normal except that the layers were more than usually well defined by interposed bands of connective tissue. The greatest change was noted in the subserous coat. Here was a thick layer of a dense, fibrous structure, extending over the greater part of the fundus, representing Nature's effort to assist in supporting the great weight imposed on the stomach walls and to protect the peritoneum from injury.

In a few instances there was complete destruction of the mucous membrane over a well-defined surface, apparently from pressure by one of the large foreign bodies, probably for a long period of time. Here the base of the ulcer was formed by dense scar tissues.

The mucous membrane of the esophagus was greatly eroded and numerous ulcers were found, with extensive round-cell infiltration. The muscular layers were hypertrophied and sharply defined.

Foreign Bodies.—The weight of the stomach contents removed at autopsy, after repeated washings to remove all food material, was 2,268 gm. One needle was found in the esophagus and one in the lower border of the left lung. Below is a classified list of the articles removed, as shown in the illustration:

NAILS		
20-penny	5	
16-penny	21	
10-penny	24	
8-penny	80	
5-penny	113	
3-penny	210	
Total	453	453
SCREWS		
2 1/2 in.	4	
1 1/2 in.	11	
1 1/4 in.	5	
1 in.	9	
3/4 in.	6	
1/2 in.	7	
Total	42	42
BOLTS		
3/8 x 1 in.	3	
3/8 x 1 3/4 in.	1	
5/16 x 2 1/2 in.	1	
1/4 x 2 in.	1	
5/16 x 1 in.	3	
Total	9	9
MISCELLANEOUS		
Teaspoon handles	5	
Nail-file, 3 1/2 in.	1	
Pieces of steel, 2 3/4 in.	3	
Thimbles	5	
Salt-shaker tops	3	
Taps for 3/8 in. bolts	10	
Buttons	63	
Safety-pins	105	
Hairpins	115	
Carpet-tacks	52	
Common pins	136	
Large white-headed pins, 2 1/3-1 1/2	16	
Needles	37	
Broken coat-rack hooks, 2 x 1 1/4 in.	7	
String beads, small, 4 ft. long	1	
Larger beads, loose	70	
Small stones and pieces of glass	85	
Prune seeds	7	
Pieces of metal, combined weight 3 oz.	54	
Hooks and eyes	19	
Grape and other small seeds	148	
Total	942	942
Making a combined total of		1,446

This case is remarkable for the number and weight of the articles removed as well as for the size and peculiar forms of some of them; especially so when considered in connection with the fact that there had never been any symptoms suggesting trouble with the stomach.

Jaundice not Pathognomonic in Cholelithiasis.—The impression is prevalent that jaundice is pathognomonic of gall-stone. This is not so and much valuable time is lost in waiting for its appearance in patients suffering from cholelithiasis; 80 per cent. do not have it.—A. L. Wright, in *Iowa Medical Journal*.

THE DIAGNOSTIC VALUE OF LOCAL TUBERCULIN REACTIONS *

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Three years ago, on May 15, 1907, von Pirquet announced, at a meeting of the Berlin Medical Society, his discovery of the cutaneous tuberculin test, which consists of a superficial scarification of the skin through a drop of the old tuberculin and the subsequent appearance (in those afflicted with tuberculosis) of a characteristic papule at the point of the inoculation.

The demonstration of this new diagnostic procedure was made possible by the researches of von Pirquet (and B. Schick) into the general law of "allergy" or the altered reaction of the organism toward infective agents on their reintroduction.

The "early vaccinal papule" appearing on revaccination, as well as the cutaneous papular reaction, following the application of tuberculin to the skin of tuberculous individuals, were both ascribed by von Pirquet to the contact of the infectious agent with "antibodies" lodged in the integument as the result of previous infection. The "hypersensibility" of the infected organism, displayed on reinfection, was shown to be a factor in the production of the reaction, the mechanism of which is supposed to consist of the digestion of the introduced virus by the antibodies and the liberation of a toxic substance, with its inflammatory effect on the skin at the point of inoculation. While this and Wolff-Eisner's explanation of the local reaction (substituting "bacteriolysins" for "antibodies") are at present quoted by various writers, the entire question, in its theoretical and practical aspect, is still a subject of extensive investigation.

Contemporaneous with the announcement by von Pirquet of the cutaneous tuberculin reaction, came the demonstration by Wolff-Eisner and Calmette of a similar phenomenon in the conjunctivæ of tuberculous individuals, and this was soon followed by various modifications of the original von Pirquet test by a number of investigators, as Moro (percutaneous test with salve containing 50 per cent. tuberculin), Lignières (rubbing 5 to 6 drops of undiluted tuberculin into the skin), etc., all these tests being based on the now accepted idea of the wide distribution of specific antibodies in the organism of the infected individual.

