

THE ,
BLOOD SEDIMENTATION RATE
IN
DIABETES MELLITUS.

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University of Glasgow.

Degree of Doctor of Medicine.

T H E S I S

Submitted, June 1937, by

WILLIAM MORTON, M.B., Ch.B..

"Strathyre",
Stepps,
Glasgow.

CHAPTER 1.

T H E B L O O D S E D I M E N T A T I O N T E S T. -----

When an anti-coagulant, such as citrate solution, is added to fresh blood, clotting does not take place. In such citrated blood the cells soon begin to separate out from the plasma and slowly settle towards the bottom of the container. Eventually the cells form a column of "sedimented cells", and leave above, a clear layer of serum.

The speed at which this cell settling takes place has been called the Blood (or Erythrocyte) (i) Sedimentation Rate, and was described by Fahreus, in 1918. He observed that the sedimentation rate was not constant, but that it varied in different individuals and that it was markedly increased in certain conditions, especially during pregnancy.

Fahreus obtained the blood by veno-puncture and ran it directly into a tube containing Sodium Citrate solution.

He measured the column of settled, or sedimentated, red cells after a given time, and named this reading, the sedimentation rate.

Other workers were attracted by his investigations, and they introduced different methods, and modified techniques, for the performance of the test. For example, Westergren (2) collected the blood in a syringe containing a solution of Sodium Citrate, mixed it and transferred it to a calibrated tube, now known as the Westergren Tube. He investigated the sedimentation rate in tuberculosis. The readings of the methods of Fahraeus and Westergren were similar, in that both expressed the rate as the distance through which the erythrocytes had settled in a given time.

Linzenmeir (3) using a different technique, recorded his results as figures representing the time taken for the cells to sediment to a given distance.

These two principles of time and distance were combined by Cutler (4) who then recorded results graphically.

Numerous other methods and modifications have since been described, but of these the micro-method (5) alone requires mention. The necessary amount of blood for this method can be obtained by finger-prick, and this is of advantage in the investigation of children, and in

conditions where repeated veno-puncture is difficult, or inadvisable.

Many corrections and refinements of the test have been suggested. For example, it was found that the sedimentation rate was influenced by the concentration of the blood; the greater the dilution of the blood, the more rapid was the rate. By making simultaneous blood counts, Walton (6) prepared a table from which it is possible to correct the sedimentation rate to the degree of anaemia present. Again, after a certain time of cell sedimentation the rate is reduced, the already settled cells obstructing further settling. When this occurs, "Packing" is said to have commenced. By placing the sedimentation tube in a centrifuge as soon as this packing is noticed, the haematocrit can be obtained. Rourke and Ernstene (7) compare the height of this haematocrit with their standard normal reading, from this they calculate the blood concentration, and so obtain, what they have termed, the "Corrected Sedimentation Rate".

Briefly, these are the more common methods of performing the sedimentation test, and it would appear that all these methods give comparable results, although the results are differently recorded. In a study by Greishelmer, Treloar, and Ryan (8) three different methods are compared. They ^{state} ~~are~~ :-

"Blood sedimentation in 99 men and 102 women

selected without regard to age or health from University students and ambulatory patients, has been studied to establish the inner-relationships between the Linzenmeir, Cutler, and Westergren methods. The average sedimentation in one hour for "normal" subjects appears to be concordant with the three methods despite the wide difference in tube width, anti-coagulant concentration, and length of fluid column, although the difference between the means for the three methods are significant statistically".

More recently, Beaumont and Dodds (9) made simultaneous sedimentations using the methods of Zeckewer, Westergren and the Finger-prick technique. They found that "the results agree very closely".

Thus, from the accuracy of the results there would seem to be but little to choose between the various methods and this makes it more difficult to explain the great number of "new" techniques which have been, and continue to be, described. It is eighteen years since Fahraeus first published his observations, and even now there is no generally accepted method, either of technique, or of expressing results. This total absence of uniformity makes it extremely difficult to correlate the findings of previous workers, and handicaps further investigations.

Moreover as the sedimentation rate is not a specific test for any one disease, but is of greatest value when repeated tests are made on the same patient, many of the corrections and refinements can be dispensed with. If the time does come when it is held to be necessary to perform blood counts, obtain the haematocrit, or consider other

possible influencing factors, before the sedimentation rate can be determined, by that time I fear that the complexity of the test will vitiate its usefulness.

In this investigation the Westergren method was chosen because of its simplicity and accuracy, and because it was possible to find some references for comparison and guidance.

2. The Westergren Sedimentation Test

Apparatus : Record syringe and an intra-venous needle.
Small blood specimen tube.
Westergren Sedimentation Tubes and stand.
Anti-coagulant.

The Westergren tube is a glass tube, 30cm. in length, with a 2.5mm. bore. It is calibrated in millimetres, 0-200. The tubes are held vertically in the special stand, which holds 12 tubes.

The apparatus was supplied to me by Messrs. Baird and Tatlock, London.

Collection of Blood :

5cc. of blood are obtained by veno-puncture: the needle and syringe must be dry.

2.5cc. of the blood are immediately transferred to the dry specimen tube containing the anti-coagulant substance. The remaining 2.5 cc. of blood may be used for Wassermann test, or other blood investigation.

After an interval of not less than 10 minutes and not more than 60 minutes, the specimen tube is shaken again and the blood drawn up into a Westergren tube. To ensure thorough mixing it is drawn up several times, finally to the zero mark. The tube is then inserted in the stand, and the readings taken.

Anti-coagulant :

Westergren used a 3.8% solution of sodium citrate. This necessitates an accurately

standardised solution and a specially graduated syringe to ensure proper proportions.

In this enquiry solid potassium and ammonium oxalate were used to prevent clotting of the blood. After a comparison of various anti-coagulant substances, Wintrobe and Landsberg recommend oxalate, in the proportion of 4mgm. solid potassium oxalate and 6mgm. solid ammonium oxalate to 5cc. of blood. As only 2.5cc. of blood were used for sedimentation, half the above amount of oxalate was placed in each specimen tube. I obtained the accurate amounts of potassium and ammonium oxalate made up in gelatine capsules. (Trade name "Slipules"). In this way the powder was kept dry, and was ready for immediate use.

It is essential, if any credence is to be given to a subsequent comparison, that each test of a series should be made in the identical manner and under the same conditions. The method described above was strictly followed, and for a common set of conditions the postulates made by Wintrobe and Landsberg (10) were accepted. These were :-

"Venous blood is collected by means of a dry syringe and needle and mixed in a small bottle containing solid potassium and ammonium oxalate. This concentration of oxalate does not alter the sedimentation rate."

"Since sedimentation rate increases with increasing temperature, the sedimentation test should be carried out at a temperature not less than 22° nor greater than 27° Cent.. Within this range variations resulting from differences in temperature are small".

"The haematocrit (tube) should be kept in an exact vertical position during the sedimentation of the blood corpuscles, for when the instrument stands at an angle of even 3" from the vertical, significant acceleration of sedimentation occurs."

It was observed that when the sedimentation tube had been cleaned with ether, the sedimentation rate was increased, so this practice was discontinued. The tubes were thoroughly washed with water, and dried in a dry oven.

Determination of Sedimentation Rate.

The erythrocytes soon commence to settle from the top of the column of blood, and a clear column of serum is left above. The distance through which the cells sediment is measured from the zero mark, to the junction of cells and serum. Readings are made, either at five minute intervals, or, at the end of the first hour. The total distance at the end of the hour is given as the sedimentation rate. For example, a sedimentation rate of 20mm. means that the cells have settled to the 20mm. mark, and indicates that there is a column of serum measuring 20mm. above, and 180mm. of sedimented blood, below.

With the Westergren method readings are sometimes taken at the end of the first and second hours, and the mean rate calculated. Certain fallacies may enter into sedimentation during the second hour, also as it does not appear that any advantage is gained by the second reading, it was not used.

Chapter 1.

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CHAPTER 11

NORMAL AND ABNORMAL RATES

of

BLOOD SEDIMENTATION.

1. The Normal Blood Sedimentation Rate.

In order to determine the sedimentation rate in health and to define the limits of variation of normal rates, the test was performed upon male and female members of the hospital staff. The selected subjects gave a history of recent good health, and on examination were found to be free from such conditions as dental caries, respiratory system infection, skin disease, etc.,

It was found that in the male members of the staff the average sedimentation rate was 2.5mm. at the end of the first hour; in the females, the average rate was 6.5mm. The actual limits of sedimentation of these "normal" bloods were from 1.0mm. to 6.4mm. in males; 2mm. to 10mm. in females. Westergren gave 3mm. as the average normal reading for men, and considered that readings from

4mm. to 6mm. were doubtful indications, and certainly that all rates above 12mm., in men, indicated a pathological condition. Similar findings have been recorded by other investigators. Also, it is agreed that the sedimentation rate in women is twice as rapid as the rate in men. Actually even higher rates in women appear to be consistent with good health, Wintrobe and Landsberg (2) take 15, or even 20mm, as the extreme range of normal variation.

For the purpose of this investigation normal limits have been taken as 1 to 7 millimetres in men; and 1 to 15 millimetres in women; and any reading obtained by the end of the first hour which is beyond these limits has been taken to be abnormal.

3. The Process of Sedimentation of Normal Blood.

A study of the process of sedimentation in normal blood reveals certain characteristics. First, it is noticed that visible sedimentation of the cells does not commence immediately, but is delayed for ten, or even twenty-five minutes. Thereafter, settling of the red cells takes place at a steady rate. In normal rates of sedimentation, which are comparatively slow,

there seldom is a phase of "packing".

By plotting the distance settled at five minute intervals the process of sedimentation can be recorded. Graphs illustrative of normal rates of sedimentation are shown in Figs. 1 & 2. In the graphs the time variable is expressed along the upper, horizontal axis; the distance through which the cells sediment, along the vertical axis.

Normal Men	See Fig.1.	-	over
Normal Women	" "	2.	"

BLOOD SEDIMENTATION RATE.

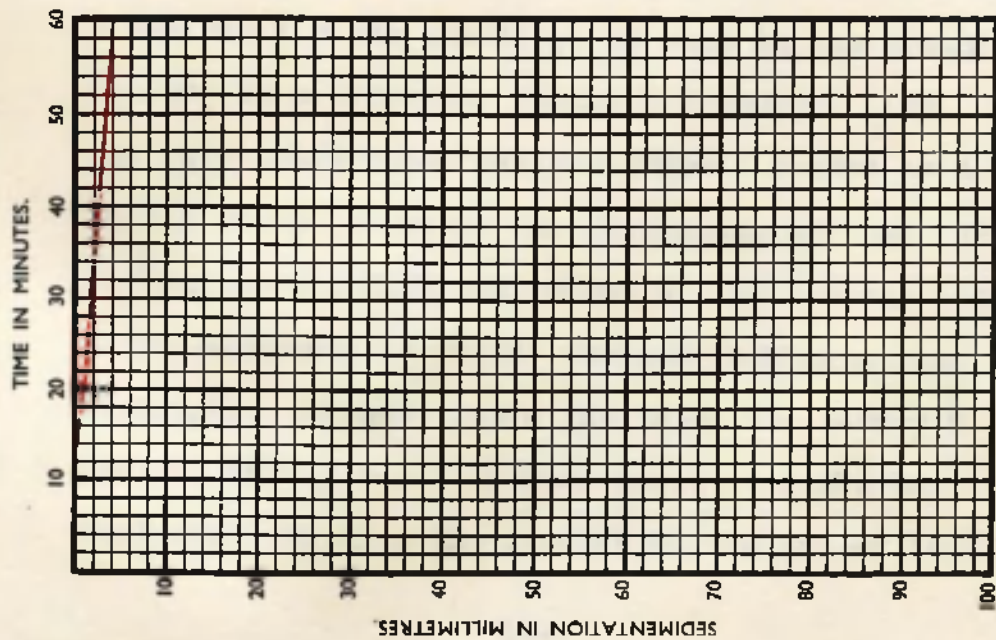


FIG 1

BLOOD SEDIMENTATION RATE.

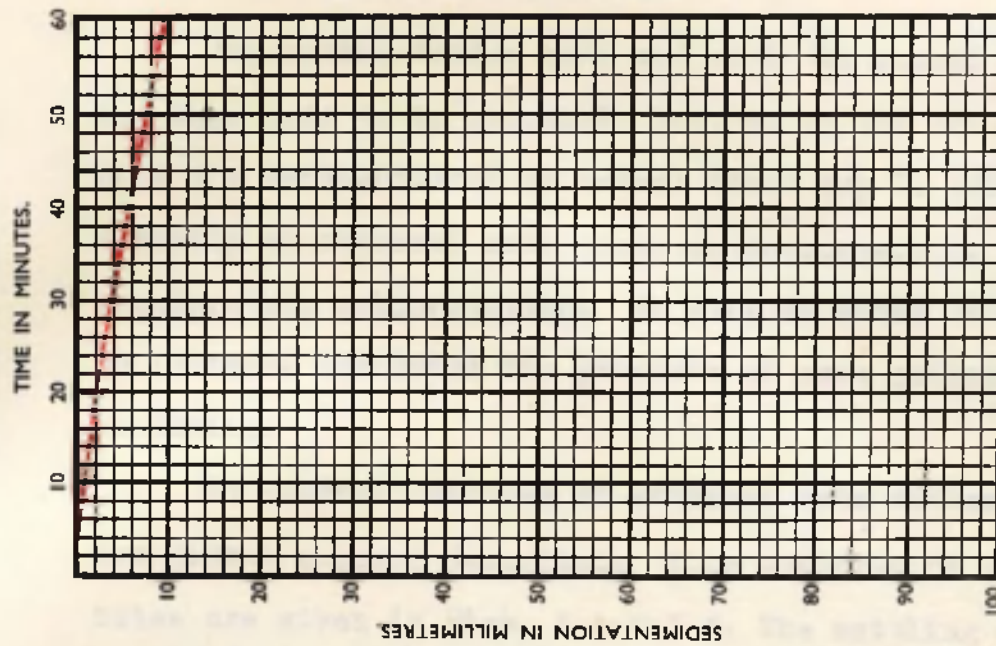


FIG 2

3. Abnormal Sedimentation Rates.

Any sedimentation rate out-with the normal limits has been said to be abnormal, but, as by the end of an hour the sedimentation of normal blood may be nil, actually an abnormal rate means an increased, or accelerated, sedimentation. As will be shown later such an increase indicates the presence of some pathological condition.

In several features an abnormal rate differs from the normal process described. Four examples of increased rates are given in Figs. 3,4,5 & 6. The settling of the cells begins earlier, or even immediately, so that the initial "lag" period seen in normal sedimentation, is of short duration. Thereafter, sedimentation takes place rapidly and steadily, so that in the graph it appears as a straight, downward dropping, line. Finally, the rate again slows and the graph finishes as a curve. This slowing is due to the phenomenon of "packing". Packing occurs when the volume of the already settled cells commences to impede further sedimentation. Obviously, the more rapid the rate, the sooner will packing take place. In many cases it would be fallacious to give the reading at the end of the first

hour, for if packing had commenced early, a false reading would be obtained. In these cases of rapid rate and early packing, the sedimentation rate is given as the distance settled before packing commences.

In Figs. 5 & 6 - two examples of packing are shown.

The result in the first, Fig. 5, would be given thus :-

S.R. - 68 mins. Pack 45 mins.

The second result, Fig. 6 as :-

S.R. - 80 mins. Pack 40 mins.

BLOOD SEDIMENTATION RATE.

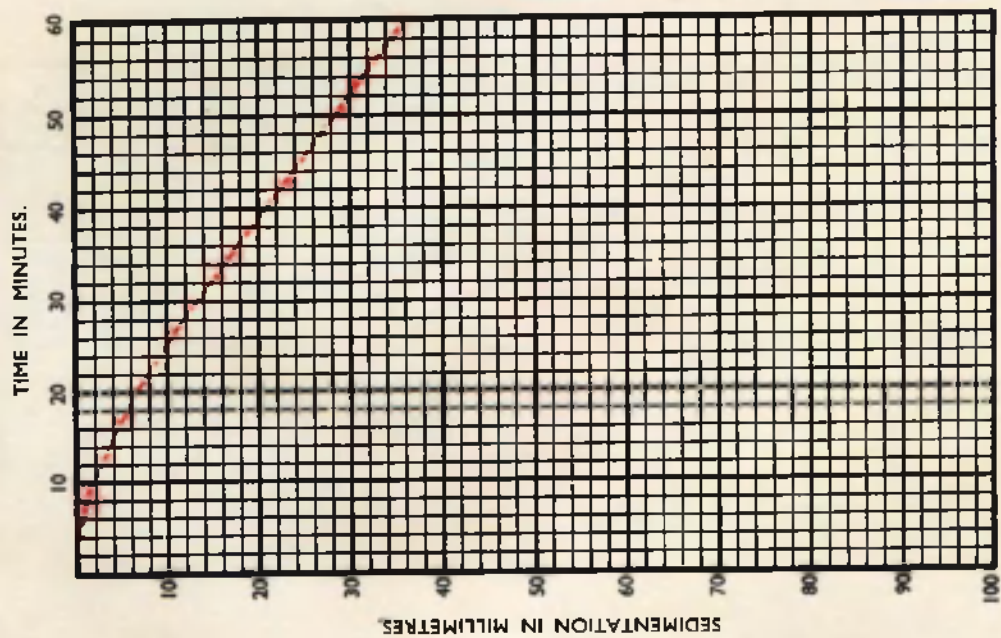


FIG 3

BLOOD SEDIMENTATION RATE.

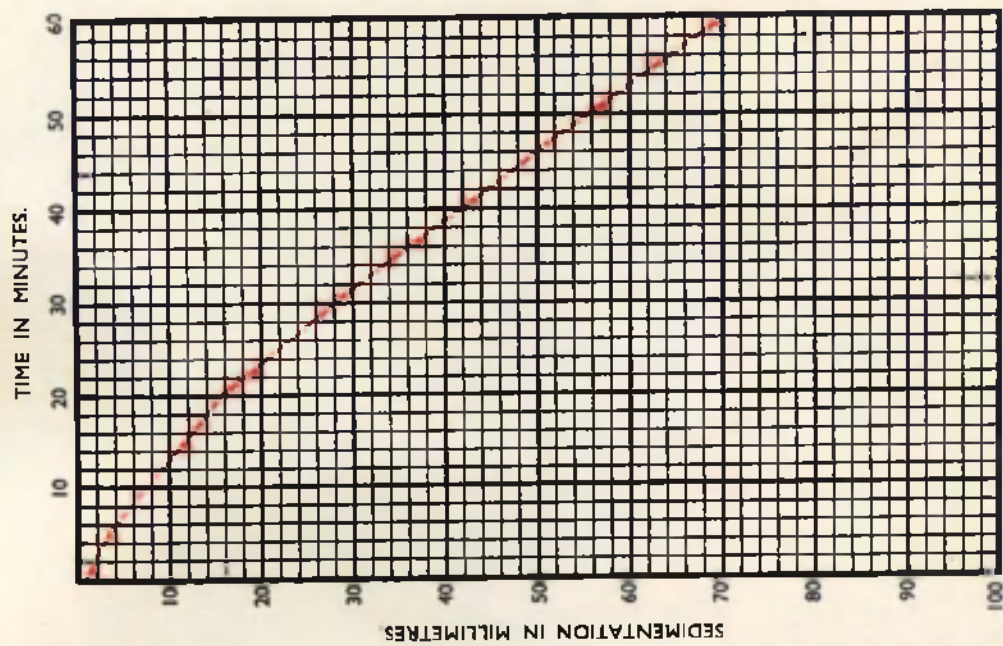


FIG 4

BLOOD SEDIMENTATION RATE.

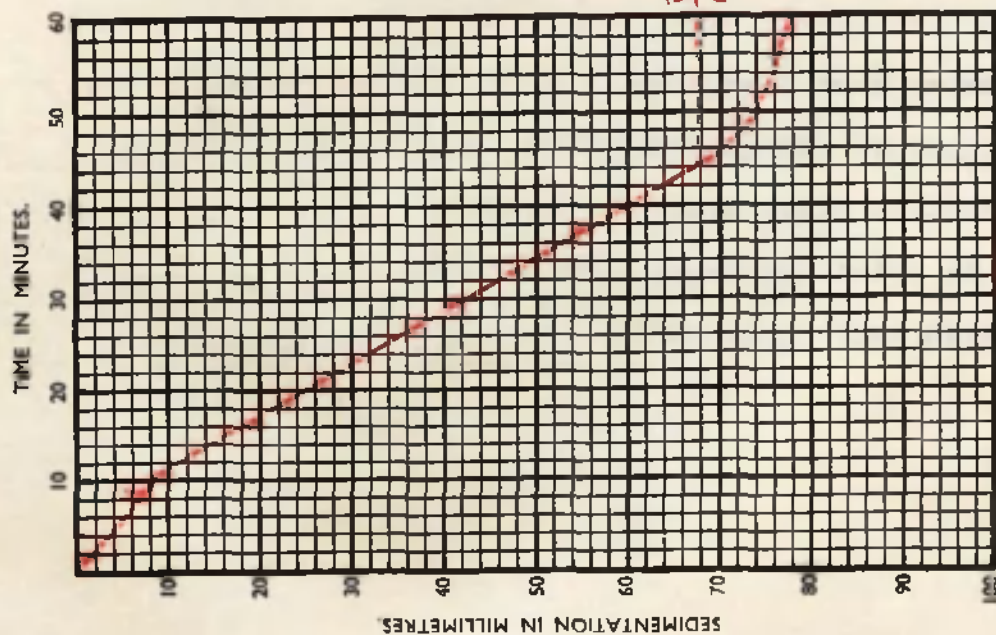


FIG 5

BLOOD SEDIMENTATION RATE.

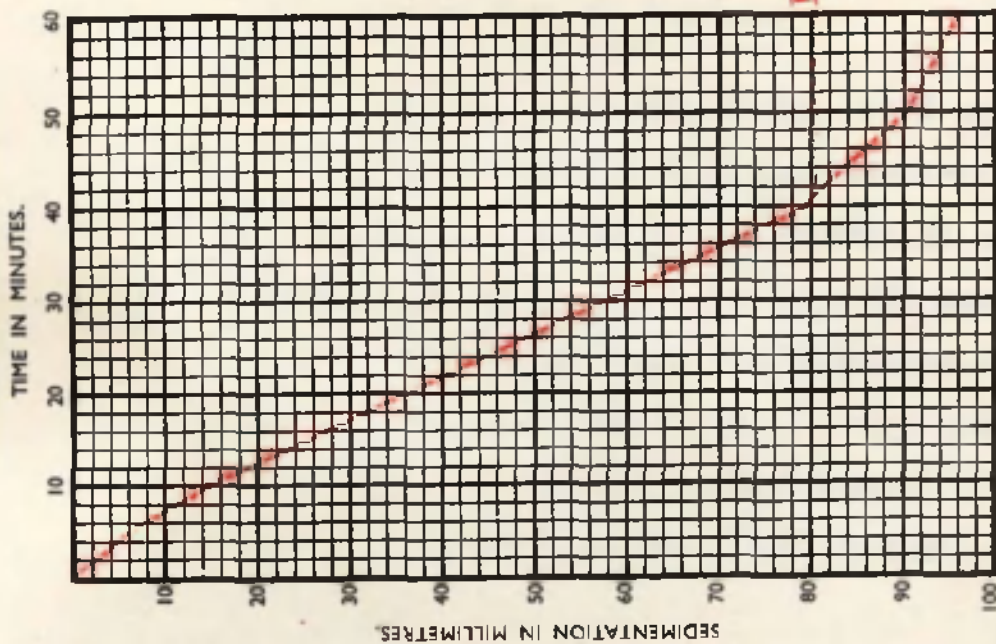


FIG 6

4. The Sedimentation Rate in Disease.

Before beginning the study of the blood sedimentation rate in Diabetes Mellitus it was considered necessary to gain some knowledge of sedimentation rates in other common pathological conditions. To acquire this experience, and to practise the technique of the test, 200 patients were investigated. These cases were chosen as being representative of the type of illness to be found in the general medical and surgical wards of any hospital.

The total numbers of any one disease were small, and so, it is not possible to formulate definite conclusions on the results. However, as in many of these cases the test was repeated several times, and as the findings were found to be in agreement with previously published results, some observations may be permitted.

Results illustrative of these cases are given in Table 1., and as the markedly increased rates of sedimentation are the most informative, they have been given first.

Table. 1.

No.	Case	Sex	Condition	Sed. R. mm
Group	C.		Very Rapid Sedimentation.	
1.	T.C.	M	Pulmonary Tuberculosis.(Acute)	88 (pack 35)
2.	J.F.	M	Advanced Bi-lateral Pulmonary Tuberculosis	80 (pack 40)
3.	E.K.	F	Bi-lateral Pulmonary Tuberculosis with cavitation	86 (pack 40)
4.	G.B.	M	Miliary Tuberculosis with Epilepsy. (since died)	86 (pack 30)
5.	W.H.	F	Pulmonary Tuberculosis, recent haemoptysis	80 (pack 50)
6.	A.J.	M	Tuberculosis Meningitis, Miliary Tuberculosis	83 (pack 30)
7.	E.F.	F	Extensive Pulmonary Tuberculosis	78
8.	F.B.	M	Acute Rheumatic Fever. (1st wk)	80 (pack 40)
9.	E.M.	M	Acute Rheumatic Fever with Carditis. (3rd Week)	86 (pack 50)
10.	L.C.	F	Rheumatic Fever (3rd week)	62
11.	A.C.	M	Acute Rheumatic Fever with Carditis. (5th week)	50
12.	J.J.	M	Lobar Pneumonia (3rd day)	83
13.	A.K.	F	Lobar Pneumonia (5th day)	80 pack 50)
14.	C.B.	M	Erysipelas of face. (5th day)	82
15.	B.M.	M	Erysipelas of face. (7th day)	80
16.	L.T.	F	Pyelonephritis	76
17.	S.T.	M	Empyema (2nd week)	86

Table 1. (contd.)

No.	Case	Sex	Condition	Sed. R.
18	E.C.	M	Acute Cystitis, and Vesical Calculus	48
19	J.S.	M	Acute Gastro-enteritis (age 4)	46
20	A.S.	M	Primary Chancre of Lip, and Alveolar Abscess	46

Group B.		Moderately Increased Sedimentation Rates.		

21	F.W.	M	Chronic Pulmonary Tuberculosis	36
22	B.B.	F	Bi-lateral Tuberculosis, fibrotic.	28
23	I.P.	M	Pulmonary Tuberculosis, few scattered deposits.	27
24	M.C.	M	Subacute Rheumatism. (Poly-cyclic)	29
26	A.N.	M	Rheumatoid Arthritis	37
26	A.W.	M	Rheumatoid Arthritis	29
27	J.M.	M	Cellulitis of arm	35
28	J.S.	M	Bronchiectasis	38
29	N.G.	F	Acute Bronchitis, and Arthritis	42
30	A.R.	F	Erythema Nodosum	40
31	T.T.	F	Erythema Nodosum	35
32	T.M.	M	Tonsillitis	29
33	R.W.	M	Quinsy. (3rd day)	41
34	N.H.	M	Impetigo Contagiosa	17
35	T.S.	F	Haemoptysis (cause undiagnosed)	32
36	G.A.	M	Arterio-Sclerotic Ulceration	38

Table 1. (contd.)

No.	Case	Sex	Condition	Sed. R.
37	L.M.	M	Acute appendicitis (Gangrenous)	41
38	T.L.	M	Acute appendicitis (haemorrhagic)	24
39	J.S.	F	Acute appendicitis (obstructive)	20
40	E.H.	F	Bi-lateral Salpingitis	37
41	E.C.	F	Bi-lateral Salpingitis & Pelvic Peritonitis.	39
42	M.H.	F	Carcinoma of Breast	28
43	S.S.	F	Carcinoma of Cervix	24
44	G.A.	M	Bronchial Carcinoma	24
45	W.J.	M	Peptic Ulcer, non-malignant (Secondary anaemia)	14
<hr/>				
Group	A.	Normal	Sedimentation Rates.	
46	C.N.	M	Chorea, uncomplicated (age 7)	6
47	N.B.	M	Chorea, " (age 8)	3
48	O.R.	F	Chorea, " (age 12)	5
49	J.S.	F	Chorea, " (age 11)	2
50	N.A.	F	Neurasthenia, with functional fixation of hip.	5
51	C.B.	M	Neurasthenia, (early Dementia praecox)	3
52	J.C.	F	Non-malignant tumour of breast	6
53	R.C.	M	Progressive Muscular Atrophy	7
54	T.H.	M	" Common cold "	6
55	H.P.	M	Septic Finger	5

The Sedimentation Rate in Disease. (contd.)

The results shown in Table 1. have been divided into three groups C, B, & A. This is an arbitrary grouping, and is suggested in the hope that it may simplify the interpretation of the findings. 90mm. is the highest recorded reading at the end of the first hour before the commencement of visible packing; and so it has been taken as the maximum result obtainable in rapid sedimentation. 0mm. obviously is the lowest possible reading. Therefore 45mm. is the mean reading, and this forms one of the dividing lines. Previously, normal readings have been stated to be 1-7 mm. in men, and 1-15mm. in women; these levels necessitate another dividing line. The result is that the rates are divided into three groups :- Group A, "Normal" sedimentation rates; Group B. "moderately increased" rates up to 45mm.; and Group C. "very rapid" rates, above 45mm. It is not intended that any exact significance be attached to the appearance of the sedimentation rate of one case of a disease within a certain group. For example a reading of 46mm. in one blood, which reading would place the rate in Group C. is not to be compared unfavourably with another reading of 38mm. obtained in another case suffering from the same illness. It has

been shown the sedimentation rate varies in normal individuals. Similarly, in disease the response of the individual varies, so that the sedimentation rate can never be specific for any one condition. However, the excursions of rate which occur are excursions of reasonable distance, and the suggested grouping is offered as a guide, by which it is possible to forecast the "expected" rate in any one case, within the wide margins of the arbitrary divisions.

Briefly, to discuss the findings of each group, beginning with Group C.- Very rapid sedimentation rates.

The first seven results illustrate the sedimentation rates obtained in acute Pulmonary Tuberculosis. In each of these cases the condition was said to be "acute" when clinical examination, positive sputum tests, and radiological examination, warranted such a classification. In all, 40 cases of Pulmonary Tuberculosis classified as acute, have been examined, and in each of these cases the sedimentation has been of the very rapid type. In another patient a sedimentation rate of 78mm. preceded a severe, and from the absence of other evidence of activity, totally unexpected, hemoptysis. In two other cases of chronic cough, the sedimentation rates were within normal limits and were in accordance with other negative findings.

The sedimentation rate in Pulmonary Tuberculosis has been the subject of countless investigations, in fact the test has received so much attention in Tuberculosis that its possible application to other diseases has been neglected. However, this is in accordance with the general "Tuberculo-Cancer" phobia which so long has obsessed popular medical investigations. It is agreed that acute Tuberculosis gives a markedly increased rate of sedimentation, some even go so far as to maintain that a normal rate is inconsistent with active infection. The place of the sedimentation test in Pulmonary Tuberculosis as an aid to progress and prognosis is admirably summed up by Freidman (3) thus :-

" I have come to rely greatly upon it, (the S.R.) feeling that it reinforces physical, radiological and symptomatic evidence, and frequently presages oncoming evil, or on the other hand gives one information of the ultimate outcome when the clouds loom dark on the clinical horizon."

The truth of this quotation will be shown when the other groups are discussed.

In Table 1. the sedimentation rate in acute Rheumatic Fever is given in Nos. 8-11. From personal observations, this disease, during the acute stage, gives as consistently as Tuberculosis, a very rapid rate of blood sedimentation.

Other conditions examined whose sedimentation rates fall within the limits of Group C. are Pneumonia,

Erysipelas, Pyelitis and Pyelo-nephritis, etc.

All the conditions appearing in this group (with the possible exception of No.20) are acute, severe and not infrequently fatal, illnesses, and are typical of the pathological processes producing very rapid rates of sedimentation.

(Case 20 has been mentioned as a possible exception, for neither syphilis, nor alveolar abscess usually produce a very rapid rate. But after all, a rate of 46, allowing for individual response, possibly should have been placed in the next group. Or, the double infection in this case might explain the increase beyond the "expected" rate.)

Group B. Moderately Increased Rates.

In this group are found cases of chronic Tuberculosis, the less acute forms of rheumatism, (excepting Chorea), cancer, and some localized inflammatory processes. The pathological conditions producing this moderately increased rate of sedimentation, with the exceptions of appendicitis and salpingitis, are less virulent and more localised in their effects than the conditions which appear in Group C. Two of the cases of Pulmonary Tuberculosis had repeatedly negative sputa; in the third, the sputum test gave Tubercle Bacilli in small numbers. At first sight it is surprising to find such acute conditions as Appendicitis, and Salpingitis included in Group B., instead of being among the illnesses of very rapid sedimentation rates. But in these conditions the appearance of symptoms occurs

early, and with correspondingly early diagnosis, and immediate treatment, there is little general constitutional up-set. At least such constitutional disturbance is small when compared to the wasting, prolonged fever, toxicity and exhaustion of Acute Pulmonary Tuberculosis, Lobar Pneumonia, or even Erysipelas.

Thus, two factors seem to have a direct effect upon the increase of sedimentation rate, namely the duration of the illness, and whether or not the condition is localized. The influences of duration of disease and general effect have been suggested in America as an indication for the use of the sedimentation test as a diagnostic aid. Smith, Harper and Watson, (4) report a series of 19 cases of salpingitis and 31 of appendicitis, and after making certain allowances for the known duration of the condition, they state that in Appendicitis the sedimentation rate is lower than in Salpingitis. They attribute this to the longer "pre-symptomatic" period in Salpingitis, and suggest that the test might be used to differentiate between the two conditions. But the reported differences are so slight, and the essential additional examinations so numerous, that one cannot visualize either surgeon or patient acclaiming the test as a reliable method of differential diagnosis.

In America new methods of investigation appear to

be received with greater enthusiasm than we accord to them in this country.

Group A. Sedimentation Rates within Normal Limits.

In this group the first four cases are of Chorea, These represent the typical results of a group of 14 examined, all of which have returned a normal sedimentation rate. Yet all other manifestations of rheumatic infection give an increased rate, par eg. acute Rheumatic Fever, Subacute rheumatism, Rheumatoid Arthritis, and Erythema Nodosum. This strange anomaly has been noted by Bruce Perry (5) and by Warner. (6) Is it possible, that after all, we are mistaken in regarding Chorea as a true manifestation of rheumatism. or is it possible that with the onset of Chorea some factor appears in the blood, which factor has a retarding influence upon the already increased rate of sedimentation ?.

The other six cases given require no explanation.

5. Discussion of Results.

From the foregoing examples and from many other conditions which have been tested, it does seem probable that the sedimentation rate mirrors, though at times rather imperfectly, the "attacking power" of a pathological condition, when consideration is given to the duration, extent, general effect, and severity of the infection or malignant growth.

If this be a correct assumption, then sedimentation rate should alter with the progress of disease. Without doubt this does occur, and is demonstrated by a series of tests made during the course of an acute illness.

In pulmonary Tuberculosis the repetition of the sedimentation test is regarded by many authorities as the truest and most dependable indication of increasing severity, or response to treatment, of the disease. Periodic tests upon such illnesses as Pneumonia, Rheumatic Fever, Carcinoma, etc., reveal that as the disease progresses the sedimentation rate accelerates; as it regresses, the sedimentation rate slows. It might be argued that the course of such conditions is revealed by clinical change, but there are other pathological processes where it is extremely difficult on clinical evidence alone, to determine progress. Such a condition is Rheumatic Carditis, and in this disease the sedimentation test supplies a most helpful, and much needed, additional control. In this hospital the test now has become a routine examination in all cases of rheumatic infection.

Figs. 9, 10, & 11 show the changes in sedimentation rate which occurred during acute rheumatic illnesses. Case F.B. (Fig. 9) was a man, age 19, suffering from a first attack of Rheumatic Fever. The first sedimentation

BLOOD SEDIMENTATION RATE.

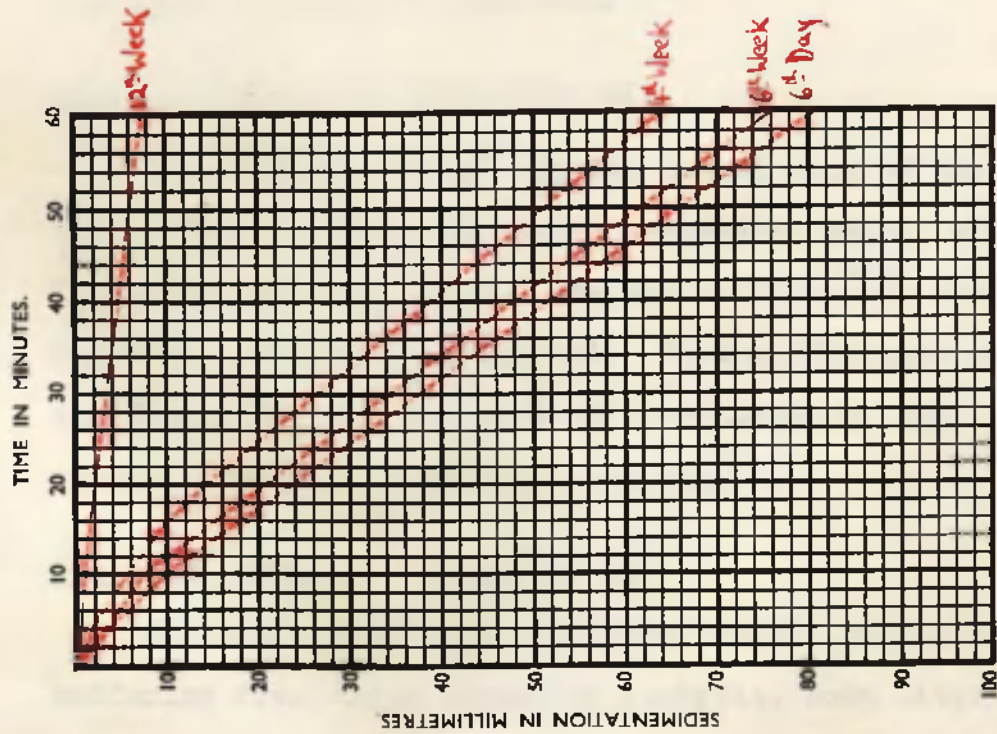


FIG 9

BLOOD SEDIMENTATION RATE.

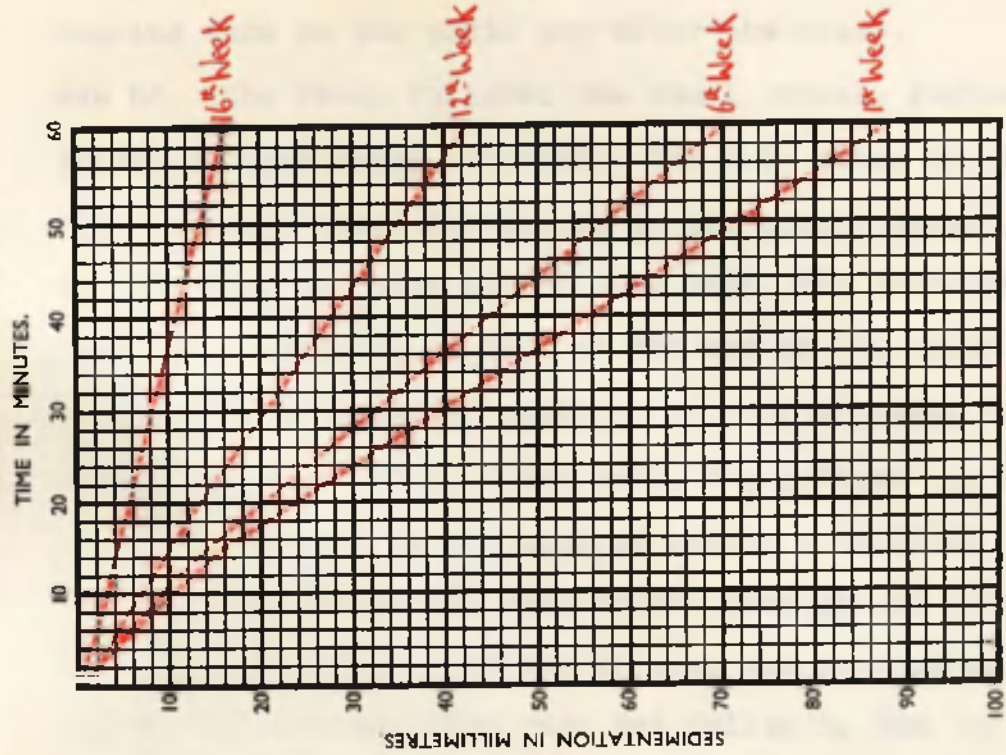


FIG 10

reading made on the sixth day after the onset, was 80. The fever followed the usual course, various joints in turn being affected. The S.R. after fourteen days was again 80. By the end of the fourth week, satisfactory progress having been made, the sedimentation test gave a reading of 64. At the end of the sixth week the rate again had risen to 76, and although on the actual day that the test was made, the patient was free from pain and had no symptoms of active infection, two days later the left knee became swollen and painful. The subsequent course of the illness was uneventful, and as the sedimentation rate had fallen to 7mm. by the twelfth week he was allowed out of bed. At no time was there evidence of carditis.

Case J.M. (Fig.10) Male, age 21.

Rheumatic Fever and, in the second week of the illness, right sided rheumatic pneumonia. Later, Mitral Valvulitis was diagnosed. The sedimentation^{rates} at monthly intervals are shown in Fig. 10. By the sixteenth week the rate still was above normal, registering 16mm. but against advice he insisted on getting up.

Case A.C. (Fig.11) Male, age 12.

Rheumatic Fever one year previously. He was admitted suffering from Acute rheumatic carditis, both Mitral

BLOOD SEDIMENTATION RATE.

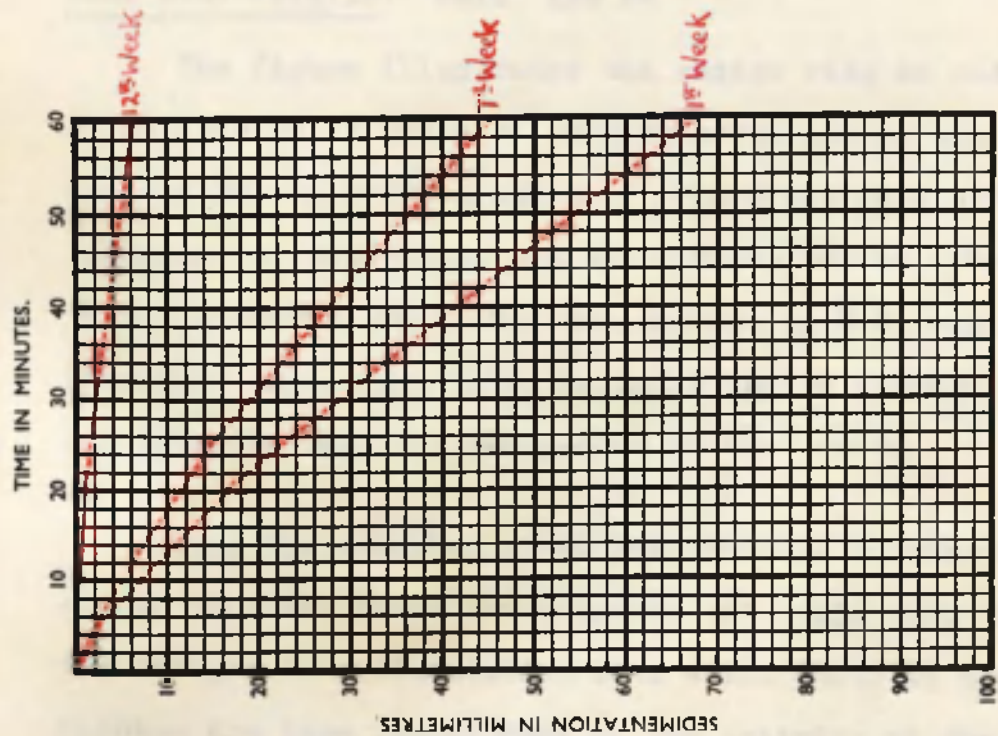


FIG 11

BLOOD SEDIMENTATION RATE.

