properly controlled by x ray, we are possessed of an invaluable method of diagnosis in cases of sterility, far superior to any previous technique. Its only contraindications are septic cervicitis or pregnancy, and the latter is quite disregarded by Hueser,¹¹ but Bécère⁴ advises against using this method of diagnosis owing to the bad effects of the x rays (not the lipiodol) on the pregnancy.

Apart from sterility, I think it is a useful, but by no means necessary, adjunct to diagnosis, for the reason that a pelvic tumour usually calls for operation, and the mistaken diagnosis of a fibroid for a parovarian cyst is of small moment to the patient, however annoying it may be to the surgeon concerned.

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THE PRODUCTION OF IMMUNITY TO TUBERCULOSIS IN MAN AND ANIMALS.*

BY

NATHAN RAW, C.M.G., M.D., F.R.S.Ed.,
LORD CHANCELLOR'S VISITOR.

BEFORE discussing the problem of immunity to tuberculosis it will be necessary to consider very briefly some of the outstanding facts about this disease. Tuberculosis, unlike other infectious diseases, advances slowly and progressively, and though it may be arrested in its march at the lymph glands—the first natural barrier—only to become active again later, its progress, as in pulmonary tuberculosis, is more often continuous. It is probable that in addition to the human, bovine, and avian tubercle bacilli there are certain intermediate types, and that the human body may be attacked by a mixture of types. Each type of tubercle bacillus is selective and can live only in the host to which it has become accustomed for centuries.

From twenty-five years' experience of subculturing and growing tubercle bacilli, I am inclined to the opinion that the bovine bacillus is the original and true tubercle bacillus, and that the other types have evolved from long residence in different hosts. This view cannot be proved by investigations on animals, as they are generally not susceptible to infection by human bacilli. The human body is readily infected by both human and bovine bacilli; avian bacilli, which infect chicken and birds, do not infect the human subject. In the light of our present knowledge we cannot determine with certainty the exact origin of every infection of the human body by tubercle bacilli. Cytological differentiation between human and bovine bacilli is not possible; mankind, from its consumption of milk, butter, and cheese, has become so accustomed for centuries to infection from cattle that the bovine bacilli have adapted themselves to their new environment and grow well in human tissues; yet the human bacilli will not grow in the tissues of cattle.

In studying tuberculosis it is necessary to consider what may happen to an invading organism in a foreign host. Bovine bacilli introduced into the body of a child may, after a few years, undergo a modification of type; their virulence may be reduced and they may assume the characteristic properties of the human bacilli. Should such modification occur it would obviously be difficult by ordinary laboratory methods to determine with accuracy whether or not the bacilli belonged to the human or the bovine type.

* Summary of paper read before the Liverpool Medical Institution, March 21st, 1929.

A child infected with bovine bacilli in infancy might possibly be certified ten or fifteen years later as suffering from a human infection, owing to the transmutation of the organism in human tissues.

In 1901 I published a paper in the *British Medical Journal* stating the following views. (1) That human and bovine infections produce separate and distinct diseases in the human body, and that they are antagonistic to each other. (2) That human bacilli cause primary pulmonary tuberculosis, while the bovine type cause enlarged glands, mesenteric disease, bone and joint lesions, etc. (3) That patients suffering from pulmonary tuberculosis rarely develop bone, joint, or gland lesions, and vice versa; in fact, that the human subject is protected by one infection against the other. (4) That cattle and pigs are immune against infection by the human bacilli, but that the human subject is susceptible to both. It was evident to me at that time that it would only be possible to immunize animals by using human bacilli. A series of animals were tested in this way, but the bacilli used were too virulent and every animal was killed.

