INFLUENZA SURVEILLANCE IN THE PACIFIC BASIN

Seasonality of Virus Occurrence : A Preliminary Report

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INTRODUCTION

This report represents an initial analysis of data presented in a session on influenza surveillance held during the 1st Asia Pacific Congress of Medical Virology, November 1988, Singapore. About twenty countries were represented, and participants had been asked to provide summaries of data available from about the past ten years. To the best of our knowledge, this is the first time that influenza surveillance results from so many countries in Asia or bordering the Pacific Ocean have been compared to establish long term trends about the seasonal occurrence of influenza infections. We have also reviewed previously published data concerning the known appearance of pandemic strains in the latter half of the century, for comparison with the information presented about recent interpandemic influenza.

Most information relates to the laboratory isolation of influenza viruses from either outbreaks of respiratory disease, or from routine cases seen in hospitals, clinics, etc. The methodologies used for virus isolation or identification varied. Chicken eggs were commonly used to grow influenza virus, and hemagglutination inhibition tests used to identify isolates. Some countries are now using imported primary monkey kidney cells, or continuous cell lines such as MDCK and LLC-MK2 cells in place of eggs to isolate viruses. In these cases, fluorescent antibody techniques were possible for preliminary typing, usually followed by hemagglutination inhibition tests for sub-typing. Most countries send a sample of their isolates to a WHO Collaborating Center for a more complete analysis.

Other types of data have been used to different extents in various countries. These include : 1. Numbers of deaths from pneumonia and influenza; 2. Numbers of clinic, hospital or physician office visits due to acute respiratory illness (ARI); 3. Rates of school absenteeism; and 4. Serologic diagnosis.

Some of the participants have had extensive surveillance programs during this period, while others were just beginning to initiate programs. Despite these variations, and the lack of presentation of all available data due to constraints of time or resources, important historical trends were demonstrated, and the groundwork established for data collection and analysis in a more rigorous fashion in the future.

The general approach to organising the order of data presentation was to commence with countries aligning the North Western area of the Pacific Ocean (i.e. North East Asia), and to proceed

TIME OF DETECTION OF PANDEMIC INFLUENZA A VIRUSES
IN REPRESENTATIVE COUNTRIES AROUND THE PACIFIC BASIN

VIRUS SUB-TYPE	CHINA	SINGAPORE	INDIA	JAPAN	AUSTRALIA	UNITED STATES	CHILE
H2N2 ("Asian Flu")	FEB '57	APR '57	MAY '57	MAY '57	APR '57	JUN '57	JUL '57
H3N2 ("Hong Kong Flu")	JUL '68*	AUG '68	AUG '68	AUG '68	SEP '68	SEP '68	SEP '68
H1N1 ("Russian Flu")	MAY '77	NOV '77	UNKNOWN	DEC '77	JUN '78	JAN '78	MAR '78

* Based on reports of outbreaks in China, and subsequent isolation of virus in Hong Kong.

counter-clockwise around the Pacific.

SURVEILLANCE RESULTS

Korea and Japan

The four main islands of Japan, and Korea, have a temperate climate with clearly demarcated summer and winter seasons, from about June to September, and from about November to March respectively. Influenza surveillance in Japan is very extensive, and information on morbidity collected by the Ministry of Health and Welfare is correlated with laboratory reports collected by the National Institute of Health, which also conducts reference analysis of viruses submitted from Prefectural laboratories.

At times when pandemic viruses have appeared, such viruses have been detected early in the course of the pandemic period, although widespread outbreaks of the new virus subtype may not have occurred until some months later. This was the case in 1957 when type A (H2N2) virus was first detected in May; the subsequent epidemic in Japan occurred during September. Similarly, type A (H3N2) virus was first isolated during August of 1968, but the actual epidemic occurred during January and February of 1969. Influenza A (H1N1) viruses were detected during December of 1977, when they co-circulated with type A (H3N2) strains. Subsequently these type A (H1N1) viruses were predominant strains in 1978, 1979 and 1980.

Seasonality of influenza virus infections in Japan since 1981 is summarised in Figure 1. The majority of influenza virus

