PULMONARY TUBERCULOSIS AND INTESTINAL STASIS.¹

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I HAVE been asked to-night to lecture on the surgical treatment of pulmonary tuberculosis. If I were to deal with the various operative procedures only, I should be dealing with but part of the subject. I want therefore to say something about the relationship of intestinal changes to pulmonary tuberculosis: that is to say, the relationship of abnormal conditions of these two parts of the body as it affects tuberculosis of the lungs and as it affects also the surgical treatment of the disease. It is a branch of the work which has been interesting me greatly during the last 15 months. It is work which is begun only and which is far from complete. There are a few facts which I have learnt, there are some conclusions which I have drawn, but by far the largest part of this field of work requires a great deal of further investigation. It is partly because of this that I want to talk about it, as it will promote controversy, may elucidate further points and may help to stimulate further investigation.

While I am quite prepared to be dogmatic in much that I shall say as regards surgical treatment, I wish you to understand that most of what I propose to say about the relationship of intestinal changes to pulmonary tuberculosis is put forward in a very tentative way—not in so far as the actual observations are concerned (these I think are accurate) but as far as the interpretation of these observations.

Up to 15 months ago, I was getting very depressed working among my patients, as there were groups of conditions and observations which appeared to be forming a barrier which must be crossed before further success could be expected. Why, for instance, were these periodic outbursts of infection, causing increase in fever, associated with certain other symptoms (attacks which were labelled usually by the patient as "chill," "cold," "gastric influenza," "gout" or "rheumatism"); and whence was the origin of these infections? Why did some patients who had never had a rise of temperature after an injection of gas in the production or maintenance of an artificial pneumothorax, suddenly develop one? Why did one patient always and another seldom show a reaction when undergoing this treatment? Why should the temperature of one always be higher if up and about, and that of another be lower?

In July, 1920, Dr. White Robertson came down for a visit and he urged on me the importance of intestinal stasis and of coli and streptococcal infections in my patients. At the end of the following month he

¹ Being part of a lecture delivered before the University College Hospital Medical Society, October 19, 1921.

very kindly gave up the last 10 days of his holiday to the investigation of the blood, sputum and urine of all my patients, 32 in number: his results being added to my clinical and radiological findings, to my knowledge of the cases and to the charts showing the course of the disease, extending in some cases over several months. In the examination of the urine, tests were made for albumin in its coagulable and its non-coagulable forms, for sugar, for acetone and for the sulpho-ether derivatives of the amino-acids—tryptophane as indican, skatoxyl and indol; tyrosine as tyromine—also for bile salts and pigments, for phosphates on boiling and neutralizing and for bacilli. These tests now form part of my routine examination of every patient. At the end of Dr. White Robertson's visit, I was left with a mass of observations, with a feeling of profound confusion but with a strong conviction that, despite what at first sight appeared to be numberless contradictions, there was something there that was worth further study. I therefore proceeded to make constant and repeated examinations of the urine both in straightforward cases and whenever there was any change in the character of the temperature or of the symptoms in any patient: also I tried the effects of drug and diet on the sulpho-ethers both on the patients and on myself.

The presence of these amino-acid derivatives in the urine is an indication of intestinal stasis and of the invasion of the lower coils of the ileum by bacteria which normally should be localised to the large intestine. As Nathan Mutch says,¹ "To put the matter briefly; the upper alimentary tract is specialised for aseptic absorption of food, and the colon for bacterial destruction of residues. The invasion of the ileum in constipation by a restricted number of bacteria, not too versatile in their chemical potentialities, gives rise to various food decompositions, and the nature of the toxins elaborated depends on the particular combination of organisms present."

The presence then, as I have said, of these amino-acid derivatives in the urine affords an indication, easily available, of the state of the intestinal tract at any period of time. My frequent examinations have enabled me to make what appear to me to be some extremely useful deductions as to the influence of intestinal stasis on the course of pulmonary tuberculosis, on the course of the complications of that disease and on the necessity of certain precautions during the treatment by operative measures, which I propose briefly to set forth. I do not intend to discuss the much debated problem of intestinal stasis as the predisposing cause of tuberculosis.

My observations have been mainly of tuberculous patients, but they include a few non-tuberculous and apparently healthy subjects, and a few cases of bronchiectasis. In a few of these, single tests only have been made, but in most of them there have been repeated tests varying up to 16, and in one case up to 32.

The first two facts I established were: (1) the great frequency of skatoxyl in patients suffering from tuberculosis of the lungs. (2) The ineffectualness of drugs to produce more than a temporary diminution of the sulpho-ethers, but the magic charm (though not infallible) as a tem-

¹ Intestinal Stasis. Arbuthnot Lane.

