form when he is given more proteid food is exactly paralleled by what occurs in phloretin diabetes. In one experiment on a cat the sugar excretion was with the same dose of phloridzin, when no food was given, 2.2 grs. per kilo.; when proteid food was given, 6.34 grs. per kilo.

Above all interesting is the occurrence of "phloretin" diabetes when the drug has been administered after prolonged periods of inanition. The details of the researches I have made upon this subject under Professor Külz's guidance are, I hope, to be published by him very soon. They show, I think, beyond the possibility of a doubt that the sugar in the urine cannot be entirely derived from the glycogen that has been stored up in the body, and they therefore give countenance to von Mering's view that the sugar is derived from the body proteid.

Von Mering originally asserted that an animal becomes glycogen-free after only five days' inanition combined with phloridzin diabetes. He has in a later paper modified the statement, and added one or two additional days to his original five. Von Mering's statement that the animal becomes glycogen-free is not correct. Prolonged and repeated phloridzin diabetes combined with absolute inanition does not necessarily cause an animal to become glycogen-free; on the contrary, there is sometimes under such circumstances still a large quantity of glycogen in the body. Nevertheless, von Mering is probably right in the main in deriving the sugar in such cases of phloridzin diabetes from the body proteids, even although the particular proof he adduces can easily be invalidated. The proteid derivation of the sugar may be safely assumed from such considerations as the following: Given an animal after prolonged inanition, and given the quantity of sugar excreted in the urine during the phloretin diabetes that is now induced, and given also the amount of glycogen found in the body when the animal is killed, is it possible to assume that a quantity of glycogen equivalent to the sum of these amounts of carbohydrate can have been present in the starving animal as residual glycogen? The figures show that this assumption is impossible.

With regard to the place where the sugar that appears in phloridzin diabetes comes from, there is as yet no information; experiments, however, which I have made seem to show that the liver of an animal killed in active phloridzin diabetes, when thrown into boiling water immediately after death, may contain large quantities of preformed sugar, thus indicating that we have in the liver, at any rate, one of the sources of the sugar that appears in the urine in phloridzin diabetes.

Another point which constitutes a link between phloretin diabetes and human diabetes is the appearance in the urine in the phloretin diabetes induced during inanition of the same morbid products of proteid metabolism as are found in human diabetes. Von Mering has seen oxybutyric acid and acetone produced under these circumstances. Though I have looked for these, I have failed to find them, but I have seen in two cases the red-brown coloration in urine which is obtained by ferric chloride where acet-acetic acid is present.

There is one more subject which I desire just to glance at before concluding this sketch of the researches I have been able to undertake in connection with diabetes. This is the subject of the influence of an increased or diminished degree of venosity of the portal blood upon the glycogenic function of the liver. That the degree of venosity of the portal blood should have a great influence on the hepatic functions is *a priori* very probable, and this is borne out by Ebstein's experiments, in which he showed that the *post-mortem* conversion of glycogen into sugar was much retarded in an atmosphere of CO_2 .

I think I have succeeded in finding a method by which the question can be studied. It is a method which it would take me too long to explain here in detail, and I am only desirous of mentioning it here because it is connected in a peculiar manner with the research scholarships of this Company, and with this Company's research scholar, the late Dr. Wooldridge, who when he died left behind him the beginnings of many things of which others will gather in the fruit. I refer to Dr. Wooldridge's method of coagulating the blood within the vessels of the living body. I have, in a communication

which is to appear in the next number of the *Journal of Physiology*, adduced, I think, sufficient reason to believe that this coagulation takes place everywhere in the body where the carbonic acid is in excess, and only there. If it turns out that I am correct in this, we shall have at our disposal in Dr. Wooldridge's method of coagulation one more method for investigating the obscure problems of diabetes, and of seeing a little further into that darkness of our ignorance of Nature which my co-research scholar, Dr. Wooldridge, made it his life work to strive to penetrate.

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 II.

Evidence that the terms "Tuberculous" Bone and Joint Disease and "Strumous" Bone and Joint Diseases are Synonymous (continued)—From their Association with Phthisis, etc.—From the Production of Tuberculosis in Animals by the Morbid Tissues—From the Production of Similar Bone and Joint Diseases in Animals with Tuberculous Material.—Experiments with Phthisical Sputum.—Experiments with Tuberculous Pus.—Experiments with Tubercle Bacilli on Rabbits.

ANOTHER point which supports the view of the tuberculous nature of these diseases is their frequent association with phthisis, tuberculous meningitis, etc. It is a well-known fact that many patients suffering from strumous joint diseases are affected, or are very liable to become affected, with phthisis; while tuberculous meningitis and general tuberculous are, unfortunately, by no means rare terminations of these diseases, especially after operation or injury.

