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SOME CASES OF PYREXIA WITHOUT PHYSICAL SIGNS.*

BY

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LADIES AND GENTLEMEN,—The title of my lecture is perhaps chosen more because it is trite than because it approaches to an exact description of the cases I have in mind. It would be more accurate to say pyrexia without adequate signs and symptoms. I say this in order that you may be familiar with the type of case with which I am going to concern myself. It is a very common and very important type of case, one which taxes our resources to their utmost. It is important because we never know whether the condition underlying an obscure pyrexia is going to turn out to be trivial, or very serious. It taxes our resources because it is very difficult to prove a negative; and when we are asked—as we invariably are by anxious relatives and friends—What, exactly, is it doctor? we are often placed in a position where either we have to manufacture names which do not carry conviction to ourselves, or we have to risk losing the confidence of those who put the question to us by suspending our opinion. An instance of that is the very familiar one—with which I shall not be dealing to-day, but I mention it in passing—of the invasion period of some acute pyrexial illness. We are expected, long before there are any signs or symptoms which are in any sense committal, to say what is the nature of the illness. To the more intelligent we point out that measles before the fourth day is a pyrexial illness and very little else, or that influenza has no strict clinical criteria, that a child may have a pyrexial period of ten days or more before we realise that the cough is becoming rather characteristic of pertussis, and that paratyphoid fever may run its whole course without proof, either clinical or bacteriological, of its true nature. In other words, there are plenty of acute febrile diseases in which it is quite impossible, with our present knowledge, to say what is the nature of the illness unless and until certain symptoms and signs have developed. I am not so much concerned with that group of acute

infections this evening as with conditions accompanied by subacute or chronic pyrexia.

I. Most cases of pyrexia without adequate signs or symptoms are due to microbic infection. There is the exception of *the nervous patient*, the neurotic, whose thermo-taxis mechanism is unstable, and who, without infection, may run a mild grade of pyrexia as an expression of this unstable nervous system. This position is queried by some practitioners, and I think the query is a reasonable one, but it perhaps reduces itself to rather a quibble if one says that in this type of patient the pyrexia is really due to some sub-infection by an organism which, in persons with a more stable nervous system, would not show this effect. These cases are a great trial in practice, as you will agree. We feel we cannot afford to take risks. The relatives or friends of these patients bring us charts showing a mild pyrexia lasting week after week; we examine the patients carefully, but we can find nothing adequate to explain the raised temperature. The patients are, however, highly nervous, and they become more and more nervous the longer this pyrexial state goes on and the more numerous the investigations that are undertaken. The longer these patients remain under observation, the more nervously unstable they become.

What is the way out of this particular difficulty? I think the way out depends on the individual case. My own feeling about many of them is, that they will be no worse if they become more definitely ill in order that they may be treated on some proper basis in regard to the diagnosis. I often say quite plainly to them, or (more often) to their responsible relatives, "This is a very unsatisfactory state of affairs. Life cannot be lived without small risks. Are you prepared to take a little risk? You have had very exhaustive and expert examinations, and nothing has been found, except this highly nervous state of the patient. I propose, therefore, to stop taking the temperature and to start on a system of gradual and encouraging re-education of these toneless muscles and this toneless nervous system, and see what comes of it. I promise you I will interrupt this programme so soon as something develops which can be definitely treated." That is an attitude which I not uncommonly adopt, and in the cases in regard to which due care has been exercised to exclude organic disease, things do not go wrong. If it be true that the proof of the pudding is in the eating, it must be a sound method, seeing that the results seem to justify the wisdom of it, for most of the cases go straight ahead and get well.

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I leave the question of the neurotic who runs a temperature easily by repeating that it matters little whether we take the view that the pyrexia is an expression purely of an unstable nervous system, or whether it is that *plus* the operation of some feebly pathogenic organism. I think the method of treatment is the same and should be undertaken on general lines, not on local or specific lines.

