Diagnostic Methods in Early Pulmonary Tuberculosis

with special reference to the opsonic-index and complement fixation technique

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Note:- Section V: sub-section B. has been published as a separate article in the British Journal of Tuberculosis Oct. 1914. entitled "The 'Albumin-Reaction" of the sputum in Pulmonary Tuberculosis."

SECTION I.

INTRODUCTORY AND DIFFERENTIAL DIAGNOSIS.

Of probably no disease other than pulmonary tuberculosis could it be said that increased attention to methods of diagnosis and prophylaxis would give rise to a vicious circle in treatment: yet this statement is open to comparatively simple demonstration.

Within the last ten years and particularly during the last two of these, a more or less systematic campaign has been entered upon with a view to reducing the incidence of tuberculosis amongst the population.

As a result of this there has been a speeding-up of methods of early diagnosis in the hope that possible centres of infection might thus be avoided: diagnosis in the so-called pre-bacillary stage has been made the criterion of good practice: examination and frequently prophylactic treatment of contacts has been made as far as possible a routine measure and finally great efforts have been made to educate the lay public as to the infectivity and means of eradication of the disease.

Moreover at the initial stages of development of this phase, the recognised and approved means of treatment of pulmonary tubercle happened to be, for good or ill, residence over a lengthy period in open-air sanatoria, with the natural result that as early diagnosis became more common and contact isolation more strict, such sanatoria sprang up all over the country.

Unfortunately the education of lay opinion was a very incomplete process, and the general public developed

and still retains a rather unwholesome dread of the dangers of association with either the phthisical subject or the contact.

This fear when confined to householders within an area of a few miles around a tuberculosis sanatorium was merely of academic interest, but when the bulk of employers became influenced by the same conception, the matter became of vital importance.

Previously the average employer of labour had estimated the significance of tuberculosis in terms of incapacitation of the workman: it had often been noted for instance that the working life of the consumptive — probably in those days the moderately advanced consumptive — ran from two to five years. With the education of lay opinion, however, and the increased responsibilities in the relation between the employer and workman, the point of view entirely changed, and now the position is practically this:- the bulk of employers will not, if they can avoid it, employ consumptive patients, and they frequently refuse to re-employ consumptive subjects either after their first spell of treatment or at any rate on their first breakdown after treatment. Now while this may simply add to the responsibilities of the particular tuberculosis centre involved and may be merely an unavoidable hardship, in the case of the contact or the suspected subject, another element deserves consideration. In the earlier period

suspects and contacts were not even recognised and the problem simply did not exist: to-day treatment of the contact or the suspect in sanatoria is liable to engender an economic ostracism even should the case ultimately prove to be negative. Now the subsequent mode of life of people, who can with difficulty obtain employment is, more often than not, the mode most predisposing to pulmonary tuberculosis - or at any rate most likely to light up an old tubercular focus. Here then is the vicious circle:

DIFFERENTIAL DIAGNOSIS.

The most urgent problem confronting the organisers of the anti-tuberculosis campaign is, then, increase in the accuracy of differential diagnosis: and here again pulmonary tuberculosis is found to present almost unique difficulties.

Even if one were to put aside the classical list of diseases and abnormal conditions simulating phthisis, there still comes up for settlement the question of relative activity or obsolescence of the disease itself at any particular time.

It is not customary to include obsolete or healed tubercle in the list of diseases to be distinguished from active tubercle, but the writer has been so impressed by the frequency with which this difficulty arises, that he not only includes these conditions in a consideration of differential diagnosis but gives them pride of place.

Next in importance comes a group of rather vaguely defined maladies, which might be classified as indeterminate toxaemias: this group includes practically every cause of general ill-health and constitutes quite a large percentage of those cases of suspected phthisis which are ultimately proved to be negative. Lastly comes the classical group of diseases simulating phthisis.

I. RECENTLY HEALED AND OBSOLETE PULMONARY TUBERCULOSIS.

It must be clearly understood that this group does not include those cases which although unhealed are in such a quiescent condition as to give no definite clinical or bacteriological signs of activity.

It has been a subject of controversy whether such quiescent cases should undergo the full course of treatment given to the ordinary consumptive, but the writer is not concerned for the moment with this point: the question in his view is one of 'healing' or 'non-healing' at the time of examination.

Similarly he is not concerned with the validity or otherwise of von Behrings (x) theory that phthisis in the adult, whether curable or terminal, is simply a

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(x) von Behring: Deut. Med. Woch. 1904 XXX.

recrudescence of an old infection: such very probably is the case, but here again the question for the diagnostician is simply: - Does the patient at the time of examination suffer from active disease? It is necessary however, to prove that healed disease is really a common source of error in diagnosis.

The proposition put in general terms is as follows:

If it can be proved that the most individuals have had at one time or other in some part of their systems, a definitely tuberculous lesion and further if it can be shown that a definite percentage of lung lesions, either fresh or recrudescent, become spontaneously healed - spontaneously in the sense of becoming healed without any treatment - and still further if it can be shown that definite extensive lesions of the lung do become healed after appropriate treatment, then it is not unreasonable to say that examination of any individual at any time may indicate the presence of a pulmonary lesion varying in extent from a few cubic centimetres to the greater part of a lobe, which lesion is giving rise to no definite symptoms and which is in fact at the time of examination a healed lesion.

Proof of the first contention can be established only from a review of the results found in the literature, results based mainly on Post-mortem examinations of subjects of various ages and on specific tuberculin testing of children.

The work of Escherich (⊗), Hamburger (◎), and Monti on the incidence of tuberculosis, as shown by the cutaneous tuberculin test, amongst the school-children of Vienna gives the following results (abbreviated).

Amongst	children	of	14	years	of	age	the	incidence	was	90%
"	"	"	7-8	"	"	"	"	"	"	70%
"	"	"	3	"	"	"	"	"	"	25%

Daske working in Dusseldorf did not obtain such striking result with the von Pirquet reaction, but his figures are nevertheless interesting

Of	children	12	to	14	years	of	age	49.9%	were	positive
"	"	9	to	11	"	"	"	43.7%	"	"
"	"	6	to	8	"	"	"	40.7%	"	"

Lapage (⊕) dealing with 1000 hospital children found that 32% of those under 2 years and 60.8% of those between 10 and 14 were positive.

Out of a series of 91 children with no manifestations of tubercle Harbitz (∈) found that 18, (10 being under 1 year) were actually infective as

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(⊗) Escherich: Wein. Med. Woch. 1911 lxi.

(◎) Hamburger: Wein. Klin. Woch. 1907 xx

(⊕) Lapage$ Brit. Med. Journ. 1912 ii 1375.

(∈) Harbitz: Untersuchung. über die. Häufigkeit. der Tub. 1905 (quoted)

proved by guinea-pig inoculations, and ten of these inoculations were made from cervical glands alone. In addition Hamburger found that 38.3% of 848 necropsies performed on subjects of all ages gave evidence of tuberculosis: Lubarsch (⊗) proved that out of 1820 cases of all ages 60.6% were tuberculous, 297 of these cases being children, of whom 21.2% were positive. The most striking results were obtained by Naegeli (◎), who found that 97% of his series of cases had some tuberculous lesion: up to the age of 15, 50% were positive: there was a sudden rise in the 18th year to 96% and above 40, a tuberculous focus was found in every body.

With regard to the second contention that a definite percentage of cases become spontaneously healed without any pressing symptoms and without any treatment, although this condition would seem to follow the establishment of the previous point, no very general opinion can be found.

Fishberg (⊕) says that such cases healing without treatment within three months are common and labels them 'abortive cases': Neisser and Brauning of the Breslau

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(⊗) Lubarsh: Fortschr. der Med: Berlin 1904 XXII.

(◎) Naegeli: Uber Haufigkeit, etc. der Tub: Virchow Arch. 1900. clx (quoted)

(⊕) Fishberg: Medical Record. 1913 I. 921.

Clinic found that 300 out of 1900 cases were of this abortive type, but the proof of definite healing does not seem to have been quite conclusive.

It might be argued, for instance, that these cases were in a quiescent stage at the time of examination and to meet this objection, the writer has given the results of detailed examination of series of cases coming under his own observation.

These cases, (20 in all) were selected from a series of 100 doubtful cases, all of whom were admitted to Sanatoria as cases of suspected phthisis.

In the twenty cases detailed, a reliable history was given of Tubercle Bacilli having been found in the sputum prior to admission (in every instance within three months) and as the sputa on admission proved to be negative, each case was investigated by serum methods and finally tested with subcutaneous tuberculin: in each case the sputum was examined by the sedimentation method of Ellerman and Erlandsen: the following are the results.

Table showing condition of twenty cases within three months of a Bacillary find.

Case	Sputum		Tuberculin Test		Serum Reactions	Sputum on Dismissal	Diagnosis
	Before admission	On admission	General Reaction	Focal Reaction			
1	T B +	T B -	+	+	+	T B +	Active Disease
2	+	-	+	+	+	-	Quiescent "
3	+	-	±	+	+	0	Quiescent "
4	+	-	+	-	±	-	Quiescent "
5	+	-	+	-	+	-	Quiescent "
6	+	-	+	-	-	-	Healed lesion
7	+	-	+	-	-	0	" "
8	+	-	+	-	-	-	" "
9	+	-	+	-		-	" "
10	+	-	-	-	-	-	" "
11	+	-	-	-	-	0	" "
12	+	-	-	-	-	-	" "
13	+	-	-	-		-	" "
14	+	-	-	-	-	-	" "
15	+	-	-	-	-	-	" "
16	+	-	-	-	-	-	" "
17	+	-	-	-	-	-	" "
18	+	-	-	-	-	-	" "
19	+	-	-	-	-	0	" "
20	+	-	-	-	-	-	" "

It will be noted that 15 cases (75%) showed no signs of activity within three months of a bacillary find, but it is necessary to add that no deductions can be drawn as to the spontaneous curability of the average case of phthisis from these figures. As a matter of fact of the remaining 80 cases, without any positive bacillary find before admission and either with a negative sputum examination or without sputum on admission, 13 on further examination showed signs of active disease, although usually of minimal activity.

But although no such general conclusion can be drawn from the figures, they may be held to prove the possibility of so-called spontaneous cure in a definite percentage of cases.

The third contention that even definitely active and moderately advanced cases will after special treatment become healed is so generally accepted as a fact and so generally attested by the after-histories of Sanatorium cases that no proof of it need be brought here.

One more statement, however, is necessary before stating any conclusion, and it is that in the experience of most diagnosticians a very substantial impairment of the lungs, either affecting the greater part of a lobe or smaller parts of 2-3 lobes is frequently found in cases giving a very recent history of ill-health.

SUMMARY.

A consideration of these facts leads the writer to the following conclusions:

(1) that examination of any individual may and frequently does indicate the presence of a pulmonary lesion, varying in size from a few cubic centimetres to the greater part of a lobe, which is at the time of examination a healed lesion.

(2) that the frequent occurrence of this condition makes healed tuberculosis the most important section of differential diagnosis.

II. GENERAL ILL-HEALTH OF UNDETERMINED CAUSE.

It may be said in criticism of the last section that such a condition is not likely of itself to give rise to symptoms necessitating examination but to grant this is simply to demonstrate the disadvantage of a relatively arbitrary classification.

The writer is prepared to admit that although 'contact-examination' frequently gives rise to the difficulty, many cases would not come up for examination were it not for a co-incidental state of general ill-health: as this general health, however, is frequently the sole pathological condition found, he is forced to include it in a separate section. It is one of the disadvantages of specialization particularly in tuberculosis that a suggestive history almost invariably

stirs up in the specialist what French would call a 'concealed complex'.

Given a general history of ill-health and a particular history of cough with or without sputum, the tuberculosis expert immediately begins to paw the ground and snuff the air; with the frequent outcome for the patient of a spell of treatment, even if only prophylactic in nature; and in sanatorium experience at any rate, it is not the classical list of diseases which comes up for exclusion. Much more common is a history of vague ill-health; varying degrees of asthenia; gradual loss of weight perhaps; persistent low fever, chronic cough: occasional traces of sputum: persistent mucoid spit: less frequently night sweats.

These symptoms may be roughly divided in two groups depending usually on the after history.

They may be the forerunners of a very definite disease; as, for instance in progressive bowel conditions such as mucous colitis, in mild cases of cystitis and in most forms of chronic anaemia: more frequently they are associated with vague, ill-defined chronic toxaemias. The researches of Arbuthnot Lane and Hale White have proved that chronic intestinal toxaemia may simulate almost any disease, particularly tuberculosis where there is a co-incidental history of cough and spit, and it is well known that, in the female, slight disorders of the genital system will give rise to equally perplexing conditions of ill-health. In the writer's

own experience about 50% of doubtful cases which ultimately proved to be negative belonged to this group.

III. DISEASES OF THE CHEST SIMULATING PHTHISIS.

Many of these diseases have become more of academic than of practical significance since the introduction of concentration examinations of the sputum, and there is no necessity to detail the usual lengthy list.

Apart from the rarity, for instance, of tuberculosis as a complication of advanced mitral disease, the examination of the blood-stained sputum will give an opportunity of differentiation. The same may be said nowadays of acute apical bronchitis, of chronic bronchitis, of bronchiectasis, of abscess, actinomycosis, gangrene and of pneumoconiosis.

There remain, however, three types of cases likely to give rise to difficulty in diagnosis:

A. Collapse - induration of the right apex associated with naso-pharyngeal catarrh. This has been extensively worked out by Gottfried Maier, Blumel (⊗) and Kronig(◎) and recently de Wesselow(⊕) points out that 8 out of 30 completely negative tested cases gave

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(⊗) Blumel: Munch. Med. Wochenschr. 1908. No 30.

(◎) Kronig: Deut. Klin. 1907. Band. XI.

(⊕) de Wesselow: Proc. Roy. Soc. Med. 1914, Vol VII.

evidence of this condition, including impairment of note and movement, harsh breath sounds at the right apex, a history of cough and spit and an unhealthy naso-pharynx.

B. Malignant disease: It is, of course, natural to expect that malignant disease of the lungs might give rise to any of the signs simulating phthisis, but in addition the writer has come across cases (2) where a malignant liver by upward pressure and ultimate ulceration of the diaphragm caused almost unmistakeable signs of phthisis.

A case of gastric carcinoma, on the other hand, whilst giving no clinical signs came under his notice owing to a history of cough and spit, progressive weakness and emaciation, night-sweats and haemoptysis (actually haematemesis).

C. Syphilitic ulcerations of the lung: Without attaching any weight to Carl Spengler's statements as to the intimate connection of pulmonary tubercle and syphilis, one has to exclude this disease in a definite percentage of cases and the difficulty is increased where the larynx is atypically affected.

D. Apical induration in heart disease. Fishberg (X) pointed out that of 38 mitral cases, 27 gave signs suggestive of phthisis: 22 had crepitations at one or other apex: 5 had a large haemorrhage and one a slight haemoptysis.

(X) Fishberg: New York Med. Journ. 1913 II 14.

As has already been stated in the case of the haemoptyses sputum examination would give definite means of differentiation.

Conclusion: The frequency of healed tuberculosis of the lungs, makes this condition of the first importance in differential diagnosis: vague chronic toxaemias associated with some pulmonary symptoms are extremely common and difficult to distinguish from phthisis; syphilis, carcinoma, naso-pharyngitis may give rise to difficulty in diagnosis.

In all of these groups the clinical manifestations may be misleading and it is important to find if any other test or series of tests can give a positive or negative diagnosis within a reasonable time and without either danger or great discomfort to the patient.

S E C T I O N II.

SYMPTOMATOLOGY.

It is perhaps not an unfair criticism of the practice of that mysterious entity - the 'instinctive clinician', that whereas he frequently hits the nail on the head, just as frequently he hits the wrong nail on the head; and [redacted] this happy-go-lucky diagnosis is made more commonly in pulmonary tuberculosis than in any other disease.

A glance at an ill-nourished or poorly developed subject, a few leading questions eliciting a history of cough with or without spit, associated with, say, recent ill-health, some loss of flesh and perhaps an occasional night-sweat, and presto! the diagnosis is made - to be subsequently clinched by the discovery of impairment at ~~the~~ an apex.

Indeed, it is rather unfortunate that pulmonary tubercle should be supposed to possess to such a degree the so-called 'classical picture.'

It is not the writer's intention to consider in detail individual symptoms, but it is desirable to review a few of the more traditional suspicious signs.

For instance, the significance of cough with or without sputum may be greatly over-rated.

Cruice (⊗) in dealing with this section makes the statement that 'the existence of cough over a longer period than two months is gravely suspicious of pulmonary tuberculosis', but it should not be forgotten that such a symptom might also be gravely suspicious of gastric carcinoma, particularly if the sputum were largely mucoid in character. And again, a chronic cough even with muco-

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(⊗) Cruice: Medical Record, 1912, ii, 334.

purulent sputum may have no deeper origin than a pharyngitis with occasional intercurrent bronchitis.

In much the same way loss of flesh, general ill-health, marked asthenia, occasional night-sweats, anaemia, may simply be pointers to conditions distinct from tuberculosis.

There are, however, three points in history and symptomatology deserving of definite consideration, and these are a history of pleurisy, a history of haemoptysis and the existence of persistent pyrexia of varying degree.

Pleurisy.

The work of Osler (⊗), Hedges (⊕) and Allard and Köster (◎) in the subsequent history of pleuritic cases, the investigations of Zebrowski (⊘) and le Damany (⊜) on the bacteriology of pleuritic fluids, Beck's work on tuberculin-testing of pleuritic subjects, and the abundant post-mortem investigation of these cases have established firmly the conclusion that the large majority of cases (varying in different works from 30% - 40% to 70%) are of tuberculous origin.

Haemoptysis.

It is possible that popular dread of haemoptysis has influenced to some slight degree the attitude of the clinician as to its diagnostic value.

Cruice (⊙), for instance, states that all haemoptyses

(⊗) Osler: System of Medicine, 1908.
(⊕) Hedges: Bart's Hosp. Rep. 1895- 31.
(◎) Allard and Koster: Hygiea, Oct. 1911 (quoted)
(⊘) Zebrowski: Deut. Med. Woch. 1904, 342.
(⊜) le Damany: Presse Medicale, 1897, 329.
(⊙) Cruice: Medical Record, 1912, ii, 334.

should be considered of tuberculous origin until otherwise explained, and Riviere (⊗) considers that where other causes can be excluded this symptom is 'well-nigh pathognomonic' of tubercle.

Stricker's figures for the Prussian Army during the years 1890-95 are largely quoted in most text-books, but in the light of modern methods they probably require some revisal.

His records dealt with 900 cases of haemoptysis, and he concluded that where the haemorrhage took place apart from undue exercise 86% of the cases were tubercular; that when it occurred after moderately hard exercise 75% were positive, and that when after violent exercise 50% were cases of tubercle.

At the same time it must be remembered that out of the 480 cases included in the first class, in only 221 cases (45%) was the diagnosis conclusively confirmed.

This, of course, alters entirely the significance of the figures, because it is precisely the after-history of the remaining 55% of cases that would throw any light on the relative significance of haemorrhage.

Kidd (⊕) points out that the significance is far greater when the amount of blood brought up is considerable, but on the other hand the figures for the Brompton Hospital show that of 4,125 cases of haemoptysis, in 69% the amount was under half an ounce, and from the theoretical point of view the significance of streaks of blood when in

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(⊗) Riviere: Diagnosis of Tubercle, 1914.
(⊕) Kidd: Allbutt's System of Medicine, 1909.

definite association with the act of coughing, should, if haemorrhage be such an important indication, be worthy of just as much consideration as any larger amount.

The writer's own experience has led him to the conclusion that haemoptysis is not of such diagnostic importance as is generally believed.

In the first place, in reading through various textbooks he has found that roughly only 70% of cases of definite pulmonary tuberculosis are subject to bleeding and in the next, a very small percentage of definite cases give a history of a beginning with haemoptysis unassociated with any other symptom.

Bartlett (x), for instance, found it in 6% only out of 400 cases, although it has been said to occur in as many as 20% of cases.

Again, before any cases of haemorrhage can be said to be due to tuberculosis, a large group of diseases require to be excluded, of which the following are but a few: - mitral disease, embolism, aneurysm, bronchiectasis, bronchitis, malignant disease, actinomycosis, pneumoconiosis, syphilis and anaemia.

But putting the claims of these diseases aside,— and it may be admitted that the likelihood of their confusing any diagnosis for long is not very great,—it does not follow that where these possible causes have been excluded, the occurrence of haemorrhage is an indication either of active tuberculosis or of a tuberculosis requiring prolonged or any treatment.

(x) Bartlett: Boston Med. and Surg. Jour. 1911 - clxv.

In the following table the writer gives details of the diagnosis in 27 cases with a history of haemoptysis out of 100 doubtful cases, all of which were fully tested with subcutaneous tuberculin and most by serum methods.

In each case the history was given of a definite haemoptysis, the average amount of which was one to two teaspoonfuls, and which occurred within two months of admission.

All cases were excluded where after cross-examination some obvious fallacy could be detected.

A note is made in each case of the results of sputum examination prior to admission.

Table showing ultimate diagnosis of 27 doubtful cases, giving a recent history of haemoptysis.

	Sputum before admission	Tuberculin Reaction		Serum	Sputum on	Ultimate diagnosis of condition on admission
		Focal	General	Reactions	dismissal	
1.	TB+	+	+	+	-	Tuberculosis:active
2.	+	-	+	-	-	" arrested
3.	+	-	±	-	-	" "
4.	+	-	-	-	-	" "
5.	+	-	-	-	-	" "
6.	-	±	±	+	-	" active
7	o	+	±	±	-	" "
8.	-	+	±		-	" "
9.	o	+	+	+	-	" "
10.	o	+	+	+	-	" "
11.	-	+	+	±	-	" "
12.	-	-	+	-	-	Negative
13.	-	-	+	-	-	"
14	-	-	+	-	-	"
15.	-	-	+	-	±	"
16.	o	-	+	-	o	"
17.	-	-	+	-	-	"
18.	-	-	+	-	o	"
19.	-	-	+	-	-	"
20	-	-	-	-	-	"
21.	-	-	-	-	-	"
22.	-	-	-		-	"
23.	-	-	-	+	-	Tuberculosis:arrested
24.	-	-	-	-	-	Negative
25.	-	-	-	-	-	"
26.	-	-	-	-	-	"
27.	-	-	-	-	o	"

It will be seen that out of 27 such cases only seven on subsequent examination gave evidence of active disease, and one had had T.B. in the sputum before admission.

In five cases a condition of arrested disease was diagnosed, although in four T.B. had been found in the sputum prior to admission and in the fifth case the complement fixation reaction was positive.

Fifteen (15) gave no evidence of disease of any kind.

It may be said in criticism of these figures that the negative sputum examinations before admission may not have been trustworthy, and that therefore the number of "arresteds" might have been greatly increased.

Although this criticism would be quite valid, it would not alter the fact that even if all of the sputa had been positive before admission only seven of the 27 were on admission found to have active disease, and on the same grounds the positive findings before admission might be similarly criticised.

Pyrexia.

Pyrexia, according to Kidd, (⊗) is a symptom hardly less significant from the point of view of diagnosis, than cough; and on the whole it is the general teaching that a slight evening rise may be one of the earliest symptoms; also that in young people whose health is poor and whose weight is decreasing a slight persistent pyrexia is of definite import. It is conclusively established that the only satisfactory method of taking the temperature is per rectum and after a period of at least one hour's rest in

(⊗) Kidd: Allbutt's System of Medicine, 1909.

the recumbent position with the mind in a condition of relative vacuity, but there is no absolute agreement as to the limit of temperature above which a state of pyrexia may be inferred..

The writer's experience of temperatures in Sanatorium practice and elsewhere inclines him to agree with Bardswell and Chapman (⊗) that in the normal the temperature practically never rises above 99° F, although this is by no means accepted by other observers.

Whatever difference of opinion there may be on this point, there can be no question that the persistence of a temperature of over 99° F. for more than two or three weeks is, particularly in the male, indicative of some chronic toxaemia, although not necessarily a toxaemia of tuberculous origin.

In Sanatorium practice the pyrexia met with in doubtful cases can be divided into three classes.

(1) A regular persistent swinging temperature with a range of from 2°- 2.5° - 3° F. rising at its highest point to 99.4° or 99.6° F., most commonly found in cases with a previous history of pleurisy, and frequently of tuberculous origin.

(II) A cyclical temperature in women associated with the period of menstruation, rising seldom beyond 100° F. and running as a rule for about seven days before the appearance of menstrual fluid.

Occasionally this condition is so marked that only for a week after the appearance of the menses is the temperature swinging within normal limits.

⊗ Bardswell and Chapman: Brit. Med. Journ: 1911. 1. 1106.

This condition has been frequently observed in tuberculous women, but its existence does not necessarily point to tubercle.

Bezançon (x) states that it is not peculiar to tuberculpus women, also that as menstruation stimulates all latent infections, these infections must be excluded before a diagnosis of tubercle is made.

In addition, it is frequently present in convalescence from other diseases.

This type of fever is most difficult to recognise when one is studying the temperature from day to day, but a single glance at a chart giving the daily temperature for, say, two to three months is sufficient to prove its association with menstruation.

(III) A type which might almost be called a 'Perpetually irregular' temperature, occasionally within normal limits but mofe often rising at night to 99.2° - 99.6° - 100° or even 100.5° F.

It is probably found more often in the male, chiefly because, in the female, most temperature charts tend to show cyclical variations. It is, in the writer's experience, rarely associated with tuberculosis.

On the whole, then, a persistent regularly swinging temperature is relatively of most importance as regards indications of tubercle, but even then very definitely non-tuberculous subjects are found to show such a regular swing, the cause in one of the writer's cases being a mucous colitis.

In addition, he has rarely found that any of these types unless occasionally the first has been notably altered by

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(x) Bezançon: Le Bulletin Medicale, No. 83, 1913.

variations in exercise and rest even where the subsequent diagnosis showed the case to be one of tuberculosis.

The immediate practical importance of these pyrexias is that they often render diagnostic methods difficult of application.

The subcutaneous tuberculin test may have to be discarded and exercise for a tuberculo-opsonic index estimation may be contra-indicated.

As regards subcutaneous tuberculin, the writer has evolved a method which, he thinks, will overcome this difficulty, at any rate partially, and a description of which will be found in the section dealing with tuberculin testing.

Summary.

A summary of conclusions as to the value of various points in history and symptomatology comes to the following:-

(1) That practically no individual symptom with, on the whole, the exception of pleurisy, is even roughly pathognomonic of tubercle.

(2) That a history of haemoptysis is by no means so indicative of pulmonary tubercle as is generally supposed and that as small a proportion as 27% of these cases may ultimately show active disease.

(3) That, unless with a previous history of pleurisy, no low persistent fever can be said to be even probably tubercle.

Finally, there is one point entirely beyond dispute and it is that any individual one of the symptoms mentioned, although not necessarily an indication of tubercle, is a very urgent indication for a thorough examination of the patient.

SECTION III.

CLINICAL EXAMINATION.

It is not proposed to enter into a discussion of clinical methods of examination of the chest, but a few theoretical considerations may be taken into account.

It is indeed impossible to criticise methods of clinical examination as such on the score of refinement. From the point of view of strict tabulation of clinical facts there is no limit to the desirability of delicate examination, but when it comes to the interpretation of these facts from the point of view of diagnosis, differences of opinion may arise.

To revert to the arguments dealt with in the introduction if we grant that most people have had tubercle at some time in their life without clinical manifestations, that many have had tubercle of the lung with only the slightest clinical manifestations, and that of those who suffer definite and extensive attacks of pulmonary tuberculosis, a certain percentage become ultimately healed, it is a fair deduction to make that a section of the population on suitable examination will give clinical manifestations of impairment of the lung, involving a space varying in size from a pea-nut to a whole lobe, which manifestations are no more than evidence of either an obsolete lesion or a recently healed lesion.

Let us consider how the admission of the validity of this deduction would modify the significance of clinical signs.

The questions of inspection or palpation of the chest require no detailed consideration. In the first place there are obvious sources of fallacy from the point

of view of natural and acquired deformity and in the next, signs such as asymmetry or flattening, asymmetry of movement or limitation of expansion can scarcely be called early signs of phthisis.

It is a different matter when one comes to consider the question of light percussion, which, since Goldschieder's (x) work has greatly increased in importance.

Indeed Rivière (o) who in this country has on every occasion emphasised its value states that "some alteration to skilled percussion can be made over every diagnosable lesion" and that "a diagnosis of phthisis can rarely be made without it."

From the writer's point of view, however, the more delicate the percussion, the greater the likelihood of those people who possess a small obsolete or recently healed lesion, being charged with harbouring active tuberculosis and of their being treated accordingly.

And this criticism might be applied to the various modes of topographical percussion. Kronig's (e) delimination of the area of resonance at the apices has now superseded Goldschieder's measurement of the extreme height of apical resonance, and has become part of the routine examination of every chest.

(x) Goldschieder. Berlin. Klin. Woch. 1907. Band XL

(o) Rivière: The Diagnosis of Tubercle, 1914.

(e) Krönig: 'Die Fruhdiagnose', Deut. Klin. 1907 Band XI.

It is undoubtedly a most valuable method of examination and the claims of its advocates that it will detect most minute foci can be easily granted, but here again in the case of the recent or obsolete lesion the very refinement of the method proves its own invalidation.

