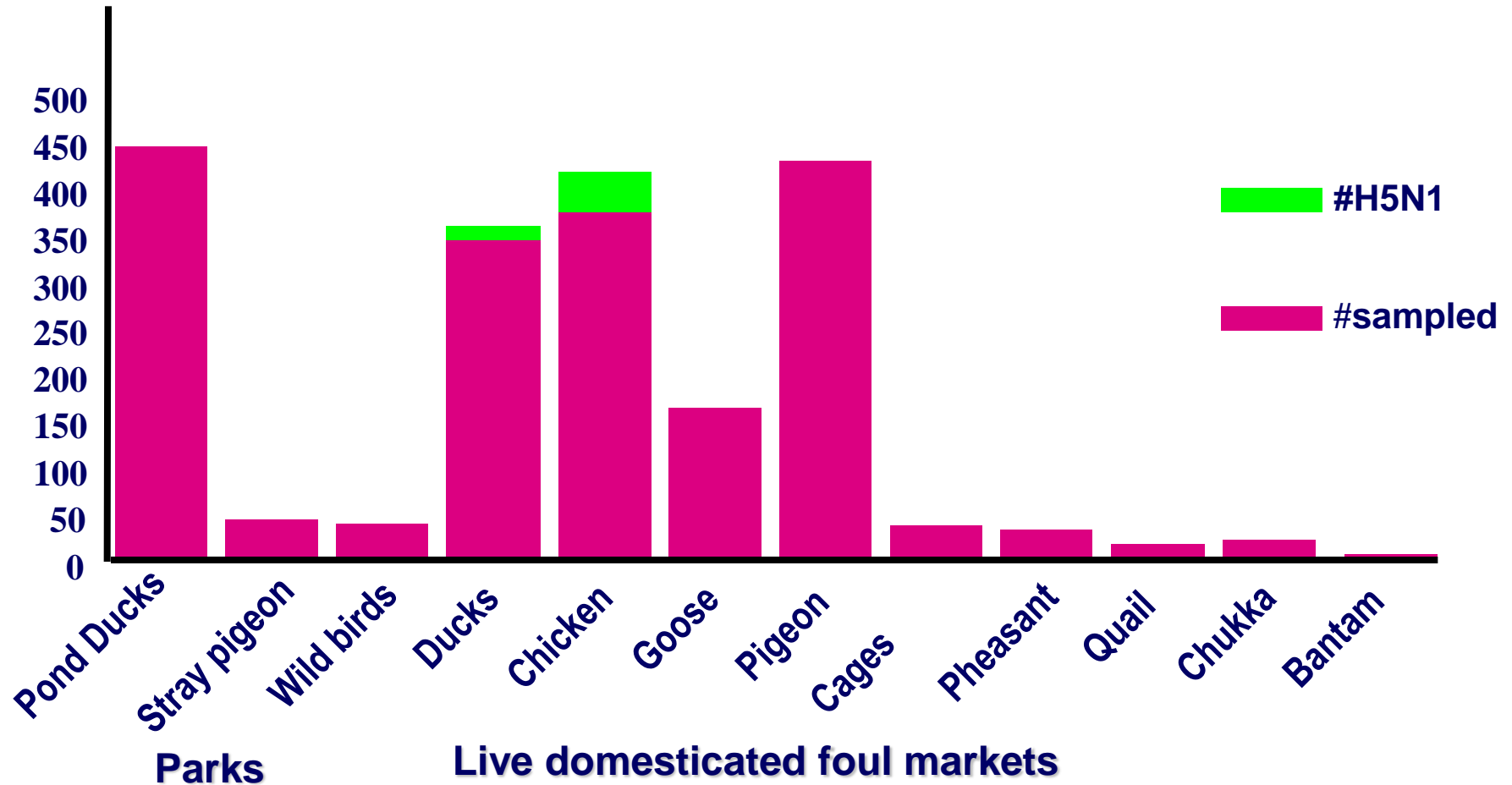


Trends of Pandemics in the 21st Century

H5N1 influenza, Hong Kong, 1997: 18 human infections/6 deaths



Source: HK University/WHO

H5N1 avian influenza

Or will viral reassortment occur as occurred in 1957 and 1968 pandemics?

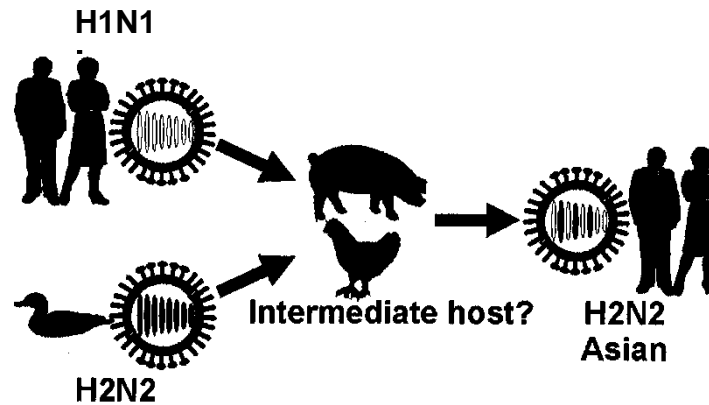


Fig. 2. Origin of the 1957 Asian influenza pandemic. The genomes of human H1N1 and avian H2N2 influenza viruses have probably reassorted in an intermediate host. The resulting H2N2 virus consisting of five gene segments of human origin and three of avian origin was the cause of the pandemic of 1957.

Reports of respiratory infection, China, 2002–2003

- 16 November, 2002
 - **Guangdong** : outbreak of respiratory illness/government recommending isolation of anyone with symptoms (**GPHIN**)
 - official government report of normal influenza B activity, 7 Dec. 2002
- 11 February, 2003
 - **Guangdong**: outbreak of atypical pneumonia among health workers (**GPHIN, text message WHO**)
 - official government report of atypical pneumonia outbreak with 305 cases and 5 deaths, influenza virus not isolated, 14 Feb. 2003
- 19 February, 2003
 - 33 year male and 9 year old son in Hong Kong reported with Avian influenza (H5N1), source linked to Fujian Province, China (**Global Influenza Surveillance Network**)

Intensified surveillance for respiratory infections, Asia, 2002–2003

- 26 February
 - **Hanoi:** 48-year-old business man with high fever ($> 38^{\circ}\text{C}$), atypical pneumonia and respiratory failure with history of previous travel to China and Hong Kong (**WHO country office**)
- 4–5 March
 - **Hong Kong and Hanoi:** 77 medical staff (Hong Kong) plus 7 (Hanoi) reported with atypical pneumonia, not influenza (**WHO team/liaison**)

First Global Alert: Atypical Pneumonia South Asia

WHO issues a global alert about cases of atypical pneumonia

12 March 2003

Cases of Severe Respiratory Illness may spread to hospital staff

12 March 2003 | GENEVA -- Since mid February, WHO has been actively working to confirm reports of outbreaks of a severe form of pneumonia in Viet Nam, Hong Kong Special Administrative Region (SAR), China, and Guangdong province in China.

In Viet Nam the outbreak began with a single initial case who was hospitalized for treatment of severe, acute respiratory syndrome of unknown origin. He felt unwell during his journey and fell ill shortly after arrival in Hanoi from Shanghai and Hong Kong SAR, China. Following his admission to the hospital, approximately 20 hospital staff became sick with similar symptoms.

The signs and symptoms of the disease in Hanoi include initial flu-like illness (rapid onset of high fever followed by muscle aches, headache and sore throat). These are the most common symptoms. Early laboratory findings may include thrombocytopenia (low platelet count) and leucopenia (low white blood cell count). In some, but not all cases, this is followed by bilateral pneumonia, in some cases progressing to acute respiratory distress requiring assisted breathing on a respirator. Some patients are recovering but some patients remain critically ill.

No link has so far been made between these outbreaks of acute respiratory illness in Hanoi and Hong Kong and the outbreak of `bird flu,` A(H5N1) in Hong Kong SAR reported on 19 February. Further investigations continue and laboratory tests on specimens from Viet Nam and Hong Kong SAR are being studied by WHO collaborating centres in Japan and the United States.

Until more is known about the cause of these outbreaks, WHO recommends patients with atypical pneumonia who may be related to these outbreaks be isolated with barrier nursing techniques. At the same time, WHO recommends that any suspect cases be reported to national health authorities.

