

THESES ON TUBERCULIN TREATMENT.¹

BY PROFESSOR DR. SAHLI.

I SUBMIT the following propositions to the Congress on Tuberculosis:—

First: All the various tuberculins are essentially identical. The apparent differences are dependent on the various degrees of admixed impurities. The active principle of all tuberculins is the protein of the tubercle bacilli. There is no proof of the existence of a tubercle exotoxin. The fact that it is impossible to produce high sensibilisation for tuberculin by previous tuberculin injection in healthy animals is no argument against tuberculin being actually the toxin of tuberculosis. The best tuberculins are those prepared from cultures as free as possible from adventitious albumins.

Second: To avoid disastrous mistakes in therapeutic dosage it is advisable to provide the practitioner with tuberculin in suitably graduated dilutions as is done in the case of Beranek's tuberculin. Not only the absolute dose, but also the concentration of the dilution is of importance. The same dose will prove more active in concentrated solution than when further diluted, because of the greater rapidity of absorption.

Third: The use of tuberculin for diagnostic purposes ought to be condemned. It is unreliable both positively and negatively. Diagnostic injections are dangerous. The only diagnostic procedure I advise is the cutaneous reaction with graduated dilutions. Its purpose is not diagnosis in the ordinary sense, but the determination of tuberculin sensibility in order to fix the proper initial dose for treatment.

Fourth: Tuberculin treatment is free from danger only if more obvious clinical reactions are avoided. In this case it is so harmless that it may be undertaken even when the diagnosis is not absolutely certain in order to effect prophylaxis in cases where infection is probable, although the disease is quiescent. Only such a mild method allows us to derive all the benefit possible from tuberculin treatment. Tuberculin treatment is chiefly valuable in incipient cases.

Fifth: In advanced cases tuberculin treatment may sometimes produce a certain symptomatic effect, but this effect does not compare with the utility of tuberculin in incipient cases.

Sixth: In order that tuberculin treatment should be widely available for the most favourable incipient cases, it is indispensable that the general practitioner, and especially the family physician, should render himself proficient in tuberculin treatment.

Seventh: Correct tuberculin treatment is only possible if based on a solid and thorough knowledge of the action of tuberculin. I have laid special emphasis on this point in my monograph on the subject, the fourth edition of which I present to the Conference.

Eighth: The theory of the therapeutical action of tuberculin may now be regarded as well established. The therapeutical action is essentially of the same kind as the tuberculin reaction. Even so-called reactionless tuberculin treatment is based on reactive processes. The reaction of tuberculin consists in stimulation of the natural healing forces. The significant factor is the increased production of what I have called inflammatory antibodies and the specific tuberculin amboceptor. The latter has the effect of increasing both the local counteraction in the foci by the production of tuberculin-opyrin and the general detoxication of the pre-formed tuberculin. This detoxication depends upon the decomposition of the tuberculin by the amboceptor over the intermediate stage of tuberculin-opyrin into innocuous and inactive products. This detoxication is especially the cause of the antithermic effect of small doses of tuberculin.

Ninth: Tuberculin acts favourably only in cases where the human organism is not already sufficiently under the influence of absorbed tuberculin—that is, generally in slighter cases.

Tenth: It is not necessary to increase the doses of tuberculin to the furthest limit of tolerance. Many cases improved more with a much smaller dose, which I term the individual optimum dose. This optimum dose ought not to be overstepped.

Eleventh: The large doses of tuberculin recommended recently for the purpose of reducing temperature have no curative action. The reduction of the temperature depends in these cases only on an artificial production of an anti-anaphylactic state—that is, the same condition of things which causes the advanced cases not to react to tuberculin.

Twelfth: Tuberculin treatment has not the character of a true immunisation, though it produces immunisatory effects in the organism. In actual immunisation we try to produce as completely as possible a state (I wish to emphasise the word *state*) of immunity. This is impossible of attainment in tuberculosis. In tuberculin treatment we only look for stimulation and activation of the counteractions of the body at each injection. To try to express the mode of action I have called the therapeutical action of tuberculin an immunisatory healing action, in opposition to actual immunisation, which is a final state never obtained in tuberculosis.

