AN ADDRESS ON THE KOCH METHOD OF TREATMENT FOR TUBERCULOSIS.

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I HAVE never hitherto ventured to give public expression to my opinions on the subject of the Koch cure of tuberculosis which, since the autumn of last year, has excited so much interest, not only among the general public, but also in the medical profession. I have been an amused and sceptical spectator, but I have held my peace; in the first place, because I did not care to take any part in the grave experimental inquiry to which Dr. Koch invited the profession while withholding from them the facts and inferences which justified it to his own mind; and, in the second place, because, since he has begun to take us into his confidence by instalments, the enthusiasm with which his supposed discovery was greeted has subsided, and a general sense of distrust in it has arisen and prevails.

I should not have ventured to say anything on the subject even now had it not been for the kind invitation of your excellent Honorary Secretary (Dr. Mackenzie) that I would open the discussion which had been arranged for this evening; for my actual experience of the treatment has been limited to a few cases which have lately been under my care, and it has been arranged that our hospital experiences (including my own) shall be brought before you collectively by some of my younger colleagues; but the subject has really interested me, and I propose, therefore, to give you my thoughts concerning it.

Specific infective diseases (all of which most of us believe to be due to specific living organisms) may, it seems to me, be somewhat roughly divided into those which tend to last a limited time, and of which one attack confers more or less complete immunity against subsequent attacks, and into those which tend to last indefinitely, and which cannot, therefore, in any sense be regarded as self-protective. Of the former class, typical examples are afforded by small-pox, scarlet fever, and measles; of the latter class, typical examples are tuberculosis and leprosy. There are many infective diseases, no doubt, the behaviour of which in the above respects has not been fully determined. Thus, there are many persons, I should suppose, who, having regard to the inevitable fatality of natural hydrophobia, would hesitate to admit it into the self-protective class, although there is much in the collective phenomena of the disease to suggest that it does really belong to this class, and for those who accept (as I do) the efficacy of Pasteur's treatment there can be no doubt on the point; and there is much reason to believe that epidemic cholera, typhoid fever, and diphtheria are self-protective in only a very slight degree. I may remark, however, in this connection, that the very fact of an infective disease having a natural tendency to get well is a proof that it has a tendency to be self-protective, for, if it were not so, the specific germs which cause it would tend to multiply indefinitely, and, sooner or later, to destroy their host. The question of the duration of the protective influence is another matter, and different self-protective diseases may, and doubtless do, vary within wide limits both as to duration and as to degree.

Now, upon what this self-protective influence depends we have, so far as I know, no knowledge whatever. But notwithstanding this, we have been enabled in certain striking and well-known cases so to avail ourselves of it, as by imparting a mild or attenuated form of disease by inoculation, to confer protection against subsequent and more severe attacks. In the last century, by inoculating and thus perpetuating a mild sort of small-pox, characterised by little febrile disturbance and scanty eruption, persons thus treated were systematically rendered proof against the severer form of the disease; and,

since the time of Jenner, the inoculation of cow-pox (which is doubtless small-pox attenuated by passage through the cow) has conferred similar, though perhaps less powerful, protection against the same disease. More recently, as we all know, Pasteur, working on these lines, has discovered methods by which the contagia of anthrax and of hydrophobia may severally be so reduced in virulence as to impart on inoculation a manageable affection which is protective against the unmanageable and fatal attacks of the natural diseases. I need not go into particulars; it is sufficient for my purpose to remark that, in the case of the former disease, he devised a special mode of cultivating the bacillus anthracis, which reduces its virulence to such a degree that inoculation with the attenuated bacilli imparts an attenuated, though still protective, attack of the malady; that, in the case of hydrophobia, he discovered a process of treatment of those tissues of the rabid animal which are the selective sites of the virus, and are presumably therefore the special habitat of the hitherto undiscovered rabid organism, in virtue of which portions of these tissues may be inoculated on other animals so as to impart to them an attenuated and non-fatal, yet still protective, form of hydrophobia. It may be presumed that all the cases above cited fall under the same law, namely, that the attenuation of the disease is due to an attenuation of the specific virus or disease germs which cause it, both disease and germs remaining nevertheless potentially unchanged.

