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POST-GRADUATE COURSE AT QUEEN'S COLLEGE, BIRMINGHAM.

Two Lectures on the General Pathology of Tubercle, with especial Reference to the Question of Infection.*

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Gentlemen—

In the time at our disposal it is not possible always to give in full detail the arguments upon which some of my statements are founded, and, as a result, it may appear that my observations are more dogmatic than is appropriate when addressing a post-graduate class. The busy life you lead, however, prohibits me from making undue demands upon your time, and as an excuse for observations that may savour of dogmatism I may plead that I make them only after careful thought and examination of the work that has been done on tuberculosis during the last eight years. When possible, I shall give references to the original papers in which any point has been elucidated, so that those desiring to do so may weigh the evidence for themselves. My first task to-day must be to define what I mean by tuberculosis, and definitions, as you know, are proverbially difficult and unsatisfactory, and none the less so when we have to include in a terse description very various clinical conditions.

Tuberculosis, then, may be defined as an infective disease due to a specific virus, the tubercle bacillus, the presence of which in the tissues sets up a chronic inflammation. You will observe that this definition is a very general one, and that three points are put prominently forward. They are that tuberculosis

* The Lectures were illustrated by the aid of Photographs and the Lantern. For the loan of many of the Photographs the Lecturer is indebted to Mr. Watson Cheyne.

is infective, that it is due to a specific poison (the tubercle bacillus), and that the bacillus excites inflammation. The importance of establishing the first two points is so great that they will necessarily occupy most of my first two lectures. Before however proceeding to discuss them, it is necessary to devote a little time to the tubercles which have so long been identified as characteristic of tuberculosis.

I said just now that the tubercle bacillus sets up a chronic inflammation in the tissues, and it is these chronic inflammatory products, aggregated usually into small nodules—recognised generally as tubercles—from which the name tuberculosis is derived. It is however very important to bear in mind that the chronic inflammatory products may take the form of an "infiltration" rather than that of well-defined nodules or tubercles; and this is particularly so in bone and synovial membrane, as has been pointed out by Mr. Watson Cheyne in his admirable lecture at the College of Surgeons. This "infiltration" is not so easily recognised as the orthodox tubercle, and it may, by the naked eye, be overlooked.

The tubercles are found in varying conditions; sometimes, in the early stages, in small, greyish, semi-translucent nodules, known as grey miliary tubercles, scattered widely through the viscera; at others, as the yellow tubercle—that is, the first variety which has undergone caseative necrosis. Sometimes the tubercles are tiny masses, none larger than a pea; at others, they may be aggregated into a well-defined mass the size of a pigeon's egg; or, as in synovial membrane, a gelatinous thickening of the part may be found, in which the unaided eye can detect no definite nodules or tubercles; and, lastly, the appearance of any tubercular formation may be greatly changed by a process of softening supervening on caseation, or else calcification may occur.

Remembering, then, that the inflammatory cells are sometimes found as tubercles, at others as an "infiltration," we proceed to the histology of these conditions. With ordinary powers of the microscope and ordinary staining methods, the

inflammatory formations in tuberculosis are found to consist in the main of three varieties of cells—giant cells, epithelioid cells, and leucocytes. All these cells are found in what may be called a typical tubercle, the giant cell or cells in the centre, the numerous epithelioid cells surrounding these, and again more externally a zone of leucocytes; but it does not follow that all tubercular tissue contains giant cells. In addition, there is sometimes a slight fibrillar matrix in between the cells, but rarely is there any distinct vascular supply. These cells are the result of the irritation of the tissue by the bacilli, or by the products formed in their growth; the intrusion of the micro-organism is resented by the tissues, and that resentment is expressed by a cellular hyperplasia. In these cells *individually* there is nothing that is *absolutely* characteristic of tubercle, but when one sees them aggregated into a regular nodule and presenting the appearance shewn in the photographs, one has little doubt of the presence of tuberculosis. (Numerous photographs were here shewn.)

The one thing that is needed to establish positively the existence of tuberculosis is the presence of the bacillus, which is to be found only by special methods of staining, to be described later on. If the bacillus, then, be found associated with all or some of the various cell elements mentioned above, however diverse the lesions may appear to the naked eye, and however much the clinical characters may vary, the diseased condition must be classified as a tuberculosis. It is the remarkable diversity of the tubercular lesions in appearance, together with the extreme variations in the course the disease runs when different parts are affected and the different degrees of danger implied to the life of the individual affected, that makes it so difficult to accept the *unity* of the tubercular lesions. For example, contrast the naked eye appearance of this tubercular tumour of the brain with what is seen in the lung and in this kidney and in this epididymis, and one is struck by the varying appearances shewn in the different parts.

Again, contrast the rapid dissemination and death in a case

of acute general tuberculosis with what occurs in the ordinary tubercular gland affections. In the one we have a general disease infecting all the viscera very rapidly, well-marked tubercles being found widely distributed, and the patient's life brought to an end in a few weeks; in the other we have a few lymphatic glands in the neck affected, and subsiding in a year without having infected distant parts or produced even an abscess or in any way seriously damaged the patient. Standing half way between the two extremes we have cases of tuberculosis of the lungs existing for years, producing slow destruction of the organs, and eventually wearing out the patient's life by the chronic suppurative process induced in the lungs.

