INFLUENZA AS A NATIONAL PROBLEM*

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IN the course of this symposium it has become clear that different people use the term 'influenza' with different meanings. The clinician is concerned with a specific form, or with a variety of similar forms, of febrile illness with involvement of the respiratory tract. The laboratory worker is looking for evidence of infection by a specific group of viruses. While each of these two concepts is valid in its own right, it does not necessarily follow that they should coincide. Fig. 1 illustrates this point schematically. If we can imagine an ideal situation, in which a population is under continuous clinical observation and virological investigation for a given period, a certain number of influenza-like illnesses will develop and a certain number of influenza virus infections will be detected. The area of overlap of these two findings, coinciding in time in the same individuals, represents cases of clinical influenza virologically confirmed. The remainder of the field of influenza-like illnesses may be interpreted as composed partly of cases of true influenza, in which laboratory tests fail to reveal evidence of influenza virus infection, and partly of illnesses resembling influenza but due to other causative agents. The field of influenza virus infections will comprise some individuals with no signs of illness and some with illnesses not recognized clinically as influenza. The latter may arise either because the clinician cannot recognize the full range of manifestations of influenza virus infection or because influenza virus infection is a coincidental finding in an illness due to other causes.

To complete this schematic presentation it is necessary to introduce a third, and rather more difficult, concept, that of 'epidemic illness'. This concept lacks the precision of the clinical or virological diagnosis, but is nevertheless real. Its importance lies in the fact that outbreaks of disease in a community often present in an ill-defined way before their clinical pattern or aetiological associations can be elucidated. In the early part of March 1963 the Medical Officer of Health (Grant, 1963) of a large County Borough wrote as follows:

FIG. 1

FIG. 2

'... among a great deal of vague upper respiratory infection, genuine influenza seems to be present in this town. Practitioners describe the illness as being of rapid onset with severe headache, dry throat, aching limbs and fever. The attack appears to be very sharp and the patients are very ill for about 48 hours. . . . There is also a considerable amount of so-called gastric "flu" characterized by sickness and severe diarrhoea and it appears to be difficult to separate this from the other condition; some patients have one condition but others appear to have symptoms of both. Parents and children are affected by both conditions

This is the kind of complex situation which presents itself not infrequently in public health practice. There is an outbreak of 'genuine' influenza and associated with it, superficially forming a part of the epidemic, illnesses occur which neither clinician nor virologist would accept as falling within their own definition of that term.

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FIG. 3.—January to March 1959: Weekly deaths assigned to influenza and to other causes.

Fig. 2 shows epidemic illnesses, in this broad sense, superimposed on the clinical and virological findings in our ideal population. This schematic presentation indicates four different possibilities: (1) Illnesses not associated with evidence of influenza, (2) illnesses regarded clinically as influenza without evidence of influenza virus infection, (3) illnesses associated with evidence of influenza virus infection but not accepted clinically as influenza, and (4) epidemic influenza clinically and virologically confirmed. In an actual population in real life a complete breakdown into these four components is impossible, since virological investigations can be undertaken only in a small proportion of cases. Moreover, these form a highly selected sample in which, on clinical grounds, there is usually strong presumptive evidence in favour of influenza virus infection.

In order to unravel this complex epidemiological picture it would seem logical to start from the most precise of our concepts, that of influenza virus infection, and to examine the effects which this can produce in the community. Table 1 shows morbidity and mortality statistics for England and Wales in the first quarter of each of

the years 1957 to 1963 inclusive and for the three months September to November 1957, which covered the main wave of the epidemic of Asian influenza. New claims for sickness benefit shown in the table are totals of weekly new claims, recorded by the Ministry of Pensions and National Insurance, for the 13 consecutive weeks most closely corresponding with the three-monthly periods. The mortality statistics are derived from those published by the General Register Office. During the first quarter of 1957 and 1960 laboratories throughout the country reported little evidence of influenza virus infection. Influenza virus A2 (the Asian variant) was prevalent in the first quarters of 1958, 1959, 1961 and 1963 and influenza virus B in the first quarters of 1959 and 1962.

The morbidity and mortality statistics for the first quarters of 1957 and 1960 establish a rough and ready base line for this time of year in the absence of evidence of widespread dissemination of influenza virus. Deaths assigned to influenza were in the 300 to 600 range, total deaths fewer than 150,000 and new claims to sickness benefit of the order of 2 million. During periods of

TABLE I
COMPARATIVE STATISTICS—ENGLAND AND WALES, 1957-63

Year	Period	New Claims to Sickness Benefit (Thousands)	Deaths From All Causes	Influenza Deaths	Virus Prevalent
1957 ..	January-March	1,948	134,557	357	—
1957 ..	September-November	3,596	133,400	5,449	A2
1958 ..	January-March	2,433	163,595	1,891	A2
1959 ..	" "	3,064	176,880	6,902	A2 and B
1960 ..	" "	2,254	149,037	508	—
1961 ..	" "	2,915	177,043	6,410	A2
1962 ..	" "	2,896	178,204	2,858	B
1963 ..	" "	3,042	196,913*	2,411*	A2

* Provisional figures.

