

THE VALUE OF TUBERCULIN IN PULMONARY TUBERCULOSIS.¹

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IN considering the value of a remedy in the treatment of any disease it is obviously necessary to be certain that the cases treated are examples of that disease. The only certain test during life that a person is suffering from pulmonary tuberculosis is the presence of tubercle bacilli in the sputum, and all statements dealing with the value of tuberculin in that disease which are based upon any other test are for the particular purpose fallacious. The results of a prolonged and careful trial of old tuberculin in pulmonary tuberculosis conducted by eight physicians at the Brompton Hospital in the year 1891 were summarised thus: 1. That tuberculin, if introduced under the skin, speedily causes inflammatory changes in and around tubercular lesions. 2. That the action of tuberculin in lung tuberculosis is to cause breaking down of the tubercular masses and of the lung tissue in the neighbourhood, and thus to promote the formation of cavities. That this is the case is proved by (a) the appearance of lung tissue in the sputum, where it was previously absent, and (b) by the physical signs of cavity replacing those of consolidation. 3. That tuberculin increases the amount of expectoration, but that there is no proof that it diminishes the number of tubercle bacilli contained therein, for in some of the patients, they apparently increased under its use. 4. That in many cases tuberculin injections are followed by a distinct extension of disease, as evidenced by physical signs. 5. That the reactions due to tuberculin are exhausting to the patient and cause loss of weight and strength. 6. That this treatment is specially contraindicated in lung tuberculosis accompanied by pyrexia, as likely to convert intermittent into continuous pyrexia. 7. That lung excavation accompanying the use of tuberculin may be followed by contractile changes, due to increase of fibrosis. This was shown in two of the cases under observation, where diminution of cough and expectoration and gain of weight took place. 8. That the tuberculin did not favourably influence the course of the disease in the majority of cases; that in some the effects were detrimental; and that even in the stationary and improved cases it was difficult to ascribe any distinct improvement to the injections which might not have been equally attained under the treatment ordinarily employed in the hospital.

The public have recently been led to believe that tuberculin in the form and doses at present administered is a remedy of great value in the treatment of this disease, and that those who are opposed to its general use are either actuated by prejudice or old-fashioned and unable to appreciate the recent advances of medical science. The provisions of the National Insurance Act relating to tuberculosis are now being, in part at least, carried out, and a system of so-called dispensaries is being established throughout the country, and at these and in sanatoria tuberculin treatment is being extensively employed by medical men, many of whom have had but little experience of its use and of the great dangers attending it. This appears to me to be such a grave situation that it is the duty of all who have had a prolonged hospital experience of consumption and its treatment to come forward and state their views.

In an interim report on tuberculin treatment recently presented to the consulting staff of the King Edward VII. Sanatorium at Midhurst by Dr. N. D. Bardswell, the medical superintendent, of which he has communicated an abstract to this Conference, there is a section dealing with the suggested use of tuberculin in dispensaries and in general practice throughout the country. In this section the history is given as regards tuberculin treatment of 10 patients prior to their application for admission to the sanatorium, and from these histories it is apparent that in the 23 years which have elapsed since 1890, when Koch first announced his discovery, tuberculin, although possibly it has

in some cases become an agent for good, has lost none of its capacity for evil. All these cases, which have been seen during the past 12 months, will be subsequently published. Every single statement contained in the Brompton Hospital Report of 1891 of the ill-effects of tuberculin in cases attended with fever and in cases in which reactions occurred is exemplified in the history of these 10 cases, and their number could easily have been greatly increased. One of these cases had not been examined by the physician responsible for her treatment with tuberculin; she had never seen him; she had been "treated by post." The tuberculin and the syringe had been received through the post. She had had written instructions as to when she was to give herself an injection and what the dose should be. Her temperature charts were to be sent to the physician. It is to be hoped that this is not one of the modern advances in medicine which we old-fashioned people are expected to approve. I will endeavour in a few sentences to epitomise these cases.

CASE 1.—Male, adult. Tuberculin treatment continued for four months in spite of violent reactions. "When not in bed with fever, too exhausted to do anything." On admission very extensive disease.

CASE 2.—Male, adult. Tuberculin treatment for 14 months with "a fair number of reactions of moderate severity." "Steady loss of weight, amounting to 28 lb." Very extensive disease; markedly febrile on admission.

CASE 3.—Female, adult. Six weeks' sanatorium treatment, followed by arrest and convalescence. When afebrile and walking several miles daily, tuberculin treatment commenced. Followed by slight and severe reactions culminating in a febrile attack lasting eight weeks; on admission, extensive disease. After 14 weeks at Midhurst no appreciable improvement.

CASE 4.—Female, adult. Five months' sanatorium treatment without tuberculin followed by apparently complete recovery. During a relapse, tuberculin treatment commenced and continued for four months in spite of numerous severe reactions; active disease of lungs and larynx. No appreciable improvement after admission.