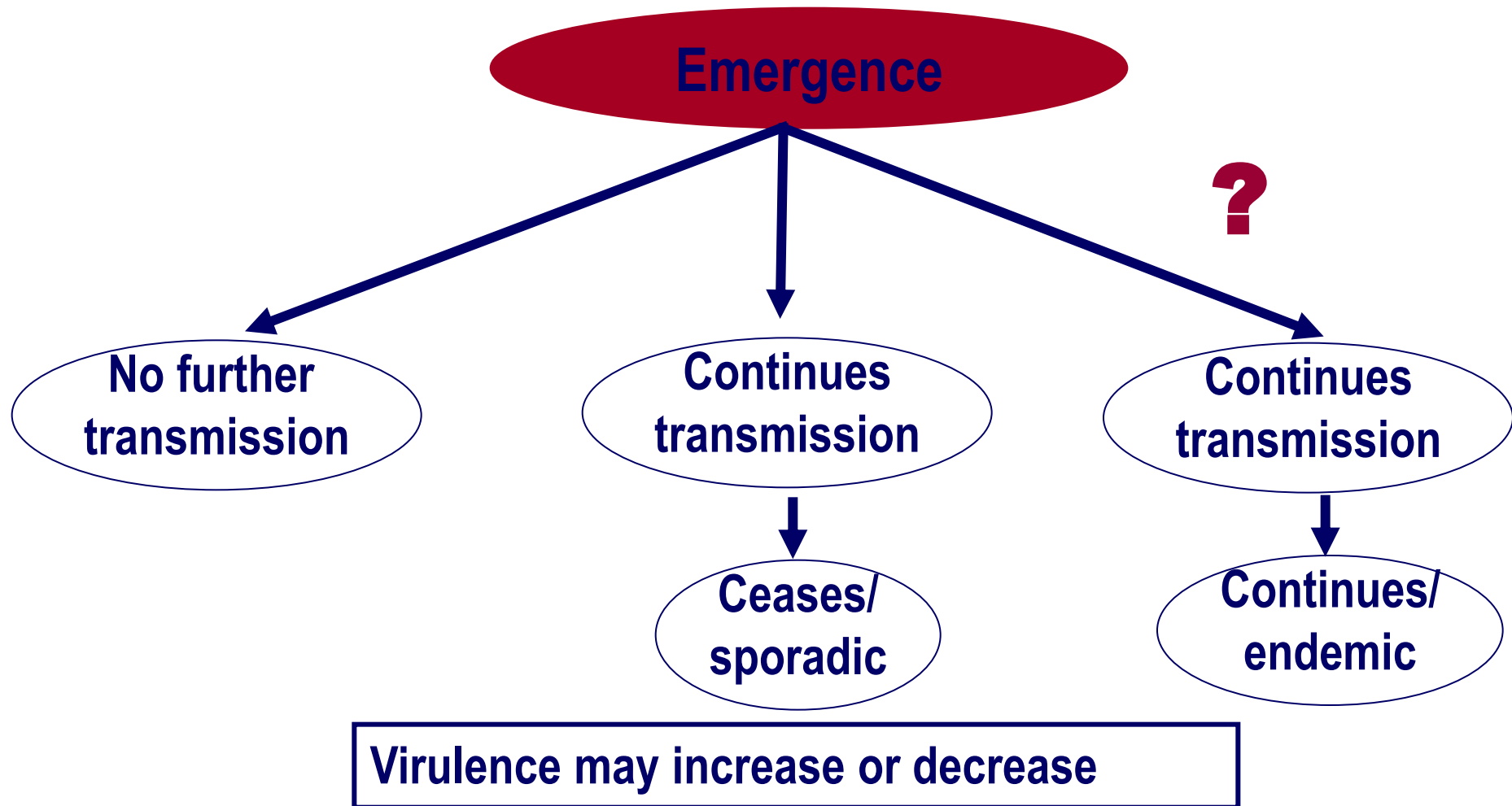
Global Alert: Severe Acute Respiratory Syndrome (SARS)

- **12 March: First global alert**
 - Described atypical pneumonia in Viet Nam and Hong Kong
- **14 March**
 - 4 persons Ontario, 3 persons in Singapore, with severe atypical pneumonia fitting description of 12 March alert reported to WHO
- **15 March**
 - Medical doctor with atypical pneumonia fitting description of 12 March reported by Ministry of Health, Singapore on return flight from New York

Situation on 15 March, 2003

- **Atypical pneumonia with rapid progression to respiratory failure, none yet recovered**
- **Health workers appeared to be at greatest risk**
- **Unidentified cause, presumed to be an infectious agent**
- **Antibiotics and antivirals did not appear effective**
- **Spreading internationally within Asia and to Europe and North America**

Emerging infections: potential transmission pathways/virulence



SARS case definition, March 2003



World Health Organization

World Health Organization issues emergency travel advisory

15 March 2003 | GENEVA -- During the past week, WHO has received reports of more than 150 new suspected cases of Severe Acute Respiratory Syndrome (SARS), an atypical pneumonia for which cause has not yet been determined. Reports to date have been received from Canada, China, Hong Kong Special Administrative Region of China, Indonesia, Philippines, Singapore, Thailand, and Viet Nam. Early today, an ill passenger and companions who travelled from New York, United States, and who landed in Frankfurt, Germany were removed from their flight and taken to hospital isolation.

Due to the spread of SARS to several countries in a short period of time, the World Health Organization today has issued emergency guidance for travellers and airlines.

"This syndrome, SARS, is now a worldwide health threat," said Dr. Gro Harlem Brundtland, Director General of the World Health Organization. "The world needs to work together to find its cause, cure the sick, and stop its spread."

There is presently no recommendation for people to restrict travel to any destination. However in response to enquiries from governments, airlines, physicians and travellers, WHO is now offering guidance for travellers, airline crew and airlines. The exact nature of the infection is still under investigation and this guidance is based on the early information available to WHO.

TRAVELLERS INCLUDING AIRLINE CREW: All travellers should be aware of main symptoms and signs of SARS which include:
high fever (>38°C)
one or more respiratory symptoms including cough, shortness of breath, difficulty breathing
AND
one or more of the following:
close contact* with a person who has been diagnosed with SARS
recent history of travel to areas reporting cases of SARS.

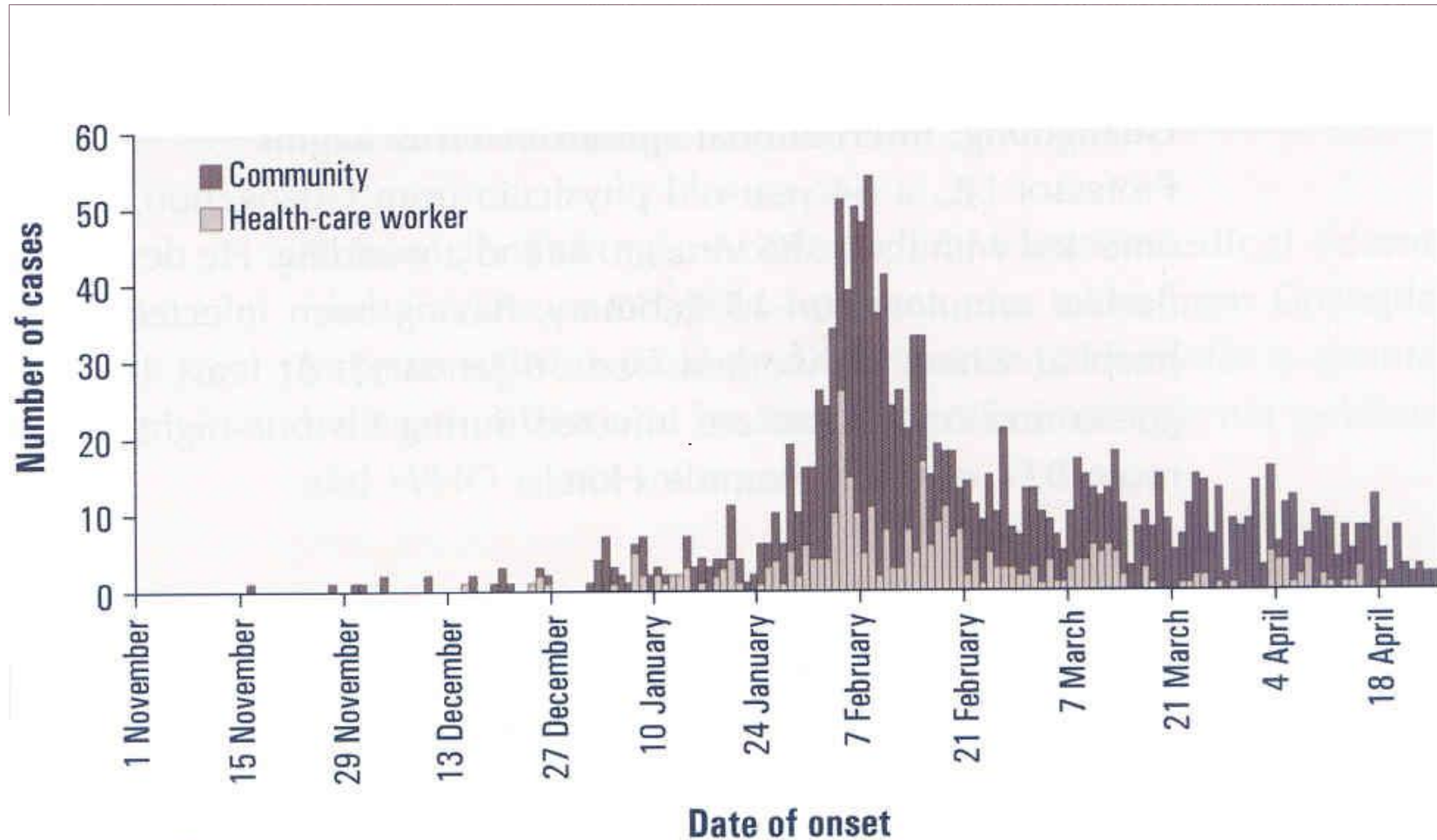
In the unlikely event of a traveller experiencing this combination of symptoms they should seek medical attention and ensure that information about their recent travel is passed on to the health care staff. Any traveller who develops these symptoms is advised not to undertake further travel until they have recovered.

