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SUMMARY REPORT ON THE ASIAN INFLUENZA EPIDEMIC IN JAPAN, 1957

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SYNOPSIS

The epidemic of Asian influenza began in Japan in May 1957, reaching a peak towards the end of June, subsiding, and showing a second, equally serious, wave in November-December. The method and place or places of its introduction into the country are not clear, but the important role of schoolchildren in its spread seems well established. While the average attack-rate for the country as a whole was some 26% in the first epidemic wave, it was as high as 50%-60% in concentrated communities such as schools and military camps. The severity of the illness was not very great in the population as a whole, but the death-rates among infants and the aged were remarkably high. The main causes of death were acute pneumonia and cardiac insufficiency. Vaccination of the general population was not carried out on a wide scale.

Course of the Epidemic

In Japan, an influenza epidemic prevailed in the winter of 1956-57. This epidemic was found to be due to the viruses of both A (A/Netherlands/56 type, according to Dr. A. Isaacs) and B types. In the Tokyo area the number of schools affected by the A-type virus was not very different from that of the schools affected by the B-type virus, as far as can be estimated from the results of virus isolations and serological diagnoses ; There were also some schools where cases due to A and B viruses were found at the same time in one and the same outbreak. The epidemic, which had started at about the end of November 1956, had almost subsided by the end of the year in the Tokyo area, but seems to have lasted until March 1957 in some of the rural areas. There were no reported outbreaks of influenza thereafter, and consequently no further trouble due to influenza was expected until the next winter. Suddenly, however, at about the end of May 1957, reports of influenza outbreaks again started to come in, first from the larger cities and then from various other places including rural areas. At the end of May we isolated several strains of influenza virus from cases in a school in Tokyo, which were identified as the A type by complement-fixation with soluble antigen, but had no common antigen

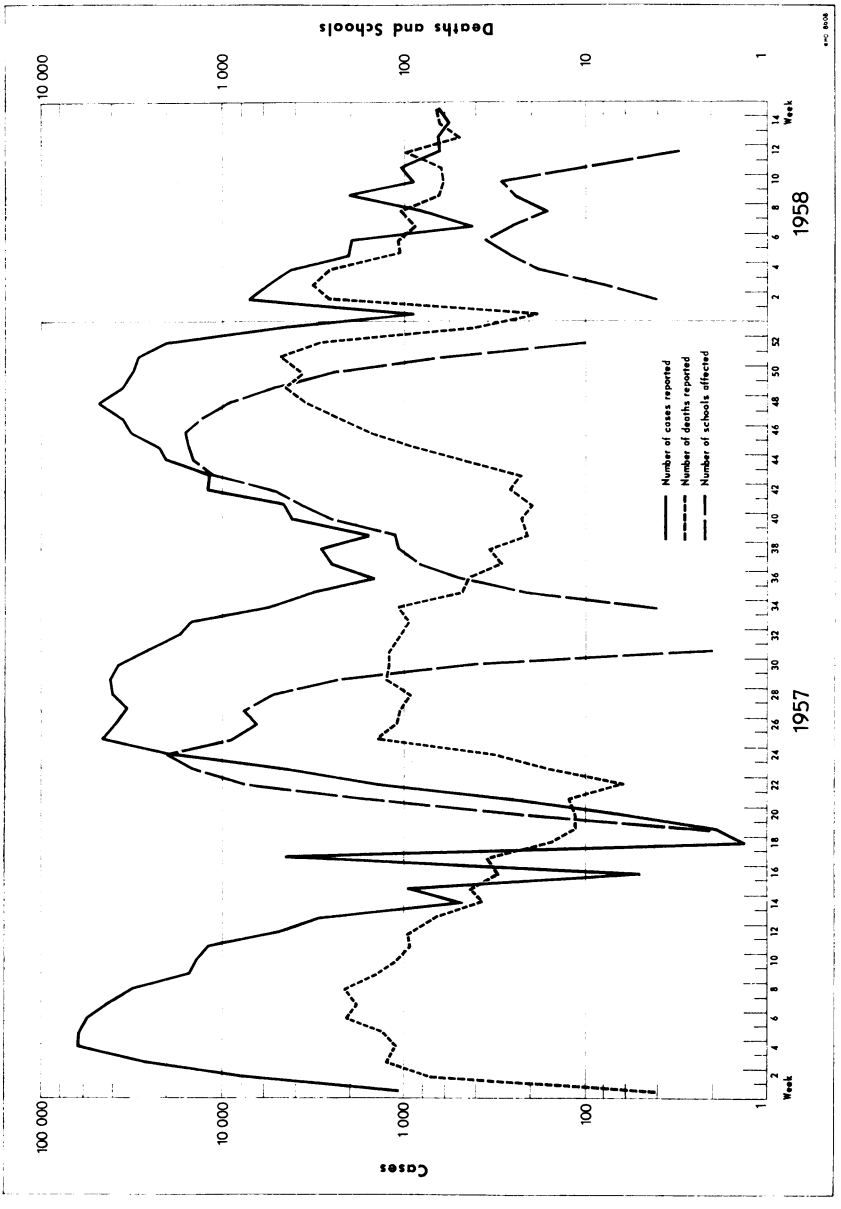
with any of the old A-type viruses in the haemagglutination-inhibition reaction. At about the same period, we received information, through newspapers from the United States of America, that a new type of influenza virus had been isolated from cases among the naval personnel in Hong Kong, and a little later formal information from the World Influenza Centre that viruses having the same characteristics had been isolated in Singapore.

