

well recognized. In many cases, fortunately, the infection shows little tendency to progress in the body, so that we constantly see in practice patients who have suffered from tuberculosis for twenty or thirty years. In other cases the infection is virulent and rapid, and kills the patient in two or three weeks.

In the former cases the bacilli are of low virulence, in the latter they are highly virulent, giving the body no chance to offer any resistance to the attack.

#### *Treatment by Tuberculin.*

It is in the avirulent bacillary infections that tuberculin is of such great service, and I have found it of little or no value in acute virulent infections.

The whole object of treatment by tuberculin is to produce an immunity in the blood against infection by tubercle bacilli; and, what is even more important, to prevent the further spread of the bacillary infection in the tissues. Whether or not it is possible to ever produce a complete lifelong immunity against tubercle is a matter of doubt.

As a result of my experience I have found that the lesions in the body which are caused by the *Typus humanus* are benefited more quickly and certainly if a tuberculin prepared from the opposite strain—namely, bovine tuberculin—is used; and in all cases of pulmonary tuberculosis I now only use bovine tuberculin. It is less toxic, and does not so readily cause reaction, is more easily tolerated, and causes the bacilli to disappear from the sputum more quickly. For the lesions caused by the *Typus bovinus*—namely, lymph glands, tuberculous peritonitis, lupus, tuberculous disease of the bladder, bones, and joints—I invariably use Koch's old tuberculin prepared from human cultures.

The question of dosage is of vital importance, and my routine practice is to administer a course of tuberculin in twelve weekly injections, then resting for a month, and, if necessary, repeating the maximum injection every week. My dosage is as follows of either human or bovine tuberculin:

0.0001 mg.	0.0006 mg.	0.006 mg.
0.0002 "	0.0008 "	0.0075 "
0.0004 "	0.001 "	0.008 "
0.0005 "	0.004 "	0.01 "

A special watch must be kept on the temperature, pulse, and blood.

It is rare to observe a general reaction if the above dosage is carefully followed.

In a great many cases the tubercle bacilli disappear entirely from the sputum at the end of a course of injections, but, unfortunately, if the tuberculin is not persisted in they in many instances speedily return—so that in some cases of pulmonary tuberculosis the injections should be continued for an indefinite time.

Whilst tuberculin *per se* cannot be expected to heal cavities in the lung or replace damaged tissues, yet it undoubtedly has the power of preventing the spread of the tubercle to healthy parts by means of its immunizing effects. Time is thus given for repair of the affected tissues.

In conclusion, I would like to express my opinion, after treating over 600 patients with injections of tuberculin, that it is a remedy of the greatest value, especially in early cases and where the deposit of tubercle is localized, as in one apex or in a lymph gland or single joint; but where the tuberculosis is disseminated and complicated by secondary infections the use of tuberculin cannot be expected to be of much avail. It ought, however, to be tried in every case with the hope of some relief or possible benefit, as we cannot allow the patient to suffer and die without making every effort to arrest the progress of the disease.

Tuberculin is not going to revolutionize the treatment of tuberculosis. It is a valuable aid to the other methods of treatment, hence it must be used with care and discrimination and with a full knowledge of its dosage and therapeutic effects.

I would conclude by saying that the best treatment we can offer to-day to a person infected with tuberculosis is a prolonged open-air life, preferably in a well-conducted sanatorium, excess of nutritious food, gentle exercise followed by plenty of rest, and a course of tuberculin by a careful physician.

## ON THE "CONTROLLED" THERAPEUTIC USE OF NEW TUBERCULIN IN THE TREATMENT OF PULMONARY TUBERCULOSIS.

BY

E. E. A. T. RIGG, M.B., B.S.LOND., ETC.,

LATE HOUSE-PHYSICIAN TO THE BROMPTON HOSPITAL FOR CONSUMPTION AND DISEASES OF THE CHEST.

#### *Introductory Remarks.*

THE success claimed for various tuberculins used in various methods in the treatment of pulmonary tuberculosis has been considerably discounted by the fact that many do very well on ordinary hospital or sanatorium treatment or even at home at work, without tuberculin, and this discount is emphasized by the fact that the advocates of the use of tuberculin (or at any rate some of them) say that only such cases of pulmonary tuberculosis as are afebrile and up and about are fit subjects for the treatment.

With these considerations in mind, Dr. Batty Shaw (upon whose patients and at whose instigation these investigations were carried out) suggested that I should carry out observations on the comparison of afebrile cases of pulmonary tuberculosis treated for three months, half with tuberculin and half without, the cases being compared at the beginning and end of this period. The plan of *controlling* the therapeutic use of tuberculin in the way described in this paper is entirely due to Mr. W. Palin Elderton, F.I.A.

