of the method, or even having seen anybody use intra-ocular injection, had condemned it. No doubt the most competent critics were those who knew nothing practically about it—of course, they were far better able to judge of it than one who had been using it for three years in a public institution, open to the profession, and who had, on every occasion possible, demonstrated its utility to students and medical men. As to the cases mentioned by other speakers, they only amounted to six or seven, and they were not to be taken into serious consideration in face of the details Dr. McKeown gave in his paper, and of the experience of the most distinguished Continental ophthalmic surgeons. Mr. Priestley Smith inquired respecting the size of the nozzles. It was well known that, if water be driven with force through a very small opening, the force exerted on a limited area was very much greater than if the same force were exercised through a wide opening. The object was to direct a pretty uniform force on the whole of the internal surface of the capsule, and not a strong force on any one point. The nozzle being broad and the slit long, this was accomplished. Besides, the broad nozzle gave support to the vitreous humour. The capacity of the body of the syringe was considerable, as it was a mistake to have only a few drops when force had to be used. When the operator had more than he required, he need not use it; when he had too little, he had to remove the instrument, and replenish it.—Mr. SNELL, replying to the remarks made on the treatment advocated in his brief communication, pointed out that many of the subjects raised had been dealt with in his former article. The mode of cutting the plaster allowed for the escape of tears, and patients did not complain of any discomfort; but those who had been treated otherwise on previous occasions acknowledged the greater comfort of the plaster treatment. He was not aware that Mr. Priestley Smith had used plaster so much in his practice. The method he had advocated, however, appeared more complete than had previously been adopted. Referring to Dr. Little's paper, he remarked that he had not seen the danger from using the suction curette which in some hands had been experienced. For some time he had used suction very little because it appeared unnecessary, for if the lens were well hooked up, the softened matter readily escaped through a small corneal wound. His rule was to introduce as few instruments as possible into the eye.

A CONTRIBUTION TOWARDS THE ETIOLOGY OF PHTHISIS.

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It is not my intention to discuss the morbid anatomy of the phthisical lesions, nor the dependence of the phthisical process on the presence of the tubercle bacillus, nor the important questions of heredity and of climatic and other influences, which bulk so largely in the etiological chapter.

For the present, I start with an acceptance of the doctrine of the unity of the phthisical process, and of the immediate dependence of the process on the presence of the bacillus. The rigidly exact observations and experiments of Koch and others have, in my judgment, placed this beyond doubt. I prefer, at least, not to raise the question now. But, in spite of the comparative fulness and clearness of our knowledge in these lines, it appears to me that we are far from a rational conception of the actual cause of death in phthisis. It was with the view of further elucidating this higher etiological problem that the present investigation was undertaken.

A glance through the literature of the subject reveals how seldom the attempt has been made to solve the problem, how comparatively seldom, indeed, the question has been raised. Where the matter has been discussed, explanations have been offered, which may be classified roughly under four heads, namely: (1) progressive asthenia; (2) loss of hæmatisis; (3) the lighting up of fresh inflammatory foci; (4) the absorption of waste products. Now, I have no desire to depreciate the value of these as integral factors in the process. My contention is that, in view of the comparative regularity of the clinical phenomena, and in the light of more recent work, they do not afford sufficient explanation. Each of them was fully discussed prior to the discovery of the tubercle bacillus, and Jacoud, more especially, has the credit of emphasising the importance of the fourth, namely, the absorption of waste products. Since the announcement of the tubercle bacillus, comparatively little has been added in this

direction, though the features and clinical course of an ordinary case of phthisis and those of experimentally induced tuberculosis are well defined and strikingly similar.

What, then, is the *modus operandi* of the tubercle bacillus in leading towards death? Its fatal properties cannot, I think, be regarded as merely irritant or privative. In all probability they are attributable to a power possessed by it of elaborating new products, which are afterwards absorbed.

Before explaining on what facts I base that statement, I ought to mention that Dr. Hermann Weber has hinted at the probability of such elaboration and absorption. In the Croonian Lectures (1885) Dr. Weber speaks of "the chemical poison which probably is originated by the development of the tubercle bacillus in the tissues in an analogous manner, as, according to the researches of Gaspard, Panum, Billroth, Burdon Sanderson, and others, a powerful chemical poison—sepsin—is developed in the process of septicæmia." I am not aware, however, that up to the present any attempt has been made to treat the matter more seriously. Whether the supposititious product or products are secreted by the bacillus or are elaborated from the tissues which it infects raises another question which must be discussed later. It is enough, meanwhile, if we recognise the probable dependence of these new products on the presence and action of the bacillus.