Note.—The deaths shown for 1957 have been classified by month of occurrence, those for subsequent periods by month of registration.

FIG. 4.—January to March 1963. Weekly statistics—London area.

influenza virus prevalence deaths assigned to influenza were numbered in thousands, total deaths in the first quarter exceeded 150,000 by amounts which ranged from about 13,000 to about 47,000 and new claims to sickness benefit were generally about 3 million. From September to November 1957 new claims to sickness benefit exceeded 3½ million. The total mortality during this autumn epidemic was relatively low, though markedly higher than is usual at that season of the year, while the number of deaths assigned to influenza approximated to that experienced in the worst of the succeeding winter epidemics.

It would seem reasonable to conclude that a substantial proportion of excess deaths not assigned to influenza were, in fact, attributable to influenza virus infection and that much of

the increase in morbidity shown by new claims to sickness benefit proceeded from the same cause. This conclusion is strengthened when trends in weekly figures are compared. Fig. 3 shows weekly influenza deaths and deaths assigned to all causes other than influenza for the first 12 weeks of 1959. The steep rise and fall in influenza deaths is paralleled by a similar rise and fall in deaths due to other causes. Fig. 4 shows weekly new claims in the Ministry of Pensions and National Insurance Inner London Region and influenza deaths in the administrative county of London for the first 13 weeks of 1963. The steep rise in new claims which began in the fourth week was closely followed by a steep rise in influenza deaths. Fig. 4 also shows for the same period weekly admissions to hospital through the

FIG. 5.—E.B.S. London: Weekly hospital admissions—pneumonia and bronchopneumonia.

Emergency Bed Service for London. Bed Bureau statistics or ambulance returns of hospital admissions are useful indices of epidemic influenza because of the speed with which the information can be made available.

Fig. 5, which has been reproduced from the Chief Medical Officer's Annual Report for 1958, shows weekly hospital admissions for pneumonia and bronchopneumonia through the Emergency Bed Service for London from the week ended August 24, 1957, to the week ended March 22, 1958. The graph is of particular interest in that it shows the complex nature of the epidemic situation in that autumn and winter. The first peak of admissions, which corresponded to the main wave of Asian influenza, is remarkable for the high proportion of patients in the 15- to 44-year age-group and for the small, but significant, rise in the 5- to 14-year age-group. Rises of this order are quite exceptional in either of these age-groups. The second peak shows the usual age structure of the winter epidemic period with a preponderance among the old and the very young. The third peak is confined solely to the 0- to 4-year age-group. This corresponded with an epidemic of bronchiolitis among infants at a time

when the incidence of respiratory diseases in all other age-groups was on the decline.

The impact of the 1957 epidemic of Asian influenza on the working population of Great Britain is illustrated in Fig. 6, reproduced from the Chief Medical Officer's Annual Report for 1957. The figure shows new claims to sickness benefit from the week ended 9th July to the week ended December 17. Fig. 7, reproduced from the same Report shows provisional notifications of pneumonia and deaths from pneumonia and influenza from the week ended August 24 to the week ended December 28.

When considering the measures which might be advocated to control epidemic influenza and to mitigate its effects vaccination would appear to offer the most promising line of attack. A report, published in 1959, by the World Health Organization's Expert Committee on Respiratory Virus Diseases included the following statement on influenza vaccine:

"The application of vaccination as a public-health measure for selected groups is now a practicable proposition. In general vaccine prepared from strains of one family of viruses gives reasonable protection against other members of the same sub-groups. Major anti-

FIG. 6.—Registrar-General's weekly returns—160 great towns.

genic shifts of the influenza virus while unpredictable seem to have occurred at intervals of 10 to 15 years in the past. It is, therefore, probable that for several consecutive years at least, vaccine can be made which will give significant protection against the strains causing epidemics in the next influenza season'.

As regards Great Britain the Joint Committee on Poliomyelitis Vaccine, under the chairmanship of Lord Cohen of Birkenhead, appointed in 1961 a sub-committee to consider whether advice should be issued to the medical profession on the best use of the influenza vaccines generally available. The sub-committee recommended an inactivated influenza A and B saline vaccine for use in specified circumstances. The Joint Committee on Poliomyelitis Vaccine endorsed this recommendation which has since been incorporated in the booklet on Active Immunization against Infectious Disease prepared by the Standing Medical Advisory Committee.

The sub-committee's view was that routine use of influenza vaccine cannot be expected to

make a significant contribution to the control of outbreaks of influenza but may be indicated for the protection of persons suffering from certain chronic diseases in whom an attack of influenza might aggravate their disability or prove fatal. For instance, those with any of the following complaints might benefit from annual inoculation with a saline vaccine during the early part of the autumn:

Chronic pulmonary disease, e.g. chronic bronchitis and emphysema, asthma, bronchiectasis, pulmonary tuberculosis and fibrosis.

Chronic heart disease, e.g. valvular and hypertensive heart disease.

