As Colonel Gunter points out, tuberculin injections undoubtedly lead to auto-inoculations from tuberculous foci, and this consideration should be regarded as ruling out tuberculin treatment in all cases in which auto-inoculations are already taking place to an excessive degree.

It is undoubtedly true that tuberculin has become much less popular of recent years in the treatment of pulmonary tuberculosis, and that it has been altogether discarded in many sanatoria and hospitals devoted to the treatment of this disease. My personal opinion is that, used with great care in carefully selected cases, it tends to give valuable results; but whoever attempts to use it should have the fullest and clearest knowledge of the strength of the preparation which is employed and also of the precise state of the patient whom he is attempting to treat.

SIDE-LIGHTS ON TUBERCULOSIS.

By LIEUTENANT-COLONEL F. E. GUNTER, D.S.O., M.D.

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WILKINSON says ("The Principles of Immunization in Tuberculosis") "every few years we should recast our ideas and bring our knowledge up to date."

In the past we have spent too much time over the physical signs in the lungs. If we wait till the appearance of definite signs of activity in the chest we have waited far too long. To give an example of this. Recently I examined the case sheets of fifty-eight ex-officers treated at Margaret Street Hospital. These officers all had tubercle bacilli in the sputum. In only 40, or 69 per cent, were there physical signs of activity, an error of 31 per cent.

The X-ray readings were somewhat better—53, or 91 per cent, showed activity from the radiographer's view-point. Still there was an error of 9 per cent.

With the modified von Pirquet, as described in detail below, all or 100 per cent reacted to dilutions of old tuberculin of 1 in 500 or 1 in 100.

The Modified von Pirquet Test—The value of the old von Pirquet reaction is not great. It is too sensitive and, consequently, the reaction occurs in too many healthy adults to be of real use in diagnosis. For this reason at Margaret Street Hospital we use the following modification:—

Old tuberculin is made up in the following dilutions: 1 in 10, 1 in 100, 1 in 500. Normal salt solution is used as a control. A drop of each solution is placed upon the forearm of the patient. The skin beneath the drops is scarified with a very sharp scalpel so as to draw blood, and a dressing is applied. Two days afterwards the arm is examined for signs of reaction.
The test as used in this manner is of value, as may be seen from the accompanying table:

**Effect of the Modified von Pirquet on 209 Ex-Officers under Observation for Tuberculosis.**

<table>
<thead>
<tr>
<th>Highest dilution in which a positive reaction was obtained</th>
<th>Number who gave reaction</th>
<th>Showed clinical or X-ray activity</th>
<th>Percentage of proved activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1—500</td>
<td>65</td>
<td>55</td>
<td>84</td>
</tr>
<tr>
<td>1—100</td>
<td>117</td>
<td>75</td>
<td>64</td>
</tr>
<tr>
<td>1—10</td>
<td>22</td>
<td>2</td>
<td>under 1 per cent</td>
</tr>
<tr>
<td>Negative</td>
<td>5</td>
<td>nil</td>
<td>0</td>
</tr>
</tbody>
</table>

(It is hardly necessary to say that the figures under heading "Highest dilution" are "end reactions," i.e., 1 in 500 reacted also to 1 in 100 and 1 in 10 and 1 in 100, also to 1 in 10, and the 1 in 10 did not react to higher dilutions.)

From the above table it will be gathered that dilutions of 1 in 10, or stronger, are useless for diagnostic purposes, but higher dilutions, such as 1 in 100, or 1 in 500, are of decided value.

Unfortunately, I cannot give control figures, but I know that many patients who come to Margaret Street for diagnosis are negative, clinically, radiographically and also to the modified tuberculin test. I, myself, use only one form of tuberculin, "tuberculin albumose frei," both for testing and treatment. I hold no special brief for this preparation, but it has served me well and I see no reason to change it. The great thing is to get your tuberculin from a reliable source, such as Meister, Lucius and Brinning.

**The Subcutaneous Test of Koch.**—I used to employ this constantly, but I find now that I can get quite sufficient information for practical purposes from the modified cutaneous test, especially if taken in conjunction with X-ray findings.

