

THE PUBLIC HEALTH LABORATORY SERVICE *

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THE Public Health Laboratory Service (P.H.L.S.) is designed to make the laboratory investigations needed to provide a continuous picture of the communicable microbial diseases of this country. These diseases must be accurately defined by identifying the agents that cause them, by continuously seeking out and recording their whereabouts, and by investigating what really matters in promoting or limiting their spread. The activities of the P.H.L.S. allow useful advice to be offered to the central and local health authorities and to others concerned with the control and prevention of these diseases.

In each of the past three decades successively fewer people have suffered and died from microbial diseases. Broadly, three kinds of measure have secured this improvement: hygiene, immunisation, and chemotherapy. But the successful application of these measures depends on a full and proper understanding of the communicable microbial diseases themselves. Mere approximations to scientific knowledge and to sound practice will not yield satisfactory dividends; indeed, action based on such approximations will often prove to be both expensive and disturbing to the community. Moreover, the pattern of communicable microbial diseases is not static, and many of our current microbial diseases and the problems associated with them remain to trouble us precisely because they present greater technical difficulties in the way of understanding and control than those that have been reduced or removed. Therefore the need for the work of the P.H.L.S. is no less today than when the Service was begun.

Structure and Organisation

The P.H.L.S. was set up under Section 17 of the National Health Service Act, 1946 (Great Britain 1946). It was made a permanent feature of the medical life of the country because its predecessor, the Emergency P.H.L.S. (E.P.H.L.S.) of the 1939-45 war, proved beyond all doubt the usefulness of having such an organisation. The E.P.H.L.S., and the P.H.L.S., were administered by the Medical Research Council (M.R.C.) for the Ministry of Health until the administration was transferred in 1961 to the independent P.H.L.S. Board by the Public Health Laboratory Service Act of 1960 (Great Britain 1960). (For accounts of the debates leading to the passing of this Act, see *Hansard* 1960.)

Two of the reasoned arguments put forward in 1938 for the setting up of the E.P.H.L.S. (Medical Research Council 1947a) may be briefly repeated. The particular service and organisation were required: (1) to augment existing facilities to meet the laboratory work required to

detect the presence of outbreaks of infection and define their extent; (2) to provide this service on a national basis so that epidemiological intelligence might be securely based on reliable laboratory findings from many areas. The national character of the organisation was essential for effective action against sources of infection causing outbreaks not confined within administrative boundaries.

REGIONAL AND AREA LABORATORIES

Throughout England and Wales 60 regional and area laboratories of the P.H.L.S. (see accompanying figure) provide a bacteriology and virology service free of charge to local health authorities and general practitioners. The work of these constituent laboratories represents the basic service of the P.H.L.S., and it is the main source of the material upon which the Service makes its investigations and offers its advice. Work is also received from other organisations whose activities and products have or may appear to have a bearing on the spread of communicable microbial diseases. Each laboratory is under a medically qualified director, and the duty of the Service is to gather as good a sample of relevant information as can be secured and dealt with. Private organisations seeking advice on how to make a bacteriologically safe product, or to follow bacteriologically safe methods, are given a free service, often in collaboration with the local health authority. Any investigative work required to define and establish bacteriologically reliable and acceptable procedures is also



Distribution of the laboratories of the Public Health Laboratory Service (February, 1965).

* Communication to the Royal Medico-Chirurgical Society of Glasgow on Feb. 19, 1965.

given free of charge. Routine laboratory control of the product itself, however, thereafter becomes the responsibility of the private organisation.