The specific character of these local reactions found considerable substantiation: (1) in the post-mortem statistics of von Pirquet (demonstrating tuberculous lesions in 123 out of 124 children reacting to the cutaneous tuberculin test, and 161 negative post-mortem findings in 190 children with negative reactions) and in the post-mortem statistics of Wolff-Eisner, Calmette and others; (2) in the almost constant occurrence of these reactions in clinically tuberculous individuals, barring a large number of very advanced cases, miliary tuberculosis, complications by other diseases (as measles) and a few other conditions still unexplained.

The percentage of the positive conjunctival reactions in the clinically tuberculous is given as 92 by Calmette (2,894 cases), 90 per cent. by Wolff-Eisner (435 cases) and 80 to 95 per cent. by numerous other observers; the percentage of the positive cutaneous reactions in tuberculous adults is given by von Pirquet as 90.

* Read at the Sixth Annual Meeting of the National Association for the Study and Prevention of Tuberculosis, Washington, D. C., May 2-3, 1910.

Considerable difference between the occurrence of the conjunctival and cutaneous reactions was observed in the "apparently healthy" class, the cutaneous reaction being positive in 70 per cent., even at the age of 10 (von Pirquet), while of the apparently healthy adults only 15 per cent. respond to the conjunctival test (Wolff-Eisner).

This observation led to Wolff-Eisner's and Calmette's interpretation of the positive conjunctival reaction as occurring only in active cases of tuberculosis, the comparative infrequency of the positive conjunctival reaction in the "apparently healthy" class being used by Wolff-Eisner as one of the chief arguments in favor of this contention.

The relation between the positive conjunctival reaction and the activity of the tuberculous process has not been, however, so far established (neither has it been absolutely disproved) and the most that can be said, in the light of the present experience, is that a positive local tuberculin reaction, conjunctival or cutaneous, signifies probably in all cases a preëxistent tuberculous infection, without furnishing any conclusive information as to the active or latent character of the process.

The cutaneous test is recommended by von Pirquet for diagnosis of tuberculosis in children under 2 years of age, a positive reaction signifying an active tuberculous process, latent tuberculous lesions being rare in this period of life. The test, in his opinion, is not appropriate for adults, in whom positive reactions occur in a large percentage of cases, corresponding to the increasing frequency of latent tuberculous lesions, from childhood up to maturity and old age.

The percutaneous (Moro's) test has no material advantage over the v. Pirquet procedure (as stated by Bandelier and Roepke and others), and is less reliable because of such drawbacks as (1) the variable power of absorption of the skin of different individuals, and (2) a number of conditions varying with each operator (force used in application, etc.). The last objection is equally applicable to the cutaneous test; the manner of its application in all its details must be agreed on, the scarification never to exceed the mere removal of the superficial layer and all unnecessary injury to the skin to be avoided.

The conjunctival test, because of the possibility of its harmful effect in a certain percentage of cases, is not employed at present as extensively as before. With certain precautions, the occurrence of untoward developments may be reduced, however, to a minimum or possibly excluded altogether. In 6,303 conjunctival tests, as reported by Calmette at the International Tuberculosis Congress in Washington in 1908, he encountered three cases of phlyctenular keratitis, twenty of conjunctivitis and seventy-two prolonged reactions. Wolff-Eisner observed very few harmful effects with the use of a 1 per cent. solution of the old tuberculin in a large number of cases. Similarly, with the use of a 1 per cent. solution of old tuberculin in 500 cases (187 positive reactions; physiologic salt solution employed as diluent; cases of ocular disease and conjunctivitis, chronic or acute, excluded) I have seen only two instances of prolonged violent reactions, and these without any permanent injury to the eye. Further research as to the utility of the conjunctival test may, however, be well carried on in the future, particularly by animal experimentation, until all conditions determining the conjunctival reaction are more or less fully established and a harmless method of its application is evolved.

The local tuberculin reaction is but a link in a chain of evidence pointing to the tuberculous character of a suspected lesion and the value of its occurrence can be adjudged only by a comprehensive study of the entire evidence in each individual case; the clinical history, physical signs, etc.

