SESSION I

EPIDEMIOLOGY OF HONG KONG INFLUENZA

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Origin and Progress of the 1968–69 Hong Kong Influenza Epidemic [1]

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The Hong Kong strain of influenza virus A2 may have originated in the mainland of China but this is not certain. It caused a very large epidemic in Hong Kong and spread rapidly to countries as far as India and the Northern Territory of Australia—as happened in the 1957 epidemic. Later its progress slowed down but epidemics occurred in many countries in the northern hemisphere in the winter of 1968–69. In all these countries except the United States of America the disease was mild and not associated with a large increase of deaths. In the United States of America, however, the number of "excess deaths" was similar to the number in 1957–58.

In the southern hemisphere epidemics began in May–June 1969; they have been clinically mild and the reported incidence of disease has been only moderately high.

In many countries the infection has spread slowly and smouldered instead of bursting into the usual sharp epidemics.

The smouldering spread and the contrast in the behaviour of the disease in the USA compared with the rest of the world are the outstanding features of the Hong Kong strain of virus. Satisfactory explanations of these observations might lead to the development of more effective means of control of influenza.

The World Health Organization's information on influenza is obtained through its influenza programme which was established in 1947. The working of this programme has been described frequently (see, for example, Payne, 1954; WHO Scientific Group on Respiratory Viruses, 1969) and here it is only necessary to remind the Conference that its main objective is to obtain as rapidly as possible strains from cases or outbreaks in any part of the world so that these strains can be examined quickly to determine their characteristics and their similarity or otherwise to previously identified strains.

Unquestionably this is the most important contribution that WHO can make in helping national health services to obtain early and accurate information on the behaviour of the viruses and thus enable them to develop and apply measures for dealing with the disease. The second objective of the programme is to collect and distribute as much epidemiological information as it is possible to obtain from national authorities.

Collaborating in the programme are 85 national influenza laboratories in 55 countries which are in contact with the organization in Geneva and with the 2 international centres—the World Influenza Centre, London, and the International Influenza Center for the Americas, Atlanta. In Geneva all the laboratory and epidemiological information is consolidated and published weekly in the WHO *Weekly Epidemiological Record*, which is widely distributed to health authorities, influenza centres and to other interested institutions and persons, and which is available to all on subscription.

In 1968, our first intimation of a possible new epidemic strain of influenza virus was a report in *The Times* of London for 12 July that a widespread outbreak of acute respiratory disease was occurring in south-eastern China. Five days later the health authorities in Hong Kong and Dr Chang, Director of the Influenza Centre there, reported a sudden increase in influenza-like illness and, most important, the isolation of viruses which by preliminary tests appeared to be similar to influenza virus A2. The strains were despatched as infected tissue-culture fluids on wet ice to the World Influenza Centre,

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where strain-specific sera were prepared in ferrets, and by this means it was determined that the antigenic pattern of the Hong Kong strain differed markedly from previous strains of virus A2. Similar findings were obtained in the International Influenza Center for the Americas to which Dr Chang had also sent specimens.

ORIGIN OF THE EPIDEMIC

We are dependent on a single newspaper report that the outbreak in Hong Kong was immediately preceded by an epidemic of acute respiratory disease in south-eastern China. There is no information on the etiology of this outbreak in China but its close temporal relationship to subsequent events makes it possible that it was due to the Hong Kong strain. It will have escaped none of the members of the Conference that the 1957 pandemic first came to light in southern China, and the experience in 1968, though very tenuous, adds a little more information to the often-expressed hypothesis that strains of influenza virus which have the capacity to spread widely and rapidly often arise in that part of the world. Unfortunately contact between health authorities in China and other countries is even more difficult than in 1957 and it is impossible to obtain information on the possible origin or behaviour of the epidemic prior to its appearance in Hong Kong. However, it is known that in Hong Kong about half a million cases occurred by the end of July.

By mid-August quantities of virus were prepared at the 2 international centres and were made available to research and vaccine production laboratories wishing to have them. The national influenza centres were informed of the emergence of the strain and of the possibility of widespread epidemics.