Relations with Hospitals

A number of hospitals are served by the laboratories of the P.H.L.S. Sometimes this is arranged on an informal basis, especially if the help of the P.H.L.S. is desired mainly to study the communicable microbial diseases of the hospital—a subject of great importance to the hospital and to the general public. Work of this kind has made it clear that effective contact between a P.H.L.S. laboratory and a hospital may provide a useful and early source of information about what communicable microbial diseases are in the area. In some places, especially if there is not enough work for a separate hospital laboratory, the P.H.L.S. enters formally into a joint arrangement with the hospital authorities whereby costs are shared and scarce resources are used economically. These arrangements have been most beneficial; but they do not represent either a universal pattern or a new P.H.L.S. policy aimed at taking over the work of hospital laboratories wherever this can be secured. In many places, for a variety of good reasons, joint arrangements are not either practicable or desirable. Everywhere, however, it is the hope of the P.H.L.S. that relationships between hospital laboratories and those of the P.H.L.S. will be complementary and mutually helpful. Many hospital laboratories, although not operating a formal joint agreement, collaborate with the P.H.L.S. by providing regular information about their isolations of significant microbes and by exchanges of scientific and technical staff for training.

Personal Consultation and Field Investigations

An essential characteristic of the working of the P.H.L.S. is the ready availability of the laboratory staff for personal consultation on a very great variety of problems and issues and for joining in field investigations, when desired, with an equally wide variety of persons and interests. These were two well-marked features of the work of the E.P.H.L.S., especially in the early days of the 1939–45 war; and they are so important for the kind of work that the P.H.L.S. has to do that any failure to safeguard their continuation on an adequate scale would so change the P.H.L.S. that its true character would be lost. Close personal consultation and extensive field work have often been required to get at the hidden reservoirs of particular infections.

REFERENCE AND SPECIAL LABORATORIES AND UNITS

There are now 16 reference and special laboratories and units, of which 11 are on the site of the Central Public Health Laboratory at Colindale in North London. The heads of these laboratories and units, together with reference experts—some within and some without the Service—act in a general way as consultants to their colleagues. They carry out the kind of specialised laboratory and epidemiological investigation and research that arises directly out of the work of the P.H.L.S. They collect, analyse, and distribute information, and they help to watch over the development and application of technical methods used in the Service. This includes the issue of reliable cultures, sera, antigens, and other special reagents. Because, for tracing the spread of infection, it is essential wherever possible not merely to identify but also to type the causative microbe, the backroom and bench work of the public health laboratories tends to be more than usually

exacting and time-consuming (Anderson and Williams 1956). Many specialised methods, especially when they are first introduced, are essentially matters for experts; and the experts can be kept in good practice only if they receive enough work from other laboratories. Moreover, the collection and study of such material on a wide scale gives insight into possible local variations in the microbes themselves and in the incidence of particular diseases throughout the country. Sometimes the use of a new method is initiated and developed by a member of a regional or area laboratory; and such a person may acquire a role as a reference expert. By and large, however, it is the function of the reference and special laboratories and units to keep the P.H.L.S. up to date on methods and to supervise their translation, whenever that becomes practicable, from specialised centres to the laboratories of the Service as a whole. As a result of free exchanges of material between laboratories there is every chance that errors of method will be discovered and eliminated from the work of individual laboratories instead of being built into their life—a constant risk for those whose inclination is to be self-sufficient.

