the cortex, will cause nausea, vertigo, hyperacidity or subacidity of the stomach, and intestinal indigestion. These are matters of daily experience in the practice of every ophthalmologist. That long neural band, the fasciculus longitudinalis, originating anterior to the nuclei of the third nerve and extending back till it is lost in the medulla is probably the medium by which the root organs of the various cerebral nerves are connected. That some such connection exists has been clinically demonstrated. When the eyes are organically different an excess of energy, equal to the difference between the better and the most abnormal eye, must be sent to both. Under such conditions the endeavor to maintain the parity between accommodation and convergence results in ciliary spasm or ciliary relaxation. It is probable that the one is associated with esophoria, the other with exophoria. The unconscious effort or paresis, as the case may be, of one set of muscles or fibers is reflected to other and remote sets. If one makes a strong effort to clench one hand very tightly he will find that he is unconsciously closing the other. The effect of tension within the eye, or of relaxation, seems to be reflected particularly to the non-striated muscular tissue, and as a result a contraction or a relaxation of circular fibers follows. This is true of the vasodilators or vasoconstrictors of the capillaries, of the circular fibers of the stomach or of the intestines, of the urethra and of the uterus. Hence follow local congestions or local anemias, cramp of the stomach or catarrh of the stomach, constipation or diarrhea, incontinence of the urine, and in several instances I have seen pregnancy, after many years of sterility, follow the relief of an eyestrain that could be explained only on the basis of a relaxation of a persistent contraction of the circular fibers of the cervix. With these far-reaching nervous involvements, inadequacy of metabolism as an element in tuberculosis assumes an added importance whether or not Ravenel⁴ is correct in his contention that "the alimentary tract is a frequent port of entry for the tubercle bacillus," for the same conditions that disturb the nervous functions of the digestive tract will involve nerve supply of all of the essential organs, and given a neuropathic diathesis we have the conditions prepared for the reception and culture of the infective organism.

CONCLUSIONS.

The essential propositions which these conclusions warrant are:

1. The inadequacies of focus or the motility of the eyes may give rise to and be responsible for disturbances of digestion and assimilation.

2. Lowered vitality, especially in the neurotic, predisposes to tuberculous infection, and as superalimentation is of first importance in effecting a cure, an exact and complete examination of the refraction and of the motility of the eyes should constitute an essential part of the examination of every patient suspected of having this disease.

3. If these are the views of the ophthalmologist on this subject they are of such vital importance to a vast number of sufferers that resolutions to that effect should be adopted, and the recommendation made to this Association that it is the sense of the members of this section that no examination for tuberculosis can be considered complete until it shall include the refraction and the motility of the eyes.

4. Am. Jour. Med. Sc., October, 1907.

OCULAR REACTION TO TUBERCULIN.*

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At a meeting of the Berlin Medical Society, May 8, 1907, von Pirquet¹ described his method of vaccinating, using a preparation of tuberculin, and reported 360 cases, all children, in which it had been tried. Of these clinically diagnosed "tuberculosis" a positive result was obtained in 88 per cent. The negative 12 per cent. occurred in the miliary cases or in those patients with cachexia, while 167 of the "unsuspected" gave positive results. In the discussion Wolff-Eisner¹ called attention to the possibility of obtaining a reaction to tuberculin when applied locally to other parts of the body and reported having observed such when a 1 to 10 dilution was used in the eye of a hay fever patient. This he had observed frequently and he described the reaction as consisting of a conjunctivitis, a chemosis, while in some cases the patient presented the condition observed in a general reaction from the subcutaneous administration of tuberculin.

Vallée² was able to confirm this statement by his work on cattle and horses, but doubted its utility or feasibility as a test in man, or even in the lower animals, on account of the pronounced inflammatory reaction. Calmette,³ of Lille, France, at a meeting of the Académie des Sciences, described the method as modified by him, in which he advocated a 1 per cent. solution of purified tuberculin, the reaction being so mild that it could be used in man. Since that time much work has been accomplished, principally by the French and Germans. More recently reports have appeared in the English and American journals.

The reaction described by Calmette, aside from the name of the author, is also known as the "Ophthalmic tuberculin," the "Oculotuberculin" and the conjunctival or ophthalmic reaction to tuberculin. At this time it may be of service to consider some of the factors of importance in connection with the work.

DESCRIPTION OF THE REACTION.

