becomes a practical question, might not school children who exhibited suspicious symptoms and who gave a positive ophthalmo-reaction be segregated and kept under observation?

Some rather interesting points suggest themselves from a study of my results. In a few cases not suspected to be tuberculous, but whose family history was bad, I have obtained pronounced reactions. Is it possible that this reaction not only reveals the presence of an actual lesion, but also a condition of tissue which is susceptible to the development of tuberculosis? What is the meaning of this reaction? Clearly to the conjunctiva of the tuberculous it is an irritant. To the eye of the healthy it is bland. I have been rather surprised to get a positive reaction in some cases of lupus that had been treated by the subcutaneous injections of the "old" tuberculin, from the smallest to the largest doses, till all local and general reactions had ceased. In such cases one would have expected that the tissues would have acquired an immunity to tuberculin. Are we to assume from this test, when positive, that there is always present an actual tuberculous lesion, or may we get it in the absence of a lesion in those susceptible to the disease? This point can only be settled by prolonged observation and by following the future history of those cases in which the ophthalmo-reaction has been positive. Parallel results are obtained by the cuto-reaction of von Pirquet. Here, again, the introduction of tuberculin into the skin causes in the tuberculous a characteristic lesion. The tuberculin proves itself an irritant to the skin in the same way as to the conjunctiva. Both in the case of the eye and the skin the action is an evidence of tissue resistance to tuberculin in the tuberculous. Is the tuberculin elaborated in the living tissue the same as that manufactured *in vitro*? One would expect that tuberculin instilled into the eye, scratched into the skin, or injected hypodermically, would "react" only in the healthy, for is not the reaction a sign of tissue resistance that we would expect to find better developed in the healthy than in the unhealthy? It seems apparent that tuberculin, or some other toxin developed in the tuberculous, imparts to the tissues a resistance to tuberculin, as expressed by the inflammation in the eye or skin, that is absent in the healthy. Von Pirquet holds that the reaction is due to the presence of an antibody.

Chantemesse, in a paper read at the Académie de Médecine (July, 1907), described an analogous reaction in enteric fever to a strong solution of typhoid toxin. The toxin was precipitated by absolute alcohol, and the powder obtained dissolved in distilled water ($\frac{1}{8}$ mg. in mjl). In non-typhoid cases in from two to three hours there occurred a slight redness and lacrymation, a reaction which was quite evanescent, all trace of hyperaemia disappearing in from four to five hours. But in enteric cases the reaction was much more pronounced, and at its maximum in from six to twelve hours, and remained till the following day. When very severe it even lasted for two to three days. There was hyperaemia, lacrymation, and a sero-fibrinous exudation—in all respects very similar to the ophthalmo-reaction of Calmette. No constitutional disturbance was observed. Chantemesse could not affirm whether this reaction is, or is not an early sign of enteric, but the reaction has been got in the eye of rabbits injected forty-eight hours previously with enteric bacilli.

I have to acknowledge with thanks my indebtedness to Dr. J. Montgomery Anderson, late House-Physician in the wards of Sir Thomas McCall Anderson, without whose assistance it would have been impossible for me to record those observations on the ophthalmo-reaction.

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NOTES ON 121 CASES TESTED WITH
CALMETTE'S TUBERCULIN.

BY

J. S. WEBSTER, and J. A. KILPATRICK,
M.B., Ch.B. Manc., M.R.C.S., L.R.C.P.,RESIDENT MEDICAL OFFICERS, MOUNT VERNON HOSPITAL FOR
CONSUMPTION AND DISEASES OF THE CHEST, HAMPSTEAD.

The diagnostic value of the ophthalmo-reaction recently introduced by Professor Calmette, of Lille, has yet to be determined, and it is in slight endeavour to assist in this that the following observations have been made. Of the importance of the early recognition of tuberculosis, especially of the lungs, little need be said, and if this reaction succeeds in placing in our hands, as it apparently gives some promise of doing, a definite and trustworthy indication of that dread disease it will amply justify any position that it may take in the future and add to our armoury another weapon that we may use in our long combat with tuberculosis.

We desire to express our indebtedness to Dr. J. E. Squire, the Senior Physician of the Mount Vernon Hospital, who first brought this reaction to our notice some little time ago, and on whose cases in this institution it was first used, for his kindness in granting us permission to publish these results, and also for the accompanying comments with which he has favoured us.

Altogether we have attempted to obtain the reaction in 123 instances, 6 of which were in presumably healthy individuals used as controls, the remaining 117 being in individuals actually suffering from or else suspected to have pulmonary tuberculosis. In all but the first few of our observations we have used the dry form of tuberculin made into a solution with distilled water.* One drop of this solution placed in the lower conjunctival sac is quite sufficient for any doubtful case, and in several instances it has appeared to be more than sufficient, judging by the intensity of the reaction produced in six of our cases. It is, of course, necessary to first examine the conjunctiva and observe that it is healthy.