AIRLINES: Should a passenger or crew member who meets the criteria above travel on a flight, the aircraft should alert the destination airport. On arrival the sick passenger should be referred to airport health authorities for assessment and management. The aircraft passengers and crew should be informed of the person's status as a suspect case of SARS. The passengers and crew should provide all contact details for the subsequent 14 days to the airport health authorities. There are currently no indications to restrict the onward travel of healthy passengers, but all passengers and crew should be advised to seek medical attention if they develop the symptoms highlighted above. There is currently no indication to provide passengers and crew with any medication or investigation unless they become ill.

SARS: international spread from Hong Kong, 21 February, 2003



SARS Epidemic curve, China, 2002 - 2003



SARS transmission, health care workers (HCW), 2003

Areas	Total cases	Case fatality ratio (%)	Number of HCW affected (%)
Canada	251	17	109 (43)
China	5327	7	1002 (19)
Hong Kong	1755	17	386 (22)
China, Taiwan	346	11	68 (20)
Singapore	238	14	97 (41)
Vietnam	63	8	36 (57)

WHO real time guidelines, SARS, 2003: www.who.int/csr/sars/



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Communicable Disease Surveillance & Response (CSR)

Location: WHO > WHO sites > CSR Home > Severe Acute Respiratory Syndrome (SARS)

Severe Acute Respiratory Syndrome (SARS)

WHO sites

CSR Home

Alert & Response Operations

Diseases

Drug Resistance

Global Outbreak Alert & Response Network

International Health Regulations

Laboratory & Epidemiology Strengthening

Preparedness for Deliberate Epidemics

Public Health Mapping

Latest information:

- Update 71 - Status of diagnostic tests, training course in China - 2 June
- Cumulative number of reported probable cases - 2 June
- Case definitions for surveillance of SARS
- SARS Travel Recommendations, Summary Table - 2 June
- Map of current probable cases - 2 June
- China: Daily Report of SARS Cases - 2 June (.pdf)
- As provided by Ministry of Health, People's Republic of China
- China:SARS Case Distribution by Prefecture(City) - 31 May (.pdf)
- As provided by Ministry of Health, People's Republic of China
- Map of current probable cases in China - 2 June

MORE INFORMATION

- Guidelines, recommendations, descriptions
- WHO Collaborative Networks
- Travel advice
- Media
- Other information resources: links, images

WHO Global Conference on Severe Acute Respiratory Syndrome

17-18 June 2003
Open for registration

WHO plans to hold an international conference in Kuala Lumpur, Malaysia to review the epidemiological, clinical management and laboratory

HIGHLIGHTS

Severe Acute Respiratory Syndrome (SARS) main page

2 June 2003
Cumulative Number of Reported Probable Cases Of SARS
[Full text](#)

2 June 2003
Update 71 - Status of diagnostic tests, training course in China
[Full text](#)

[SARS Travel Recommendations Summary Table](#)
2 June

[Summary of WHO measures related to international travel \(French\) \(Chinese\)](#)
23 May

[Lab testing; PCR primers](#)

DISEASE OUTBREAKS

Severe Acute

Update 79 - Situation in China

China's Executive Vice Minister of Health, Mr Gao Qiang, and WHO's Executive Director for Communicable Diseases briefed the press this morning on the situation of SARS control in China. Also in attendance were Dr Qi Ziaoqiu, Director-General of the Department

Cumulative Number of Reported Probable Cases Of SARS

From: 1 Nov 2002¹ To: 2 June 2003, 18:00 GMT+2
Revised: 3 June 2003, 9.00 GMT +2

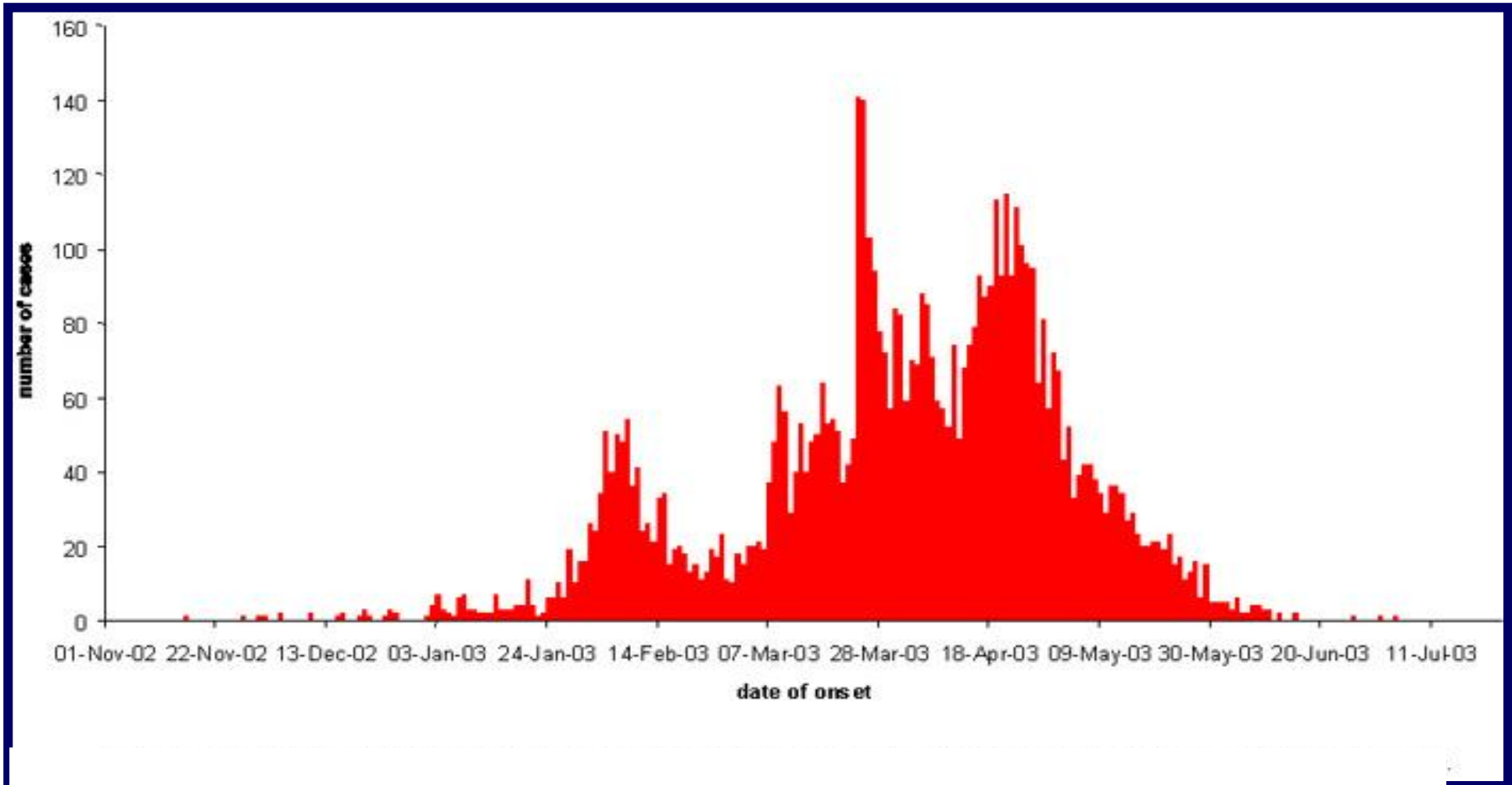
Country Cumulative number of case(s)² Number of new cases

Brazil	2	0	0	2	10/Apr/2003	24/Apr/2003
Canada	198	10	30	116	1/Jun/2003	1/Jun/2003
China	5328	2	334	3495	1/Jun/2003	2/Jun/2003

SARS Travel Recommendations Summary Table

This table, updated daily, indicates those areas with recent local transmission of SARS for which WHO has issued recommendations pertaining to international travel.