As described by Calmette, the reaction consists of a slight redness and swelling, chiefly of the caruncle and the inner canthus, but also involving the conjunctiva. Aubaret and Lafound,⁴ Aubaret and Magne⁵ have subdivided these cases into four classes, depending on the degree of the reaction. Sabrazés and Dupérie⁶ classified them as mild, medium and severe.

Varying according to circumstances and conditions, various results appear in the eye when the test is made. When the reaction is negative no changes whatever occur. A negative reaction may become positive by repeated instillations, even in the normal individual, or a negative reaction may become positive after the subcutaneous administration of tuberculin. When the reaction is positive the appearance is quite variable. In some only a very slight swelling and redness of the caruncle or surrounding portion of the conjunctiva may occur. The vessels, particularly those of the bulbar conjunctiva, are distended and appear more distinct.

* Read before the Chicago Medical Society, Feb. 26, 1908.

1. Berl. klin. Wchnschr., 1907, xlv.

2. Acad. d. sci., 1907, cxliv, No. 24.

3. Acad. d. sci., 1907, cxliv, No. 24; Presse méd., 1907, No. 49.

4. Gaz. hebdom. d. sc. méd. de Bordeaux, Aug. 4, 1907.

5. Jour. de méd. de Bordeaux, Aug. 25, 1907.

6. Gaz. hebdom. des sc. méd. de Bordeaux, July 21, 1907.

When the reaction is more pronounced the swelling and redness become much more marked, resulting in an inflammatory condition. The lids may become much swollen, the eye partially or completely closed, and a chemosis may be present. The congestion is more pronounced than in the mild cases, and on the involved surface a deposit of fibrin may be found. An increased lachrymation and photophobia are associated features. In the severe reactions the changes become more marked, sometimes extreme. Actual pus formation with ulceration has occurred in the severest cases. In only two of the observed cases did the reaction become marked and severe, and even then not sufficient to require special attention.

The fever and other conditions manifest in a general reaction to the subcutaneous injection of tuberculin are absent. Pupillary changes are not obtained as a rule. Generally the patient complains of little or no discomfort in the eye, more than a very slight burning, a scratching or a sensation of fullness or tightness, unless the changes are pronounced.

TIME OF THE REACTION.

The time that elapses between the administration of tuberculin and the reaction varies from three or four hours to thirty-six hours or even longer. In the majority of cases the reaction reaches the acme in eight to fourteen hours. Usually by the third or fourth day the eye has returned to apparently normal. Wiens and Gunther,⁷ Eisen,⁸ G. Serafini,⁹ A. Napier¹⁰ and others report cases in which the reaction has been much prolonged and with resulting effects in the eye. In one of the cases reported by Serafini, a young man with mild pulmonary and glandular involvement, the local findings were much intensified.

FORM OF TUBERCULIN EMPLOYED.

In some of the earlier cases dilute old tuberculin was employed. This was done partially from lack of knowledge and partially from the difficulty of obtaining a proper preparation. The ordinary tuberculin is not suitable, as the contained glycerin, as well as perhaps other substances, may produce a condition simulating a positive reaction. McLellan¹¹ claims that 1 per cent. of the old tuberculin is non-irritating to the eye.

Calmette, in his original communication, recommended the use of the precipitated or purified tuberculin, which may now be obtained in powder, tablet or liquid form ready for immediate use. The tablets contain 10 mg. of the dry purified tuberculin, and added to 1 c.c. of sterile water or physiologic salt solution make a 1 per cent. suspension, as the tuberculin is insoluble. As sterile water is irritating to the normal eye, physiologic salt solution is to be preferred. Since the preparation is only a suspension, it is necessary that it be frequently agitated, otherwise the supernatant fluid will contain little or no tuberculin and produce questionable results. It is best always to make a fresh preparation, although one several days old has given positive results. The liquid form is marketed in glass containers similar to the vaccine tubes. Of the three, the tablet form is probably the most convenient and was employed in the present work.

THE DOSAGE AND TIME OF ADMINISTRATION.

Calmette recommends that one drop be instilled into the eye. Wiens and Gunther, as the result of their experience, urge that a 0.5 of 1 per cent. suspension be used, as in a number of their cases the patients presented severe reactions and changes in the eye that continued for at least three months. Schenck and Seiffert¹² used three strengths, 1 per cent., 2 per cent. and 4 per cent., using the weakest first and stronger for subsequent tests if a negative result was obtained.