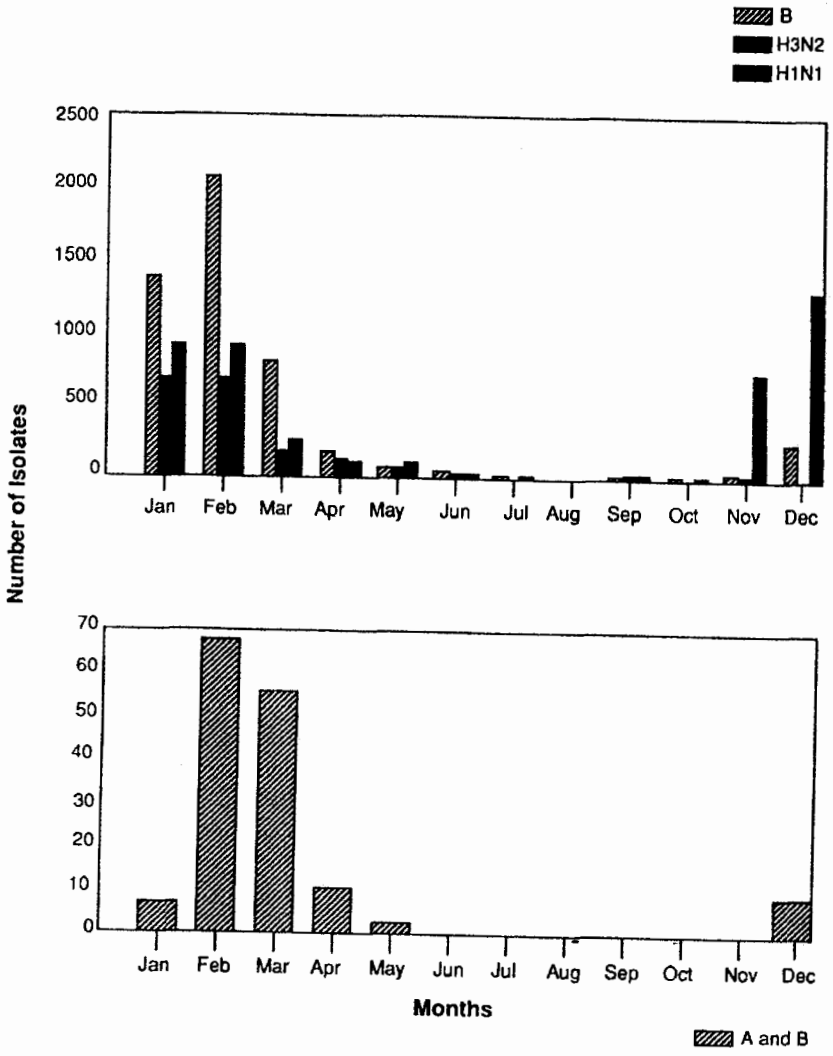

Figure 1. SEASONALITY OF INFLUENZA IN JAPAN AND KOREA. Total number of virus isolates, by month, from Japan, 1981-1988 (upper panel) and Korea, 1972-1987 (lower panel).

isolates are reported in the winter months during January, February and March. During interpandemic periods, it has often been observed that a virus which is in the minority as the cause of outbreaks or epidemics in one season, particularly towards the end of the winter, appears as the next season's epidemic strain.

Influenza surveillance in South Korea is carried out through the Ministry of Health and Social Affairs by the National Institute of Health. Surveillance records are available since 1957 and retrospective serological studies have been undertaken. The majority of influenza isolates are obtained from the General Hospital in Seoul. However, reports of influenza activity, and a few isolates, are also obtained from the City and Province Health Laboratory.

Influenza A (H2N2) viruses were first isolated in Korea during May, June and July of 1957. In contrast, influenza A (H3N2) virus was first isolated during December 1968, and influenza A (H1N1) virus during February 1978. As can be seen from Figure 1, the majority of isolates in the interpandemic years occur during the winter months.

China, Hong Kong and Taiwan

This area encompasses a very wide range of geography and climate. Beijing, representing northern China, is further north in latitude than Seoul, Korea and clearly has a temperate climate. Of the other areas discussed, Shanghai, centrally located on the coast of China, is on a parallel with the southern tip of Japan. Guangdong Province and Hong Kong are adjacent areas with tropical

or sub-tropical climates, as does the island of Taiwan. Some of the highest population densities in the world are found in cities in these areas.

Surveillance in China is conducted by several Provincial Health and Anti-Epidemic Centers, which investigate outbreaks of respiratory disease or collect specimens from hospital patients. A National Influenza Center in Beijing is responsible for receiving information and strains from these centers. It is believed that all the recent pandemic strains of influenza A virus had their origin in China. Thus, the first reported outbreak of influenza A (H_2N2) virus occurred in late February, 1957, in Guizhou Province, near Kweiyang, in southern China. The disease had spread to many parts of China by the end of the month and by early April was epidemic in Hong Kong. Similarly, in mid-July, 1968, reports appeared of an outbreak of acute respiratory disease in south-eastern China. Although no isolates were obtained from the Chinese outbreak, at about the same time there were reports from Hong Kong of epidemic levels of influenza illness, and the causative agent was confirmed to be a new sub-type of influenza A virus, later known as "Hong Kong 'Flu", or H3N2 subtype. Finally, influenza A (H1N1) viruses which had not been active in man since 1957, were isolated at the end of May and early June, 1977, from Liaoning Province and Tientsin Municipality in Northern China.