Such a process of elaboration or secretion has its analogue in the more evident varieties of fermentation, which have been studied by Pasteur, Schützenberger, and others; for example, the alcoholic, the lactic acid, the butyric acid, and the ammoniacal. More particularly the view appears to me substantiated by the following weighty evidence. The association of special forms of microzymes with special forms of fermentative action has been conclusively demonstrated by Pasteur and a large school of subsequent observers. A distinct variety of fermentation as certainly follows the admission into a suitable medium of a given microbe, as the exclusion of the same microbe excludes the possibility of its occurrence. Further, the rearing of pure cultivations has shown that different effects are obtained, though some of the observations in this direction are open to question, and, certainly, marked differences in the rate of growth are observed, according to the constitution of the medium in which the cultivation is attempted, while certain organisms are most exclusive in their selective affinities. Moreover, if the same medium, say Koch's gelatine, be utilised for the cultivation in different tubes of different microparasites, the effects produced on the medium are very different in the several instances. Even in the gross, such differences, for example, in the rate and amount of liquefaction in the production of certain gasses are marked. And it is in the highest degree probable that careful examination of the medium after cultivation has been carried on for some time would show important alterations in its chemical constitution, as occurs in the better known forms of fermentation. In other words, the living organism has the power of disturbing, or rather, in order to the preservation of its own life, the organism is compelled to disturb, the molecular arrangement of the elements in the medium of cultivation.

These considerations open up a wide and promising field for investigation. This appears the aspect of bacteriological observation, which is pregnant with most results. In illustration of this, the work of Panum, Selmi, Gautier, Brieger, Bergmann, and Schützenberger, need only be cited.

In practically applying this hypothesis to the problem of phthisis, I directed my attention first of all to the urine. The results obtained, which have been given elsewhere, were not sufficiently definite in character to warrant their citation here. Examinations of portions of the diseased organs, or of their glandular appendages, was abandoned, as it was found impossible to have these sufficiently fresh to avoid the objections that would inevitably assail successful results so obtained. This led to the adoption of the sputum as the *materies morbi* for investigation, and that, on the following, among other, grounds:—

1. The sputum is the constant accompaniment of the morbid condition, and stands in a peculiar relationship to the diseased organs.
2. It is always accessible in large quantity, fresh, and, therefore, as much as possible free from such contamination as might be supposed to introduce fallacy.
3. It has been shown that the maximum amount of the contagious element resides in the sputum.
4. Having regard to the conditions of growth of the tubercle bacillus, it seems likely that the muco-purulent secretion is a peculiarly good medium for cultivation.
5. It has been proved that tubercular sputum retains its virulence for months.
6. The presence of the tubercle bacillus can be comparatively easily determined, while with greater care its relative abundance in different specimens may be gauged.
7. The sputum

can readily be subjected artificially to similar conditions outside the body as within the chest. 8. Much of the experimental work already carried out with reference to tuberculosis has been done by the subcutaneous and intravenous injection of unaltered phthisical sputum (cf. the work of Villemin, Chauveau, Biffi, Veza, Semmer, Tappener, etc.). 9. Collateral evidence from the side of other ptomaine investigations seems to imply that the ready access of oxygen to the centre of ptomaine production aids considerably in their rapid and abundant development.

After approaching the subject in a variety of ways, with a remarkable constancy of results, I thought it best to institute a series of experiments with extracts obtained from different phthisical sputa by such methods as could be least open to objection in respect of complications introduced from without.

Method.—The sputum was carefully collected in a clean vessel, preferably a closed jar, with central hole for the entrance of the expected material, such as is used in some of the Edinburgh Royal Infirmary wards. In the selection of the patient the greatest care was exercised. *a.* Only such cases were made use of as showed undoubted signs of advancing phthisis. *b.* No case was accepted where the temperature chart did not record a more or less persistent elevation. *c.* After the first two or three examinations it was found best to restrict the selection to subjects where possible impurities from smoking were absent.

Similar care was taken in the selection of the sputum. *a.* The sputum was rejected when any foreign admixture was present, such as vomited materials. *b.* It was rejected when saliva was present in appreciable amount. *c.* The reaction of the sputum was tested, and only such admitted as gave an acid or neutral reaction. This last condition was found always associated with a peculiar odour which may be regarded as *sui generis*. *d.* The presence, and approximately the relative abundance of the tubercle bacillus was in every instance ascertained.