But nothing that I have hitherto said throws any light on the nature of the protective influence which certain of the infective diseases exert against recurrence of themselves; neither do I pretend that I can throw any light on the subject; yet there are some things which may, perhaps, have some relation to it, to which I may briefly advert. There is no doubt that disease germs cause mischief in the body, not by the mere fact of their presence therein, but in consequence of some poisonous matter which they manufacture or secrete, or some other deleterious influence which they exert over the fluids or tissues in or among which they lie. Dr. Burdon Sanderson and others demonstrated some years ago that while some septic organisms enter the system and multiply in it, causing symptoms of septicaemia, which tend to continue or increase and terminate in death, in other cases the septic organisms flourish only in unhealthy sores, and produce symptoms of septic poisoning not by their actual presence in the blood or tissues, but by means of a poison which they discharge, and is absorbed more or less abundantly, and distributed by the circulating fluids; that, in the former case, the symptoms are maintained in consequence of the continued presence and multiplication of the bacteria in the tissues; that, in the latter case, the symptoms, being only the consequence of the absorption of chemical poison from a restricted area, cease with the restoration of that area to health; and further that, in this latter case, the poison is soluble, and can be obtained in solution, entirely free from bacterial or other organisms, and from putrefactive taint or tendency; that it is of extreme virulence (the effects being proportionate to its dose), and has exactly the same effect on the system as the material containing bacteria from which it is derived. The symptoms to which it gives rise are, I may add, very much like those which are induced by the injection of Koch's fluid.

Dr. Sanderson also, in 1883, "reporting as to chemical agents capable of destroying the material of infection, dwelt upon the circumstance that many of the chemical products of bacterial life are endowed in a very remarkable degree with the power of putting an end to the life of bacteria themselves."¹

More recently observations have been made by Wooldridge, Hankin, Sidney Martin, and other observers, which throw additional light on this interesting subject. It has been shown, for example, that the bacillus anthracis, acting on albuminous tissues, produces an albumose or toxalbumin (a proteid substance) possessing special and characteristic poisonous properties which seem to be identical with those belonging to the bacilli themselves, and, not only so, but that the injection of this albumose into the system has the same influence in preventing a subsequent attack of anthrax as has the injection of the attenuated but living anthrax bacilli. It

can hardly be held that this albumose is the actual poison which the bacilli discharge; but, at any rate, it is a substance infected with it, and possibly holding it in chemical or mechanical solution or suspension. It may be added that recently Sidney Martin has succeeded in producing an alkaloid from anthrax bacilli which, equally with the anthrax albumose, produces poisonous effects on mice, only much more rapidly. The points, however, to which I wish to direct attention are that these observations confirm the earlier observations of Sanderson, and accord with what *a priori* reasoning might have justified one in believing—namely, that disease germs produce disease through the poisons which they yield or manufacture; that specific symptoms of the same kind as those due to the organisms themselves may be induced by the injection of the chemical poison derived from them; and that the protective influence of infective diseases against their own subsequent attacks would seem to be mainly, if not solely, due to the influence of the specific poisons which they discharge, and not to their own direct and personal influence.