The usual pattern of influenza virus isolation in Northern China, as seen since 1977, follows that expected for a temperate climate (not shown). Most virus isolations and outbreaks of

disease occur during the winter months. In contrast, Shanghai, which is about midway between Beijing and Guanzhou, often experiences two peaks of influenza activity each year. One occurs in summer-autumn and the other in winter-spring (Figure 2). The influenza isolation patterns reported in South China, as exemplified by Guangdong Province (Figure 2), indicate that viruses are isolated year round, with peak activity in summer (May-July).

Laboratory surveillance in Hong Kong was, until recently conducted only through the Government Virus Unit at Queen Mary Hospital on Hong Kong Island. Samples were obtained from hospital patients, as well as being submitted from clinics in Hong Kong and Kowloon. More recently, a virology laboratory has also been functioning in the Chinese University Hospital in the New Territories. The pattern of virus isolations in Hong Kong is fairly similar to that in Guangdong Province, and an earlier peak in later winter/spring may also occur (Figure 3).

Influenza surveillance data for Taiwan comes from both the National Institute of Preventive Medicine and the Veterans General Hospital, both located in Taipei. Influenza A (H2N2) virus was first detected in Taiwan in April of 1957 and type A (H3N2) virus during late August 1968. However, the Veterans General Hospital reported obtaining the first isolates of type A (H1N1) virus during October-December of 1977. For the last ten years, both laboratories have reported isolating type A (H1N1) and (H3N2) strains, and influenza B viruses. Combined seasonality data from both reporting institutions is shown in Figure 4. The only period

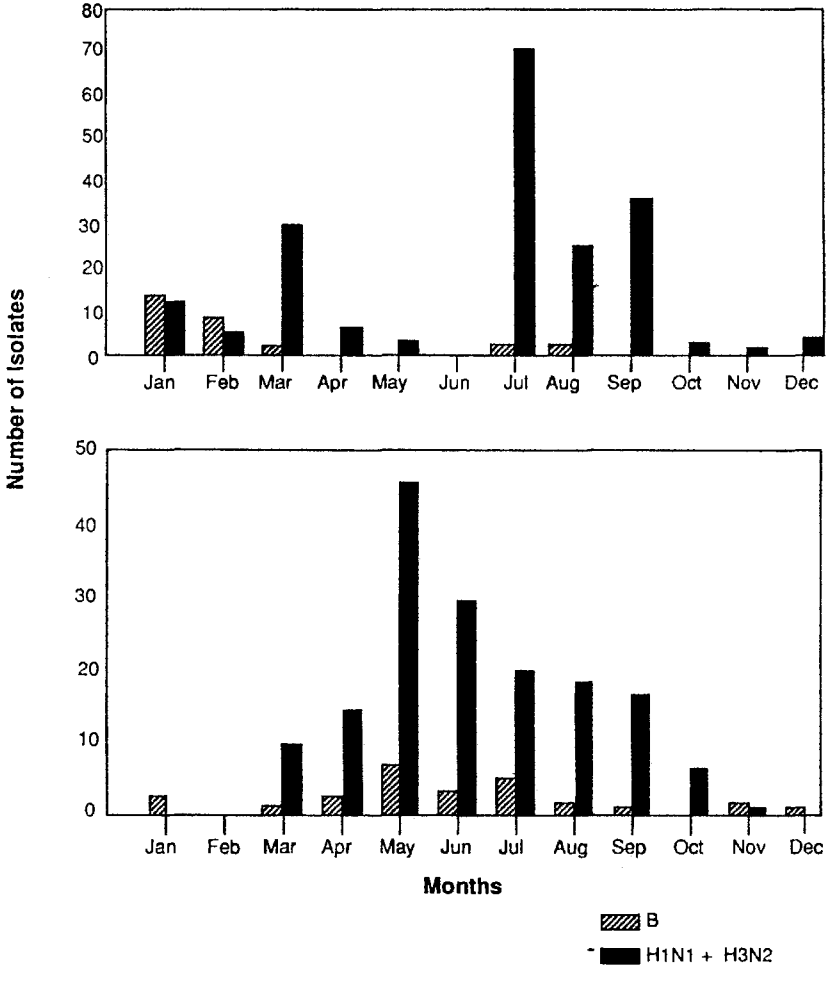

Figure 2. SEASONALITY OF INFLUENZA IN CENTRAL AND SOUTHERN CHINA. Total number of virus isolates in the People's Republic of China, by month, from Shanghai, 1975-79 (upper panel), and Guandong Province, 1982-1987 (lower panel).