It is difficult to ascertain the frequency of general tuberculosis, phthisis, etc., in cases of tuberculous joint disease; for patients who, when discharged, showed no symptoms of phthisis, may, and often do, develop it in later life. In my own statistics, many of the cases were not under observation for a sufficient length of time to be of value in determining this point; the average duration of the disease up to the termination of the treatment being about three years. Nevertheless we find that, during this period of time, of 386 patients, 42, or 10.8 per cent., had become affected with, or had died of, phthisis or tuberculous meningitis. Of a large number of statistics which have been published, I may mention the following. Billroth and Menzel found, on searching the *post-mortem* records at Vienna for a period of fifty years (1817-1867), that there had been 2,106 cases of carious disease of bones and joints, and of these more than half (1,143, or 52 per cent.) were complicated with tuberculosis of the internal organs. It must, however, be noted that these were chiefly adults, and also that the *post-mortem* examinations were made at a time when the views on tuberculosis were very imperfect. In Billroth's Zürich statistics, extending over a period of seven years (1860-67) it is stated that he operated on 71 cases, of which 26, or over 36 per cent., died of tuberculosis and phthisis. Neumeister has put together a large number of cases from the Würzburg clinic, and also from published papers; and gives a total of 438 cases, with 66, or 15 per cent., of deaths from tuberculosis and phthisis, and 10, or 2.2 per cent. from acute tuberculosis. Willemer states that, in the case of the knee-joint, 1 per cent. of the patients die of tuberculosis during the first year of the disease, 6 per cent. during the second, and 7 to 8 per cent. during the third.

I believe that, apart from the fact that the cases in the above statistics were observed for a long time, the septic condition of the wounds in many cases aided the generalisation of the disease, but this is a point to which I shall again refer.

Suffice it to say that, speaking roughly, something like 20 to 30 per cent. of the patients suffering from strumous disease of the larger joints ultimately die of internal tuberculosis. Further, there is only a comparatively small percentage of the cases—König says about 21 per cent.—in which the joint disease is the only tuberculous trouble.

Further proof that these diseases are of a tuberculous nature, and the same as tuberculous phthisis of the lungs, only modified by situation and other conditions, is furnished by the fact that inoculation of animals with the morbid products from the joints sets up tuberculosis in exactly the same manner as when material from the lungs is employed. I have on many occasions inoculated portions of synovial membrane and pus from strumous joints subcutaneously, or into the anterior chamber of the eye, in rabbits and guinea-pigs, and have invariably produced typical tuberculosis by this means. The same has been the experience of a number of other workers, though in a few cases negative results have been obtained. Much of the success depends on the care taken in introducing the material, more especially care that it shall keep its place and not slip out again through the opening made, and also on the employment of a sufficient amount of the material.

The last proof of the tuberculous nature of these diseases to which I need refer is the fact that similar affections may be induced in animals by the introduction of tuberculous material into bones and joints, and also by injury to joints in tuberculous animals. Tuberculous bone and joint affections have been produced by phthisical sputum, material from tuberculous joints, the pus of chronic abscesses, etc. I have obtained absolute proof of their tuberculous nature by setting up similar processes in animals by the injection of pure cultivations of tubercle bacilli derived from human tuberculosis. Such cultivations injected into the joints of rabbits and goats set up typical strumous disease of these joints; injected into the blood vessels supplying the bones they caused tuberculous deposits in the bones and disease of the neighbouring joints; and injected into the epiphyses or medulla of bones they caused tuberculous inflammation with, in some cases, expansion of the bone and new formation of bone from the periosteum, and, where the disease has extended to the joints, the typical disease of the articulation.

As these experiments¹ have not yet been published, as they were at the time they were performed the first which, so far as I am aware, had been made with pure cultivations of tubercle bacilli, and as they are of great importance with regard to the etiology of the disease, I propose to devote the remainder of this lecture to their consideration. In describing these experiments I shall, however, only mention those in connection with which I have photographs to show.

Attempts were made some years ago by Schüller to demonstrate the tuberculous nature of these affections by injecting tuberculous material into the air passages and at the same time, or subsequently, injuring the joints, and in his opinion some positive results were obtained in this way. For various reasons I did not follow out this line of research, and, in fact, have only performed one experiment of this kind. In it a guinea-pig was inoculated subcutaneously with tuberculous sputum, and on the same day, under chloroform, both knee-joints were contused, but without any positive result.