What I have referred to as "the unity of tubercular lesions" has been worked out with infinite toil by pathological observations, aided by experimental observations on animals. The connecting link is the constant presence of the tubercle bacillus, which can be demonstrated in all tubercular lesions, which can be obtained from them by cultivation, and which thus obtained can be used with certainty to set up the disease anew in animals.

Clinically we are frequently reminded, sometimes quite tragically, of the connection there is between the most acute and the most chronic and apparently unimportant lesions of tuberculosis, and we are not allowed to forget that the latter always contain the potentiality of the former. A man is affected with tuberculosis of the epididymis for years, the trouble so quiet that he has forgotten it, when suddenly an acute tubercular meningitis arises which ends his life in two or three weeks; or a child with a little tubercular osteitis of a metacarpal bone or a caseous tubercular gland suddenly develops acute general tuberculosis, or a lupus which has existed for years eventually lights up a pulmonary tuberculosis which runs a course of months only.

We have recently received important evidence pointing to the unity of all tubercular processes by the method of treatment published by Dr. Koch. Whatever the lesion may be, whether tubercle of the skin (lupus) or of a lymphatic gland, or of a synovial membrane, or of the lung, the injection of Koch's fluid

gives rise, practically always, to characteristic constitutional and local changes, the constitutional consisting in the usual phenomena of fever, and the local changes in swelling, heat, and, when it can be seen, in redness. Not only do these conditions arise in tubercular lesions, but they appear rarely in any other disease.

Although I have dwelt thus at length on the identity of all tubercular lesions I do not for one instant mean to assert that tubercle in different individuals, or in different parts of the same individual, is of the same lethal significance or that it always tends to the same local destructive effects. It is as essential that we should study the life history of tubercle in different parts and different tissues of the body, as it is that we should make out the extreme differences between epithelioma of the lip and the same disease in the tongue, or between a periosteal sarcoma of the femur and a similar growth in the radius; as everyone knows or should know the significance of these growths of different parts varies greatly, and so it is with the formations in tuberculosis.

I have already said that the one necessary point to be established before any lesion is regarded as tubercular is that it contains the tubercle bacillus. In searching for this it is necessary to resort to special methods of staining; these may vary in small details, and many modifications have been suggested since Koch's original plan was published, but the details will be more appropriately explained at the practical classes. I propose here only to explain the general principles; they are that the bacillus is effectively stained only by the aniline dyes in the presence of an alkali; that the organism resists the penetration of even this stain for some time, but once it has taken up the stain it holds it very tenaciously. To take an example:—A definite proportion of the red colour fuchsin is dissolved in an alkaline solution, and the tubercular matter is placed in contact with the stain thus made. For bacilli in sections it is advisable that the staining process should be continued for some hours, in material such as sputum or pus. The staining may be considerably curtailed,

especially if the staining fluid be warmed, and for clinical purposes a few minutes is sufficient.

We now have the whole section or layer of sputum coloured red, and the stained material is exposed for a brief period to the action of a rather strong acid and subsequently is washed in alcohol. The effect of this is to remove the red stain from practically everything but the bacilli, which, as I have already mentioned, hold their stain tenaciously once they have received it. For convenience of examination it is usual to employ what is known as a counter stain, for example, methylene blue. A dilute solution of this stain is applied to the section or sputum, and the material (with the exception of the bacilli which are still red) absorbs the blue stain. The specimen is then mounted in the usual way for examination by the microscope. For this examination a good lens, an 8th or a 10th is desirable, or what is still better, a 12th oil immersion; and it is of advantage, indeed in some cases a necessity, that a special illumination of the specimen shall be made by an Abbe's substage condenser or some similar arrangement, the advantage gained being that the structure picture is obscured and the colour picture well brought out, the stained bacilli being thus more readily discovered.

The bacillus is rod-shaped, in length about $\frac{1}{7000}$ of an inch (somewhat less than half the diameter of a red blood corpuscle) and it is generally somewhat bent, sometimes distinctly curved. With high powers of the microscope, a 12th oil immersion, or with a first-rate 8th or 10th, the bacillus is sometimes seen to be distinctly nodular, the appearance being probably due to spores by means of which the organism is reproduced. The spores resist staining even more strongly than the rest of the bacillus, we thus have parts of the rod-shaped body stained and part unstained, the effect being sometimes to give the appearance of a chain of micro-cocci. So far as is known at present the tubercle bacillus has no power of independent movement, and it is either carried passively by the blood or lymph stream, once it has found its way into those channels by the breaking down of the tubercle; or it is taken up into the interior of a wandering

cell or leucocyte and transported into the tissues by the migrations of its host.