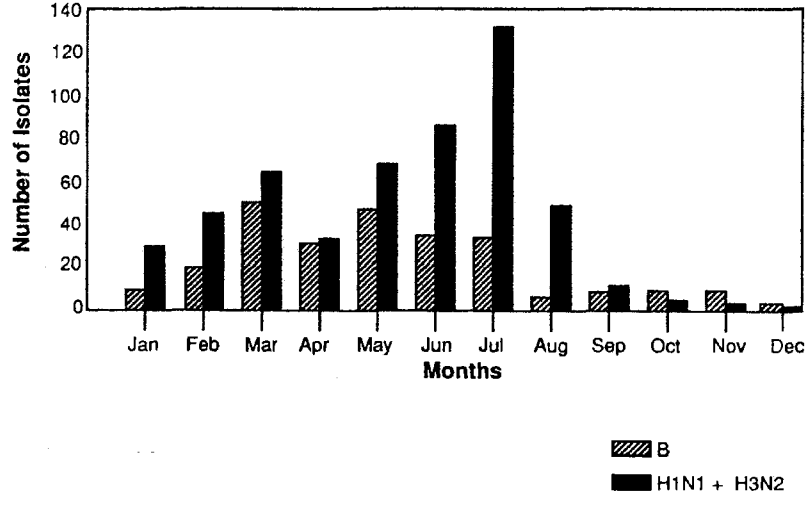

Figure 3. SEASONALITY OF INFLUENZA IN HONG KONG. Total number of virus isolates, by month, in Hong Kong, from 1978-1988.

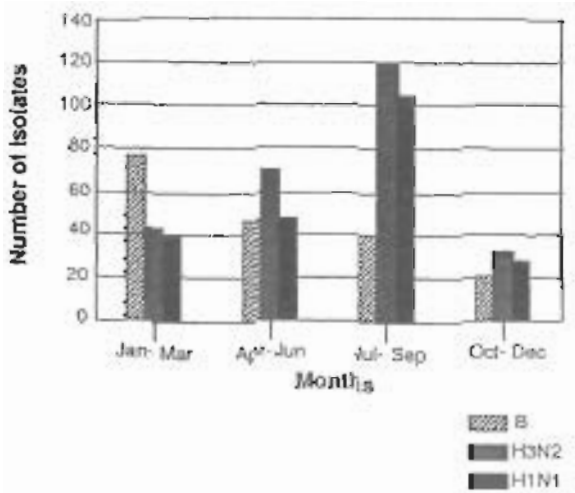

Figure 4. SEASONALITY OF INFLUENZA IN TAIWAN. Total number of virus isolates, by quarter, in Taiwan, Republic of China, 1979-1988.

of decreased influenza activity appears to be usually from October through December.

Malaysia, Singapore and Thailand

These countries all have a predominantly tropical climate with the seasons related to the extent of rainfall, i.e. wet or dry.

Laboratory surveillance for influenza in Singapore is conducted by the National Influenza Center, in the Government Pathology Laboratory. Since 1972, the following types of surveillance data have been collected routinely : admissions to government out-patient clinics for acute respiratory infection (ARI); isolation rates of influenza viruses from patients at these clinics, performed on a year-round basis, and reports on influenza-pneumonia deaths. The morbidity and mortality data are collected by the Department of Health.

Singapore reported isolating influenza A (H2N2) viruses in April of 1957, and influenza A (H3N2) virus was reported at the beginning of August, 1968. Type A (H1N1) virus was not isolated until November 1977, and the first outbreaks did not occur until December-January.

Based on surveillance from 1972 until 1986, influenza is endemic in Singapore (Figure 5). There is often a major peak of influenza activity from April to June or July, with a second period of increased activity in October to January.

Influenza surveillance in Malaysia has been undertaken since 1954 at government clinics and the outpatient clinic and student

