CLINICAL PATHOLOGY IN GENERAL PRACTICE

THE PUBLIC HEALTH LABORATORY SERVICE

BY

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There is a growing demand from general practitioners for direct access to the laboratory. Since the Public Health Laboratory Service already provides the practitioner with assistance in the diagnosis of infectious diseases it may be appropriate to discuss the scope and usefulness of this service.

Some practitioners make much more use of the laboratory than others. A number of severe infections have now become rare, many respond to various of the new drugs, and difficult cases can usually be transferred to hospital without delay. Therefore many practitioners find it possible to carry on with little or no help from the laboratory. Others make regular use of the facilities provided, and believe that this enhances the quality and interest of their work. They realize that they have a responsibility to prevent disease as well as to cure it, and that outbreaks of infection cannot be controlled unless their existence is promptly recognized. They find that the identification of the organism causing an infection often enables them to make more intelligent use of antibiotics. The regular use of the laboratory assists them to form and control their clinical judgment and to assess the results of their treatment. The interest of the work is increased when they can obtain assistance in the investigation of new and unusual conditions.

There is a tendency to belittle what is called "postal pathology," in which the pathologist does not see the patient either in his bed or in the laboratory, but if laboratory facilities are to be widely available some such practice is inevitable. It leads to undesirable results only when the practitioner uses the laboratory as a slot-machine to deliver mechanical answers to a few questions, and when the pathologist reports with a rubber stamp. Much of the work of the P.H.L.S. is of a "postal" nature, but this does not prevent a good deal of valuable co-operation between the practitioner and the pathologist. The practitioner must have enough knowledge to request the appropriate investigation at the right time, must have been trained to collect specimens efficiently, and must provide the pathologist with sufficient information to allow him to assess the significance of his findings. The pathologist does not content himself with mechanical reporting, but takes every opportunity to discuss his results with the practitioner, usually over the telephone, but occasionally in the laboratory or at the bedside. He welcomes inquiries about appropriate investigations for particular cases and encourages visits to the laboratory to establish personal contact.

It is often desirable to transmit specimens to the laboratory by some means quicker than the post. In suitable cases relatives can be detailed to take them to the laboratory or to put them on a bus or a train. Many public health departments have collecting centres for specimens, and in some populous districts the P.H.L.S. organizes "specimen collection rounds" with calls at a number of such centres. The practitioner should con-

sult the nearest public health laboratory or health department about the arrangements available in his area.

Nature and Scope of the Services Provided

There are 60 area and regional laboratories of the P.H.L.S., and in areas in which a laboratory has not yet been established arrangements have usually been made for the work to be done at the local hospital laboratory. The laboratories provide help in the diagnosis, prevention, and control of infectious diseases in the following ways: (1) with the general practitioner, by assisting in the diagnosis of suspected cases; (2) with the medical officer of health, by taking part in the investigation of established outbreaks and in the routine control of water, milk, food, and other environmental factors; and (3) on a national scale, with the central reference laboratories of the service, and with the Ministry of Health, by making observations on the spread of disease.

The diseases with which the service concerns itself are those that can be transmitted from man to man and from animals to man. The diagnosis of venereal disease is the one exception to this rule. Although this is generally the responsibility of the hospital laboratory service, arrangements differ from one area to another, and in some places the public health laboratories continue to carry out this work. Certain bacterial diseases, such as coliform infections of the urinary tract, are not strictly infectious. Their investigation is also the concern of the hospital laboratory service. It is best to make inquiries locally if there is any doubt about the correct laboratory for any particular specimen. Public health laboratories provide outfits for the collection of specimens, but do not pay the postage on packages returning to the laboratory.

The local laboratories of the service carry out a wide range of bacteriological investigations. In addition, they avail themselves of facilities at the reference laboratories for the more unusual and difficult tests.