Considerable clinical study and further extensive autopsy experience is still needed in order to establish the relation of the local reaction to the active and latent tuberculous processes and the various types of tuberculous disease. The conditions determining the reaction itself as well as the rapidity and degree of its development in various types of cases are still a fruitful field for research, if the local reaction is to gain the position of a practical diagnostic procedure.

During the last two years I have employed (at the Edward Sanatorium, at Naperville, Ill., and in my dispensary and private practice) the local and subcutaneous tuberculin reactions in a variety of tuberculosis cases. For the conjunctival test a drop of a solution of Koch's old tuberculin in an 0.8 per cent. sterile physiologic salt solution was used; for the cutaneous test, undiluted old tuberculin; dilutions of old tuberculin of various strengths (in 0.5 phenol solution) were employed cutaneously for differential study of results with various dilutions in the same individual. For the percutaneous test (Moro) an ointment consisting of equal quantities of Koch's old tuberculin and hydrated wool fat was employed.

In applying the conjunctival test the technic, as recommended by Wolff-Eisner, was closely followed; for the cutaneous reaction the superficial layer of the skin of the forearm (anterior surface) was gently scarified, by turning the von Pirquet inoculation needle through a drop of the old tuberculin; in applying the percutaneous (Moro) test a piece of the ointment the size of a pea was rubbed into the anterior surface of the forearm. The results were generally observed at the end of twelve and twenty-four hours and, after that daily for several days.

The conjunctival reactions were classified in their degree according to the scheme of Citron.¹ Similar classifications are offered by Comby, Edward R. Baldwin, and others. In this scheme + = means reddening of the caruncle and palpebral conjunctiva; ++ = means intenser reddening with involvement of the ocular conjunctiva and increased secretion; +++ = means intense reddening of the whole conjunctiva with chemosis, much fibrinous and purulent secretion, small ecchymoses, etc.

For the results of the percutaneous test, Moro's classification was used.² It is as follows: Slight reaction: single, isolated, more or less distinct, reddened spots, visible twenty-four to forty-eight hours after the inoculation and only on careful inspection, disappearing in a few days; well-marked reaction: papules indistinguishable in degree of hyperemia and exudation from those of the cutaneous inoculation, or coalescing red nodules on inflamed base; intermediate: thirty to fifty or more discrete, miliary nodules with reddened areola. The size of the papule, the degree of redness and elevation were recorded in describing the cutaneous reactions.

This paper deals with some of the features of the local tuberculin reactions, as influenced by the site of

1. Bandelier and Roepke: *Tuberculosis in Diagnosis and Treatment*, p. 24.

2. Bandelier and Roepke: *Tuberculosis in Diagnosis and Treatment*, p. 17.

the inoculation, the degree of the tuberculin dilution, the stage of the disease and the state of resistance; in a group of cases the local tuberculin reactions are compared with the results of the subsequent subcutaneous injections of tuberculin.

THE SITE OF THE LOCAL TUBERCULIN INOCULATION AS A FACTOR DETERMINING THE DEGREE OF THE REACTION

In applying the von Pirquet test to the skin, the degree of the reaction varies frequently, according to the site selected, in its extent, injection, elevation and rapidity of development. Exceptions, however, occur to the observations stated below, the reaction at times being more marked in locations where the reverse is usually the rule.

In all, 140 applications of tuberculin were made in fifty-five cases of pulmonary tuberculosis (mostly in the first stage of the disease). In ten cases tuberculin was applied simultaneously to the anterior surface of the arm and the interscapular space, the dilutions of 10 and 25 per cent. and undiluted tuberculin (2 inches apart) being used in a straight line in both locations. In five of these cases the reactions were slightly more pronounced in size in the interscapular space; in three there was practically no difference; in two the reactions were slightly more marked on the arm.

In twelve cases undiluted tuberculin was applied to the anterior surface of the forearm and the interscapular region on the same side. Invariably the reaction in the interscapular region was more extensive, generally redder and in two cases more elevated (the average diameter of the interscapular reaction 16.5 mm., forearm 10 mm.).

In twelve cases undiluted tuberculin was applied to the posterior surface of the left leg and anterior surface of the left forearm, with a resulting more marked reaction in the first-named location in nine cases (average diameter 12.5 mm., forearm 9.5 mm.). Slightly more marked reaction was observed on the left forearm in four cases, in which undiluted tuberculin was simultaneously applied to the anterior surfaces of left and right forearm.

In twelve cases, a 25 per cent. dilution of tuberculin was simultaneously used on the anterior surfaces of the thigh and arm, with a resulting more marked reaction on the thigh in nine cases (average diameter 12.5 mm., arm 9.5 mm.). More marked reactions were also observed below the mammary gland than on the anterior surface of the forearm.