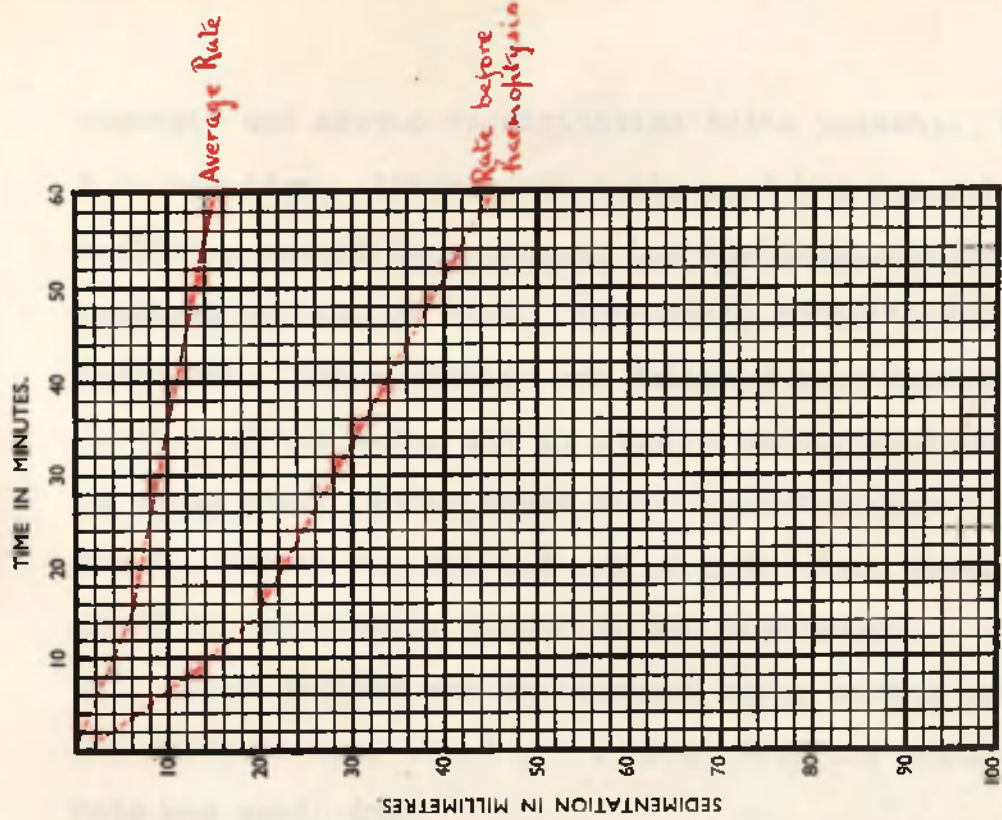


FIG 12

stenosis and Aortic regurgitation being present. His S.R. was 68mm. After seven weeks rest his general condition showed improvement, but the sedimentation rate remained as high as 45mm. Eventually tonsillectomy was performed. The operation was followed by a dramatic slowing of the S.R., and an equally significant fall in pulse rate. Three weeks after operation the S.R. was 4., and he was allowed out of bed. Four weeks later his S.R. still being normal he was discharged.

This patient was re-examined three months later, the Aortic murmur could not be detected; the sedimentation rate was again 4mm.

Case G.A. (Fig.12) Male, age 24

The figure illustrates the sudden rise in sedimentation rate which preceded an unexpected hemoptysis, in this case of Pulmonary Tuberculosis. There was considerable fibrosis of both lungs and the disease was believed to be quiescent, until the sudden rise in S.R. was observed. Five days later he had a severe haemoptysis, and Tubercle Baccilli reappeared in the sputum.

From the examples given and from the information gained in other cases investigated, it would seem that the changes in sedimentation rate which occur in acute illness are true indications of the activity of the

disease. Possibly, the return of the sedimentation rate to normal levels may lag behind the clinical evidence of recovery; on the other hand an accelerated rate may forestall clinical evidence of activity of a fresh infection, or an exacerbation of an existing one.

6. The Use of the Sedimentation Test

In certain conditions the sedimentation test may be used as an aid to diagnosis of an obscure condition, when, and only when, it is correlated with the findings of a full clinical examination. In Table 1. there are reported two cases, labelled "neurasthenia", in which the sedimentation rates were normal. Such readings, agreeing with other negative findings, might be invoked further to justify the diagnosis of "neurasthenia", a diagnosis no less negative than the investigations which give rise to it. But, to advocate the use of a single sedimentation reading in the investigation of pathological conditions, would lead to so numerous, and such dangerous mistakes, that general condemnation would undoubtedly follow. The sedimentation test is not a diagnosis test for any one, or type, of disease, neither does a normal sedimentation rate prove the absence of pathological conditions. Professor Witts (7) recently delivered a timely warning, and cited a case where the sedimentation

rate was - normal, yet on operation the patient was found to be suffering from an advanced spheroidal celled carcinoma of the stomach.

It is not as a diagnosis test, but as an additional method of controlling the progress of a pathological state that the sedimentation test is of undoubted value. Perry (5) in an exhaustive study of the sedimentation rate in rheumatic carditis, comes to the conclusions, that :-

"Acute Rheumatic Carditis is always associated with a high sedimentation rate."

"The Sedimentation Rate is an accurate index of active infection in Rheumatic Carditis."

The importance of such findings is obvious, and may supply an answer to the oft' repeated question, "when to allow a patient suffering from Rheumatic Carditis to get up"? Where ever possible, a patient should not get out of bed until the sedimentation rate has regained a normal level. This may mean a more prolonged stay in bed that is warranted by the evidence of pulse rate, response to exercise, etc., but at least this procedure errs on the side of safety; at greatest, it may avoid the life long tragedy of a "rheumatic heart".

The recent success of gold therapy in Rheumatoid Arthritis, suggests another use of the sedimentation test as a control of the success, or otherwise, of the

treatment. Hartfall and Garland (8) report that the sedimentation rate originally raised, was slowed after injections of gold in the majority of their series of Rheumatoid Arthritis.

Another possible use of the test would be by measuring the time taken for the rate to return to normal, to estimate the damage done by the disease process, and the resistance of the patient. Even in the acute specific fevers it is not at present known for how long after infection does an increased sedimentation rate persist. It is accepted that the rate is accelerated in the majority of cases of malignant disease. Does the rate return to normal after the conclusion of successful treatment, and if so, could it be utilised as a control of the efficacy of radium, or surgical treatment.

In short, the sedimentation test already has won its place in the clinical laboratory, and ~~I believe~~ ~~that~~ as we gain further knowledge of the reaction, so shall we find further uses for it.

7. The Nature of the Phenomenon of Blood Sedimentation.

Before concluding this section a note on the various theories of the causation of the phenomenon of blood sedimentation, may not be out of place.

Fahraeus (9) in his original contribution wrote of the "suspension stability of the blood" and suggested that changes of sedimentation rate were due to disturbances of this "suspension stability". This is a logical, but not illuminating, description of the process.

Cutler, (10) accepting the Fahraeus definition, attempted to find the factors which produced the disturbance of "suspension stability", and he put his findings as follows :-

"Should the amount of tissue destruction pass beyond normal, then the stability of the blood is seriously disturbed, and the red cells settle out quickly from the plasma."

So far, it has been suggested that an alteration in sedimentation rate is produced by a disturbance of blood stability, and that this disturbance is found in conditions where there is much tissue destruction, but the actual disturbing element is not described.

What is meant by "tissue destruction" ? Surely in any patient where there has been loss of weight, to an

extent that the patient might be as said to be "wasted", then in that patient there must be "abnormal tissue destruction". Yet, in all such cases of wasting, the sedimentation rate may not be increased. For example, in such types as Involutional Melancholias, Maniac Depressives, and the more common "neurasthenias" the investigator has yet to find one case with an increased sedimentation rate, although the destruction of bodily tissue is most marked. Also, as will be described in the next section of this report, Diabetes, though a wasting disease, does not invariably produce an increased rate. However, the explanation of tissue destruction was well received, and Bortee (11) endeavoured to name the intermediate factor between cause and affect. He wrote :-

"..... In conditions involving the rapid destruction of tissue there is found in the blood an excess of fibrinogen. In any case where the content of fibrinogen in the blood is above normal, the speed of sedimentation is increased."

In "Recent Advances of Medicine, 1934" (12) the statement is made, that :-

"A reduction in the suspension stability of the blood is brought about by an increase in the fibrinogen or globulin protein fractions. Breaking down of tissue protein fractions may therefore account for an increased rate of sedimentation."

It is significant that this explanation does not appear in the 1935 edition of the same volume (13), nor is any

other explanation vouchsafed. In addition to the fibrinogen suggested by Bortee, the globulin fraction now also is suggested as a cause.

Then comes Cherry (14) with a further subdivision of globulin and eugobulin factors.

"Two factors apparently influence the change in rate, cell volume and the plasma variations in fibrinogen, eugobulin, and globulin in the plasma."

It has already been proved that the cell volume does have a direct effect upon sedimentation speed. But, here is the conclusion reached by Alfred Brown and Munro (15), after an examination of the variations in the plasma.

"..... The graphs illustrating the values show clearly that no parallelism exists between the Sedimentation Rate and the fibrinogen percentage, the globulin percentage, or the euglobulin percentage, of the plasma proteins. Further that the Sedimentation Rate has no connection with the globulin-albumin ratio, the fibrinogen-globulin ratio, or the ratio of fibrinogen plus globulin, to albumin and to total proteins."

Such intricacies of blood chemistry not only are beyond the scope of this investigation, but also, they are beyond the understanding of the investigator, and will not be discussed. However, it would appear safe to deduce from the above extracts, that the findings do not agree.

In order to prove that the cause of increased sedimentation rate lies in plasma changes, rather than in alteration of cell constituency, some ingenious

experiments have been made. For example, cells of a fast sedimenting blood have been washed, then crossed with the serum of a slow rate, and vice versa. The unnaturalness of such experiments precludes much credence being accorded to the results achieved.

A more reasonable, but less easily demonstrated, theory, is that the phenomenon is due to changes either in the electrical burden of the particles, or to the colloidal dispersion of the serum constituents.

At present there is a total lack of unanimity in the views held as to the causative factors, and the exact nature of the phenomenon is not known.

It is necessary to return to the first offered explanation, that changes are due to disturbance of the blood stability, and is it not probable that this stability is the result of a fine balance between all the blood constituents, and that any change, whether it be in cell, or serum, may disturb the inter-relationship of the two, and thus lead to an increased rate of cell settling, or as it now is known, rate of blood sedimentation.

S U M M A R Y.

of Chapters 1 and 11.

1. Various methods and techniques of performing the Sedimentation Test are discussed.
2. The Westergren Test as used in this investigation is described.
3. The normal rate of blood sedimentation is shown to be 1-7mm. in men; 1-15mm. in women.
4. The process of blood sedimentation is illustrated.
5. Examples are given of sedimentation rates in 200 patients suffering from common illnesses.
6. It is found that the more active, or acute, the condition, the greater is the increase in rate of sedimentation.
7. It is suggested that rates of sedimentation be divided into three groups, according to the reading at the end of the first hour of sedimentation.
8. It is noted, that, alone in rheumatic manifestations, the sedimentation rate in Chorea, is not increased.
9. There are given the accepted uses of the test, and some possible additional applications are mentioned.
10. The nature of the phenomenon of blood sedimentation is discussed.

Chapter 11.

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SECTION TWO.

THE BLOOD SEDIMENTATION RATE. in DIABETES MELLITUS.

CHAPTER 111.

The Blood Sedimentation Rate in Diabetes Mellitus.

It has been stated in Section One that in the majority of pathological conditions there is found an increased rate of blood sedimentation, and that this increase is an indication of the severity of the disease. Could then the sedimentation test be applied to the study of Diabetes Mellitus ?

To determine this question the following investigation was undertaken. Few references to the rate of sedimentation in diabetes were found, and as these appeared to reach no definite conclusions, this study was commenced without preconceived ideas of the results to be expected.

As is the way with such investigations the field of enquiry has been greatly enlarged, for each group of findings suggested further possible methods of investigation.

Also, within the past year there have been published

many new observations on the physiology, course and treatment of Diabetes, and certain most important conclusions and theories have been formulated. Without reference to these it was felt that no investigation at the moment would be complete.

The 45 cases investigated either were attending the Diabetic Out-patient Clinic, organized by the Hull Public Health Committee, or, were admissions to Anlaby Road Hospital, Hull. The great majority of these patients were in poor social circumstances, and as is the rule, unfortunately, in such classes the incidence of malnutrition and minor infections, was unusually high. These factors, in addition to the difficulty of obtaining a suitable, yet economically possible, dietary, will have to be allowed for when any interpretation of the findings is made.

In this section of the investigation dealing with Diabetes, 507 blood sedimentation tests have been made, and 324 blood sugar percentages determined. The sedimentation tests were made by the Westergren method, in accordance with the technique already described. The single blood sugar readings were determined by colorimeter method, using a Blutzucker-Kolorimeter (Zeiss Ikon). A number of the sugar tolerance curves were prepared in the Pathological Department of the Royal Infirmary, Hull, using

the method of Folin and Wu. The urinary sugar was estimated by Benedict's Test; the urinary acetone by Rothera's Test; Gerhart's ferric chloride reaction for diacetic acid, also being occasionally used. The Wasserman Reaction was determined for each patient examined.

1. The Sedimentation Rate in Diabetic Patients.

The sedimentation rate and the blood sugar level were determined in 45 patients known to be suffering from diabetes. These readings were obtained from a sample of blood in the fasting state, during the preceeding 15 hours neither food nor insulin had been taken.

The results are shown in Table 2., and following the classification suggested in Section 1, they are grouped in accordance with their sedimentation rates.

At the time of examination a record was made of the patient's age, sex, general condition and the presence of focal infection, local sepsis, diseased tonsils, respiratory disturbance, rheumatic manifestations, or any other condition which might influence the rate of sedimentation. Also, each was questioned about the duration of the diabetes, and whether any other members of the family had suffered from the disease. Notes giving briefly the essential particulars, and the glucose tolerance-test curve for each case, will be found at the end of this report.

Table. 2.

Blood Sedimentation Rates in 45 Diabetic Patients.

Group	No.	Case	Sex	Age	Blood Sed.R	Fasting B.S.
A	1	F.U.	F	50	3 mm.	0. 154.%
	2	A.S.	F	40	4 mm.	0. 250.%
	3	R.M.	F	51	5 mm.	0. 125.%
	4	A.F.	M	65	6 mm.	0. 120.%
	5	T.C.	M	68	6 mm.	0. 127%
	6	B.J.	F	34	8 mm.	0. 161.%
	7	S.E.H.	F	63	12 mm.	0. 256.%
	8	L.C.	F	51	13 mm.	0. 185.%
	9	F.S.	F	56	14 mm.	0. 105.%
	10	A.T.	F	64	15 mm.	0. 160.%
	11	C.M.	F	49	15 mm.	0. 160.%
	12	A.C.	F	48	15 mm.	0. 165.%
B	13	M.M.	M	58	9 mm.	0. 185.%
	14	A.H.	M	46	12 mm.	0. 310.%
	15	B.S.	F	67	16 mm.	0. 145.%
	16	J.G.	F	56	20 mm.	0. 180.%
	17	F.A.S.	F	64	20 mm.	0. 180.%
	18	E.F.	F	49	20 mm.	0. 143.%
	19	J.L.	M	61	20 mm.	0. 255.%
	20	A.W.	F	53	20 mm.	0. 175.%
	21	B.B.	F	66	20 mm.	0. 165.%
	22	G.S.	F	71	23 mm.	0. 180.%

Table. 2. (Continued)

Blood Sedimentation Rates in 45 Diabetic Patients.

Group	No.	Case	Sex	Age	Blood Sed. R	Fasting B.S.
	23	G.L.	M	34	20 mm.	0. 160.%
	24	S.C.	F	53	20 mm.	0. 275.%
	25	L.B.	F	52	21 mm.	0. 156.%
	26	W.B.	F	56	21 mm.	0. 215.%
	27	M.L.	F	63	22 mm.	0. 210.%
	28	A.B.	F	65	24 mm.	0. 240.%
	29	E.S.	F	21	24 mm.	0. 250.%
	30	M.R.	F	58	24 mm.	0. 145.%
	31	G.H.	M	70	25 mm.	0. 200.%
	32	E.L.	F	51	28 mm.	0. 235.%
	33	F.T.	F	52	30 mm.	0. 200.%
	34	S.B.	F	66	33 mm.	0. 227.%
	35	B.H.	F	69	33 mm.	0. 175.%
	36	A.J.	F	71	36 mm.	0. 225.%
C	37	E.B.	F	66	50 mm.	0. 250.%
	38	C.L.	F	58	71 mm.	0. 285.%
	39	C.W.	F	59	75 mm.	0. 300.%
	40	A.B.	F	66	80 mm.	0. 215.%
	41	S.H.	F	60	80 mm. p	0.242.%
	42	A.K.	M	73	80 mm. p	0. 255.%
	43	J.S.	M	60	80 mm. p	0. 183.%

Table. 2. (Continued)

Blood Sedimentation Rates in 45 Diabetic Patients.

Group	No.	Case	Sex	Age	Blood Sed.R	Fasting B.S.
	44	■ A.W. 2	M	16	80 and 30 mm.p	0.300.%
	45	■ B.H.	F	39	80 mm.p p/ packing	0.152.%

■ These two cases are discussed later.

2. Discussion of the Results Shown in Table 2.

In the 45 diabetic patients examined the sedimentation rates were, normal in 12, increased in 33, cases. That is 73.3 % had abnormal rates of sedimentation. Was this increased rate in the majority of the cases due to the diabetes 'per se' ? The fact that 12 out of a total of 45 had normal rates, immediately suggests that it was not so. Could it be that the more severe types of diabetes produced an acceleration of sedimentation rate, in this case severity, being judged by the fasting blood sugar level, and the presence of marked diabetic symptoms ? Or did such factors as age, duration of the diabetes, and family incidence, influence the response to the sedimentation test ? Or, more simply, could the increase in rate in the majority of cases be explained by the presence of other disease conditions ?

In an endeavour to answer these questions the three groups have been examined. From the information given in Table 2, together with the particulars of each case, the results have been correlated and are shown below in Table 3.

Under the heading "Number of cases with known cause of increased sedimentation rate" are included these patients who were found to be suffering from pathological conditions, other than diabetes, which conditions were known to cause an increased sedimentation rate. (See

Section 1. of this report.)

By the presence of diabetic symptoms are meant such indications of the disease as :- excessive thirst, polyuria, pruritis, neuritis, lassitude, loss of weight, and diabetic retinitis. Because the majority of the patients are elderly, Arterio-Sclerosis has not been included as a diabetic manifestation.

Table 3.

	Sedimentation Groups		
	A	B	C
Average age. (Years)	53.25.	55.5	60.1
Average duration of the diabetes (Years)	3.66.	4.4	3.75
Number of cases with a family history of diabetes.	1	4	1
Number of cases with marked symptoms of diabetes.	6	19	8
Average reading of fasting blood sugar determination. (%)	0.164	0.203	0.223

Number of cases apparently healthy apart from diabetes.	11	3	0
Number of cases with known cause of increased Sed. R., apart from diabetes.	1	21	8
Total number of cases.	12	24	8

(x Case No.44, differs in so many ways from the usual diabetic, that it has been omitted from the above table.)

Before discussing further the figures given in table 3 it must be stated that 45 cases is too small a number on which to base definite conclusions. However, in another investigation, referred to later, the reported results of the examination of a large number of diabetic patients are so similar to the findings given above, that it would seem permissible to take the group of cases under discussion as typical and representative of diabetes in general.

First, to consider the possible influence of age upon blood sedimentation. It will be seen in Table 3, that, in the three groups the average age shows a increase as the sedimentation rate rises above normal level. But the difference between the groups is small, and as three patients in group A are over 70 years of age, and as the ages of the cases in group C vary from 39 to 80 years, the actual age does not appear greatly to influence rate of sedimentation: certainly it does not control it.

Again, there is no apparent parallelism between duration of the diabetes and increase of rate of blood sedimentation. This is an expected conclusion, for it is well known that the severity of a case of diabetes cannot be measured by the known duration of the condition.

In only 6 cases a positive family history of diabetes was ascertained. This is too small a proportion

to warrant any observation.

As the average rate of sedimentation increases, so does the prevalence of marked diabetic symptoms. Manifesting such symptoms, there are in Group A. 6 out of 12 cases; in group B, 21 out of 24; and in group C, all 8 cases. This would seem to be worthy of note.

It is open to question whether the fasting blood sugar level is invariably a true indication of the type of diabetes present; this is discussed in the next chapter. But although a comparatively low reading does not always mean a mild type of diabetes, a reading higher than that of the normal renal threshold always implies that the case is one of fairly severe diabetes. In the three groups shown in Table 3, the average reading in Group A is 0.164 %; in group B 0.203 %; and in group C 0.223 %. These suggest that the higher the rate of sedimentation, the higher should be the fasting blood sugar level. But if the individual fasting levels are examined, (see Table 2), it is found that there are no less than nine exceptions to the above hypothesis. That is too great a number of exceptions in a small total to justify the suggestion.

Thus far, it does appear that neither age, nor duration, nor family incidence, have any influence upon rate of sedimentation, but that severity of diabetic symptoms and considerable increase beyond normal, of fasting blood

sugar levels, are more prevalent in the cases with accelerated sedimentation rates, than in the group of normal sedimentation.

The findings do not encourage the formulation of more definite conclusions, at least not until the second part of Table 3, dealing with the incidence of other disease processes, has been considered. To take the cases where a condition known to increase the rate of blood sedimentation was found on examination, there are 1 in Group A, 21 in group B, and 8 out of 8 in group C. These figures do suggest a definite connection between increasing incidence of disease, other than diabetes, and increasing rate of sedimentation.

Examining in more detail the incidence of infection in each group, it is found in Group A. that in only one case did a normal rate of sedimentation appear to contradict the clinical findings, for it was known that this patient (Case F.U.) had a positive Wasserman reaction, and in the past she had been treated for Syphilis. However, after a second, full course of anti-specific treatment the blood Wasserman still gave a positive reaction. Since there were no symptoms of active syphilitic infection, it may be that this is one of the few cases where, after treatment, the blood reaction remains positive, although the disease may never again manifest its presence. In which case it

could be said that all 12 cases in group A were healthy, apart from diabetes.

In Group B, only three cases were found to be "healthy" apart from diabetes: these were cases Nos. 14, 15 & 44. Case No. 14 has a rate of sedimentation of 12 mm., which reading is only slightly more rapid than the accepted rate for "normal" men; case 15 has a rate of 16 mm. but remembering that the divisions of rate are discretionary and adopted for convenience, 16 mm. in a woman possibly should have appeared in Group A.

Allowing for individual variation, these two cases may be normal, at least the increases in rate are too small definitely to indicate the presence of a pathological condition. Case No. 44 without doubt has an abnormal rate of sedimentation, and apart from the condition of diabetes repeated examinations have failed to reveal any other cause. Not only has this case a sedimentation rate which varies, but it is a type of diabetes which is severe and difficult to classify. Later it will be dealt with separately.

21 cases in Group B were found to be suffering from some condition known to increase rate of sedimentation. In order of frequency these conditions were : sub-acute rheumatism and rheumatoid arthritis; pyorrhea and oral sepsis; skin disease; chronic cholecystitis; recent

"chills"; one case of uterine haemorrhage; one case of poststatic enlargement, possibly malignant. The sedimentation rates vary from 20mm. to 36mm. and are typical of the rates for such conditions in non-diabetic patients.

To consider the cases comprising Group C where there was a very marked acceleration of sedimentation rate. Case No. 37 was suffering at the time of examination from a large septic ulcer of her foot, which subsequently healed, where upon the rate of blood sedimentation fell to 18 mm. Case No. 38 was suffering from a septic and extensive diabetic gangrene of the right foot and leg. She died soon after admission, before surgical treatment could be instigated. Case No. 39 is suffering from carcinoma of the uterus; and has received radium treatment. No. 40 has chronic bronchitis, emphysema, advanced myocarditis, and is extremely ill but refuses to come into hospital. Case No. 41 had been admitted for surgical treatment of uterine fibroids and at the time of examination was very anaemic. No. 42 and No. 43 both were cases of diabetic gangrene of legs, and both died after amputations. Case No. 45 is one of advanced pulmonary Tuberculosis and Diabetes.

Thus it does appear that the sedimentation rate in diabetic patients depends not upon the Diabetes, but upon the presence or absence of other pathological

condition. With the possible exception of two cases, and the definite exception of one, in group B., the increase in blood sedimentation rate has been explained in each case. If this be true, then if a local inflammatory process subsides, does the sedimentation rate return to normal level ? In several of the patients under review this has occurred. To quote one case, of severe diabetes, (No. 29, E.S.) who at the time of the first test was suffering from acute pyorrhoea, and gave a B.S.R. of 21mm. After rigorous dental treatment, the rate had fallen to 8mm., well within the normal limits, and although the severity of the diabetes has not diminished, subsequent tests continue to show a normal reading.

The blood Wasserman reaction was negative in every case except No. 1. The comparative rarity of syphilis in diabetics has been commented upon by Elliott Joslin (2) Labbe and Tauflet (3) and others.

As previously remarked, the class and social position of the majority of the patients in this series must be considered, also the comparatively high age incidence might explain the prevalence of infection. And so, it was with great interest that it was found that a close similarity existed between these results and those of Kramer, who investigated a series of 366

diabetic patients.

David W. Kramer, (3) (from the Dept. of Medicine, Jefferson Medical College) using a different sedimentation technique, and approaching the subject from a different stand point, concludes :-

" 510 sedimentation tests were performed upon 366 diabetic patients; 67.8 % (346) showed abnormal readings. ---- The explanation for this high percentage must be either the diabetes or the presence of infections or both."

" A study of the duration of the diabetes showed that the maximum difference in the various diabetic groups was only 5.3 % These figures evidently do not permit us to attach much significance to the effect of the diabetes upon the sedimentation rate."

" The possible influence of the blood sugar was also studied. There was a striking similarity of the percentages in the hyperglycaemic group and those whose Blood Sugar was 180 mgm. or below. ----- From our studies we concluded that the blood sugar per cent had no influence upon the Sedimentation Rate."

" Since the duration of the diabetes and the blood sugar cannot explain the high incidence of the abnormal Sedimentation Rate, the inference is that the most likely explanation is infection."

These conclusions by Kramer, which so closely resemble my findings, also were based upon an examination of the blood in the fasting state. But in diabetes the blood sugar content is far from stable, and in severe cases it is subject to comparatively large variations. Surely then, it would be necessary to compare blood sedimentation rates against fluctuations of blood sugar level, before it could definitely be stated that "blood sugar per se had

no influence upon the Sedimentation Rate." This has been investigated and the results are given in chapter V. Further discussion on this subject will be postponed until then.

3. Observations : To recapitulate the results which emerge from the findings of this part of the inquiry, it has been found that;

In a series of 45 diabetic patients 73.3 % gave an abnormal response to the sedimentation test. (In Kramer's 365 patients 67.8 % had abnormal rates.)

The increase in rate in the majority of the patients cannot be explained by the age groups, the duration of the diabetes, or the family incidence. In the groups of increased rate the more severe types of diabetes are frequent but there are many exceptions to this rule.

There is no direct relationship between fasting blood sugar and sedimentation rate.

The presence of infection or other pathological process other than diabetes, is found in practically all the cases with increased rate of blood sedimentation.

Like Kramer's, the above conclusions are rather negative when considered solely from a scientific standpoint.

Yet they are clinically applicable, and useful. First, they once again stress the very great prevalence of minor infections in diabetes, and second, they suggest a simple method of determining the presence of such conditions. The fact that the diabetes itself has no influence upon the rate of blood sedimentation makes the method practicable. The simplicity of the test is a

strong recommendation, for as a sample of blood is obtained for blood sugar reading, simultaneously a quantity is taken for the sedimentation test. The importance of minor infection to the prospect of satisfactory treatment of diabetes, is generally agreed, and an increased blood sedimentation rate indicates that some such condition is present. Thereafter repeated sedimentations determine the response to treatment. Moreover as the ^{is} patients' general condition improves, although the blood sugar readings may show little change, in almost every case of initially increased sedimentation, the rate subsequently returns to normal level.

Chapter 111

S U M M A R Y . .

Forty five cases of Diabetes Mellitus have been examined and their blood Sedimentation Rates determined.

Twelve cases had normal rates of sedimentation; twenty-five cases had increased rates; eight cases had rates of the "very rapid" type.

The possible influences of age, duration of Diabetes, the severity of the symptoms and the fasting blood sugar level have been considered.

The incidence of co-existent disease has been found to be very high and corresponds to the number of cases with increased rates of sedimentation.

Similar results obtained by Kramer are noted.

It is concluded that Diabetes does not influence the blood Sedimentation Rate. Because of this, the Sedimentation Test is a valuable indication of the presence of infection, and an important guide to the treatment of such.

Chapter 111.

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CHAPTER IV.

Changes in the Blood Sugar Percentage

and

The Sedimentation Rate.

In normal, non-diabetic, persons the blood sugar content is subject to variations within certain defined limits; in diabetic patients these variations are relatively much greater, and exceed the normal limits. In the previous chapter the conclusion, that Diabetes does not influence the sedimentation rate, was based on the examination of fasting bloods, thus no allowance has been made for the possible influence upon sedimentation of rapidly changing blood sugar percentage. It is surprising that such a likely influence upon rate of sedimentation, has not previously been investigated.

From the group of diabetic patients already examined, there were chosen fifteen cases, representing the three sedimentation groups. The sedimentation rate and blood sugar percentage in the fasting state were determined. Each was given 50 gm. of glucose in solution, and thirty minutes later the blood sugar, and rate of sedimentation,

again tested. As this re-examination took place two, to seven, weeks after the date of the previous test, it allowed a comparison of the rates of sedimentation after an interval of time, and between altered fasting blood sugar readings. To facilitate such comparison the previous "fasting" results for these patients are repeated below.

Table 4.

Blood Sedimentation Rates and Blood Sugar Percentages
Before, and After, Oral Glucose.

		First Examination.		Second Examination.			
				Fasting.		After Glucose.	
No	Case	S.R.	B.S.	S.R.	B.S.	S.R.	B.S.
1	F.U.	3	0.154	4	0.165	2	0.246.
6	B.S.	8	0.161	7	0.220	4	0.273.
8	L.C.	13	0.185	13	0.200	11	0.220.
10	A.T.	15	0.160	13	0.165	4	0.235.
11	C.M.	15	0.162	16	0.125	10	0.165.
12	A.C.	15	0.165	17	0.145	9	0.220.
18	E.F.	20	0.143	21	0.143	15	0.200.
23	G.L.	20	0.160	17	0.145	6	0.200.
27	M.L.	22	0.210	38	0.200	34	0.330.
31	G.H.	25	0.200	21	0.155	14	0.245.
32	E.L.	28	0.235	32	0.220	13	0.283

First Examination.				Second Examination.			
				Fasting.		After Glucose.	
No	Case	S.R.	B.S.	S.R.	B.S.	S.R.	B.S.
33	F.T.	30	0.200	34	0.220	30	0.235.
34	S.B.	33	0.227	32	0.200	5	0.235.
37	E.B.	50	0.250	52	0.235	29	0.290.
43	J.S.	80	0.183	81	0.185	57	0.255.

S.R. - Blood Sedimentation Rate.
B.S. - Blood Sugar Percentage.

1. Comparison of Results Obtained from First and Second Investigations of "Fasting" Blood.

The patients selected for repeat examination had, for various reasons, received no insulin treatment in the interval between the times of investigation, many were as yet on no strict diet, and could be regarded as examples of "uncontrolled Diabetes". The fact that at this time the Diabetic Clinic was only in the process of organization, made it possible to obtain such examples. As expected in such untreated cases, there are only slight variations in the individual fasting blood sugar readings. The Sedimentation rates also are fairly constant, with the exception of case No. 27, who at the time of the second test, was suffering from an alveolar abscess which caused

an increase in rate. In the other fourteen cases the greatest recorded difference is 4 mm. and this is of no significance in the "rapid" groups. Further, there is no parallelism between the changes in sugar percentages and the difference in sedimentation readings.

The above results again suggest that no comparison can be made between Sedimentation rate and sugar percentage in fasting blood. Also, that the "fasting" sedimentation rate for each diabetic patient is fairly constant, when no complications have arisen, or disappeared, between the times of investigation.

2. Comparison of Sedimentation Rates. Before and After.

Oral Glucose.

As expected, after 50 gm. of glucose the blood sugar percentage shows increase; in some cases a slight increase, in others a considerable one, is recorded.

In each case, 30 minutes after the ingestion of glucose, the sedimentation rate is reduced. An examination of the results shown in table 4. reveals that the difference in sedimentation readings vary from 2mm. to 30mm; that these variations always show reduction in rate at the time of the second reading; and that the wide divergences of the retardation of rate are incomparable with, either the fasting, or the alteration of, blood sugar percentage.

As blood sugar increases, sedimentation rate

decreases, that at first sight would appear to be the logical conclusion; but several other factors must be considered.

Firstly, since the above results had been found in diabetic patients, were they only applicable to diabetic bloods ? The identical tests were applied to non-diabetics.

3. Results of Oral Administration of Glucose upon Blood Sugar Sedimentation Rate, in Non Diabetics.

A group of normal, healthy individuals was examined to determine Blood sugar percentage and sedimentation rate in the fasting state; then after oral glucose. The results were varied and inconclusive. In health the sedimentation rate has been shown to be slow, thus any further retardation of rate is scarcely perceptible. Moreover, 50 gm. of glucose does not increase the sugar percentage above 0.17 %. These two facts might explain the inconclusiveness of the results obtained.

Patients suffering from some pathological condition known to increase sedimentation rate were next examined. As the initial Sedimentation Rate was rapid, the subsequent excursions of rate were more marked. Also as mild "lag" curves are obtained in many debilitating diseases, in this group larger variations in sugar percentage were possible. The results in six selected cases are shown in Table.5.

Table. 5.

	Condition	Fasting		After Glucose.	
		S.R. mm.	B.S. %.	S.R. mm.	B.S. %.
1.	Pulmonary Tuberculosis	72	0.142	55	0.183
2.	Acute Rheumatic Fever	60	0.120	45	0.170
3.	Arterio-sclerotic Ulcer of Foot	50	0.100	38	0.180
4.	Bronchitis	20	0.110	18	0.157
5.	Rheumatic Carditis	26	0.113	32	0.175
6.	Tonsillitis	12	0.097	12	0.140

These results again show that as blood sugar is increased, half an hour after glucose, sedimentation rate is slowed. Cases 4,5, & 6 are not conclusive, but there are very definite retardations in rate in cases 1,2 & 3.

The results in non-diabetic patients agree with the results of the same test in diabetics. Therefore, the causative factor of the decreased sedimentation rate is not peculiar to Diabetes.

4. Consideration of Other Possible Causes of Retardation of Sedimentation Rate After Oral Glucose.

If glucose were administered by intravenous injection, did the sedimentation rate again show a reduced speed ? Or, did the primary fasting condition of the patient influence

the findings ? These two questions were investigated by giving intra-venous glucose, after a normal breakfast had been taken. There were slight differences between the sedimentation readings of, the fasting blood, and the specimen obtained after breakfast, and there was a general and constant slowing of the rate after intravenous glucose. This slowing appeared to occur as early as ten minutes after the injection. Thus, irrespective of fasting or non fasting state; or whether the blood sugar was raised by the ordinary metabolic processes following the ingestion of carbohydrate, or by the artificial method of intra-venous injection, hyperglycaemia occurred and the Sedimentation Rate was reduced.

After, either glucose, or ordinary carbohydrate meal, by counts of the red and white blood cells, it has been found that a slight leucocytosis takes place, but that the numbers of the erythrocytes remain unchanged. Therefore neither gastric reflex, nor change from fasting state, nor alteration in blood cell volume, explain the reduced rate of sedimentation.

In several publications (1) reference is made to an "increased stickyness" of blood of high sugar content, but no proof nor explanation of this fact are given. The increase in blood lipoids, or raised cholesterol percentage, which occur in the more severe diabetic states, can scarcely be applied to many of the milder

cases investigated. Moreover, the fact that sedimentation rate is increased in pregnancy, when the blood cholesterol also is increased, does not suggest that diminished sedimentation rate is influenced by increased cholesterol content of hyperglycaemic blood.

From personal observations, blood of high sugar content does appear to be "sticky" and presumably such increased viscosity would lead to decreased sedimentation, but this is a most unscientific explanation for the phenomenon of :- increased blood sugar - retarded blood sedimentation.

Cherry (2) makes reference to the effect of glucose on blood sedimentation.

" The glucose tolerance test shows a decreased rate with an increase in the blood sugar percentage in controls; (ie. non-diabetics) the reverse seems to be found in diabetics. "

The first part of his conclusion is an agreement with the results given above, unfortunately it is difficult to correlate this opinion with his published figures. The second statement, that " the reverse seems to be found in diabetics", is based on an investigation that makes no mention of the presence of infection. That it is not true for the majority of patients would seem to be proved by the results of this investigation.

5. The Blood Sedimentation Rate as an Indication of the Progress of Diabetes.

At present, this series of diabetic patients has not been under observation for a sufficient length of time to decide whether the Sedimentation Rate is slowed after satisfactory treatment of the disease, but, the results so far obtained do not encourage such an opinion. The fact that increased blood sugar causes a reduction in rate might suggest that vice versa, a decreased blood sugar should lead to an increased sedimentation. This does not appear to be the case, where fasting bloods are tested. Further, it is noted that in several of the cases where the sedimentation rate is much decreased after glucose, this is not necessarily matched by an equal increase in blood sugar. Again there would appear to be no comparison between increase in blood sugar and decrease in Sedimentation Rate. Buchanan (3) having made examinations of diabetic patients for several years, finds that in certain cases, which ~~the sedimentation rate~~ ^{the sedimentation rate} following treatment, showed improvement in the diabetic state, actually increased. Of one case he writes "when the clinical condition is bad the Sedimentation Test is low, and at present, when he is in fairly good condition the test is high". It is uncertain what he means by "fairly good condition"; nor does he say that the test has been made on fasting blood. He makes no mention of infection which may be present. Such results are difficult to discuss.

On the other hand Krarup (4) in an inquiry into the action of Protamin Insulinate considers that a reduced rate

is indicative of satisfactory progress. Again no mention is made of presence of other disease, which if present would also receive treatment and so give a more normal rate. Therefore, the sedimentation test as an indication of the response to treatment does not seem to be applicable to Diabetes Mellitus, other than as a control of the activity of co-existent disease.

5. Discussion of Possible Conclusions.

The results of this part of the investigation concerned with the Sedimentation Rate in increased blood sugar percentages, seem to show that increasing hyperglycaemia is accompanied by a slowing of the rate of sedimentation. But, in the preceding chapter it was concluded that Diabetes had no effect upon Sedimentation Rate. These two conclusions appear to be contradictory. Yet, there may be a possible explanation of this contradiction; namely, that in Diabetes two different sets of sedimentation readings can be obtained ? It has been noted repeatedly that sedimentation rate has no connection with fasting blood sugar percentage. Also, that it is fairly constant for each individual examined under the same conditions, i.e. in the fasting state. Later it will be shown that in all 45 cases investigated the rate at first slowed, as the blood sugar increased after glucose, then as the blood sugar reading tended to return

to fasting level, so did the sedimentation tend to resume its fasting rate.

The sedimentation rate obtained in fasting blood, might be called the "True Sedimentation Rate" of diabetic patients. This rate which is sensitive to infections etc. but which is unaffected by the diabetic state, or the fasting blood sugar percentage.

The influence of increasing sugar percentage of the blood in diabetics, which occurs after high carbohydrate, or glucose, meals, produces a definite retardation of blood sedimentation, such lowered sedimentation rates might be termed, the "Retarded, or Uncontrolled," Sedimentation Rates.

In Diabetes, excluding the very transient periods of hyperglycaemia which are associated with "lag" curves, after carbohydrate intake the blood sugar is raised, and maintained, for a variable time, above 0.18%, the recognized maximum blood sugar reading in normal individuals. But, during ^{of the life of} each day of a diabetic patient the blood sugar tends to remain fairly constant, for after all, the hyperglycaemia which follows meals does not exist for more than 12 hours out of 24, during the other hours the blood sugar is fairly steady, although above the normal level. This percentage is variable, and is no indication of the severity of the diabetic symptoms which may be present,

and so, there does seem to be some evidence to support the suggestion that there is an individual limit to hyperglycaemia. For example, there is no uniform, nor constant, sugar percentage at the onset of coma in different cases, but the blood sugar readings obtained in the same patient during successive comas are closely alike. When 50 gm. of glucose are taken by a Diabetic there is a rapid, and considerable, rise in the blood sugar percentage above the individual sugar level. It is not known what exactly takes place when there is this sudden increase of blood sugar, but it is generally agreed that the increase is at first greater in the blood serum than in the cells. (Joslin) 1. Later the sugar content of serum and cells becomes the same. Whilst this transference of sugar from serum to cells is taking place, there must be a not inconsiderable disturbance of the blood stability; would this not explain the reduction in rate of blood sedimentation ?

It seems a reasonable supposition on which to found the proposition that there are "Uncontrolled Rates of Sedimentation in Diabetes" and that these are obtained during the time when the excessive hyperglycaemia is being adjusted. With the present knowledge of the process of sedimentation, these rates cannot fully be used for the investigation of Diabetes.

In the recent book on Endocrinology by Wolf (5) he

states that " The importance of this test(ie. sedimentation test) as far as endocrine disturbances are concerned lies in the fact that it may be utilized to apprise one of the infections of diabetes".

If to this he had added a condition, that blood in the fasting state must be used for determination of the sedimentation test, lest "Uncontrolled Rates" occur, then our conclusions would have been in agreement.

CHAPTER 1V

S U M M A R Y.

To determine the changes if any, which take place in blood sedimentation rate after the administration of glucose, 15 diabetic patients were re-examined.

The re-examination showed that the individual sedimentation rate was fairly constant, in the fasting state.

30 minutes after oral glucose solution, the blood sugar percentage was increased; the blood sedimentation rate was reduced. The same phenomenon was found in non-diabetics.

The reduction in sedimentation rate did not depend, on a gastric reflex, a change from the fasting state, or alterations in blood cell volume.

The alteration in sedimentation rate 30 minutes after glucose is no indication of the severity of the diabetes, nor can successive sedimentation readings indicate the response to treatment, other than the progress of infection, etc.,

It is suggested that in the fasting state, a "true" sedimentation rate is obtained. During times of rapid increase in blood sugar, "retarded, or uncontrolled", rates of sedimentation may occur.

Chapter 1V

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C H A P T E R V

The Glucose Tolerance Curve and The Blood Sedimentation Rate.

In Diabetes the blood sugar usually continues to increase for 60, 90, 120, or even 180 minutes, after a meal of 50 gm. of glucose, was this increase accompanied by further retardation of sedimentation rate?

The routine glucose tolerance test was performed on 43 diabetic patients; that is, the fasting blood sugar was determined, and there after redetermined at half hourly intervals, until two hours had elapsed since the taking of 50 gm. of glucose. As each specimen of blood was obtained the sedimenation rate was tested. The results are shown in the charts which appear at the end of this thesis. The glucose tolerance curves are given in the usual graphic way, and opposite are shown the sedimentation readings.. The numbers of each figure correspond to the case numbers of the patients previously examined.

Since an increasing blood sugar at the end of the first half-hour coincided with a reduced rate of sedimentation it was anticipated, that, as the blood sugar increased still further at later readings, the blood sedimentation rate would show still further retardation. In other words, that the sedimentation graph would illustrate a series of "Retarded or Uncontrolled" readings. Such expected results were found in the majority of the cases examined, and are shown in charted results of each case. (See Figs. No. 1, 2, 3, 4, 5, 6, 9, 10, 11, 12, 15, 16, 18, 20, 21, 22, 23, 25, 27, 29, 30, 31, 32, 33, 35, 39, 40.)