The argument which applies to percussion methods applies to the various changes in breath sounds.

Apart from the fact that abnormal conditions such as coarseness or feebleness of breath sounds, broncho-vesicularity or interruption of breath sounds are only of significance when persistently localised, they are not of themselves indicative of active disease.

The presence of adventitious sounds on the other hand is of much deeper significance, particularly when localised and persistent.

The quarrel between the 'percussion' and the 'auscultation' schools of diagnosticians has become almost classical and requires no enlargement.

But although there may be a difference of opinion as to whether slight impairment of percussion note or slight impairment of breath sounds can claim right of precedence, there can be no doubt that the presence of adventitious sounds heard at the end of inspiration after coughing or an increase after coughing of previously heard adventitious sounds is at the same time an early and a fairly definite sign of active pulmonary tuberculosis. There are, however, a few objections to such an absolute interpretation of added signs.

Unfortunately the moist sounds of phthisis go by no standard, and examination of many advanced cases will after the evidence of almost every possible variant

of the added sound.

This adds to the difficulty of differential diagnosis of chronic apical bronchitis or of apical collapse following naso-pharyngeal troubles, but it is of even more importance in the diagnosis of healed tuberculosis.

It is common experience (the writer can remember about 7 cases in his own experience) that cases of definite tuberculosis which have been arrested for periods varying from 4 to 15 years will still show on examination of the periphery of the old lesion, sounds called indifferently 'dry' or 'fibrotic' more on account of their association with dried up disease or fibrotic tracts than from any particular sound-character. These may vary from an isolated click to a simulation of abundant moisture.

One might mention also the rather baffling variations of added sounds obtained from old patches of pleurisy.

It is true that there is practically never any increase of these added sounds after cough, which is a valuable distinction, but with cases of this type, the physician is confronted with a dual responsibility indicated by the possibilities either of dismissing an unarrested case as healed or of sending for prolonged treatment a really arrested case.

Finally one must consider the type of case which, with T.B. in the sputum presents for a period at any rate, no physical signs whatever.

Riviere would, of course, deny the existence of such cases, but the writer claims that he has come across

at least one such, and the theoretical possibility of their existence he will demonstrate under the section dealing with sputum examination.

A summary, then, of criticism of the validity of clinical signs in early diagnosis might, without running to extremes, be put as follows: Granting for the moment that clinical signs are invariably present can it be proved that any one of these signs with the possible exception of adventitious sounds after cough, is sufficient grounds on which to base a diagnosis of active pulmonary disease?

S E C T I O N IV.

TUBERCULIN TESTING.

SUB-SECTION. A.

SUBCUTANEOUS METHOD

FOCAL REACTIONS

Whatever theory one may hold concerning the rationale of the tuberculin reaction, whether one inclines to Wasserman's (x) theory of the attraction to the focus by anti-tuberculin of the injected substance, to the subsequent modification of this theory by (o) Citron, to the toxin theory of Hertwig (4). Ehrlich (5) with its variations by Meyer and Schmitz (8) or to Wolff-Eisner's (7) lytic-amboceptor theory or again to the hyper-susceptibility theory of Friedberger (9) the important point for the diagnostician is that the theories of non-specific action of tuberculin are now discredited.

Equally important from the point of view of pulmonary tuberculosis is the fact that of all the reactions due to tuberculin, the focal reaction gives the most positive aid in establishing a diagnosis of active disease.

The relative importance of local and general reactions will be referred to later, but it may be said now that a judgment of the value of tuberculin testing stands or falls by the finality of the focal reaction.

And this finality must be determined not on the completely positive or completely negative results but

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(x) Wasserman & Bruck: Deutch. Med. Woch. 1906. Nr 12.

(o) Citron: Berl. Klin. Woch. 1909. Nr 51.

(4) Hertwig: Die Grundlage der Tuberkulin wirkung. 1891.

(5) Ehrlich: Int. Kong. für Hygien. 1903.

(8) Meyer und Schmitz: Deutsch. Med. Woch. 1912 Nr. 42

(7) Wolff-Eisner: Die Fruhdiagnose. 1909.

(9) Friedberger: Deutsch. Med. Woch. 1911 Nr. 11.

on the percentage of cases tested where no definite finding could be come to.

A Focal Reaction as generally defined by Bandelier and Roepke (x), consists of the appearance of râles or where these were present before an increase in frequency: well marked alteration in the breath sound over the affected spot in the sense of impurity, jerkiness, roughness or sharpness; extension or increase in the markedness of diminished resonance, the increase of localised pleuritic symptoms.

There is still acute controversy concerning a standardised means of recognition of the focal reaction, the 'percussion' schools being pitted against the advocates of 'auscultation', but this is simply a reflex of the same disagreement over primary examination of the chest.

Against the views of Otten (o) von Romberg (+) in favour of the percussion method, one must put those of Waltershöfer (w), Bandelier and Roepke and Rivière (r) in favour of auscultation.

When one considers how varying and almost incommensurable are symptoms such as cough or traces of sputum, how difficult in standardizing from day to day the strength of percussion and how relatively easy is

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(x) Bandelier & Roepke: Lehrbuch. d. Spez. Diag. pp. 104-105.
(o) Otten: Med. Klin. 1910. Nr. 28
(+) von Romberg: Wiesb. Kong. fur. inn. Med. 1910.
(w) Waltershöfer: Beiträge z. Klin. d. Tub. Bd. XXI. heft 2.
(r) Riviere: Diag. of Pul. Tub. 1914.

the localizing or even approximate enumeration of râle ~~s~~, one is inclined to agree with Rivière that only very decided changes can be accepted as evidence, and to lay down for oneself the following standards. of a ~~f~~ focal reaction.

(i) Presence of moist râle where not previously heard.

(ii) Definite increase in previously heard râle.

(iii) Marked impairment of percussion note where previously there was no impairment.

The question of the maximum dose too is of the greatest importance.

It may be put thus: What dose can be given without causing any ~~danger~~ risk to the future course of the disease and without at the same time being too small to cause a definite focal reaction?

Now whilst Ulrici's (x) statement as to the dangers of the focal reaction cannot be altogether accepted chiefly because many of his bad results were noted from cases of known tuberculosis, the whole of his criticism cannot be passed over.

Against Ulrici's claims may be put the experience of Baudelier and Roepke, Penzoldt (o), von Romberg, Otten, Junker, who state that given properly the test never causes any harm.

(x) Ulrici: Beiträge z. klin. d. Tub. 3 sup. Band.

(o) Penzoldt: Wiesb. Kong. für inn. Med. 1910.

At the same time Baudelier and Roepke, of whom it is not unfair to say that they are enthusiastic protagonists of the method, make this interesting statement concerning two particular cases, that after no reaction whatsoever to the 1st, 2nd, and 3rd doses (.0002 cc. A F:, .001 cc. A F .005 cc A F), they gave typical reactions to the 4th (.01 cc A F) when Tubercle Bacilli were for the first time found in the sputum.

J Tunker also reports 4 cases where test doses produced bacilli in the sputum, otten gives three and Lowenstein observed this phenomenon in almost 5% of his tested cases.

It is claimed that when this happens, it is only a temporary condition and that no ultimate harm is done, but this is a statement that the writer cannot pass unchallenged. It is allowed by general consent that one of the most definite signs of improvement in phthisis is the disappearance of bacilli from the sputum, and whatever opinion one may hold concerning the stimulation of an active focus to the point of producing an increased bacillary output as a matter of specific treatment the question still arises: Is one justified under any circumstances in producing bacilli in the sputum for purposes of diagnosis?

It may be said in reply that such would not occur were proper precautions followed, mainly those, that no febrile case should be tested and that the slightest febrile reaction even .2° F. should be an indication for repetition of the exciting dose. But should the repetition of the dose, instead of producing a focal,

give a general reaction either of similar or even slightly increased intensity, what is to be the next step in the test, taking for granted, of course, that the focal reaction is to be considered the final proof of activity? Can repetition of the dose go on indefinitely and even so what deduction can be made from continued reactions? It is necessary to refer here to the purely cumulative method of testing pursued by Löwenstein and Kauffman (x) which consists in repeating the same small dose (say .0002 A.F-) four times within ten days.

The results of this method have been considered unsatisfactory after extensive experiment by Baudelier and Roepke, and lay themselves open to two entirely opposite criticisms, on the one hand, of establishing a tuberculin tolerance and on the other of producing an anaphylactic state. Moreover it is generally agreed that reactions may not evidence themselves in any way until the final test is reached. (i.e. in a progressive series of doses: — ·01 cc 1:f (1/10 mgm))

It is evident then that there is at least a possibility of some cases not giving a satisfactory result on account of awkward general reactions and therefore any consideration of the serviceability of the test is, in effect, a consideration of the percentage of cases in which this indefinite result is arrived at by reason of the probable danger of pursuing the full course of injections.

In the literature of the subject, whilst dangers are discussed in general terms, it is not common to find

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(x) Löwenstein & Kauffman: Zeit. fur Tub. Band. XHI.

detailed description of cases illustrating difficulties or dangers in the method which are not quoted with a certain amount of bias one way or the other.

In view of this the writer, before tabulating his own series of cases, has detailed 5 cases taken from the earlier records of the King Edward VII Sanatorium, 2 of which came under his own observation.

They have no pretence to be examples of properly tested cases. Indeed three of them are open to damaging criticism from the point of view of technique but, that apart, they are interesting examples of the conflicting results often obtaining in testing suspicious cases.

In criticising each case the writer has for the sake of argument deliberately generalized from the particular.

The previous history of these cases is omitted because whilst this might help in deciding whether or not to test a case, it does not help to decide the course of the tests, and in any case practically all histories are suspicious.

Case I. Miss C. aet 17 was admitted in moderately good condition with slight cough and sputum, negative to sedimentation examination for bacilli and with no definite signs of any kind in the chest.

1st day of Test. Dose .0002 cc A.F no reaction

3rd " " " " .001 " " " "

5th " " " " .005 " " with violent local and general reactions: temperature 100° 4.F. which rose next day to 101° F; local and general reaction still

violent. These subsided.

9th day of Test. Dose. .01 cc. A F followed by a more violent local and general reaction: headache: temp. 103°F. but no focal reaction of any sort.

All other evidence was negative and she was dismissed as a negative case, (Charts No I... and ~~_____~~)

It is to be particularly noted that in spite of a violent general reaction there was no repetition of the exciting dose.

Case II. Miss K. aet. 18. was admitted in good condition with slight cough ahd traces of sputum: T.B.- by sedimentation. Her clinical signs consisted of impaired resonance and impaired breath sounds at the apices of Rt. upper and lower lobes.

1st day of Test: .0002 cc. A F : no result

3rd " " " : .001 cc. A F : slight local reaction.

5th " " " : .005 cc. A F : marked local and general reaction: temp 100°4° F: cough increased: next day temp. 101° F: general reaction: subsided next day.

7th day of test: .01 cc. A F : with violent L.R. and G.R., on

9th day of test: focal reaction at Rt. apex: on 10th " " ": T.B. were found in the sputum. Some days later a general disturbance set in(Charts Nos. II. & III.) and T.B. continued in the sputum until dismissal.

A comparison of these cases is highly illuminating.

From No. II one would be entitled to say that a violent general reaction with a marked rise in temperature is an indication for repetition of the exciting dose and that to ignore such reaction is to court injury to the future course of the case; but one could say equally truly that absence of focal reaction after the 3rd test (.005 cc. A F) does not necessarily mean absence of active disease.

It must be noted, however, that in No I absence of focal reaction at the 3rd Test did mean, as subsequent events proved, absence of active disease and that a violent general reaction might be ignored without injury to the future course of the case. The difference between the two cases actually was that in the one case there were no physical signs, in the other the signs were definite and moderately extensive.

To leave these for the moment, there are other difficulties of which the next case is a good instance.

Case III. Mr W. aet. 25 was admitted in good condition with some cough and spit: T.B.- by sedimentation: there were signs of impairment of the upper 1/3 of Rt. upper lobe, including some so called "fibrotic" creps. which were not increased on cough: some impairment of resonance at apices of Lt. upper and lower lobe.

On 1st day of test: Dose .0002 cc. A F: no reaction

" 3rd " " " " .001 A F: no reaction

" 5th " " " " .005 A F: slight local reaction but no general symptoms: temp rise 0.3° F : which immediately subsided.

On 7th day of test: Dose .01 cc. A F: No local Reaction

no general symptoms: only slight rise in temp: and no clinical focal reaction yet 3 days after T.B. were present by sedimentation only: a week after, moist sounds gradually developed at the impaired portions: T.B. found by ordinary method and continued present until dismissal. (Charts No IV and V)

The important point here is that the general reaction did not act as a warning signal. Indeed even with the last dose, there was little general disturbance: taken in conjunction with Case II, however, it shows the risk of instituting tests in cases where, impairment, although not necessarily active, involves the greater part of one lobe or smaller portions of more than one lobe.

Case IV. Miss M. 29 was admitted in good condition with some cough and sputum: T.B.- by sedimentation: signs of impairment of Rt. lower lobe including so-called "fibrotic" creps. not increased on cough and partial impairment of Lt. upper lobe.

On 1st day of Test: Dose .0002 cc. A F: no result

" 3rd " " " : " . 001 cc. A F: no result

(interval due to domestic circumstances)

" 7th " " " : repeat .001 cc. A F: no result

" 9th " " " : .005 cc. A F: slight local reaction

Slight general reaction: temp. rise 1°F: this subsided.

" 11th day of Test: Dose. . 01 cc. A F: marked local reaction; marked general reaction with rise of temp. but no focal reaction: sputum taken on 12th day gave T.B+ by sedimentation, but these disappeared within a week and patient was dismissed after a course of treatment with unaltered signs. (Charts No VI)

Considering these four cases on their own merits the following conclusions might be stated:

(i) It is never justifiable to produce T.B. in the sputum as a diagnostic measure.

(ii) Cases should not be tested at all where the clinical signs indicate involvement of one lobe or sections of more than one.

(iii) Although a marked general reaction does not necessarily indicate risk in the administration of a higher dose, a higher dose should never be given, most particularly where the clinical signs or history are more than usually suspicious.

(iv) Absence of a focal reaction clinically does not necessarily mean absence of a focal reaction bacteriologically.

(v) It is necessary if possible to give the 4th injection .01 cc. A F before a definite negative result can be established. || Practically they would modify a testing technique in two ways:

A. Doses exciting even small general reactions would be repeated.

B. After a second repetition, if there was still no focal reaction, the test would be abandoned.

With these general considerations in view and recognising the precautions laid down in the literature, the writer carried out most of his tests of which 100 are detailed below.

Before going far, however, he found that a rigid interpretation of the temperature rule, i.e. repeating

all exciting doses, led to almost a deadlock in a large proportion of cases of which the following example is interesting.

Case V. Mr O. was admitted in good condition with no cough or sputum. There was a slightly impaired note at left apex and breath sounds were prolonged, but no other signs in the chest.

On 1st day of test: Dose .0002 cc A F: no result

" 3rd " " " : - . 001 cc. A F: with no immediate result but a delayed reaction at the site of 1st injection; next day local reaction became very marked: temp. 100° F: marked general malaise: no focal reaction. There symptoms subsided and on

6th day of test: Repeat dose .001 cc. A F: followed by a very violent local and a violent general reaction: temp. 102°2°F. which lasted over 2 days, but no focal reaction of any sort. Owing to the violence of the reactions the tests were not continued. The chest remained negative and all other evidence including serum reactions was negative. He was dismissed as a presumable negative, but without those most desirable finality of diagnosis which a completed test would have given. (CHART No VII)

This is an outstanding example but in a large percentage of cases small reactions were met with, which tended to prolong the tests over an impossible period.

A working mean was then adopted to the effect that where the clinical signs, the history and the serum reactions were uniformly negative or almost negative a slight general reaction might be safely ignored and this was found to work out satisfactorily.

RESULTS OF 100 TESTED CASES

CASE	DOSE	TEMP.	L. R. (Local Reaction)	G. R. (General Reaction)	FINAL RESULT (i.e. Focal + or −)
1.	.0002 cc. A F	99^8	−	−	−
	.001 " "	99^4	−	−	−
	.005 " "	100^0	+	−	−
	.005 " "	103^8	+ +	+ Pains in head shivering	A few doubtful inconstant creps. Rt. Lower apex.
2.	.0002 cc. A F	99	−	−	−
	. 001 " "	99^6	+	−	−
	. 001 " "	101	+	Malaise	Focal reaction A few creps R. upper Lobe post & Lower apex
3	.0002 cc. A F.	99^2	−	−	−
	. 001 " "	99^4	−	Tired. Headache.	Cough +
	. 005 " "	99^8	+		+
	. 01 " "	103	+	−	More cough. No sputum No focal reaction.
4.	.0002 cc. A F	100_8	−	−	−
	. 001 " "	99^8	−	Headache & faint	Cough +
	. 005 " "	99^6	−	−	−
	. 01 " "	99^8	−	−	+ No focal reaction
	. 01 " "	100	+	No malaise.	No focal reaction
5.	.0002 cc. A F	99^6	−	−	−
	. 001 " "	99	−	−	−
	. 005 " "	101	−	−	−
	. 01 " "	100^2	−	No symptoms.	No focal reaction.
6.	.0002 cc. A F	98^8	−	−	−
	. 001 " "	98^6	−	−	−
	. 005 " "	99	+	−	−
	. 01 " "	99^8	+	Headache. Malaise.	More cough. No increase in sputum. No focal Reaction
7.	.0002 cc. A. F	98^6	−	−	−
	. 001 " "	99	−	−	−
	. 005 " "	98^8	−	No symptoms.	No sputum. No focal reaction
8.	.0002 cc. A F	99^2	−	−	
	.001 " "	99^6	−	−	−
	. 005 " "	98^8	−	−	−
	. 01 " "	99	−	No symptoms	No Focal Reaction
9.	.0002 cc. A F	99^8	+ Slight	−	−
	. 001 " "	100^4	+	Malaise. Headache.	Traee of sputum.
	. 001 " "	100	+	+ +	F.R? A trace of stickiness at post appect Rt. apex.

CASE	DOSE.	TEMP.	L. R.	G. R.	FINAL RESULT
10	.0002 cc. A.F.	99^{2}	-	-	-
	.001 " "	99	-	-	-
	.005 " "	101^{2}	-	Headache	
	.005 " "	102^{6}	+ +	+	No focal reaction.
11.	.0002 cc. A F	98^{6}	-	-	-
	.001 " "	98^{2}	-	-	Slight sputum
	.005 " "	98^{8}	-	-	-
	.01 " "	99	+ very slight	Headache	No focal reaction
12.	.0002 cc. A F	99^{2}	-	-	-
	.001 " "	99^{2}	-	-	-
	.005 " "	99	-	-	-
	.01 " "	101	-	No symptoms	No Focal Reaction
13.	.0002 cc. A F	99^{2}	-	-	-
	.001 " "	98^{4}	-	-	-
	.005 " "	99	-	-	-
	.01 " "	100	+ v. s.	Headache.	No cough or sputum, some pain L. arm. No Focal Reaction.
14.	.0002 cc. A F	99	-	-	-
	.001 " "	99_{8}	-	-	-
	.005 " "	99^{4}	-	-	-
	.01 " "	101^{4}	-	No Malaise.	No Focal Reaction.
15.	.0002 cc. A F	99^{4}	-	-	-
	.001 " "	99^{6}_{8}	-	-	-
	.005 " "	99^{8}	-	-	-
	.01 " "	99^{8}	+	No symptoms.	No Focal Reaction.
16.	.0002 cc. A F	99	-	-	-
	.001 " "	98^{6}	+	-	-
	.005 " "	99^{8}	+	-	-
	.01 " "	100^{2}	+	No Symptoms.	Slight increase in cough & sputum, No Focal Reaction
17.	.0002 cc. A F	98^{2}	-	-	Slight increase in cough.
	.001 " "	98^{4}	-	-	No cough,
	.005 " "	98^{6}	-	-	-
	.01 " "	99^{6}	-	No Symptoms.	No focal Reaction.
18.	.0002 cc. A F	99	-	-	-
	.001 " "	99	-	-	-
	.005 " "	98^{8}	-	-	-
	.01 " "	100	+	Headache	No focal Reaction

CASE	DOSE	TEMP.	L. R.	G. R.	FINAL RESULT
19	.0002 cc. A F . 001 " " . 005 " " . 01 " "	98^{8} 98^{4} 99^{6} 99	- - + -	- - - No Symptoms.	- - - No Focal Reaction.
20.	.0002 cc. A F . 001 " " . 005 " "	99^{4} 99^{4} 101^{2}	+ - -	- Headache +	- Pain in R. Base No Focal reaction. Complement Fixation Negative.
21.	.0002 cc. A F . 001 " " . 005 " " . 01 " "	99^{4} 99^{8} 101^{2} 101^{4}	- + + +	- - -	- - More cough & Sputum. Slight Focal Reaction R. apex Front and behind.
22	.0002 cc. A F . 001 " " . 005 " " . 01 " "	98^{8} 99 99^{2} 100	- - + +	- - - No Symptoms	- - - No Focal Reaction Com. Fix. —
23.	.002 cc. A F .001 " " .005 " " . 01 " "	.100 100^{2} 100^{2} 101^{8}	- - - +	- - - No Malaise	- Slight cough. No Sputum. No focal re- action
24.	.0002 cc. A F . 001 " " . 005 " " . 01 " "	99^{6} 100^{2} 99^{2} 104	- - - +	- - - Headache & earache	 No focal reaction.
25.	.0002 cc. A F .001 " " .005 " "	99^{2} 99^{2} 101	- - +	- - Headache.	 No creps. but breath sounds harsh. Almost bronchial at Rt. apex.
26.	.0002 cc. A F . 001 " " . 005 " " . 01 " "	98^{4} 98^{6} 99 101^{4}	- - + + +	- - Headache -	 More Cough & Sputum No cough or sputum No Focal. Complement Fixation negative.

CASE	DOSE	TEMP.	L. R.	G. R.	FINAL RESULT
27.	.0002 cc. A F . 001 " " . 005 " "	99^{6} 100^{2} 101^{4}	- + +	- - Malaise.	Some cough. No focal reaction. Com. Fix. Negative.
28.	.0001 cc. A F .0005 " " .0005 " "	99^{8} 100^{4} 101	- + +	- - -	Some dry cough. Focal Reaction + R. lower lobe Com. Fix. -
29.	.0002 cc. A F . 001 " " . 005 " " . 005 " " . 01 " "	99^{8} 99^{2} 99^{4} 99^{4} 99^{8}	- + v.s + + +	- - - - No symptoms	Slight cough. No sputum. No Focal Reaction. Com. Fix.
30.	.0002 cc. A F . 001 " " . 005 " " . 005 " " . 005 " "	98^{8} 99^{2} 100^{6} 102 101^{6}	+ - + + + + +	- - Some malaise Headache & Malaise. +	No increase cough & sputum Some pain over site of old pleurisy. No sputum, slight increase cough. Pain R. side. Definite rub R. base nil at apex. F.R. Nil definite.
31.	.0002 cc. A F . 001 " " . 001 " "	98^{8} 99^{2} 101	+ + + +	Headache. - Headache & malaise.	- No Focal Reaction.
32.	. 0002 cc. A F . 001 " " . 005 " " . 005 " "	98^{8} 98^{4} 102 103^{6}	+ slight + " + +	- - Malaise headache + +	- - No Focal Reaction. Complement Fixation Negative.
33.	.0002 cc. A F . 001 " " . 005 " "	99 99 100^{4}	- - 	- Headache Off Colour.	T.B. + on 1st admission No focal reaction. Slight moisture at Rt. apex, small amount of sputum. Complement Fixation. Positive.

CASE	DOSE	TEMP.	L. R.	G. R.	FINAL RESULT
34.	.0002 cc. A F	99	-	-	Sputum increased
	.001 " "	99^4	-	Headache	
	.005 " "	99^6	+	-	
	.01 " "	102	+	Headache	More cough & sputum, no Focal Reaction. Com. Fix.
35.	.0002 cc. A F	99^2	-	-	
	.001 " "	99^2	-	-	
	.005 " "	99^8	+	Headache	Focal reaction + History of Pleurisy and Bronchitis.
36	.0002 cc. A F	99^2	+	-	-
	.001 " "	99^6	+ +	Headache & Malaise.	-
	.005	100^8	+	-	
	.01 " "	100^6	-	No Symptoms.	No focal Reaction. Complement Fixation negative.
37	.0002 cc. A F	99^2	-	-	Two days later.
	.001 " "	101	+	Malaise	The slightest suspicion of stickiness at R. apex.
	.001	99^4	-	-	Slight increase cough. No Sputum. F.R?
	.005 " "	104^2	+ +	No Malaise.	
38.	.0002 cc. A F	98^8	-	-	
	.001 " "	98^8	-	-	
	.005 " "	99^2	+	-	
	.01 " "	102	-	No Symptoms	Focal Reaction + (T.B. - E. & E.) Complement Fix. doubtful.
39	.0002 cc. A F	99^2	-	-	
	.001 " "	99^2	-	-	
	.005 " "	99^6	-	-	
12 days later	.01 " "	101	+	-	No Focal reaction
	.0002 " "	100_2	-	-	
	.0002 " "	100^2	-	-	
5 days later	.0005 " "	99	-	No Symptoms	No Focal Reaction.

CASE	DOSE	TEMP.	L. R.	G. R.	FINAL RESULT
40.	.0002 cc. A F	$99_{}$	-	-	
	. 001 " "	100^{2}	+	Headache & sickness.	No cough.
	. 001 " "	99^{4}	+	-	
	. 001 " "	102	+ +	Headache & Nausea.	Focal Reaction + R. apex in front. T. B. -
41.	.0002 cc. A F	99	-	-	
	. 001 " "	99^{4}	+ +	-	
	. 005 " "	99^{8}	+	Headache	
	. 005 " "	101^{8}	+	Malaise	No Focal Reaction An occasional inconstant crep. over R. supra scapular fossa. No cough. No sputum. Complement Fixation - negative.
42.	.0002 cc. A F	$100_{}$	-	-	
	. 001 " "	101^{2}	+	No malaise	
	. 001 " "	103	+	Malaise.	Focal Reaction + a few creps. Post R. apex.
43	.0004 cc. A. F	99^{4}			
	.0002 " "	99^{2}	-	-	
			-	-	Slight increase pain L. side of neck.
	.001 " "	99^{2}	-		
	.005 " "	99^{2}	+	No symptoms	No Focal Reaction. Has disease of cervical glands.
44	.0002 cc. A F	99	-	-	
	. 001 " "	99^{2}	-	-	
	. 005 " "	99^{2}	-	-	
	. 01 " "	102^{6}	+ +	No symptoms.	Slight cough & sputum. No Focal Reaction. Com. Fix. -
45	.0002 cc. A F	98^{8}	-	-	Wasserman -
	. 001 " "	$99_{}$	-	-	
	. 005 " "	100^{2}		No malaise	No Focal Reaction Epithelioma of Larynx Too large for removal.
46	.0002 cc. A F	98^{2}	-	-	
	. 001 " "	101^{2}	-	Headache	
	. 001 " "	101^{4}	-	-	No Focal Reaction.
47	.0002 cc. A F	98^{6}	-	-	
	. 001 " "	99^{4}	+	Malaise	
	. 001 " "	100	+ +	Headache and Malaise	Slight cough. No sputum. Focal Reaction + R. apex. Com. Fix. + T. B. -

CASE	DOSE	TEMP.	L. R.	G. R.	FINAL RESULT
48	.0002 cc. A F . 001 " " . 005 " " . 01 " "	98 98^{8} 99^{2} 99	- - - -	- - - No Malaise	No Focal Reaction.
49.	.0002 cc. A F . 001 " " . 005 " " . 005 " "	99^{8} 99^{6} 102_{4} 101^{4}	- + + + +	- - Shivering. Headache.	Slight increase of cough No Focal Reaction.
50	.0002 cc. A F . 001 " " . 005 " " . 005 " "	99^{2} 99 100^{8} 100^{8}	- - + +	- Headache Malaise -	Slight increase cough and sputum. No Focal reaction.
51.	.0002 cc. A F . 001 " " . 005 " " . 01 " "	98^{8} 99 98^{8} 99^{2}	- - - -	- - - No symptoms.	No Focal Reaction. Complement Fixation negative.
52.	.0002 cc. A F . 001 " " . 001 " "	99 100 102^{2}	+ - + +	- Malaise +	No Focal Reaction.
53	.0002 cc. A F . 001 " " . 005 " " . 01 " "	98^{8} 99 99^{2} 99^{4}	- - - +	- - - Malaise	Cough and Sputum + No Focal Reaction. Com. Fix.
54	.0002 cc. A F . 001 " " . 005 " " . 005 " "	98^{4} 98^{3} 100_{8} 99^{8}	- - + -	- - Malaise +	No Focal Reaction Complement Fixation - Negative.