#### *Criteria.*

The question arose as to what criteria should be used in estimating the improvement or the reverse of the cases after their course of treatment.

1. *General Condition.*—This, as judged by the patient's own feelings and the observations of the medical attendant, was self-evidently too fallacious to place stress upon, as a patient quite often says he or she is better when the temperature has risen or the physical signs show extension of the disease in the chest. This therefore was relegated to a secondary place.

2. *Increase of Weight.*—This also was evidently fallacious, as it might easily coexist with extension of disease and not be present, or to a much less extent, in a case which was in all other respects much improved.

3. *Functional Capability.*—An attempt is made to estimate this partly at the Brompton Hospital by registering the number of miles per diem a patient walks, but this also self-evidently will vary with the natural constitution and habits of the patient.

4. *Occurrence or Non-occurrence of Relapses.*—In a period of three months this could not well be judged of, and the occurrence of temperature, if maintained for more than a day or two, was considered as disqualifying the patient from the conditions of the experiment. No reliance was placed upon the disappearance of tubercle bacilli from the sputum as a sign of improvement, for the extrusion of phlegm is so obviously under the control of the patient, and temporary absence of tubercle bacilli in the sputum of patients suffering from active pulmonary tuberculosis is not infrequent.

5. *Physical Signs.*—The only criterion that remained, therefore, was alteration in the physical signs—that is, whether there was extension or retrogression of them during the three months—and of these the greatest attention was paid to rales as being the most definite indication of the extent of disease which could easily be demonstrated to another observer. Therefore, at admission, the rales were estimated and diagrammatized to the actual intercostal spaces and parts of intercostal spaces (outer and inner ends) in which they were heard. This was done for the front and back of both lungs. These observations were made independently by Dr. Batty Shaw and by myself, and in nearly every case substantial agreement was arrived at. At the end of three months, the cases were again examined by Dr. Batty Shaw (without examination in the interval, and, as far as possible, without his knowing whether the patient had been treated with tuberculin or not). The examination was carried out in the same way, rales being diagrammatized to the space without reference to the first diagram, and then the two diagrams compared. The cases were examined independently by

me, and I made separate diagrams which were afterwards compared with those of Dr. Batty Shaw. Out of 19 cases there was substantial agreement in 17 cases, and minor differences in 2, which were afterwards adjusted. In some cases the extent of rales had increased, in some retrogressed, and in others remained stationary, while in still others there had been increase of rales in one lung and diminution in another. In such cases a balance had to be struck between the two, and the case adjudged as worse, stationary, or better accordingly.

Physical signs were, therefore, taken as the main criterion, and alteration and increase of weight, amount of exercise, and general condition correlated secondarily.

#### Choice of Cases.

In agreement with one of the safest recognized methods of giving tuberculin, it was adopted as a *sine qua non* that all the cases should be afebrile when up and about all day, and that rise of temperature maintained for more than a day or two should disqualify the patient from being one of the series.

Another point now cropped up, which was that many cases are adjudged suffering from pulmonary tuberculosis on slight and often equivocal signs at one apex, or on no signs at all, and on some haemoptysis which may very possibly have not been haemoptysis at all, but have been concealed epistaxis or bleeding from gums, teeth, or posterior naso-pharynx. Therefore, as the second *sine qua non* it was resolved to take only those patients into the scheme who had expectorated sputum in which tubercle bacilli had been found.

The third point was the distribution of the cases between the two methods of treatment, and where a number of cases presented all grades of involvement of the lungs from very slight to extensive (1 apex to 5 lobes), and where some showed fibrosis and some not, it would be almost impossible to apportion the cases fairly between the two treatments so as to be free from any suspicion of bias. To obviate this, the patients were chosen by lot. In this way two series of nine were chosen, but, because of rise of temperature or because they left the hospital, three soon fell out from the names not treated by tuberculin. To replenish these, the next four patients fulfilling the conditions of afebrile tuberculosis drew lots, one to have tuberculin treatment, and three not. The final result was that ten patients were treated with new tuberculin (T.R.) and nine were not, the one out of the latter ten cases being set aside, as she left the hospital before the expiration of three months.

#### Method of Giving Tuberculin (T.R.).

As before mentioned, tuberculin was only given to afebrile cases.

*Dosage.*—Treatment was commenced with a very small dose, increased every second day at first, and afterwards at intervals of four days.

*General Scheme.*—The dose given was as follows in milligrams every second day: 0.00001, 0.00003, 0.00005, 0.00007, 0.0001, 0.00015, 0.0002, 0.0003, 0.0005, 0.0007, 0.001, 0.0015, 0.002, 0.003, 0.005, 0.007, 0.01, 0.015, 0.02, 0.03, 0.05, 0.07, 0.1.