In the experiments which I have made as to the effects of the local injection of tuberculous material, I performed a few with phthisical sputum, and also with the pus resulting from the injection of this sputum, but the great majority were done with pure cultivations of tubercle bacilli.

I.—EXPERIMENTS WITH PHTHISICAL SPUTUM.

The sputum was obtained from a case of advanced phthisis, but did not contain many bacilli, about two or three in each field. The sputum was diluted with boiled distilled water. The syringe employed was the ball syringe introduced by Dr. Koch, and now so well-known in connection with his recent work. When the animals were killed the limbs were frozen and sawn up, one half being preserved and the other prepared for microscopical examination. The experiments with phthisical sputum were performed on rabbits and guinea-pigs. In two experiments on rabbits a small quantity of the sputum was injected into the right knee-joints. Both experi-

ments yielded positive results, and I may describe Experiment II in detail.

EXPERIMENT II. (November 8th, 1887).—*Injection of Phthisical Sputum into the Right Knee-joint of a Rabbit.*—The knee became gradually swollen, and on November 21st there was a large fluctuating swelling in the knee-joint, chiefly at the posterior part. On November 30th this swelling had much increased; the animal was very lame, and, as it was suffering from the epidemic diarrhoea of rabbits, it was killed; it lived 22 days.

On examination of the internal organs, no tuberculous lesions were visible to the naked eye, nor were the inguinal glands swollen; the knee-joint was distended with cheesy matter, and at the upper and anterior part the pus had evidently burst through the capsule and passed upwards underneath the rectus muscle. At the posterior part of the joint there was great swelling, due to thickening of the synovial membrane, with cheesy patches scattered here and there throughout it, as well as to distension of the capsule by the pus in the joint. In front the capsule was not markedly thickened, but between the tibia and the femur there was a fold of synovial membrane, which was greatly thickened and of a gelatinous appearance, and seemed to be closely adherent to the bone.

Fig. 1.

This photograph (Fig. 1) shows the appearances on making a complete section of the joint; we see that the capsule has been greatly distended, especially at the posterior part (to the left) with cheesy material, which has fallen out during the preparation of the section. The wall of this cavity is composed of caseating tuberculous tissue. The tuberculous growth has spread to the posterior part of the femur, destroyed the cartilage, and penetrated into the bone; the posterior part of the epiphysis has, in fact, been destroyed. The cartilage over the lower part of the bone is intact, but on the anterior surface it is destroyed, and here also the tuberculous material is extending into the superficial cancelli. The remaining trabeculae of the epiphysis of the femur are somewhat

¹ The expenses of these experiments were defrayed by the British Medical Association.

sclerosed. The epiphysis of the tibia is similarly affected. The articular cartilage over the centre of the bone has been destroyed, and the growth has penetrated into and broken up the middle part of the epiphysis. The centre of the epiphysal cartilage is also undergoing destruction. There was a considerable number of thin, feebly staining, and fragmentary bacilli in the thickened synovial membrane.

In two rabbits, holes were drilled in the upper part of the tibia and sputum introduced into the interior of the bone. In the first experiment the result was very slight; the second I may give in detail.

EXPERIMENT IV. (November 8th, 1887).—Two holes were bored, one at the upper and inner part and one on the outer side of the right tibia of a young rabbit, and sputum injected. A fluctuating swelling formed on the outer side of the upper end of the tibia in the course of about ten days, and steadily increased in size till the animal was killed on December 9th, 31 days after the inoculation.

There was no evident tuberculosis of the internal organs. There was an abscess around the upper part of the tibia, especially on the outer side. There was no pus in the knee-joint, but the synovial membrane at the posterior part was thickened; the lower end of the femur appeared healthy, but the upper end of the tibia showed the following changes. The bradawl with which the hole in the bone was made had entered the upper part of the shaft of the tibia, and had not penetrated into the epiphysis, but in the epiphysis there was a small collection of soft gelatinous material, which was in parts undergoing caseation. Beneath the epiphysal cartilage there was a line of congested bone, and the whole of the upper end of the bone was yellow, dense, and much expanded. The hole in the bone was full of cheesy material, which was continuous with the cheesy material in the external abscess.