HEADQUARTERS ORGANISATION

To coordinate and administer the affairs of the 76 laboratories and units of the P.H.L.S.—which means the work of 1200 people—to maintain essential contacts of many kinds, and to carry out the policy and directives of the P.H.L.S. Board, the London H.Q. staff of the P.H.L.S. consists of 24 people who work in an area of 3000 sq. ft. The proportionate cost of this H.Q. is remarkably low, especially for a relatively small organisation and above all if it is realised that the H.Q. staff relieves the laboratories of such tasks as payment of salaries and maintenance of accounts. During the financial year 1963–64 the cost of the H.Q. was £46,551, out of a total budget for current expenditure for the whole Service of £1,756,378 for the same period—that is, 2.6% of the total. These figures are worth quoting because, more simply than any other evidence, they emphasise that, in the P.H.L.S., the central administrative machinery has not become an end in itself. With only a minimum of direct guidance it is left to the heads of individual laboratories to judge and advise on the best application of their particular talents and resources to their local problems and opportunities. But this and every other matter of the same kind is handled in the fashion of a community. The members of the central administration themselves go in for personal consultation and visits to the laboratories; and they apply themselves to three aspects in particular of the community life of the P.H.L.S.—namely, the five meetings in each year of the staff committee and all the work that flows therefrom; the formation and effective functioning of working parties; and the recruitment and arrangements for training of new staff. These problems and methods keep the centre and the periphery of the P.H.L.S. in effective contact with each other; and they guarantee that good insights are shared, that eccentric notions are heard (and sometimes adopted with refreshing benefit), and that some superficially unattractive-looking work is nevertheless done because it clearly ought to be done. It can be endured within the P.H.L.S. because it is to be shared; because its acceptance as a public duty is a deliberate decision; and because it can be more quickly assessed because many laboratories take part.

New Staff

The recruitment and training of new staff is of the utmost importance to the P.H.L.S. The search is for men

and women of good intelligence and basic training who have a real capacity for investigation linked with a willingness to apply this rare quality, often as part of a rather large team and often to problems which would probably not attract individual investigators. In finding and training the right people, the P.H.L.S. has been enormously helped and encouraged by the willingness of the staff of university departments and medical schools both to encourage their students to consider the P.H.L.S. as a career and to accept its trainees for systematic courses and for individual tuition and inspiration. A great many of the first members of the E.P.H.L.S. were already experienced and distinguished members of universities and research institutes. They went out, often to improvised laboratories, to look for signs of bacteriological warfare and great epidemics. Finding none, they turned their skills against the ordinary problems presented by the epidemic diseases then prevalent. The harvest of things discovered and of problems solved was so impressive that the new service came to stay. Now the problems are more difficult; the experienced research-workers available for our particular tasks are fewer; and the work expected has so increased that time for thought is often impossible to find. Against this background the need for finding the right staff and getting them the most useful training is a matter of continuous concern and uphill effort.

The P.H.L.S. in Action

During 1963, 153 scientific papers, books, or reports were published by members of the P.H.L.S. (Public Health Laboratory Service 1964a). These papers and those of earlier years give a balanced although not a complete picture of the contribution of the P.H.L.S. to medicine. However, although this makes invidious distinctions, it may be useful to describe the P.H.L.S. in action in four different fields to illustrate the special kind of contribution which it can readily make because its distinctive organisation not only encourages collaboration but makes this both normal and effective.

Virology as a Routine

Until after 1945 virology was studied only in laboratories able to treat such work as a research project. The advent of manageable methods of tissue culture for the growth of viruses in the early 1950s opened the way to a considerable expansion of virology. Even then, however, a laboratory was not likely to undertake virology unless it was well favoured and wished to do something regarded as rather special. Tomlinson and Mitchell (1956) made an important contribution, therefore, by isolating poliomyelitis virus in a routine laboratory of the P.H.L.S. without the use of human serum and without expensive reagents. Quickly a number of other laboratories of the P.H.L.S. showed that they also could handle viruses. Virological methods suited to routine laboratories were worked up within the Service, and now there are only a few laboratories which cannot yet tackle any virology. As a result, during epidemic periods of influenza the P.H.L.S. probably isolates more strains of virus than most countries and it has been able to cooperate with the World Health Organisation (W.H.O.) by rapidly producing strains of influenza virus for analysis in the all-important search for new types. In the continual world-wide look-out for new epidemics of influenza, speedy identification of the rapidly changing type strains responsible may enable effective vaccines to be ready in time to meet advancing epidemics. The P.H.L.S. has also cooperated with the M.R.C. in a

long series of trials of various influenza vaccines. (For an account of the development of a virological diagnostic service within the P.H.L.S., see Bradstreet et al. 1964.)