Thirteenth: All localised tuberculosis is suitable for tuberculin treatment, provided that the patient's system is not already overloaded with tuberculin, and he is, therefore, too seriously ill. As a rule acute cases cannot be treated by tuberculin.

Fourteenth: Tuberculin treatment by means of multiple cuti-reactions after the method described by me at the International Congress on Tuberculosis in Rome, 1912, has been proved harmless, and useful especially for incipient cases. It is based on the principle of enlarging the reactive surface. The strongest local (cutaneous) reaction is produced with the smallest amount of tuberculin.

Fifteenth: Well-diluted tuberculin treatment constitutes a real and great therapeutical progress.

Berne.

REMARKS ON THE TECHNIQUE OF ELECTROCARDIOGRAPHY FOR CLINICAL PURPOSES.

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I.—The Electrodes. The Compensator and the Condenser.

In the Oliver-Sharpey lectures on the Electrical Action of the Human Heart as delivered and published,¹ I did not find time or space for any description of the technique of electrocardiography. But since then I have learned from various inquiries that have been addressed to me, as well as from trade catalogues containing approved directions for the pursuit of electrocardiography, that the simplified technique which I now follow is not generally known. It may be of service therefore to describe as briefly and untechnically as possible the simplified procedure that I consider to be best adapted to clinical use.

It has been assumed by recent clinical authorities on the technique of electrocardiography that it is necessary to use unpolarisable electrodes and a compensator in order to balance what are called "skin-currents" in circuit. I made use of these accessories 30 years ago in my first investigation of the subject, and they are in daily use in my laboratory for other purposes, but for taking electrocardiograms I have long since abandoned them.

At the Brussels Congress of Physiology in 1905 Professor Max Cremer showed that a condenser in the circuit gets rid of accidental fluctuations of current without interfering with the comparatively short alternating currents of the electrocardiogram. His subsequent publications,² and those of Zwicke³ and of Gildemeister,⁴ have fully confirmed the statement. Electrocardiograms taken (1) with unpolarisable electrodes and compensation; (2) with ordinary metal electrodes and a condenser of sufficient capacity (20 to 50 microfarads) are indistinguishable from each other; theoretically, according to Gildemeister, the error caused by the condenser to the first ventricular wave amounts to 1 in 2000—i.e., is negligible.

¹ A paper read before the Fifth Annual Conference of the National Association for the Prevention of Consumption and other Forms of Tuberculosis on August 4th, 1913.

² THE LANCET, May 24th and 31st, 1913.
³ Sitzungsberichte der Gesellschaft für Morphologie und Physiologie, München, 1905.

⁴ Zeitschrift für Biologie, 1911, p. 32.

⁵ Zeitschrift für Biologische Technik und Methodik, 1913.

I had found long ago that with platinum electrodes in salt water a galvanometer was not permanently deflected by accidental currents, such as "skin currents," or by compensating currents thrown in in the usual way. Their presence in the circuit acted precisely like that of a condenser, but I did not realise until Cremer's demonstration in 1905 of the effect of a condenser that as a matter of fact a platinum electrode in saline acts as a condenser of comparatively large polarisation capacity amounting, with the electrodes I used, to between 10 and 20 microfarads. At first I had used platinum wires, of "small" surface, of a capacity that I roughly estimated at 10 microfarads. Subsequently, and in conformity with the presumption that capacity might more probably be too small than too large, I used strips of platinum foil an inch broad, and dipping into salt water to a depth of about 2 inches, giving thus an effective surface of 4 square inches and a total capacity in circuit that I estimated at about 250 microfarads. Finally, I returned for routine use to platinum wire electrodes and a separate condenser in circuit of about 20 mF.

