The significance of these many portals is evidenced in the practical tuberculinization of the community (48), and is of interest in the detection of the source of infection, both human and bovine.

The questions that yet remain to be solved concern the latency of the infection contracted in childhood. Where do the bacilli live? Do they live in the tuberculous glands and old lesions so frequently found *post mortem*? Do they there remain quiescent for indefinite periods, capable, when the time comes, of setting up disease, as exemplified in the recent attention drawn to pulmonary tuberculosis resulting from extension from tuberculous bronchial glands (54, 55)? If so, how are we to account for the negative results obtained by Cobbett (3) after inoculating animals with the tuberculous tissues? Do the bacilli live in the blood and tissues generally (50, 51, 13), having established a *modus vivendi*, wherein they are tolerated but not allowed to multiply to any extent? This may be so, and thus the vast majority of the people in this country are in reality tubercle carriers, awaiting some impairment of the powers of resistance—to quote von Behring—in order to become obvious sufferers from tuberculosis.

Much might be said regarding the view that the first infection in childhood, by conferring a partial immunity, determines that, in the large proportion of cases in adult life when tuberculosis does supervene, the disease shall run its most chronic form with cavity formation in the lungs (55, 56), and not the acute miliary form.

From what has been already brought forward it will be seen that, although the problems that tuberculosis still offers for solution are of far-reaching consequence, still the recognition of the portals of entry and the source of the infection places us in a stronger position than formerly, and enables us to say, in the words of the resolution adopted at last year's International Congress, "Prophylaxis of tuberculosis must principally be directed towards the suppression of contamination from man to man, and principally in the family, and, whilst contamination of man by bovine infection is of less frequency, it is, nevertheless, necessary to maintain all measures against infection from this source."

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THE VARIETIES OF TUBERCULIN IN THE
TREATMENT OF TUBERCULOSIS.

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IN the paper which I published in the BRITISH MEDICAL JOURNAL in 1903 I ventured to suggest that a considerable amount of tuberculosis in children was caused by the bovine tubercle bacillus. Since that time a great amount of scientific investigation has been carried out over the whole world, and especially by our own Royal Commission, with the result that we are now certain of the following conclusions:

1. That the great mass of tuberculosis occurring in the human subject in the form of pulmonary tuberculosis is caused by the human bacillus (*Typus humanus*), and is conveyed from person to person by infection.

2. That a considerable amount of so-called surgical tuberculosis in children and adults is caused by the bovine bacillus (*Typus bovinus*), received into the alimentary canal through milk and food.

Originally of a common species, the bacilli have, owing to long environment in different hosts, assumed marked characteristics, so that we are able, experimentally, to divide them into two types:

- Bacilli of the Typus humanus*, which cause :
 - Pulmonary tuberculosis and pleurisy.
 - Secondary tuberculous enteritis.
 - Tuberculous laryngitis.
 - Fistula in ano and possibly some other lesions.
- Bacilli of the Typus bovinus*, which cause :
 - Primary abdominal tuberculosis.
 - Tuberculous lymph glands.
 - Bones and joints (probably).
 - Genito-urinary tuberculosis.
 - Acute miliary tuberculosis.
 - Lupus. Meningitis.
 - Pulmonary tuberculosis (a small percentage).

I have for the last ten years separated my wards in hospital into human and bovine wards, and after an observation of over 6,000 cases of tuberculosis, I am impressed with the fact that it is rare to see lesions of the human and bovine type associated in the same patient. In fact they seem to be antagonistic to each other, so that one rarely observes a patient suffering from pulmonary tuberculosis develop any other lesions beyond those mentioned in the human group. It is also rare for cases of gland or bone tuberculosis to develop true pulmonary tuberculosis except in the course of a general systemic infection.

It is necessary to mention this clinical fact to explain my reason for using tuberculins of the opposite strain in the treatment of the disease. There seems to be little doubt that a mild infection by bovine bacilli in the human body, such as neck glands, by way of the alimentary canal, will protect against an infection by human bacilli, and it is most probable that a large number of people are immunized against pulmonary tuberculosis in after-life by having been infected in early childhood by bovine bacilli through milk or food. In all the experimental work throughout the world it has been found to be a rare occurrence to find both types of bacilli in the same body.

Variations in Virulence.

Whether or not a patient is going to be destroyed by tuberculosis seems to me to depend on two important factors: (1) Virulence of infection; (2) individual resistance.

The variability in virulence of the tubercle bacillus is

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.

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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 râles as being the most definite indication of the extent of disease which could easily be demonstrated to another observer. Therefore, at admission, the râles 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, râles being diagrammatized to the space without reference to the first diagram, and then the two diagrams compared. The cases were examined independently by