The state of matters is best seen in photographs of complete sections of the bone. Here we see that the upper end of the bone is much enlarged, and that on one side the shell is completely absent, and its place is taken by young fibrous tissue and caseous material; this is no doubt where the hole was made by the bradawl. This material extends into the medulla of the bone, which has also completely disappeared at the upper part. On the other side of the bone there has been new formation of osseous trabeculae, which are arranged in a fine network not unlike the bone seen in strumous dactylitis. There is also in places a considerable quantity of the same sort of bone formed from the periosteum. The meshes of the reticulum are filled with swollen fibrous tissue, and there is a layer of osteoblasts lining the trabeculae. In places the new growth has gone on to formation of dense bone, in other parts this newly-formed bone is being invaded by, and disappearing before, the tuberculous growth. The soft mass in the interior of the bone consists in the centre of caseous material, surrounding which is tissue of new formation, in which there are here and there fresh points of caseation, just as in the wall of a chronic abscess. In this new tissue, which is cellular, we find epithelioid cells, sometimes occurring in small groups, but only very occasionally arranged in the form of definite tubercles, as in man, and there are no large giant cells, although some of the cells have several nuclei.

On examining the epiphysis we see that at one side the epiphysal cartilage has been destroyed, and the tuberculous material has spread into the epiphysis and involved more than half of it. At the point where the cartilage has been broken through, the tuberculous tissue is seen to penetrate between the cartilage and the ossifying layer, as I pointed out last year occurred in man. The joint also shows commencing changes of a tuberculous nature, especially at the posterior part, where the tuberculous disease has apparently just reached it. At that part there is thickening of a portion of the synovial membrane, which is commencing to caseate on its surface. Over the posterior part of the head of the tibia, the cartilage is being destroyed by spread of the soft tissue over it.

Here we have all the appearances of tuberculous osteomyelitis as it occurs in man set up in this case by the injection of phthisical sputum into the bone, and in the former experiments we have produced an affection corresponding to empyema tuberculosum of joints in man.

Similar experiments were performed on four guinea-pigs,

but the results were with one exception imperfect, and not so typical as in rabbits.

I may give the results of these eight experiments with tuberculous sputum in the following tabular form:—

I.—EXPERIMENTS WITH TUBERCULOUS SPUTUM.
Rabbits.

No.	Seat of Injection.	Lived.	Result.
1	knee	35 days (killed)	Pus in knee-joint. Thickening of synovial membrane, commencing erosion of cartilage. Caseous mass in femur. Caries of the head of the tibia.
2	knee	22 days (killed)	Pus in knee-joint. Thickening of synovial membrane. Destruction of posterior part of femur and of part of the head of the tibia.
3	tibia	10 months (died)	Abscess over bone. Cheesy deposit in medulla. No expansion of bone.
4	tibia	31 days (killed)	Typical tuberculous osteomyelitis spreading into the epiphysis, and also commencing disease of knee-joint.
<i>Guinea-pigs.</i>			
5	knee	13 days (killed)	Commencing swelling of synovial membrane.
6	knee	115 days (killed)	Pus in knee-joint. Sclerosis of ends of bone. Spread of tuberculous tissue into the superficial cancelli and the upper part of the shaft of the tibia.
7	tibia	181 days (died)	Nothing found in bone on microscopical examination.
8	tibia	56 days (died)	Small whitish spots seen in bone. Nothing found on microscopical examination.

II.—EXPERIMENTS WITH TUBERCULOUS PUS.

Three experiments were performed on rabbits with an emulsion of the pus in distilled water from the knee-joint of the rabbit used in Experiment II. In the first an injection was made into the knee-joint of a rabbit, and a small collection of cheesy material was found in the joint seven months later. In the second, the emulsion was injected into the femoral artery of a rabbit. When the animal died thirty-five days later, a cheesy deposit was found in the upper part of the femur which communicated with the exterior by a small round aperture in the bone filled with cheesy material. The following is the third experiment:—

EXPERIMENT XI. (December 13th, 1887).—The same emulsion of pus was injected into the femoral artery of a rabbit at the groin; about one-third of a cubic centimetre was introduced. This animal died on January 2nd, 1888; lived 20 days. A large abscess was found at the seat of injection, another abscess extended down the outer side of the thigh, and a very large one occupied the outer side of the leg. On sawing up the bones of the leg nothing abnormal was seen with the naked eye in the femur, but a cheesy mass was found in the upper part of the tibia just below the epiphysal line, probably in connection with the point of entrance of the nutrient artery into the bone. The medulla of the tibia was dark red, and there were some small white spots in it. There was nothing abnormal in the bones of the foot, but there was a little pus in the soft tissues. There was no evident tuberculosis of the internal organs.