FIG. 1.—[In this and the subsequent illustrations, the quantities of the amino-acid derivatives are shown in numbers for the sake of clearness in comprehension. These numbers are approximately correct only. They are obtained by representing "faint trace" as 1; "trace" as 2; "slight" as 3; "one plus" as 4; "one to two plus" as 6, &c.] Patient with active disease of the right upper and middle lobes, left hilum and larynx; five months' history.

FIG. 2.—A. Patient with long history of fibrosis of three lobes which has recently developed fresh activity; B, patient with active disease in four lobes; two years' history.

porary measure, of castor oil and of calomel and of the extreme usefulness, in certain cases, of kaolin.

In almost all these cases in which there are persistent large amounts of sulpho-ethers in the urine, the temperature of that patient is of the type due to secondary infection of a high degree associated with tubercle—the morning temperature being 98° to 99° F., and the evening temperature reaching 101° to 103° F. (rectal). In each of these cases, the prognosis (based on clinical and radiological examinations) was bad, and this was corroborated by the later history of the patient (fig. 1).

In some cases in which there was very extensive disease of the chronic type but with recent and considerable activity, the sulpho-ethers were small in amount (fig. 2, A and B). In others again of much the same type clinically, the sulpho-ethers were considerable at the start but diminished very appreciably with regulation of the bowels (fig. 3). In both these types the disease in the lungs has proved fairly amenable to treatment, though the progress is not rapid. Both groups, however, but especially the latter, are very liable to slight exacerbations of fever, associated with increase of sulpho-ethers.

FIG. 3.—Patient with active disease of two lobes; 18 months' history; showing diminution of sulpho-ether after course of agar-agar.

I have not had a case of the acute miliary type since testing for sulpho-ethers, but I have had two patients of the acute pneumonic type. The only one of these whom I have been able to watch for any length of time has also a tuberculous larynx. He had had a gastro-enterostomy done for ulcer some years previously. I have never been able to effect any permanent diminution of the amino-acid derivatives in his urine. I collapsed the affected lung by artificial pneumothorax, but it took a long time to effect this satisfactorily because of the consolidation, and it took

12 months to reduce his temperature to a maximum evening rise of 99° F. (rectal). For several months it was an open question whether I could save his life. Now he is extremely fit, in his general health. He has no evidence of any active disease in his lungs. His larynx is not yet quite healed. His urine is still loaded with sulpho-ethers. He has a pleural effusion on the side of his pneumothorax which I find impossible to prevent recurring. This does not inconvenience him, and he is able to live at home and lead a fairly normal life without work. Yet I feel that the prognosis in his case is most doubtful.

I must now turn to certain complications which occur from time to time in cases under treatment for pulmonary tuberculosis; some of them more so perhaps in a private than in a public sanatorium, as in the former the diet is richer and there is less control over the constant tucking into sweets, chocolates and other oddments between meals. The examination of the urine will help materially in differentiating between these complications and in indicating the right line of treatment.

(1) There is nausea. This may be due to indiscretion in diet or to irritation of the gastric mucosa. It may be accompanied by yawning and even by sighing respirations, and is then probably due to acetone. The presence of acetone in the urine is much commoner than I had imagined. The acetone, and necessarily the symptoms consequent on it also, can be very easily abolished by large doses of sodium bicarbonate and potassium citrate, to the very great relief of the patient.

(2) There are the gastro-intestinal group of disturbances, often referred to by the patient as "bilious attacks." There may be nausea or vomiting, anorexia, furred tongue and possibly offensive breath. There is little or no rise of temperature, possibly no acetone, whilst the increase in the sulpho-ethers depends on whether the gastric or the intestinal symptoms predominate. These cases usually respond to free purgation, but they may need some intestinal antiseptic such as dimol or salol (fig. 4).

(3) There are the "short fevers." In these the chief symptoms are malaise, aches and pains in the limbs, possibly shivering, nausea, coryza, and an increase in bronchitis. There is an increase in fever, the temperature rising especially in the late afternoon. The urine always shows a considerable increase in the amino-acid derivatives. Such attacks which last three to five days are referred to as "severe chills," or "gastric influenza" (fig. 5). One patient who had spent eighteen years in Burma referred to them as attacks of "malaria."¹

These short fevers are most prevalent in the autumn and winter months and are liable to occur during the first hot spell in the spring. They appear at times to spread from one patient to another in the manner of an irregular epidemic.