CASE	DOSE	TEMP:	L. R.	G. R.	FINAL RESULT
Re-admission. 55.	.0002 cc. A F	98^4	-	-	-
	.001 " "	98	-	-	
	.005 " "	98^4	-	-	
	.01 " "	98^8	+ slight	No malaise	No Focal Reaction. Complement Fixation - negative.
56.	.0002 cc. A F	99	-	-	-
	.001 " "	99^6	-	-	
	.005 " "	101^2	+	Malaise	Focal Reaction + A few fine creps above and below outer end of R. clavicle.
57	.0002 cc. A F	99^2	-	-	
	.001	99^2	-	-	
	.005 " "	99^2	-	-	
	.01 " "	99^2	-	-	No Focal Reaction. Complement fixation. -
After 9 weeks. 58.	.0002 cc. A F	100^2	+	Headache & general pains.	Sputum increased.
	.0002 " "	100	-	-	-
	.001 " "	99^6	+	-	
	.005	100^2	+	-	
	.01	100	+	No symptoms	No focal reaction.
59.	.0002 cc. A F	99^2	-	-	
	.001 " "	99^2	-	-	
	.005 " "	100	+	Malaise	-
	.005 " "	98^8	+	-	Focal Reaction (+ slight)
	.01	99^4	-	Nil	R. Lung Com Fix. -
60.	.0002 cc. A F	99^4	-	-	Focal Reaction +(slight)
	.001 " "	99	-	No symptoms	On Tuberculin A F .00005 cc. .07 "
61.	.0002 cc. A F	98^6	-	-	
	.009 " "	98^8	-	-	
	.005 " "	98^8	-	-	
	.01	102^8	-	No symptoms	No Focal Reaction. Complement fixation +

CASE	DOSE	TEMP:	L. R.	G. R.	FINAL RESULT
62	.0002 cc. A F	99^2	+	-	Cough & sputum increased
	. 001 " "	100	+	Malaise & headache	+ + +
	. 001	98^6	+	+ +	-
	. 005	99	+	No malaise or headache.	No Focal Reaction.
63	.0002 cc. A F	100^4	-	-	
	. 001 " "	99^8	-	-	
	. 005 " "	100	-	-	
	. 01 " "	100	-	No symptoms	No Focal Reaction.
64	.0002 cc. A F	99^2	-	-	Slight increase Cough & sputum.
	. 001 " "	99^4	+	-	+
	. 005	100^6	+	Malaise	Focal Reaction + slight increase in creps.
	. 005	101^4	-	+	
65	.0002 cc. A F	99^2	-	-	
	. 001 " "	99	-	-	
	. 005	99^8	+ s.	-	
	. 01	99^4	-	No symptoms	No Focal Reaction
66	.0002 cc. A F	99^2	-	-	
	. 001 " "	99^4	+	Headache	More cough.
	. 005	99^4	+	+	-
	. 01 " "	99^8	+	+	No Focal Reaction. Complement fixation negative.
67.	.0002 cc. A F	98^2	-	-	
	. 001 " "	99	+ slight	-	
	. 005 " "	99^2	+	Headache	-
	. 01	99^4	+	" "	No Focal Reaction.
68	.0002 cc. A F	99^2	-	-	
	.0002 " "	99	-	-	
	. 001 " "	99^4	-	No symptoms	No Focal Reaction.
69.	.0002 cc. A F	98^2	-	-	
	. 001 " "	98^6	-	-	
	. 005 " "	99^2	+	-	
	. 01 " "	99^6	-	No symptoms.	No Focal Reaction Complement Fix. negative.

CASE	DOSE	TEMP	L. R.	G. R.	FINAL RESULT
70.	.0002 cc. A F	98^{6}	-	-	
	.001 " "	98^{8}	-	-	
	.005 " "	101^{6}	-	-	
	.01 " "	99^{6}	-	-	No Focal Reaction.
71. 3 weeks later.	.0002 cc. A F	100^{6}	+	Malaise	
	.001 " "	99^{2}	-	+	
	.005 " "	101	+	+	
	.0002	99	-	-	
	.001 " "	99^{4}	-	No symptoms	No Focal Reaction.
72.	.0002 cc. A F	99	+ slight	-	
	.001 " "	99^{2}	-	-	
	.005 " "	99^{6}	+	-	Focal Reaction+ No sputum
73	.0002 cc. A F	99	-	-	
	.001 " "	99	+ slight	-	
	.005 " "	99_{6}	+	-	
	.01 " "	103^{6}	+	Malaise	No Focal Reaction
74	.0002 cc. A F	99^{4}	-	-	
	.001 " "	99^{2}	-	-	
	.005 " "	99^{2}	-	-	
	.005 " "	103^{4}	+	Malaise. Pains in chest.	More cough. No sputum.
	.01	104^{4}	+	+	Sputum increased. No focal reaction.
75.	.0002 cc. A F	99	-	-	
	.001 " "	99^{2}	-	-	
	.005 " "	99^{2}	-	-	
	.01 " "	101^{4}	-	-	No focal Reaction.
76.	.0002 cc. A F	98^{8}	+	-	
	.001 " "	98^{4}	-	-	
	.005 " "	101	+	-	
	.01 " "	102^{4}	+	Malaise	No Focal Reaction.

CASE	DOSE	TEMP.	L.R.	G. R.	FINAL RESULT
77.	.0002 cc. A F	99	-	-	
	.001 " "	99^4	+	Headache	
	.005 " "	99^6	+	+	
	.01	99^8	+	-	
	.01 " "	100^4	+	Headache.	No Focal Reaction.
78.	.0002 cc. A F	99	+	-	
	.001 " "	99	+	-	
	.005 " "	98^8	+	Malaise	
	.005 " "	101^4	+ +	-	
	.005 " "	102	+ +	No Malaise	No Focal Reaction Complement Fixation Positive.
79.	.0002 cc. A F	99^2	-	-	
	.001 " "	99^4	+	-	
	.005 " "	99^6	+	-	
	.005 " "	99^2	-	No symptoms.	Focal Reaction + No cough or sputum
80	.0002 cc. A F	99	-	-	
	.001 " "	98^4	-	-	Cough increased.
	.005 " "	99	-	-	No cough. No focal reaction. Complement fixation. negative.
81.	.0002 cc. A F	99^4	-	-	
	.001 " "	99^2	+	-	
	.005 " "	100	+	-	F.R? + very slight
	.01 " "	100^6	+	Headache	No Focal reaction.
	.01 " "	100	+		No cough.
82.	.0002 cc. A F	98^8	-	-	
	.001 " "	99^2	-	-	
	.005 " "	99	-	-	
	.01 " "	99	+	No symptoms.	No Focal Reaction. Complement Fixation negative.
83.	.0002 cc. A F	99	-	-	
	.001 " "	99^2	-	-	
	.005 " "	99^6	±	Headache.	
	.005 " "	99^8	+	Slight malaise.	Pleural Friction L. only.
	.005 " "	99^4	+	-	No cough. No Focal reaction.

DASE	DOSE.	TEMP.	L. R.	G. R.	FINAL RESULT
84.	.0002 cc. A F	99^4	-	-	Focal Reaction +. A few creps L. apex.
	.001 " "	99^4	-	No symptoms	
85.	.0002 cc. A F	98^8	-	-	
	.001 " "	98^6	-	-	
	.005 " "	98^8	+	-	
	.01 " "	101^4	+	No symptoms.	No Focal Reaction Complement Fixation Negative.
86.	.0002 cc. A F	99^6	-	Malaise	More cough
	.001 " "	99^8	-	-	No "
	.005 " "	99^8	+	-	-
	.01 " "	101^8	+	Malaise	No Focal Reaction.
Re admission 87.	.0002 cc. A F	99^8	-	-	
	.001 " "	99	+	-	
	.005 " "	102	+ +	Slight malaise.	No Focal Reaction. Complement Fixation Negative.
Re admission 88.	.0002 cc. A F	99^2	+	-	
	.001 " "	99	+	-	
	.005 " "	100^4	+ +	Malaise & Headache.	-
	.005 " "	99^6	+	No malaise	No Focal Reaction
Re admission 89.	.0002 cc. A F	98^8	-	-	
	.001 " "	98^4	+	-	
	.005 " "	98^8	+	-	
	.01 " "	100	+ +	Slight malaise.	No Focal Reaction. Complement Fixation positive.
90	.0002 cc. A F	99^4	+	-	
	.001 " "	102^4	+	Headache	No Focal Reaction.
	.001 " "	102^2	-	〃	
	.001	102^6	-	〃	
	.005 " "	104^4	-	No symptoms	
91	.0002 cc. A F	99	-	-	
	.001 " "	99	-	-	
	.005 " "	99^6	-	〃	
	.01 " "	99^4	-	No Symptoms	No Focal Reaction.

CASE	DOSE	TEMP:	L. R.	G. R.	FINAL RESULT
92.	.0002 cc. A F	99_4	-	-	
	.001 " "	99^4	-	Malaise	
	.001 " "	99^4	+	-	
	.005 " "	104^2	+	Malaise	No Focal Reaction Complement Fixation -
93.	.0002 cc. A F	99^2	-	-	
	.001 " "	99^4	+	-	
	.005 " "	99^2	+	-	
	.01 " "	100	+	Headache	No Focal Reaction.
94.	.0002 cc. A F	98^8_2	-	-	
	.001 " "	99^2	+	-	
	.005 " "	99	+	-	
	.01 " "	99^6	+	No Malaise	No Focal Reaction
95	.0002 cc. A F	99_4	-	-	
	.001 " "	99^8	+	-	
	.005 " "	100	+	-	
	.005 " "	103^2	+	Malaise	No Focal Reaction Complement fixation.
96	.0002 cc. A F	98^6	-	-	
	.001 " "	98^6_4	-	-	
	.005 " "	99	+	-	
	.01 " "	100	+	No symptoms	No Focal Reaction.
97	.0002 cc. A F	99^2_4	-	- -	
	.001 " "	99^4	+	-	
	.005 " "	100^4	-	Pains in back	
	.01 " "	100	-	Headache	No Focal Reaction.
98	.0002 cc. A F	99	-	-	
	.001 " "	99_4	-	-	
	.005 " "	99^4	-	-	
	.01 " "	100^4	+	-	
	.01 " "	102^4	+	Malaise	Some cough. No sputum No Focal reaction.
99.	.0002 cc. A F	99^2	-	-	
	.001 " "	99^2	-	-	
	.005 " "	99	+ slight	-	
	.01 " "	99^4	+ "	Slight headache	No Focal reaction
100	.0002 cc A F	99	+	-	More Cough. No sputum
	.001 " "	99	+ +		No " Slight sputum
			Very severe	Some headache	No Focal Reaction

The following summary will help to indicate the value of the test in the light of the five illustrative cases.

DEFINITE FOCAL REACTION.

Dose	.01(2)	.01	.005 (2)	.005	.001(3)	.001(2)	.001	.0005(2)	.0002
Cases	-	3	2	4 (x)	1	3	2	1	-

DOUBTFUL FOCAL REACTION

Dose	.005 (2)	.005(1)	.001 (2)
Cases	1	3	1

NO FOCAL REACTION
Maximum dose not given!!

Dose	.01 (2)	.01	.005 (3)	.005 (2)	.005	.001 (2)	.001	.0002
Case	4	49	4	7	10	4	1	-

Definite 16%
Doubtful 5%
Negative 79%

Considering the negative results more in detail it will be seen that if one considers as properly tested only those cases where the 4th dose was given (.01 cc A F) only finds that 53 cases out of 79 come under this category, that is to say, the others (32.92%) were for the sake of safety not sufficiently tested to justify any definite conclusion being drawn. [redacted]. Include as properly

---

(x) One of these gave no clinical focal [redacted] reaction, but T.B. were found.

tested the 4 cases where .005 cc A F was given three times and the percentage shrinks merely to 27.85%. Include those where .005.cc.A F was given twice, and there are still 19% of the results unsatisfactory.

On the other hand add to the "negatives" the "doubtful focals" (the highest dose being .005 (2)) and we have actually 36.92% of cases with an unsatisfactory finding. And it is necessary to point out in defence of this statistical criticism of the value of the test that Bandelier & Roepke in dealing with such doubtful results, do come to a definite diagnosis in each case, taking into consideration the history and physical signs and ignoring their own crisp statement that the focal reaction is the diagnostic reaction par excellence. (Lehrbuch. 106-115).

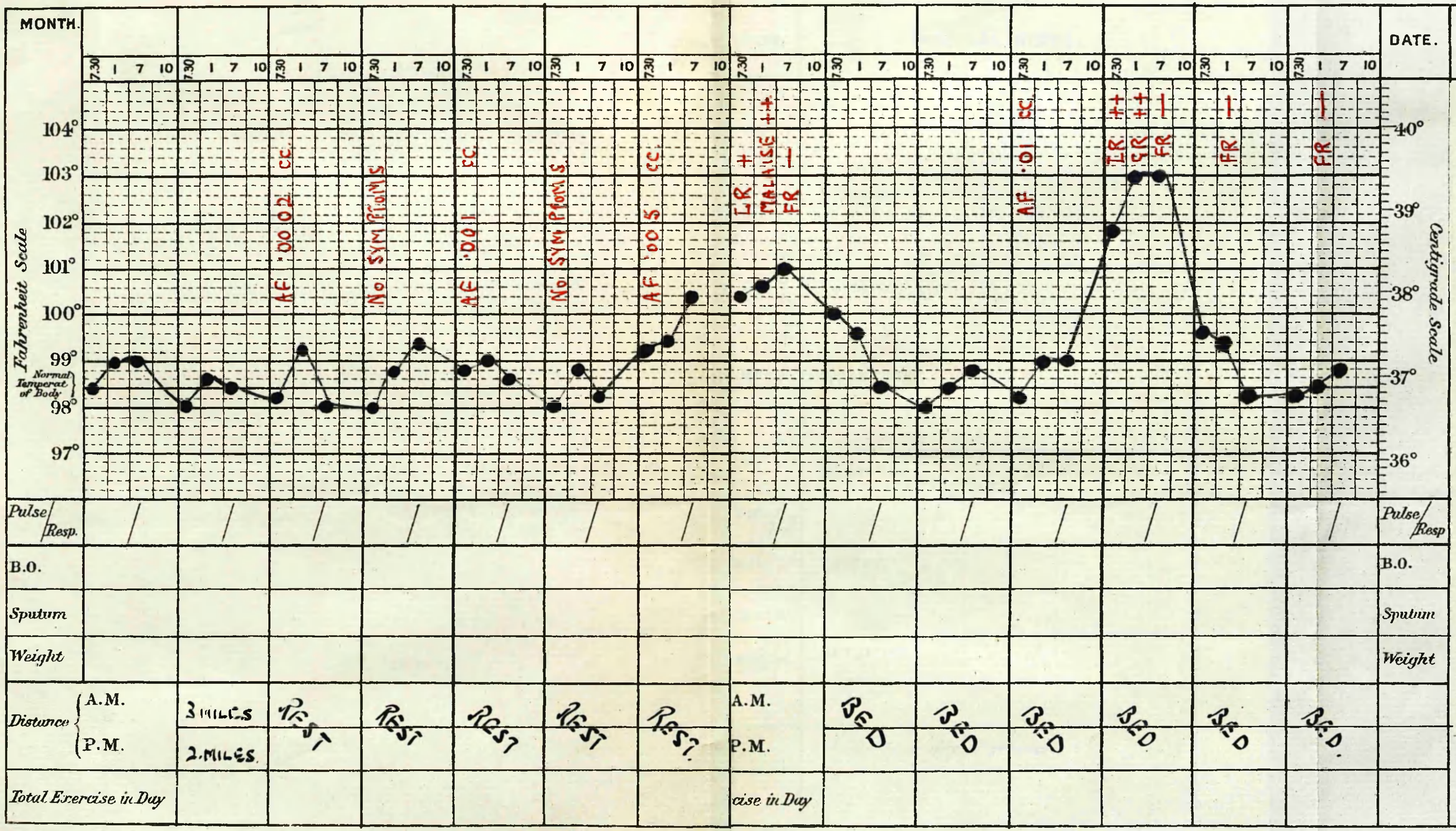
SUMMARY: A focal reaction set up by doses of sub-cutaneous tuberculin is definite proof of active pulmonary disease: where a dose of .01 cc. A F (1/10 mgr. Koch Tuberculin) has been given without any focal reaction arising, the case may be said to be negative: no case can be considered fully tested unless this maximum dose has been given at least once: in the large majority of cases slight general reactions are set up by early doses, which reactions can be, with proper precautions, ignored, indeed must be ignored if any more than a small minority of cases are to reach the deciding maximum dose: in a considerable percentage of cases. (33% - 37%) reactions, which cannot be ignored, are set up by later doses and by the repetition of these later doses, with the consequence

that those cases cannot, with safety, have administered to them the final deciding dose (.0. cc A F) and are therefore insufficiently tested.

Finally it may be said without fear of contradiction that the test as a whole if, with proper precautions, it does no harm, can and almost always does set up feelings of deep discomfort over a period ranging from days to two or three weeks.

MARGIN FOR BINDING. MARGIN FOR BINDING.

Patient's Name .... Case?   No. ....



MEDICAL NOTES.

Chart No I.

Shows a violent local and general reaction to the 3rd Test Dose, which was nevertheless ignored.
The final dose (·01 cc AF) produced a still more violent general reaction but no local reaction.
The serum reactions were negative.
Note: That violent general reactions do not necessarily indicate active disease.

See Page 35

Weekly Summary of progress

Malby & Sons, Lith.

MARGIN FOR BINDING. MARGIN FOR BINDING.

Patient's Name King 's Name King No.

MONTH.

Fahrenheit Scale: 104° 103° 102° 101° 100° 99° Normal Temperat of Body 98° 97°

Centigrade Scale: 40° 39° 38° 37° 36°

7.30 1 7 10

AF .00 02 cc

No Symptoms

AF .00 1 cc

LR + NO MALAISE FR —

AF 100 S cc

LR + Cough + Sputum + FR —

AF .01 cc.

LR + GR + Cough + Sputum +

Focal Reaction At Rt. Apex

T.B. +

DATE.

MEDICAL NOTES.

CHART. No II

Shows (as in No I) the ignoring with of a violent General reaction to the 3rd Test dose. (.005 cc AF).: a Focal Reaction was noted two days after the final dose. (.01 cc). and T.B. were found in the Sputum.

Chart III shows the subsequent course of the disease.

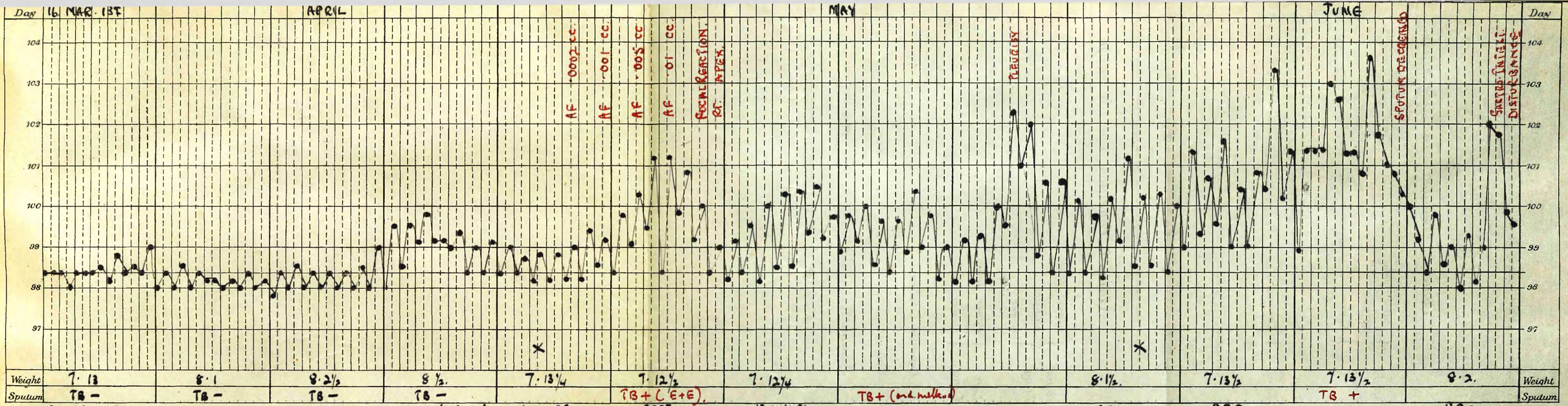
The case differed from No I in having definite clinical signs.

See page 35

Pulse / Resp.															Pulse / Resp.
B.O.															B.O.
Sputum															Sputum
Weight															Weight
Distance A.M.		2 MILES.	Rest	Rest	Rest	Rest	Rest	A.M.	Rest	Rest	Rest	1 MILE	2 MILES	3 MILES	
Distance P.M.		2 MILES.						P.M.				1 MILE	2 --	3 ---	
Total Exercise in Day								ercise in Day							

Weekly Summary of progress

Malby & Sons. Lith.



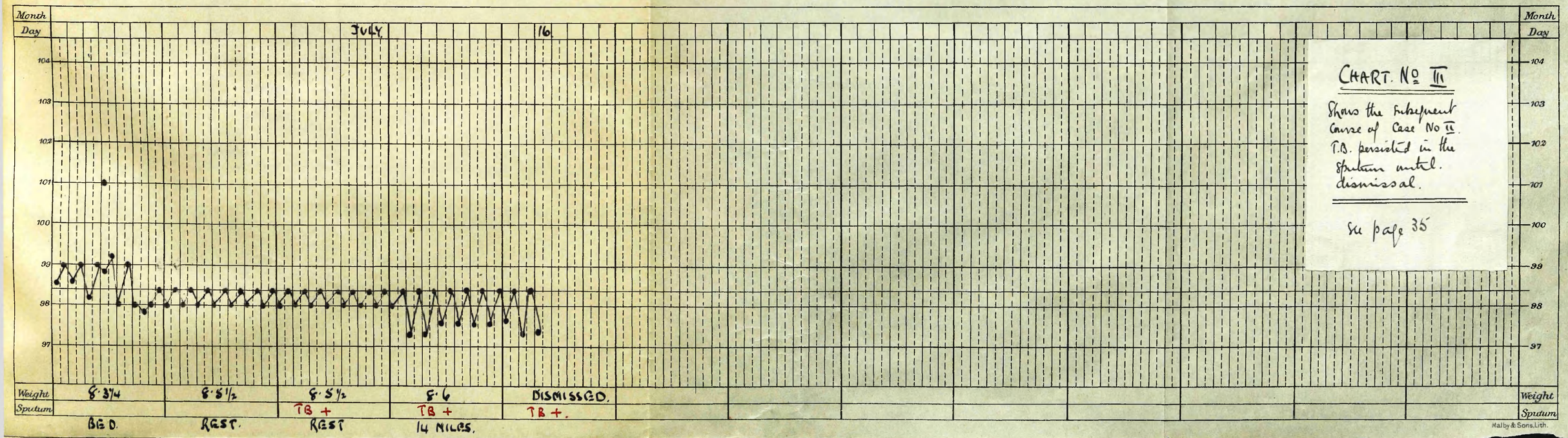


CHART. No III

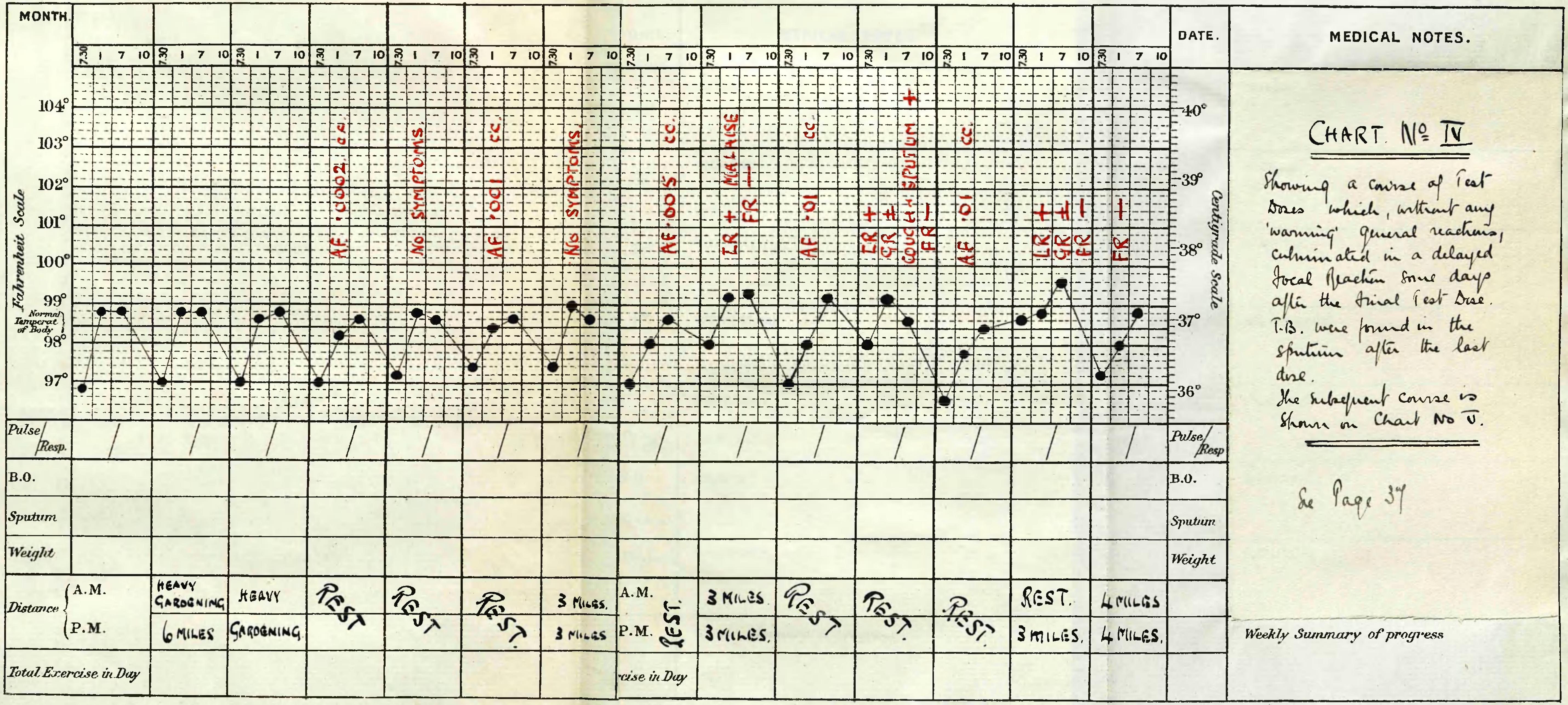
Shows the subsequent course of Case No II. T.B. persisted in the sputum until dismissal.

See page 35

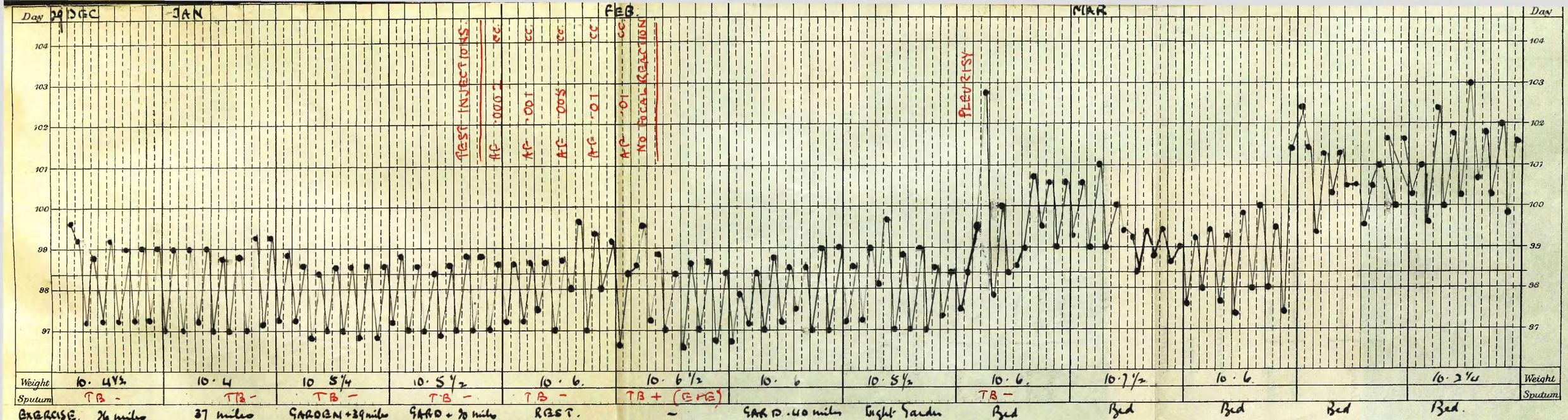
Malby & Sons, Lith.

MARGIN FOR BINDING. MARGIN FOR BINDING.

Patient's Name .... 's Name .... No. ....



Malby & Sons, Lith.