Respiratory Infections

Sore Throat.—In the past, the main purpose of sending a throat swab to the laboratory was to exclude the presence of diphtheria. Now that this disease is less common, more attention can be given to identifying other causes of sore throat. However, the exclusion of diphtheria is still a matter of importance. It is unlikely that this country can be kept permanently free of the disease, even if the present level of immunization is maintained, and there is a danger that recrudescences might not be recognized promptly. Diphtheria in immunized persons is often clinically atypical, and the examination of the throat swab may be of most value in those cases in which the disease is not seriously suspected. Most laboratories issue a provisional report by telephone on the morning after the receipt of a swab, unless it arrives very late in the day. This report will state whether diphtheria bacilli, haemolytic streptococci, or Vincent's organisms are present, and will usually indicate whether they are few or many. On the following day the cultures are re-examined for diphtheria bacilli. A small proportion of previously negative cultures are then found to be positive, but fortunately this occurs rarely in clinical cases of diphtheria. On the second day, also, the haemolytic streptococci will have been grouped and the final report will be issued by post. When submitting a swab, the practitioner should include a brief account of the illness, and state

whether antibiotics or sulphonamides have been given. If diphtheria bacilli are found in the absence of typical symptoms, the laboratory will carry out a virulence test. The giving of penicillin locally or systemically may result in a false negative result for diphtheria. Small numbers of haemolytic streptococci are found in the throats of 10% of normal people in winter, but large numbers are usually present in streptococcal sore throat. Only a few may be present if the swab is badly taken (from the mouth rather than the fauces), or if specific therapy has been employed. A small proportion of swabs from undoubted cases of streptococcal infection, even of scarlet fever, will be negative. Haemolytic streptococci of groups A, C, and G are pathogenic for man, and the other groups can be disregarded as causes of upper respiratory infection. All are penicillin-sensitive. Vincent's organisms are found in large numbers in association with a well-defined clinical type of throat infection, and also occasionally in some blood diseases and in glandular fever. Small numbers may be present in the normal throat. The interpretation of a positive result is therefore a matter of clinical judgment. The laboratory does not usually mention the other types of bacteria present in throat swabs, as none of them is known to be associated with any particular disease of the throat. Swabs from about 50% of cases of sore throat are negative for any recognized pathogens.

Nose and Ear Infections.—All organisms grown from swabs of nasal and aural discharges will be mentioned in the report, with the exception of *Staphylococcus aureus* and non-pathogenic types of *Neisseria* in the nose, as any or all of them may be of clinical significance. As treatment will probably be directed to their elimination, it is usual to perform antibiotic sensitivity tests.

"Pneumonia."—Requests for bacteriological examinations in connexion with uncomplicated cases of lobar pneumonia are rarely made nowadays, as prompt response to chemotherapy is the rule. However, culture of the sputum may be very valuable if the case is unusually severe, clinically atypical, or does not respond to treatment. In addition to pneumococci, the examination may reveal *Staph. aureus*, Friedländer bacilli, or *Haemophilus influenzae* in large numbers, and in such cases the sensitivity to antibiotics should be determined. Sputum examination in more chronic conditions may result in the detection of an unexpected case of tuberculosis or fungus infection. Since the remarkable change in the prognosis of lobar pneumonia more attention is being given to the so-called atypical pneumonias. In addition to a routine sputum culture, the practitioner may request an examination of the patient's serum for various antibodies. Two of the diseases detectable by this means are of animal origin (and therefore preventable) and one is susceptible to antibiotic treatment. Serological tests for the following diseases are now in routine use: (1) "primary" atypical pneumonia, which is associated with cold agglutinins and the agglutination of streptococcus MG; (2) Q fever, a rickettsial disease which in this country is probably transmitted from cattle to man in milk or in dust; (3) infection with viruses of the lymphogranuloma-pestis group, which follows contact with many species of birds and is susceptible to aureomycin treatment; and (4) pneumonia following a recent influenza A or B infection.

Tuberculosis.—The laboratory will examine sputum, pus, urine, cerebrospinal fluid, and other materials for tubercle bacilli when requested, or when the history or pathological findings suggest the advisability of doing so. First, a microscopic search will be made, either on untreated or on concentrated material. There is usually little doubt that the acid-fast bacilli present are tubercle bacilli, though many strains of saprophytic mycobacteria are morphologically indistinguishable from tubercle bacilli. The laboratory ensures that its collecting receptacles are free from such saprophytes, and doctors obtaining specimens should take similar precautions. In some materials, such as urine, saprophytic mycobacteria occur commonly, and here a

positive microscopic finding should be confirmed by culture or animal inoculation. Few pathologists like to report "Tubercle bacilli present" on a microscopic examination of any material, and most prefer the phrase, "Acid-fast bacilli present." However, they will generally make it clear when they consider that confirmation of the microscopic findings is necessary. Practitioners should not hesitate to ask for confirmation when the clinical condition and the result of microscopy appear to conflict. Culture and guinea-pig inoculation are also used to detect small numbers of tubercle bacilli when the microscopic examination is negative, but the result is not available for three to six weeks. The laboratory should be left to decide which of the two tests to employ.