¹ White Robertson says in his article on "Hidden Sepsis": "It was my experience in India that practically all acute fevers were hastily labelled 'malaria,' and on my return to England I found the same fevers, this time labelled 'influenza.' In 1910, I classified, after exhaustive clinical and laboratory investigation, 1,000 consecutive fevers in my own practice, and as a result was able to show that, while malaria was found to account for only 33 per cent. of these, the fevers due to coli bacteræmia representing practically the whole of the remainder. They are equally common in this country."—*Lancet*, November 20, 1920.

FIG. 4.—Showing the absence of increase of sulpho-ethers with increase of activity, but the increase of them during a "bilious attack."

FIG. 5.—Showing the amount of sulpho-ethers present before and during a "short fever" also the effect of castor oil and of kaolin on the fever.

If treated at the onset by castor oil or calomel, and then by large doses of kaolin and oil of peppermint as recommended by White Robertson, the attack may be cut short. One patient whose progress was constantly interfered with at intervals of about six weeks by the appearance of these symptoms, has not had a real "short fever" attack for over a year, as now, at the first indication, he doses himself with castor oil.

(4) Lastly, there are two groups of cases which show at first a very close similarity. In both the temperature which may previously have been steady rises slowly to a slightly higher level each night and morning. There may be no other symptoms except that the patient feels "off colour," or more tired than usual. These symptoms are most usually due to intestinal stasis, in which case the urine will show an increase in sulpho-ethers and the temperature will return to its old level after free purgation (fig. 6). They may, however, be the result of an exacerbation

FIG. 6.—A rise of temperature due to intestinal intoxication and not to changes in the chest.

of the tubercle bacilli, in which case no change in the physical signs in the chest can be detected till possibly three or four days later. This cause for the rise in temperature must be strongly suspected if there is no change in the character of the urine.

I now come to the question of the importance of intestinal stasis in surgical treatment. We all know the necessity of castor oil before an operation. I did not realise until some months ago that purgation might be essential also before an injection of gas in the production of an artificial pneumothorax. I was for long extremely puzzled as to why in some cases there was no reaction, in others a short sharp reaction as indicated by the rise of temperature, and in others again a prolonged reaction with shivering, with considerable malaise and with pains in the limbs. My investigations of the urines helped to elucidate this problem.

Patients without intestinal stasis usually give no reaction if the dose of gas injected is regulated; or, if they do give one, it is manifested by a quick rise and a quick fall in temperature, which is due to a sudden increase of the tuberculous toxin (fig. 7A). There is no appreciable amount of sulpho-ethers passed in these cases. When, however, intestinal stasis is present and considerable, and the urine constantly shows the presence of large amounts of the amino-acid derivatives, then there is almost always a profound reaction. The picture resembles closely that of a "short fever," but the time taken before the temperature returns to its old level may be a week to 10 days or more. There is usually no change in the chest to account for these disturbances, but sulpho-ethers are always present in increased quantities in the urine (fig. 7B). So constant is the association, that it seems that the responsibility must be put down to the intestinal condition.

FIG. 7.—A. A reaction due to toxins of tubercle bacilli; B, a reaction due to toxins of secondary organisms; C, rise of temperature associated with pleural effusion.

Occasionally it happens that a patient who has had several injections of gas in the production of an artificial pneumothorax without ever giving a reaction, will, for no obvious reason, suddenly give a reaction of the "short fever" type. The patient whom I mentioned as describing these attacks as malarial always had abundance of sulpho-ethers in his urine on these occasions. Another interesting point about this patient is that, whereas while in the sanatorium traces of sulpho-ethers only were found between the attacks, since he has left they have increased greatly in amount, and are constant. If, now, when he returns for his refill I omit to purge him thoroughly the day before, he will get one of his "malarial" attacks. When he is purged, however, there is a rise of temperature after the refill, but it is not so high nor so prolonged and it is unaccompanied by the shiverings and by the aches and pains.

Another patient who had never previously had a reaction (there had been 11 previous injections) developed a big reaction similar to a "short fever" but more severe and more prolonged. He admitted later that he had noticed the initial symptom of one of the febrile attacks to which he was subject, earlier in the day. His urine, usually clear, was on this occasion loaded with sulpho-ethers. He developed a pleural effusion which had to be replaced by oxygen. Since then he has had no recur-

rence of fluid nor of a similar reaction, nor of an excess of sulpho-ether, but precautionary measures have invariably been taken. I have once recently given him a refill with impunity, two days after the onset of a definite "short fever" attack; this attack had however been controlled from the start by castor oil and kaolin.