In two cases of presumably healthy individuals some slight reddening of the lower palpebral conjunctiva was noticed after two days at least had elapsed since the date of inoculation. In a tuberculous individual well-marked changes occur which are of varying intensity, ranging from a little lacrymation to the most acute injection of the conjunctival vessels accompanied by marked epiphora. In five cases the palpebral conjunctiva was noticed to redden as early as the second hour, but in two cases at least this may have been due to the irritation produced by rubbing the eye, because the degree of injection diminished shortly afterwards, but the individuals themselves denied touching their eyes. We have noticed that in many cases the first indication of any reaction was afforded by the plica semilunaris, which is situated just to the outer side of the caruncle, and the swelling and slight reddening which this undergoes occupies a fairly prominent place throughout the whole of the reaction: In one case this fold was the only part of the conjunctiva to show any signs of reaction, and in this particular individual it was evidenced not so much by reddening (present only in a slight degree) as by swelling, especially obvious when the two eyes were compared. By the fourth hour from the time of inoculation 15 more cases commenced to show the reaction, and from this hour onwards the remaining cases giving the reaction commenced to show some slight reddening, the longest latent interval between the placing of the drop in the eye and the time when the reaction was first noticed being twenty hours; unfortunately a night intervened and we were unable to note the onset of the maximum reaction. In the most severe case the maximum reaction was noticed to be present sixteen hours after the application of the test. The reaction in some slight cases lasted only two days, but in the more severe as long as a week, and even longer. The palpebral conjunctiva usually reddens before the ocular and through.

* The dry tuberculin is supplied in small tubes containing such quantity that 10 drops of distilled water give a solution which is said to be of proper strength for ordinary use, and will, of course, serve for ten observations. We have found that this solution is stronger than necessary, and appears to produce in some cases a reaction of undesirable intensity; in our later cases we diluted with 15 drops instead of 10, and have formed the opinion that this weaker dilution is more convenient, and gives equally satisfactory results.

out shows a greater degree of reaction, leading in many cases to swelling; the caruncle is usually the last place to show any sign of reaction, but in one case it was apparently the only place to show any reaction at all. The majority of the patients did not complain of any pain, but noticed some slight discomfort in the inoculated eye, best described in their own words as "it feels as if there was a little grit in my eye"; there was also a general complaint of watering of the eye, accompanied by epiphora, which lasts for a varying period and is of varying severity, corresponding usually with the severity of the reaction. In only the most severe reactions was there any purulent discharge; it was only noticed in 5 cases, but nearly all the patients giving the reaction complained either of a slight amount of discharge or else that their eyelids on the inoculated side were glued together when they awoke on the morning following the day when their eyes were inoculated. It was probably due to the fibrinous exudation which occurs normally during this reaction and not to any purulent discharge.

Five patients complained of a little intolerance of light; they were those who gave the most severe reactions. In some cases complaint was made of a soreness at the back of the nose, which made the patient feel as if he had caught cold; in only one of these cases was there any rise of temperature, and the question naturally arises whether, before the epiphora commenced, some of the tuberculin solution diluted by the lacrymation had been washed down the nasal duct into the nose and thence into the pharynx. The fact that the soreness was first noticed in the morning of the day following the application lends a little colour to this view.

Despite the statement that there is no general reaction, 7 of the cases showed very definite rises of temperature after inoculation. In 4 the temperature went up on the evening of the day when the solution was applied, but in the others it was noticed in the evening of the following day; it was not accompanied by any headache or malaise, and these patients were not those who exhibited the greatest amount of local reaction. The temperature quickly came down to its usual level in all the cases; two of them are detailed below.

One patient after recovering from the reaction caused by the tuberculin became affected with the phlyctenular conjunctivitis to which tuberculous individuals are especially prone, but she is now making fair progress towards recovery.

Altogether we have tried the reaction in 123 persons, the majority exhibiting signs of pulmonary tuberculosis; in these the amount of lung involved and the degree of its activity varied very much; many were in a comparatively early stage of pulmonary tuberculosis and not expectorating at all, so that we could not attempt to find the tubercle bacilli; it is in cases such as these that the reaction if it prove to be reliable will be of most value.

CASE I.

C. B., aged 44, male, ironworker by occupation, was admitted with a ten months' history of cough and expectoration; had pleurisy in March, 1907, but never had any haemoptysis. The

T = One drop of tuberculin placed in eye.

physical signs were dullness, with feeble breathing and prolonged expiration at right apex. Tubercle bacilli have been discovered in the sputum.