All the discoveries above alluded to in respect of the prevention of certain specific infective diseases have had reference to diseases which are themselves self-protective, and their recognised effects are not to cure these diseases in the sense in which the word cure is ordinarily used, but to render persons invulnerable to future attacks. They are in their application protective, and not curative. But, as I have already observed, tuberculosis and leprosy and other such diseases differ from the diseases against which protective inoculations have hitherto been found successful in the important facts that one attack of either of these affections is, as a rule, the beginning of a lifelong ingravescence of it; that they can in no sense be regarded as self-protective, for, on the contrary, every new focus of disease is, as in cancer, the starting point of further infection; and that, in respect of them, inoculations, if they act beneficially at all, must act curatively, and not by way of prevention. It seems clear, therefore, that such diseases must be attacked on different principles from those which have been found successful in the case of diseases of the other class; that is to say, that if we are to treat them successfully by inoculation, we must either discover something which, injected into the healthy body, will render it thenceforth invulnerable (and this something can scarcely be any modified or attenuated form of the specific virus), or must discover something which, injected into the body already diseased, destroys or neutralises, or otherwise gets rid of, the specific morbid organisms.

When Koch's alleged discovery was first announced—and, indeed, for some little time after it had become the rage in Berlin, and doctors and patients were flocking thither from all quarters—we were kept in ignorance not only of the nature and mode of preparation of the fluid employed for the purpose of inoculation, but also of the scientific explanation of the mode in which its manufacturer considered it to exert a beneficial or curative influence. It was announced, no doubt, and soon became sufficiently obvious, that the injection was a potent poison, which produced, or tended to produce, some febrile disturbance of limited duration, and at the same time produced, or tended to produce, aggravation of inflammation in tissues already the seat of tuberculous growths. And it was generally admitted that the injection was derived from tuberculous guinea-pigs; but as to its specific action we had no clue. For my own part, I was under the impression, and I believe that this was the impression of many others who gave thought to the subject, that Koch—working on lines already referred to—had discovered a method of separating a form of albumose instinct with the poison of tubercle bacilli, and that his aim in injecting it was to destroy the bacilli present in the patient's system.

But when, about the middle of November, Koch gave the world an instalment of his confidence, and stated with respect to the action of his fluid on tuberculous tissue: "In what way this process occurs cannot as yet be said with certainty, as the necessary histological investigations are not complete. But so much is certain, that there is no question of a destruction of the tubercle bacilli in the tissues, but only that the tissue enclosing the tubercle bacilli is affected by the remedy"; I must acknowledge that the scepticism which I had hitherto entertained with respect to the efficacy of his

treatment became largely increased, partly because of the important admission herein contained that his remedy had no direct influence on the cause of the disease, partly because his account seemed to me to imply that he had hitherto been working in the dark and was still in search of a working hypothesis.

Two months later, namely, in January last, Koch unburdened himself a little more fully. He told us then that "the remedy with which the new therapeutic treatment of tuberculosis is carried out is a glycerine extract of pure cultivations of tubercle bacilli;" and further that, "the constitution of the active principle can as yet only be a matter of conjecture. It seems to me to be a derivative of albuminous bodies, and to be in close relation to them, but it does not belong to the group of so-called 'toxalbumins,' as it can withstand high temperatures, and in the dialysator passes easily and quickly through the membrane." He also explained more fully the mode in which he believed its curative influence was effected, and how he had been led to his discovery. Briefly his account is as follows. He found, in the course of some experimental inquiries, that the injection of either living tubercle bacilli or tubercle bacilli which had been destroyed, ground down and suspended in water, produced a different local effect according as it was injected beneath the skin of healthy guinea-pigs, or of guinea-pigs already inoculated and tuberculous: that, whereas in the former case it produced a nodule which after a time ulcerated and remained ulcerated down to the time of the animal's death, in the latter case it formed no nodule but led to a necrotic change extending for some distance around, and finally resulting in the separation of an eschar and the healing of the sore; that, further, the injection of even large quantities of the solution of defunct bacilli produced no effect in healthy guinea-pigs beyond local suppuration, while in guinea-pigs already tuberculous, small doses rapidly proved fatal, but if largely reduced below the amount required to kill and repeated at short intervals caused only little local ulceration, but gradual shrinking of already tuberculous lymphatic glands, and notable improvement in the general health. And he suggested, in explanation of the curative effects of his remedy, that the injection of the fluid led to inflammatory changes and a necrotic process in the outlying tissues in which the bacilli were embedded, analogous to, if not identical with, what we know as caseation; and that the bacilli becoming thus imbedded in, or overwhelmed by, the wide-spread ruin in which they were involved, became, though not killed, checkmated, and in deep seated or solid tissues imprisoned, at the surface of organs or in organs accessible to air thrown off and an eschar formed of the surrounding necrotic tissue.