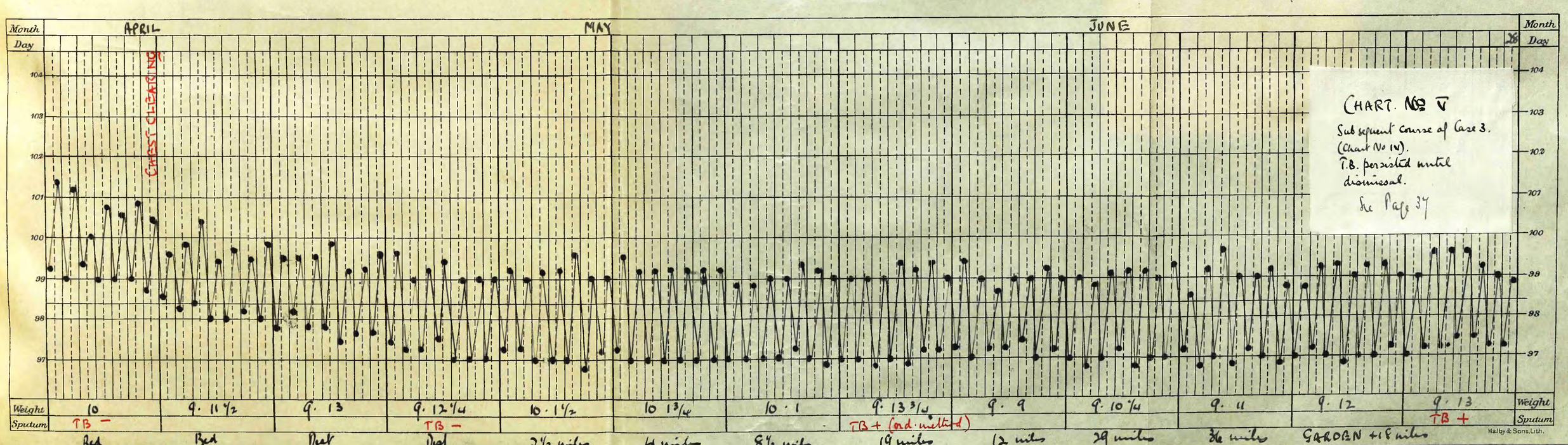


CHART. No V

Subsequent course of Case 3. (Chart No IV). T.B. persisted until dismissal.

See Page 37

Mail by & Sons. Lith.

MARGIN FOR BINDING.

MARGIN FOR BINDING.

Patient's Name Merici

's Name Merici

No.

MONTH.

DATE.

Fahrenheit Scale — Centigrade Scale

104° 103° 102° 101° 100° 99° 98° 97°

Normal Temperat. of Body

40° 39° 38° 37° 36°

7.30 1 7 10

AF .0002 cc.

No SYMPTOMS

AF .001 cc

No SYMPTOMS

AF .001 cc.

No SYMPTOMS

AF .005 cc.

ER + (slight)
GR ± MALAISE +
FR +

AF .01 cc.

LR ++
GR ++ MALAISE ++
FR +

FR +

Pulse/Resp.																	Pulse/Resp
B.O.																	B.O.
Sputum																	Sputum
Weight																	Weight
Distance A.M.		REST.	2 MILES	REST	REST	REST	REST	A.M.	REST	REST	REST	REST	REST	REST	REST		
Distance P.M.			2. -					P.M.									
Total Exercise in Day								ise in Day									

MEDICAL NOTES.

CHART. No. VI

Showing no reaction of any kind to the first three doses, but a focal Reaction (T.B. in the Sputum) to the trial dose (.01 cc AF).

Note: That cases not given this dose are not necessarily negative in spite of absence of Focal Reaction

See page 37

Weekly Summary of progress

Malby & Sons, Lith.

MARGIN FOR BINDING. MARGIN FOR BINDING.

Patient's Name Oxley   's Name Oxley   No.

MONTH	DATE.	MEDICAL NOTES.

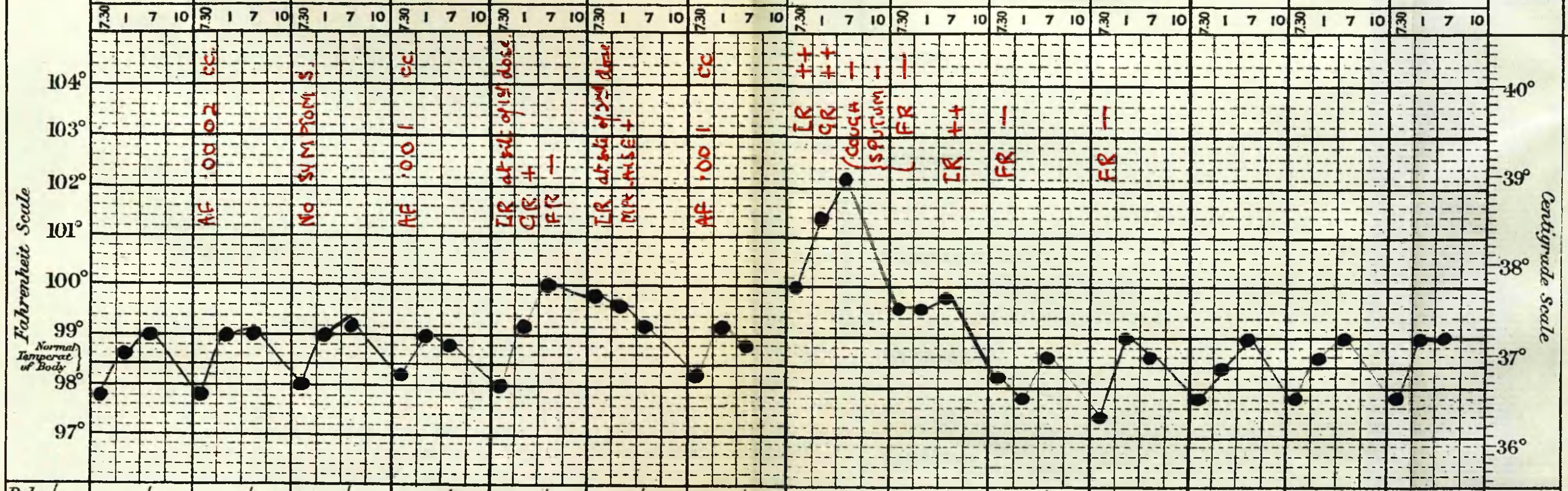


CHART No VII

Showing a typical incompletely-tested case. Doses discontinued owing to violent local and general reactions. Onset doubtful but serum reactions negative.

Pulse/Resp.	/	/	/	/	/	/	/	/	/	/	/	/	/	Pulse/Resp	
B.O.														B.O.	See Page 37
Sputum														Sputum	
Weight														Weight	
Distance A.M.		REST	REST	REST	REST	REST			REST	REST	2 miles	3 miles	4 miles	GARDEN	
Distance P.M.											2 —	3 —	4 —	4 miles.	Weekly Summary of progress
Total Exercise in Day															

Malby & Sons, Lith.

S E C T I O N IV.

SUB-SECTION. B.

GENERAL

AND

LOCAL

TUBERCULIN

REACTIONS.

No consideration of tuberculin testing can be considered complete which does not refer to the various cutaneous per-cutaneous and conjunctival tests, and with these might be included the local and general reaction after sub-cutaneous tuberculin, inasmuch as all of them are concerned primarily with the degree of sensitiveness of each case. The main question here also is one of finality. How far can a definite diagnosis be made on the strength of any or all of the local and general reactions?

The simple cutaneous test needs no consideration except in the case of children, and the conjunctival while no longer considered as once a dangerous test, (although this is not the view held by Wiens and Gunther (X)) and while giving satisfactory results in known cases of tuberculous, (Calmette (O), Smithies and Walker(+), Hamman (R) and Cohn (=)) gives most unsatisfactory results in cases of early phthisis varying from 25% unsatisfactory cases of Wolff-Eisner (±) to the 40% of Hamman and the 45 - 50% of Bandelier and Roepke (@)

(X) Weins and Günther: Munch. Med. Woch. 1908. Nr.36.

(O) Calmette: Int. Cong. of Tuberculin, 1908 Vol. I.

(+) Smithies & Walker: Journ.Amer.Med.Ass.1909 LII.

(R) Hamman: Arch.Intern.Med.1909.III.

(=) Cohn: Berl.Klin.Woch.1907.Band.XLIV.

(±) Wolff-Eisner: Die. Fruhdiagnose. 1909.

(@) Bandelier and Roepke: Lehrbuck. spec. Diag. 1913.

Except in the case of children the per-cutaneous test of Moro lends no finality to the diagnosis and there are left for consideration the quanti-Pirquet test, the intra-cutaneous test of Mantoux and Roux, the local and general reactions after sub-cutaneous injection and the needle-track reaction of Escherich.

It is still a question for discussion how far all these tests are strictly comparable.

The literature on this point is not so extensive as on other sections of the same subject.

Rivière is unable to find any relationship between skin and sub-cutaneous reaction, but Carpenter and Gordon found a very close relationship.

The writer's own experience on this point, and it is not at all extensive, is on the side of some general relationship but he has found the occurrence of Local Reaction a most variable quantity and has experienced a great difficulty in standardizing, particularly the local sub-cutaneous reaction.

But even if one considers each reaction as having a special significance of its own, the results are none too satisfactory. For instance Hamman and Wolman, using the quanti-Pirquet test found 16% non-active cases reacting positively to 1% tuberculin and 44% of incipient cases negative to the same dilution and 22% of incipient negative to a 5% dilution.

The intra-cutaneous test of Mantoux and Roux(x) whilst giving more satisfactory results than the

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(x) Mantoux and Roux: Münch. Med. Woch. 1908. Nr. 40.

cutaneous in children as shown by Monti(⊙) and Engel(⊗), does not afford in the adult any more information than the cutaneous and is besides more painful and more difficult to standardize.

The needle-track reaction of Escherich(⊕) is also limited in value to the examination of children and then chiefly as a means of investigating further a negative cutaneous reaction in a still suspicious case or a slightly febrile case. In the adult needle-track reactions are of no definite value.

This will be appreciated by anyone who has had opportunities of observing numbers of local reactions to sub-cutaneous injections.

In 14 of the writer's 100 test cases, no local reactions were obtained with the highest dose where local reactions had already been present with a lower one, and in two or three cases a focal reaction was obtained without any local reaction being noted at all.

It is the writer's belief after observation of many thousand injections given as test doses or as specific treatment that the production of varying degrees of local reaction depends to a large extent on the technique of injection.

It has been very striking to him to note that whilst injections in the upper part of the arm give

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(⊙) Monti: Wien. Med. Woch. 1912. Nr. 7.

(⊗) Engel: Deut. Med. Woch. 1911. Nr 36.

(⊕) Escherich: Jahrbuck. F. Kinderheilk. XXXIII.

very frequent and severe reactions, these are much less marked when given in the abdomen and are reduced to a minimum when given in the loose skin between the scapula and the spine.

The explanation seems to be twofold (1) the relative immobility of the last two areas, (2) the ease with which in the back at any rate injection can be made in the loose areolar tissue.

The most minute difference in the mode of injection will produce in the same person with almost the same dose great variations in reaction, e.g. the vigorous rubbing of the skin with spirit before and after injections; the injection by accident into dense fatty layers or into muscle; the injection immediately above the elbow as compared with that in the deltoid groove.

That being so it can be understood that little reliance can be placed on the local reactions.

We are thus brought to the consideration of the value of the general reaction following sub-cutaneous injections.

As has already been seen, if the focal reaction to sub-cutaneous tuberculin is established as the sole criterion of active pulmonary disease, and if the precautions as to testing are carried out, we are met with a considerable bulk of cases where the result is quite indefinite.

Can one then deduce activity or otherwise from the character of the general reaction?

It has also been pointed out that Bandelier and

Roepke whilst laying down the focal reaction as a standard actually conclude diagnosis of active disease in many instances on the result of general reactions particularly to earlier doses.

It is true that these diagnoses were made after a sharp rise in temperature after a single dose or after a cumulative dose, that they excluded as far as possible any neurasthenic condition, and that the reactions were considered in conjunction with the history etc., but they are still open to the criticism of Bandelier and Roepke's own statement that the test of pulmonary tuberculous par excellence is the clinical focal or the production of a bacteriological focal. It can be freely admitted that acute rise after an early dose points coeteris paribus to an early attack but it might also be fairly considered to point to a recently healed lesion, and of course in this case the temperature rise of a cumulative reaction would be even less final evidence. The febrile reaction to the larger doses is admitted after the work of Fränkel, Neisser and Hamman to have in the majority of cases no clinical significance. The writer's investigations lead him to the same conclusion as the following tables will show.

It will be remembered that in carrying out his tests a middle course was steered between the rigid "temperature rule" of Bandelier and Roepke which adds so many to the doubtful list and the ignoring of "danger signal reactions." This mean was taken after a consideration of the physical signs, history and the results of serum

examinations in each case, and on the whole it did not work out badly.

A certain number of small general reactions were ignored and higher doses given where the history and clinical signs were markedly negative.

Tables have been made out showing the results of this course and incidentally showing the questionable value of the general reactions.

TABLE I.

Shows the ultimate results in test cases where reactions to the 1st (.0002 A.F.) or 2nd (.001 A.F.) tests were ignored and also in cases where the exciting dose was repeated.

	Positive(Focal)		Doubtful		Negative	
	Reaction		Reaction		Reaction	
	slight	severe	slight	severe	slight	severe
Reaction ignored	7	1	2		28	2
Dose repeated	4	1		3	3	4

TABLE II.

Shows results where reactions to 3rd (.005 A.F) and on three occasions to the 4th (.01 A.F.) were ignored and where the exciting dose was repeated.

	Positive(Focal)		Doubtful		Negative	
	Reaction		Reaction		Reaction	
	Slight	severe	slight	severe	slight	severe
Reaction ignored	1		1	2	33	3
Dose repeated	3		1	1	7	4

TABLE III.

Cases with no reaction to 1st, 2nd, or 3rd, giving result to 4th. Dose. (·01 cc AF).

Positive	Doubtful	Negative.
2	—	14

TABLE IV.

	Positive	Doubtful	Negative
Cases stopped at 2nd dose	1	—	1
Cases " " 3rd "	5	1	7

The points illustrated by these tables may be put in a more convincing fashion thus:- In the great majority of cases where a reaction, slight or severe, was caused by the early test doses, the ultimate result was negative: in the great majority of cases where a general reaction slight or severe, was caused by the larger doses, the ultimate result was negative: in some cases where no general reactions at all were noted to the previous doses, a focal reaction was set up by the final dose (A F .01 cc).

The deductions to be drawn from these facts are respectively, (1) that general reactions to the earlier test doses are no indication of an active process, and incidentally that, using proper precautions, they may be ignored with safety, (2) that reactions to the later doses are no indication of an active process, (3) that

absence of general reaction to any but the final test dose and even then, is not indicative of absence of disease.

SUMMARY:

In the adult, the various cutaneous reactions cannot be taken as proof of active pulmonary tubercle: reactions at the site of injection of subcutaneous tuberculin are of no significance: general constitutional reactions to small or large doses of subcutaneous tuberculin do not necessarily indicate an active process.

S E C T I O N IV.

SUB-SECTION. C.

TUBERCULIN TESTING IN FEBRILE CASES.

Apart altogether from the limitations of subcutaneous tuberculin testing from the point of view of insufficiently tested cases, there is a still greater limitation to its usefulness in that no persistently febrile cases can be tested at all, at any rate by the usual methods.

This is due chiefly to the fact that no safe deductions can be drawn in such cases from rise in temperature after any dose, and that therefore the 'temperature' safeguard from danger is not trustworthy.

Now, persistently febrile cases form quite an appreciable percentage of any series of doubtful cases - in the writer's experience about 10% of doubtfuls show some persistent febrile condition - and consequently it is important to find if any modification of the rule as to testing such cases could with safety be made.

It will be remembered that in the section dealing with symptomatology, three types of pyrexia were described: (1) a steady, swinging temperature, (2) a cyclical temperature associated with menstruation, and (3) a perpetually irregular temperature, and it was also noted that practically all examples of these types occurring in doubtful cases showed no improvement with variations in the amount of exercise.

At the end of this section charts are appended as follows: - illustrating Type No. 1 (Charts Nos. XVIII); illustrating Type No. 2 (Charts Nos. VIII, IX, X, XI, XII); illustrating Type No. 3 (Charts Nos. XIII, XIV, XV).

A consideration of these will show that at any rate in the instance of temperatures associated with menstruation the ordinary course of infections can be pursued.

It is of course necessary to keep the case under observation for at least two or three months, and to observe at what period the temperature is likely to fall within normal limits.

At the first indication of a fall, test doses are commenced and as a rule can be carried through without any more than the ordinary difficulty.

((Charts No. X · XI · XII) are examples of this method and it may be noted how the final result was in those cases negative.))

We are still left, however, with the regular swinging temperature and the irregular type.

It is, of course, possible to keep these cases under observation for several months on the chance of ultimate settling of the temperature (as is shown by Charts No. XIII · XV) but such a lengthy period of observation is not always feasible, and some other method of dealing with such cases would seem highly desirable.

In the course of his experience of the therapeutic action of tuberculin in definite cases of tubercle, the writer was struck with the specific anti-pyretic effect of minimal doses of tuberculin - notably of Bacillary Emulsion (Koch) - on slightly febrile cases.

(Charts XVI - XVII are excellent illustrations of this effect) It occurred to him that use might be made of this specific anti-pyretic action of Bacillary Emulsion in cases where the ordinary method of testing could not be satisfactorily carried out.

The following case is an example: -

Case No. VI Mr H. was admitted in fair condition

with a history of previous pleurisy three months before and a subsequent cough without sputum.

Physical signs indicated an old pleurisy over the right lower lobe. The temperature was persistent though slightly febrile, rising very steadily to 99.4° F.

After two months' observation a modified course of test doses was given.

On 1st day: AF .0001 cc. injected: no symptoms.

On 3rd day: AF .0005 cc. injected: local reaction +; general reaction 100.4° F. and some malaise.

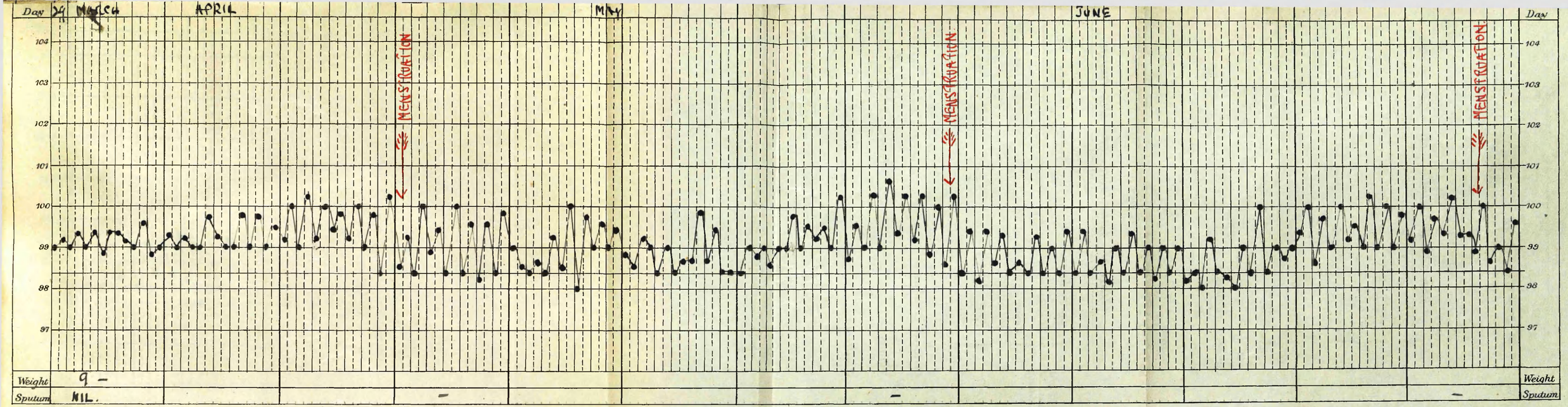
On 5th day: AF .0005 cc. repeated: local reaction ++ general reaction ++: Temperature 101° F. There was some doubt as to a focal reaction, but the tests were not continued.

A fortnight later a series of test injections of Bacillary Emulsion were given beginning with .000001 cc. and continued at the rate of two per week over a period of ten weeks, rising to .0001 cc. Bacillary Emulsion.

The temperature gradually subsided during the later doses, and the case was diagnosed as one of tuberculous pleurisy in a condition of minimal activity. (Chart No. XVIII)

Admittedly such a method is not always practicable from the point of view of time, but it is more satisfactory than leaving the case quite untested, and it is certainly without any danger.

In any case such febrile cases usually spend considerable periods of time under observation, and even if no definite result should be come to within such periods it is possible that a course of injections of this type might aid in clearing up the diagnosis.



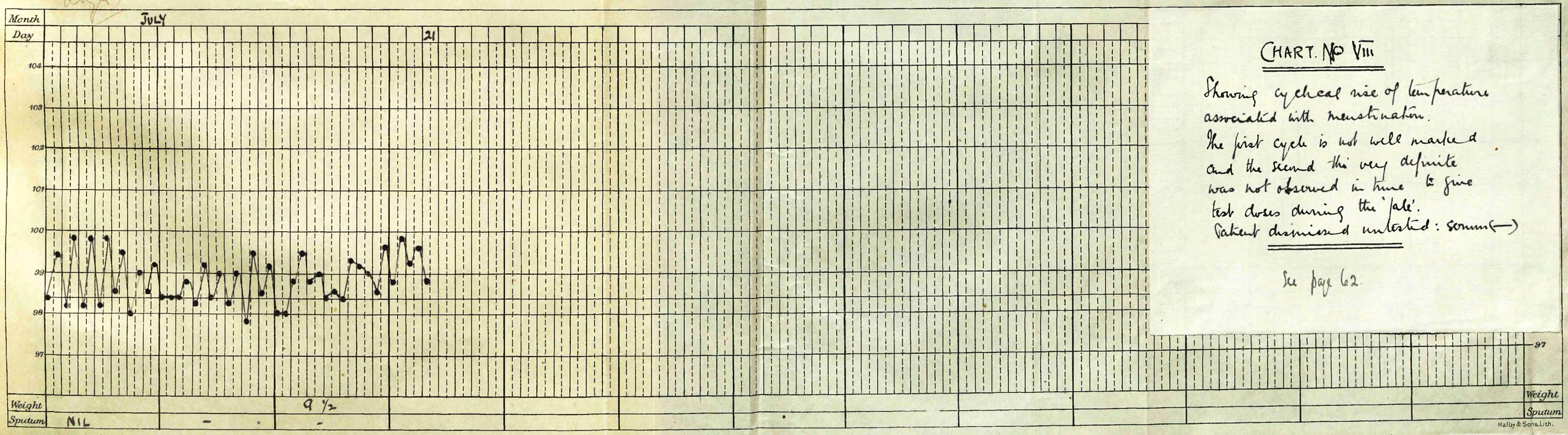


CHART. No VIII

Showing cyclical rise of temperature associated with menstruation.
The first cycle is not well marked and the second the very definite was not observed in time to give test doses during the 'pale'.
Patient dismissed untested: somm(—)

See page 62.

Malby & Sons, Lith.

Month APRIL MAY JUNE JULY Month

Day 5 Day

MENSTRUATION MENSTRUATION MENSTRUATION

104 103 102 101 100 99 98 97

Weight 9. 4½ 8. 6½ Weight

Sputum nil Sputum

12 Miles | 8 miles | Bed. | Bed. | Rest | Strolls | 4 miles | 16 miles | 21 miles | 16 miles | 18 miles | 12 miles | 12 miles

Month Day 13 Month Day

MENSTRUATION

104 103 102 101 100 99 98 97

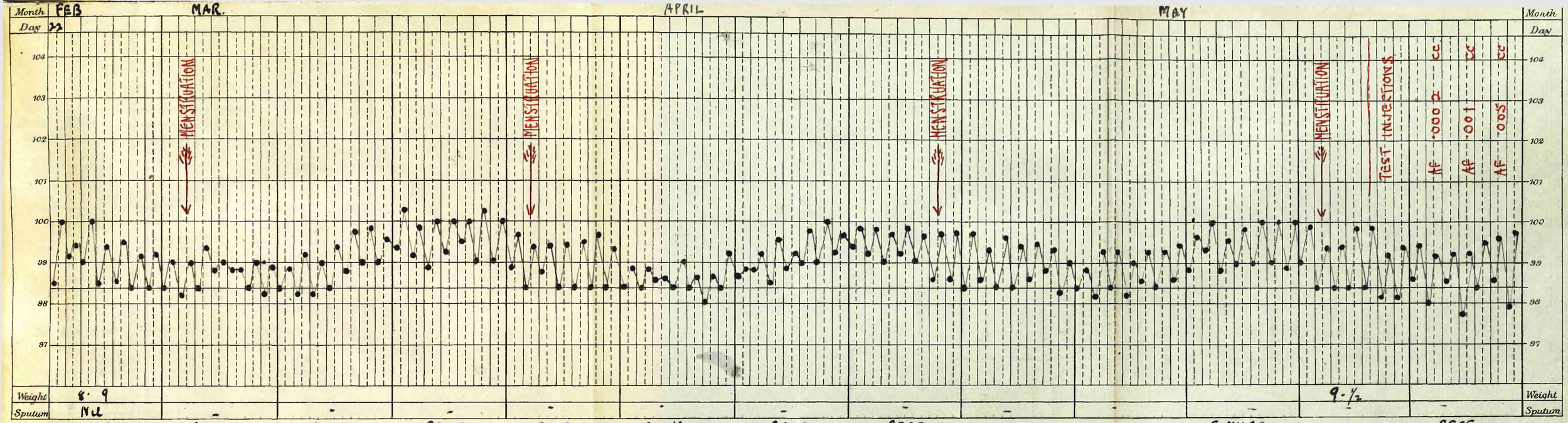
Weight 8. 6 Weight

Sputum nil Sputum

CHART No. IX

Showing cyclical rise of temperature associated with menstruation.
Patient dismissed untested
Sputum reactions negative and clinical signs nil.

See page 62



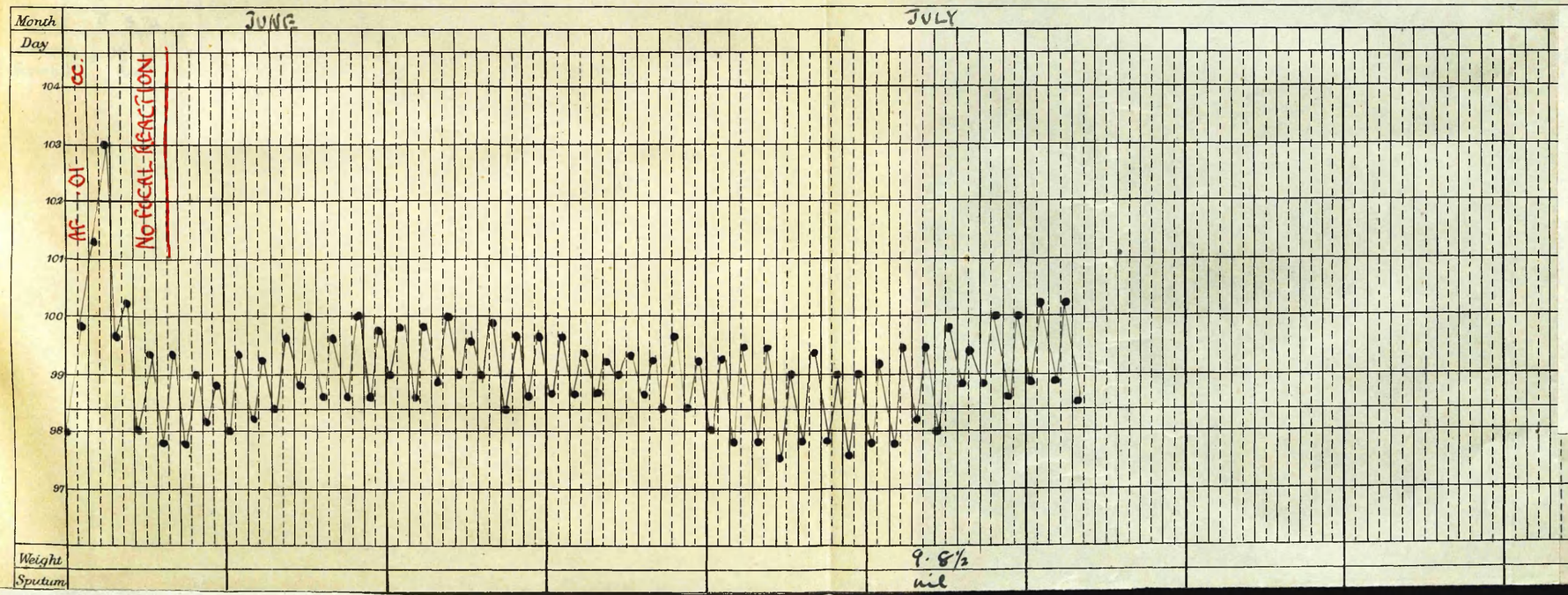
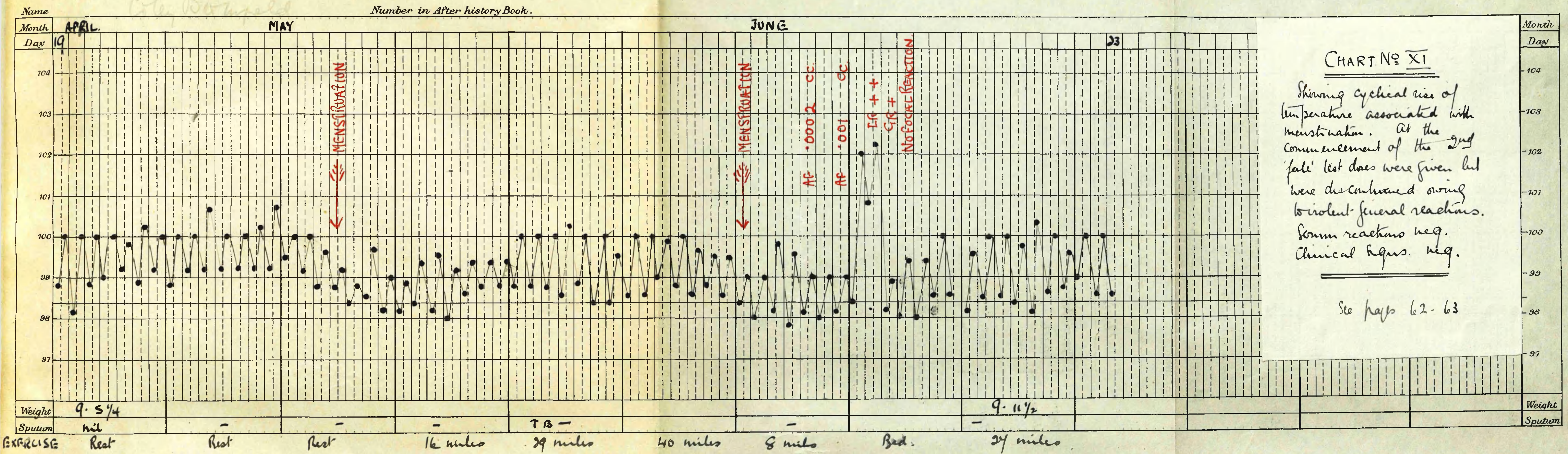
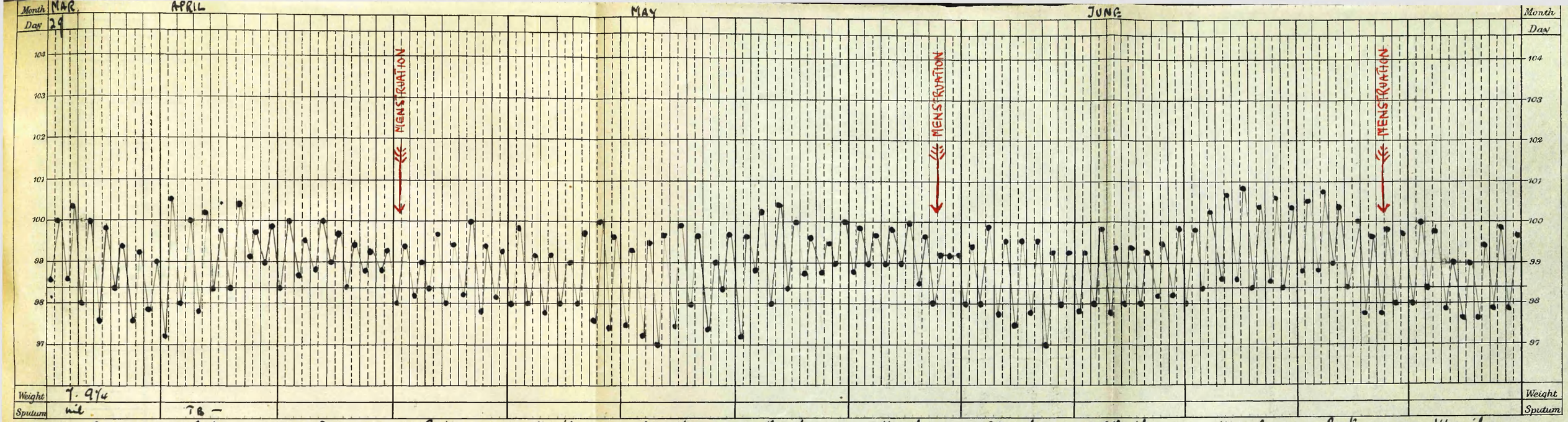


CHART. No X

Showing cyclical rise of temperature associated with menstruation. The periodicity was noted and test doses commenced at the 4th 'pale' with negative result. Temperature unaltered subsequently.