It is evident from observations made by numerous investigators that the anatomic conditions of the skin and mucous membrane in various locations of the body (the histologic structure, circulation, lymphatic system, nerve-supply, etc.), as well as greater cutaneous sensitiveness displayed by some individuals to the slightest mechanical or chemical irritation, have their influence in determining the degree of the reaction; they are factors of importance and an accurate interpretation of the local reactions is impossible without giving due consideration to these varying conditions.

THE STRENGTH OF THE TUBERCULIN SOLUTION AS A FACTOR DETERMINING THE DEGREE OF THE CUTANEOUS REACTION

One hundred and four cutaneous applications of tuberculin, of various dilutions, were made, according to von Pirquet's directions, in forty-six cases of pulmonary

tuberculosis (twenty in the incipient stage, twenty-six moderately advanced). In thirty-four of these cases, a 25 per cent. solution and one of undiluted tuberculin were simultaneously applied to the anterior surface of the left forearm, 2 inches apart, the scarification being made with a separate instrument through a drop of each dilution. The resulting reactions were as follows: (1) size of the papule with undiluted tuberculin decidedly larger in fourteen cases (with undiluted tuberculin the diameter was 12.5 mm.; with 25 per cent. it was 7.5 mm.); smaller in twelve (with 25 per cent. 13.5 mm., with undiluted 9.5 mm.); same size with both dilutions in eight cases; (2) elevation of the papule, with undiluted tuberculin, greater in ten cases, smaller in six, same in eighteen; (3) redness, with undiluted tuberculin, more pronounced in four cases, same in thirty.

In twelve cases, a 10 per cent. dilution, a 25 per cent. and undiluted tuberculin were simultaneously applied to the anterior surface of the left forearm. The resulting papule was larger in size, with undiluted tuberculin, in six cases; larger, with 10 per cent. in four; the same with all dilutions in two. The elevation was more marked with undiluted tuberculin in six, with 10 per cent. in two, the same in four. Redness was more pronounced with undiluted tuberculin in eight, with 10 per cent. in two, the same in two.

The manner of the application and the actual amount of tuberculin absorbed are seemingly important factors in determining the degree of the reaction.

In all our cases, an attempt was made to make the scarification superficial and uniform, with all dilutions. The drop was left undisturbed for five minutes after the inoculation, the excess of tuberculin around the point of inoculation being removed at the end of that time.

A more reliable interpretation of the cutaneous reaction may be possible with an improved technic, in which a small, measured quantity of tuberculin should be used for cutaneous inoculation, under conditions facilitating its complete absorption.

THE ANATOMIC EXTENT OF THE DISEASE AND THE STATE OF RESISTANCE OF THE INDIVIDUAL AS FACTORS DETERMINING THE DEGREE OF THE LOCAL TUBERCULIN REACTION

From the experience of numerous observers we know that, as a general rule, reactions on application of tuberculin grow less pronounced and occur less frequently with the anatomic progress of the disease from the incipient to the far-advanced stage. The "antibody" theory of tuberculin reactions explains this by the gradual failure of the organism to respond to tuberculin stimulation. The anatomic extent of the disease is, however, not always indicative of the coexistent state of resistance of the individual. In numerous cases, with most extensive signs, particularly in those in which the process is very chronic and the general condition is favorable, the local tuberculin reaction is frequently very pronounced, while the reaction fails or is very slight in a certain percentage of anatomically incipient cases.

In statistics covering thousands of cases, the classification "first," "second," "third" stage is synonymous of course with the gradual impairment of resistance and decline of response to tuberculin, from stage to stage (as various factors counterbalance each other in large groups of cases). In observation of individual cases, however, this power or failure of response to local tuber-

culin application is frequently at variance with the stage of the disease.

I append here, as an example, an experience with a group of cases classified according to stage³ and observed for periods of one to two years subsequent to tuberculin application. This group included a number of advanced cases characterized by chronicity of process and favorable general condition.

In 165 cases of pulmonary tuberculosis (ninety-nine incipient, thirty-six moderately advanced, thirty far advanced), the conjunctival reaction was positive (traces of reaction included) in 67 per cent. of the incipient, in 33 per cent. of the moderately advanced and 67 per cent. of the far advanced; the cutaneous reaction was positive (diameter above 5 mm.) in 69 per cent. of the incipient, 41 per cent. of the moderately advanced and 67 per cent. of the far advanced.