There were two epidemic peaks of infections due to A/Asia/57 virus in 1957 in Japan, and one more small peak in the early part of the year 1958, which might rather be considered a protraction of the second wave. Fig. 1 shows the number of cases and deaths due to influenza reported to the authorities, according to the data at the Bureau of Statistics in Japan, and the number of schools involved in the epidemic, according to the reports to the rural authorities, which do not include the epidemic in early 1957, caused by both the old A-type and the B-type viruses. The two distinct waves of influenza after the eighteenth week in 1957 and a small recurrence in early 1958 are clearly seen from this figure. As already mentioned, the first peak of the curves of cases and deaths, which occurred in the fourth to sixth week, reflects the epidemic due to the old type A and B viruses. Attention must be drawn here to the fact that these dates are not those on which the cases had fallen ill but on which the reports were made, while the dates referring to the schools are those of the onset of the outbreaks in the schools. It is reckoned that, on the average, cases were reported about a week or ten days after their onset. Even if this delay is taken into consideration, the waves shown by the number of affected schools run a little ahead of those shown by the number of reported cases. This might, in part, be an indication that schoolchildren play an important role in spreading influenza by conveying the infection from their school to their families. In addition, it must be kept in mind in explaining the epidemic waves that in Japan the schools are generally closed for the summer and winter vacations from the latter part of July to the early part of September and during the period from the last week of the year to the first week of the next year.

It is quite clear that A/Asia/57 virus was introduced into Japan from one or several other countries, because, according to information received from the World Health Organization, several places in Asia (Hong Kong, Singapore, Taiwan, etc.) had already been affected in April 1957, while the epidemic first started in Japan at the beginning of May. From analysis of the dates of onset of the outbreaks in schools—the first being reported in a Tokyo school on 10 May—it is evident that the epidemic started first in large cities and then spread to the smaller cities and rural areas.

It is not clear from what outside country or countries the virus was imported for the first time in Japan, to what city or cities it was introduced, or in what way or ways its introduction occurred, but the possibilities are numerous. There must have been many chances of virus introduction

FIG. 1. INFLUENZA CASES AND DEATHS REPORTED AND SCHOOLS AFFECTED IN ASIAN INFLUENZA EPIDEMIC IN JAPAN, 1957*



* A Asia 57 influenza virus is not incriminated in the peaks of cases and deaths shown during the first weeks of 1957.

by patients arriving by air or sea from places already involved in the epidemic. It is possible that the virus was introduced many times from outside and that the epidemic in Japan started as a multicentric outbreak. There are also many reports indicating that educational trips of school-children played an important role in transporting the virus from area to area within the country.

