

was in the sigmoid and probably due to cancer, so an incision was made over the cecum with the idea of making an artificial anus and doing a radical operation for cancer of the sigmoid later on; an artificial anus in the region of the sigmoid would have made a subsequent radical operation in this region much more difficult. After opening the peritoneum a considerable amount of brownish fluid was evacuated. Toward the median line a large cystic mass was felt. Another incision was made in the median line and disclosed an enormously dilated, slate-colored sigmoid which was at first difficult to identify. The gas it contained was evacuated by a trocar and canula and the intestine drawn into the wound. It was found to be a volvulus of the sigmoid which had turned through 180 degrees. The whole of the sigmoid, the upper part of the rectum, and the descending colon were gangrenous. Along the mesenteric border of the affected intestine were numerous black thrombotic areas. Healthy bowel was found about the splenic flexure of the colon, which was pulled down and the intestine divided at this point. The proximal end was temporarily clamped and all of the gangrenous intestine excised, after ligating the mesentery in sections, down to the rectum. The rectum was gangrenous as far as it could be inspected, and it was not thought proper to leave the rectal stump free in the pelvis, so the intestine was amputated through the affected area and the lower portion, which consisted of the upper part of the gangrenous rectum, was sewed in the lower angle of the wound. A tube was inserted in this stump and was packed around with iodoform gauze. The rest of the wound was approximated with sutures except at the upper angle, where the clamped end of the colon was brought down and sewed to the skin. The end of this bowel was drawn snugly around a tube with a purse-string suture. A large drainage tube was put in the primary opening over the cecum to drain the peritoneal cavity and a liberal amount of gauze surrounded the openings of the intestines in the median line to prevent infection of the wound.

Postoperative History.—The patient stood the operation very well. He was put to bed and the head of the bed elevated about two feet. He was given salt solution by hypodermoclysis. There was an abundant fecal discharge within a few hours. By the next day the patient had improved markedly, though there was some difficulty in respiration, and on September 19, two days after the operation, his pulse was only 100 and of good volume, with a temperature of 100. He made an uninterrupted recovery from this time on. The part of the rectum that was sutured in the wound gradually sloughed away. The patient was up and walking about three weeks after the operation and was discharged in good condition on Sept. 11, 1908, twenty-five days after admission to the hospital. On account of the affection of the rectum and the amount of sigmoid and colon removed it will be impossible to restore the continuity of the intestine and the artificial anus will be permanent.

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THEORETICAL AND PRACTICAL CONSIDERATIONS CONCERNING THE SIGNIFICANCE OF THE CONJUNCTIVAL REACTION (OCULAR TUBERCULIN TEST)*

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The new tuberculin reactions have opened up a wide field in connection with both theory and practice and have revived the discussion of many questions that had come to a standstill. I do not regard it as my task now to take up all of the theoretical questions; the lack of space would preclude this. I shall occasionally refer to the papers in which those interested may find further data that may interest them. I believe it would be best

to pick out a few practical questions and try to come to a conclusion concerning them.

Recently a number of new tuberculin reactions have been placed at our disposal for the diagnosis of tuberculosis. A large amount of literature has followed the first publication about these matters, a great part of which is worthless because of an insufficient knowledge of the fundamental basis of the reactions on the part of the observers. A recital of such examples is not in place. Such publications have caused confusion and dispute, a fact which has made the practitioner avoid this field of contest. But the time of toil and trouble will pass. It was the unavoidable result of an unsubstantiated approval of methods, from which I kept aloof, as is shown in my first communication on the subject.

We have now first the old subcutaneous method of Koch; second, the *Stichreaction*, just as old, but newly applied; third, the cutaneous and the conjunctival reaction; fourth, a series of so-called "new" reactions which I will not discuss.

The subcutaneous reaction is a specific one; it is a very sensitive test. A positive result indicates the presence of tuberculosis, but does not demonstrate necessarily an active or clinically evident tuberculosis. The occurrence of a positive reaction in 50 to 80 per cent. of clinically healthy individuals tested by the subcutaneous method should guard against such an error. I would not mention such a self-evident fact before this assemblage were it not that such errors are made daily in practice and being stated in literature. (Cf. Röpke and others.)

On the whole, the cutaneous and the *Stichreaction* give the same results as the subcutaneous method, which fact establishes their importance for clinical purposes. They are simple, safe methods which can be substituted for the subcutaneous method, demonstrating the same facts. They demonstrate a tuberculous focus, which, however, may be inactive or latent.