The average diameter of the inoculation papule in the first stage cases was 12 mm.; second, 13 mm.; third, 11.5 mm.; the comparison showing very little variation for the three stages of the disease.

With the conjunctival test, more pronounced reactions were obtained in the second stage (48.5 per cent. of the positive cases more than +) than in the first (28 per cent. more than +). Very slight difference in the degree of the percutaneous reaction was observed in forty first stage cases and twenty-nine second. These figures have reference of course only to a limited number of cases divided according to stage; their analysis suggests, however, that the mere anatomic extent of the disease does not give a definite idea of the resistance of the patient and sensibility that may be displayed on application of tuberculin.

Dividing these 165 cases into three groups, regardless of the anatomic extent of the disease—(1) progressive cases, good general condition, (2) stationary, good general condition, (3) far advanced, hopeless—the percentage of the positive reactions is readjusted in the following way: first class, conjunctival, positive in 75 per cent., cutaneous in 70 per cent.; second class, conjunctival, positive in 35 per cent., cutaneous in 82 per cent.; third, conjunctival, trace in 10 per cent., cutaneous, positive in 33 per cent.

Observations on various groups of cases lend support to the general idea that the tuberculin reaction fails with the gradual exhaustion of the defensive elements of the organism, and the anatomic extent of the disease is important only in the measure in which it is operative in producing this condition. This is offered as an observation, familiar to many, without any attempt at evolving a general diagnostic or prognostic scheme based on the degree of the local tuberculin reaction. Experience, however, tends to substantiate in a large number of cases the dictum of Wolff-Eisner, that a negative local tuberculin reaction, in the presence of decided physical signs, is of unfavorable augury, pointing as it does to the inability of the organism to counteract the toxins of the tubercle bacilli; while a positive reaction means simply that the defensive elements still exist, the battle is still being fought, but the result cannot be predicted.

REPETITION OF THE LOCAL TUBERCULIN TEST DURING THE COURSE OF THE DISEASE: INTERPRETATION OF THE RESULTING REACTION

It is evident from the consideration of the conditions determining the occurrence and the degree of the local

reaction, that various factors influence the result of the repeated local tuberculin test. Of these the following may be considered:

1. The hypersensibility occasioned by a previous inoculation of tuberculin into the skin or conjunctiva is a factor of considerable importance. Fritz Levy⁴ was the first in Germany to call attention to the fact that, on the second application of the conjunctival test, hypersensibility is manifested in 70 per cent. of cases, the condition becoming operative three days after the first instillation; this phenomenon was observed also on repetition of the cutaneous reaction. The exact duration of this hypersensibility is still undetermined. Experience shows that in a large percentage of cases the conjunctival test repeated in the other eye is positive, while the first reaction was negative, and the same is true of the cutaneous test. To what extent and in what manner the first introduction of tuberculin influences the result of the second application at another site, is still a question open to further investigation. We know, however, that the local changes produced by the first application of tuberculin are operative for a considerable period of time, as manifested by the re-inflammation of the local tuberculin reactions on subcutaneous injection of tuberculin, months after the local test was performed. In 90 subcutaneous injections of tuberculin in a corresponding number of incipient closed cases of pulmonary tuberculosis, with the resulting characteristic constitutional reaction in 80 cases (doses O.T. from .0002 c.c. to .005 c.c.), re-inflammation of the conjunctival reaction occurred in 54 cases, cutaneous in 74. The re-inflamed conjunctival reaction was more pronounced than the original in 46 cases, same in 6, slighter in 20; cutaneous, more pronounced in 46, same in 8, slighter in 20. The size of the re-inflamed cutaneous spot in many cases was two to five times larger than the original, and this with the injection done two to four months after the application of the local test. Approximately the same experience was obtained with the percutaneous (Moro) test. The re-inflammation of the reaction spots may be due to the presence of a larger number of antibodies or bacteriolysins near the cutaneous or conjunctival focus of deposited tuberculin. In what measure or manner this focus of deposited tuberculin influences the result of subsequent tuberculin inoculation at another cutaneous or conjunctival site is still a matter of speculation.

