

ridden in a hospital with a chronic affection diagnosed as myocarditis, died from that disease on the second day of treatment. There appears to be no possible connection between the treatment and the patient's death.

The question comes up as to who shall receive the Pasteur treatment. Any person who has been bitten by a rabid animal, or who has fresh open wounds or scratches contaminated with the saliva of such animals, should receive the treatment. The possibility of danger from the milk of rabid cows is remote, since inoculation from the sound digestive tract does not take place. Persons bitten by animals showing suspicious symptoms should have the animal put under observation for 10 days, whenever possible. Though rabies among animals is very prevalent in California, human deaths will be exceedingly few if the rules here laid down with regard to the methods of diagnosis in animals and the prompt treatment of human beings, are followed.

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COMMENTS ON TUBERCULIN.*

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The program demands from me a paper on tuberculin tests. Such a paper would be largely academic, mere quotation from so-called authorities. With your permission, I will, instead, endeavor to give a rambling talk on certain phases of tuberculin that have impressed me in my daily work. No man has any right to express an opinion upon a subject he has not investigated. My interest in this subject dates from Koch's first announcement, because I was then suffering from tuberculosis. Experience soon convinced me that tuberculin was too dangerous for me to use in general practice. For some years I wrote and spoke against it. About fifteen years ago I began to restudy it and to use it—cautiously. I have always been prejudiced against its use, but for a long series of years I have made from 7,000 to 10,000 injections annually. Regarding many points connected with it I have been unable to arrive at definite conclusions. Some few questions I have definitely settled in my own mind.

To those interested I wish to recommend two books, recently published. One is a special plea for the use of tuberculin in treatment; written by one of the most enthusiastic advocates of the remedy, our own Pottenger. The other, by Hamman and Wolman, of Johns Hopkins, presents a judicial view of our present knowledge of tuberculin, and will bear reading and rereading.

The friends of tuberculin advise its use for three purposes, diagnosis, prognosis and treatment.

A fourth purpose, prophylaxis, has been more recently emphasized; notably by Von Ruck and Friedman. This prophylactic idea is by no means new. The present theory is that inoculation of very young children, prior to infection, will prevent infection. Obviously, this is the most important purpose to which tuberculin can be put. So far, the preparation to be used, the methods and conditions of use, the repetition of dose and other essential problems are embryotic in the minds of the pathfinders. Obviously, too, the value of any method of prophylaxis can only be determined after a lapse of twenty or thirty years.

My time limit precludes reference to other than salient points. The various preparations of tuberculin now exceed one hundred. Their several originators laud them separately. The users of tuberculin prefer one or another, just as various syphilographers prefer different preparations of mercury. Those in common use are O. T., T. R., B. E. and, perhaps, I. K. and watery extract. I will premise three propositions, regretting lack of time to debate them.

1st. All forms of tubercle bacilli, human, bovine, avian, even those infecting cold-blooded animals and fish, are one. Their differences depend upon adaptation to environment. This function of adaptation is common to other forms of parasitic vegetable life.

2nd. All forms of tuberculin are one, no matter how prepared. Each of them must possess the elements essential to the production of a tuberculin reaction, otherwise it is not tuberculin.

3rd. The action of tuberculin is specific. That is, no reaction will ever occur, no matter what dose may be administered, unless the subject of that dose is tubercular. Please note this statement does not necessarily imply active tuberculosis.

Practically all my work is sent to me by other doctors. Some of them write that a given patient has or has not tuberculosis, because he has or has not reacted to some tuberculin test. None of them ever describe the symptoms of the reaction. Few of them name the test. The latter is important information; for instance, if the doctor has made the conjunctival test and has secured a reaction, a second application to the same eye might result seriously. Likewise, the dose given subcutaneously should be stated. Tuberculin tests are invariably given for diagnosis or prognosis. No test should ever be made for the former purpose when the diagnosis is obvious without the test. If T. B. can be demonstrated; if the physical signs are conclusive; if the lesion is manifestly tubercular to the eye, as in the larynx, there is no need of further evidence. The tuberculin test is not justifiable. If the diagnosis is doubtful further evidence is requisite. The tuberculin test, however, is not conclusive in these doubtful cases. It is not necessary to discover whether the patient has ever been infected. It is needful to know whether there is active disease, whether the condition existing is menacing and requires treatment. From sixty to eighty per cent. of adults have been infected but only a much smaller per-

* Read at the Forty-eighth Meeting of the Southern California Medical Society, May, 1913.

