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GLOBAL EPIDEMIOLOGY OF INFLUENZA

Since the World Influenza Centre was set up in London four years ago, with collaborating laboratories arranged by the World Health Organization in many parts of the world, two influenza outbreaks have occurred and have been investigated. The report on the 1949 epidemic[1] and that in the opening pages of this issue by Drs. A. Isaacs and C. H. Andrewes on the pandemic of 1950–1 clearly show that this global strategy is opening up a new approach to the fundamental epidemiological problems of this disease. Mere description of epidemics, however useful as an historical record, has not solved the problem of how epidemics arise and spread. Moreover, as Isaacs and Andrewes point out, the important question whether influenza arises by recrudescence from within or whether it comes from without cannot be solved by descriptions of events unaided by bacteriology. But the combination of world-wide observation with the use of delicate technical methods for the labelling of strains of influenza virus gives promise of valuable results.

In a report to the World Health Organization Freyche and Klimt[2] have gathered together information on the influenza epidemic of 1950–1 from all parts of the world. This was no mere European outbreak, for from the summer of 1950 onwards epidemics affected at intervals large parts of Africa and South America, the U.S.A., Japan, and Oceania, and most countries in Europe. The northern hemisphere was chiefly affected from November onwards, and Great Britain was involved shortly before Christmas. Unlike the epidemic of 1949, which reached southern Britain via France and Italy from a focus of origin in Sardinia, the outbreak of 1951 struck first at the northern ports of Liverpool, Belfast, and Newcastle almost simultaneously. Moreover, the outbreaks in Liverpool and Belfast achieved a ferocity, so far as both morbidity and mortality were concerned, which has been unequalled in the recent past. Except in northern Britain the outbreak, though extensive, was not exceptional, nor indeed was the epidemic in Scandinavia, which preceded that in Great Britain by at least two months. Again, in contrast with experience in 1949, when the virus strains recovered from many European countries and forwarded to London were all close cousins of each other, those recovered in 1950–1 were not so homogeneous. Although they all belonged to the serological group of influenza A-prime viruses, they could be classified into two main subtypes by the haemagglutination-inhibition test with ferret sera. One of these subtypes—the "Scandinavian"—was recovered from Sweden and Denmark in November, 1950, and was closely similar to the virus recovered from local outbreaks in Sweden in the previous June. It differed from the second subtype recovered from Liverpool and Belfast (the "Liverpool") in being a poorer antigen and in combining relatively feebly with antibody in the *in vitro* test. Isaacs and Andrewes recall that Veen and Mulder[3] described similarly distinct subtypes ("Q" and "P") in 1950 during their detailed analysis of a large number of strains of influenza virus. The Liverpool subtypes ("P" strains) were closely similar to each other serologically and were recovered from Northern Ireland, France, Spain, Greece, Turkey, and Israel. Moreover, strains recovered from Johannesburg in July, 1950, belonged to this category, thus raising the possibility that spread had occurred across the Equator from the southern hemisphere. The Scandinavian outbreak clearly seemed to have its roots in the previous summer epidemic in Sweden, but "Q" strains similar to those from Sweden were recovered from several countries in Europe; and both Liverpool and Scandinavian viruses were found side by side in Eire, England, Holland, and Italy.

The interpretation of these findings by Isaacs and Andrewes is that the epidemics in the northern hemisphere began in two distinct ways. That in the Scandinavian area could have arisen by reactivation of virus dormant in the area between June and October, whereas a fresh importation of virus from the southern hemisphere may have occurred in the Liverpool–Belfast areas. In either case, subsequent spread seemed to be directly from one geographical area to another rather than by established lines of communication. It seems a little premature to comment upon these findings, particularly because some unexplained circumstances exist—such as the recovery of both subtypes of virus from Capetown and Melbourne in June–July, 1950. But laboratory experiments with the 1951 strains showed that it was possible to convert the one subtype into the other by particular methods

[1] Chu, C., Andrewes, C. H., and Gledhill, A. W., *Bull. World Hlth Org.* 1950, **3**, 187.
[2] W.H.O. Epidemiological and Vital Statistics Report, 1951, IV, p. 141.
[3] *Studies on the Antigenic Composition of Human Influenza Virus A Strains*, 1950, Leyden.
[4] *Brit. J. exp. Path.*, 1944, **25**, 130.

of cultivation. "Q" strains, which are less well neutralized by sera, were derived from "P" virus by passage in eggs in the presence of antiserum, and the converse transformation was brought about by passage of "Q" virus in mice. It seems likely that such variations may also occur in nature under epidemic conditions and that the formation of "Q" type strains may represent an adaptation by virus to permit it to survive in an immune population. In the meantime it is abundantly clear that the laborious collection of epidemiological data undertaken in Geneva is not enough, and that continued laboratory study of outbreaks is essential.