This in great part is determined by circumstances. As the early and slight reactions may appear within five or six hours, it is best employed early in the day. This permits of the examination being made in daylight, which is often of great assistance in the doubtful cases. When possible all patients should be examined every two hours and in the best of light. In private and dispensary work the time may not be a matter of choice and the result often must be determined by an assistant or nurse. The dispensary cases are not included in the report.

METHOD OF ADMINISTERING.

This is not so simple as it may first appear. With a sterile medicine dropper one drop of the suspension is instilled into the inner canthus of one eye only, the other acting as a control and a means of comparison. There is no immediate discomfort from the instilled drop, but frequently the patient will close the eye quickly or forcibly or perhaps rub the eye. To prevent this the lower lid is drawn downward and held for some seconds until the drop is well distributed and the patient has become accustomed to its presence. In all instances the patient is cautioned not to rub or irritate the eye. When a negative result occurs the test may be repeated after the lapse of from six to ten days. As the examined eye, even in the normal, becomes sensitized by repeated tests it is advisable and necessary to try first one and then the other, never the same eye for two successive examinations.

In order to determine as far as possible the efficiency of the reaction a rather wide range of cases were selected. Only those under constant observation in hospital practice have been included in order that the findings may be more accurate. At least one-third of the tuberculosis cases were rejected as unsuitable for the test on account of the presence of a conjunctival hyperemia, conjunctivitis or some other eye disease. Referring to the tables it will be found that 153 patients have been examined, many receiving two or more instillations. Of these 54, or 35.4 per cent., gave a positive reaction.

In some of the patients with typhoid, cerebrospinal meningitis, gonorrheal rheumatism or secondary syphilis, and in whom tuberculosis was neither suspected nor revealed on careful examination, a well marked positive reaction occurred. Where it might have been expected to be positive, as in the cases of pleurisy, tuberculosis of the knee, hip, spine and cervical glands, it was negative. Pulmonary tuberculosis in some form was diagnosed in ninety-five cases, with a positive reaction in forty, or 42.1 per cent. It may be urged that the negative reaction indicates an absence of tuberculosis or a faulty diagnosis. Examination of the tables, however, will show that, in addition to the physical findings, the bacilli were present in forty-two cases. Here the con-

7. München. med. Wchnschr., 1907. liv.

8. Beitr. z. Klin. d. Tuberk., viii.

9. Gior. d. r. Accad. di med. di Torino, November, 1907.

10. Glasgow Med. Jour., January, 1908.

11. Brit. Med. Jour., Dec. 7, 1907.

12. München. med. Wchnschr., 1907. liv.

dition can be hardly questioned, and of these just 50 per cent. gave a positive reaction. An attempt was made to determine in which form of pulmonary tuberculosis the reaction was most constant, but as far as could be judged there was no marked and constant difference which is not in accord with the findings of P. Eisen,⁸ Wolff-Eisner and Teichmann,¹³ and others.

TABLE 1.—FINDINGS IN MEDICAL CASES.

No. of Cases.	Clinical Diagnosis.	Reaction.	Remarks.
6	Typhoid fever	—	
1	Typhoid fever	+	Two instillations; marked.
9	Croupous pneumonia	—	Two instillations in two cases.
2	Pleurisy with effusion	—	
2	Pleurisy with effusion	+	Three instillations in one case, all marked. Both patients reacted very markedly.
1	Plastic pleurisy	—	
1	Cerebrospinal meningitis, lumbar puncture, diplococcus intracellularis in culture	+	Two instillations; marked.
1	Spinal meningitis (t. b. c.) ..	+	Three instillations; marked.
3	Diabetes mellitus	—	
4	Rheumatism, acute articular ..	—	
1	Rheumatism, gonorrheal	—	
1	Rheumatism, gonorrheal	+	Two instillations.
1	Sciatic	—	
2	Acute endocarditis	—	
1	Myocarditis	—	
1	Influenza	—	
1	Delirium tremens	—	Two instillations.
2	Hepatic cirrhosis	—	

TABLE 2.—FINDINGS IN SURGICAL AND ORTHOPEDIC CASES.