See pages 62. - 63


Name
Number in After history Book.
Month
Day
APRIL
MAY
JUNE
19
23
104
103
102
101
100
99
98
97
MENSTRUATION
MENSTRUATION
AF ·0002 cc.
AF ·001 cc
LR ++
CR +
No FOCAL REACTION
Weight
9. 5¾
9. 11½
Sputum
nil
TB —
EXERCISE
Rest
Rest
Rest
16 miles
29 miles
40 miles
8 miles
Bed.
27 miles
CHART No. XI
Showing cyclical rise of temperature associated with menstruation. At the commencement of the 2nd 'fall' test doses were given but were discontinued owing to violent general reactions. Serum reactions neg. Clinical signs. neg.
See pages 62 - 63.



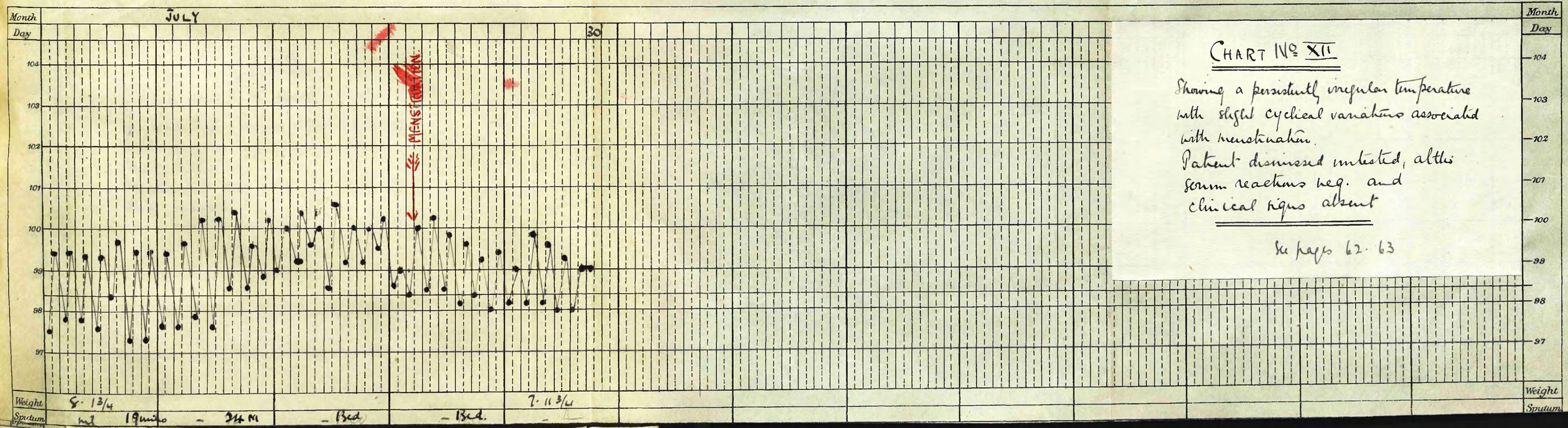


CHART No. XII

Showing a persistently irregular temperature with slight cyclical variations associated with menstruation.
Patient dismissed untested, all the serum reactions neg. and clinical signs absent

See pages 62. 63

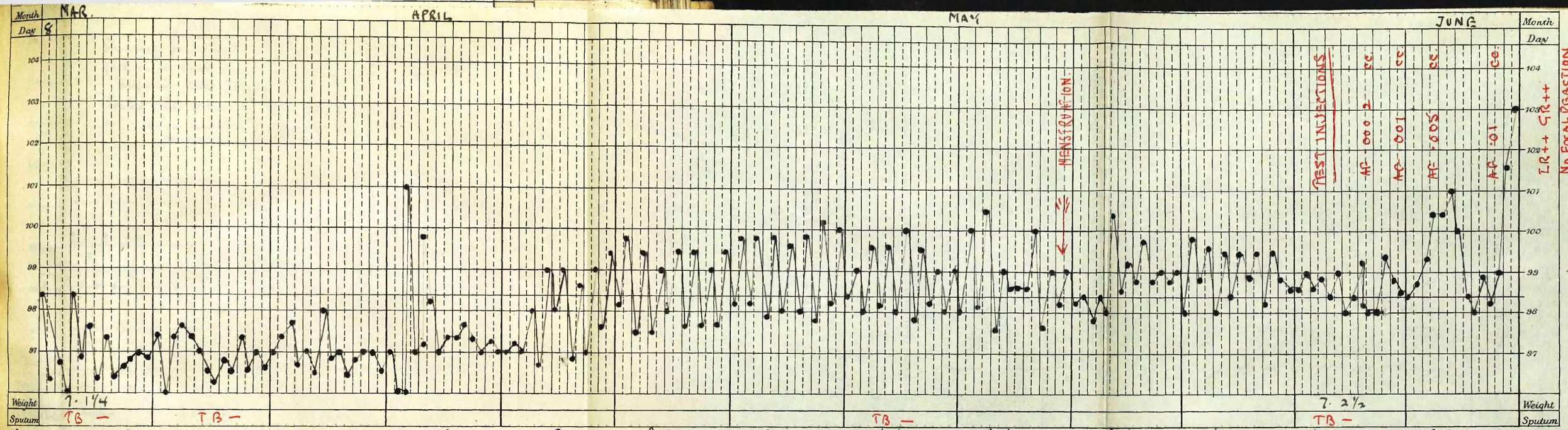


CHART. No XIII

Showing persistently ~~mega~~ irregular temperature, tested after 2½ months interval with negative results. (Case I. Section T.D).
Menstruation very irregular and at with long intervals.

See page. 62.

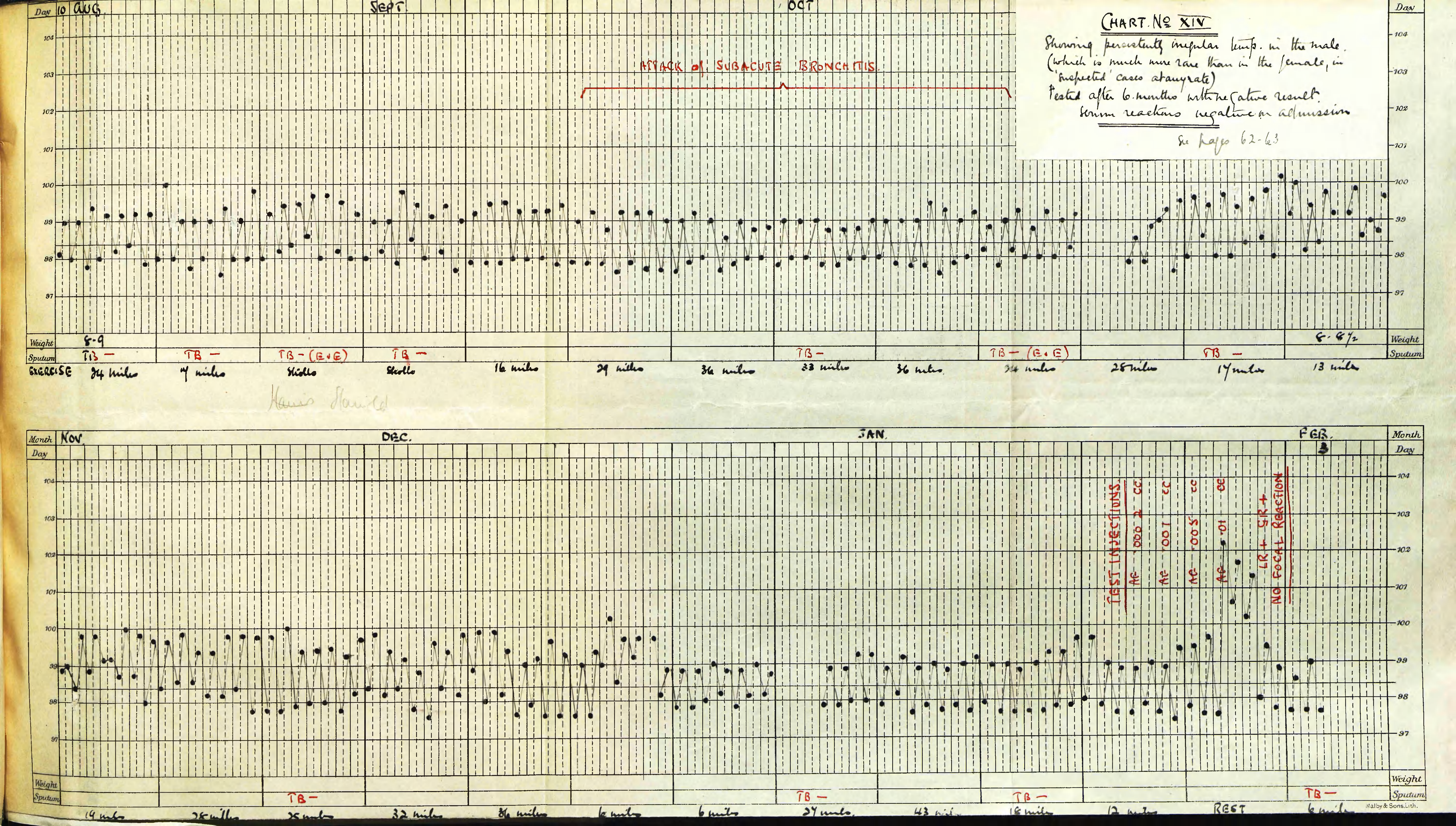
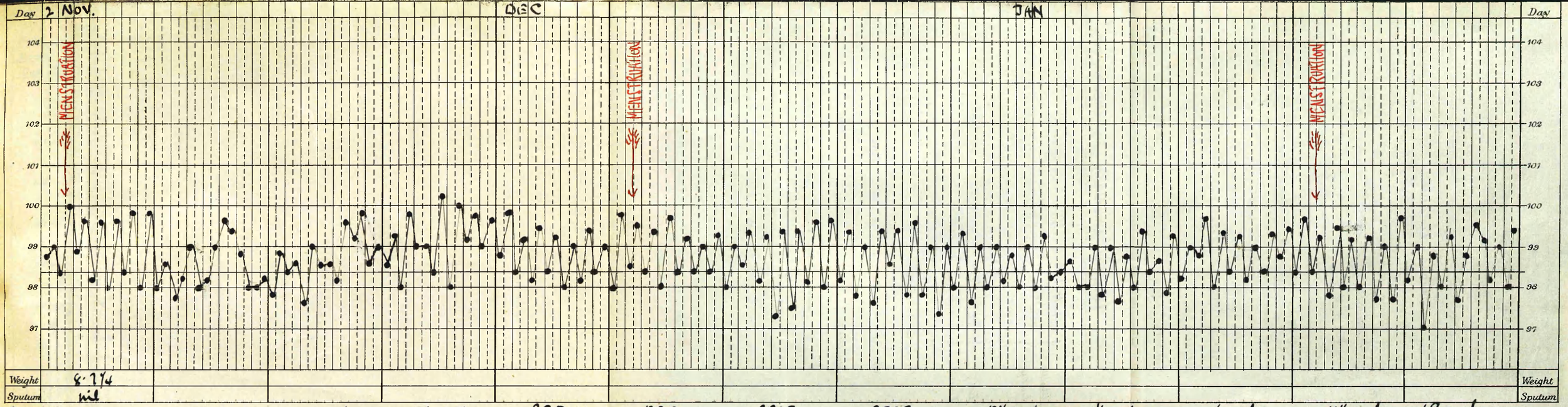


CHART. No XIV
Showing persistently irregular temp. in the male. (which is much more rare than in the female, in 'suspected' cases at any rate)
Tested after 6 months with negative result.
Serum reactions negative on admission
See pages 62-63
ATTACK of SUBACUTE BRONCHITIS
Day
10 AUG.
SEPT.
OCT
Weight
8-9
8-8½
Sputum
TB —
TB —
TB — (E+E)
TB —
TB —
TB — (E+E)
TB —
EXERCISE
24 miles
7 miles
Strolls
Strolls
16 miles
29 miles
36 miles
33 miles
36 miles
34 miles
25 miles
17 miles
13 miles
Month
NOV
DEC.
JAN.
FEB.
TEST INJECTIONS.
AE .0002 cc
AE .001 cc
AE .005 cc
AE .01 cc
LR + GR +
NO FOCAL REACTION
TB —
TB —
TB —
TB —
14 miles
28 miles
25 miles
32 miles
36 miles
6 miles
6 miles
27 miles
43 miles
18 miles
12 miles
REST
6 miles
Malby & Sons. Lith.



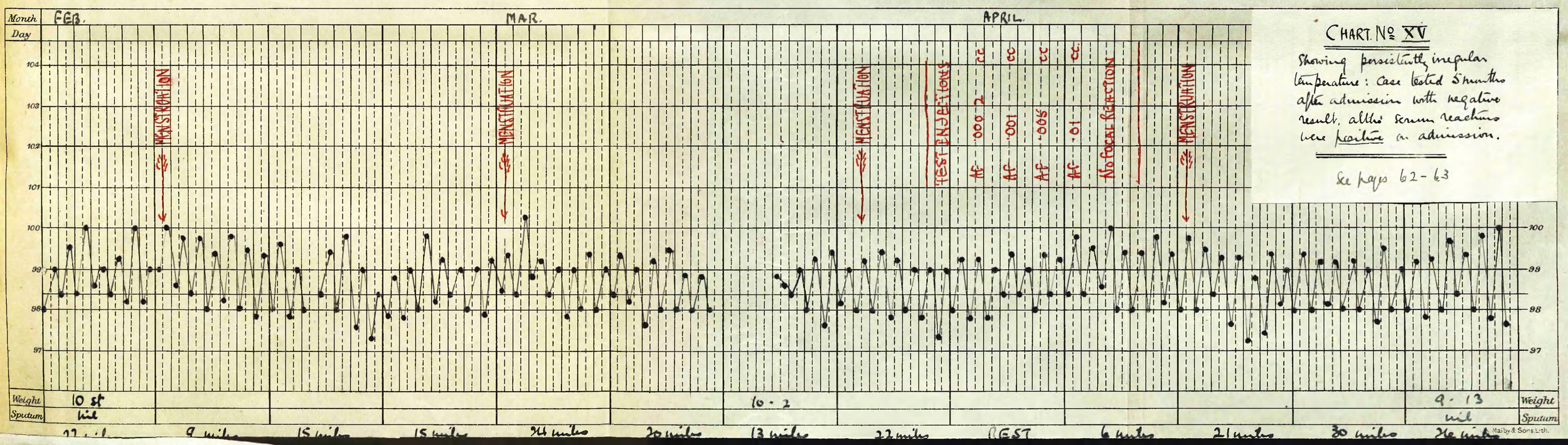


CHART. No. XV

Showing persistently irregular temperature: Case tested 5 months after admission with negative result, altho serum reactions were positive on admission.

See pages 62-63

Maiby & Sons Lith.

Name

Number in After history Book.

Month JUNE JULY AUGUST SEPT OCT.

Day 15

104

103

102

101

100

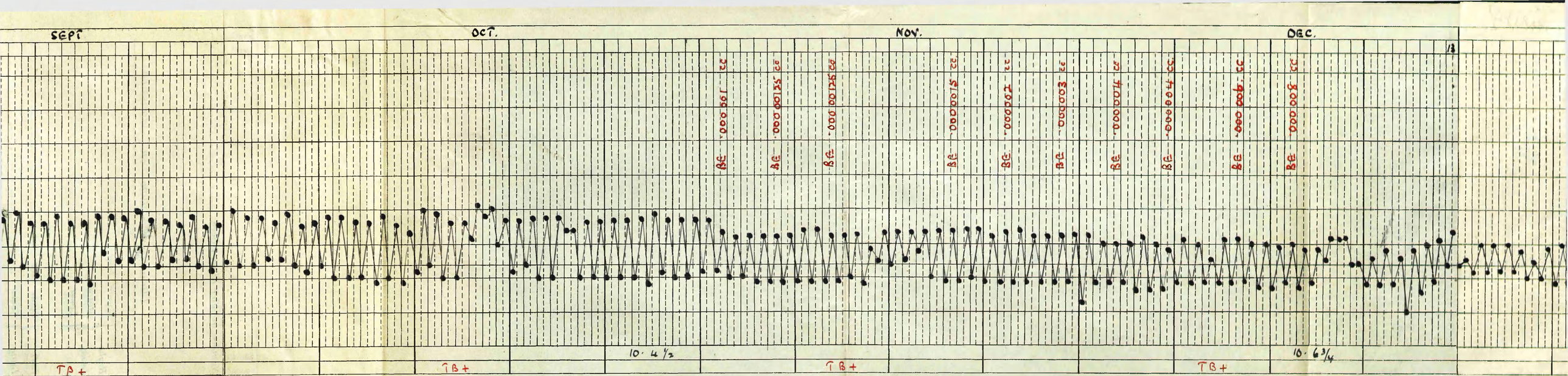
99

98

97

Weight 9. 11

Sputum TB + TB + TB + TB + TB +


SEPT
OCT.
NOV.
DEC.
TB+
TB+
10. 4 1/2
TB+
TB+
10. 6 3/4

Number in After history Book.

DEC. JAN. FEB.

B.E. ·000 005 cc

B.E. ·000 008 cc

99

98

97

TB + TB + TB + TB +

10·6¾ 10·7

Weight

Sputum

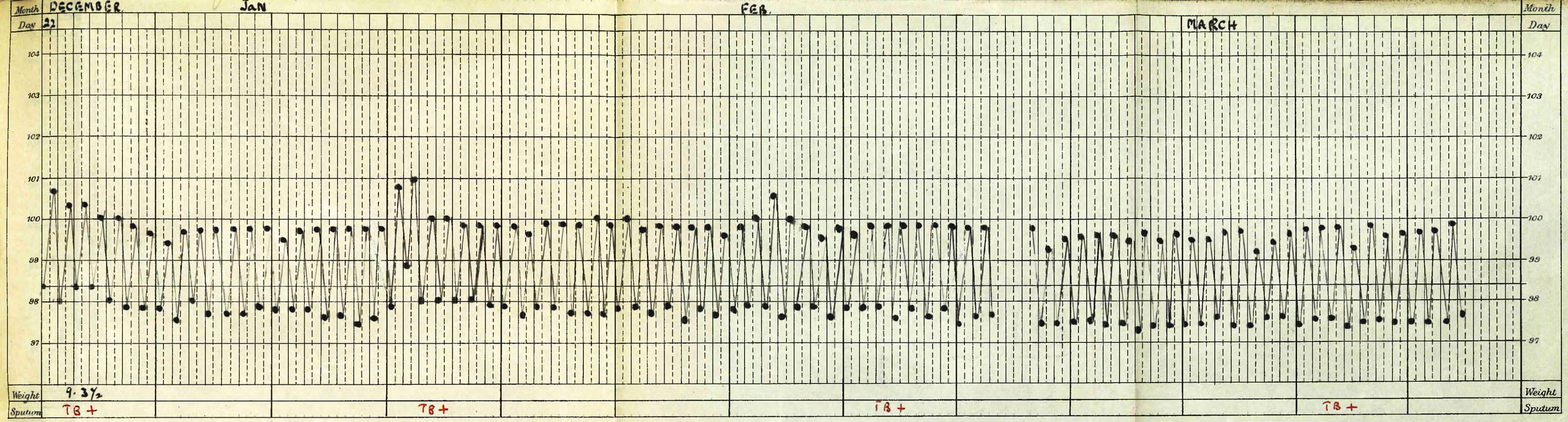
Mailby &

CHART No. XVI

Showing the specific anti pyretic effect of Koch's Bacillary Emulsion in small doses on a Case of Pulmonary Tuberculosis.

To avoid fallacy, the case was kept under observation for four months before and after the period of Inoculation.

See page 64



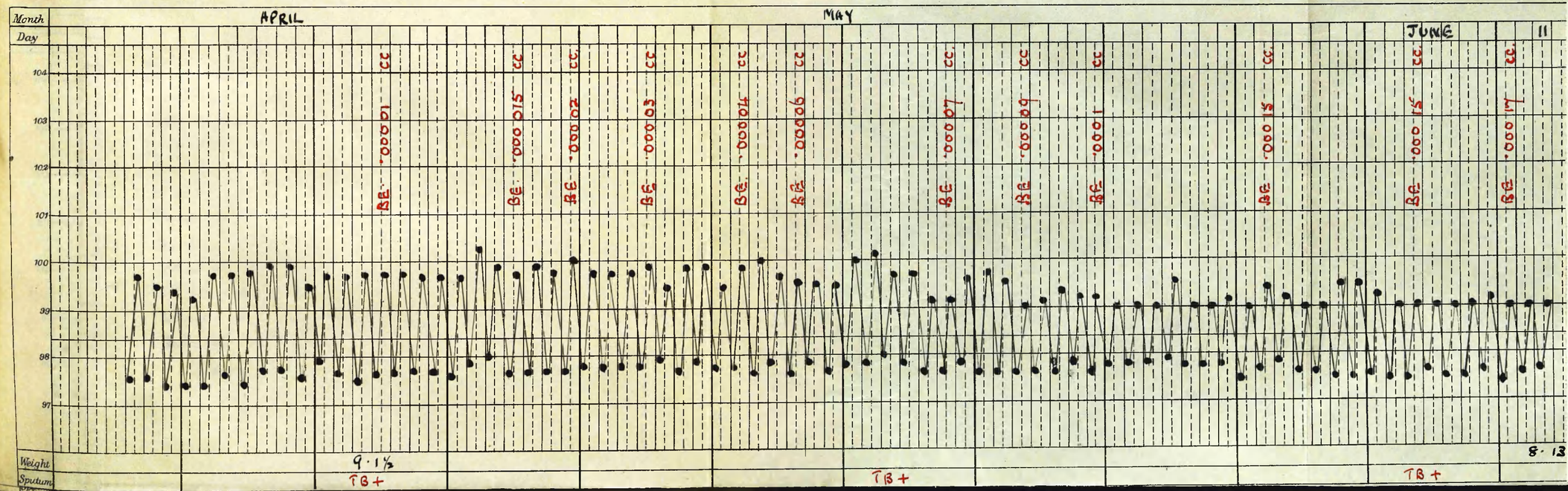
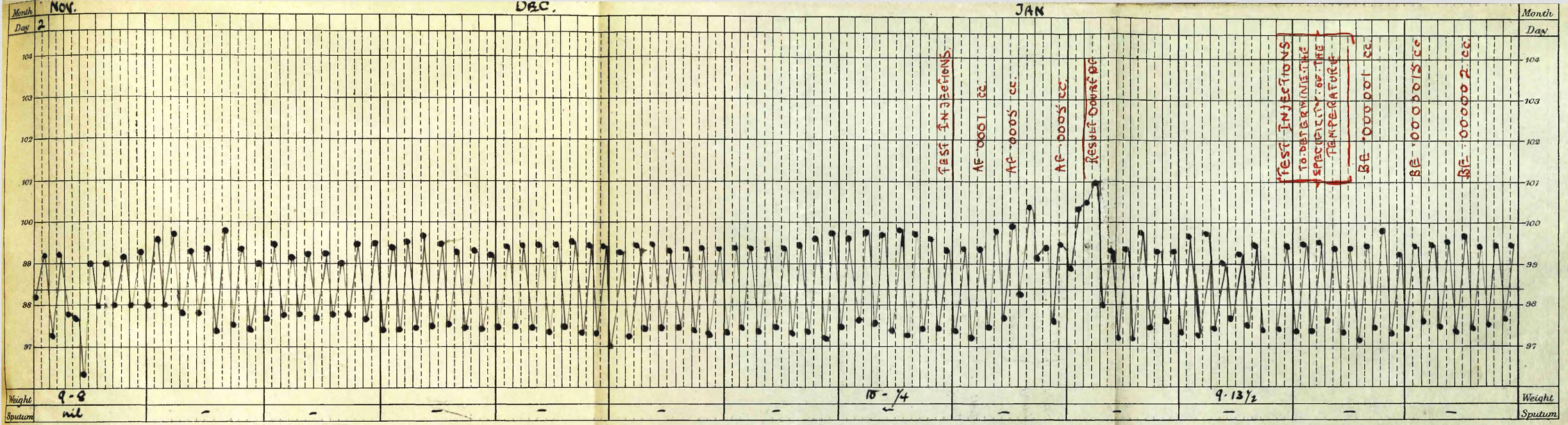


CHART. No. XVII

Showing the specific antipyretic effect of Koch's Bacillary Emulsion in a case of Pulmonary Tuberculosis.
Case kept under observation for 3½ months prior to Inoculations

See page 64



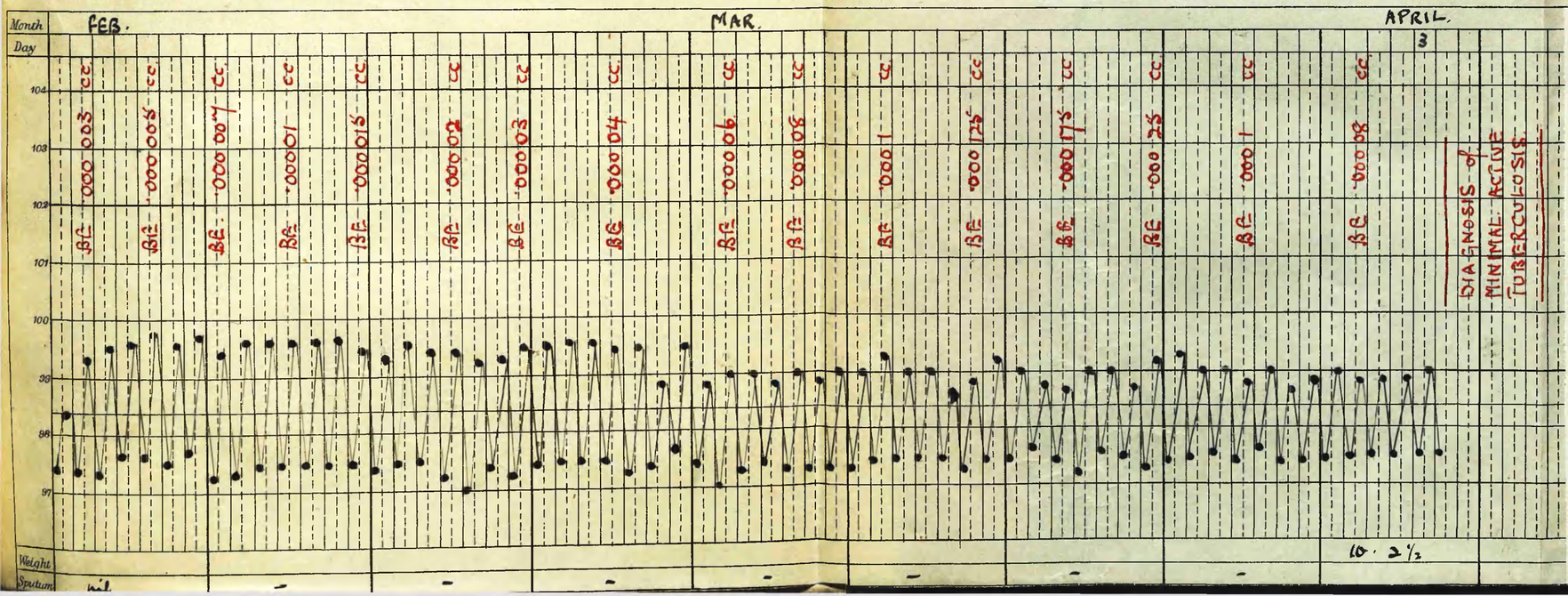


CHART № XVIII

To illustrate a method of giving diagnostic injections of tuberculin where the temperature curve indicates the ordinary course of test doses (i.e. ·0002 – ·01 cc. AE).