The number of bacilli found in any tubercular tissue may vary greatly, the variations depending upon whether the tubercular lesion is acute or chronic and slowly advancing. The age and amount of degeneration in the tubercular matter also influences the number of bacilli seen. In a section of lung from a case of acute tuberculosis the number of bacilli in a field may be counted by thousands; in a section from a tubercular tumour of the brain half a dozen may be found in a field; and in lupus it may be necessary to examine half a dozen sections or more before finding a single bacillus.

The bacilli are found most readily where the tubercular process is spreading, and should be looked for especially in the interior of the giant cells or epithelioid cells, though they are often found between rather than within them; and this is especially so in the more acute manifestations. If the portion under examination should be caseous, no bacilli may be found; yet this material, when inoculated into animals, gives rise to tuberculosis, the explanation being that the caseous matter contains the spores of bacilli which have broken up; the spores though not staining, yet have the power of giving birth to fresh bacilli.

Koch's original papers shewed that whether the part examined was a tuberculous lung, gland, bone or joint, or a tubercular ulcer of the tongue or bladder, or lupus, the bacillus was found—and this has been confirmed over and over again by others—whilst sections from other and non-tuberculous diseases failed to shew tubercle bacilli. (Numerous photographs of bacilli were here shewn.)

The only micro-organism closely resembling the tubercle bacillus is that found in leprosy, which is similar in appearance, and is capable of being stained in a like manner; but it is differentiated from the former by cultivation, and practically it is of little importance to us owing to the rarity of leprosy in this country.

Whilst the characters of the tubercle bacillus which I have related are amply sufficient to enable us to recognise it in any suspected material, before it can be accepted that this bacillus is the absolute cause of the disease, it is necessary to do much more than simply to shew its presence in tubercular lesions. It must, in addition, be possible to cultivate in material outside the body the micro-organism already identified by staining, etc. When the micro-organism thus separated by cultivation is introduced into the body of another susceptible animal, it must there multiply and produce tuberculosis; and on examination of the diseased tissues by staining and the microscope, the same micro-organism must be identified that was found in the original tubercular lesion.

All this has been done in the first instance by Koch, and has been confirmed by other observers; and it is now my purpose to place concisely before you the steps by which these conclusions have been arrived at. And to those who wish to study the matter at length, I will recommend Koch's admirable and exhaustive paper on the "Etiology of Tuberculosis," translated by Mr. Stanley Boyd, in a work published by the New Sydenham Society in 1886, and titled "Micro-parasites in Disease."

Now to describe briefly that most important point the method of cultivation of the tubercle bacillus. You are all familiar with the fact that it is possible to grow on suitable material various germs—the yeast fungus, for instance, in a solution of sugar from malt, the various moulds on certain kinds of cheese. What happens in these every-day rough and ready sort of ways is carried out more carefully and with greater precision in the case of many germs capable of producing disease in man and animals. Some of these germs or micro-organisms will grow on bread, some on potato, others on gelatine-peptone, and so on; some cannot be cultivated at all—for instance, the bacillus of leprosy. Some of these micro-organisms — the anthrax bacillus, for instance — will grow on almost any medium or cultivation material, and others are very selective. This is especially the case with the tubercle bacillus. The best medium on which it

can be grown is blood serum prepared as follows:—An animal is bled into a sterilised glass vessel, and when coagulation has occurred, the serum is removed by a pipette and placed in test tubes, which are filled about one-third full. To ensure this serum being sterile and non-infected by germs in the air, etc., the test tubes are plugged with cotton wool and are placed in this steam steriliser and heated for several successive days for an hour each day to a temperature of 58° C. This does not damage the serum for our purpose, and it destroys any accidental infection from extraneous sources. The serum is then coagulated by exposure to a temperature of 65° C. for about an hour, the test tubes being sloped so as to make as large a surface as possible for inoculation, as you see in these tubes sent round.

The inoculation of the serum is performed as follows:—As soon as possible after the death of a tuberculous animal or the removal of a piece of tuberculous tissue, the part affected is exposed with properly sterilised instruments, and a portion of the tubercular matter conveyed by means of a sterilised platinum wire on to the surface of serum, in a tube, and there spread out as I here shew you. Now you may imagine all is ready for the bacilli in the tubercular matter to commence their growth on the serum. Not yet; the bacillus is not only select in its feeding, but it requires a temperature maintained pretty constantly at our body heat for days before growth visible to the naked eye takes place on the serum. The inoculated tube is therefore placed in an incubator, such as I shew here, and the temperature maintained at 100° F. by means of a gas regulator and thermometer. If the temperature rises above 106° or falls below 86°, growth ceases. The temperature, then, being maintained at about 100° F. for some eight or ten days, small whitish points and grains appear on the surface of the serum; these are presently more distinct as tiny dry scales. The appearances vary slightly according to the solidity of the serum and the acuteness of the lesion from which the cultivation was started. At the end of about four weeks any particular cultivation ceases

to develop, but from it other test tubes may be inoculated and successive cultivations kept going *ad infinitum.* In addition to the scaly appearance of the cultivation to the naked eye, the colonies of bacilli, examined under a low power of the microscope, present characteristic groupings in the shape of strongly curved lines like the letter S, and somewhat spindle-shaped, thicker in the middle and tapering at the ends (see diagram); and under a much higher power the individual bacilli, when stained, can be easily recognised. (The photograph now on the screen is from a cultivation on agar-agar which had been carried on for seven generations.)

