Peripatetic patients and pathologists¹

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There are two aspects of pathology in which I have a special interest: these are the pathology of tropical diseases and the fostering of a closer relationship between the pathologist and the patient, a matter of great importance to this Association.

Because the general pathologist is obsolescent, some have assumed the consequent death of clinical pathology; this is nonsense. The idea that only a general pathologist can practise clinical pathology comes from that fact that in the past most hospital laboratories outside teaching hospitals employed only one consultant pathologist: he had to be proficient in all disciplines, and, owing to the small size of the hospitals, he had close contact with patients. Pathologists in large teaching hospitals were able to specialize in one discipline but they were usually ill-housed in buildings remote from the wards and rarely emerged except at night or to give a lecture. As a result clinical pathology was commonly assumed to be synonymous with general pathology. Nothing could be further from the truth.

Any pathologist dealing with routine diagnostic pathology, as opposed to pure research, should see and examine patients, no matter how specialized he may be. If he does this, discusses his laboratory results with the clinicians, and advises on what further investigations might be helpful, he is a clinical pathologist.

Unfortunately, for technical and economic reasons, there is a rapidly growing tendency to centralize laboratory tests, and pathologists are becoming more remote from the hospitals which they serve and more interested in analyzers than in patients.

Until now, pathologists have been the main contributors to advances in technique and have assumed responsibility for technical supervision; this has been because the old style laboratory assistant had little educational or scientific background. Now laboratory assistants have become technicians and are on the brink of becoming technologists; there is also a great increase in the numbers of medical scientists. But pathologists are

reluctant to surrender any part of their spheres of influence. It is time we asked ourselves whether the development and supervision of scientific techniques should continue to be a major activity of medically qualified pathologists. It is their preoccupation with these duties which has prevented them from taking their rightful place as clinical consultants; they should now gladly surrender the bulk of this work to medical scientists and technologists and devote themselves more to filling the widening gap between available techniques and their clinical application.

A laboratory result reported without reference to the clinical condition of the patient can be produced just as well, if not better, by a good technician or a medical scientist as by a medically qualified pathologist. The centralized laboratory concerned with multiple routine tests is more properly the sphere of the science graduate; the pathologist should be in the hospital, seeing patients, discussing results and the need for further investigations with the clinicians, and assessing the validity and value of the laboratory procedures.

It is my contention, therefore, that this Association has an even greater responsibility now than it has had in the past to get pathologists out of their lairs and into the wards, to encourage them to have closer contact with clinicians, and to make them think in terms of patients instead of specimens; in fact to become clinical and peripatetic.

This liaison between clinical medicine and pathology was actively pursued by the father of pathology in the R.A.F., Captain Whittingham, now Air Marshal Sir Harold Whittingham and an honorary member of this Association. Sir Harold developed a special interest in tropical medicine and in that sphere the liaison became officially blessed by the establishment of the Consultant in Pathology as also the Consultant in Tropical Medicine. It is from this somewhat unique position that I have had the opportunity to practise clinical tropical medicine as well as its pathology.

It might be thought that with the loss of our Empire, tropical medicine would be of diminishing importance to doctors practising in Britain; but travel to distant places is now regarded as part of the normal way of life by a large proportion of

¹An abbreviated version of the Presidential address to the Association of Clinical Pathologists to the meeting held in London in October 1966.

the population either on duty in the Services, or in search of pleasure, or as an essential part of business relationships, or in the cause of international scientific bonhomie; most of this travel is by air with a consequent reduction in the time spent in transit, so that diseases with short incubation periods can be expected to appear in non-endemic areas. Add to this the mass migrations of labour from places of underemployment to those of labour shortage, and it can readily be seen that we must think in terms of world epidemiology and forget our British insularity.

There have been several prophets crying for more attention to be paid to exotic diseases in this country—Professor Maegraith on the clinical side and Professor Hill from among pathologists—but patients still die through faults on the part of clinicians and laboratories.

How great is this problem? The following deaths from some of the major exotic diseases are recorded in the Registrar General's tables for the period 1955–64: malaria 41; amoebiasis 50; suppurative hepatitis and liver abscess 273 (this probably includes a considerable number of amoebic liver abscesses); schistosomiasis 16; leishmaniasis 3; trypanosomiasis 2.

Malaria is a notifiable disease and during this same 10-year period there were 1,257 notifications, which gives a case mortality rate of 3.2% compared with an average case mortality rate of 2 per 1,000 for the R.A.F. during the six war years 1940–45. Leaving out the ill-defined group of suppurative hepatitis and liver abscess, you may think that the total of 112 deaths in 10 years is small and hardly worth worrying about. But at least 90% of these patients should not have died; they died from diseases which are easily cured provided the diagnosis is made in time and the correct treatment is given.