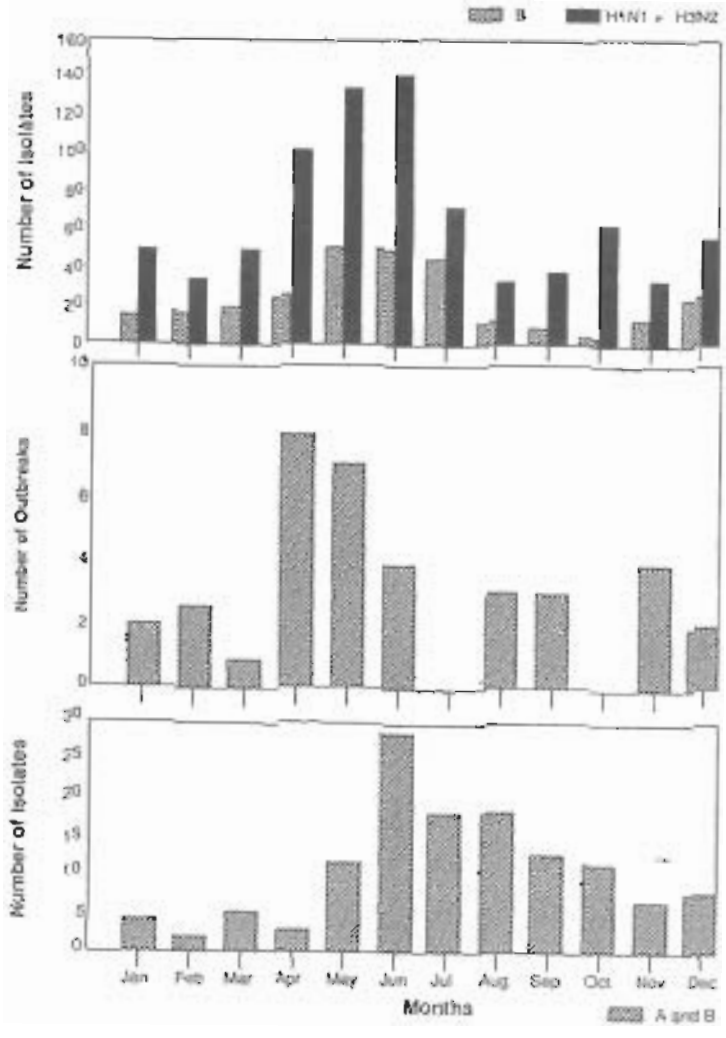

Figure 5. SEASONALITY OF INFLUENZA IN SINGAPORE, MALAYSIA AND THAILAND. Total number of virus isolates, by month, in Singapore, 1972-1986 (upper panel) and Thailand, 1979-1988 (lower panel). Number of confirmed outbreaks of influenza in Malaysia from 1954-1987 is shown by month in the middle panel.

health clinic at the University of Malaya. In May, 1957, outbreaks of type A (H2N2) virus were reported. Type A (H3N2) viruses were first reported in August, 1968, from an outbreak of febrile respiratory illness at a US Air Force Base. In contrast to other countries, influenza A (H1N1) viruses were not reported until 1980, although it is probable they were in fact present undetected in 1977/1978.

Like Singapore, Malaysia usually has its peak influenza activity during the months of April to June, judged by investigations of outbreaks of influenza-like illness (Figure 5). As in Singapore, influenza viruses have been isolated in most months of the year, from outbreaks or sporadic cases occuring outside the peak months.

Surveillance in Thailand has been conducted mainly by two organisations, the Government Virus Research Institute, and Mahidol University, in the Bangkok area. The US Armed Forces Research Institute for Medical Services has participated in the past. Most specimens for laboratory diagnosis have come from pediatric out-patients in Bangkok. Surveillance sources are being expanded, and potentially include : deaths from pneumonia and influenza, virus isolations, numbers of clinic or hospital visits for ARI, school absenteeism, serological studies and active physician reporting of influenza-like illness, including provincial areas.

Dates of first reports of type A (H2N2), (H3N2), and (H1N1) viruses in Thailand were May 1957, September, 1968, and November, 1977 respectively. Data for the years 1982-1986 shows that the isolation of influenza viruses peaks in the period May to October

(Figure 5). However, influenza virus has also been isolated at other times of year, as in Singapore and Malaysia.

Indian Sub-Continent

While not technically bordering on the Pacific Ocean, the Indian sub-continent is likely to be epidemiologically important in the spread of influenza viruses in the Asian-Pacific region. The climate in the region varies considerably with geography, but large areas are dominated by tropical monsoons. In these regions, four seasons are recognized : cold weather (December to March); hot weather (April to May); the rainy season (June to September); and the season of retreating southwest monsoon (October and November).

Surveillance information from India has primarily come from the National Institute of Virology, Pune, which has conducted extensive surveys for several years in clinics in the city. Other sources include : The National Institute of Communicable Diseases, Delhi, which is now establishing a new program in respiratory diseases; and the Department of Virology, Christian Medical College Hospital, Vellore, which has studied pediatric respiratory disease epidemiology on various occasions.

Influenza A (H2N2) virus was first detected in India in May of 1957. Influenza A (H3N2) virus was probably present by August, 1968. This is not too dissimilar from the pattern in many normal years, when positive influenza virus isolations are often made in July and August coinciding with the rainy season. In addition,

the period March-April is often a time when influenza virus outbreaks occur.

Information about long-term surveillance activities in Pakistan was not available for this report. Only recently has influenza laboratory diagnosis been undertaken in Bangladesh. Preliminary information from the Institute of Public Health in Dakar describes the isolation of influenza viruses during both the warm and cold months, with peak activity occurring during the July to October season.

Australia, New Zealand, Papua New Guinea and Fiji

These island nations have a wide variety of climates. New Zealand and much of the populated regions of Australia are temperate, although the north of Australia is subtropical to tropical, as is Papua New Guinea and Fiji.

National Influenza Centers have been designated in Melbourne, Australia , and Wellington, New Zealand. In conjunction with other laboratories in major cities, comprehensive laboratory diagnosis of influenza has been undertaken for many years in these countries. In Papua New Guinea, virus isolation is undertaken at the Research Institute of Medicine in Goroka, and in Fiji the National Influenza Center is established at the Wellcome Virus Laboratory in Suva.

Summary reports suggest that influenza A (H2N2) viruses may have been isolated in Australia in May, 1957, and spread to all regions of the country by August. The H3N2 virus, was first detected in Australia in September, 1968 but the first epidemic

of this virus did not apparently occur until July-August of 1969. Type A (H1N1) viruses reached Australia by March, 1978, and caused outbreaks in the next few months.