SUBSEQUENT PROGRESS

The subsequent spread of infection is of considerable interest. At first it resembled closely that of the 1957 pandemic. At the beginning of August, a large outbreak was observed in Singapore. Later the same month, epidemics occurred in the Philippines, Taiwan and the Republic of Viet-Nam, and localized outbreaks in Malaysia. In September, epidemics were reported in Thailand, India (Madras and Bombay), the Northern Territory of Australia and in Iran, where the well-authenticated outbreak among the participants at the Congresses of Tropical Medicine and Malaria in Teheran took place (Saenz, Assaad & Cockburn, 1969).

Up to this point the speed and pattern of spread were sufficiently similar to the 1957 experience to make it a reasonable prediction that extensive epidemics would occur in the rest of the world in due course. However, there were differences which should perhaps have received more attention than they did. One was the behaviour in Japan, where the disease failed to spread in August and September in spite of numerous introductions of virus by sea travellers. Later in the year, in the autumn, many separate foci developed, often in schools, but coalescence into a general epidemic (which was only of moderate extent) was delayed until mid-January.

Other differences from the 1957 experience were soon apparent. Between the end of September and the end of the year very little evidence of spread in new areas was reported despite the occurrence of small foci in these areas associated with importation of infection from countries in which epidemics were present.

This, however, was not the case in the United States of America. Here the first apparently indigenous outbreak occurred at about the end of October, in California. Infection spread rapidly in November in a roughly West–East direction and by Christmas outbreaks had been reported from nearly all the States. The epidemic was extensive and the peak occurred at about the end of the year. It was associated with a great increase in deaths from pneumonia–influenza in each of the administrative divisions. The peak of deaths was recorded about 2 weeks after the peak of the epidemic. On the basis of excess deaths (i.e., the number of deaths above the average for the same weeks in previous years), the epidemic was as severe as that of 1957–58 when the original A2 virus was prevalent.

This experience of widespread infection associated with a high level of excess mortality was unique. It did not occur in other temperate-climate countries in the Americas. Canada, for example, experienced a relatively slight increase in incidence of disease and practically no excess deaths.

In Europe, the rise in incidence began later than in the United States of America and continued into April. Nearly all the European countries reported outbreaks but these were of variable extent. The largest was in Poland (onset mid-January), where it was estimated that 3–4 million cases of influenza-like disease occurred.

Generalized epidemics were also reported from Bulgaria, Czechoslovakia, parts of the Federal Republic of Germany, Finland, Hungary, Iceland, the Nether-

lands, Sweden and parts of the USSR. In all these countries, however, the disease was reported to be mild and no great excess of deaths was observed. In the other European countries the presence of infection made little difference to death rates and, compared with other epidemics, had a relatively slight influence on sickness-absence. This was well shown in the United Kingdom, where the Public Health Laboratory Service provides readily available virus diagnostic facilities over the whole country, and where there was evidence that infection was frequent and widespread but not clinically severe. Other European countries also reported that the disease caused predominantly focal outbreaks or spread relatively slowly instead of in the usual clearly recognizable explosive pattern. In the temperate countries of the northern hemisphere, outbreaks ceased by the end of April.

Some tropical countries not affected during the first wave became involved by the end of 1968 or early in 1969. Outbreaks were recorded in Kenya and epidemics in Brazil and Ceylon. Indonesia obtained serological evidence of infection.

In the southern hemisphere, no large outbreaks were reported in 1968. In 1969, epidemics began about mid-March in South Africa and since mid-May outbreaks have been reported from Argentina, Australia, Chile, New Zealand, and Uruguay. They have been uniformly mild.