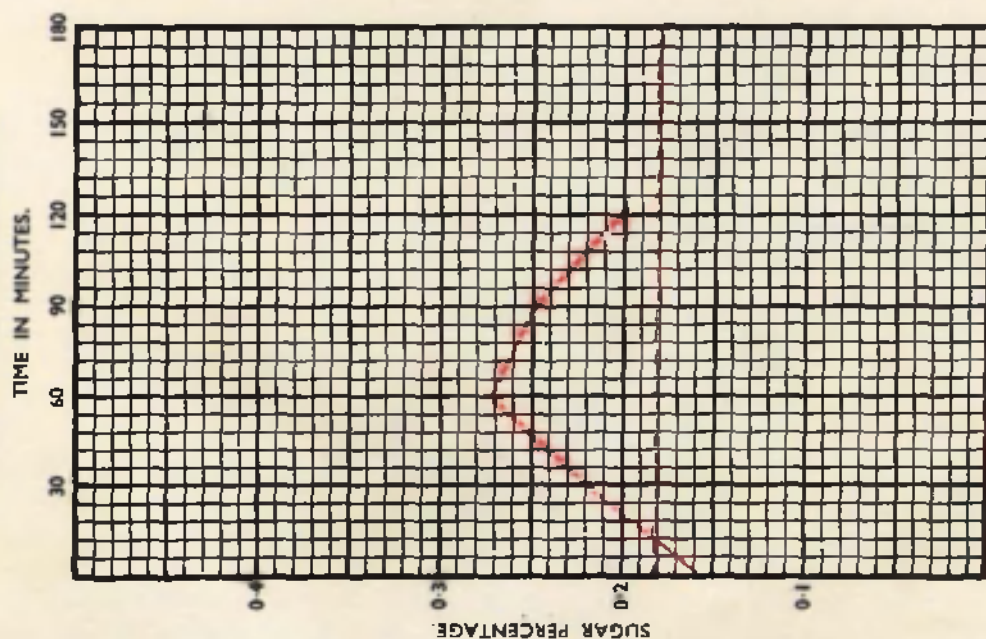
In each of these twenty-eight cases the sedimentation rate was slowed at the first reading, and further reduced at one, or more, later readings. Then as the blood sugar, past the maximum peak, commenced to return towards fasting level, the sedimentation rate was increased, but at no time did the rate of sedimentation exceed that obtained from the first, fasting, reading. The increasing sugar percentage did not invariably continue to coincide with further reduction of sedimentation, for in several cases the sedimentation rate started to increase towards its initial rate, before the blood sugar showed any indication of a commencing fall. Thus, once again, change of blood sugar level is accompanied by change of sedimentation rate, but the changes are not in direct, or even close, proportion

to each other. Also the amount of the blood sugar increase, appears to be entirely dissociated from the extent of the slowing of the sedimentation rate.

Below, in Fig. 13 there is illustrated, a result typical of the cases under discussion, and the points mentioned above. Thus, in the majority of the cases examined, the results of the investigation correlating the glucose tolerance test and the sedimentation rate, show that increasing hyperglycaemia is associated with a slowing of blood sedimentation, and that as the blood sugar tends to return to the fasting level, so does the sedimentation rate tend to regain its initial speed.

But, in 14 of the other cases very different results were obtained, and these results were similar to one another, but dissimilar to those described above, and seemed to form a second group. If the first group might be called the group of "expected results", or the typical results, then the second group might be termed the group of "atypical results". The difference between the two, is, that in the group of typical results the sedimentation rate is at first slowed, and no subsequent reading showing a increase in sedimentation rate is recorded; whereas in the second group there is an initial slowing of rate, but at a later reading a sudden and marked increase in blood sedimentation is found.

GLUCOSE TOLERANCE CURVE.



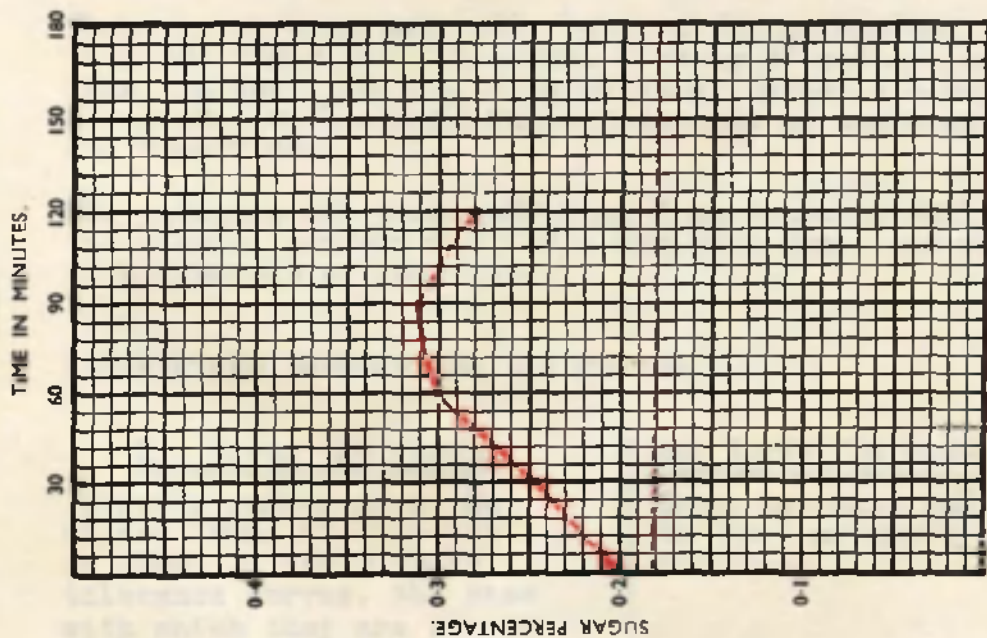
BLOOD SEDIMENTATION RATE.



GROUP N (typical result)

FIG 13.

GLUCOSE TOLERANCE CURVE.



BLOOD SEDIMENTATION RATE.

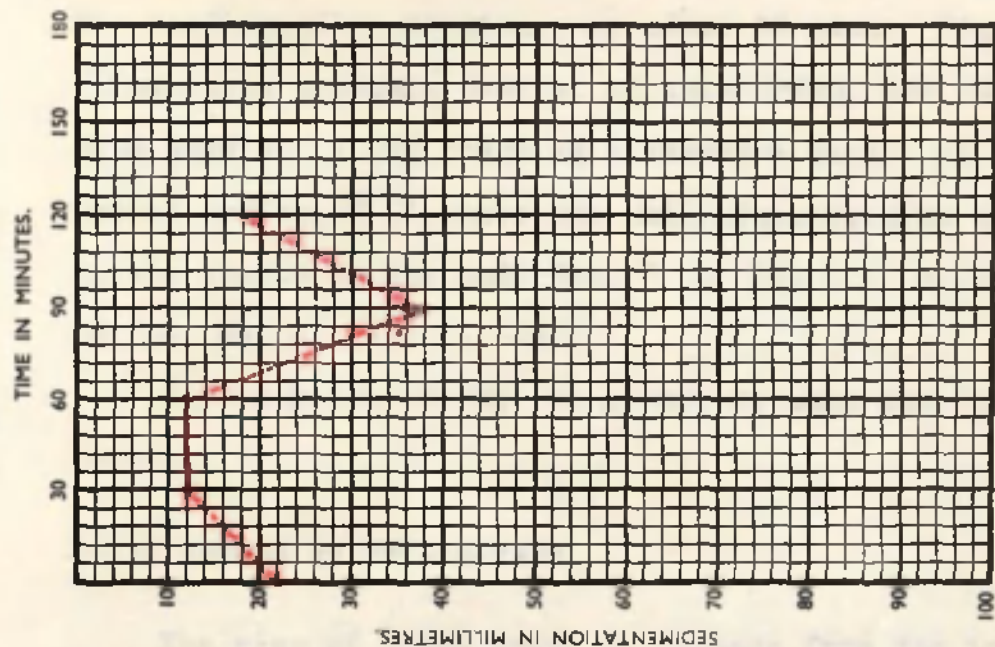


FIG 14.

GROUP X (atypical result.)

This acceleration of sedimentation rate occurs at either the reading after 60 mins., or after 90 mins. Fig. 14 illustrates a result typical of this group, the increased rate showing in the graph as a downward peak. In this second series of 14 cases the individual results are shown in the charts at the end, Nos. 7, 8, 14, 17, 19, 24, 26, 28, 34, 36, 37, 38, 41, 43.)

A comparison of the two groups reveals the following facts :-

Facts common to both groups.

The rise of blood sugar percentage from the initial, fasting level is associated with a reduction of blood sedimentation rate.

The fasting blood sugar percentage does not influence the subsequent behaviour of the sedimentation rate.

There is no apparent ratio between the percentage increase in blood sugar and the actual slowing of sedimentation rate. A small initial rise in sugar percentage may be associated with considerable reduction of sedimentation, and vice versa.

The patients all were suffering from Diabetes Mellitus, the disease had existed for a variable time, and was of alldegrees of severity.

Differences between the two groups.

1st Group (28 cases)

Patients suffer from the milder forms of Diabetes as shown by their sugar tolerance curves, the ease with which they are standardized, and the absence

2nd Group (14 cases)

These patients suffer from the more severe types of Diabetes.

of severe diabetic symptoms.

They have made satisfactory progress with diet and insulin treatment.

The Glucose Tolerance Curves show a sudden rise in sugar percentage and a fairly rapid return to fasting level.

i.e. "Peak" tolerance curves.

Many of the fasting sugar percentages were below 0.18%

With two exceptions the cases were normal, or below normal, weight.

The blood sedimentation curves are concave. i.e. there is a slowing of rate followed by a return to fasting speed.

Case No. 44 is a most difficult type and possibly may be one of "Pituitary Diabetes" Case No. 45 is suffering from advanced Pulmonary Tuberculosis. Neither of these cases have been included in the above two groups.

Before examining further the findings described above, other considerations have to be examined. For example, what was the sedimentation response to a similar investigation in non-diabetic individuals; did insulin affect the sedimentation of hyper-glycaemia produced by the administration of Adrenaline? These and other questions were examined and briefly are reported below; the results will be discussed later.

"Unsatisfactory Diabetics".

The Glucose Tolerance Curves show a state of sustained hyper-glycaemia, with a slow return to fasting level. (Except Case No. 27). Flattened tolerance curves.

12 of the 14 cases were definitely over-weight.

The blood sedimentation curves have a peak caused by a sudden acceleration in rate. This peak approximately corresponds to the highest point in the sugar tolerance curve.

The Glucose Tolerance Test and Blood Sedimentation Rate in Non-Diabetics.

The investigation made on the diabetic patients was repeated on four non-diabetics, one a case of renal glycosuria, one suffering from arterio-sclerotic gangrene of the foot, one, healthy, the fourth healthy but obese.

The results are given for these cases in charts Nos. 46 to 49.

In the patient suffering from renal glycosuria (Fig.46) the blood sugar percentage rose from the fasting level of 0.1% to 0.18% at the reading, made one hour, after glucose had been taken; whilst the sedimentation rate was reduced from 20 mm. to 10mm., Fig. 47 illustrates the results in a man, age 72 years. He was suffering from a chronic perforating ulcer of the foot and advanced arterio-sclerosis. Again, as the blood sugar percentage increased the sedimentation rate slowed from 50 mm. to 28 mm. The two healthy cases showed similar results, only the reduction in sedimentation rate was less.

Thus in the non-diabetic cases examined the findings were identical with these of the first group of diabetics that is, as the sugar percentage increased the blood sedimentation was reduced. It is worthy of note that in neither the obese case, nor in the patient suffering

from arterio-sclerotic gangrene, was the sedimentation rate increased beyond that of the fasting state as was found in the second class of diabetics, reported above.

The Blood Sedimentation Rate after Insulin.

If the sedimentation rate is reduced by increasing blood sugar, is the corollary true, that sedimentation would be increased by reducing the sugar content? To test this, several of the previously examined patients were given insulin (20 - 30 units) by subcutaneous injection, then at half hourly intervals the blood sugar and sedimentation rates were tested. The resultant graphs of two representative cases are shown in Figs. 50 and 51. The first graph shows a rapid and considerable reduction in blood sugar percentage after the injection of insulin; this was the more common finding. In the next it will be noticed that the insulin action is delayed, and that the blood sugar did not reach such a low level. (So far I have not had the opportunity of making an "Insulin Curve" on the majority of the patients, to date 13 have been examined in this way, therefore I will not give figures for so small a number.) However, the findings illustrated above do appear to be in agreement with the recently suggested division of Diabetics into two classes, the "Insulin Sensitive" and the "Insulin Insensitive". (H. P. Himsworth) (7). In the treatment of diabetic

patients, especially those who are liable to hypoglycaemic reactions or "Insulin Shock" possibly it will eventually be realized that the "Insulin Curve" may be as informative as the Glucose Tolerance Test, and certainly when they are compared together, the times of, and the reasons for, the onset of hypoglycaemic symptoms often become obvious. But, to return to the sedimentation test after the injection of Insulin.

Although only a small number of cases have been investigated, the constancy of one finding is worthy of note. That is, that although in all cases there is some reduction in blood sugar content by 60 minutes, in no case does the sedimentation rate change. Therefore, a lowering of blood sugar does not affect the blood sedimentation.

Five of the cases examined had a peak, similar to that found in the second group of glucose tolerance charts. This acceleration of sedimentation took place at the 90, or 120 minutes reading. In Fig. 50 and 51, two examples are given of such charts, and it is of interest to compare these with the charts of the same patients' glucose tolerance tests. (Figs. 29 and 41)

The sedimentation response in four cases who are being treated with Protamine Insulinate (Leo Insulin Retard - Hagedorn) (2) have also been examined.

Throughout tests over a period of twelve hours, no change of note, has been found in the sedimentation rates.

At the moment all that can be stated, is that sedimentation is not affected immediately ~~xxxx~~, either by the administration of insulin, or by the subsequent reduction of blood sugar. This finding is constant to all the cases examined, and is incomparable with the results recorded after the administration of glucose. In some of the cases there occurred an acceleration of sedimentation rate one hour, or later, after the injection of insulin. It is noted that these closely correspond to the cases of the second group of glucose tolerance tests.

Adrenaline and the Sedimentation Rate.

It is well known that the administration of Adrenaline causes liver glycogenolysis and thus increases the blood sugar percentage. Did then, the injection of Adrenaline lead to a reduction of sedimentation rate ? Six patients were given 20 minims of Adrenaline and the blood sugar and sedimentation recorded. The results were similar to these obtained after glucose, only the reduction in sedimentation rate took place almost immediately. The later behaviour of the sedimentation rate showed considerable variation. But since Adrenaline produces a leucocytosis, then an erythrocytosis, (Levy Simpson) (2) as well as a little

understood reaction upon endogenous insulin, the possible influences upon blood sedimentation are so numerous that they would require a separate investigation. Therefore, the only conclusion drawn, is, that following the injection of Adrenaline the blood sedimentation rate is decreased at first, as happens in all states of increasing hyperglycaemia, however produced.

Sugar Content of Blood Serum and Cells.

An attempt was made to estimate separately the percentages of sugar in the blood serum and in the cells. It was found that the two figures did not always coincide. This investigation requires considerable technical skill, and the possible sources of error are so numerous, and the differences in readings so small, that it was not considered safe to place any reliance upon the various findings.

The Sedimentation Rate During Coma.

It had been hoped that some information would be obtained from the investigations of blood sedimentation rates during coma. But, fortunately for the patients, and unfortunately for the investigator, the occurrence of diabetic coma now is rare. Also, the routine treatment by the administration of glucose and insulin made it impossible to obtain a series of uninfluenced results.

On the other hand the frequency of hypo-glycaemic reactions in patients of the class under observation ,

who think nothing of taking 25 units of insulin and then postponing the next meal for an indefinite time, yielded no more helpful information.

Apparently, the blood sedimentation rate during the time of hypo-glycaemia, may be normal, retarded or accelerated. One patient who suffers from severe and frequent insulin reactions, and whose fasting blood sedimentation rate is fairly constant at 12mm. per hour, has had at various times during hypo-glycaemic comas, the following sedimentation readings - 8mm, 42mm, 12mm, and 60mm,. There is no uniformity of results, and the author can offer no explanation of this lack of uniformity.

Ketosis, as shown by the presence of Acetone in urine.

As true diabetic coma was so great a rarity, there was no opportunity to study the effect, if any, of ketosis, upon blood sedimentation rate. But in group N., frequently the presence of acetone was demonstrated by Rothera's test, such small quantities had no apparent effect upon blood sedimentation.

It was rare to find acetone in the urines of the second group X.

Discussion.

It has been shown that the results obtained by testing the blood sedimentation rate after a glucose test meal in the diabetic patients examined, appear to conform to two distinct types.

The first type of results was found in the majority of the cases, and fulfilled the expectations of the single examinations of blood sedimentation after glucose. That is, that as the blood sugar percentage increased, the blood sedimentation rate was reduced ; as the glucose curve began to fall, the sedimentation rate rose. Thus, a graph of the sedimentation rate appeared as an inverted picture of the glucose tolerance curve. This group shall be referred to as Group N., and includes the results in non-diabetics.

In 14 cases, (ie. 34%) the results revealed a distinct, and common difference, to the above, for at some time after glucose, a reading was obtained which recorded a sudden acceleration in sedimentation rate, beyond fasting level. This group shall be known by the letter X.

The patients examined were suffering from diabetes mellitus, and previously it has been concluded that diabetes ' per se ' has no effect on sedimentation rate, why then did the results fall into two separate classes ? All the available data concerning each patient was carefully re-examined, and the two groups compared. Infections and disease other than

diabetes, occurred in both groups, though in group N, the incidence was lower. There were no explanatory differences, in either, fasting blood sugar percentages, or in fasting sedimentation rates. Did the two groups of results indicate that two different types of diabetes had been examined ?

The fact that diabetes does not influence the sedimentation rate when tested under standard conditions, namely, in fasting blood, does not necessarily preclude that the sedimentation rate will be unchanged under varying conditions, such as rapid changes in blood sugar. The actual amount of change seems to be governed by individual response. Therefore, as two classifications of results have been found, the possibility of two types of individual response must be considered. Flimsy evidence on which to base a theory of separate types of diabetes mellitus, however, the possibility of the existence of such different types of diabetes, has been presented in several publications.

Until recently it had been taught that Diabetes Mellitus was a disease caused by a pathological condition of the pancreas, which lead to impaired carbohydrate metabolism an increased blood sugar percentage, glycosuria, and the consequent symptoms and complications. But, in non-diabetics it now is known that hyper-glycaemia, and glycosuria, can be produced by factors other than disease of the pancreas. For

example, the "lag curve" after gastro-enterostomy; (R. D. Lawrence (4); C. Wallace Ross; (5) D. Emberton; (6).) Or the same temporary hyper-glycaemia which follows a carbohydrate meal after a period of starvation, or greatly restricted carbohydrate intake. (C. W. Ross; (5) H. P. Himsworth; (7). Similarly, in diabetes the blood sugar response can be modified by alteration of the food constituents, as illustrated by the work of Rabinowitch (8) on "high carbohydrate diets".

Still more recently, after a study of the action of injected insulin, it has been found that in diabetics there is no uniform response. Himsworth (9) goes so far as to state, that, "it became evident that a type of diabetes might exist which was due, not to lack of insulin, but to insensitivity of the body to insulin".

Here is one suggested division of diabetes into two classes, which Himsworth calls the "insulin sensitive" and "insulin resistive" types. The latter group in his opinion, either lacks an insulin "activator", or is hindered by the presence of an "inhibitor" of insulin. Tuttle (10) concluding an argument based on very different premises; makes a similar suggestion but holds that insulin has a double action, and that it requires an activator, which he believes to be phosphorus.

The relationship between diabetes and the Thyroid, the Pituitary, and the Adrenals, is but little understood, but that such a relationship does exist, is apparent.

(Levy Simpson; (2) H. P. Marks; (14). On endocrinological causation a further subdivision of the disease might be based.

Today the concensus of opinion appears to be, that, no longer can Diabetes Mellitus be accepted as a pathological entity, but that it can arise from various sources, and that it is manifested in different types. Otto Leyton (15) makes the suggestion, that "Diabetes might be a syndrome produced by several different lesions". Possibly this is carrying the argument too far.

And so, fortified by such authoritative opinions, the possibility of distinguishing two types of diabetes, by the response to glucose of the sedimentation rate, may be considered. The patients in group N. showed the usual symptoms of diabetes and gave typical histories of onset and progress. But, when group X were tabulated from clinical evidence, a striking fact appeared. Namely, that with one exception, all these patients were over-weight. On further interrogation it was discovered that the prevalent obesity was not a recent development, moreover in no case was there a history of previous loss of weight. This was a very different history from that usually given, and very different from the course of the disease in the first, "typical" group.

Diabetes is a wasting disease, why did the patients in group X not lose weight; when each was clinically, and by blood analysis, proven to be suffering from Diabetes Mellitus?. Their blood sugar levels were higher than

those of group N; glycosuria was common; the incidence of arterio-sclerotic ulceration and gangrene was high; if the usual standards are accepted, the patients in group K were suffering from a more severe type of diabetes. Yet, there was no wasting, except in two fatal cases of gangrene. The prevalence of gangrene and arterio-sclerotic changes points to a possible explanation. If the peripheral storage mechanism was impaired, or more important, if the actual processes of carbohydrate combustion were slowed, then there would be a lessened demand for glycogen. It has been recently suggested by some investigators that insulin may have a double action, first, to convert or aid the conversion of, blood glucose into glycogen, and second, to assist in the oxidization of glycogen. This second suggested action presumably would be peripheral rather than circulatory and if impaired, might even produce obesity.

In the patients of group K. the response to treatment has been most unsatisfactory, for although they are receiving large doses of insulin compared to the majority of the first group, yet hyperglycaemia and glycosuria persist. Also few, if any, admit to any improvement after ten months treatment. They are listless, take no exercise, and suffer from "eye symptoms", "neuritis", and headaches. Even with the injection of 80 units of insulin daily, in three of the cases, insulin reactions or hypo-glycaemic

reactions, are almost unknown. In two patients admitted to hospital, the insulin response as indicated by a glucose curve after insulin, showed only a slight reduction in blood sugar level, and at no time did it fall below the normal fasting reading.

When these facts are compared to the clinical findings of the other group a striking difference is apparent. The patients in group N. show definite improvement to diet and insulin, and most of them feel much better. Weights have increased, they are more active, and generally once again feel life worth while. Subject to temporary remissions, their urines remain sugar free: vague aches and pains are relegated to a less pleasant past; diabetic coma is unknown. In a few, traces of acetone occasionally appear. Hyperglycaemic attacks, even insulin comas, unfortunately still are rather common in this group of patients and remain the main cause of concern. Possibly Protamine Insulinate will solve the problem in some cases.

Thus, not only as a result of differing blood sedimentation response, but also from clinical standards, it does seem that two separate types of diabetes have been examined. Previously, it was questioned whether in some patients there does not exist an individual level of hyper-glycaemia, and the clinical signs of the patients in group X. again give rise to such a possibility, and lead one to wonder if any advantage is obtained by the continuance of large doses of insulin.

The causes of the alteration in blood sedimentation rate, in all, a primary retardation; in group X. a subsequent acceleration, are unknown. If the changes in rate which followed the injection of insulin had been consistent, some guide to a likely answer might have been found, but it was not so. Whether the change in sedimentation is brought about by the change in blood sugar percentage, or, whether with an alteration of blood sugar content, some simultaneous change in the blood serum or cells, or in both, leads to a more rapid, or a slower rate of sedimentation - that cannot be explained. Previously it was suggested that changing sugar content between cells and serum might produce a retarded rate. It does not appear that this explanation fits the acceleration, which takes place in group X. However, as there is no agreement as to the controlling factors of increased blood sedimentation in non-diabetics, it is scarcely reasonable to expect any clear account of the causation in diabetics. Once again, in view of the results in diabetics, it is difficult to accept the theory of "tissue destruction" as a complete definition.

Chapter V.

S U M M A R Y .

The Glucose Tolerance Test, and simultaneously obtained blood sedimentation rates, were compared in 43 diabetic patients.

There occurred a reduction in sedimentation rate corresponding with the increase in blood sugar percentage, 30 minutes after glucose had been taken, in each case. The subsequent behaviour of the sedimentation rate was not consistent, but was of two definite types.

In the first group, comprising 28 cases, the sedimentation rate continued to show an inverted picture of the graph of the glucose tolerance curve. (Group N.)

In the second group, 14 cases, after an initial reduction in rate, at a subsequent reading the sedimentation rate was increased, and increased beyond the rate of the fasting reading. (Group X.)

A comparison of the two groups obtained by the above classification based on sedimentation rates, revealed certain characteristic differences in history and clinical condition.

Similar tests repeated in non-diabetic patients showed results similar to those obtained in Group N. cases.

The response of diabetic patients to insulin and adrenaline was examined, but, no constant changes in blood sedimentation rate were found.

A discussion of the results suggests the possibility of the existence of two separate types of Diabetes Mellitus, both on the grounds of clinical difference, and on the different changes which occur in the sedimentation rate after a glucose test meal. Reference is made to recent theories on the above subject.

CHAPTER V

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The
Blood Sedimentation Rate In
Diabetes Mellitus.

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C O N C L U S I O N .

To present this thesis as a history of the various stages of the investigation, has been the endeavour of the author. But, as has already been stated, when the investigation was begun there was no intention of ultimately directing the inquiry to a comparison of blood sedimentation rates and blood sugar percentages, as found in the glucose tolerance test results.

Hence, as each stage of the investigation arose from the findings of the preceeding part, the report of the investigation also had to be divided into sections, with the result, that three different lines of inquiry have been made, and three separate, but complimentary, sets of findings had to be described. These three parts were, the description of the test, the application of the test and the results in various conditions; secondly, the blood sedimentation test in Diabetes Mellitus, and the assessment of the value, if any, of the test, in this disease; thirdly, a comparison of sedimentation rates and blood sugar percentages, after a glucose meal.

The findings reported in each chapter have been discussed and summarized. It would be adding redundant matter, to this, already over lengthy thesis, if these findings again were stated in full. So, with a very brief recapitulation of the conclusions drawn from the three parts of the inquiry, this report will be concluded.

In Section I. the findings reported require no further discussion, but it is of interest to note, that, since this investigation was commenced two years ago, many publications on the subject of blood sedimentation have appeared in the medical press. In some of these the results reported have been verified, in others, several of the uses of the test suggested in Chapter II have now been adapted. It may be added that subsequent experience of the test has fully supported the conclusion, that, the sedimentation rate mirrors the activity of many disease processes, and that the simplicity, and reliability of the sedimentation test make it a most welcome addition to the methods of clinical investigation.

The second part of the inquiry, reported in Chapter III, deals with the sedimentation rate in Diabetes Mellitus. The very definite conclusion arrived at, is, that the sedimentation rate of fasting blood is no measure of the severity of the diabetes, nor is it influenced by the blood sugar percentage, but, that it is a valuable guide to the presence, or absence, of other infections.

The results of the final part of the investigation which are discussed in Chapters IV and V, are more difficult to assess:

A retardation in rate of blood sedimentation follows ingestion of 50gm. of glucose solution, and seems to coincide with the initial rise in blood sugar percentage. That would appear to be a definite conclusion based on the uniformity of the results obtained.

When the customary routine glucose tolerance test is compared to repeated sedimentation rates, two types of sedimentation response occur. In one, the majority, group, as the blood sugar percentage continues to rise, the sedimentation rate continues to fall. In the other group, the sedimentation rate, at one reading shows a marked acceleration beyond its initial speed.

This division, in the absence of other possible explanatory factors, leads to the suggestion that two types of diabetes have been examined. This suggestion is supported by clinical differences, and the different response to treatment, of the two groups.

Other lines of investigation, such as the examination of the sedimentation rate during coma, or after the administration of insulin, failed to give conclusive results, and no conclusions could be drawn from them.

The disappointing fact must be admitted, that this part of the investigation failed to give the results anticipated from earlier findings, however, the very

unexpectedness of the results, appeared to warrant their inclusion.

If in time, there is gained a greater knowledge of the process of blood sedimentation, it is possible that such investigations might be of value in the study of the haematology of conditions such as Diabetes Mellitus.

CHARTS OF
GLUCOSE TOLERANCE TESTS
and
BLOOD SEDIMENTATION RATES.

Abbreviations Used.

- F.B.S. - Fasting blood sugar percentage.
Sed. R. -Blood sedimentation rate.
W.R. -Blood Wassermann Reaction.
Sp. Gr. -Specific Gravity.
W.B.C. -Number of white corpuscles.
R.B.C. -Number of red corpuscles.
M. -Male.
F. -Female.
-

No. 1. Case F.U.

Age 50. (F)

One year ago was admitted to hospital in diabetic coma. Since then has been treated with insulin, 10 units m., 5 units n., Several years ago she received a full injection course of anti-specific treatment.

General Cond.. Good. Some buccal leukoplakia, no symptoms of neuro-syphilis. Weight 162 lbs.

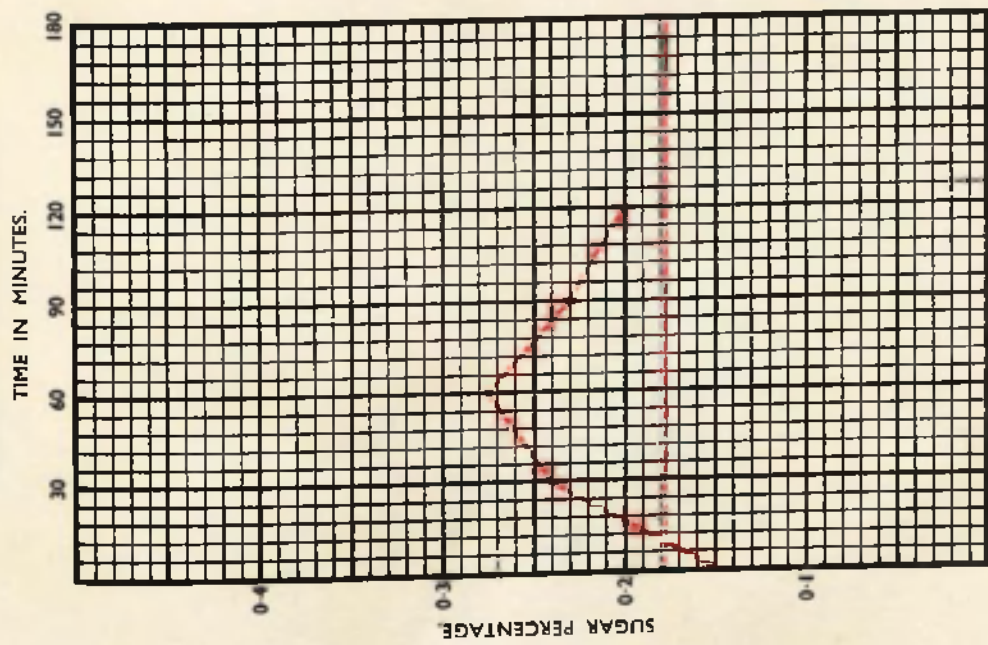
Blood F.B.S. 0.154. Sed. R. 3mm. W.R. ~~+~~x.

Urine Sp. Gr. 1030. Sugar 0.5% No Acetone.

Treatment 10 line diet, and insulin, 10 units b.d..
Course of Kharsulphan begun.

Progress Very satisfactory. On high carbohydrate diet she remains sugar free, and the insulin has been reduced to 5 units b.d.. After the injection course the W.R. remains positive, but there is no evidence of active syphilitic infection.

GLUCOSE TOLERANCE CURVE.



BLOOD SEDIMENTATION RATE.

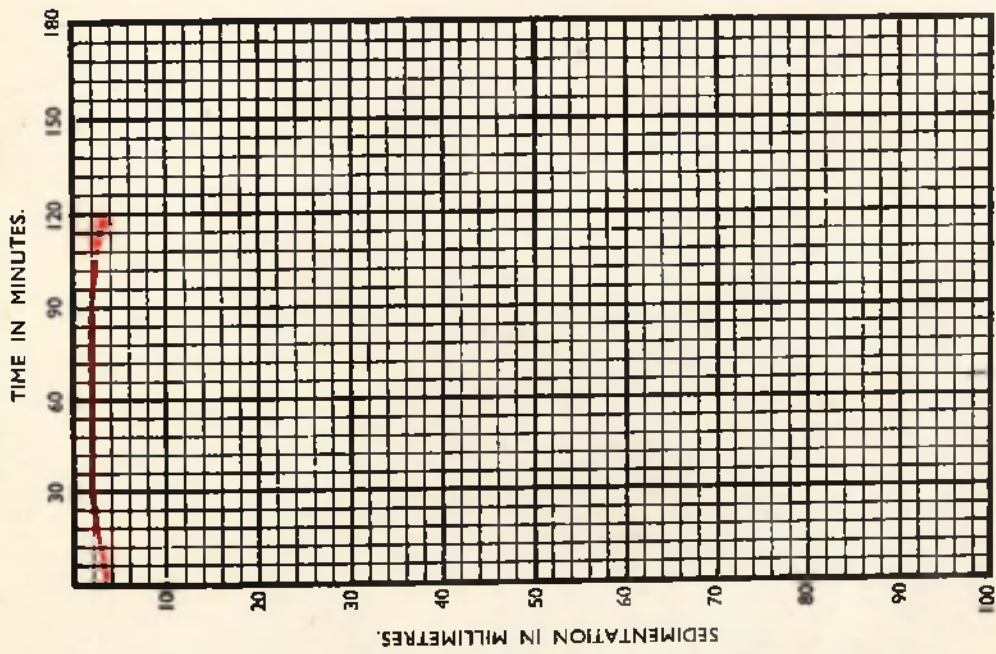


FIG 1.

No. 2 Case A.S.

Age 40. (F)

Two years history of Diabetes; first symptoms, thirst, loss of weight and general debility. No family history of diabetes.

General cond. Thin and nervous. Has a simple adenoma of Thyroid gland.
Weight 109 lbs.

Blood F.B.S. 0.25% Sed. R. 4mm. W.R. -ve.

Urine Sp.Gr. 1.030 Sugar 1% Acetone present

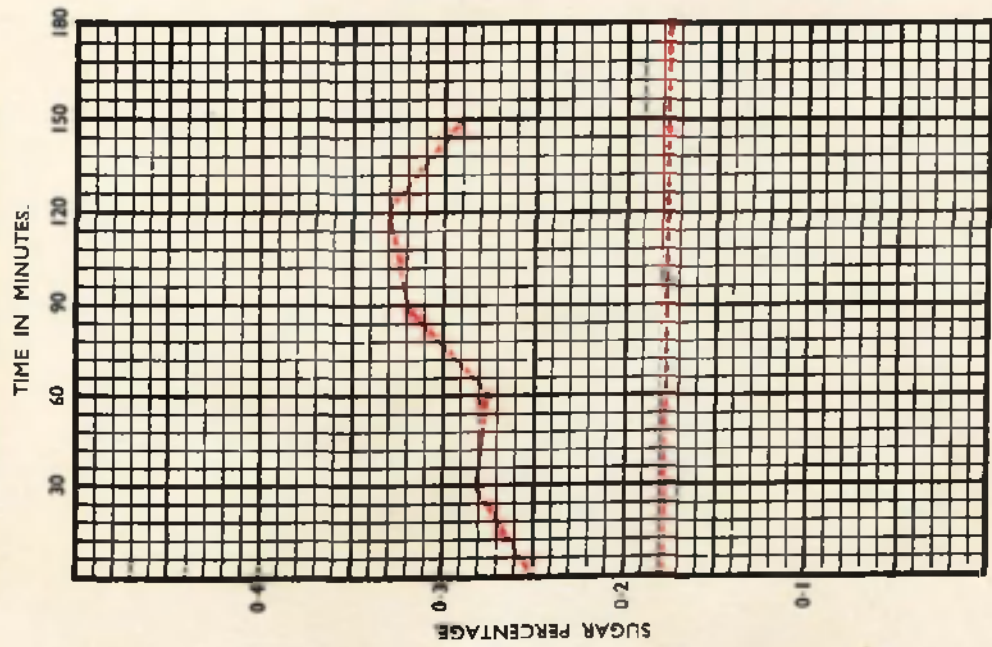
Treatment High carbohydrate diet and Insulin, units 30m., and 20n.,

Progress Has not been satisfactory. Urine seldom sugar free. Began to have frequent hypoglycaemic attacks, so Insulin divided into three doses. Frequently acetone in urine. Still losing weight.

Adenoma of Thyroid enlarging - for operation.

GROUP N.

GLUCOSE TOLERANCE CURVE.



BLOOD SEDIMENTATION RATE.

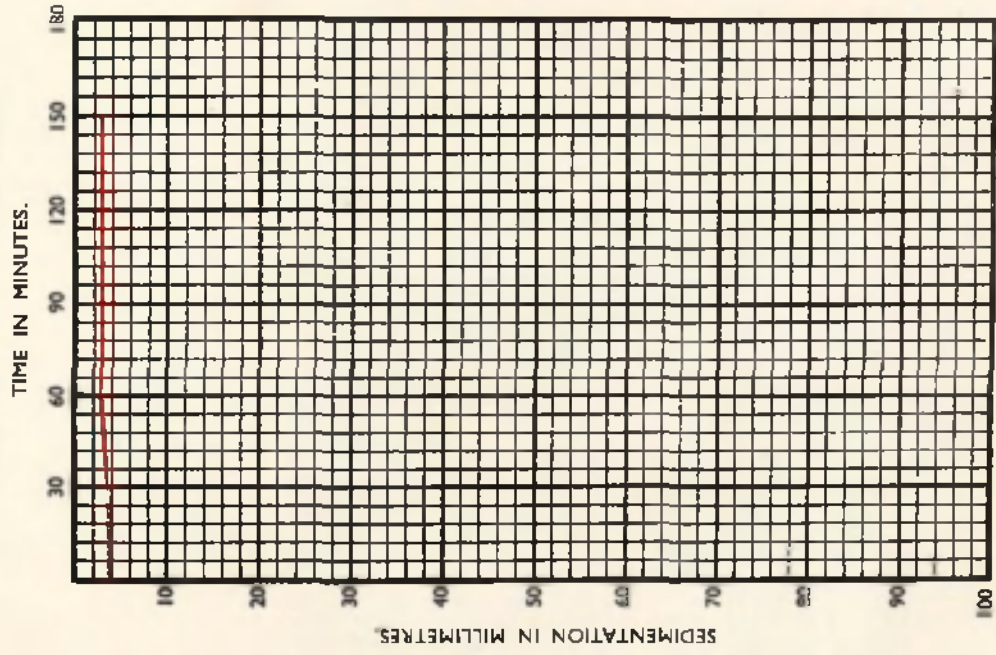


FIG 2.

No. 3 Case R.M.

Age 51. (F)

One year ago suffered from increasing lassitude, associated with thirst and polyuria. Recently has lost much weight. No family history.

General cond. Very thin. No abnormalities found. Weight 106 lbs.

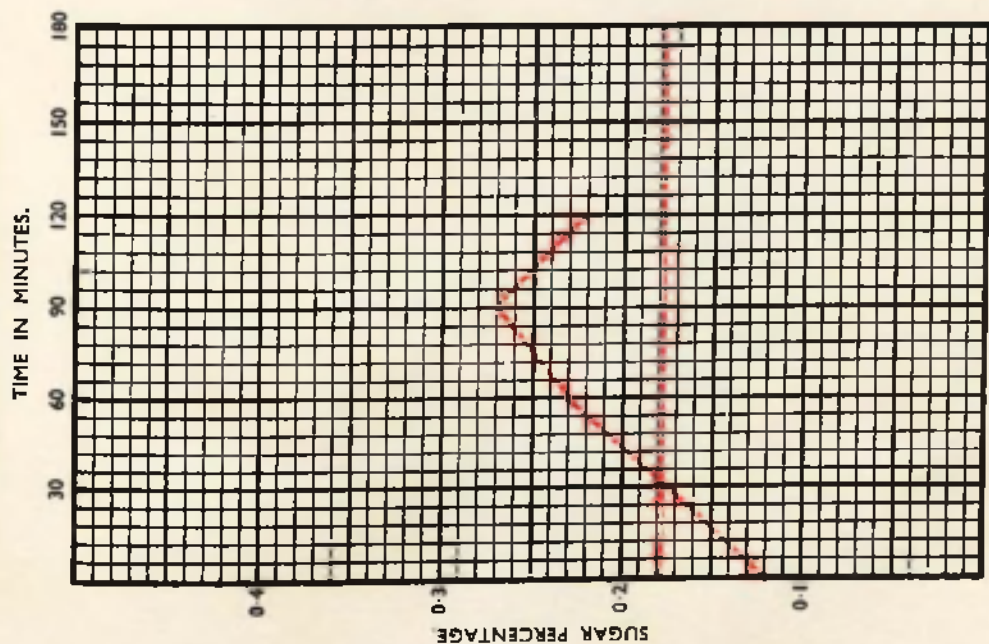
Blood F.B.S. 0.125 %. Sed. R. 5mm. W.R. -ve.

Urine Sp. Gr. 1018. Trace of sugar. No acetone.

Progress On full 10 line diet without insulin she remained practically sugar free. At the date of her discharge she felt much improved and obviously had gained weight; but unfortunately there was no record of her weight on admission.

GROUP N.

GLUCOSE TOLERANCE CURVE.



BLOOD SEDIMENTATION RATE.

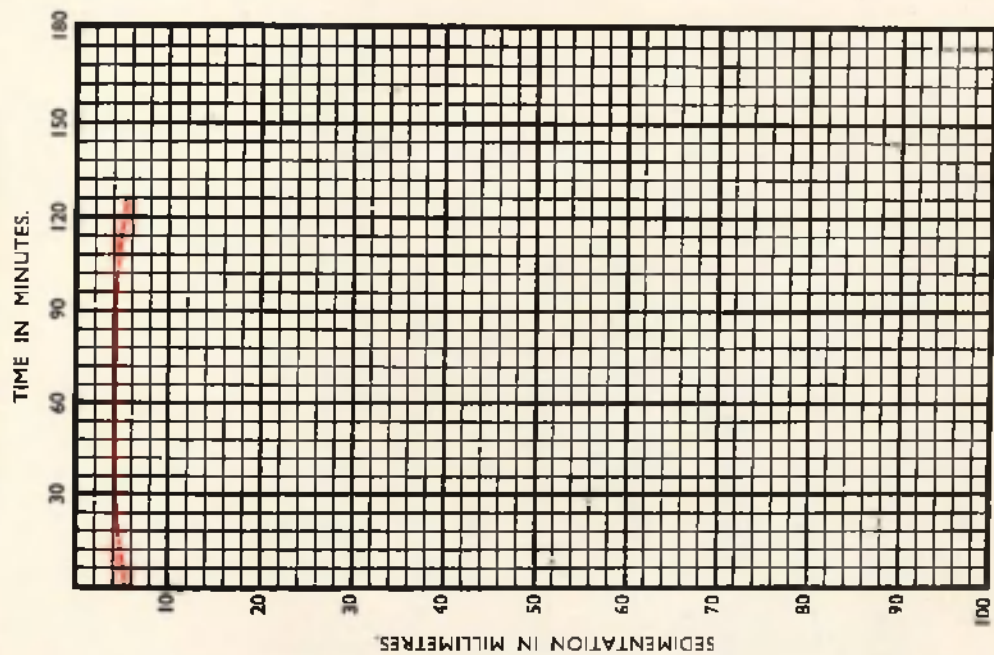


FIG 3.

Age 55. (M)

Diabetes discovered one year ago. Since been treated with diet and Insulin; still losing weight. No family history.

General cond.

Fairly good for age. Subject to dizzy attacks.
B.P. 195/140. Weight 117 lbs.

Blood

F.B.S. 0.1 %. Sed. R. 6mm. W.R. -ve.

Urine

Sp. Gr. 1020 Sugar and acetone free.

