Leading Articles

Virus Disease and the Nervous System

The control which we have gained over bacterial disease is bringing the virus diseases into greater prominence than ever before. They probably now account for a greater proportion of the working time of the general practitioner than any other single class of illness. G. I. Watson (1955) found that they accounted for 25% of his visits over the last five years.

In spite of their importance it is perhaps not sufficiently realised that there is hardly a pathogenic virus which may not affect the nervous system. It is not necessarily those particles which have ordinarily the greatest virulence that cause the damage. The virus of herpes simplex for example may cause encephalitis. The virus of chicken-pox is believed to cause herpes zoster, and both these conditions may be complicated by encephalomyelitis. The incidence of encephalitis among 6,774 cases of chickenpox at the Willard Parker Hospital in the decade 1941-50 was 0.26%, (Appelbaum *et al.* 1953). Glandular fever may produce acute meningitis, diffuse encephalitis, acute polyneuritis and peripheral neuropathy. Banks (1954) states that glandular fever should be considered in every case of infection of the central nervous system of obscure origin.

In measles a recent survey gives the incidence of encephalitis as 1.5 per thousand with a case fatality rate of 28.6%. Of those who had survived it was found that 22 had recovered and were well; one had choreiform movements for one year with frequent headaches, dizzy spells and vomiting since that time; one had persistent tremors involving the extremities; one was epileptic; one had residual cord damage affecting the bladder, foot-drop and myopia; one had poor co-ordination; three were mentally defective, and six showed personality changes (Fox *et al.* 1953).

In a series of 564 cases of mumps investigated in Stockholm (Bengtsson and Orndhal, 1954) lumbar puncture was performed not only when neck rigidity was present but also when there was vomiting, dizziness and headache. Pathological changes in the cerebrospinal fluid or in the electro-encephalographic tracings were found in 54% of these cases. Of 19 boys affected in a residential school there were eleven cases of clinical and laboratory evidence of meningitis (Henderson, 1952).

In the 1951 epidemic of Bornholm disease reported from Birmingham by Disney and his colleagues (1953), six of the 104 typical cases had meningitis and in 27 atypical cases with suggestive symptoms seven had pleocytosis in the spinal fluid. In the Oxford epidemic of the same year there were seven cases (2.6%) of proved benign

meningitis and nine other cases had severe persistent headache together with photophobia and neck rigidity (Warin *et al.* 1953).

A fully documented case of rubella complicated by neurological and mental symptoms has recently been reported (Mitchell and Pampiglione, 1954) and the authors state that more than 60 similar cases have been reported in the literature to date.

The report of Dr. I. M. Scott on the psychological symptoms consequent on infective hepatitis published on another page is of more than passing interest. Cullinan (1952) in describing the post-hepatitis syndrome notes that patients may suffer from lassitude, have fits of depression and be unable to make decisions; that the disease may simulate menigitis has been noticed (Newman, 1942) but, possibly because of the expected gloomy outlook of the patient, the question as to whether the mental changes experienced in these cases were due to the effect of jaundice or of the virus does not appear to have been put.

The natural history of virus infection in general is instructive in this context. The virus is capable of growth only within a living cell. The first essential to the causation of disease is entry into a susceptible cell. This achieved multiplication is surprisingly rapid and a hundred particles may appear within a few hours. They then burst out from the cell, which may or may not be destroyed in the process, and either enter the blood-stream or directly invade the neighbouring cells.

If the rapid local growth is followed by invasion of the blood-stream the state known as " primary viraemia " occurs. The virus particle from the blood-stream are trapped in the cells of the liver, spleen and lymph glands, where active proliferation again occurs. This is followed by a " secondary viraemia " resulting in the dissolution of the attacked cells and consequent liberation of the organisms in huge quantities. When this secondary viraemia occurs the incubation stage is over and all susceptible cells in the host are invaded. Thus in measles the rash appears, the bronchial tubes are inflamed, the gastric mucosa and the gut are irritated. These are the outward and visible signs surely of a disease which in some degree affects all the organs of the body. The delirium of measles with its pyrexia is so common as not to be considered a complication, yet it must indicate a disturbance of the brain cells.

If we turn to the virus of poliomyelitis which has perhaps the greatest affinity of any for the nerve cell, we find evidence that its initial behaviour is similar to other pyrexia-causing virus particles. Not so long ago this virus was considered to be a specific inhabitant of the nerve cell, which it was thought to enter by passing along the olfactory nerve fibres from the nasal mucosa (Walshe, 1938). It is now believed by many that the invasion of the central nervous system takes place during the stage of secondary viraemia (Meenan,

1953). In epidemics of poliomyelitis which have been carefully studied, it has been shown that there are usually many more non-paralytic than paralytic cases and the general practitioner has always been confronted with difficulty in establishing a diagnosis in these cases. Dr. G. I. Watson writing of "*Virus Disease in General Practice*", grouped together "P.U.O." and poliomyelitis and wrote "the lesson cannot be preached too widely by general practitioners that every fever during the summer and autumn months should be considered as due to poliomyelitis until events prove it otherwise." The prodromal symptoms—fever, vomiting and headache—are common to all systemic virus infections.

In some conditions there is little or no leakage into the blood-stream—molluscum contagiosum and trachoma are examples—and in these the spread is from the surface of one epithelial cell to another. It is thought that the spread of the virus of influenza takes place in this manner and that from the first infected area—the bronchial epithelium—spread occurs rapidly over the broncial tree into the lung by passing over a "sheet of susceptible cells." This type of propagation cannot however account for the onset of complications such as meningitis.

The mechanism of spread of the virus of the common cold has not yet been worked out, but all of us can from personal experience recall the malaise and the gastro-intestinal dysfunction which so often preceeds the onset of the coryza by two distressful days.

More and more virus diseases are proving to fall into the group in which spread occurs through the blood-stream. Should not virus disease be considered as a general disease, each specific type showing a greater predeliction for certain types of cell, but having no exclusive affinity in its selectivity? In any severe virus infection any or all the organs of the body may be damaged, some to a greater, some to a lesser extent. Such a concept would help to explain the post-influenzal depression, the delirium of measles, the prolonged inanition of glandular fever and the jaundiced outlook of the patient with infective hepatitis. A review of the remote psychological consequences of virus disease might yield interesting information.

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