The conjunctival reaction differs materially from the cutaneous and the *Stichreaction*, being a reaction on a mucous membrane. It is positive in active tuberculous processes which are not too far advanced, and does not react in those cases in which a clinical examination is negative. It has already been shown that some of the apparently healthy people who gave the reaction had active tuberculosis. The future will tell whether or not tuberculosis is present in the remaining 5 to 8 per cent. But we can say to-day that, in contradistinction to the other tuberculin reactions, the conjunctival reaction is the one which indicates an active tuberculosis. An apparently healthy individual showing a positive conjunctival reaction is to be regarded in a suspicious light as being afflicted with an active tuberculosis.

These facts are proved by the records of reaction in 4,000 cases obtained under all precautions. The diagnostic value can be found only in the positive reaction. I have never stated that the negative conjunctival reaction excluded the presence of active tuberculosis, but it is improbable, except in cases in which clinically an active tuberculosis is present. For this reason the conjunctival reaction has a greater diagnostic value than the subcutaneous reaction. At first we considered them of equal value, but comparative examinations in about 100 cases have convinced us of the greater clinical value of the conjunctival reaction.

The inherent difference between the tuberculin local reaction and the subcutaneous method lies in the pro-

*Read by invitation at the meeting of the New York Pathological Society, Oct. 14, 1908.

duction of a typical tuberculin reaction far from the seat of the existing disease, that is, the avoidance of the lighting up of a fresh process at the seat of the original lesion. The rise of temperature in the subcutaneous method is not the element of danger, but the starting up of activity at the seat of the old lesion is the serious consequence, a process the progress of which can not be limited. In the recognition of this specific advantage of the conjunctival reaction the contraindications become evident; to these I have adhered from the beginning, having neglected them only once, in consequence of an error. In a paper read before the Berlin Ophthalmological Society, Jan. 7, 1908, I stated the contraindications. This was before the time when unfortunate experiences proved the correctness of my theoretical deductions. The prevention of reaction in the primary focus of the disease is the cardinal point.

Therefore, the conjunctival reaction is contraindicated if the eyes are or have been the seat of tuberculous diseases, or even if there is a suspicion of the existence of such lesions in the eye. Again, the application of the conjunctival reaction in an eye which has reacted is inadmissible and useless, because it would bring about a reaction at what is practically a tuberculous focus. This would not have any diagnostic value. It would act just like a cutaneous reaction, indicating a process which may have been latent. Another contraindication lies against the use of too concentrated preparations, especially the so-called "test" preparations. Their harmfulness especially appears when, as sometimes occurs, the conjunctival reaction is contraindicated for one of the reasons given above.

I recommend for use for the conjunctival reaction the "Rüete-Enoch tuberculin" for ophthalmo-reaction" in 1 to 2 per cent. solution, the efficacy and safety of which I have tested; as to its activity I can vouch. With more concentrated solutions better statistics can be obtained, because in persons with active tuberculosis a higher percentage of positive results will be produced. But I consider such statistics valueless, because they enforce a reaction in cases which are clinically evident.

In cases of tuberculosis in the early stages the reaction used according to my directions gives such distinct signs that no reason exists to vary my form of using the reaction, so often proved to be absolutely harmless. (A negative result of conjunctival reaction, in using the solutions I suggest, gives important prognostic evidence which is not to be obtained by the use of other concentrations.)

I admit freely that ophthalmologists are competent to judge the value of the conjunctival reaction, but they must recognize the above-mentioned contraindications and must get their experience from general medical cases. I am sorry to say that the ophthalmologists have hardly ever studied the contraindications, in consequence of which the conjunctival reaction will become prominent only after overcoming many prejudices founded on ophthalmologic publications.¹ It is not a mere coincidence that the ophthalmic clinic of Silex obtained very favorable results by using the method exactly according to my directions (tests made by Erlanger).

I have already said that the conjunctival reaction can be employed in diagnosis in internal medicine. But

you will hear occasionally that the reaction is uncertain because it may be negative in tuberculous patients and positive in clinically healthy persons. This only confirms my statement and shows the clinical inexperience of the observer, because he does not appreciate that these negative reactions may be found in consumptives and that healthy people who give positive conjunctival reactions should be regarded with ten times as much suspicion as those who react positively to a subcutaneous injection of tuberculin. And you know that many clinicians consider even such a subcutaneous reaction as quite important from a diagnostic standpoint.