I believe that the above is a fair summary of Koch's published views; and I proceed to make a few remarks upon them. In the first place I am disposed to believe (though this is a matter that requires confirmation) that the fluid, even though it be not an albumose, does really contain the specific poison which tubercle bacilli yield, and which, by its local influence, causes the inflammatory growth which we know clinically as tubercle. In the second place, I think we ought to have had furnished to us full details, and not a mere summary, of his experimental researches with respect to the effects of the injection of his fluid into healthy and into tuberculous guinea-pigs respectively. I am not, of course, in a position to deny the accuracy of his statements, but, on the other hand, I am not prepared to accept them on the evidence which has been placed before us. It is the less necessary, however, to go into this matter at length since we now have a great deal of evidence of more or less value with regard to the influence of so-called "tuberculin" on human beings. As I have already stated, so soon as I learnt that Koch himself allowed that his injections had no directly injurious influence whatever upon the bacilli themselves, the essential cause of tuberculosis, the scepticism I had from the first entertained became at once profound; for I could not bring myself to believe that a mere aggravation of the natural inflammation that attends the tuberculous process, even if succeeded by extension of necrotic changes, could in any true sense lead to the cure of tuberculosis. It is not the bacilli as simple living bodies which cause this disease. The progress of the affection involves, first, the multiplication and diffusion

of these bodies; next, the development of granulation tissue, and sooner or later, in a greater or less degree, more acute and widespread inflammatory changes, all arising directly or indirectly out of the irritation to which the bacilli give rise; and, lastly (unless they dry up and become effete), the disintegration and excavation of the diseased patches. And it is these superadded conditions which make tuberculosis the dangerous and lethal malady we know it to be; it is to them that are due the breaking down of the lung tissue into cavities, the ulceration of the bowels and larynx, and the graver phenomena in tuberculous meningitis and peritonitis, and even in lupus. Moreover, not only did it seem probable that the remedy might aggravate the tuberculous process in these respects, but (notwithstanding the theoretical suggestion as to the imprisonment of the bacilli and the consequent neutralisation of their destructive tendencies) it seemed on theoretical grounds at least as probable, if not more probable, that the softening and disintegration of the tissues in which they were embedded might really tend to liberate them and to allow of, or even to promote, their multiplication and diffusion. It is no doubt true that it has been shown by clinical experience that the inoculation of patients suffering from lupus tends first to produce aggravation of inflammation in the inflamed part, and then to exfoliation of the over-inflamed tissues, and to a certain amount of healthy reaction or apparent improvement; though, after all, such results amount to nothing more than the fits of amelioration which those who are in the habit of treating this disease not infrequently witness under other circumstances, and which unfortunately only very rarely result in real and permanent cure. But, on the other hand, no one could contemplate with equanimity such aggravation of inflammation in the cases of tubercle of the lungs, bowels, brain, kidneys, or serous membrane, even though the temporary aggravation, failing to cause death, should lead to temporary improvement. In such cases as these, the only justification for such treatment seems to me to be the assurance of a reasonable hope that the temporary aggravation of mischief should be followed by an actual cure, and not merely by a lull in the progress of the malady. All that seems to have been demonstrated by Koch's experiments, in fact, is that the fluid has a notable influence in temporarily aggravating the tuberculous process, followed in the case of superficial parts by exfoliation of the affected tissues and some apparent local improvement, and that it has a notable influence in causing aggravation of mischief in internal parts affected with tuberculosis. He has never shown that the tuberculous bacilli in tuberculous patients are actually bound in fetters, as he suggests they are, or that they do not, as a matter of fact, become more potent and virulent under the conditions in which he places them than they were before.