Inspection of a longitudinal section of the upper end of the tibia shows that immediately below the epiphysal line there is an irregularly-shaped, somewhat triangular caseous mass, surrounded by a layer of tissue undergoing caseation. Outside the actual caseating layer there were groups of largish cells. At one part the cellular growth has destroyed the epiphysal cartilage and is spreading into the epiphysis. There were numerous tubercle bacilli in and around the caseous mass. Throughout the medulla, both of the tibia and femur, lighter stained collections of cells were seen, some of which were undergoing caseation.

In this case we have an example of chronic abscesses in the soft parts and tuberculous osteomyelitis set up by the injection into the blood stream of pus from a joint infected by phthisical sputum. In the pus used I failed to discover tubercle bacilli in the thickened synovial membrane; they were fragmentary and feebly stained, corresponding in this respect to what is seen in man. These last experiments are also of im-

portance as showing that the disease set up by the phthisical sputum was in reality tuberculous disease with its characteristic infective properties.

III.—EXPERIMENTS WITH TUBERCLE BACILLI.

I did not pursue these experiments with tuberculous material further, because the real test of the matter was whether these effects could be produced with the pure tuberculous virus—the tubercle bacillus—quite isolated from the tuberculous tissue. As I did not happen to have cultivations of tubercle bacilli, and as a year at least must have elapsed before I could get a sufficient number of removes from the first culture to do away with the objection that something besides the tubercle bacilli had been carried over, I asked Dr. Koch to send me some tubes, which he very kindly did. The following is the previous history of these tubes. In the autumn of 1886 a guinea-pig was inoculated with sputum from a patient suffering from phthisis. The guinea-pig, having become tuberculous, was killed on October 22nd, 1886, and blood serum was inoculated from the tubercles with the usual precautions. When growth had occurred a small portion was transferred to a fresh tube of serum, and so on from tube to tube of serum or glycerine agar till October 14th, 1887, when the tenth series of tubes was inoculated. It was the growth in this tenth series of tubes that was employed in the following experiments. In preparing the material for injection a few scales of the bacillary growth were removed from the tube and rubbed up with sterilised distilled water to form a fine emulsion, and from 2 to 4 minims of this emulsion were injected. All the usual precautions were of course taken, and the experiments were performed on rabbits, guinea-pigs and goats. I shall, as before, only detail those experiments of which I can show photographs.

A.—EXPERIMENTS ON RABBITS.

EXPERIMENT XII. (January 11th, 1888).—The emulsion of tubercle bacilli was injected into the right knee-joint of a rabbit. A week later there was considerable swelling of the knee-joint and redness of the skin over it. The animal was found dead on February 13th, 1888; lived 33 days.

No disease was visible to the naked eye in the internal organs, but the knee-joint was full of pus, which was more fluid than in the former experiments. The synovial membrane was not much thickened, and there was nothing apparent to the naked eye in the bones. The microscopical appearances of the part were similar to those previously described in connection with Experiment II, namely, infiltration of the synovial membrane with small and large cells, and spread of the soft tissue over the articular cartilages and their destruction from the surface. Patches of tuberculous infiltration undergoing caseation were seen in various parts of the epiphysis of the femur, as shown in this photograph, and similar appearances were seen in the head of the tibia, though not so advanced.

EXPERIMENT XIII. (January 11th, 1888).—A small quantity of the same emulsion was injected into the right knee-joint of a rabbit. A week later there was marked swelling and heat of the knee-joint. The animal was killed on May 10th, 1888, when the swelling of the knee was still considerable, though not so great as it had been; lived 120 days.

There was marked tuberculosis of the lungs, but in none of the other organs were tubercles visible to the naked eye. The right knee-joint was distended with cheesy material which had burst through the capsule and burrowed down the leg. In the joint there was a large quantity of pus, more especially above the patella and also behind the joint.

On making sections of the bones (see Fig. 2) several small cheesy deposits were seen in the femur just above the epiphysal line, and in front there was a small hole in the shell of the bone containing cheesy matter and communicating with the cavity of the joint on the one hand, and with these caseous deposits in the interior of the bone on the other. At one part of the epiphysis of the femur, just beneath the articular cartilage, the bone was yellow and dense. In the head of the tibia there were two small yellow tubercles, and there was pus around the upper part of the shaft of the bone. The cartilage over the head of the tibia had disappeared, and its place was taken by soft tissue.

On microscopical examination of sections of the lower end

of the femur the articular cartilage was seen to be almost entirely destroyed, the surface being covered with fibrous tuberculous tissue caseating at the edge. Where cartilage

Fig. 2.

was still present it was seen to be undergoing fibrillation and destruction. Over the centre of the end of the bone the tuberculous tissue was penetrating into it, and there were one or two large tuberculous nodules in the cancelli; the trabeculae were also thickened. Here and there were collections of epithelioid and small giant cells, but the chief form was tuberculous infiltration. In the caseating patches numerous imperfectly stained and fragmentary tubercle bacilli could be made out.

