Influenza in Asia

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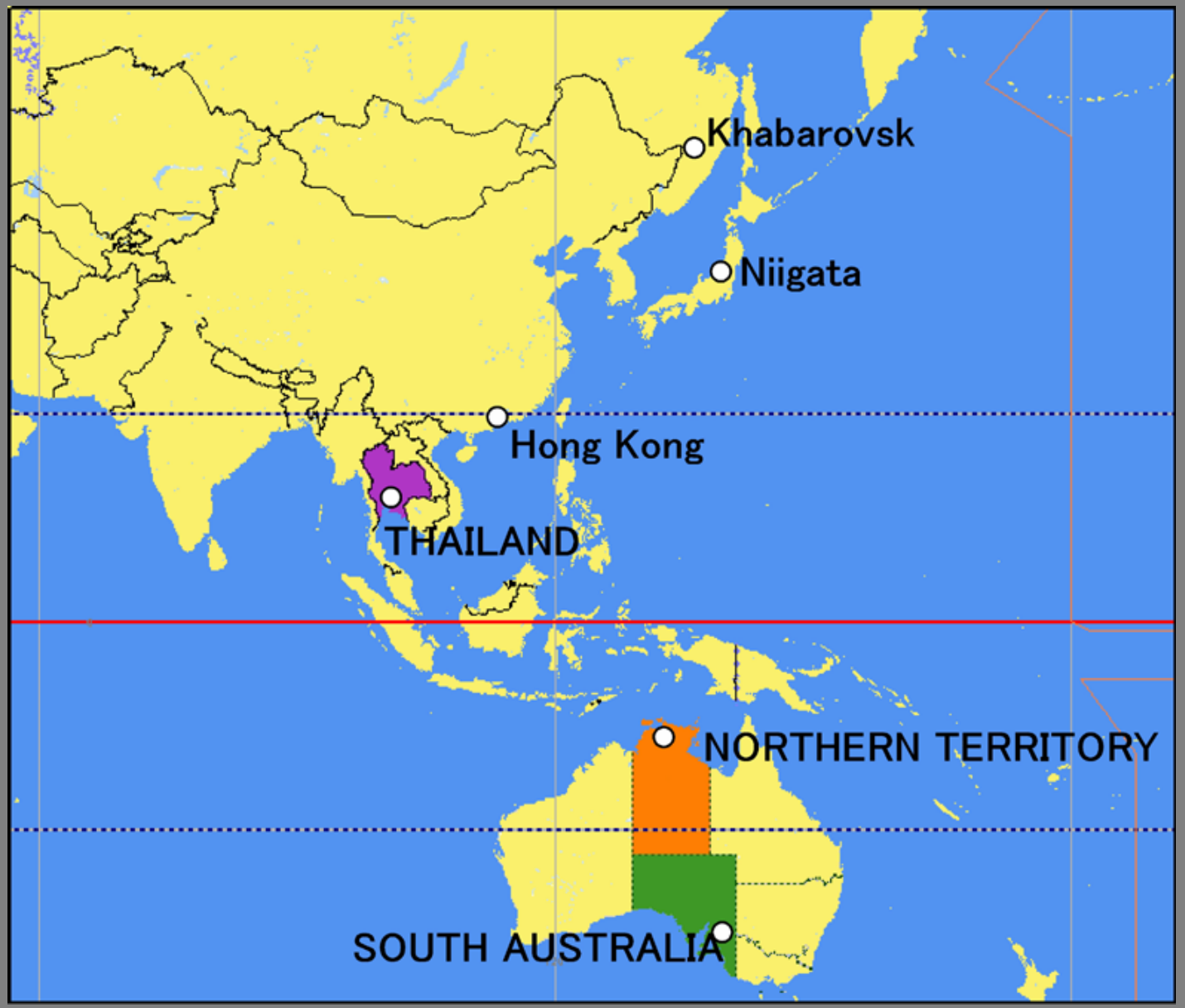
Influenza in zones with a temperate climate is characterized by the occurrence of one annual epidemic during the winter months.

But, that is not always true in different climates, especially in tropical and subtropical areas.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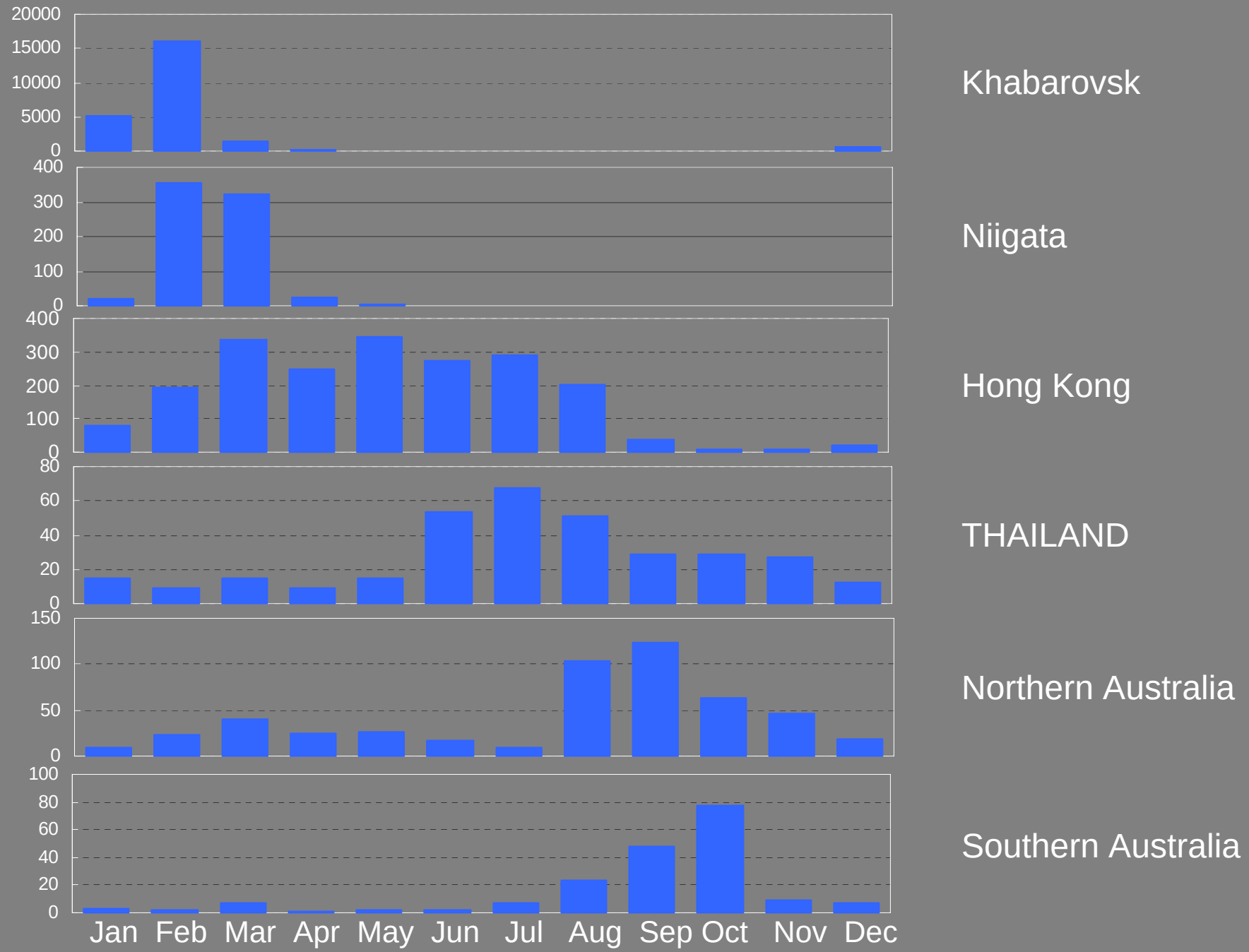
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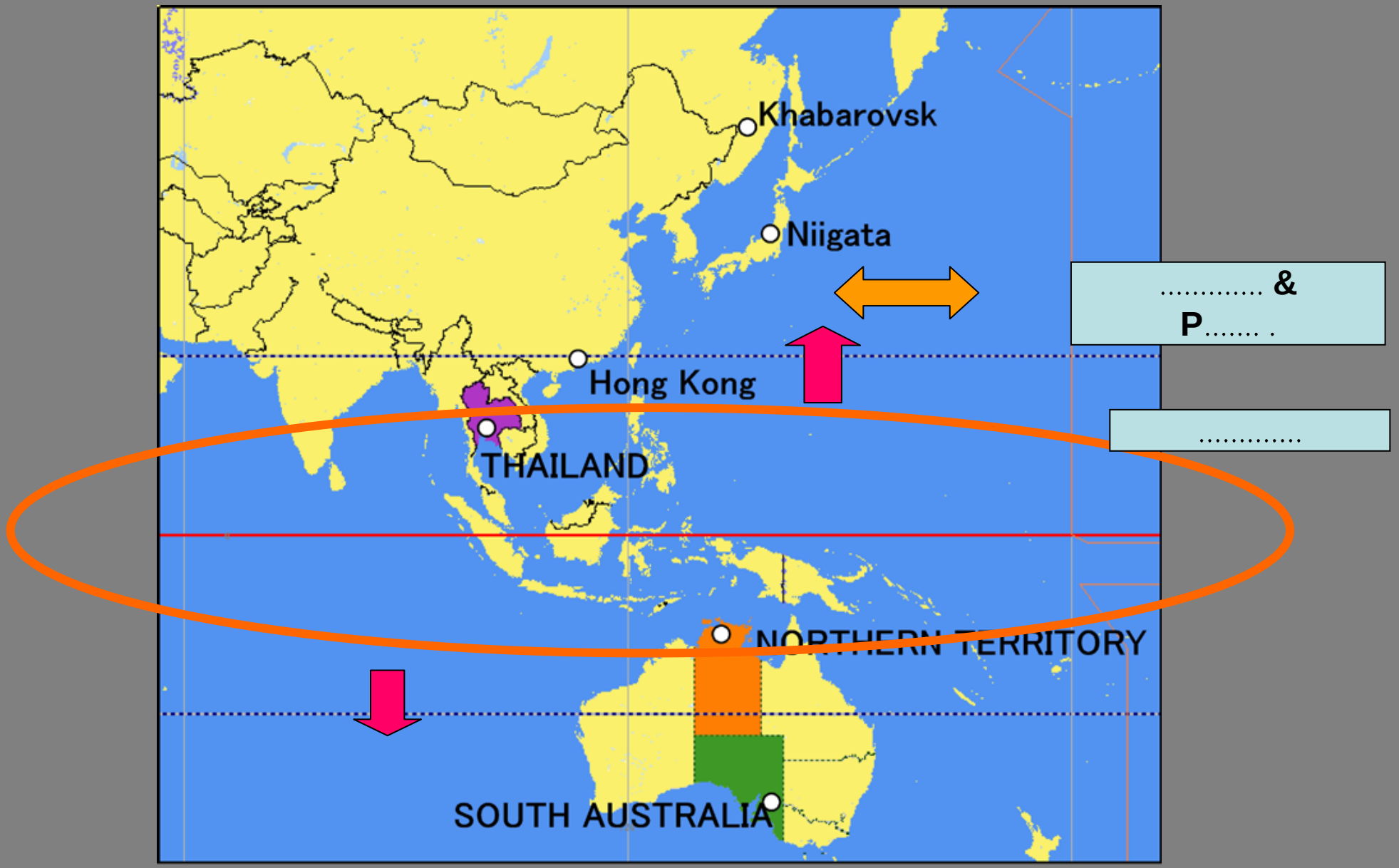
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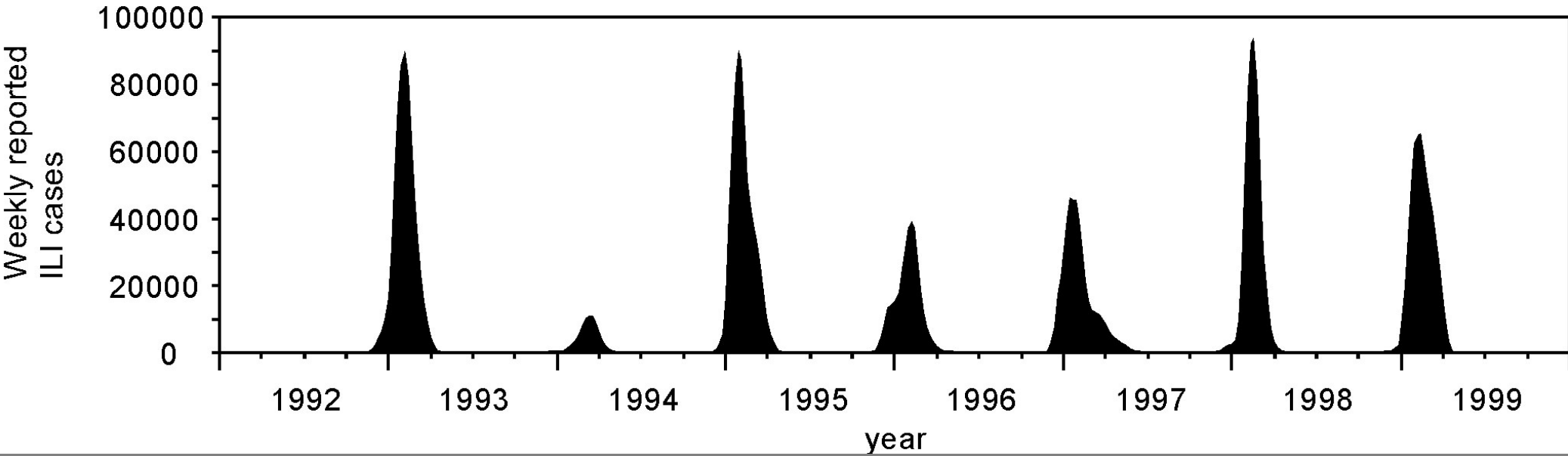
Spatial patterns of influenza virus infections in Japan, using a geographical information system (GIS)

