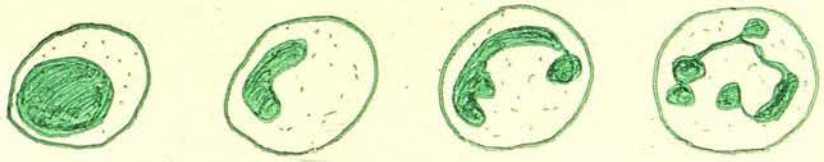
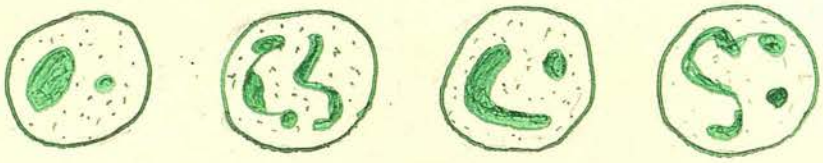
CLASSIFICATION OF NEUTROPHILES.

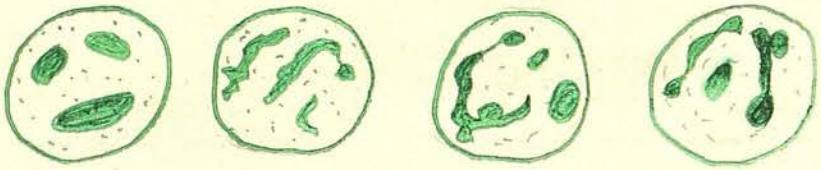
CLASS I.



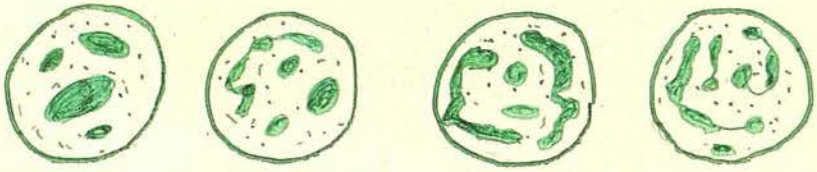
CLASS II.



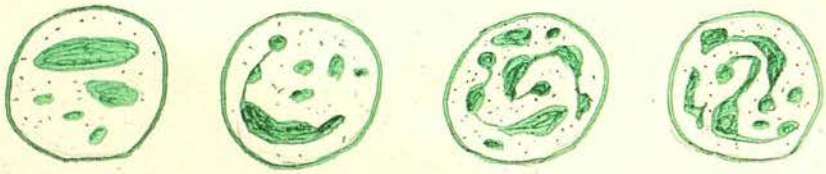
CLASS III.



CLASS IV.



CLASS V.



THE EFFECT OF TUBERCULIN ON THE BLOOD.

Its Value in the Diagnosis, Prognosis,
and Treatment of Pulmonary
Tuberculosis.

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by

WILLIAM LESLIE BURGESS, M.B., Ch.B.

M.D. 1912.

THE EFFECT OF TUBERCULIN ON THE BLOOD.

Its Value in the Diagnosis, Prognosis, and Treatment of Pulmonary Tuberculosis.

The object of the present thesis is to shew that certain changes in the blood occur during the course of treatment with Tuberculin: also that these changes may be used not only as guides to treatment, but likewise as aids to diagnosis and prognosis.

My thesis is founded on Arneth's teaching, which has reference to the classification of the poly-:morpho-nuclear leucocytes into different varieties. Wright has shewn the value of the Opsonic Index in the treatment of certain diseases. But while the Opsonic Index is of undoubted value, it must be confessed that it has its limitations. For instance, the Index is easily /

easily influenced by exercise etc. It is subject to rapid fluctuations. In the hands of the busy general practitioner the estimation of the Opsonic Index is well-nigh impossible, not only owing to the technical difficulties involved, but also because it requires great care and monopolises much time.

When the treatment is controlled by means of examination of the blood according to Arneth's method, as I shall attempt to shew, reliable results may be secured, and after a little practice rapidity of operation may be assured.

Present Day Methods of Treating Tuberculosis by means of Tuberculin.

At the present time there are two chief methods of administering tuberculin in the treatment of tuberculosis. In the first, manifest reactions are intentionally produced, and the doses of tuberculin are rapidly increased to a maximum, which is very large. In the second, or "reactionless method", manifest reactions are avoided as much as possible, and only very minute quantities of tuberculin are injected with a very cautious increase of dose to a maximum, which is not very large.

While it is certain that reactions to tuberculin may do a patient good, it must not be forgotten that /

that they may do the patient a great deal of harm. The general reaction evidenced by fever etc. is frequently accompanied by a local reaction at the site of the tuberculous disease. Changes take place at these foci which really consist in an increased activity of the disease. This may be only temperary and may finally end in an improvement of the local condi:tion by the stimulation of the production of antibodies. If this occurs the reaction has done good, and if we could always be certain of securing such a result, everything would be in favour of the first method of treatment. It frequently happens however that a severe reaction does so much damage that the local defensive powers are diminished to such an extent that the increased activity, instead of being only temperary, becomes permanent. This may not happen very often, but the fact that it does occur, shews that by producing a reaction, we are exposing the patient to danger.

The first method of treatment may therefore occasionally have successful results, but it exposes the patient to the discomforts and possible dangers of bad reactions, which are quite unnecessary.

In the "reactionless method" we avoid reactions altogether, and in so doing give the tuberculin in extremely minute doses and with a very gradual increase /

:crease of dose. In this method we are apt to err on the side of over-cautiousness. Certainly this is more advisable than rashness, but on the other hand we may not get the full use of the remedy, and the stimulation necessary for the adequate production of antibodies is not applied because of the constant dread of the production of a manifest reaction. In this method the patient experiences no discomfort whatever.

What is wanting in these methods of administer-:ing tuberculin, is some means of control. I have already shewn that the Opsonic Index cannot be trusted, and clinical evidence is of no use in a proper treat-ment, because if the treatment is a correct one no clinical signs are produced.

It should be remembered that reactions may occur without being clinically evident. These re-actions do as much good as manifest reactions, and they are absolutely devoid of danger.

What should be aimed at in a course of treat-:ment is the production of reactions, but these re-actions should not be clinically manifest. It is these irritative actions that help to bring about a cure, but when they exceed a certain optimum they aid the progression of the disease.

I shall attempt to shew how such a course of treatment may be carried out by using the classifica-:tion of the neutrophiles as a control.

CLASSIFICATION OF NEUTROPHILES.

(See Frontispiece.)

As the result of the researches of Arneth, we have reached a much more advanced stage in the classification of leucocytes. To him we owe the classification of neutrophiles according to the forms of their nuclei. He has studied this classification in various diseases, including pulmonary tuberculosis. This subject has not been investigated to any extent, and indeed its value has not been proved. It has been found valuable as an aid to prognosis in certain acute diseases e.g. typhoid, pneumonia, diphtheria, etc. Its value in pulmonary tuberculosis has not been appreciated.

I shall try to prove its value in pulmonary tuberculosis not only as a help in <u>prognosis</u>, but also along with tuberculin as an aid in <u>diagnosis</u>. It also serves as a guide to appropriate <u>treatment</u> especially in the exhibition of tuberculin.

As has been mentioned, the classification of neutrophiles depends upon the forms of their nuclei. Arneth /

Arneth has formed five classes:-

In the first class the nucleus is composed of one part.

In the second class the nucleus is composed of two parts.

In the third class the nucleus is composed of three parts.

In the fourth class the nucleus is composed of four parts.

In the fifth class the nucleus is composed of five parts.

That is to say, the number of each class indicates the number of separate parts composing the nucleus e.g. in the first class, no matter how complicated the nucleus is, if the nuclear matter is continuous all through it, the nucleus consists of one part.

The separate parts of the nucleus may be of various shapes - looped, ovoid, etc. - regular or irregular in outline.

In classes two to five a separate part is only considered as separate if there is a loss of continuation of nuclear matter except by a single thread. Two parts of the nucleus may be leaning against one another or overlapping though the nuclear matter is not continuous. These of course are considered as separate parts.

It must be noted that the number of lobes of which ~~is~~ the nucleus is made up is not considered unless these lobes are distinctly separate from one another except by a very fine thread.

A nucleus, though consisting of only one part, may be very much lobed. It belongs to Class I.

This distinction is necessary because otherwise it would be difficult to decide to which class certain polymorphs belonged. It prevents a large amount of overlapping.

Arneth in his investigation of the neutrophiles of the blood, not only subdivided these into five classes, but subdivided each class according to the shape of each separate part of the nucleus e.g. - Class I he divided into three sub-classes which he called:-

(1) myelocytes (M)
(2) slightly indented (S)
(3) deeply indented (D).

The other classes are subdivided according to whether the separate parts of the nucleus consist of loops or ovoids e.g. - Class II is divided into three parts viz.-

(1) two ovoids (2,O);
(2) two loops (2,L);
(3) one ovoid and one loop (1,O; 1,L).

Similarly, the other classes are divided up and are represented by letters as shewn in the following /

:lowing table which represents that of a normal blood:-

CLASSIFICATION OF POLYMORPHS.

1			2			3				4					5				
M	S	D	$_2O$	$_2L$	$_1O_1L$	$_3O$	$_3L$	$_1L_2O$	$_2L_1O$	$_4O$	$_4L$	$_3O_1L$	$_3L_1O$	$_2O_2L$	$_5O$	$_4O_1L$	$_3O_2L$	$_4O_2L$	$_3O_3L$
	5	14	3	30	23	4	7	8	2	2		1			1				
19%			56%			21%				3%					1%				

It requires the study of a large number of blood films to gain confidence in one's judgment of these corpuscles and to enable one to rely on one's observations so as to produce comparable results.

In making the films special care must be taken and a most important matter is the proper choice of stain.

The blood film is prepared in the usual way, dried, and then stained. Arneth used Ehrlich's triacid stain because it is specific for neutrophile granules, but I find that it is not intense enough for the nuclei. I have tried numerous stains and have chosen Wrights as the best for this work. I have found that it stains nuclei more definitely and more markedly than any other; clearness of outline being of the greatest value in this investigation.

It is necessary to use the oil immersion lens to examine these films. The first hundred neutrophiles are carefully examined and relegated to their various classes. A percentage is thus obtained of the number of polymorphs in each class.

Arneth /

Arneth has published a table of the neutrophile classification of normal blood, his table being the average of fifteen normal cases. My normal table is the average of twenty normal blood films. It does not agree with Arneth's. Appended will be seen Arneth's classification as well as my own.

CLASSIFICATION OF POLYMORPHS. (Arneth)

1			2			3				4					5				
M	S	D	$_2O$	$_2L$	$_1O_1L$	$_3O$	$_3L$	$_1L_2O$	$_2L_1O$	$_4O$	$_4L$	$_3O_1L$	$_3L_1O$	$_2O_2L$	$_5O$	$_4O_1L$	$_3O_2L$	$_4O_2L$	$_3O_3L$
	2	5	2	23·4	11·6	2·2	5·6	16·66	16·4	3·8	·07	6·4	·6	4·7	1	·4	·4	·07	·07
5%			35%			41%				17%					2%				

CLASSIFICATION OF POLYMORPHS. (my own)

1			2			3				4					5				
M	S	D	$_2O$	$_2L$	$_1O_1L$	$_3O$	$_3L$	$_1L_2O$	$_2L_1O$	$_4O$	$_4L$	$_3O_1L$	$_3L_1O$	$_2O_2L$	$_5O$	$_4O_1L$	$_3O_2L$	$_4O_2L$	$_3O_3L$
	4	14	1	33	20	3	5	9	6	2	1	1				1			
18%			54%			23%				4%					1%				

The differences in the two tables may be accounted for by my regarding every nucleus as consisting of one part unless the parts composing it are absolutely separate or connected only by the finest thread.

This accounts for my larger number of corpuscles in classes I and II and the smaller number in Classes III, IV, and V.

The subdivision of the five classes into subclasses according to the shape of the component parts is a refinement which I do not consider necessary.

I have used it in all my blood examinations till recently, but I have found that it is not of much value and that simple classification into Arneth's five original /

original classes is all that is required.

Examination of numerous films of blood from phthisis patients shews various blood pictures whihh on investigation may be tabulated to demonstrate the various classes of neutrophiles. The total number of leucocytes varies also, but I do not propose to investigate this to any extent.

It may be mentioned however that in pulmonary tuberculosis the total leucocyte count seems to alter within a very short period of time. Thus, if the leucocytes are counted at various periods of the day, large variations may be found, the total count sometimes being nearly doubled in the space of two hours. What this variation is due to it is difficult to say, as it does not seem to vary in proportion to temperature, exercise, nor food. This variability makes the total count of little value.

We can associate the condition of the patient with a certain blood picture. The very acute case of pulmonary tuberculosis shews a large number of corpuscles in Classes I and II, especially so if the case is not only acute but very advanced. In the early case with very little general disturbance the blood table may be practically normal.

The value of the dassification of a particular blood depends on the amount of leucocyte destructim which /

which is taking place. When an infective process is actively proceeding, there is presumably much destruction of leucocytes. These leucocytes are replaced as rapidly as possible. The new corpuscles are however much younger members whose nuclei are much less complex.

Therefore although leucocytes belonging to all classes are destroyed, they are replaced only by leucocytes belonging to Class I.

Thus it is that when an infective process is very active the percentage of neutrophiles in Class I is very high.

But not only are the nuclei of the new leucocytes composed of only one part but they are very re:gular in outline. They are mostly simple loops without any lobes.

The following are some examples of classifications from actual cases:-

(a) Very early case. No general disturbance. Diagnosis made by Tuberculin Test.

1			2			3				4					5				
M	S	D	$_2O$	$_2L$	$_1O_1L$	$_3O$	$_3L$	$_1L_2O$	$_2L_1O$	$_4O$	$_4L$	$_3O_1L$	$_3L_1O$	$_2O_2L$	$_5O$	$_4O_1L$	$_3O_2L$	$_4O_2L$	$_3O_3L$
	6	19	5	33	20	4	1	9	0	1		1							
	25%		58%			15%				2·%					0 %				

(b) Early case. No general disturbance. Diagnosis made by Tuberculin Test. Slightly more active than (a).

1			2			3				4					5				
M	S	D	$_2O$	$_2L$	$_1O_1L$	$_3O$	$_3L$	$_1L_2O$	$_2L_1O$	$_4O$	$_4L$	$_3O_1L$	$_3L_1O$	$_2O_2L$	$_5O$	$_4O_1L$	$_3O_2L$	$_4O_2L$	$_3O_3L$
	6	27	4	20	30	2	1	8	1			1							
	33%		54%			12 %				1%					0%				

(c) Early case. Febrile with temperature of 100-101° F. every evening.

1			2			3				4					5				
M	S	D	$_2O$	$_2L$	$_1O_1L$	$_3O$	$_3L$	$_1L_2O$	$_2L_1O$	$_4O$	$_4L$	$_3O_1L$	$_3L_1O$	$_2O_2L$	$_5O$	$_4O_1L$	$_3O_2L$	$_4O_2L$	$_3O_3L$
	7	25	3	28	27	1	1	7	0			1							
32%			58%			9%				1%					0%				

(d) Case - stage II. Mixed infection. (Staphylococcus aureus). Evening temperature 100-102° F.

1			2			3				4					5				
M	S	D	$_2O$	$_2L$	$_1O_1L$	$_3O$	$_3L$	$_1L_2O$	$_2L_1O$	$_4O$	$_4L$	$_3O_1L$	$_3L_1O$	$_2O_2L$	$_5O$	$_4O_1L$	$_3O_2L$	$_4O_2L$	$_3O_3L$
1	20	43	3	10	20		1	2											
64%			33%			3%				0%					0%				

(e) Very advanced case. Both lungs - stage III. Died 22 hours after blood film taken.

1			2			3				4					5				
M	S	D	$_2O$	$_2L$	$_1O_1L$	$_3O$	$_3L$	$_1L_2O$	$_2L_1O$	$_4O$	$_4L$	$_3O_1L$	$_3L_1O$	$_2O_2L$	$_5O$	$_4O_1L$	$_3O_2L$	$_4O_2L$	$_3O_3L$
2	20	50	5	3	19			1											
72%			27%			1%				0%					0%				

Reliability of the Neutrophile Classification.

I have found that this classification is remarkably constant. It is not subject to accidental fluctuation in any way. The same classification will be found day after day. If any marked change takes place, it may be assumed that something radical has occurred to produce it.

I /

I have examined films taken at various times after a meal and have come to the conclusion that diet does not affect the classification in any way.

As regards exercise, no effect is produced in the blood of a healthy individual, no matter how much energy is expended. In a tuberculous individual, however, if the exercise is excessive, auto-inoculation occurs. If this is very marked, it has an effect on the classification of the neutrophiles. It causes a deterioration.

A dose of tuberculin has no effect on the blood of a healthy individual. If however the individual be tuberculous, a dose of tuberculin has a marked effect on the blood. This will be discussed fully later.

Sleep has no effect.

If any change is produced in the classification, some time is required to bring it about. An hour or two is not long enough to effect a change. It requires at least twenty four hours before the alteration becomes appreciable.

FORMS of TUBERCULIN.

There are now numerous varieties of tuberculin. Undoubtedly, these tuberculins differ in value if they are all used in the same manner. This difference however is probably only one of degree as they all contain the same active principle viz. the toxin of the tubercle bacillus, but the amount of this toxin varies in the different forms of tuberculin. The amount of foreign matter, especially foreign albumin (non-specific) present in tuberculin also alters the effect produced on the body. In other words, some tuberculins are purer than others.

It may be concluded therefore that all tuberculins contain the same active principle, but that they differ in strength and purity according to the method of their preparation. As long as we remember this and use a preparation accordingly, we can meet with success by using any form of tuberculin.

I have always used Koch's preparations.

Koch's Old Tuberculin is a filtered glycerine extract of virulent bacilli (human) reduced by evapo-

:ration to 1/10th its original bulk. I use this preparation in both diagnosis and treatment. For the sake of convenience, in this thesis, I will designate this tuberculin "T.K." (Tuberculinum Kochi).

Another preparation which I use in treatment is one made in exactly the same manner as T.K., but for its preparation bovine bacilli are used. This tuberculin I will call "P.T." (Perlsucht-Tuberculin). Similar to this but not evaporated to 1/10th of its bulk is "P.T.O." (Perlsucht- Tuberculin-Original).

The above three preparations are those which I have been using for some time and I have found them quite satisfactory.

I think it safer to begin the treatment with a bovine preparation, as the patients do not have the same tendency to react to it as in the case of a human preparation. I therefore always begin treatment with a small dose of P.T.O. with increasing doses up to 1 c.c. I next proceed with P.T. and continue with it until the patient has had 1 c.c. I then follow this up with T.K. up to 1 c.c. This forms a complete course of treatment, but, as will be shewn later, every patient does not undergo a complete course.

I have also used Koch's Tubercle Bacilli Emulsion ("T.E.") made from human bacilli, but have now given it up, having found the other forms more satis-:factory.

Method /

Method of Dilution of Tuberculin.

Tuberculin in the pure state keeps indefinitely, but the dilution, especially the weaker dilutions, do not keep well. It is therefore advisable that these should be made up immediately before use.

I prepare my dilutions in strength of the value of multiples of 10. This simplifies the process very much.

The diluent is normal saline solution to which is added sufficient pure carbolic acid to make the resulting fluid a .5% carbolic solution. The carbolic acid acts as a preservative.

I store the solution in rubber-stoppered glass bottles of about 12 c.c. capacity.

Several 1 c.c. glass pipettes and one 10 c.c. glass pipette are required for the dilution, which is carried out as follows:-

To 1 c.c. of the pure tuberculin 9 c.c. of the diluent are added so that 10 c.c. of a 1-10 dilution are produced. If 1 c.c. of this dilution is made ~~is made~~ up to 10 c.c. with the carbolic saline solution we get a dilution of 1-100. Similarly, we can get a dilution of 1-1000, 1-10,000.

From these dilutions we can measure any dose we require by means of a syringe accurately graduated into tenths. Thus:-

.1 /

.1 c.c. of dilution	1-10	= .01 c.c.	tuberculin
.2 c.c. "	1-10	= .02 c.c.	"
.35 " "	1-10	= .035 "	"
.1 " "	1-1000	= .0001 "	"
.2 " "	1-1000	= .0002 "	"
.95 " "	1-10000	= .000095	"

In this way we can accurately measure any dose we require.

By the above method we make up at least 10 c.c. of each dilution. If we have not many patients under treatmen t, most of this would be wasted as it would be too old before we could use it up. In this case it is better to make up smaller quantities. This is best done by means of a 1 c.c. glass pipette accurately divided into tenths. By adding .9 c.c. of the diluent to .1 c.c. of the pure tuberculin we get 1 c.c. of dilution 1-10. If 1 c.c. is not enough for the occasion then another 1 c.c. can be made up at once. The other dilutions can be made up in the same way. We can thus make our dilutions every mornin g, and feel satisfied that we are using absolutely fresh solutions.