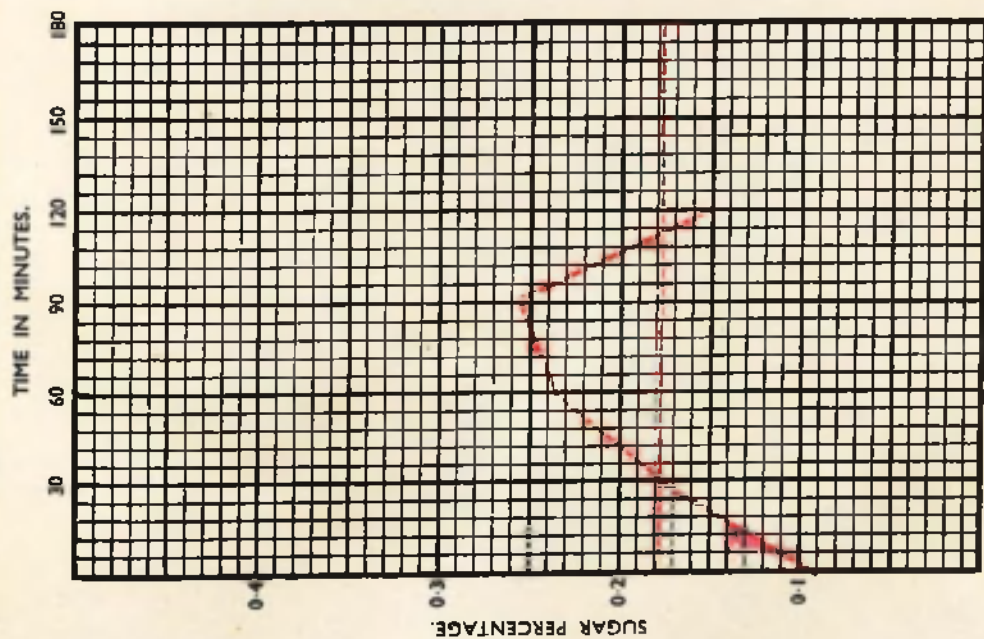
Treatment

Increased diet and insulin 5 units B.D.

Progress

Case of mild diabetes who had not been receiving sufficient food. Only recently referred to clinic. Now gaining weight and making satisfactory progress on 10 units Protamine Insulinate.

GLUCOSE TOLERANCE CURVE.



BLOOD SEDIMENTATION RATE.

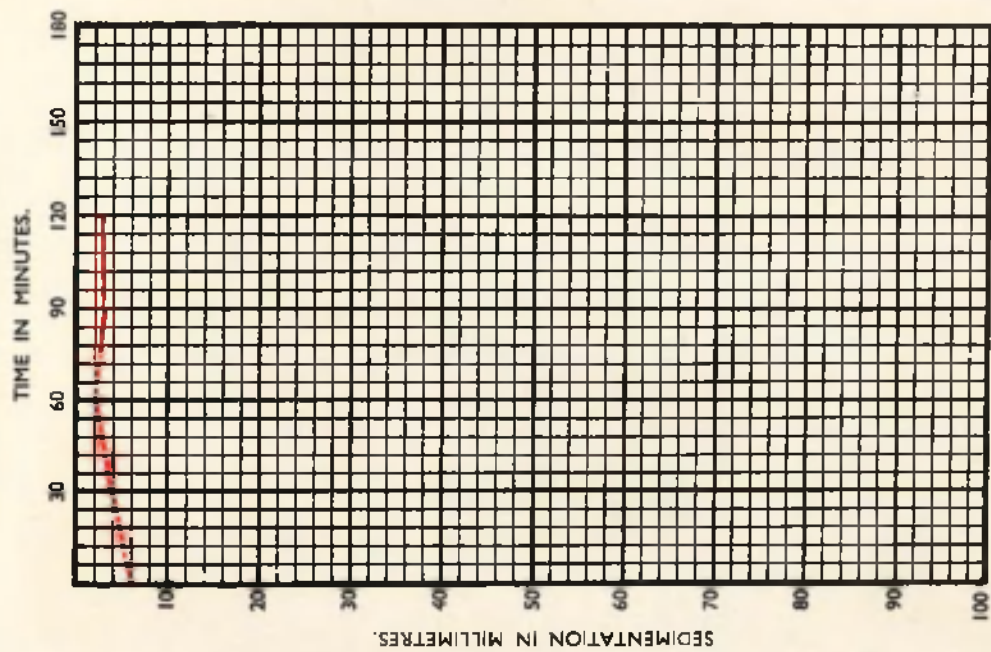


FIG 4.

No. 5 Case T.C.

Age 68. (M)

Admitted to hospital complaining of polyuria and pruritis and loss of weight.

General Cond. Rather thin, otherwise appears well. Weight 139 lbs.

Blood F.B.S. 0.127 %. Sed. R. 6mm. W.R. -ve.

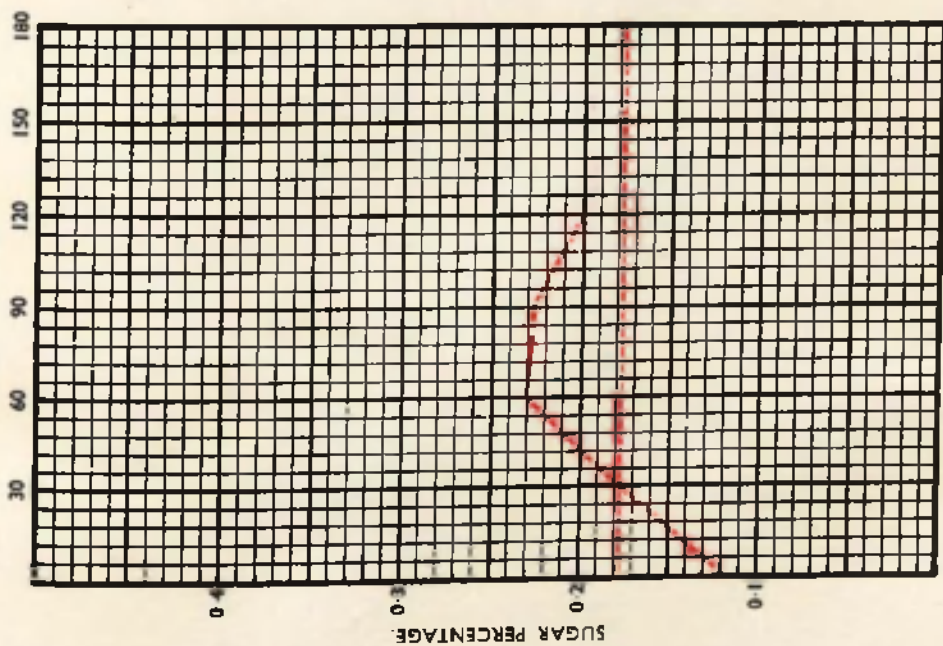
Urine Sp. Gr. 1024. Sugar .5% Trace of Acetone.

Treatment Now on high carbohydrate diet and Insulin 15 units m., and 10 units n., He appears to be making a satisfactory response.

GROUP N.

GLUCOSE TOLERANCE CURVE.

TIME IN MINUTES.



N.

BLOOD SEDIMENTATION RATE.

TIME IN MINUTES.

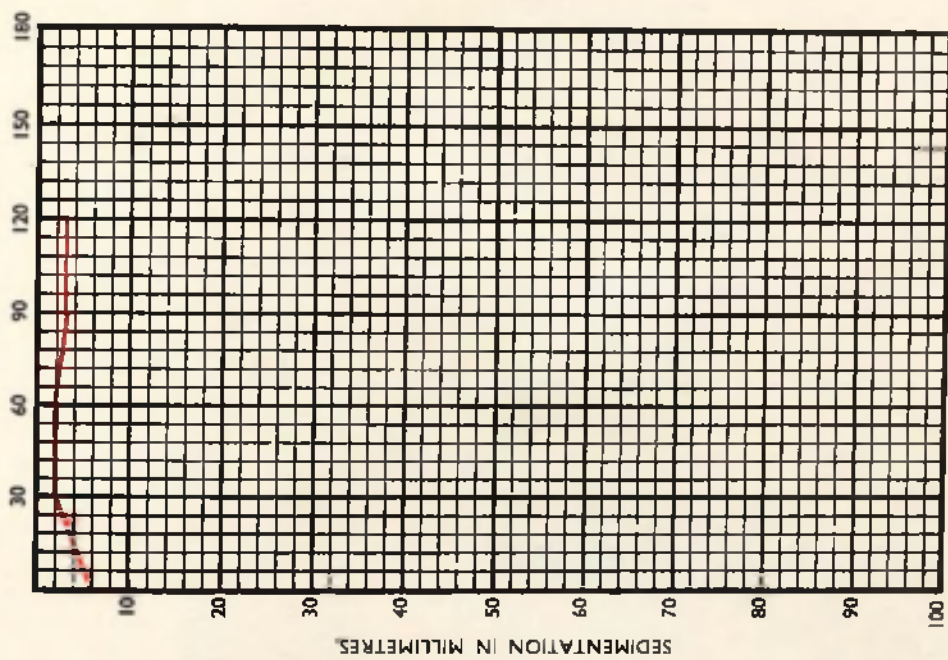


FIG 5.

No. 6 Case B. J.

Age 34. (F)

One year ago Diabetes commenced with symptoms of thirst, polyuria, pruritis and lassitude. Since treated with Insulin and diet. No Diabetes in family. Has been losing weight.

General Cond.

Rather thin. Edentulous. Easily tired and subject to attacks of faintness. Pruritis and neuritis at times severe. Weight 132 lbs.

Blood

F.B.S. 0.161 %. Sed. R. amm. W.R. -ve.

Urine

Sp. Gr. 1030 Trace of sugar. Acetone free.

Treatment

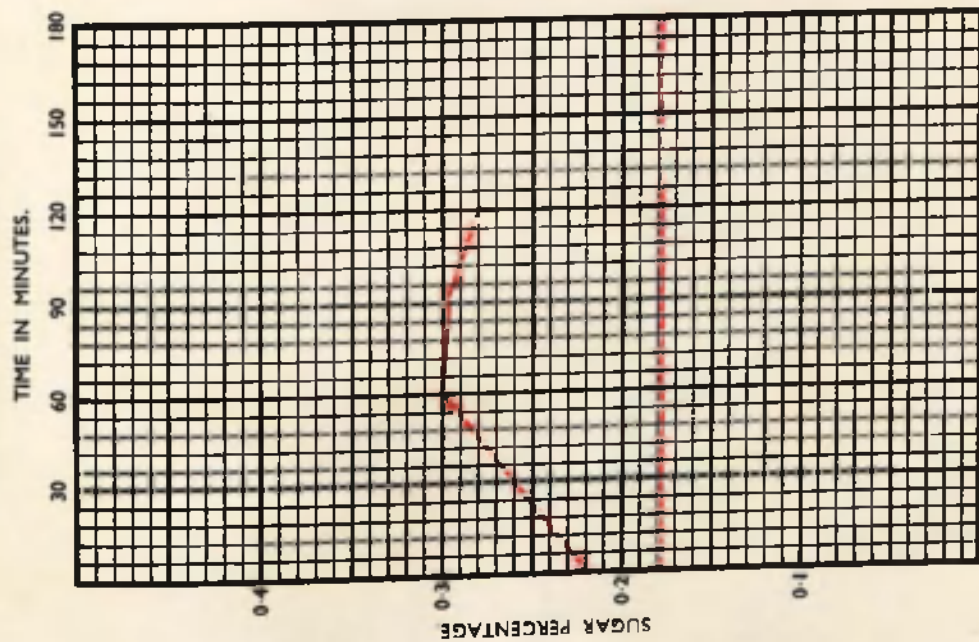
Placed on 10 line diet and Insulin, 20 units m., 20 units n.,

Progress

Recently has ^{not} been taking suitable diet, sugar present in urine, 2-3 %. Has lost some weight.

GROUP N.

GLUCOSE TOLERANCE CURVE.



BLOOD SEDIMENTATION RATE.

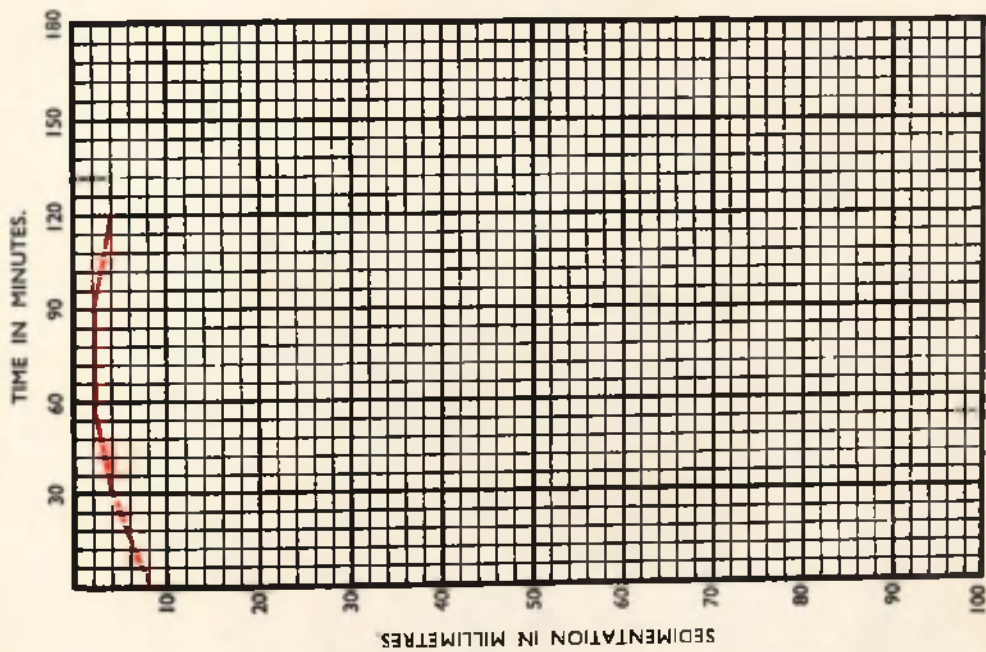


FIG 6

No. 7 Case S.E.H.

Age 63. (F)

Fifteen years history of Diabetes. Always has suffered from severe pruritis. No known family history of Diabetes. Always stout.

General Cond.

Overweight. Edentulous. Chronic varicose ulcer of leg, practically healed. B.P. 150/90. Arterio-sclerosis present

Blood

F.B.S. 0.256 %. Sed. R. 12mm. W.R. -ve.

Urine

Sp. Gr. 1032. Sugar 3% Also acetone.

Treatment

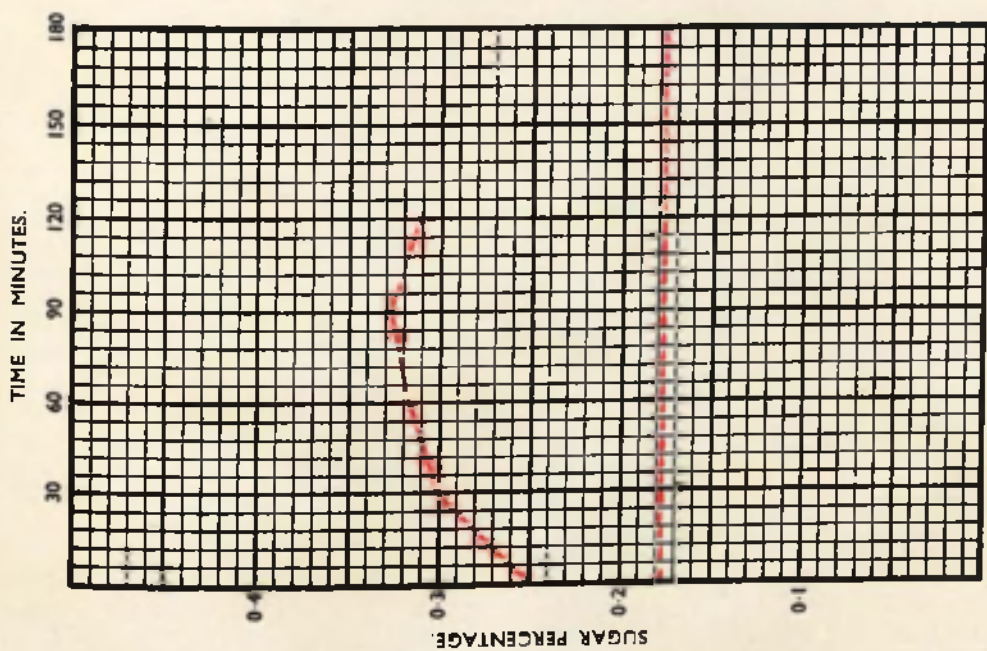
Diet and Insulin 15 units b.d..

Progress

Not satisfactory. Does not keep to diet, and seldom is sugar free. Varicose ulcer keeps breaking down.

GROUP X.

GLUCOSE TOLERANCE CURVE.



X.

BLOOD SEDIMENTATION RATE.

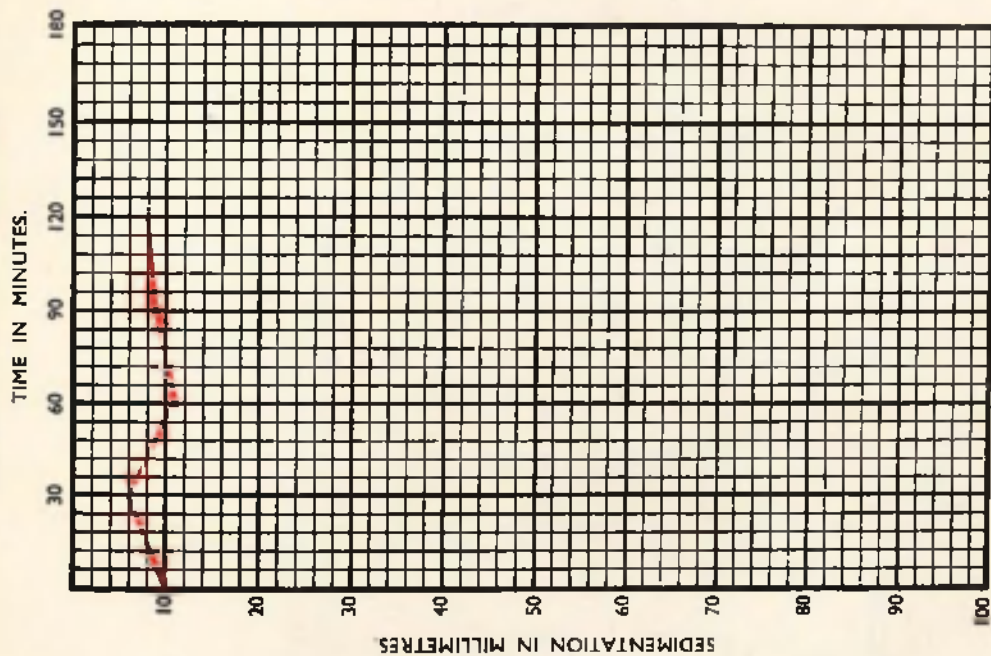


FIG 7.

No. 8 Case L.C.

Age 51. (F)

Diabetes found when patient was in hospital for surgical treatment seven years ago. Since then she has received neither Insulin nor dietary treatment. No family history of diabetes. Always stout.

General cond. Some arterio-sclerosis. B.P. 140/100. Complains of dizzy attacks and neuritis. Weight 232 lbs.

Blood F.B.S. 0.185 %. Sed. R. 13 mm. W.R. -ve.

Urine SP. Gr. 1024. Sugar present 2%. Trace of acetone.

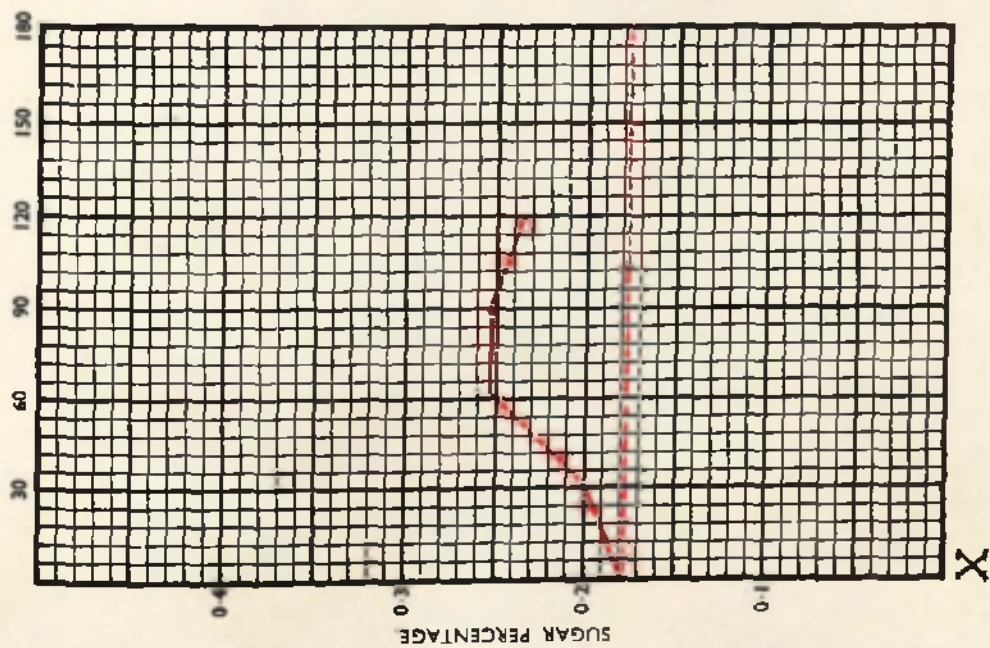
Treatment Placed on Insulin, 10 units m., and 5 units n.,

Progress Insulin dosage raised to 15 units b.d.. now sugar free and satisfactorily stabilized.

GROUP X

GLUCOSE TOLERANCE CURVE.

TIME IN MINUTES.



BLOOD SEDIMENTATION RATE.

TIME IN MINUTES.

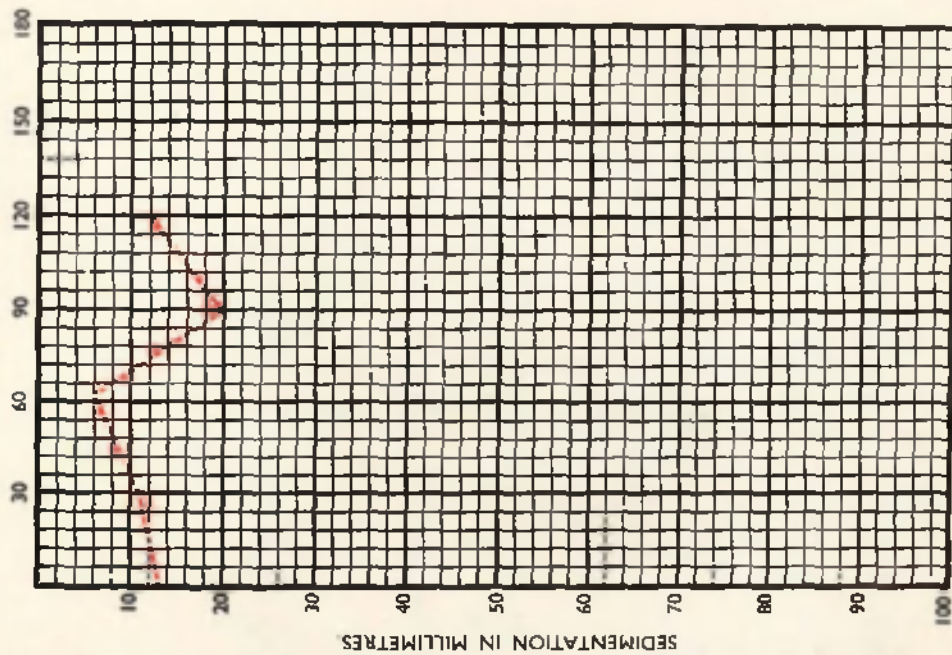


FIG 8.

No. 9 Case F. S.

Age 56. (F)

Admitted to hospital for surgical treatment of uterine prolapse. Suffered from diabetes for the past six years. No blood sugar determinations had been made, but she was taking a restricted diet and 16 units of Insulin daily, but still losing weight. No family history of diabetes.

General Cond. Fairly good. Uterine prolapse with both cystocele and rectocele. Weight 128 lbs.

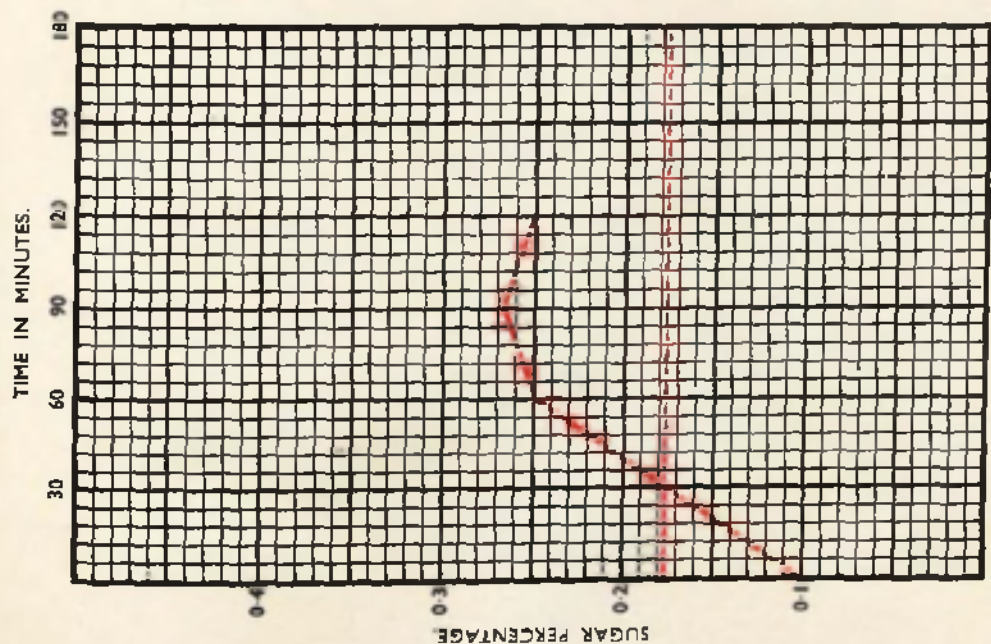
Blood F.B.S. 0.1 %. Sed. R. 14 mm. W.R. -ve.

Urine Sp. Gr. 1022. Trace of sugar. No acetone.

Progress Satisfactory. Successfully operated upon, and eventually discharged on 10 line diet and no Insulin.

GROUP N.

GLUCOSE TOLERANCE CURVE.



BLOOD SEDIMENTATION RATE.

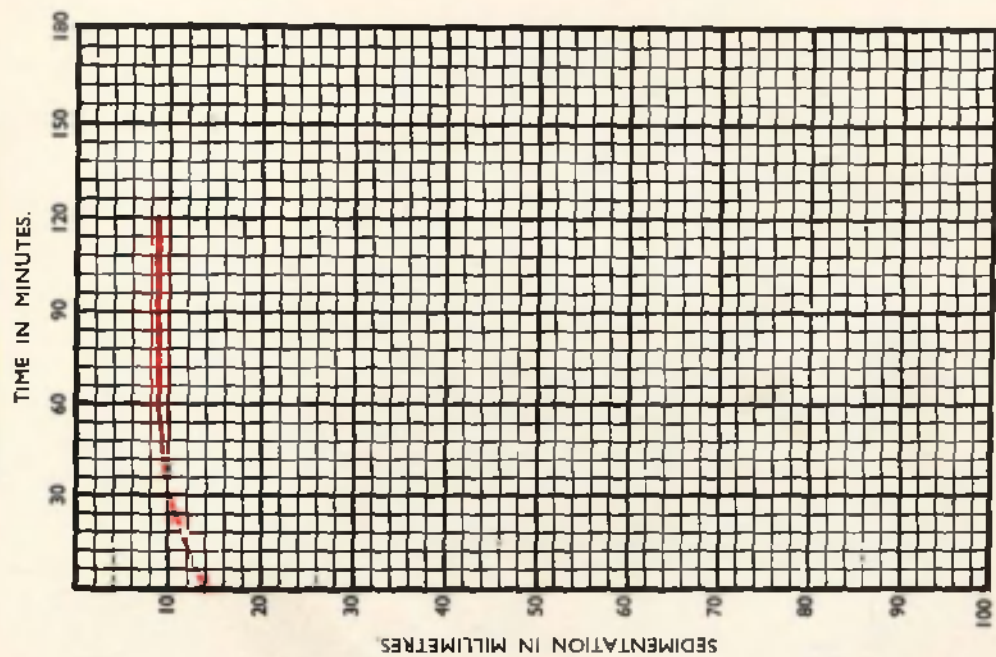


FIG 9.

N.

No. 10 Case A.T.

Age 64. (F)

Two years ago admitted to hospital suffering from septic foot, Diabetes diagnosed. Since treated with diet and Insulin No F.H. of Diabetes.

General cond. Fairly good. Heart and lungs normal. B.P. 140/100.
Cataract of left eye. Weight 128 lbs.

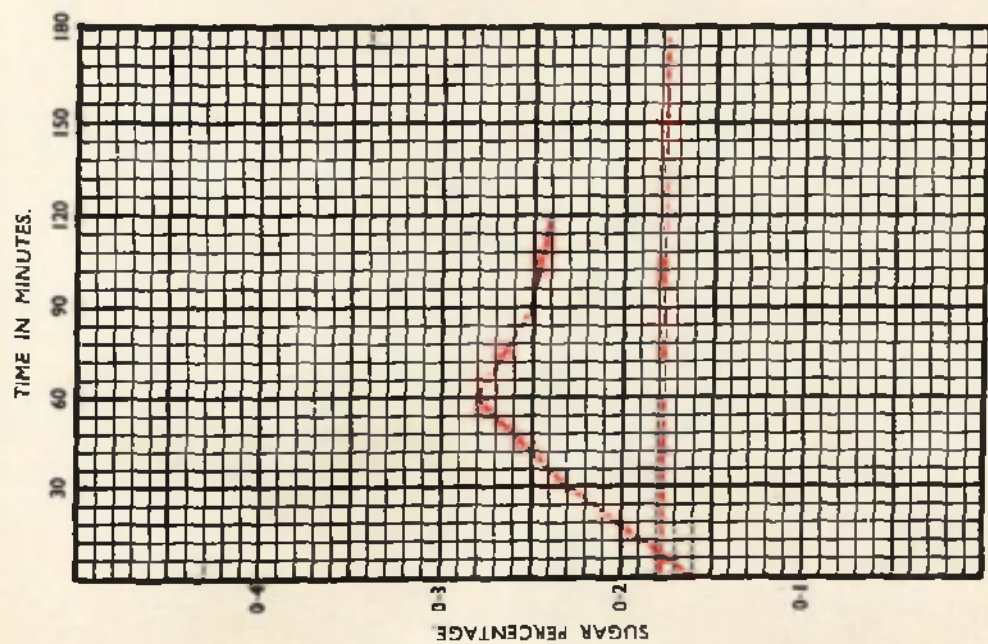
Blood P.B.S. 0.16 %. Sed. R. 14 W.R. -ve.

Urine Sp. Gr. 1030. % sugar present. No acetone.

Treatment 10 line diet.
Insulin, 15 units m., 10 units n.,

Progress Satisfactory, after three months Insulin reduced to 10 & 5. After eight months, feels well, gaining weight, and urine is sugar free. Mild hypo-glycaemia attacks have ceased since Protamine Insulinate was substituted for ordinary Insulin.

GLUCOSE TOLERANCE CURVE.



BLOOD SEDIMENTATION RATE.

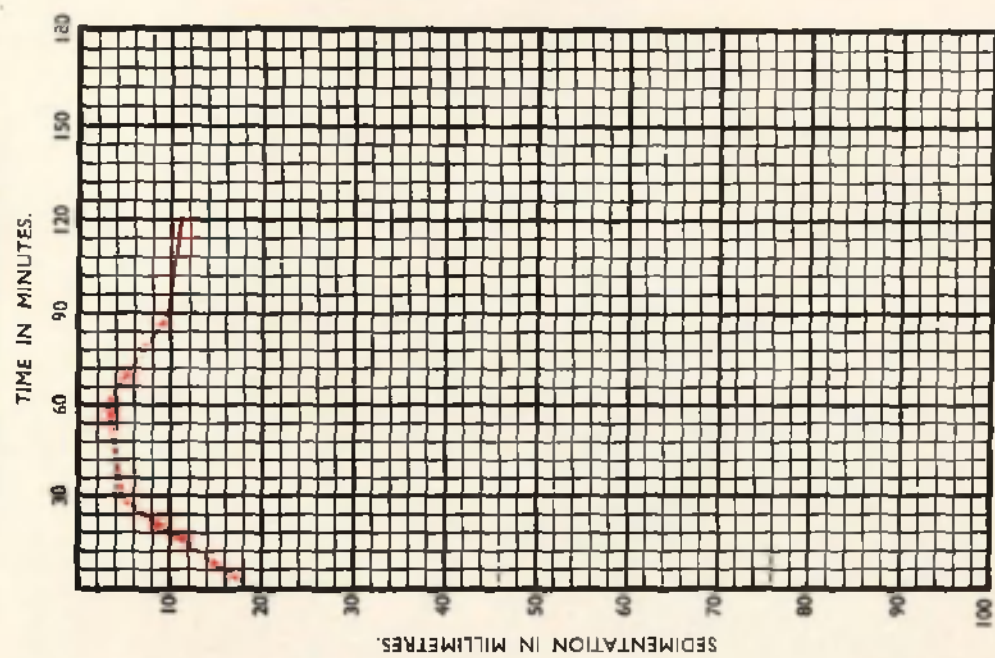


FIG 10.

No. 11 Case C.M.

Age 49. (F)

Three years ago patient suffered from severe pruritis vulvae. Diabetes diagnosed. At one time very stout, she has lost a great deal of weight. For past six weeks before attendance at Clinic she has been receiving 50 units of Insulin in the morning.

One brother and one sister suffer from Diabetes.

General cond.

Fairly well nourished. Heart and lungs normal. Edentulous. Varicose veins both legs. Weight 128 lbs.

Blood

F.B.S. 0.16 %. Sed. R. 15mm. W.R. -ve.

Urine

Sp. Gr. 1030. Sugar present 2%. Acetone present.

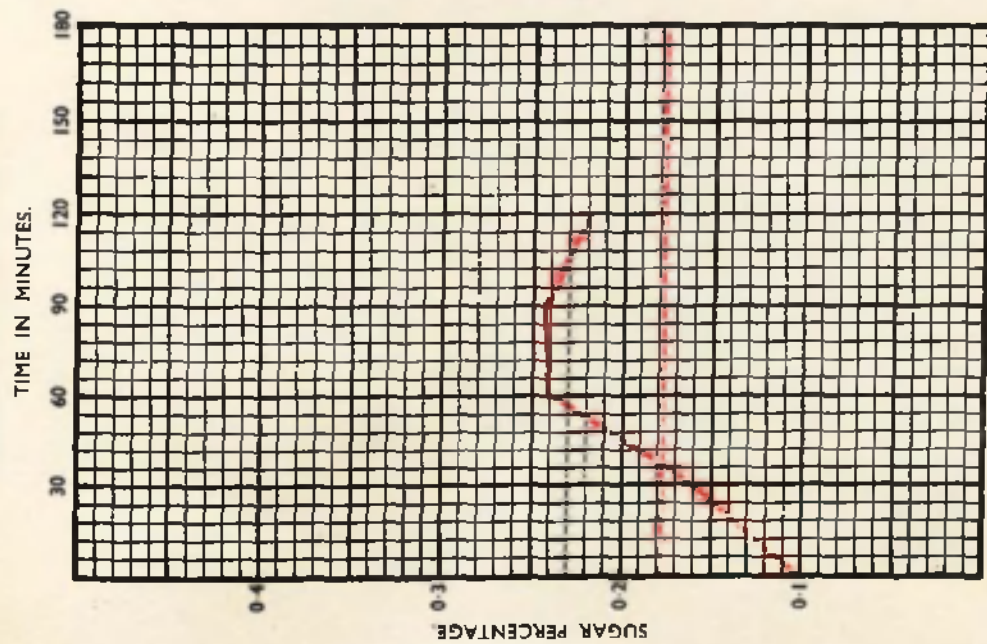
Treatment

10 line diet.
Insulin, 25 units m., 20 units n.,

Progress

Seven months later, very satisfactory. Weight now 145 lbs. (a gain of 17 lbs.) and keeps sugar free on 10 units m., and 10 units n., of Insulin.

GLUCOSE TOLERANCE CURVE.



BLOOD SEDIMENTATION RATE.

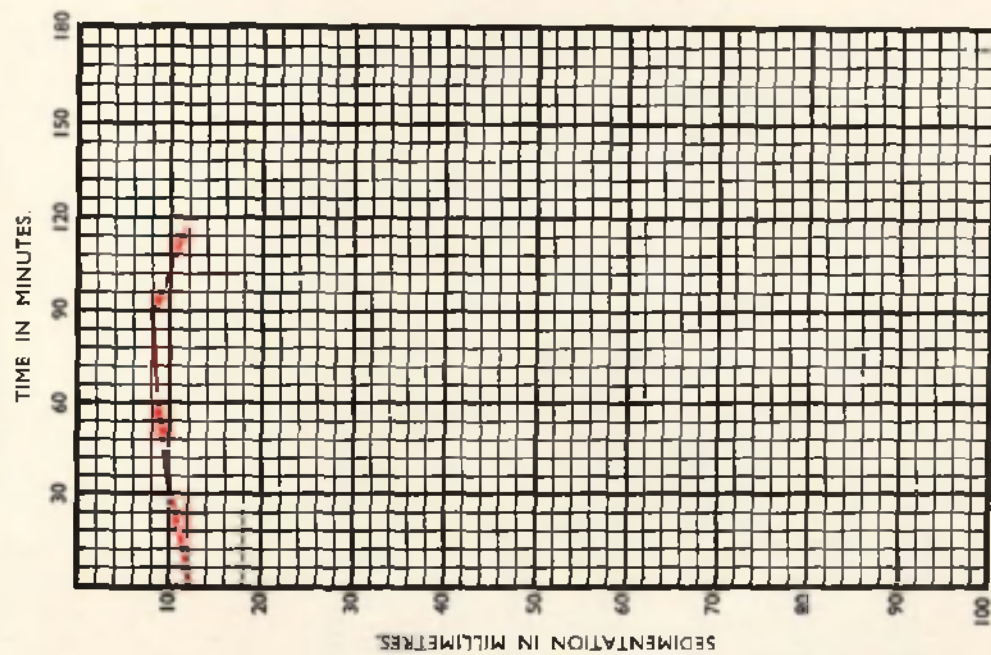


FIG 11.

No. 12 Case A.C.

Age 48. (F)

Diabetes first diagnosed five years ago. Since then she has been receiving 15 units of Insulin daily. No family history of diabetes.

General Cond.

Fairly good. Mild arterio-sclerosis, subject to headache. Weight 157 lbs.

Blood

F.B.S. 0.16%. Sed. R. 15 W.R. -ve.

Urine

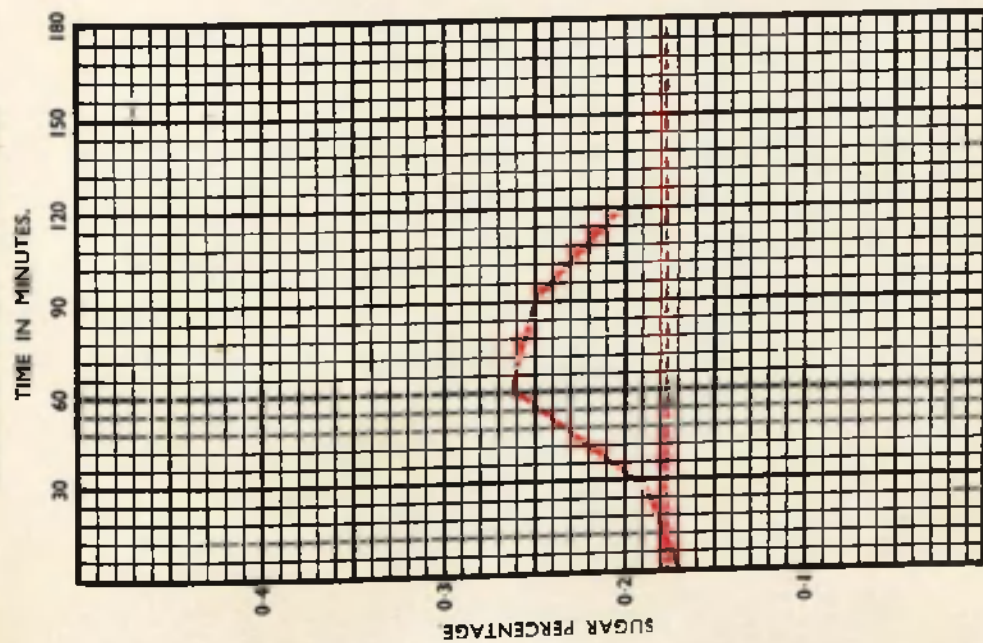
Sp. Gr. 1030. Sugar present 1%. No acetone.

Treatment

Mild diabetic who remains well, and sugar free, on 5 units of Insulin m., and 5 units n.. Insulinate 10 units daily Three months later put on Protamine

GROUP N.

GLUCOSE TOLERANCE CURVE.



BLOOD SEDIMENTATION RATE.

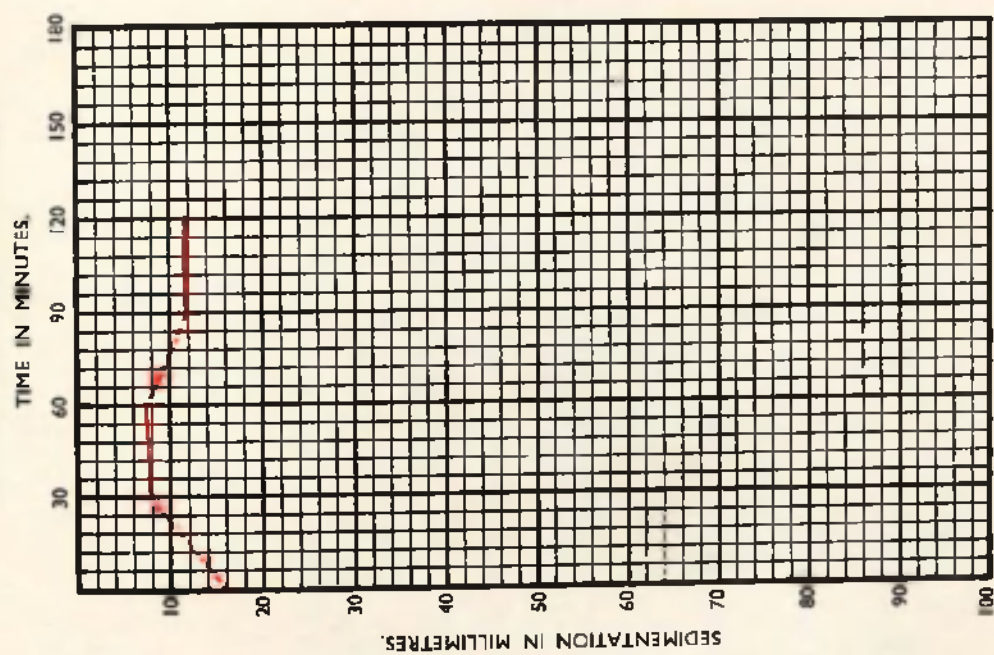


FIG 12.

No. 14 Case A.H.

Age 46. (M)

Typical symptoms of diabetes for many years, not diagnosed until patient was admitted to hospital, 6 years ago, in coma. No family history.

General cond.

Fairly good. Subject to headaches and sickness.
B.P. 130/100. Weight 149 lbs.

Blood

F.B.S. 0.31%. Sed. R. 12mm. W.R. -ve.