Mistakes are also made concerning my opinion that there is a prognostic value to the reaction. Nevertheless, I can state that this opinion, so seriously opposed, is coming slowly but surely to the front. Therefore, I am anxious to correct mistakes in literature. I declared that a negative conjunctival reaction is to be taken as evidence of unfavorable prognosis in manifestly tuberculous individuals (where bacilli are found), but I never said that a positive reaction indicates a favorable prognosis. Furthermore, I never stated that a negative conjunctival reaction occurring with a positive subcutaneous one indicated an unfavorable prognosis. In such cases I decide on a latent tuberculosis, while Röpke² actually states that I believe the opposite. This can be satisfactorily explained by the fact that Röpke and I differ³ in the interpretation of what constitutes an active tuberculosis.

The prognostic conclusions of Teichmann and myself⁴ are based on the course which the cutaneous reaction pursues. I wish it clearly understood that the prognostic deductions which I pointed out from the first have at least as great importance as the diagnostic ones, and have not been changed in any important features. This prognostic application is the reason why I practice both the cutaneous and the conjunctival reaction in all cases at the same time.

There is not, as may seem, anything mystical about making the prognosis depend on the course of the reaction. Let us consider a continued reaction (*Dauerreaction*) which indicates, according to my conclusions, a cure or a favorable course. Such a reaction indicates that at the point of reaction the tuberculous poison causes a connective tissue formation. It is only necessary to suppose that the seat of disease reacts or has reacted in the same manner through the incorporation of these poisons, and then the result obtained by the continued reaction is easily understood. It is not to be wondered at if empirical observations have led to the same conclusions.

Here we find a strictly logical state of facts whose correlations are not at first recognizable. Wolfson and I have made a great number of opsonic examinations, and we arrived at the conclusion that this trying procedure gives no better diagnostic results than an exact clinical examination in combination with the use of local reactions. The control of a tuberculin treatment by the determination of the opsonic index is another matter.

We supposed that we would find a high opsonic index in cases of strong tuberculin reactions, and particularly in cases showing a *Dauerreaction*. This was not at all the case, and it only gradually developed why this was

* Manufactured in Hamburg, Hermanstrasse, 5.

1. Die Gefahren der Ophthalmoreaction und ihre Vermeidung, Wien. klin. Wchnschr., 1908, No. 33.

2. Beitr. z. Klin. d. Tuberk. (Brauer's), ix, No. 3.

3. Röpke and Wolff-Eisner: Beitr. z. Klin. d. Tuberk., 1908, x, 2.

4. Die prognostische Bedeutung der cutanen und conjunctivalen Tuberkulinreaction, Berl. klin. Wchnschr., 1908, No. 2.

so. A high opsonic index is produced by absorption of tuberculous poison from the focus of disease. This is prevented by the formation of connective tissue and explains, therefore, the absence of a high opsonic index.

These opsonic experiments, together with our experiments concerning the binding of complements in tuberculous subjects,⁵ prove that the poisons from the tubercle bacilli are absorbed, being identical in their effect with tuberculin. This fact is of great fundamental importance, because it explains the difference in the opinions of many observers which could not otherwise be explained. It is well known that to-day there are adherents and opponents to the tuberculin treatment, both from a diagnostic and therapeutic standpoint, the one side continuously reporting injurious effects which have not been observed by others.

The above-mentioned facts demonstrate that when a patient is injected with tuberculin the same process takes place in him which would eventually develop as the result of absorption of tuberculin from his own tuberculous lesions. Under these circumstances it is dependent on the point of view of the observer whether he holds the tuberculin injection or the disease itself accountable for the result. The same fact explains, it seems, what is apparently paradoxical, that the statistics of the adherents of tuberculin do not differ greatly from those of its opponents. I wish to state, in passing, that no good basis exists for the compilation of statistics of pulmonary disease. I shall discuss this on another occasion.⁶

Inasmuch as in all tuberculous subjects tuberculin appears in the circulation, it can be easily understood that the results with or without tuberculin treatment can not differ very materially. It will remain for the future to determine which individual will require a tuberculin treatment. The observation of the local reaction, the study of the opsonins and the clinical course of the illness will be the determining factors.

Numerous experiments, the observation of local reactions and the work of others have convinced me that there is a certain immunity to tuberculosis, an immunity against poisons which have become soluble and another against the bacilli themselves. The latter is most likely a bacteriolytic one. The immunity against poisonous matter, freed by lysis, is not an antitoxic one, but corresponds to the mechanism of the natural immunity against toxins which I have recently described.⁷

The toxin immunity of the naturally non-susceptible animal consists of the binding of the poison by organ receptors. (This stands in contrast to active immunity of an animal originally susceptible.) If endotoxins are bound, as described above, for natural immunity, the fixation seems often to occur by means of the receptors in connective tissue.