In the administration of tuberculin I pay no attention to the actual weight of tuberculin in each di-:lution. I know that each dilution always contains the same amount, and I know the amount in volume of a particular dilution which I can safely inject. The weight varies in the same proportion as the volume. The consideration of the actual weight is therefore not necessary and only leads to confusion.

Site /

Site of Injection.

I always inject tuberculin into the upper arm. By plunging the needle of the syringe straight through the skin, no pain is experienced. The choice of the upper arm is merely for convenience - especially in the Dispensary.

A reaction at the site of injection so seldom occurs that none of my patients ever lose a day's work because of a painful arm.

The /

THE EFFECT OF TUBERCULIN ON THE BODY.

When tuberculin is exhibited in proper doses hypodermically it produces certain effects on the body if the individual be tuberculous. The sum of thes e effects is known as the Tuberculin Reaction. The same doses of tuberculin given to a healthy person produces no effect. The Tuberculin Reaction presents the following leading features.

1. A General Reaction distinguished by fever with temperature rising to 100° F. or higher. There may be shiverings, headache, vague pains in various parts of the body e.g. limbs, joints, back and occasional nausea and vomiting. Accompanying this reaction there is also some reaction in the blood with which I propose to deal more fully later.

2. A Focal Reaction which occurs at the site of the tuberculous disease and consists of an exacerbation or increase of symptoms and signs, for instance, in tuberculosis of the lung there is increased cough and spit with the appearance or increase of crepitations /

:tions in the part affected; in tuberculous glands, redness and signs of inflammation ensue.

3. A Local Reaction, which occurs at the site of injection and consists of redness, swelling, hardness and pain, not unlike the onset of an abscess, though an abscess never occurs. This is also called by some the "Needletrack Reaction".

Under "General Reaction" I alluded to chan ges which occur in the blood. These changes I consider of such importance that they form the chief subject matter of the present thesis.

Effect on the Blood.

In the first place the changes which take place as the result of a dose of tuberculin only occur in tuberculous individuals. The chief change occurs in the leucocytes, the erythrocytes shewing no change of importance. First of all, the total leucocyte count is increased. Secondly, there is an alteration in the proportion of the varieties of leucocytes. Third, and most important, there is an alteration in the classification of the neutrophiles.

As regards the first the increase of leuc ocytes is not marked after one dose of tuberculin, even a re:acting dose, but the total count may be increased by about 25%. Occasionally I have seen a very ma rked leucocytosis occurring after a dose of tuberculin.

As /

As I have already noted, the total leucocyte count varies within very short periods of time. This makes it difficult to estimate the changes due solely to the tuberculin.

As regards the second, there are four chief varieties of leucocytes viz.-

(1) polymorphs or neutrophiles;
(2) lymphocytes;
(3) eosinophiles;
(4) basophiles.

We have also what are considered as varieties of lymphocytes -

Large mononuclears

and

Transitionals.

If we make them separate varieties of leucocytes we have six varieties.

There seems to be a slight decrease in the proportion of lymphocytes in the total count.

In the eosinophiles there is a marked increase.

The basophiles seem to shew no change.

The mononuclears shew a marked increase.

The transitionals shew a very marked increase.

The changes in these corpuscles are not of any importance in relation to the value of the blood in the administration of tuberculin.

The proportion of neutrophiles remains practically the same or if anything is slightly decreased; but the actual /

II

BLOOD.

Name, John Chapman Age, 13 Disease, Phthisis

Time.		Leucocytes.					Classification of Polymorphs.																					Remarks.
Date.	Hour.	No. per CMM	Varieties.				1			2			3				4					5						
			P	L	E	B	M	S	D	$_2O$	$_2L$	$_1O_1L$	$_3O$	$_3L$	$_1L_2O$	$_2L_1O$	$_4O$	$_4L$	$_3O_1L$	$_3L_1O$	$_2O_2L$	$_5O$	$_4O_1L$	$_3O_2L$	$_4O_2L$	$_3O_3L$		
3-4-12	10 a.m.	9,500	77	20	3	0		6	26	3	24	24	4		6	5			1			1						6 days after
								32%			51%				15%				1%					1%			
4-4-12	10 a.m.	10,600	65	33	2	0		1	25	7	23	24	2	1	5	10	1		1									7 " "
								26%			54%				18%				2%					0%			
5-4-12	10 a.m.	10,400	67	32	0	1		3	24	6	21	26	2	1	6	10			1									8 " "
								27%			53%				19%				1%					0%			

I

BLOOD.

Name, John Chapman Age, 13 Disease, Phthisis.

Time.		Leucocytes.					Classification of Polymorphs.																											Remarks.
			Varieties.				1			2			3				4					5													
Date.	Hour.	No. per CMM	P	L	E	B	M	S	D	$_2O$	$_2L$	$_1O_1L$	$_3O$	$_3L$	$_1L_2O$	$_2L_1O$	$_4O$	$_4L$	$_3O_1L$	$_3L_1O$	$_2O_2L$	$_5O$	$_4O_1L$	$_3O_2L$	$_4O_2L$	$_3O_3L$									
26-3-12	3·15 p.m.	12,000	66	33	1	0		2	22		29	27	1	2	9	4	1		2		1													Before Tuberculin
								24%			56%				16%				4%					0%									
27-3-12	10 a.m.	10,000	69	30	0	1		3	24		23	31	2	4	8	3	1						1											" "
								27%			54%				17%				1%					1%									
27-3-12	7 p.m.	11,000	72	25	2	1		3	22		25	33	3	2	9	2			2															" "
								25%			58%				15%				2%					0%									
28-3-12	11-30 a.m.																																	
								T. K. 001 c.c.																											
28-3-12	5-30 p.m.	9600	60	40	0	0		2	22	1	26	18	7	3	15	3			2				1											6 hours after
								24%			45%				28%				2%					1%									
29-3-12	9 a.m.	10,700	70	30	0	0		5	34	2	13	22	1	1	8	10	2			1	1													20 " "
								39%			37%				20%				4%					0%										T = 100·2°F.
29-3-12	5-30 p.m.	11,500	64	35	1	0		1	37	4	18	26	2	2	6	2			2															30 hours after
								38%			48%				12%				2%					0%										T = 103·0°F.
30-3-12	10 a.m.	12,700	70	20	8	2	0	4	42	2	18	24	1	1	2	5			1															46 hours after
								46%			44%				9%				1%					0%									
30-3-12	5-30 p.m.	10,300	71	22	7	0		1	51		21	20	1	2	3	1																		54 " "
								52%			41%				7%				0%					0%									
31-3-12	9 a.m.	11,200	68	26	5	1		5	61	1	16	15			2																			69 " "
								66%			32%				2%				0%					0%									
1-4-12	6 p.m.	9,800	56	40	3	1		3	34	3	26	23	2	2	5	1			1															4 days after
								37%			52%				10%				1%					0%									
2-4-12	4 p.m.	9,500	57	40	3	0		2	34	1	23	29	3	2	4	1	1																	5 " "
								36%			53%				10%				1%					0%									

actual number of neutrophiles is probably increased.

Changes in the Classification of the Neutrophiles.

In the first place, I will shew the changes which occur as the result of a single dose of tuberculin which has produced a general reaction. For this purpose I have appended a chart shewing the result of examination of the blood at various times before and after the dose of tuberculin was administered.

Case 1. John Chapman, age 13, had a suspicious right apex. Slight morning cough and spit. Sputum negative. No fever. I decided to give him a diagnostic dose of tuberculin.

On March 28th 1912 at 11.30 a.m. I injected .001 c.c. T.K.. The following morning his temperature rose to 100·2° F., and that evening to 103°F. He had also other signs of reaction viz. - . headache, pain and redness at site of injection. There also appeared a few crepitations at the right apex.

I therefore concluded that the patient was suffering from phthisis.

As can be seen by his blood chart, the classification of the neutrophiles before the dose of tuberculin was injected was nearly normal.

After the dose of tuberculin, his blood gradually deteriorated. Six hours after there was no appreciable /

:ciable change. Thirty hours afterwards a change became evident, a great number of the neutrophiles being included in Class I. Class III remained about the same as before, but the number of neutrophiles in Class II was reduced. At forty six and fifty four hours afterwards this change became more evident, the neutrophiles in Class I increasing at the expense of Classes II, III, and IV. Sixty-nine hours afterwards i.e. practically three complete days after the dose of tuberculin, the blood count reached its lowest value. As can be seen on the chart the classification at that time was :-

1	2	3	4	5
66%	32%	2%	0%	0%

Most of the leucocytes were now in ClassI. This shews a marked change from the original classification

From this time the blood gradually returned to its previous value. This occupied about four days.

The complete cycle therefore lasted seven days.

In this case the temperature rose to 103° F. A study of the blood chart will shew that the blood began to change just before the temperature began to rise.

The temperature reached its highest point thirty hours after the tuberculin was injected, whereas the blood reached its lowest value sixty-nine hours after the injection. This is probably accounted for by the fact that the blood-forming organs require more time /

II

BLOOD.

Name, John Borland Age, 6 Disease, Phthisis.

Time.		Leucocytes.					Classification of Polymorphs.																			Remarks.
Date.	Hour.	No. per CMM	Varieties. P	L	E	B	1 M	S	D	2 $_2O$	$_2L$	$_1O_1L$	3 $_3O$	$_3L$	$_1L_2O$	$_2L_1O$	4 $_4O$	$_4L$	$_3O_1L$	$_3L_1O$	$_2O_2L$	5 $_5O$	$_4O_1L$	$_3O_2L$	$_4O_2L$	$_3O_3L$	
3-3-12	10 a.m.	8.400	60	35	3	2		25	28	20	20	6		1													3 days after 2nd dose.
								53%			46%			1%				0%				0%				
4-3-12	10 a.m.	8,100	64	31	4	1		20	33	11	16	14	3	1		1				1							4 " " "
								53%			41%			5%				1%				0%				
5-3-12	10 a.m.	7.500	55	38	6	1		25	24	12	17	13	4	1	4												5 " " "
								49%			42%			9%				0%				0%				
6-3-12	10 a.m.	9000	65	31	2	2	1	13	26	9	19	13	5	3	8	1	2										6 " " "
								40%			41%			17%				2%				0%				
7-3-12	10 a.m.	7.900	62	32	3	3		5	19	5	29	20	2	3	13	2			1								7 " " "
								24%			54%			20%				1%				1%				

I

BLOOD.

Name, John Borland *Age,* 6 *Disease,* Phthisis

Time.		Leucocytes.					Classification of Polymorphs.																					Remarks.
Date.	Hour.	No. per CMM	Varieties. P	L	E	B	1 M	S	D	2 $_2O$	$_2L$	$_1O_1L$	3 $_3O$	$_3L$	$_1L_2O$	$_2L_1O$	4 $_4O$	$_4L$	$_3O_1L$	$_3L_1O$	$_2O_2L$	5 $_5O$	$_4O_1L$	$_3O_2L$	$_4O_2L$	$_3O_3L$	
21-2-12	10 a.m.	7.600	60	38	1	1		3	18		28	29	1	4	10	4	1			1			1					Before Tuberculin
			21%								57%				19%				2%				1%			
23-2-12	6 p.m.	7,000	65	32	3	0		4	19	5	25	29	2	4	9	2	1											" "
			23%								59%				17%				1%				0%			
25-2-12	2 p.m.	8000	70	28	2	0		5	15	2	35	23	3	4	11	1	1											" "
			20%								60%				19%				1%				0%			
26-2-12	11 a.m.																											
										T. K.			·0001 c.c.															
27-2-12	10 a.m.	7.900	62	35	1	2		7	18	4	29	27	1	6	7	1												1 day after.
			25%								60%				15%				0%				0%			
28-2-12	10 a.m.	8.500	60	37	2	1		9	22	10	31	20	1	2	4	0	1											2 " "
			31%								61%				7%				1%				0%			
29-2-12	10 a.m.	8600	57	36	5	2		14	28	9	24	19	2	3	1	0												3 " "
			42%								52%				6%				0%				0%			
29-2-12	11 a.m.																											
										T. K.			·0005 c.c.															
1-3-12	10 a.m.	9.100	61	32	5	1		12	28	9	23	19	4	0	3	1			1									1 day after 2nd dose
			40%								51%				8%				1%				0%			
1-3-12	6 p.m.	9.000	57	33	9	1		14	30	12	31	7	3	1	1	1												1½ " " T. 100·8° F.
			44%								50%				6%				0%				0%			
2-3-12	10 a.m.	7.100	59	34	7	0		12	38	7	29	10								1								2 " "
			50%								46%				3%				1%				0%			

time to produce and send new leucocytes into the blood stream after being stimulated to increased activity by the destruction of the already acting corpuscles.

This case shews very well the effect of a reacting dose of **T.K.** As will be shewn later exactly the same changes occur with a reacting dose of P.T.O. or P.T.

I will now shew the effects on the blood of a patient who had two doses of tuberculin with an interval of three days. The chief point to be noted is that the first dose did not produce a clinically evident reaction. A second larger dose was therefore given which produced a general reaction.

Case 2. John Borland, age 6, had very little cough; no spit. He did not take his food well and frequently vomited immediately after meals. No fever. Impaired note at the right apex, with bronchial breathing. I decided to give him test doses of tuberculin.

On February 26th 1912 at 11 a.m. I injected .0001 c.c. T.K. This produced no effect. Three days afterwards (29th February) at 11 a.m. I injected .0005 c.c. T.K. At 6 p.m. the following evening his temperature was 100.8° F. He had also headache and a marked reaction at the site of injection.

I therefore concluded that he was suffering from phthisis.

The /

The changes in the blood which occurred as the result of these doses of tuberculin are seen in the accompanying blood charts.

Before tuberculin was injected the classification of the neutrophiles was practically normal. The first dose of T.K., though it produced no clinically evident reaction, caused a marked change in the blood. One day after the first injection the blood was practically the same. Two days after, however, a change became evident, and exactly three days after the first dose, and immediately before the second injection was given, the changes were very marked. The number of leucocytes in class I was double the original number. The number in Class III was reduced to six.

The second dose of tuberculin which caused the general reaction, produced a further degeneration of the classification of the neutrophiles. The blood reached its lowest value three days after this dose. It then gradually recovered, and reached its original classification seven days after the second dose of tuberculin was given.

This case is very instructive. It shews that, although the first dose of tuberculin was not sufficient to produce a reaction (temperature etc.) it was enough to produce marked changes in the blood, and as these changes only occur if the individual be tuberculous /

BLOOD.

Name, Jean O'Mally Age, 23 Disease, Phthisis

Time.		Leucocytes.					Classification of Polymorphs.																					Remarks.
Date.	Hour.	No. per CMM	Varieties. P	L	E	B	1 M	S	D	2 $_2O$	$_2L$	$_1O_1L$	3 $_3O$	$_3L$	$_1L_2O$	$_2L_1O$	4 $_4O$	$_4L$	$_3O_1L$	$_3L_1O$	$_2O_2L$	5 $_5O$	$_4O_1L$	$_3O_2L$	$_4O_2L$	$_3O_3L$	
10-6-12	6 p.m.	8.000	60	38	0	2		19	25	13	17	16	4	1	1	1	1										Before Tuberculin
			44%							48%			7%				1%				0%					
11-6-12	2 p.m.	7.550	59	40	0	1		22	25	9	19	21	4														" "
			47%							49%			4%				0%				0%					
12-6-12	10 a.m.	8,790	67	33	0	0		13	29	17	27	7	2	3	0	2											" "
			42%							51%			7%				0%				0%					
12-6-12	11 a.m.																										
										T.K. .001 c.c.																	
13-6-12	10 a.m.	7.000	62	36	1	1		23	23	21	19	12	2														1 day after
			46%							52%			2%				0%				0%					
14-6-12	10 a.m.	7,550	56	40	3	1		25	20	18	20	5			1				1								2 " "
			55%							43%			1%				1%				0%					
14-6-12	11 a.m.																										
										T.K. .005 c.c.																	
15-6-12	10 a.m.	8.900	53	46	1	0		31	23	9	19	13	3		1		1										1 day after 2nd dose
			54%							41%			4%				1%				0%					
16-6-12	10 a.m.	9200	50	44	4	2		30	33	17	12	5	1	1			1										T. 101.2 07.
			63%							34%			2%				1%				0%					2 " "
17-6-12	10 a.m.	9.100	45	48	6	1		35	49	7	7	2															3 " "
			84%							16%			0%				0%				0%					
21-6-12	10 a.m.	8,500	50	46	3	1	1	27	23	11	18	16	2		2												7 " "
			51%							45%			4%				0%				0%					
24-6-12	10 a.m.	8,720	52	47	0	1		13	20	9	23	26	1	2	5	1											9 " "
			33%							58%			9%				0%				0%					

:culous, they are of great importance.

In both the above cases the classification of the neutrophiles before tuberculin was injected was very nearly normal. If the blood is of a lower value changes are produced in exactly the same way. The blood chart opposite shews this very well.

Case 3. Jean O'Mally, age 23, had a very suspicious right apex. Sputum negative. I therefore gave her test doses of tuberculin.

On 12th June 1912 I injected .001 c.c. T.K. which produced no clinical reaction. On 14th June I gave her .005 c.c. T.K., which on the following evening caused a temperature of 101.2° F. The reaction was therefore positive.

Her classification before tuberculin was far below normal as can be seen on the chart. After the first dose the blood deteriorated, although the temperature did not rise. The second dose caused the blood to deteriorate very markedly. On the third day after this dose the blood reached its lowest value At this time 84% of the polymorphs came under Class I and 16% under Class II. The other classes had none.

In this case the blood reached a lower value as the result of the tuberculin than the two previous cases, but it degenerated in the same proportion.

In Cases 2 and 3 it is seen that the second dose of tuberculin increased the changes in the blood which had /

BLOOD.

Name, Dora Saatmann Age, 24 Disease, Phthisis.

Time.		Leucocytes.					Classification of Polymorphs.																						Remarks.
Date.	Hour.	No. per cmm	Varieties. P	L	E	B	1 M	S	D	2 $_2O$	$_2L$	$_1O_1L$	3 $_3O$	$_3L$	$_1L_2O$	$_2L_1O$	4 $_4O$	$_4L$	$_3O_1L$	$_3L_1O$	$_2O_2L$	5 $_5O$	$_4O_1L$	$_3O_2L$	$_4O_2L$	$_3O_3L$	
26-3-12	12 a.m.	7.800	76	20	2	2		2	17	5	25	20	9	1	14	3	2		1		1						Before Tuberculin
								19%			50%			27%				4%					0%			
28-3-12	6 a.m.	6.500	80	20	0	0		4	16	4	29	20	3	2	13	7	2										" "
								20%			53%			25%				2%					0%			
11-4-12	10 a.m.	8120	70	25	2	3		3	15	9	26	19	1	4	17	3	1		1		1						" "
								18%			54%			25%				3%					0%			
12-4-12	11 a.m.																										
										P.T.O.			.0005. c.c.														
15-4-12	10 a.m.	8.200	65	30	5	0		7	32	9	24	12	3	1	2							1					3 days after.
								39%			45%			6%				0%					1%			
16-4-12	11 a.m.																										T. 99.6°7. following night.
										P.T.O.			.001. c.c.														
19-4-12	10 a.m.	8.100	64	32	4	0		14	39	11	16	17	2		1												3 days after 2nd dose
								53%			44%			3%				0%					0%			
22-4-12	10 a.m.	8.600	60	35	3	2		17	29	13	14	3	7	2	9	2	1		2					1			6 " " "
								46%			30%			20%				3%					1%			
25-4-12	10 a.m.	7.900	65	33	2	0		4	19	3	27	24	6	7	8	1			1								7 " " "
								23%			54%			22%				1%					0%			

had been initiated by the first dose. In the same way if a third dose had been given while the blood was suffering from the effects of the previous doses, the blood would deteriorate still further. If a general reaction had been produced by the second dose, this reaction would be accentuated by the third dose.

This is the course of events, if the blood is at or about its lowest value as the result of the previous doses.

Cases illustrating this will be found under DIAGNOSIS.

So far I have shewn the effect of T.K. on the blood. If P.T.O. or P.T. be given in doses which produce reactions, then exactly the same effect is produced on the blood. It is therefore unnecessary to repeat in detail what has already been said in regard to T.K. It will however be advisable to give one illustration as I always use P.T.O. and P.T. for treatment, and this effect on the blood is of importance in regulating the doses and the periods of time between the doses.

Case 4. Dora Saatmana, age 24, had right apical phthisis. I began her treatment with P.T.O., her initial dose being .0005 c.c. which I injected at 11 a.m. on 12th April 1912. She felt no bad effects from the dose and there was no rise of temperature. Four days later, on 16th April 1912, I gave her P.T.O. .001 c.c. i.e. double the previous dose. Her temperature rose the /

the following evening to 99.6° F. She had a slight headache and her arm was rather painful at the site of injection.