The sputum, thus carefully collected for twelve or twenty-four hours, is at once subjected to further examination. Its bulk is measured, and three volumes of rectified spirits are added to it. The mixing process is carried out *guttatim*, so that the separation of the elements of the sputum may be rendered complete, and the admixture made as intimate as possible. If the sputum be neutral, or but faintly acid, a trace of tartaric acid is added to the rectified spirits previous to mixing. The whole is transferred to a Florence flask. Its mouth having been protected by a fine muslin rag, the flask is placed in a Koch's steam steriliser, and exposed to a gentle moist temperature of 36° to 40° C. for twenty to twenty-four hours. At the end of this time the fluid is carefully filtered, first once or twice through fine muslin, and then three or four times through filter paper, till the filtrate runs off perfectly clear. Its volume is then measured, and the whole evaporated down in open beakers to one-fifteenth of its bulk (*circa*). This reduces it to the consistence of a more or less muddy extract, varying in colour according to that of the original sputum. The latter part of the process is conducted slowly, with the view of driving off all remaining trace of spirits, and to prevent the escape of other volatile products.

The extract thus obtained was utilised for injection. With regard to its constitution, it must be observed that it is as pure an extract as can well be obtained of the carefully-selected sputum. The only additions made are measured quantities of faintly acidulated rectified spirit. This, in the process of slow evaporation to one-fifteenth of its original volume, was presumably entirely given off; so that, in observing the results, we have to deal with the effects of a fairly purified extract of phthisical sputum—that is, sputum minus the coagulable elements, separated out by the addition of the rectified spirits and the after-process of filtration.

It should be further mentioned that the extract, when properly prepared, is most unstable; and, being extremely liable to the attack of fungi, breaks down in a few days, giving rise to new products. The extract was, therefore, never used for experimental purposes after it had been prepared for three or four days.

Four series of experiments were conducted with the extract so obtained:

1. To observe its effects on the system generally.
2. To observe its effects on the circulation; that is, on the cardiac rate.
3. To test the antagonistic effects of certain drugs, especially atropine, as regards the system generally.
4. To test these antagonistic effects as seen more especially in the cardiac rate. It is impossible here to give details of the numerous experiments conducted under these heads, but the general results may be summarised.

SERIES I.—*A. On Frogs.*—Thirteen experiments carried out with varying quantities, and under a variety of conditions, yield results of striking uniformity, and point to the presence in the extract of a

toxic principle, or of toxic principles, of considerable potency. The results differ only in degree, a progressive increase in the intensity of the symptoms being observable with the increased dosage. The general line of symptoms is that of the gradual development of voluntary motor depression. In no instance was a stage of excitement traceable. This condition of depression appears, in part, explicable by a toxic influence exerted on the higher centres. This is evidenced by the general character of the depression, by the sluggish nature of the movements while co-ordination remains little affected, and by contraction of the pupils. The spinal cord appears to be unaffected, the reflexes remaining normal throughout in the less severe cases, and in the graver being unaffected till later on.

B. On Mammalia.—In mice it was found possible to induce distinct symptoms with 0.3 cubic centimetre of the extract. These symptoms resembled in general character those observed in the frog, and passed off gradually in the course of an hour or two. With increased injection, the intensity and duration of the symptoms were correspondingly increased. As in the frog, the scope of the symptoms suggested implication more especially of the higher centres. There was the same early appearance of gradually advancing depression. This, as before, was not preceded by any trace of excitation. In the course of ten minutes the animal invariably became quieter, the stage of quiescence passing on to more or less complete passivity and disinclination for movement, according to the amount injected. In the lighter cases this was gradually recovered from. In the more severe cases it deepened into death, or death followed after more or less complete approach towards recovery. In addition to these symptoms, common to frogs and mice, certain well-marked phenomena were observed. Among the more striking of these should be noted fibrillary twitching of the surface of the body, and convulsive movements of the trunk and limbs. Regarding changes in the respiration, it has to be borne in mind that the estimation of the rate of breathing is always difficult in mice. The general impression, however, was that after the preliminary excitement there remained a certain increase in the respiratory rate, to be followed later, when symptoms were sufficiently prolonged, by retardation. In those animals which died after prolonged symptoms, anorexia was a conspicuous feature, while water was drunk freely.