centage have existing tubercular disease. Almost all who have been infected will respond to some dose or other; the exceptions will be referred to later. The test is an index of infection, not of disease, clinically speaking. Reaction only implies previous infection, not existing disease. The test, therefore, may raise more doubts than it allays. Many have held that the time, the severity or the character of the reaction is the determining factor; or, perhaps, all combined. Those who are willing to base diagnosis and prognosis upon tuberculin tests depend on the theorem that "the higher the grade of hyper-sensitiveness the more acute the infection." In my experience this is only true in a very general sense. I agree with those who maintain that "unfortunately, the degree of hyper-sensitiveness does not vary in direct proportion to the activity of the disease, but depends upon so many unknown factors that we are unable accurately to formulate its conditions." When we observe that healed lesions, or patients artificially immunized or far advanced cases may or may not react; that tests usually fail in acute miliary, meningeal and floral tuberculosis, and during the co-existence of acute infectious diseases, we feel obliged to pause and reflect. Reaction following a minute dose is supposed to signify a higher degree of hyper-sensitiveness, but that may occur in the presence of a healed lesion. A delayed reaction may occur in acute active tuberculosis. Severe general reaction may be noted when no anatomical lesion can be detected. I am sure that early diagnosis of tuberculosis is more of an art than a science; that tuberculin tests are an aid but do not reveal certainties. They are, doubtless, of more value to the expert than to the tyro, as are all other diagnostic measures. Tests have been applied to all parts of the body, the rectum, vagina, urethra, scalp, toes, etc. A few have become standard. Tuberculin reactions are various, uncertain and an unknown quantity to many medical men. We note three major divisions.

1st. The local reaction. It assumes many forms. An erysipelatous blush may appear; it may be one-quarter to several inches in diameter, painful or painless, flat or raised. It must not be confounded with erysipelas or streptococcus or other infection, any of which may follow a skin puncture or abrasion. It may consist of pimples or papules, having a pale or red base. It may be in the form of an induration, circumscribed or diffuse, beneath the skin, at the site of the needle point. One only learns the appearance and feel of these local reactions by experience. The novice may mistake many accidental conditions for the real thing. Pus never forms. Pus always means some other infection. Indeed, I have never seen even a pin-point abscess from any hypodermic injection I have given. A local reaction is never dangerous, no matter how severe it may be. It is rarely painfully annoying, but is likely to be tender to the touch.

2nd. The focal reaction. It is best observed in the larynx or in joint or skin lesions. It is

characterized by redness, heat, swelling and pain; or by each, some or all of these accompaniments of inflammation. It only occurs at some focus of infection, hence its name. In the lung it is manifested by fresh rales, with increase of excretion; maybe increased dulness. Any evidence of increased activity in the lung denotes focal reaction. Of course, the increase of activity may be merely a coincidence. We are too apt to assume "post hoc, ergo propter hoc." The debate anent the danger of tuberculin tests has centered around the focal reaction. Some have argued that only good can result; that the stimulus is followed by destruction or encapsulation of the focus. Others claim that focal reaction invariably disseminates the disease, at least to contiguous parts. Personally, I have never observed permanent ill results. At the same time, I would object to the production of a focal reaction in my own lung.

3d. The general reaction. Fever is its main characteristic, but fever, also, may be a coincidence. It appears in from four to thirty-six hours, preceded or not by a chill. There may be focal pain, or general aching, or various degrees of malaise. The reaction may be so mild that the patient fails to observe it, or so severe that his physician becomes alarmed. We often commit the error of assuming that because we have injected tuberculin the symptoms which follow are due to it. All consumptives are subject to just such general symptoms and only long experience will enable us to attribute them to the real cause.

The tuberculin reaction is specific, therefore does not depend on the form of tuberculin used. Different observers contend that some particular form is best for a given test, especially for the conjunctival test. Personally, I use O. T. for all. As happens with any potent substance, the mode of its introduction into the body seems to influence the severity and character of the resultant symptoms. The subcutaneous test, made by injecting tuberculin under the skin, produces typical reactions, local, focal and general. The intracutaneous test, made by injecting tuberculin into the skin, will usually produce typical local but less marked focal and general reaction. I will not refer to the ascending doses used to produce these reactions nor otherwise describe them, because details can be found in the text books. The cutaneous test, known as Von Pirquet's vaccination, produces beautiful local results, but still fewer focal and general symptoms. In using this test it must be remembered that the skin seems to be unequally sensitive in various parts of the body. The percutaneous test, the product of Moro's ointment, which consists of equal parts of O. T. and lanolin, produces a peculiar form of local reaction and, usually, no other result. The conjunctival test seems to restrict its action to the conjunctiva. I have ceased using it owing to a couple of severe inflammatory reactions due, probably, to the presence of pathogenic cocci in the eye when the test was made. Any of these tests, however, may produce any grade of reaction in hyper-sensitive patients.