If her blood chart be examined, it will be seen that her classification was of very good value before tuberculin was given. The first dose of P.T.O. lowered the value considerably although it did not produce any clinical signs of a reaction. The second dose of P.T.O. which was given four days later when the blood was still suffering from the effects of the previous dose, caused a further deterioration in the blood, and also produced a general reaction.

I need not in the meantime give any more illustrations as they will be met with frequently under TREATMENT.

This shews that P.T.O. acts in the same way as T.K. in regard to its effect on the blood. The point of value to be noted is that THE BLOOD GIVES US A WARNING OF THE PROBABILITY OF A REACTION.

Having described the effect of a reacting dose of tuberculin and of succeeding doses of tuberculin each of which is given when the blood is suffering from the effects of the previous doses, I will now proceed to shew the course of events when we wait until the effect of one dose on the blood has passed off before we inject another dose.

For this purpose I will shew the effect when P.T.O./

II

BLOOD.

Name, Mrs Ross *Age,* 29 *Disease,* Phthisis

Time.		Leucocytes.					Classification of Polymorphs.																					Remarks.
Date.	Hour.	No. per c.mm.	Varieties.				1			2			3				4					5						
			P	L	E	B	M	S	D	$_2O$	$_2L$	$_1O_1L$	$_3O$	$_3L$	$_1L_2O$	$_2L_1O$	$_4O$	$_4L$	$_3O_1L$	$_3L_1O$	$_2O_2L$	$_5O$	$_4O_1L$	$_3O_2L$	$_4O_2L$	$_3O_3L$		
14-6-12	10 a.m.	8.000	69	30	0	1		3	23	7	24	25	4	1	9	1												
								26%			59%			15%				0%					0%					3 days after
15-6-12	11 a.m.																											
											P.T.O.	.003. c.c.																
18-6-12	10 a.m.	7900	65	33	2	0		9	18	9	25	26	3	1	7	1			1									
								27%			60%			12%				1%					0%					3 days after
19-6-12	11 a.m.																											
											P.T.O.	.004. c.c.																
22-6-12	10 a.m.	13.000	59	40	1	0		11	15	5	29	25	3	2	9	0			1									
								26%			59%			14%				1%					0%					3 days after
23-6-12	11 a.m.																											
											P.T.O.	.006. c.c.																

I

BLOOD.

Name, Mrs Ross *Age,* 29 *Disease,* Phthisis

TIME.		LEUCOCYTES.					CLASSIFICATION OF POLYMORPHS.																				REMARKS.
Date.	Hour.	No. per CMM	VARIETIES.				1			2			3				4					5					
			P	L	E	B	M	S	D	$_2O$	$_2L$	$_1O_1L$	$_3O$	$_3L$	$_1L_2O$	$_2L_1O$	$_4O$	$_4L$	$_3O_1L$	$_3L_1O$	$_2O_2L$	$_5O$	$_4O_1L$	$_3O_2L$	$_4O_2L$	$_3O_3L$	
8-5-12	7 p.m.	7500	75	25	0	0		2	26	4	27	26	3	0	10	0	1		1								Before P.T.O.
								28%			57%			13%				2%						0%			
9-5-12	10 a.m.	8.000	70	26	1	3		5	20	5	25	26	4	1	16	1	2							1			" "
								25%			56%			16%				2%						1%			
29-5-12	10 a.m.	7.900	69	28	2	1		3	15	7	29	27	3	2	13	0		1									" "
								18%			63%			18%				1%						0%			
30-5-12	11 a.m.																										
								P.T.O.					·001. c.c.														
2-6-12	10 a.m.	7.500	70	26	4	0		17	32	13	16	15	2	1	2	1		1									3 days after
								49%			44%			6%				1%						0%			
4-6-12	10 a.m.	8.100	71	27	0	2		2	16	3	39	20	3	9	5	1	1	1									5 " "
								18%			62%			18%				2%						0%			
5-6-12	11 a.m.																										
								P.T.O.					·0015. c.c.														
8-6-12	10 a.m.	8.500	65	32	3	0		26	24	13	13	16	3	4	0	1											3 days after
								50%			42%			8%				0%						0%			
10-6-12	10 a.m.	8.300	64	30	5	1		17	20	15	26	13	5	3	1	0											5 " "
								37%			54%			9%				0%						0%			
11-6-12	10 a.m.	7.900	63	29	7			16	19	17	39	6	2	3	5	3											6 " "
								25%			62%			13%				0%						0%			
11-6-12	11 a.m.																										
								P.T.O.					·002. c.c.														

P.T.O. is administered. I do this because my method of treatment depends on this principle. T.K. however acts in exactly the same manner.

In the first place it must be noted that if the dose of tuberculin is small enough, no appreciable effect will be produced in the blood. It will be advisable however to give first of all an illustration of a case in which the first dose lowered the value of the classification of the neutrophiles.

Case 5. Mrs Ross's blood charts will be seen opposite. She had right apical phthisis. Very early. I began her treatment with .001 c.c. P.T.O. which she took very well. It caused no rise of temperature and no discomfort. Examination of her blood however shewed that it had been affected to some extent as the value of her neutrophile classification was lowered. I waited until the blood had recovered its original value, which required five days, and on the sixth day after the first dose I gave .0015 c.c. P.T.O. This dose caused her no discomfort and no rise of temperature followed. Again however there was an effect on the blood. As can be seen by the chart the blood again deteriorated to the same extent as previously. I again waited until the blood had recovered. This required six days. I then administered .002 c.c. P.T.O. which produced no effect on the blood. Four days later I gave P.T.O. .003 and in other /

other four days .004. None of these doses produced any deterioration in the neutrophile classification.

In this case I increased the dose every time even although the previous dose had affected the blood but I waited each time until the blood had recovered before injecting another dose. In this way I not only prevented a reaction from occurring but made the blood less liable to be affected by the tuberculin, as the larger doses produced no effect on the classification, although the smaller ones had produced a marked effect.

If the first dose of tuberculin administered has no effect on the blood, the next dose may, or may not, have an effect. If any of the succeeding doses cause some deterioration, then the changes are exactly the same as occur if this dose is considered as the initial dose. These points are more fully considered under TREATMENT.

Neutrophile Classifications which are not affected by Tuberculin.

In the above patients the changes in their blood are quite evident. The value of their neutrophile classification makes marked changes possible. If however we have a case whose blood is already of very low value, for instance:-

1	2	3	4	5
60%	37%	3%	0%	0%

it /

it is evident that a very marked change cannot possibly take place. In these cases however tuberculin does not produce any effect. The classification remains much about the same, or it may degenerate to a very slight extent.

As will be pointed out later, these cases are not suitable for tuberculin treatment, and their diagnosis is usually settled by other means as they are almost certain to shew the tubercle bacillus in the sputum. The blood does not usually have such a low value if the disease is very early, even although it is acute. In those cases therefore we do not require to give tuber-:culin at all.

Measurement of Blood Change.

In comparing the neutrophile classification before and after a dose of tuberculin, there may be some difficulty in measuring the actual change which has taken place, owing to the fact that there are five classes.

The section in which the most important change takes place is Class I. This is so because the new corpuscles come into this division. Leucocytes belonging to all the classes are destroyed and these are re-:placed by corpuscles which come under Class I.

It is therefore chiefly by Class I that I measure any change which has taken place.

For instance, if the number of neutrophiles in Class /

Class I is doubled then I consider that the blood is now of half its original value. At the same time this may be modified if the number of corpuscles in Classes III and IV has remained the same or has increased. I pay little attention to Class II because the alteration in its number is evident by the alteration in the other classes.

Time Taken for Changes to Occur.

This is a matter of importance because by paying attention to it we can save ourselves a great amount of time and trouble.

As regards the time taken for the blood to reach its lowest value, it has been already noted that three days is the usual period. Therefore, if we examine the blood at any time during the third day after the dose of tuberculin we can be sure that if any change is going to take place we will not miss it. Not only so, but the examination at this time reveals the maximum change which will take place as the result of that dose of tuberculin.

It is therefore quite unnecessary to examine the blood every day after an injection.

The time taken for the blood to recover after a dose of tuberculin is however very variable. No definite period of time can be mentioned as being the usual /

usual.

First of all, if the change in the blood is very slight, the time taken to recover is usually very short - it may be one or two days. If there is a marked change in the blood, then it takes longer - it may be nine or ten days.

If the alteration of the classification is the result of several doses of tuberculin, each dose given while the blood is suffering from the effects of the previous dose, a much longer period is required for recovery than if the deterioration is due to a single dose of tuberculin. This is so even though the maximum degeneration in both cases is the same.

It is therefore often necessary to examine the blood on more than one occasion to discover when it has returned to its normal state.

My rule is to examine the blood every day after it has reached its lowest value if the change in the blood is slight. If there is a marked alteration, I examine it every second day until it has returned to its original condition.

The cases given under DIAGNOSIS and TREATMENT are all illustrations of this, and it would be superfluous to give examples here.

In the blood charts which I have shewn up to this point /

point, I have included the finer classification suggested by Arneth. As I have already mentioned this refinement is of no assistance, and in the remainder of this thesis its use will be dispensed with.

D I A G N O S I S.

Physical examination of the chest and the symptoms from which a patient may be suffering are not sufficient evidence of the presence of pulmonary tuberculosis. It is therefore necessary to have some means of clinching the diagnosis.

To secure this, we can employ two methods:-

1. Examination of the sputum for tubercle bacilli.

2. Administration of tuberculin in one of the following ways:-

   (a) Subcutaneous injection (Koch).

   (b) Opthalmic (Calmette).

   (c) Cutaneous

   by Vaccination (Von Pirquet)

   or Inunction (Moro).

1. Every case which comes under my observation has the sputum, if any, examined for tubercle bacilli. First of all by the Ziehl-Neelsen method, and if negative to this test, by the antiformin method.

If /

If no tubercle bacilli are found after three such examinations, or if the patient has no sputum, the patient is then subjected to the tuberculin test.

2. Of the various ways of administering tuberculin for the purposes of diagnosis I have found the subcutaneous method the most satisfactory.

Till recently I have used the temperature and other clinical signs as the evidence of a reaction. I now pay chief attention to the changes produced in the blood.

Temperature as Guide.

For the sake of clearness I will first of all give a short outline of the technique of the test in which the temperature is used as the indication of a reaction.

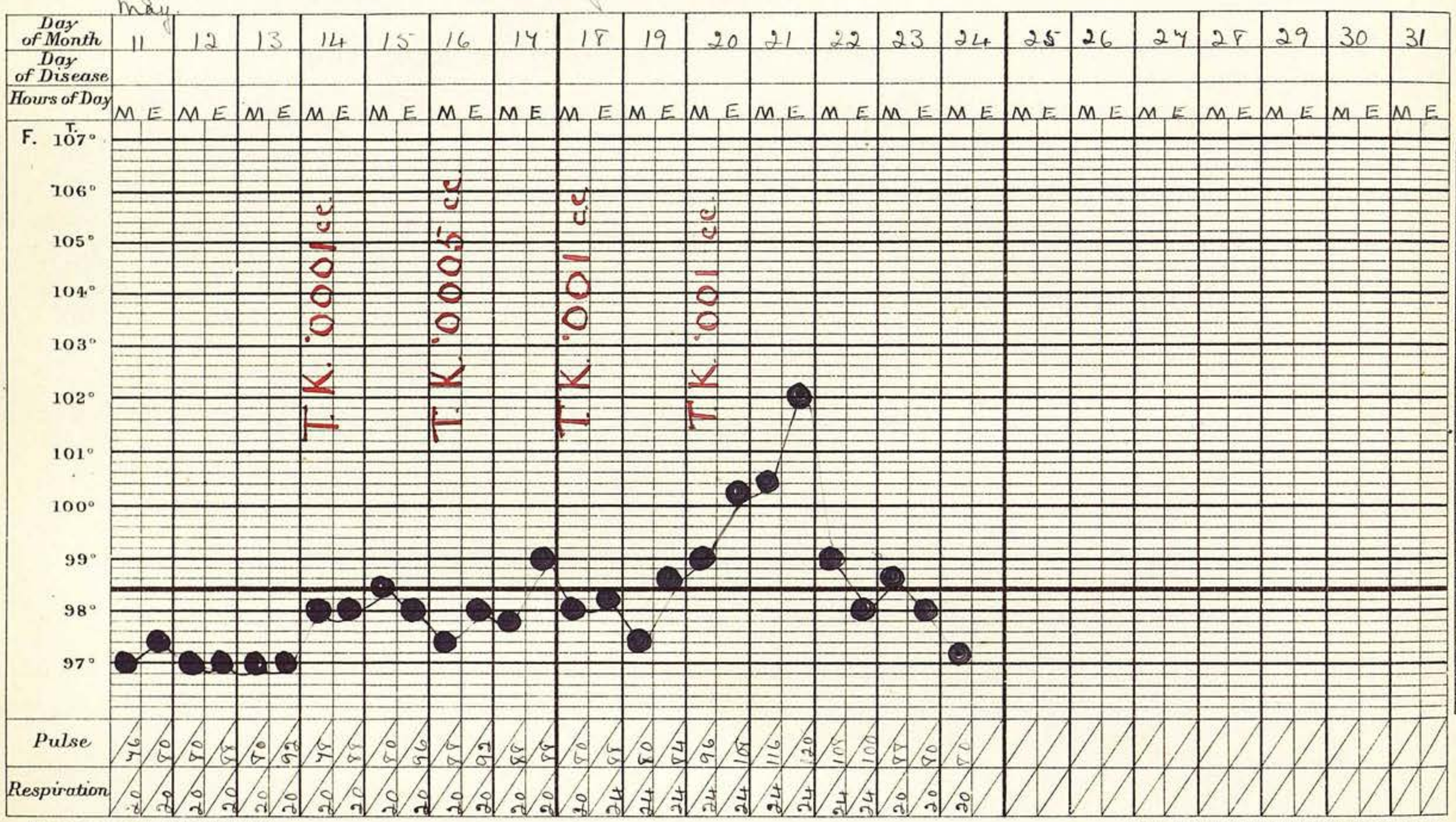
For all my test doses, I use Koch's Old Tuberculin (T.K.).

The temperature must be carefully noted at four hourly intervals for at least three days before a dose is given. If the temperature rises above 99° F. it is necessary to wait till it becomes, and remains, normal before a test dose is injected.

To be certain of a reaction the temperature must rise to 100° F. It is therefore necessary to take the temperature every four hours after the tuberculin is administered.

If the patient is under ten years of age .0001 c.c. T.K./

Name Agnes Ruthven Age 8 years Disease Phthisis Index No.



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T.K. is injected. If the temperature does not rise to 100° F. within forty-eight hours .0005 c.c. is injected. If this dose fails to produce the required temperature then .001 c.c. T.K. is given, and this is repeated in forty-eight hours if the necessary rise has not occurred. If these four doses fail to produce the required reaction, it may be taken for granted that the patient is not tuberculous.

In a patient of more than ten years of age, the technique is exactly the same, but the four doses given are :- .001; .005; .01 and .01 c.c. T.K.

Besides the temperature reaction, we may have of course other signs of reaction referred to in a previous paragraph. The most important of these is the Focal Reaction. This consists of an exacerbation of symptoms at the site of the tuberculous focus. In the case of the lungs, we have the appearance or increase of already present rales in the affected part, increase of sputum etc., etc.

Case 1. I have annexed a temperature chart to illustrate this test. An explanation is unnecessary.

Blood as Guide.

I will now describe the method I use for diagnosis in which the change produced in the blood is used as the indication of a reaction to the tuberculin. This method is made possible by the fact that tuberculin, unless given /

given in extremely large doses only causes changes in the blood of a tuberculous person. The value of it depends on the fact already demonstrated that changes are produced in the blood by a smaller dose of tuberculin than that necessary to cause a temperature reaction.

The blood charts shewn under EFFECT ON THE BLOOD are all illustrations of this method of test dosing. It is necessary however to go rather more fully into the subject.

I still consider T.K. the most suitable tuberculin for diagnostic purposes, and I still use the same sequence of doses.

If the temperature is taken as the indication of a reaction to a test dose, it is necessary that it should rise to 100° F. Anything under that, e.g. 99.6° F. is not conclusive. In the same way a certain degree of change in the classification of the neutrophiles is necessary before we can conclude that the test is positive.

We cannot say that the blood must deteriorate to a certain given value in every case before deciding that the test is positive, because the classification of the neutrophiles is so different in different individuals before the test doses are given. It is therefore necessary that the resulting classification should be measured as a proportion of the original classification /

Name John Peuthrer. Age 14. Disease Phthisis Index No.

Day of Month	25	26	27	28	29	30	31	1	2	3	4	5	6	7	8	9	10	11	12	13	14
	March.							April													
Day of Disease																					
Hours of Day	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E
T.	0	0	0		0	0	0			0				0							
Pulse	100 104	98 100	92 96	100 98	92 104	98 104	98 108	98 120	112 108	100 98	92 98	92 100	98 92	88 92							
Respiration	24 24	24 24	24 24	24 24	24 24	24 24	24 24	24 24	24 24	24 24	24 24	24 24	24 24	24 24							

F. 107° 106° 105° 104° 103° 102° 101° 100° 99° 98° 97°

C 41° 40° 39° 38° 37° 36°

21·60·18·1 | 22·61·17·0 | 19·58·21·2 | T. ·001 c.c. | 39·46·16·0 | 44·44·8·1 | T. ·005 c.c. | 45·45·9·1 | 62·33·4·1 | 54·35·10·0·1 | 40·48·11·1

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:tion.

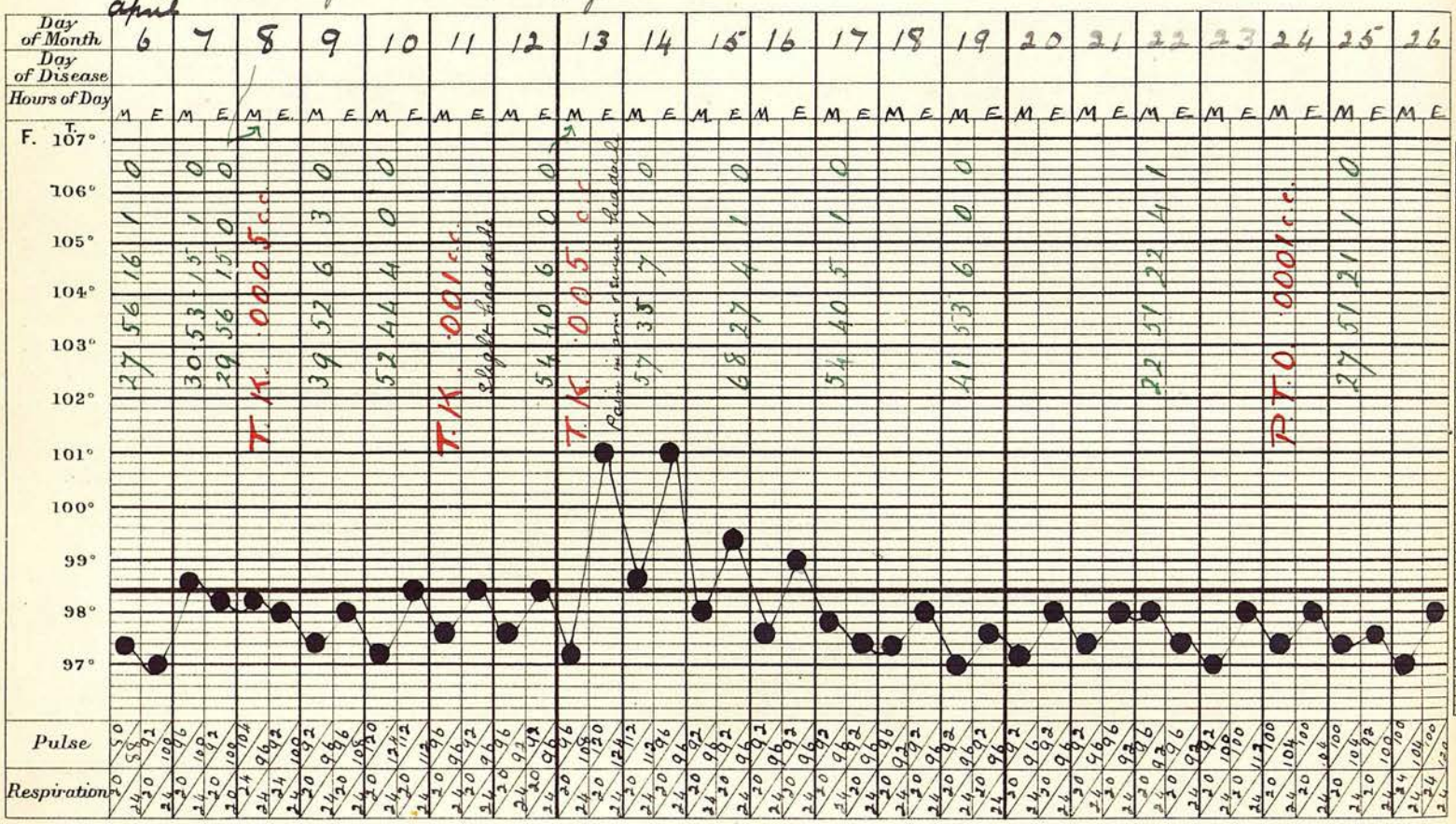
It may be taken as a general rule that the blood must degenerate to about half its original value before we can be certain that the test is positive. This rule requires modification in certain cases. These will be referred to later.