In 1906 I decided to attempt attenuation of bacilli by repeated subculturing and thus reduce their virulence and lower their toxicity. The only certain method of permanently attenuating virulent cultures of tubercle bacilli is by long-continued and systematic subculturing spread over a number of years. For this purpose I used a pure culture on glycerin agar of human bacilli from a virulent case of pulmonary tuberculosis, a virulent bovine culture from the mesenteric glands of a cow, and a culture of avian bacilli from the liver of a chicken. These cultures have been grown on glycerin potato and transferred to glycerin agar every month for twenty-two years, the present growths representing the two hundred and sixtieth generation. The growths are still profuse and true to type, but they are now completely non-pathogenic to animals. Every year since 1906 I injected these bacilli into animals, and until the year 1913—that is, until the eighty-fourth generation of subcultures—I observed no change in their virulence. After that time attenuation became marked, and in a series of animal inoculations carried out in 1914 the subcultures were observed to be avirulent.

A further series of animals was inoculated a year ago with a protective vaccine prepared from attenuated cultures of human bacilli, and these animals, together with unprotected controls, were given each half a milligram of virulent bovine bacilli. All the unprotected animals rapidly developed general tuberculosis and died within four months, while the protected animals showed only local and non-progressive lesions. An animal which can resist the laboratory dose of virulent bacilli can certainly resist the comparatively mild infection it may meet in everyday life. If, then, we can produce artificial immunity in man and in animals sufficient to enable them to resist ordinary infection we shall have gone a long way towards stamping out tuberculous infection.

Calves that are to undergo immunization should be separated from the mother at birth, and having been fed on healthy milk or on the pasteurized milk of the mother for a week should be given the first dose of vaccine, the second dose following a week later. They should then associate with the other animals. This method of immunization is applicable only to non-infected animals. During the past three years it has been applied to over 2,000 calves in valuable pedigree herds, and careful records have been kept. These calves have been tested at the end of a year, and in many cases again at the end of a second year, with Pasteur's tuberculin, and in practically all cases the result has been negative.

The production of immunity in the human subject is complicated by the fact that children are susceptible both to human and to bovine infection. A year ago, at the request of their parents, I inoculated all the children—about one hundred—living in a large tuberculosis colony, where all the male parents were suffering from pulmonary tuberculosis, with two doses of protective vaccine prepared from bovine bacilli. So far these children appear to be quite healthy, and though it will require years of observation before we can form any opinion as to the efficiency of the vaccine, I believe that in time it will be possible to

immunize children, especially those who are directly exposed, against tuberculous infection.

Since 1902 tuberculin has fallen into disrepute, but I have no doubt that it will come into its own again, and that preparations from non-virulent attenuated cultures which produce no reactions will be recognized to be of the greatest service in the treatment and prevention of all forms of tuberculosis. Attenuated cultures retain the quality of producing tuberculin, and, being deprived of their virulence and toxicity, are perfectly safe in use. A very small amount of vaccine prepared from such cultures is sufficient to protect a person from infection. Professor Calmette, in his prophylactic treatment of infants a few days after birth, uses a living attenuated culture of bovine bacilli to produce immunity against human infection. It is still too early to estimate correctly the results of his work, but there is a fundamental objection to using a living bacillus, as we do not know whether or not it may be reactivated after long residence in the human host.

In my view, all cases of tuberculosis should be treated by some form of tuberculin, which is the natural specific remedy; but this tuberculin should be prepared from attenuated, avirulent, non-toxic cultures. Pulmonary tuberculosis should be treated with tuberculin prepared from bovine cultures, and surgical tuberculosis with tuberculin from human cultures. Given in early cases of pulmonary tuberculosis tuberculin seems to limit the spread of the infection and to enable the patient to resist the disease. In no case can its administration do the least harm, and given scientifically it has often produced wonderful results. I have treated a large number of cases in this way, and have never seen any untoward effects. The best results are only seen in early cases. The method of stamping out tuberculosis is to immunize children of tuberculous parents and to produce active immunity in early cases of tuberculous infection.

Memoranda :

MEDICAL, SURGICAL, OBSTETRICAL.

CALCANEAL SPURS OF TRAUMATIC ORIGIN.