EXPERIMENT XIV. (January 18th, 1888).—An emulsion of tubercle bacilli was injected into the left knee-joint of a rabbit. The knee swelled up as usual, and on March 4th, 1888, it was still considerably swollen; but on May 10th, 1888,

Fig. 3.

this swelling was less and more to one side of the joint. The animal was killed on June 13th, 1888; lived 147 days. The lungs were found to be much infiltrated with tubercles, but the other organs appeared healthy to the naked eye. On

sawing up the limb two large abscesses were found in the thigh, and there was some pus in the joint. There were dense yellow masses in the epiphysis of the tibia, and also in that of the femur, and the articular cartilages were apparently destroyed. The synovial membrane was thickened and villous on the surface, as seen in this photograph of a drawing made at the time (Fig. 3), where the patella has been turned outwards, the pus washed away, and the surface of the synovial membrane exposed.

I may pass on next to experiments in which the parts were examined at an earlier stage after the injection.

EXPERIMENT XX.—In this experiment three rabbits (A, B, and C) were injected with an emulsion of tubercle bacilli in the following manner:—On the right side injections were made (1) into the lower epiphysis of the femur through a hole bored with a bradawl; (2) under the periosteum of the tibia. On the left side injections were made (3) into the knee-joint; (4) into the medulla of the tibia. A was killed ten days later, and on the right side there was a small cheesy deposit in the epiphysis of the femur, and an abscess behind the tibia, the periosteum being swollen and detached from the bone. On the left side there was a good deal of cheesy pus in the knee-joint; the tibia was not sawn up at the time, and has been lost. B. was killed sixteen days after the injection, and the following were the naked eye appearances: On the right side there was a carious patch in the epiphysis of the femur, and a small abscess outside the bone; there was, apparently, nothing abnormal about the periosteum of the tibia, but there was a small abscess in the soft tissues. On the left side there was a good deal of pus in the knee-joint, especially at the posterior part, and there was a patch of caseation, about the size of a small pea, in the medulla of the tibia, and a smaller point just below it.

In this photograph we see the appearance of a complete section of the right limb. The sections have been made to one side of the joint, so that the caseous deposit in the centre of the epiphysis is not shown, and the bradawl has apparently penetrated at this part quite up to, if not through, the cartilage. Hence the deposit here is at the edge, and communicates freely with the joint; in fact, the soft tissue in the defect in the bone is connected by a band of new material with the anterior part of the fibro-cartilage. There is much sclerosis of the bone around the deposit, and patches of caseation in the new tissue. The posterior part of the capsule of the joint is considerably swollen, and undergoing caseation at the surface, and other parts of the capsule also show commencing disease. As regards the tibia, a small abscess is seen in the muscles in front, but the shaft of the bone has not been hit in the sections. This abscess has, no doubt, formed along the track of the needle.

Fig. 4.

C died twenty-three days after the injection, and the following were the naked-eye appearances. On the right side (Fig. 4) there was a caseating patch, the size of a large pea, in the epiphysis of the femur, thickening of the synovial membrane of the knee-joint, and some pus in the joint. In the drawing the artist has distorted the appearances by pulling the bones apart. There was no change visible to the naked eye in the periosteum of the tibia, but, as will be immediately mentioned, changes were found on making sections. On the left side there was a good deal of pus in the knee-joint; the medulla of the tibia contained an elongated caseous patch.

The following is a table of the experiments on rabbits with tubercle bacilli, and their results:—

