in a column 50 mm. high. Therefore the sedimentation at the end of one hour in this case is 48% and next it has to be corrected for the blood count.

The photo is life size.

IV. APPLICATION OF SEDIMENTATION RATE TO STUDY OF ACUTE RHEUMATISM.

Since Frahaeus (18) accidentally discovered that there was an increase in Sedimentation rate in pregnant women, this phenomenon has been used in the study of all types of disease.

All workers agree that there is no evidence to show that the S.R. can be considered as diagnostic of any specific disease.

McDonagh (37) states that the rate of sedimentation of blood runs "pari passu with active dehydration of protein particle of blood" and as the chemico-physical change may be brought about in various methods the test is not a diagnostic one of any particular condition.

It must be classified along with rise in temperature or an increased leucocyte count, neither of which are of definite diagnostic value but are of great help in diagnosis and treatment of the patient. It is in the study of a disease in its intensity, its reaction to treatment and its prognosis that the sedimentation rate is of value and of very great value in certain conditions.

Cutler (32) reviewing 5,000 cases where sedimentation rate was estimated makes the following classification of conditions according to their S.R.

A./

A. Abnormal Sedimentation rate.

1. Chronic infections, - Tuberculosis and Syphilis.
2. Acute infections, - pheumonia, septicaemia, acute endocarditis and the exanthemata.
3. Malignancy.
4. Localized suppuration.
5. Acute intoxication, - lead and arsenic poisoning.
6. Certain endocrine disturbances, - thyrotoxicosis.

B. Doubtful increased Sedimentation rate.

1. Simple catarrhal inflammation, appendicitis and colitis.
2. Chronic ulcerations - gastric and duodenal ulcers.

C. No change in Sedimentation rate.

1. Functional disorders.
2. Certain nervous disorders including dementia praecox.
3. Focal infection - an apical root abscess.
4. Metabolic diseases, - uncomplicated diabetes, and essential hypertension.
5. Allergic diseases, - asthma and Hay fever.
6. Most skin diseases.
7. Simple cysts and growths.
8. Chronic valvular heart disease.

Consequently classified widely the only conditions giving an increase are infection and malignancy.

The/

The sedimentation rate is a test widely used on the Continent, in America, and in Canada, but has not the same wide field of application in the study of disease in this country. There are, however, one or two particular conditions in which it is used constantly.

One definite use to which it has been put is in the differentiation between pyosalpinx and an ectopic pregnancy for there is a marked increase in the suppurative condition whereas the pregnancy is not to a stage where the S.R. is increased. Gynaecologists recognise this as a very useful and important guide in cases where such a diagnosis is difficult.

There is another line in which it has been of some use in the control of cases of tuberculosis treated by artificial pneumothorax. When such cases are progressing favourably the S.R. falls and this is very useful in cases which are afebrile and showing little or no signs or symptoms.

The application to the study of rheumatism is rather similar in nature to its method of application to tuberculosis.

As already pointed out it is to estimate any latent active process that is not manifesting itself by very much in the way of physical signs and symptoms.

Before/

Before being able to state what is a pathological rate one must first define the limits of normality. It will be quite understood after all the different methods that use the figures given as normal are not in any way uniform.

Normal Sedimentation as given by various workers at the end of 1 hour.

Cutler. (31) 5 cc. tubes 50 mm. column.

Males: 2-8 mm. Av. 3-4 mm.

Females: 2-10 mm. Av. 5-6 mm. Menses up to 12 mm.

As percentage Males 4-16% Av. 6-8%.

Females 4-20% Av. 10-12%.

This is over a series of 5,000 cases and appears to be the most reliable series although not corrected for red cell count.

Average limit 6-12%

Outside limit 20-24%.

Walton (20) 32.5 mm. column. 6 mm. internal bore and expressed at 5,000,000 red blood cells per cubic mm.

Males 0-5.5 mm. Av. 2.0 mm.

Females 0-5.5 mm. Av. 3.5 mm.

As percentage Males 0-17% Av. 6%.

Females 0-17% Av. 11%.

Here/

Here the average limit is 6-11%

and outside limit 17%

But expression of rate at 4,500,000

Males 0-25% Av. 15%.

Females 0-25% Av. 20%.

and outside limit 25%.

Zeckwer and Goodell (30).

In the group labelled healthy give figures from 8-20% and an average of 14.4%.

The outside limit is given as 45% ! This can be explained by the fact that no correction was made for the blood count and the dilution with citrate was one-fifth of the volume not one-tenth as in Cutler and Walton's figures.

The following are figures of capillary types of tubes and were therefore not correlated to the previous ones.

Westergren (26) Males 1-7 mm.

Females 1-11 mm.

Gram (38) Males 2.5 - 6.0 mm. Av. 3.9 mm.

Females 2.5 - 7.25 mm. Av. 4.7 mm.

Kreindler & Popper (39) Males 3-6 mm. Av. 4.5 mm.

Females 4-8 mm. Av. 6 mm.

It/

It will be seen on referring to the table that where possible the results have been reduced to a percentage expression and so correlated to one another as far as possible. As regards the experiments performed in this enquiry the important figures are those of Cutler and Walton as it was following their experimental findings as already stated that the present work was performed.

It will be seen that the results are very much the same by the two workers and the average result of normal is up to 12% and outside limit being about 20%.

Therefore any sedimentation rate of over 20 - 24% at 4,500,000 r.b.c's can be considered as above the outside normal limits. In most of the cases on which S.R. was performed and who were in a healthy condition the rate was found to be less than 10%.

In cases of acute rheumatic fever it is difficult to be dogmatic as to the adequate duration of treatment and to decide how long a patient should remain in bed. It is impossible to state a period that is adequate for all cases especially as relapses commonly occur without warning.

In the application of the S.R. to the study and control of rheumatism it is thus of main interest in the recovery or convalescent stage. All the acute febrile conditions appear to cause an increase in the S.R./

S.R. and from that alone it may be reckoned in the acute stage that the S.R. will be raised to about 50%. It will be wise in most cases, if possible, to estimate the rate when the condition is fairly acute, as this will give a figure for comparative purposes during recovery. Nevertheless the important stage is when the patient is clinically better, and the question of continuance of treatment arises.

The other type of case where the estimation is of value is in doubtful ambulant ones where if the sedimentation rate is increased it would appear to be a definite suggestion that adequate treatment in bed is essential.

One point must always be kept in mind and that is the possibility of some concurrent condition which is causing an increase of the sedimentation rate.

In regard to prognosis it would appear that it is of value in showing the immediate changes that are to take place. Its value as regards the ultimate condition lies in its demonstrating if the patient has made a rapid immediate recovery or not.

V. ILLUSTRATIVE CASES.

In the following series of cases an attempt is made to show how and in what type of case the sedimentation rate is of value in the regulation of treatment.

First is a series of cases, all of polyarticular rheumatism, in which the sedimentation was watched over a period of several weeks and the effect of the treatment on the rate studied. The five cases shown, together with a chart of the temperature and the sedimentation rate, are selected as representative of a typical reaction found in all the cases that responded well to treatment. All the sedimentation rates are given as the percentage of plasma at the end of one hour, and corrected to a red blood content of 4,500,000 per cmm. The actual figures showing the blood count and the sedimentation rate will be found in the table on page 64 .

