FIRST SESSION

Communicable diseases

WELCOME

Dr R. A. B. Rorie, M.D., F.R.C.G.P., D.P.M. (*Chairman*)

IT is my privilege and pleasure as provost of the East Scotland Faculty of the Royal College of General Practitioners to welcome you to this Symposium. I do so on behalf of our sponsors Messrs Geigy (U.K.) Limited, Pharmaceuticals Division, who, over the past 15 years have done so much to support these postgraduate ventures, and I welcome the opportunity of thanking them for their help. A special welcome must go to our undergraduate colleagues, who have come here to help with and enjoy our meeting. It is also my pleasure to introduce Dame Annis Gillie who is to take the chair this afternoon.

I could spend much time in thanking those who have contributed to this meeting, our team of speakers, our consultants—Dr Jamieson, Dr Morrison Dorward and Dr John Langlands who have done so much on the secretarial side, but time is short and our programme is very full. The subject is 'Communicable diseases', and who better to open the proceedings than one who has occupied chairs in both infectious diseases and public health, Professor Tom Anderson.

Virus diseases in man

Professor T. Anderson, M.D., F.R.F.P.S., F.R.C.P. (*Professor of public health*)

SO long as man lives in groups—and at the present time our focus of attention is on the family rather than larger groups—he is bound to encounter micro-organisms with which he must come to terms. We need to remind ourselves that whereas the bacterial parasites have a comparatively simple metabolism and are, for that reason, now easily treated we are moving into a period when the main concern will be the virus infections. As a result, there is increasing interest in the cell for this is the ultimate point of virus attack. Getting into the cell in the first place represents quite a feat on the part of the virus, which has to stick itself on to the surface of the cell, then break the cell envelope and without doing too much damage, enter the cell which will supply its metabolic energy. When this process has taken place, the virus to all intents and purposes disappears; it becomes intimately concerned in the metabolism of the cell. After an interval replication of the virus particles will take place. One of two things then happens. Either the virus continues to live in that cell indefinitely, or else there is an explosion of virus particles from the cell, infecting other cells of, or other people in close contact with, the host.

In this paper I want to look at the methods by which viruses enter cells. There are three main ways. First, many respiratory tract infections and, indeed, some skin

infections arise because the virus has *direct access* to the cell. When we breathe the air of a room full of people it is almost certain that we inhale virus particles which reach the upper or lower respiratory tract. They are not interfered with by circulating antibody though substances covering our mucous membranes may have a protective effect. Burnett and his co-workers described some time ago the possible importance in virus infection of the kind of mucus secreted. It may well be that in a state of high humoral immunity—perhaps shortly after immunization—mucous membranes are covered with mucus rich in antibody. In that respect antibody may play some part, but the point I want to emphasize is that in most of these infections the virus reaches the cell directly, adheres to it, enters it and when the cell 'explodes' the virus is coughed out into the environment or infects other cells lower down the respiratory tract.

The second kind of virus infection might be described as *systemic.* Here the virus gets in probably more often than we yet realize through the conjunctiva, but perhaps also by passing through the chinks between the cells of the respiratory tract. For a short period, possibly to be measured in minutes and hours rather than days, the virus circulates in the blood stream, and then centres on certain types of cell in which it prefers to live. It takes some time for the virus to replicate in these cells, and this is what we call the incubation period of such classic infections as measles, smallpox and chickenpox. In other words the virus enters on day one, there is a brief viraemia before it settles in some specialized cells, replicates and then at day 14 (or whatever the incubation period is) virus particles suddenly burst into the blood stream. There may now be a considerable viraemia, sometimes producing classical signs and symptoms that enable us to diagnose these infections on clinical grounds. Measles, chickenpox and smallpox can as a general rule be diagnosed as well by the clinician as by any virologist and a good deal faster.

This ease of recognition contrasts with local or 'direct access' virus infections. The ways in which the cells of, for instance, the respiratory tract can respond to any noxious stimulus are limited; they either produce increased quantities of mucus or, if the cells are severely damaged they produce no mucus and the membranes become exceedingly dry. In this respect one needs to remember that no clinician can differentiate on signs and symptoms alone the precise aetiology of respiratory tract infections; the common cold can mimic influenza and *vice versa.*

The third form of virus infection is a combination of both types, direct access and systemic. The best example is in some enterovirus infections, such as classical poliomyelitis, where the virus is accepted locally by the cells of the intestinal tract and invades the body to some extent, perhaps producing a viraemia; but the virus penetrates further to produce anterior poliomyelitis only when there is inadequate host resistance. Despite the apparent victory over polio, we need to recall that this is still an important route by which viruses enter the body; important because perhaps it is less the virulence of the virus that occasions the serious infection than some impairment of host resistance which allows a completely casual infection of bowel cells to become a serious and life threatening illness.

If a virus infection cannot be recognized prior to the onset of physical signs, the patient's cells will already be heavily impregnated with the virus at this early stage. We are therefore faced with a difficult therapeutic problem. A chemotherapeutic substance that enters the cell and influences its metabolism in such a way as to disturb virus replication, will almost certainly get very close to what the virus would have done, namely destroy the cell. This makes me hazard a guess that chemoprophylaxis may prove more important than chemotherapy. In other words, we will have to wait until some people are infected, identify the virus responsible, and then give prophylactic chemotherapy to contacts.

Indeed, the therapy of all virus infections is likely to be in the rather precarious

position of harming either the patient or the virus. This has emerged already with one or two of the few chemicals that have been suggested for virus therapy.