Attack-Rates

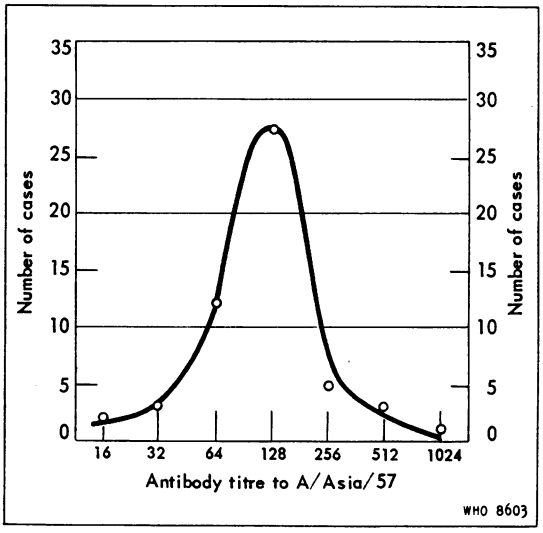
In order to determine the attack-rates in different areas, populations, and age-groups, questionnaires were distributed to the workers in the health centres of each prefecture and to the members of their households at the end of the first wave of Asian influenza, asking whether or not they had suffered from the disease. From the answers to these questionnaires, it was apparent that there was considerable variation in attack-rates between the prefectures; the average value was 26.4% with a range of from 11.4% to 35.0%.

It is well known that the data from questionnaires are seldom quite accurate, at least as far as influenza is concerned, because there are many diseases whose symptoms are sometimes fairly difficult to differentiate from those of influenza, and during influenza epidemics, the figures for reported influenza cases sometimes include cases due to such other diseases. For example, we found that about 40% of those clinically diagnosed as influenza in a certain institute were serologically negative. In this instance these serologically negative cases might have been poor in antigenic response though having real influenza infection. However, the fact must also be emphasized that the haemagglutination-inhibition antibody titres were distributed normally among the serologically positive cases (i.e., they showed a normal distribution curve) at the convalescent stage (Fig. 2), and the serologically negative cases must therefore constitute a population which is qualitatively rather than quantitatively different in antibody response. We rather favour the view that the serologically negative cases really had no influenza infection but some other disease showing similar symptoms, and that if there were patients with poor antigenic response, they were few in number—constituting a very small percentage as calculated from the antibody distribution curve after infection.

Considering this, it seemed more reasonable to calculate the attack-rates from the serological data than from the data derived from questionnaires; this kind of survey experiment was possible owing to the fact that the majority of people had had no haemagglutination-inhibiting antibody against A/Asia/57 virus before the epidemic.

At the end of July 1957, when the first wave of Asian influenza had almost subsided in the majority of the prefectures in Japan, sera were taken from almost all the workers in certain health centres selected by us.

FIG. 2. ANTIBODY DISTRIBUTION AMONG STUDENTS* SUFFERING FROM ASIAN INFLUENZA DURING FIRST EPIDEMIC WAVE IN JAPAN



* Students in Obirin school, Kanagawa Prefecture

Further sera were collected in the same way in February 1958, i.e., some time after the second wave. The serological examinations of the first collections of sera were made by the respective prefectural health laboratories, but the second collections of sera were examined by the members in the Japanese Influenza Centre with the collaboration of the workers in the Medical Service School, Self-Defence Forces of Japan (Lieut.-Col. T. Sonoguchi), because some erroneous results had been found in the examinations of the first sera. Table 1 shows the summarized results of the above examinations. Though there are considerable variations from area to area, the average attack-rate is about 20% in the first wave and rises to about 50% after the second wave.

It is reasonable to suppose that the attack-rate would be much higher for those in establishments more crowded than the health centres. In a nursery home, the attack-rate was 55% among the children and 28% among the adults. In the dormitory of a school for students 15-20 years of age, the attack-rate was about 60% in the first wave, as calculated from serological examinations. From these and other data based upon laboratory experiments, we estimate on an average an attack-rate of about 50%-60% in the first wave in schools, dormitories, orphanages, etc.