It must be noted that it occasionally happens that the dose of tuberculin required to produce the degree of change in the blood may also cause some rise of temperature. This however is very seldom the case. Case 1 (George Chapman) under Effect on the Blood illustrates this. The first dose caused the temperature to rise and also the blood to change.

To make this method of test dosing clearer I have annexed the temperature chart of a patient. In it the classification of the neutrophiles is marked in green ink, and the doses of tuberculin in red ink.

Case 2. John Peutherer, age 14 years, complained of weakness. He could not take his food well and had been losing weight for three months. On percussion the right apex was slightly tympanitic and the breathing was broncho-vesicular. He had no sputum. I could not say definitely that he was suffering from phthisis, and I therefore decided to give him test doses. As can be seen from the accompanying chart, I examined his blood on three occasions on different days before giving tuberculin. I found that his neutrophile classification /

Name Fraser Fordyce Age 14 years Disease Phthisis Index No.



:fication was practically normal.

On March 28th 1912 I injected .001 c.c. T.K. This produced a change in the blood, and on the evening of 30th March the classification of the neutrophiles was of less than half its previous value. Class I had been doubled, and Class III was reduced to less than half the original number. I therefore considered the test positive.

The temperature had not risen above 99° F. as the result of this dose. Merely for experimental purposes I gave another larger dose, viz. .0045 c.c. T.K. three days after the previous dose. This produced a temperature of 101.4° F. and also rather severe pains in the arm and head. The blood degenerated much further as the result of this dose.

In this case the second dose of tuberculin was quite unnecessary as I had clinched my diagnosis by means of the first dose although no temperature had been produced. It must also be noted that the first dose caused the patient absolutely no discomfort.

Case 3. To emphasise the importance of this I have appended the chart of another patient viz. Fraser Fordyce. In this case, although the first dose of tuberculin was quite sufficient to produce the required change in the blood, yet it was not sufficient to cause a temperature. It was not until the third dose had been /

Name Mrs Ross Age 29 years Disease Phthisis Index No.

Day of Month	may 6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26
Day of Disease																					
Hours of Day	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E
T.																					
Pulse	50 54	58 54	50 52	96 84	88 80	88 96	90 92	96 92	88 80	80 96	90 90	80 88	100 108	96 92	88 80	80 84	84 80	80 80	88 80	80 88	84 84
Respiration	20 20	20 20	20 20	20 24	20 20	20 20	20 20	20 20	20 20	24 24	24 24	20 20	20 24	24 20	20 20	20 20	20 20	20 20	20 20	20 20	20 20

	24 58 16 2	29 50 21 0	28 57 13 2	T.K. .001 c.c.		31 58 9 2	T.K. .005 c.c.		37 54 4 0	T.K. .01 c.c. Headache. Slight.		58 40 2 0	T.K. .01 c.c. Headache and pain all over body.		80 19 1 0				61 34 5 0	28 58 12 2	

F. 107° 106° 105° 104° 103° 102° 101° 100° 99° 98° 97°

C 41° 40° 39° 38° 37° 36°

been given that the temperature rose. The first injection caused no discomfort. The second caused slight headache. The third caused severe headache and pain in the arm as well as a temperature of 101° F. and also slight fever for the succeeding night or two.

As regards his blood the first dose did not quite double the leucocytes of Class I, but it reduced the numbers in Classes III, IV, and V to much below half. Altogether this change was quite sufficient to settle the diagnosis. The second dose caused the blood to deteriorate still further, as also did the third.

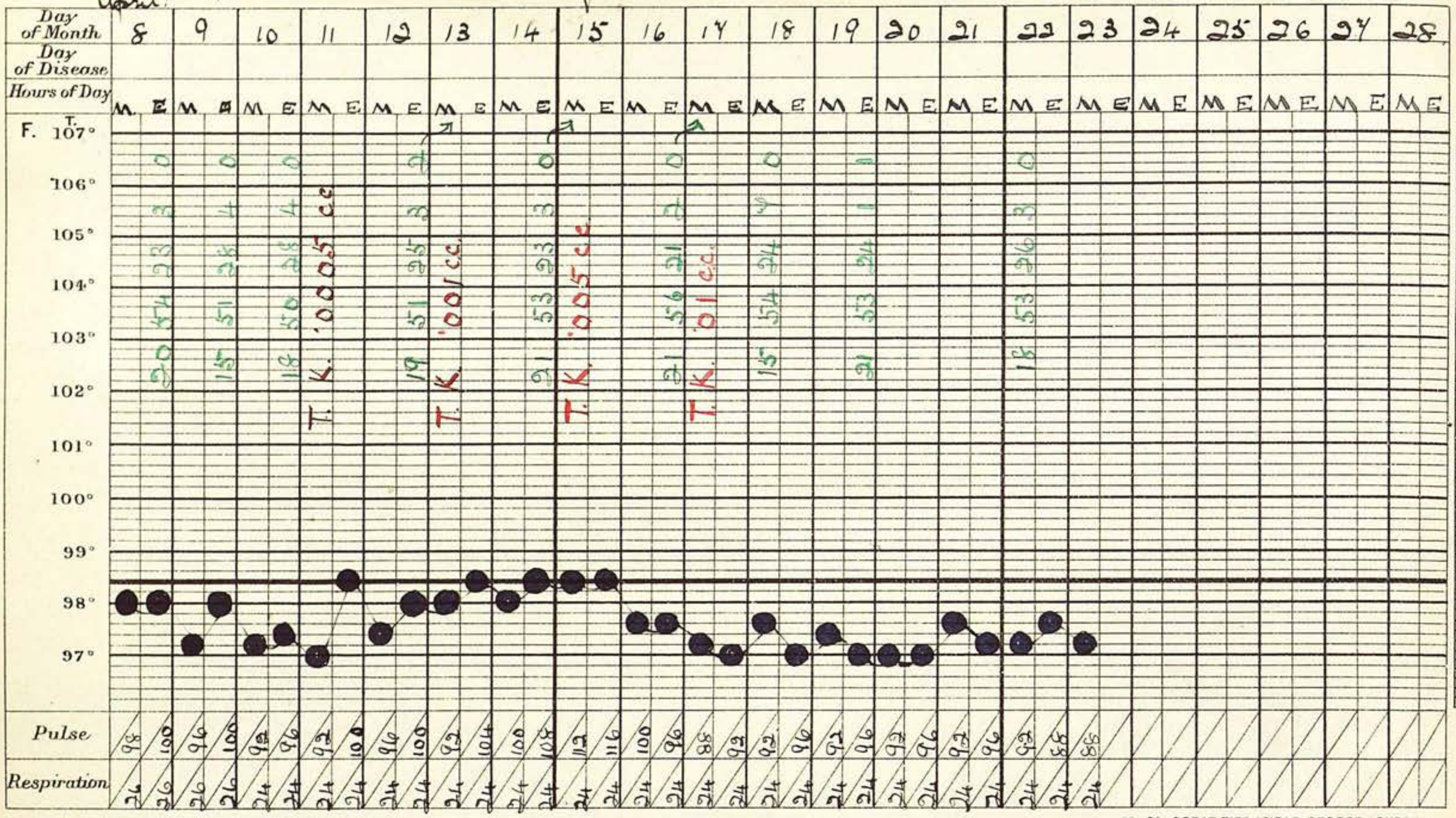
In this case also one dose was all that was required. The others were quite unnecessary and only caused the patient severe discomfort, and also exposed him to the possible danger of a bad reaction. It is however not always the first dose that causes the required change in the blood, but it is very unusual that more than two doses are required.

Case 4. Mrs Ross, age 29. In this case it was not until the fourth dose was given that the temperature rose. The third dose produced a satisfactory blood change.

Negative to Test Doses.

The cases I have already given to illustrate this method of diagnosis have all reacted to the test. I now give the chart of a patient who did not react to the /

Name Marjory Stuart. Age 4 Years. Disease Phthisis. ? Index No.



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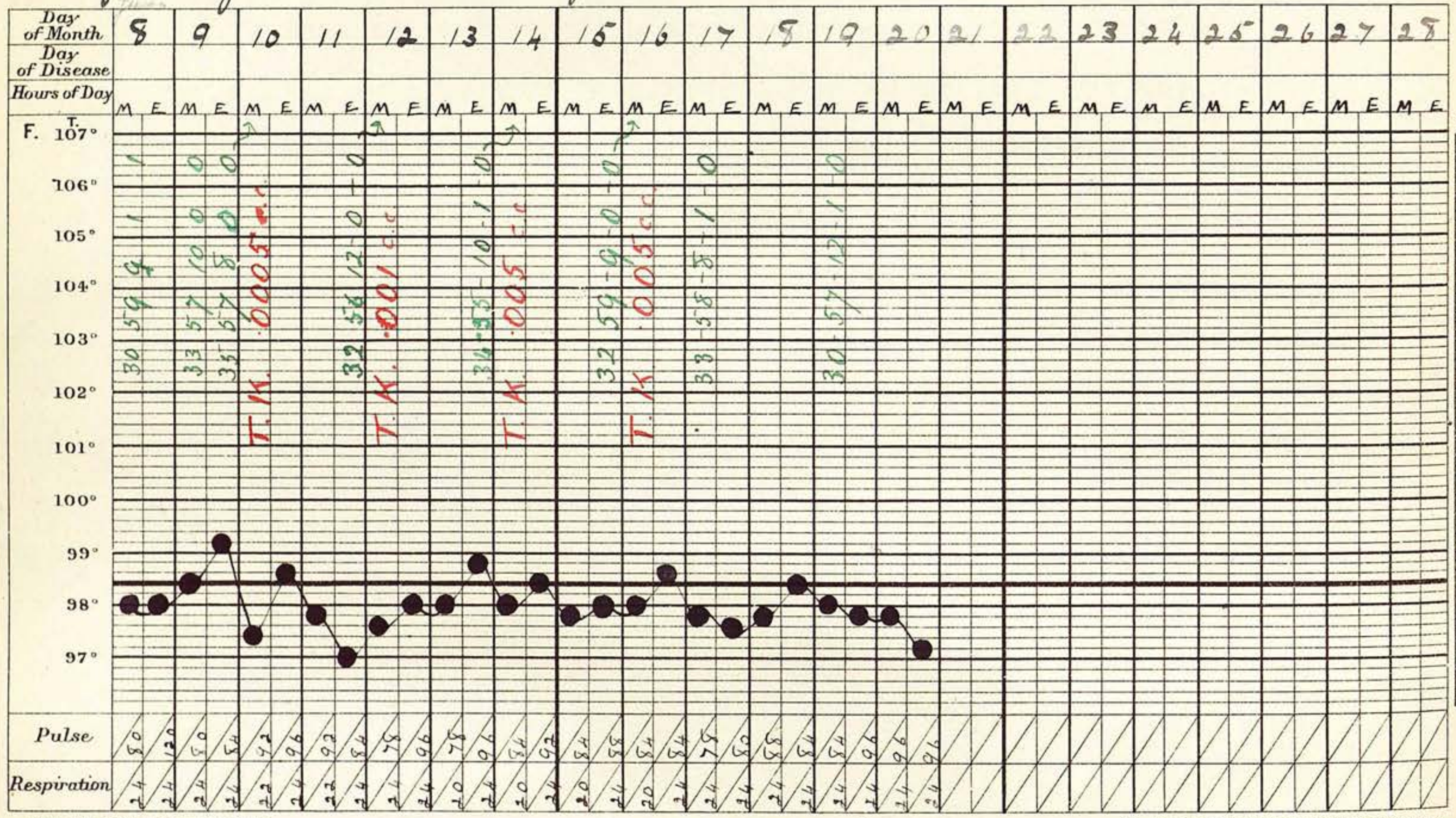
Name John Gordon Age 9 years Disease Phthisis ? Index No.



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the tuberculin neither by blood nor by temperature after having the four injections of tuberculin.

Case 5. Marjory Stuart, age 7 years, came to me on 8th April 1912 complaining of cough. She had been losing weight for two months. Three years ago she had an attack of pneumonia. Her mother suffers from phthisis. No sputum. Examination of the chest revealed nothing but broncho-vesicular breathing at the left apex.

On April 11th, I injected T.K. .0005 c.c. On the 13th, .001 c.c.; on the 15th, .005 c.c., and on the 17th, .01 c.c.. None of these doses caused any rise in temperature, nor was any effect produced in the blood. It can be seen from the chart that the classification of the neutrophiles was quite good before tuberculin was given, and remained quite good after the test doses were given.

I therefore concluded that she was not suffering from tuberculosis. I dismissed her from the Sanatorium. Four months later I saw her again. She was in excellent health.

Case 6. Another case similar to the above is that of John Gordon, age 9 years. He complained of morning cough and spit. Sputum negative. I gave him four test doses (See Chart). These caused no temperature and produced no change in the classification of the neutrophiles.

The last two cases are examples from a large number /

Name Janet Parves Age 35 years Disease Phthisis. Index N°

Day of Month	July 24	25	26	24	28	29	30	31	August 1	2	3	4	5	6	4	8	9	10	11	12	13
Day of Disease																					
Hours of Day	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E
T. F. 107°		0	0		0	0	0 1 cc		0	0		0		0							
106°		0	0		0	0			0	0		1		1							
105°		9	11		0	8	T. K.		4	2		6		8							
104°		38-53	35 54		53	54	0		39	33		43		53							
103°																					
102°					38	36			64	65		50		38							
101°																					
100°																					
99°																					
98°																					
97°																					
Pulse	96	100	96	100	100	96	88	96	100	104	96	88	108	96	98						
Respiration	22	22	22	22	22	22	22	22	22	22	22	22	22	22	22						

C 41° 40° 39° 38° 37° 36°

number which have led me to conclude that tuberculin produces no effect on the blood of a healthy person unless very large doses are given.

Test Dosing in Febrile Cases.

If the temperature is used as the indication of a reaction, a difficulty arises in those patients who are already running a temperature because any febrile reaction to the tuberculin cannot be distinguished from the pre-existing fever.

My method of test dosing overcomes this difficulty in most cases.

As a general rule if a patient is running a temperature the classification of the neutrophiles is of a lower value than in the case of an afebrile patient. If however the disease is fairly early, the classification is not of such a low value that a marked change in it cannot be observed.

In febrile cases, then, we can use the blood as the indication of a reaction in exactly the same way as in afebrile cases.

Case 7, is a good illustration of this. Janet Purves, age 35 years, was sent to me for diagnosis. She complained of cough and spit. She was losing weight, and suffered from breathlessness. She frequently vomited, and had no appetite for her food.

Physical /

Physical examination of her chest shewed slight dulness at the right apex with bronchial breathing.

She had an occasional rise in temperature in the evening (See Chart).

On July 30th I injected .001 c.c. T.K. This was followed by a slight headache and mild pains all over the body. The temperature continued to rise in much the same fashion as before. No importance could be attached to the temperature because it was impossible to tell how much, if any of it, was the result of the tuberculin injection.

A study of her blood however made it clear that she had reacted to the test doses and proved she was suffering from tuberculosis.

Before tuberculin was given her neutrophile classification was much below normal (See Chart). After the test dose the blood deteriorated markedly, the lowest value being reached on the third day, when the classification was of less than half the previous value.

Although the temperature charts of the above cases are twice daily records, the temperatures in every case were taken at four-hourly intervals before and after the test doses, by trained nurses.

Test /

Test Dosing in the Dispensary.

This method is of great value if we require to give patients test doses in their own homes or at the Dispensary.

It has already been noted that if the rise of temperature is used as the indication of a reaction, a four-hourly record both before and after injecting the tuberculin is necessary.

This is easily obtained if the patients are in the Sanatorium with a Staff of trained nurses. If howeverthe patients are living in their own homes, it becomes a serious difficulty.

It would scarcely be possible to expect trained nurses to visit the patients' homes every four hours, and if the patients are left to take their own temperatures, we cannot feel confident that they take them properly, or even that they take them at all.

By using the change in the classification of the neutrophiles as the indication of a reaction to tuberculin, we can neglect the temperature altogether. All that is necessary is to examine the blood before tuberculin is given and on the second or third day after each dose has been injected. It is better to make two examinations of the blood on different days before injecting the tuberculin.

I /

TUBERCULIN.

Aug. NAME George Muir Sept. AGE 16. DISEASE Phthisis.

DATE.	30	21	22	23	24	25	26	27	28	29	30	31	1	2	3	4	5	6	7	8	9
TUBERCULIN.			T.K. ·0001 c.c.			T.K. ·0005 c.c.		T.K. ·001 c.c.													
POLYMORPHS. 1	23	25	25			32		49		60			34		22						
2	67	64	63			60		44		35			58		59						
3	10	11	10			8		7		4			8		17						
4	0	0	2			0		0		1			0		2						
5	0	0	0			0		0		0			0		0						
REMARKS.								No discomfort.													

I prefer that patients should stay in bed during the period of test dosing, and this is the rule in the Sanatorium. In the case of out-patients however I do not press this point, and I have given test doses to patients who have been working all the time. They come to me for the injection of tuberculin, and return in three days, when I examine the blood, and if necessary give them another dose.

The fact that the test doses causes them no discomfort is of great weight in persuading them to attend regularly.

Case 8. I have appended the chart which I use for these patients in diagnosis. They take their own temperatures, but I attach very little importance to their records, unless the blood shews a corresponding change.

In this patient the test was positive. The temperature did not rise above 99° F.

Intervals between Test Doses.

When the blood has suffered from the injection of a dose of tuberculin it usually reaches its lowest value on the third day. It is therefore only necessary to examine the blood once, that is, on the third day after the dose has been given, to get the maximum effect of that injection. If the required change has /

has not been produced in the blood, a second dose is given immediately and the blood again examined in other three days. We should therefore give the test doses at intervals of three days.

If however the necessary loss of value is going to be produced by an injection the blood begins to change within a few hours, and if we examine the blood in forty-eight hours the loss of value is quite evident. If the examination in forty-eight hours shews no, or very little, alteration in the classification of the neutrophiles, we can take it for granted that the change necessary to denote a positive reaction will not take place with that dose, and we can immediately proceed to give another.

We can therefore frequently give test doses at intervals of forty-eight hours, but the only advantage in doing so is the saving of time. This is only possible however in the Sanatorium where we have facilities for frequent examination of the blood. In the Dispensary the three days interval is the most useful.

Cases of Pulmonary Tuberculosis which do not React to Test Doses.

There is a certain class of cases in which it is useless to give tuberculin for diagnostic purposes. This class includes those patients whose neutrophile classification is of such a low value that a dose of tuberculin /

tuberculin produces no appreciable effect on it, and the necessary alteration in the classification cannot possibly take place. These cases have already been mentioned under Effect on the Blood where it has been shewn that in a classification such as this:-

1	2	3	4	5
60%	37%	3%	0%	0%

tuberculin has practically no effect and the change necessary for a positive test cannot possibly take place.

If this classification is due to pulmonary tuberculosis the case is so acute and usually so advanced, that a positive diagnosis is always arrived at by other means, as the sputum is almost certain to contain tubercle bacilli. In fact these cases are so advanced that they do not react to tuberculin at all (vide "Tuberculin Reaction").

Cases in which a less marked Blood Change must suffice to denote a Positive Reaction.

If the classification of the neutrophiles before giving tuberculin is about the following value:-

1	2	3	4	5
47%	46%	6%	1%	0%

we cannot expect the blood to deteriorate to half that value. We must be content with a less marked change in /

in the neutrophiles. In these cases, if the test doses cause the blood to deteriorate to about the following value:-

1	2	3	4	5
80%	16%	3%	1%	0%

we may take it that the test is positive.

It is not often that we require to give test doses in these cases as they are usually diagnosed definitely by other means.

Value of Tuberculin in Diagnosis.

By giving test doses of tuberculin, we can tell whether there is a tuberculous focus in the body or not. It gives us no indication as to the site of this focus, and it does not help us to decide whether the disease is active or quiescent.

If a recognisable localised reaction occurs as the result of a test dose, for instance, the appearance of crepitations in the lungs, we can be certain that tuberculous disease is present in that situation. This however occurs in a very small percentage of patients, and it is my object in the administration of tuberculin to avoid a clinical reaction altogether as I believe it exposes the patient to danger unnecessarily.

If the tuberculous focus is latent, it causes no symptoms, the patient suffers no discomfort, and therefore /

:fore he requires no treatment. I consider it absurd to give diagnostic tuberculin to a person who has no complaint. If we did so, we would find that a majority reacted to the tuberculin, and we would be tempted to give tuberculin treatment when it was quite unnecessary, the disease being to all intents and purposes cured.