A somewhat similar type of reaction, but with less diurnal variation in the temperature, is seen when a pleural effusion follows an injection of gas. The patient feels out of sorts and has usually vague pains about the chest. The sulpho-ethers are, however, not necessarily increased (fig. 7c).

I have made no mention of the organisms in the intestinal tract which, in cases of stasis, are responsible for the appearance of sulpho-ethers in the urine. Nor do I propose to do more than to mention that these are mainly of the coli group. I would however call your attention to the fact that the dominant organism may be in a few cases the streptococcus. In these, sulpho-ethers are not a feature. The chief characteristics are the swinging temperature (showing diurnal variations and a switchback curve extending over periods of ten days or a fortnight, and rarely dropping below 98° F.), and the associated symptoms such as sore throat and pains about the body and in the joints. These increase with the increase in fever and die down with the lowering of it.

I have spoken already of the charm of castor oil; calomel possesses it also but perhaps to a less degree. It must be understood, however, that neither of them is invariably infallible even in the same person. Much depends on the character of the intestinal stasis. If there is long established chronic intestinal stasis with advanced secondary infection of the lungs, I have found no drug, no diet, no amount of colon irrigation effect much apparent change either in the temperature or in the outpouring of intestinal toxins. In the less extreme cases, either of the purgatives mentioned will produce a temporary improvement and this improvement may be of great value in diminishing the reaction of an injection of gas.

I have found kaolin, paraffin, agar, dimol and salol to be the most satisfactory drugs for continued administration. The former particularly in acute cases, paraffin and agar in the chronic cases, and dimol or salol in that type of disturbance which is gastro-intestinal as opposed to purely intestinal.

I may add that, now, previous to a major operation on the chest, I give the patient a course of kaolin and oil of peppermint before the final dose of castor oil.

Colon irrigation has not proved such a success as I had hoped it might be, though a few cases have responded well.

Before leaving this part of the subject I must say a word about diet. In the majority of the cases from which I have drawn the illustrations, the diet has been more or less uniform. In the more acute cases there has naturally had to be considerable modification; and the same applies to acute exacerbations occurring either as the result of injections of gas or independently of (or despite of) treatment, e.g., "short fevers." Two patients responded well to a much reduced proteid diet (no butcher's meat); in one of these the diet had a most marked beneficial influence on his general health.

A consideration of the above evidence would suggest that the organisms in the intestinal tract are in close rapport with those causing secondary infections in the lungs, and that stimulation of the one group may affect the other group as well. Also that the changes produced in the lungs by injection of gas may cause an excitation, not only of the tubercle bacilli and an outpouring of tuberculous toxins, but also an excitation of the secondary organisms in the lung which pour out their toxins and in turn set off those in the intestinal tract. The reverse process of this would also hold good. This is supported by the frequency with which intestinal symptoms are associated with increase in bronchitic symptoms in those subject to bronchitis, or with a mild bronchitis, and coryza in those who have no definite changes in their bronchial tubes. It would account moreover for the close relationship of excessive sulpho-ether excretions in cases with extensive secondary infection.

Finally, if there is any truth in the above observations and deductions, it becomes evident that to treat tuberculosis of the lungs as an isolated lesion, leaving out all consideration of the gastro-intestinal tract, is to treat a part only of the disease and to be therefore but inviting failure.

I would urge, therefore, that in investigating a case of pulmonary tuberculosis, in addition to the study of the chest symptoms and signs, of the bacteriological characters of the sputum, of the radiological appearances of the thorax, of evidences of tuberculosis elsewhere, it is necessary to investigate the condition of the intestinal system as regards stasis (and ptosis), and also, although it is a subject I do not propose to discuss to-night, the functioning capacity of the endocrine glands.

May I, however, again emphasise what I said at first. What I have put before you about the sulpho-ethers and the secondary infections and tuberculosis, is offered tentatively. A larger mass of observations may show that my deductions are wrong. I hope at any rate that I may have made you realise that pulmonary tuberculosis is not a simple disease which can be regarded as a morbid change affecting the lungs only, but rather that the local pathology is a part only of a much more general pathology of the body.

HÆMOPTYSIS AND ITS TREATMENT.

I.—CLASSIFICATION AND SOURCE.

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THE treatment of hæmoptysis cannot be considered a creditable chapter in the book of medicine, and we should most of us like to see it re-written—by an enemy for preference! In particular we should rejoice to lose the familiar faces of ergot, and of acetate of lead, tannic acid, perchloride of iron, *et hoc genus omne*—the children of false analogy and unsound reasoning! But when an attempt is made to substitute a system of rational therapeutics for the present chaos, we find that our foundations have still much of the character of a quicksand, and the stability of our