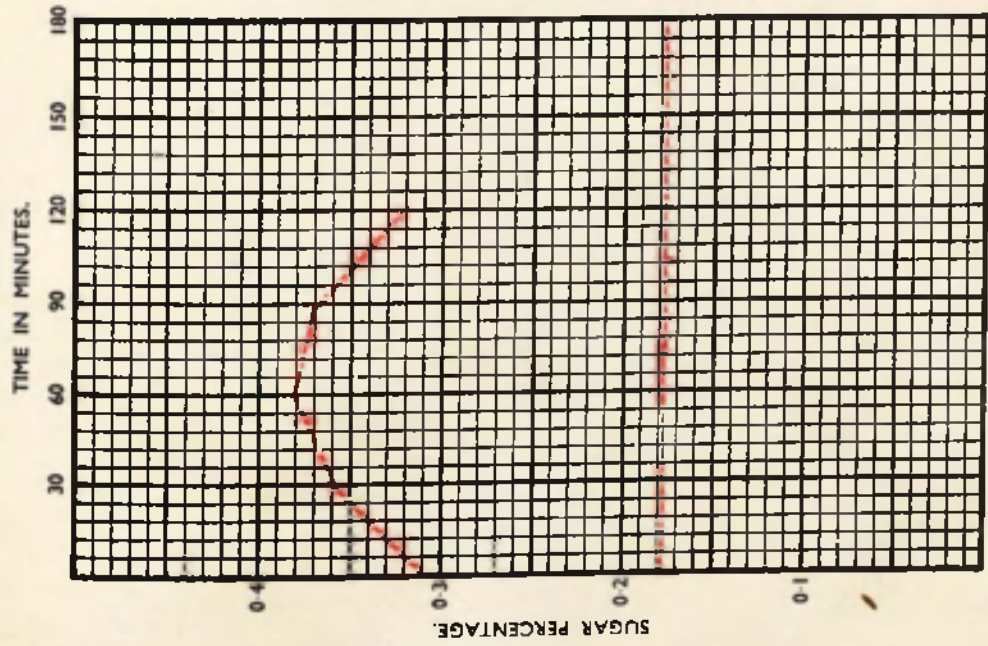
Urine

Sp. Gr. 1032. Sugar 3 %. Acetone present.

Treatment

Subject to severe hypo' attacks, so placed on Insulin 15 units t.d.s. Even with this dosage he still has occasional hypo' attacks, but his general condition is improved.

GLUCOSE TOLERANCE CURVE.



BLOOD SEDIMENTATION RATE.

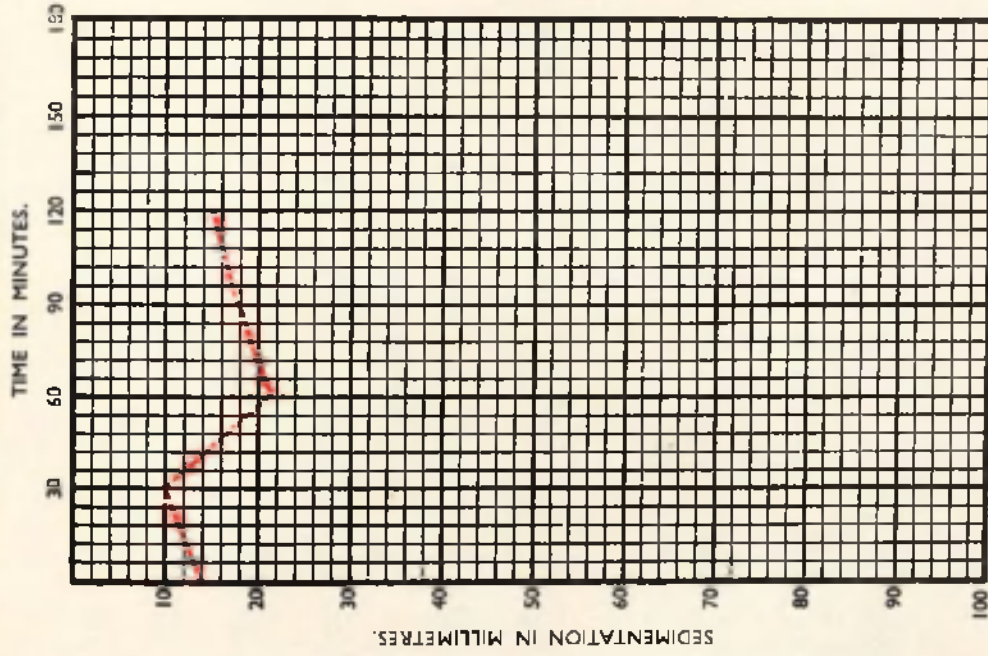


FIG 14

X

No. 15 Case B.S.

Age 67. (F)

Four years history of diabetes. First symptoms, thirst, pruritis, and loss of weight.

No family history of diabetes.

General cond. Rather obese; slight arterio-sclerosis. Nil else of note. Weight 177 lbs.

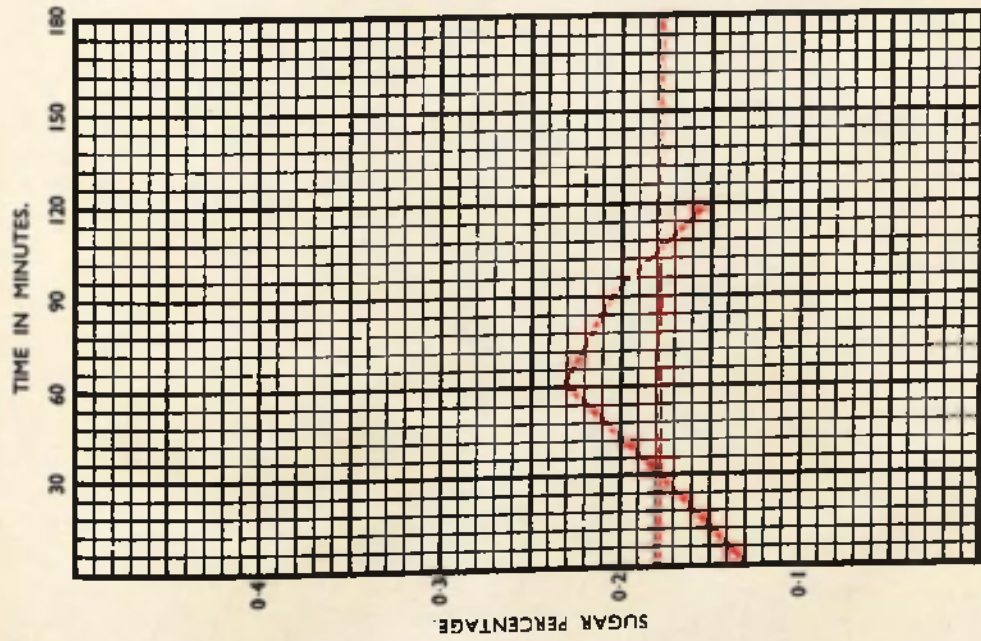
Blood F.B.S. 0.14 %. Sed. R. 16mm. W.R. -ve.

Urine Sp. Gr. 1030 Sugar 0.1 %. No acetone.

Treatment Low carbohydrate diet and Insulin, units 10m., and 5 nocte.

Progress A mild type of diabetic, now feels well and is sugar free on 5 units of Insulin b.d.

GLUCOSE TOLERANCE CURVE.



BLOOD SEDIMENTATION RATE.

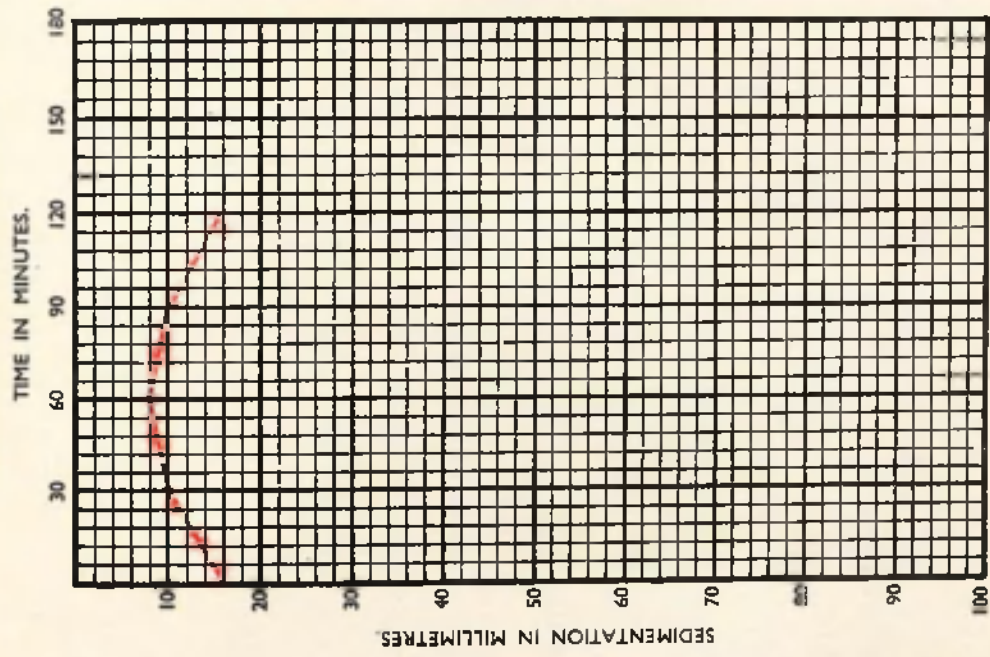


FIG 15.

N.

No. 16 Case J. G.

Age 56. (F)

Two years ago patient weighed 14 stone. Then commenced to lose weight rapidly. Also suffered from severe pruritis. Diabetes diagnosed six months ago, since when she had been on diet and Insulin, 15 units b.d.

No Diabetes in family. Weight 144 lbs.

General cond. Severe pruritis, also extensive Dermatitis Herpetiformis. Some arterio-sclerosis. B.P. 125/90.

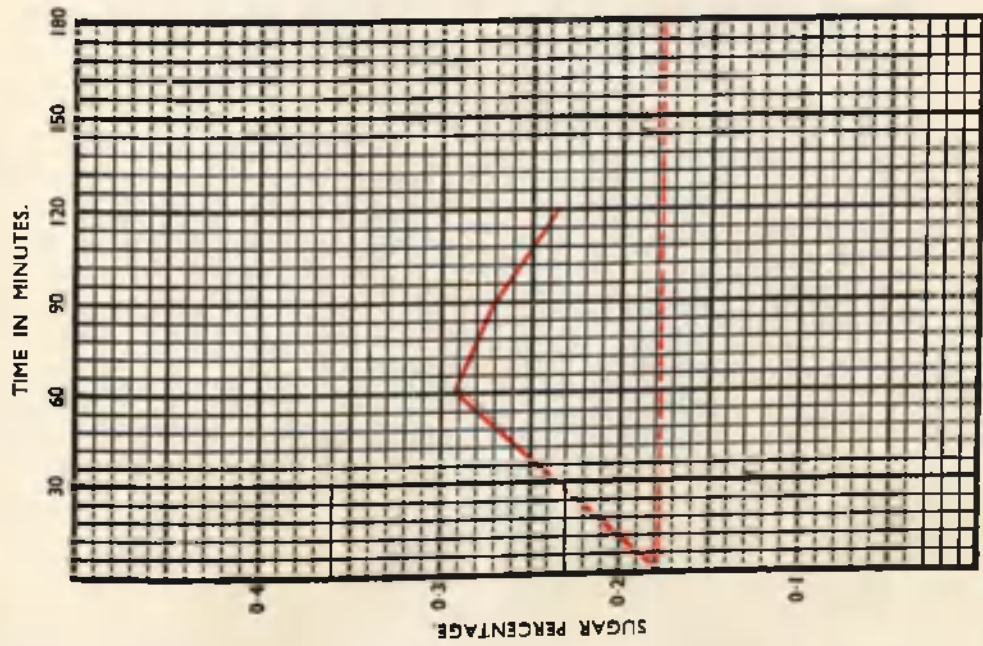
Blood F.B.S. 0.14% Sed. R. 20mm W.R. -ve.

Urine Sp. Gr. 1020. Trace of sugar. No acetone.

Treatment 10 line diet.
Insulin 15 units n. & 10 units n., this dosage produced Hypo. Sym.

Progress Three months later feels much improved, urine sugar free and weight increasing. Insulin reduced to 10 and 5 units. Then P.I. 10 units b.d.

GLUCOSE TOLERANCE CURVE.



BLOOD SEDIMENTATION RATE.

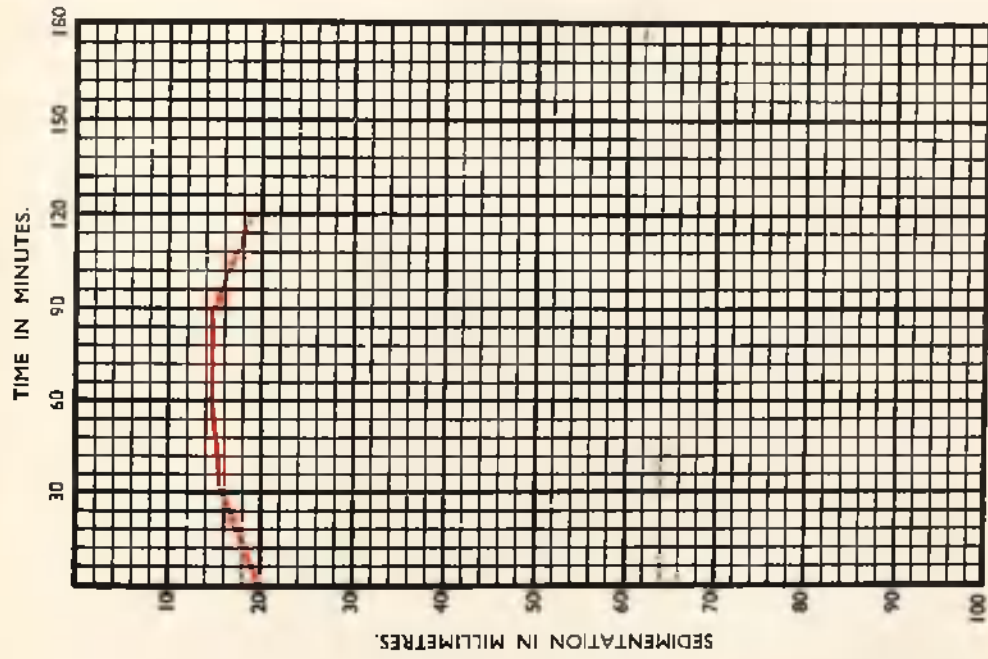


FIG 16.

N.

No. 17 Case F.A.S.

Age 64. (F)

Six years ago right leg amputated for diabetic gangrene.
Two years ago left foot " "
Has been receiving 30 units of Insulin b.d.
No known family history.

General cond.

A cripple owing to double amputations, rather stout.
Feels fairly well. Suffers from extensive Acne Rosacea.

Blood F.B.S. 0.18 %. Sed. R. 20mm. B.W. -ve.

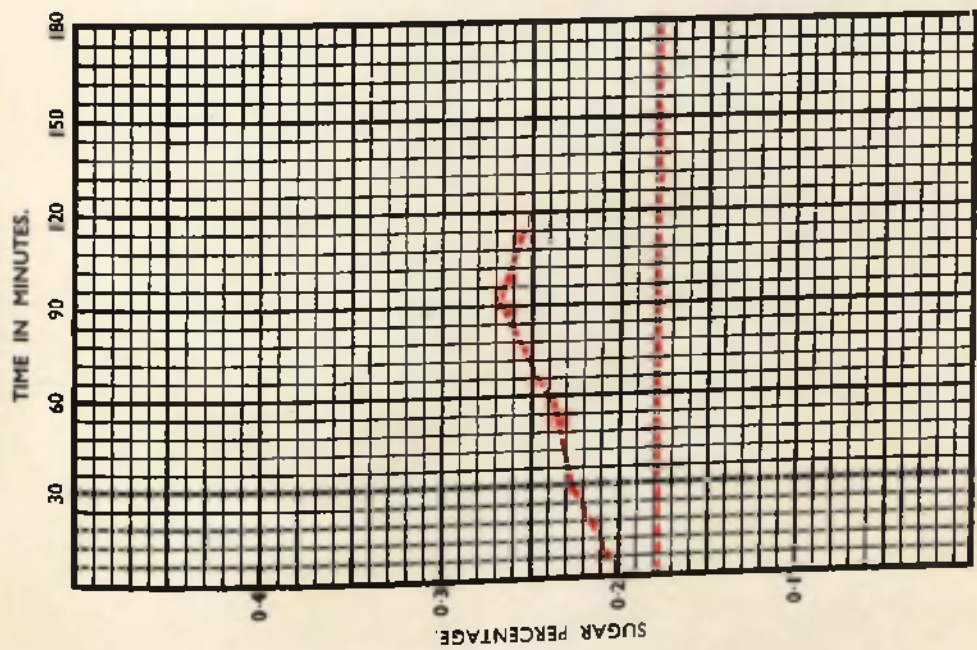
Urine Sp. Gr. 1024. Sugar present 1%. Acetone free.

Treatment Diet and Insulin continued as previously

Progress Has made satisfactory progress, Insulin increased to
35 units b.d., and carbohydrate ratio in diet raised.
Six months later urine sugar free.

GROUP X.

GLUCOSE TOLERANCE CURVE.



BLOOD SEDIMENTATION RATE.

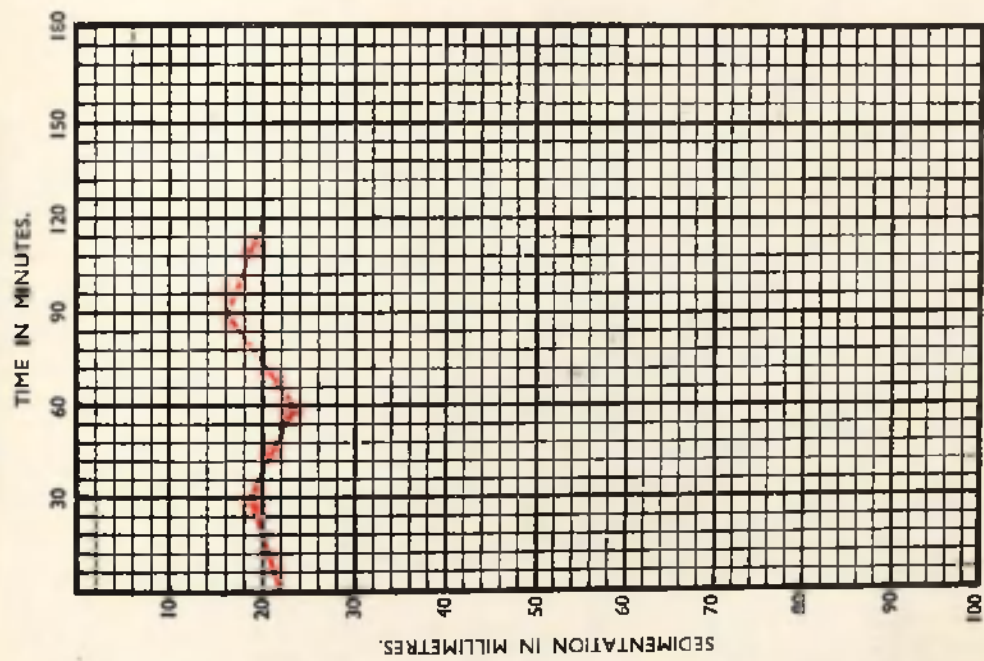


FIG 17.

X

No. 18 Case E.F.

Age 49. (F)

Two years history of Diabetes. Has been taking 70 units of Insulin. No family history of Diabetes. 14 pregnancies, 9 died of "convulsions".

General cond.

Fairly good. Edentulous. Lower abdominal pain, and some vaginal discharge. Weight 136 lbs.

Blood

F.B.S. 0.143 %. Sed. R. 20mm. W.R. -ve.

Urine

Sp. Gr. 1025. Trace of sugar. No acetone.

Treatment

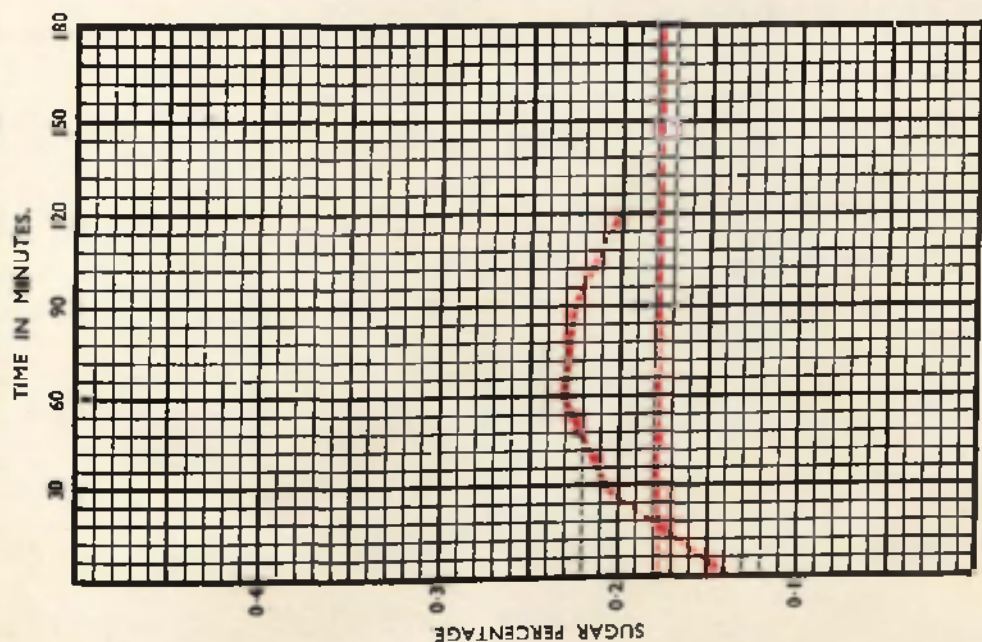
Placed on 10 line diet and Insulin 30 units b.d.

Progress

As a diabetic satisfactory. Developed some Hypo. Sym. so was advised to take Insulin three times daily, Total dose now reduced to 40 units which keeps her sugar free. But has had three severe uterine haemorrhages, and although advised to come into hospital for investigation has not yet done so. Has gained 26 lbs. in weight.

GROUP N.

GLUCOSE TOLERANCE CURVE



N.

BLOOD SEDIMENTATION RATE.

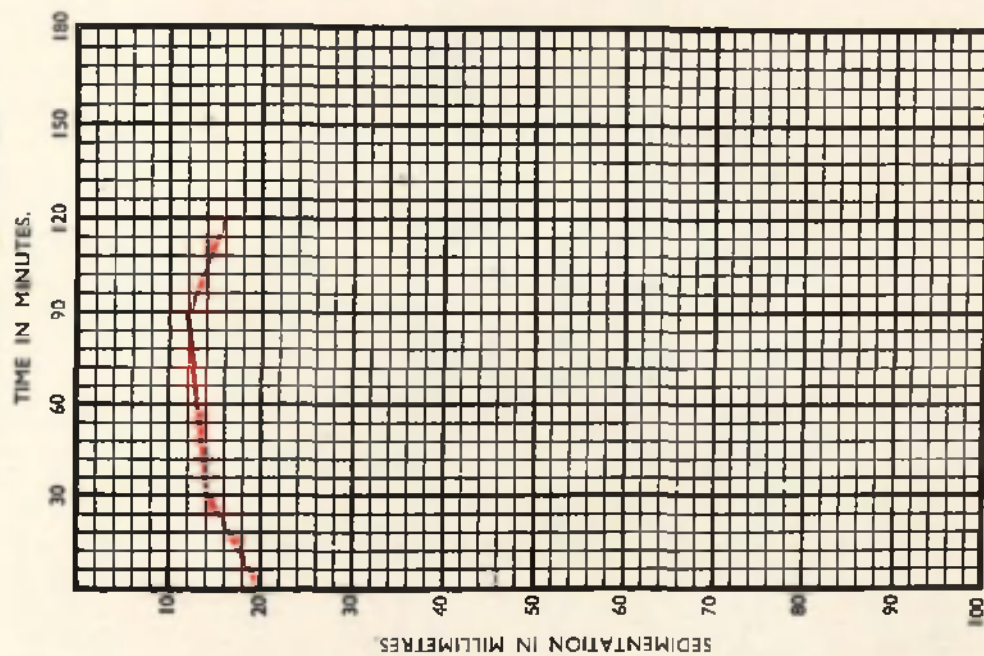


FIG 18.

No. 19. Case J.L.

Age 61. (M)

Ten years ago patient was admitted to hospital in diabetic coma.
Since then he has taken 40 units of insulin b.d..
No family history of diabetes.

General cond. Thin, feels ill, no energy. Suffers from chronic rheumatoid arthritis.

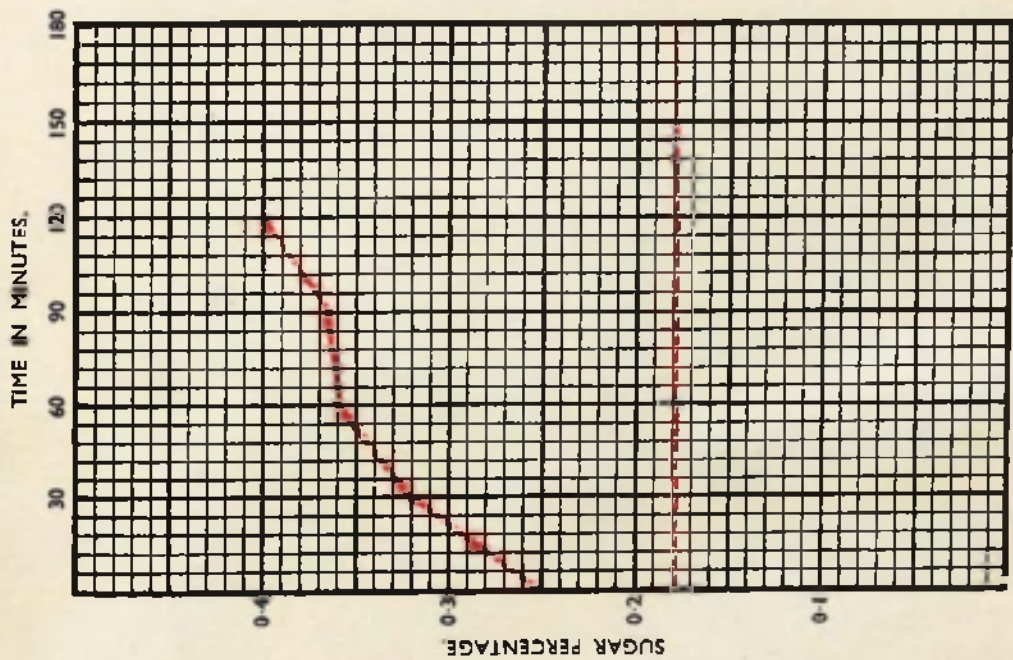
Blood. F.B.S. 0.25%. S.R. 20mm. W.R. -ve.

Urine. Sp. Gr. 1028. Sugar $\frac{3}{4}$ %. Acetone present.

Progress. Most unsatisfactory. He alternates between hyper-glycaemia and insulin reactions. Protamine Insulinate tried, but it does not control the diabetes.

Group X.

GLUCOSE TOLERANCE CURVE.



BLOOD SEDIMENTATION RATE.

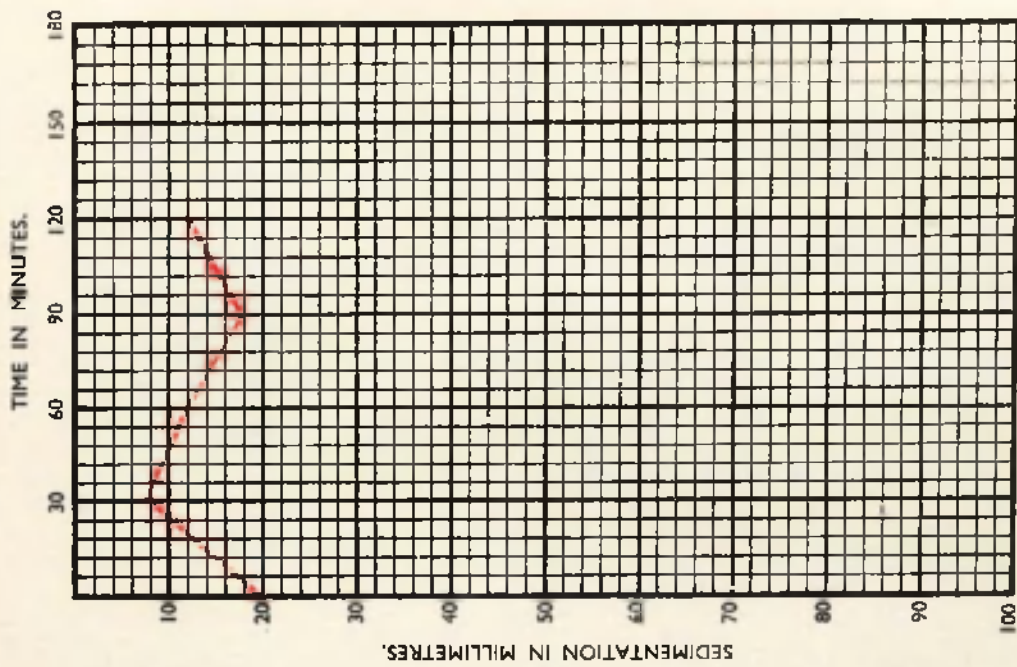


FIG 19.

No. 20 Case A.W.

Age 53. (F)

History of Diabetes for two years. Admitted for treatment for Ulcer of leg one week ago.

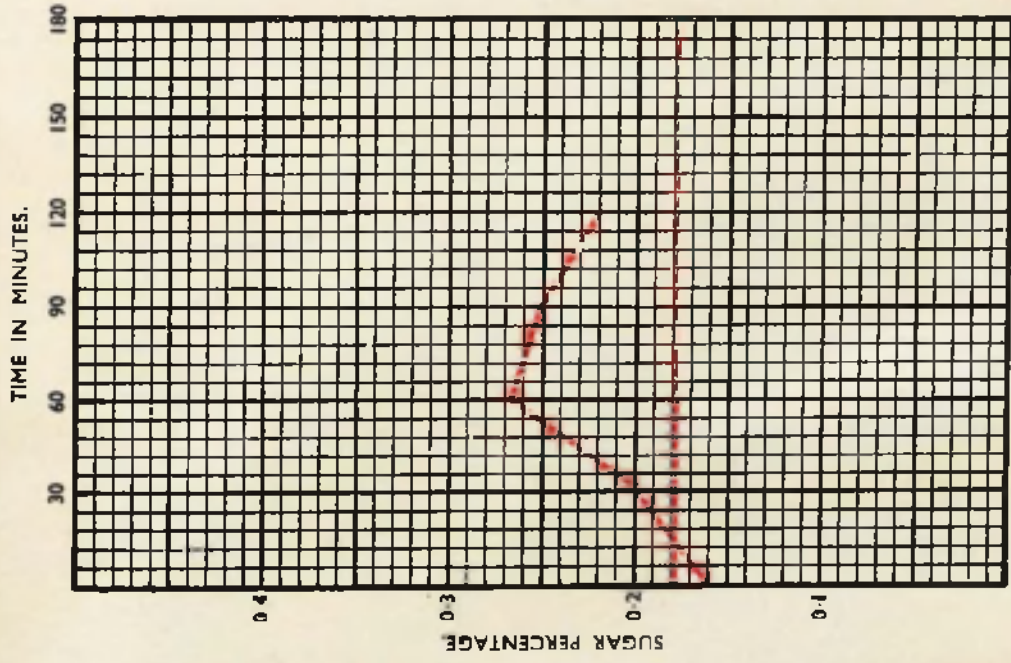
General cond. Fairly good. Arterio Sclerosis present, and Arterio Sclerotic ulceration of leg.

Blood P.B.S. 0.175 %. Sed. R. 20mm. W.R. -ve.

Urine Sp. Gr. 1030 Sugar 1 %. Trace of Acetone.

GROUP N.

GLUCOSE TOLERANCE CURVE.



N.

BLOOD SEDIMENTATION RATE.

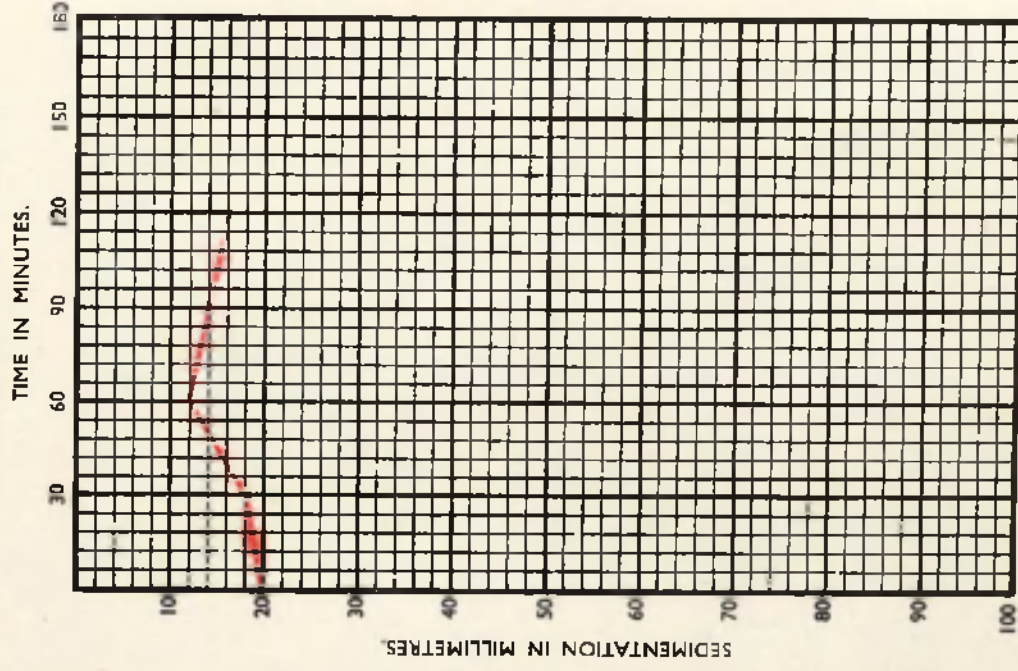


FIG 20.

No. 21. Case B. B.

Age 66. (F)

Gangrenous patch developed on foot six months ago. Has suffered from excessive thirst and polyuria for years. Unable to obtain any reliable history.

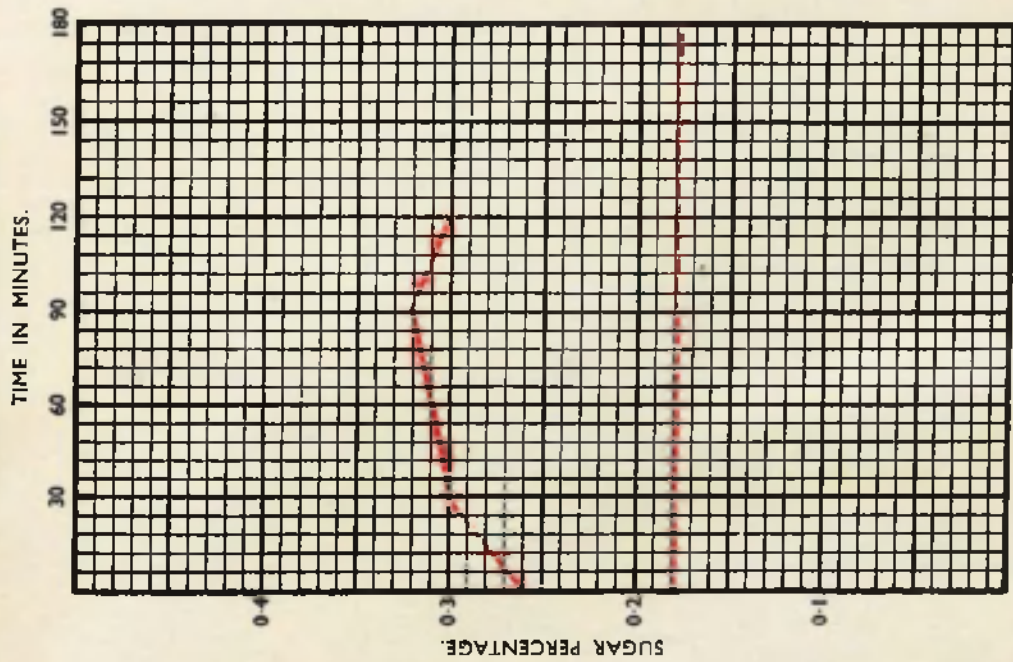
General cond. Poor. First attendance at clinic, to be examined later.

Blood F.B.S. 0.165 %. Sed. R. 20 mm. W.R. -ve.

Urine Sp. Gr. 1028. Sugar 3.0 %. Trace of acetone.

GROUP N.

GLUCOSE TOLERANCE CURVE.



N.

BLOOD SEDIMENTATION RATE.

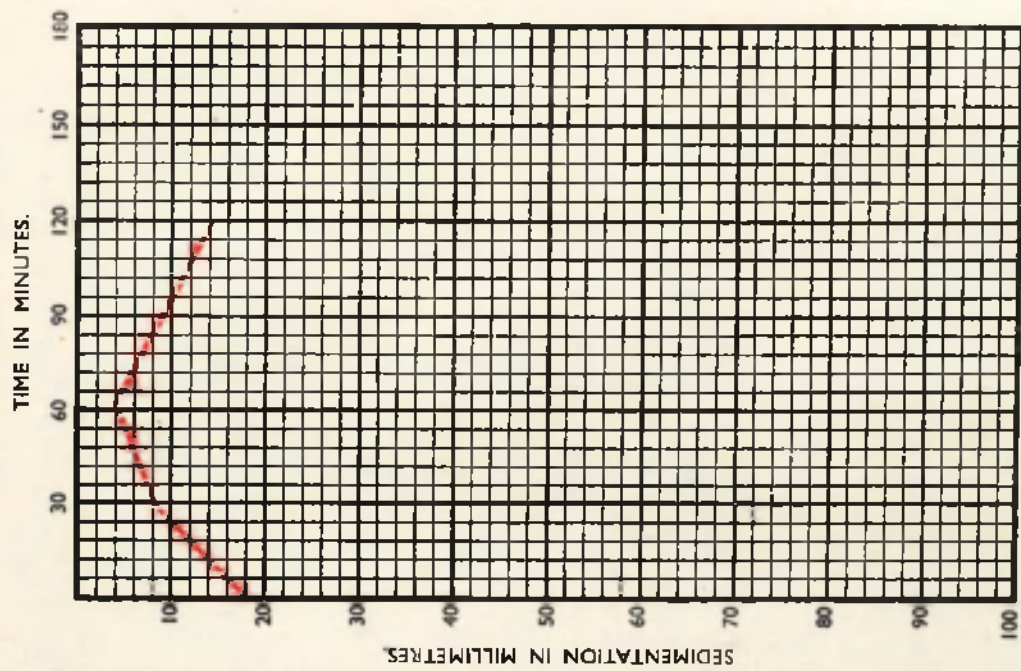


FIG 21.

Age 71. (F)

Three years ago patient was very stout, but for the past two years she has steadily lost weight. On account of severe pruritis, and headaches, she consulted her doctor who diagnosed Diabetes.

Known duration of Diabetes - 6 weeks.

General cond.

Fair, mild arterio-sclerosis, with slight arterio-sclerotic retinitis.
Rheumatoid arthritis of both knees. B.P. 155/120.
Weight 149 lbs.

Blood F.B.S. 0.18 % Sed. R. 23mm. W.R. -ve.

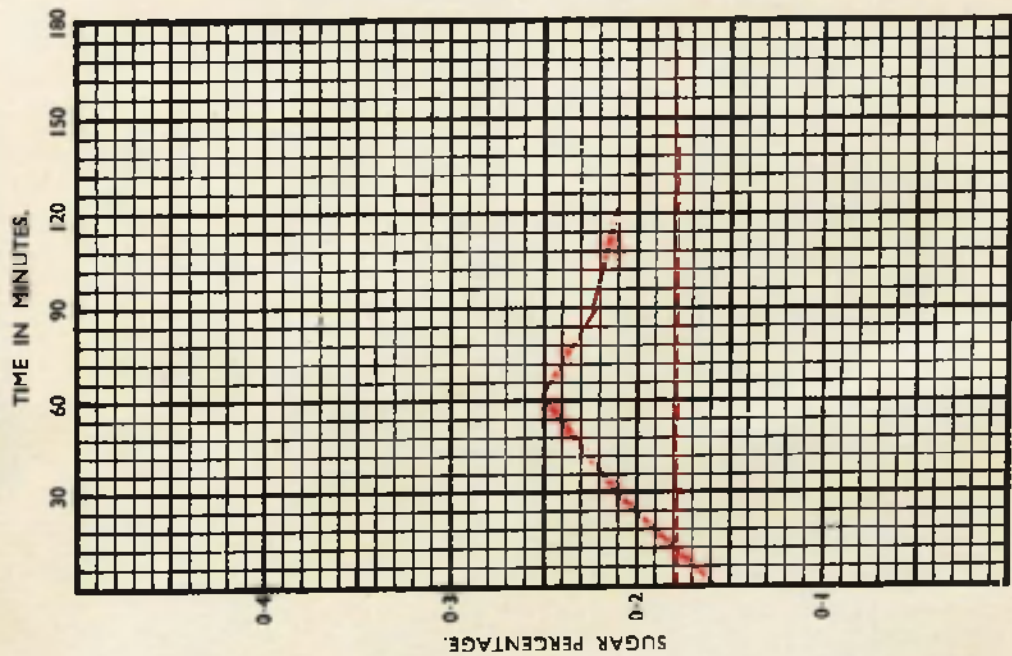
Urine Sp. Gr. 1020 Sugar 0.5 % No Acetone.

Treatment Placed on 10 line diet, with 10 units Insulin, morning, and 5 units, night.

Progress four months later

Fairly satisfactory, urinary sugar 1 %. Weight 169 lbs.
a gain of 20 lbs. Suffers from rheumatic pains.

GLUCOSE TOLERANCE CURVE.



BLOOD SEDIMENTATION RATE.

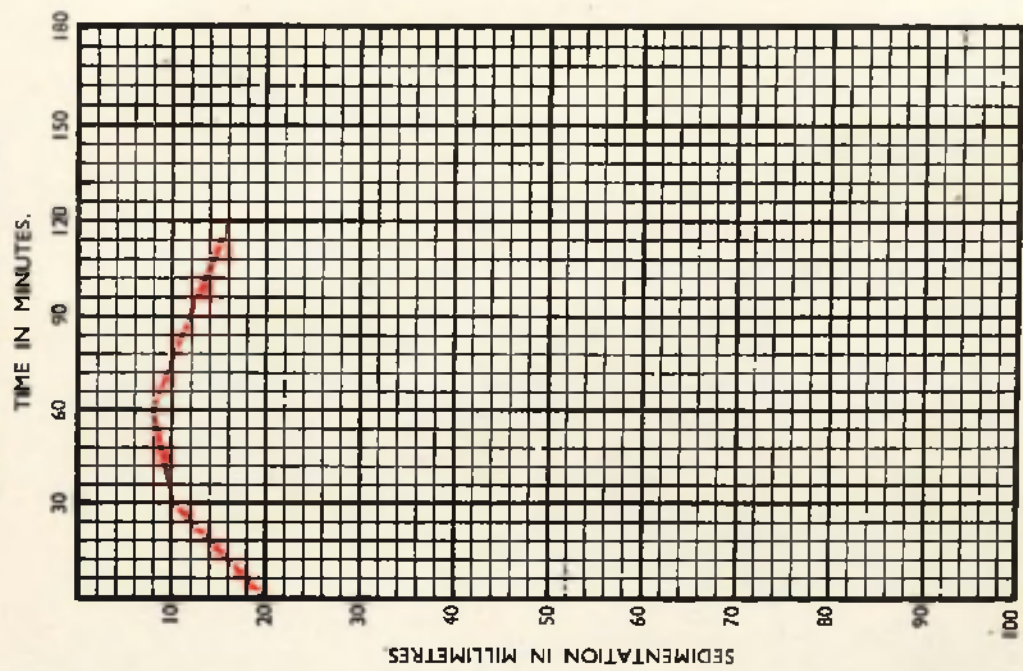


FIG 22.

No. 23 Case G.I.

Age 34. (M)

Admitted to hospital suffering from general debility. Diabetes diagnosed, one year ago. Since treated with diet and Insulin 10 units b.d. No known Diabetes in family.

General cond. Well nourished, but complains of headache and general weakness. Dental caries. Weight 143 lbs.

Blood F.B.S. 0.16 %. Sed. R. 20mm. W.R. -ve.