It is now necessary to shew that these bacilli provided by cultivation, when introduced into healthy animals, set up tuberculosis invariably; but it is necessary to use, for experiment, animals which are really capable of becoming tuberculous, and the most suitable are guinea-pigs and rabbits, both of which are very susceptible to the disease, whereas dogs or cats are much less so; and, as shewing the curious selective power of the disease, it is worth mentioning that field mice readily fall victims to it, whereas white mice have an almost complete immunity. I dwell upon this question of susceptibility because at this juncture it is very important—a fact which is illustrated by reminding you of the difficulty in inoculating syphilis into the lower animals, whilst everyone knows that in the susceptible human subject infection is easily produced.

In the experiments about to be mentioned from Koch's report, cultivations of tubercle bacilli on blood serum were used; and in all of them, just to shew that the blood serum had nothing to do with producing tuberculosis, some of the animals had simply blood serum without bacilli introduced into them without any effect whatever. These are known as control experiments. The first experiment I relate is inoculation from a cultivation made from tubercle in the human being, the bacilli being taken from the fifth generation of test tubes inoculated. Six healthy guinea pigs were selected, and four of them were inoculated in the subcutaneous tissue of the abdominal wall; in fourteen days

there was swelling of the inguinal glands, and ulceration occurred in the seat of inoculation; on the thirty-second day one of the guinea pigs died, and three days later the remaining five were killed. All the animals inoculated shewed extensive tuberculosis, the two not inoculated remaining healthy. Numerous other cultivations from various tubercular lesions gave similar results. Amongst them I may mention a cultivation from lupus, which was kept going for twelve months in test tubes, and then, when inoculated, the bacilli proved as virulent as those from any other source. These inoculation experiments could be watched with great exactness when the bacilli were introduced into the anterior chamber of the eye of a rabbit, the development of the tubercular nodules on the iris being easily seen; and it is important here to mention that the tubercular disease was much more acute and rapid when a large number of bacilli were injected than in those cases where only a few were introduced. Other infections were produced by injecting some of the cultivated bacilli into the peritoneal cavity of various animals, some of them, such as guinea pigs, dying of an intensely rapid tuberculosis; others, such as dogs and rats, living for months before they succumbed. It was, however, when introduced directly into the venous circulation that the most rapid and certain infection was produced, and a condition was induced resembling closely that which obtains in the most acute miliary tuberculosis in the human subject.

The method of infection which will be of the greatest interest to you though is that by inhaling the bacilli. In a large loose box were placed eight rabbits, ten guinea-pigs, four rats, and four mice, and into this box a spray was made to play, the reservoir of which contained a mixture of tubercle bacilli and distilled water. The animals were exposed to the spray on three successive days for half an hour each day, and after the inhalations were finished the subjects of experiment were kept in separate roomy cages and well looked after. Symptoms appeared in some of the animals in ten days time, and nearly half the rabbits and guinea pigs had died by the twenty-fifth day, whilst the remainder

were killed three days later; in every instance the animals were found to be tuberculous. (Some photographs lent by Mr. Watson Cheyne were here shewn to illustrate experimental infection of joints.)

It is convenient here to mention that several experimenters have used ordinary tubercle from lung and other organs for the purpose of inoculating or otherwise infecting animals, and the proof is overwhelming that tuberculosis can thus be set up.

Accepting then the proposition that tubercle bacilli *alone* can give rise to tuberculosis, the question which next meets us is, whence come the bacilli? Must they be obtained from the body of some man or animal that has already fallen a victim to the disease, or can they arise *de novo*, or do they develop from some other micro-organism?

Whilst it is perfectly certain that many bacteria concerned in producing disease can flourish outside the human or animal body on putrefying animal and vegetable matter, it is equally clear that the tubercle bacillus cannot do so. It requires first of all a very special nourishment; secondly it needs a constant temperature of at least 86° Fahrenheit to enable it to grow; and supposing both the above conditions complied with, the tubercle bacillus would, owing to its slow development, be stifled and overrun by the more rapid developing bacteria around it and its growth would be choked, as has been established in artificial cultivations.

The next point is, do they arise *de novo*? that is, do we accept spontaneous generation? In answer to this enquiry I may say that there is not a tittle of reliable evidence to shew that this is possible. Lastly, do other bacteria develop into tubercle bacilli? Although it has been assumed that this is possible no facts support it whilst there are many against it; for example, no such transformation has been established in the case of other bacteria. Again, cultivations of tubercle bacilli for two years on blood serum have failed to shew any deviations in the naked eye appearances of the cultivations, in the microscope and staining characters of the bacilli, or in their virulence when inoculated.