I chose platinum for the electrodes because it keeps clean, or is easily cleaned; gold has the same advantage, and I have found that it answers equally well; zinc plates are unsatisfactory, being apt to get oxidised when left in salt water and to give accidental currents. Other metals or alloys, such as silver or German silver, might, no doubt, be found to answer equally well, but I have been satisfied with platinum, and thus to be independent of shunting and compensation. Standardisation of deflections by a millivolt in circuit must, of course, be practised at frequent intervals to verify the instrument and to know the electromotive-force of an observed deflection.

II.—The Galvanometer.

A good many models of apparatus have passed through my hands during the last 25 years, from Lippmann's capillary electrometer to Einthoven's string galvanometer in various models, and the Bock-Thoma oscillograph; of course, any galvanometer when used in combination with a condenser of not too great capacity becomes substantially an electrometer. I have often been asked which is the best instrument for clinical purposes, and I do not find it easy to give a short answer. The Cambridge model is obviously good, if somewhat expensive. So are the various Edelmann models. In my laboratory one of them is set up for demonstration in the lecture room, and another very handy little model, with gold electrodes, as a travelling instrument; in this last form the instrument is suitable to the consulting-room table; no compensator or condenser nor any photographic accessories are necessary. The patient dips his or her fingers into a couple of finger glasses and the physician inspects the electrical pulse under the microscope. A.-V. dissociation and extra-systole, coupled beats, and disturbances of rhythm are plainly to be seen with this instrument by an accustomed eye.

The Bock-Thoma model—which by some clinical authorities is said to be "very bad"—is in my opinion excellent. The accessories are conveniently arranged, and it presents the advantage of permitting two or more records to be taken simultaneously, e.g., of the heart-sounds and the electrocardiogram (*vide* Fig. 1). It consists of four strings side by side in four magnetic gaps, each string acting as a separate galvanometer. The advantages of this are obvious. A spare galvanometer is always at hand. Double, treble, or at a pinch quadruple records of pulse, heart, and respiration can be obtained if one cares to take the trouble. The principal advantage of the Cambridge model is the fact that the fibre is hermetically enclosed in a removable fibre-case which protects it from dust and from draughts of air. In the Bock-Thoma the fibre is not completely enclosed.⁵

The essential quality of all such instruments consists in the sensitiveness of the fibre and the rapidity of its deflection. Comparing in this respect (1) the Cambridge model and (2) the Bock-Thoma, we have in the former a single silver-coated glass fibre, in the latter a loop of platinum with a minute glass mirror. The magnification in the former case is by means of an optical system, and amounts to $\times 500$ or $\times 600$; in the latter it is by virtue of the "optical lever,"

and amounts to $\times 1000$ to $\times 4000$. The mass of the moving part in the former case is smaller than in the latter; it is therefore easily made dead-beat, the difficulty being to make it quick enough. With the Bock-Thoma, by reason of the double fibre and mirror, the mass is greater, the movement is easily made quick, the difficulty being to make it dead-beat. It overshoots. And I may say that before I had had experience of the Bock-Thoma I was very suspicious as to the possible effect of this overshoot.

Fortunately, however, the time relations of the heart currents are such as to allow a considerable margin in the physical properties of these instruments as regards overshoot. The sharpest to-and-fro movement of the electrocardiogram, that of the systolic spike V_1 , occupies a time of 0.04 to 0.05 sec.; in a case where I measured it as accurately as I could, the rise of V_1 took 0.03 sec., and the fall 0.015 sec.⁶ Thus while the nearly instantaneous change of potential of 1 millivolt caused by an ordinary contact key can develop "overshoot," a change gradually developed in 0.03 sec. will not do so to any appreciable extent. Overshoots occur, indeed, at intermediate points in the rise of V_1 , since the period of the oscillograph (1/80th sec. or 0.0125) is shorter than the time of rise of V_1 (about 0.03 sec.). But at ordinary speeds of the recording surface (about 1 inch per sec.) their effect is invisible and negligible. They become apparent only when the record is drawn out at higher speeds (3 to 5 inches per sec.) as slightly darker spots on the recording line marking the period of the oscillograph, and incidentally serving the useful purpose of an automatic chronograph. The "true" electromotive value of the spike is much more likely to be underestimated with the single string by reason of air damping than overestimated with the oscillograph by reason of overshoot. As a matter of fact the electrocardiogram taken by an oscillograph with, e.g., a period of 80 per second and an overshoot of 1 in 5, exhibits no appreciable overshoot, and is scarcely distinguishable from an electrocardiogram taken by a dead-beat string-galvanometer of sufficient rapidity.