CASE II.
W. C., male, shop assistant. Was admitted with a thirteen months' history of cough. Haemoptysis on one occasion, only

T = One drop of tuberculin placed in eye.

six weeks ago, and then only slight. The physical signs are impaired resonance at left apex with slight catarrhal signs at both apices.

It has been found convenient to group the cases with regard to the ophthmo-reaction into: (1) Those which gave a definite reaction. (2) Those which did not give a reaction. (3) Doubtful cases in which the subjective symptoms—for example, epiphora and a feeling of grit in the eye—were present, but in which there were no objective symptoms or only very doubtful reddening of the palpebral conjunctiva.

Out of the 121 individuals 4 were presumably healthy. Of these 2 did not give any reaction and 2 gave doubtful reactions; one of these had had pleurisy with effusion twice and the other had had a cough for the last twelve months, but neither had been submitted to a physical examination. Both were exceedingly anxious to have the reaction tried again. One case giving a doubtful reaction ten days earlier gave a definite one when inoculated again, whilst the other gave a most intense reaction with some swelling of the eyelids, the second inoculation in this case taking place eight days after the first.

Forty-three cases of pulmonary tuberculosis with very definite physical signs and with tubercle bacilli present in the sputum were subjected to the test, and in every case a positive result was obtained which was absolutely definite.

Of the remaining cases, 58 had comparatively definite signs of pulmonary tuberculosis, one lobe of lung being affected in the majority. In all these cases the disease, by observation of the temperature chart, was judged quiescent, and in none of them had any bacilli been recently found in the sputum. The results obtained were somewhat contradictory. In 36 cases definite reactions were observed; in 18 cases no reaction to Calmette's test was observed; whilst in the remaining 4 cases doubtful results were obtained. These results naturally suggest that this reaction will indicate slight degrees of activity when the temperature chart indicates none at all, but only the future with many more results will show this. One case, however, was very suggestive, since bacilli were isolated from his sputum about a month ago; but recently repeated examinations have failed to reveal any bacilli. This patient did not give any reaction. His temperature is somewhat irregular, but he suffers from attacks of malaria, which may account for it.

The remaining 16 individuals were all doubtful cases of suspected pulmonary tuberculosis without any definite physical signs, and without any expectoration or sputum from which no bacilli have been isolated. They all, however, had a suggestive history. From these 6 gave a very definite reaction, whilst 7 gave no reaction at all; the remaining 3 gave doubtful results, consisting of subjective signs only.

SUMMARY OF RESULTS.

All definite cases with definite bacilli in the sputum gave the reaction. In cases with physical signs of pulmonary tuberculosis but quiescent as judged by temperature, some gave the reaction and some did not, and there was no obvious cause for this variation.

In doubtful cases some gave the reaction, some did not; some were indefinite, but we have for the present no definite evidence to confirm or disprove the indications of the tuberculin inoculation.

In presumably healthy individuals two reacted and two did not, but in the absence of physical examination no

evidence for or against the presence of tuberculosis in those who gave the reaction can be offered.

It is difficult to draw any conclusions as to the relation between the intensity of reaction as compared with the amount of lung involved, that is, the extent of the tuberculous lesion.

In five cases very severe reactions were obtained, and these cases presented marked differences in the physical signs. The most intense reaction of all was obtained in one of the control cases—an individual who was unaware that he had any tuberculosis, and who, because he gave an indefinite reaction when first inoculated, asked us to repeat it eight days later; he refuses to have any physical examination, but he has no symptoms beyond a slight cough for the last twelve months.

A severe reaction also occurred in the case of a patient with advanced and extensive pulmonary tuberculosis, whose temperature chart is satisfactory when he does not attempt any exercise, but whose condition, judged by its irregularity whenever he attempts exertion, appears a little unstable. His case, however, is complicated by the presence of a large amount of albuminuria ascribed to a tuberculous kidney. This patient has no adventitious sounds in the lungs.

Another case giving a severe reaction was that of a woman with doubtful disease at one apex and severe and persistent pleuritic pain on that side, accompanied by a friction sound; her temperature is a little raised (about 1° F.) above what it should be. Since she was subjected to the ophthalmic-reaction about four weeks ago some adventitious sounds have made their appearance at the apex, and rendered the diagnosis more definite.

From these cases the difficulty in determining any relation between the amount of tuberculosis present and the degree of reaction will be apparent, and many more cases could be cited to show this.

As regards the intensity of reaction as compared with the degree of activity shown by the tuberculous disease, a similar difficulty exists for the cases with the highest temperatures, and therefore the most active tuberculosis did not show the most intense reactions.