It is suggested in the lecture of Professor Fraser, in the issue of March 2nd (p. 383), that calcaneal spurs are the result of a trauma. On the other hand, Mr. A. H. Tubby, in his contribution on deformities in the *Encyclopaedia Medica* (second edition, vol. iii, p. 380), states that the general conditions associated are gonorrhoea, subacute gout, rheumatism, arthritis deformans, excessive standing, and, rarely, epiphysitis, tuberculous and syphilitic, of the os calcis. The two cases described below were recipients of compensation, and the questions to be decided in arbitrations under the Workmen's Compensation Acts were what final settlements were to be awarded.

The first case was that of a stevedore, who was working, on October 20th, 1925, in the hold of a lighter receiving sets of timber. A set which was being lowered got out of hand, and crushed his left ankle and foot against timber already in the hold. Swelling and pain were caused, and he ceased work. Subsequently he tried to do light work, but had to knock off owing to pain. He was examined on July 23rd, 1926, when the case came up on arbitration. Slight pain was complained of on extreme flexion of the left ankle, and some tenderness on pressing the middle of the left heel. Applicant was slightly lame, and, with his heel on the ground taking the weight of his body (13 st.), everted the foot. X rays showed on the left os calcis a small spur, situated on the fore part of the inferior surface, not on the most dependent part. There was also a second spur at the insertion of the tendo Achillis. The onus was on the applicant to prove that the condition was due to injury arising out of, and in the course of, his employment, but the case was settled on payment of £275 and costs offered by the respondent.

In the second case a workman who fell from a height of 11 feet badly bruised his heels, and was said to have fractured both calcanea. This accident occurred early in 1925. X rays showed enlargement of these bones, opacities, spurs on the inferior surface, and thick spurs at the insertion of both the tendines Achillis. The effect was to produce pain on standing and inability to work. A final settlement of £425 and costs was made on March 8th, 1928.

It would appear that these cases drag on, compensation being paid all the time; medical men advising those concerned would be justified in suggesting an early settlement, since otherwise the mental element comes in, and it is difficult, even after treatment similar to that recommended by Professor Fraser, to get the workman to return to full work. Both patients were middle-aged men, and no signs of rheumatism or arthritis could be found.

J. S. WARRACK, M.A., M.D., D.P.H.,

Gravesend.

Barrister-at-Law.

FIBRO-SARCOMA OF ISCHIUM TREATED WITH RADIUM.

The following case seems worth recording, not only on account of its rarity in such a position and the success attending treatment, but on account of the history.

A healthy boy of 15 was sent to me in April, 1926, by Dr. V. Ll. Jones of St. Clears, with a somewhat tender swelling about the size of a small walnut connected with bone in the right perineum at or behind the junction of the pubic and ischial rami.

The history was that of a so-called chill in the previous December, with pains in the lower limbs, for which he stayed in bed two or three days. On getting up he suffered from acute pain in the right perineum and inner side of the right thigh, for which he was kept in bed a further three or four days. After

this he continued to get the same pain, though less severely, on walking or running. The swelling could be distinctly felt per rectum, though not so pronounced as through the perineum. X-ray examination showed the bone to be expanded in cyst-like form. He walked with a limp, there was some atrophy of the thigh muscles, the movements of the hip were free, and jarring on the heel caused pain in the right perineum. The diagnosis was cyst of bone or chronic abscess.

On April 19th the swelling was exposed by incision, the shell of bone broken into, and the contents, evidently new growth of tough consistence, removed with a sharp spoon. The wound was closed round a small drainage tube, the deep end of which occupied the cavity. The growth was examined by Dr. A. F. Sladden, director of the Beck Laboratory, Swansea Hospital, who reported that sections showed "mainly organized fibrous tissue with areas of fibro-sarcoma, specially in relation to bony tissue; order of malignancy low."

On April 22nd 25 mg. of radium screened by 5 mm. of silver were introduced along the track of the tube into the bony cavity and left for twenty-four hours.

The boy has enjoyed perfect health since. Nothing is now felt per rectum, and only some slight irregularity of bone in the perineum.