PERSONAL EXPERIENCES IN THE DIAGNOSIS AND TREATMENT OF CONDITIONS APPARENTLY OF TUBERCULAR ORIGIN.[1]

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WITH SOME REMARKS

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Mortality from tuberculosis is rapidly decreasing. Morbidity from this cause is still, however, high. One cannot but be impressed by the number of applicants for life insurance who have a history of T.B. confirmed or suspected. Insurance companies, probably rightly, rely greatly upon mortality statistics for their ratings: hence they are alive to the possibility of T.B. in young applicants of light weight, with a bad family history. They are prone to treat applicants of older ages comparatively leniently. Statistics, however, from their very nature, cannot be up to date, and their source is sometimes open to question. Even physical signs are not very reliable, for, as Dr. Brady points out, signs resembling T.B. can be produced by other organisms besides T.B. To make a really accurate prognosis we require a skiagraphic report and a tuberculin test in all cases of doubt. It is probably impracticable for insurance companies to obtain these data, but without them liens or ratings will often be placed on some of the younger lives which should be taken as standard, and many older lives will be accepted as standard which should be liened or rated.

Though a thorough examination may not be practicable from a life insurance standpoint, in private and hospital practice we are on a different footing, for here we have ample time and means for making a satisfactory diagnosis. A diagnosis of tuberculosis in the early or easily curable stage can only be made by having recourse to the tuberculin reaction, skiagraphy and a record of symptoms. If we wait till we are able to make our diagnosis by physical signs we are making that diagnosis too late. If we wait till T.B. appears in the sputum we are very much too late.

To take up these three aids to diagnosis, viz., the tuberculin test, skiagraphy and a study of the symptoms in order:—

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The Tuberculin Test.

I do not propose to discuss the merits of the various tuberculin tests, for they all appear to give similar information. They all furnish very accurate data as to hypersensitiveness or not to tuberculin, and so are an indication as to dosage in tuberculin therapy. To a lesser extent they give some indication as to activity. At Margaret Street we use the modified Von Pirquet test which was introduced into this country by Dr. H. A. Ellis [1]. It is very simple and is sufficiently accurate for practical purposes.

In order to obtain some data on the value of this test as to activity, I made some observations on officers attending Margaret Street Hospital [2]. I first examined the case sheets of fifty-eight officers who had tubercle bacilli in the sputum and who were, therefore, presumed to be actually tubercular. They all reacted to 1 : 500 or to 1 : 100 dilutions. I next took the cases of 209 officers in whom the sputum was negative to T.B.; of those who reacted to 1 : 500, 84 per cent had clinical or radiographic evidence of activity; of those who reacted to 1 : 100 but not to 1 : 500, 64 per cent showed activity; of those who reacted to 1 : 10 only, and not to higher dilutions, less than 1 per cent showed any evidence of activity. I have since had ample opportunity of confirming these findings, and I am convinced that a modified Von Pirquet which gives reactions with dilutions of 1 : 100 or higher is an indication that there is a probability of an active tubercular focus somewhere. It is often argued that as most of us at one time have been infected with T.B., the majority of adults will react to tuberculin. In my experience this is not the case, provided the test is only trusted in the higher dilutions and provided there be other evidence of the patient being tubercular. To say a man is tubercular because he reacts to tuberculin and has no other evidence of ill-health beyond the tuberculin reaction is manifestly absurd. On the other hand, a negative reaction to tuberculin or a reaction to a 1 : 10 dilution only practically rules out tuberculosis.

X-ray in Diagnosis.

I do not propose to say much about this. It is essential that the readings be made by an expert in skiagraphy. X-rays are useful in checking the progress that is being made under tuberculin. My general impression is that, from an X-ray point of view, hilum gland tuberculosis improves to a remarkable extent under tuberculin therapy. The same improvement is not seen with regard to the fibrotic condition. Does not this point to fibrosis, in some cases, being due to a mixed infection rather than to T.B. pure and simple? If so, it must be an argument in favour of dealing with mixed infection as well as with T.B.

Symptoms.

Amongst the most important symptoms in the early stages are: Loss of weight, pain sometimes referred to the abdomen, dyspepsia, loss of energy,

neurasthenia, protracted colds, hæmoptysis, rapid pulse, low blood-pressure. Of course, many of these symptoms simply point to a toxæmia and may be due to other causes than T.B., but a combination of certain of them with a well-marked modified Von Pirquet points to the probability of early T.B. The indication is then for treatment by tuberculin. In the more advanced stages, with definite physical signs and T.B. positive sputum, I have found treatment with tuberculin, on the whole, to be disappointing.

A word as to blood-pressure. Though it is the rule to have a low blood-pressure in early tuberculosis, it is by no means always so in the more chronic cases. I found [3] that the average systolic blood-pressure in 100 tubercular officers was 135 millimetres; if there was much fibrosis it tended to be considerably higher. Dr. Francis Brook [4] states that rises in blood-pressure may be due to sepsis. I have frequently found in studying insurance reports that a history of fairly recent sepsis is frequently accompanied by high blood-pressure. The question is not purely academic. It is a further indication that the fibrosis may be due to so-called secondary organisms, and this may have an important bearing on treatment.