Poliomyelitis and enterovirus surveys have also been made possible; and the ready availability of the necessary laboratory and epidemiological surveillance allowed the M.R.C. and the Ministry of Health to press forward trials of a killed British vaccine of Salk type, and later of the attenuated live Sabin vaccine, with confidence, at times when incidents and observations abroad were of such a character that—but for the effective guarantee of surveillance made possible—misgivings and hesitations might have held things up seriously (Medical Research Council 1957, Public Health Laboratory Service 1961, 1965).

The handling of the laboratory work needed in the control of major episodes of infection is also made more effective because of the wider practice of virology in peripheral laboratories of the P.H.L.S. For example, the work of the P.H.L.S. in the poliomyelitis outbreak at Hull in 1961 (Ministry of Health 1963) was generally acknowledged as of great value. In the smallpox outbreak of 1962, three P.H.L.S. laboratories were particularly involved in essential diagnostic work: Colindale for London and Birmingham cases; Leeds for Bradford cases; and Cardiff for South Wales cases.

Two Studies of Postoperative Infection

The first is that reported by Blowers et al. (1955) in which the help of a great variety of experts was very quickly mobilised to reinforce a small, newly opened P.H.L.S. laboratory called upon for help in an important outbreak of staphylococcal infection in two associated thoracic surgical units. Besides much hard, although ordinary, routine work, in which neighbouring laboratories readily joined, the investigation required skilled epidemiology, phage-typing, air-sampling, and the measurement of ventilation and air movement. Apparatus, advice, and experts converged from many quarters. This joint effort not only established the extent of, and the way to control, the particular outbreak, but it left behind a continuing impetus to the further study of the difficult and important questions governing the safety and efficacy of the methods used for ventilating operating-theatres (Blowers and Crew 1960, Lidwell and Williams 1960, Medical Research Council 1962).

With so much interest in postoperative infection, it was clearly necessary to define the extent and character of the problem, and this was done in a survey which covered twenty-one different hospitals and drew in twenty-three laboratories, only one of which was not a laboratory of the P.H.L.S. (Public Health Laboratory Service 1960).

Immunisation in the Field

Right from the earliest days of the E.P.H.L.S., the Service has keenly investigated methods of immunisation so that these could be used in a sound manner on a wide scale. One of the first contributions was the evidence that combined active and passive immunisation could be used to halt localised outbreaks of diphtheria (Downie et al. 1941, Fulton et al. 1941).

It was important to establish the principle that these two kinds of immunisation could be used together and also to dispel the expressed fear that immunisation might be all very well for the immunised individual but dangerous for any unprotected members of the community at risk. Wrongly, it had been feared that immunisation would

cause a dangerous increase in the number of symptomless carriers; instead it was shown that their number decreased as a result of immunisation. The whole methodology of mass immunisation that has been developed and followed right up to the present time owed a lot to the fundamental work of these early days and to the work of the P.H.L.S. in later trials, most of which were collaborative efforts involving the P.H.L.S., the M.R.C., the Ministry of Health, and the Society of Medical Officers of Health. Without a generous and cooperative attitude all round, these and other similar trials could not have been undertaken. Two among many examples are the introduction into this country of immunisation against whooping-cough (McFarlan et al. 1945, Medical Research Council 1951, 1959), and an investigation into the association between paralytic poliomyelitis and previous recent inoculation (Medical Research Council 1956). The results were in each case important in the formulation of government policy on immunisation of children.