2. The interval between the first and second applications of tuberculin. Improvement in the general condition of the patient as a factor influencing the degree of the repeated reaction. With the progress of a large proportion of tuberculosis cases under sanatorium or home care toward improvement, it is interesting to note the difference between the results of the first and the following local tuberculin tests as applied at various intervals. In 52 cases of pulmonary tuberculosis (34 incipient, 10 moderately advanced and 8 far advanced) the conjunctival test was repeated in the other eye at intervals not exceeding one month from the date of the first application, with the resulting increase in the degree of the reaction over the first test in 30 cases out of 52 (this includes also cases found negative on the first application and positive on the second); of 26 cases, in which the second instillation was performed from one to six months later, an increase in the degree of the reaction was noted in 8, suggesting the explanation that the larger number of more pronounced second reactions in the first month following the first application is dependent on the hypersensibility resulting from the first instillation, a hypersensibility, the duration of which is yet undefined.

Approximately the same result was obtained with the cutaneous test: increase in the degree of the reaction in 22 cases out of 38, with repetition of the test during the first month; and in 18 cases among 42, with the second test applied from one to five months later.

In analyzing the effect of the improvement of the general condition of the patient on the result of the repeated

3. Provisional Scheme of the National Association for the Study and Prevention of Tuberculosis.

4. Wolff-Eisner, Alfred: The Ophthalmic and Cutaneous Diagnosis of Tuberculosis. Chapter on the Repetition of the Reaction.

local tuberculin test, the proximity of the dates of both tests shows itself again to be a factor of great importance. With a gain of less than 10 pounds in weight, subsequent to the first tuberculin application, the second conjunctival reaction was more pronounced in twenty cases out of thirty-two; with a gain of 10 to 30 pounds, in fourteen out of thirty-eight; an increase in the degree of the cutaneous reaction occurred in the first class of cases in eighteen out of thirty-six, in the second class in twelve out of twenty-six, the smaller increases in weight occurring in the first few weeks subsequent to the first tuberculin application, the greater increases in the following four to five months.

A proportionately larger number of more pronounced second reactions was observed in incipient cases; the least deviation in the far advanced, regardless of gain in weight.

It may be expected that the improvement in the general condition of the patient, presumably productive (always?) of an increase in the defensive elements of the organism, would show itself in a more vigorous reaction on the introduction of tuberculin, and this is probably the case; in many instances, however, a mere increase in weight may not be coincident with a greater production of defensive antibodies, as shown by the progressive course of a large percentage of tuberculosis cases regardless of enormous increases in weight.

The relative influence of (1) the state of hypersensitivity resulting from the first tuberculin application, and (2) of the increased resistance (as suggested by improved nutrition, recession of the physical signs, etc.), on the result of the repeated local tuberculin test, is still a matter in need of further investigation.

In studying the results of the local tuberculin tests, when applied (1) to various groups of tuberculosis cases (differing in extent and activity of the process, state of resistance, previous use of tuberculin, etc.) as well as (2) at the various stages of improvement or further progress of individual cases, it becomes evident that numerous conditions operate in determining the occurrence and the degree of the resulting reaction. If the present theory of the local tuberculin reaction (based on the assumption of the wide distribution of specific antibodies or bacteriolysins in the infected organism) is correct, all the above-mentioned conditions are factors to the extent to which they stimulate the production of these specific substances and influence the sensibility of the organism to the infectious agent and its toxins.

THE DIAGNOSTIC SIGNIFICANCE OF THE LOCAL TUBERCULIN REACTION AS CONTROLLED BY A SUBSEQUENT SUBCUTANEOUS INJECTION OF TUBERCULIN

1. In 30 incipient pulmonary closed cases in which the conjunctival reaction was positive (21+, 9++), and the cutaneous at the end of forty-eight hours fully developed and strong (average diameter 13.5 mm., pronounced redness and distinct elevation in 60 per cent.), the percutaneous positive in 14 out of 18 (4 slight, 4 intermediate and 6 marked), the subcutaneous test was positive in all: six responding to 0.2 mg. O.T., eighteen to 1 mg., six to 3 mg.; average rise of temperature, 0.9 F.; symptoms in 24; focal reaction in 4; average dose of O.T., 1.2 mg.; marked reinflammation of the conjunctival and cutaneous reaction in 30 (18++, 12+; average diameter of the reinfamed cutaneous spot, 27.5 mm.).

2. In 12 cases of the same class, with the conjunctival = trace in 12, the cutaneous rapid and marked in all (average diameter 13.5 mm.), the percutaneous positive in 9 (3 slight, 4 intermediate, 2 marked), the subcutaneous test was positive

in ten: 9 cases responding to 1 mg. and 1 to 3 mg.; focal reaction in 1; symptoms in 8; average rise of temperature after the injection, 1.5 F.; average dose of tuberculin used, 1.4 mg., still showing that regardless of the doubtful conjunctival reaction in these cases, the subcutaneous test was positive with approximately the same dose of tuberculin as in the first group of cases; reinflammation of 6 conjunctival reactions (6+) and 9 cutaneous (average diameter 42 mm.).