Timing of peak influenza virus activity by week

Sakai, Emerging Infect Dis. 10;1822-26, 2004

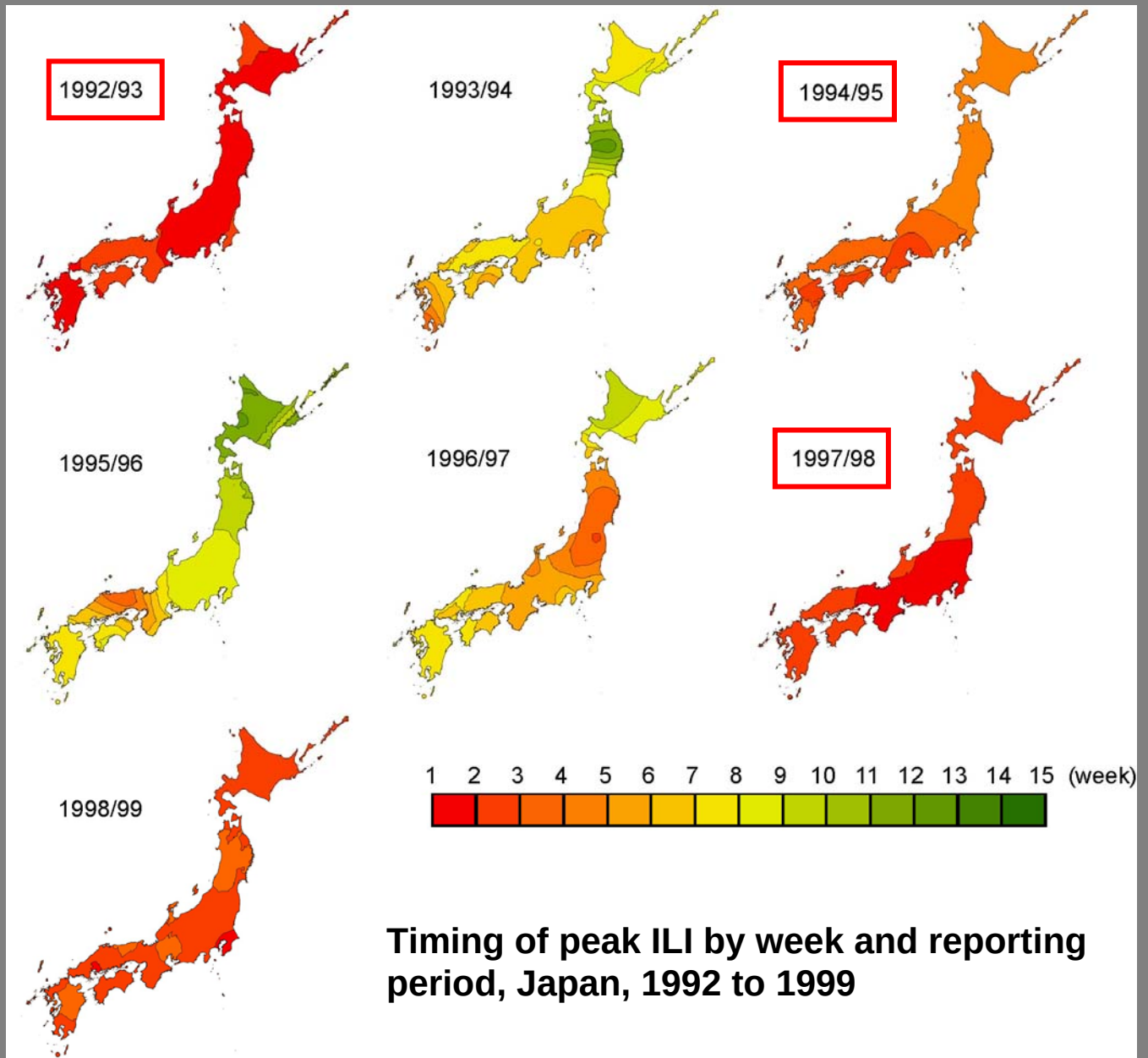
Moving average of weekly reported ILI cases in Japan

H3N2 B | H3N2 | H3N2 B | H1N1 | H3N2 B | H3N2 | H3N2 B



A/H3N2: A/Kitakyusu/159/93 | A/Wuhan/359/95 | A/Sydney/5/97

Timing of peak ILI epidemic activity by week in Japan



Timing of peak ILI by week and reporting period, Japan, 1992 to 1999

Two spreading patterns of epidemics:

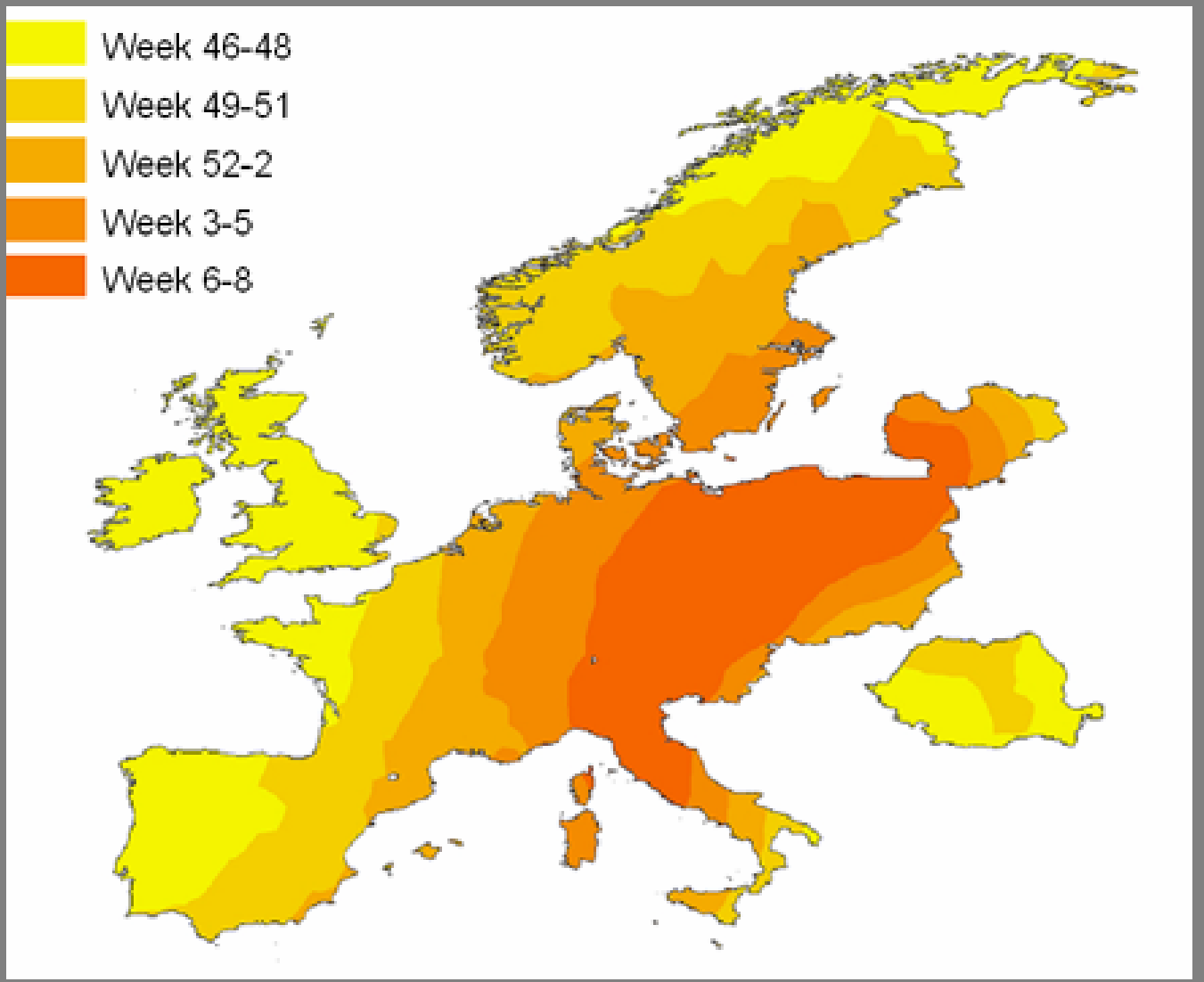
1) Monotonous spreading patterns;

peak influenza activity covered all Japan within 3 to 5 weeks in large epidemics with new antigenic variants of A/H3N2

2) Multitonous spreading patterns;

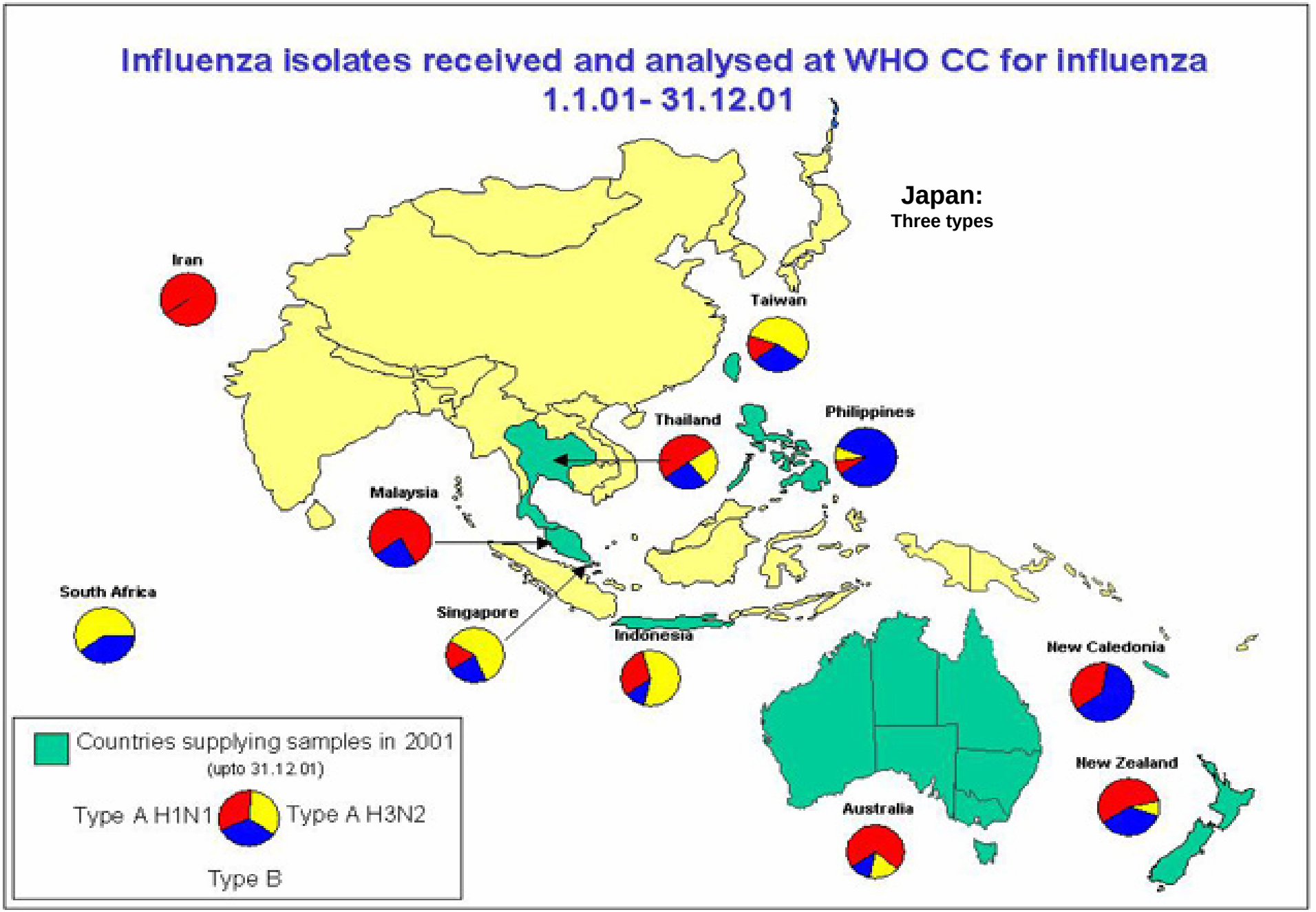
the peak influenza activity covered within 12 to 15 weeks in small epidemics without new variants in the other five seasons