The normal seasonality of influenza virus, outside of pandemic periods, is that of a temperate climate with a single peak period in the winter months of June to September (Figure 6). Based on available data, there is little variation in seasonality of influenza viruses in different regions of Australia.

In New Zealand, pandemic viruses of type A (H2N2), (H3N2), and (H1N1) were first detected in July, 1957; May, 1969; and June, 1978 respectively.

When cumulative data over several recent years of interpandemic influenza are compared, it can be seen that the normal seasonal peak of influenza activity in New Zealand precedes that for Australia by approximately one to two months (Figure 6). Thus, the influenza season in New Zealand may best be regarded as May to September, on average. However, from the period 1975 to 1984, six epidemics were "in season" while four fell slightly outside these seasonal limits. Isolations have been made in other months of the year. It is not unusual for isolates outside the peak season to be related to importation by recently returning travellers.

Laboratory information from Papua New Guinea is intermittent. Type A (H2N2) viruses were reported there in September, 1957, but reports from 1968 and 1977 have not yet been identified. From 1983 to the present, prospective studies have been conducted, and although the total numbers of isolates are quite small, the major

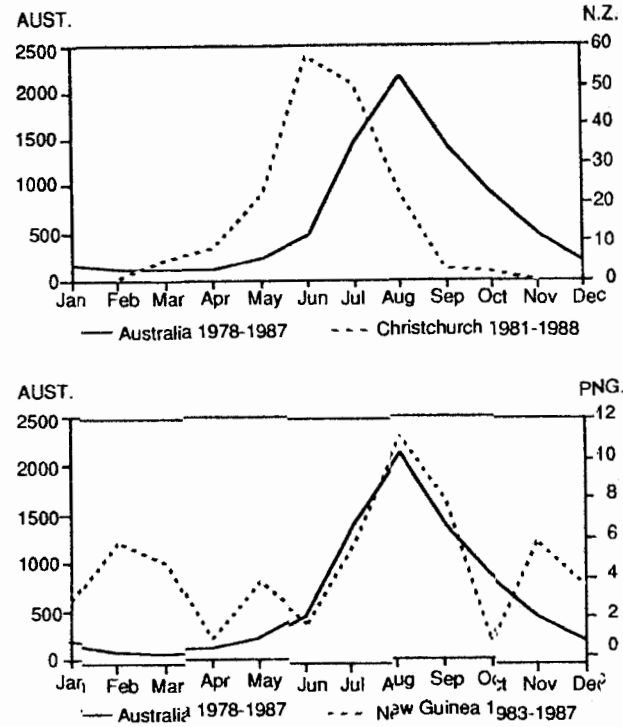

Figure 6. SEASONALITY OF INFLUENZA IN OCEANIA. Total number of virus isolates, by month, in Australia, 1978-1987, vs. Christchurch, New Zealand, 1981-1988 (upper panel), and in Australia, 1978-87, vs. Papua New Guinea, 1983-1987 (lower panel).

peak appears similar to Australia, i.e. from about July to September. The A/Victoria/3/75 (H3N2) variant of influenza is also known to have caused outbreaks with severe illness in rural populations in Papua New Guinea in about June-July. As in other countries located in the tropics, however, isolation of influenza viruses appears to occur throughout the year (Figure 6).

In Fiji, type A (H2N2) viruses are reported to have been detected in July, 1957, and type A (H1N1) viruses in April, 1978. During the interpandemic years, outbreaks of laboratory confirmed influenza have occurred in Fiji typically in about March-April, or July to September (not shown). However, there is usually only a single wave of influenza in any one year.

South and Central America

The climate among the Pacific countries of South and Central America ranges from temperate, in Chile, to tropical, for example in Panama; these two countries being nations with particularly active influenza diagnosis and surveillance programs.

Influenza A (H2N2) virus was first isolated in Chile in July 1957, and type A (H3N2) outbreaks began in about mid-May, 1969. When type A (H1N1) viruses reappeared in 1977, it was not until June 1978 that outbreaks began in Chile. During interpandemic years surveillance primarily involves monitoring clinics and hospitals, as well as investigating specific outbreaks. There is a single epidemic season each year, and as in the case of pandemic years, most isolates are obtained from about May to August (not shown).

In Panama, outbreaks believed to be due to influenza type A (H2N2) virus were reported during June-July 1957, but attempts to isolate the virus were unsuccessful. During September to October 1968, only mild influenza epidemics were observed in association with isolation of influenza A (H3N2) viruses. The re-emergence of type A (H1N1) viruses had little effect in Panama until March of 1978. In recent years, weekly reports of influenza-like illness have been obtained for pediatric patients who present at sentinel outpatient clinics, and a peak is seen between about May and August. Laboratory diagnosis has confirmed that outbreaks of influenza occur at this time, although isolates may be obtained at other times too in some years.