We may take it that once the tubercle bacillus is expelled from the body of man or animal it either dies or lies dormant until again taken up into the body of another host; and seeing that in the living tissues spore formations occur, and so the cycle of its existence is completed and provided for, one may regard the tubercle bacillus as leading a purely parasitic existence. There is comfort in the fact that there exist such checks to the development of this powerful infection as are implied in the demand for special food and temperature before it can grow; but as a set off against these requirements we find that the bacillus and its spores are decidedly resistant to destructive changes; that to kill them extreme heat and cold are necessary; that sputum containing them may be dried for six months or allowed to putrefy for six weeks without destroying their virulence if they be used for inoculation.

I think we may believe without hesitation that the tubercle bacillus is the cause of tuberculosis, and that when man or brute becomes the subject of the disease it is owing to the entrance into the body of tubercle bacilli which have been set free from some other man or brute.

So far all that I have said on the question of infection has been devoted to experimental observations on animals, of which you may be rather tired, so I turn to what one may call the clinical evidence; and I should like to remind you that one positive observation fully described and made by a reliable observer ought to outweigh a number of negative observations.

The first point I wish to elucidate is whether one human being can be inoculated either directly from another or indirectly by means of the sputum coming in contact with a wound.

Here is a case in point, reported by Elsenberg (*Berlin. klin. Woch.*, No. 35, 1886). A child, born September, 1885, of healthy parents, was circumcised on the eighth day, the wound being sucked two or three times. Suppuration followed, and two months after the operation the wound had increased in size and the inguinal glands had swelled. When first seen, on Feb. 28th, 1886, at the seat of operation there was an ulcer covered with thick yellow exudation, and there was an infiltra-

tion into the prepuce; the edges of the foreskin were thick and rigid from infiltration, and there was undermining of the outer layer. The inguinal glands on both sides were very large, and especially on the left side, where they had broken down. There was also an abscess behind the left ear. The child died March 12th, 1886, but no *post mortem* examination could be obtained. Examination of the foreskin and glands, however, shewed typical tubercular structure and the presence of tubercle bacilli. Examination of the operator shewed that he was suffering from a cough, that he had tubercle of the larynx, and that he had phthisis of the left apex, his sputum containing tubercle bacilli. Elsenberg states that he has had three other patients under his care inoculated in a similar manner; and Eve, of the London Hospital (*Lancet*, vol. i., 1888), has recorded some cases similarly infected, as have other observers.

Here is a case, in which the inoculation was indirect, related by Tchering (*Fortschrift der Med.*, 1885). A woman, aged 24, nursed her employer, who died of phthisis. A few days before his death she wounded her third finger by breaking his sputum pot. Fourteen days later a whitlow appeared, which did not suppurate but left a painful and œdematous induration, and this was erased with a sharp spoon. Some time after, the pain, swelling, interference with movement, the thickening of the tendon sheath, and the enlargement of epitrochlear and axillary glands determined Professor Studzgard to operate. The middle finger, the sheath of the tendon, and the glands were removed, tubercle structure and bacilli being found in them. The patient was well two months after.

Pfeiffer (*Zeitschrift für Hygiene*, vol. iii.), quoted by Heron, relates the case of a veterinary surgeon who wounded himself whilst making a *post mortem* examination of a tuberculous cow. As a consequence, he developed local and, later on, lung tubercle. Tubercle bacilli were found both in the *post mortem* wound and in the lung lesions.

I could quote many other similar instances, but want of time forbids; and in my lecture on tubercular skin lesions I shall refer again to the question of surface inoculation.

There is only one other point to which I will allude here, and it is to the possibility of auto-infection. The bacilli, separated at one point of the body and on the way to be expelled, inoculate on their way the passage by which they travel. Examples of this are seen in secondary affections of the larynx in cases of phthisis, of the bladder in tuberculous kidney, of the intestines in patients who swallow their tuberculous expectoration. These auto-inoculations of themselves point strongly to the infectivity of tubercle.

I turn now to another possible source of infection, viz., to the use of the flesh and milk of tuberculous animals. To anyone who would like to look fully into this matter I would recommend the book on "The Propagation of Tuberculosis," by Lydtin, Fleming, and Hertsen. London: Baillière, Tindall, and Cox. It is of course impossible to get such positive evidence of infection in these ways as it is by the skin, for we cannot see the initial lesion produced, and often the source of the infection cannot be traced.

The following case, quoted by Heron ("Evidence of Communicability of Consumption"—London: Longmans & Co.—in the Appendix), is of great interest. A healthy infant, without hereditary tendency to tuberculosis, was fed on the unboiled milk of a certain cow. The child became thin, shewed symptoms of inflammation of the bowels, and died in four months. *Post mortem* there was disclosed marked tubercle of the mesenteric glands. The cow was at once slaughtered, and at the *post mortem* advanced tubercle of the lung was found, and in the milk contained in the udder tubercle bacilli were discovered.

From the same observer Heron also quotes a collection of four cases of children under observation at the Jenner Children's Hospital, in Berne, 1882, all of whom suffered from abdominal phthisis after consuming the uncooked milk of a tuberculous cow.

From the reports of the same hospital another case is mentioned. An infant, the child of healthy parents, was suckled by his mother during the first five months of his life, and was subsequently fed on milk from one cow, the milk being only

warmed, not cooked. The child died of tubercle of the intestine and mesenteric glands, the lungs, meninges, and other organs being healthy. During the same summer the cow also died, and was found to have extensive tubercle of the lungs and pleura.