The second lesson we might learn is in regard to the prevention of virus infections. In the systemic and mixed groups protection by means of a vaccine can be valuable. A person well immunized against one of the systemic infections will respond to the slight initial viraemia (at the time of infection) with rapid outpouring of antibody, so that by the time the secondary, massive viraemia occurs antibody has been mobilized and the disease will be prevented.

However, in some mixed (systemic and local) infections such as poliomyelitis we have learned that perhaps 1,000 persons may have to be infected in order to produce one or two cases of overt disease. In such circumstances a virus vaccine must be absolutely safe, because it will be administered to thousands of people who would probably never have contracted the disease. Virus vaccines for such infections will have to be much more carefully tested even than, for example, those for the 'normal' systemic diseases.

We are encouraged here by the fact that we may be entering a period when chemoprophylaxis of some of these infections will be possible. For example experiments in Madras and South America have shown that we now have a drug which, administered in the early incubation period of smallpox, will prevent the disease. This interesting work fits in well with the stages of systemic infection; in order to cover one or two generations of the virus in the cell, the drug needs to be given over a period of only about 24 hours. It is not necessary to keep on giving it throughout the incubation period.

Many problems remain to be worked out in regard to virus chemoprophylaxis. Chemicals may be quite specific within a very small range, and smallpox is the only disease for which there is an active substance at present; but just as sulphonamides in the early 1930s seemed an almost incredible advance, the encouraging thing about the thiosemicarbazone story is that it has opened the door just a small amount—as it were—to let us see what the future may hold.

We were all brought up to believe that the cause of typhoid fever was *Bacillus typhosus*, and that once you knew the cause the whole process of control was easy. It took quite a long time for us to appreciate that this is only a partial truth. Infectious diseases are due to an interplay of three factors, host, parasite, and environment. The features of an infectious disease can be altered as easily by changing the environment as by changing either the host or the parasite; yet most of us are almost unconscious of the great changes that are taking place in our environment and take little account of them until we start to write history 20 or 30 years later.

The very large outbreak of *Salmonella typhimurium* infection which has been sweeping across the middle of Scotland recently is something which we may have to learn to live with if we insist on feeding our animals in a particular way and to use slaughterhouses which are better suited to the nineteenth than the twentieth century.

However, one or two features of this host–parasite–environment relationship are worth noting in regard to viruses. The first is that as we begin to live rather different kinds of life we shelter our children and especially our infants from early experience with many of the agents which produce infectious diseases. I am inclined to think that the systemic virus infections must have been among the earliest agents that man had to contend with. Serious as some of them may have been their presence was marked, because intimate exposure to the viruses occurred during the first three or four months of life. Some passive immunity was transferred from the mother so that an active immunity could be attained under the cover of this passive immunity by the continuous exposure to infection during the first five or six months. But, as we became more

hygienic and prevented our children eating each other's or their own faeces we began to nurture them more carefully and to reduce family size so that we had two or three children instead of 15 or 16. Poliomyelitis was then called 'infantile paralysis', because it was never seen except in young children. But as the years passed, so the age group of the persons affected advanced. I think we may be entering a period when some of what were regarded by the older of us as almost automatic infections (like herpes simplex in infancy and childhood) are going to emerge in the future as infections of considerable importance in older people who, because of a changed environment, escape earlier infection. In this respect inherited characteristics are important because the smaller our families the more likely we are to be careful in their nurturing and to delay their experience of the common viruses.

Last of all, one of the great epochs in medicine was the eradication of a group of infections following the remarkable improvement in sanitation that took place in the second half of the nineteenth century. All the magnificent methods that we now have for dealing with sewage and ensuring a safe water supply are very good for bacteria, but quite often they are useless in regard to viruses. The contamination of our water supply with viruses is something of which we are practically unaware. We may well have, in the second half of the twentieth century, just as big a problem in eliminating viruses from our water supply as we had with bacteria at the end of the nineteenth century.

Virus prevalence in Scotland

Professor N. R. Grist, B.Sc., M.B., Ch.B., F.R.C.P.E., F.C.Path. (*Professor of infectious diseases*)

You might be forgiven these days for wondering whether the enormous range of weird and wonderful new viruses with unfamiliar names is genuine or just a by-product of the fact that numerous virologists are working away with increasingly elaborate techniques, and more or less inventing the problems as they go along. Actually there is a bit of both. To get some idea of the prevalence of viruses we need initially to take a glance at the methods of detection that are available. First, evidence can be obtained from the traditional notification schemes: for example, that for Glasgow in 1963 shows emphasis on respiratory infections and some of the childhood exanthemata.

A similar analysis of infections in the Ruchill Infectious Disease Hospital, Glasgow in the same year again shows strong emphasis on pneumonia, then some of the rashes and a few cases recorded as polio, mumps and so on. In addition to these more traditional ways of recording infectious diseases, one must now depend also on laboratory data to get more aetiological detail. The WHO Virus Reports for 1964 show enteroviruses associated with neurological disease, numerous adenoviruses especially affecting the respiratory tract, influenza and para-influenza, and then herpes simplex, mumps in its proper relationship to the neurological disease, and respiratory syncytial virus appearing seventh in the list. Of course this is a biased sample; these are the kinds of things that laboratories were able to pick up at the time, but at least we are getting a little more detail.

Respiratory viruses pathogenic to man include the myxovirus group–influenza A B and C, the para-influenza viruses causing croup and various, usually minor, respiratory illnesses, and respiratory syncytal virus affecting infants. There are also