This is based on the specific anti-pyretic action of Koch's Bacillary Emulsion as illustrated on Charts XVI & XVII.

Ten days after a doubtful result to a modified series of test doses, a series of small doses of BE. was given and the temperature, which had previously remained stationary, subsided to the later dose.

A diagnosis of active pulmonary disease was made.

See pages 62-64

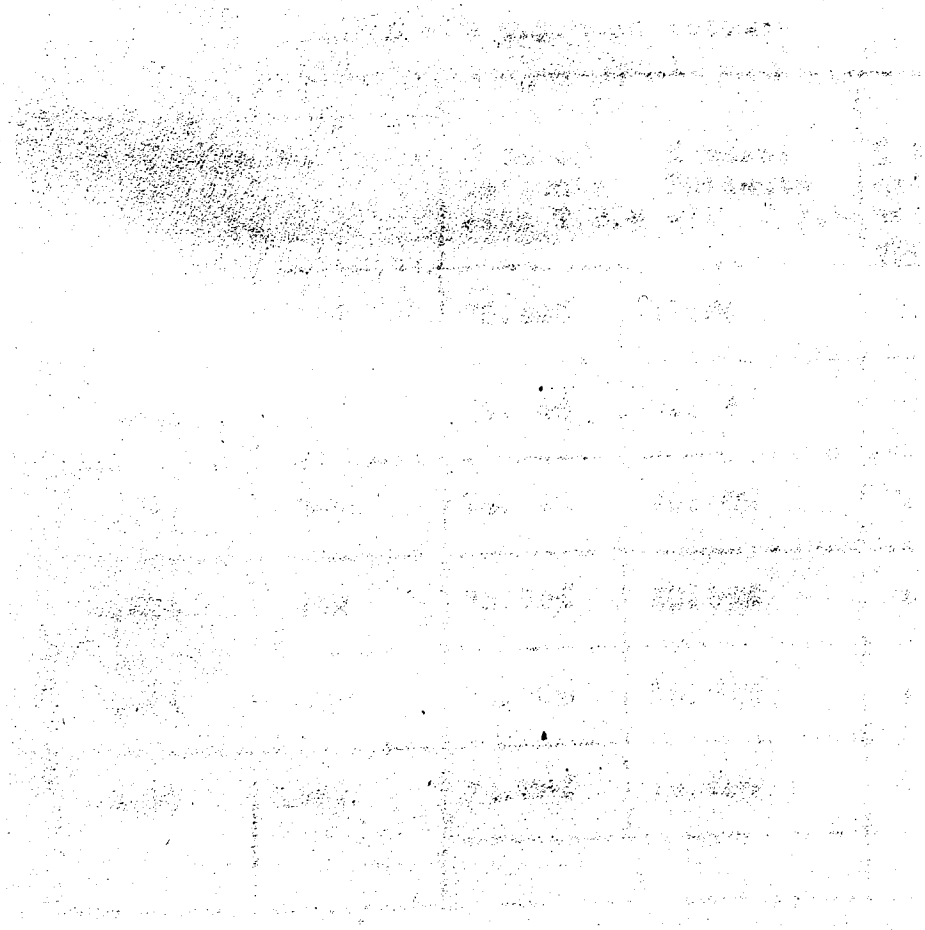
S E C T I O N V.

SPUTUM

EXAMINATION

SUB-SECTION. A.

BACTERIOLOGICAL.



Of all the methods of rapidly establishing or negativing a diagnosis of active pulmonary tuberculosis requiring treatment, the examination of the sputum for Tubercle Bacilli is the most important, and to trespass for a second into the region of prognosis, it is, since the adoption of sedimentation methods, the most accurate means of foreshadowing the course of the disease.

The writer has been permitted through the kindness of Dr. Radcliffe (Bacteriological Laboratory, King Edward VII Sanatorium) to review the results of sputum examinations carried out there for a period of five years. The results are appended below:-

Year	No. of Specimens	No. of Patients.	% No. of patients with T.B.+	% No. of Patients with T.B.-	% No. of patients without sputum	Total % without T.B.
1907 - 8	1328	334	75.44%	17.08	7.48	24.56
1908 - 9	1439	388	71. 4%	21. 6	7. 0	28. 6
1909 -10	1695	339	74. 4%	20. 0%	5. 6%	25. 6%
1910 -11	1884	412	73.78%	20.88%	5.34%	26.22%
1911 -12	1844	409	75.30%	16.63%	8.07%	24. 7%
Total average	8190	1932	74.06%	19.23%	6.69%	25.92% average

In the year 1907 - 8 the ordinary methods of examination were employed, but next year those cases which gave

negative results to ordinary examinations, were further investigated by the sedimentation methods which had then been described: to wit, the Antiformin procedure of Uhlenluth, the Ligroin method of Lange and Nitsche, and the method of Ellerman and Erlandsen (⊗).

Next year 1909 - 10 and since then the Ellerman and Erlandsen method or 'E. and E' method as it is called for convenience has been continued.

This was done because Radcliffe's results so closely followed those of Herzfeld (◎) which are given below:-

Sputum	Antiformin	Ligroin	E. and E.
	Average Number of T. B. in four preparations		
1	0.5	0.0	2.5.
2	1.25	1.0	3.0
3	26.25	-	42.0
4	13.75	4.25	218.25
5	32. 0	4. 5	59.75
6	132. 5	11. 0	Innumerable
7	very numerous	35. 6	Innumerable
8	0. 0	0 . 0	3.25
9	45. 0	20. 0	Innumerable

In addition in two consecutive years by using the E. and E. method Tubercle Bacilli were demonstrated in 36.48% and 40% respectively of cases where by repeated ordinary examinations no Bacilli were found (Radcliffe).

(⊗) Ellerman & Erlandsen: Zeitscr.für.Hygien.Baud.61.p.219

(◎) Herzfeld: " " " 66.p.340

At various times at Midhurst the staining methods of Much. & Karl Spengler have been investigated (Radcliffe de Wesselon and the writer) but although the number of cases investigated was small and there were no opportunities of animal inoculation, the results obtained did not show any advantages over the Ziehl-Nielson method. In any case it is a simple matter to stain at least one of the sedimentation films after the Gram-Much. method.

To turn to the first table of results it will be noted that on the average each year 25.92% of cases admitted never had any bacilli or had no sputum at all.

The importance of this will be seen from the following fact that an examination of the After-history records of these cases made at Midhurst (the figures have not yet been officially published) shows that the death-rate amongst them is coeteris paribus no larger than that of the average adult. To put it at the least, the death-rate of these cases is very much lower than of those where with an equally small lesion, bacilli were found.

In the next place the death-rate of patients who lose their bacilli during Sanatorium treatment is smaller than that of patients who are dismissed with bacilli present. (Midhurst, umpublished).

From this last fact it is fair to deduce that the absence of bacilli has some prognostic significance, and it is a short step to state that therefore absence of bacilli must have also some diagnostic significance.

Applying this reasoning to the interpretation of the very definite differences in death rates, one is

forced to the conclusion that of the 25.92% of cases with negative bacillary find a very small proportion can have been in what is called the 'prebacillary stage' i.e. suffering from incipient phthisis. And after all mere theoretical considerations would point to the same conclusion.

As de Wesselow (x) points out any tuberculous infection cannot, from anatomical considerations, be far from an air-passage and we must expect therefore the appearance of bacilli in the sputum at an early stage.

In addition if the lesion begins in the smaller bronchi bacilli would appear in the sputum, according to Cornet, before the appearance of physical signs.

It is not unfair, then, to claim that where physical signs are present bacilli should, as a general rule, be found present in the sputum if the lesion is active.

These considerations cannot be held as in substantiation of the non-existence of the pre-bacillary stage, but they are put forward in criticism of that long drawn out pre-bacillary stage which is the happy hunting ground of many diagnosticians, and in support of the statement of the great diagnostic value of a positive or a negative bacillary find.

(x) de Wesselow: Proc. Roy. Soc. Med. 1914. Vol 7. p.159.

SECTION V.

SUB-SECTION. B.

CHEMICAL.

THE ALBUMIN REACTION.

A detailed consideration of the so called 'albumin reaction' of the sputum is the more necessary that in addition to the support of many French writers, it has received from Riviere and others in England the stamp of their approval.

If, as all observers agree, albumin can be detected in the sputum in various definitely non-tuberculous affections of the lungs, such as passive congestion, etc. or if, as has been asserted by Wanner, Remlinger (1), Bezançon and de Jong (2), traces of albumin can be found in practically all sputa, it is clear that the significance of its presence in pulmonary tuberculosis can be satisfactorily based only on routine quantitative estimations. Going on this assumption, 210 quantitative examinations of the sputum were made in 149 cases coming under observation in the King Edward VII. Sanatorium at Midhurst.

TECHNIQUE OF THE REACTION.

The accurate separation of albumin from the sputum, and the subsequent testing of the same, present at times considerable difficulty. The technique is as follows: The sputum is collected in a Petri dish, and to avoid as

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(1) Remlinger: Société de Biologie, March 12, 1911.

(2) Bezançon et de Jong: "Traité de l'examen des Crachats", 1913.

much as possible either the dissociation of true albumin present by proteolytic ferments, or the setting free of albumin from protein molecules by decomposition, is examined within three hours of collection. Separations of albumin are always to be made from the entire sample, and not, as by Ridge and Treadgold (⊗), from the purulent portions only, because in the bulk of doubtful cases and in many tubercular cases the various elements of the sputum are almost entirely homogenized, and it is not possible to separate even small quantities of purulent material.

In an ordinary filtration of the sputum in tuberculous cases the substances requiring definite consideration are the following: (1) Mucin, from the goblet cells of the mucous tract; (2) nucleo-albumin or phosphoglobulin; (3) nucleo-proteid, from the disintegration respectively of the cell-plasm and nucleus of pus-cells; (4) albumoses, especially deutero-albumoses, and sometimes hetero-albumose; (5) serum albumin and serum globulin. The original method of Wanner, diluting the sputum with an equal volume of 3 per cent. acetic acid; or of Roger and Lévy-Valensi (◎), adding a few drops of acetic acid to a watery solution of sputum, serve to exclude the first three substances, although it is to be noted that, if the acidification is not strong enough, phosphoglobulin will pass through the filter and subsequently coagulate with heat. The albumoses, too, pass through in this method - a fact which renders all tests inaccurate

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(⊗) Ridge and Treadgold: Lancet, August 9, 1913.

(◎) Roger et Lévy-Valensi: Soc. Méd. des Hôp. July 23, 1909; La Presse Médicale, April 20, 1910; May 20, 1911.
Roger: Soc. Méd. des Hop., October 15, 1909

except the heat test, and even then the addition of quantities of saturated salt solution to act as electrolyte will bring down the albumoses with heat, and although these may be dissolved out, yet the delicacy of the test, particularly in the presence of small traces of albumin, is impaired.

The method adopted by Lesieur and Privey (⊗), and later by Ridge and Treadgold, of adding to 1 volume of sputum 4 volumes of 0.85 per cent. solution NaCl, shaking, and acidifying slightly to litmus with a few drops of 3 per cent. acetic acid, is more satisfactory as far as the ultimate test is concerned, but in the examination of about thirty cases by this method it was possible still to separate from the filtrate some phospho-globulin and some albumoses, usually deutero-albumoses, and sometimes hetero-albumoses.

In the course of our investigation, tests were made with Witte's peptone with a view to finding the optimum acidification and strength of salt solution necessary to salt out the albumoses. Equal parts of half-saturated salt solution, acidifying with 6 per cent. acetic acid, gave the maximum precipitation in twenty-four hours, although the same result could be obtained by heating the mixture in an incubator at 57° C. for one hour. Too strong a salt solution, however, if added to a thick

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(⊗) Lesieur: "L'Albumino Reaction des Crachats", June, 1911 (Soc.Méd.des Hôp.de Lyon).

Privey: De l'Albumoptysie, Thèse Lyon, 1911.

Lesieur et Privey: Paris Médicale, 1911, vol.XIV.

purulent sputum, renders homogenization and subsequent filtration difficult. It has been found practicable to treat the sputum either by adding equal volume of water, shaking, adding 1 volume of half-saturated salt solution, shaking, and adding 1 volume of 3 per cent. acetic acid, or by adding 2 volumes of half-saturated salt solution directly, shaking thoroughly, and then adding 1 volume of 3 per cent. acetic acid. In the first instance there may be a partial precipitation of the globulins, but in any case too great stress cannot be laid on the globulin content, as a globulin-like body, probably one of the myosin group, has been demonstrated in leucocytes by Halliburton (⊗) and others.

It is extremely difficult to thoroughly separate true albumin from the other albumins, unless by a boiling process, which is, of course, out of the question in this stage of the test. By salting-out methods, however, these other albuminous bodies may be fairly thoroughly removed, and if the filtration is properly carried out a clear filtrate should be obtained. Filtration is most satisfactory with a double ply of moistened Swedish paper. Chardin paper is sometimes useful in a preliminary filtration. It is important to obtain a clear filtrate, and it might be advisable, should the quantity of fluid permit, to take it through a candle-filter. Should the filtrate still contain precipitable albuminous substances, not true albumin, an hour's heating at 57° C. and re-filtration will usually serve to remove them.

(⊗) Halliburton: Journ. of Physiol., 15, 90 (1894).

TESTS FOR ALBUMIN IN SPUTUM.

Boiling. - Any or all of the methods indicated for separating the albumin in solution are satisfactory, provided the ultimate estimations are based on the boiling test; but should acetic acid have been used in any quantity, it is necessary at this stage to add sodium hydrate until the solution is just acid to litmus. This has been insisted on by Bezançon and de Jong, who state that otherwise traces of albumin will be overlooked. Small quantities of albumin, too, require relatively greater quantities of salt solution to insure proper precipitation, and in doubtful cases the solution should be reboiled at intervals over a period of fifteen minutes. Finally, each precipitate must be tested for its insolubility in strong acid.

Nitric Acid Test. - Apart from the fact that strong nitric acid will partly dissociate even true albumins, the ring test does not give such delicate results as boiling, and is, moreover, unsatisfactory from the quantitative point of view. Potassium ferrocyanide precipitates also albumoses and nucleo-albumin, and is in any case not so delicate as the boiling test.

Heavy Metal Precipitation. - Salts such as mercuric chloride precipitate immediately and entirely all the albumin present and the albumoses and nucleo-albumins, if present, although some of the albumoses are soluble in excess. It is extremely delicate, but can be used in sputum examinations only in the absence of all but the

true albumins. Tanret's solution ($HgCl_2$, 1.35 grms.; KI, 3.32 grms.; glacial acetic, 20 c.c.; water, 50 c.c.) gives a method of rapidly estimating the approximate amount of albumin in a solution for subsequent confirmation by boiling. In the presence of quantities of salt solution the whole of the mercury albuminate is not thrown down.

Phosphotungstic Acid is an extremely delicate reagent and has the advantage that in excess of a strong solution the albumoses are soluble. In the form of the Wolff-Junghaus reagent it, too, is useful for rapid approximate estimation.

Biuret Test, although useful sometimes in distinguishing by colour between albumins and albumoses, is only suitable where there is a moderately strong solution of albumin. It is most delicate in peptone examinations. Millon's Reagent, too, is insufficiently delicate. Trial was made of Jacquemet's (⊗) method of investigating the albuminoid content of sputa, which consists in precipitating from the non-acidified filtrate the mucin by ammonium chloride, and, after refiltration, the albumin by boiling with a few drops of acid, and, similarly, the nucleo-albumins by saturated citric acid, and the albumoses by trichloracetic acid. The results were not satisfactory, from the quantitative point of view.

(⊗) Jacquemet: Province Mèdicale, 1912.

METHOD OF QUANTITATIVE ESTIMATION.

Using ordinary test-tubes and graduated pipettes, 1 c.c., 2 c.c., and 9 c.c., dilutions in series of the filtrate can be made with accuracy, and, taking into account the original dilution of the sputum, a fairly accurate estimate can be made of the weakest dilution in which albumin can be detected. A portion of each dilution is kept, and the rest is boiled and then contrasted, in strong light against a black background, with the unboiled portion. In this way minute traces can be detected. Artificial light against a white background serves equally well. In dealing with very weak dilutions of the filtrate, it is advisable to re-estimate the reaction to litmus, and it must also be remembered that the salt content is then very small.

DELICACY OF TEST AND ITS RELATION TO WEIGHED QUANTITIES.

The boiling test, although less delicate then precipitation by heavy metals or phosphotungstic acid, is less open to error. The delicacy of the boiling test may be gathered from the fact that guinea-pig serum and sheep serum from which the globulin fraction had been split by CO_2, showed traces of albumin in a dilution of 1 in 6,000. Human serum also was tested, and showed traces in dilutions of 1 in 9,000 and 1 in 10,000, although in these tests the globulin was not removed with the view to finding how far the albumin reaction in sputum could be influenced by the presence of minute

quantities of blood, say, from the gums. Attempts, too, were made to estimate the weight of these traces. The albumin was precipitated by heat, measured quantities of acid and salt solution being added, and was collected on a dried tared filter-paper. To avoid the fallacy due to included salt in the dried filter-paper, another paper of equal tare was subjected to similar treatment, except that the solution contained no albumin. Both papers were washed and dried at 60° C. for equal periods, and it was found that a dilution of 0.000014 gram of albumin per c.c. will give definite traces on boiling.

Throughout the following series of cases quantitative estimations were made with the boiling test, but in each case as many confirmatory tests were carried out as the quantity of fluid would allow. In doubtful cases the sputum was examined for tubercle bacilli by the sedimentation method of Ellerman and Erlandsen, and the patient was tested where possible by subcutaneous tuberculin.

The following table shows the number of cases giving various definite quantities of albumin in the sputum, excluding those where blood or food was present macroscopically:

T A B L E I.

Dilution showing Albumin.	Nil.	1 in 1 to 1 in 3	1 in 3 to 1 in 5	1 in 5 to 10.	1 in 10 to 20.	1 in 20 to 50.	1 in 50 to 100.	1 in 100 to 200.	1 in 200 to 400.	Total
Cases of active tuberculosis..	1 (?)	4	9	11	11	10	24	13	17	100
Cases of arrested tuberculosis..	---	1	-	2	1	2	-	-	-	6
Cases <u>non</u>-tubercular..	1	1	1	3	3	2	3	-	-	14
Examinations of mouth contents	4	3	3	4	2	2	-	-	-	18

Regarding these results from the qualitative point of view, albumin found only in dilutions up to 1 in 5 would be considered a mere trace. The results of examination of mouth-contents of healthy individuals are interesting. Some specimens were simply normal saliva, others contained possibly some pharyngeal secretion, and others were taken after thoroughly brushing the teeth or shortly after a meal. In all except the purely salivary specimens traces of albumin were demonstrated. Kuhne (x), as far back as 1866, noted the presence in saliva from albuminous glands of a globulin-like body, alkali-albuminate, and a small amount of serum-albumin.

Table II shows the average amount of albumin found in different groups of cases. All the examinations made are included in this table, except those of the contents or normal mouths.

TABLE II.

Number of Exams.	Class of Case.	Albumin Content.	
		Average Quantity.	Range.
100	T.B.+ on ordinary examination	1 in 121	trace to 1 in 400
19	T.B.+ by sedimentation only	1 " 64	" " 1 in 300
18	T.B.- but focal reaction to tuberculin	1 in 20	nil " 1 in 100
34	Completely negative to tuberculin	1 " 28	" " 1 in 100
10	Arrested but still with sputum	1 " 14	1 in 5 " 1 in 30
6	Blood present macroscopically	1 in 408	1 in 50 to 1 in 1,000
5	Food present macroscopically	1 " 33	1 " 10 " 1 in 80

(x) Kühne: Lehrbuch d. Physiol., 1866.

This table has some bearing on the significance of the albumin-reaction, because, taking the average amount of albumin present in cases under suspicion, but proved to be non-tubercular, as 1 in 28, there were to be found amongst actively tubercular cases 39 giving a smaller quantity. This would seem to point that the significance of albumin in the sputum does not rest wholly on the tuberculous nature of the case.

With a view to clearing up this point, a table was made of the average amount of albumin in groups of sputa differing widely in their constitution. The character of the sputum having been noted in each case, it was found that these sputa could be divided into four classes: (i) consisting entirely of muco-pus; (ii) consisting almost entirely of muco-pus, but with an admixture of mucus and saliva; (iii) consisting of muco-pus, mucus and saliva intermingled in almost equal quantities; (iv) consisting of mucus and saliva only.

The following are the results:

TABLE III.

Sputum	Class I.	Class II.	Class III.	Class IV.
T. B. + ...	1 in 221	1 in 114	1 in 40	1 in 13
T. B. - ...	1 in 100 (1 case)	1 " 61	1 " 29	1 " 8

This would seem to show that the amount of albumin in sputum could almost be judged by a superficial examination of the constituents of the sputum, the character of the sputum being taken as an indication of damage to the

epithelial surfaces in the respiratory or buccal tract. It also shows that the tubercular case having a greater damage to his epithelial surfaces, has on the average a larger quantity of albumin in his sputum.

In considering the significance of the above results, it must be remembered that in this Sanatorium the differential diagnosis of pulmonary tubercle and chronic bronchitis does not often arise. In only three or four of these cases was chronic bronchitis an important element of the diagnosis. Moreover, during the last year in this Sanatorium there were at least seventy cases admitted in which the diagnosis was doubtful, and of these seventy thirty-eight had no sputum at all - i.e., in 54 per cent of the cases the test was inapplicable.

CONCLUSIONS.

1. That the sputum of phthisical patients contains, on the average, a larger amount of albumin than that of the non-tuberculous, but that the amount present in T.B. cases is often less than that usually found in the non-tuberculous. 2. That injury to the epithelial surface of any part of the respiratory or buccal tract may give rise to the presence of albumin in the sputum. It may be remarked, in conclusion, that a sputum test, the delicacy of which may be impaired by the vigorous brushing of teeth prior to expectoration, does not give promise of conclusive results or material assistance in the diagnosis of doubtful cases of pulmonary tubercle.

S E C T I O N VI.

BLOOD CELL CHANGES. THE ARNETH COUNT.

Originally the method of blood-examination known as the 'Arneth count' was looked upon as a criterion either for estimating the prognosis in any case of pulmonary tubercle or for the estimation of the results of Tuberculin inoculations.

Recently, however, claims have been made on behalf of this method that it is of the greatest value in early diagnosis: Holroyd (⊗) for instance is strongly in favour of its use as a diagnostic measure and Cooke (◎) considers that it is of considerable value in clearing up the diagnosis in doubtful cases.

Statements such as these make it necessary to refer to the subject in some detail.

In his original work Arneth (⊕) drew attention to the importance of careful blood-counts during a course of tuberculin, and in particular of the nuclear differentiation in neutrophile polymorphonuclear leucocytes: these he divided into five classes according to their nuclear divisions. As difficulty frequently arose on the point of what constitutes a bona-fide nuclear division he laid down the rule that if there is any band of nuclear tissue except a thin chromatin filament connecting the different parts of a nucleus, the nucleus cannot be said to be divided.

(⊗) Holroyd: Brit. Med. Journ. 1913. ii 927.

(◎) Cooke: Brit Journ of Tub. Oct. 1914.

(⊕) Arneth: Munch. Med. Woch. 1905 lii 542.

Proceeding on these lines he found that neutrophile polymorphs show five distinct conditions of division, namely those with one undivided nucleus and those with two, three, four and five divisions: a certain number of cells could not be distinctly differentiated and these were discarded as doubtful.

Arneth found in healthy people, fifteen normals being averaged , the following count.

Cells of Class I.	Cells of Class II.	Cells of Class III	Cells of Class IV.	Cells of Class V.
5%	35%	41%	17%	2%

In cases of tuberculosis he found a marked increase in percentage of cells of Classes I and II: for instance,

Class I.	Class II.	Class III.	Class IV.	Class V.
46%	49%	5%	0	0

in a fatal case of phthisis: in a number of cases improving with a course of tuberculin, he noted that the swing to the left became less marked and that the count gradually returned to normal.

The increase to the left is supposed to be an indication of the amount of toxaemia.

The writer's experience of the test has not been extensive but such as it is has not led him to lay any great stress on a positive count in the diagnosis of doubtful cases. As regards technique there are some possible sources of fallacy.

It must be remembered that a number of 'doubtful'

cells are found in practically every examination, cells whose nuclear divisions are so heaped together as to make accurate differentiation impossible, and it will be obvious that depending on the percentage of these cells, is the relative percentage of cells in Class I. and Class V.

In the writer's series of cases, this percentage of doubtful cells varied a good deal from 4% to as many as 22%.

Moreover by artificial means the number of doubtfuls can be decreased and by the same means the number of cells in Classes III and IV and V. increased.

As is well known if blood films are made by rolling out the drop of blood between two cover-slips, great variations can be made in the amount of pressure, with the result that most of the white cells can be with sufficient pressure greatly flattened and even ruptured; and this would obviously tend to disintegrate 'doubtfuls' and artificially increase the number of cell divisions where the connecting filaments of chromatin were very slender.

A good example of a 'faked' count is the following taken from a control. An ordinary film gave the following count

Class I.	Class II.	Class III.	Class IV.	Class V.
15%	40%	41%	4%	0

Percentage of 'doubtfuls' to all cells 13%.

A cover-slip film of the same case made with unnecessarily great pressure was as follows:

Class I.	Class II.	Class III.	Class IV.	Class V.
16%	37%	36%	6%	5%

Percentage of 'doubtfuls' to all cells 6%.

It is necessary therefore to standardise as far as possible the film technique and this is best done by using Wright's opsonic 'spreader', which has the additional advantage of collecting the white corpuscles at one end of the film: also in each case a note should be made of the percentage of 'doubtful' cells to all cells counted. In the next place the number of neutrophile cells counted should be at least 400, and finally suspected cases should always be done in batches the unstained films being re-marked by an outsider.

In this way alone i.e. counting unknown slides, can unconscious bias in counting be avoided.

As regards the results obtained in straightforward cases of tuberculosis, the writer's experience agrees very strongly with that of other observers.

He has in every case noted a more or less marked swing to the left i.e. increase in the cells of Classes I and II., but he has not been able to confirm the very definite increase of the swing in proportion to the severity of the case as noted by Cooke, at any rate in the earlier and middle stages. In the following table the percentage of 'doubtfuls' noted is always calculated on the total cells counted, and the groups are in accordance

with the Turban-Gerhardt classification.

Table Showing Nuclear Counts in different stages of Phthisis.

	Class I. %	Class II. %	Class III. %	Class IV. %	Class V. %	Doubtfuls %
GROUP I. Lowest	29	38	27	5	1	5
	24	54	19	3	-	5
	46	42	12	-	-	15
Highest	32	56	12	-	-	6
Average (20 cases)	34	48	16	2	-	8
	20	44	28	6	2	19
Lowest	16	53	28	3	-	15
GROUP II.	48	40	12	-	-	3
Highest	34	40	26	-	-	10
Average (19 cases)	29	46	22	2.5	.5	9
	36	33	28	3	-	7
Lowest	40	34	26	-	-	8
GROUP III.	58	33	9	-	-	13
Highest	43	47	8	2	-	9
Average (18 cases)	47	38	11	1	-	10
Average all cases	37	44	17	1.8	.2	9

It will be seen that the swing to the left is more marked in advanced cases, but that there is little

difference between the count in an early case and in a moderately advanced one.