Photographic development is a subordinate matter that is usually left to the judgment of a laboratory assistant, who, however, like most photographers, brings out sharper records black on white than white on black. The string galvanometer gives across the photographic slit a thin vertical shadow in a bright field, which develops out as a "white" on "black." The oscillograph gives across the slit a vertical bar of light, which develops out as a "black" on "white." The records in both cases can be taken on a reel of paper or of gelatin film or on a glass plate. For an occasional record that is to be manifolded it is preferable to use a film or a plate from which contact prints can be taken. But for systematic recording purposes, when cases are to be taken by the hundred, and their records filed, it is far more expeditious and economical to take them on paper, and for this purpose the black-on-white records of the oscillograph are preferable to the white-on-black records of the string galvanometer. The former are clearer than the latter under equal conditions of light and development. The magnification is greater by the oscillograph than by the string, and the more distinct record of the former appears, therefore, more irregular than the finer and less distinct record of the latter instrument; but if the two records are brought to the same degree of distinctness and magnification there is not much to choose between them in this respect. The coarse tremor evident on

⁶ At these time-values of the spike V_1 , the record given by the oscillograph (with a semi-vibration period of 0.006) is slightly more accurate than that afforded by the single string (with a deflection-time of 0.02 for the millivolt-centimetre and a return-time to zero of 0.03 to 0.04 sec.). The two notches that sometimes precede and succeed the spike ("Q" and "S") are more pronounced with the quicker oscillograph than with the slower string. According to some clinical observers the depth of the notch "S" is an index of irritable heart, and I have heard it called "the neurasthenic notch." Without going so far as to deny altogether the nervous character of the "S" notch, I venture to invite attention to the fact that its absence or presence and its size can be determined by purely instrumental conditions. Slight alterations of tension such as are constantly occurring from alterations of temperature and moisture will as their first visible effect produce alterations in the depth of S and in the relative magnitudes of "P," "R" and "T." If the string happens to be slightly tighter and quicker than usual, "S" is favoured; if slightly looser and slower, "S" is disfavoured. With a string that is excessively loose and slow, T can be as big as, or bigger than, R, as with a capillary electrometer. It is futile to take elaborate measurements of the relative magnitudes of P, Q, R, S, T without checking the tension before and after each observation.

⁵ I learn that in the latest models the enclosure is complete. I also learn that a careful comparison between the string-galvanometer and the Bock-Thoma apparatus was made two years ago by Grödel and Meyer-Lierheim. (Berliner Klinische Wochenschrift. 1911. No. 24.)