**Blood-pressure Readings.**—It is sometimes stated that a high systolic blood-pressure is against the diagnosis of tuberculosis. It has very little influence. The average systolic blood-pressure in 100 of the above-mentioned officers was as follows: T.B. +, 135. T.B. −, but signs of activity, 140. T.B. −, but no signs of activity, 130. From a reading of the X-ray reports, I find that in cases in which there is much fibrosis there is a tendency to higher blood-pressure, and this is what one would expect.

**Weight.**—This is of importance. "The American Medico-Actuarial Mortality Investigation," vol. v, 1914, gives the following table:

<table>
<thead>
<tr>
<th>Age of insurance</th>
<th>Ratio of actual to expected deaths from T.B., taking 100 per cent as normal 5 to 20 lb. under weight</th>
<th>5 to 20 lb. over-weight</th>
<th>5 to 20 lb. over-weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>15—24</td>
<td>186 per cent</td>
<td>114 per cent</td>
<td></td>
</tr>
<tr>
<td>25—29</td>
<td>116 &quot;</td>
<td>96 &quot;</td>
<td></td>
</tr>
<tr>
<td>30—34</td>
<td>100 &quot;</td>
<td>87 &quot;</td>
<td></td>
</tr>
<tr>
<td>35—39</td>
<td>92 &quot;</td>
<td>88 &quot;</td>
<td></td>
</tr>
<tr>
<td>40—44</td>
<td>77 &quot;</td>
<td>89 &quot;</td>
<td></td>
</tr>
<tr>
<td>50 and over</td>
<td>73 &quot;</td>
<td>79 &quot;</td>
<td></td>
</tr>
</tbody>
</table>
That is to say, in the young subject light weight is of importance but lessens in significance with age. It is of special import if there be a history of mortality from tubercle bacilli in the parents. The Americans consider that in men over six feet two inches the mortality is greater.

**Family History.**—From the mortality tables it would not appear that a bad family history is of significance in people over 45 years of age. The death-rate in those insuring from 15 to 25 is actually less with a tubercular history in one parent than when a brother or sister is affected.

**Question of Heredity.**—It is generally conceded that tuberculosis is not directly inherited, but that it is contracted after birth. Wilkinson considers that some people are born with cells with poor fighting power. Ellis (see below) considers that these individuals are born with a poor biochemical make-up, and that the fault lies in the chemistry of the cell.

**The Importance of Symptoms.**

Symptoms, from the point of view of diagnosis, are of more value than signs, for, as I have said, if we wait till signs appear we have waited too long. The list of symptoms is protean and may affect any system of the body. I would go so far as to say, "exclude tuberculosis before making a diagnosis in cases of chronic toxæmia." I have gone on this system for some years with the happiest results.

At this stage it may be well to summarize in as few words as possible the present views as to the tubercular process as stated by Wilkinson. Infection occurs in childhood and may be considered a blessing, provided the dose be small, as it confers immunity against massed infection in later life. He says: "Tuberculosis is the result of action and reaction of two units of vital energy, the cell of the host and the cell of the parasite." The earliest lesion occurs anywhere in the air passages. The bacillus travels by the lymphatics and is carried to the tracheo-bronchial glands. The essential weapons of defence are the cells of the tissues, not the blood.

The first line of defence is the mucous membrane lining the air passages. The second, the tracheo-bronchial glands. It is then that secondary symptoms occur, especially endotoæmia. If the second line of defence breaks, the tubercle bacilli burst through the lymph gland structure and spread along the lymphatic ducts that lead to the veins of the neck. They then get into the right heart, lungs and general circulation. In chronic phthisis tubercle bacilli are in the blood, but are inert in the vessels. Later, for reasons not yet known, tubercle bacilli settle down in the apices of the lungs.

Wilkinson likens tubercle to syphilis and divides it into three stages. The third stage is chronic apical phthisis which he compares to a gumma. He emphasizes the folly of waiting till the third stage before making a diagnosis. The time to diagnose tuberculosis is in the secondary or symptomatic stage. But diagnosis is impossible without the use of
F. E. Gunter, S. L. Cummins and H. A. Ellis

Mode of Action of Tuberculin.