With regard to colds in the tubercular [5], I have not had good results by treating them with stock vaccines, and of 28 cases 16 did well, but in 12 the colds became worse and I gave up the treatment. I have since realized that my dosage was probably too large initially, and too rapidly increased. The same care is needed in administering a "cold" antigen to the tubercular as with tuberculin itself.

Below I give a résumé of my results of cases treated with tuberculin during the past six years.

T.B. Positive Cases.

Twelve cases. Four were definitely improved, 4 slightly or not at all improved, 4 died.

As far as it is possible to judge no case was made worse by tuberculin, at the same time I do not consider it is the most satisfactory way of treating open tuberculosis. The chief danger in open tuberculosis is the mixed infection and it seems reasonable to treat this by autogenous vaccines. Dr. Brady deals with the rationale of this method of treatment at the end of this paper.

T.B. Negative Cases but with X-ray Evidence of Lung Changes.

Thirty cases. Of these 11 showed fibrotic changes of which 4 were definitely active, 7 not active; 14 showed changes in the hilum glands, 2 definitely active, 4 not active; 4 cases showed mere haziness; and 1 case showed a cavity not active.

Results.—Twenty-two cases were treated by tuberculin injections, eight by some form of tuberculin inunction. Every case improved to a remarkable extent. Certainly more brilliant results were attained by injections, but the simplicity of the method of inunction far outweighs the problematical

advantages of injection. I am of the opinion that the high state of immunity obtainable by injection is unnecessary in the majority of cases of this class.

T.B. Negative Cases and X-ray Normal.

Twenty-seven cases. These consisted of a miscellaneous group. Enlarged cervical glands 4, constant cough 7, loss of weight 2, T.B. abdomen 1, neurasthenia 4, bronchitis 2, colds 2, "run down" 2, hæmoptysis 1, T.B. testicle 1, T.B. spine 1.

Results.—Eight were treated by injection, the remainder by inunction. All did remarkably well. I never now treat this class of case by injections.

Tubercular Asthmas.

I would define a tubercular asthma as asthma occurring in a patient who reacts definitely to tuberculin or has X-ray or other evidence of T.B., and in whom there is no discoverable cause of the T.B. beyond the tubercular factor. The following are the main characteristics of tubercular asthmatics :—

(1) They all react to tuberculin and, as a rule, they are not particularly sensitive; for example, of 51 cases who were tested 10 per cent only reacted to 1 : 500, 60 per cent to 1 : 100, and 30 per cent to 1 : 10.

(2) The blood-pressure is about normal for the age.

(3) *Skiagraphic Appearances.*—I find that of these 51 cases 66 per cent were normal to X-rays, in 11 per cent there was definite fibrosis, in 7 per cent the hilum glands were enlarged and in 16 per cent the apices were definitely affected. The comparatively large number of apical affections is significant.

(4) *The age of onset* seems to vary considerably. I have seen cases in which it began at the age of 4, and others in which it started at over 50.

(5) A definite family history of asthma is rare, but of T.B. not uncommon.

(6) The general health of these patients is not, as a rule, good. They seem to be suffering from a mild degree of toxæmia. This is contrary to what one usually finds in other forms of asthma in which the patient is often in good health between the attacks.

Treatment.

Tuberculin seems to act almost as a specific, though the effect is seldom immediate; there is at first an improvement in health, then the attacks get less severe and finally cease. At one time I used tuberculin injections but equally good results are obtained by skin medication in the form of "Santubin" ointment. Out of fifty-one cases only four could be said to be failures. I agree with Dr. Gordon Tippett [6] that better results are got by combining tuberculin therapy with a mixed vaccine of other organisms grown from a swab of the tonsils or from the sputum.

Conclusions.

Up to about a year ago I had come to the following conclusions :—

(1) That tuberculosis in the early stages or when quiescent is amenable to treatment by tuberculin.

(2) That for practical purposes some form of skin medication is preferable to injections.

(3) That open tuberculosis should not be dealt with by tuberculin.

(4) That asthma of tubercular origin is commoner than is usually supposed and is particularly amenable to tuberculin therapy.

(5) That treatment of catarrhal conditions in the tubercular by stock vaccines is unsatisfactory.

(6) That tuberculin has little effect on fibrosis and that frequently after a course of tuberculin the X-ray shows evidence of activity.

In other words the value of tuberculin, though great, was more limited than, at one time, I supposed. I began more and more to confine my field to very early cases and to tubercular asthmas. About a year ago I had the good luck to meet Dr. Brady. We are now working in collaboration. The general principle on which we work is for Dr. Brady to deal with the mixed infection, tuberculin, when thought desirable, being administered by skin medication. The results have been most happy and are much better than when the treatment was with tuberculin alone.

References.