Calculations were also made of the percentages of serologically positive cases in various camps of the Japanese Self-Defence Forces (data from

TABLE 1. PERCENTAGE OF HEALTH CENTRE WORKERS SHOWING A/ASIA/57 VIRUS ANTIBODY AFTER FIRST AND SECOND WAVES OF ASIAN INFLUENZA, 1957

Locality	After the first wave		After the second wave	
	number	%	number	%
Prefecture:				
Hokkaido			123/199	61.8
Iwate	63/182	34.2	51/93	54.8
Yamagata	58/291	20.0	103/251	41.0
Gumma			134/290	46.2
Tokyo	76/304	25.0	153/287	53.3
Kanagawa			136/262	51.9
Niigata	21/457	4.6	126/365	34.5
Nagano			110/214	51.4
Shizuoka	43/297	14.5	108/224	48.2
Gifu	98/257	38.2	92/184	50.0
Aichi	23/276	8.3	113/203	55.6
Kyoto	54/305	17.7	46/87	52.9
Osaka	69/259	26.6	61/144	42.4
Hyogo	25/255	9.8	87/182	47.8
Shimane	29/212	13.8	29/113	25.7
Okayama			105/220	47.7
Kochi	44/250	17.6	87/159	54.7
Fukuoka			112/193	59.1
Saga	36/276	13.3	74/175	42.3
Miyazaki	17/173	9.8	71/155	45.8
City:				
Osaka			51/101	50.5
Kyoto	49/155	30.6	99/184	54.7
Nagoya			111/206	53.9
Average	705/3949	18.2	2182/4491	43.0

Lieut.-Col. T. Sonoguchi). Blood was taken from about 100 individuals selected at random in each camp for serological examination (haemagglutination-inhibition titrations against influenza A/Adachi/2/57 virus strain) during the period from 20 September to 10 October 1957, when the second influenza wave had not yet generally started in the majority of camps. It was found that in these military camps as well an average of about 50%-60% of the people were attacked in the first wave.

For various reasons the attack-rate must also be different in different age-groups, and this difference may be of importance in the epidemiology of influenza. Table 2 shows the attack-rates by age of A/Asia/57 influenza in

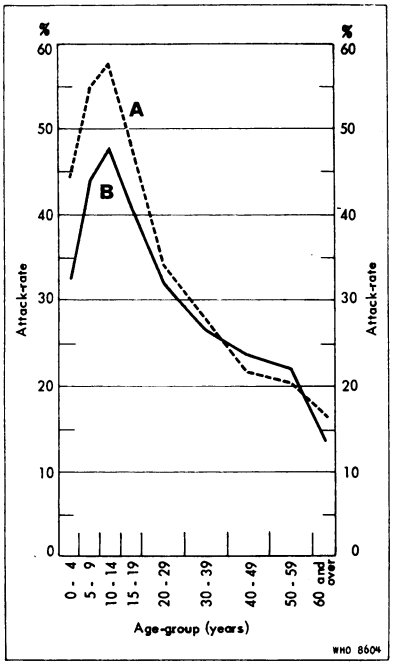
TABLE 2. AGE-SPECIFIC ATTACK-RATE OF INFLUENZA IN FIRST EPIDEMIC WAVE IN JAPAN, 1957 *

Age-group (years)	Number of individuals	Number of cases	Attack-rate
0–4	1 285	361	28.1
5–9	1 482	623	42.0
10–14	1 319	477	36.2
15–19	1 059	295	27.9
20–24	982	220	22.4
25–29	1 690	383	22.7
30–34	1 566	327	20.9
35–39	1 073	203	18.9
40–44	829	152	18.3
45–49	654	98	15.0
50–54	586	86	14.7
55–59	516	58	11.2
60–64	415	37	8.9
65–69	328	33	10.1
70 and over	413	43	10.4
Total	14 197	3 396	23.9

* Based on data from questionnaires to workers in health centres and members of their households.

the first epidemic wave for the whole of Japan, calculated from the data obtained from the questionnaires distributed among the health centre workers and their households (see above). Fig. 3 and 4 present the same kinds of data for Tokyo Prefecture and for Kyoto City. The curves B in these figures are based on the data obtained from the questionnaires to the health centre workers in each area. The curve A in Fig. 3 is based upon data from questionnaires to students in six elementary schools, five middle schools and four private schools in Tokyo, and their families; while the curve A in Fig. 4 is based on questionnaires to 3765 individuals selected at random in 10 health centre districts in Kyoto City. These curves all show that the ages 5-20 years, in which the majority of the individuals are attending school, had the highest attack-rate in the first wave. This fact can be explained largely by the high rate of exposure to influenza of the individuals of this age-group, especially through school life, but not by their high