3. In 24 cases of the same class, with the conjunctival trace in 24, the cutaneous slight (average diameter 7.5 mm.), the percutaneous positive in 2 out of 7 (one trace, one slight), the subcutaneous test was positive in 21 cases (6 responding to 1 mg., 6 to 3 mg., 6 to 5 mg. and 3 to 10 mg.); average dose of tuberculin, 4 mg.; average rise of temperature after the injection, 0.6 F.; focal reaction in one, symptoms in 15; reinflammation of 8 conjunctival reactions (3 traces, 5+) and 13 cutaneous (average diameter, 12.5 mm.).

4. In 12 cases of the same class, with the conjunctival positive in all (7+ and 5++), the cutaneous positive in 6 (average diameter 6.3 mm.) and negative in 6 (positive on repetition; average diameter 9.5 mm.), the percutaneous applied to 3 (3 traces), the subcutaneous test was positive in 9 cases (one responding to 0.1 mg., 2 to 0.5 mg., 2 to 3 mg. and 4 cases to 5 mg.); average rise of temperature after the injection, 1.5; average dose of tuberculin used, 3 mg.; no focal reactions observed; symptoms in 7; reinflammation of 6 conjunctival (3+, 3++) and 4 cutaneous (average diameter, 25.4 mm.).

5. In 9 cases of the same class, with the conjunctival test negative (6+ on repetition in the other eye), the cutaneous rapid and marked (average diameter 16.9 mm.), the percutaneous applied to 3 (3 slight), the subcutaneous was positive in 9 (3 cases to 1 mg. and 6 to 3 mg.); focal reaction in 2; symptoms in 9; average rise of temperature after the injection, 0.9 F.; average dose of tuberculin, 2.3 mg.; reinflammation of 4 conjunctival reactions (3+, 1++) and 6 cutaneous (average diameter, 25.4 mm.).

6. In 12 cases, with the conjunctival negative in 9, trace in 3 (6 of the negative+ on repetition); the cutaneous negative in 9, trace in 3 (5 of the negative became positive on repetition, with 9.5 mm. as the average diameter); the percutaneous positive in one out of 4, the subcutaneous test was negative in 6 (to 5 mg.) and positive in 6 (one to 1/5 mg. and 5 to 5 mg.). The average rise of temperature after the injection was 1.6 F.; average dose of tuberculin, 4.7 mg.; symptoms in 4; focal reaction in one (with 1/5 mg.); reinflammation of 5 conjunctival (2 trace, 3+) and 4 cutaneous (average diameter, 9.5 mm.).

An analysis of these cases points to the high probability of positive subcutaneous reaction with correspondingly smaller doses of tuberculin in a large number of cases reacting promptly and distinctly to the cutaneous test; hence the relative value of the marked cutaneous reaction as a positive test in cases in which the subcutaneous test cannot be applied for various reasons.

The focal reaction occurred in only 10 per cent. of cases tested subcutaneously; adding to this number an experience with thirty more positive hypodermic tests in incipient pulmonary cases, we get in all 12 per cent. of focal reactions under the average conditions of observation.

In the light of the autopsy experience of von Pirquet, Wolff-Eisner, Calmette and others, the cutaneous tuberculin reaction in adults discloses tuberculosis only in the anatomic sense; the test, with its present method of application, sheds little or no light on the active or latent character of the tuberculous lesion.

Where a focal reaction is desired (and that can be obtained in only a certain percentage of cases) the cutaneous test cannot supplant the hypodermic. It can be used, however, as a preliminary diagnostic measure, being absolutely harmless, compared with the conjunc-

tival test, and more reliable than the percutaneous reaction, which fails in a large number of cases.

CONCLUSIONS

1. A vast amount of clinical experience, gathered by numerous observers and substantiated in a proportion of cases by post-mortem findings, points to specificity of the local tuberculin reactions.

2. The verdict of to-day is that a positive reaction, following the local application of tuberculin (conjunctival or cutaneous) signifies the existence of a tuberculous focus somewhere in the organism, without giving a definite idea of the active or latent character of the process.

3. Reactions occurring on application of tuberculin differ in their degree according to various sites of the body selected as points of inoculation; a comparative study of the results obtained by numerous observers is possible only with a clear description in each individual case of the site practiced on.