If however physical examination of a patient shews signs of the possible presence of tuberculosis in the lungs, even if the patient appears in good health and has no complaint, then I think it advisable to administer tuberculin for diagnostic purposes.

We meet such cases now and again in the examination of contacts.

In the case of a person who has an active focus of tuberculosis in the lung, it may affect him in a variety of ways. It may shew itself in the form of stomach trouble, heart weakness, nervous trouble, or the first sign may be in the joints as an arthritis. It may be that a general weakness is all that is complained of. In fact any organ or tissue in the body by shewing disturbance of function, may be the first to shew signs of the presence of tuberculosis in the lungs.

It is of the utmost importance that this peculiarity of tuberculosis should be kept in mind, and if we are called on to explain the presence of any such disturbance which cannot be accounted for in any other way, the /

the possibility of tuberculosis should always be in our thoughts. This possibility becomes stronger if ordinary means are not successful in getting rid of the troublesome symptoms. A thorough physical examination should be made. The sputum should be carefully examined for tubercle bacilli. Heredity and exposure to infection must be investigated.

If we cannot come to a definite diagnosis from information collected by the above means, the patient should be subjected to the Tuberculin Test.

It is in these cases that diagnostic tuberculin is of value. If the test is negative, we can eliminate tuberculosis as the ~~cause~~ *cause* of the mischief. If the test is positive, we have proof of the presence of a tuberculous focus in the body. This focus may or may not be in the lung, but in any case, it is more than likely the cause of the trouble, and if it is, treatment by means of tuberculin will complete the proof by causing the disappearance of the symptoms.

The test, if carried out as I recommend, can do the patient no harm, and it causes him no discomfort.

Therefore it may be conclusively asserted that the Tuberculin Test, if not considered alone, but as a link in the chain of evidence, is of extreme value.

P R O G N O S I S.

It is a matter of extreme difficulty to gauge the actual improvement taking place in a case of phthisis.

The examination of a patient may reveal to us the presence of pulmonary tuberculosis, but from it we cannot by any means form a true opinion as to the future course of the disease.

Examination of the patient at intervals during the course of treatment gives us a better idea as to the degree of improvement, if any, which has taken place, but it must not be forgottem that physical signs, weight, general condition of the patient &c may, by supplying us with untrustworthy evidence, lead us to form a false opinion as to the real course of events.

Examination of the blood by Arneth's method gives us a means by which we can measure the actual improvement which has taken place, and thereby the success or otherwise attending our method of treatment.

It must be clearly understood that a single examination of the blood gives us no more idea of the future course of the disease than does one examination of the patient. If this examination of the blood reveals to /

to us a neutrophile classification of good value, we can take it for granted that the disease is not in the meantime very active, but we cannot say whether it will remain so or not. If we find a neutrophile classification of very low value, we know that an infective process is actively proceeding. This infective process may be purely tubercular, or there may also be a superimposed infection, due to some other organism such as the staphylococcus aureus. We cannot tell however what the result of this infectious process will be. According to the result of the blood examination we get an idea as to the activity of the disease at the time, but that is all.

If we wish to get reliable information regarding the progress of a patient, we must make repeated examinations of the blood at intervals and compare the results obtained. By this means we procure valuable information of the effect produced by our method of treatment, and of the results likely to be obtained if we continue such treatment.

In the case of a patient whose neutrophile classification to begin with is practically normal, and continues to be so, the patient is progressing favourably. If however the classification gradually deteriorates in value, that is, if the nuclei of the polymorphs become gradually less complicated, the disease is becoming more active, our treatment is not meeting with success /

:cess ,and may really be the cause of the increased activity.

On the other hand, in the case of a patient whose neutrophile classification to begin with is of very low value, and shews no sign of improvement after repeated examination, we know that the disease is not improving. If, however, the nuclei becomes more complicated, we can be assured that the infective process is abating, and that our treatment is meeting with success.

Therefore, we must choose a method of treatment which will produce a change in the neutrophile classification in the right direction. If this change is taking place, then we know that we are doing the best we can for the patient.

The form of treatment most suitable for a particular patient can thus be found by watching the effect produced on the neutrophiles, and any treatment which causes a bad effect must be abandoned. A fair trial must of course be given and a conclusion should not be arrived at within too short an interval of time.

It is by this means that I measure the degree of improvement produced by tuberculin. I also use this principle in choosing the cases of pulmonary tuberculosis which are likely to be improved by tuberculin; but as harm may be caused in certain patients even by a few doses, I propose to go into this matter more fully.

T R E A T M E N T .

I will first of all give a short outline of my method of treatment and follow this up by notes of a few cases as illustrations.

When to Begin Tuberculin Treatment.

When the diagnosis has been arrived at by the discovery of the tubercle bacillus in the sputum, tuberculin treatment may be proceeded with at once, provided the case is a suitable one for this form of treatment (vide Choice of Cases).

If however it has been necessary to give diagnostic doses of tuberculin, we will have to wait until the effects of these doses have completely passed off. If we begin treatment before this has occurred we will find that the first dose will be followed by a reaction. We cannot trust clinical evidence to tell us when it is safe to begin treatment, and we cannot mention a certain number of days as being necessary for the disappearance of the effects of the test doses, because the time necessary is so variable in different cases according to the severity of the reaction, number of test /

test doses given etc.

The best method of finding when it is safe to begin the course of treatment is by means of the blood. We must make it a rule never to commence tuberculin treatment until the neutrophile classification has returned to its original state after being disturbed by the diagnostic tuberculin. To carry this out it is advisable to examine a blood film every second day after the blood has recovered in order that treatment may be begun with as little delay as possible.

Initial Dose.

My initial dose in most cases is .0001 c.c. P.T.O. I findthat this dose can usually be given with safety If however the patient is very young, under five years of age, I usually begin with .00001 c.c. P.T.O. Occasionally my initial dose is .001 c.c. P.T.O. This can be given without harm resulting if the neutrophile classification is of good value and especially if a third or fourth dose of old tuberculin has been required to produce the change in the blood necessary to arrive at a definite diagnosis.

Subsequent Doses.

The method of increasing the dose is quite readily understood if the charts of the illustrative cases are studied. I do not propose therefore to give a description /

description.

The only objection to this method is that the graduation of dosage is not quite regular. This however I do not consider a drawback as I have never had any trouble follow any dose as long as I regulate the interval between the doses by means of an examination of the blood.

As can be seen from the charts, I never have to reduce a dose of tuberculin, and I very seldom repeat the preceding dose. In nearly every case I increase the dose to some extent. The only variable item is the interval between the doses.

That is to say, my series of doses are alike in nearly every case, but the intervals between the doses vary, and it is by them that I control the treatment.

Intervals Between the Doses.

The intervals between the doses are entirely regulated by the blood. No therapeutic dose of tuberculin should be given until the blood has recovered from any effects produced by the preceding dose. Attention to this is of the greatest importance, and it forms the whole idea of my method of treatment. By this means we can avoid clinical reactions altogether, as the first evidence of the probability of a reaction is seen in the blood, and by waiting until the neutrophile classification returns to its previous state, we know /

know that the effects of that dose have passed off, and we can now with safety give another injection of tuberculin.

Minimum Interval.

Most of the tuberculin injections given during a course of treatment cause no effect on the blood and therefore are far from producing any clinical evidence of a reaction. However, it is necessary to examine the blood at least once after every therapeutic dose of tuberculin. The best time to do so is some time during the third day after the dose has been administered.

My rule is as follows:- I give the injection at 11 in the morning. On the third day after this before 11 a.m., I take a film and examine it at once. If there is no change in the neutrophile classification I give another dose immediately. Therefore as long as there is no effect produced in the blood, the interval between the doses is three days. This is therefore the minimum. A shorter interval is not advisable as it requires three days to produce the maximum change in the neutrophile classification, and if this change is slight it could not be recognised in less than that period of time. There is no necessity to make the interval longer if there /

there is no change in the blood because we know that in that case a larger dose can safely be given without causing any general disturbance. At the most, a larger dose will only cause a change in the neutrophile classification.

Longer intervals are necessary when a change in the neutrophile classification has been produced by an injection of tuberculin. This change is recognised by an examination of a film on the third day after the dose has been given. We must now wait until the blood recovers, and the time taken varies according to the degree of deterioration, the more severe the change the longer the interval.

If the change in the blood is very marked, I examine a film every second day until the classification has resumed its original value. If It is slight, I examine a film every day.

Whenever the blood has recovered I give another injection of tuberculin increasing the dose according to the process illustrated in the charts. If the change is very marked I repeat the previous dose, I only reduce the dose if the blood change has been accompanied by a general reaction - rise of temperature etc. This however is very seldom necessary, and we can usually go through a whole course of treatment without a single rise of temperature occurring from any dose of tuberculin if we know the condition of the neutrophile /

neutrophile classification before every injection.

The longest interval between therapeutic doses of tuberculin is very seldom more than ten days. If the blood has not recovered within that time, the patient is probably not a suitable case for tuberculin. This however will be discussed under Choice of Cases for Tuberculin Treatment.

Interruptions in the Course of Treatment.

In an interruption occurs during the course of treatment from any cause, e.g. the patient having a holiday in the country, we must not resume the treatment where we left off. It is necessary to reduce the dose, and if the interval is a lengthy one it will be advisable to begin the treatment at the beginning.

It will be found however that we can rapidly increase the dose until we reach the one at which we left off, as no change is produced in the blood by the repetition of these early doses, and therefore no delays occur.

Complete Course of Treatment.

This consists of a course of P.T.O. up to 1 c.c P.T. up to 1 c.c., and finally Old Tuberculin up to 1 c.c.

The time taken for this course is usually about six months, but it may be much longer, or it may be shorter /

shorter depending on the manner in which the patient takes the tuberculin.

Every patient does not go through this complete course, in fact very few do, as their optimum dose is often reached before it is completed.

Maximum Possible Dose.

This is 1 c.c. T.K. - the final dose in the complete course of treatment. I never give more than this to any patient.

Maximum Individual Dose.

This may be reached at any period in the course of treatment. It is recognised by the fact that every attempt to go beyond it results in a change in the neutrophile classification. When I have reached this dose I repeat it once a week for some time and make another attempt to increase the dose. If this is again unsuccessful, being followed by a change in the neutrophile classification, I continue with the same dose giving an injection once a fortnight.

I have had numerous patients who could not tolerate more than .5 c.c. P.T.O.

Although a patient cannot tolerate a large dose of tuberculin it is not an unfavourable sign by any means. Most of them do just as well with a repetition of their optimum dose as the patient who can tolerate 1 c.c. T.K.

Temperature.

I pay no attention to a rise of temperature unless it is accompanied by a change in the neutrophile classification /

SANATORIUM CHART.

Extending over 3 months.

NAME & AGE Mr. Ross. age 29

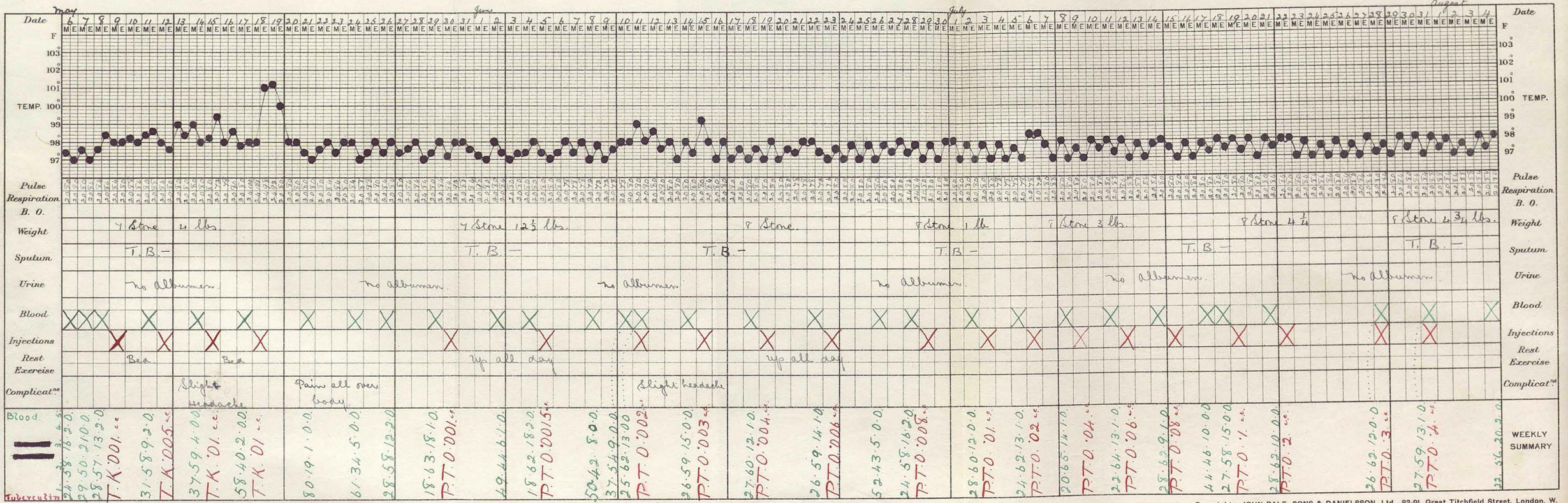
DATE

CASE-BOOK Nº

NORMAL WEIGHT

HEIGHT

CHEST { INSPIRATION / EXPIRATION



:fi cation. If a rise of temperature is due to the tuberculin, the blood will shew a corresponding deterioration. Frequently during a course of treatment we have a rise of temperature in the evening, but we cannot be certain whether it is due to the tuberculin or not. Examination of the blood however gets rid of this difficulty.

Illustrative Cases.

Case 1. Mrs Ross. Age 29. Admitted 6th May '12.

Complaint. - Cough and Spit. Severe pain between shoulder blades - worse on coughing. Loss of weight.

Duration - 7 months.

Physical Examination shewed nothing but a slightly impaired note and broncho-vesicular breathing at the right apex.

Sputum - T.B. negative. Afebrile.

Neutrophile classification was practically normal.

Diagnostic doses of Old Tuberculin produced a satisfactory reaction (See Chart). The fourth injection caused a temperature of 101° F. This dose was not necessary as the third test dose gave conclusive proof, since it produced a change in the neutrophile classification sufficient to denote a positive test. There was no focal reaction.

This patient had therefore a tuberculous focus somewhere in the body, and I determined to treat it by means of tuberculin, hoping thereby to get rid of the troublesome symptoms especially the pain in the back /

back which had annoyed her for several months and had resisted all other forms of treatment.

The neutrophile classification had returned ~~had returned~~ to its previous value after the test doses on 29th May and on 30th May I began her treatment by injecting .001 c.c. P.T.O. I considered that this dose would be quite safe as her neutrophile classification was of good value and because she had required three test doses of T.K. before the necessary change was produced in the blood.

The first dose of P.T.O. caused a slight deterioration in the classification of the neutrophiles which recovered in a few days when I injected .0015 P.T.O. This dose also produced a slight effect, but the following dose had no effect. I proceeded with the treatment according to the method I have described above. Only occasionally did the tuberculin cause any change in the blood.

After the first six weeks of treatment the cough and spit improved greatly and the pain in the back entirely disappeared. On July 22nd she left the Sanatorium quite healthy - no cough, no spit, and no pain. At that time she had reached .2 c.c. P.T.O. I continued the treatment at the Tuberculin Dispensary upto 1 c.c. P.T.O. and proceeded with P.T. beginning with .02 c.c. and finally reaching 1 c.c. She has had no return of the pain and has been in excellent health since /

since. She comes to see me every month at the Dispensary.

A study of her chart shews my method of increasing the doses and also the state of the blood after every dose.

During the whole course she had one rise of temperature viz. 99.2° F. on the evening of 15th June. She had an injection of tuberculin the same morning, but as this dose produced no change in the blood I paid no attention to this temperature and gave the next injection at the usual interval and no fever resulted. This temperature was therefore not a sign of a reaction to the tuberculin as the following largerdoses would certainly have caused a further rise of temperature.

She never suffered any discomfort except from the fourth test dose which caused pain all over her body. I have already shewn that this dose was unnecessary.

This case demonstrates the value of the test doses of tuberculin. They proved the presence of a tuberculous focus in the body. The course of treatment made it evident that this focus was the origin of the troublesome symptoms by causing their entire disappearance. I cannot say whether the focus was in the lungs or not, but I consider that there probably was tuberculous disease in that situation as the /

II

SANATORIUM CHART.

Extending over 3 months.

NAME & AGE James Sharp. Age 16.

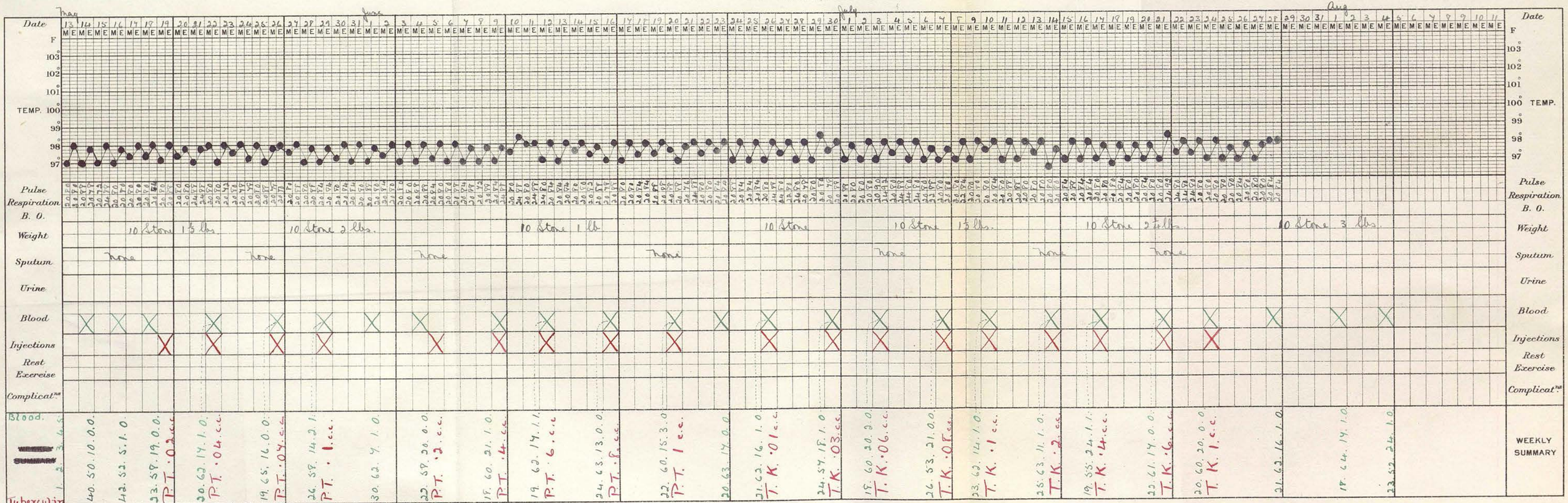
DATE

CASE-BOOK Nº

NORMAL WEIGHT

HEIGHT

CHEST { INSPIRATION / EXPIRATION



When ordering please quote } Chart No. 19.

NAME & AGE James Sharp. Age 16.

DATE

CASE-BOOK Nº

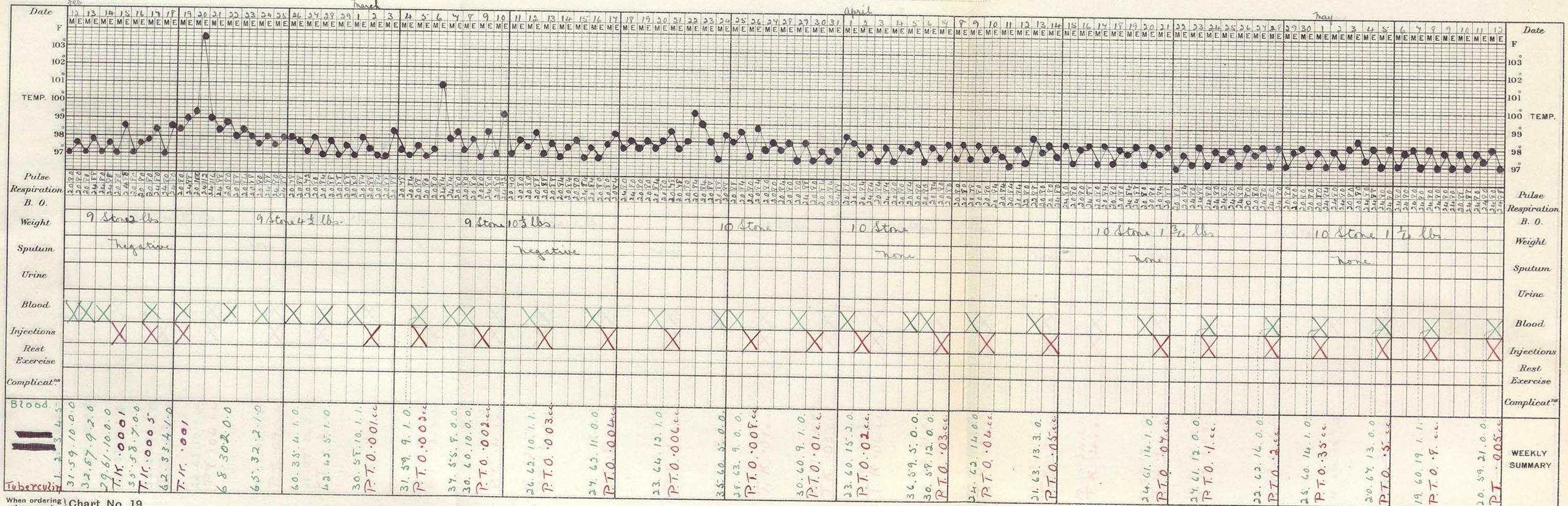
SANATORIUM CHART.