Chronic renal disease, e.g. chronic nephritis
Diabetes and, possibly, other less common endocrine disorders, such as Addison's disease.

This list is not intended to be exhaustive and anyone who wishes to be vaccinated against influenza should discuss the matter with his family doctor and be guided by him on its desirability.

FIG. 7.—New claims to sickness benefit, Ministry of Pensions and National Insurance. Weekly totals for Great Britain (including Scotland).

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Discussion

A QUESTIONER asked about influenza-spotting trials so that the surrounding area could be warned of a small wave of influenza arising.

DR. RODEN said that there had been two influenza-spotting schemes: (1) Where the general practitioner notified the medical officer of health of his district that influenza was appearing, and (2) The special spotting scheme of the Public Health Laboratory Service in connection with influenza vaccine trials.

THE QUESTIONER referred to an influenza-spotting scheme in the county of Lancashire which was run by the University of Manchester and the medical officer of health. He thought the grouping at present was too small. The idea was that the surrounding area of Lancashire should be warned of coming disease and suggested that the scheme might be carried further.

DR. RODEN said that was an interesting idea, though such a warning would probably come too late.

DR. FLEWETT, referring to Dr. Roden's paper, asked whether with the increased load on hospital beds and the extra load of work on the staffs which people had mentioned earlier in the programme there was anything we could do to minimize this load by a programme of vaccinating chronic bronchitic patients and hospital staff against influenza; would this be likely to achieve any significant reduction?

DR. HEARN said this was most important if it could be done.

DR. RODEN said that influenza vaccination had shown some effect against influenza but was effective against influenza virus infections only. A really scientific approach had been made to this by the Medical Research Council's Committee on Influenza and Other Respiratory Virus Vaccines. The most effective antigen was one put up as a water and oil emulsion. A living attenuated vaccine had been tried upon a small scale but its value could not yet be fully assessed. For any vaccine one must ask, first, does it prevent the spread of influenza; secondly, does it prevent people from falling sick; and thirdly, does it prevent people already with damaged lungs from dying when they catch influenza. In between pandemics one should use vaccine for the individual case specially at risk, especially those with chronic chest disorders. The vaccine was probably ineffective in preventing spread in the community. It was doubtful whether one could expect great things from vaccinating the public at large.

DR. BEALE said that his job was making influenza vaccines effective in preventing disease. There was concrete evidence that the vaccine was capable of stimulating antibodies. Two doses of vaccine were

better than one. Clearly for a vaccine to be acceptable for general industrial use, for example, it must be reasonably free from side-effects. The oil and water emulsion vaccine now available gave much less in the way of reactions. The problem of the manufacturer came in selecting the right strain to put in the vaccine and for this they were dependent on the World Influenza Centre to provide them with strains of the most recent isolations of those which were liable to turn. His information so far was that the Japanese strain at present causing influenza was similar to the A/Eng. 68 strains. About the B strains there was this new variant of influenza B virus in Taiwan which had been reported, but nothing so far was known about whether it was going to spread or what was happening.

The Chairman, DR. KER, asked Professor Stuart-Harris if he would like to sum up.

PROFESSOR STUART-HARRIS said that we had forgotten our uninvited friend the influenza virus who was sitting on the ceiling at the back of the hall and who had been laughing all day yesterday and today until the last five minutes of Dr. Roden's paper this morning. It was quite clear from what all the speakers said that we were utterly incapable of dealing with its activities. The person who suffered most was the person who for years had been afflicted with chronic respiratory disease. Yesterday we were dealing with the end-product of the influenza virus attack. Today he had been struck by the number of speakers admitting their inability to predict the appearance of influenza; whether or not the weather mattered we did not seem to have any real evidence. Studies by a worker in his own laboratory had shown that respiratory disease behaved in much the same way in Trinidad where the climatic conditions were certainly very different. There certainly was no easy solution to our problems when an epidemic occurred. Nowadays the Ministry of Health had the most rapid information about the progress of an influenza epidemic. It was, however, desirable to bring the general practitioners into the picture and devise a system so that the Ministry and general practitioners could work more closely together. He referred to the suggestion that the appearance of bronchiolitis in babies might be used to predict an ensuing influenzal epidemic and suggested that Dr. Flewett might like to look into the possible connection between the two. It was quite clear that work on influenza had by no means ended. We needed some quick and efficient method of controlling it; a live attenuated vaccine was undergoing trial at present.

DR. HEARN proposed a vote of thanks to the organizers of the symposium and to all the speakers.

reviewed and the incidence of neuropsychiatric manifestations is assessed. Attention is drawn to the occurrence of focal neurological signs in a small proportion of such patients in the absence of localized pathological changes in the brain. The difficulty of excluding a treatable lesion when the patient is in hepatic failure is stressed, and it is

suggested that, if recovery from the acute illness occurs and the neurological signs persist, detailed investigation is warranted.

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ERRATUM

'Influenza as a National Problem', A. T. Roden, October 1963. It is regretted that in this article Fig. 1 and Fig. 2 were transposed, and the caption to Fig. 6 applied to Fig. 7 and vice versa.