Two cases will illustrate this. The cutaneous reaction was applied to both subjects. They then received 1, 3 and 5 mg. tuberculin by subcutaneous injection and reacted with increasing fever. When 7 and 9 mg. were used, the general reaction did not occur, but in place of it an intense inflammation of the old cutaneous reaction appeared (in one case erysipelas and in the other an intense furuncle). I have repeatedly pro-

duced these phenomena in cattle. Their interpretation involves great difficulty and is only possible for those who have an experimental training in the fundamental work of natural immunity against toxins. The tuberculin, which has probably been made absorbable by lytic processes, is carried to those points at which the receptors are located. These are essentially the foci of disease, but other places can act as foci with receptors. If all the tuberculin is bound here, a tuberculin injection will cause a local reaction. If it is only partially bound there will be a weakened or delayed reaction and a late general reaction. We are thus enabled to protect the general organism from the influence of the tuberculin poisons by directing their action to less vital tissues, as, for instance, connective tissue, and we shall probably be enabled to make therapeutic use of the fact. Taking it for granted that the production of such receptors in the connective tissue will be of most advantage, and considering the numerous observations made by Holländer, Joseph and others, that certain forms of skin tuberculosis preclude tuberculosis of the lungs, we can understand⁸ that after an injection of tuberculin the local reaction can appear before the general reaction, or even that the general reaction that is to be expected, does not appear at all or is influenced by its progress. For some time past I have been enabled by intracutaneous injections of small doses of tuberculin, or through the inunction of tuberculin ointment, to obtain in patients with lung disease artificial skin foci. In my second edition of my "Ophthalmodiagnose"⁹ it is my intention to give more accurate reports of the fundamental principles involved in this therapeutic measure, but I shall not allow myself to be misled into reporting successful results too soon.

It can be easily seen how in this field purely theoretical are most intimately connected with practical results, of which the conjunctival reaction, the initial step in our observations, is the most palpable proof.

I should like to call the attention of veterinarians to the fact that the application of the conjunctival method in cattle presented points of extreme difficulty. In the experiments that I have made with the aid of the royal Prussian agricultural department, the principal difficulties have been overcome. It is to be hoped, therefore, that in the veterinary practice the conjunctival reaction will be developed in as exact a degree as in the human species.

SUMMARY

Let me give a summary of my remarks:

1. The subcutaneous and the cutaneous methods are specific reactions for tuberculosis. As they both demonstrate active and latent tuberculosis, their use is extremely limited for clinical diagnosis.

2. The positive conjunctival reaction shows only active tuberculosis.

3. The conjunctival reaction in clinically healthy individuals makes the suspicion that they are affected particularly strong.

4. A negative result in those manifestly tuberculous justifies a bad prognosis.

5. In advancing tuberculous disease negative reactions become more frequent.

6. A positive conjunctival reaction does not justify a good prognosis, but this is the case only in the so-

5. Ueber Ergebnisse der Komplementablenkung mit Tuberkelbazillenderivate als Antigen bei Tuberkulose und Infektionskrankheiten, Wien. klin. Wochenschr., 1908, xxi, No. 37, p. 1296.

6. Die Bedeutung der lokalen Tuberculinreaktionen für die Heilstättenfrage, Ztschr. f. Tuberk., December, 1908.

7. Die Bindungsverhältnisse der Organgewebe gegenüber Toxinen, Centralbl., 1908, xlvii.

8. c. f. Wolff-Eisner: Ophthalmodiagnose, Würzburg, 1908.

9. Issued January, 1909, by A. Stuber, Würzburg, and entitled "Frühdiagnose und Tuberkuloseimmunität."

called *Dauerreaction* (continued reaction), a form of the cutaneous reaction.

7. It is possible to create receptors in tissues that are indifferent as regards life, such as connective tissue, these receptors attracting tuberculin and localizing the toxic action. This observation is of therapeutic value.

SUPPLEMENTARY REMARKS

My paper could not include all the investigations concerning the theory of the action of tuberculin, especially the lytic theory of the tuberculin reaction. Some facts are given in the first edition of my book, which was published in New York by Wood & Co., Oct. 10, 1908; new facts will be found in the *Berliner klinische Wochenschrift*, 1908, No. 30, p. 317. The second German edition will be published as mentioned above.