Extending over 3 months.

NORMAL WEIGHT

HEIGHT

CHEST { INSPIRATION / EXPIRATION



as the tuberculin entirely got rid of the cough and spit. Wherever it was, it is now either cured or latent, and the patient is in excellent health. If the focus is latent, the possibility of it again becoming active need not trouble us, as she is getting a small dose of tuberculin every month which will keep her defensive powers in readiness to cope with any such emergency, and will also serve as a warning to us if these defensive powers fail, and the focus again threatens to cause mischief.

Case 2. James Sharp. Age 16 Admitted 12th February 1912.

Complaint. Cough. Occasional spit. Severe haemoptysis in December 1911. Sputum frequently blood-stained.

Duration. 4 months.

Physical Examination shewed some dullness at the right apex with bronchial breathing. No rales were present.

Sputum negative. Afebrile.

The neutrophile classification was of moderate value.

I gave three diagnostic doses of T.K. The second of these produced a satisfactory deterioration in the neutrophile classification. The third dose (which was not necessary) produced a temperature of 103.6° F. and other signs of a general reaction, including a focal reaction at the right apex evidenced by /

by the appearance of a few crepitations at that situation.

The test was therefore positive, and the site of the tuberculous focus was evidently at the apex of the right lung.

The neutrophile classification returned to its original value within ten days after the final test dose, and on March 2nd, I began his treatment by injecting .001 c.c. P.T.O. I reached .8 c.c. P.T.O. on May 8th and I then proceeded with P.T. the first injection being .005 c.c. On 20th January I injected 1 c. c. P.T. and on 26th June I began with Old Tuberculin by injecting .01 c.c. I finished the course on July 24th when I gave 1 c.c. T.K., i.e. the maximum possible dose.

This patient had therefore a complete course of tuberculin treatment which lasted twenty two weeks. He was an inmate of the Sanatorium only for the first eight weeks, after which he attended the Dispensary twice weekly. On leaving the Sanatorium he started work as a gardener and was never off work for a single day. I examined his blood every time he came to the Dispensary and according to the result of this examination I decided whether to give him a dose or not.

All his symptoms had disappeared before he left the Sanatorium, and there has been no recurrence of any of them since. He gained over a stone in weight.

As /

As regards his temperature , his chart shews that he had an occasional rise at the beginning of the treatment. The first of these was on the evening of March 6th when it rose to 101° F. This was accompanied by only a slight degeneration of the neutrophile classification which had recovered by 9th March , when I repeated the previous dose. I considered this quite safe , as , although the rise of temperature was very marked , the change in the neutrophile classification was very slight. The injection of 9th March was followed by a temperature of 99.4° F., but there was no change in the neutrophile classification and I accordingly increased the succeeding dose at the usual interval. There was no further rise till March 22nd when the temperature again rose to 99.4° F but the neutrophile classification only necessitated an interval of five days. The temperature never rose above normal during the remainder of the course (See chart). He never suffered the slightest discomfort either from the diagnostic doses or from the treatment.

Before the commencement of the treatment the neutrophile classification was of moderate value. During the course it gradually improved , and at the end , was quite normal , where it has remained since.

The optimum dose in this patient was evidently larger than the maximum possible dose. He comes to me once a month when I examine his blood and give him a small dose of T.K.

Tuberculin /

SANATORIUM CHART.

Extending over 3 months.

NAME & AGE Hugh Dall. age 24.

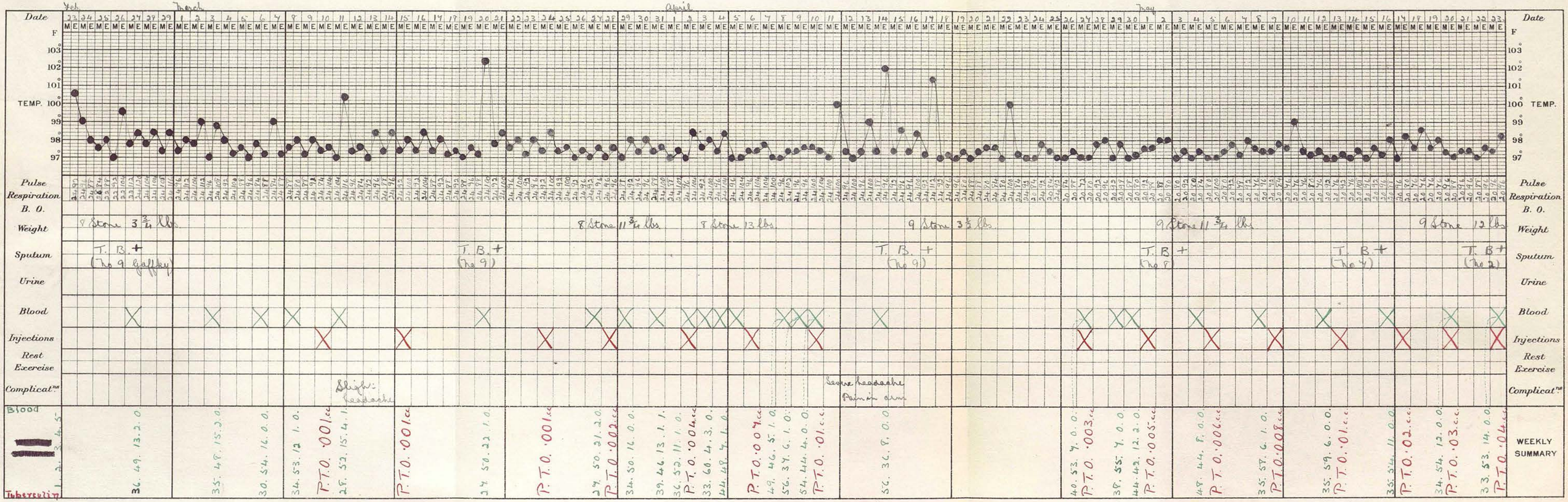
DATE

CASE-BOOK Nº

NORMAL WEIGHT

HEIGHT

CHEST { INSPIRATION / EXPIRATION



When ordering please quote Chart No. 19.

Tuberculin did this patient a great deal of good, as is evidenced by the disappearance of the symptoms and the improvement in his blood. It caused him no inconvenience, as he worked all day and every day after the first eight weeks when he was in the Sanatorium.

Case 3. Hugh Dall. Age 27. Admitted 23rd Feb. '12.

Complaint. Cough and copious spit. Shortness of breath. Loss of weight. Frequent haemoptysis.

Duration. 4 years.

Physical Examination. Right lung Stage II; Left lung Stage I. Numerous crepitations at both apices.

The patient was slightly febrile, having a temperature of 99-100° F in the evenings.

Sputum - T.B. positive (No. 9 Gaffky).

Test doses were of course unnecessary.

The neutrophile classification was of moderate value (See Chart).

In this case duringthe first few weeks, I administered the tuberculin in the ordinary way i.e. although I examined the blood after each injection, I did not allow the result of this examination to regulate my treatment but trusted entirely to the clinical evidence to prevent a bad reaction.

I began treatment on March 10th by injecting .001 c.c. P.T.O. This resulted in a temperature of 100° F and a slight headache. I therefore waited five days and repeated the same dose. Five days later the temperature rose to 102.2° F. but on that date the patient was out of bed for an hour for the first time, and this probably /

:bably accounted for the temperature. After an interval of ten days I repeated the same dose again. I then gradually mounted to .01 c.c. P.T.O.

During this time the blood had gradually been deteriorating in value (See Chart) but I neglected this warning with the result that a violent reaction occur:red after the injection of .01 c.c. P.T.O. The temperature rose every evening to between 99 and 102° F. The patient suffered intense discomfort from headache and pain at the site of the injection. On auscultation I found rales everywhere in the chest. The sputum was very copious, and on two occasions there was severe haemoptysis. Clinically, I got no warning of this reaction and therefore could not prevent it. If however I had used the blood as a guide it is evident that this reaction would never have occurred, as the deterioration of the neutrophile classification was initiated by an injection of tuberculin administered more than a week before that dose which precipitated the general reaction.

The patient recovered in about ten days and the blood returned to its original condition in sixteen days. I now began the treatment again, using the blood as guide, my first injection being .003 c.c. P.T.O. I reached .5 c.c. P.T.O. without having a single rise in temperature and without causing him any discomfort. This dose proved to be his optimum, and I therefore repeated it at intervals.

The /

SANATORIUM CHART.

Extending over 3 months.

NAME & AGE Fredrick Cowley, Age 37

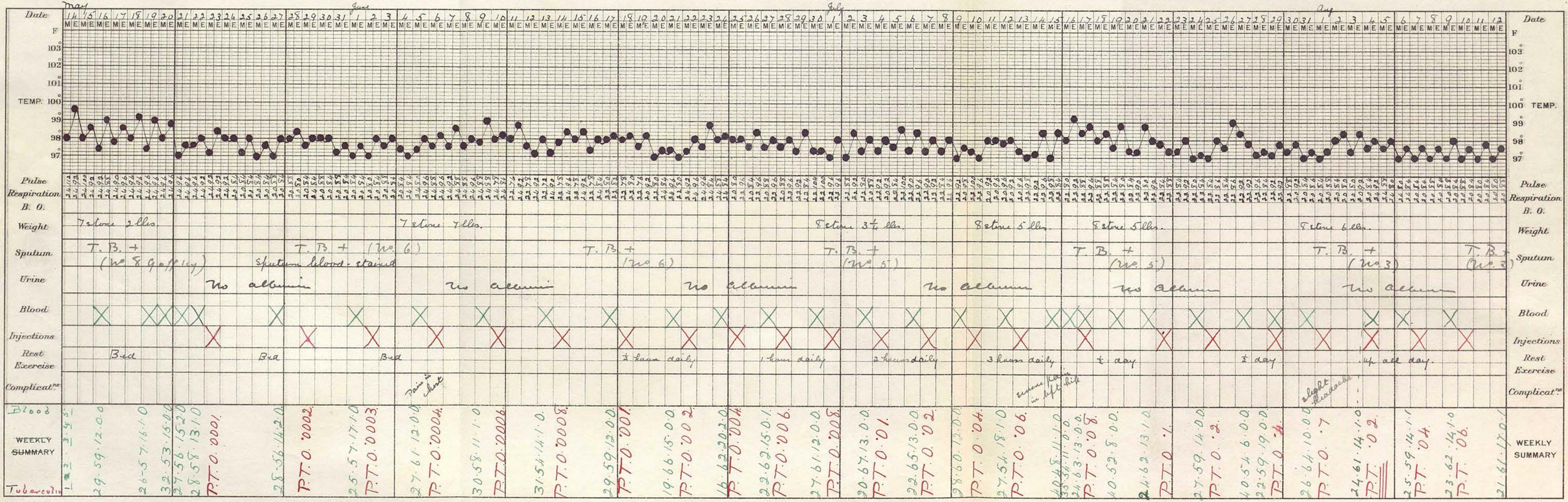
DATE

CASE-BOOK Nº

NORMAL WEIGHT 8 stone 4 lbs

HEIGHT 5 ft. 4"

CHEST { INSPIRATION / EXPIRATION



When ordering please quote Chart No. 19.

The tuberculin did the patient an immense amount of good. He increased in weight to the extent of more than two stones. His cough practically disappeared. He had very little sputum which contained only a few bacilli (no. 1 Gaffky). There was never any blood in the sputum. Before treatment he was slightly febrile, but after the first attempt at treatment his temperature never rose above normal.

This case shews excellently the value of the blood as a guide in the administration of tuberculin compared to clinical evidence and also shews the value of tuberculin, when correctly given, in an advanced case of phthisis. This patient was not cured, but he was very much improved. He had been treated for several months in a Sanatorium by purely open air measures before he came to me, but he did not benefit much from it. The tuberculin however did him much more good, and after the completion of the course, he felt better and was heavier than he had ever been since he first took ill, over four years previously.

Case 4. Frederick Cowley. Age 37. Admitted 14th May 1912.

Complaint. Cough and spit, chiefly in the morning. Loss of weight. Haemoptysis frequently.

Duration - 14 years.

Physical Examination. Right lung Stage II; Left lung Stage II. Numerous rales all over the chest.

The patient was slightly febrile with evening temperature from 99-100° F.

Although /

TUBERCULIN.

V

August. NAME Myles Flynn. AGE 32. September DISEASE Phthisis

	DATE.	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
TUBERCULIN.		T. K. .04 c.c.							T. K. .06 c.c.							T. K. .08 c.c.							T. K. .1 c.c.							T. K. .2 c.c.							T. K. .3 c.c.							T. K. .5 c.c.			T. K. .7 c.c.			T. K. 1 c.c.		
POLYMORPHS.	1	24							20							24							23							29							24							37			20			24		
	2	52							50							57							52							56							56							50			54			53		
	3	22							25							22							23							14							20							19			23			21		
	4	2							4							3							2							1							0							3			1			2		
	5	0							1							0							0							0							0							1			2			0		
REMARKS.		9. Stone 11½ lbs.							9. Stone 11 lbs							9. Stone 12 lbs.							9. Stone 11¾ lbs.							9. Stone 12 lbs.							9 Stone 12½ lbs.							9. Stone 12¼ lbs.									

TUBERCULIN.

IV.

NAME Myles Flynn AGE 32. DISEASE Phthisis

	June 16	17	18	19	20	21	22	23	24	25	26	27	28	29	July 30	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	August 1	2	3
TUBERCULIN.	P. T. 1. c.c.							P. T. .2. c.c.							P. T. .4. c.c.							P. T. .Y. c.c.							P. T. 1. c.c.							T. K. .01. c.c.							T. K. .02. c.c.						
POLYMORPHS. 1	30							26							29							31							23							30							22						
2	54							53							57							58							54							50							54						
3	16							19							14							11							21							19							22						
4	0							2							0							0							2							0							1						
5	0							0							0							0							0							1							1						
REMARKS.	only comes once weekly. 9. Stone 11. lbs.							9. Stone 11. lbs.							9. Stone 11½. lbs.							9. Stone 11 lbs.							9. Stone 10½. lbs.							9. Stone 13¼. lbs.							9. Stone 11½. lbs.						

TUBERCULIN.

111

April. NAME Myles Flynn. AGE 32. yrs. DISEASE Phthisis

May June

DATE.	28	29	30	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
TUBERCULIN.	P.T.O. ·4. c.c.							14 days Holiadays							P.T.O. ·4. c.c.							P.T.O. ·4. c.c.			P.T.O. 1. c.c.				P.T. ·02. c.c.		P.T. ·02. c.c.				P.T. ·04. c.c.		P.T. ·06. c.c.				P.T. ·08. c.c.		P.T. ·08. c.c.						
POLYMORPHS. 1	24														30		43					32			25				26		23				30		26				24		24						
2	59														57		57					50			53				59		61				53		54				60		61						
3	15														12		5					17			18				14		15				15		18				16		12						
4	1														1		1					1			3				1		0				2		2				0		0						
5	1														0		0					0			1				0		1				0		0				0		0						
REMARKS.	9 Stone 8 lbs							9. Stone 7. lbs							9 stone 6. lbs.							9. Stone 9. lbs.							9. Stone 8½. lbs.						9. Stone 9. lbs.						9. Stone 8½. lbs.								

TUBERCULIN.

II

NAME Myles Flynn AGE 32. DISEASE Phthisis

DATE.	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27
	march																						april																												

TUBERCULIN.

I

NAME Myles Flynn. AGE 32. DISEASE Phthisis

DATE.	January 21	22	23	24	25	26	27	28	29	30	31	February 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	March 1	2	3	4	5	6	7	8	9
TUBERCULIN.				P.T.O. .001. c.c.				P.T.O. .002. c.c.							P.T.O. .002. c.c.			slight cold			still slight cold.	P.T.O. .002. c.c.		P.T.O. .003. c.c.					P.T.O. .004. c.c.		T. 99. ℉.	P.T.O. .004. c.c.				P.T.O. .005. c.c.					P.T.O. .006. c.c.		P.T.O. .008. c.c.						
POLYMORPHS. 1	35	33	30					36		46					31		34					29		37					32		37					33		51					34		30				
POLYMORPHS. 2	54	58	60					57		54					57		35					62		52					56		58					65		46					53		60				
POLYMORPHS. 3	9	9	8					7		3					11		11					9		10					10		11					10		2					12		9				
POLYMORPHS. 4	1	0	2					0		0					1		0					0		0					1		2					1		1					1		1				
POLYMORPHS. 5	1	0	0					0		0					0		0					0		1					1		0					1		0					0		0				
REMARKS.	9. Stone 8 lbs.							9 Stone 7 lbs.							9. Stone 8½ lbs.							9. Stone 6½ lbs.							9. Stone 6¼ lbs.							9. Stone. 7 lbs.							9. Stone 8 lbs.						

Physical Examination - Right lung Stage I; Left lung Stage I.

Sputum T.B. positive (No. 3 Gaffky).

Afebrile.

Neutrophile classification moderately good. I began treatment on January 24th 1912, when I injected .001 c.c. P.T.O. and gradually increased the dose to 1c.c. P.T.O. I then proceeded with P.T. up to 1 c.c. and T.K. up to 1 c.c. (See Charts).

The tuberculin did him a lot of good. His cough and spit disappeared. He gained several pounds in weight. As far as one could say, he is now quite cured, but whether he will remain so or not remains to be seen. I still keep him under observation.

During the whole course of his treatment this patient worked very hard as a labourer in a brewery. He never lost a single day's work, and never suffered the slightest discomfort from the treatment.

The records of his doses and blood examinations are seen in the accompanying charts, which I have had printed for use in those cases in which the treatment is regulated by means of the neutrophile classification.

CHOICE OF CASES FOR TUBERCULIN TREATMENT.

As every case of pulmonary tuberculosis is not suitable for tuberculin treatment, it becomes necessary to eliminate those cases which are not likely to benefit from this form of treatment.

In some patients, the administration of tuberculin actually does harm, and it is the indiscriminate fashion of giving tuberculin to every case of pulmonary tuberculosis which has caused so much discredit to be attached to this method of treatment.

Physical examination of the chest cannot permit us to say definitely that a patient is or is not likely to benefit from tuberculin.

Though tuberculin may not cure an advanced case of phthisis, it may relieve troublesome symptoms and render the disease latent. At the same time there are many cases of advanced phthisis in which tuberculin does no good, and indeed often does serious harm.

On the other hand, every early case of phthisis is not necessarily suitable for tuberculin treatment, and certain of these clinically slight cases are made more active by means of tuberculin.

Because /

Because a case is febrile, we cannot say that it is unsuitable for tuberculin treatment as many of these cases derive great benefit from it, while others are adversely affected.

It is therefore of great importance that we choose the cases that are likely to be improved by tuberculin, because otherwise the harm we may do would counter-balance the good, and it would be wiser for us to give up the use of tuberculin altogether.

Examination of the blood by Arneth's method provides us with a means by which we can divide up our cases into two sections - those which are likely to benefit by tuberculin; and those which are not. If we do begin treatment, by watching the blood carefully after each dose, we can tell whether we are likely to have good results or not.

Every case of phthisis which comes under my observation has the blood examined by Arneth's method three times on different days before treatment of any kind is begun. According to the result of this examination the patient is or is not treated with tuberculin. I associate each particular patient with a certain blood picture which under treatment must either retain its present value or improve, but must never deteriorate.

If the classification of the leucocytes, is below a certain value which I have decided on after treatment of numerous cases, I never begin treatment with tuberculin knowing from experience that my efforts would /

SANATORIUM CHART.

Extending over 3 months.

NAME & AGE Mrs Neilson Age 36.