Food-poisoning and Enteric Fevers

In collaboration with medical officers of health, public health inspectors, food manufacturers, caterers, shopkeepers, port health authorities, veterinarians, and administrators, the P.H.L.S. has made great efforts to clarify the problems of food-poisoning and the enteric fevers. Reports on food-poisoning in England and Wales published each year in the *Monthly Bulletin* (Public Health Laboratory Service 1964b) give an indication of some of the efforts and good results. In this difficult matter, a complexity of conflicting interests and long-established habits of mind and of practice have required a continuous process not only of investigation but of persuasion and education. Recent as well as past events make it clear that much has still to be done before sound bacteriological principles become universally accepted as the basis of practice. Both for the safe production and handling of food and for the most efficient management of outbreaks it is obvious that a much wider understanding of bacteriology is required. Unfortunately the practical situations are seldom simple, and a few incompletely understood facts of bacteriology may prove quite insufficient as a guide to comment or action. In these matters the P.H.L.S. has now a rich store of accumulated experience and is both willing and anxious that its local and central resources should be fully drawn upon by all who are responsible for decisions on policy and for the conduct of day-to-day affairs. The P.H.L.S. has been and still is deeply involved in learning about the sources and tracing and preventing the spread of food-poisoning salmonellæ—by meats (W. B. Moore 1950, Hobbs and Wilson 1959, Public Health Laboratory Service 1964c), egg products (Medical Research Council 1947b, Newell 1955, Public Health Laboratory Service 1958), desiccated coconut (Anderson 1960, Galbraith et al. 1960), and animal feeding-stuffs and fertilisers (Walker 1957, Public Health Laboratory Service 1959). The role of staphylococci in food-poisoning has been examined (Allison 1949, Parker 1953, Anderson and Stone 1955, Hobbs 1955, 1962). The facts about *Clostridium welchii* food-poisoning have been established (Hobbs et al. 1953, Hobbs 1962, Hobbs and Wilson 1959). The reasons for the almost complete freedom of the United Kingdom from botulism are being analysed. Much effort has been put into tracing and following up carriers of typhoid and paratyphoid bacilli (among numerous examples, see, for instance, King 1944, Wallace and Mackenzie 1947, Thomas et al. 1948,

B. Moore 1948, 1950, Moore et al. 1952) and in defining the much-discussed and topical problem of the association of canned foods with food-poisoning salmonellæ, staphylococci, and typhoid fever. A series of important papers from 1951 onwards (Public Health Laboratory Service 1951, Sandiford 1954, Couper et al. 1956, Bashford et al. 1960) may be held to have reached their climax with the publication of the Milne Report on the Aberdeen outbreak of typhoid fever (Scottish Home and Health Department 1964).

Discussion

The organisation, methods, and objectives of the P.H.L.S. are not always fully understood—even by its friends. It is not wholly a routine service, although it provides one for those whom it serves. Nor is it just another research body; but it cannot hope to do its work without the kind of people, methods, and resources made available for research. Its duty is to define the agents of communicable microbial diseases, to discover their distribution and method of spread, and to investigate and advise on how these diseases may be controlled. To do this in any effective manner it must recruit and train investigators, and it must make special efforts to keep its laboratory methods up to date and in reliable order. Its members must freely share duties and insights in the manner of a community. It is not so easy as it may seem to apply on a national scale the outlook and methods of a research team to the day-to-day problems of infection as they are met in ordinary life; but nothing less will serve. Success in the enterprise demands hard work and a sense of dedicated purpose from the members of the Service together with a general understanding that the P.H.L.S. can live and work only if its organisation, like its duties, can be more than a little different from the ordinary run of things.

Conclusions and Summary

The function of the Public Health Laboratory Service (P.H.L.S.) is to make a continuous study of how communicable microbial diseases are spread and what advice may be offered about how to control them.

Such a study is necessarily based upon the use of reliable laboratory methods, now so numerous and complex that no single laboratory could ever hope to be able to maintain them all in good working order. Another requirement is an up-to-date and comprehensive knowledge of bacteria, viruses, fungi, protozoa, immunology, and epidemiological methods, such as no microbiologist, however confident, would be likely to claim for himself.

These considerations, together with the indifference of bacteria and viruses to man-made subdivisions of the country (and indeed of the world) dictate the organisation of the P.H.L.S. as a nation-wide community of investigators.