No. of Cases.	Clinical Diagnosis.	Reaction.	Remarks.
1	Tuberculosis of knee	—	
2	Tuberculosis of knee	+	One instillation, slight.
1	Tuberculosis of hip	—	Two instillations.
1	Tuberculosis of spine	—	
2	Tuberculosis of spine	+	One very marked.
1	Ochritis (t. b. c.)	—	
1	Cervical adenitis (t. b. c.) ..	—	Two instillations.
1	Tuberculosis of spine or syphilis	—	Two instillations.
1	Tuberculosis of hip with sinus-bacilli in pus	+	
1	Rectal carcinoma	—	

TABLE 3.—FINDINGS IN DERMATOLOGICAL CASES.

No. of Cases.	Clinical Diagnosis.	Reaction.	Remarks.
1	Lupus	—	
1	Syphilis, secondary	—	
3	Syphilis, secondary	—	One very marked.
1	Syphilis, tertiary	—	

TABLE 4.—FINDINGS IN ALL STAGES OF PULMONARY TUBERCULOSIS WITH PHYSICAL SIGNS.

No. of Cases.	Condition.	Reaction.	Remarks.
21	Bacilli in sputum	+	
21	Bacilli in sputum	—	
19	No bacilli in sputum	+	
34	No bacilli in sputum	—	
4	Bacilli in sputum	+	Instillations at first all negative; 1 mg. tuberculin given subcutaneously and positive ocular occurred in 4 (50 per cent.) without a second instillation.
4	Bacilli in sputum	—	

In two of the cases in which a very incipient tuberculosis was present repeated tests were all negative. If any difference existed the negative reactions occurred most frequently in the far advanced. Where the anemic condition was pronounced practically all were negative. In eight cases the subcutaneous administration of tuberculin produced a most positive ocular reaction in four, or 50 per cent.

These findings, compared with those of Calmette and many of the earlier investigators, are not as encouraging, while with the later reports the difference is not so great. P. Eisen obtained a positive reaction in 66.6 per cent., where the diagnosis of tuberculosis was cer-

tain and 31.1 per cent. of non-tuberculous affections also reacted.

On account of the limited number of cases and the incomplete state of the work I feel that I am not justified in making any positive statements, but a review of the reported cases and of my own forces me to certain conclusions which appear fair and just.

CONCLUSIONS.

1. As a diagnostic method Calmette's test is by no means positive or even specific. In a varying proportion of tuberculous cases of various forms a positive reaction will occur, but not in all. In differential diagnosis it can be of but limited service as it appears, apparently, in non-tuberculous affections. When the subcutaneous use of tuberculin in doubtful cases of tuberculosis is not possible on account of fever the ocular test may be employed. In my incipient cases in which an early positive diagnosis was most desired it was of no service.

2. Wolff-Eisner and Teichmann¹³ have employed and suggest the reaction as a means of prognosis. They determined that when an active reaction took place in patients in the incipient and early stages of tuberculosis it indicated an active effort at protection and consequently was a favorable sign. A weak, slow reaction was found in the far advanced, in the first and second stages, when the resistance was poor. When no reaction took place it indicated that the resistance was still less. It would appear to me that a diagnostic means of so little value can have still less value as a means of prognosis.

3. In a review of the literature no reference is made to the therapeutic possibilities in this method of administering tuberculin. The absorption by the conjunctiva is rapid and considerable, as can be demonstrated in the use of other drugs. Just what effect ocular administration of tuberculin has on the powers of resistance as indicated by the opsonic index has not been determined. If the ocular reaction is analogous to the local or general reaction produced by subcutaneous injections of tuberculin, and it is found feasible to administer it in this manner, it may be found necessary to avoid the pronounced and severe reactions.

4. Concerning the cause of the reaction I have nothing definite to offer, as the work along this line has not yet been sufficient. Wolff-Eisner and Teichmann¹³ in their work in determining the prognostic value of the test, consider the presence and intensity of the reaction due to the development of an endotoxin. Smithies and Walker¹⁴ have suggested that the inflammatory reaction in the eye is produced by the action of endotoxins which are liberated by the action of the antibodies on the dead bacilli in the eye. As the reaction occurs apparently in patients in whom no tuberculosis can be demonstrated it may, like the reaction from subcutaneous use of tuberculin, belong to the "group reactions."

5. From all we can now judge, the ocular reaction to tuberculin must be considered simply as confirmatory and must always be considered secondary to the findings as determined by a careful physical examination.

I take this opportunity to thank various members of the attending and resident staffs of Cook County Hospital, especially Dr. Miller, superintendent of the County Tuberculosis Hospital, for the use of cases and the assistance rendered in the present work.

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