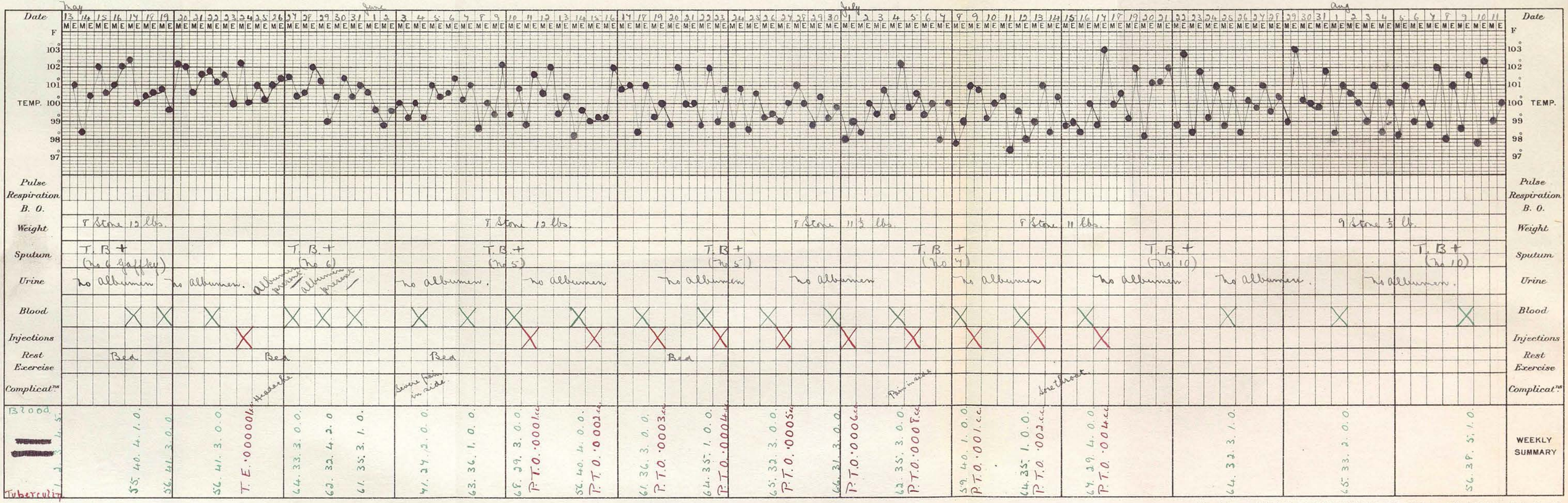
DATE

CASE-BOOK Nº

NORMAL WEIGHT 9 Stone 12 lbs.

HEIGHT

CHEST { INSPIRATION / EXPIRATION



would not be attended with success but in all probability the tuberculin would lower the value of the blood. If it is above that value, I begin treatment with tuberculin feeling confident that, if not bringing about a cure, I will at least improve the patient's condition and quite satisfied that I can do no harm as long as I examine the blood frequently during the course of treatment.

The following is the classification which I have decided on as beingthe above mentioned value:-

1	2	3	4	5
40%	50%	8%	2%	0%

This classification is of course not absolute and a certain latitude must be allowed in both directions.

Cases Unsuitable for Tuberculin.

I shall first of all consider those cases which have a neutrophile classification value far below that of the deciding classification of which the following are examples:-

Case 1. Mrs Nielson; Age 36,;Admitted 13th May 12.

Complaint. Cough and spit. Shortness of breath. Night sweats. Loss of weight. Loss of appetite.

Duration. Three months (?)

No previous illnesses: Family history good.

Her sputum contained large numbers of tubercle bacilli (No. 6 Gaffky). She had irregular fever, the temperature frequently reaching 102° F. (See Chart).

Physical examination of the chest shewed disease of both lungs. Right lung, - Stage II; Left lung - Stage /

Stages I-II. Numerous rales were present at both apices.

I considered the possibility of the presence of some other organism as well as the tubercle bacilli, but after several careful examinations of the sputum, I came to the conclusion that no mixed infection was present. The case was therefore one of pure tuberculous infection.

Examination of the blood shewed a neutrophile classification of very low value (See Chart-green ink).

I decided to try the effect of a few doses of tuberculin. Accordingly on May 26th I injected .000001 c.c. Bacillary Emulsion (T.E.). This dose was followed by the appearance of albumin in the urine. The temperature continued as before. Severe pain was produced in the head and left side. The blood rather de-creased in value. Altogether this dose had a bad ef-:fect on the patient.

I did not give any more injections of the emulsion, but seventeen days after that dose I began treatment with P.T.O., the initial dose being .0001 c.c. My reason for stopping the T.E. was chiefly because of the effect produced on the kidneys. A study of her Chart shews that I gave her ten injections altogether, the last being .004 c.c. P.T.O.

These doses had absolutely no effect on the temperature which continued to swing as before. The

number /

II

SANATORIUM CHART.

Extending over 3 months.

NAME & AGE Janet Allan. Age 19.

DATE

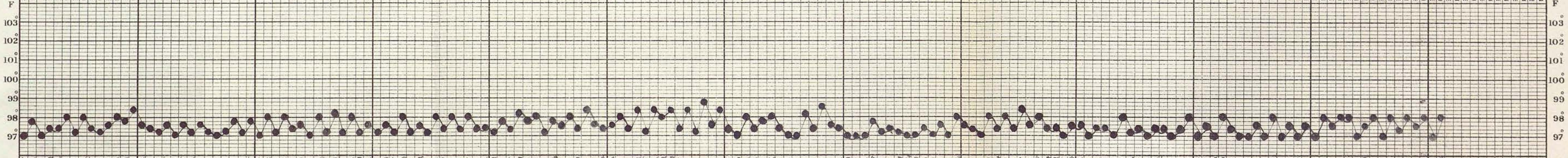
CASE-BOOK No

NORMAL WEIGHT

HEIGHT

CHEST { INSPIRATION / EXPIRATION

Date: June – July – Aug



Weight: 7 Stone 2 lbs. — 7 Stone 1¾ lbs. — 7 Stone 2 lbs. — 7 Stone 2 lb. — 7 Stone 1½ lb. — 7 Stone 2¾ lbs. — 7 Stone 3¼ lbs. — 7 Stone 4 lb. — 7 Stone 4 lbs.

Sputum: T. B + (No 5) — T. B. + (No 10) — T. B. + (No 10) — T. B. + (No 9)

Rest / Exercise: Up for 4 hours daily — Up for ½ day — Up for whole day, rest during afternoon

WEEKLY SUMMARY (Blood 1. 2. [redacted] 3. 4. 5. / Tuberculin)

80. 20. 0. 0. 0.
P. T. O. ·001 cc.

63. 34. 0. 0. 0
P. T. O. ·002 cc

60. 38. 2. 0. 0.
P. T. O. ·003 cc

64. 29. 4. 0. 0.
P. T. O. 0·004 cc.

66. 30. 4. 0. 0
P. T. O. 0·006 cc.

58. 41. 1. 0. 0.
P. T. O. ·008 cc

59. 34. 4. 0. 0.
P. T. O. ·01 cc

61. 36. 3. 0. 0.
P. T. O. ·02 cc

58. 38. 3. 1. 0.
P. T. O. ·04 cc.

63. 35. 2. 0. 0.
P. T. O. ·07 cc.

64. 30. 3. 0. 0.
P. T. O. ·1 cc

72. 27. 1. 0. 0.
P. T. O. ·2 cc.

64. 25. 8. 0. 0.
P. T. O. ·4 cc.

65. 28. 6. 1. 0.
P. T. O. ·7 cc

60. 34. 6. 0. 0.
P. T. O. 1. cc.

64. 32. 1. 0. 0.
P. T. ·02 cc.

60. 35. 5. 0. 0.
P. T. ·04 cc.

63. 34. 2. 1. 0

60. 34. 6. 0. 0

57. 37. 6. 0. 0

55. 35. 9. 1. 0.

When ordering please quote } Chart No. 19.

SANATORIUM CHART.

Extending over 3 months.

NAME & AGE Janet Allan. Age 19.

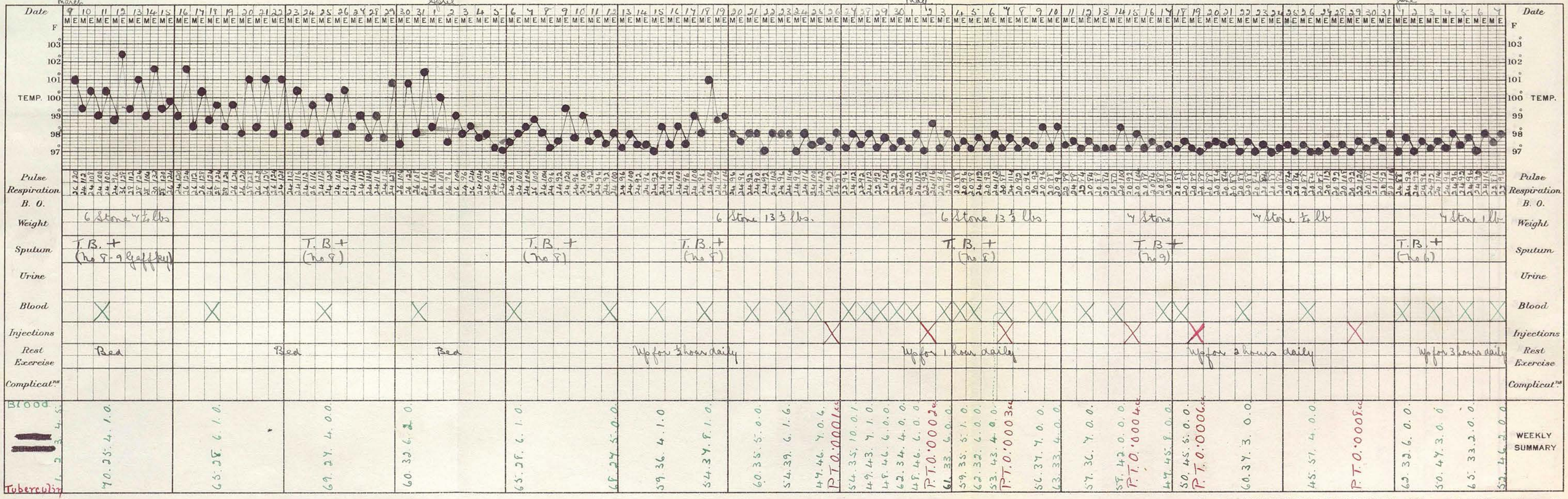
DATE

CASE-BOOK Nº

NORMAL WEIGHT

HEIGHT

CHEST { INSPIRATION / EXPIRATION



When ordering please quote Chart No. 19.

number of tubercle bacilli in the sputum was increased (from No. 6 to No. 10 Gaffky). Physical examination shewed no improvement, numerous crepitations still being present. Her weight was practically the same as before. As regards the blood, the average classification of the neutrophiles was now of rather lower value than it was before the commencement of the treatment.

Apart from any improvement having taken place as the result of the administration of tuberculin, the patient was not so well as she was. The tuberculin caused her practically no discomfort. In fact, each individual dose did not seem to have any effect on her at all.

Case 2. Janet Allan, age 19; Admitted 9th March 1912.

Complaint. - Cough and copious spit. Shortness of breath Night sweats. Loss of weight. Occasional severe pain between shoulder blades.

Duration. - Six months.

Her sputum contained large numbers of tubercle bacilli (No. 8 Gaffky). Physical examination of the chest shewed disease in both lungs. Right lung-stage II; Left lung-stage I. Numerous rales were present in both lungs.

On admission she had a swinging temperature rising to 101-102° F. in the evenings (See Chart). This fever was the result of a mixed infection. Examination of the sputum (with the necessary precautions to eliminate mouth bacteria) shewed the presence of staphylococcus aureus. The neutrophile classification was of a very low value.

By means of fresh air etc., I got rid of the mixed infection in about six weeks, after which the temperature ran quite a normal course. She was quite suitable for tuberculin treatment except for the fact that the disease was fairly severe. The neutrophile classification though it had improved slightly on the disappearance of the mixed infection was still very low in value, much below the deciding value.

I decided to try the effect of P.T.O., and began her treatment with .0001 c.c. As can be seen from the Chart, I gradually mounted until I had injected 1 c.c. P.T.O. without once causing any rise of temperature. None of these injections caused her the slightest discomfort. She also gained a few pounds in weight

The duration of this course was sixteen weeks.

During the treatment I examined the blood at least once after each injection. I found that the tuberculin did not improve the neutrophile classification in the slightest, indeed at the end of the course it was of rather lower value than previously. Altogether the patient shewed no improvement, the disease being just as active as ever. She began to shew signs of improvement after the treatment was stopped, when the neutrophile classification increased in value to a slight extent.

This patient serves as a very good illustration of those severe cases of pulmonary tuberculosis which do

not /

not react to large doses of tuberculin. The case was afebrile before I began treatment and remained so all through the course. She took the tuberculin remarkably well, and not one of the injections caused her the slightest discomfort. Nevertheless the tuberculin did her no real good, and in all probability retarded her recovery, the disease being as active as ever.

It is in cases such as this, that we are tempted to push the tuberculin because of the encouragement offered us by the splendid way in which the patients take the tuberculin, there never being the slightest sign of a reaction.

I have found that this insensitiveness to tuberculin is really a bad sign, as it is by means of a reaction, though clinically not evident, that we hope to bring about a cure. In these cases tuberculin tends to aggravate the condition. This matter will be more fully dealt with under Tuberculin Reaction.

These cases can always be recognised before treatment is begun by means of the blood. Therefore if the neutrophile classification is of such a low value as in the case of Mrs Nielson and Janet Allan, tuberculin treatment should never be attempted as it does the patient more harm than good.

It should be noted that we may meet with cases similar to the above in which the disease is not very severe. It is the blood alone that we should use as our guide. If it contra-indicates treatment by tuberculin /

SANATORIUM CHART.

Extending over 3 months.

NAME & AGE David Dawson age 37

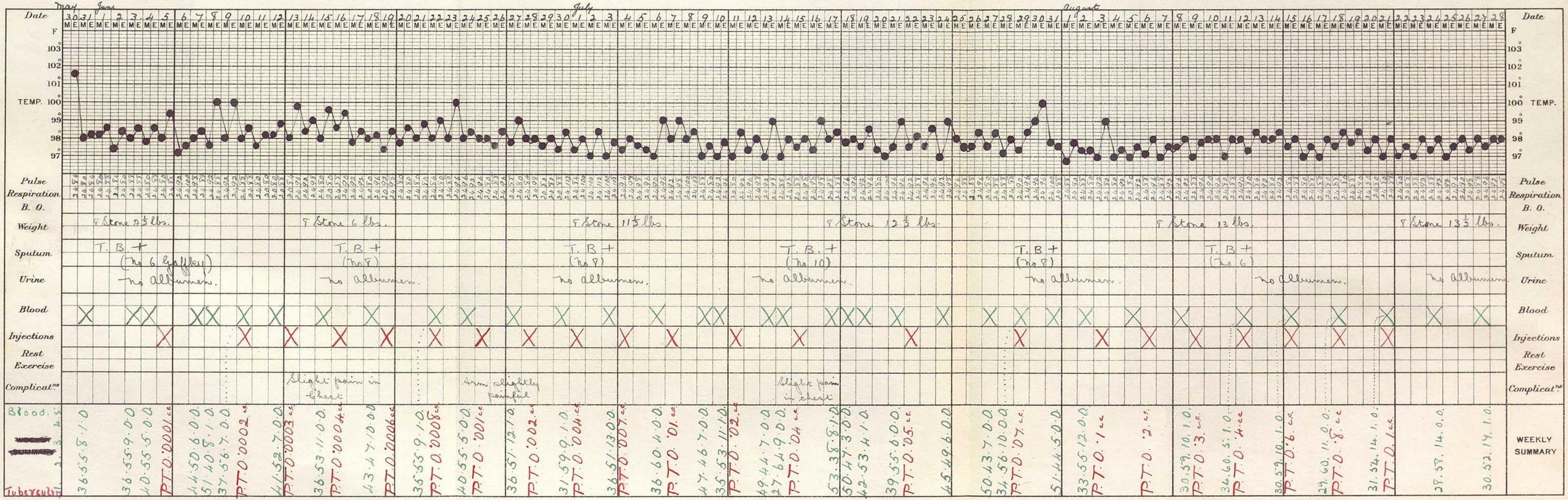
DATE

CASE-BOOK Nº

NORMAL WEIGHT

HEIGHT

CHEST { INSPIRATION / EXPIRATION



When ordering please quote } Chart No. 19. Treatment.

:culin, no matter what the physical signs are, some other form of treatment must be employed.

Mixed Infection.

Under the category of cases considered as unsuitable for tuberculin treatment are usually included those cases in which there is besides the tubercular infection, an infection by some other organism such as the staphylococcus aureus. In the majority of these patients the neutrophile classification is of such a low value that tuberculin treatment is contra-indicated. This low value may be the result of either infection alone or of both together.

This however is not always the case as wefrequently find a classification of fairly good value. The infections in these cases are not usually very severe. Tuberculin treatment may do these cases a vast amount of good and can safely be tried if we control our doses by watching the effect of each injection of tuberculin on the blood.

Case 3. The chart facing this page is that of a patient (David Dawson) who had a mild mixed infection, the invading organism being the staphylococcus aureus. I made myself sure of this by careful examination of the sputum (including cultivation) after getting rid of the mouth bacteria by washing.

That the infection was mild was evident by the temperature, which seldom rose above 100° F. and also by the blood, the neutrophile classification being of quite /

quite moderate value.

The lungs were not extensively affected, Right lung Stage II; Left lung Stage I - early. Numerous crepitations were present in both apices.

Tuberculin treatment was not contra-indicated by the blood and I determined to try it. My initial dose was .0001 c.c. P.T.O. which produced a slight deterioration in the neutrophile classification. I accordingly waited until the blood returned to its previous state when I injected .0002 c.c. P.T.O. I then gradually increased the dose up to 1 c.c. P.T.O. which I injected on 21st August 1912. (See Chart).

Only occasionally did the blood deteriorate after an injection. When it did so I waited until it had returned to its previous state before giving another. These "invisible" reactions were sufficient to shew that the tissues of the patient were doing their best to fight against the toxin and accordingly I was pleased to observe them.

At the beginning of the course, the temperature continued to rise as before, but after the first three weeks of treatment it never rose above 99° F. except on one occasion when it rose to 100° F (on July 30th) On that day I had allowed the patient to go home for a few hours, and I have no doubt he abused the liberty granted.

His symptoms improved to a large extent. He was still short of breath but not nearly so bad as he was before /

before treatment. His cough had almost entirely disappeared.

Staphylococci were still to be found in the sputum, but they were not nearly so numerous, the tubercle bacilli had also diminished in number. (See Chart). The classification of the neutrophiles had improved considerably.

On the whole the patient, though not cured, had greatly benefited from the course of treatment, and was brought to such a condition that he could more readily resist the infections.

In all probability, in cases such as the above the tubercular infection has not been rendered so acute by the presence of the invading organism that it could not be influenced by a course of tuberculin in which the technique was carefully considered and controlled by examination of the blood after each dose. We may therefore conclude that cases of mixed infection will derive great benefit from tuberculin if the neutrophile classification is not of too low a value.

Cases in which we cannot come to a Decision without giving a few Doses of Tuberculin.

I will now consider those cases in which the classification of the neutrophiles is of a somewhat similar value as the "deciding classification".

In these patients we cannot at once say definitely whether they are suitable for tuberculin treatment or not. One or two injections of tuberculin accom-

panied /

TUBERCULIN.

Name: Mrs. Dickson Age: 42. Disease: Phthisis

Date	Tuberculin	Polymorphs 1	2	3	4	5	Remarks
July 7		40	51	8	1	0	
July 8		46	49	5	0	0	
July 9		42	54	4	0	0	
July 11	P.T.O. ·0001 c.c.						
July 14		43	54	4	0	0	
July 15	P.T.O. ·0002 c.c.						
July 18		58	41	1	0	0	
July 19		58	40	2	0	0	
July 20	T. 99°F						
July 21		55	44	1	0	0	
July 22		56	40	4	0	0	
July 24		60	37	2	1	0	
July 26	T. 99°F	56	40	4.	0	0	
Aug 2		60	34	5	1	0	
Aug 3	T. 101°F						Sore throat.
Aug 9		54	39	7	0	0	
Aug 16		54	40	2	0	1	
Aug 22		52	43.	5	0	0	

:panied by examination of the blood will however enable us to come to a conclusion.

My method is as follows:-

I inject .0001 c.c. P.T.O. and watch any effect that is produced in the blood. When this effect, if any is produced, has passed off I inject .0002 c.c. I then proceed as in ordinary treatment never giving a dose while the blood is suffering from the effects of the previous dose. If in this way we manage to give three or four injections, we can proceed with the treatment, feeling confident that the case is a suitable one for tuberculin.

If however one of the first few doses produces a change in the blood and the blood does not return to its original state, we must stop the treatment as this case is not a suitable one for tuberculin treatment. Persistence in giving tuberculin to these patients, neglecting the blood, will bring them to a simi-:lar state as that of Mrs Nielson or Janet Allan recorded under Cases Unsuitable for Tuberculin.

We can proceed with the tuberculin even if each dose produces a change in the blood as long as it recovers again within reasonable time.