Secondary reactions may puzzle us. Thus, if a cutaneous test is made, with or without reaction, and weeks or months later a test be made elsewhere on the body, the site of the first test may exhibit a marked local reaction, providing the second test reacts. We may, indeed, term this result a focal reaction and assume that the first test has established a focus without the introduction of living bacilli. This view will, of course, be combated by many, for it introduces a new and an unknown element of danger, as well as a bizarre idea of pathology. I have several times noted this phenomenon.

A brief reference to treatment. A large number of patients sent to me have received tuberculin, but how much only the Lord knows. The milligram and its fractions constitute the basis of dosage. One tells me he has taken one C.C. and is surprised that I do not know what dose he has had. Another talks of No. 1 or of No. 6, all of which is nonsense. One C.C. of pure O. T. contains 1000 Mgrs. of tuberculin. One C.C. of Parke, Davis & Co.'s T. R. contains one Mgr. but one C.C. of Von Ruck's T. R. contains ten Mgrs. and one C.C. of Cutter's contains two Mgrs. It is confusion confounded. The best exposition of this subject is a short paper and table by Dr. Geo. H. Kress, to be found in the *Journal of the A. M. A.* for April 29, 1911. Buy the crude preparation and make your own dilutions. Make them with the same observance of asepsis that you would if arranging for a laparotomy. You will then, at least, know what you are giving and how much. Dr. Kress' paper is indispensable to any one who wishes to begin the use of tuberculin.

A patient was sent to Banning with a box containing six vials of Cutter's tuberculin and directions to use one after the other; also to call on King, if need be. The need was great. Whether the poor fellow began at the wrong end of the series I do not know. I do know that I have never seen such a deplorable result. I would as soon think of giving a patient six vials of graduated rattlesnake venom, with directions to inject them one after another. One doctor wrote to inquire what I would charge to administer two injections of tuberculin per week, stating that if the price was above a certain figure the patient could only afford one per week. Such people make a fetish of tuberculin. No doctor on earth can tell, in advance, whether the patient will require a dose every day or one each month. The effect, positive or negative, of the last dose is the only criterion that can determine the time or the amount of the next dose. I give an injection every day to all to whom I give tuberculin. The injection may consist of tuberculin or of salt water; that is my affair. I must have the patient under daily observation. One doctor told a patient to come to me and receive tuberculin for three or four weeks, when he would be well, and wrote the same statement to me. No one ever has been cured of an active tuberculosis in four weeks. Friedman to the contrary notwithstanding.

The cure is a matter of months, perhaps years; and tuberculin, if useful at all, is only one of the essentials. In my Sanatorium I would drop tuberculin before any one of a number of other measures. Another doctor sent his wife to me on condition that I should not administer tuberculin to her. Still another insisted that I must not give more than the dose he specified. In my institution I am master of the situation. Patients obey or leave. I never care much which, because I seek results and cannot get them if the patient is permitted to dictate measures. The dose of tuberculin is never a fixed quantity. To give one vial of so-called No. 1 and to follow it by No. 2 and 3 and 4, seriatim, is foolish. The patient who may need one Mgr. to-day may require only 1/1000 of a Mgr. next week.

The one absolutely essential thing is never to do harm. If harmful reactions cannot be avoided then quit using tuberculin. At the beginning of treatment one never knows the degree of sensitiveness existing. I therefore, always start with a dose of one hundred millionth of a Mgr., which, in my experience, has never produced perceptible reaction. This dose is slowly increased, not in accordance with any fixed scale or at fixed intervals of time, but as the patient will bear. The maximum dose I do not know. Doses of several hundred Mgrs. have been reported. I have never exceeded fifty Mgrs. I now have three patients in my Sanatorium who are taking ten Mgrs. daily. None of them have reacted from these large doses. Two of them were pretty far advanced when they came, a year ago, but are now arrested cases. The third was an early case and is now free from signs or symptoms of disease. I am able to report as large a percentage of cures as any I have seen published, from reputable sources, although I make it a rule not to report any patient cured unless well three years after the cessation of treatment, but how much of my results may be attributed to tuberculin I do not know.

Many who have successfully used tuberculin insist upon some scientific explanation of its action. The fact that equally qualified men have advanced quite different theories is evidence that our knowledge is imperfect. The same statement is true of most therapeutic agents. I have practiced medicine long enough to know that the science of to-day may be the rubbish of to-morrow. Our knowledge is ever increasing, never complete. My own use of tuberculin is empirical and based upon clinical experience alone. Of one thing I am assured. Tuberculin is a two-edged sword and no one can learn to use it safely by simply reading about it. After having given, perhaps, 100,000 injections I still meet with surprises and am eager to learn more about it. I would not decry any form of scientific investigation but, as a matter of fact, we know so little about the so-called physiological or any other action of tuberculin that we are not justified in basing treatment upon any theory of it.