

## **The pathological effects of dead tubercle bacilli / by Stewart Stockman.**

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THE PATHOLOGICAL EFFECTS OF DEAD TUBERCLE BACILLI.

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Experiments have been undertaken to determine the effect of dead tubercle bacilli injected subcutaneously. The results show that dead tubercle bacilli produced an abscess in the subcutaneous tissue of the guinea pig, which was indistinguishable from that produced by living tubercle bacilli. The abscess produced by dead tubercle bacilli was indistinguishable from that produced by living tubercle bacilli in its histological features, in its reaction to the various tubercle bacilli tests, in its reaction to the various tubercle bacilli tests, and in its reaction to the various tubercle bacilli tests.

By subcutaneous inoculation they produced an abscess in from two to six weeks. Tubercle bacilli, obtained by the ordinary methods were found in the pus. If intraperitoneal and pleural inoculation with a milky emulsion of bacilli they produced nodules of various sizes on the serous membranes. These were made up of a central creamy-looking part surrounded by fibrous tissue. The central part consisted of epithelioid cells and giant cells. Tubercle bacilli were abundant in the central part; well-marked caseation was not found.

Intravenous inoculations were made into the cranial veins of rabbits. The animals were killed and examined at intervals of from one to sixty days. A few died after the third week. In animals killed after one day the bacilli were found in the lungs, liver, and spleen, most abundantly in the first mentioned organ. The other tubercle bacilli were found in the lungs, some being macroscopic, others quite visible to the eye. They were passed upon the sixth day, the longest period of observation. The structure consisted of epithelioid cells, giant cells, and leucocytes. Bacilli were found between the cells and among giant cells. Later the nodules were denser and made up of epithelioid cells and loose connective tissue. After three weeks microscopic nodules, apparently having their origin mainly in the capillaries, were found in the liver. After five or six weeks visible nodules were found in the latter organ. Treadwell and Hallock describe that the nodules deposited in a position of the vascular endothelium under the condition of dead and disintegrating tubercle bacilli. They say that "the dead bacilli seem to act as foreign bodies simply, causing a surrounding of it, it is true, but only because bodies other than bacilli in the same form of the foreign body question. Every foreign body does not produce this tissue reaction, although the power to do so may not belong exclusively to the tubercle bacillus. The action of the dead tubercle bacillus is, in large part, at least, similar to it, and it is the foreign body of this order that we are most likely to meet with in the tissues."

At the conclusion of their paper these authors offer some suggestions as to the influence of the products of the living germ on the degenerative changes in a true tubercle. They suggest, too, the possibility of the more fibrous tubercles being due to dead bacilli.

Curiously enough it was this last idea which was to further form an opinion which I had formed as to the origin of interstitial giant cells. That led me to undertake some experiments with dead bacilli. I had conceived the idea and started experimenting with dead bacilli before I knew of their paper. I have since read it very carefully, and wish here to acknowledge my indebtedness to the authors. I have performed most of my experiments on different animals, but many of the results confirm those of Treadwell and Hallock.

I read also mention that Stress and Goetschke have in some extent confirmed the results of the American authors by experimenting on guinea-pigs, rabbits, and dogs. They say little about lesions in the liver. They do not state that giant cells are the nodules. That may be because in their experiments the few bacilli were injected in one part, or because the courses of the nodules were not examined. Many of their animals wasted and died. When the changes of bacilli were broken up and well distributed in the fluid the animals wasted and died all the same, but no lesions were found. Evidently several dead bacilli are necessary to see quite produce a lesion. If the number of bacilli was very small the animals wasted, then recovered, and appeared quite healthy, but if a second inoculation was administered they died of the dead bacilli they mentioned the animal against it. With the products of the bacilli in artificial culture they could produce no lesions.

TUBERCLES OF THE LUNG.

