Epidemiological research on the phenomenon
of the influenza herald wave

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Among the many kinds of respiratory infectious diseases caused by viruses, influenza is thought to be one of the most important factors affecting human social life. Since 1980, we have continued surveillance on influenza epidemiology among children in part of a thickly inhabited area of Tokyo Metropolis, around Kamata in Ota Ward. Influenza epidemics occurred every winter in this surveillance period all over Japan including around Kamata. In those epidemics, type A (H1N1), A (H3N2) and B influenza viruses were involved either as a single causative agent, or two or three of them cocirculated in a single epidemic. During the past eight years, we observed the so-called influenza herald waves¹⁻³ several times. These were detected as small epidemics or sporadic infections after the main epidemics around Kamata. The influenza herald wave is considered to be an indicator of what the prevailing influenza virus in the next epidemic season will be.

The materials examined in this study were collected from out-patients who visited the pediatric clinic of the Social Insurance Associations Kamata General Hospital. Virus isolation and identification were carried out by the methods described previously⁴. The sole exception was that the nasopharyngeal swabs were inoculated into monolayer cultures of primary cynomolgus monkey kidney cells and/or Madin-Darby Canine Kidney (MDCK) cells. Patients' acute and convalescent sera were examined for the HI antibody titers with the micromethod after RDE-treatment. As antigens for HI test, both prototype strains of currently circulated viruses, inside Japan or outside when an epidemic of Kamata occurred, and one of the isolated strains in the epidemic were used.

Case numbers of influenza detected in this surveillance are shown in Fig. 1. In the winter of 1979/80, an influenza epidemic caused by three types of A (H1N1), A (H3N2) and B virus broke out at the end of February, 1980 and continued until April of the same year, and each type of virus disappeared from the surveillance population almost simultaneously.

In the winter of 1980/81, an influenza outbreak occurred at the beginning of February, 1981, when both A type viruses were isolated but B type virus infections were identified only by a serological test. Epidemics caused by both A type viruses almost ceased in mid-March. However, type B virus was isolated first from a patient in March, and the virus prevailed and then
Fig. 1 Number of influenza cases detected by the surveillance in Kamata

The number of cases is the total of those in virus isolation and/or increase of HI antibody titers (more than fourfold).
smoldered on until the end of April. In the next winter of 1981/82, a big influenza epidemic of type B virus broke out in mid-January and continued to the beginning of March. Therefore, the circulation of type B virus during March through April, 1981 is regarded as a herald wave of the epidemic of the same type during the months from January to March, 1982.

A small outbreak of type A (H3N2) virus infection occurred in mid-February, 1982 in mid course of a type B virus prevalence, and A (H3N2) virus remained to circulate in the area until April after the type B epidemic ceased. In the next winter of 1982/83, a big A (H3N2) influenza epidemic broke out. In this case too, a herald wave of A (H3N2) virus was observed in late winter, 1982.

In the winter of 1982/83, we had a big A (H3N2) type epidemic from January to March, but could not isolate any virus strain of the other types of A (H3N2) during and after this epidemic, except for a few seroconversion cases of A (H1N1) infection during the epidemic. Therefore, in the period between the winter of 1982/83 to 1983/84, we could not observe clear evidence of the herald wave among the subject population.

The influenza epidemic from November, 1983 to February, 1984, was caused almost exclusively by A (H1N1) type, but after the epidemic, in June, one type B influenza virus strain was isolated from a patient of the subject area, and in the next winter, 1984/85, a big type B influenza virus epidemic was observed. This might well have been a typical herald wave, because it was observed in June when acute respiratory illness is not common, though the number of the virus isolates was only one.

After the type B virus epidemic prevailed from January to April, 1985, one virus strain of type A (H3N2) was isolated in mid-July, 1985, and at the beginning of November, 1985, a type A (H3N2) influenza epidemic broke out, flourished during the year and disappeared at the beginning of 1986. Thus, a herald wave of A (H3N2) was clearly observed as in June, 1984.

From April to July, 1986, an unambiguous outbreak of type A (H1N1) influenza occurred around Kamata, and in the following winter from December, 1986 to March, 1987 we observed an A (H1N1) type influenza epidemic in the same subject area. This is a very definite case of the herald wave.

During our surveillance period including eight successive influenza seasons, we observed up to five times the phenomenon of the influenza herald wave as described above. In these five herald waves, three were clearly observed, while two were somewhat obscure as only one virus strain was isolated in each. However, if we had collected more specimens, we would have been able to isolate more virus strains. The pattern of influenza epidemics all over Japan from 1980 to 87 closely resembles what was observed in our surveillance around Kamata. Presumably, the phenomenon of the influenza herald wave must be observed in other areas of Japan, as well.

It is rational to confirm whether or not the virus in the herald wave was an ascendant of that in the following major epidemic in the successive winter. In our previous study of antigenic analysis of virus isolates using monoclonal antibodies and of whole viral RNA oligonucleotide mapping, we were unable to obtain a clear substantial conclusion to this problem.

There exist several hypotheses about the ecology of influenza virus especially concerning the survival of the virus in interepidemic seasons. For example, the virus of the herald wave will be transported to and circulate in the other Hemisphere, where winter and summer are in reverse, or
in the Tropical zones, and it is reintroduced into the original Hemisphere at the beginning of the next epidemic season\(^8\). However, another possibility may not be excluded, which is that the influenza virus hides itself in a certain unknown condition in the original area during the off-season, and at the beginning of the next favourable season, a reactivated virus causes a major epidemic\(^9\). The results of our survey favor the latter possibility, because the herald waves were clearly observed in the small area of Kamata.

The phenomenon of the influenza herald wave — At the latter half of or after a main epidemic period, a small wave of influenza will be caused by such viruses as (1) other types than the main epidemic virus, (2) antigenically drifting from the main epidemic virus, or (3) one of the types which remains and smolders on, providing two or three types are included in a main epidemic. The virus included in the wave will herald the type or antigenic character of the next epidemic virus. — has been confirmed in different areas and at different times, including this report of ours, and can be regarded as a milestone of influenza virus ecology.

References


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