The first four are typical cases of the reaction to treatment with salicylates and the last a case that was treated with anti-streptococcal serum.

CASE No. 1./

CASE NO. 1.

J.R. aet 20. Admitted 20/1/34.

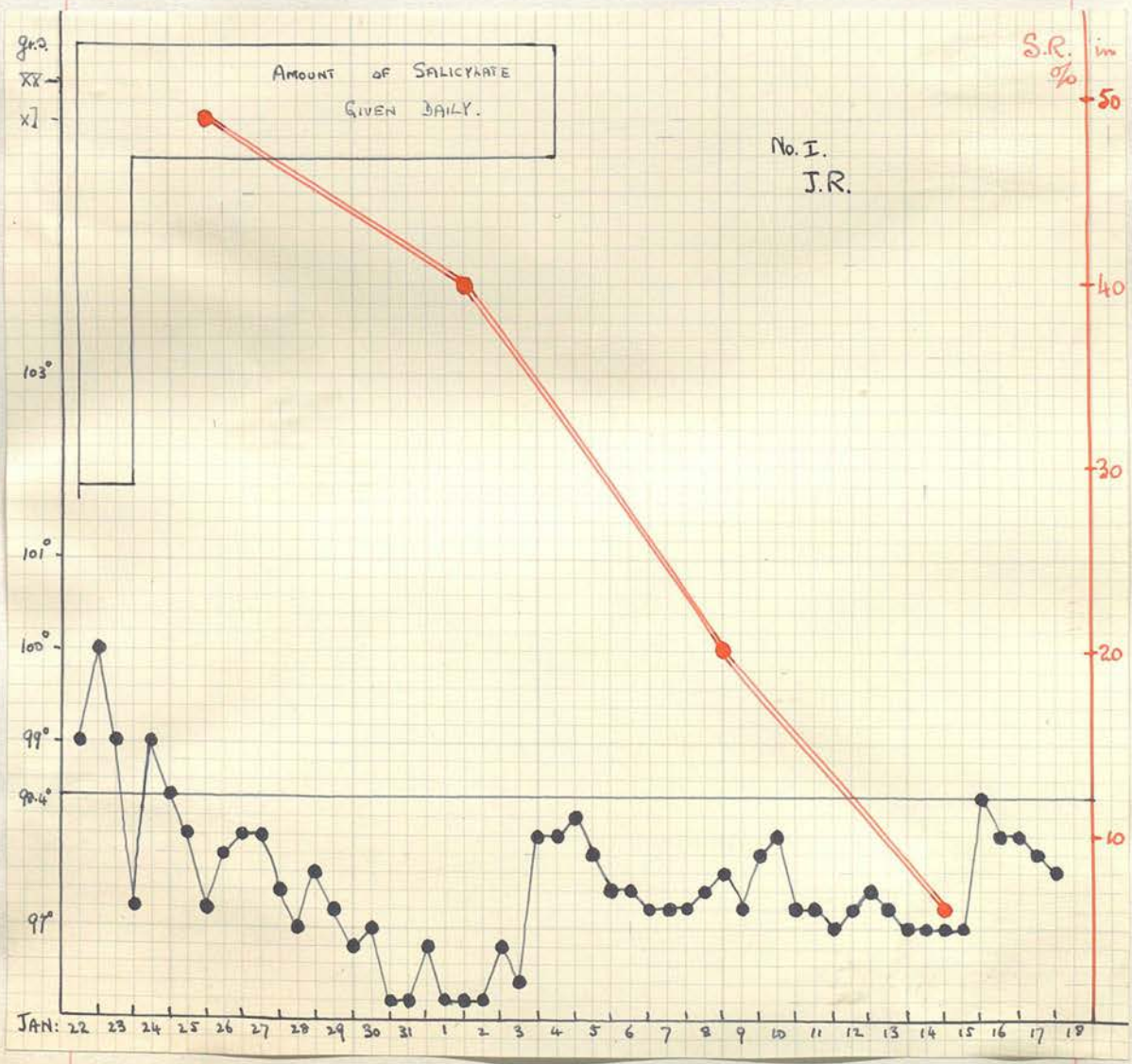
Complaint.

Repeated and constant "colds" for several months.
Pains in the joints for 7 days.

On examination.

She was found to have a polyarthritis with some degree of febrile reaction and at the same time an erythema nodosum on the anterior aspect of the legs. Tonsils enucleated, throat rather congested.
She was treated with salicylates and made a good recovery. No evidence of endocarditis was found. There was some previous history of growing pains.

The Sedimentation Rate will be seen to be increased but rapidly drops as the patient recovered.



CASE NO. 2.

J.G. aet. 36. Admitted 24/1/34.

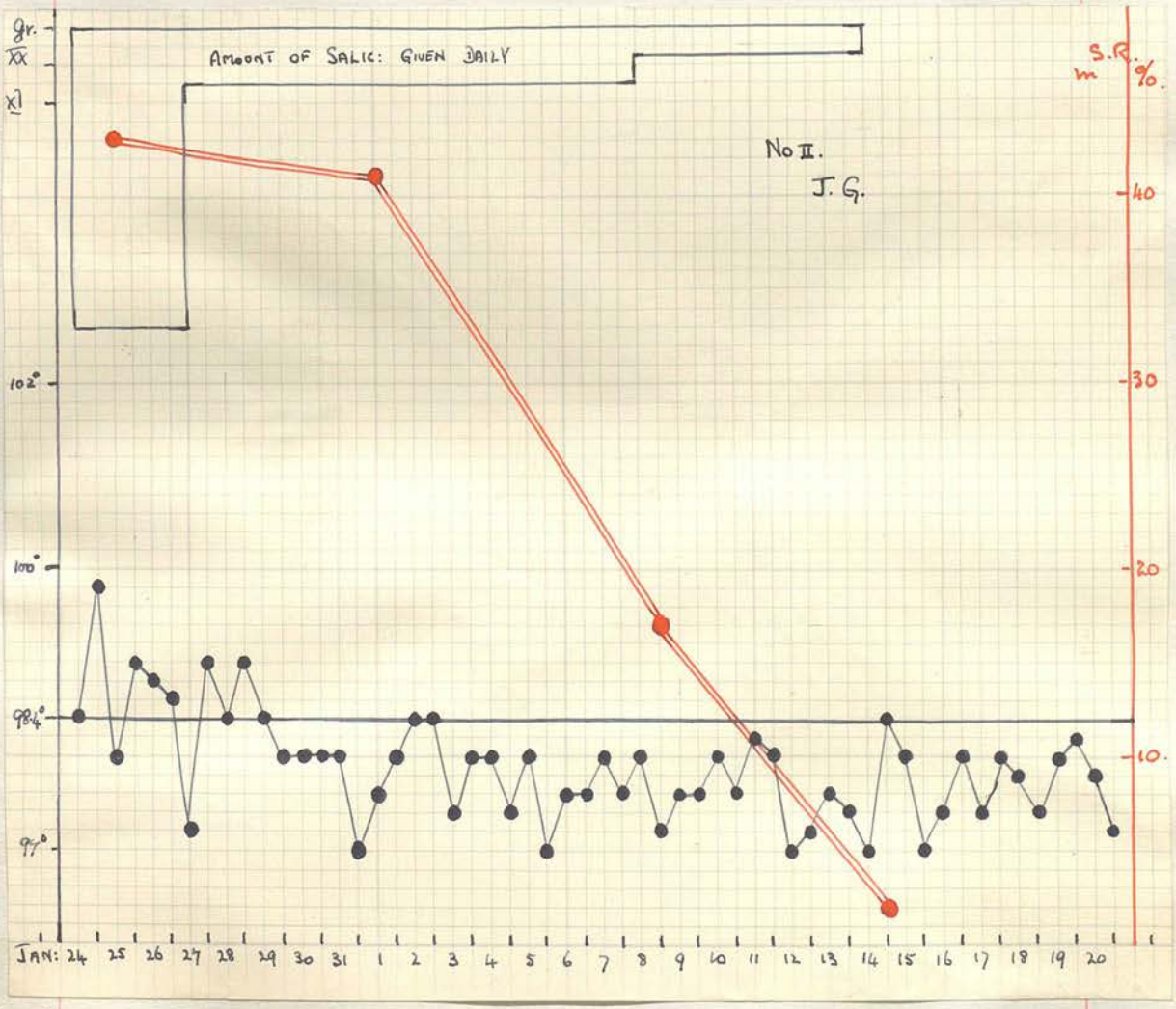
Complaint.