What then are the basic causes of the failure to diagnose these diseases or to diagnose them sufficiently early? The faults lie about equally divided between clinicians, teachers, examiners, and pathologists. Clinicians frequently fail to ask patients the simple question, 'Have you ever been out of this country and if so where and when?', and even if they get a positive answer they may fail to pass on the information when sending specimens for examination to the laboratory. Many teaching hospitals give no instruction on tropical diseases and most newly qualified doctors coming into the Services are completely ignorant even about those likely to be seen in the United Kingdom. Examiners fail in that although some knowledge of tropical medicine is included in the syllabus of all qualifying examinations, relevant questions are sufficiently rare for the examinees to take a calculated risk in ignoring the

subject. Pathologists are in much the same position: few ensure that they are informed of the geographical history of their patients, few know enough about the simpler diagnostic tests, and even fewer see that their technicians can deal with such tests. I am therefore devoting a large part of my address to mentioning some simple clinico-pathological pointers which are not easily available to the casual reader of textbooks of tropical medicine, but which are of importance in the diagnosis of some of the exotic diseases which may be seen in this country; they also serve to illustrate the importance of the pathologist having close contact with patients.

First let us consider malaria because it is the disease above all which should not be allowed to kill. Malignant tertian or falciparum malaria is a killing disease if treatment is delayed and can provide one of the few medical, as opposed to surgical, emergencies; a patient can die or reach a stage from which there is no return within 24 hours of the onset. Malignant tertian malaria, like syphilis, is a great mimic of other diseases and the diagnosis should be suspected in any febrile patient who has recently visited an endemic area and stopped taking suppressive therapy. The commonest initial diagnosis of those who die in this country is influenza, because the doctor has failed to elicit the history of residence in an area endemic for malaria. But even when the clinician suspects malaria the laboratory is quite likely to miss the presence of parasites in blood films. This is partly due to inexperience in scanning films for parasites and partly to technical faults. Blood films for malaria parasites should be stained at a pH of 7.2 and for routine use Giemsa is the best stain. The technical details for achieving the best results are given in an excellent article by Shute (1966); I strongly recommend all those in charge of departments of haematology to get a reprint or photostat of this article and see that their technicians are fully conversant with it.

The presence of malignant tertian parasites should always be reported immediately to the physician in charge and the potential urgency of the situation be tactfully but firmly stressed; when more than 10% of the red cells are infected, it should be seen that emergency parenteral treatment is given, even in the absence of clinical indications.

Quartan malaria has a particular relevance to pathologists. Parasites are always very scanty, the infection can persist for many years, and the incubation period may be long. I have recently heard of a patient with Christmas disease who had multiple transfusions of blood and fresh plasma and subsequently developed quartan malaria. All the donors claimed never to have had malaria but detailed investigation revealed that one had been in many parts

of the tropics during the war and had suffered from malaria up to 1946, and another was a West African. Shute (1944) recorded the history of a woman who had quartan malaria 21 years after she had returned to England from Calcutta.

The other infection which mainly accounts for deaths due to exotic diseases in this country is amoebiasis. Here the term 'exotic' is not entirely justified because a proportion of the patients have never been abroad. There is evidence that many patients suffering from amoebiasis remain undiagnosed. Population surveys show that the amoebic carrier rate in England is about 5%, but how often do hospital laboratories report the presence of amoebae or their cysts?

According to the Registrar General's mortality figures amoebiasis causes more deaths than malaria, yet amoebiasis is a far less fatal disease than malaria so that the higher death rate should be associated with a much higher incidence. As some of you will know, I have collected figures of the recorded incidence of various exotic diseases during the period 1961-65 from a sample of 30 hospitals throughout this country; the results show twice as many records of malaria as of amoebiasis. It is interesting that an article by Wright (1966) gave the details of eight patients with severe amoebiasis seen at the Radcliffe Infirmary, Oxford, between 1957 and 1964; on two of them the diagnosis was made after death, and on three others only after surgical operations had been carried out; one had never been abroad and another only as far as Calais. The stools of only one of the eight patients were examined microscopically and they were reported as negative before the diagnosis was made on other grounds. It is perhaps a result of the awareness of amoebiasis occasioned by these patients that, of the 52 records of amoebiasis reported from the 30 hospitals to which I wrote, 13 (a quarter) were from the Radcliffe Infirmary. Surely the conclusion from these figures must be that a patient suffering from amoebiasis is unlikely to be diagnosed unless he has acute, severe symptoms or he dies.