That infection is undoubtedly conveyed to animals by their eating flesh and milk from tuberculous sources admits of no doubt whatever. Johne (*Deutsche Zeitschrift für Thiermedicin*, 1883) gives most positive results from experiments on alimentation. Of 117 animals fed with raw *tuberculous matter* from a heifer, over 60 per cent. became infected; of 46 fed with the *raw flesh* of tuberculous cows, 13 per cent. were infected; and of 91 fed with *milk* from tuberculous cows, over 30 per cent. were infected.

These experiments have been confirmed by Gerlach, Bollinger, and others, and I think we may formulate these conclusions:—

1. If animals are fed on raw tuberculous matter, such as mesenteric glands, over 50 per cent. become infected.

2. If they are fed on uncooked flesh from a tuberculous animal, though no tubercles can be recognised in the flesh eaten, infection may still take place, though with much less frequency than in the last case.

3. If the tuberculous material or the flesh be *thoroughly* cooked the risk of infection is greatly diminished if not abolished.

4. Animals fed on uncooked milk from tuberculous cows become infected, but not in the majority of cases.

5. Boiling the milk may destroy the chance of infection by killing the bacilli, but if spores are present simply boiling is not sufficient to destroy them and the milk is dangerous.

It has been pretty generally believed that for the milk of tuberculous cows to be infective the udder itself must be tuberculous; that part being healthy, no danger of infection exists. Unfortunately we must now regard this as incorrect.

Observations made by Hirschberger and Bollinger seem quite conclusive. They removed the udders of cows just slaughtered and drawing milk from the ducts by means of a syringe they injected it into the abdominal cavity of guinea-pigs. In the case

of nine cows, suffering from tuberculosis of the lungs only, in three instances positive results were obtained from the inoculations, and in six negative results. The result however is amply sufficient to shew that milk from an animal may be infectious when the disease is localised to a part other than the udder. (See Heron).

In milk taken from a tuberculous udder the danger is much greater, for it is possible in such milk to demonstrate a large number of bacilli. On this question there is some very interesting information in a pamphlet by McFadyean and Woodhead on "Micro-parasites of the Domesticated Animals."

It is worth while in connection with the use of milk from tuberculous cows to recall to your minds the large number of children under a year old who die of tubercular disease of the abdominal lymphatic glands. This is a matter that has not yet been thoroughly threshed out, and I recommend it as a subject well worth investigation to anyone who is seeking one.

I must now ask your attention to a matter of the greatest importance. So far I have not touched upon the possibility of human tuberculosis being conveyed from one person to another by the inhalation of bacilli. Direct evidence of infection in this way is difficult to obtain, mainly from two causes. Assuming that tubercle bacilli *can* infect when inhaled into the lungs, the numerous occasions on which this may occur prevent us from identifying the particular time at which the bacillus is inhaled; and when infection has actually been produced it may be months before the disease has made such progress as to attract the patient's attention to his condition, and at such a distant time it is useless to attempt to trace the infection in the majority of cases.

It has been proved, I think, beyond reasonable doubt that animals may be infected if they are placed in a limited space and made to inhale a spray containing bacilli or broken up tubercular matter. But those who do not believe in the possibility of infection, argue that the conditions in these experiments are not analogous to what obtains in the every-day life of human beings, so we must seek evidence of infection of a different

kind. Many of us have probably been struck by the fact that a phthisical person introduced into a previously healthy household may be the forerunner of phthisis in those previously healthy. A very striking case of this kind is recorded by Ogston. One son out of a healthy family of ten persons who had no hereditary taint, contracted consumption abroad and returned home to be nursed. His two sisters, who nursed him, and a brother, who shared his room and slept with him, all died of consumption, as did the patient; whilst the parents and four other sons remained healthy. Other cases similar to this might be quoted.

I will now remind you of those cases in which phthisis arises in healthy persons thrown in contact with those who are not blood relations. I know of nothing more convincing than the cases published by Dr. Hermann Weber in the Clinical Society's Transactions, 1874. He mentions that he has the history of sixty-eight persons, male and female, who, with a more or less consumptive taint, married healthy partners. In ten out of these sixty-eight cases one or several of the partners became consumptive. When, however, we examine the cases more closely, it appears that there were thirty-nine husbands who were consumptive, and in the case of nine of them the wives became diseased. Of these nine husbands one lost four wives, one lost three, four lost two each, and three lost one each—all of them from consumption—and in every case the wives were free from consumption, as far as is known, at the time of marriage, and had almost invariably a family history free from tubercular tendency.

Dr. Wade has kindly furnished me with another example. A Miss ——, aged 20, left Birmingham in January, 1888, to live in the country. She found existence there very dull, and she felt depressed and listless, but presented no symptoms of disease. About March, a girl reputed to have phthisis came to stay with her, and shared the same bed. About six weeks after, Miss —— began to lose flesh, to have a cough, and in a little time grey expectoration. Later, there were physical signs of phthisis, and the sputum contained bacilli. The patient died in September, 1889.