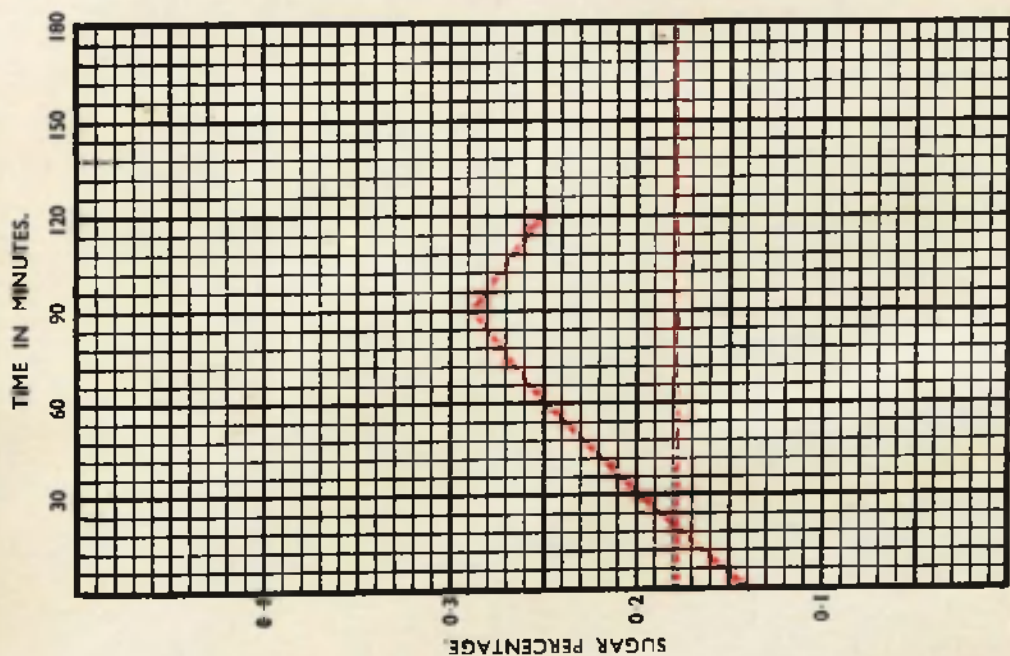
Urine Sp. Gr. 1035. Sugar 1%. Trace of acetone.

Treatment 10 line diet. Insulin 15 units b.d.

Progress Nine months later, keeps very well apart from slight Hypo.Sym. Weight increased, now 151 lbs. Carbohydrates in diet increased, Insulin 15 units b.d. Urine free from sugar and acetone.

GROUP N.

GLUCOSE TOLERANCE CURVE.



BLOOD SEDIMENTATION RATE.

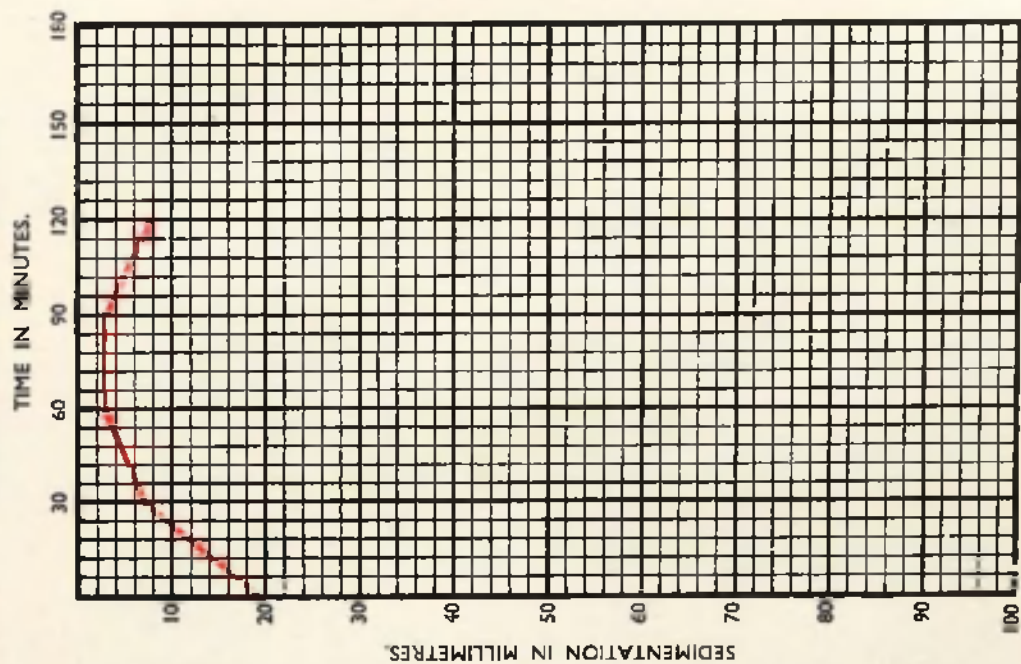


FIG 23.

No. 24. Case S.C.

Age 53. (F)

Diabetes diagnosed eight years ago. Seven years ago left arm amputated for gangrene of hand. Since then has endeavoured to follow diet chart and has received 60 units of Insulin daily. Four members of her family have had Diabetes. Always stout.

General cond. Very stout. Weight 234 lbs. Slight pressure sore on toe.

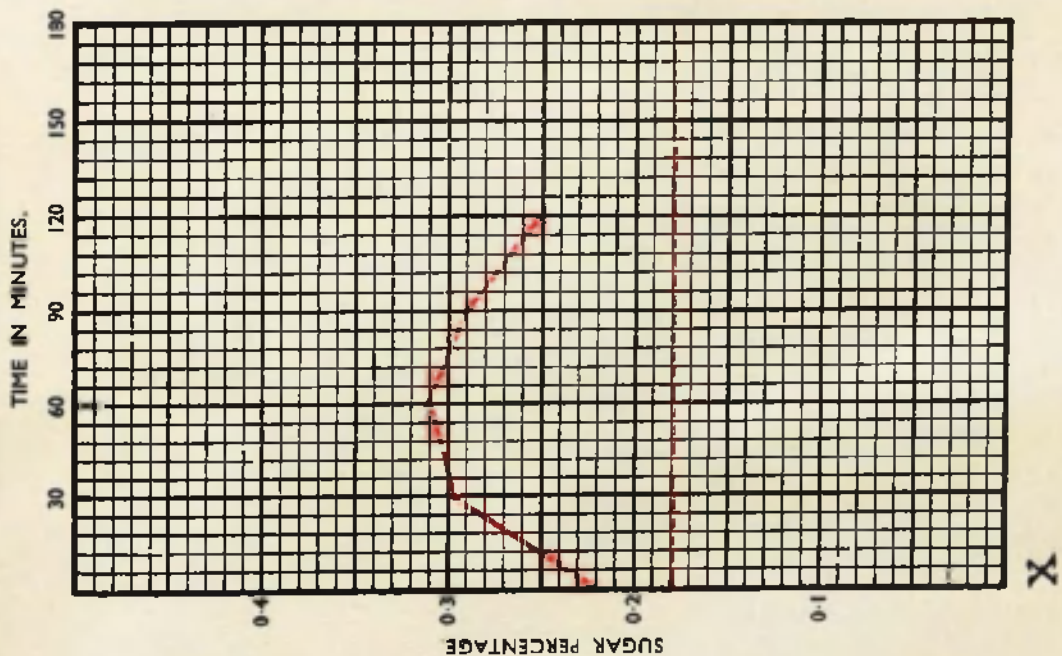
Blood P.B.S. 0.275 %. Sed. R. 20mm. W.R. -ve.

Urine Sp. Gr. 1034. Sugar present 3 %. Acetone present.

She is a most difficult patient, makes no endeavour to follow diet, and takes her Insulin at irregular intervals. She has made no progress since her first attendance six months ago, and although gangrene of the foot is imminent she refuses admission to hospital.

GROUP X.

GLUCOSE TOLERANCE CURVE.



BLOOD SEDIMENTATION RATE.

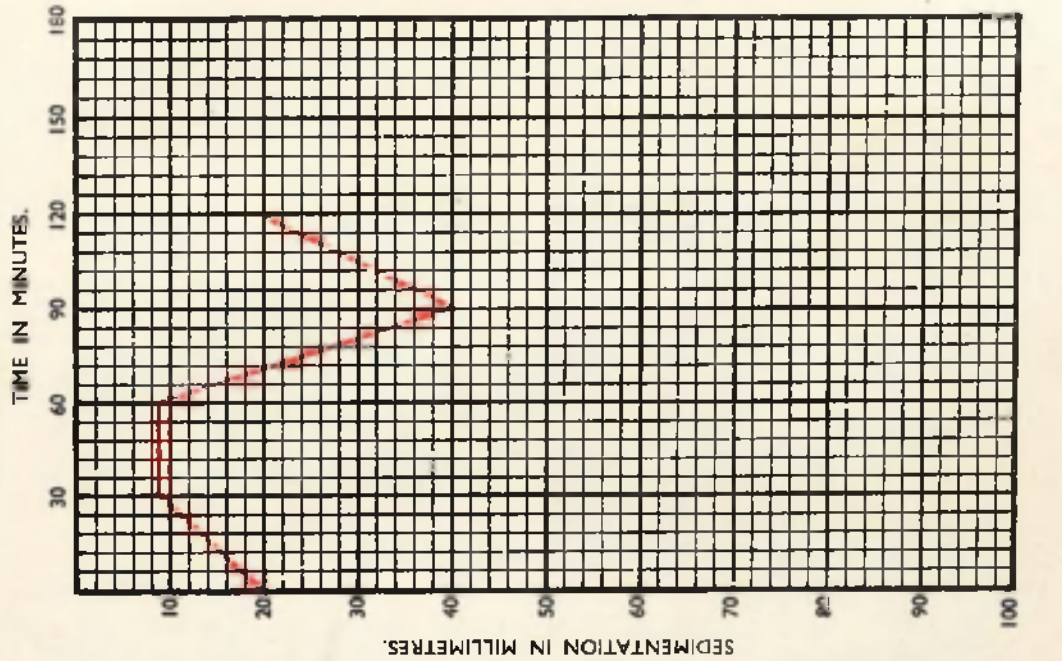


FIG 24.

No. 25 Case J. B.

Age 52. (F)

One year's history of Diabetes; first symptoms - thirst and polyuria, loss of weight and later severe lenteric diarrhoea. No known family history.

General cond. Not good, Obese. Rheumatic nodules on neck, advanced arterio-sclerosis for age. B.P. 190/90
Weight 183 lbs.

Blood F.B.S. 0.156 %. Sed. R. 21 mm. B.W. -ve.

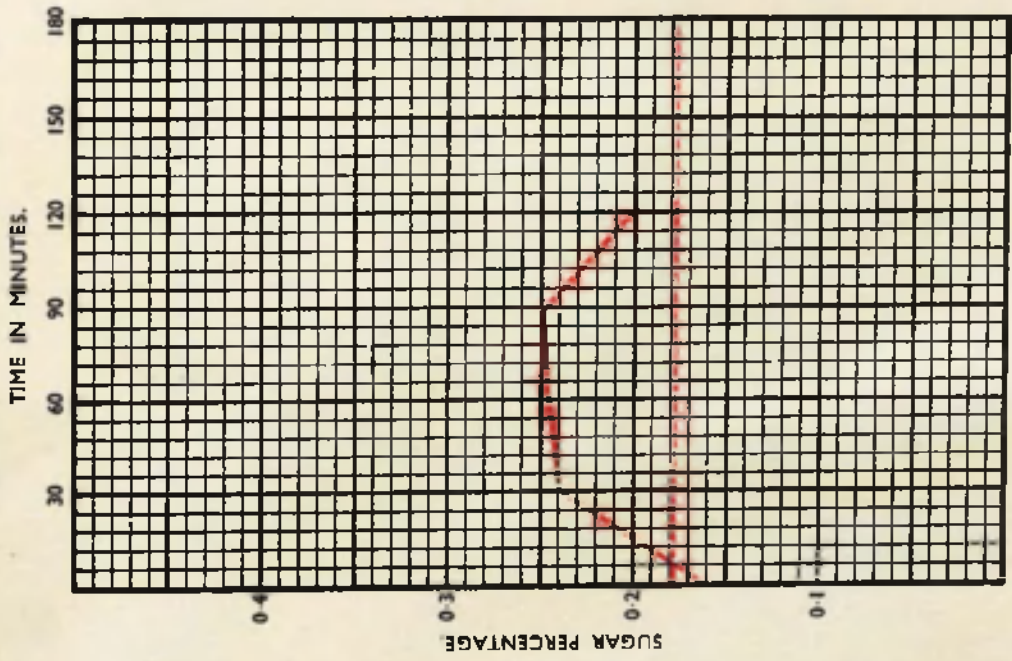
Urine Sp. Gr. 1028. Trace of sugar. No acetone.

Treatment Placed on restricted 10 line diet, proportion of fats reduced. Insulin 5 units b.d.

Progress Six months later feels much improved. Urine sugar free. Now weighs 176 lbs.

GROUP N.

GLUCOSE TOLERANCE CURVE.



BLOOD SEDIMENTATION RATE.

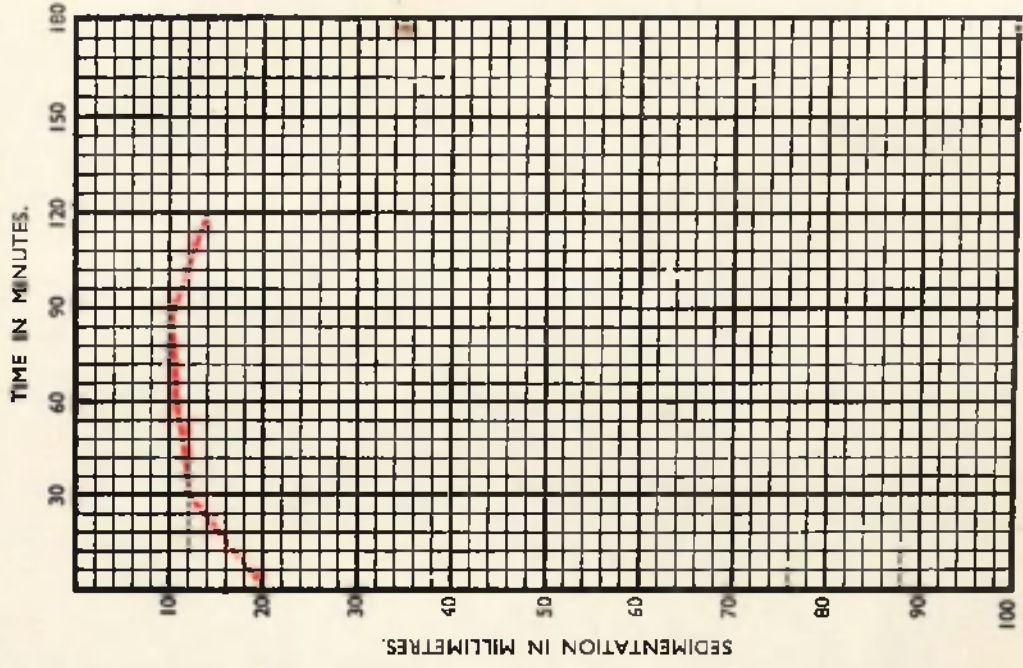


FIG 25.

N.

No. 26 Case W. B.

Age 56. (F)

Three year's history of Diabetes. First symptom was Pruritis. Has been on diet and Insulin 15 units b.d. for past year. No known family history. Weight 153 lbs.

General cond. Poor. Chronic bronchitis and rheumatism. Much dental sepsis. Weight 153 lbs.

Blood F.B.S. 0.215. Sed. R. 21mm. W.R. -ve.
Count :- R.B.C. 4,720,000. W.B.C. 8,500. Haem 80%.

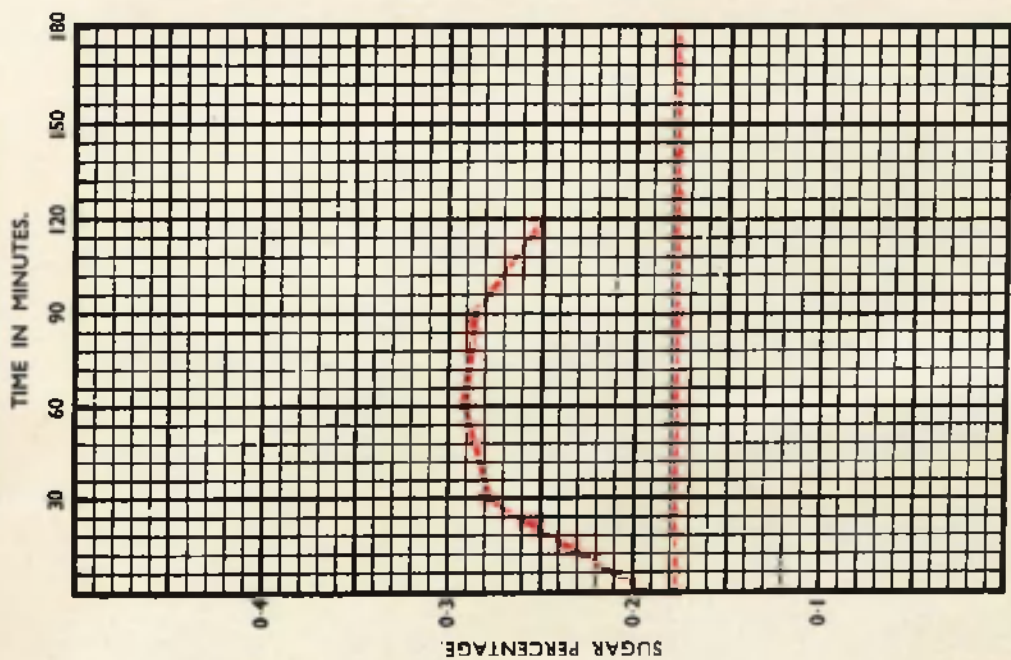
Urine Sp. Gr. 1050. Sugar present 2-3% Acetone present.

Treatment 10 line diet and Insulin 20 and 15 units. Advised to have teeth extracted.

Progress Unsatisfactory. Refuses dental treatment. Has gained weight and now is receiving Insulin, 15 units b.d. Three months later, F.B.S. 0.185. Sed. R. 20 mm.

GROUP X.

GLUCOSE TOLERANCE CURVE.



BLOOD SEDIMENTATION RATE.

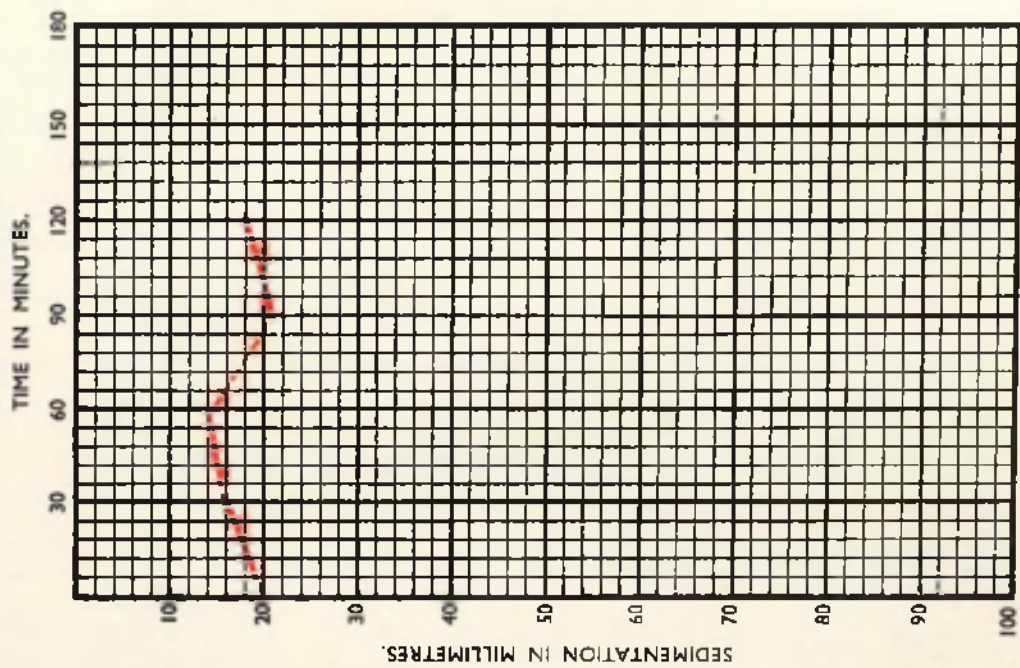


FIG 26.

X.

No. 27 Case M.L.

Age 63. (F)

Two year's history of Diabetes. On so called "low carbohydrate" diet, and 15 units of insulin b.d. Used to weight 12 stone.

General cond. Poor. Suffers from frequent attacks of sickness and diarrhoea. Underwent operation for gall stones many years ago, does not think that gall bladder was removed. Pyorrhoea. Weight 173 lbs.

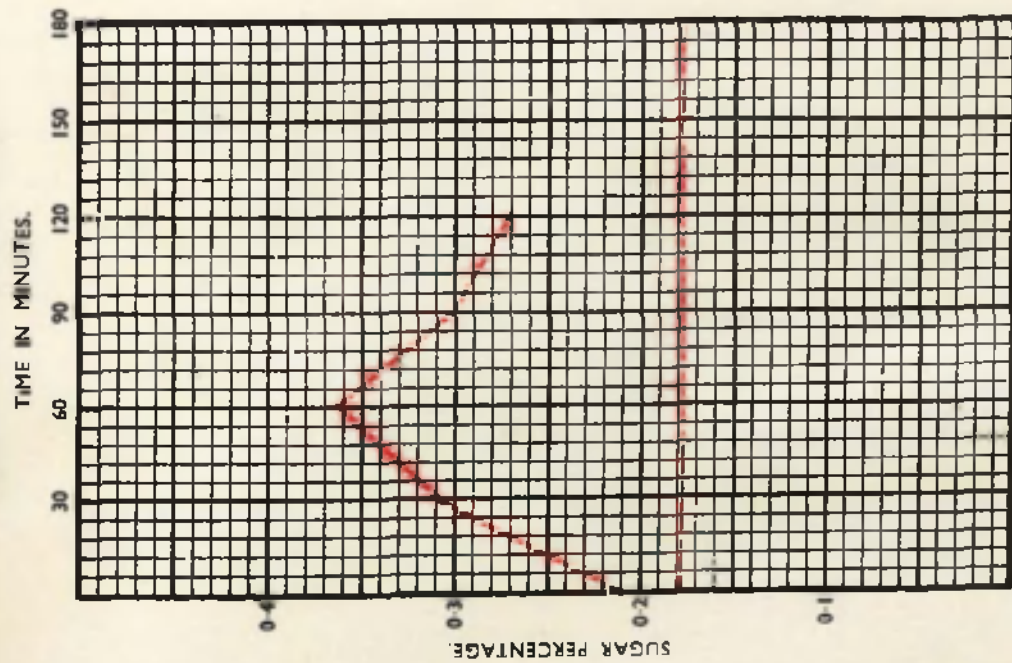
Blood F.B.S. 0.215%. Sed. R. 22 mm. W.R. -ve.

Urine Sp. Gr. 1028. Sugar, 2% present. Trace of acetone.

Treatment Placed on a line diet, and Insulin 20 units b.d.
Restricted fats.

Progress After eight months there is a marked improvement, urine is sugar and acetone free. Sickness less frequent, now receiving Insulin 15 units m., and 10 units n.,

GLUCOSE TOLERANCE CURVE:



BLOOD SEDIMENTATION RATE:

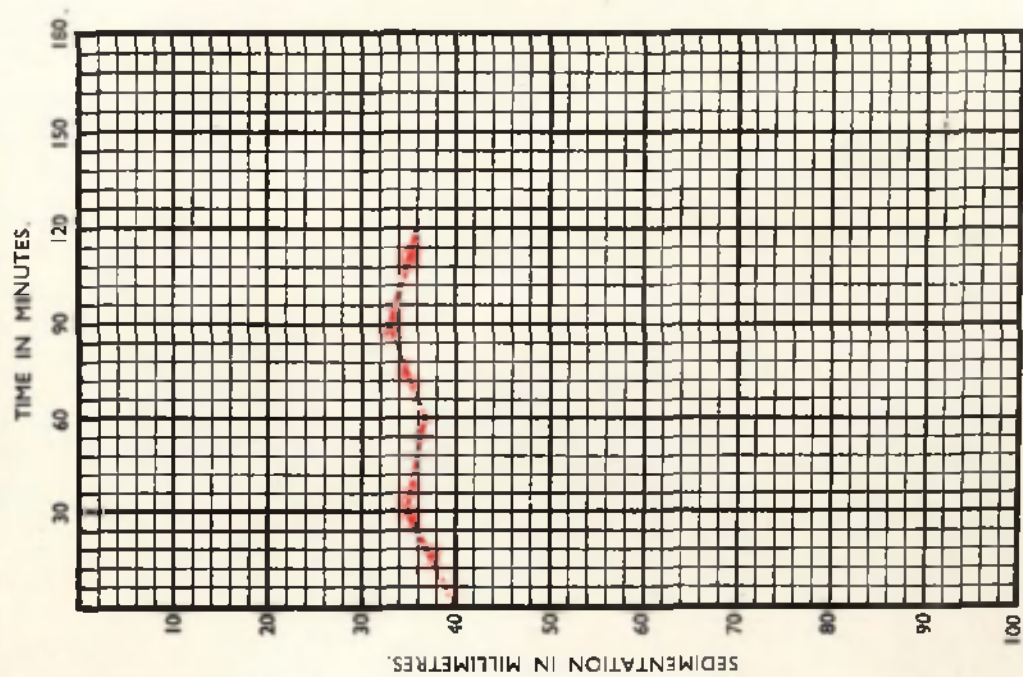


FIG 27.

N.

No. 28 Case A.B.

Age 65. (F)

Admitted to hospital 10 years ago for operation. cholecystectomy
Diabetes found. Has been on diet since. No family history.

General cond.

Poor. Rheumatism, pruritis and arterio-sclerosis.
B.P. Weight 244 lbs.

Blood

F.B.S. 0.24 %. Sed. R. 24mm. W.R. -ve.

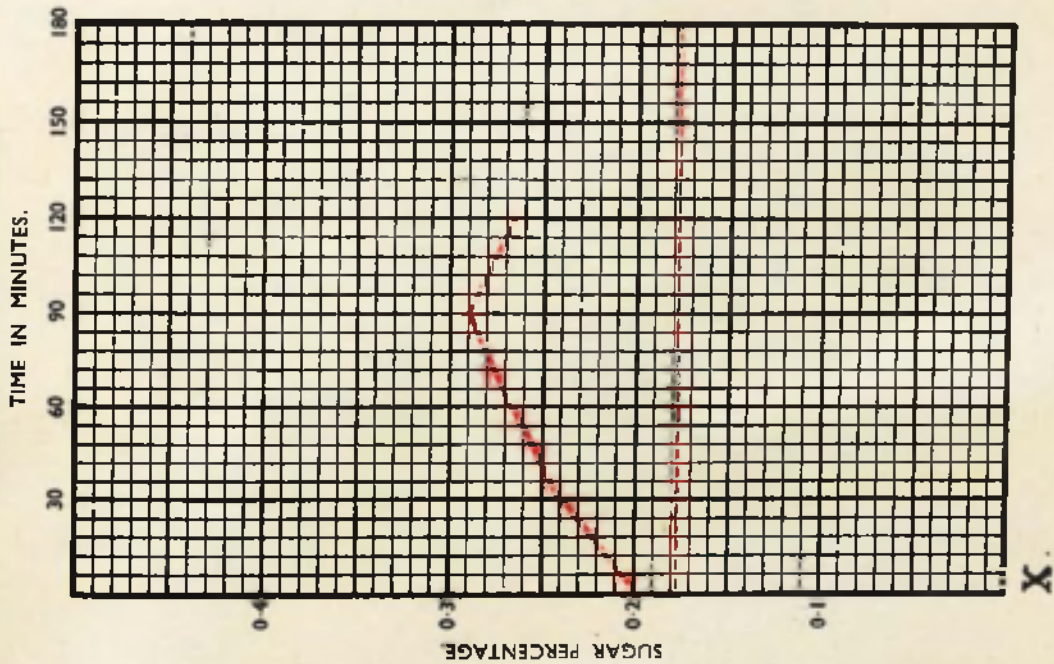
Urine

Sp. Gr. 1040. Sugar 3% present. No acetone.

Treatment

5 units of Insulin b.d. and 10 line diet,

GLUCOSE TOLERANCE CURVE.



BLOOD SEDIMENTATION RATE.

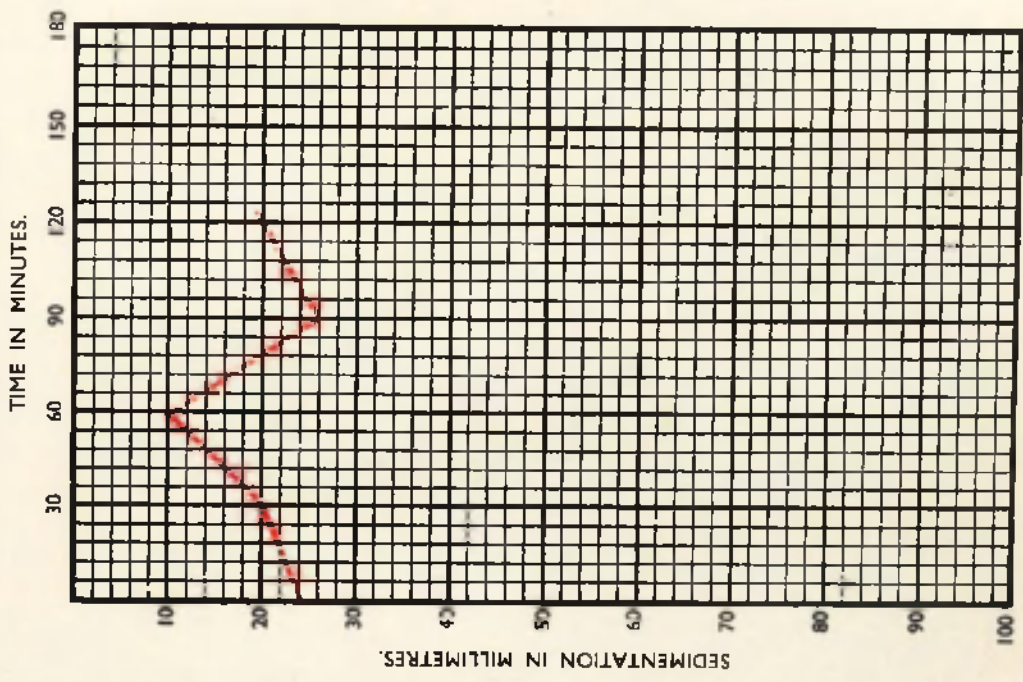


FIG 28.

No. 29 Case E.S.

Age 21. (F)

Four years history of Diabetes. First symptoms were thirst, polyuria and pruritis. Was not placed on strict diet but has been receiving 30 units of Insulin daily. No history of Diabetes in family.

General cond. Rather thin. Septic gingivitis. Weight 122 lbs.

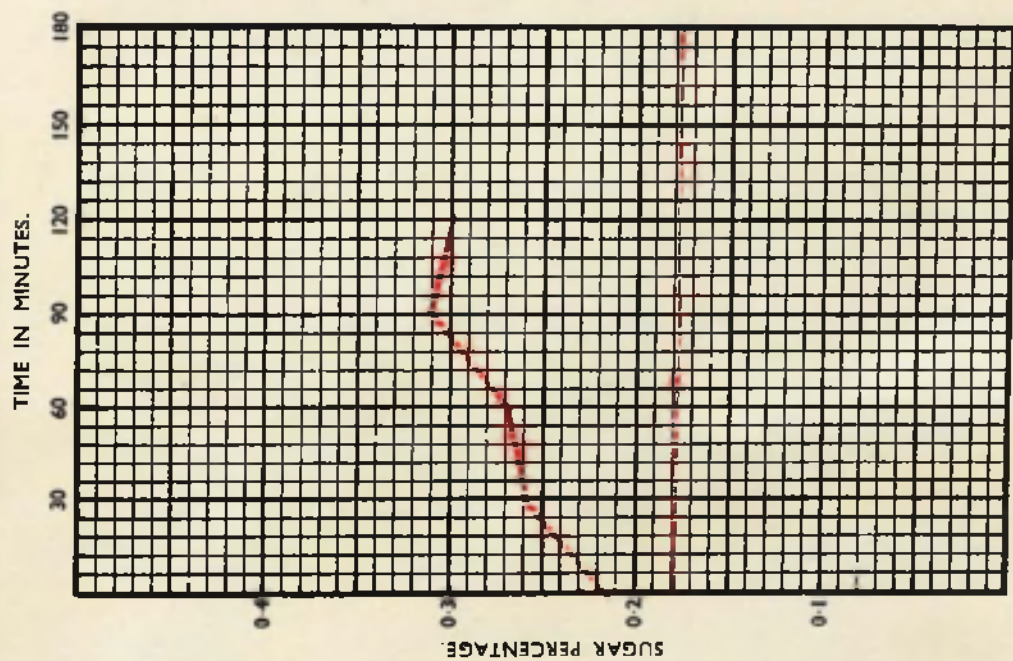
Blood F.B.S. 0.25 %. Sed. R. 24mm. W.R. -ve.

Urine Sp. Gr. 1036. Sugar 4% present. Large amount of acetone.

Progress Ten months later, she looks and feels better. Gingivitis cured. Sed. R. now 11mm. Weight 130 lbs.

GROUP N.

GLUCOSE TOLERANCE CURVE.



BLOOD SEDIMENTATION RATE.

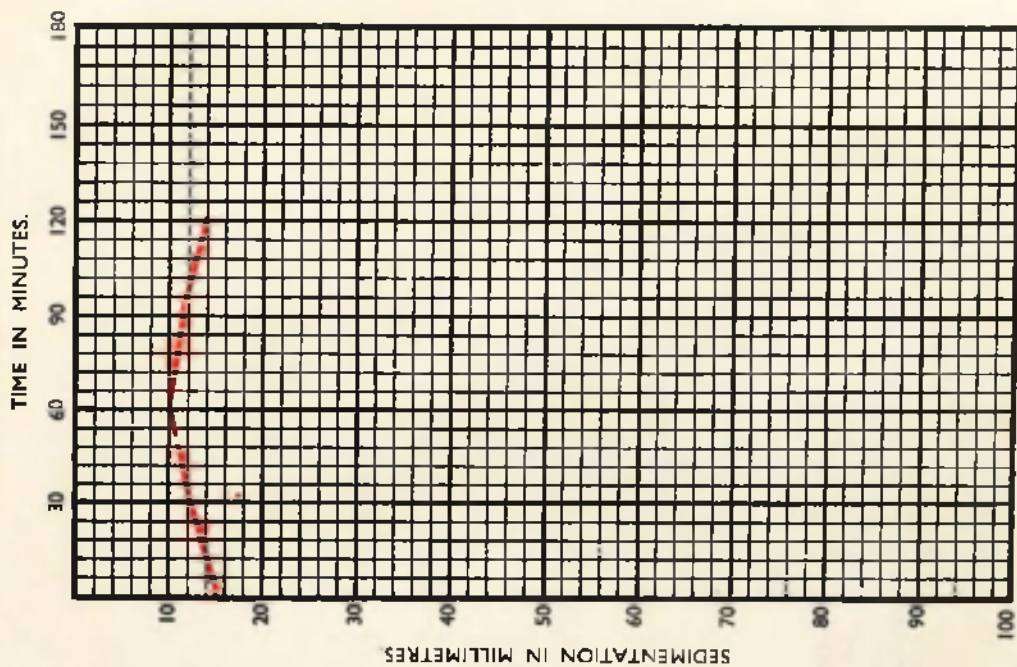


FIG 29.

N.

No. 30 Case M.R.

Age 58. (M)

Eight months ago consulted doctor on account of failing eyesight. Cataract found, and subsequently diabetes diagnosed, family history -ve.

General cond.

Chronic rheumatism, mild bronchitis, and a very slight degree of exophthalmos.
Weight 180 lbs.

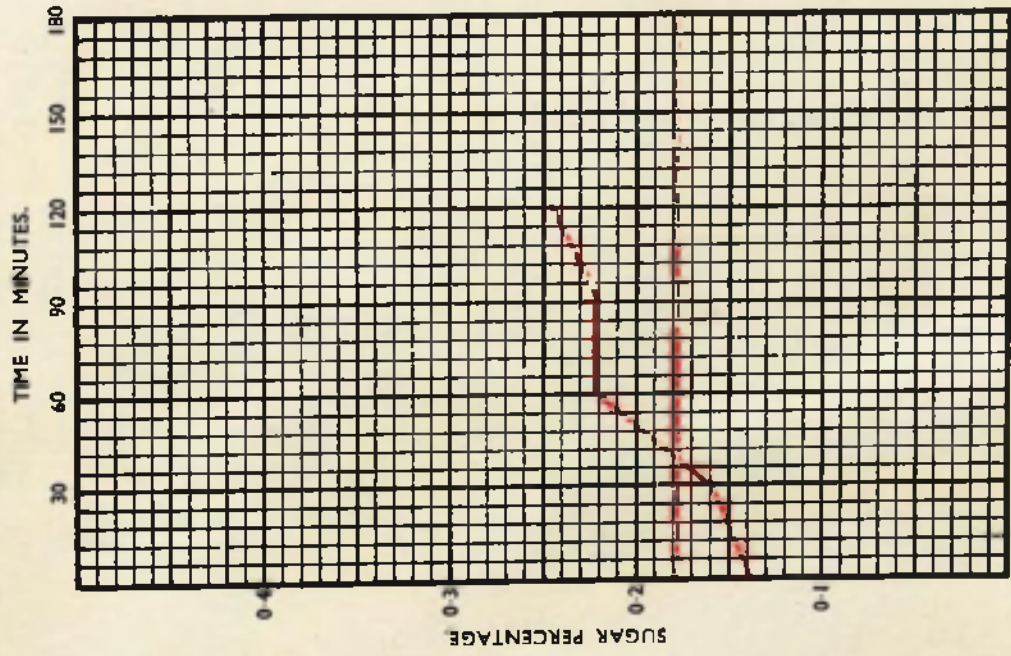
Blood F.B.S. 0.145%. Sed. R. 24mm. W.R. -ve.

Urine Sp. Gr. 1026. Sugar 1 %. present. No acetone.

Treatment Diet and 10 units of Insulin b.d.

GROUP N.

GLUCOSE TOLERANCE CURVE.



BLOOD SEDIMENTATION RATE.

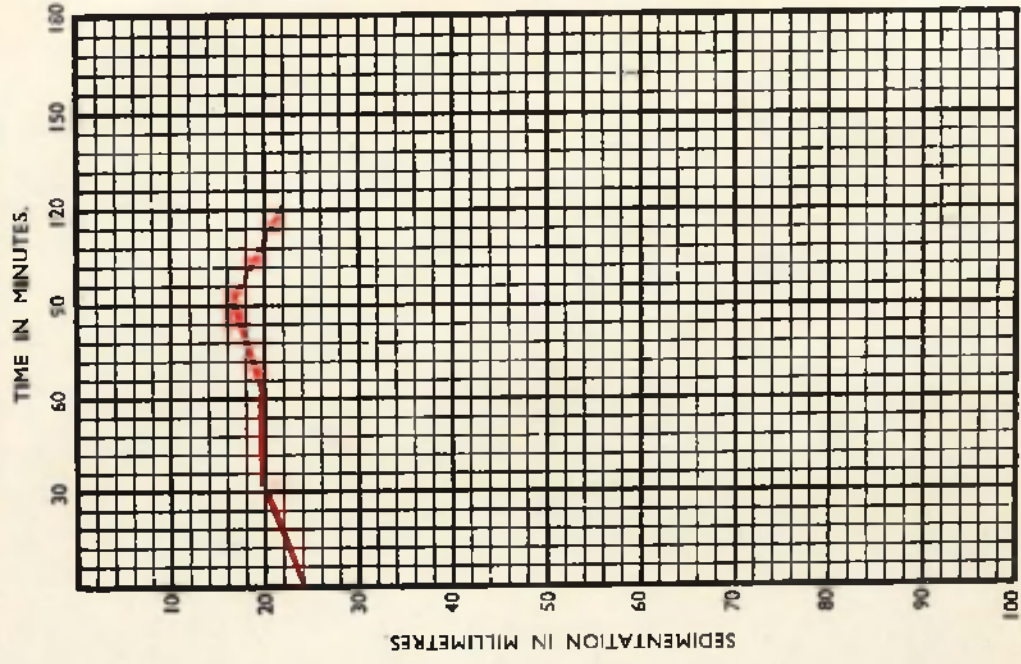


FIG 30.

N.

No. 31. Case G.H.

Age 70. (M)

Five years history of Diabetes. First symptoms, excessive thirst and polyuria. Has been treated with diet and 15 units of Insulin daily. Mother suffered from Diabetes.

General cond.

Cardio-vascular system normal for age. Easily tires, and subject to "fatness" Weight 127 lbs. Some enlargement of Prostate.

Blood F.B.S. 0.2%. Sed. R. 25 mm. W.R. -ve.

Urine Sp. Gr. 1.02A. Sugar present 2%. No acetone

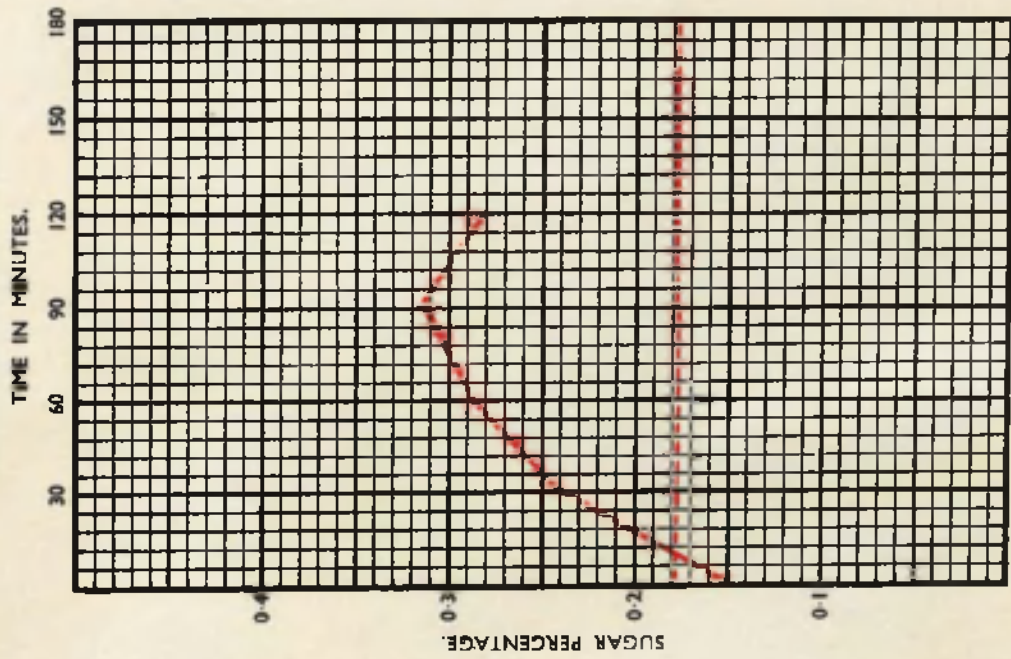
Treatment

Was difficult to stabilize with Insulin as small doses did not prevent glycosuria, and larger amounts lead to frequent and severe Hypo-Sym. Insulin dosage increased to 20 units b.d. His economic position made it very difficult to get a satisfactory diet.

Progress

Still not satisfactory, frequent glycosuria, but he feels improved and has gained 7 lbs. in weight.

GLUCOSE TOLERANCE CURVE.



BLOOD SEDIMENTATION RATE.