When it comes to the diagnosis of doubtful cases by this method the writer's cases have not been satisfactory.

Arneth himself did not claim specificity for the test, which he found positive in cases of pneumonia, measles and chicken-pox: Cooke also does not claim specificity, and even the cases he quotes in favour of the diagnostic value of the test are not beyond criticism.

In one of his two cases reported, the patient had no signs of tuberculosis except a very slight impairment of percussion note over an area about the size of a penny in the right base. His count was as follows:

Class I.	Class II.	Class III.	Class IV.	Class V.
33%	34%	29%	4%	0

and he states: 'a radiograph fully confirmed the diagnosis of active tuberculosis.'

In the following table are set out the counts in seven cases which were sent in as suspected phthisis, were fully tested by tuberculin and serum methods, and found to be negative:

Table showing results in Negative Tested Cases.

Case.	Class I. %	Class II. %	Class III. %	Class IV. %	Class V. %	Doubtful %
1	20	62	16	2	-	8
2	27	57	15	3	-	12
3	15	43	32	9	1	11
4	21	48	27	3	-	15
5	23	52	21	4	-	5
6	24	43	26	7	-	6
7	30	52	18	-	-	9
Average	23	50	22.8	4	.2	9

The important fact in this table is that, although the cases were negative the average does not differ materially from that of positive cases in the first and second stages.

The last table shows the counts in six normal controls: these counts are the average of a series of four counts made in each case.

Table showing counts in non-tubercular Individuals.

Case	Class I. %	Class II. %	Class III. %	Class IV. %	Class V. %	Doubtful %
1	35	46	19	2	-	12
2	20	56	19	5	-	8
3	24	47	28	1	-	22
4	9	41	41	8	1	15
5	11	39	40	10	-	4
6	16	44	31	9	-	11
Average	20	47	27	5.8	.2	12

Here again there is no substantial difference between the average count and those in the early stages of the disease, although it is but fair to add that the films were taken from a hospital population which although non-tubercular may not have been in the best of general health.

The question of the normal count indeed needs further investigation.

Finally there is one very definite criticism of the validity of the test in early diagnosis.

Arneth himself stated that the real value of the test lay in establishing a criterion of the result of tuberculin inoculations when if the case improved, the abnormal count gradually returned to normal, and most observers claim that improvement from any treatment leads

to the establishment of a more normal count.

When one remembers then that many doubtful cases which come up for diagnosis are either on the high road to recovery or actually spontaneously healed, it follows that it many cases a fairly normal count does not indicate a non-tuberculous condition.

The diagnostician cannot eat his cake and have it: a test of value in prognosis cannot a priori be of great value in diagnosis.

CONCLUSIONS: That the Arneth count although very strikingly positive⊗ in the general run of cases of phthisis is not in the first place a specific test and in the next has not the 'negative' value which would give it a large sphere of usefulness in diagnostic methods.

⊗ positive, that is, in comparison with Arneth's 'normal'.

S E C T I O N VII.

URINARY EXAMINATION.

A. ACIDITY REACTION (MALMEJAC)

B. MORIZ-WEISZ REACTION.

It does not seem reasonable to expect that chemical investigation of the urine will afford an accurate and ready means of diagnosing pulmonary tuberculosis in its earliest stages; to put it another way, even if an accurate and early diagnosis of tubercle could be made by chemical examination of the urine, it is not unreasonable to expect that a more accurate and earlier diagnosis could be made by examination - not necessarily chemical - of the blood.

As a matter of fact most of the 'urine reactions' which have been boomed as a means to this end have come to nothing, but there are two methods of examination which have attracted more attention lately, viz., Malmejac's Acidity Reaction and the Moris-Weisz Reaction.

A brief description of these two methods of examination is given below, along with a rough valuation of their probable usefulness.

I. Persistence of Urinary Acidity.

Malmejac (x) states that it is possible to make a diagnosis of pulmonary tuberculosis even in its earliest stages, by simply estimating the total acidity of the urine and the number of days this acidity lasts. According to this author the urinary acidity is much higher in cases of tuberculosis than it is in normal individuals, and in addition it persists for a longer time. For normal urines the time given is on the average 7 days: for pulmonary tuberculosis,

Stage I	(Turban-Gerhardt)	17 days.
Stage II		26 days.
Stage III		40 days.

Technique: 10 cc. of urine are diluted with 50 cc. of

(x) Malmejac: La Presse Medicale, 1909, No. 76.

neutral distilled water; 3 drops of a 1% solution of Phenolphthaleine are added and titration carried out with a decinormal sodium hydrate solution, the results being expressed as grammes of sulphuric acid per litre. A 24-hour specimen of the urine is collected in each case and kept in a sterile bottle.

The following table shows the results in 15 cases of pulmonary tuberculosis, one of renal tuberculosis and a few controls.

Table showing persistence of Urinary Acidity

Case	Acidity in Grammes of H SO per litre	Duration of Acidity in Days	Degree of Disease
1.	1.2985	24	Group I (Turban-
2.	2.989	49	" I Gerhardt)
3.	2.940	49	" I
4.	1.225	10	" I
5.	2.597	48	" I
6.	2.107	24	" II
7.	3.087	24	" II
8.	2.401	10	" II
9.	2.205	30	" II
10.	1.813	28	" III
11.	2.352	17	" III
12.	2.5357	43	" III
13.	2.352	19	" III
14.	3.038	63	" III
15.	2.205	42	" III
16.	2.2417	26	Renal
17.	1.274	6	— Control
18	.539	12	— "
19.	2.940	66	— "
20.	1.911	46	— "

It will be seen that the results do not correspond with those of Malmejac, as there is practically no difference between the various groups as regards total acidity or length of time during which this persists. The controls, too, vary just as much as the patients.

Table showing average acidity in each Group

Group	Cases	Acidity in Grams. of H_2SO_4 per litre.	Duration of Acidity in days.
I	5	2.2099	38
II	4	2.45	22
III	6	2.3492	33
Renal	1	2.2417	26
Normal	4	1.666	32

These cases may not be comparable, inasmuch as they were examined at different times and it may be that the temperature at which the specimens are kept has a definite influence on the onset of ammoniacal fermentation.

The results seemed entirely disappointing and the investigation was discontinued.

II. Moris-Weisz Reaction.

The original reaction of Weisz consisted in the addition of three drops of 1 in 1000 potassium permanganate solution to fresh urine diluted with two volumes of tap-water when, in phthisical cases a yellow coloration appeared due to the oxidation of urochromogen into urochrome.

The latest modification of this method is that of Martelli and Pizzetti (x) who dilute the urine with 3 volumes of tap-water, take one third of a test tube full of the diluted fluid and add five drops of fresh 1 - 1000 permanganate. If no result is obtained, they repeat the test with less diluted urine until equal parts of urine and water are tested. In all cases diluted urines untested are put up as colour controls. The yellow coloration in positive cases should last 24 hours.

(x) Martelli and Pizetti: Il Polyclinico: Rome, 1914, xxi, 182 (quoted)

This is one of those reactions which are the despair of any investigator with leanings towards accurate quantitative estimations.

In the writer's experience of 83 cases, a really satisfactory reaction was obtained in only two instances: in the others a positive reaction where present was of such a faint character that quantitative estimations on a colorimetric plan were out of the question.

With the exception of the two cases referred to, the positive reactions were obtained only with an equal parts dilution of urine and distilled water.

In constructing the following table, the benefit of the doubt was invariably given to the positive side of the reaction and the faintest shades of colour were held to be positive; in spite of this the results were very unsatisfactory.

Table showing results in Different Stages.

Group (Turban Gerhardt)	Positive	Doubtful	Negative
I	8	10	20
II	5	6	7
III	5	-	1
Negative Cases	2	5	14

These results, which conform roughly with those of other observers, show conclusively that no diagnostic aid can be afforded by the reaction, and that even from the point of view of prognosis, a positive reaction, unless perhaps extremely well marked, is of small significance.

S E C T I O N VIII.

RADIOGRAPHIC EXAMINATION.

Röntgen ray diagnosis in pulmonary tuberculosis is practically closed territory to all except the expert and the writer has no intention of trespassing thereon, but the claims of radiologists to accurate diagnosis by this means have recently become so pressing that no review of diagnostic methods which passes them over can be considered in any way complete.

A review of the recent literature on the subject discloses that whilst all experts agree as to the value of X-ray examination in diagnosis, there is much difference of opinion both as to the mode of examination and as to the interpretation of the various appearances noted.

There is, for instance, the controversy as to the importance of the radiographic negative, which throws light on the condition of the hilus, of the lymphatic and peribronchial tissue and of the peripheral substance of the lung, compared with that of the screen examination which affords information as to inspiratory brightening of the apices and diaphragmatic movements.

At the International Congress of Medicine, 1913, Wenkebach and Walsham stated that both screen and plate are necessary in order to get the full value of this method of examination, Köhler, Finzi and Haemisch advised against the screen, Lebard favoured the use of the screen, whilst Owen considered the plate the more satisfactory of the two.

Elsewhere Lees (x) states that no sound conclusion

(x) Lees: Brit. Med. Journ. Sept., 1914.

can be based on a screen examination without the aid of a photograph. Even as to the interpretation of the various results of examination there seems to be no definite conclusion except on one or two points.

It appears to be agreed that failure of apical brightening may depend on causes other than phthisis, also that lagging diaphragmatic movement (Williams' sign) is frequently absent in cases of early phthisis.

In the case of the radiographic negative there is general agreement that, in the adult at any rate, signs of hilus disease and peribronchial infiltration do not necessarily indicate activity, but that on the other hand certain woolly shadows and mottled spaces in the substance of the lung do indicate an active process.

As far as diagnosis is concerned, this latter statement is the crux of the matter, because the existence of old lesions, more or less extensive, in the apparently healthy is definitely agreed upon, and the only question one wishes to ask of the radiographer is whether or not he can diagnose activity in either an old extensive lesion or a fresh minute focus.

It is unfortunate that all radiographers should be agreed on the many sources of fallacy of the 'woolly outline', fallacies of focus, of photographic development, of perspective and of many technical details in the manipulation of the apparatus.

Putting these sources of fallacy aside there are still conflicting statements of experts as to the interpretation of 'mottling.'

Lees, (⊗) on the one hand, says that fine mottling is "all-important" in the diagnosis of active tuberculosis, whilst Overend (⊕) states that "in itself mottling is a sign of phthisis but not of activity."

Again, there is one obvious defect in the X-ray examination, that only a very definite degree of infiltration or, one might say, of concentration will give rise to a shadow.

The work of Ziegler and Krause (◎) showed a piece of tissue must have a bulk of at least 4 c.c.m. before being visible, and Lees, (⊗) discussing the subject, says: "careful percussion will detect the small areas of incipient pulmonary tuberculosis when even the best X-ray photograph shows little or nothing definite."

As opposed to this we have Morton's (⊛) statement that in many cases the X-ray gives a positive and in others a tentative diagnosis of tuberculosis where clinical signs are so slight as to make a positive diagnosis out of the question.

Kidd (◍) notes this ground of disagreement and concludes that it is still a matter of dispute whether skiagrams or screen observations give as early indications as the older methods of physical examination.

But if there is any difference of opinion as to the right to "diagnosis of activity" where the physical signs are very slight, this difference becomes

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(⊗) Lees: Brit, Med. Journ. Sept. 1914.
(⊕) Overend: Brit. Med. Journ. Dec. 1914.
(◎) Ziegler and Krause: 'Rontgenatlas' Wurzburg, 1910.
(⊗) Lees: Brit. Med. Journ. Sept. 1914.
(⊛) Morton: Brit. Med. Journ. July, 1913.
(◍) Kidd: Allbutt's System of Medicine.

more acute with cases where the physical signs are fairly extensive.

Haemisch (⊗) has referred to the difficulty in distinguishing tumours of the lungs and tubercle from one another, and Owen (⊕) says, as regards the distinction of active from obsolete tubercle: "It is very difficult to gauge the activity of the lesion from a study of the radiogram alone or to distinguish the fibrosis of tubercle from that due to other causes."

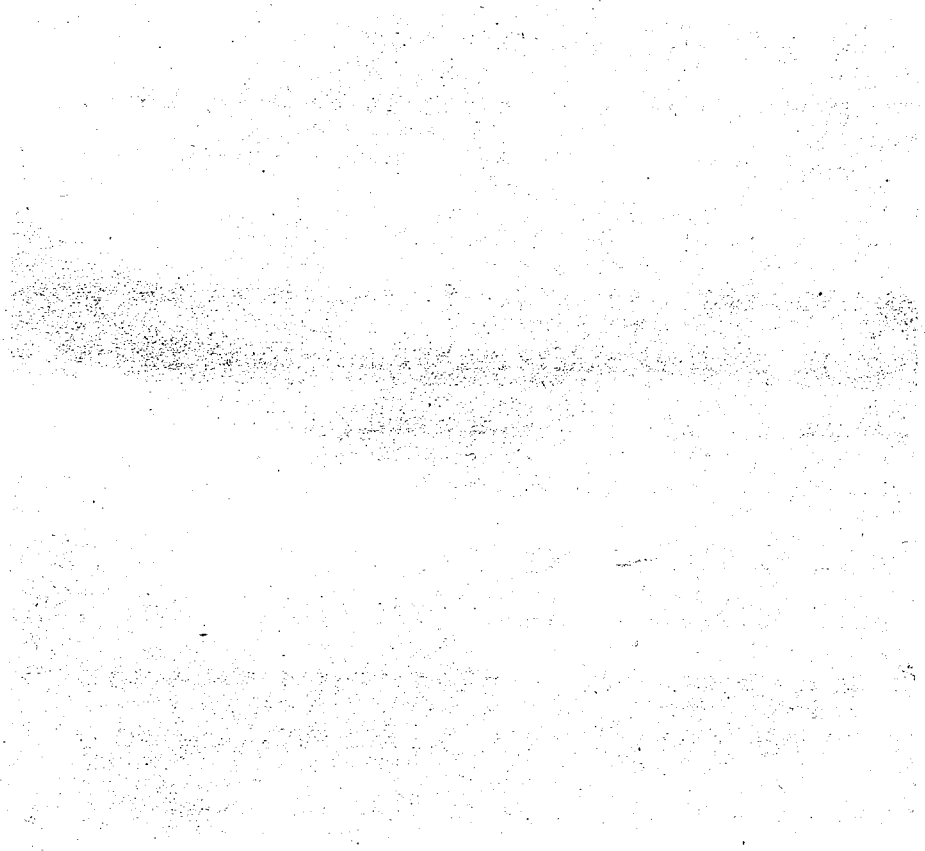
Moreover, it was pointed out by Jordan (◎) that X-ray examination may show fibroid and calcareous changes in roots of lungs passed as healthy in the Post-mortem room.

This question of diagnosing recrudescence of activity in an old infiltration - a very common occurrence in pulmonary tubercle - is of great importance and it does not seem probable that the plate or screen could be of much assistance in cases where an extensive adherent infiltration of an upper lobe came in question as to a possible break down in the centre of its mass.

It may be agreed that limitation of movement, apical brightening, bronchial glands shadows, lymphatic, arterial or peribronchial striations, all point to the existence of phthisis at some time or other, but it can still be argued that they so not necessarily indicate immediate activity: indeed, they may be the cause of many misjudgments, simply because indications of old disease, if extensive enough, are apt to bias succeeding observers.

(⊗) Haemisch: Proc. Int. Med. Cong. 1913.
(⊕) Owen: Proc. Int. Med. Cong. 1913.
(◎) Jordan: Practitioner, 1912: 248.

The matter is summed up by Lindsay (x) as follows: - "Unfortunately the sources of fallacy are numerous; the skiagram does not help us to differentiate between old healed lesions and recent active lesions."



(x) Lindsay: Brit, Med. Journ. Dec. 1914, 957.

S E C T I O N IX.

SERUM METHODS.

A. OPSONIC INDEX.

B. COMPLEMENT FIXATION.

Before considering in detail the most modern method of diagnosis of early pulmonary tuberculosis, to wit, serological examination, it will be well to review in a few sentences the findings suggested by the previous sections. In the view of the writer each method of examination detailed must be subjected to this test: Does it enable one to distinguish between active and inactive disease?

That is not to say that the method must stand or fall at the bar of this criterion, because in most of the cases referred to, the examination must be made as a matter of routine.

History and symptomatology fall into this category and need no further consideration: refined methods of clinical examination whilst absolutely essential as a routine, do not of this necessity remove us from the quandary: a negative sputum examination has unfortunately not the deciding value of a positive bacillary find and even to grant the greatest diagnostic significance to albumin reactions and cytological examinations would not help in cases where sputum is absent: urine reactions and blood cell reactions have something of the vagueness which surrounds metabolic processes: radiographic examination, valuable as it is, cannot have the final say in the matter of activity. We are left, therefore, with the specific tuberculin test, which is, in a large percentage of cases, a test of the greatest value and finality.

Even then we find a large minority of unsettled cases, which fact taken in conjunction with the admitted discomforts of the test - if only to the patient - serves to detract somewhat from its universal applicability.

There remain for consideration then two distinct lines of investigation, viz. by the opsonic index technique and by that of complement fixation.

The writer was fortunate in being able to work in the Laboratory at Midhurst at a time when the technique of complement fixation had just recently been brought to a high degree of accuracy, and when it had been decided to make detailed trial of its value, in conjunction with the opsonic index method in diagnosis.

The trial was arranged in the following lines:—

Doubtful cases were carefully recorded as regards history and clinical signs; the sputum, if any, was examined as often as possible by the sedimentation method of Ellerman and Erlandsen; if negative the opsonic index was estimated, and finally the patient was given subcutaneous doses of tuberculin on Baudelier's scale (.002.cc A.F.001: .005: .01 cc) The results were then compared with those of the complement fixation test which had been frequently observed prior to the diagnostic injections. As far as possible the one observer was kept in ignorance of the other's result.

For instance in the following 47 cases noted, the clinical examination was made, the tests carried out and the opsonic index estimated by the writer, whilst

Dr Radcliffe carried out the sedimentation and complement fixation tests.

The sedimentation examination of the sputum has already been referred to, but it may be added that each sputum was tested frequently by the ordinary method, and by the sedimentation method when possible before and immediately after test injections.

The opsonic index technique followed by the writer was that of Wright (X), and every attempt was made to minimise the margin of error either in actual technical details or in counting methods.

The pipettes, for instance, were standardized as to bore on a fine wire gauge, and the slides were re-numbered before staining by some other member of the staff.

Samples were taken from the case under investigation, before exercise and one, six and twenty-four hours afterwards. The exercise given was as heavy as the patient's interest would allow (?) and was combined with deep breathing. [redacted]. Two normal control sera were put up in each batch and unity was taken as the mean of these separately counted controls.

In view of the writer's experience of the addition of débris to the emulsion - that whilst in some cases the exaggeration of the swing was most gratifying, in others the counts were erratic - all the sera were tested,

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(X) Wright. Technique of the Teat and Capillary Pipette.

(?) as a rule one hours 'heavy gardening'

without any additions being made to the emulsion.

It is not proposed to enter into a defence of the accuracy of the opsonic index. That has been very thoroughly considered by Wright in his book, but it may be said that the accuracy of the index depends on the honesty and patience of the observer. He alone can say whether his results are of the slightest value, and the only satisfactory course to follow where the technique has been at all 'ragged' is to commence the estimation of a fresh index.

After a long series of experiments with known cases and known controls, the writer estimated his margin of error and established as his own standard that an index giving a swing of .27 or over was definite evidence of active disease.

A consistently low or consistently high index, requiring a more severe standard, he set for himself as .7 below and 1.3 above.

It is impossible here to describe in detail the technique of complement fixation as carried out in these cases by Dr. Radcliffe. A short reference to it is nevertheless necessary on account of the variations in the character of the antigen used by different observers and also on account of such statements as were made so late in the day as Dec. 1914 by Lindsay (x), that 'complement' fixation is still in the experimental stage' and that

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(x) Lindsay. Brit. Med. Journ. Dec. 5. 1914.

'it would be premature to express any opinion upon its probable usefulness'.

It is admitted that until recently the results of investigation by this method have been very unsatisfactory, the best giving positive findings in roughly 50% of definitely positive cases. The results in bovine cases were just as unsatisfactory, except those of Hammer (⊗) which have not been confirmed. With the employment of new antigens however the results became more promising. Besredka (◎) using an antigen grown in special egg-bouillon obtains about 90% of positive findings in definite cases of tubercle, although the value of these observations is greatly impaired by the fact that syphilitic cases would also give positive results. Genaux claims to have got over this by extracting the fatty bodies from the antigen. Calmette and Massol (≡) using as antigen a concentrated extract of washed tubercle bacilli with 1% Witte peptone, claim to have obtained 92.5% of positive results. Radcliffe, using as antigen a freshly prepared unsterilized emulsion in salt solution (.85%) of living tubercle bacilli grown on glycerine-egg medium (the strength of the emulsion being 1:500) obtains a positive finding in 88.6% of positive cases.

(⊗) Hammer: Deutch. tierärzt. Woch., Bo.39, 1912.

(◎) Besredka. Annal de l'Inst. Pasteur: Nov.1913.No.1009. Comptes rend. de la Soc. de Biol., Feb.6th 1914. No 180 and Feb 13th 1914, No.197

(≡) Calmette et Massol. Annal. de l'Inst. Pasteur April 1914. No. 338.

Here is one of his latest (unpublished) returns:

No. of cases.	Group (T.G.)	Complement Fixation.			
		+			-
96	I	87	=	90.6%	9
281	II	256	=	91.1%	25
118	III	96		81.3%	22
495		439		88.6%	56

MacIntosh and Fildes (x) using practically the same antigen get 76.7% positive cases in 43 cases of phthisis: 80.7% positive in 26 cases of surgical tuberculosis with the exception of tuberculous glands, where 37.5% only out of 16 cases.

In addition Radcliffe has examined the serum of 52 healthy persons on 187 occasions with invariably a negative result: MacIntosh and Fildes have examined 87 controls from healthy and diseased (non-tuberculous) individuals, all being negative except 3 (2 cases of leprosy and 1 of Addison's disease).

So far then as specificity is concerned the figures of MacIntosh Fildes and Radcliffe, even neglecting those of Besredka or of Inman who used Besredka's antigen, are of themselves satisfactory evidence. But it is quite a legitimate point to raise, whether or not complete 'fixation' is definite evidence of an active process, as compared say with an arrested lesion.

MacIntosh and Fildes answer this very definitely in the affirmative, and on that grounds that since fixation

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(x) MacIntosh and Fildes. Lancet. Aug. 22. 1914.

does not occur in the case of the average person who gives a positive cutaneous reaction to tuberculin and since even in undoubted cases of tubercular glands the percentage of 'fixations' is small, it is fair to claim that complete fixation in a suspected case of pulmonary disease, means active disease.

Radcliffe's opinion, however, is not so definite. He is inclined to think that where the history and symptomatology are recent a positive result means active disease, but that where there has been an old history of substantial impairment of the lung, it is possible to find fixation for some time after, even when the condition and symptoms do not point to a progressive lesion. Whether again this latter condition is due to the fact that the lesion although seemingly healed is only quiescent, although a probable contingency is not in his opinion sufficiently definite for any final statement. So far there are no figures obtainable on the point, nor can there be until the reaction has been as fully exploited as was the Wasserman Reaction on the population of general hospitals.

At the same time an investigation such as the present one of the relations of 'fixation' to the opsonic index and of both to the results of test injections might throw some light on the following points:

(i) Is the complement fixation reaction alone proof of active disease: if not

(ii) Is the fixation reaction, along with the

opsonic index sufficient proof of this or

(iii) must in any case test injections be given: finally

(iv) What indication do all three tests together give of the amount of activity to be deduced from the presence of lesions detected by the various methods of clinical examination?

As an answer to the first two points can be obtained simply from a short summary of his results, the writer has arranged the details of his cases in a form which will give some information as to the last two. He has divided them in four sections as follow:

(i) cases giving no focal reaction and no general reaction (or practically none) to test injections.

(ii) cases giving no focal reaction but a marked general reaction to test injections.

(iii) cases giving a focal reaction to test injections.

(iv) cases which for various reasons were not tested.

TABLE I: Cases giving no Focal Reaction.

No.		T. B.	Focal Reaction.	Opsonic Index	Complement Fixation.
1.	Family history neg: vague general ill-health: no definite clinical signs in the chest: no sputum. Final test dose .01 cc. A F: slight local reaction: no sputum. Opsonic Index: 1.17 - 1 - 1.1 - .99.	0	-	-	-
2.	Family history neg.: run down after influenza: cough developed: no sputum: impaired note. Rt. apex: increased V.R.: no adventitious sounds. Final test dose: .01 cc. A F.: slight local reaction: no sputum. Opsonic Index.: 1.04 - .97 - 1 - 1.12.	0	-	-	-
3.	Family history neg.: pleurisy 5 months before: 2 pints of effusion tapped (? pneumococcal); deficient movement Rt. side. B.S. generally diminished. P.N. dull: increased V.R. generally: no adventitious sounds: sputum neg. by 3 ordinary exams: E and E (-): Final test dose .01 cc A F.: local reaction slight: very slight general reaction: sputum E and E (-). Opsonic Index: .91 - 1 - .97 - 1.06	-	-	-	-

No.		T.B.	F.R.	O.I.	C.F.
4	Family history neg: progressive ill-health associated with gastric disturbances: history of slight cough: no definite clinical signs in lungs: well marked presystolic murmur at mitral area: no sputum. Final test dose .01 cc A F. no reaction at all: no sputum. Opsonic Index: 1.23 - 1.11 - 1.06 - 1.23	0	-	-	-
5.	History of contact: some low fever: sent in on suspicion, no clinical signs in chest: no sputum. Final test dose .01 cc A F: no reaction of any kind: no sputum. Opsonic Index: 1.09 - .98 — .99 - .97	0	-	-	-
6.	Family history neg: history of pleurisy 3 mths before: sputum at that time neg: P.N. dull lower half of Rt. lung: loss of movement: B.S. diminished: no adventitious sounds: sputum neg. by 2 ordinary exams: E & E - : Final test dose .01 cc A F: no reaction of any kind: no sputum: Opsonic Index: .81 - .87 - .8 - .94	-	-	-	-
7.	Family history doubtful: general ill-health for 6 months: chronic cough and sputum: persistent low fever: V.R. increased at Rt apex. no adventitious sounds: sputum E & E (-). Final test dose .01 cc A F: no reaction of any kind. No sputum. Opsonic Index: 1.07 - 1. 11 - 1.06 - 1.	-	-	-	-

No.		T.B.	F.R.	O.I.	C.F.
8.	Family history neg: general ill-health: some chronic cough. No sputum: P.N. impaired Rt. apex: B.S. harsh to 2nd rib: V.R. +: no adventitious sounds: no sputum. Final test dose: .005 cc A F: no local reaction: no sputum. Opsonic Index: 1 - 1.03 - 1.2 - 1.12.	0	-	-	-
9.	Family history negative: some cough and sputum after a bad cold. P.N. impaired Rt. apex: B.S. bronchial: no adventitious sounds: sputum neg. to ordinary exam.: E. & E. (-) Final test dose: .00 5 cc. A F: some local reaction: sputum E. & E. (-). Opsonic Index: .98 - 1.03 - .98 - .98.	-	-	-	-
10.	Family history negative: some cough and spit general ill-health for some months: no definite physical signs. Sputum neg. to 4 ordinary exams E. & E. (-) Final test dose: .005 cc A F: some local reaction: E. & E. (-) Opsonic Index: .9 - .95 - .9 - 98.	-	-	-	-

TABLE II: Cases giving a General Reaction.