There are various theories, but the most feasible appears to be that of Wolff Eisner. He considers tuberculin to be a foreign albuminous substance of low toxicity. This, however, becomes more toxic when it comes in contact with a specific lysin. A tubercular patient has in his body what Sahli calls tubercular lysin, and so gets reactions as a result of lytic action, whereas the healthy patient does not. The reason why tuberculin is not always satisfactory in diagnosis is because we do not directly diagnose tuberculosis, but the lysin content or hypersensitiveness.

You may get a reaction in the apparently cured because there is enough lysin in the body to produce it. Sahli points out that there is a very close connection between hypersensitiveness to tuberculin and immunity to tuberculosis. Hypersensitiveness is due to excess of lysin. He points out that in all endotoxic affections, it is probable that the antitoxic substances remain localized in the foci and do not get into the blood-stream. Hence they cannot be isolated, so their existence is difficult of proof. One significant fact, however, is that increasing doses of tuberculin diminish sensitiveness. This must be due to an antitoxin; were it not so, each dose of tuberculin would tend to increase the hypersensitiveness. The action of tuberculin in treatment is probably as follows:—

By progressive inoculation lysin is increased and tuberculo-lysin is formed, hence reactions, but, as the dose of tuberculin is increased, antibodies are formed in a higher proportion than in the tuberculo-lysin.

If this theory be correct the aim in tuberculin therapy will be, first of all to overcome hypersensitiveness by frequent small but gradually increasing doses, and then, when reactions cease, to push the doses fairly rapidly till large doses, say 1 c.c., of tuberculin, are tolerated, so as to establish a high immunity. This is the practice of Camae Wilkinson, and I have followed his methods with good results.

Hypersensitive cases are by no means unfavourable so far as prognosis is concerned, but they require caution in treatment. According to Sahli, these cases have an excess of lysin, and if you start treatment with large doses of tuberculin, you are apt to get a dangerous amount of tuberculo-lysin set free before sufficient antibodies have been formed. For this reason I prefer to begin treatment in these hypersensitives with tuberculin inunctions. By this method reactions are avoided. When hypersensitiveness is overcome one can safely proceed to injections. Ellis says these cases are calcium deficient. They certainly improve rapidly on calcium or parathyroid.

Wolff Eisner explains fever and night sweats in tuberculosis as due to hypersensitivity. He considers them to be due to the lytic action on the products of the tubercle bacillus. He also thinks that rises in temperature
Side-lights on Tuberculosis

as the result of exercise are due to the fact that more blood is brought to the tubercular focus. Hence more tuberculin is absorbed and lysinized. This is most important. I have studied Patterson's charts on the effect of exercise on temperature, and have been much struck by the similarity they have to tuberculin temperature charts. In both series, in most cases, benefit is observed as the result of graduated treatment, and in both series also the harmful effect of tuberculin or exercise in unsuitable cases is obvious.

Concluding Remarks.

My chief object in this paper is to emphasize the importance of the early diagnosis of a tubercular affection, i.e., a tuberculosis that is showing activity. Most of us at one time have had a mild tubercular infection and, for this reason, may react mildly to tuberculin. Owing, however, to the protective influence of this infection and possibly also to the chemical condition of the tissues, little or no harm accrues, but, if for any reason activity is lighted up, it will show itself in symptoms and the diagnosis should be confirmed in the only way possible (at an early stage), i.e., by tuberculin. Tuberculin in diagnosis is not easy, and tuberculin in treatment is full of pitfalls, but once you have mastered the technique, which can only be learnt by studying for some months under a man who has experience, then you will be in possession of a very valuable addition to your medical equipment. As your knowledge of the subject increases, you will probably adhere less and less closely to your teacher's methods, for your plan of treatment must vary with the class of case with which you are dealing and the conditions under which you work, but once having learnt the principles of tuberculin therapy, you will not lightly discard them.¹

Postscript.

By H. A. Ellis, M.B.
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Although there is no doubt that there is no heredity in transmission of tubercle, there is a question of hereditary constitution in its liability to occur. In this connection constitution can be divided into three types:—

1. The normal, in which there is a balance between assimilation and elimination, between intake of fuel and output of waste.
2. When there are difficulties of assimilation or a deficiency of intake of fuel.
3. Where there is a difficulty of elimination of waste products and therefore an accumulation of ashes.

¹ I shall be glad to show my methods to any officer of the Corps at the Hospital, on any Thursday, at 11.30 a.m.