- **Peak influenza activity mostly started in Prefectures or areas of western, central part of Japan during seven seasons except the 1996/97 season.**

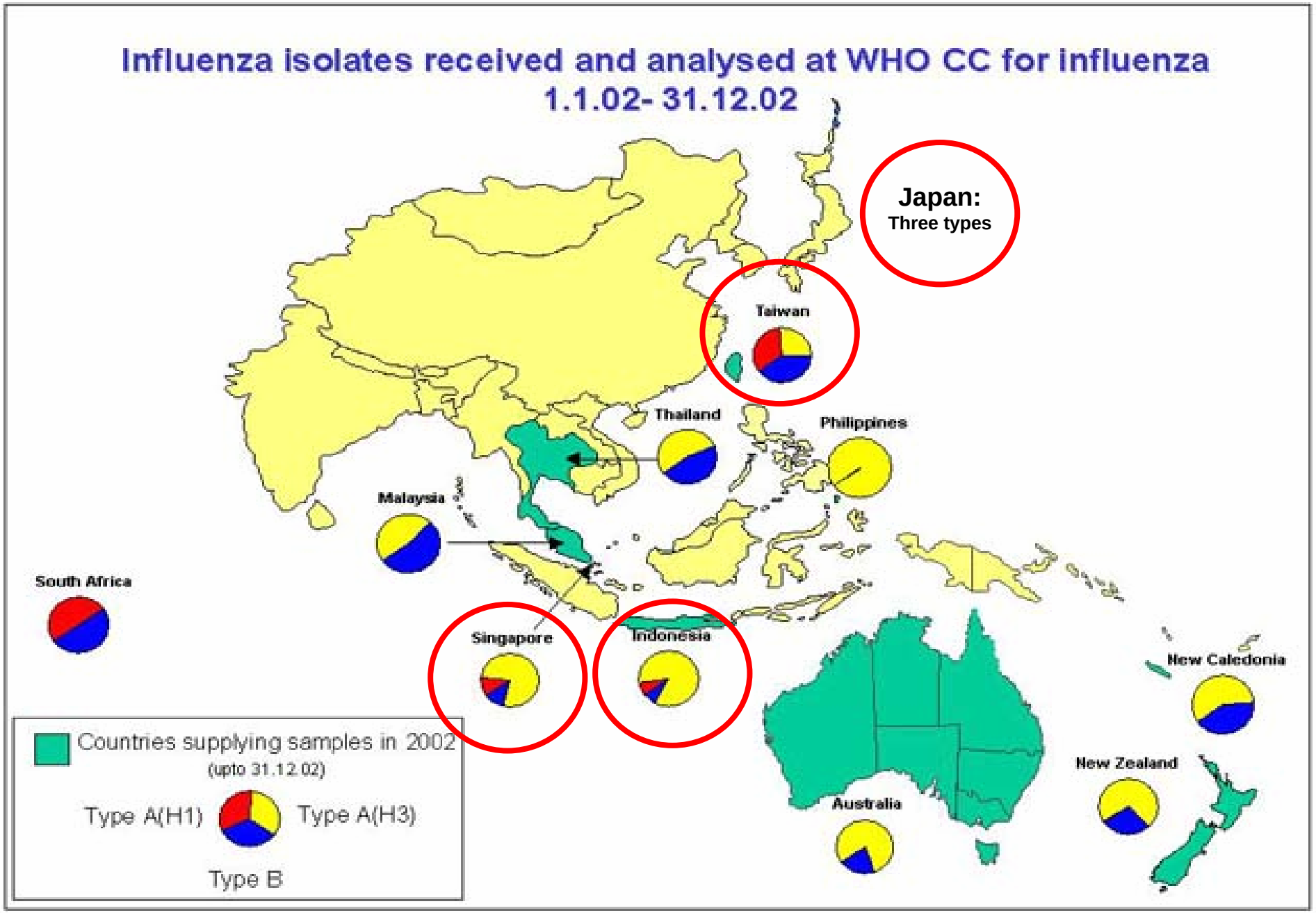


The kriging map clearly demonstrated possible west-east as well as south--north spread of influenza across Europe in the season.

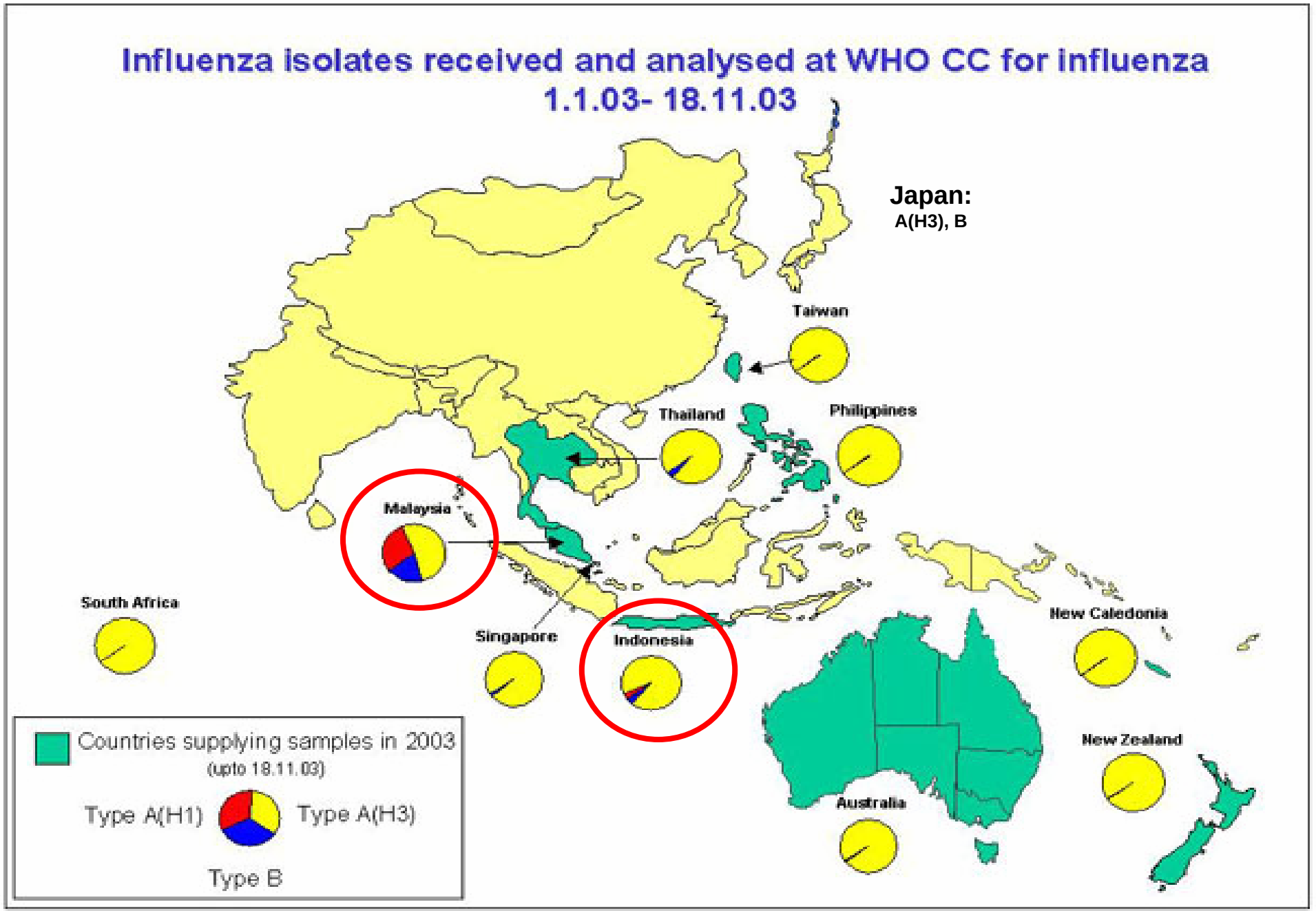
- **There is a paucity of data from tropical and subtropical countries regarding the relative importance of influenza in contributing to epidemic and sporadic disease.**
- **Understanding the epidemiology of influenza viruses in this region is important to document the potential burden of disease, compared with that of other respiratory illnesses, such as bacterial pneumonia.**
- **Surveillance activities can provide useful baseline data for measuring local epidemics and can generate critical information regarding the circulation strains that could have an impact on the annual selection of appropriate vaccine strains (i.e. Northern vs. Southern hemisphere formulation).**



WHO Collaborative Center, Melbourne



WHO Collaborative Center, Melbourne



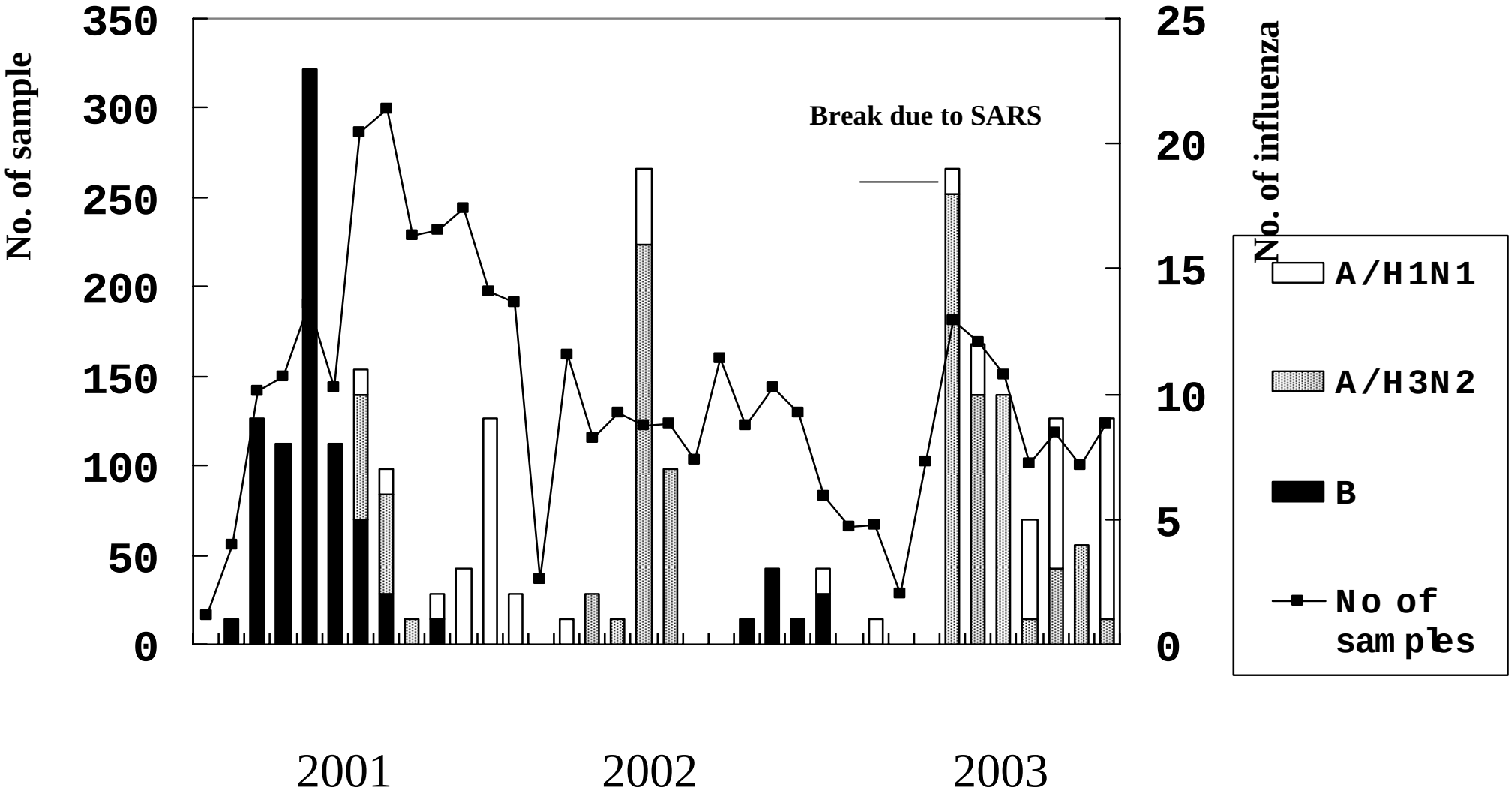
WHO Collaborative Center, Melbourne

Epidemiological study in tropical and subtropical countries

- **The WHO Influenza Program was established in 1952.**
  4 WHO Collaborating Centers
  (USA, UK, Australia, and Japan)
  112 national centers in 83 countries

- **Tropical and subtropical counties showed the inadequacy of surveillance due to lack of the requisite epidemiological and laboratory capacity**

Monthly distribution of influenza viruses in Hanoi, Viet Nam, from 2001 to 2003.