FIG. 3. AGE-SPECIFIC ATTACK-RATE OF ASIAN INFLUENZA DURING FIRST EPIDEMIC WAVE IN TOKYO

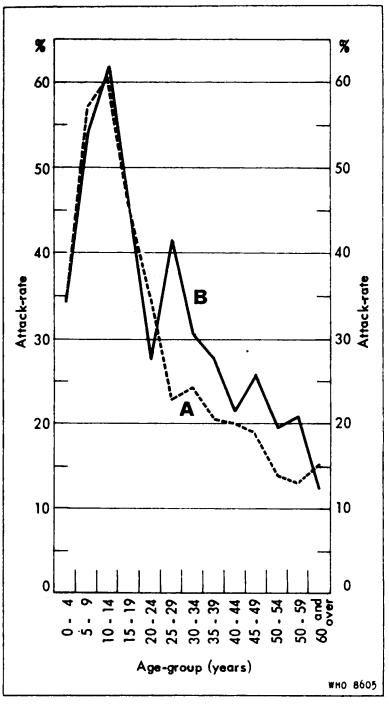


A = data based on answers to questionnaires distributed among Tokyo schoolchildren.

B = data based on answers to questionnaires distributed among health centre workers and their families in Tokyo.

susceptibility to the disease. As is known, it was presumed that every individual, of no matter what age, had the same susceptibility to the first attack of A/Asia/57 virus, because practically nobody had neutralizing antibody to this virus before the first attack. Table 3 shows the secondary intrafamilial attack-rate in different age-groups; the data are based on questionnaires to all the students in a particular class in all the middle schools, and to their families, in Saitama Prefecture. In this case, intrafamilial secondary attack is defined as the development of symptoms in a family member four or more days after the first case, while those who fell ill within less than four days are regarded as simultaneous attack. In this case also a higher attack-rate is seen in children at school, but it would be rash to conclude from these data that this age-group has a high susceptibility. The possibility that some of the cases regarded as

FIG. 4. AGE-SPECIFIC ATTACK-RATE OF ASIAN INFLUENZA DURING FIRST EPIDEMIC WAVE IN KYOTO



A = data based on answers to questionnaires distributed among 3765 persons in Kyoto, selected at random.

B = data based on answers to questionnaires distributed among health centre workers and their families in Kyoto.

TABLE 3. INTRAFAMILIAL SECONDARY ATTACKS OF ASIAN INFLUENZA IN DIFFERENT AGE-GROUPS IN FIRST EPIDEMIC WAVE IN JAPAN, 1957 *

Age-group (years)	Number of patients [a]	Number of persons in the families of the patients	Number of intrafamilial secondary attacks [b]	Number of first cases and simultaneous attacks [c]	Number of persons exposed [d]	Intrafamilial secondary attack-rate (%)
0–4	122	394	33	89	305	10.8
5–9	462	1 272	102	360	912	11.2
10–14	779	2 073	181	598	1 475	12.3
15–19	351	1 462	91	260	1 202	7.6
20–24	192	928	29	163	765	3.8
25–29	69	376	15	54	322	4.7
30–34	41	281	8	33	248	3.2
35–39	106	614	21	85	529	4.0
40–44	127	957	25	102	855	2.9
45–49	114	1 050	23	91	959	2.4
50–54	77	611	19	58	553	3.4
55–59	20	285	5	15	270	1.9
60–64	14	148	5	9	139	3.6
65–69	18	146	4	14	132	3.0
70–74	7	159	3	4	155	1.9
75–79	5	121	1	4	117	0.9
80 and over	2	95	1	1	94	0.1
Total	2 506	10 972	566	1 940	9 032	6.3

* Based on data from questionnaires to all students in a given class in all middle schools in Saitama Prefecture, and to all families of those students.

[a] Patients are those having a fever of more than 38°C.

[b] Intrafamilial secondary attack is the development of symptoms by a member of the household 4 or more days after the first case.

[c] Simultaneous attacks are those occurring within 4 days of the first case.