In your presence, Sir,[†] I hesitate to enlarge on the nervous type of pyrexia when the patient is a child, except to say, from my own experience, that the nervous child "puts up temperatures," as one expresses it, even more readily than does the nervous adult. The position is not easier, it is, perhaps, more difficult, because in the pyrexial child who has no adequate symptoms and signs for the time being we always have in the background the possibility of that ubiquitous condition tuberculosis, generally glandular. In the case of children who have just had acute illnesses the anxious parents keep on the nurse, and the nurse has to justify her position and goes on taking the temperatures. It is often found that the temperatures are not normal; the thermometer registers a temperature a little higher than immediately after the subsidence of the specific fever—scarlet fever, whooping-cough, acute rheumatism, or whatever the illness may have been. And then the position arises of which I have just spoken. The "dark horse" is tuberculous adenitis affecting a group of glands which cannot be very well, or at least not very convincingly, examined: those in the thorax or abdomen. We had hoped, so far as the thoracic group is concerned, that the radiologist could help us out of this particular difficulty. Perhaps I ought not to say that he has driven us further into the difficulty, but he certainly has not got us out of it, the reason being, I think, that the criteria of the normal in respect of the size of the hilum glands in the child are still lacking. I am not seldom consulted about such cases; often they are the children of doctors, and in most of them the parents have already had X ray investigations made. Oftimes they were satisfied with the progress of the child up to the time that the X ray picture was taken; and then the whole household was plunged in a state of gloom because a report was received which was very serious in its significance in reference to the size of the hilum glands. Our trouble, I say, is that we have not got proper criteria. If we had, I think a lot of these cases would be passed as within the range of the normal for a child who has recently had an acute infection, which is likely to cause swelling in these glands. In other words, I think it is too glibly assumed that swelling or enlargement of the bronchial or hilum glands in a child is necessarily due to tuberculosis. But we know clinically that these children do, after a latent period from their recovery from measles, pertussis, and other specific fevers, every

now and then develop active tuberculosis. We have only to remind ourselves of the common sequence of events in tuberculous meningitis: measles in January, February spent in convalescence, in March the child was almost fit, in April it was rather slack and not so fit, in May headache, squint, peevishness, and the development of tuberculous meningitis. So long as one is faced with a definite sequence of events of that kind and not infrequently, it behoves us to be extremely careful before we say in February and March "This is only the residue of the acute illness and does not mean that the child is tuberculous." I find it is less difficult to deal with the adult who is running a mild degree of pyrexia than it is with a child under similar conditions, and for the reason stated.

I spoke of the nervous type of pyrexia. We are all familiar with the factitious pyrexia which, one feels generous, one calls neuromimesis, and one is not it is labelled malingering, but anyway some psychosis, whether involving morale or not which leads to a factitious temperature. I will not go into that, because I have to speak about things which are more important, except to say, as I have hinted, that it is not always a moral or criminal proceeding. One of the most instructive cases of this type that I ever saw was the widow of a medical man who had died of pulmonary tuberculosis. When I saw her she was imitating most of the symptoms that she had seen in her husband over a long period, and imitated them extremely well. The hæmoptysis, as we were able to show, was of a spurious form produced by sucking her gums, and occasionally by pricking them. The stuff expectorated was not frothy, though it was pink, it was a watery fluid, such as a person with active pyorrhœa often produces in the early morning. The loss of weight was probably associated with the anorexia and under feeding, and the cough was of the barking kind, which, from its sound and its purposeless character, suggested a nervous origin. When we came to consider the temperature we found that it was only necessary to see that the nurse sat near the bed the whole time that the thermometer was in situ to break up a very marked quotidian intermittent fever.

II. Rather than deal with specific instances of pyrexia due to microbic infection, I will speak of one or two general considerations which are, I think, helpful in dealing with these cases. One line of thought is, that *there are certain situations in the body where infection occurs but often remains "cryptic" for a long time.* The tissue or the organ in which such tissues comes the *endocardium*, which is very important if only for the reason that subacute bacterial endocarditis often shows itself first by the discovery of a pyrexia of unknown origin, the patient has a mild and rather casual illness, the temperature is found to be raised, and the illness,

[†] Dr. Bernard Myers took the chair upon the occasion of this lecture.

whatever it may be—influenza, catarrh, sore-throat—subsides though the temperature goes on. It turns out to be the pyrexia of a latent subacute infection of the endocardium. You may say there are physical signs, but you will remember that I said I am speaking of physical signs which are not adequate to carry conviction. We are faced with a situation where one morning we feel sure there is a systolic bruit at the apex, and next day we feel sure there is not, and the case drifts on. But there are certain stigmata which are more important than the question whether there is a systolic bruit at the apex, which is not, after all, a very committal thing. There are more committal points which are often overlooked if not borne in mind. For example, there is the complexion of the patient. Some observers are very sensitive to complexions, others are not. The complexion of the subacute endocardial patient is called the *café-au-lait* complexion, and I consider that it is a very good term; it is a curious muddy, greyish appearance, and it is often present very early in the disease. Then certain other stigmata should be looked for, or asked for; petechiæ about the shoulders or neck or elsewhere, which would otherwise be meaningless, but which, in association with this pyrexia, become very significant. Then, most significant point of all—almost pathognomonic in fact—is the appearance, suddenly, of one or more tender reddish spots on the pulp of the fingers or the toes, preceded by pain and followed by a little blueness, disappearing after 48 hours or three days, and, at the time of one's examination, nothing of all this may be present. One asks "Have you had any pains at the tips of the fingers?" and often the answer is "Yes." The typist finds she could not use one finger because of tenderness; she thought she must have pricked it with a needle. Equally significant are fleeting pains in the left hypochondrium, due to splenic infarction, and red blood cells in the urine, requiring the microscope for their discovery.