CASE 5.—Female, adult. Eighteen months' tuberculin treatment by post. Numerous severe reactions, ultimately followed by continuous fever. On admission, very extensive and active disease. Favourable progress after two months of complete rest.

CASE 6.—Female, adult. Chronic disease of four years' duration, with periods of complete arrest. Three courses of tuberculin, the last, accompanied by severe reactions, extending over a period of three months, during which she was very ill. No substantial improvement after admission.

CASE 7.—Female, adult. "After six months' treatment by rest, convalescence was in a considerable measure established." Then followed a course of tuberculin with severe reactions, ending in acute pleurisy with effusion. No improvement after admission.

CASE 8.—Female, adult. Onset in 1910. Recovery after spending a considerable part of 1911 in a sanatorium. Relapse after pregnancy and miscarriage. Tuberculin treatment begun in 1912. Ten injections; last eight followed by severe reactions. Malaise, hæmoptysis, weakness, and faintness throughout treatment. Treatment discontinued after tenth inoculation on account of cardiac weakness and continued faintness. Temperature fell after admission.

CASE 9.—Female, adult. Onset in February, 1913. Tuberculin treatment commenced at once. No reaction to first five inoculations; sixth and all subsequent inoculations followed by severe reactions; pyrexia became continuous. "For last four weeks of treatment felt very ill and tired, lost weight, cough and sputum doubled in amount." On admission evidence of extensive and active disease.

CASE 10.—Female, adult. At Midhurst from August to November, 1912; discharged "with signs of arrested disease, in excellent general health, 10 lb. above average weight and walking six miles daily." A few weeks later began tuberculin treatment under the advice of a practitioner. From the first inoculation the temperature rose and very soon became definitely febrile. With the fever were associated constant malaise, shivering, nausea, and not infrequently vomiting. After the thirteenth inoculation the temperature for a week ranged between 101° and 103° F. Tuberculin was then discontinued, but for ten weeks the patient was confined to bed. Ultimately recovered after prolonged rest at the seaside.

I could supplement this experience with much of my own of a like character, but will restrict it to a single recent case, as it illustrates what is now taking place possibly all over the country.

CASE 11.—A man, aged 30 years, a foreman labourer, got wet through in November, 1911. Four days later he shivered. He remained at work, but developed "a cold upon the chest." Subsequently he noticed gradually increasing shortness of breath, especially elicited by playing a wind instrument. In February, 1912, he was found to have a pleural effusion on the left side; he was in bed for three months. In March, paracentesis of the left chest was performed and four pints of fluid removed. The operation was repeated in May, and six pints were removed. In September tubercle bacilli appeared in the sputum. In October he was admitted into a sanatorium. Tuberculin treatment was commenced a few days later, and injections were given weekly for three months; no reactions appear to have been produced.

This man was not aware that there was any question as to the value of this treatment, or that I had any opinion on the matter. I only discovered by chance towards the end of the interview that he had been submitted to tuberculin treatment. The following conversation then took place. He said, "I was the only one who could stand it." "How many others were treated?" "About 20." "Why was it

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omitted?" "In some it would bring on a small hæmorrhage. It made some feel very bad—bodily ill, headaches; they couldn't eat their food." "What was the effect upon their temperature?" "Used to send it up." "There were only about four of us who could stand it week after week, but I was the only one who stood it all through." He left the sanatorium on Jan. 9th, 1913, and had no tuberculin treatment up to June 14th, when a second course was commenced at a county tuberculosis dispensary, and is now in progress. His weight at the commencement of this course was 10 st. 12 lb. On July 6th it was 10 st. 8 lb. No reactions have been produced; he has had no appetite for seven weeks; states that he will be on the highest dose next week.

When I saw him on July 14th, 1913, the left pleura was so full of fluid that the heart's apex was in the right mammary line. There was evidence of tuberculous infiltration of the left upper lobe and of the right upper, middle, and lower lobes. This case is not cited to prove that this man has been injured by the treatment, as, although it has certainly done him no good, everything that has happened might have occurred if he had not been subjected to it. But I would ask you to think of this travesty of "sanatorium treatment" in which all that is being done for a patient in such a condition—"an ambulant case"—is an attempt to immunise him against tuberculin! This is, indeed, "fiddling whilst Rome is burning"!

The reports of the results obtained at the Frimley Sanatorium of the Brompton Hospital by the system of graduated labour introduced there by Dr. Marcus Paterson and those of the King Edward VII. Sanatorium at Midhurst during five years without the use of tuberculin are, in my opinion, absolutely trustworthy and unbiased. The same can be said of the interim report from the Midhurst Sanatorium on the results of the use of tuberculin, but it must not be forgotten that it deals with only 130 *selected* cases, whereas the results of sanatorium treatment at Midhurst without tuberculin are based upon the experience of 764 *unselected* cases. It is unnecessary to dwell on the fallacies attending any statement of percentage results when the numbers dealt with are small and the cases are selected. The figures, as Dr. Bardswell has already informed the Conference, show that whilst the use of tuberculin has had no appreciable effect upon the general results, there has been a difference as regards the cases discharged free from bacilli. This difference is stated as an increase of 5 per cent., a very small margin, which, with larger numbers, may increase or disappear; but it is sufficient to justify a continuance of the treatment, provided that every possible precaution is taken against harm being done.