Hot rainy seasons and winter: "Acute respiratory syndrome"


Hanoi
West highland
JSPS project:Niigata and Nagasaki Univ.

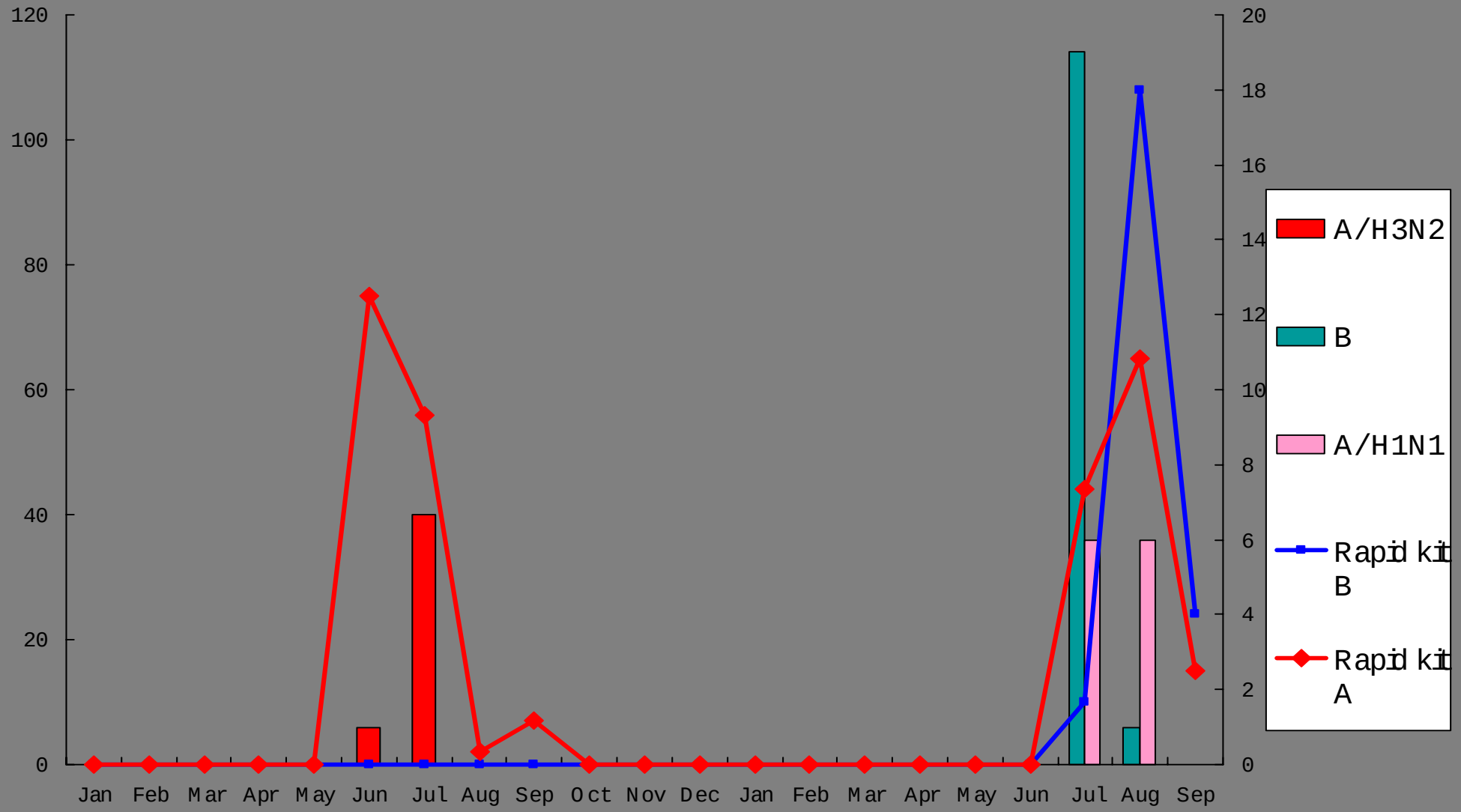
Establishment of influenza laboratory facility in Lusaka, Zambia (JICA Project: 1989-2006)

- **Laboratory condition**
  - **Shortage of staff**
  - **Small scale of laboratory facility**

- **Target infections**
  - **Influenza**
  - **RS viruses**
  - **Rotavirus**
  - **Viral hepatitis**
  - **Measles**
  - **Poliovirus**
  - **HIV/AIDS**
  - **Avian influenza**

Priority ?

Influenza seasonality in Yangon



2004

2005

Rainy season

Emerging of amantadine resistant A/H3N2 strains (Fujian-like strains)

Molecular technique

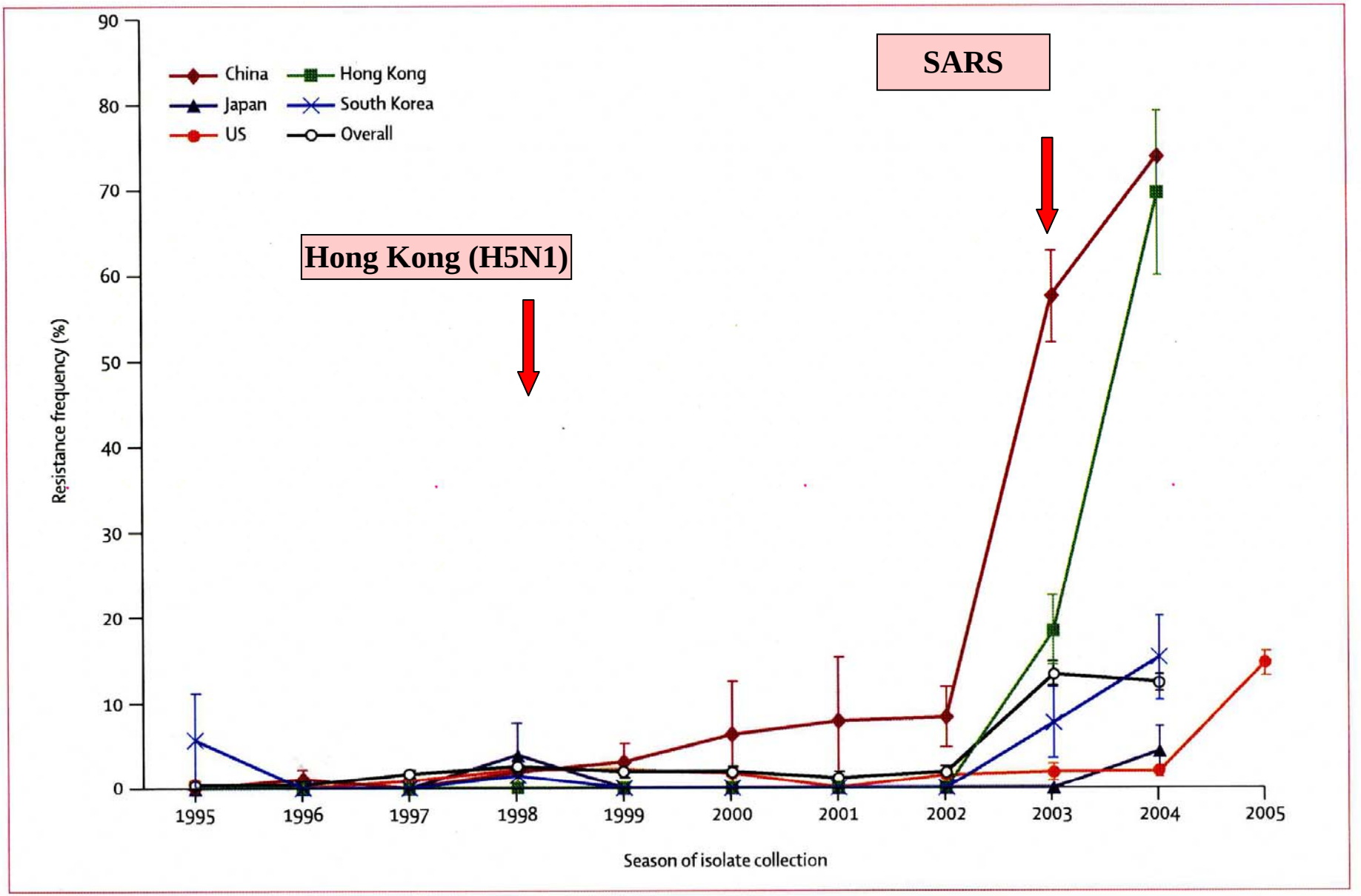
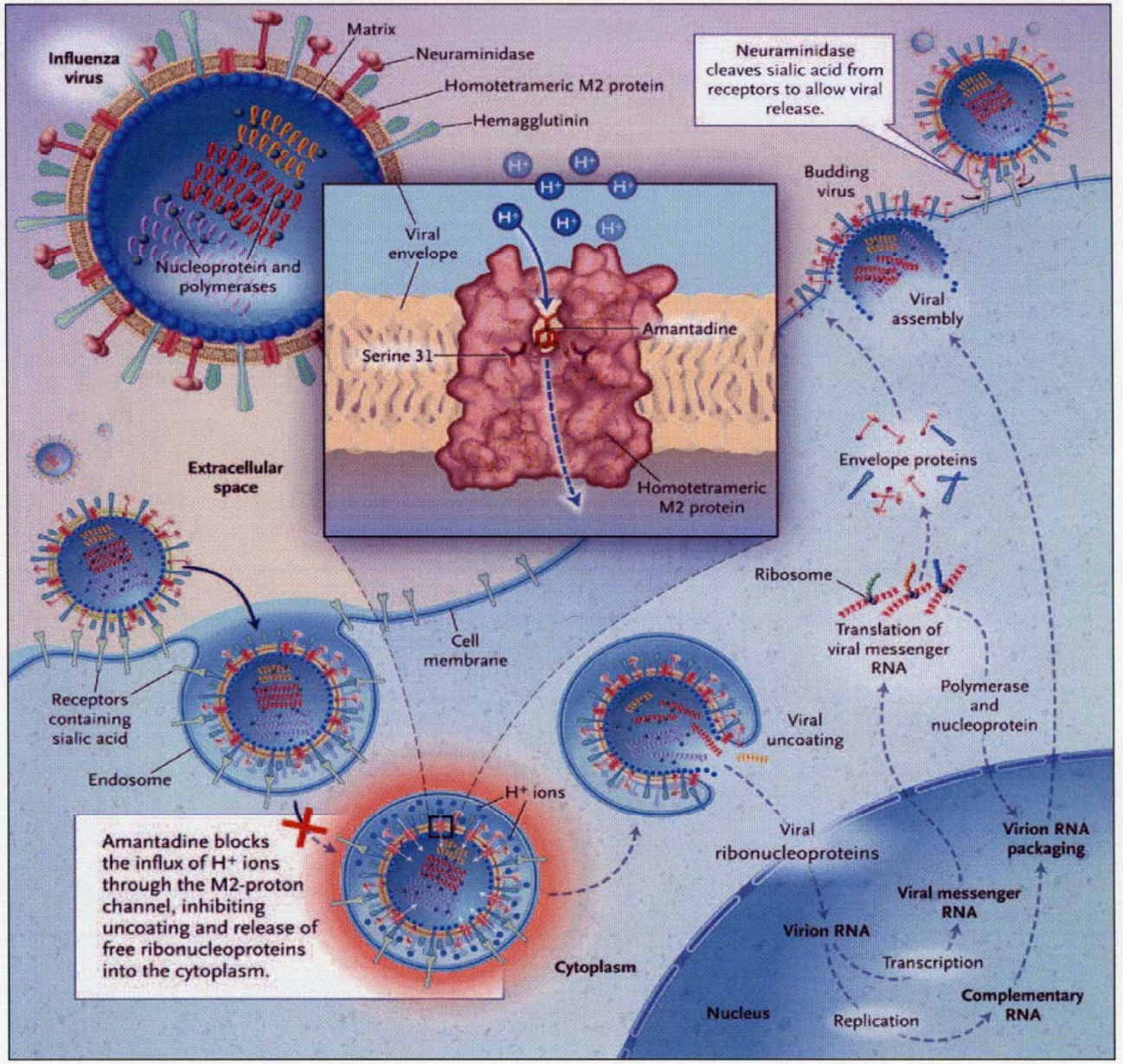