*Every Fourth Day.*—0.15, 0.2, 0.3, 0.5, 0.7. The last—0.7 mg.—was the maximum dose reached.

The injection, however, was conditioned by the occurrence of reactions. If the temperature rose to 99° F. or above with all but the smallest doses (where the temperature was possibly not due to the injection of tuberculin) the patient was put to bed until it became normal, and no further dose was given for five to ten days (five with small doses and up to ten with the larger), and then the last dose repeated. In the case of the smallest doses, the next dose was given after an interval of four or five days. If the temperature now remained normal, the original increase of dosage was gone on with. If another reaction occurred, the patient was again put to bed till the temperature was normal, and when it had kept normal for from two to seven days, the same or a smaller dose was given. If this produced a reaction a still smaller dose was given after an appropriate interval until one was found which produced no response. This dose was now repeated two or three times before increasing again.

Out of 10 cases, 2 gave no reaction till 0.7 mg. was injected. A third case reacted first with 0.1 mg., whilst the other cases reacted two to seven times with various doses.

#### A Typical Example.

##### CASE V.

First dose=0.00001 mg. This produced a reaction temperature 100° F. After eight days' interval 0.00003 mg. was given, and at two days' interval, 0.00005, 0.00007, 0.0001, 0.00015, 0.0002, 0.0003, 0.0005, 0.0007, 0.001, 0.002, 0.003, 0.005, 0.007, 0.01, 0.015, and 0.02 mg. After this last the temperature rose to 99°; five days' interval, and then 0.02, 0.03, 0.05, 0.07, and 0.1 mg. were given at two days' interval, then at four days' interval, 0.15, 0.2, 0.3, 0.3, and 0.3 mg.

At the end of three months all the 19 cases were again examined in the way described and note also made of their weight and amount of exercise taken.

#### SUMMARY OF RESULTS.

##### 1. Physical Signs:

(a) Tuberculin-treated patients. Out of 10: Improved 1, worse 4, *in statu quo* 5.

(b) Non-tuberculin-treated patients. Out of 9: Improved 4, worse 3, *in statu quo* 2.

##### 2. Increase of Weight:

(a) Tuberculinized patients (10 cases). Gained 10–20 lb. 4, gained less than 10 lb. 4, *in statu quo* 2.

(b) Non-tuberculinized patients (9 cases). Gained over 20 lb. 2, gained 10–20 lb. 3, gained less than 10 lb. 4.

In (a): Average per cent. of increase of weight, 6.3 per cent.

In (b): Average per cent. of increase of weight, 10.3 per cent.

##### 3. Exercise—capacity of walking, maximum amount per diem:

(a) Tuberculin patients (10 cases). Two miles and over, 3; 1–2 miles, 5; less than 1 mile, 2.

(b) Non-tuberculin patients (9 cases). Two miles and over, 6; 1–2 miles, 3; less than 1 mile, 0.

4. *General Condition.*—This is a difficult criterion, but, generally speaking, in (a) only 5 out of 10 were in thoroughly good condition; in (b) 8 out of 9 were in thoroughly good condition.

The net result of these observations is to show that the administration of new tuberculin by one of the more popular approved methods is not followed by greater improvement in the *physical signs*, nor by greater increase in weight, nor by more greatly increased capacity for physical work, nor by a greater improvement in the general condition, as compared with the results of ordinary hospital methods.

The observations on the signs do not support the idea that new tuberculin in any way lessens the activity of the local lesion. It is possible that the less favourable influence on weight, the less capacity for work, and the falling off of the general condition are due to the disabilities imposed on the patient by being treated with tuberculin, as they so often were kept in bed to help restore the temperature to normal.

## ORGANIC ACID RATIO OF URINE AFTER TUBERCULIN.

By ARTHUR H. GREGSON, M.B., B.Ch.Vict.,  
BLACKBURN.

A GIRL, born in 1892, had suffered from lupus vulgaris of the left cheek from 1895 to 1905. Roentgen rays were tried, but did not benefit. Curetting was successful in 1905, but afterwards the glands of the neck and beneath the jaw on both sides enlarged.

She consulted me, and on December 4th, 1909, received an injection of  $\frac{1}{10000}$  mg. T.R. This was repeated weekly in increasing dose until, on February 1st, 1910,  $\frac{1}{100}$  mg. T.B.E. was given; after this the temperature rose to 103° F., the patient became delirious, and suffered from severe abdominal pain and tenderness. The temperature was intermittent for months; various methods were tried to reduce it, including administering on May 3rd and 22nd of  $\frac{1}{10000}$  mg. T.R. of human origin, as before, but without benefit.