As examples of this, the case of the presumably healthy individual may be mentioned first. In this person his temperature for the short time that he was under observation was quite normal, never rising above 98.4° F., and yet he gave the most marked reaction of all. Whether the fact that it was the second inoculation within eight days has anything to do with this or not cannot be stated. The case of the woman, already mentioned, who gave a severe reaction, also illustrates the difficulty, for she showed no marked degree of activity, her temperature being 1° F. above the proper range; out of the total number of cases on which observations were made 24 were classed as subacute cases of pulmonary tuberculosis. Of the 24 cases, 7 gave a fairly severe reaction, but 17 gave only an ordinary amount of reaction, such as the majority of the cases classed as quiescent showed. In the classification of cases with regard to their activity the temperature chart has been our guide throughout.

From the above results it seems to us that this reaction gives some promise of utility, but its reliability can only be ascertained by a much more extended series of observations on both healthy and tuberculous individuals. The chief value seems to lie in the fact that we have obtained the reaction in several cases in which the presence of tuberculosis was suspected, but where there were no definite signs of it; whether it has any value in recognizing the quiescence of a tuberculous lesion cannot be stated, for some cases judged quiescent gave the reaction, and others also judged quiescent did not.

In conclusion, we wish to express our thanks to the resident medical officers at the Northwood Hospital for their kindness in supervising some 50 patients on whom an attempt to obtain the ophthalmic-reaction of Calmette was made.

REMARKS BY DR. SQUIRE.

Those who, like myself, have not felt justified in advocating the hypodermic injection of tuberculin for diagnostic purposes in cases of suspected pulmonary tuberculosis have based their objection on the possible risk of lighting into activity a tuberculous focus in a dangerous situation. A dose of tuberculin sufficiently large to cause a general reaction not only reduces for a time the resisting power of the body—a negative opsonic phase—but may activate a latent tuberculous focus which may then get beyond control, and may also lead to auto-infection. Calmette's ophthalmic-reaction promised to obviate this disadvantage, for absorption through the conjunctiva would not infect the body to the extent of a hypodermic injection, and a purely local reaction in the eye would not appear to have the disadvantages

or risks of a general reaction. I was therefore anxious to test as far as I could, first, whether the reaction with Calmette's tuberculin was purely local; and, secondly, whether the test could be relied upon to indicate the presence of tuberculosis which could not otherwise be detected, and the activity or arrest of recognized lesions due to tuberculosis. The interesting report of Drs. Webster and Kilpatrick of their investigations seems to indicate that, though in the great majority of cases the reaction is confined to the conjunctiva, a general reaction is occasionally produced. As to the value of the test as an indication of the presence of active tuberculosis, the results, though they suggest that the test is reliable, are not conclusive. In those cases in which active tuberculosis was proved to be present by other methods of examination, a reaction was obtained in every instance. Of the doubtful cases, some reacted, some did not; we may, I think, conclude that when a reaction was obtained, tuberculosis was present and active; but in some, at least, of the negative cases I should hesitate to accept the absence of reaction as conclusive proof that there was no tuberculosis. Calmette's method of using tuberculin certainly seems to be the best for diagnostic purposes yet suggested.

MEMORANDA: MEDICAL, SURGICAL, OBSTETRICAL

A CASE OF ACHONDROPLASIA.

THE patient here reported, a girl aged 16 years, came under my notice recently. She is one of a family of eight, all of whom, with the exception of herself and one sister, are normal. This sister, who immediately precedes the patient in point of age, is slightly under medium height, and is affected by rickety curves of the bones of the lower extremities. The patient's father and mother and other near relatives are all normal.

History.—The patient was 2½ years old before she began to speak, and was 4 years old before she began to walk, crutches being required at first to aid her in so doing. The elder sister already referred to was 7 years old before she could walk. In addition to the usual illnesses of childhood, none of which affected her seriously, the patient suffered from general ill-health. She sweated much about the head, was always feeble, and deformity of the bones began to appear about the time she first attempted to walk.

Appearance.—She is now 3 ft. 6 in. in height, markedly stunted, and of heavy build. On the other hand, she is quite

active, and her intelligence practically perfect. The head is large, and she has a decidedly "old" look. The depression of the root of the nose and prognathism are slightly marked. The hair of the head is abundant and glossy. The limbs are markedly affected. In the upper extremities the humeri, as is well seen in x-ray examinations, are much curved, as are likewise the radii and ulnae. The ends of these bones are much enlarged, and the "trident hand" is well marked although the fingers are a little long. In the lower extremities the curving of the femora and tibiae is pronounced, indeed it was principally on account of the deformity of the lower limbs, associated with a degree of pain in the knees, that she came to see me. There is marked lordosis, with consequent protuberance of the abdomen. The central point of the body lies well above the umbilicus, the skin is smooth and pliable, and there is a thick layer of subcutaneous adipose tissue throughout.