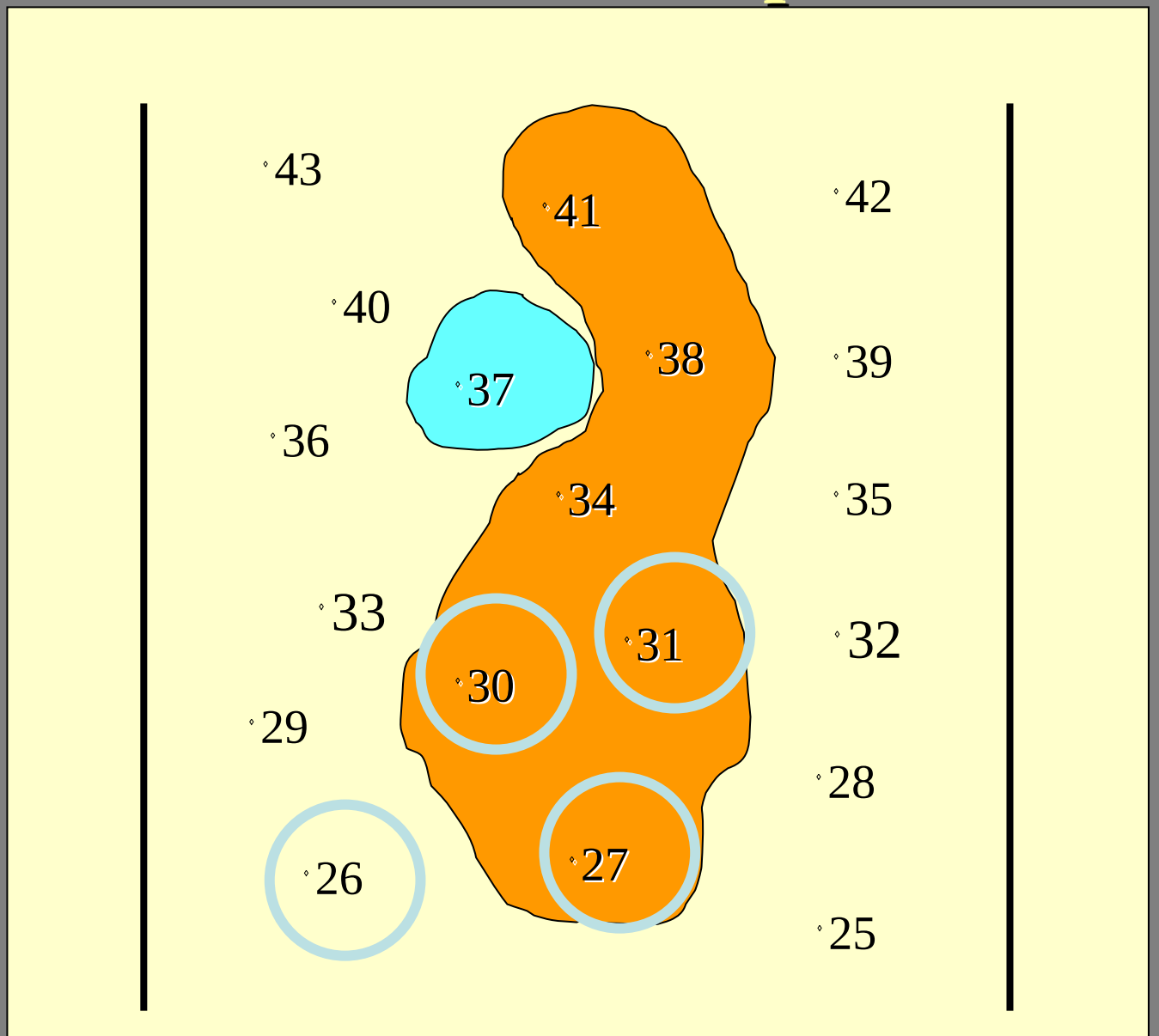
Figure: **Trend of adamantane-resistant H3N2 viruses, 1994–2005**

Each point represents the percentage of resistant viruses of the total tested. Error bars represent the 95% CI for the proportion of resistant viruses out of the total tested.



Mechanism of Action of and Development of Resistance to M2 Inhibitors.

Postulated projection of transmembrane domain in M2 protein



L.Holsinger et al.
Influenza A virus M2 ion channel protein: a structure-function analysis
J. Virology 68:1551-63.1994

Prevalence of amantadine resistant H3N2 strains in Niigata city

Season	No. of resistant H3N2/No. of isolates (%)
1997/98	0 / 33 (0)
1998/99	0 / 22 (0)
1999/00	6 / 179 (3.4)
2000/01	0 / 80 (0)
2001/02	1 / 104 (1.0)
2002/03	2 / 179 (1.1)
2003/04	1 / 175 (0.6)
2004/05	1 / 336 (0.3)
2005/06	91 / 153 (59.5)

Prevalence of amantadine resistant H3N2 strains from 2002/03 to 2005/06 season in Okinawa, Japan

Season	No. of Resistant H3N2/No. of isolates (%)
2002/03	4/50 (8.0)
2003/04	4/44 (9.1)
2004/05	21/31 (67.7)
2005/06	28/38 (73.7)

They had no history of prior amantadine administration

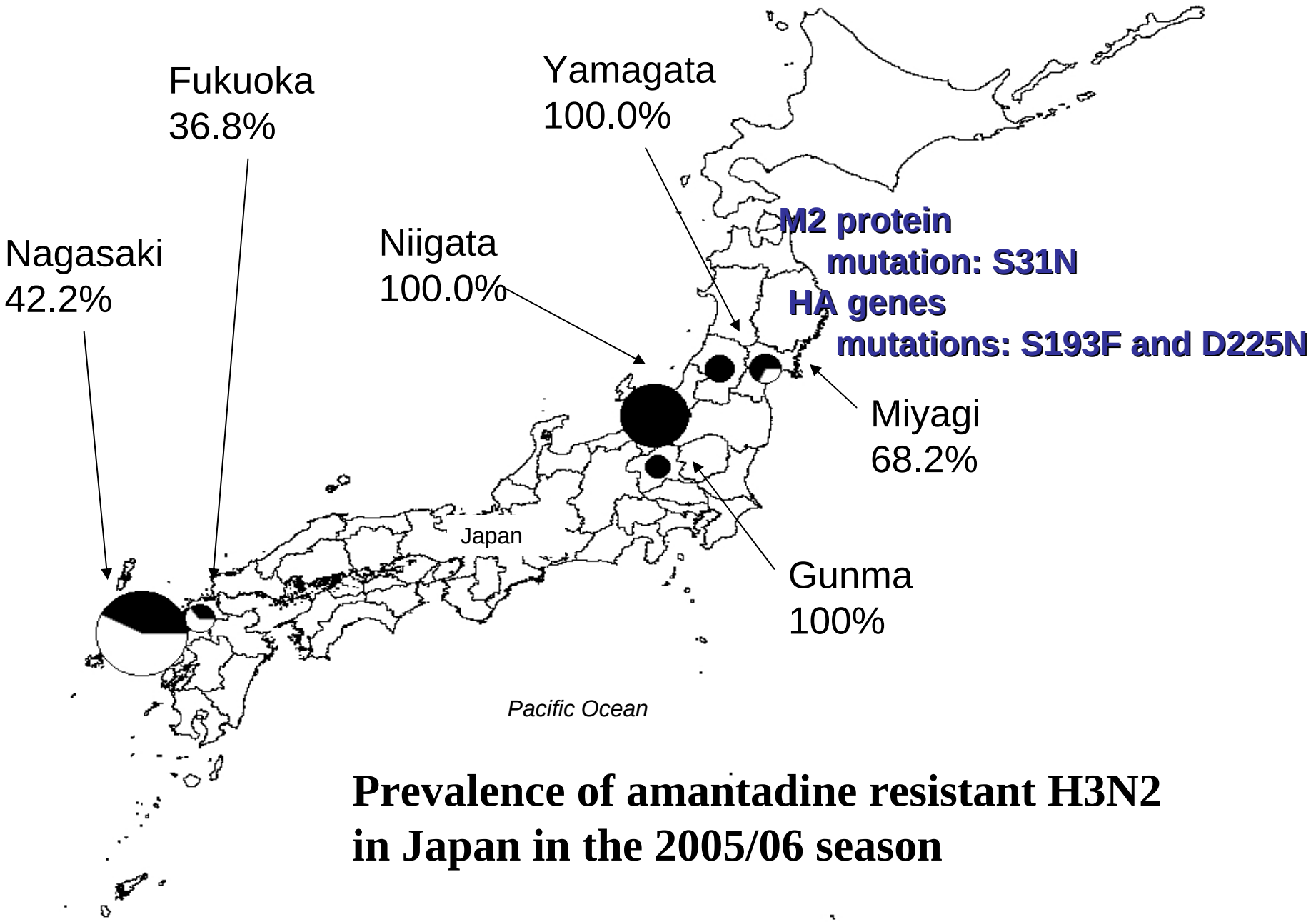
Prevalence of amantadine resistant H3N2 strains in the2005/06 season

Niigata city

Subtype	Am resistant strains /Isolated strains	%
H1N1	0 / 50	0.0
H3N2	91 / 102	89.2

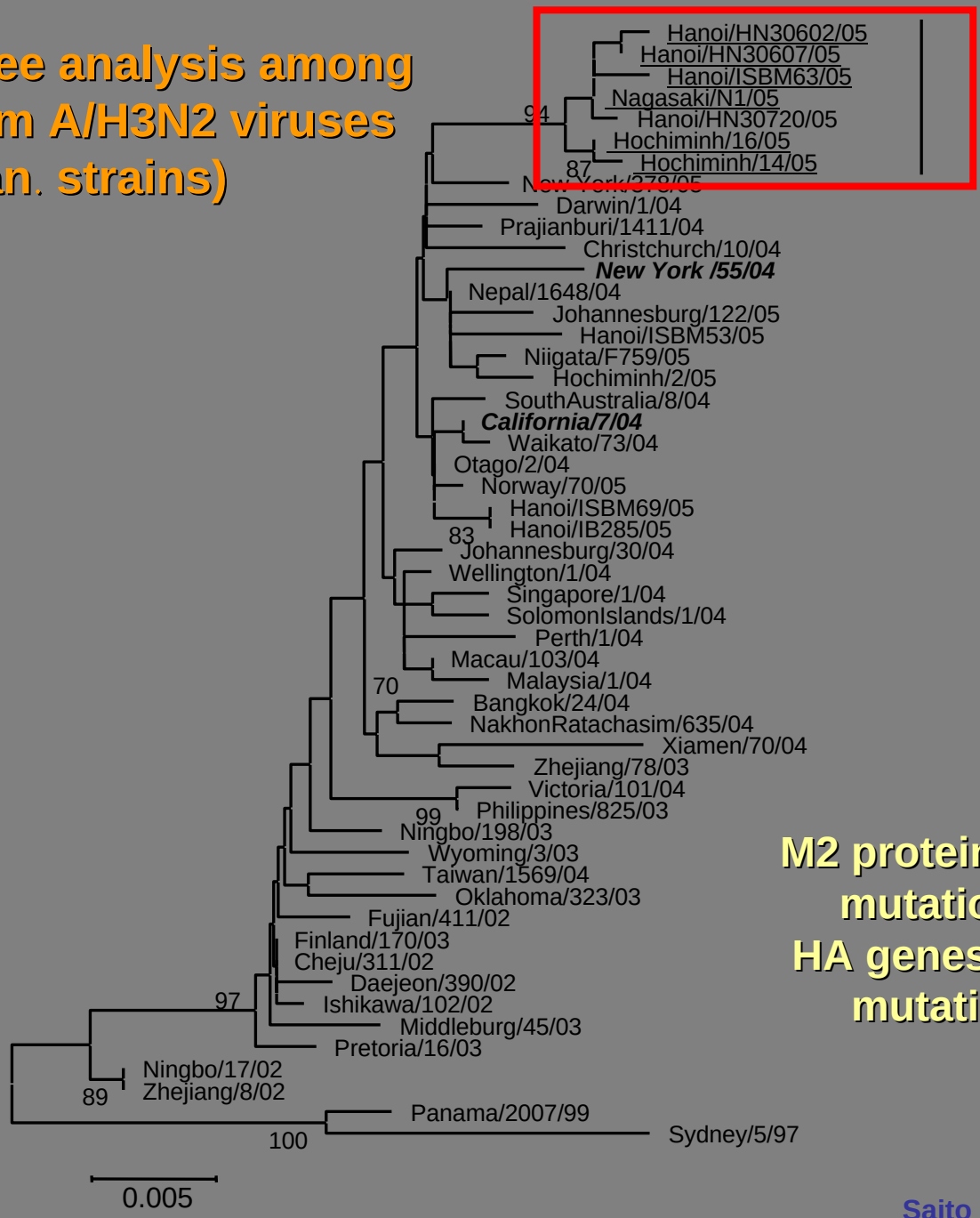
Nagasaki Pref.