But amoebiasis is rarely acute and the symptoms of intestinal amoebiasis may mimic most abdominal conditions from functional diarrhoea or dyspepsia to acute appendicitis or neoplasm. In the R.A.F. all stools sent to the laboratory for culture are also examined by direct microscopy. I believe that the minimum requirements for every patient with abdominal symptoms and blood in his stools is to search six faecal specimens by direct microscopy; if the symptoms are still unexplained, he should be examined by sigmoidoscopy and scrapings from any lesions should be immediately examined on a warm slide.

The diagnosis of amoebiasis is much more difficult

than that of malaria. Amoebae in either the vegetative or cystic forms are difficult to find, and long experience is necessary to make an accurate identification. The finding of *Entamoeba histolytica* in a patient's stools is by no means proof that the patient's symptoms are due to amoebiasis; many of the 5% carriers are symptomless. Here therefore we have the perfect situation for the proper practice of clinical pathology: a correct assessment of the significance of the pathological findings can only be made by relating them to the clinical picture.

In the diagnosis of intestinal amoebiasis regard must be paid not only to the identification of *E. histolytica* but also to the type of exudate accompanying the infection; this may be extremely helpful in deciding the significance of amoebae. Where the naked-eye appearances and microscopic exudate have the characteristics associated with acute amoebic dysentery, an active amoeba containing red cells may reasonably be assumed to be *E. histolytica*. Even experts will not positively identify an actively amoeboid object as *E. histolytica* in the absence of a typical amoebic exudate, and macrophages in a bacillary exudate provide a dangerous trap for the unwary. When an amoebic exudate is not present, positive identification of *E. histolytica* can be made only on the cystic form.

The identification of cysts needs considerable experience and there is only one finding which by itself is sufficient for identification: the presence of a sausage-shaped chromatoid body in the saline preparation; in many cysts, no chromatoid bodies can be seen. But lack of experience should not be allowed to lead to a defeatist attitude. There is no difficulty in preserving active amoebae or cysts in order to obtain expert opinion by post: for active amoebae, faecal smears should be fixed in Schaudinn's solution, and for cysts a portion of the suspected specimen should be emulsified in 10% formalin.

One of the curious features about amoebiasis is the long latent period commonly found between the probable time of infection and the onset of symptoms. This is particularly so in the case of liver abscess. The latent period between the original infection and the onset of hepatic symptoms is usually several years, and often many years, and by this time the gut infection may no longer be present; in fact in only 50% of patients with liver abscess can amoebae be found in the stools. Nevertheless, a patient complaining of malaise, loss of weight, drenching sweats, and pain in the right hypochondrium, should be suspected of having an amoebic liver abscess even if he has never been abroad; if in addition he has an enlarged, tender liver and a raised right diaphragm visible on the radiograph, the diagnosis is almost certain. If these

precepts had been observed in the series from the Radcliffe Infirmary the correct diagnosis would have been considered from the start in six out of the eight patients.

Before leaving amoebiasis mention must be made of the rare and interesting lesion known as amoeboma. An amoeboma usually occurs at one of the colonic flexures and presents clinically as a tumour: it is caused by localized amoebic invasion with consequent inflammatory swelling and oedema of the gut wall; it may be superimposed on a neoplasm. If the correct diagnosis is not made, the 'tumour' may be removed surgically and the patient is then likely to die from amoebic peritonitis; an uncomplicated amoeboma resolves completely during treatment with emetine.

There are three other conditions on which I wish to comment at some length because in each case a clinical suspicion can readily be confirmed in the laboratory: they are schistosomiasis, leishmaniasis, and trypanosomiasis.

There is often a latent period of several years between the time of infection and overt clinical symptoms of schistosomiasis. The commonest form of the disease is that due to haematobium infection which often presents clinically as an end-of-stream, symptomless haematuria. The eggs can usually be found in the centrifuged deposit of an end-of-stream specimen of urine; when the history is suggestive but eggs are not found, success may be achieved by examination of a urine specimen passed after prostatic massage or after bicycling on a physiotherapy static bicycle. Infections with *Schistosoma mansoni* or *japonicum* give rise to earlier more generalized signs such as hepato-splenomegaly with dysenteric symptoms; the ova can be found in the stools or in a snip of rectal mucosa. All types of schistosomiasis may be accompanied by an eosinophilia. As with other exotic diseases, the most important factor in reaching the correct diagnosis is to think of the possibility. I remember a patient with haematobium infection complaining of symptomless haematuria, who was investigated at three different hospitals before the diagnosis was considered, in spite of the fact that there was no need to ask him if he had ever been overseas since he was a native African.