Pacific North America and Hawaii

There is considerable variation in climate from the warm, dry areas in Southern California, through cooler, temperate areas of Northern California, Oregon and Washington States, as well as British Columbia, merging into arctic regions of Alaska. Hawaii can be considered to have a temperate or semi-tropical climate. Within each of these states or provinces, there is also considerable variation between coastal, mountain or intermediate areas. Influenza surveillance is well developed throughout the different regions. State, provincial, or large country health departments routinely identify viruses from outbreaks or from surveillance sites such as sentinel physicians or clinics, as well as isolates

from major hospital laboratories.

At the time of the 1957 Asian influenza pandemic, much influenza surveillance in the US was conducted under the auspices of the Armed Forces Epidemiological Commission on Influenza, with a strong emphasis therefore on military bases, which are the site of many returning travelers from the Far East. Thus, the earliest cases of influenza A (H2N2) viruses on the West Coast of the USA were reported in June, 1957, from military personnel in California, at about the same time as the virus was identified in military personnel on the East Coast.

Similarly the first isolates of influenza A (H3N2) in the US occurred in September, 1968, among military personnel in Atlanta, Georgia, San Diego, California, and Alaska and Hawaii. Most of these were directly traceable to persons returning from Asia. By 1977, when type A (H1N1) viruses reappeared, the majority of influenza surveillance in the US was no longer conducted among the military, but civilian populations. The type A (H1N1) virus was thus first isolated in the US during January of 1978 from students in Wyoming, although in an area with important military bases. By March, the virus had been isolated across the US, including all Pacific areas of the country. However, in isolated areas of Alaska, the A (H1N1) virus was apparently not necessarily introduced in the first wave in 1977/78. Thus, in December 1988, an explosive outbreak of type A (H1N1) virus occurred on St. Paul Island, shortly after the return of students from a residential school in Anchorage.

Routine surveillance during interpandemic periods indicates that influenza normally occurs in outbreaks or epidemics during a single season each year in winter. The peak months of virus isolation in California, Oregon and Washington states have been December to February (Figure 7). In Alaska there have been several years when influenza has begun about one to two months earlier (Figure 7). In all these states, isolation of influenza has occasionally occurred during May or June. The seasonality of influenza isolation in Hawaii (Figure 7) is very similar to that in the Pacific regions of the US described above. Occasionally, influenza is isolated before the usual season from travelers returning from Asia. These episodes can provide early warning of the impending epidemic in the coming winter.

Other Countries

Influenza virus isolations have been obtained in some years from other countries around the Pacific, including Indonesia (mainly through the Naval Medical Laboratories, Unit 2, based in Djakarta), and the Philippines (mainly through the US Air Force Base near Manila, and more recently from the Research Institute for Tropical Medicine, Manila). Observations in these countries are similar to those of other areas in the tropics. Outbreaks on Pacific Islands such as American Samoa, Guam, and Palau have also occasionally been reported and investigated, usually with the cooperation of the virology laboratory in the State Health Department in Hawaii. Such activity often corresponds to a period