The *lymph glands* I have already mentioned in referring to tubercle. But I think that *lymphadenoma* is a disease often overlooked as a cause of obscure pyrexia. I believe that the lymphadenomas—there is probably more than one type of disease going under that name—are more often met with than formerly. And there is this important point about many of the cases one sees, that they are not the frank cases which Hodgkin described, they do not present the picture which he portrayed so graphically. The disease is prone to be more diffuse, that is to say, the lymphadenomatous process is prone to involve deep-seated glands or the lymphoid tissue in the viscera, without obvious glandular enlargement at all. So that, although it is right to scour the patient's body carefully for enlarged glands in any case of obscure pyrexia, we must not say, when no enlarged glands are found, that therefore the disease is not lymphadenoma; we have to remember the liver and spleen and, of course, the hilum glands, and the lung and

pleura itself. The first definite physical sign in this type of lymphadenoma may be of pleurisy or of ascites, whilst as yet there are no enlarged glands on the surface of the body.

The *liver* comes under consideration in another sense. It is a large organ, and a mild degree of hepatitis, or even a small abscess in the depth of the liver, may be the actual focus from which obscure pyrexia may arise. There are two types of case which one comes across. One is disease of the liver following dysentery of the amœbic type, amœbic hepatitis, with perhaps nothing incriminating about either the size of the liver or its tenderness, but there is a history of residence in the tropics, or, more helpful, of actual dysentery. In a doubtful case of that sort, examination of the stools and a trial of emetine are indicated. The other type is that in which the liver is affected by deep-seated suppuration, generally due to *Staphylococcus aureus*. In such a case I have seen pyrexia going on for two months with nothing that could be found as an explanatory condition. Then perihepatitis developed with sudden pain over the liver region.

The *peri-renal tissue* comes into this category of tissues or organs, which are somewhat deep-seated and have to be borne in mind in the presence of an obscure pyrexia; again the infecting organism is *Staphylococcus aureus*; in other words, perinephric abscess as the sole expression of general staphylococcal infection is not at all uncommon. The pathology, as you probably know, is that the abscess is pyæmic. The patient is suffering from a general staphylococcal infection which has perhaps not revealed itself until this focus begins to appear in the perinephric tissue. And we know what happens, because the stages are clearly demonstrable. A pyæmic infarct occurs beneath the capsule of the kidney, which infects the capsule, spreading to the perinephric tissue; the kidney seems able to dispose of the small degree of infection in the cortex, but the perinephric tissue, being very lacking in resistance to pyogenic infections, flares up and an abscess forms. If the patient is operated upon and the pus is let out, most of these cases do very well. Recently I suggested exploration of the loin in a boy who had had a temperature of an obscure kind for three weeks; during the third week he was found to be tender in one loin and not in the other. I also thought that on this particular day there was a little surface œdema. We had nothing else to go upon, except that we found on inquiry that he had had a boil on his head six weeks before this illness, and it gave some trouble at school, that is to say, it was not very satisfactorily treated, because the hair was not shaved sufficiently to make a good job of it, though eventually it healed. During the exploration the surgeon said, "There is nothing here." I said, "Are you actually on the kidney?" He replied, "I do not know that I am." He was in the perinephric tissue. Then he pushed his finger further, and he said, "Yes, I think there is something

here," and there was a spurt of pus. He had evacuated a small subcapsular abscess which had begun to spread to the perinephric cellular tissue.

Whilst I am speaking of *Staphylococcus aureus* infections I ought to mention *bone* among deep-seated and rather cryptic tissues. We all know from experience the cases of osteo-myelitis occurring in children or young adults. Sometimes it is easy to diagnose with pain and tenderness in a common situation. But there are cases which drift on past the acute stage and it may be some weeks before the abscess becomes manifest, and so we have to search and think of the various parts of the skeleton where osteomyelitic areas may possibly occur.