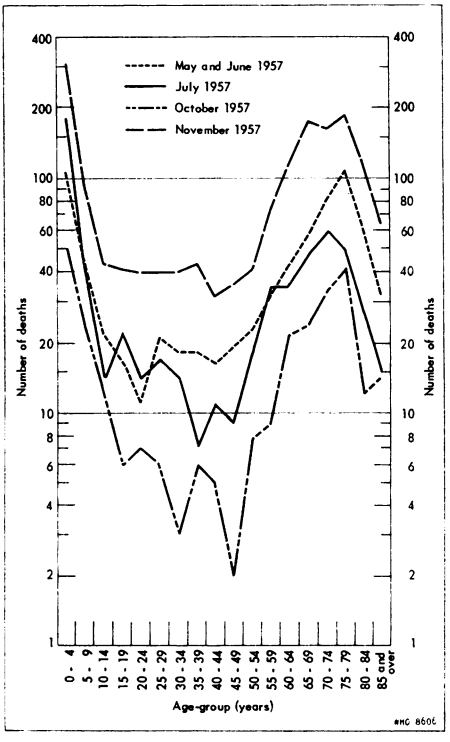
[d] The number of persons exposed is the number of persons in the families of the patients minus the number of simultaneous attacks.

being of intrafamilial secondary attack might have become infected outside the household cannot be excluded; and even within the household there may be some differences in real exposure to the virus between different age-groups because of the differences in their household activity.

Death-Rates and Causes of Death

There was considerable discussion about the severity of the infections due to A/Asia/57 virus during the epidemic period in Japan, and it was feared by some that the pathogenicity or virulence of the virus might increase

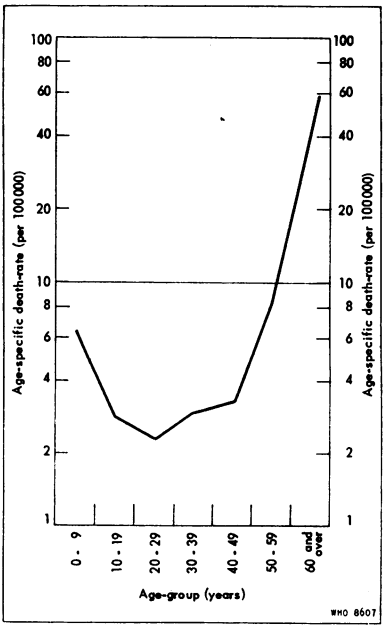
FIG. 5. DEATHS FROM ASIAN INFLUENZA ACCORDING TO AGE-GROUP IN DIFFERENT MONTHS IN JAPAN



during the course of the epidemic. Special attention was therefore paid to the deaths due to influenza and influenzal pneumonia during the epidemic period. The time-occurrence curve of the influenzal deaths in 1957-58 is shown in Fig. 1. Though there was some increase in the number of influenzal deaths in the second wave as compared with the first, that may be attributed to the unfavourable season rather than to any increase in virulence. The number of deaths from influenza according to age-group for the period May-November 1957 is shown in Fig. 5. It is clear from this figure that the death-rate is remarkably high both in infants and in old people. This is also obvious from Fig. 6, which gives the age-specific death-rates (per 100 000 individuals) for the whole epidemic period (May 1957 to January 1958) in Tokyo.

The direct causes of death among influenza patients during the epidemic have also been studied, and it was found that in Tokyo, for instance, out of over 580 deaths, 316 were caused by acute pneumonia and 133 by cardiac insufficiency. Among the other causes were, in decreasing order of frequency, influenza, senility, cardiac asthma, bronchial asthma, bronchitis, pulmo-

FIG. 6. AGE-SPECIFIC DEATH-RATES FROM ASIAN INFLUENZA IN JAPAN (MAY 1957—JANUARY 1958)



nary oedema, meningitis, encephalitis, enteritis, nephritis, hepatitis, and dyspepsia.

Very few of the deaths from influenza were subjected to post mortem examinations during the epidemic. The only available report deals with accidental deaths which happened to include those due to influenza. The pathologist concerned did not systematically conduct bacteriological and virological examinations, but succeeded in isolating the influenza virus twice and pneumococci three times from fatal influenza cases. Histopathologically, he found haemorrhagic pneumonia in the left lower lung and bilateral lung oedema in a 46-year-old male, and bronchitis, bronchiolitis and mild bronchopneumonia (mainly interstitial) in a 6-year-old female. They were both virus-positive.