I have examined a number of tuberculous livers from the cow, one generally held distinct massive nodules, but that is not the only form that the tubercles assume in this animal. At the Edinburgh slaughter during the last five years I have found a considerable number of very circumscribed nodules without any appearance of a caseous nucleus in these substances. On examining these microscopically I have found tubercle bacilli and tuberculous giant cells, although the former were not very numerous. For that reason I think that the percentage of tuberculous nodules has been slightly underestimated. These nodules, however, will not very much increase the amount of tubercle-infected milk, because the affected portions give little or no milk, and the cow is soon to be sent to the slaughter-house under the order by way of the blood vessels, and it is highly probable that at an earlier date there were distinct caseous tubercles in these nodules. Two possible explanations of the difference in these two livers suggest themselves:

1. The bacilli might have been overcome by the tissues in such an extent that they could no longer produce distinct caseation, but were still able to excite a proliferation of the tissues and cause the formation of giant cells.

2. The bacilli might have arrived in the gland in an exhausted condition, and were thus no longer able to produce the distinct caseous lesion.

There is nothing wildly imaginative in these suggestions if we think on what we know of the tubercle bacillus. It is well known that the bacillus first acts by exciting a proliferation of the tissues. The new cells, instead of completing their development, however, tend to become caseous. Still, we know that the cells do sometimes complete their development and form fibrous tissue. This is especially the case in the old tubercles found in the cow and pig. They are often surrounded by a ring of fibrous tissue, which is invading the caseous center. However, the tuberculous lesions of the muscles—namely, it contained a bad medium for the growth of the tubercle bacillus—which I have described in the pig were distinctly chronic.

I may say, too, that I have once found tubercle bacilli in fibrous nodules under the various conditions of the fourth month of the cow, and have several times found them in fibrous thickenings on the subcapsular regions of the ovary. These are mainly the observations which have led me to undertake these experiments.

Experiment I.—Tubercle bacilli. I began to experiment on this subject for the purpose of trying to make the various animal tuberculosis by using the killed tubercle bacilli. I first injected two guinea-pigs with a dose varying from 0.2 cc. to 1 cc. They were kept separate from those inoculated with tubercles of the fresh culture of tubercle bacilli in glycerine fluid, from which the nodules had been prepared by diffusion through gauze without previous heating. The cultures were allowed to go on for a few months and began to degenerate with a view to being used as a source of bacilli, without, however, the usual 40° C. with 24 hours the temperature was 24° C., but was still above the physiological temperature. I used pure buttermilk as the medium, and added the fluid. This began to degenerate in a few months. It produced a very low temperature of 24° C. in 48 hours. The whole of the tubercle bacilli had been killed. Thinking that the nodes prepared in the ordinary way will not result in general caseation, but will produce a local lesion, whenever it has been from the possible explanation of the effects of dead bacilli. These I have been thinking of for some time. I secured a small quantity of tubercle bacilli killed by these nodes, allowing the bacilli to grow in a glycerine fluid, which had been heated for five months. An abscess formed and burst three days afterwards. A month later a second injection of bacilli in that medium was given under the skin. The latter came from a glycerine fluid culture that had been in the incubator for four months, and afterwards killed by heat before inoculation. On the third day a swelling about the size of a hen's egg formed at the site of inoculation. The skin over this swelling was unaltered, and only very soon thickened into a fibrous covering of greater or less extent. Every day progressive nodules with the pus slowly increased with tubercle bacilli. In other nodules were present. Attraction for tubercle bacilli with the pus was not strong. The changes were caused by the tubercle bacilli, which were killed and dead. The abscess burst on the fifth day, and the nodules took a considerable time to heal up. The temperature rose to 39° C. on the morning after the second injection. It fell to 38° C. on the third day. On the afternoon of the sixth day it rose to 40° C. a small tubercle nodule was noticed. The temperature rose, however, had risen to 40° C. and had taken 24 hours after. These results are the most striking of dead bacilli. The temperature rose, however, had risen to 40° C. and had taken 24 hours after. These results are the most striking of dead bacilli. The temperature rose, however, had risen to 40° C. and had taken 24 hours after.

One might draw the following conclusions from this experiment: (1) That the soluble products of the tubercle bacillus exert a decided effect on the healthy organism, although they have a very decided action on animals whose bodies contain the tubercle bacillus, living or dead. (2) That the dead bacilli are far more active than the tubercle bacilli, although this may be an account of their retaining a strong toxin in their bodies.

This latter conclusion suggested perfect health for ten months afterwards. I was anxious to see if the world still owed to the dead bacilli.



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