Leishmaniasis in either the cutaneous or the visceral form is a disease with a long incubation period, usually six to 18 months. It is therefore quite common for the onset to occur away from the endemic area. The Army have recently had some 40 cases of oriental sore and six of kala-azar developing in this country following service in the Radfan area of Aden. A patient with kala-azar often has such a characteristic appearance that the diagnosis can be suspected at first glance. He presents a paradoxical

picture: he has skin pigmentation, obvious loss of weight, and the look of a very ill man, and yet he is bright of eye, mentally alert, and on enquiry is found to have a voracious appetite. The disease should always be suspected in a patient who has been to an endemic area within the last three years, and is suffering from a chronic pyrexial illness with loss of weight, a palpable spleen, and a total white count of under 5,000. The parasites may be found in the peripheral blood but are usually much more easily seen in marrow smears; in two of the recent Army patients no parasites could be found in marrow smears but they were easily demonstrated in smears from splenic puncture.

Attention has recently been drawn by Duggan and Hutchinson (1966) to the incidence of African trypanosomiasis as an exotic disease. The endemic areas are clearly defined and the diagnosis need not be considered in patients who have not visited them. The early symptoms are very varied and even at this stage personality changes may occur. Failure to diagnose the disease has frequently been due to use of inappropriate techniques. Lymph node biopsy is useless but aspiration of a few drops of gland juice may reveal the causative organism; the E.S.R. is nearly always markedly raised and in the majority of patients the organisms can be found in thick blood films. In late stages of the disease the findings of a raised cell count and protein content in the cerebro-spinal fluid call for very careful search for the parasites.

Conditions which are becoming of increasing clinical importance in Britain are those associated with the presence of abnormal haemoglobins. Patients with sickle cell anaemia and homozygous thalassaemia are most affected but those with other disorders of haemoglobin synthesis may complain of mild to moderate symptoms. These conditions should be considered whenever a patient presents with a refractory anaemia associated with a bizarre blood picture, especially the presence of thin target red cells, and particularly if the patient is of foreign extraction. We have been carrying out the haemoglobin electrophoresis for Dr. Pitcher on suspected cases from Stoke Mandeville Hospital for the last 18 months; we have collected 24 cases of thalassaemia, three of haemoglobin S and two of haemoglobin C out of 59 samples from suspected patients. The largest single national group has been 11 Italians but one patient was a navigator who lost consciousness at altitude; he was of pure Norfolk descent.

Admittedly these conditions are not at present amenable to specific treatment, but their recognition can at least save the patients from over-transfusion or poisoning with iron.

One of our most recent patients was a young African boy, born and brought up in England; he visited Ghana on holiday and started a pyrexial illness 14 days after his return. He had malignant tertian malaria with thalassaemia. This illustrates the point that the old adage, never to diagnose a double pathology when one will account for the symptoms, should not be followed when dealing with patients who have lived in the tropics; in tropical medicine never be satisfied that the diagnosis is complete when only one causative agent has been found.

I hope that the few precepts and technical hints I have offered in relation to exotic diseases may help to reduce the mortality from these eminently curable diseases. Even if they have little direct effect, perhaps they will indirectly achieve the same result by stimulating examiners to include an effective proportion of questions on tropical medicine in their papers.

My plea for pathologists to become clinical is urgent. The widening gap between clinical medicine and the scientific techniques available must be bridged if patients are to have the full potential benefit of modern knowledge. Some seem to think that batteries of routine tests analysed by computers can fill this gap; this is an example in its extreme form of much erroneous modern thinking whereby a patient is put in the same category as an unknown substance requiring analysis. A result of slot-machine diagnosis by large numbers of routine tests may be the discovery of many irrelevant abnormalities under which the effective diagnosis is buried.

In case I have overemphasized the need for pathologists to become clinicians let me make it

clear that I am not advocating that they should completely abandon all interest in techniques and scientific methods; every pathologist should have a sound knowledge of these matters, sufficient to give a critical assessment of their accuracy and proper application, but he should not need to be concerned with their routine performance.

One of the obstacles to true clinical pathology is that many clinicians treat pathologists as little more than medically qualified technicians. Unfortunately this status is sometimes merited by reason of a lack of clinical interest or by an exaggerated feeling on the part of the pathologist that patients are no more than a tiresome source of interesting research material. Either outlook inevitably leads to the misapplication of science to medicine and to a lack of attention to the patient's return to health.

As a corollary to the pathologist's obligation to take a clinical interest, I believe that he has a right to be supplied with adequate clinical details; he is also just as entitled to visit and examine the patient on whom a laboratory request has been made, as is any other consultant whose opinion has been sought.

It is my fervent hope that in the future this Association will make its chief aim the encouragement of true clinical pathology so that patients may benefit from the application of the best in scientific medicine and from the acumen of the medical scientist at his best.

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