No.		T.B.	F.R.	O.I.	C.F.
11.	Family history positive: 3 months before admission brought up some blood. Slight persistent cough and sputum. P.N. impaired Rt. apex: B.S. harsh: no adventitious sounds sputum negative to 4 ordinary exams. E. & E. (-) Final test dose .01 cc A F. Temp. 101° F: malaise: L.R. +. no sputum. Opsonic Index: 1.02 - 1 - 1.05 - 1.09.	-	-	-	-
12.	Family history negative: 6 mos. before admission gradually developed cough and spit: 4 mos. before brought up some blood: sputum examined then and T.B. said to be found: some retraction and limitation of movement of Rt. side: P.N. dull at Rt. apex: B.S. weak: V.R. & V.F. increased: (?) occasional click: some bronchophony: B.S. faint left side. Sputum negative to 2 ordinary exams: E & E (-). Final test dose .01 cc A F: temp 101° F: malaise: L.R + sputum E & E (-). Opsonic Index: 1.05 - 1.16 - 1.06 - 1.14.	-	-	-	-

No.		T.B.	F. R.	O.I.	C.F
13.	Family history positive: contact positive: history of chronic cough over 8 years: occasional traces of sputum said to be T B - : associated chronic gastric trouble: no definite physical signs in chest: no sputum: cyclical menstrual temperature. Final Test dose .01 cc A F: Temp. 102° F: malaise: L.R.+ no sputum. Opsonic Index: 1.13 - .95 - .96.	0	-	-	-
14.	Family history positive: contact positive: cough and traces of sputum for over a year: T.B. said to be (-): associated anaemia. No definite clinical signs in chest: no sputum. Final test dose: 1.01 cc A F: Temp. 103° F: malaise ++. L.R. ++ no sputum. Opsonic Index: .85 - .94 - .83 - .88	0	-	-	-
15.	Family history positive: always subject to catarrh: six weeks before admission 3/7 haemoptysis and occasional traces of blood in sputum: P.N. impaired at Rt. apex: V.R. increased. No adventitious sounds: sputum negative to 4 ordinary exams. E & E (-). Final test dose .01 cc A F: Temp 100. 8° F. malaise marked L.R: marked: sputum E & E (-) Opsonic Index: .71 - .85 - .72 - .86.	-	-	-	-

No.		T.B.	F R.	O.I.	C.F.
16.	Family history negative: ill-health for 2 yrs. 2 months before admission dry cough for a few days: brought up 3/4 blood: no sputum since: P.N.impaired at Rt.apex: U R & U F increased: no adventitious sounds: no sputum. Final test dose: .005 cc A F: Temp.101° F: no sputum. Opsonic Index: .96 - 1.06 - 1.08 - .98.	0	-	-	-
17.	Family history positive: contact positive: sent for inspection: P.N.dull at Rt.apex: V.R.increased: V.F. (+ +): some broncho-phony: no adventitious sounds: sputum negative to 2 ordinary exams: afterwards none. Final test dose: .005 cc A F (Repeated): Temp. 100.6° F: malaise marked. L.R x x: no sputum. Opsonic Index: 1.05 - 1.1 - 1.13 - 1.06.	-	-	-	-
18.	Family history doubtful:liable to catarrh: slight ill-health for some months;slight cough and sputum for over a year:sputum said to be T B - : P.N.very slightly im-paired at Rt.apex: V.R.& V.F.increased sputum E.& E.(-) Final test dose:.005 cc A F:temp.103° F:malaise marked: L.R.+: some increase in cough:sputum E.& E.(-). Opsonic Index: .94 - .89 - .76 - .89. NOTE:- This index was not satisfactory but there was no opportunity for repetition.	-	-	-	-

No.		T.B.	T.R.	O.I.	C.T.
19.	Family history negative: some haemorrhage a year before: streaking of sputum (T.B. said to be absent): no physical signs in chest: sputum E.& E (-). runs a persistent temperature unaltered by rest or exercise: tested carefully during a remission. Final test dose: .001 cc.A F: Temp 102° F: malaise marked local reaction: no focal reaction. Opsonic Index: .98 - 1.08 - .98 - 1.02.	-	-	-	-
20.	Family history positive: contact positive: some chronic cough for 2 years with occasional sputum (T.B. said to be found 1 year before): P.N. slight impaired at both apices: V.R. & V.F + at both apices: no adventitious sounds: no sputum: Temp. rather irregular. Final test dose: .005 cc.A F: Temp 101.4° F: malaise some cough: local reaction marked: no focal reaction. Opsonic Index: 1 - 1.13 - 1.04 - 1.	0	-	-	-

No.		T.B.	F R.	O.I.	C.F
21.	Family history negative: pleurisy (Rt) 11 years before and again 2 years before: some cough and sputum following last attack (T.B. said to be absent); general signs of thickened pleura over Rt. side: no moist sounds: no sputum. Final test dose: .001 cc.A.F.: Temp.100.4° F: malaise marked: L.R. +++: no focal reaction: same result to a repeat dose: No focal. Opsonic Index: .96 - .92 - .93 - .91.	0	-	-	-
22.	Family history negative: some cough and spit for a few months before: P.N. impaired Rt. apex: B.S. faint to first interspace: no moist sounds: sputum negative to 2 ordinary exams E & E (-). Final test dose: .005 cc.A F: Temp 102° L.R.+: no sputum. Opsonic Index: 1.05 - 1.15 - 1.04 - 1.	-	-	-	-

No.		T.B.	F.R.	O.I.	C.F.
23	Family history negative: always subject to colds: one month before admission some cough and spit: sputum examined (T.B. said to be found) P.N. dull at Rt. apex: B.S. harsh and blowing. V.R. and V.F. ++: some bronchophony: no adventitious sounds: sputum negative by 5 ordinary exams. E.& E.(-): Final test dose: .01 cc A F: Temp 102.8° F: malaise marked: cough and sputum slightly increased: L.R. ++. No focal reaction: Sputum E. & E - . Opsonic Index: 1.07 - 1.24 - .9 - 1.02.	-	-	+	-
24.	Family history negative: some cough and spit over a period of 18 months: some impairment of P.N. at left apex: no added sounds: sputum negative on 3 ordinary exams. E. & E. (-). Final test dose: .01 cc A F.: Temp 100.6° malaise: local reaction +: no focal reaction. Opsonic Index: .74 - 1 - .84 - 1.14.	-	-	+	+

No.		T.B.	F.R.	O.I.	C.F
25.	Family history positive: cough for over a year: no sputum: progressive loss of weight: on admission P.N. impaired to 3rd space: B.S. harsh: crepitations after cough over same area and all over Rt. upper lobe and apex of Rt. lower lobe behind: on left side in front 'creps.' to 3rd space and to level of 3rd spine behind. Patient not tested until 5 months after admission. Final test dose: .01 cc. A F: L.R.+ : G.R. + : Temp 100° F. No focal reaction. Opsonic Index: .9 - .78 - .97 - 1.3.	0	-	+	+

TABLE III: Cases giving a Focal Reaction.

No.		T.B.	F.R.	O.I.	C.F
26.	Family history negative: gradual ill-health: cough and spit for some months before admission: P.N. impaired at Rt. apex: B.S. bronchial: no adventitious sounds: sputum negative to 3 ordinary exams. E. & E. (-): Final test dose: .001 cc A F: Temp 103° F: G.R.+: L.R.+. Focal Reaction at Rt.apex: E. & E. (-). Opsonic Index: 1.12 - .99 - 1.1 - 1.25.	-	+	+	+
27.	Family history positive: history of cough for over 2 years: sputum for 6 months. P.N. dull Rt. apex: B.S. bronchial, some crepitations above clavicle also at apex of Rt. lower lobe behind: sputum negative to 4 ordinary exams' E. & E. (-). Final test dose: .005 cc.A F: Temp.101.8° F. G.R. +: L.R. +: Focal reaction at both apices involved. E. & E. (-). Opsonic Index: 1.41 - 1.35 - 1.3 - 1.45.	-	+	+	+

No.		T.B.	F.R.	O.I.	C.F.
28	Family history negative: cough & spit for some months before admission: P.N. dull Rt. apex to 2nd rib. B.S. bronchial: V.R.+: some scattered clicks to 2nd rib. not increased on cough: sputum neg. in 3 ordinary exam. Final test dose: .01 cc. A F: Temp 102° F: G.R.+: L.R.+. Focal reaction at Rt. apex: sputum (E. & E) T.B.+. Opsonic Index: .81 - .99 - 1.09 - .74.	- +	+	+	+
29.	Family history negative: cough and spit following influenza. P.N. dull at Rt. apex: B.S. harsh to 3rd Rib. no adventitious sounds. Sputum neg. 3 times by ordinary method. (E. & E.) (-) Final test dose: .01 cc. A F: Temp 100.2°F. G.R.+: L.R.+: Focal reaction Rt. apex: sputum E. & E. (-). Opsonic Index: 1.03 - .94 - .84 - 1.13.	-	+	+	+
30.	Family history strongly positive: contact positive: influenza 3 mos, before: cough & sputum since: sputum said to be T.B.+. Deficient movement left side: supraclavicular retraction. B.S. deficient: some fine crepitations to 2nd left rib in front V.R. & V.F. increased. No sputum. Final test dose: .005. cc. A.F: Temp 101° F. malaise slight: cough increased: no sputum: Focal reaction increase and extension of crepitations to 4th rib. Opsonic Index: 1.33 - 1.26 - .92 - .76.	0	+	+	-

No.		T.B.	F.R.	O.I.	C.F.
31.	Family history negative: 2 years before haemoptysis 1/2 pint sputum then said to be T.B. (-): 3 months before admission 1 pint haemoptysis: sputum again said to be negative. P.N. slightly impaired over left apex: some crepitations after cough to 3rd space in front and to 4th spine behind: sputum negative to 2 ordinary exams: thereafter none. Final test dose: .01 cc. A.F. Temp 100.6° F. malaise marked L.R.+ : Focal reaction in left upper lobe (increase in moisture) Opsonic Index: .85 - .98 - .87 - .91.	-	+	-	+
32.	Family history negative: chill 1 month before admission: Haemorrhage 3/IV : traces of sputum: T.B. said to be found. P.N. impaired. Rt. apex. V.R. & V.F. increased: some bronchophony ? adventitious sounds: sputum negative to ordinary exam. thereafter none. Final test Dose: .001.cc. A.F. very marked malaise L.R. +++. increase in cough: no sputum. Focal reaction at Rt.apex (Presence of crepitations) Opsonic Index: .91 - 1.06 - .91 - .95.	-	+	-	+

No.		T.B.	F.R.	O.I.	C.F
33.	Family history negative: pneumonia 1 year before: no cough or sputum on admission: P.N. impaired Rt. apex: V.F. increased: some rhoncus. Query some crepitations at Rt. apex. behind: Query left apex: Final Test dose: .005 cc.A.F.: L.R.-: G.R.-: Temp. normal. Focal Reaction both apices. Opsonic Index: 1. - 1.09 - .9 - 1. (NOTE: Patients temperature after exercise on opsonic test was 99.2° F. which is presumptive evidence of insufficient auto-inoculation).	o	+	-	-

TABLE IV: Cases not tested.

No.		T.B.	O.I.	C.F.
34.	Family history positive: contact positive: Pleurisy Rt. side one year before: dry cough ever since: no sputum. P.N. slightly impaired Rt. apex: B.S. deficient Rt. apex in front and behind: V.R. increased over same area: no adventitious sounds: patient runs a persistent irregular temp. at night up to 100.4° (Rectal) which did not settle after 5 months observation: not tested on that account. Opsonic Index: 1.04 - 1.12 - .93 - 1.07. Provisional diagnosis: Negative. After history 10 months later: still negative: no cough.	-	-	-
35.	Family history negative: chronic ill-health for 2 years: dry cough for 1 year: gastro-intestinal disturbances, constipation etc. for same period. No sputum: no physical signs in chest runs a persistent low fever up to 100° F. (Rectal) did not settle after 6 months' observation: not tested on that account. Opsonic Index: 1 - 1 - .96 - .89. Provisional diagnosis: Negative. After history 9 months later: still negative.	0	-	-

No.		T. B.	O.I.	C.F.
36.	Family history negative: history of (?) pneumonia Rt. side with ? septicaemic symptoms: thought to be (?) miliary tuberculosis ? hysteria: P.N. impaired Rt. apex: no adventitious sounds: sputum (T.B.-) on 3 exams: temperature very irregular, independent of exercise: not tested on that account. Opsonic Index: .91 - 1.03 - 1.02 - .99. Provisional diagnosis: Negative.	-	-	-
37.	Family history negative: pleurisy 4 years ago: 3/1 haemoptysis then: cough and traces of sputum for 2 years: 3/1 haemoptysis 6 mths. before: P.N. impaired Rt. apex: B.S. harsh and blowing: crepitations after cough to 3rd space in front (Rt) and over upper and apex of lower lobe behind: sputum negative to ordinary examination. Patient kept under observation without testing owing to extent of signs: 2 months later sputum exam gave T.B. +. Opsonic Index: .86 - .82 - 1.04 - .73.	+	+	+

No.		T.B.	O.I.	C.F.
38.	Family history positive: contact positive: for some years past cough and spit every morning: 3 months before cough much increased: sputum increased: T.B. said to be found. P.N. dull Rt. apex. B.S.harsh: V.R. and V.F increased: ? some crepitations on cough: sputum negative to 3 ordinary exams: kept under observation without testing: 6 weeks later T.B.+. Opsonic Index: .79 - .71 - .98 - .76.	+	+	+
39.	Family history positive: contact positive: 2 years before Rt-sided pleurisy: cough and occasional spit ever since: T.B. said to have been found 3 months before. P.N. dull Rt. apex: B.S. markedly diminished over Rt. front and behind from apex to base. Some crepitations increased on cough opposite scapular process. No sputum on admission but kept under observation without tests for 2 months when an isolated specimen gave T.B. +. Opsonic Index: 1.11 - 1.29 - 1.01 - 1.	+	+	+

No.		T.B.	O.I.	C.F.
40.	Family history negative: some cough and spit for about 4 months back: T.B. said to be found: marked retraction of Rt. apex: limitation of movement Rt. side: P.N. dull to 3rd rib. B.S. generally diminished over upper lobe in front and behind: no adventitious sounds: sputum negative to 2 ordinary exams: often absent : Kept under observation without tests for 1 month: sputum by E. & E. gave T.B.+. Opsonic Index: 1 - .83 - 1. - 1. 24.	+	+	-
41.	Family history query: Pleurisy (Rt) 8 yrs before: chronic cough and occasional spit ever since: P.N. impaired to 3rd rib in front and to 5th spine behind: abundant crepitations over same area: P.N. impaired to 2nd rib on left side: also abundant crepitations: sputum negative to ordinary and E.& E. examination, but patient not tested and a subsequent E.& E. gave T.B.+. Opsonic Index: 1.15 - .99 - .85 - 1.01.	+	+	+

No.		T.B.	O.I.	C.F.
42.	Family history positive: pleurisy (Rt) 3 months before: cough and sputum (T.B. said to be found): P.N. generally dull Rt, side marked flattening and restriction of movement: V.R. & V.F. increased crepitations after cough throughout: P.N. dull left apex: some crepitations sputum E.& E.(-): not tested on account of extensive signs. Opsonic Index: - 1.42 - 1.29 - 1.23 - 1.03. Provisional diagnosis: positive.	=	+	+
43.	Family history positive: haemorrhage 3 months before (1/2 pint): sputum gradually developed. P.N. dull Rt. front: V.R. increased crepitations all over front and to angle of Rt. scapula behind. Some crepitations at 1st left interspace: sputum E.& E. (-) not tested on account of extensive signs. Opsonic Index: 1.26 - 1.19 - 1.44 - 1.05. Provisional diagnosis: positive.	-	+	+

No.		T.B.	O.I.	C.F.
44.	Family history negative: Influenza 6 months before: followed by cough and spit: on admission P.N. dull over left front: B.S. bronchial, some superficial crepitations all over front increased on cough: no sputum: temperature liable to sudden violent fluctuations.	O	-	+
	Opsonic Index: (Estimated on temperature alone i.e. without exercise) .9 - .93 - .99 - .86.	O	+	+
	One month later Rt. sided pleurisy with effusion (1½ pints) still no sputum: serous fluid gave positive fixation.			
	Opsonic Index re-estimated (this time on (exercise) 1.17 - 1.01. - .9 - 1.14.			
45.	Family history negative: some haemoptysis 4 months before admission and again at 2 mths. some cough and sputum (T.B. said to be found before admission): some impairment at Rt. apex and occasional crep. at apex: some creps at level of 5th spine behind on Rt. side and at 6th spine on left: no sputum: not tested on account of extensive signs.	-	+	+
	Opsonic Index: 1.16 - .86 - 1.12 - 1.03. Provisional diagnosis: positive.			

No.		T.B.	O.I.	C.F.
46.	Re-admission of old case (3 years standing): T.B. last found 1 year before: P.N. dull to 2nd rib Rt: some crepitations over Rt. upper lobe slightly increased on cough: V.R. and V.F. increased: sputum E.&.E.exams (-) not tested. Opsonic Index: .9 - 1.44 - 1.1 - 1.05. Provisional diagnosis: quiescent disease not yet arrested.	-	+	-
47.	Re-admission of old case (2½ years standing) T.B. last found 6 months before: P.N. dull Rt. apex: B.S. deficient: occasional click at apex not increased on cough: some fine creps, at left apex not increased on cough: no sputum or cough. Opsonic Index: .96 - 1.01 - 1.89 - .93. Provisional diagnosis: arrested disease.	0	-	+

The following tables show in a more compact form the results of this investigation.

TABLE V. Cases tested with Tuberculin.

Result of test injection.	Cases	Opsonic Index.		Complement Fixation.	
		+	-	+	-
No reaction	10		10		10
General reaction	15	3	12	2	13
Focal reaction	8	5	3	6	2

TABLE VI. Untested Cases.

Diagnosis	Cases	Opsonic Index.		Complement fixation.	
		+	-	+	-
Negative	4		4	1	3
Positive	10	10		8	2

TABLE VII. All Cases

Diagnosis	Cases	Opsonic Index		Complement Fixation	
		+	-	+	-
Negative	29	3	26	3	26
Positive	18	15	3	14	4

Although the number of cases fully investigated is small, it may yet serve to give some indication of the diagnostic value of serum methods.

It will be noticed that all of the cases giving completely negative results to test injections, gave also negative results to serum examination.

Of the 15 cases giving no focal but a marked general reaction to tuberculin, 3 gave a positive index and 2 of these 3 a positive complement fixation.

One case therefore (No. 23) was negative to all except opsonic methods, and it is interesting to note that this case gave a history of T.B. in the sputum before admission.

Of the 2 remaining cases giving a positive index and positive fixation one (No.24) had practically no physical signs and the other (No. 25) although admitted with extensive signs, was not tested until 5 months after admission when a definite degree of arrest might reasonably be presumed.

Of the 8 cases giving a focal reaction to tuberculin, 5 gave a positive index and 6 positive fixation.

It is important to note, however, that in only one of these cases (No. 33) were both serum methods negative, and there the auto-inoculation in the opsonic test was not above suspicion. Against this one case may be put the 3 cases giving a positive serum examination but no focal reaction.

In considering the value of serum reactions, it must be remembered that in a large group of definitely positive cases, 10% may give for some reason or other, a negative complement fixation and this same fact may account for the negative

fixations, amongst those doubtful cases giving a focal reaction. With this fact in view the following conclusions may be stated concerning cases where the history or clinical examination points to involvement of the lung:-

(i) positive complement fixation is strong presumptive evidence of active or quiescent disease.

(ii) positive complement fixation plus a positive opsonic index is definite evidence of active disease.

(iii) a positive opsonic index is definite evidence of active or quiescent disease.

(iv) negative complement fixation is in nine cases out of ten evidence against active disease.

(v) negative complement fixation plus a negative opsonic index is almost definite evidence against active disease, and

(vi) a repeatedly negative opsonic index is definite evidence against active disease.

The bearing of these conclusions on the use of tuberculin test injections is evident.

To repeat the conclusions of the section on test injections: even if, in suitable cases, there be no danger from such injections, there follows from their use in the bulk of cases, a very definite amount of discomfort and, more important still, in a large minority of cases, either they cannot be given or they cannot be fully carried through.

On the other hand serum reactions - certainly complement fixation and almost invariably the opsonic index - can be carried out in every case.

It would seem justifiable therefore to conclude that where both serum reactions can be carried out, if necessary, on more than one occasion, there is no necessity to give test injections at all.

This conclusion is borne out still further by the result of serum reactions in untested cases.

Of 14 such cases, 4 were considered to be negative. Three of these could not be tested owing to fever and the fourth was an old case presumably arrested. (No. 47).

All four gave a negative index, and all except the arrested case negative fixation.

Ten were considered to be positive and none of these could be tested on account of the extent of clinical signs.

All ten gave a positive index and eight of them positive fixation. Five of these later on developed T.B. in the sputum and a sixth a tuberculous pleurisy.

In addition, when the combined results of serum reactions and test injections are considered, they will be found to afford some indication of the diagnostic value of various degrees of clinical involvement of the chest.

In the following tables, clinical signs have, for sake of convenience been divided into 3 categories: (1) where they were completely absent, (2) slight; where the apex of one lobe, say, was definitely impaired, (3) marked: where the clinical involvement corresponded with Groups II and III of the Turban-Gerhardt classification: i.e. extensive involvement of all of one lobe, or part involvement of 2 lobes, or involvement of three or more lobes.

TABLE VIII: Clinical Signs in Tested Cases.

Result of Test	No signs	slight involvement	marked involvement	Total
No reaction	4	4	2 (pleurisies)	10
General reaction	3	9	3	15
Focal reaction		2	6	8

TABLE IX: Clinical Signs in Untested Cases.

Diagnosis.	No signs.	slight involvement	marked involvement	Total
Negative	1	2	1 (arrested case)	4
Positive		1	9	10

TABLE X: Clinical Signs in All Cases.

Diagnosis	No signs	slight involvement	marked involvement	Total
Negative	8	15	6	29
Positive		3	15	18
Total	8	18	21	47

It will be seen that out of 47 doubtful cases investigated only 8 had no physical signs, 4 of these 8 gave no reaction to tuberculin, 3 a general reaction only and one (No. 35) was not

tested owing to fever, but gave no serum reactions.

Eighteen cases showed a slight degree of clinical involvement and of these 4 gave no reaction, 9 a general reaction, 2 were not tested but were otherwise negative, and 3 alone were positive (2 giving a focal reaction and one T.B.) The degree of involvement was practically identical in all the negative cases, i.e. the percussion note was impaired or dull above one clavicle, the vocal resonance was increased, the breath sounds were harsh, or the breath sounds were very faint and tubular. Some cases, however, had merely an alteration in resonance whilst others might give some slight pectoriloquy or an impairment at another apex.

In none of the cases was there any moisture before or after cough, whereas in the 3 positive cases, two had some suspicion of moisture after coughing at an apex.

The cases showing marked impairment are even more interesting. Of 18 cases with extensive signs, 6 alone were negative. 3 of the 6 were old pleurisies with extensive impairment of lung surface, 1 was an old arrested case with large fibrotic tracts, 1 (25) had not been tested until 5 months after admission and was probably originally positive, and the remaining case had some suspicion of moisture at the Rt. apex.

The 15 positive cases on the other hand gave in every instance evidence of moisture, usually increased on cough at any rate over the most of one lobe and occasionally all over one side.

To sum up: of 29 negative cases, 26 showed no signs of moisture before or after cough, whilst all of 18 positive cases presented various degrees of moisture varying from a few clicks to abundant râle.

Before making any statement as to the value of early clinical signs in the light of these figures, it will be well to recall the standpoint of the purely clinical school, as instanced by followers of Krönig's light percussion method. The careful mapping of Krönig's area, the noting of shortening of the area or of blurring of its inner margin or of relative dulness at both margins is held to be sufficient evidence in which to demonstrate in any apex disease as small in area as a cherry. It is admitted by many that the method is very suitable for detecting old or healed lesions, but in spite of that when a doubtful case comes to be considered, alterations in this area are considered to be strong evidence in favour of active disease.

The writer's series of cases is admittedly small, but it is at least typical of the run of doubtful cases in Sanatorium practice and in 19 out of his 29 cases, a very definite alteration in Krönig's area was noted.

Indeed in 3 only of the cases showing signs limited to one apex, were positive results obtained.

But apart from the question of distinguishing obsolete from active lesions, there are other points in differential diagnosis which have already been referred to.

Four of these cases for instance which proved to be negative, gave a history of naso-pharyngeal catarrh and were in all probability instances of collapse induration of an apex following obstruction of the higher air passages.

Three negative cases had a history of chronic gastro-intestinal disturbances, and 2 of these showed impairment of an apex: one suffered from chlorosis; one from mitral stenosis

(early); one from metrorhagia; one from salpingitis; and six from chronic ill-health, slow fever with which was associated some cough and sputum and after examination an impairment of one apex.

It would seem then that, however common it may be to find early cases, with T.B. in the sputum, having signs confined to one apex, it is not common to find active disease of one apex in cases where the sputum has been repeatedly negative.

Moreover when such cases are established, it will be found almost invariably that there is some degree of moisture, however small, to be heard, before or after coughing, at the impaired area.

SUMMARY.

The following conclusions are based on the results of this investigation:

(1) that about 62% of cases coming under observation as supposed early phthisis, but with no bacilli in the sputum, prove to be negative: nevertheless

(2) that such negative cases may present clinical signs of impairment of percussion note, breath sounds and resonance at, at least, one apex: and

(3) that moist sounds in such cases are almost invariably absent: therefore

(4) it is not justifiable to diagnose active tuberculosis on the strength only of impairment of an apex

(5) that active disease confined to one apex with a repeatedly negative sputum is not common.

(6) that where moist sounds are present, further investigation is needed to exclude or confirm the presence of active disease

(7) that when this investigation takes the form of the complement fixation reaction along with the estimation of the opsonic-index (if necessary, repeatedly) a final diagnosis can be made without recourse to test injections of tuberculin.

S E C T I O N X.

CONCLUSION.

It is not proposed to recapitulate here the conclusions arrived at in the different sections of this essay, because although of individual importance, they are not essential to a broad survey of the present condition of diagnostic methods. Such a survey must of course be incomplete and is certainly like all other surveys of early diagnosis in pulmonary tubercle, disappointing.

The history of diagnosis in this disease has been a history of sanguine expectations as to the finality of one test after another, followed by slight qualifications, gradual disillusionment and frequently scepticism.

Even the most ardent protagonists of individual tests are usually compelled to admit that in quite a large percentage of obscure cases, their particular diagnostic measure is not of itself final; and as a rule in such instances they fall back on what is really a scientific subterfuge. They will say for instance that when such a deadlock is arrived at, it is necessary to take into account the family history, the history of the illness, the general health and physical signs, all of which is tantamount to an admission that their particular test is only of importance as an additional factor in diagnosis. Absolute finality in biological diagnosis is admittedly inconceivable, but the writer claims that during the past year the increase in accuracy of diagnostic methods over those previously followed is in the approximate ratio of 9:1, and that this increase is due wholly to

the improvement of blood-serum technique, particularly that of complement fixation. The limitations of this serum examination are obvious, and at present there are still cases where in spite of such examination an element of doubt enters and an appeal for confirmation has to be made to other tests, but these instances, it is claimed, are 9 times less frequent than before.

This deficiency besides is probably not so annoying as the over-efficiency of the von Pirquet reaction, and there is some likelihood that further improvement in technique will not only set up a criterion of activity by quantitive methods, but will elimate the number of instances where a negative serum result is obtained in positive cases: until that stage is reached the laborious technique of the opsonic-index forms the only satisfactory confirmatory evidence. The position may be summed up that by the use of both these methods, the diagnosis of early tubercle has risen nearly to the high-water mark of possible accuracy.

It must be made quite clear that this statement casts no reflection on the value of other methods of examination, particularly, careful inquiry into history and symptomatology, painstaking and accurate clinical examination, and thorough bacteriological examination of the sputum: such a view is untenable. These methods are and always will be indispensable and the more refined they become, the smaller the group of obscure cases! but if and when they have all drawn blank, it is

not fair to make a positive or negative diagnosis unless recourse has been made to serum examination.

Perhaps the best conclusion to an essay of this kind is to give a brief description of the writer's routine examination of any one doubtful case: it is as follows:

The clinical history and symptomatology are carefully investigated, but no unfavourable deductions are made from any statements with the exception of a story of pleurisy or of frequent haemoptysis.

Cough, spit, night sweats, loss of weight, isolated haemoptyses, fever, positive family history, none of these are held to justify any deductions as the ultimate nature of the case, with one reservation that should there have been a definite haemoptysis and should the case ultimately be tested by subcutaneous tuberculin, great caution will need to be exercised in dosage. A thorough physical examination is made of all systems and the condition of the chest is noted with care for subsequent reference during a possible tuberculin test. Measurement of areas of dulness and localization of patches of moisture are noted on suitable charts, but still no deducations are made even from the presence of moisture at some part of the chest unless marked alterations are heard in its amount following cough. The sputum is then examined for Tubercle Bacilli by the Ziehl-Neelson method, and, should the result be negative after frequent examination, the sedimentation

test of Ellerman and Erlandsen is carried out. A negative sedimentation test is of the first importance, and definite deductions are here drawn for the first time during examination.

If the history and clinical signs are negligible and the sputum negative the chances are that the ultimate result will be negative.

Sputum however may have been absent and in any case the serum is now examined by the complement fixation technique and the opsonic-index, over two days on varying exercise, is estimated.

At this stage in most cases the diagnosis can be concluded. A positive fixation and positive index are taken to indicate active or quiescent disease; a negative fixation and negative index mean healed or obsolete disease. If, however, there is any doubt as to the result of the serum reactions, or if the patient wishes to obtain some idea as to the relative activity or quiescence of his disease, subcutaneous test doses of tuberculin on Bandelier's scale (A F. .002, .001, .005. 01. ccs.) are given. Here the history and clinical signs are reviewed and no doses are 'pushed' where there is a previous history of haemoptysis or where the involvement of the chest as measured by clinical examination seems extensive.

Need for additional caution is indicated where there has been a history of a positive bacillary find prior to admission because such a history does not, as might be expected, contra-indicate diagnostic test-doses if after admission bacilli cannot be found by concentration examination.

These tests are considered satisfactory proof of a negative condition only where the maximum dose has been given without any suggestion of a focal reaction. If a suitable installation be at hand, radiographic examination of the chest is carried out but no great stress is placed on the results where there is evidence of extensive fibrotic changes.

The Arneth count, albumin-reaction, urinary reactions and per-cutaneous tuberculin reactions are not investigated.

Finally should the diagnosis be a negative one, the patient is instructed to observe simple hygienic rules in the future and is dismissed the sanatorium with a clean bill of health.