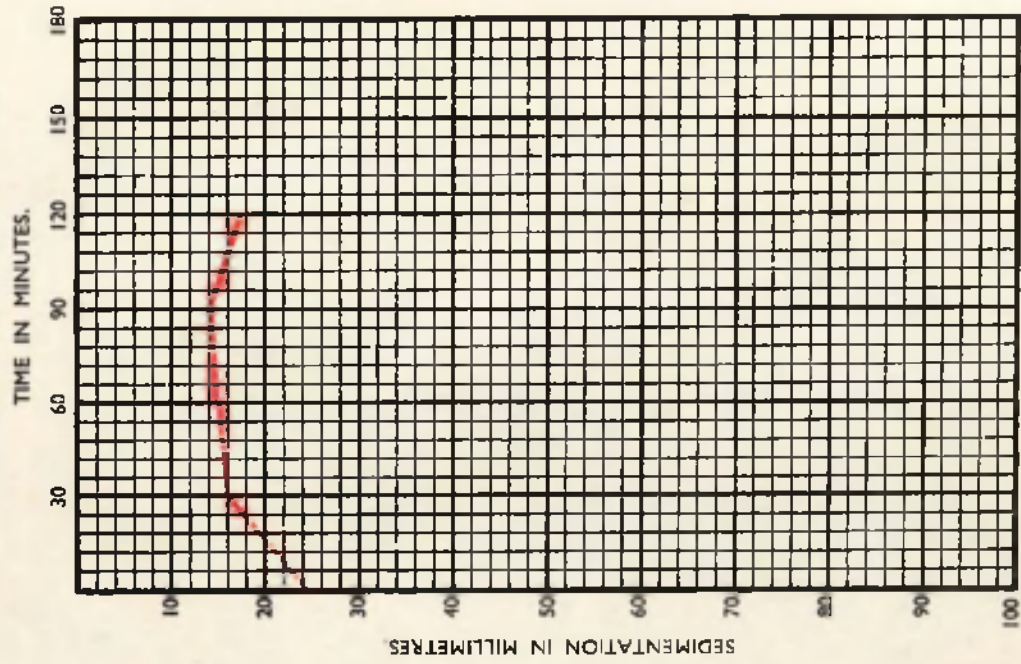


FIG 31.

N.

No. 32 Case E.L.

Age 51. (F)

Four years history of Diabetes, suffered from polyuria, thirst, and pruritis. Has since been treated with Insulin and diet, and is much improved. Mother, and uncle were diabetics.

General cond.

Fairly good. Heart and lungs normal. Varicose veins. Does not feel well and eyesight is failing rapidly. Chronic Rheumatism. Weight 150 lbs.

Blood F.B.S. 0.235%. Sed. R. 28 mm. W.R. -ve.

Urine Sp. Gr. 1028. Sugar 2%. Trace of acetone.

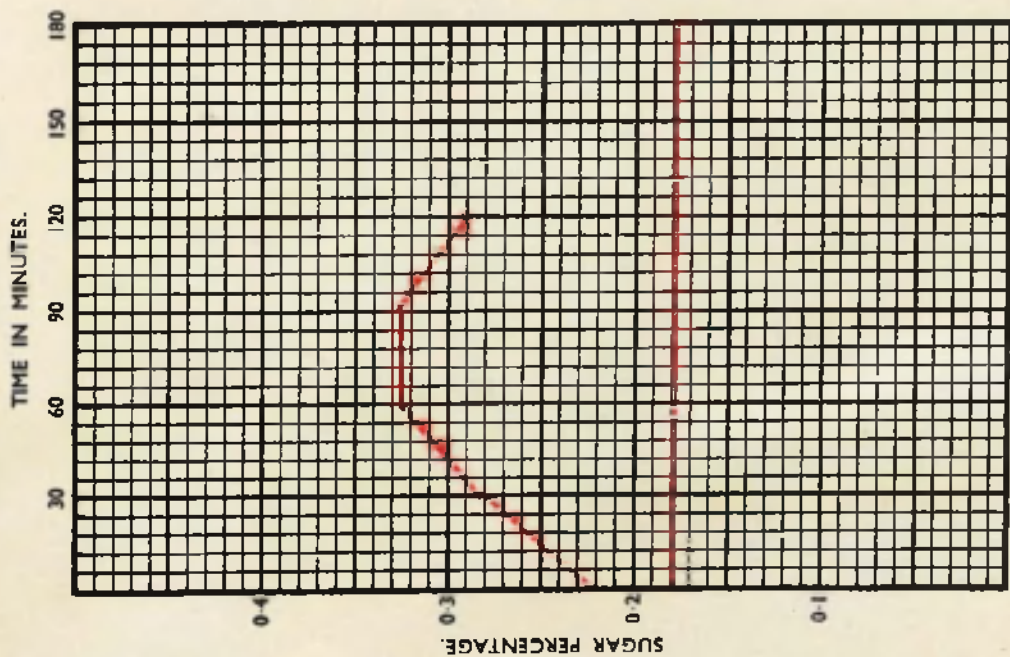
Treatment

She was a very difficult case to stabilize and eventually was placed on Insulin, three times daily - 20, 10, & 20 units. This dosage kept her almost free from sugar.

Progress

Not satisfactory. She has advanced diabetic retinitis. Still suffers from severe neuritis, and recently sugar has reappeared in the urine. To be admitted for further examination.

GLUCOSE TOLERANCE CURVE.



BLOOD SEDIMENTATION RATE.

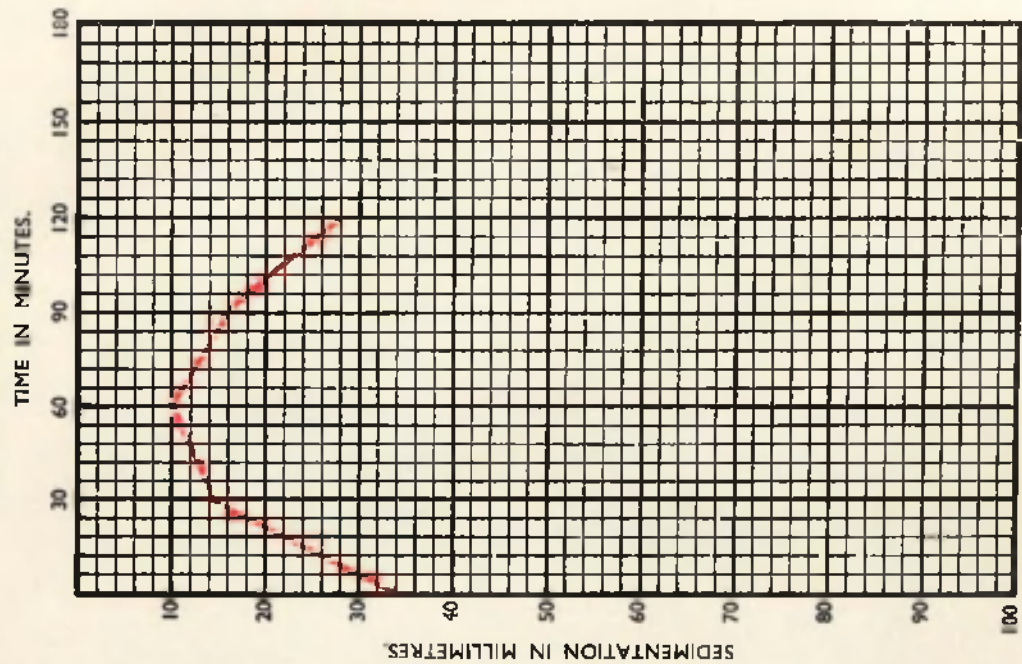


FIG 32.

No. 33 Case F.T.

Age 52. (F)

Diabetes diagnosed 10 years ago. Has since been on diet. (unsatisfactory) and Insulin. No known family history of Diabetes.

General cond.

Edentulous. Slight degree of arterio-sclerosis.
B.P. 135/80. Weight 151 lbs.

Blood

F.B.S. 0.2 %. Sed. R. 30 (Recent "chill") W.R. -ve.

Urine

Sp. Gr. 1028. Sugar present 1.5 %. No acetone.

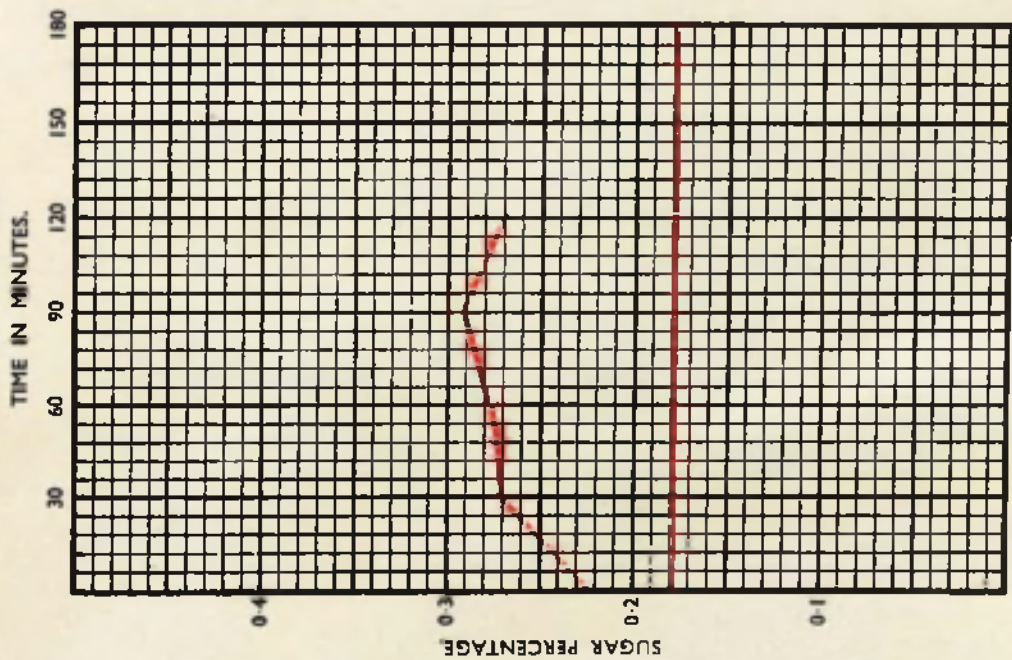
Treatment

Placed on 10 line diet and Insulin 20 units b.d.

Progress

Feels well, apart from eyesight. She is myopic, but there is no evidence of diabetic change. Now sugar free on insulin 20 units m., and 15 units n., Weight stationary.

GLUCOSE TOLERANCE CURVE.



BLOOD SEDIMENTATION RATE.

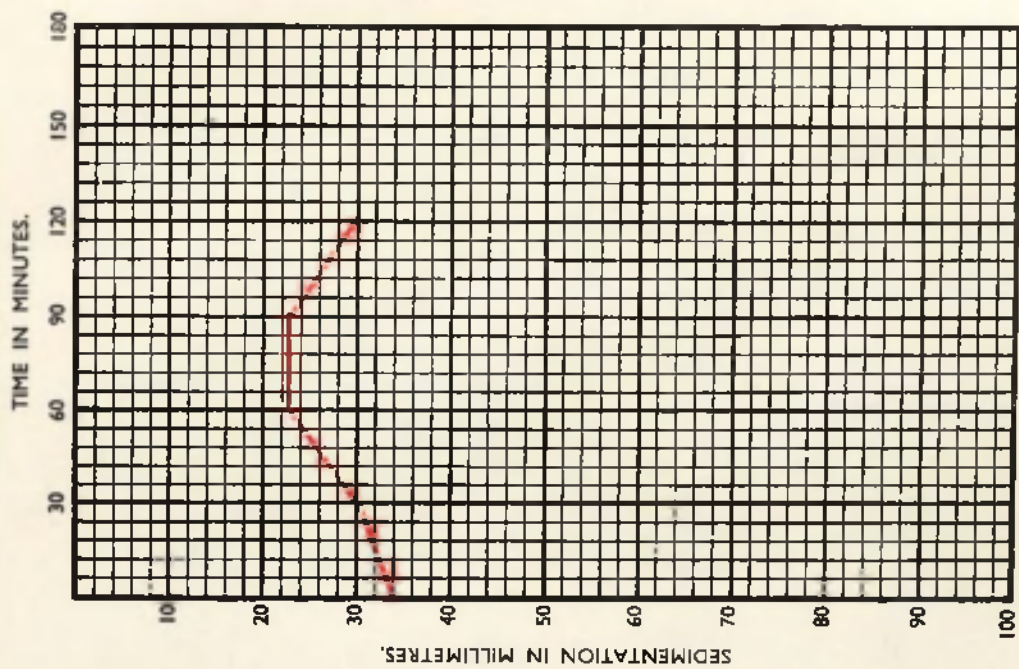


FIG 33.

No. 34. Case S.B.

Age 56. (F)

Nine years history of Diabetes. Initial symptoms, thirst, polyuria and pruritis. Has been on diet and Insulin for years. No family history of diabetes.

General cond. Poor, rheumatism, neuritis and arterio-sclerosis.
Weight 196 lbs.

Blood F.B.S. 0.227 %. Sed. R. 33 mm. W.R. -ve.

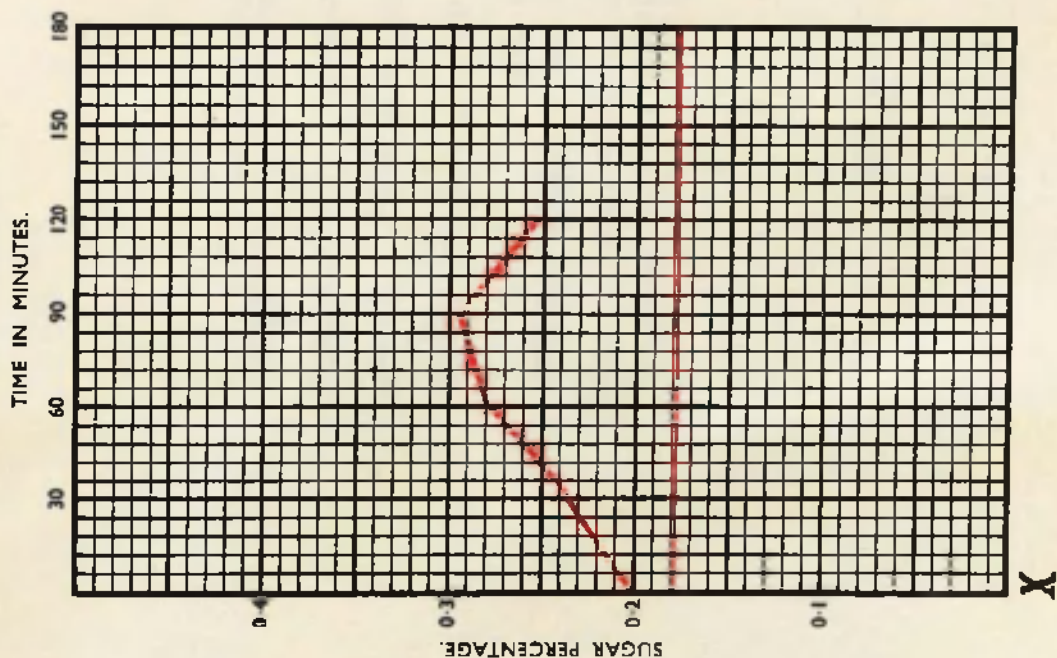
Urine Sp. Gr. 1034. Sugar present 2.5 %. No acetone.

Treatment Insulin 20 units b.d. Diet 10 lines.

Progress Satisfactory from the diabetic point of view. Three months later Insulin reduced to 15 units m.; and 10 units n., F.B.S. 0.18 %. Sed. R. unchanged. Suffers from articular rheumatism, and a course of gold injections has been started.

GROUP X.

GLUCOSE TOLERANCE CURVE.



BLOOD SEDIMENTATION RATE.

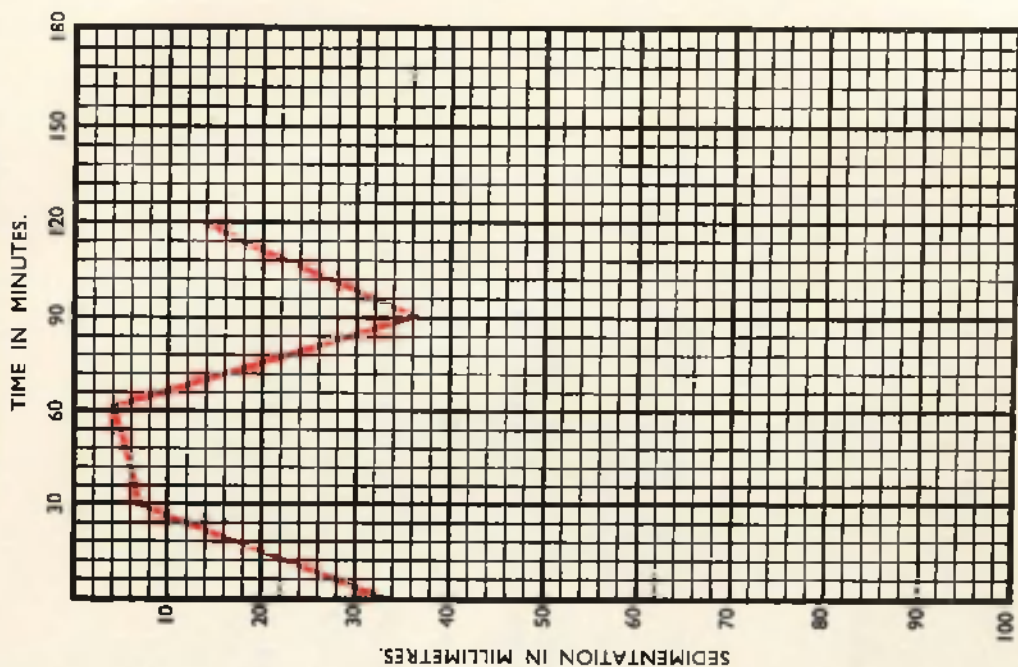


FIG 34.

No. 35. Case B.H.

Age 69. (F)

Known to have diabetes three years ago, since when has been on diet, but no Insulin. Last over 2 stone in weight, in the past 18 months. No family incidence.

General cond. Not good. Has polyarticular arthritis. and Arterio-sclerosis. Weight 142 lbs.

Blood F.B.S. 0.223 Sed. R. 35 mm. W.R. -ve.

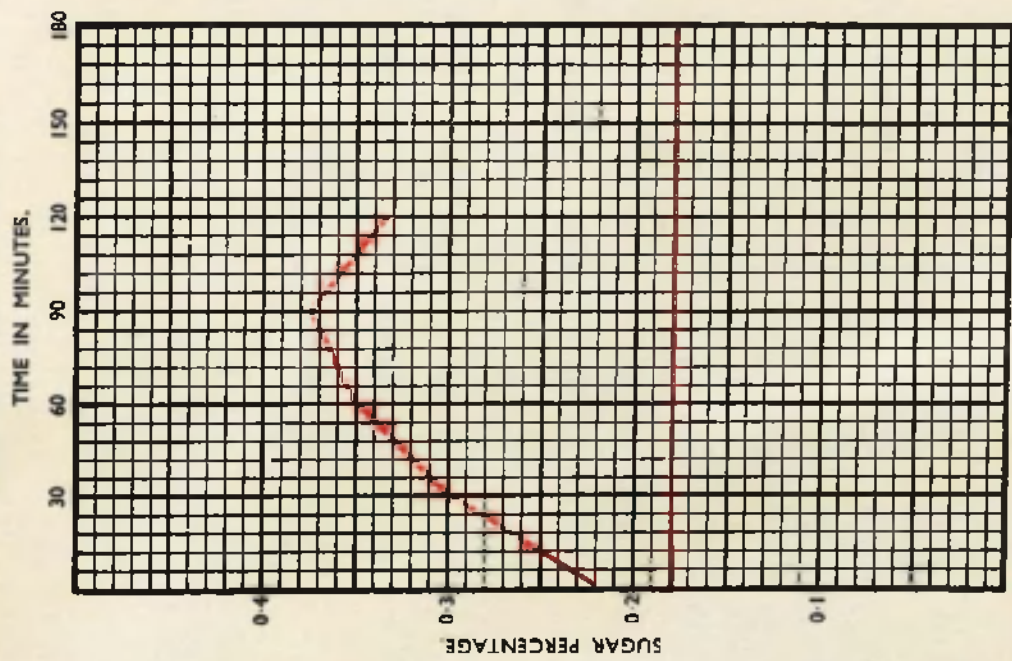
Urine Sp. Gr. 1027. 2%. Sugar. Trace of acetone.

Treatment Insulin 15 units b.d. and 10 line diet.

Progress Insulin dosage raised to 25 units b.d. subsequent progress satisfactory.

GROUP N.

GLUCOSE TOLERANCE CURVE.



BLOOD SEDIMENTATION RATE.

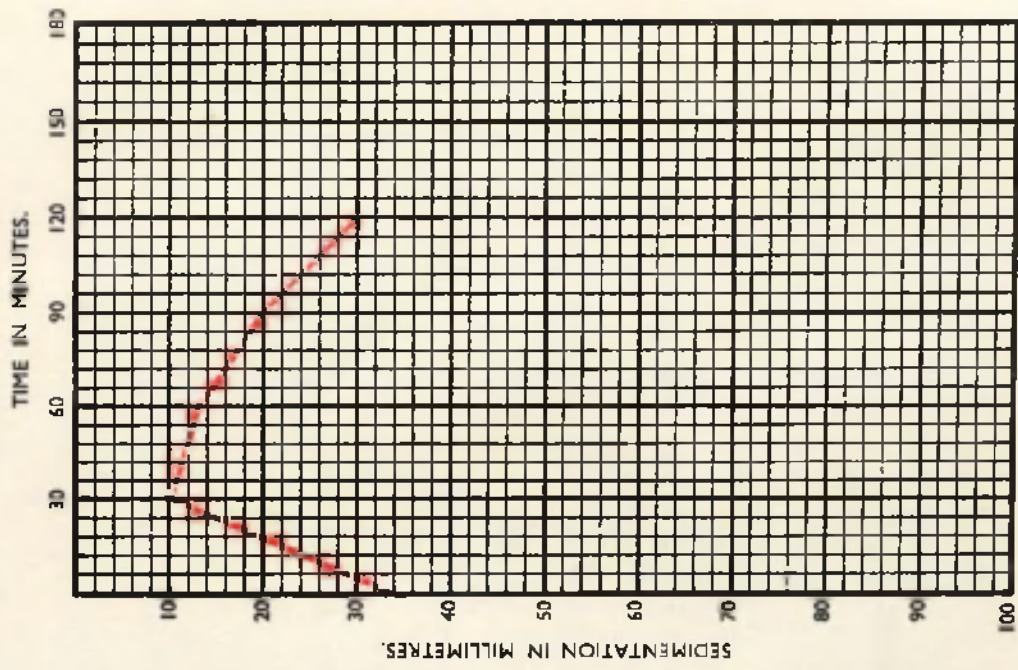


FIG 35.

No. 36 Case A.J.

Age 71. (F)

Five years history of Diabetes. Chief symptom, failing eyesight. Always stout. No family history of Diabetes.

General cond. Poor. Suffers from frequent attacks of sickness.

Blood F.B.S. 0.225 %. Sed. R. 36mm. W.R. -ve.

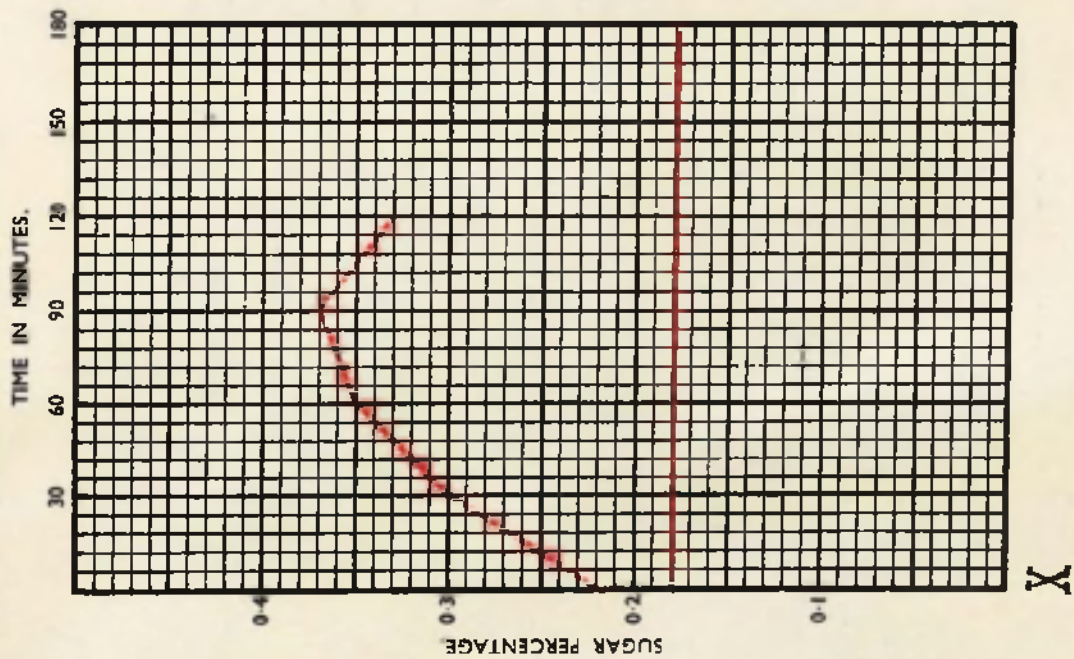
Urine Gr. Sp. 1030. Sugar present 3%. Trace of Acetone.

Treatment Insulin, 10 units b.d.

Progress Patient has not recently attended Clinic, is confined to bed at home.

GROUP X. (The Sed. R. at 2 hrs. is greater than fasting rate.)

GLUCOSE TOLERANCE CURVE.



BLOOD SEDIMENTATION RATE.

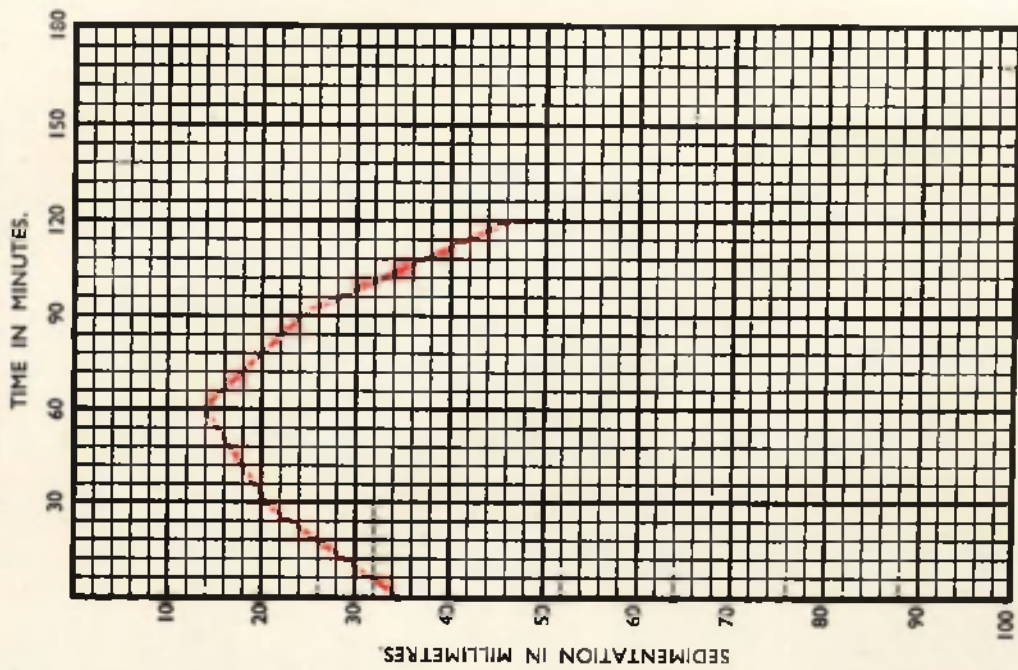


FIG 36.

No. 37. Case E. B.

Age 66. (F)

Diabetes diagnosed seven years ago. On diet and Insulin since, no regularity about either. Family history negative.

General cond.

Overweight. Edentulous. Cardio-vascular system normal. Bronchitis, and emphysema. Septic ulcer of great toe, no evidence of gangrene.

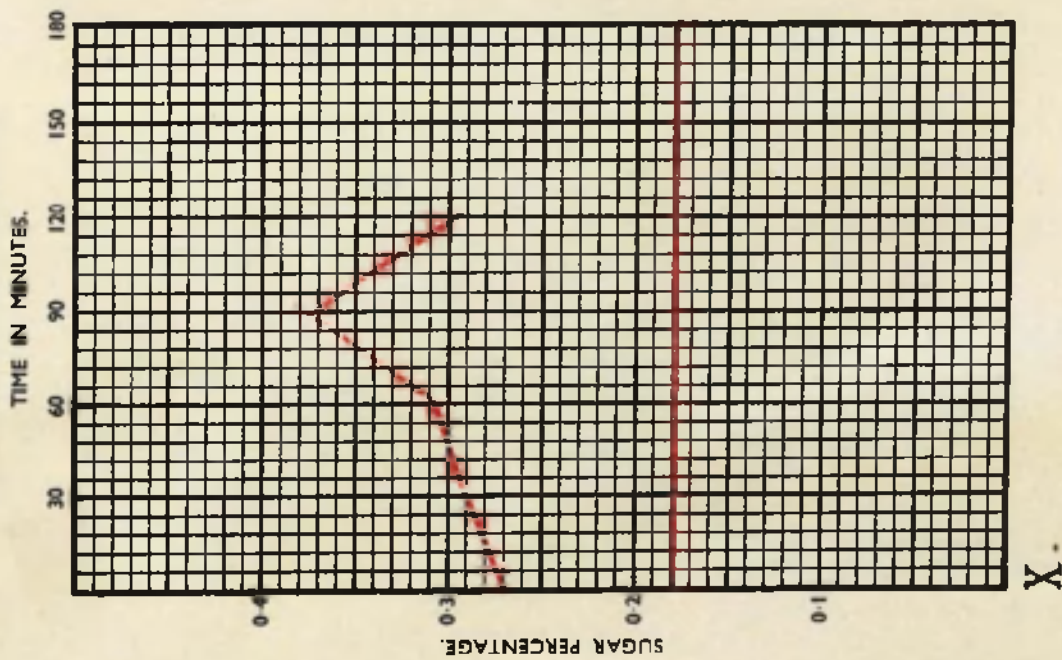
Blood F.B.S. 0.25 %. Sed. R. 50. W.R. -ve.

Urine Sp. Gr. 1034. Sugar 3%. present. No acetone.

Treatment Diet and Insulin 15 units m., and 10 units n.,

Progress Diabetes is controlled, but the ulceration of leg recently has recurred.

GLUCOSE TOLERANCE CURVE.



BLOOD SEDIMENTATION RATE.

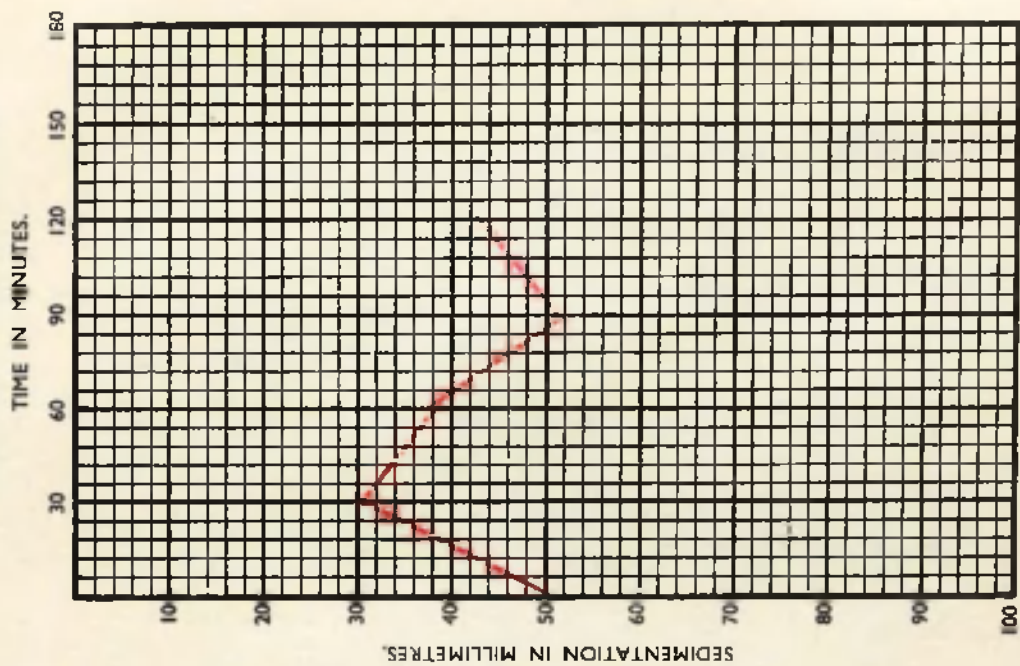


FIG 37.

No. 38 Case C.L.

Age 58. (F)

Five years history of diabetes, had never received satisfactory treatment. Always stout.

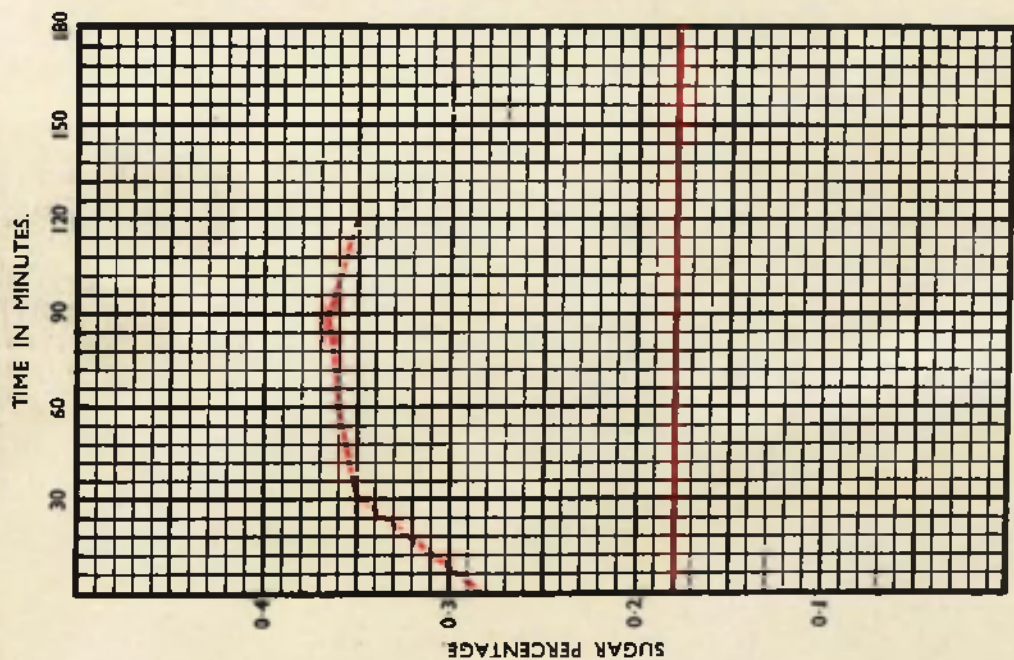
On admission to hospital she had septic gangrene of her left foot with cellulitis of the leg. Also there was chronic cystitis.

Blood F.B.S. 0.235 %. Sed. R. 71 mm. W.R. -ve.

DIED

GROUP X.

GLUCOSE TOLERANCE CURVE.



BLOOD SEDIMENTATION RATE.

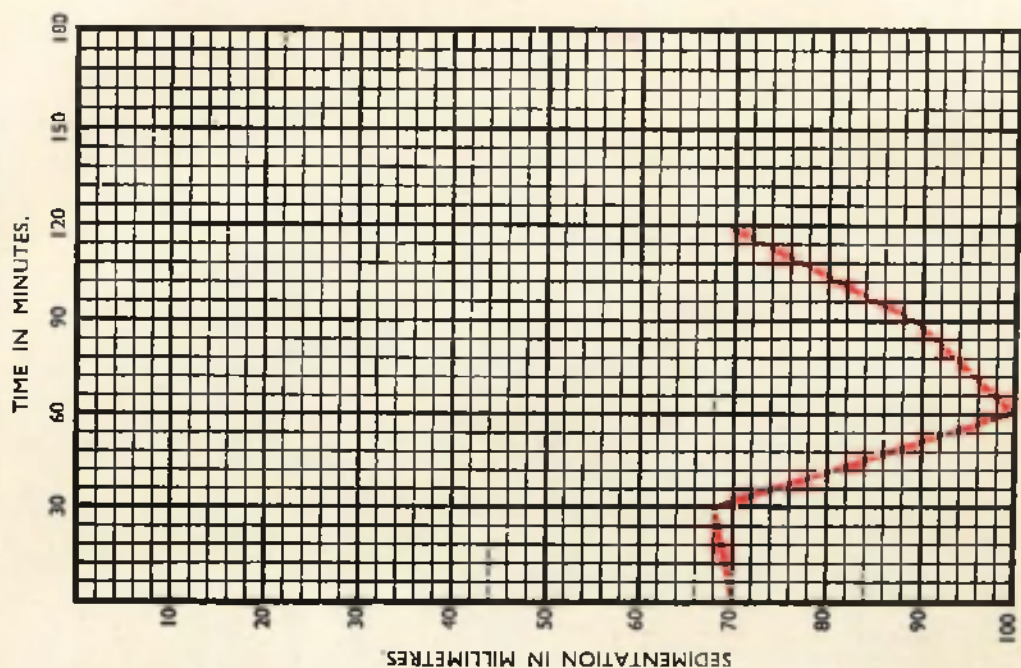


FIG 38.

X

No. 39. Case C.W.

Age 59 (F)

Recently admitted to another hospital for Radium treatment of carcinoma of cervix. Diabetes found.

General cond.

Fairly good. Weight 170 lbs.

Slight chronic Bronchitis. Considerable erosion of the Cervix.

Blood

F.B.S. 0.3 %. Sed. R. 76 mm. W.R. -ve.

Urine

Sp. Gr. 1030. 0.3% sugar. Trace of acetone.

Treatment

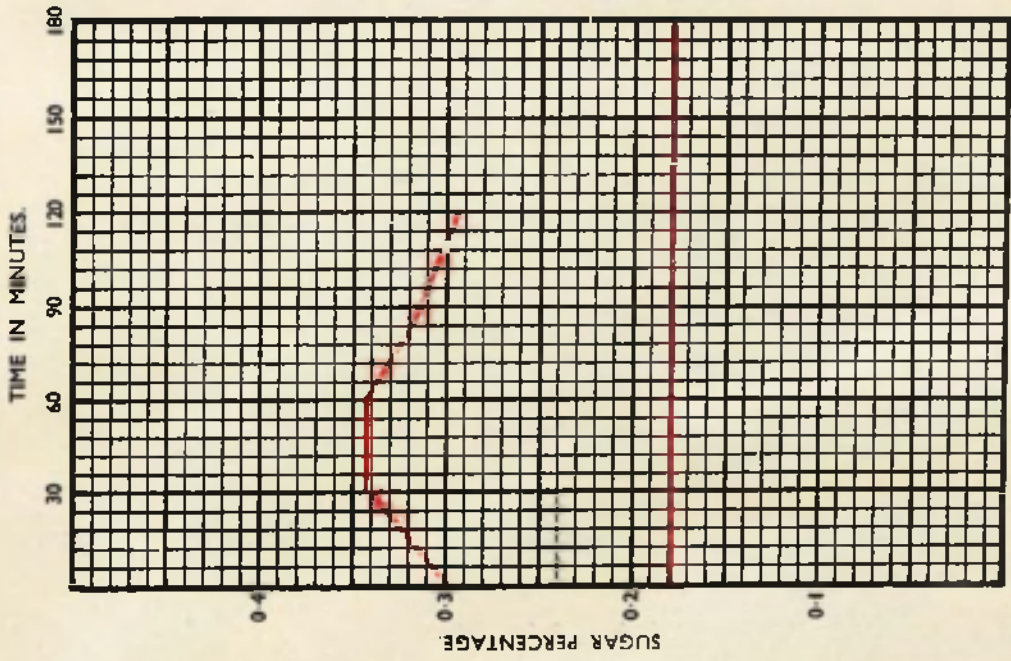
Flexible dietary allowed. Insulin 25 units B.D.

Progress

Recent symptoms suggest the development of intra-abdominal secondaries.

GROUP N.

GLUCOSE TOLERANCE CURVE.



BLOOD SEDIMENTATION RATE.

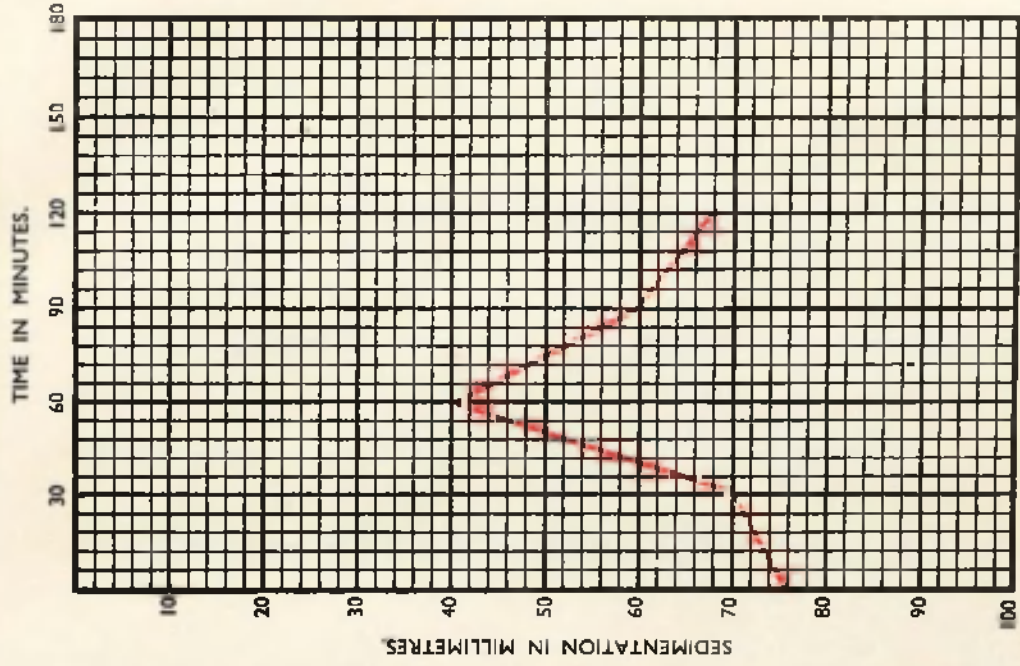


FIG 39.

No. 40. Case A.B.

Age 66. (F)

Known duration of Diabetes - one year.

Has been receiving Insulin, 25 units as a single dose, and not surprisingly, has been suffering from severe Hypo. Sym.

General cond.

Very poor. Advanced myocardial degeneration, and chronic bronchitis and emphysema. Weight 160 lbs.

Blood

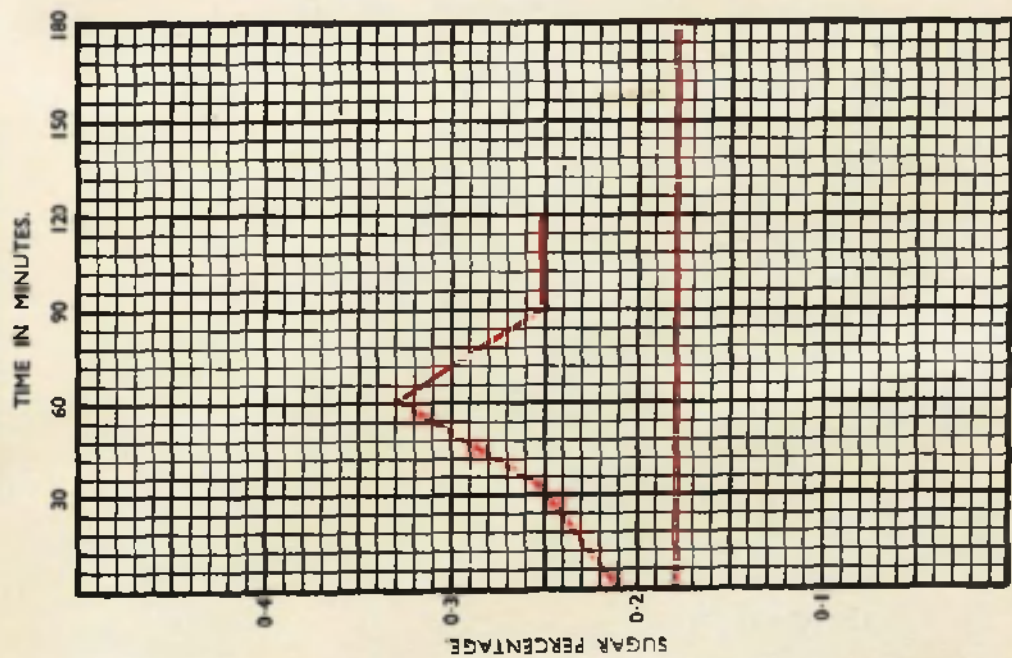
F.B.S. 0.215 %. Sed. R. 80 mm. W.R. -ve.