Pains in the knees and feet for 3 weeks.

On examination.

He was found to be suffering from an arthritis of both knees and of the left shoulder. Slight febrile reaction. There was a soft systolic murmur in the mitral area on admission but this disappeared before he was discharged. Treated with salicylates and made a good recovery. Previous rheumatic fever at aet. 14. No history of sore throats.

The Sedimentation Rate was increased and fell rapidly as the patient progressed favourably.



CASE NO. 3.

H.McD. aet. 21. Admitted 13/12/33.

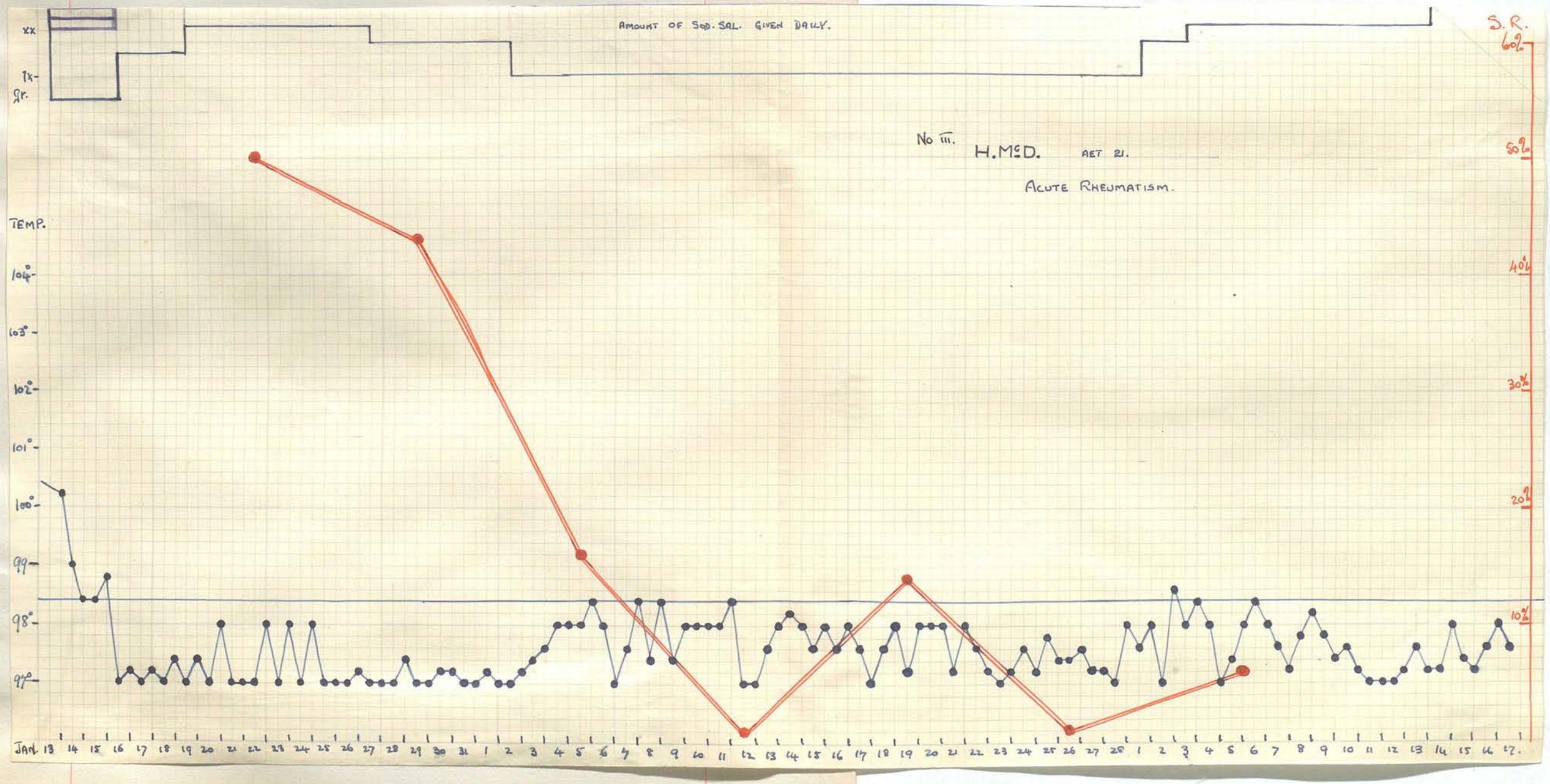
Complaint.

Pains in the knees and arms for 5 days.

On examination.

Found to have a polyarthritis with some fever. Soft blowing systolic murmur present in the mitral area. Previous history of occasional sore throats and of growing pains. Treated with salicylates and made a good recovery as far as the pains were concerned.

The Sedimentation Rate was definitely increased and fell as the patient progressed and remained slow.



CASE NO. 4. P.C. aet. 54. Admitted 15/1/34.