Probable cases of SARS by date of onset worldwide, 1 March – 27 June 2003



Source: WHO

SARS and the economy: impact on global travel, April 2003

Time Flight	Destination	Gate	Status
17:00 GA 859	Singapore Jakarta	18	Est at 19:10
17:20 MU 598	Shanghai/Pudong		Cancelled
17:45 KA 894	Shanghai/Pudong		Cancelled
17:50 KA 430	Kaohsiung		Cancelled
17:50 KA 604	Xiamen		Cancelled
17:50 KA 904	Beijing		Cancelled
17:55 KA 700	Gulin		Cancelled
17:55 MU 5020	Nanjing	66	Now Boarding
18:00 CA 420	Chongqing	64	
18:00 MU 204	Xian	26	Boarding Soon
18:00 PR 307	Manila	24	
18:05 AI 315	Delhi Mumbai	33	Boarding Soon
18:05 KA 660	Fuzhou		Cancelled
18:20 CX 402	Taipei	67	
18:25 MU 510	Shanghai/Pudong	19	
18:30 SQ 885	Singapore	23	Boarding Soon
18:35 KA 622	Hangzhou		Cancelled
18:40 AC 008	Vancouver Toronto		Cancelled
18:45 CI 616	Taipei	28	
18:50 TG 633	Bangkok	42	
18:55 KA 812	Nanjing		Cancelled
19:10 CX 111	Sydney	47	
19:10 CX 135	Melbourne		Cancelled
19:10 OF 088	Melbourne	18	
19:15 MU 538	Shanghai/Pudong	15	
19:15 NZ 070	Auckland	35	
	LH 9810		
19:20 KA 906	Beijing		Cancelled
19:20 SQ 899	Singapore		Cancelled
19:25 BR 872	Taipei		Cancelled
19:25 CZ 3078	Haikou	32	
19:40 5J 119	Manila	21	
19:40 CA 116	Beijing		Cancelled
19:40 CX 468	Taipei		
19:40 CX 913	Manila		Cancelled
19:45 CI 642	Taipei	25	
19:50 MU 7002	Taiyuan		Cancelled
20:00 CX 715	Singapore		Cancelled
20:00 UA 805	Singapore		Cancelled
20:05 CI 616	Kaohsiung	28	
20:10 CZ 3078	Guangzhou	30	
20:10 OF 068	Brisbane Sydney		Cancelled
20:15 KA 806	Shanghai/Pudong	29	
20:15 TG 630	Taipei		Cancelled
20:25 CX 107	Auckland	1	
	BA 4551		
20:35 KA 438	Kaohsiung		Cancelled
20:45 CX 464	Taipei		Cancelled
20:45 TG 607	Bangkok	42	
20:50 CI 618	Taipei		Cancelled
20:50 CZ 3032	Gulin	32	
21:00 BR 858	Taipei	38	
21:05 PR 311	Manila		
21:10 OF 128	Sydney	19	
21:45 KA 434	Kaohsiung	27	
21:45 KA 488	Taipei		Cancelled
21:50 CX 408	Taipei	4	
21:50 CX 905	Manila	31	
21:55 CI 672	Kaohsiung		
21:55 SQ 002	San Francisco		
22:00 VN 763	Ho Chi Minh		
	CX 763		
22:05 CI 666	Taipei		Cancelled
22:05 CX 709	Bangkok		Cancelled
22:25 EK 383	Bangkok Dubai	62	
22:55 CX 462	Taipei		Cancelled
23:10 LH 731	Munich		Cancelled
	NZ 4631		
23:20 CX 103	Cairns Brisbane		

Coronavirus infections, thought to be asymptomatic, animal handlers, China

BMJ 2003;327(7415):582 (13 September), doi:10.1136/bmj.327.7415.582-a

BMJ 2003;327:582 (13 September), doi:10.1136/bmj.327.7415.582-a

News extra

Asymptomatic animal traders prove positive for SARS virus

Hong Kong Jane Parry

The microbiology team from the University of Hong Kong has published a paper on the origins of the coronavirus that causes severe acute respiratory syndrome (SARS). The paper, published online in *Science* (www.sciencemag.org/cgi/content/abstract/1087139) on 5 September, presents the results of testing eight species of wild and domestic animals sourced from a live animal market in Shenzhen, southern China, in May 2003. The paper also showed that eight traders of wild animals and three workers who slaughtered wild animals were positive for the virus, despite never having shown symptoms of SARS.

A total of 25 animals were tested, and researchers isolated a SARS-like coronavirus from four civet cats, as well as from a raccoon dog. Antibodies were also found in three palm civets, a raccoon dog, and a Chinese ferret badger.

The genetic sequences of the human SARS coronavirus and the virus detected in the civet cat and other animals were very closely related, according to Dr Guan Yi, associate professor at the University of Hong Kong's faculty of medicine. "The virus detected in animals was a little different to the human one, so we called it a SARS-like virus," he said.

The team also took blood samples from 1500 workers and for the research paper published results of testing on 55 workers. Of these, eight wild animal traders, three workers who slaughtered wild animals, and one vegetable seller were seropositive for the SZ16 coronavirus, but none of them had reported SARS-like symptoms in the previous six months. "We don't know why the workers didn't show symptoms. They could have been infected, several

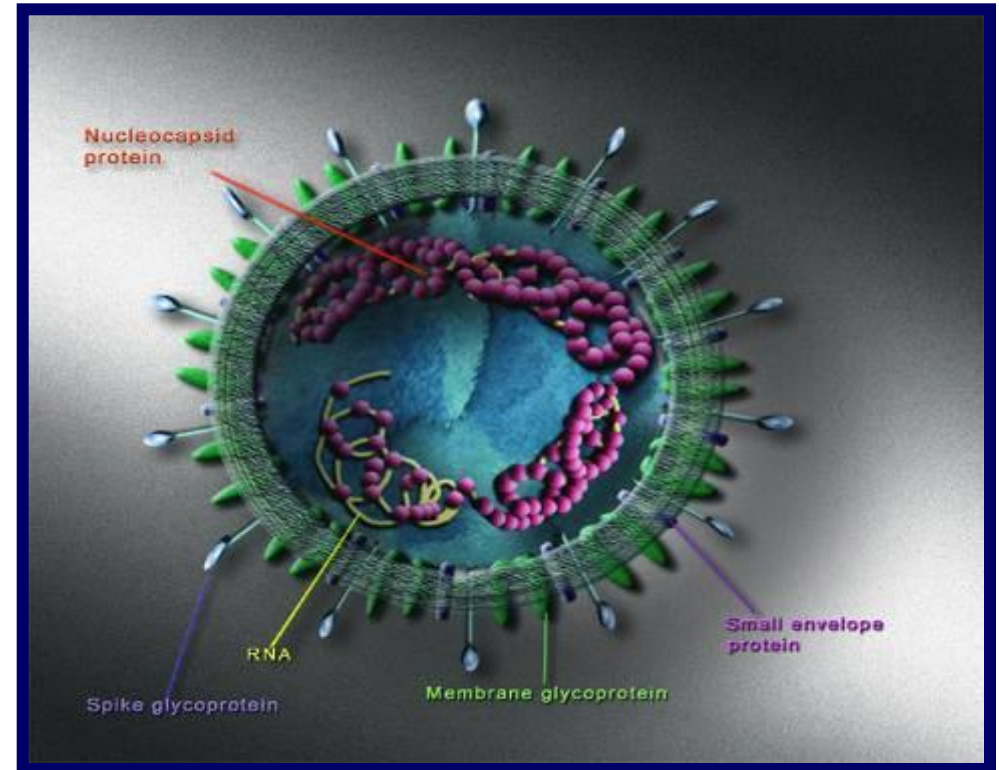
Source: BMJ 2003, online

Severe Acute Respiratory virus, 2003



Suspected animals in the chain of transmission

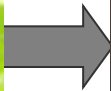
The SARS Coronavirus



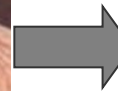
Nipah virus (emergence 1999): proposed transmission chain