No.	Seat of Injection.	Lived.	Local Result.
12	knee	Days. 33 (died)	Pus in joint, commencing destruction of the cartilage of the femur and tuberculous infiltration in various parts of the epiphysis.
13	knee	120 (killed)	Pus in joint; destruction of the lower end of the shaft of the femur in front; destruction of the articular cartilage of the femur; caseating tubercles in the epiphysis, and thickening of the trabecula of the bone.
14	knee	147 (killed)	Pus in the joint; synovial membrane thickened and villous; extra-articular abscesses in the thigh; destruction of the articular cartilages; dense yellow masses in the epiphyses of the tibia and femur.
15	knee	197 (died)	Pus in the joint; capsule thickened and villous; pus around the joint and extending down the leg; articular cartilages destroyed; destruction of the anterior surface of the femur; a cavity containing caseous material in the epiphysis of the femur and several points of yellow sclerosed bone.
16	knee	137 (died)	No disease of the joint. The material used was extremely dilute, and possibly no bacilli were injected.
17	femoral artery	(not killed)	Apparently no effect. Very dilute material was used.
18	right knee	9 (died)	Swelling of the synovial membrane and a few specks of cheesy material in the posterior part of the joint.
"	left knee	"	The same.
19	right knee	10 (died)	The same.
"	left knee	"	Thickening of the synovial membrane, villous projections on the surface; patches of caseation in its substance and also at the surface; these characters most marked posteriorly. Articular cartilage of femur destroyed for a considerable distance.
20 A	epiphysis of right femur	10 (killed)	Small cheesy deposit in the epiphysis.
" b	under periosteum of right tibia	"	Periosteum swollen and detached from the bone.
" c	left knee-joint	"	Cheesy pus in the joint and swelling of synovial membrane.
" d	medulla of left tibia	"	?
20 B	epiphysis of right femur	16 (killed)	Cheesy deposit in epiphysis extending into the joint; sclerosis of the bone around. Posterior part of the capsule thickened and caseating.
" b	under periosteum of right tibia	"	Small abscess in the muscles along the track of the needle. Not examined microscopically.
" c	left knee-joint	"	Pus in the joint; thickening and caseation of the synovial membrane; destruction of the articular cartilages in places, and spread of the tuberculous tissue into the superficial cancelli.
" d	medulla of left tibia	"	Two small caseous patches in the medulla and a caseous mass in the muscles along the track of the needle.
20 C	epiphysis of right femur	23 (died)	Caseating patch in the epiphysis; sclerosis of the bone around; abscess in the thigh. Synovial membrane of knee-joint thickened and caseating in places. Articular cartilage of the femur undergoing destruction in front and behind, and commencing changes in the cartilage of the tibia.
" b	under periosteum of right femur	"	Thickening of periosteum with caseous patches in it, and sclerosis of the bone beneath.
" c	left knee-joint	"	Pus in the joint. Swelling of the synovial membrane.
" d	medulla of left tibia	"	An elongated caseous patch in the medulla of the tibia.

In all, there were 12 cases in which tubercle bacilli were injected into the knee-joints of rabbits, of which 11 yielded

a typical result, the exact changes which occurred depending on the length of time which the animals lived, and the number of bacilli injected. The earliest change which is noted is swelling of the synovial membrane, with the formation of a villous condition of the surface, and the appearance of small caseating patches here and there on the surface, especially at the posterior part, probably where the bacilli had collected in greatest numbers. Soon the joint becomes full, and often distended with caseous material, the synovial membrane being in a condition of tuberculous infiltration, and caseating at the surface. If the animal lives longer the cartilages are attacked and destroyed from the surface, as in man, and the tuberculous material extends into the bone, giving rise to soft caseous deposits, or leading to sclerosis of portions of the bone. In only 1 case did the injections fail, and in that instance an extremely small number of bacilli, and possibly none at all, was injected.

In 3 cases injections were made into the lower epiphysis of the femur, in each instance with positive results. The result of the injection was the development of a caseous tuberculous deposit in the epiphysis, with sclerosis of the bone around. In all the cases the joint had also become affected, and the changes in the synovial membrane and articular cartilages just alluded to were commencing. In 3 cases injections were made into the medulla of the tibia; in 2 of these caseous deposits were formed, 1 has not been examined. In 3 cases injections were made under the periosteum. In 1 of these there was considerable swelling of the periosteum, when the animal died ten days later. In the second the sections did not hit that part of the tibia, but the caseating needle track was seen. In the third there was great thickening of the periosteum with caseous patches in it, and sclerosis of the bone beneath. Similar changes were also seen in one of the cases where the bacilli were injected into the epiphysis of the femur. In 1 case a very dilute material was injected into the femoral artery apparently without effect.

It is thus evident that the result of the injection of pure cultivations of tubercle bacilli into the bones and joints of rabbits is the same as was obtained when phthisical sputum was employed, and corresponds in all respects with the changes in strumous diseases of bones and joints in man. We see similar thickening of the synovial membrane, similar caseation of the new tissue, similar accumulation of cheesy material in the joint, similar destruction of the cartilage, and, when the tuberculous growth has penetrated into the bone, similar formation of soft caseous deposits or thickening of the osseous trabeculae and commencing formation of sequestra.

(To be continued.)

ON THE TREATMENT OF HYDATID DISEASE BY INCISION AND EVACUATION OF THE CYST WITHOUT DRAINAGE.