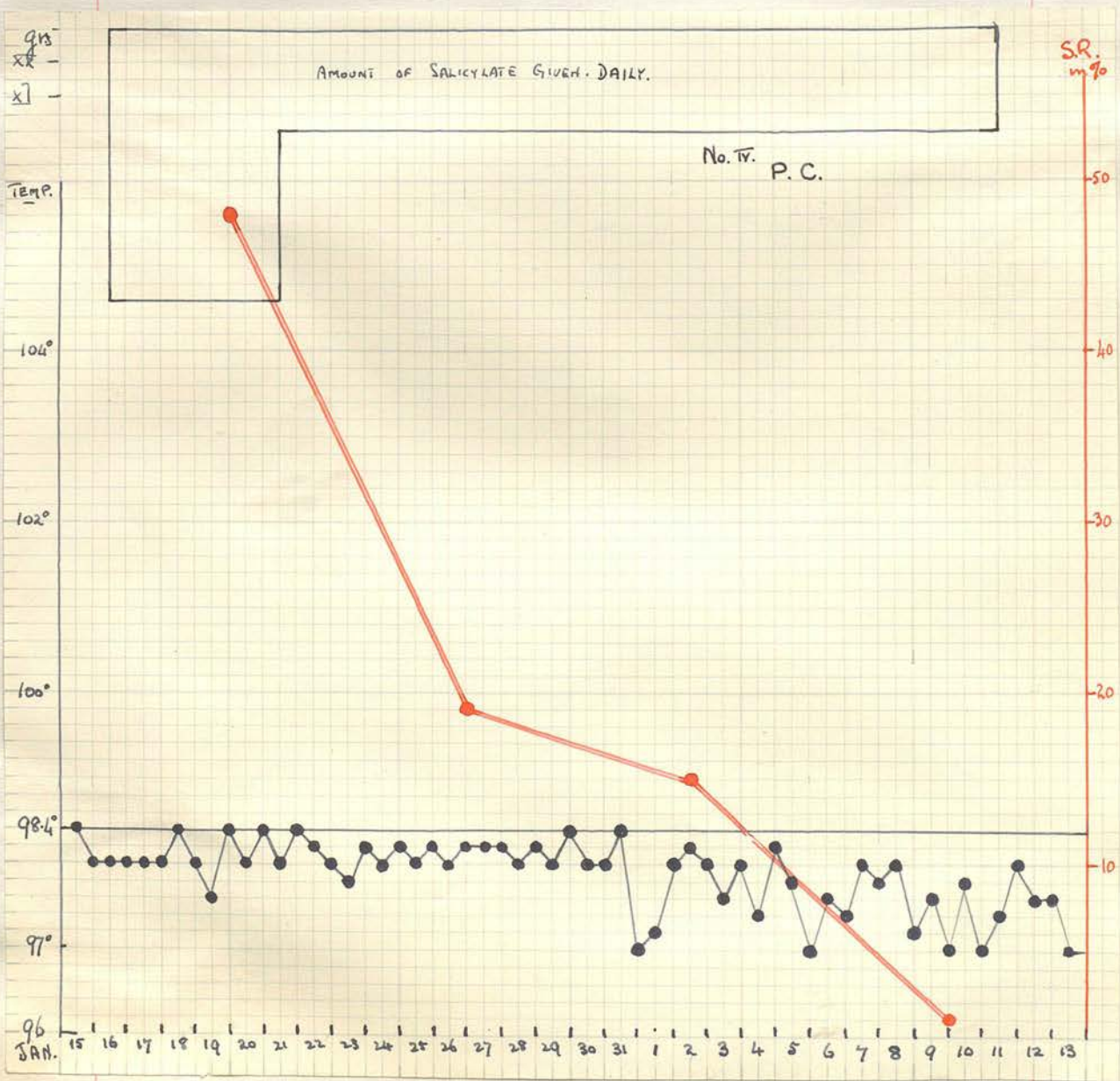
Complaint.

Pains in the joints for 12 weeks.

History. This patient is rather of a different type and his illness apparently started with an injury to his eye with a resultant "hypopyon" 4 months before his admission. He had recovered from this but had not been in quite the best of health when he developed pains in all his joints.

On admission he had some congestion of his fauces and enlargement of his right tonsil. There does not appear to be any previous history of rheumatism. No evidence of carditis. Treated with salicylates which certainly relieved his joint pains. He was afebrile during his spell in hospital. He made a good recovery.

It will be seen that the Sedimentation Rate was markedly increased on admission and fell as in the other cases, as the patient recovered.

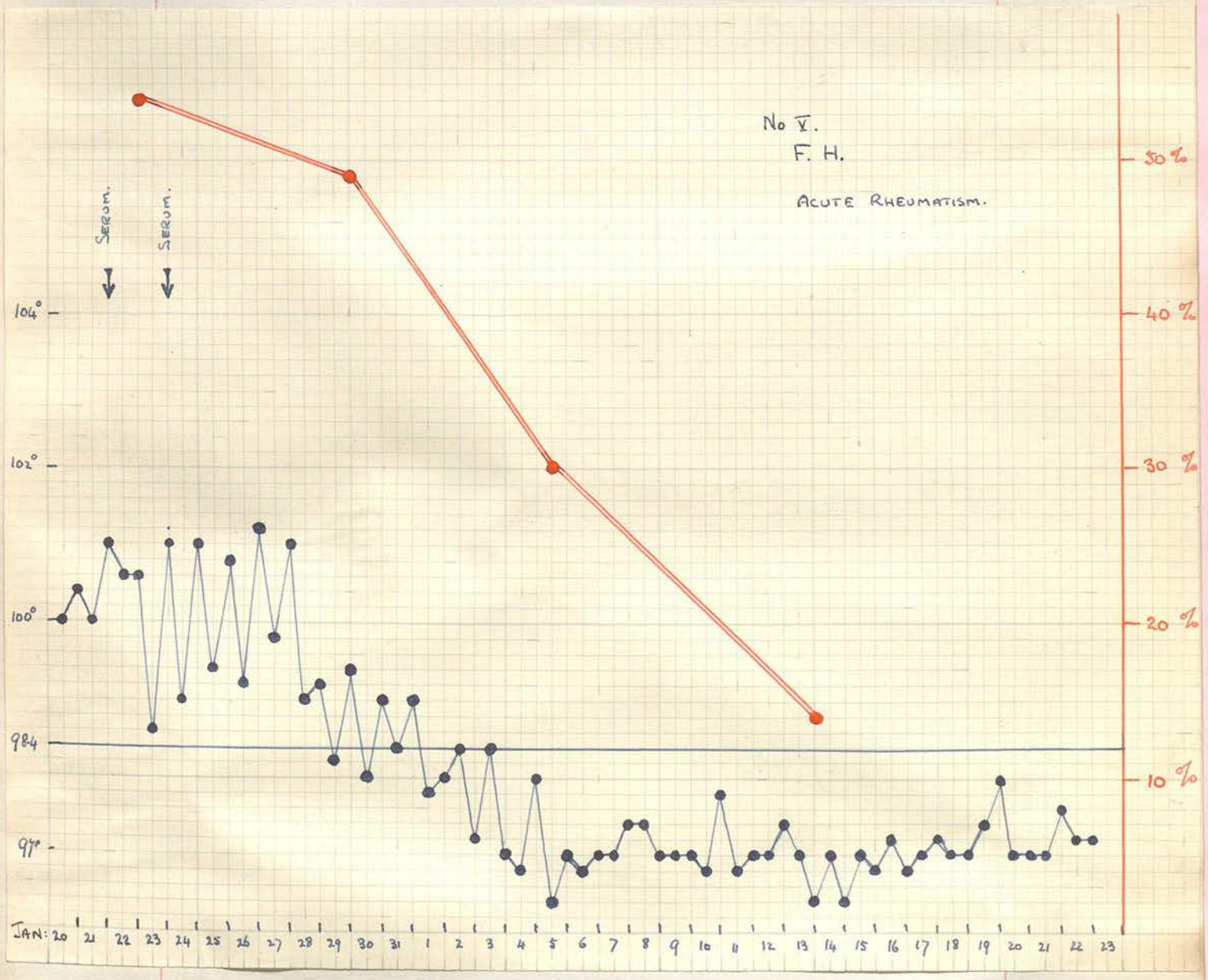


CASE NO. 5. F.H. aet. 36. Admitted 20/1/34.