Fruit bat



Domesticated swine



Human

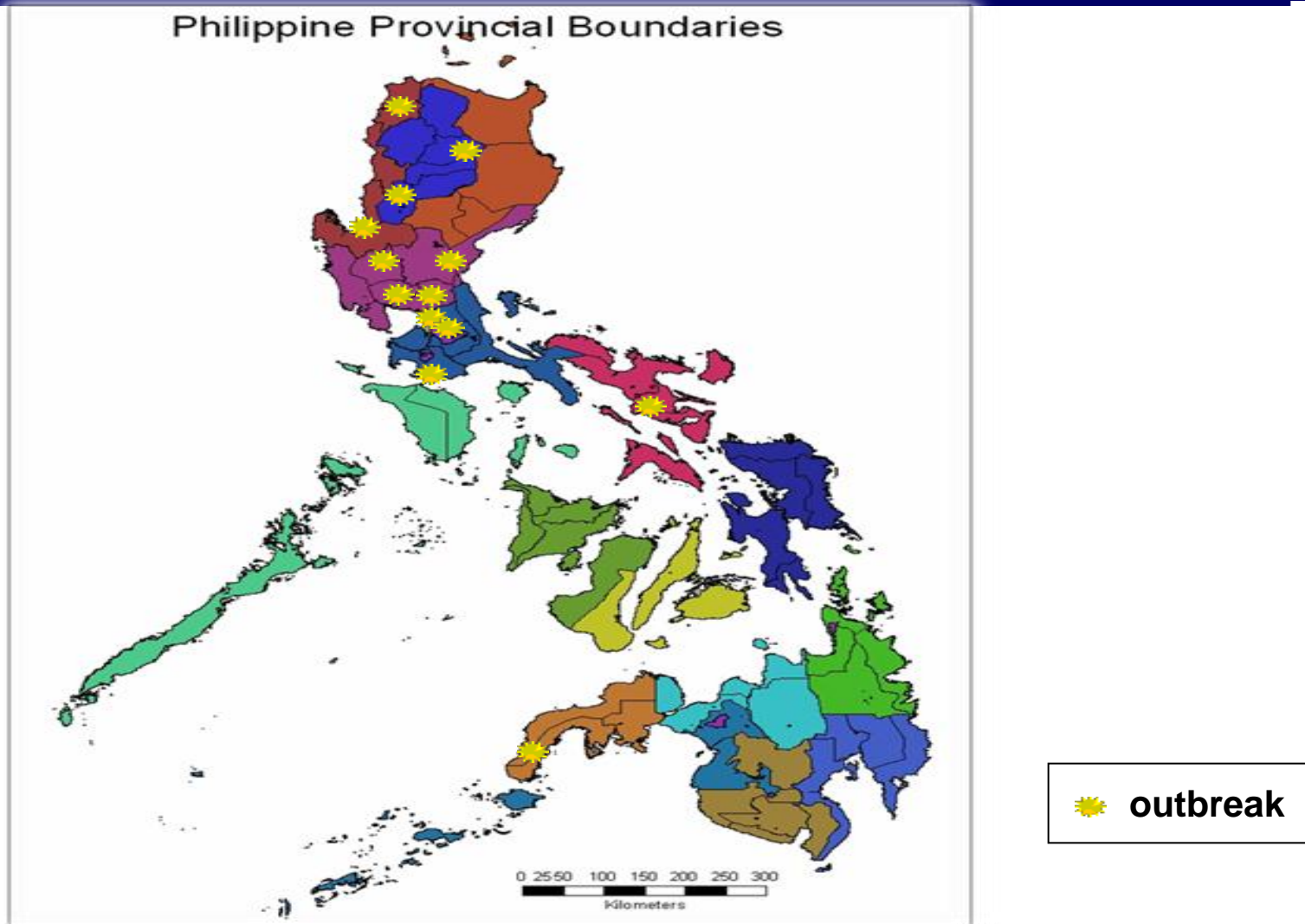
Nipah virus outbreaks, 1998 - 2008

Dates	Location	No. cases	No. deaths	CFR(%)
1998-1999	Malaysia;	265	105	40
1999	Singapore	11	1	9
2001	W. Bengal, India	66	45	68
2001	Bangladesh	13	9	69
2003	Bangladesh	12	8	67
2004	Bangladesh	29	22	76
	Bangladesh	36	27	75
2005	Bangladesh	12	11	92
2007	W. Bengal, India	5	5	100
2007	Bangladesh	15	8	54
2008	Bangladesh	11	6	54

Changing Nipah virus epidemiology: Bangladesh and India

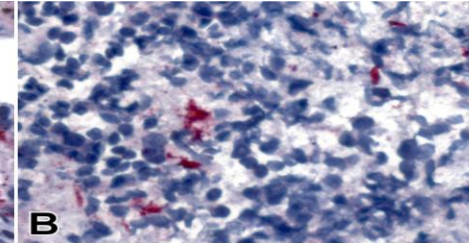
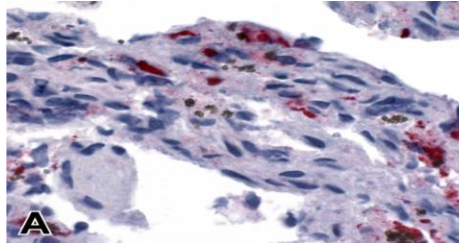
- **Human-to-human transmission first suspected 2001, hospitalized patients, India**
- **Human to human transmission suspected again in 2003, 2005, and 2007, Bangladesh**
 - **cases could not be linked to domestic animal exposure, including pigs**
 - **index cases not identified: one potential exposure to bat guano in palm wine**
- **Risks to human health poorly understood**

Philippines, Porcine Reproductive and Respiratory Syndrome, July 2007 – June 2008



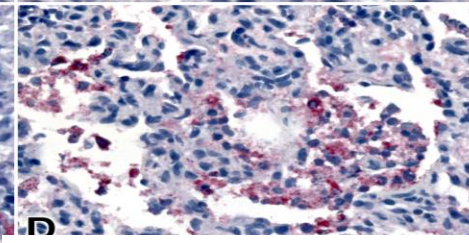
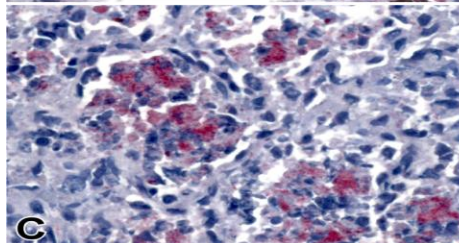
Swine tissue specimens and cell culture specimens, Philippines, 2007-2008

Lymph node capsule stained for EBV



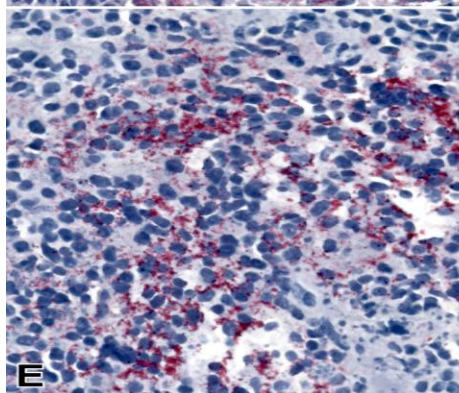
Lymph node tissue stained for EBV

Lung tissue stained for EBV

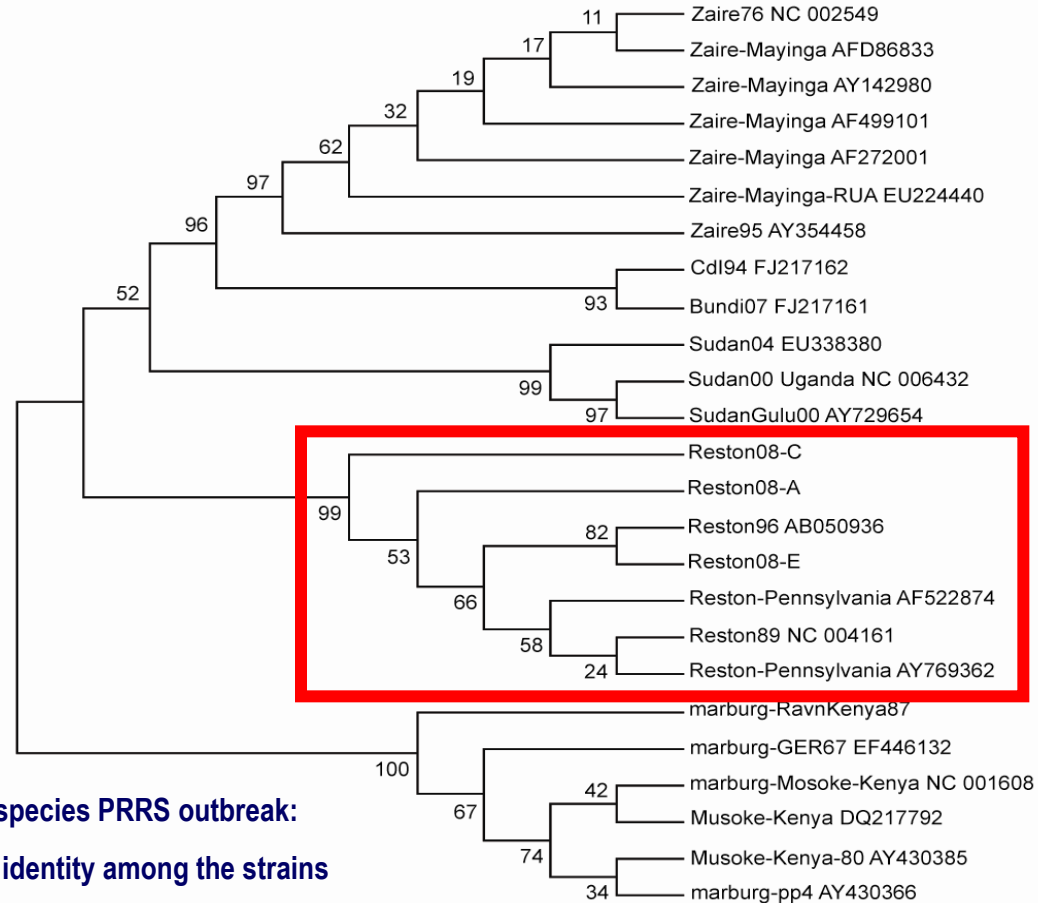


Lung tissue stained for PRRSV antigens

Lymph node germinal center stained for PRRSV antigens



Ebola Reston Virus, 1998 - 2008



3 separate strains of Ebola Reston Virus species PRRS outbreak:

4% mean difference in nucleotide identity among the strains

2.5% difference from 1989 isolate from laboratory monkeys imported from Philippines in USA

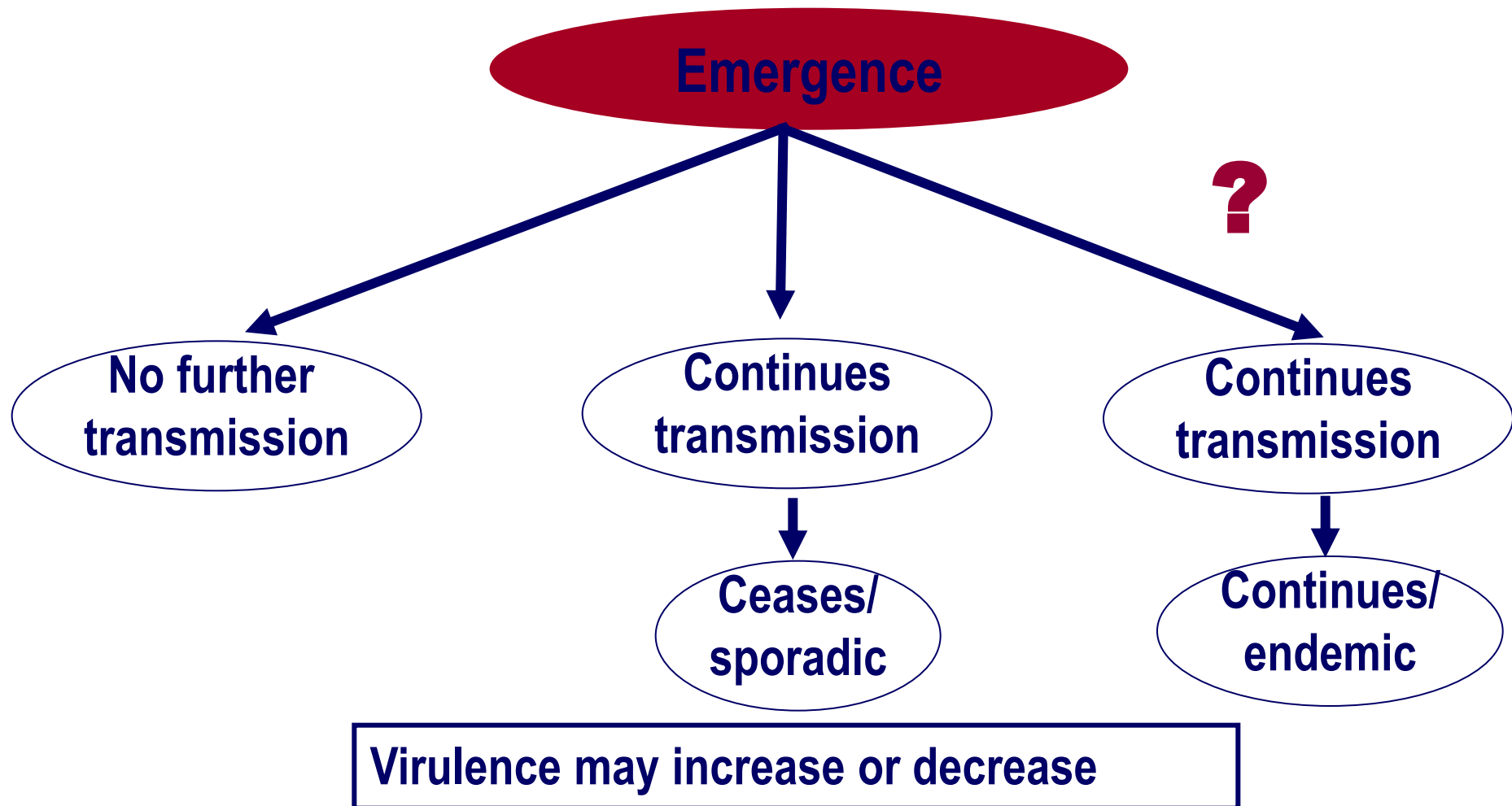
Human Infections, Ebola Reston Virus (ERV), 1989-2008

	Occupation	Risk exposure	Location of likely exposure
Mr X	Backyard pig farmer	Close contact and care for sick pigs Collection and use of boar semen	Metro Manial and Bulacan farm
Mr DZ	Farm worker	Close contact and care of sick pigs	Bulacan farm
Mr SB	Farm worker	Close contact and care of sick pigs	Bulacan farm
Mr WZ	Farm worker	Close contact and care of sick pigs Collection of boar semen	Pangasinan farm
Mr JD	Slaughterhouse worker	Slaughtered on average 4 pigs(day	Pangasinan – backyard farms
Mr Y	Slaughterhouse worker	Slaughtered pigs daily	Nueva Ejica -commercial farms Bulacan – backyard farms

Epidemiological investigation, pigs at slaughter (n = 70), January 2009 - present

- **19/70 (27%) PCR positive for Ebola Reston Virus in blood specimens**
- **19 PCR positive pigs not reported as overtly ill at time of slaughter**
- **Organs investigated:**
 - **13/19 spleen samples tested PCR positive**
 - **12/19 lung samples tested PCR positive**