The *nasal sinuses* come into the group of cryptic organs and tissues. We all search the sinuses for focal sepsis of the chronic type when faced with some toxic condition. In most cases of focal sepsis pyrexia is not conspicuous; but every now and then a case presents itself—and I have just seen one—in which pyrexia is a marked feature. In the case I refer to the sinuses were examined twice, because the patient presented no physical signs but had a headache, the features of which were very suggestive of sinus infection: the headache was referred to the root of the nose, between the eyes and through to the occiput. On the second occasion the laryngologist said, "I feel certain there is something there," but he could not demonstrate anything. The patient got worse, developed rigors and had meningitic symptoms. A second lumbar puncture was done—the first having been negative—and streptococci were demonstrated in the slightly turbid fluid. The patient died. We had a *post-mortem* examination, and found the sphenoidal sinus full of pus, and the body of the sphenoid necrotic. So this was a case of very obscure focal sepsis, which, though we bore in mind the possibility of what turned out to be the actual cause, we could not diagnose.

III. I now pass to another general consideration. There are certain *test drugs* which, I suppose, we all, at times, try in certain pyrexial cases. It is worth while to remember that they exist. Everybody gives quinine to the Anglo-Indian who has a shivering fit and a high temperature, headache, and sweats. Whatever the bacteriologist's report may be, we test the case with quinine, and we say, with Osler, that a fever of regular type which does not yield to quinine is not malaria. There are other test drugs. I spoke just now of emetine; that is a good test drug for dysenteric or post-dysenteric pyrexial conditions— $\frac{1}{4}$ to $\frac{1}{2}$ gr. hypodermically twice a day. The assumption—not so complete as in the case of malaria—is that we are not dealing with an active amœbic dysentery infection if emetine produces no good result. Sodium salicylate as a test for acute rheumatism is another instance. I think it is correct to say that if the efficient

exhibition of salicylates fails to bring down the temperature in a patient suspected of acute rheumatism, the practitioner has a big presumption in favour of a pyrexial illness not being rheumatic, always supposing there is no complication such as serous membrane inflammation, for which salicylates are not specific, as they are for uncomplicated rheumatism. I say the *efficient* exhibition of salicylates—not 10 gr. three times a day, given during the day and not at night, but 10 gr. given every two hours during the day and every four hours during the night. If salicylates, given in that manner for three days, make no impression on the temperature, it may be taken as fairly certain that the pyrexia is not due to acute rheumatism.

Still another useful test drug in pyrexial conditions is hexamine. If we suspect coliform infection of the urinary tract, the exhibition of hexamine without results upon the pyrexia in three or four days gives a considerable presumption that the cause is not of this nature. If sodium bicarbonate in full doses also fails, the presumption becomes still greater.

The next test drug I shall mention is novarsenobillon, or neokharsivan, for spirochætal conditions which are associated with pyrexia. I am not thinking now of syphilis, though occasionally one sees pyrexia, even in these days, due to syphilis; but it is not common. The cases I am thinking of are better illustrated by such a disease as *relapsing fever*, which seems less uncommon than when I described it 15 years ago. That is a relapsing fever which, though it has a characteristic skin eruption, comes into the group of obscure pyrexias. One dose of 0.4 g. of novarsenobillon is generally lethal to the spirochæte of this infection. Therefore, arguing along the same lines, two doses at intervals of five or six days, having no effect on a relapsing temperature, would indicate that the cause was not a spirochæte infection of that type. Lastly, there is *santonin*. To a child who is running a temperature which is rather baffling and a little odd and meaningless I sometimes give a dose of *santonin* to see what will happen.

IV. After considering the probable place of infection it is desirable to think of the *probable* *microbe* causing it. I spoke just now of coliform infection. I doubt if there is anything more likely to be the cause of a very sharp rise of temperature in a patient who, on critical examination, gives no physical signs, than a coliform infection, generally, but not always, of the urinary tract. Most of us are now aware of this, but it is not so very long ago that cases were rather frequently met with in which it was not known that examination of the urine was necessary to decide this point. Little children are very prone to this infection, little girls more than little boys; and babies suffer from it. My youngest case, which I remember very well, was aged 14 days, a very interesting infant with a characteristic

baecilluria. It is difficult to collect the urine of such a patient, but the characteristic smell of the diaper was sufficient, indeed it was decisive. Some practitioners are less sensitive to this odour than others, but it is characteristic, so that sometimes one can make a diagnosis in the dark, or at any rate in a room so badly lighted that one cannot see the urine properly. The patient, at the time of the febrile bout, is very ill, sometimes even stuporose; therefore the question of meningitis or encephalitis often arises. There is generally a foul tongue, but on examination nothing can be made out. Another common feature about the cases is the rapidity with which they recover after the storm is over, whether treated or not treated, and the completeness with which the return to health takes place. I mentioned hexamine as a test drug, but in the very acute cases a more crucial test is by large doses of sodium bicarbonate. I do not remember to have seen a case of the acute fulminant type which did not respond to 20 gr. of bicarbonate of soda every two hours until the urine was alkaline.