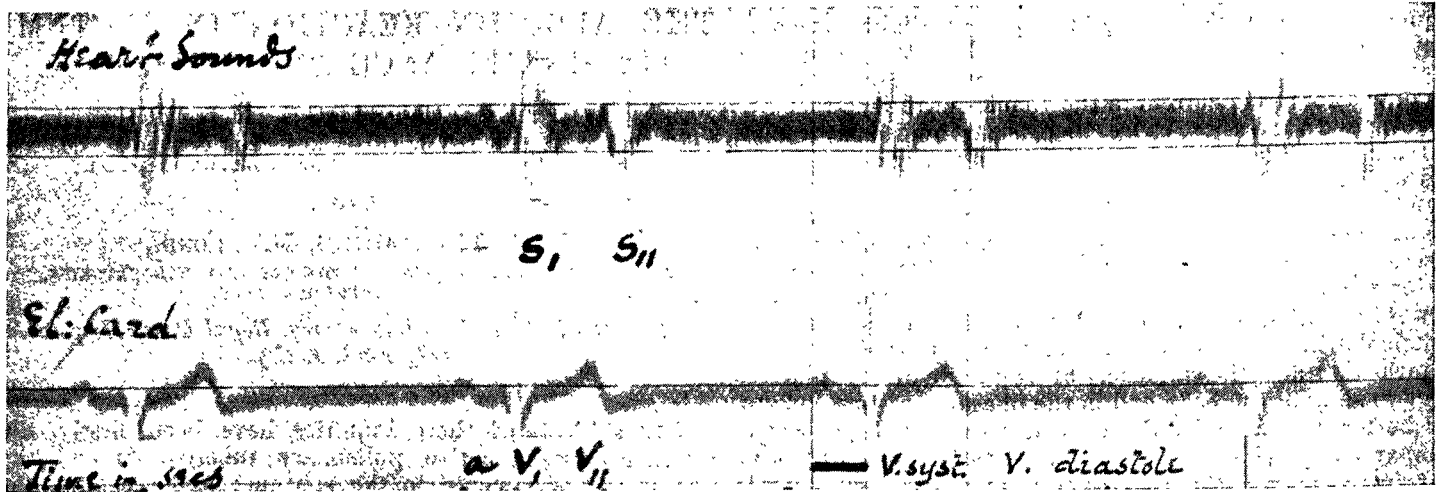


FIG. 1.—Bock-Thoma oscillograph. Simultaneous record of the heart sounds of T. H. K. (upper line) and of the electrical changes (lower line). S_I, S_{II} indicate the first and second sounds, V_I and V_{II} indicate the first and second ventricular waves, a is the auricular wave, and the length of the auriculo-ventricular interval is indicated below the third cycle by a horizontal bar. This subject, with an unusually slow pulse of 50 per minute, consulted a medical man for pain in the left shoulder, and was diagnosed as having serious heart disease with complete absence of the first sound. His anxiety was increased by frequent auscultation and percussion, but has been (for a time at any rate) allayed by the demonstration to him of his typically normal record. Duration of the aV interval, 0·17; duration of ventricular systole, 0·32; duration of ventricular diastole, 0·87; duration of cardiac cycle, 1·19; relation of systole to cycle, 27 per 100, or 6·5 hours per 24. Pulse-frequency = 50 per minute. The length of the aV interval is measured from the beginning of a to the beginning of V_I. The length of the ventricular systole is measured from the beginning of V_I to the end of V_{II}.

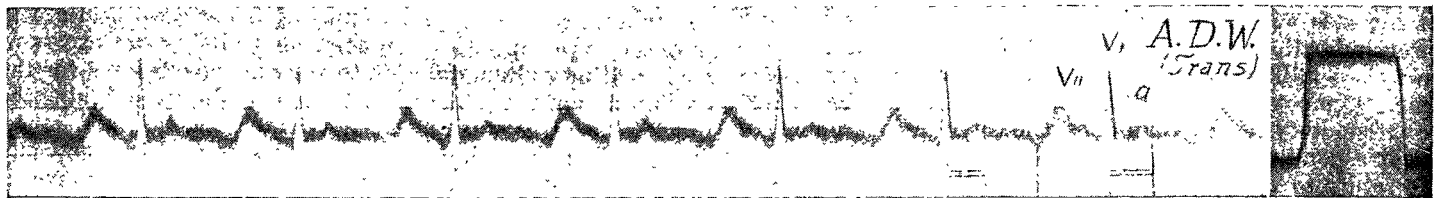


FIG. 2A.—Cambridge string galvanometer. (Read from left to right.)