There is, of course, abundant evidence to show that Koch's fluid has certain striking therapeutic properties. It causes a temporary febrile attack of more or less intensity and of limited duration; it causes aggravation of inflammation in tuberculous tissues, and this inflammation does in some cases—and more especially in superficial parts—lead to some disintegration and removal of the affected tissues, and to this extent to some, at any rate temporary, amendment. But the general febrile disturbance is very uncertain in its occurrence. Often it fails when it might reasonably be expected to occur; and it occurs not only in tuberculous patients, but also in persons who are free from tubercle. The local reaction, again, is also very uncertain. Often, even in tuberculous cases, there is no local reaction whatever, even though the general febrile disturbance is considerable. In many cases of tubercle—as often, for example, in the case of scrofulous glands—it is impossible to get any local reaction. And, further, it has now been, I think, satisfactorily shown that local reaction occurs not only in the case of tuberculous diseases, but also in leprosy and some other affections. In reference to these matters, I should like to repeat what I have already said, that the general symptoms caused by the introduction of Koch's fluid have a close resemblance to those due to the influence of septic poison, and to suggest that it is highly probable that any poisonous influence evoking high fever would tend to cause aggravation of inflammation in parts already the seats of inflammatory mischief, and that hence such effects might be expected to follow the introduction of any poison

of the class to which Koch's fluid belongs; and further, that had Koch's fluid been used as extensively in the treatment of the granulomata—such as syphilis and leprosy—as it has been in that of tubercle, one might have observed equivalent results. There seems, indeed, to be some real evidence accruing in support of the latter view; and it is interesting that Mr. Hutchinson observes that in two cases at least (of lupus thus treated), during the febrile reaction old chilblains became again inflamed.

But, after all, the real question to be decided is whether or not Koch's fluid cures tuberculosis. Now, in answer to this question much valuable evidence has accrued. In the early days many persons—not only among the general public but also in our own profession—seem fairly to have lost their heads. Scrofulous joints and lupus have been cured, not only in Berlin, but all over Europe, the only grounds for the allegations of these successful results being an unreasoning faith in Koch's infallibility, and the obvious fact that local increase of inflammation was followed sooner or later by some degree of temporary amendment. The successful treatment of phthisis and other internal tuberculous affections was less widely and noisily, but not less confidently, proclaimed—less widely and noisily, because happily there was a wholesome dread that, at any rate in advanced cases, the remedy might prove dangerous, and therefore few such cases were treated; not less confidently, because in certain early cases of phthisis in which it was employed some improvement of health followed—as improvement of health frequently does, for a time at least, attend almost any kind of treatment, and even the treatment at all; and on the principle of "*omne ignotum pro magnifico*," the apparent improvement in the general health was assumed to represent the total elimination of that unknown quantity, the local pulmonary lesion, and the curability of consumption was proclaimed as a fact. But amidst all this chorus of jubilant credulity, discordant voices were here and there heard, and as time has progressed these have become more and more abundant and obtrusive. Of great interest in this connection seem to me the recent lecture of Mr. Hutchinson on lupus, and especially the remarkable address by Virchow on the effect of Koch's remedy on the internal organs of tuberculous patients. Mr. Hutchinson was at considerable pains to ascertain how cases of lupus treated in this country, and supposed to be benefited, have gone on. He says: "If we are obliged to report that nothing that can be called a cure has yet been obtained in London practice, it may seem unnecessary to ask whether cures are lasting. On this point too, however, I am sorry to say that some evidence is already forthcoming. I fear it is the fact that relapses occur very quickly. The patient who was taken to Berlin by Mr. Malcolm Morris and Dr. Pringle, and was for a time supposed to be almost cured, is now, I am assured by both the gentlemen concerned, in a condition almost as bad as before the treatment." Virchow's address dealt with the pathological conditions observed in some 27 or 28 deaths in subjects of tuberculosis who had been actively treated by Koch's process, of which 16 were cases of pulmonary phthisis, and 1 a case of tuberculous meningitis. It would take too much time to recapitulate his observations. But the collective results go to show, that in the lungs, bronchi, membranes of the brain, and other internal parts (as in lupus and scrofulous joints) the use of Koch's fluid tends to cause more or less intense and widespread inflammation around the tuberculous deposits; that this inflammation in no degree tends (as Koch assumed to be the case in order to explain the supposed curative action of his remedy) to envelop and imprison the living bacilli in caseous cocoons, and so to prevent them from doing further mischief; but that, as happens in the case of lupus, the inflammation in some cases becomes from its very severity (witness his case of meningitis) a source of serious danger; that largely it induces the disintegration and destruction of tissue—in the lungs the formation and enlargement of vomicae, in the bowels the extension of ulcers and tendency to perforation; and that associated with the above conditions there is a rapid and large development of miliary or submiliary tubercles, not only in the organs primarily affected, but also in other parts of the body, and even in such unusual situations as the pericardium. It is certain that Virchow's calm, philosophical, and business-like account not only gives no support to Koch's