Passing from coliform infections of a local character to general coliform infections leads me to mention the prevalence of paratyphoid, and to remind you that the physical signs and symptoms are much less marked in many of the cases than they are in typhoid fever. We used not to have very much difficulty in making a diagnosis of typhoid fever when that disease was more common than it is now. Even if the agglutinations were not very decisive and even if the bacteriologist did not succeed in getting *B. typhosus* from the stools, we felt fairly confident from the character of the pyrexia, the pulse, the enlarged spleen, the spots, the patulous abdomen, the râles over the chest, the facies, &c. But paratyphoid is a very different affair. Some of the patients are not even ill, the tongue is clean, there is a little headache at the beginning, but it passes off more quickly than in typhoid, the abdomen seems natural, there is no bronchial catarrh. But we notice the relatively infrequent pulse-rate, which is useful, and the absence of leucocytosis, or the presence of a leucopenia. The cases sometimes relapse, which in itself is a useful fact in the diagnosis, because a continued fever which relapses once or twice makes it extremely likely that the infection is in the typhoid group. The bacteriologist generally reports that it is paratyphoid B, less often that it is paratyphoid A. But I have seen three cases in the last month in which skilled bacteriologists have reported no positive agglutination to *typhosus* or *paratyphosus A* or *B*, and have failed to recover a non-lactose-fermenting organism in the stool, that is to say, no organism in this group had been identified. Yet the clinician was able to be quite sure of his diagnosis because the evidence was overpowering.

Consider the evidence in one of these cases. The girl lived for a time in a Paris hotel, and was taken ill 14 days after she left Paris. (Paris

contains at the present time a good deal of paratyphoid.) The significance of both of these facts is obvious. When she was taken ill she was at a theatre, and she said, "Need we stop? It is dull." "Aren't you well?" said her mother. She replied, "I have a headache." In the morning the headache was much worse. Her temperature was found to be 102° F. The spleen was palpable on the tenth day of the illness. After defervescence by lysis there was a relapse of the fever. One said that she was suffering from a general infection by a member of the coliform group, and though the bacteriologist said it could not be paratyphoid A or B, I was willing to call it a pathogenic coliform bacillus X, and leave it at that for the time being. I feel certain that coliform infections of a general kind are at present rather common. We have been through a period, in the last 10 or 15 years, in which coliform infections of a focal kind have been very rife, and perhaps we may now experience coliform infections of the septicæmic type.

V. Neoplasms occasionally cause obscure pyrexia. In my experience they are odd neoplasms, neoplasms which are prone to undergo necrosis and presumably form toxic products as the result of this. Therefore they are not straightforward carcinomata, they are more likely to be sarcomata, and I am not sure they are not as likely to be benign tumours, such as fibroids. You have seen pyrexia associated with necrobiosis of a large fibroid. As an illustrative case I may mention that last year I was consulted about a very obscure case of pyrexia. The working diagnosis was tubercle of the kidney, and this view seemed to be confirmed at first, when improvement occurred with treatment at a sanatorium and small doses of tuberculin. Tubercle bacilli were not demonstrated in the urine. There were pain and aching in the loin, and there was some doubt about the size of the left kidney. These were all the data there were to go upon for several months. But on coming home to London the pyrexia became higher, the patient wasted, and diarrhoea started. The diarrhoea was very troublesome, and the abdomen was tympanitic. It was then decided to explore the upper left quadrant of the abdomen from the front. It was found that the kidney was large, but it was very firm, and felt more like a tumour than a tuberculous kidney. It was removed, but with great difficulty. It was very adherent, and there were many vessels running into it. It was found that there was a hypernephroma embedded in the kidney as large as my fist, and on opening it the greater part of it was found to be necrotic; it consisted of soft, cheesy material, and that was the only thing found, except that examination of the intestine clearly demonstrated amyloid change. That patient's pyrexia lasted 15 months. This case shows that obscure pyrexia is sometimes due to absorption of toxic material due to degenerative changes in a neoplasm.