Whooping-cough.—A correct diagnosis of whooping-cough is usually made by the practitioner or the patient's mother. Laboratory help is valuable in the atypical case, particularly where symptoms are modified by vaccination. Since chloramphenicol appears to be effective only when given within a week of onset, it is important to establish the diagnosis of an atypical case if there is an infant among the family contacts. The pernasal swab—a fine flexible wire swab which is passed backwards along the floor of the nose—is the most convenient and effective means of collecting material. Unfortunately it takes three to four days to complete the bacteriological examination. With present methods 80 to 90% of cases give a positive result in the first two weeks of the disease. The number of positives will be increased by taking two swabs, one through each nostril. Specimens should reach the laboratory on the same day unless a special transport medium is used.

Gastro-intestinal Infections

Diarrhoea with or without vomiting and fever is due to a variety of agents, including the dysentery bacilli, the salmonellae (including *S. paratyphi B*), staphylococcal enterotoxin, certain strains of *Clostridium welchii*, and, in infants, some serological types of *Bacterium coli*. Though it is often possible from the clinical picture to suspect the nature of the infection, bacteriological examination alone can reveal this with certainty. Failure to establish a bacteriological diagnosis seldom does much harm to the patients, as most recover during or some time after a course of treatment. However, there are great variations in severity from case to case of the same disease, and a mild attack of dysentery or salmonella infection may be followed by a severe or even fatal infection among the patient's associates. Bacteriological examination may reveal an unexpected connexion between a number of cases and lead to the identification and elimination of a source of infection. Although fairly rapid transmission of faeces specimens to the laboratory is desirable, most pathogens survive well enough to make postal specimens highly effective in acute cases. In the occasional case in which amoebic dysentery is suspected, a specimen should be examined within a very short time of being passed: it may be possible to arrange for the patient to defaecate at the laboratory. Rectal swabs are useful in some circumstances, as they can be conveniently and quickly collected. Some laboratories provide a special apparatus, but a moistened throat swab is quite effective if it really reaches the rectum. In acute cases of diarrhoea the results are good, but in convalescent cases and in typhoid fever they are inferior to those of faeces culture. Rectal swabs must reach the laboratory within a few hours. In most acute salmonella and dysentery cases a provisional report may be given on the day after the specimen is received. A final negative report is usually given at 48 hours and the exact identification of a pathogen may take longer.

Unexplained Pyrexia

There are a number of febrile conditions in which the laboratory can be very useful. The blood can be examined for evidence of typhoid fever, Weil's disease, undulant fever, glandular fever, infectious endocarditis, and a number of

other diseases. The laboratory will supply outfits for the collection of blood for culture and for serological tests, together with a sterile syringe. Many practitioners find it convenient to keep such an outfit in readiness. The pathologist will always be pleased to give advice on the appropriate investigations in cases of unexplained pyrexia.

Infections of the Central Nervous System

The practitioner may not often be called on to investigate infections of the central nervous system, as such cases are usually admitted to hospital at an early stage. Investigation usually begins with a general examination of the cerebrospinal fluid to exclude pyogenic and tuberculous meningitis. In cases of lymphocytic meningitis there are various valuable serological tests, including those for lymphocytic choriomeningitis, canicola fever, and mumps infection.

Skin Infections

Bacteriological examination may be of value in some skin diseases. In unusual or intractable pyogenic conditions, a culture and sensitivity test, together with a search for the focus of infection, may be useful. The examination of scales or hair from suspected cases of ringworm may help in prognosis and may indicate a possible animal source of infection. Swabs from suspected cases of anthrax, especially among those not known to handle dangerous materials, may be of vital importance in securing early treatment.

Other Activities of the P.H.L.S.

Supply of Sera, Vaccines, etc.—The service takes no part in the supply of therapeutic sera, but holds stocks of certain prophylactic and diagnostic agents. It supplies vaccine lymph direct to the practitioner, and diphtheria prophylactics indirectly through the local health departments. It keeps stocks of scarce prophylactic agents such as typhus vaccine, rabies vaccine, gamma globulin, and anthrax antiserum, but typhoid, plague, and cholera vaccines are obtained from commercial sources. The laboratory staff will be pleased to advise about immunization procedures, but will not, as a rule, carry out inoculations. Skin-testing reagents, including Frei antigen, brucellin, Trichinella, and hydatid antigens, are available for suitable cases.