theories and holds out no hope of the successful treatment of tuberculosis by Koch's method, but proves beyond question that all the fears of its most sceptical opponents are more than justified.

For reasons already stated I have purposely refrained from discussing my own cases which have been subjected to treatment by Koch's remedy. I have, therefore, nothing further to say save to apologise for my language if I have anywhere expressed myself unduly strongly, and to thank you for your kind attention.

LECTURES ON THE PATHOLOGY OF TUBERCULOUS DISEASES OF BONES AND JOINTS.

Delivered at the Royal College of Surgeons of England.

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LECTURE III.

Factors which aid in the production of Tuberculous Disease.—

Points of Entrance of the Bacilli into the Body.—Heredity.—Influence of Injury.—Relative Frequency of Disease in Different Bones and Joints. Influence of Chronic Inflammation, Movement, and Pressure.—Influence of Sepsis.—Relation to Age, Sex, and General Hygienic Conditions.

ALTHOUGH there can no longer be any doubt that the tubercle bacillus is the ultimate cause of these affections, and although without it they could not occur, the converse does not necessarily hold good, namely, that given the tubercle bacillus in the body, tuberculous disease must result. This proves, not that tuberculosis is not a contagious disease, not that the tubercle bacillus is not the essential causal agent of tuberculous diseases, but only that the bacillus cannot act except under favourable conditions—that, in fact, other factors must come into play to enable the bacillus to obtain a foothold and grow in the animal body. One of the chief problems to which we must direct our attention in the future is the nature of these accessory factors, and there is no doubt that as our knowledge with regard to them increases, so our power of dealing with these affections will become greater.

In the lectures on Suppuration and Septic Disease which I had the honour of delivering here three years ago, I attempted to point out the various factors which come into play in the production of these affections, and to estimate their relative importance. Our knowledge with regard to the conditions under which the tubercle bacillus acts is, however, by no means so full as that with regard to the pyogenic organisms, and one reason for this deficiency is that it is difficult to carry on cultivations of these organisms outside the body, while their growth both outside and inside the animal body is very slow. It is quite clear, however, that conditions exist which favour or hinder the entrance of the parasite into the body, which enable it to obtain a foothold in certain parts, and which permit or encourage it to go on growing in these parts, and cause the morbid changes characteristic of tuberculous disease.