Emerging infections: potential transmission pathways/virulence

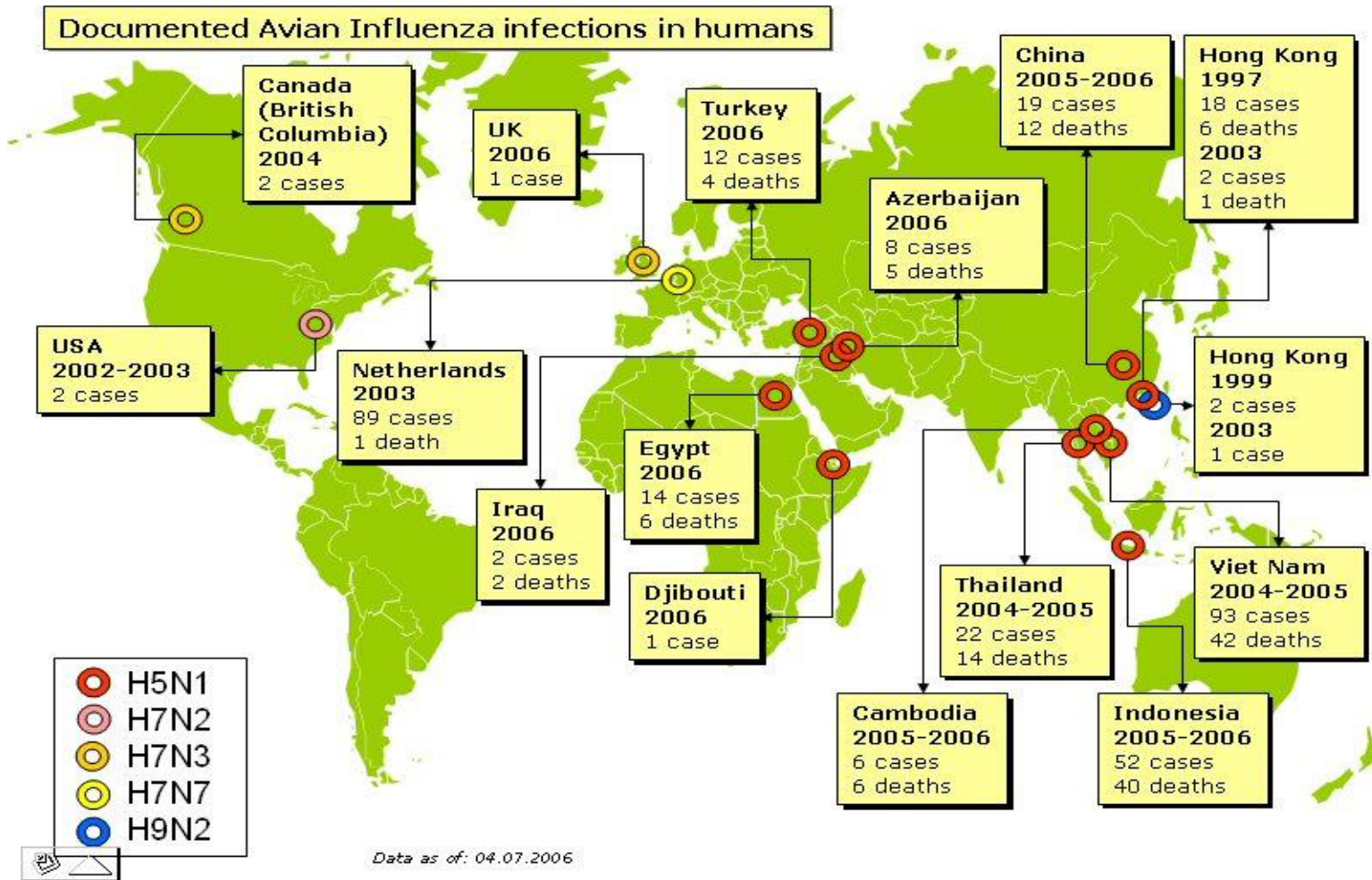


Breaches in species barrier: infections in humans identified since 1976

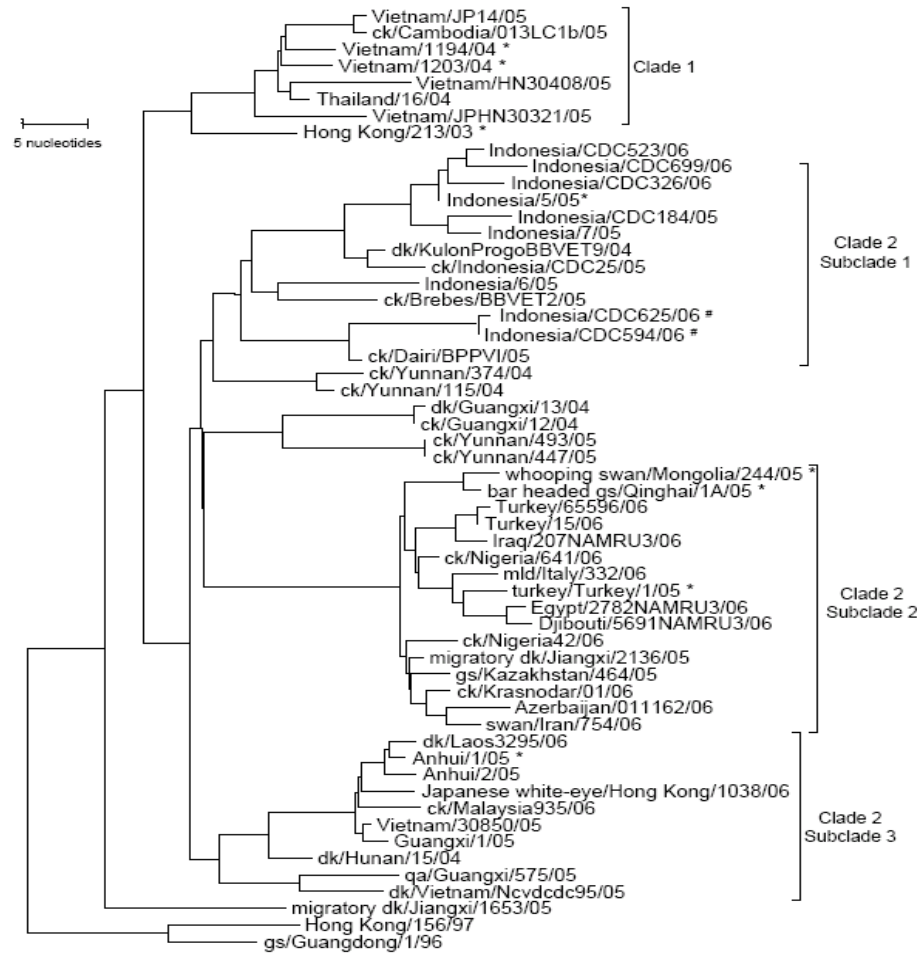


Infection	Animal linked to transmission	Year infection first reported
Ebola virus	Bats	1976
HIV-1	Primates	1981
E. coli O157:H7	Cattle	1982
Borrelia burgdorferi	Rodents	1982
HIV-2	Primate	1986
Hendra virus	Bats	1994
BSE/vCJD	Cattle	1996
Australian lyssavirus	Bats	1996
H5N1 influenza A	Chickens	1997
Nipah virus	Bats	1999
SARS coronavirus	Palm civets	2003
Influenza (H1N1)	Swine	2009

Risk assessment: laboratory-confirmed human avian influenza infections, 1999 - 2009