Let us see whether comparative pathology supports the possibility of tuberculosis arising from inhaled bacilli. Veterinary observers hold strongly that rodents and bovines, when tuberculous, communicate the disease to healthy animals who are confined in the same building and feed out of the same manger. Here are two examples quoted in the book, edited by Lydtin, to which I have already referred.

"In the territory of Taunenkirch there was a farm let for three years to a man named Gugelmaier. An average of about a dozen cows, some heifers, and a bull were kept here, all lodged in the same stable. Four years ago the farmer bought a grey cow, which soon became emaciated; consequently it was killed, and it was then found to be affected with tuberculosis to a very high degree. Since the purchase of this cow Gugelmaier had lost ten other cattle from this disease, being obliged to kill some and to sell others. The following is the succession of losses in this farm:—Three cows in 1880, one in 1881, five in 1882, and one in 1883; and another animal, a fat heifer, when slaughtered was found to have a small number of tubercles."

Lydtin also reports the following:—"In 1875 the schoolmaster of Obersasbach occupied a farm and bought some cows, but in about four years he was compelled to give up farming because of the continual losses he sustained among his cows. The first he bought in 1878, but in 1879 he sold it to a butcher, and when slaughtered it was found to be highly tuberculous, so that it could not be used as food. The second cow was bought on January 2nd, 1879, and lived in the same stable as No. 1 for fifty-four days. It was sold to a butcher December 10th, 1880, who returned the carcase, as it was tuberculous to an extreme degree. A third cow was purchased on August 11th, 1879, and lived for four months with No. 2, and it was subsequently killed on account of tuberculosis. A fourth cow, purchased in 1880, lived for some time with No. 3, and was then sold, but was returned by the buyer as probably tuberculous. The first cow came from the stable of a neighbouring farmer whose herd was infected by tuberculosis, but the second,

third, and fourth were, so far as is known, healthy at the time of purchase, and had not been exposed previously to infection. Further, the schoolmaster's stables were well kept, and the cows properly looked after."

An experiment of Koch's shews the possibility of guinea-pigs infecting one another in the way we are now discussing. He selected a number of healthy guinea-pigs. Some of them he infected with tubercle by inoculation, and then shut up with them in the same stable a number of the animals perfectly healthy and not inoculated. The result was that in three or four months' time these healthy animals became tuberculous, and *post mortem* examination shewed clearly that the disease had commenced in the lungs, and the only possible inference was that the disease started from bacilli inhaled from the destruction of tubercular lesions in the inoculated animals.

The cases and experiments I have quoted at least suggest the possibility of infection by the respiratory passages. But you may naturally enquire what evidence is there that tubercle bacilli are to be found in the atmosphere, and further whether they are still virulent? First of all as to the virulence. If animals be inoculated with tubercular sputum containing bacilli, even if it has been dried for weeks, tuberculosis is produced. As long as the sputum remains moist, the bacilli are of course kept out of the atmosphere, but when a phthisical person of dirty habits expectorates about a room or in the streets, things are different. The expectoration then dries up and becomes distributed in tiny particles, which contain bacilli, on the furniture, carpets, or any other objects, where they can be discovered by proper methods of examination.

Dr. Cornet's experiments on this point are most positive. He proceeded as follows:—With perfectly sterile sponges he washed the walls or floor of a room, or the furniture, or whatever he wished to examine. From these sponges he inoculated broth, such as tubercle bacilli could grow upon, and if when this broth was injected into guinea-pigs they shewed symptoms of tuberculosis, he concluded that tubercle bacilli were present in the

places examined in such numbers as to be a source of danger to animal life.

In twenty-one hospital wards where the majority of the patients were consumptive, fifteen of the wards yielded dust which in the way above mentioned produced tuberculosis. Examination of Lunatic Asylums and of private residences where consumptives had lived gave similar results, while other places, such as out-patient departments and surgical wards did not yield tuberculous dust, nor did he find bacilli in the rooms of consumptives who had been in the habit of collecting their expectoration in a spittoon instead of spitting on to the floor or into a handkerchief.

Whilst the sputum of phthisical patients is more than suspected of spreading disease it is improbable that the breath itself is a source of infection. Dr. Heron made several observations on this point, and he was unable to find tubercle bacilli in vessels into which phthisical persons simply breathed; if however coughing came on, although without definite expectoration, a few bacilli might occasionally be found.

I will not longer try your patience with details of this kind. The possible communicability of tuberculosis in the way I have suggested is for us and the public a question of the most vital importance, and necessarily the responsibility of arriving at a correct conclusion falls upon us. On a question of such magnitude I do not ask you to accept my judgment but to examine the evidence given in the works I have mentioned so that you may form your own conclusions; for myself I have arrived at the following:—That tuberculosis is occasionally conveyed to the human subject by external inoculation; that infection may occur occasionally by eating the flesh of a tubercular animal, but more commonly by the use of uncooked milk from such; and that the commonest method of infection is by the respiratory tract from some other human tuberculous subject; but for infection to take place the association between the healthy and the phthisical must be very close.