Subtype	Am resistant strains /Isolated strains	%
H1N1	0 / 6	0.0
H3N2	59 / 189	31.2



Prevalence of amantadine resistant H3N2 in Japan in the 2005/06 season

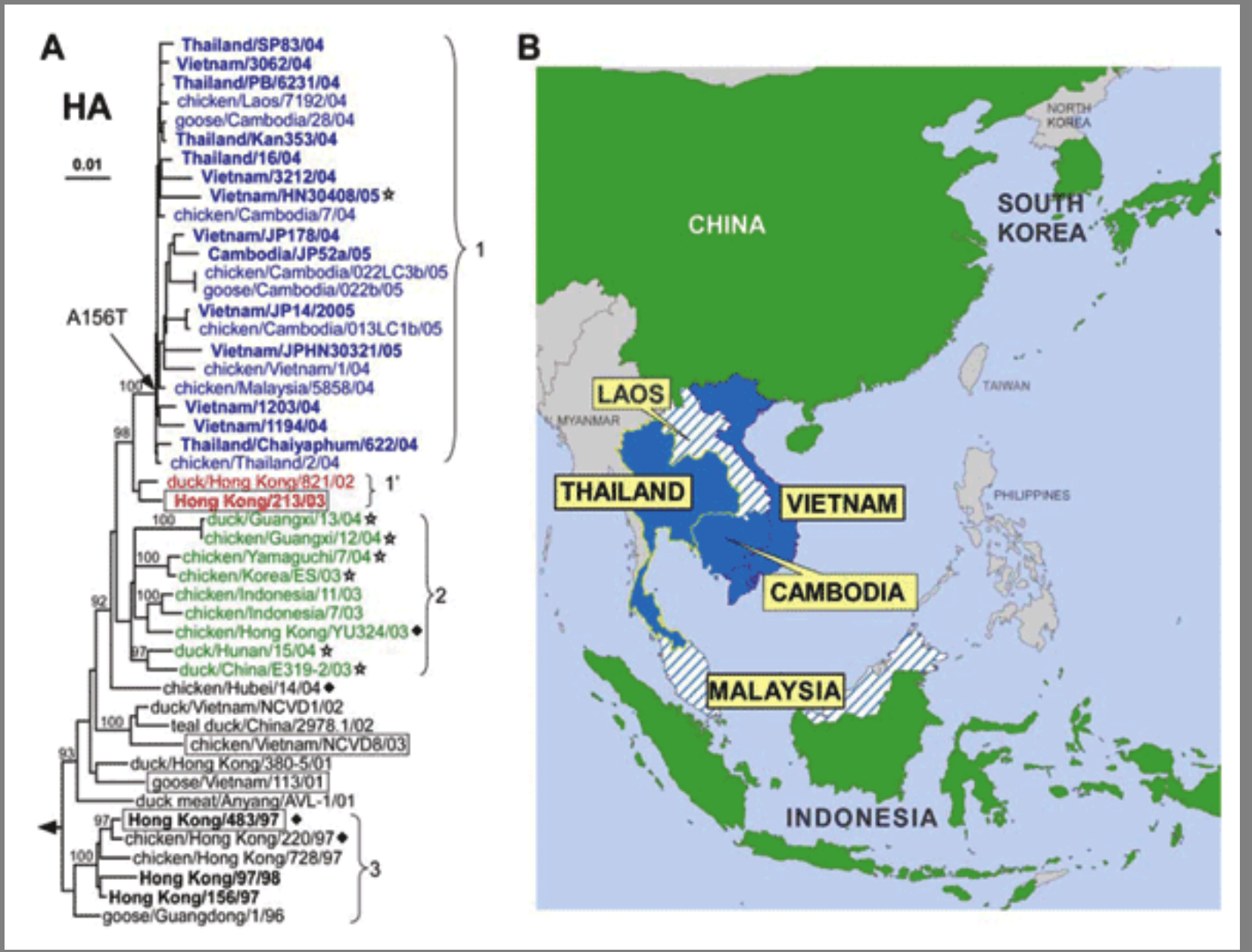
Pylogenetic tree analysis among HA genes from A/H3N2 viruses (.Fujian. strains)



Clade .N.
(amantadine resistant)

M2 protein
mutation: S31N
HA genes
mutations: S193F and D225N

Saito R et al. Tohoku J Exp Med, 2006


A
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Thailand/SP83/04
Vietnam/3062/04
Thailand/PB/6231/04
chicken/Laos/7192/04
goose/Cambodia/28/04
Thailand/Kan353/04
Thailand/16/04
Vietnam/3212/04
Vietnam/HN30408/05
chicken/Cambodia/7/04
Vietnam/JP178/04
Cambodia/JP52a/05
chicken/Cambodia/022LC3b/05
goose/Cambodia/022b/05
Vietnam/JP14/2005
chicken/Cambodia/013LC1b/05
Vietnam/JPHN30321/05
chicken/Vietnam/1/04
chicken/Malaysia/5858/04
Vietnam/1203/04
Vietnam/1194/04
Thailand/Chaiyaphum/622/04
chicken/Thailand/2/04
duck/Hong Kong/821/02
Hong Kong/213/03
duck/Guangxi/13/04
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chicken/Yamaguchi/7/04
chicken/Korea/ES/03
chicken/Indonesia/11/03
chicken/Indonesia/7/03
chicken/Hong Kong/YU324/03
duck/Hunan/15/04
duck/China/E319-2/03
chicken/Hubei/14/04
duck/Vietnam/NCVD1/02
teal duck/China/2978.1/02
chicken/Vietnam/NCVD8/03
duck/Hong Kong/380-5/01
goose/Vietnam/113/01
duck meat/Anyang/AVL-1/01
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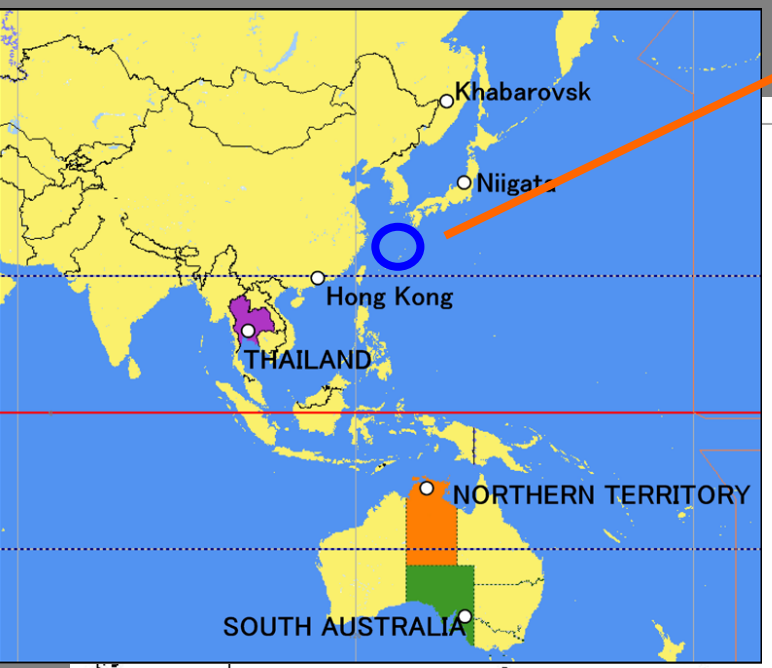
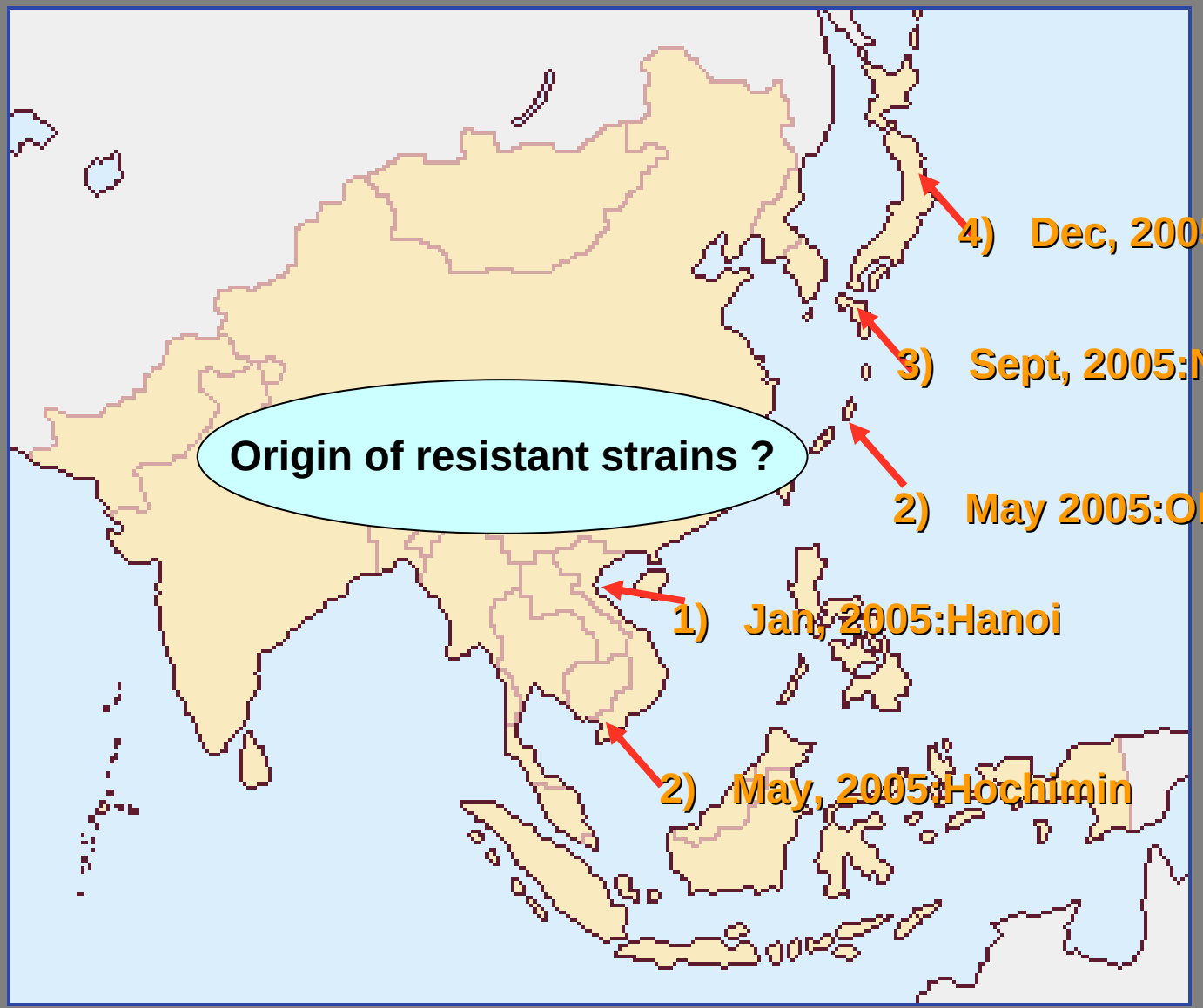
PHILIPPINES
MALAYSIA
INDONESIA