Complaint. Pains in the joints for 10 days.

History. He had apparently been a healthy man with no history of rheumatic manifestations but said to have had scarlet fever twice. He had a bad tonsillitis about a month before admission. His pains were mainly in the knees, hips and ankles. No evidence of carditis. Haemolytic streptococci cultured from a throat swab. Treated with two injections of streptococcal anti-toxin. Made a very good recovery.

The Sedimentation rate will be seen to fall in about 2 weeks, as in the previous cases.



These five cases are described to show the apparent usual effect of acute rheumatism on the sedimentation rate. They all demonstrate one or two interesting points. The first case is a typical one of acute rheumatism in a young woman who had some previous history of growing pains but no more serious manifestations. She appears to have escaped any cardiac complications. The salicylates relieved her joint pains, and she became afebrile after one or two days and made a very good and speedy recovery. The sedimentation rate, if it is to be of any value, should in such a case have shown a rapid fall, and have been normal on discharge. It will be seen that such was the result.

The second case is a very similar one but it occurs in a man somewhat older, but with a definite previous history of rheumatic fever. He is of interest because he had a definite systolic mitral murmur on admission which cleared up as he recovered, and here again there is a marked fall of the sedimentation rate as the patient makes a marked clinical recovery.

The third case is instructive as he also had a definite mitral systolic murmur which, however, did not clear up as in the last case: but it will be seen that in spite of this the sedimentation rate fell and remained low for several weeks.

From these results it would appear that in a case of acute rheumatism there is a process that causes/

causes some upset of the chemico-physical balance of the blood and that this is rectified as the patient recovers. It will be seen that in the fourth case it is not necessary to have a febrile reaction in order that the sedimentation rate be increased. This case is rather of a different nature, it must be admitted, and probably was a septic arthritis, although clinically it was very similar to the other cases shown in this series. No focus of sepsis could be found and he had a typical history of sore throat just previous to the onset of the arthritis. In the control of such a case as this one, where there are no signs but only symptoms to control the treatment, as far as one can see the sedimentation rate would be of great value.

The fifth case is included to show the effect of streptococcal anti-toxin in the treatment of cases of acute rheumatism. Here again the patient's age is rather above that typical of acute rheumatic fever, but he shows the interesting fact that he had a haemolytic streptococcus in his throat and made a very good recovery after two injections of 30 cc. of the serum. It will be seen that the sedimentation rate shows a very similar reaction in this case to that in the previous four treated with salicylates.

CASE NO. 6. T.C. 56. Admitted 15/1/34.

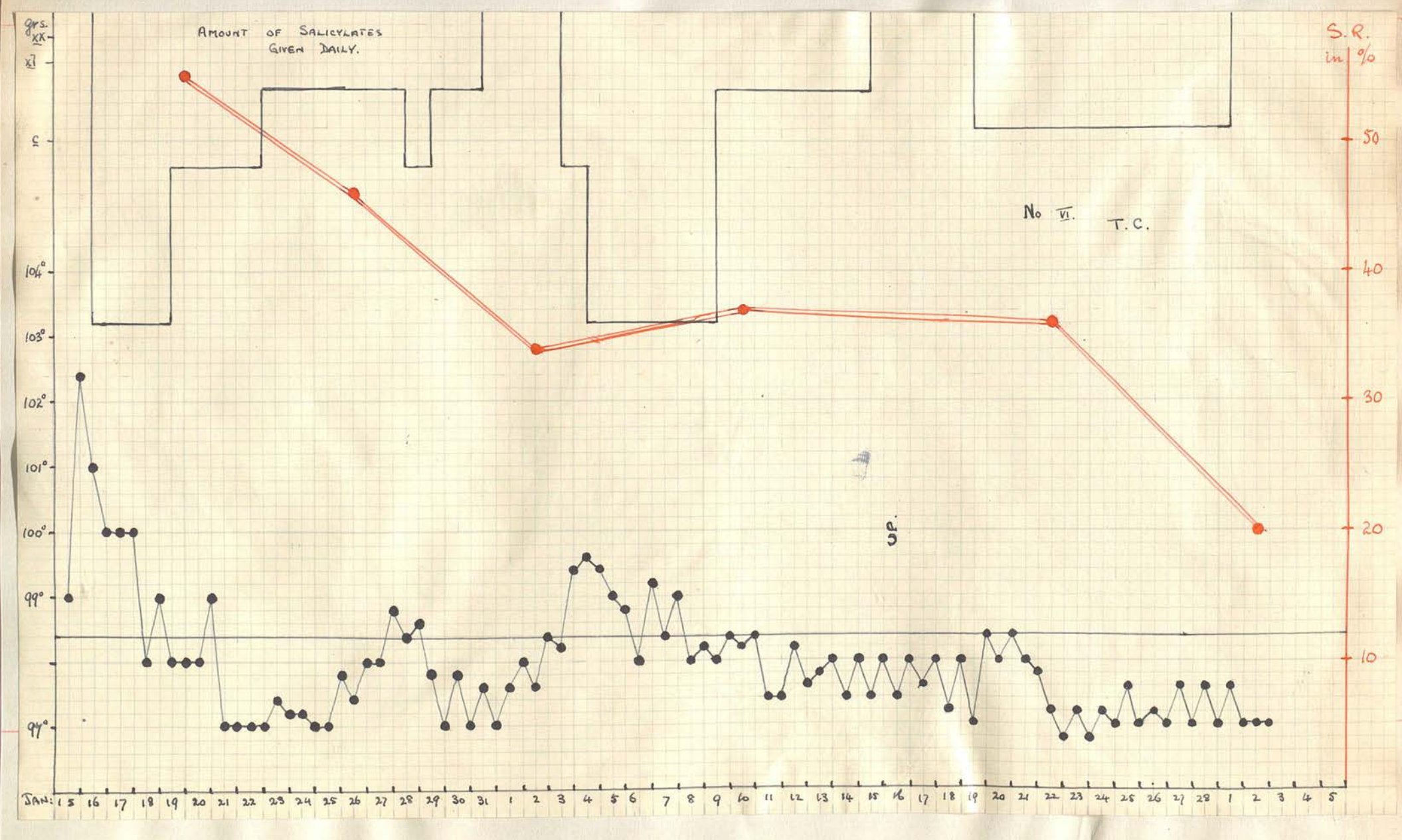
Complaint. Pains in the joints for 2 weeks.

History. Patient gives a history of previous rheumatism and that for some time lately he had had a chronic cough.

On examination he was found to have a polyarthritis effecting his wrists, knees and shoulders. No evidence of carditis was found. He was given salicylates and the dosage was entirely controlled by the symptomatology of the patient and it will be seen that the dosage is very irregular. He was allowed up after about a month in hospital when his joint pains had for the time being, abated. Immediately the pains returned and he was again confined to bed.