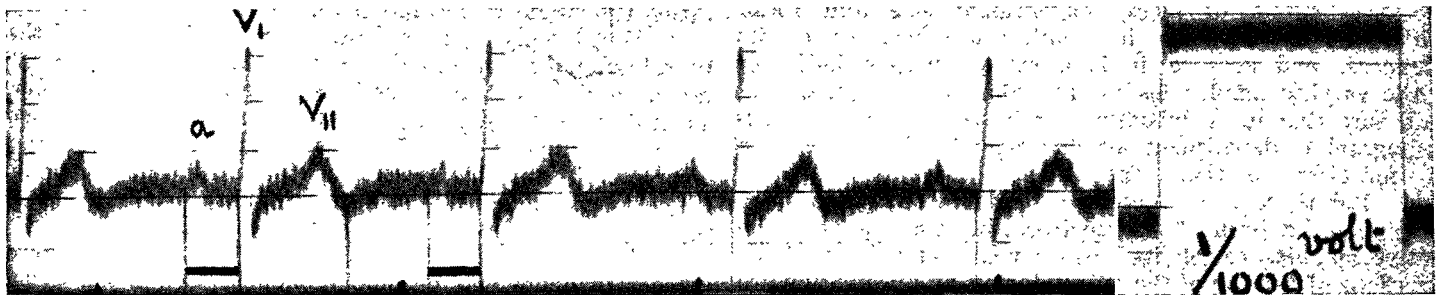


FIG. 2B.—Bock-Thoma oscillograph. A. D. W.—Transverse record. aV interval = 0·17 sec. Length of ventricular systole, 0·36; length of ventricular diastole, 0·44; cycle, 0·80; pulse frequency, 75. S/Cy = 45, or 10·8 hours per 24. The aV interval, taken from the beginning of the auricular to the beginning of the first ventricular wave, to measure the rapidity of transmission from auricle to ventricle, is indicated below the first two cycles by a horizontal bar. It measures in this case 0·16 to 0·18 sec. The square-topped deflection at the end of the record shows the deflection and overshoot by the instantaneous closure of 1 millivolt through the instrument.

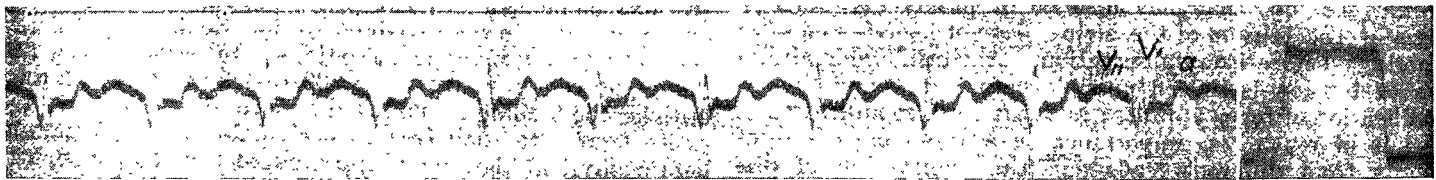


FIG. 3A.—Cambridge string galvanometer. (Read from left to right.)