Vaccination

As mentioned above, the new virus was isolated for the first time in Japan at the end of May 1957, and production of the vaccine containing the new virus was soon afterwards recommended to several manufacturers in Japan; however, they were unable to start work until July. The new vaccine was first produced in November 1957, after assay in the National Institute of Health of Japan, and general vaccinations started in that month, when the second wave of the epidemic had already reached its climax. According to the reports from prefectural authorities, vaccinations were mostly carried out in November and December. As the amount of the vaccine made available at that time was very limited, the extent of the vaccination in the prefectures was also inevitably very restricted.

Laboratory experiments of vaccine, antibody responses after vaccination and some other data available are reported in another paper.[1]

ACKNOWLEDGEMENTS

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RÉSUMÉ

L'épidémie de grippe asiatique a débuté au Japon en mai 1957. Apparue d'abord dans les grandes villes, elle s'est propagée aux bourgades et aux zones rurales. Les premiers isolements pratiqués à la fin de mai montrèrent que l'on avait affaire à un virus différent de ceux qui étaient responsables de l'épidémie hivernale de grippe, qui avait sévi de novembre 1956 à mars 1957 — avec un clocher en janvier.

[1] See page 355.

La courbe de l'épidémie présenta deux clochers, l'un à la fin de juin, l'autre en novembre-décembre, correspondant à deux vagues de la maladie. La seconde vague s'étendit jusqu'au début de 1958 avec un nouveau maximum en janvier. Il n'est pas facile d'établir de quel pays l'infection pénétra au Japon. Il est possible qu'elle vint de plusieurs côtés et se propagea à partir de plusieurs centres.

Afin de déterminer le taux de morbidité par groupes d'âge et par région, un questionnaire a été distribué aux personnes travaillant dans les centres de santé et à leurs familles. Les réponses reçues indiquent de grandes variations d'une zone à l'autre, allant de 11,4% à 35%. Ces données étaient évidemment approximatives, et cela d'autant plus qu'il s'agit de la grippe dont les symptômes rappellent ceux de plusieurs autres maladies. C'est ainsi que l'on a trouvé, par exemple, que 40% des cas diagnostiqués comme grippe étaient négatifs à l'examen sérologique, et l'on a des raisons de considérer ces cas comme non grippaux, d'après les résultats des tests d'inhibition de l'hémagglutination.

Il a donc paru plus efficace d'évaluer la morbidité par des épreuves sérologiques plutôt que d'après les réponses au questionnaire. Les renseignements ainsi obtenus devaient être d'autant plus précis que la population n'avait pas été exposée antérieurement à un virus du type causant l'épidémie.

L'auteur a groupé dans un tableau les résultats d'examens sérologiques effectués après la première vague, puis après la seconde. La moyenne des cas durant la première vague est de 20% environ, et de 50% durant la seconde — avec de grandes variations suivant les régions. Cette proportion était encore plus élevée (50-60%) dans les collectivités d'enfants, écoles, orphelinats, internats. Dans les camps militaires, on estimait à 50-60% la proportion des personnes touchées par la première vague.

L'analyse de la répartition des cas par groupes d'âge — représentée en plusieurs tableaux — d'après les réponses aux questionnaires, montre que les groupes d'âge de 5-20 ans, correspondant à l'âge de la scolarité, sont les plus atteints. La concentration des cas dans ces groupes d'âge s'explique plutôt par une plus forte contagiosité résultant de la vie en collectivité (écoles, camps, etc.) que par une plus grande sensibilité à l'infection.

La crainte d'un accroissement de la virulence du virus au cours de l'épidémie — en général bénigne — fit prêter grande attention aux décès dus à l'infection et à ses complications, la pneumonie grippale en particulier. Une légère augmentation de la mortalité durant la deuxième vague — comparée à la première — est à imputer à la mauvaise saison, plutôt qu'à une virulence accrue. Le taux de mortalité était particulièrement élevé chez les jeunes enfants et les vieillards.

Le vaccin spécifique a été mis à disposition dès novembre 1957. L'épidémie étant alors en décroissance, seuls des groupes restreints de la population ont été vaccinés.