DISCUSSION

Though, therefore, the virus has been spread widely through the world, many of the countries in which it was detected did not experience typical large epidemics, and in many of those in which epidemics did occur, their influence on absence from work and on death rates was slight or absent. The United States of America was the exception to the general rule, and the difference there is one of the most striking features of the epidemiological behaviour of the Hong Kong strain. Such differences have rarely been reported in the past. Perhaps the last occasion on which something similar was observed was in the United Kingdom in 1950–51 (Massey, 1951; Semple, 1951). There an epidemic due to the A1 strain commenced in the last days of 1950 and by mid-February was subsiding. It was first observed in Scotland and north-eastern England, then in north-western England and the London area and thereafter spread rapidly to the rest of the country. In all regions except the north-west it behaved in much the same way as other epidemics of the period, but in the north-west and particularly in Liverpool and adjoining districts of Merseyside, the number of deaths from acute respiratory disease was unusually high. In Liverpool in the second week of January almost 900 deaths were recorded, compared with a pre-epidemic weekly level of 250–300. By the fourth week in January the number had returned to normal. In the United Kingdom in 1950–51, 2 strains of virus A1 were spreading more or less at the same time (Andrewes, 1954). One was the " Scandinavian " strain, which was responsible for outbreaks in northern Europe in the autumn and which was isolated in the outbreaks in Scotland, north-eastern England, in some other parts of England and in the Republic of Ireland. In north-western England, however, the outbreaks were associated with the " Liverpool " strain. At first sight the strain difference might be considered the explanation of the different death rates. But the Liverpool strain was also prevalent in Belfast and in some parts of southern England and in a number of countries in southern Europe and in Turkey and countries to the south of it. Six months earlier it had been isolated in outbreaks in the southern hemisphere. In none of these areas except Merseyside was it associated with an unexpectedly high death rate.

It would seem that some additional factor must have been operative in Merseyside. Semple (1951) pointed out that immediately before and during the epidemic period Merseyside experienced the coldest spell for many years, the weekly mean temperature from mid-December to mid-January being 4.4°F to 7.5°F (2.5°C to 3.6°C) below the mean temperatures for the corresponding weeks in the previous 20 years. Over two-thirds of the deaths were in persons, mainly women, 65 years of age or more and most of these deaths were in persons over 75 years of age.

As long ago as 1885 Farr showed from statistics of deaths in England and Wales that " the degree down to which mean monthly temperatures fall in December, January, or February determines, to a great extent, the mortality of winter ", even when epidemics of influenza are absent. He went on to suggest minimum night temperatures for the bedrooms of the very old and very young.

In 1950–51, therefore, 2 explanations of the abnormally high death rate in Merseyside were possible: a more virulent strain, or an exceptional climatic condition occurring as the epidemic developed. Perhaps there were also other factors which were not identified.

What was the important factor in the epidemic of Hong Kong influenza in the United States of America last winter? Its identification might go far to improving our knowledge of the behaviour of influenza and might lead to the development of more effective means of preventing influenza deaths if not of preventing the disease.

EFFICACY OF THE WHO PROGRAMME

The main purpose of this presentation has been to describe in general outline the origin and progress of the epidemic.

In conclusion we should, however, like to mention again the WHO influenza programme. So far as the isolation and characterization of the virus were concerned, the programme fulfilled its objective and thanks to the efforts of the national reference centre in Hong Kong and the 2 international centres, the strain was isolated, identified and distributed to vaccine producers with all possible speed. It is difficult to imagine circumstances in which the interval from arrival of specimens in a national influenza centre to the characterization and distribution of the strain could be shortened. Contact between the national influenza centres on the one hand and the international reference centres and WHO in Geneva on the other hand is improving each year. The number of national centres has increased from 59 in 43 countries in 1962 to 85 in 55 countries in 1969. However, there are still large areas, especially in Africa, where no centres exist.

In contrast to the precise information obtained about the viruses, the quantity and quality of the epidemiological information is variable. This is partly because different countries use different methods of assessment.

In the United States of America much emphasis is placed on excess deaths from pneumonia and influenza; the United Kingdom relies mainly on claims for sickness-absence made to the Ministry of National Insurance, on increased demands by doctors for urgent admission of their patients to hospitals, and on reports of the occurrence of influenza-like disease received from members of the Royal College of General Practitioners; in Czechoslovakia information from serological surveys and clinical data from a variety of sources is collected and analysed regularly throughout the winter.

These are examples of different approaches in 3 countries in which ascertainment is practised fairly intensively. There are many countries in which the occurrence of influenza-like disease receives much less attention—which is scarcely surprising when the other important health problems which face them are taken into account.

In the past year we have introduced a scheme by which national influenza laboratories provide us with regular information on a special form. The scheme has been taken into use by most of the national centres and is beginning to work smoothly. But the separation between laboratory and epidemiological services in so many countries still hampers the free flow of information nationally and internationally.

The current interest in epidemiological surveillance and the resolution adopted by the 22nd World Health Assembly on the importance of developing national and international surveillance for specified diseases provides us with an opportunity to establish simple methods of obtaining from as many countries as possible reliable information on which valid comparisons can be made. We have already begun the pursuit of this objective.

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