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THE surgical treatment of hydatid disease has shared in the general advances in surgery, and the incision and drainage of the cyst (supposing aspiration to be undesirable or to have failed) may now be looked upon as the usual and routine treatment.

This will probably remain so in all cases in which suppuration has taken place within the cyst, and so these cases must be excluded from the method of treatment which I am about to describe.

Before, however, dismissing the subject of suppuration in hydatid cysts, it may be well to state that, although the suppuration (apart from the shrinking and calcareous changes which the contents of cysts undergo from the death of the parasite) is probably always due to septic agencies, yet it does not appear that these need always be introduced from outside the body. Thus in a recent case in which a very large cyst between the bladder and rectum was aspirated with a fine sterilised needle, and clear fluid withdrawn, no symptoms occurred for a fortnight, and the cyst appeared to be shrinking; at the end of that time, however, the cyst began to refill, and febrile symptoms occurred, and when opened later, the contents were found to be purulent and offensive.

Here, I think, there is little doubt that the needle was not to blame, but that the suppuration in the dead cyst was due to its proximity to the rectum and the osmosis of intestinal gas, the cyst being only separated from the bowel by the intestinal coats, and the pressure so great as to cause partial obstruction before aspiration.

I wish, however, in the following remarks to bring into prominence a method of treating cysts which are still living and growing, and which contain clear fluid with or without daughter cysts; and this is the method of incision and evacuation of the cyst contents without any subsequent drainage, or with only temporary drainage for a few hours after the operation in certain cases.

The first case, to which I have already referred, is that of a healthy young man, a butcher—seen with Mr. Serres, of Osgathorpe, and Dr. Hatchett—in whom there was a large cyst, situated between the bladder and rectum, beneath the peritoneum; this had grown upwards, filling the pelvis, blocking the rectum and urethra, and reaching up to the level of the umbilicus, and resembled a full-term pregnancy; the bladder was dragged up with it, and its fundus, though empty and compressed, reached to within 2 inches of the umbilicus. This caused a difficulty during the operation, for, on making a median incision, the empty bladder uncovered by peritoneum was the first thing met with. The incision was prolonged upwards and the peritoneum opened above the bladder, and thus the cyst was reached. On opening the latter—which, it will be remembered, was aspirated three weeks previously—I found the elastic cyst proper had separated from the outer cyst wall, and lay curled up loose in the cavity, together with much pus and a quantity of smaller daughter cysts; the elastic membrane and contents were removed entirely and the cavity sponged out, and to this fact I attribute the rapid closing of such a very large cavity; a large drainage tube was placed within the cavity. The more important feature in the case, however, follows. On exploring the general peritoneal cavity, I found in a reflection of the peritoneum in the right iliac fossa a small cyst, the size of a Tangerine orange. As I could not drain it, I incised the cyst and removed the elastic membrane and clear fluid, this being a growing cyst, I also scraped away some of the inflammatory adventitious cyst wall, immediately outside the elastic cyst proper; but this was, I think, unnecessary, and might lead to hæmorrhage. The remains of the cyst were then returned into the peritoneal cavity; no bad effects followed, and at a subsequent operation on the same patient—to which I shall refer—no trace of the cyst could be found. After dealing with this cyst, I discovered another much larger one in the epigastric region; but, considering the already large wound and serious character of the operation, it was decided to leave it for subsequent treatment. The patient recovered well, and at the end of three weeks the large cavity was a mere sinus, which soon healed.

He reappeared five months later, looking well, having gained a stone in weight, and without any symptoms of pressure on the bladder or rectum. On examination, however, I found that the cyst in the epigastrium had grown, and was now the size of a foetal head, and there was another cyst or cysts at the lower part and to the left of the abdominal cavity.

A week later I opened the abdomen by a median incision passing through the umbilicus. I then discovered three cysts, the larger one referred to above, which lay beneath the transverse colon and omentum, and two others the size of cricket balls, one in the left renal region apparently in connection with the left mesocolon, and one quite movable at the lower part of the cavity, situated entirely in the omentum. The upper cyst was first dealt with, the omentum being gently teased away and the surface of the cyst bared; it was then tapped with a fine trocar and cannula, and most of the clear fluid drawn off without aspiration. I then drew the less tense cyst towards the abdominal wound with artery forceps, and incised it freely. On doing this I found that the white elastic cyst proper had shrunk somewhat away from the walls or ectocyst, and lay, together with daughter cysts, in the cavity; it was easily withdrawn with ring forceps, and came out quite clean, although, from its brittleness, in several pieces. I then wiped the cavity out dry with a sponge, and allowed the cyst to fall back into the abdominal cavity. I then dealt with the