The points of entrance of the tubercle bacillus are very various. I have already referred to instances in which the bacilli entered through wounds in the skin, and, as we have seen, the characteristic lesions in such cases are the development of a sore at the point of entrance and tuberculous disease of the neighbouring lymphatic glands, and subsequently it may be other tissues and organs of the body; this mode of entrance is, however, comparatively rare. In order to inoculate the tuberculous virus on animals with certainty, it is necessary to form a pocket beneath the skin into which it is introduced, and in which it may lie at rest; moisture and the possibility of remaining in the part for some time are essential for the growth of the bacilli. If the tuberculous virus is simply rubbed into scratches in the skin, the blood containing the virus quickly dries, and in this way the growth of the

bacillus is prevented, while even where there is enough moisture the organisms are usually rubbed off or carried away before they have had time to obtain a footing in the wound.

The most common point of entrance of these bacilli is, without doubt, the mucous surfaces of the body, more especially of the digestive and respiratory tracts. Thus in children one of the most frequent seats of disease is the lymphatic glands—chiefly the cervical, mesenteric, and bronchial glands. In the case of the cervical glands, infection usually occurs from the throat, from carious teeth, from ear disease, eczema of the scalp, etc. In the case of carious teeth or otitis media, we have suppurating cavities through which the bacilli may enter, but in many instances there is no definite evidence of a primary lesion at the point of entrance, the only sign of disease being the enlarged glands in the neck, and yet in all probability the infective material has in most cases entered from the throat. In the same way it is not uncommon to find the mesenteric glands in children much diseased, although there is no tuberculous ulceration of the intestine.

Klebs found that finely-divided particles of tuberculous material were absorbed without lodging and causing disease at their point of entrance in the intestinal mucous membrane, but they were usually caught in the mesenteric glands, though in some cases they even passed them and lodged in various internal organs. On the contrary—and this was also demonstrated by Chauveau—where the animals were fed with large and firm tuberculous masses, intestinal ulcerations occurred. Just as in the experimental so in the natural infection, the virus may escape the glands and produce the first symptoms of disease in parts distant from the point of entrance.

Another common seat of infection is the respiratory tract. Apart from the local effects on the nasal passages, as manifested by the production of ulcerations, etc., grouped under the term scrofulous ozena, it is not uncommon for the virus to be inhaled into the lungs, and either set up disease in the pulmonary alveoli in the first instance, or, as in the case of the intestine, pass through the alveolar epithelium and be carried to the bronchial glands, and set up disease there without any previous affection of the lungs. Indeed, it seems very probable that in most cases the source of the joint infection is diseased bronchial glands. In order to reach the joint from these glands the virus must, of course, be carried by the blood, and it has been demonstrated that the tuberculous growth may destroy the wall of an artery or vein, project into the lumen of the vessel, and thus furnish the conditions necessary for the entrance of the organisms into the blood current; or the virus may reach the blood from the lymph stream, more especially when the disease has entered from the intestine, and has attacked the wall of the thoracic duct. When large quantities of the virus are poured into the blood in one or other of these ways general tuberculosis results, but it is perhaps most common for the bacilli to enter the blood in small numbers at a time, and then, unless they meet with conditions which favour their deposit in some suitable organ, they are quickly destroyed.

Lastly, it is held by many that the disease is often hereditary—that is to say, that infection has occurred before birth. Jani examined the generative organs of several individuals who had died of tuberculous disease, and found tubercle bacilli in the seminal tubules in 5 cases, in the prostate in 6 cases, and in the Fallopian tubes twice, and in none of these cases was there any local disease. From these facts it has been concluded that, apart altogether from tuberculous lesions of the genital organs, tubercle bacilli may be present in the genital passages of tuberculous individuals, and thus gain access to the ovum.

In connection with Jani's observations, which, however, are of doubtful accuracy, I may briefly allude to some very interesting experiments which have been performed by Maffucci. Tubercle bacilli were injected into new laid eggs, which were then hatched; 18 eggs were inoculated and at the same time a hen and a guinea-pig. The guinea-pig died after forty days with tuberculosis of various internal organs, and the hen died after two months and a half of internal tuberculosis, especially affecting the liver. Of the 18 eggs 9 proved sterile, and in one the embryo died before full time, but no tubercles or tubercle bacilli were found in it. The chickens