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EXPERIMENTS WITH INTERFERON IN MAN

A report to the Medical Research Council from the Scientific Committee on Interferon*

THE existence of interferon was reported in 1957 by Isaacs and Lindenmann. Since then it has become clear that this substance is produced in response to many virus infections and plays a part in the normal process of recovery from infection with animal viruses. Interferon may be the result of a cellular reaction to the entry of a foreign nucleic acid (Rotem et al. 1963).

This committee was constituted to encourage collaborative research on interferon, on its nature, mode of action, large-scale production and possible prophylactic or therapeutic use. An initial trial in volunteers showed that vaccinia virus will not "take" on skin injected the day before with monkey-kidney interferon (Scientific Committee 1962). It was therefore thought likely that if the human nose and pharynx were treated with interferon it

TABLE I—DOSAGE OF INTRANASAL DROPS (ml.) CONTAINING INTERFERON OR CONTROL MATERIAL AND GIVEN TO VOLUNTEERS

Virus used	Day before inoculation	Day of inoculation	Days after inoculation				
			1	2	3	4	5
Coe or PK	1 morning 1 afternoon	1 mixed with virus	1	1
Cop 222 ..	As above	As above	1	1	1	1	1
PK	Dosage by nasal spray 1 ml. divided into 11 applications between 09.30 and 20.00 hr.	Spray as before. Virus in 1 ml. saline 11.00 hr.	Spray as before 1 1

kidney-cell cultures by the Wellcome Foundation and by Glaxo Laboratories. Interferon was given as nasal drops or sprayed into the nose of volunteers at the Common Cold Research Unit, Salisbury. The titre of interferon used was measured in monkey-kidney cells just before or after use and found to inhibit the multiplication of an M rhinovirus strain at a dilution of about 200 (Sutton and Tyrrell 1961). "Dummy"

TABLE II—RESULTS OF INFECTING VOLUNTEERS WITH THREE VIRUSES CAPABLE OF CAUSING COLDS

Interferon	Virus given	Virus isolated	No. of positive specimens	Antibody rises	Laboratory evidence of infection	Colds
Yes	Coxsackie A21	6/6†	16/16	3/6	6/6	3/6
No	"	4/4	12/12	3/9	4/4	2/4
Yes	Parainfluenza 1	5/7	11/21	4/7	5/7	3/7
No	"	6/7	13/21	4/7	7/7	2/7
Yes	M rhinovirus	4/8†	6/22	3/7	6/8	3/7
No	"	1/6	3/17	5/6	5/6	3/6

† Numerator=number of positive results. Denominator=number of volunteers or specimens tested.

‡ Four volunteers were given interferon by spray—all were infected and two developed colds.

might become insusceptible to infection with respiratory viruses. Results of experiments to test this possibility are reported here.

Materials and Methods

Interferon.—Interferon was prepared as described earlier (Scientific Committee 1962) in rhesus or cynomolgus monkey

interferon consisted of fluid from uninoculated tissue-cultures similarly treated and was administered to all control volunteers.

Viruses.—Representative viruses capable of causing colds were chosen and all were shown to be unable to grow in vitro in cells treated with interferon. The strains and doses used were:

(a) parainfluenza virus type 1, Cop 222 (Tyrrell et al. 1959)—150 and 1500 T.C.D.₅₀ of virus passed twice in monkey kidney and then once in human embryo kidney.

(b) M rhinovirus strain PK (Bynoe et al. 1961)—10 T.C.D.₅₀ of virus as nasal washings.

(c) coxsackievirus A21 or Coe virus (Parsons et al. 1960)—150 and 750 T.C.D.₅₀ passed once in human amnion and once in human embryo kidney cultures.

The doses of virus were chosen to give substantial numbers of colds.

Laboratory tests.—Three nasal washings were collected for virus isolation; PK and parainfluenza virus in monkey-kidney cultures, and coxsackie A21 in HeLa or human fibroblast-cell strains. Antibodies were measured by hæmagglutination-

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