When I read my paper at the meeting of the German Medical Society last week, the chairman pointed out that the name "ophthalmo-reaction" is a misnomer for several reasons. At the same time he stated my absolute priority. At the same meeting he said that I came to America to stand up for my rights. This was not my intention, because I thought that there was no necessity; but while in the library of the Rockefeller Institute reading about one hundred papers of the American literature concerning the matter, I found only Calmette mentioned. I claim that I made known the conjunctival reaction in a discussion of the first paper of von Pirquet on May 15, 1907, while Calmette made his communication to the Academy of Sciences, June 16. To Calmette belongs the credit of having greatly assisted in having the reaction quickly adopted by the profession.

There can be no question about these facts; Calmette himself points out that the paper of von Pirquet was the cause of his investigations, and this paper contains my communication about the discovery of the conjunctival reaction. It is not generally known that on the same day on which Calmette read his paper, Vallée also read a paper concerning conjunctival reaction in cattle in which he stated that his investigations were undertaken in connection with my discovery.

I am glad to state that there is no point of difference between Calmette and myself after his publication at the International Tuberculosis Congress in Washington, but only with his above-mentioned investigators. I would like to suggest to him the appropriateness of calling the reaction by the names of both authors.

Of greater importance to me than the question of the priority of the discovery of the reaction is the part I took in building up the scientific structure which is based on it and its application for the prevention of tuberculosis. I should be only too glad to work harmoniously with all those who have the same aim.

There is no difficulty in applying the reaction, but the matter is not as simple as it may appear. It took my collaborators several months before they were able to carry out my intentions. In cases in which there is a contradictory result with the reaction, it is absolutely necessary to compare the results with the findings of the physical examinations in order to avoid the wrong interpretation. I should like to have any one who can not exclude apparent contradictions bring the matter before me. Many a physician has come to me with a very critical point of view, but no one has departed unconvinced.

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Principles of Animal Nutrition.—The natural foods of all species of animals contain more or less proteids, mineral matter, fats and carbohydrates. No matter how widely the forms of food eaten by different kinds of animals may differ, they will be found to contain these essential basic nutritive elements. The problem of nutrition is the same in all animals so far as the principle goes, but there is a great variety of methods by which the necessary food elements are obtained and digested, each species having organs specially adapted for securing and digesting its natural food.—G. R. Pisek, in *Amer. Jour. Obst. and Dis. of Women and Children*.

THE SURGERY OF SYPHILIS*

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The time allotted to me will not suffice for more than a brief survey of the conditions demanding surgical intervention occurring in syphilis.

I first desire to emphasize the fact that many practitioners overlook most brilliant opportunities in the treatment of syphilis by regarding the disease too specifically. In other words, when they meet a condition which does not yield readily to antisiphilitic medication they appear to be helpless. As I will endeavor to demonstrate, there are many instances in which radical measures of a surgical character constitute the primary indication, internal medication occupying an almost secondary position in the cure of the given lesion. It is, of course, acknowledged that in such cases, once the lesion is under control, specific medication is a *sine qua non* to complete the cure of the constitutional condition and prevent recurrence of the lesion.

CHARACTER OF LESIONS WHICH REQUIRE SURGERY

The initial lesion *per se* rarely requires the knife. Time was when some of us were hopeful that excision of the initial lesion would at least modify the subsequent course of the constitutional condition. A large experience in this direction in an experimental way convinced me long ago that such hopes were ill-founded. An occasional case arises in which the induration of the initial lesion is very persistent, defying specific medication for a long period. Under these circumstances the persistence of the lesion may be very embarrassing, especially as regards the marital relation and the necessity of concealing the patient's condition from those about him. Here a clean free excision of the indurated area is sometimes of great advantage. It must be remembered, however, that unless the primary lesion has fully matured, induration is likely to recur in the incision, forming a chancre much more formidable than the original. The more thoroughly the patient has been treated by mercurials before the excision has been made, the less likelihood there is of its recurrence. The most frequent condition calling for surgical intervention in primary syphilis is concealed chancre or a mixed sore, with phimosis.

I long ago ceased delaying in cases of this kind, and am convinced that the risk of extensive infection of the wound in case a mixed sore exists, which, by the way, can not always be proven by autoinoculation, is much less than by allowing the lesion to progress without diagnosis or proper treatment. So far as my own experience goes, I have never had occasion to regret a dorsal incision of the prepuce for the purpose of freeing the glands and inspecting and treating the concealed lesion.

Marked edema occurring in the course of chancre sometimes demands multiple punctures for drainage. Where the edema is persistent and the lesion is true chancre, this method is preferable to allowing the edema to be replaced by connective tissue hyperplasia and extensive integumentary induration—circumstances which demand the knife later on.

* Read before the South Side Branch of the Chicago Medical Society in a Symposium on Syphilis, Oct. 29, 1908.