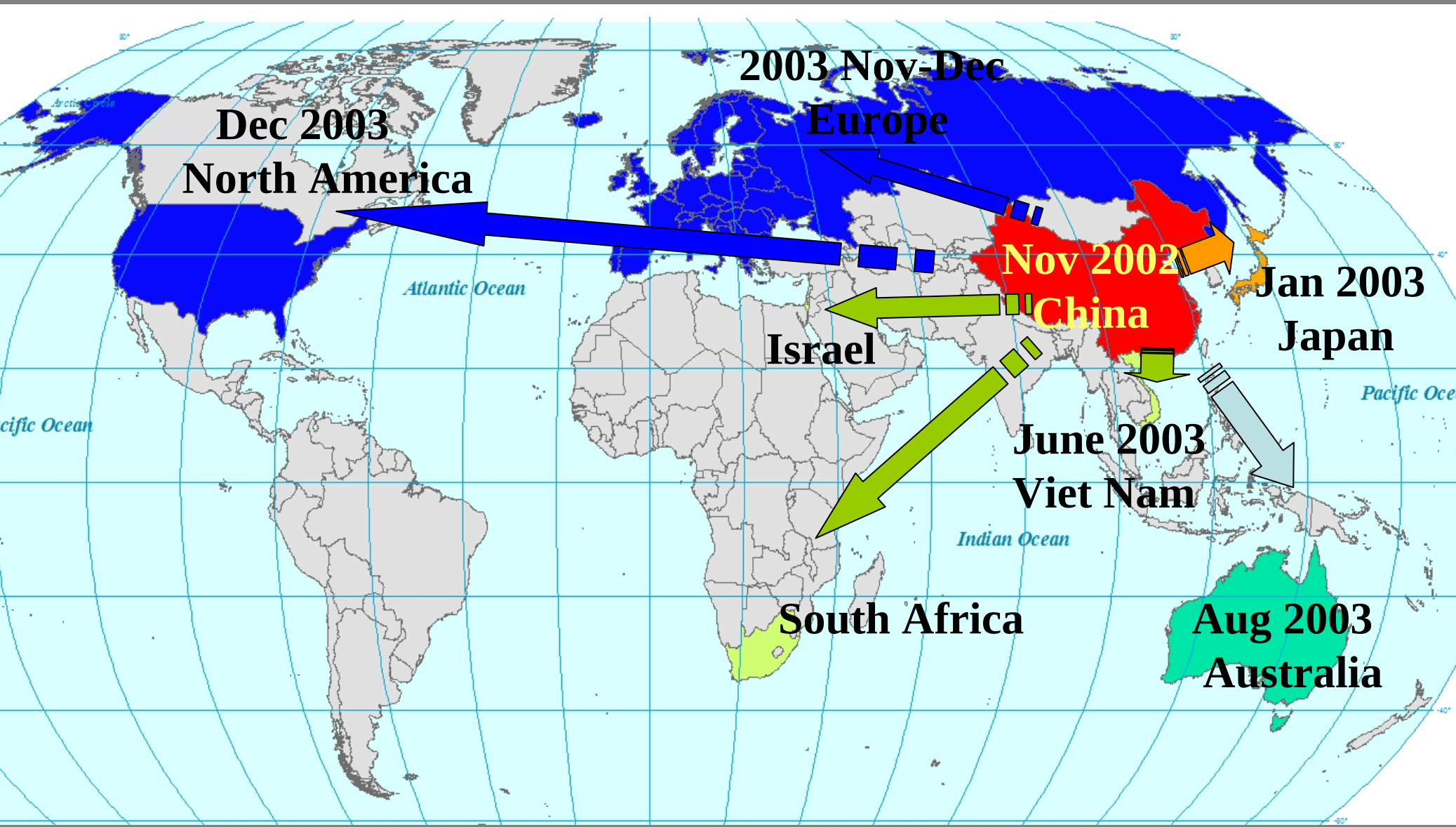
Off-seasonal Influenza outbreak, Okinawa, in 2005



Amantadine resistant A/H3N2 strains (Clade “N”) in several areas in 2005

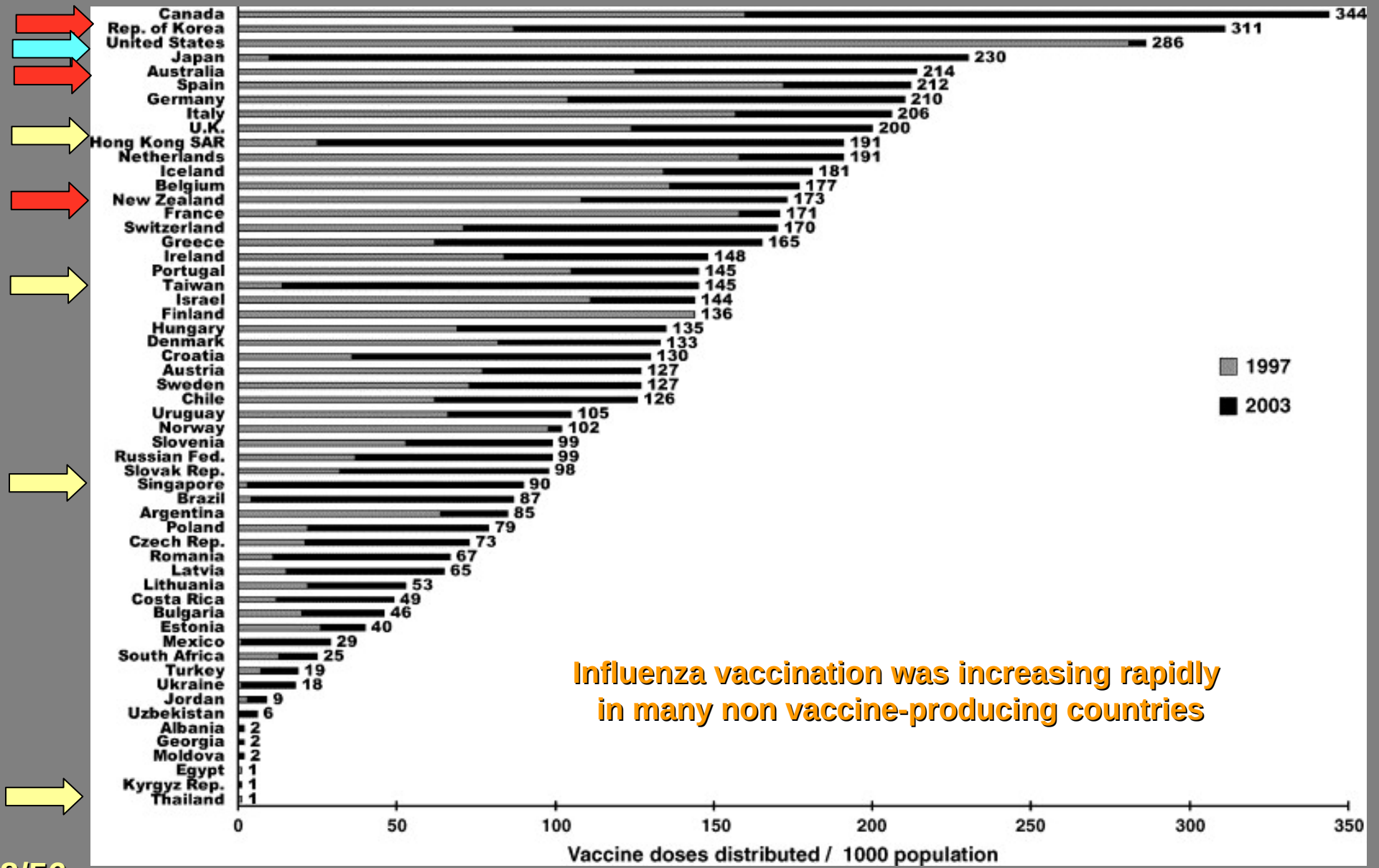


Circulation of A/Fujian/411/2002(H3N2)-like strain around the world



Influenza Vaccination in Asia

Influenza vaccine distribution in 56 countries, 1997 and 2003.



Influenza vaccination was increasing rapidly in many non vaccine-producing countries

- **Present worldwide manufacturing capacity for trivalent seasonal vaccines was estimated to be around 420 million doses per year. That capacity would fall far short of the demand during pandemic.**
- **Increased use of vaccines for seasonal influenza, in line with WHO targets, was put forward as the surest and most sustainable way to increase manufacturing capacity, as the same facilities were used to produce pandemic vaccines.**
- **Influenza vaccination was increasing rapidly in many non vaccine-producing countries, and this change has important implications for pandemic vaccination.**

Procurement of influenza vaccine

- **Globally expansion of vaccine production facilities ?**
  private or national manufacturers
  self-sufficient in vaccine
  using donated or purchased vaccine
- **Local vaccine production**
  1. Political commitment of vaccine production from government (leadership)
  2. Epidemiological data: disease burden
  3. Achievement of large-scale vaccine production
  4. QA/QC of vaccine

- **Integration into the EPI activity**

WHO Western Pacific Regional Office 1985-1990

- **Hepatitis B vaccine**
  (plasma-derived inactivated vaccine)
  1. Local vaccine production:
  China, Vietnam
  2. high-titre HBsAg positive collection scheme
  Pacific islands countries

Locally collected plasma was sent by the countries involved to Japan, where the Kitasato Institute (the WHO collaborating Center) processed it into vaccine. The vaccine was then returned to the countries which had collected the plasma.

"The cost of HB vaccines has dramatically declined from US$20 to US$0.5-2.0 per dose due to the above scheme and genetically-engineered HB vaccine."

Members; Task force meeting
Gust ID, Coursaget P, Yano M, Beasley P, Maynard JE, Xu ZY
Ghendon Y, Suzuki H, Umenai T, Nakajima H.
(China, Korea, Vietnam, Sour pacific countries, New Zealand)

WHO Western Pacific Regional Office 1985-1990

- **Japanese encephalitis vaccine**

  (mouse brain-derived inactivated vaccine)

  1. Local vaccine production:

  Vietnam

The "technology transfer" was done in collaboration with BIKEN Foundation and the WHO collaborating Center in Nagasaki

Members: Task force meeting

Igarashi A, Oya A, Fukai K, Shope RE, Fournier MJ, Yu YX

Petriciani JC, Esparza J, Suzuki H, Umenai T, Nakajima H.

The local vaccines project Vietnamese children

VABIOTECH (The company for vaccine and biological production No.1, National Institute of Hygiene and Epidemiology)

- **Produces Hepatitis B vaccine (both human plasma derived and recombinant); Japanese encephalitis vaccine (Mice brain derived-Nakayama strain); Oral whole cell cholera vaccine; Rabies vaccine (suckling mice brain derived) vaccine; Hepatitis A inactivated vaccine (Tissue culture).**

- **During the last 10 years, with the support from the Ministry of Health (MOH), Ministry of Science and Technology (MOST), VABIOTECH has been successful in conducting several National R&D Subjects and were highly appreciated and brought about wide-ranged Socio-Economic effectiveness in the Strategy of Control and Prevention of some infection disease in Vietnam :**