My reasons for the last conclusion are briefly as follows:—

(*a*) That in tuberculous man, from the lungs a large number of living bacilli are constantly being shed.

(*b*) That these bacilli can live for weeks under adverse circumstances.

(*c*) That they are dispersed in a dry state with some freedom in the apartment occupied by a tubercular patient and hence may be inhaled.

(*d*) That animals made to inhale bacilli become tuberculous, the disease commencing in the lung.

(*e*) That in a large proportion of human tuberculous subjects the disease commences in the lungs, where, by inhalation, bacilli are necessarily located.

(*f*) That there are many cases of consumption which appear to be due to living with those affected by the disease.

It may be urged as a difficulty in accepting my last conclusion that if it be correct it would be impossible for a large proportion of people to escape phthisis who do remain healthy. I acknowledge this difficulty, and whilst insisting upon the tubercle bacillus as the absolute cause of tuberculosis I do not hesitate to say that there are circumstances which greatly modify its action and which explain to some extent the difficulties.

The first of these is an inherited tendency to tuberculosis, a proposition which most people are inclined to accept without hesitation and to support by quoting instances. This predisposition is however not so readily accepted now as it was a few years ago, those who reject it endeavouring to explain many of the instances where one case of phthisis in a family is the forerunner of others as examples simply of infection through constant exposure to the reception of bacilli. For myself, I accept fully this predisposition of the tissues and regard it as of great importance.

The second modifying circumstance is "the acquisition of a generally lowered state of nutrition," such as occurs in the alcoholic, the syphilitic, and in lunatics. I imagine that it is not possible to doubt the influence of such conditions as these in the production of phthisis.

The third modifying circumstance is a condition of "local damage" to a particular part or organ in which the bacillus first establishes itself. In the lung, for example, a catarrhal state

may be the starting point of tubercular processes, in that bacilli lodged in a peripheral portion of lung may find material in which they can grow, and further are left undisturbed by the respiratory ebb and flow, which is interfered with by the narrowing of the smaller tubes from the existing catarrh. Again, in the larynx the repeated cough probably destroys the epithelium on some of the mucous membrane, these abrasions afford lodgment for bacilli which under normal circumstances would either be swept away by the ciliated epithelium or on a squamous surface would find unsuitable soil. In the knee joint a traumatic synovitis may precede the tubercular condition.

The relation between the exciting and the predisposing causes may be stated as follows:—Given all the predisposing causes, without the presence of the tubercle bacillus, and there will be no tuberculosis; given the predisposing causes, plus the presence of the tubercle bacillus, tuberculosis will pretty certainly be developed; given the tubercle bacillus, without the predisposing causes, and the development of tuberculosis is doubtful.

As a corollary of what I have said of the danger of using tuberculous food and milk and of the danger of infection from phthisical expectoration, it becomes necessary to say something of prophylaxis. The danger from tuberculous food and milk is to be met by a rigid inspection of slaughter-houses and meat markets. Any animal whose carcase was found to be infected with tubercle should be absolutely condemned as food, and should be burnt. Inspection of dairy cows, especially in the cow-sheds and byres of towns, should be systematically carried out, the inspectors being empowered to order the destruction of infected animals, reasonable compensation being in all cases provided for the owner.

With regard to the infection from phthisical expectoration, this danger can, to a very great extent, be provided against by insisting upon all phthisical sputum being received into proper vessels, the contents of which should be cremated, and at the same time the use of pocket-handkerchiefs and expectoration on the floor of buildings or elsewhere should be prohibited, the

harm likely to arise from such a cause being pointed out to the patients. It would also be a wise precaution to cremate the fæces in cases where the alimentary tract is involved, so that the bacilli from such cases may not be distributed on a sewage farm or in similar ways.

It remains now only to say a few words on the relation of the term struma or scrofula to tuberculosis. Taking the terms struma and scrofula as being synonymous in the minds of those using them, I propose to employ the first only, to save confusion. Strumous, it is perfectly clear, is a term very often used to indicate a condition which is undoubtedly tubercular. For example, a so-called strumous gland in the neck is one which contains caseating tubercles, which contains bacilli, which is capable of giving another animal tuberculosis if inoculated into it. So it is with so-called strumous disease of the knee-joint, a tubercular disease either of bone or synovial membrane or both. Such conditions had better be referred to as tubercular; the term is fuller and more definite. Strumous is however used in a second sense, being commonly coupled with another word, and so we have the term strumous tendency. What is implied by this is that the subject of it is born with a natural weakness of tissue derived by inheritance from tuberculous ancestors, and that such an one is more vulnerable to the virus of tubercle than a healthy person.

It is not possible to do otherwise at present than to accept this strumous tendency as having a real significance, derived from the fact that those subject to it have an unusual tendency to catarrhal inflammation of the mucous membranes, and probably of joints and glands, and that on to these simple inflammatory changes the tubercular inflammation may be grafted, the bacillus finding conditions suitable to its development. Congenital tuberculosis is, as far as is known, very rare in the human subject, though I am told it is not so rare in bovines.

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