The sedimentation rate will be seen to be rapid and fell to some degree after admission, but it will be seen that it did not fall altogether, but remained at a comparatively fast rate for several weeks before finally dropping to nearly normal limits.

(CHART NEXT PAGE)


Amount of Salicylates Given Daily.
grs.
XX
XI
V
No VI. T.C.
S.R. in %
50
40
30
20
10
104°
103°
102°
101°
100°
99°
98°
97°
U.P.
JAN: 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 1 2 3 4 5

CASE NO. 7. J.B. aet. 36. Admitted 19/1/34.

Complaint. Pains in the joints for 4 weeks.

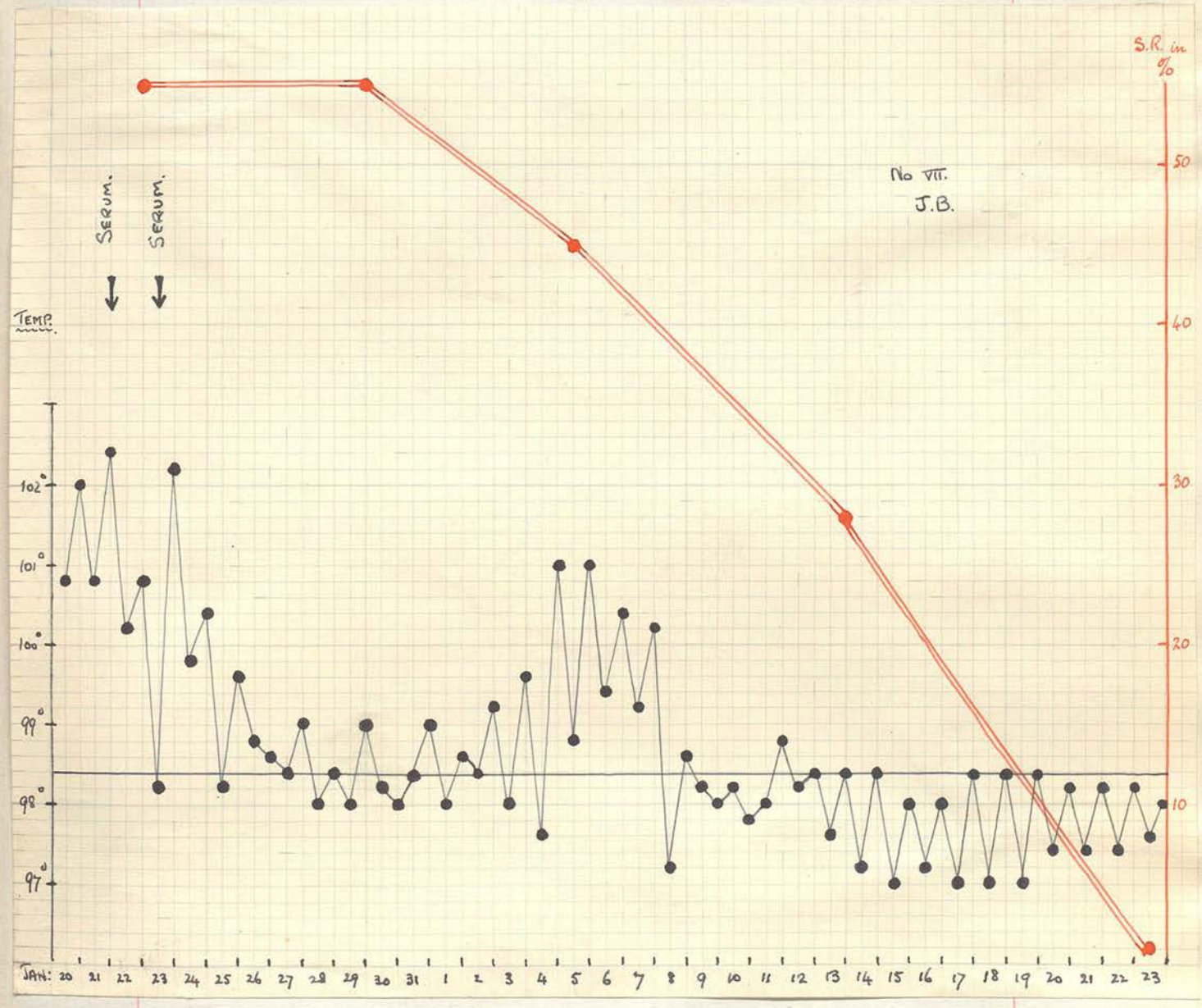
History. This patient had a sore throat about 2 months before admission after which the glands in his neck became swollen for some time. Three weeks after the swelling of the glands had subsided, he developed pains in his ankles, knees and wrists. There appears to be no previous history of rheumatism.

He was found to have a definite arthritis affecting the wrists, ankles and knees, but none of the small joints. He had a soft mitral systolic murmur. Treated with two injections of streptococcal antitoxin. About a week later he developed a bad staphylococcal boil on his buttock which delayed his progress. This, however, cleared up fairly rapidly and he made a good ultimate recovery.

The sedimentation rate in this case shows some delay in falling to normal, but the fact of his developing the boil, or rather carbuncle, would influence the rate.

The slight rise in the temperature in the middle of the chart was due to the condition of his buttock, which was then at its worst.

(CHART NEXT PAGE.)


S.R. in %
No VII.
J.B.
SERUM.
SERUM.
TEMP.
102°
101°
100°
99°
98°
97°
50
40
30
20
10
JAN: 20 21 22 23 24 25 26 27 28 29 30 31 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23

These two cases are given in full in order to show more clearly the use of the sedimentation rate in the control of the treatment of acute rheumatism. Case No.6 is of extreme interest. As pointed out in the case note, the treatment, as far as the dosage was concerned and as regards the date when the patient was first allowed up, was entirely controlled by the symptomatology and the resultant effect was that the patient relapsed on more than one occasion. The salicylates were stopped as soon as the patient was free from pain, and he immediately developed them again, and at this point the sedimentation rate had only fallen very slightly. Then a little later the drug was again stopped and the patient allowed to get up, when once more he relapsed and had to be confined to bed and the salicylates again administered. At this second point the sedimentation rate had risen very slightly, and was still moderately fast. This appears to be a very good example of a case in which the problems of when to stop the dosage and when to allow a patient to get out of bed are very difficult to decide and need for one's guide some sign rather than the symptoms of the patient. The S.R. in this case remains fast and it is suggested that had the case been controlled by that, the dosage would have been continued a little longer until the rate was getting nearer normal; but more important still the patient would not have been allowed/

allowed out of bed until the sedimentation rate was within normal limits which would have definitely stopped the second relapse.

The next case is included in order to demonstrate that, if there is evidence of a delay in the fall in the sedimentation rate, the cause may possibly be other than the rheumatic process, or in other words the possibility of complications affecting the rate must be borne in mind. In the majority of cases, the sedimentation rate has dropped practically to normal in two weeks but in this case it is slow to begin its descent. The reason was that he was developing a carbuncle on his buttock. The interesting feature is, however, that there is really no very great effect on the sedimentation rate once the boil had burst and was healing. The rate fell rapidly and the patient was very well on discharge, and it will be seen that the rate was quite normal by that time.