In rabbits, comparatively large quantities of the extract were required to produce urgent symptoms. On economic grounds this line of experimentation was less systematically carried out. So far as they go, the results obtained were in strict accord with those just detailed. Of greater interest, however, in the case of the rabbit, was the effect of daily repeated small doses. Thus, for example, two rabbits were fed on measured quantities of oats and water, and their weights registered for some days, until the daily register became fairly constant. The same conditions were continued, with the addition that once in the twenty-four hours each animal received subcutaneously small injections of the extract. Presumably as a result of this, their weights progressively decreased by amounts varying from one-fourth of an ounce up to one ounce per diem, and the amount of food consumed was reduced to one-half, and on one occasion to one-quarter, of the amount previously consumed in the corresponding time. After some days the system appeared to grow more tolerant of the morbid material, as it was found necessary to increase the dose to produce the same effect. At the end of ten days the injections were discontinued, and the weights, without increasing, remained almost constant for a week or two. Then a gradual progression downwards, apart from fresh injection, was observed, each animal continuing to lose a fraction of an ounce daily until death. It appears likely that the early loss of weight was due directly to the action of the morbid product, which doubtless led to loss of appetite, etc. This is evidenced by the daily loss of weight corresponding with the dates of injection and by return to a more constant condition when the injections were stopped. The later progressive loss of weight, apart from injection, is more difficult of explanation. We may suppose that, following the earlier injections, a condition of marasmus developed. In neither of the rabbits was there found, on *post-mortem* examination, the slightest trace of caseation to which rabbits are prone.

SERIES II.—Effects on the circulation, that is, on the cardiac rate. A considerable number of experiments were conducted under this head. They prove conclusively the presence of a powerful cardiac depressant. In each instance the fall is striking. Where large doses were used it was remarkable, the cardiac rate being reduced, in the course of four hours under the influence of the extract, from 44 a minute to 18, and even 14. Coincident with the decrease in rate, a marked lengthening of the diastolic in relation to the systolic phase was evident. These results, taken along with those of Series IV (*infra*), imply, I think, that the depressed action on the heart is produced

through the medium of the inhibitory fibres, and not by direct action on the cardiac ganglia.

SERIES III and IV.—It is convenient in this brief summary to combine the results obtained in Series III and IV. In each it was attempted to neutralise the ascertained depressant effects of the extract by the exhibition of presumably antagonistic drugs. For the present, I limit myself to the results obtained with atropine. The double series yield results in remarkable consonance with those obtained in the earlier series. In the first place, they afford strong corroborative evidence as to both the general systemic and the special cardiac effects of the extract. But, in the second place, they prove that the combined exhibition of atropine undoubtedly modifies these results in a striking manner. Of this there is evidence in all the experiments, the degree to which such modification is produced varying with the relative quantity of the antagonistic principle. Most perfect antagonism was produced by the combined injection of .55 milligramme of sulphate of atropine with 0.6 cubic centimetres of extract. Under such conditions the general systemic effects—easily produced both in frogs and in mice by 0.6 cubic centimetres of extract—were almost completely absent, while the cardiac rate, which 0.6 cubic centimetres sufficed to depress considerably, remained practically constant. The effects were similar, whether the atropine were exhibited simultaneously with the extract, or at varying intervals before or after. The antagonising influence of atropine is most strikingly demonstrated in those experiments where the injection of the extract preceded that of the atropine by a measured interval of time. In such cases the effects of the extract were first of all well defined, and gradually declined on the addition of the atropine. Similar results, though less striking, were obtained when the atropine preceded the extract. It should be added that, in every instance where counter-experiments were made with atropine, the extract was first tested, with the view of establishing its physiological action.

This experimental record is necessarily too brief, and doubtless is open to much criticism. But the results at my disposal—which I hope to publish in more extended form—appear to me to justify the statement that from the tubercular sputum there is separable one or more products possessed of well-marked toxic properties, these toxic properties being more or less completely opposed by atropine.

The remaining question is, in how far this poisonous principle is dependent on the presence of the bacillus? Might not such toxic effects be produced by extracts obtained from other sputa besides those strictly bacillar? There is, unfortunately, no time to give in full the ground for my statement, but my belief, which rests on experimental basis, is that the presence of the bacilli is causally related to the poisonous product obtained from the sputum. I incline also, for similar reasons, to the belief that there is a relation traceable between the toxicity of the extract and the abundance of the bacillar elements discoverable in the sputum.

On the line of absorption and the therapeutic indications, regarding which I had proposed speaking, I must not dwell; but it may be convenient in closing to tabulate shortly the chief points which have been briefly discussed.

Conclusions.—1. In view of the work of Koch, it is impossible to avoid admitting that a causal relationship exists between the tubercle bacillus and the phthisical process. 2. The mere predication of this relationship is not sufficient in explanation of the clinical facts and the generally fatal termination of such cases. 3. The usually received explanations of the *modus moriendi* in phthisis are insufficient. 4. It appears probable that the lethal influence of the bacillus is due to the production thereby of certain poisonous products. 5. Clinical and experimental evidence appears to indicate that the morbid secretions from the respiratory surfaces afford a good medium for the growth of the tubercle bacillus, and, presumably, for the elaboration of such products. 6. Such a product is separable from the carefully selected and prepared sputum. 7. This product is possessed of well-marked physiological properties, being eminently toxic to frogs, mice, and other animals. 8. The toxic properties of the product are, speaking generally, depressant. 9. More particularly they include a marked depressant influence on the heart. 10. This depressant influence seems to be exerted through the medium of the cardio-inhibitory mechanism. 11. The toxic action of the product is more or less completely opposed by atropine. 12. The amount of the product which may be separated appears to bear a distinct relation to the abundance of the bacillar elements present. 13. Absorption of the poisonous product most probably occurs by way of the lymphatic circulation.