Finally, the virus worker in the influenza field has a new and formidable responsibility. It is a striking fact that all but a handful of influenza-A strains isolated in various parts of the world since 1947 have belonged to the serological grouping of the influenza A-prime viruses. The evidence suggests that the classical A virus represented by the PR8 virus has disappeared. Yet this virus is still used by most laboratory workers for serological work, and there are grounds for belief that contamination of human material under test in eggs with virus already under study in the laboratory is a real danger. Instances of contamination with the WS strain of virus were reported by Andrewes and his colleagues[4] in 1944, and the question is raised whether the few instances of recovery of PR8-like virus reported since 1947 are similarly due to laboratory contamination with the PR8 strain used in the laboratory. Clearly the matter is of much more than academic interest because of its bearing upon the strains of virus used in immunization. Moreover, in the future, laboratory contamination with A-prime virus may well occur and defy detection because mouse adaptation is no longer practised as a routine. All this lays a new burden on the individual worker who may wish to assist in the world-wide study of influenza by recovering strains from human material in his locality: let him beware a fellow-traveller from his own laboratory capable of supplanting the growth of the frail virus present in the specimens collected from his patients.

SURGERY FOR INFANTILE HEMIPLEGIA

Infants rendered hemiplegic by birth trauma or other cause in the early post-natal years frequently present both parents and doctor with a serious problem. While the loss of voluntary power in the limbs of one side may be disabling it is the often associated epilepsy and mental retardation which provide the major obstacle to satisfactory management and treatment, and this is always likely to be so in view of the structural delicacy of nervous tissue and its failure to regenerate. It is none the less encouraging to note recent contributions of neurosurgery both to the prevention of brain damage in early life and to the treatment of established infantile hemiplegia.

Prevention rests on the recognition that abnormal mechanical factors must not be permitted to interfere with the rapid brain growth which occurs in the first few years of life. It has been shown that the birth weight of the brain is doubled at 7 months and trebled at 2½ years. Eighty per cent. of all brain growth is completed in the first three years of life. Premature synostosis of the cranial sutures or the presence of a subdural haematoma can, if overlooked during this period of rapid growth, so interfere with development as to give rise to mental retardation, epilepsy, and possibly other symptoms. The importance of these lesions and their recognition before they have occasioned irreparable cerebral damage have been stressed in a number of papers, including those of Simmons and Peyton[1] and of Ingraham and Matson.[2] The application of this knowledge should certainly save for a normal life a number of infants who would in the past have become mentally defective.

It used to be generally assumed that in an established hemiplegia the scar in the damaged cerebral hemisphere was but a pathological end-result, the original cause of the brain injury having long since ceased to act. It was clear that nothing could restore the function of devitalized neurones, and it seemed equally so that the scarred cerebral hemisphere was not in itself productive of further disturbance of brain function. The occurrence in these cases of severe mental retardation in the presence of a focal lesion of one cerebral hemisphere might, however, have been expected to cast suspicion on this assumption, and the recently published paper of Krynauw[3] suggests that it is in fact unjustifiable. Krynauw was impressed by the electroencephalographic finding that the dysrrhythmia in cases of infantile hemiplegia is not confined to the affected hemisphere, and he believes that the abnormality on the opposite side is the result of the spread of high-voltage discharges to it from the injured hemisphere by commissural pathways. He suggests that this bombardment of the normal cerebral hemisphere with abnormal impulses leads to disturbance of its function, and on the basis of this hypothesis he has performed excision of the pathological hemisphere in 20 cases with but one post-operative fatality.

The results of this operation are of great interest from both practical and neurophysiological view-

[1] *J. Pediat.*, 1947, **31**, 528.
[2] Ibid., 1944, **24**, 1.
[3] *J. Neurol. Neurosurg. Psychiat.*, 1950, **13**, 243.
[4] *Lancet*, 1951, **2**, 411.