Notes.

This patient only recently has commenced to attend the clinic, is ill and will have to be admitted to hospital for full investigation. Until this is done it will not be possible to explain the "very rapid" Sed. R.

GROUP N.

GLUCOSE TOLERANCE CURVE.



BLOOD SEDIMENTATION RATE.

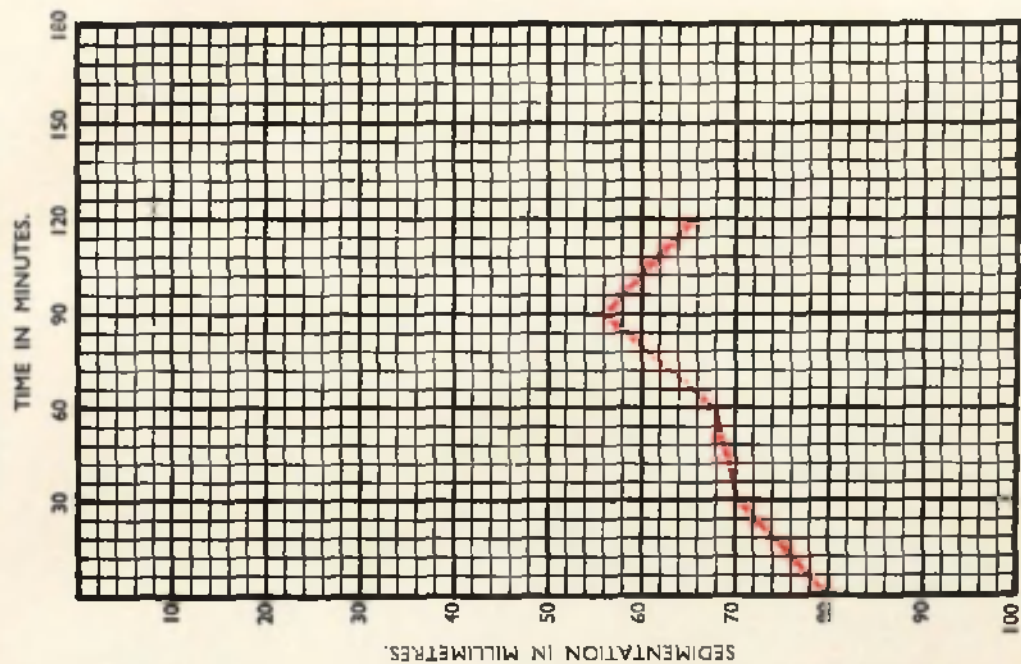


FIG 40.

No. 47. Casse S.H.

4.000.000

Has suffered from Pulmonary Tuberculosis for 12 years. Diabetes known to have been present for past 3 years.

General cond. Poor. Cavitation at right Lung Apex, with radiological signs of recent activity. Weight 116 lbs.

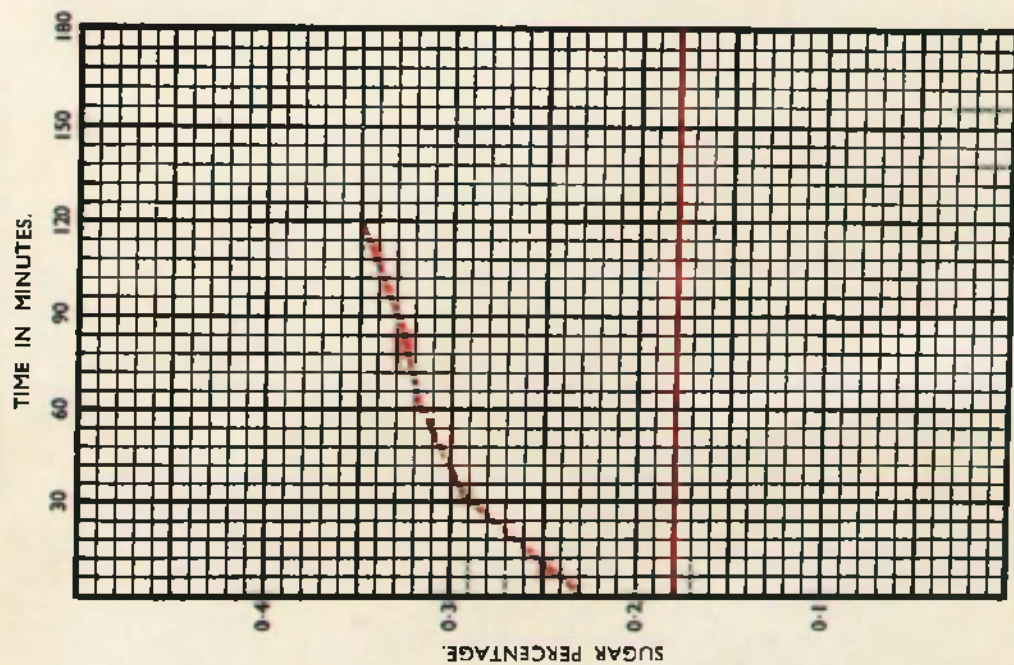
Blood	F. B. S.	0.235	Sed. R.	60 mm.	W. R.	-ve.

Urine
Sp. Gr. 1038. 0.3 %. Sugar present. Acetone heavy.

Transferred to Sanatorium.

GROUP X.

GLUCOSE TOLERANCE CURVE.



BLOOD SEDIMENTATION RATE.

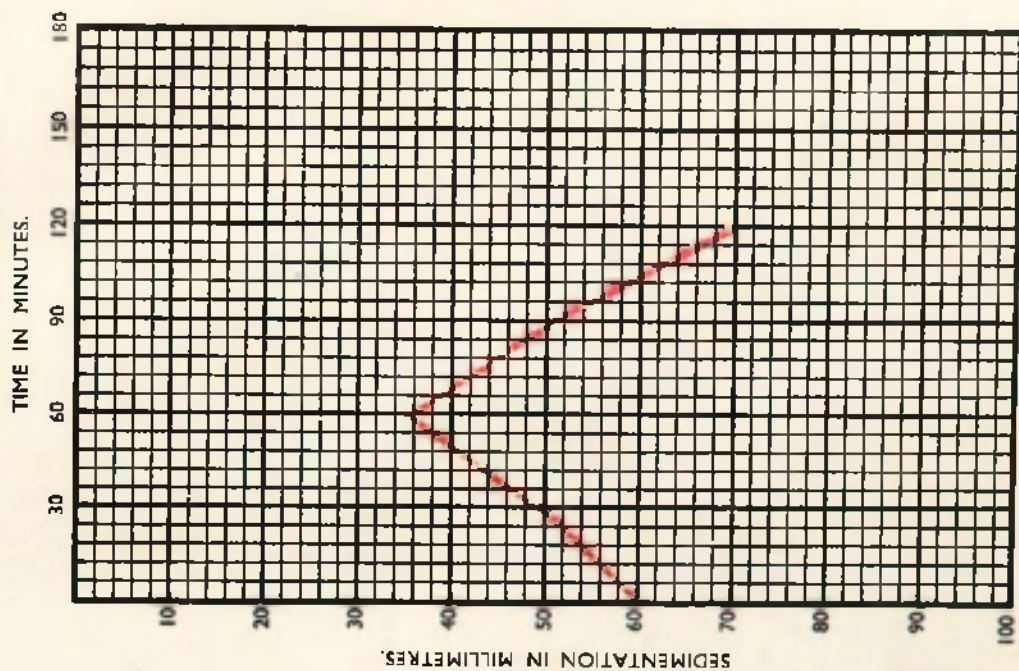


FIG 41.

X.

No. 43 Case J.S.

Age 60. (M)

Eight years history of diabetes, but had never received standardized diet or Insulin dosage.

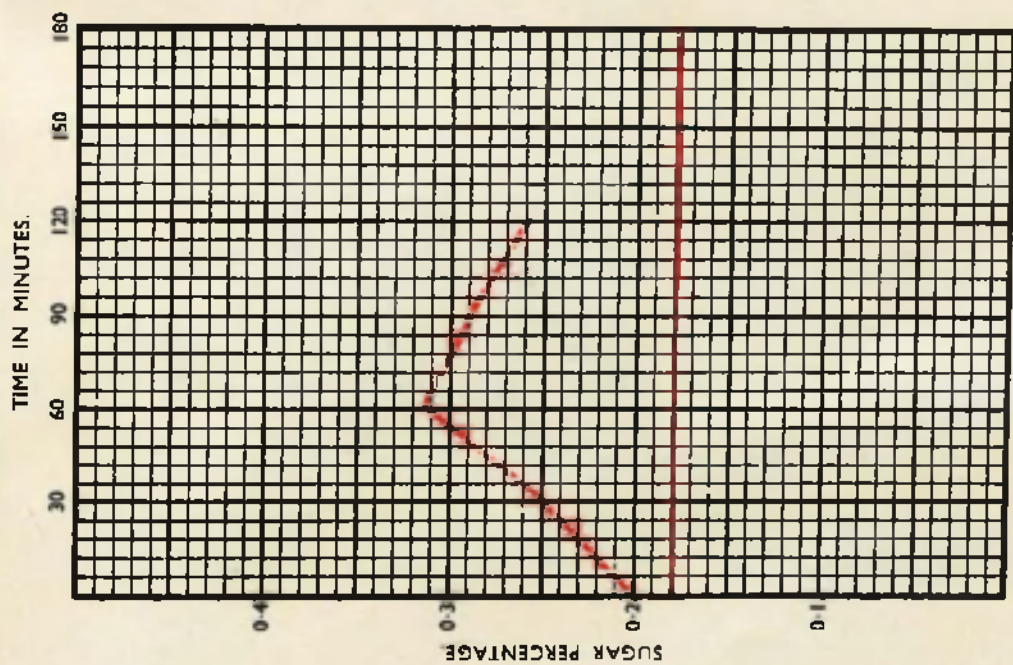
On admission to hospital both legs were cedematous, gangrene of the right foot and a perforating ulcer of the left foot. Both places were septic, and he was in a condition of profound toxæmia.

Blood F.B.S. 0.18 %. Sed. R. 81 mm. W.R. -ve.

Patient died within a few days of admission.

GROUP X.

GLUCOSE TOLERANCE CURVE.



BLOOD SEDIMENTATION RATE.

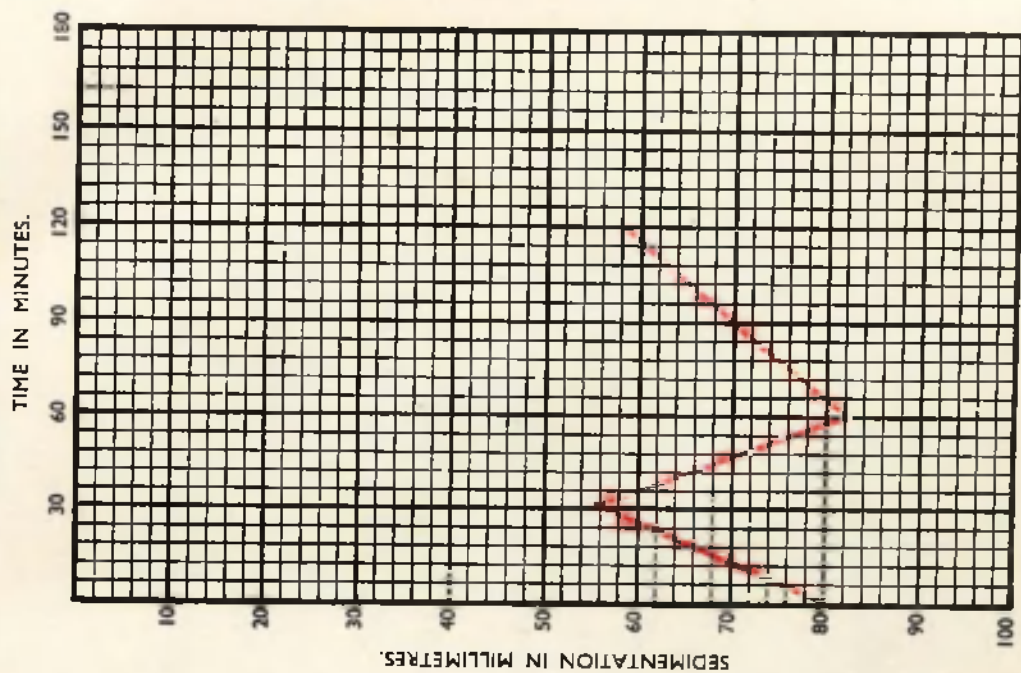


FIG 43.

X.

No. 44 Case A.W.

Age 16. (M)

Has had diabetes for the past five years. He suffers from a very severe form of diabetes and has been admitted to hospital in both hyper and hypoglycaemic attacks. No diabetes in family.

General cond. Good. Well nourished and has no complaints.
Weight 124 lbs.

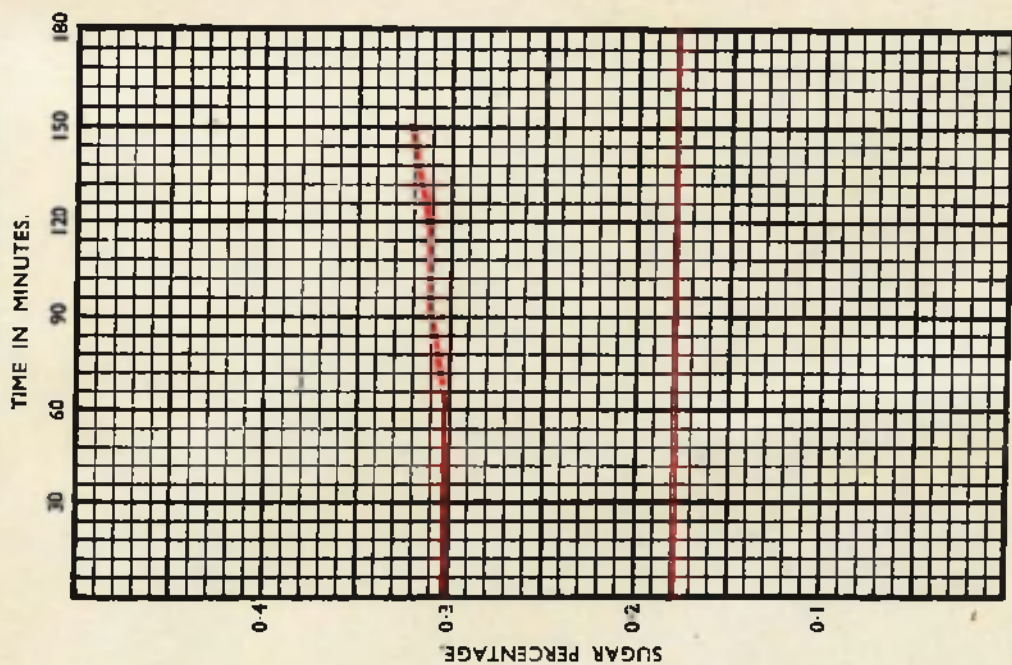
Blood F.B.S. 0.355 %. Sed. R. 15 mm. W.R. -ve.

Urine Sp. Gr. 1032. Sugar 3%. Acetone present.

Re-examination on several occasions has given very different Sed. readings

Unable to place this case in either group.

GLUCOSE TOLERANCE CURVE.



BLOOD SEDIMENTATION RATE.

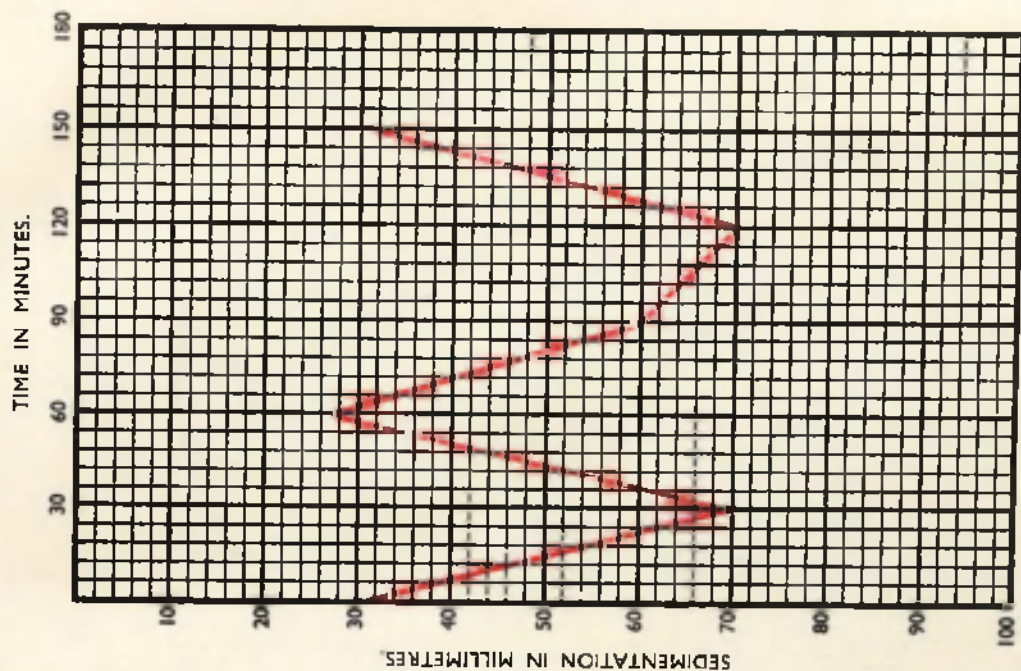
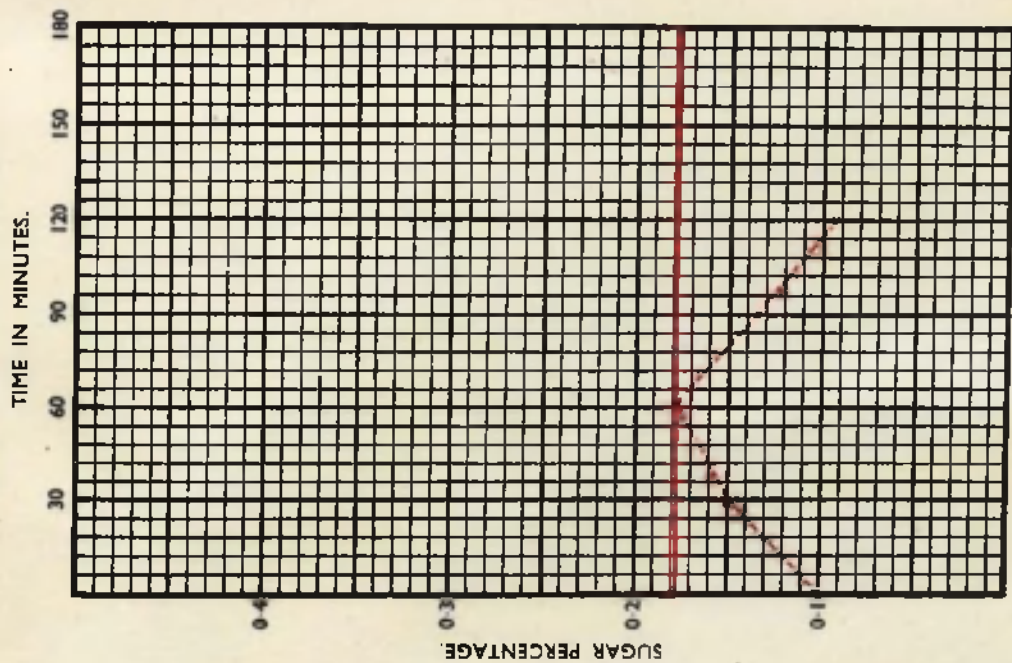


FIG 44.

GLUCOSE TOLERANCE CURVE.



BLOOD SEDIMENTATION RATE.

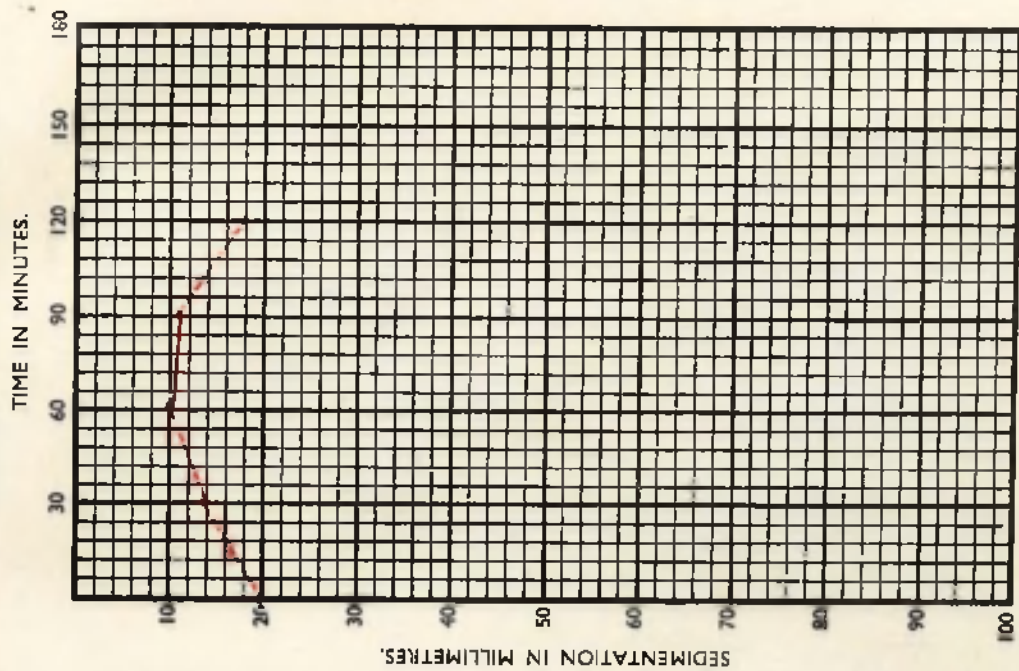
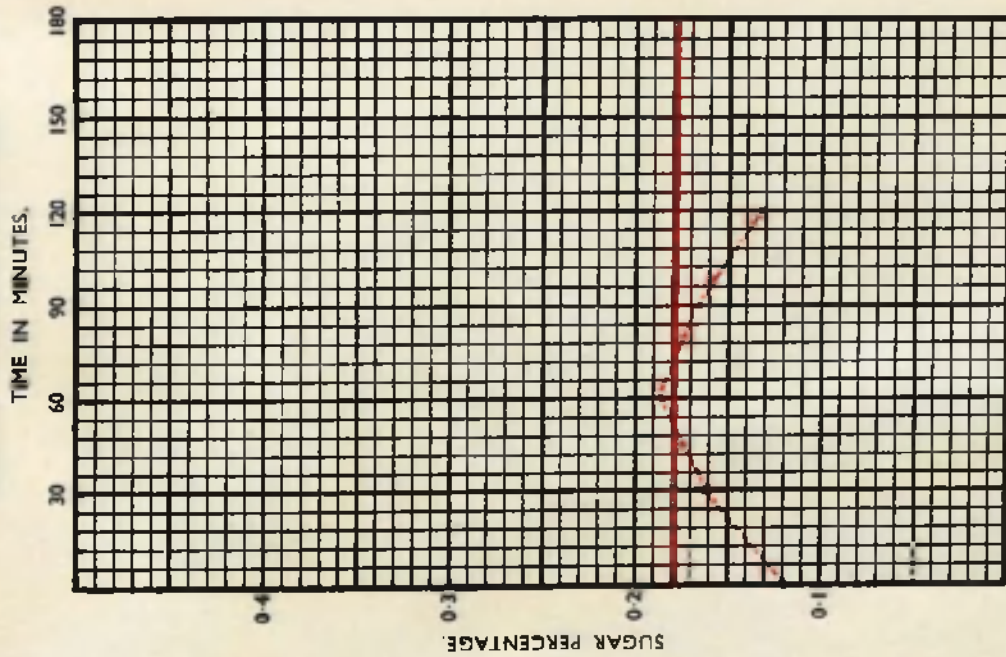


FIG 46.

Case of Renal Glycosuria. (P).

GLUCOSE TOLERANCE CURVE.



BLOOD SEDIMENTATION RATE.

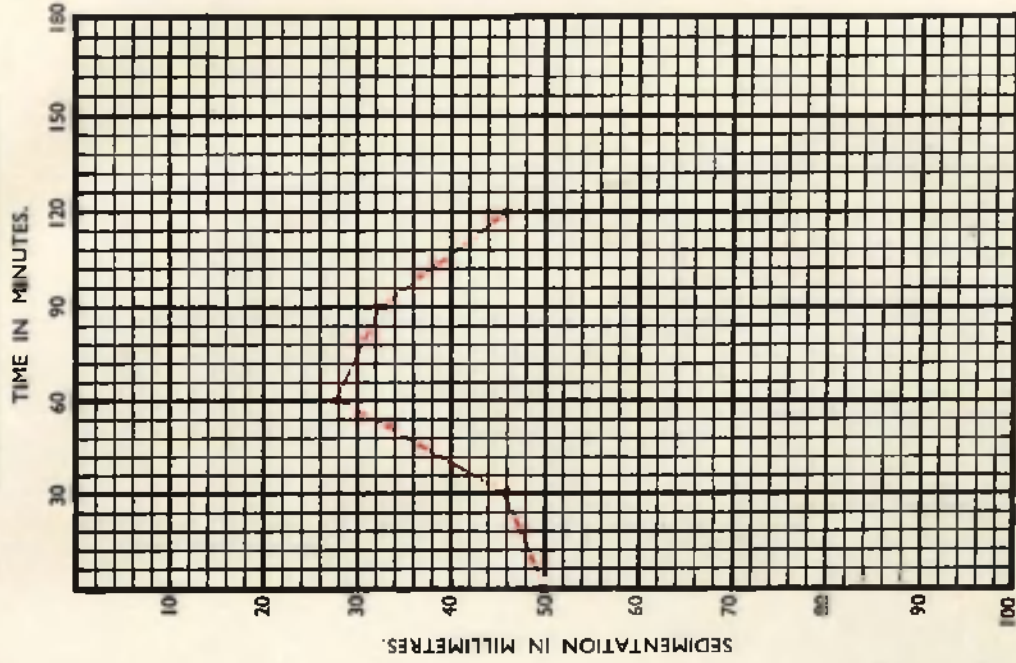
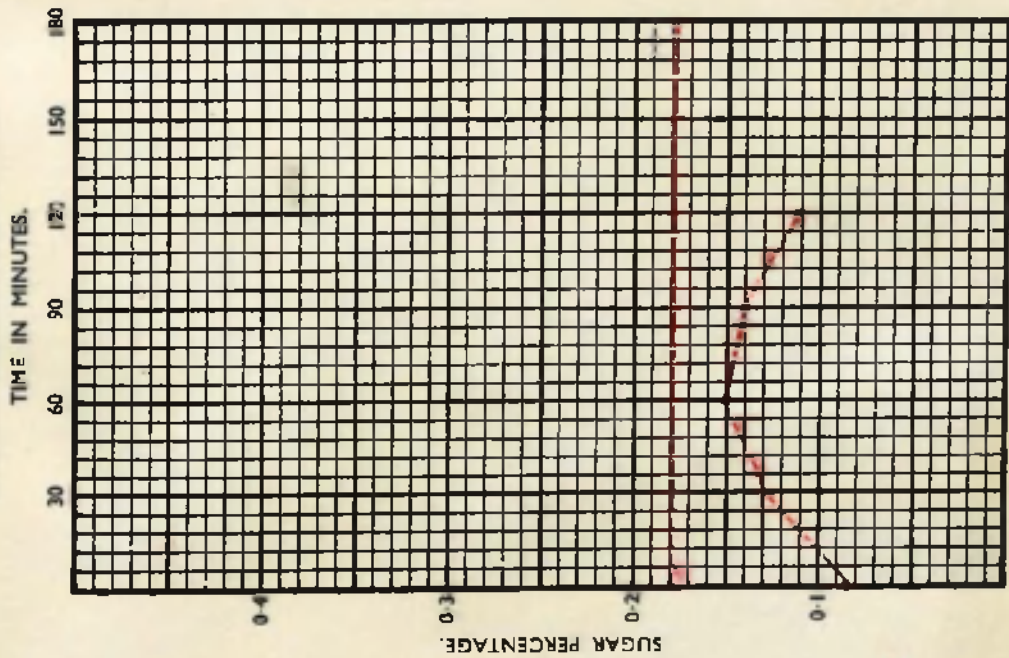


FIG 47.

GLUCOSE TOLERANCE CURVE.



BLOOD SEDIMENTATION RATE.

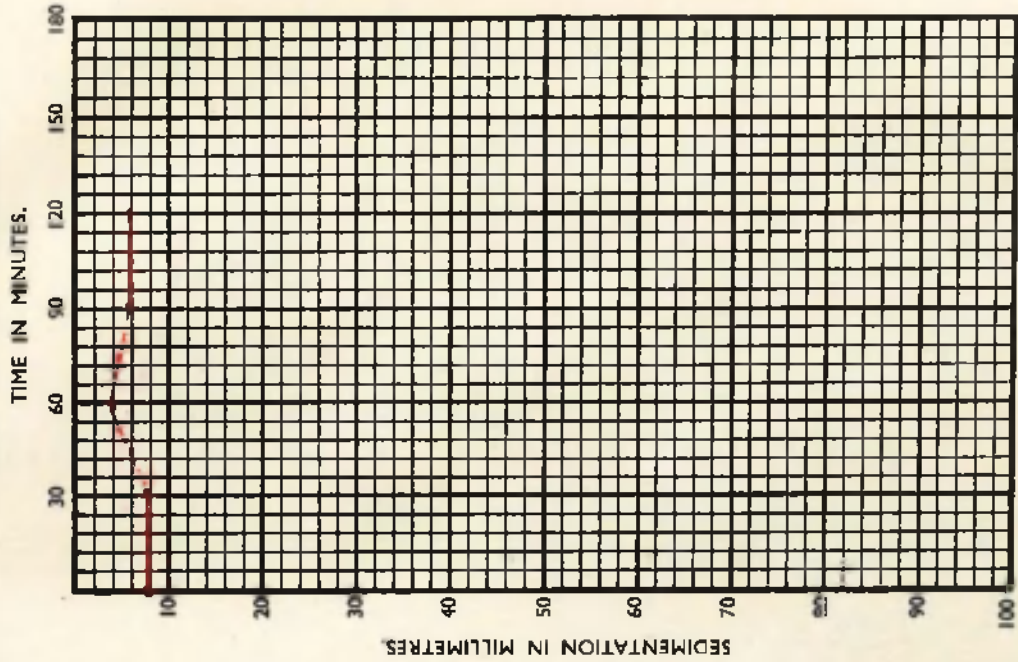
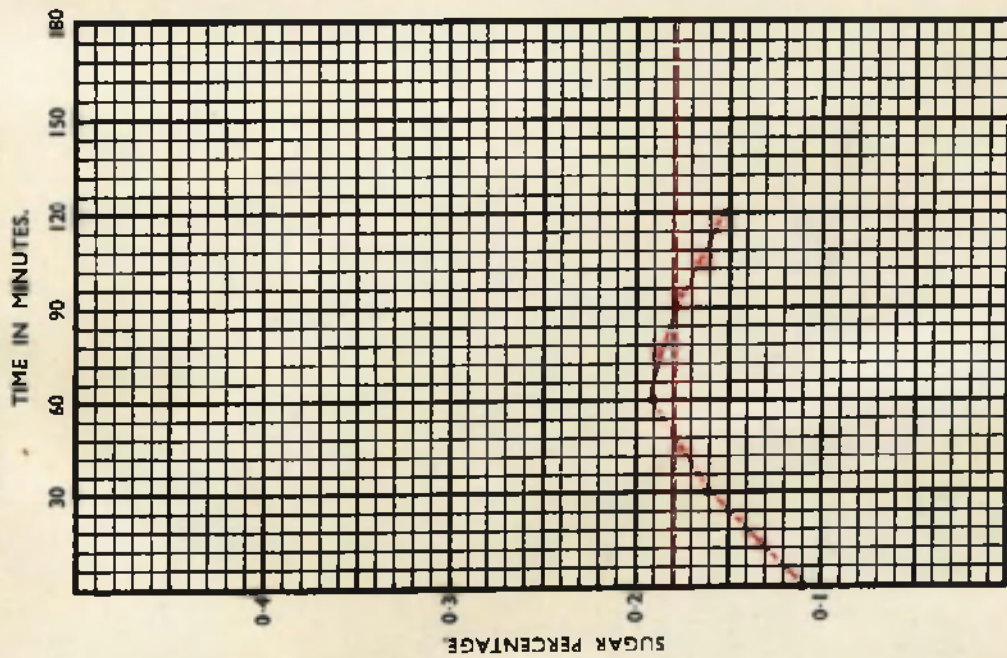


FIG 48.

Normal, healthy woman, age 47.

GLUCOSE TOLERANCE CURVE.



BLOOD SEDIMENTATION RATE.

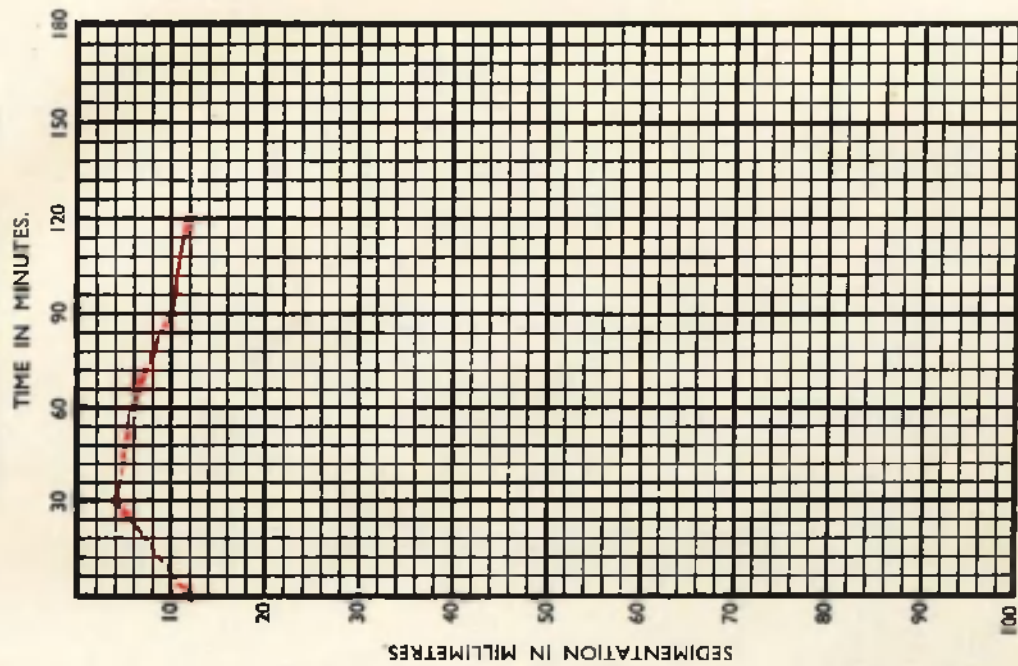
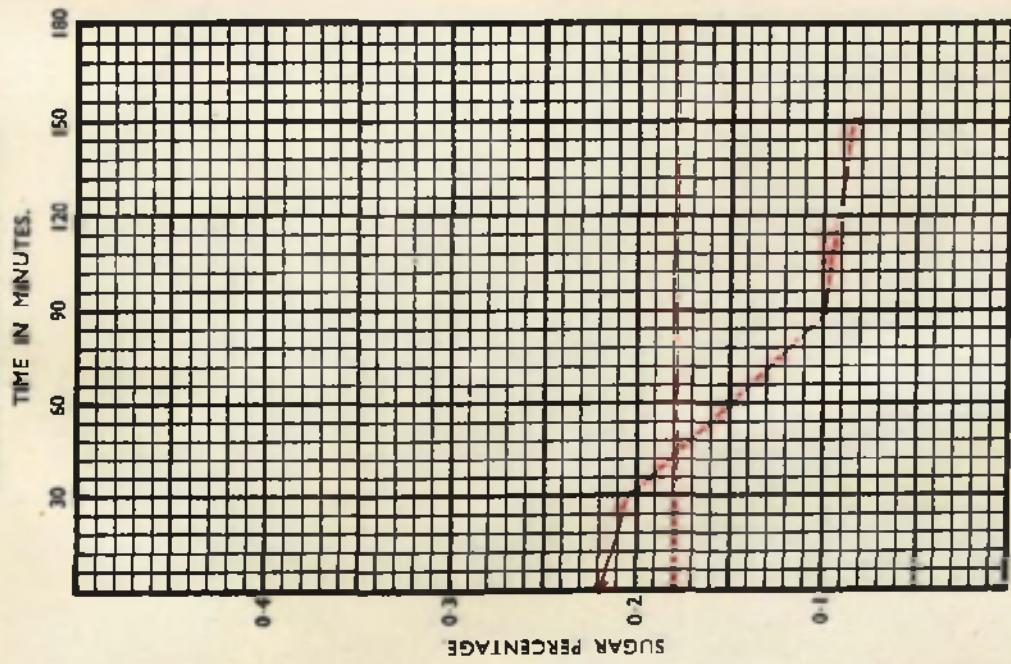


FIG 49.

Very stout, otherwise healthy woman, age 61.

GLUCOSE TOLERANCE CURVE.



BLOOD SEDIMENTATION RATE.

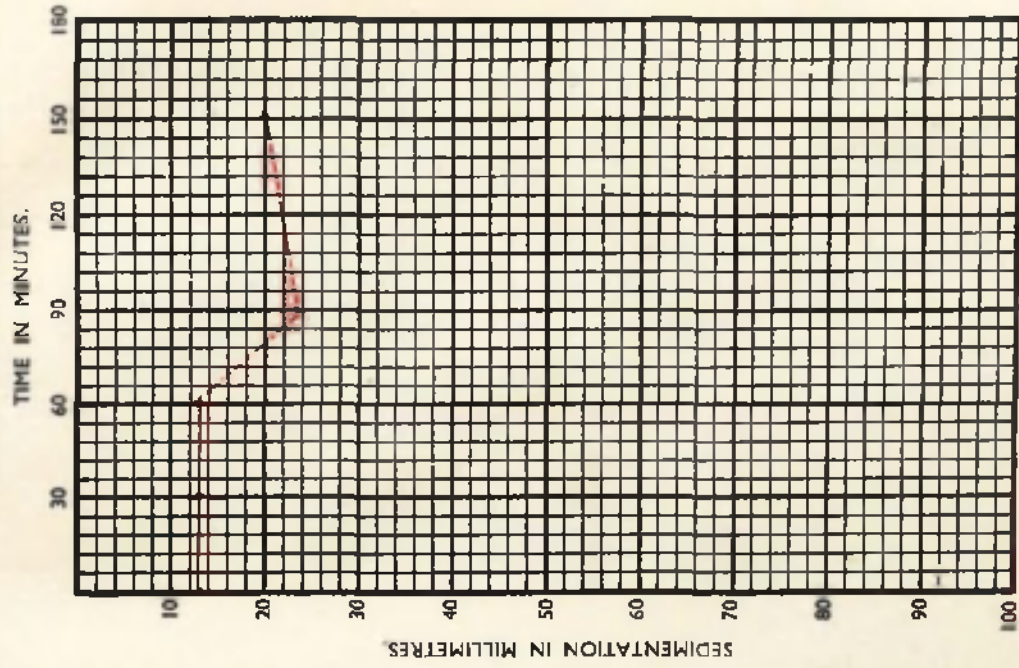
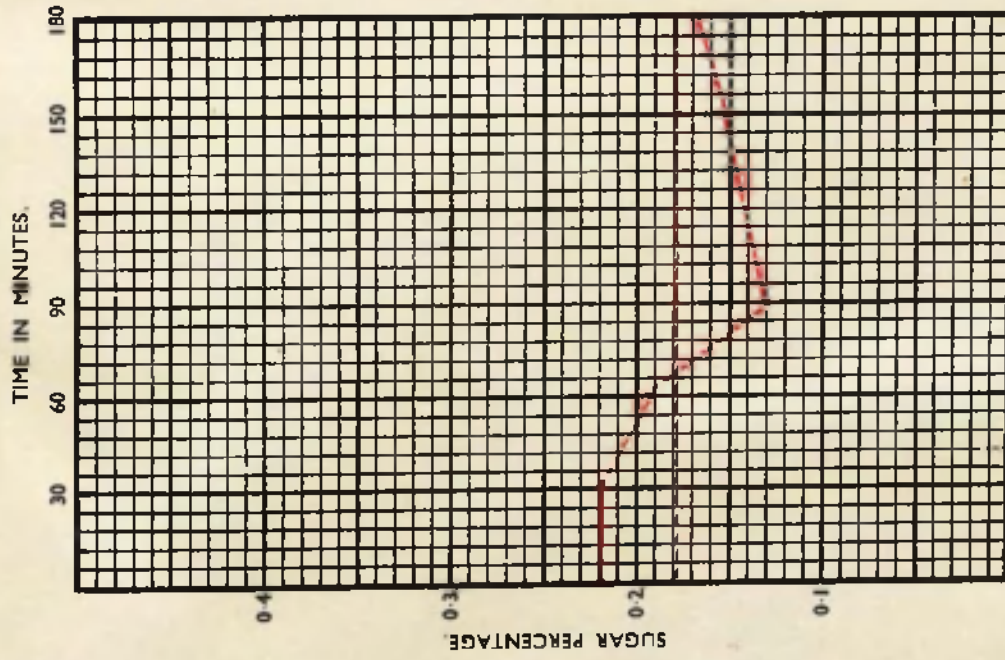


FIG 50. (case 29)

After 25 units of Insulin.

GLUCOSE TOLERANCE CURVE.



BLOOD SEDIMENTATION RATE.

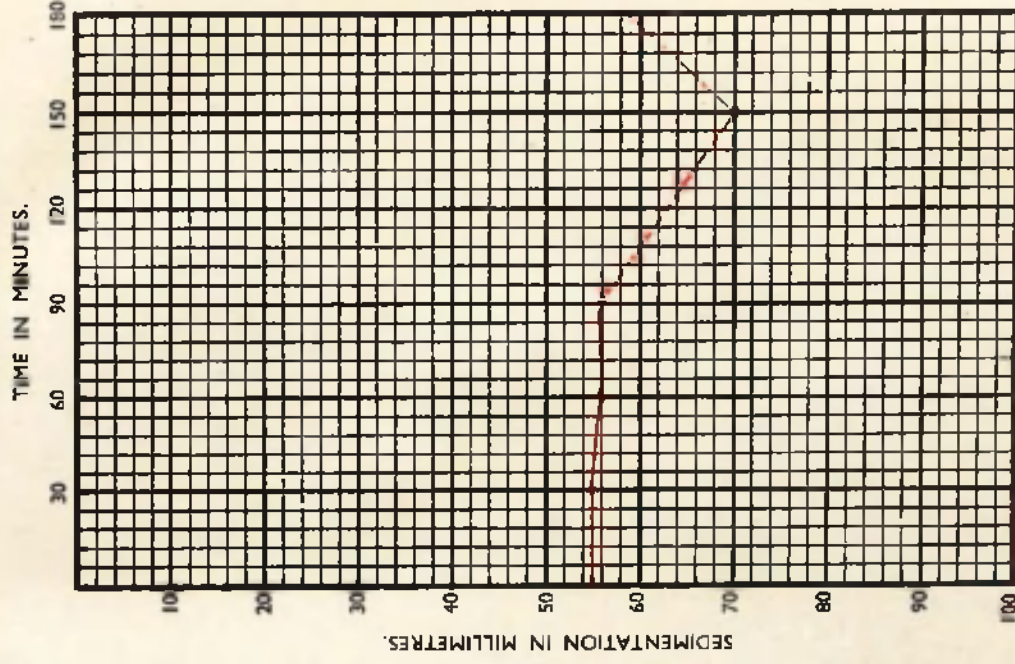


FIG 51. (case 41.)

After 30 units of Insulin.