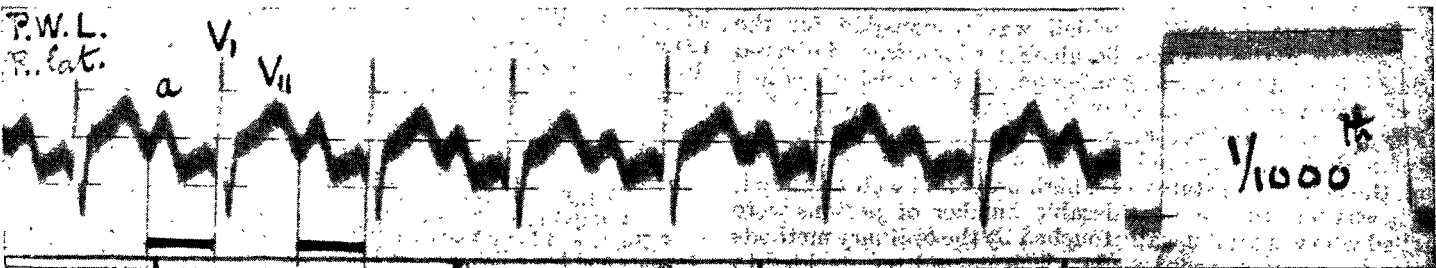


FIG. 3B.—Bock-Thoma oscillograph. P. W. L. Right lateral record taken two or three minutes after running upstairs (1050 Kg M in 15 seconds). The pulse-frequency is 120 per minute. The aV interval is not shortened in proportion with the shortening of the cycle, but is absolutely longer than normal in this subject. Normally it was measured to be 0·17 sec. at a pulse-frequency of 70 to 80 per minute. In this record the interval, as indicated by horizontal bars below the first two cycles, comes out = 0·21 sec. at the pulse-frequency of 118 to 120 per minute.

most oscillograms and on records taken by a sufficiently "quick" and sensitive string are due to slight muscular contraction or tone. Of course a tremulous tracing can be due to other causes, such as a shaky building or a spitting arc or to alternating current in the vicinity of the instrument. But over and above these causes there is a true muscular tremor which can be exaggerated at will by voluntary contraction, and which in animals can be abolished by chloroform.

But in another and more important respect oscillographs are in general preferable to string records for clinical purposes. The larger and quicker indications of the former are better adapted to measurement than are the smaller and slower indications of the latter; the lengths of the auriculo-ventricular interval and of the ventricular systole are easier to measure; and the variations of amplitude of the spike on the two sides of the body and in the phases of respiration are far better compared by the comparatively quick than by a comparatively slow recorder. And as supplied by the instrument maker, the deflection time of an oscillograph mirror does not much exceed 0.005 sec. with an amplitude of 2 c.m. per millivolt, while that of an average string is at least 0.020 sec. for a deflection of 1 c.m. The greater height of the spike, as given by the oscillograph, even if due to "overshoot," could be of no disadvantage, since it would be a proportional augmentation of all deflections; but as a matter of fact the greater height of the spike in an ordinary oscillograph record as compared with an ordinary string record is a sign that the quicker instrument has followed the development of electromotive force during this phase more perfectly than was the case with the slower instrument. The smaller and slower indications of a string adjusted to give 1 c.m. deflection by one millivolt can of course be magnified for purposes of measurement, but to do this costs time and at best gives less satisfactory results than does the direct measurement of the corresponding oscillogram.

To return to the question—"What is the best instrument for clinical purposes?" or otherwise put "Which instrument is best to buy?—the Cambridge model or the Bock-Thoma?" I can only say that I like both instruments in a laboratory. I like the Cambridge model for cases where I want to get an electrocardiogram of most conventional size and form. I like the Bock-Thoma for routine use because of its quickness, and because it is a more sensitive indicator of the varying amplitudes of the ventricular spike, and I am sure that in a laboratory or in the special electrocardiographic department of a hospital, if there is a use for either of these instruments, there is a use for both. But there is at present a tendency to lay too much stress upon the form of the electrocardiogram and upon the relative magnitudes of its various peaks and depressions. Variations of tension of the string during an observation are of frequent occurrence, and the precaution of recording the standard deflection after as well as before taking a record should never be omitted if its form is to be studied. Variations of form, such as the presence or absence of Q, the augmentation of S giving the so-called "nervous notch" of some clinicians, the relative augmentation or diminution of T, are features that may possibly be of pathological significance, but that may also be of purely instrumental origin if the tension of the string has not been tested after as well as before every observation. A considerable alteration of tension is indeed possible before gross and obvious modification of form appears; and, after all, modification of form is of much less importance than the comparison of records from different leads and the observation of disordered rhythm.

