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Epidemic Influenza and General Hospitals

If an influenza epidemic due to Hong Kong virus does reach Great Britain in the coming winter months as expected[1] the attack rate could be high, though the virulence of the organism seems to be no more than moderate.

The number of patients seeking admission to hospital in such an epidemic cannot be predicted. There might be no more than a transient rise in the usual winter intake of elderly and bronchitic patients, but previous experience of similar epidemics points to a sudden demand for hospital beds. If this happens there is much to be said for providing isolation accommodation in selected wards with a view to containing the infection. Among the more obvious reasons for this are limiting the spread of infection to patients already in hospital, protecting new admissions from resistant hospital staphylococci, and concentrating the patients in a part of the hospital where special facilities, in both staff and equipment, are available. Patients developing influenza in other wards should not be transferred to the isolation wards until examination of sputum, nasal swab, and perineal swab has shown that they are not carriers of resistant staphylococci. Until the results of these examinations are available they should if possible be nursed in their own ward's side-rooms.

Perhaps 95% of patients with epidemic influenza withstand their infections without undue inconvenience. The remaining 5%, roughly those who are admitted to hospital, may become gravely ill in three principal circumstances—namely, because of a severe viral infection, a staphylococcal superinfection, or a pre-existing disease.

A severe viral infection may lead rapidly to a state of shock. The blood pressure of all ill patients must be taken frequently. If the systolic pressure falls to about 100 mm./Hg intravenous hydrocortisone should be given in a dose of 100 mg. at once and then 200 mg. in a saline drip in the next 24 hours. Sometimes an extensive influenzal haemorrhagic exudate develops in the lungs which can cause death from drowning. Prostration, dyspnoea, and widespread confluent radiological shadowing are characteristic. Repeated bronchial aspiration of blood-stained exudate may afford relief. Among other influenzal complications are encephalitis, which is usually mild, and myocarditis.

The standard staphylococcal complication is pneumonia, with its predisposition to abscess formation. Acute laryngotracheobronchitis in patients with influenza is nearly always staphylococcal. Dyspnoea, stridor, and sucking in of the soft tissues of the neck during inspiration are evidence of the laryngotracheobronchitis, for which treatment is tracheostomy, suction, and the administration of heated and humidified oxygen or air.

The groups of patients who are known to tolerate influenza poorly include the elderly, those with chronic cardiorespiratory disease or mitral stenosis, diabetics, and pregnant women. In addition otherwise healthy

children and young adults may develop dangerously severe infections.

Any of these circumstances may lead to death within hours of the onset of symptoms of influenza. Hence a careful clinical assessment of all the possibilities must be made on admission to hospital and a radiograph of the chest taken. The possibility of staphylococcal infection is so important that a specimen of sputum must be sent to the laboratory at once. Within half an hour a report should be ready stating whether staphylococci have been seen, and their sensitivity to antibiotics should be known the following day.

During the first 24 hours after admission to hospital chemotherapy must be based on the assumption that staphylococci may be present. Patients admitted direct to the isolation wards, who are unlikely to have resistant staphylococci, could appropriately be given benzylpenicillin 500,000 units and cloxacillin 250 mg. six-hourly, both by intramuscular injection. Those already in hospital, who may perhaps have staphylococci resistant to methicillin and cloxacillin and who need chemotherapy, might best be given fucidin 500 mg. three times a day by mouth and cloxacillin 250 mg. six-hourly by intramuscular injection. For patients in either group who are sensitive to penicillin, fucidin 500 mg. three times a day by mouth and cephaloridine 250 mg. six-hourly by intramuscular injection are recommended. The treatment of all patients should be reassessed on the day after admission in the light of laboratory tests, especially those relating to staphylococci and their antibiotic sensitivities.

An influenza epidemic inevitably causes or hastens deaths in those groups of patients who are known to tolerate it poorly. The real tragedies arise from failure to recognize and treat a severe viral infection or staphylococcal super-infection before it is too late. Many lives can be saved by systematic management, particularly during the first 24 hours after admission to hospital.

[1] *Brit. med. J.*, 1968, **3**, 757.
[2] *Brit. med. J.*, 1968, **4**, 396.

Host Response to Virus Infection

The immune response that follows virus infections is well recognized as a valuable protective mechanism. Much less is known, however, of the ways in which this response can modify the course of an infection. Yet clearly there are great variations in the way in which different patients react to an infection. In most instances, for example, nothing is known of the factors which cause a few children to develop aseptic meningitis out of the many hundreds who have symptomless alimentary infection with enteroviruses. Similarly, the causes of the postinfectious encephalomyelitis which follows measles in 1 child out of every 1,000 infected are quite unknown.

Patients with a virus infection do not produce much antibody until after the acute phase of the illness, and recovery from the acute infection seems to depend upon the production of inteferon rather than on antibody. The antibody, which forms largely in convalescence, usually persists for many years and has a powerful protective action by neutralizing the infectivity of the virus. Thus re-invasion of the host with the same virus results in the virus being promptly rendered non-infectious.

There is also evidence that delayed hypersensitivity plays a part in the immune response to virus infections.[1] Children with hypogammaglobulinaemia with an associated defect in delayed hypersensitivity, for example, are particularly prone to develop chronic progressive vaccinia, since there is a failure of the normal immune response which localizes the vaccination reaction to the site of inoculation.[2]

Nevertheless, it is now becoming clear that the immune response may not always be entirely beneficial. R. R. A. Coombs has recently stated that in the absence of an immune response many organisms would show little pathogenicity, and that the lesions associated with infections may be at least partly the result of an allergic reaction in the tissues due to the antigenicity of the organisms or their products.[3] H. E. Webb and C. E. G. Smith[4 5] have suggested that the inflammatory lesions in virus encephalitis might be due less to actual virus multiplication than to an antigen–antibody reaction resulting from an unusually early production of antibody by the host. This hypothesis has been supported by the finding that the incidence and severity of encephalomyelitis in mice inoculated with arboviruses was increased in animals given specific antibody at the time when viraemia was maximal.[6 7] Since antibody in human infection with louping ill virus appears to be formed locally within the central nervous system —as well as systemically, with appearance of antibody in the blood—it is easy to see how a similar situation might arise in man.[8]

In the first of a new series of occasional articles under the general heading of " For Debate . . .", at p. 684 of this week's *B.M.J.*, Dr. Webb expands his original hypothesis and discusses some of the ways in which the immune response of the host may influence the course of virus infections. Recurrent virus infections, such as herpes simplex or zoster, are examples of virus disease occurring in hosts who are already at least partially immune but who nevertheless suffer from a reactivation of the virus and recrudescence of infection.

Further examples of atypical or unusual virus disease in partially immune hosts have come to light recently. Children previously vaccinated with inactivated measles virus vaccine have occasionally developed unusual and sometimes serious reactions upon exposure to natural measles.[9-11] In addition, some cases of subacute sclerosing panencephalitis appear to be due to reactivation of latent measles virus several years after recovery from an attack of natural measles.[12-14] This disease

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[4] Webb, H. E., and Smith, C. E. G., *Brit. med. J.*, 1964, **2**, 569.
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