4. The results of cutaneous tests performed with various dilutions of tuberculin contribute to the belief that the actual amount of absorbed tuberculin is a factor of importance in determining the degree of the reaction.

Sufficient evidence has not been produced so far to substantiate the claim that a positive conjunctival reaction signifies active tuberculous disease. The possibility, however, exists, that activity of a tuberculous process may be a factor in causing a positive local reaction with a minimal dose of tuberculin, under certain conditions of the power of response. Hence the failure of the conjunctival test in the clinically healthy and its uniform occurrence in the clinically tuberculous (barring the very advanced cases, etc.).

If this contention has any foundation, a positive cutaneous reaction ought to be possible in active cases of tuberculosis, with minimal doses of tuberculin (greater dilutions).

Further experience with the cutaneous test, with various dilutions of tuberculin, applied to various groups of cases, with a perfected technic, assuring thorough absorption of a definite quantity, may possibly lead to some method of differentiation of active and latent cases.

5. Cases of suspected tuberculosis, in which the cutaneous reaction is rapid in development and marked in degree, generally respond readily to the subcutaneous injections of minimal doses of tuberculin; hence the relative value of the cutaneous tuberculin test in cases in which the employment of the subcutaneous test is for some reason contraindicated.

6. The subcutaneous test remains the decisive diagnostic procedure in doubtful cases of tuberculosis, particularly if a focal reaction is desired. The possible unfavorable effects of this test in some cases may be avoided by the use of small doses of tuberculin (initial 1/5 or even 1/10 mg.), according to the age and condition of the patient.

7. The work of von Pirquet, Wolff-Eisner and Calmette opened a new field for further clinical and laboratory research, out of which may be evolved a safe, reliable method of diagnosis of the obscure and the very incipient cases of tuberculosis.

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Chancre.—The syphilitic chancre should never be cauterized. The destruction is often extensive and the result frequently undesirable.—A. G. Nadler, in *Yale Medical Journal*.

THE MODERN TREATMENT OF SYPHILIS, WITH REFERENCE TO THE RECENT SYNTHETIC PREPARATIONS*

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The enormous number of cases of late syphilis and parasyphilis prove that the classical treatment of lues by the old remedies, as usually employed, is inadequate. This cannot altogether be attributed to a lack of potency on the part of the drugs, but rather to a combination of factors referable to the physician or the patient, or both. It is not my desire to discuss the shortcomings of my colleagues, but rather to call attention to some of the causes which contribute to the failure to control this disease. Of these, there are two which should be especially emphasized, namely, the tendency to regard syphilis as a mild infection with laxity in carrying out its treatment, and secondly, the lack of familiarity with the possibilities of the specific drugs.

For years it was taught in one of our large institutions that the malady is an insignificant one. The dissemination of such teaching among hundreds of students certainly was not in the interest of luetic patients. Views on the benign nature of syphilis are often promulgated by men who are familiar with only one side of the affection. They encounter, for example, chronic ulcerative processes of the skin in patients otherwise in good health and parents of healthy children, and entirely forget that there is a more serious side. An observation of a large number of cases in private and hospital practice from various parts of the country has impressed me with the want of familiarity of the general practitioner with the manifestations of the disease. This is emphasized by the surgical operations frequently performed for luetic affections of the joints, tongue, larynx, testicle, etc., under the mistaken diagnosis of tuberculosis, malignant disease or some other infection. Again, ulcerating and destructive lesions are permitted to proceed to extensive deformity or loss of function before the nature of the trouble is even suspected. This is perhaps due to the fact that we do not give students in our medical schools a comprehensive knowledge of syphilis. Its teaching is scattered through so many departments that when the graduate leaves his school he is possessed, it is true, of a fragmentary knowledge of the cutaneous, nervous, surgical and visceral manifestations he has been taught by the respective chairs, but he has altogether failed to appreciate its significance or to obtain a grasp of the subject. It would seem that the establishment of a chair in syphilology, which would enable one to teach in a comprehensive manner what the infection may do, would be a decided advance in our pedagogic methods.

In seeking to account for the vast amount of uncured syphilis, we must remember, too, that the patient often is culpable in his lack of cooperation. He either fails to carry out properly directions as to treatment and hygiene, falls a prey to the various quacks, pathies, etc., or after outward manifestations disappear neglects all treatment and reverts to his old habits and indulgences.

In addition, there is the fairly large group of so-called unrecognized syphilis, which, according to Fournier's

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