The cases that are now given in detail are a series in which the patient either has or has had acute rheumatism. The sedimentation rate is thus studied in the various stages of the condition and in cases reacting in different ways to treatment. The table at the end gives the details of the Sedimentation rate and blood counts.

CASE 8. N.M. aet. 13.

This boy had had acute rheumatism in the form of an acute rheumatic fever and had developed mitral incompetence. He had a history of a previous attack 3 years before. He was treated with salicylates for 6 weeks and the S.R. of 54% was on the day before his discharge. It will be seen to be still very fast.

He was seen a week later and then had some definite return of joint pains.

Had the S.R. been taken into account in this case he might have been kept in bed and the recurrence prevented.

CASE 9. J.F. aet. 29.

This man had an acute rheumatism for 6-7 weeks and the S.R. will be seen to fall during the 7 weeks from 59% - 49%. This showed a beginning of a satisfactory fall but unfortunately he became very restless and was discharged at his own wish.

CASE 10. J.T. aet. 20.

A young woman, who had acute rheumatic fever, and the S.R. of 43% was about a month after the commencement of the condition. She was by then afebrile and had had 2 weeks treatment with salicylates. There was a definite systolic bruit.

Judging by the raised S.R. both these cases required considerable further treatment.

CASE 11. F. McC. aet. 14.

A young girl who had a previous history of sore throat and growing pains, and was admitted to hospital 6 weeks before, with a typical rheumatic fever. Her S.R. will be seen to be 20% and so had just returned to the limits of normality.

CASE 12. B.G. aet. 31.

This patient shows a very satisfactory S.R. at 2 and 3 weeks after injection of streptococcal antitoxin for an acute rheumatic fever. The readings will be seen to be 10% and 2% respectively and are well within normal limits. She had, however, developed a definite mitral systolic murmur.

CASE 13. E.J.

This is a particularly interesting case because on the two occasions she was seen she was up and about at her work. The history was one of a bad tonsillitis a/

a year previously and since then mild joint pains flitting in character off and on since. The first S.R. of 41% was after 6 weeks on salicylates and the second of 40% was a few weeks later. There was a definite systolic murmur present, and a doubtful presystolic. The increased S.R. in such a case as this demands more radical treatment and the patient should certainly have been in bed. No evidence of any other possible cause for the increased rate was found.

CASE 14. M.L. aet. 13.

This girl had a mild rheumatic fever. She had joint pains flitting in character and a mitral stenosis. Her rate is seen to be increased - 30%.

CASE 15. J.D. aet. 32.

This was a septic polyarthritis following a parotid abscess. The rate as one would expect was increased - 44%.

CASE 16. R.D. aet. 30.

This was the patient's fourth attack of rheumatic fever and he had a definite mitral stenosis and incompetence. The rate will be seen to be raised - 32% and it is recorded after patient had been ill for about 3 months but had only been in hospital one week.

CASE 17./

CASE 17. A.P. aet. 11.

Another typical case of rheumatic fever with a history of sore throat, flitting joint pains and temperature. The S.R. of 50% was recorded while he was in the acute stage.

CASE 18. W.D. aet. 23.

A case of acute rheumatism for 2 weeks and having a history of a previous attack 5 years ago. A mild systolic murmur present. S.R. was still rapid - 40%.

CASE 19. C.F. aet. 11.

This girl had an acute rheumatism a year previously and developed mitral incompetence. She was treated with streptococcal anti-toxin. Since discharge has been well except for some slight breathlessness. S.R. is slow, showing there was now no active process.

CASE 20. A.A. aet. 33.

This woman was subject to subacute rheumatism and had developed a mitral stenosis. Treated with anti-toxin as in last case, two years ago, and has been well since. S.R. normal - less than 2%.

CASE 21. M. McC. aet. 11.

This child had had chorea and a history of rheumatism and had reported back after treatment with streptococcal anti-toxin. She was well and her S.R. is seen to be slow. It was less than 2%.

CASE 22. F.F. aet. 37.

This woman had an acute rheumatism some months before the S.R. was estimated and she had been successfully treated with serum. Her S.R. is slow.

CASE 23. D. McD. aet. 20.

A case of acute rheumatic fever which had developed a mitral incompetence. He was also treated with antitoxin and the S.R. two months after is seen to be well within normal limits.

CASE 24. J.L. aet. 38.

A case very similar to the last but about 4 months after treatment. S.R. 3%.

CASE 25. D.B. aet. 38.

This man had had joint pains for 2 - 3 months flitting in character. No previous rheumatic history.

S.R. of 17% was after 5 weeks in hospital and treatment with an autogenous vaccine prepared from growth of haemolytic streptococci from his throat.

CASE 26. J.S. aet. 64.

This case is included as the patient gave such a typical history of acute rheumatism following a sore throat 5 weeks before. After he had the sore throat for a week pains began in his elbows, knees and ankles flitting/

flitting in character. It is unusual in a man of this age and his only previous rheumatic history was growing pains when young.

S.R. is seen to be increased to 32%.

CASE 27. M.J.

A case of persistent mild chorea with definite choreic movements on concentrated effort.

No cardiac involvement.

S.R. is 1.5%.

CASE 28. B.G.

Marked chorea which had persisted for a very long period in spite of various different methods of treatment. S.R. about 2%.

CASE 29. C.M. aet. 14.

A case of chorea of a few weeks standing, definite movement of both hands and while still active S.R. was about 2%.

CASE 30. C.R. aet. 14.

A marked case of chorea with constant movement of both hands and continuous grimaces of the face.

S.R., while acute, slow - about 2%. No cardiac involvement.

CASE 31./

CASE 31. E.F. aet. 10.

A case of marked chorea with gross movements of both hands. S.R. of 8% while patient was acute. He had a definite mitral systolic murmur.

CASE 32. S.M. aet. 8.

Another case of chorea with gross movements. S.R. while acute - 16%.

Although higher than in other cases is still well within normal limits.

CASE 33. A.H.

A girl who had had acute rheumatism and chorea some time after her admission. She had developed a mitral incompetence. S.R. 5%.

CASE 34. R.T. aet. 12.

This girl had chorea and while in hospital developed a tonsillitis and S.R. of 31% was recorded while she had a slight febrile reaction due to the condition of her throat.

TABLE SHOWING FULL DETAILS OF CASES.