Case 4. Mrs Dickson, age 42. Admitted 29th June 1912.

Complaint. - Cough and Spit. Occasional haemoptysis. Shortness of breath and palpitation.

Duration. - Nine months.

Physical Examination. Right lung - Stage I-II; Left lung - Stage I.

Crepitations /

TUBERCULIN.

NAME M. A. Davidson. AGE 14. DISEASE Phthisis.

DATE.	April 14	18	19	20	21	22	23	24	25	26	27	28	29	30	May 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	June 1	2	3
TUBERCULIN.		T. 99° ℉	R. T. O. ·0001 c.c.		T. 99.2° ℉						R. T. O. ·0001 c.c.					T. 99° ℉			R. T. O. ·0001 c.c.							T. 99.2						T. 99.6														T. 99.8			
POLYMORPHS. 1		49	44	44		53		48		44				64		63		53		42		58	59	54			56					64		60		63		58				56			46
2		44	49	48		45		49		44				34		32		43		26		42	39	43			40					29		36		34		41				40			49
3		4	4	4		2		3		6				2		5		4		2		0	2	3			4					4		4		2		1				4			5
4		0	0	1		0		0		0				0		0		0		0		0	0	0			0					0		0		1		0				0			0
5		0	0	0		0		0		0				0		0		0		0		0	0	0			0					0		0		0		0				0			0
REMARKS.																																															

Crepitations at both apices. Sputum T.B. positive (No. 2 Gaffky).

Afebrile.

The neutrophile classification was slightly below that of the deciding value. It was therefore doubtful whether she was a suitable case for tuberculin or not.

On 11th July I injected .0001 c.c. P.T.O. This produced a slight effect on the blood which passed off in a day or two. I then gave .0002 c.c. which produced a very evident effect on the blood. Moreover, this change in the neutrophile classification did not disappear for several weeks.

No temperature or discomfort of any kind was caused by either of these doses.

I came to the conclusion that this case was not a suitable one for tuberculin and accordingly I gave up the treatment. In the above case I increased the dose at the second injection. In all probability the same effect would have been produced if I had merely repeated the initial dose, but possibly a third dose would have been necessary before a lasting effect would be produced. The following case is an illustration.

Case 5. Mary Ann Davidson, age 17. Admitted 11th April 1912.

Her neutrophile classification before tuberculin was slightly better than that of the deciding value (See Chart).

On April 19th I injected .0001 c.c. P.T.O. which

produced /

SANATORIUM CHART.

Extending over 3 months.

NAME & AGE Richard Porteous Age 13.

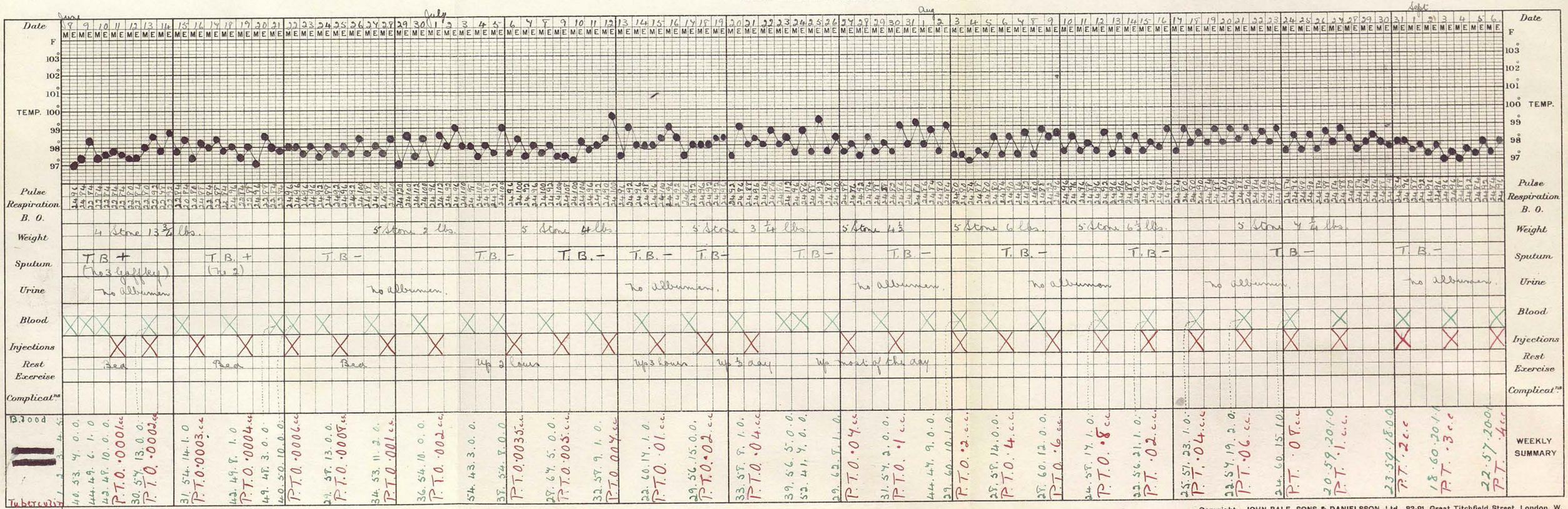
DATE

CASE-BOOK Nº

NORMAL WEIGHT

HEIGHT

CHEST { INSPIRATION / EXPIRATION



When ordering please quote Chart No. 19.

produced a deterioration in the neutrophiles. The blood recovered in a few days, when I repeated the initial dose. This also caused some deterioration in the neutrophile classification. However, recovery again resulted in a few days, when I repeated the same dose. This was followed by a more permanent effect on the blood which lasted several weeks.

To begin with, this patient had a slight temperature, but the tuberculin had no effect whatever on it.

In this case also therefore I concluded that tuberculin was contra-indicated, and I accordingly withheld it.

The following case had, to begin with, a neutrophile classification somewhat similar to the above case. In this patient however a lasting deterioration was not produced on the blood by the first few doses of tuberculin. I accordingly proceeded with the treatment which met with complete success, the neutrophile classification gradually improving to the normal condition.

Case 6. Richard Porteous, age 13. Admitted 8th June.

Complaint. Cough and Spit. Loss of weight.

Duration. Four months.

Physical Examination. Right lung, Stage II; Left lung - Stage I. Numerous rales at both apices. Sputum T.B. positive (No. 3 Gaffky).

Neutrophile classification slightly below the deciding value.

On June 11th I injected .0001 c.c. P.T.O. which caused /

caused no alteration in the classification of the polymorphs. I then gave .0002c.c. This also produced no effect and I accordingly proceeded with the treatment knowing that the succeeding doses would produce no lasting deterioration in the blood, since the earlier doses had not done so. I gradually increased the dose until I had injected 1 c.c. P.T.O. when the neutrophile classification was practically that of a normal blood. I then continued the treatment with P.T. of which I injected 1 c.c. on 16th September.

During the whole course of treatment only on one occasion did the temperature rise above 99° F. This occurred on the 12th July, but as no effect was noticeable on the blood, I paid no attention to this rise and proceeded with the treatment without delay. (See Chart). The patient never suffered the slightest discomfort.

He had now no sputum whatever. All his symptoms had disappeared, and he had gained several pounds in weight.

There were now no physical signs of activity, and the only evid ence in the lung was an impaired note at the right apex.

The patient was therefore to all intents and purposes cured. Whether he will remain so or not remains to be seen. I have made arrang-ements for him to visit me once every month at the Dispensary.

Cases Suitable for Tuberculin.

Besides cases similar to Richard Porteous (vide supra) all patients with a neutrophile classification of greater value than the deciding classification are suitable for tuberculin treatment. The nearer this classification is to the normal, the more likely will a cure be brought about by the tuberculin.

Numerous illustrations have been given under TREATMENT. It is therefore unnecessary to give any here.

Treatment of Cases Unsuitable for Tuberculin.

If by the above methods I have decided that a patient is not suitable for tuberculin treatment, I never lay the case aside as never likely to be benefited by this form of treatment. I consider that these patients require treatment by open air methods preferably in a Sanatorium. The blood should be examined by Arneth's method from time to time, and thereby the degree of improvement measured.

In this way we may find that the neutrophile classification increases in value to the necessary extent. If this occurs the patient is now suitable for tuberculin which should be given as I have recommended.

If /

If this does not occur, the patient must continue with the ordinary forms of treatment, fresh air, good food etc., as tuberculin will not do him any good, and, in all probability, will do him harm.

TUBERCULIN REACTION.

It is not my intention to discuss the nature of this reaction at any length. It is necessary, however, to account for the changes which take place in the neutrophile corpuscles during such a reaction.

There have been many theories advanced in explanation of the tuberculin reaction, but most of them leave a great deal unexplained. The Lysin Theory of Wolff-Eisner seems to me to be the most logical, and it most satisfactorily accounts for all the phenomena observed during the administration of tuberculin. It is this theory which I believe to be the most correct one, but whether it is so or not, it serves as an excellent working theory.

In order to make what follows quite clear, it will be advisable, first of all, to give a very short outline of Wolff-Eisner's theory.

Wolff-Eisner's Theory.

We may assume that albuminolysins are formed after injection of foreign albuminous substances, just as bacteriolysins are produced after injection of bacterial /

:al protein. These abbuminolysins are formed by the tissues of the body as antibodies to the injected albumin. Just as bacteria are dissolved up by bacteriolysins, so the foreign albumin is acted on and broken up by a specific lysin. This sets free a substance which has a much more toxic action than the injected albumin.

In applying this theory to the action of tuberculin, Wolff-Eisner assumes that tuberculin is itself a foreign albuminous substance. When it is injected into the body, it meets a specific lysin, and becomes lysinized. This lysinized tuberculin is of high toxicity, and it causes the toxic symptoms of the general reaction which follows the injection of tuberculin in a tuberculous individual. A local reaction may be caused by the irritative action of the lysinized tuberculin on the tubercular focus, the occurrence depending on the local capacity for stimulation.

In the tuberculous individual, the specific lysin is always present in the body formed by the reactive processes to tuberculin produced at the tuberculous focus. This accounts for the reaction in these individuals. If the focus is latent, the patient still reacts, because enough tuberculin is produced to ensure the constant presence of a small quantity of lysin in the body.

In the case of a healthy individual, however, there is no lysin in the body, and the patient, therefore, does not react to one dose of tuberculin.

He /

He may react to repeated injections, because the early doses stimulate the cells of the tissues to the production of lysin which acts on the later injections of tuberculin producing the highly toxic lysinized tuberculin. In the same way the healthy individual may react to a single large dose of tuberculin, because, after it has caused the production of lysin there is still tuberculin enough to be acted on by this lysin.

Wolff-Eisner then, believes that this lysinized tuberculin causes all the symptoms of the reaction, both local and general, and that tuberculin is not, in itself, really toxic.

I do not propose to discuss all the variabilities and anomalies of the tuberculin reaction, but these are all satisfactorily explained by the above theory.

The changes which occur in the blood after injection of tuberculin can also be accounted for by this theory. (The outline of Wolff-Eisner's theory is completed under ACTION OF TUBERCULIN.)

Its Application to the Changes in the Blood.

The shape and complexity of the nuclei of the neutrophile leucocytes is very variable. The mature corpuscle has a very complex nucleus. The younger ones have very simple nuclei. As these young members grow older their nuclei become more complex, and may finally appear to be multiple-nuclei.

When /

When any infective process is actively proceeding, toxins are circulating in the blood. These toxins cause the destruction of large numbers of leucocytes. In the case of the neutrophiles, leucocytes belonging to all classes, or it may be only the more mature leucocytes, are destroyed. The significance of this is discussed under ACTION OF TUBERCULIN. In any case, new leucocytes are rapidly formed and the younger members actively proliferate, so that we have now a large preponderance of young neutrophiles, that is, leucocytes belonging to Class I.

This is illustrated in Septicaemia, Diphtheria, etc., and, in the case of Phthisis, exactly the same thing occurs. In this disease the toxin is the lysinized tuberculin produced by the action of the specific lysin on the tuberculin formed in the body. The amount of destruction of neutrophiles is dependent on the amount of lysinized tuberculin in the blood which depends on the amount of tuberculin produced at the focus of the disease. The more active the focus, the more tuberculin is produced, and still more is produced if the disease is not only active but also very extensive.

Thus it is that the value of the neutrophile classification depends on the activity and extent of the disease. In an early case there may be sufficient toxin (lysinized tuberculin) in the blood to cause some destruction of leucocytes, but not enough to produce /

:duce toxic symptoms, temperature etc. If the case is more active there may be sufficient lysinized tuberculin in the blood to cause a rise of temperature. This causes a proportional destruction of leucocytes, and a classification of low value is found. If the case is both advanced and active, the corpuscles never reach maturity, and a very low classification is produced.

When a patient is being treated with tuberculin, the specific lysin, which is always present in the tuberculous individual, acts on the injected tuberculin producing exactly the same toxin. This lysinized tuberculin causes the Tuberculin Reaction. If only a small amount is produced, then no clinical signs result. Nevertheless, there may be sufficient to cause some leucocyte destruction, and therefore an alteration in the classification of the neutrophiles. That is to say, a very small amount of toxin causes no effect whatever; a larger amount causes an alteration in the neutrophile classification; a still larger amount makes itself evident by causing the well-known signs of the Tuberculin Reaction, their severity also depending on the amount of lysinized tuberculin present.

This explains why the blood gives us a warning of the probability of a reaction.

In the healthy individual, no specific lysin is present in the body, therefore no lysinized tuberculin is produced by the injection of tuberculin and no alteration occurs in the neutrophile classification.

Low /

Low Classification Value.

It has been mentioned that, in an active case of phthisis, especially if the disease is advanced, the classification of the neutrophiles is always of very low value. This is because the larger amount of toxic lysinized tuberculin present destroys the corpuscles before they reach maturity.

The power of forming new corpuscles may also be diminished to some extent because of the lysin interfering with the function of the blood-forming organs - bone marrow etc. This probably does not often occur to any extent, because the total number of neutrophiles is not very much reduced. If, however, the amount of toxin is excessive, this effect becomes very marked, and the function of the bone marrow is interfered with as well as the function of every other organ in the body. When this occurs, not only is the neutrophile classification of very low value, but the total leucocyte count is very low.

Another factor which helps in the production of a low classification value is the interference with the proliferation of the young corpuscles. This probably occurs to some extent in every degree of toxicity.

We have therefore three factors, either acting together or separately, which tend to lower the value of the blood. First, the destruction of corpuscles. Second, interference with the proliferation of young corpuscles /

corpuscles. Third, occasionally, the interference with the formation of new corpuscles.

The above explanation is of importance in connection with immunity.

In the administration of tuberculin, we have exactly the same effects produced, and according to the amount of tuberculin injected, one, two, or all three factors may come into play. If there is already a large amount of toxin in the body, a very small amount of injected tuberculin will be sufficient to lower the value of the blood considerably.

Cases in which Tuberculin does Harm.

When the neutrophile classification is of very low value, it is evident that there is too much toxin in the body already. The addition of more by means of the injection of tuberculin would evidently be useless and probably harmful.

When the neutrophile classification to begin with is of good or moderate value, and the administration of tuberculin lowers this value permanently, the tuberculin has done serious harm.

As I have described and illustrated above, when the classification is at or near the "deciding value", it is necessary to give one or two doses of tuberculin before deciding whether the case is a suitable one or not. If these doses cause a lasting deterioration, it must be that the tuberculin has increased the activity /

:vity of the diseased focus, because although no more tuberculin is being injected, an excess of toxin is still present and acting, as the neutrophile classification remains of low value. It is in cases such as these that we may cause serious harm by the administration of tuberculin. They also illustrate the necessity of blood examination before and during the administration of tuberculin.

Cases in which Tuberculin does Good.

If a case is suitable for tuberculin treatment, one dose may lower the value of the blood. This deterioration, however, is merely temporary, and rapid recovery follows. By increasing the dose, and arranging the intervals between the doses, as I have recommended, the classification gradually improves and very large doses of tuberculin can be administered without producing any lasting bad effects on the blood.

In these cases, I believe that the tuberculin still causes destruction of the neutrophiles, but it also stimulates the blood-forming organs to increased activity and also stimulates the proliferation of the younger corpuscles, so that, the neutrophile classification instead of deteriorating, increases in value.

It is my opinion that this leucocyte destruction has a close relation to immunity. This however is dealt with under ACTION OF TUBERCULIN.

In the same way, such a patient can tolerate very large doses of tuberculin without shewing any clinical signs of reaction.

This is not because the patient has become insensitive to the tuberculin. He is probably more sensitive than he was before the treatment was started, but the whole army of reactive forces have been brought into action, and these now work so quickly and smoothly that the toxins do not get the opportunity to make themselves evident.

ACTION OF TUBERCULIN.

In his theory, Wolff-Eisner assumes that the lysins are antibodies formed by the action of tuberculin whether originating in the body or artifically injected. This lysin acts on the tuberculin, and the product (lysinized tuberculin) probably acts on the tubercle bacilli killing or weakening them.

This lysinized tuberculin causes the formation of secondary antitoxic bodies which act against the lysinized tuberculin and lysinized tubercle bacilli. These are not only specific, but the lysinized tuberculin, by local irritative actions, calls up the non-specific curative forces - inflammatory hyperaemia etc. (This completes the outline of Wolff-Eisner's Lysin Theory.)

Blood and Immunity.

I believe that Wolff-Eisner's theory explains the action of tuberculin most satisfactorily. Of course it has not been proved to be the correct explanation.

It has been said that the lysinized tuberculin causes the production of secondary antibodies. Is it not /

not possible that these are formed in the blood-forming organs and sent into the blood stream in the leucocytes, and released by their destruction ?

It has been shewn by Wasserman and others that immune bodies originate chiefly in the bone marrow. If this is so, it is more than likely that the leucocytes carry them through the body in the blood stream, and give them up when they are destroyed by circulating toxin.

My observations of the blood of phthisis patients, and the effect of tuberculin on it, has satisfied me that a close relation exists between immunity and the changes in the neutrophile classification.

By assuming that the most mature corpuscles, that is, those with the most complex nuclei, are the most useful in resisting infection, we can explain the connection with immnuity. These corpuscles, then, carry the most active antibodies which are released when the leucocyte is destroyed. This lowers the value of the neutrophile classification which now consists of leucocytes carrying no or very ineffective antibodies. If the circulating toxin is in excess the classification remains low. If, however, the individual is improving, the classification gradually improves. This is because corpuscles are more rapidly formed and more rapidly proliferate as part of the reactive process. They rapidly reach maturity and are destroyed, releasing /

:ing their antibodies.

Tuberculin treatment produces exactly the same effect if properly carried out in suitable patients. A dose of tuberculin indirectly destroys the mature neutrophiles and thereby releases the antibodies. Another dose is not administered until the young corpuscles have reached maturity when they are in their turn destroyed, and gradually the blood-forming organs, by rapid action, and by the rapid developement of the corpuscles, the destruction of mature leucocytes, releasing antibodies, and replacement of these, goes on so rapidly that no change in the neutrophile classifi-:cation is noticeable. Thus a continuous stream of antibodies is set free to act against the poison.

When treatment by tuberculin is not carried out properly, or attempted in unsuitable cases, the mature (antibody carrying) neutrophiles are destroyed by the first dose or two of tuberculin. These are not replaced, and therefore a sufficiency of antibodies is not supplied. The treatment, therefore, rather allows the disease to get the upper hand, because the excess of toxin prevents the formation and growth of neutrophile leucocytes.

The continued presence of a good neutrophile classification indicates that there is a sufficiency of antibodies.

The /

The continued presence of a neutrophile classification of low value means that a sufficiency of antibodies is not being produced, shewing that the optimum stimulation is not being applied, or is being exceeded.

CONCLUSIONS.

Tuberculin produces a marked effect on the blood.

The effect of chief importance is that produced on the neutrophile leucocytes. This effect is recognised by the alteration produced on Arneth's classification of the neutrophiles.

This change only takes place in the blood of tuberculous individuals/

individuals.

Similar changes take place in the blood of phthisis patients during the ordinary course of the disease according to the degree of intoxication.

These changes are satisfactorily explained by an excellent theory on the action of Tuberculin.

They are probably closely related to immunity which gives them a special significance.

They can be used along with tuberculin as an aid in the diagnosis of tuberculosis. By using them we avoid the danger of clinical reactions, and the patient suffers no discomfort.

By frequent examinations of the blood by Arneth's method, we have a means of measuring the progress made, and the success, or otherwise, attending our method of treatment.

The condition of the neutrophile classification gives us a method of deciding whether a patient is or is not suitable for tuberculin treatment.

The neutrophile classification also serves as a guide in the treatment of tuberculosis especially by the administration of tuberculin. The fact that this control /

control is absolutely reliable, and not subject to accidental fluctuations in any way makes it especially valuable.

By using the method I have recommended in the diagnosis etc of tuberculosis, we get rid of the numerous difficulties associated with the administration of tuberculin in the Dispensary, and in the home of the patient.

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