The experience so far gained at King Edward VII. Sanatorium lends no support to the statements that the temperature in a febrile case can be reduced and the activity of the disease diminished or arrested by the use of tuberculin, or, indeed, that any obvious effect at all upon the patient's strength, weight, temperature, pulse, cough, expectoration, or appetite can be observed to follow its administration during a "reactionless course." I would invite you to contrast the careful scientific presentation of the case contained in the report from King Edward VII. Sanatorium just referred to with the many statements you have doubtless read, and I will venture to read a paragraph which I wrote in 1897 and published in 1898, which seems to have a bearing upon the present situation. The "announcement" refers to Koch's original paper: "The great interest excited throughout the world by this announcement is still fresh in our memories; the lamentable lack of judgment, of self-control, and of those critical faculties which should characterise the members of a scientific profession, displayed by many upon that occasion, may serve as a warning for the future."

Some of the conclusions at which I have arrived are as follows:

1. The use of tuberculin in any form in the treatment of pulmonary tuberculosis is not free from danger. Even with exceedingly small initial doses which are gradually increased the limit of tolerance may be suddenly reached and a reaction may occur.

2. Its use is absolutely inadmissible in any case in which there is fever.

3. Fever is, as I have always taught, the guide to the activity of the disease; therefore, the rôle of any remedial agent which can only be employed in afebrile cases is necessarily very limited.

4. General reactions should be avoided. If one occurs the treatment should at once cease. To continue tuberculin injections with increasing doses in spite of reactions is unjustifiable and dangerous to the life of the patient.

5. Focal reactions are also dangerous, as they cannot be controlled. They may occur in the neighbourhood of obsolete lesions, such as it is the object of all treatment to produce. I have reported a case in which, under treatment with old tuberculin, a patient expectorated four calcareous particles, one of which was surrounded by pigmented lung tissue, and also a small portion of lung tissue. Subsequently signs of excavation appeared at the apex of one lung. Calcareous particles are "sleeping dogs" which should not be disturbed.

6. The treatment likely to be attended by the best results should follow the lines of rest and exercise originated by Dr. Otto Walther at Nordrach, and further developed by Dr. Marcus Paterson at the Frimley Sanatorium of the Brompton Hospital.

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THE PLACE OF TUBERCULIN IN TREATMENT IN RELATION TO OTHER METHODS.¹

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TUBERCULIN has twice held the confidence of the medical profession in the treatment of tuberculosis, once stimulated by its discoverer, Robert Koch, and once by the researches of Sir Almroth Wright on opsonins, of von Pirquet and others on skin sensitiveness, and of many workers on anaphylaxis. Following each of these waves of enthusiasm there has been a relapse in confidence characterised by a good deal of scepticism on the part of those who have tried it. During the whole time, however, from its discovery to the present there have been those of great authority, like Trudeau in America and Philip in Edinburgh, who have never wavered in their belief in its value, in their persistent search for the truth underlying the method of administration, the choice of cases to which it shall be given, and the mode of operation of this poison in the animal body.

We are just now following the second wave of enthusiasm. This has washed to the shores of our knowledge some new truths concerning this vexed question. We are still, however, divided into two camps: those who believe—and among these are many who are best able to judge—and those who are filled with unbelief. There are so many factors entering into the problem of tuberculin administration, from the standpoint of the chemical composition of the patient and of the tubercle bacillus, and of the vital functions of both, as well as from the standpoint of the varying intelligence of our profession, to say nothing of the methods of the manufacturers who produce and exploit it, that it is small wonder that we have no universal law or opinion concerning it. I will try in this short address to outline in a general way what is known of tuberculin in its relation to the treatment of tuberculosis, to point out the flaws in our knowledge and methods of administration, to suggest the future necessities, and to give my own conviction as to its value and place.

Tuberculin has little influence on the non-tuberculous animal. It produces almost no protection against future infection with the tubercle bacillus, and acts only indifferently in the production of those phenomena known as anaphylactic which follow the introduction of a second dose of a foreign protein substance into the animal body. In the majority of tuberculous animals, however, tuberculin produces the changes which we know as "reaction." These changes, when pronounced, are characterised by sickness and fever, by inflammation at the point where the injection has been made, and also about the various tuberculous processes in the body. The dose of tuberculin to produce reaction cannot be given by mouth, but must be given directly into the tissue, and is best given by a hypodermic needle, either hypodermically or intradermally. If the reaction produced by the tuberculin is not too severe, it is often followed by an improvement in the patient's

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