No.	Name	Age.	Type.	Date.	Temp.	R.B.C.	S.R. %	S.R. 4,500,000
1.	J.R.	20	Acute polyarticular rheumatism. No evidence of carditis. Salicylates.	25.1.34	98° F.	3,400,000	60	49%
				1.2.34	98°	3,400,000	54	40%
				8.2.34	97°	3,600,000	37	20.5%
				14.2.34	97°	3,600,000	24	6%
2.	J.G.	34	Acute polyarticular rheumatism. Salicylates.	25.1.34	99°	4,100,000	48	43%
				1.2.34	97.4°	4,100,000	46	41%
				8.2.34	97°	3,900,000	29	17.5%
				14.2.34	98°	3,900,000	16	2%
3.	H.McD.	21	Acute rheumatism. Mitral syst. murmur. Salicylates.	22.12.33	97°	4,000,000	55	50%
				29.12.33	97°	4,000,000	49	43%
				5.1.34	98.4°	3,800,000	30	18%
				12.1.34	98°	4,000,000	13	1%
				19.1.34	98°	4,100,000	22	14%
				26.1.34	97.4°	4,100,000	10	1%
				2.2.34	98°	4,400,000	8	6%
4.	P.C.	54	Polyarthritis ? Septic afebrile. Salicylates.	18.1.34	98.4°	3,800,000	55	48%
				26.1.34	98	3,800,000	32	19%
				2.2.34	98.2°	3,800,000	27	15%
				9.2.34	97°	3,400,000	23	2%

5./

TABLE SHOWING FULL DETAILS OF CASES. (continued)

No.	Name.	Age.	Type.	Date.	Temp.	R.B.C.	S.R. %	S.R. 4,500,000
5.	F.H.		Polyarthritis.	22.1.34	100.4°	4,400,000	55	54%
				29.1.34	99°	4,400,000	50	49%
			Serum.	5.2.34	97°	4,000,000	38	30%
				13.2.34	97°	4,000,000	24	14%
6.	T.C.	56	Acute polyarthritis.	19.1.34	99	4,400,000	56	55%
				26.1.34	97.4	4,400,000	48	47%
			Salicylates.	2.2.34	98	3,700,000	45	33%
				9.2.34	98.4	3,700,000	48	37%
				22.2.34	98°	3,700,000	48	37%
				2.3.34	97°	3,700,000	26	20%
7.	B.		Polyarthritis.	22.1.34	100.8°	3,900,000	60	55%
				29.1.34	98.4°	3,900,000	60	55%
			Serum.	5.2.34	98.8°	3,200,000	60	45%
				13.2.34	98°	3,200,000	49	28%
				22.2.34	97°	3,400,000	23	1%

No.	Name	Age.	Type.	Date.	Temp.	R.B.C.	S.R. %	S.R. 4,500,000
8	N.M.	13	Acute rheumatism.	19.12.33	97°	4,400,000	55	54%
9	J.F.	29	Polyarthritis.	5.1.34 12.1.34	98.4° 98°	3,800,000 3,900,000	64 55	59% 49%
10	J.T.	20	Rheumatic fever.	21.12.34	98.4°	4,300,000	45%	43%
11.	F. McC.	14	Rheumatic fever.	2.1.34	98°	4,400,000	22%	20%
12	B.G.	31	Rheumatic fever (cured)	23.1.34 31.1.34	98° 98°	3,900,000 3,500,000	23 24	10% 2%
13	E.J.	30	Slight articular pains	11.1.34 22.1.34	98.4° 98.4°	4,100,000 4,100,000	46 45	41% 40%
14	M.L.	13	Slight articular pains Mitral Stenosis.	30.1.34	100°	3,200,000	50	30%
15	J.D.	32	Septic arthritis.	25.1.34	97°	4,500,000	44	44%
16	R.D.	30	Rheumatic fever.	26.2.34	98°	2,700,000	59	32%

No.	Name	Age.	Type.	Date.	Temp.	R.B.C.	S.R. %	S.R. 4,500,000
17	A.P.	11	Acute rheumatism	26.2.34	98°	3,300,000	62	50.5%
18	W.D.	23	Acute rheumatic fever	26.2.34	98°	4,000,000	46	40%
19	C.F.	11	Acute rheumatism cured.	9.2.34	98.4°	4,000,000	3	2%
20	A.A.	33	Mitral Stenosis	9.2.34	98.4°	3,100,000	11	2%
21	M. McC.	11	Chorea.	9.2.34	98.4°	3,800,000	11	2%
22	F.F.	37	Cured rheumatic fever.	9.2.34	98.4°	4,600,000	10	12%
23	D. McD.	20	Cured rheumatic fever.	9.2.34	98.4°	4,200,000	7	2%
24	J.L.		Cured rheumatic fever.	9.2.34	98.4°	4,100,000	12	3%
25	D.B.	38	Acute polyarthritic rheumatism.	2.3.34	98	4,400,000	19	17%

No.	Name.	Age	Type.	Date.	Temp.	R.B.C.	S.R. %	S.R. 4,500,000
26	J.S.	64	Acute rheumatism.	2.3.34	98°	4,000,000	40	32%
27	M.J.	10	Chorea.	4.1.33	98°	4,000,000	13	1.5%
28	B.G.	11	Chorea.	31.1.34	98°	2,900,000	34.7	2%
29	C.M.	14	Chorea.	23.1.34	98°	3,400,000	10	2%
30	C.R.	14	Chorea.	23.1.34	98°	2,600,000	17	2%
31	E.F.	10	Chorea.	14.2.34	98°	4,000,000	19	8%
32	S.M.	8	Chorea.	16.2.34	98°	4,100,000	24	16%
33	A.H.	9	Acute rheumatism.	4.1.34	98°	4,200,000	12	5%
34	R.S.	12	Chorea and tonsillitis	21.12.33	99	4,500,000	31	31%

VI. INTERPRETATION OF THE TESTS WITH CONCLUSIONS.

The cases shown in detail illustrate the typical increase in rate during the acute stage of the illness and the rapid fall as the patient progresses favourably.

The rate will be seen to be normal in 3-4 weeks and such appears to be the usual phenomenon in a straight forward case.

In the series of cases all show a rise of S.R. in the acute stage. The only exception to this is in those of chorea. It is interesting to note that in these latter the S.R. when corrected for the blood count is well within normal limits, except where there is some complication.

It is suggested that the reason for discrepancy in the findings of various workers is due to the fact that the readings have not been corrected for the blood count, in a condition where comparatively severe anaemia is commonly met with.

It would appear that there must be some active process present when the S.R. is increased. The presence or absence of carditis does not seem to be a factor determining the rate. One makes this statement on account of the fact that some of the cases of chorea in spite of an apparent carditis still had a slow sedimentation rate.

However/

However this does not entirely depreciate the value of the test for if an increase of rate is found it is surely indicative of the patient not being truly cured, and indicates that treatment should be continued.

As far as could be judged those cases in which the S.R. had fallen to normal were at least in a quiescent stage and appeared to be cured.

CONCLUSIONS.

1. There is an increase of S.R. in acute rheumatic fever and this increased rate slowly diminishes as the patient progresses favourably.

2. This increased rate does not occur in chorea.

3. The increased rate does not appear to have any connection with the presence of carditis.

4. The presence of an increased rate in a patient convalescent after rheumatic fever is a definite indication for further treatment.

5. A normal S.R. was found only in those (apart from the cases of chorea) which had been apparently cured.

VII. SUMMARY.

1. The crippling of young life by the after effects of rheumatism is stressed.

2. The problem of suitable treatment on account of the obscure etiology are pointed out.

3. The difficulty of judging the condition of a patient in the convalescent state is referred to.

4. The sedimentation rate is studied with regard to its rationale, experimental methods and factors causing alteration in rate.

5. The importance of the red blood count as a factor is stressed and a method of correction used.

6. The sedimentation rates are expressed as a percentage and corrected to a standard blood count.

7. The cases of rheumatism in which the S.R. was studied are given in detail.

8. The use of the S.R. in the regulation of such cases is demonstrated.

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