Field Investigations.—The service is constantly engaged in investigations into the source and mode of spread of infectious diseases, and in field trials of prophylactic agents. Although many of these activities are carried out in co-operation with the public health authorities, much help is obtained from general practitioners, and some schemes would be impracticable without their participation. Many practitioners are taking part in the scheme for the early diagnosis of influenza and others are collaborating in trials of whooping-cough vaccines. Those who encounter new or unusual types of infectious disease will find that the laboratory staff are anxious to assist in their investigations.

The general practitioner has direct access to the public health laboratory for the submission of specimens and for advice on the prevention and control of infections and on general problems of immunity. He will find many opportunities for useful collaboration with the laboratory, both in the solution of day-to-day problems and in the acquisition of new knowledge.

Next article on Clinical Pathology.—"Dispatch of Specimens," by Dr. Martin Hynes.

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EUROPEAN HAEMATOLOGY CONGRESS

[FROM A SPECIAL CORRESPONDENT]

The Fourth Congress of the European Society of Haematology was held in Amsterdam from September 8 to 12. Over 500 members and about 250 guests attended from at least 28 countries.

Six main topics were chosen for discussion and over a hundred papers were presented. Immuno-haematology was dealt with first, the chief contributions being by J. V. Dacie (London), J. J. van Loghem, jun. (Amsterdam), C. Gasser (Zurich), J. F. Ackroyd (London), S. Moeschlin (Zurich), W. Dameshek (Boston), and M. M. Hargraves (Rochester, Minn.). Amongst the subjects discussed were the antibody patterns and clinical syndromes of acquired haemolytic anaemia, the mechanism of drug-induced and idiopathic purpura and granulocytopenia, and the significance of the L.E. cell. Further information was available on the characterization of the antibodies of acquired haemolytic anaemia, but there was nothing new concerning its aetiology or treatment. Recent work on anti-platelet and anti-leucocyte agglutinins indicates that many cases of drug-induced or idiopathic thrombocytopenia or granulocytopenia may have a pathogenesis comparable to that of acquired haemolytic anaemia. Dr. Dameshek in his usual challenging style went so far as to suggest that Henoch-Schönlein purpura was an immunovascular disease.

Barbiturates and Porphyrinuria

The metabolism of haemoglobin and erythropoiesis were the next main topics. The chief contributions were by H. Bénard (Paris), C. Rimington (London), and J. Waldenström (Malmö). By the use of tracer techniques in particular it has been shown that haemoglobin synthesis continues in non-nucleated erythrocytes, particularly during active blood regeneration. On the purely chemical side Professor Rimington presented new work on the mechanism of formation of porphyrins from porphobilinogen. Barbiturates can cause porphyrinuria in experimental animals, and there appears to be evidence that this can happen in man also, particularly where latent porphyria exists. The same may be true of lead intoxication.

The metabolism of iron and iron-deficiency anaemia were next discussed, and the remarkable elucidation of the metabolic pathways that can be obtained by using Fe^{59} was clearly demonstrated. C. V. Moore (St. Louis) made a plea for the abandonment of the title idiopathic as a description for certain iron-deficiency anaemias: in his view iron-deficiency was always due to blood loss, to deficiency of iron in the diet, or to failure to absorb it. Haemochromatosis and the siderosis due to transfusions were next considered, and finally vitamin B_{12} and the megaloblastic anaemias. The main papers were given by L. Heilmeyer (Freiburg) and C. C. Ungley (Newcastle).

Treatment of Acute Leukaemia

On the third day of the Congress three main topics were dealt with: acute leukaemia, lymph-node puncture, and the platelets. W. Dameshek (Boston) reviewed the treatment of acute leukaemia; in his experience the most promising therapy was a combination of A.C.T.H. and aminopterin. With this regime he had had 25 successive remissions lasting from four weeks to two years in cases of acute lymphocytic leukaemia in children and young adults. Some patients had had up to four remissions. The principal papers on lymph-node puncture and blood platelets were given by A. Pavlovsky (Buenos Aires) and S. van Creveld (Amsterdam), respectively.

The last topic discussed was that of blood coagulation. R. G. Macfarlane (Oxford) described his conception of the formation of blood thromboplastin, the main point being that the so-called accelerators are thought to be participants in the reaction which produces thromboplastin and not accelerators of the reaction of thromboplastin with