[1] "The Diagnosis of Tuberculosis by Tuberculin," *Lancet*, 1916.
[2] "Sidelights on Tuberculosis," *Journ. Roy. Army Med. Corps*, 1926.
[3] *Ibid.*
[4] "Actinic Practitioner," 1929.
[5] *Brit. Med. Journ.*, 1924.
[6] *Ibid.*, 1933.

Remarks by Dr. Brady on the Secondary Infections in Pulmonary Tuberculosis.

Pulmonary tuberculosis is very rarely a pure infection when diagnosed; there is usually a second involvement due to the invasion of the T.B. focus with the micro-organisms of the respiratory tract. The history of pulmonary tuberculosis points very much to this fact. It usually begins with a cold, tonsillitis, whooping-cough or bronchitis. So much so that certain commentators are inclined to the opinion that the T.B. condition is secondary to the pathological disturbance caused by the other organisms, an opinion which is open to a considerable amount of justified discussion. One fact must be kept in mind and that is, that the tubercle bacillus itself is less virulent than any of the other organisms involved in the tubercular focus.

The authorities who hold that the other organisms in a T.B. sputum are leading a saprophytic existence in the broken-down material prepared for them by the T.B. leave themselves open to strong criticism, as all those organisms have the same morphological characteristics as those

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The authorities who hold that the other organisms in a T.B. sputum are leading a saprophytic existence in the broken-down material prepared for them by the T.B. leave themselves open to strong criticism, as all those organisms have the same morphological characteristics as those

which produce bronchitis, pneumonia and similar pathological lung conditions. Every organism in the respiratory tract is latently pathogenic. It only requires a lowering of resistance to turn it into an active pathogenic one. One or more of the catarrhal producing organisms are always to be found in tubercular sputum. They can be seen phagocyted by desquamated alveolar cells and polymorphonuclear leucocytes. The presence of a polymorphonuclear leucocytosis indicates an infection other than T.B. These microbes can be grown from a piece of sputum, the outer layers of which have been washed away.

If these microbes are infecting the lung, inoculation with a vaccine made from them should produce focal reactions. These certainly do occur. Most of the physical signs of pulmonary tuberculosis can be caused by these organisms.

The commonest organisms isolated from tubercular sputum are a mixture of the Gram-negative cocci of the *Micrococcus catarrhalis* group and streptococci. In a large number of sputa examined for T.B. the presence of a *Streptococcus longus* is very often seen. When this organism is found with the tubercle bacillus, the prognosis is nearly always bad. I am convinced that to do any good with a case like this an antigen dealing with both organisms is essential.

Now in the treatment of T.B. by the immunization method one must also realize that at the focus of infection the T.B. is also present. This being so, to get the best possible results one must provide an antigen for the T.B. as it is necessary to increase the resistance to each and every one of the organisms at the focus of infection. Tuberculin gives one the antigen for the tubercle bacillus. Every physician has his own tuberculin.

If there be much bronchial catarrh and sputum one likes to get the treatment for this under way before starting immunization with tuberculin. The initial dose of the antigen should be very small, i.e. one million of a streptococcus and one million of a staphylococcus. The effect of the vaccine is a rapid change for the better in the physical phenomena and especially in a reduction of the evening temperature. I have seen the small dose above referred to reduce a temperature of 100° to 96° F. in twenty-four hours. A negative phase with these small doses is often absent.

In estimating the value of this form of treatment one looks for the following results: (1) Disappearances of symptoms and physical signs; (2) a negative sputum after repeated examination; (3) disappearance of X-ray signs of activity.

A case illustrating the methods of treatment employed :—

Mrs. V. G., aged 36, April, 1929.

History.—Patient had tubercular glands at the age of 21. Her father was accidentally killed and at the autopsy actual tubercular glands were found in his lung. Six months ago the patient began to feel tired, lackadaisical and lost interest in life. She developed a cough with catarrh, etc.

The chest was carefully examined but no clinical signs of tuberculosis were present.

Examination of sputum revealed tuberculosis, and an X-ray plate revealed a very small cavity in the left apex which was drained by a bronchus—whence the tubercle bacillus in the sputum.

The secondary organisms were *Str. longus, M. catarrhalis, M. flavus.*

The antigen was made in the following strengths 1 (million *Str. longus*) + 1 (million *M. catarrhalis*) + 1 (million *M. flavus*), 2 + 2 + 2 and so on, doubling the dose on each successive occasion, unless a reaction occurred, i.e. rise in temperature, malaise, etc., when the next dose was reduced, leaving two clear days interval after all signs of reaction had settled down.

The tuberculin dose was given alternately with that of the antigen, taking the same precaution regarding reaction.

A plate taken after six months treatment, showed the cavity very much reduced in size with much clearer parenchyma.

A plate taken finally showed the cavity completely healed. At this time there was no sputum. The patient had put on about two stone in weight and was carry out her usual occupation.

The last report in February, 1933, showed patient maintaining improvement without any sign, clinically, of the condition.

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