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MEDICAL TEMPERANCE COMMITTEE.—The final meeting of the committee which was responsible for the organisation of the lectures on alcohol which were delivered during the recent Brighton conference of the British Medical Association was held on July 31st, and much satisfaction was expressed at the success which crowned its labours. The lectures delivered by eminent members of the profession were, the committee states, of a high order and well attended, and it was felt that a considerable number of persons were reached who were not usually touched by the ordinary methods of the temperance propaganda. The committee decided to place on record its gratitude to the medical men who had rendered such splendid service gratis, and to hand over a balance of about £6 to the United Temperance Council.

THE ALBUMIN REACTION IN SPUTUM: ITS SIGNIFICANCE AND CAUSATION.

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THE subjects of these inquiries have been, firstly, the relation between active pulmonary tuberculosis and the appearance of albumin in the sputum; and secondly, the establishment, if possible, of the pathological condition associated with albuminous sputa. The presence of albumin in the sputum was described originally by Biermer¹ in 1855. In his investigation he mixed the sputum with water, filtered, and precipitated the albumin by heat after acidification. He claimed that the amount of albumin present was proportional to the cytological content, and was present in all sputa, in contradistinction to Renk, who at a later date claimed it absent in chronic bronchitis. Wanner in 1903 investigated the question more fully. His technique consisted in diluting the sputum with an equal volume of 3 per cent. acetic acid in order to precipitate all mucin, neutralising the excess of acid, adding sodium chloride to provide electrolytes for the coagulation of the albumin by heat, and finally weighing the precipitate after washing in hot water, alcohol, and ether. His conclusions were that albumin was present in practically all sputa. More recently Roger² and Levy Valensi³ investigated the question of its presence in pulmonary tuberculosis under the title of the albumin reaction. Their technique was similar to that of Wanner, except that they mixed the sputum with an equal volume of water, afterwards precipitating the mucus with dilute acetic acid.

In 1911,⁴ replying to objections raised by Goggia⁵ that putrefaction decomposes the proteins in sputum, especially mucin, and sets more albumin at liberty, Roger and Levy Valensi maintained that they always advocated the use of fresh specimens; and in answer to Remlinger⁶ they completely deny his assertion that all sputa contain traces of albumin. Whilst agreeing that albumin is present in pneumonias, passive congestion, œdema, and all cases of pulmonary tuberculosis, they assert that it is never present in acute and chronic bronchitis, and claim that if albumin is absent from the sputum in suspected cases of pulmonary tuberculosis after two examinations it is certain that the case is not tuberculous. They then proceed to analyse the few cases of pulmonary tuberculosis in the literature, which contained no albumin in the sputum. In cases of the second and third degrees there were 4 out of 897. In one case no sodium chloride was added when the coagulation test was employed. In two others no tubercle bacilli were ever found, and in the fourth one or two doubtful bacilli were seen once after many examinations. In cases of the first degree 13 were negative out of 288, or 4.5 per cent., and they criticise the technique employed in several of the cases and quote figures to show that in early pulmonary tuberculosis, before physical signs have appeared, at least 50 per cent. to 70 per cent. of cases have albumin. They quote Dieudonné⁷ on the increased amount of albumin present in exacerbations produced by tuberculin and other causes. Of 19 cases considered as healed and examined by him 8 showed a few tubercle bacilli by antiformin only, and in these the albumin reaction was positive. In 7 tubercle bacilli had recently disappeared, and the albumin reaction was positive in all. In 4 others considered as cured for two years the albumin reaction was negative. Dieudonné claims that the test is of the utmost value in distinguishing between bronchitic and

¹ Biermer: Die Lehre vom Auswurf, Würzburg, 1855.

² Roger: Société Médicale des Hôpitaux, October, 1909.

³ Roger and Levy Valensi: Ibid., 1909, vol. xxviii., Sér. 32, p. 3.

⁴ Roger and Levy Valensi: La Presse Médicale, 1911, vol. xix., p. 409.

⁵ Goggia: Gazzetta degli Ospedali, July, 1910.

⁶ Remlinger: Société de Biologie, March 12th, 1911.

⁷ Dieudonné: Revue Médicale de la Suisse Romande, 1910, vol. xxx., p. 394.