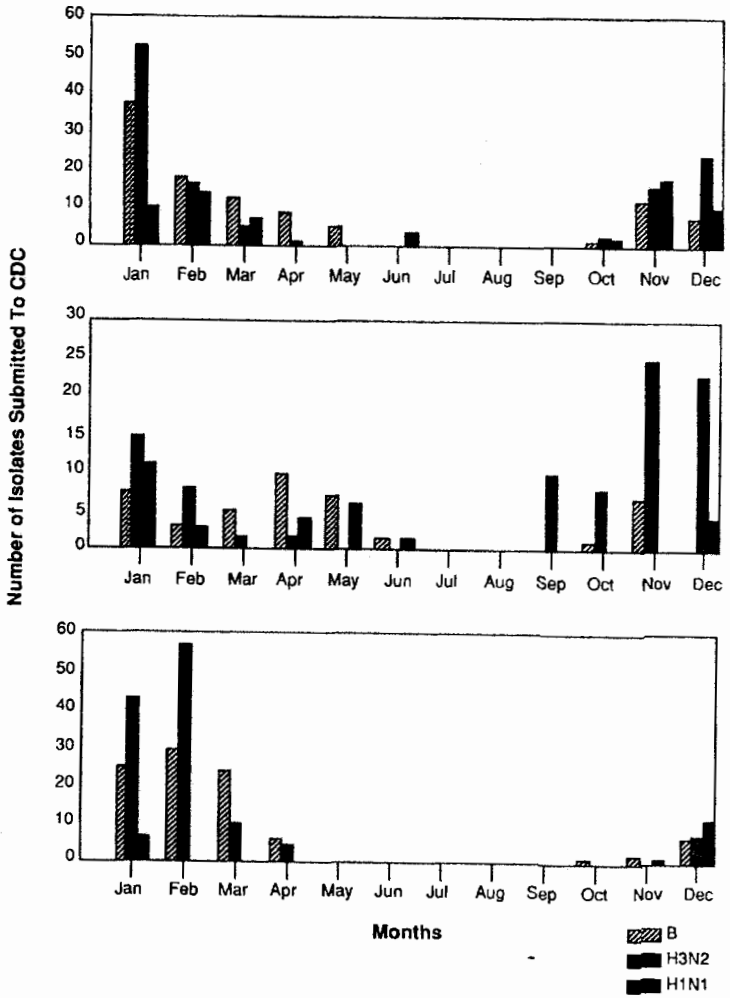

Figure 7. SEASONALITY OF INFLUENZA IN PACIFIC REGIONS OF THE USA. Number of isolates submitted to the Centers for Disease Control, by month, 1981-1988. California, Oregon and Washington States (upper panel), Alaska (middle panel) and Hawaii (lower panel).

when a new antigenic variant that has first been recognised in another area in the Pacific, is spreading.

Understanding patterns of virus spread in the Pacific Basin ultimately may prove beneficial in identifying ways to improve the early detection of strains in time to prepare and distribute vaccines, or plan public health responses to major epidemics. In addition, because new strains do appear to originate in the Asian-Pacific regions, more detailed investigation and analysis of this phenomenon is essential if we are to understand the ecology and spread of the virus as well as come to terms with methods for its control.

SUMMARY AND CONCLUSIONS

The seasonality of interpandemic influenza activity in countries around the Pacific Basin is summarised in Figure 8. Influenza viruses can be isolated from some areas bordering the Pacific during any month. The figure clearly shows that influenza viruses are actively transmitted in temperate climates in the Northern (e.g. Japan, US) and Southern (e.g. Australia) temperate regions during the winter months, which are six months apart. Unlike the temperate regions, however, year-round isolations of influenza are apparently the norm for the tropical and sub-tropical regions of Asia and the Pacific such as South China and Singapore. Here, peak activity is often found in and around the summer months. The environmental and epidemiological factors responsible for these patterns remain to be elucidated, but it is clear that influenza

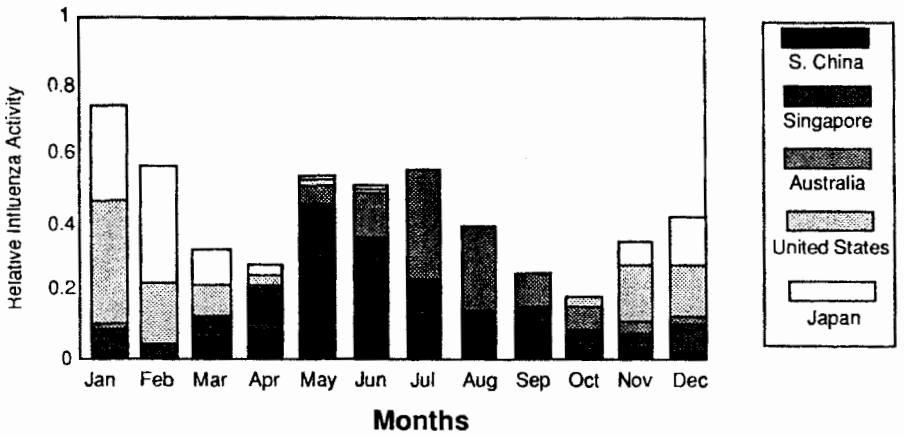

Figure 8. SCHEMATIC SUMMARY OF THE RELATIVE SEASONAL OCCURRENCE OF INFLUENZA IN DIFFERENT REGIONS OF THE PACIFIC BASIN. For each country shown, the ratio of monthly isolates of influenza to total annual isolates in that country is indicated.

cannot be considered a 'winter disease' when experience in the tropics is taken into account.

Based on preliminary review of results of reference laboratory analysis, the first occurrence of new antigenic variants of inter-pandemic influenza may often be in the mainland of Asia, with concurrent spread to the Malaysian Peninsula, the Korean Peninsula and Japan, before spread to Oceania and the Americas. This pattern would be fairly consistent with that seen during pandemics of influenza (Table 1). Further analysis of laboratory findings based on antigenic analysis of virus isolates during interpandemic years is needed, however, to substantiate this observation.

Caution must be used in interpretation of surveillance findings, which are limited by the selection and numbers of patients sampled, and by the quality of diagnostic methods used. With more intensive sampling, including periods outside those usually considered to be the 'epidemic period', the occurrence of influenza variants may be recognised before outbreaks occur. Thus, it is hoped that improved monitoring in different countries will take place in the future. If patient sampling, specimen collection, and diagnostic test procedures can be used that are less varied than in the past, information of greater certainty may be obtained as to the true dates of virus appearance in different areas, with minimal surveillance artefacts. Furthermore, application of molecular biologic approaches to study gene evolution also may help increase the precision with which the time of appearance and spread of new variants can be identified.

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