ON CERTAIN NEURALGIAS SIMULATING RENAL CALCULUS.¹

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THE purpose of the present paper is partly to draw attention to certain painful affections of the kidney which may be taken for calculous disease of that organ, and to seek for information from those who may have had a wide experience of such cases as to the distinguishing points that may be best relied on for diagnosis in cases in which doubt exists. As a rule, the diagnosis of renal calculus is easy; a time usually comes, either early or late, in which the calculus endeavours to escape by the ureter, giving rise to severe colic, and causing blood and pus to appear in the urine; to these is usually added a symptom which writers have been accustomed to consider as absolutely symptomatic of renal calculus, namely, retraction of the testicle on the side affected. Though this latter symptom is of undoubted importance, nevertheless, too much dependence must not be placed on it, since the phenomenon will appear quite independently of renal calculus, and is evoked whenever a tenacious mass of any size passes from the pelvis of the kidney down the ureter; thus, it may be observed in cases of hydatid of the kidney, or when tuberculous or scrofulous masses are passed downwards into the bladder. It is also a well-ascertained fact that a stone in the kidney may exist for a considerable time without giving rise to any of these symptoms, except pain, and that in some instances may be quite unimportant, giving rise rather to a feeling of weight and dragging than to actual suffering; whilst the urine may be examined repeatedly with only negative results. Thus, Dr. Murchison (*Diseases of the Liver*, third edition) refers to a case which was under his care, and other physicians, in which for years the painful affection of the right side was referred to hepatic neuralgia and treated as such, till after years of suffering the patient was relieved by the passage of a renal calculus. One can hardly suppose that such an acute clinical observer as Dr. Murchison would have neglected to examine the urine, and had blood or pus been present to have come to a speedy and right conclusion. An interesting illustration of a similar incident was reported in the March number of the *Chicago Review* for this year (1887), in which the patient for eighteen years had suffered from severe lumbar pain and whose urine had been frequently examined, but with negative results, till at last pyelitis was evoked, and then, after eighteen years of doubt, the nature of the case was fully revealed. I have myself (*Morbid Conditions of the Urine*, Churchill, 1882) recorded a case in which a gentleman suffering from severe lumbar pain consulted an eminent surgeon and a distinguished physician. The surgeon told him he was suffering from locomotor ataxy, the physician that the symptoms were due to syphilitic disease of the spinal cord, and placed him on a course of mercury; two years afterwards he passed an oxalate of lime calculus, which completely relieved him of his pains. He assured me that during the whole time of his sufferings his urine continued bright and clear, and that it was frequently examined by his medical attendants, and it was not till the day he passed the calculus that he noticed it thick and bloody.

It would be easy to enumerate other cases in which stone in the kidney existed without being recognised by the usual symptoms, but the converse of these cases, namely, when lumbar pains of long standing have been attributed to renal calculus, are not so numerous, and are certainly more perplexing. Thus, some years since a patient of the late Dr. Murchison, who was thought by him, and by the other physicians who also saw the case, to be suffering from stone in the left kidney, although the urine was repeatedly examined with negative results, and who went on suffering excruciating agonies of paroxysmal pain, died suddenly one night. At the inquest the *post-mortem* examination showed the peritoneum full of blood, which proceeded from the rupture of an aneurysm of one of the smaller mesenteric vessels, but which evidently pressed on some nerve plexus supplying the pelvis of the left kidney. Here, indeed, is an instance in which a correct diagnosis was impossible; but all cases of renal pain are not so obscure, and I have endeavoured to classify them in the following order.

1. Neuroses of the Kidney.—(a) A true neuralgia of the kidney is of very rare occurrence. I cannot say I have ever met with an instance. Delicate women at the menstrual period, and for some time after, suffer from aching pains in the renal region, and these pains by some have been considered neuralgic. But it has been shown that

We are informed that Mrs. H. O'D. Bartholeyns has resigned the Secretaryship of the Middlesex Hospital.

¹ Read in the Section of Medicine at the Annual Meeting of the British Medical Association held in Dublin, August, 1887.