R & D Activities in new vaccine development

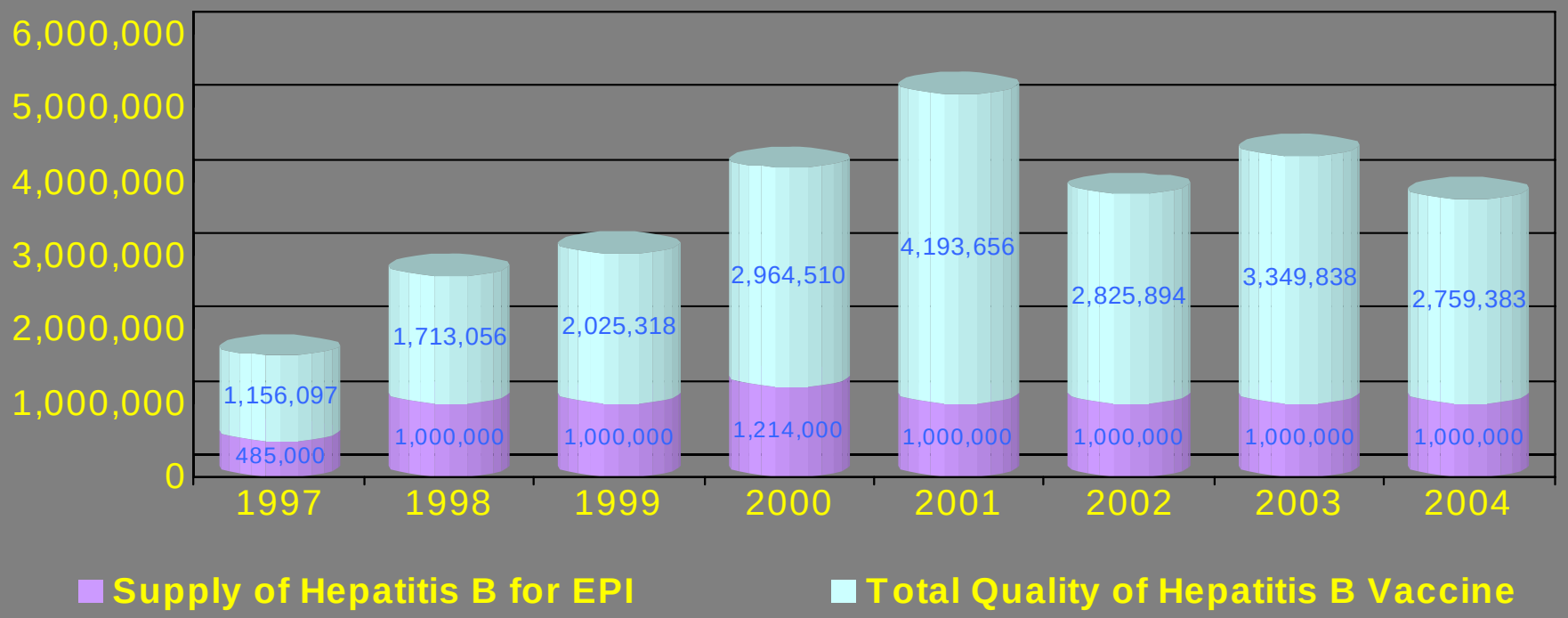
- **Apply The above mentioned Technologies in Vietnam Production Conditions with a numbers of initiatives and creation in each step of Production Process in order to produce the product with high quality and meet all WHO′s and Japanese Requirement for this vaccine.**

- **Have been successfully produced Hepatitis B vaccine, JE and Cholera vaccines and supplied for The National EPI for Immunization of new born. Millions doses of each vaccine were produced and supplied for domestic demand and for The National EPI Program since 1997.**

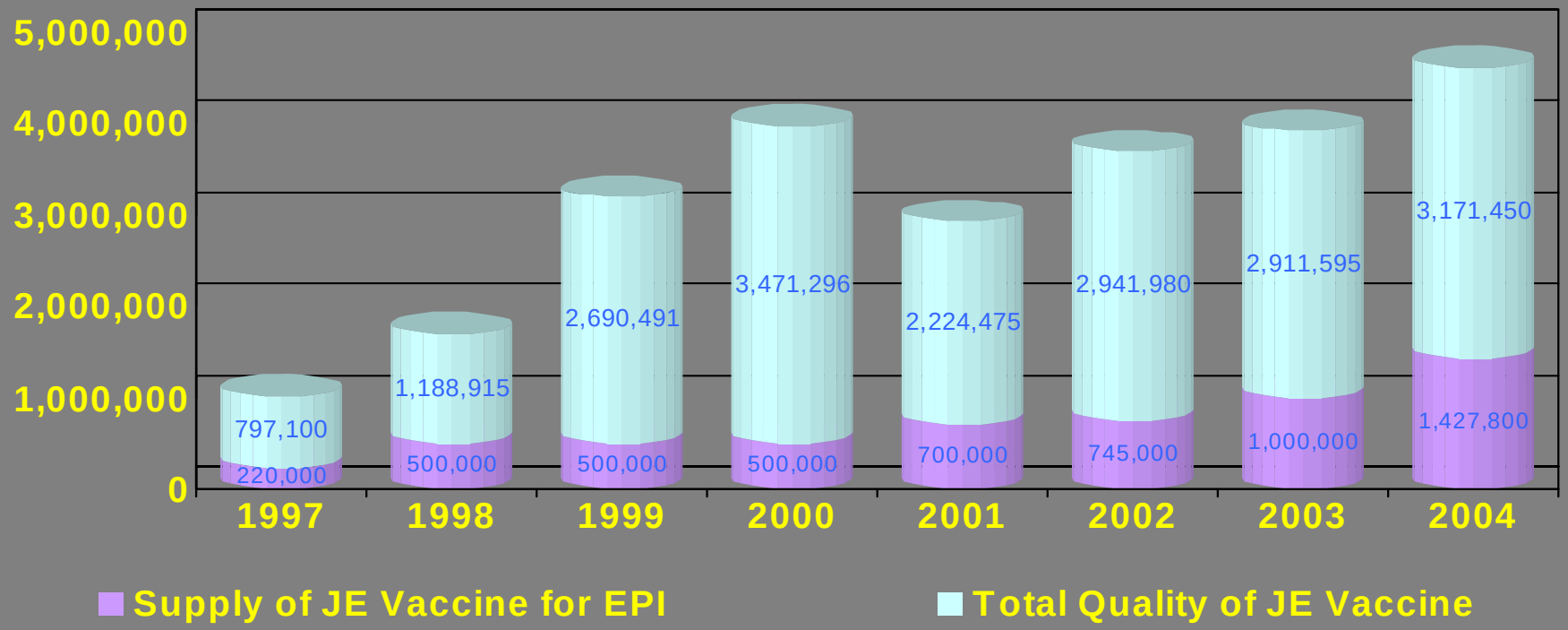
R & D Activities in new vaccine development

- **September 4, 1997 The vaccines were licensed under The Decision of Ministry of Health.**
- **August 18, 1997 Government decided to introduce the vaccines into The National EPI Program for free of charge vaccination of new born.**
- **1996-1998, Based on feasibility study and the important of the vaccines for prevention of Vietnamese children, Ministry of Science and Environment continues to support and invests for National Pilot Production Projects coded KHCN-11-DA1, KHCN-11-DA2 and DA1 for scaling up the production capacity of each vaccine.**

Consumption of Hepatitis B vaccine



Consumption of Japanese Encephalitis Vaccine

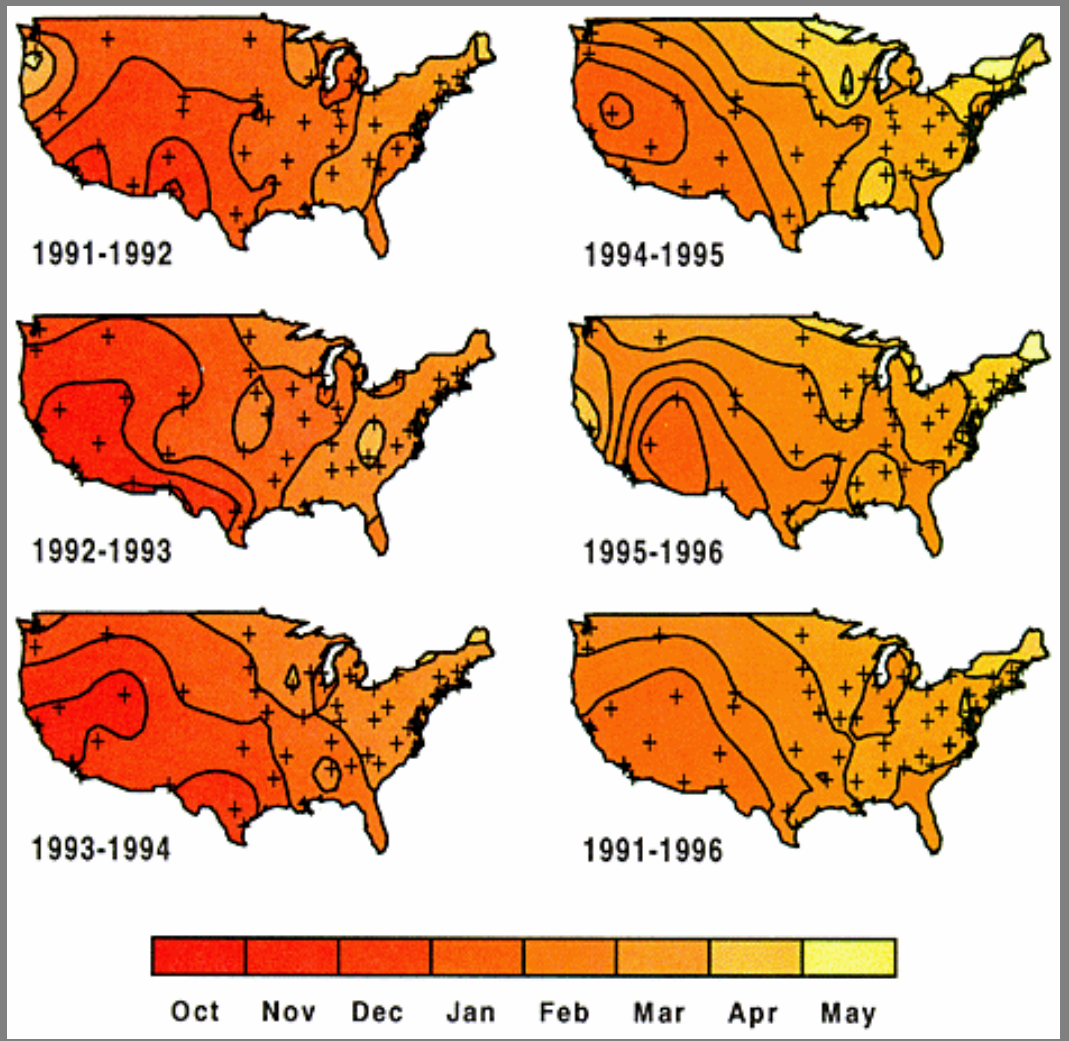


International Coordination

Acknowledgement

- Niigata Univ.: Saito R. Sakai T
- Nagasaki Univ.: Masaki C
- Infectious Disease Surveillance Center, National Institute of Infectious Diseases, Tokyo: Okabe N
- Shimomura Clinic
- National Institute of Hygiene and Epidemiology, Hanoi, Vietnam: Mai QL
- Pasteur Institute, Ho Chi Minh City, Vietnam: Tu VP
- Sendai Virus Center: Nishimura H
- Okinawa Prefectural Institute of Health and Enviromental Sciences
- Yamagata Prefectural Institute of Health and Enviromental Sciences

Kriged Map for Rotavirus Activity



Timing of peak rotavirus activity by month and reporting period, United States, 1991 to 1996. +, locations of participating NREVSS laboratories.

Torok TJ, Kilgore PE, Clarke MJ, Holman RC, Bresee JS, Glass RI.
Visualizing geographic and temporal trends in rotavirus activity in the United States, 1991 to 1996.
Pediatr Infect Dis J. 1997 Oct;16(10):941-6.

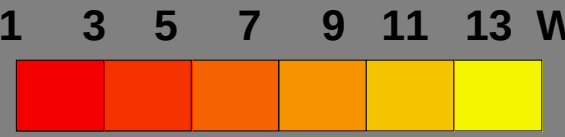
Definition

- **The peak week :**

  The biggest number of reported ILI cases/sentinel/week in individual prefectures

- **The first week:**

  In any one of 46 prefectures reached a peak of epidemic in the season. In rest of prefectures, peak weeks were numbered by difference between “the first week” and mode week of each prefecture.



Isolates and nasopharyngeal swabs collected in Nagasaki, Japan, Hanoi and Ho Chi Minh City, Vietnam in 2005, and selected strains in genetic database were included in the analysis.

Strains labeled with closed circles indicated amantadine resistant strains possessing S31N mutation in M2 protein, and open circles sensitive. Presence of HA motif in amantadine resistant strains, mutations at positions 193, serine to phenylalanine (S193F), and 225, asparatic acid to asparagine (D225N), were shown by arrows.

Phylogenetic trees were inferred from 467 nucleotide sequences by the neighbor-joining method. Bootstrap values > 70% are shown.

Influenza circulates in hot rainy seasons
Winter circulation also occur in subtropical climate

Type and subtypes similar in Asia
Antigenic and genetic characterization similar

- **Influenza is a highly contagious acute respiratory disease of global importance that has caused epidemics and pandemics for centuries. The phasing and geographical spread of influenza pandemic has important implications for future planning, and complete global spread is now likely to increase travel and urbanization. However, influenza spread in space even within one cycle of an epidemic is an important question.**
- **To better understand the movement and velocity of influenza epidemic spread in Japan, we used a GIS with several surveillance data.**