Risk assessment: H5N1 virus groups (clades) infecting humans since 2003



* Candidate vaccine reference viruses

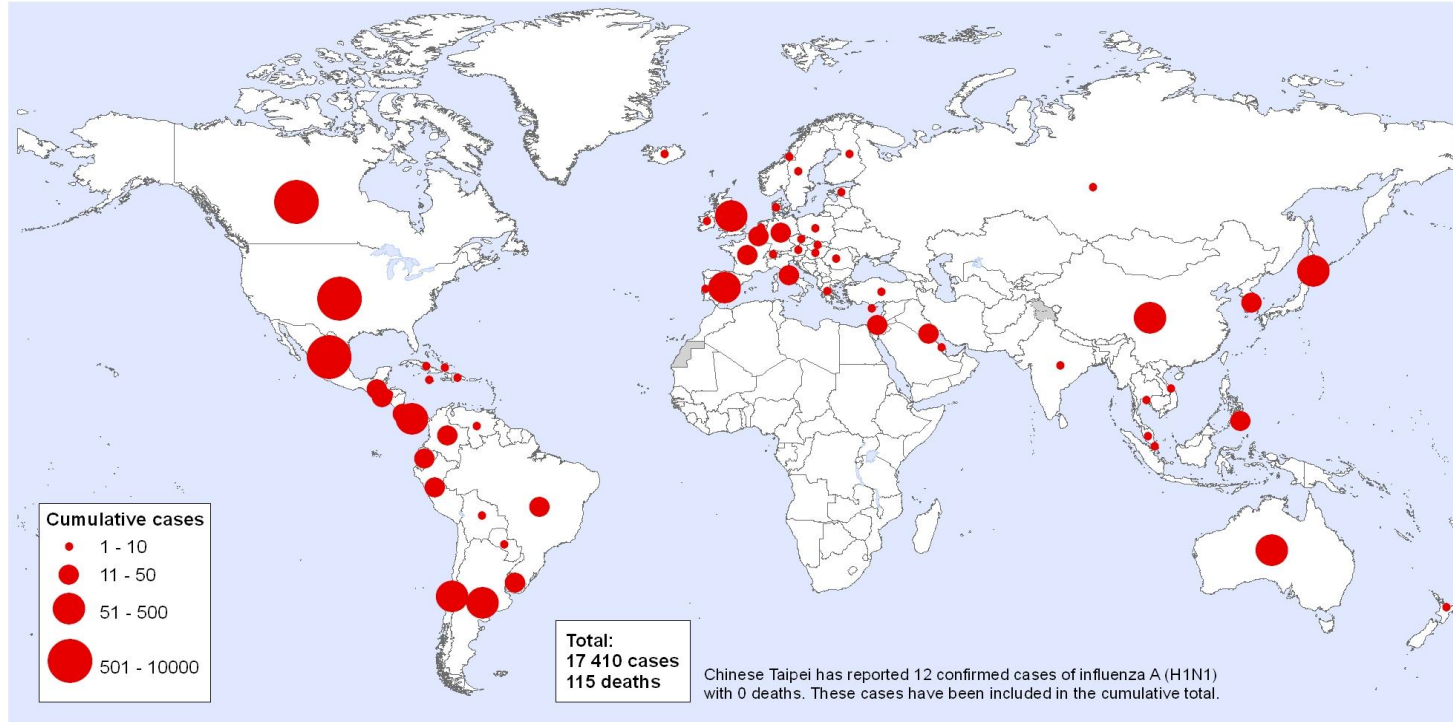
Karo family cluster



H1N1 pandemic influenza, 2009

New Influenza A (H1N1),
Number of laboratory confirmed cases as reported to WHO

Status as of 01 June 2009
06:00 GMT



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

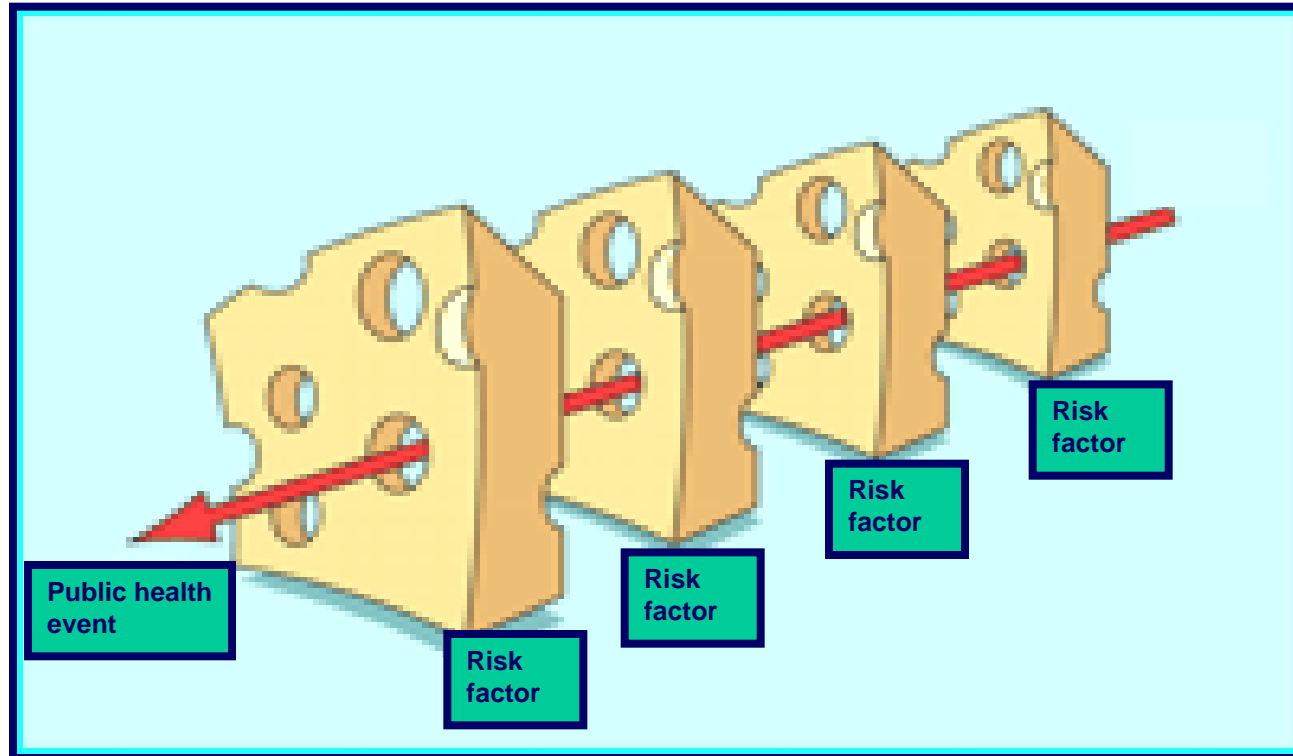
Map produced: 01 June 2009 06:46 GMT

Data Source: World Health Organization
Map Production: Public Health Information
and Geographic Information Systems (GIS)
World Health Organization



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Swiss cheese events in epidemiology and public health

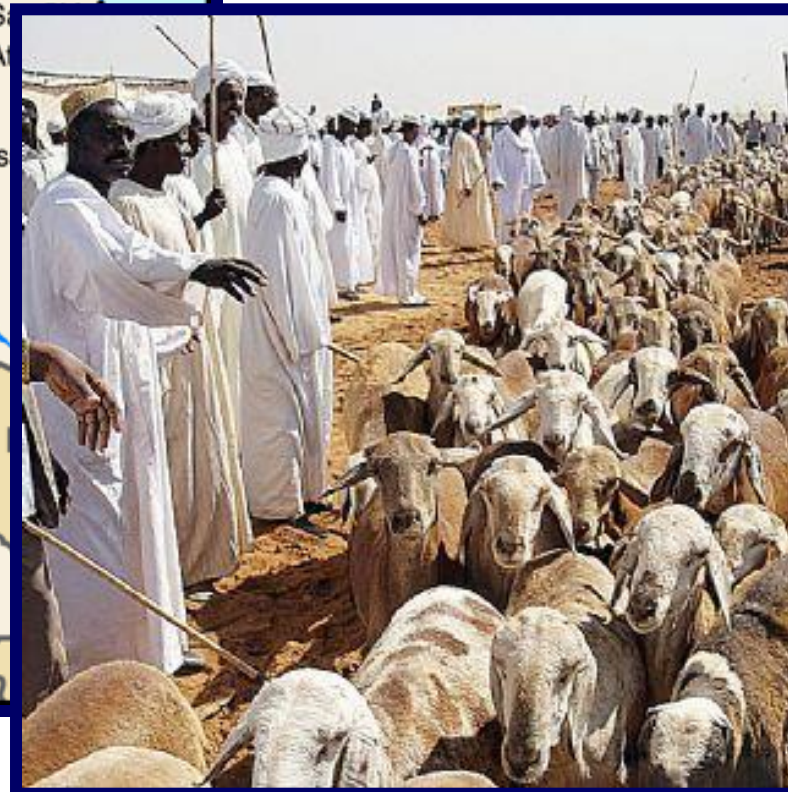


James Reason: *BMJ* 2000;320:768-770

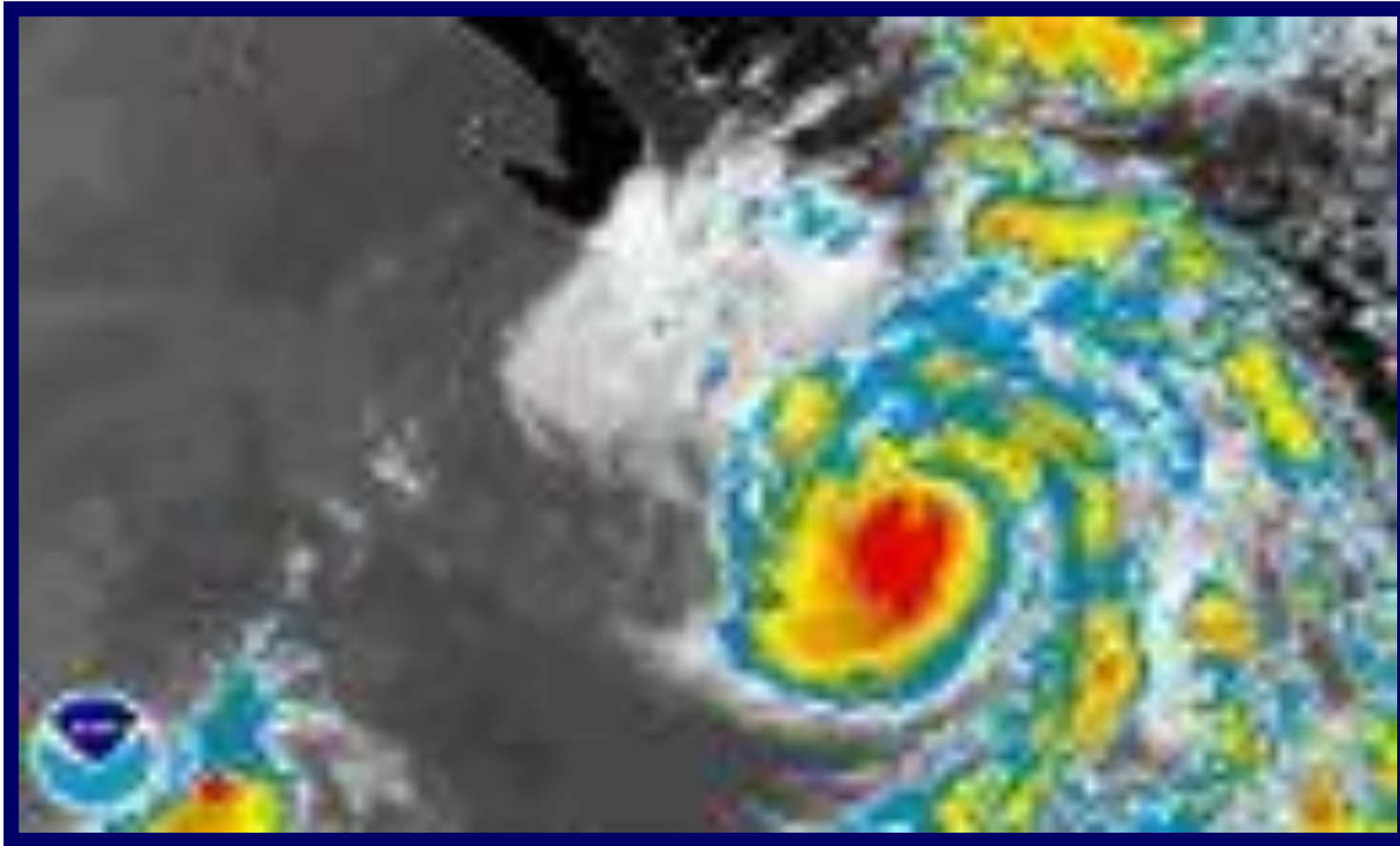
Routine vaccination of cattle against Rift Valley Fever, East Africa



Animal husbandry, Sudan and trade associated with religious festivals



Climate change and health: extreme weather events



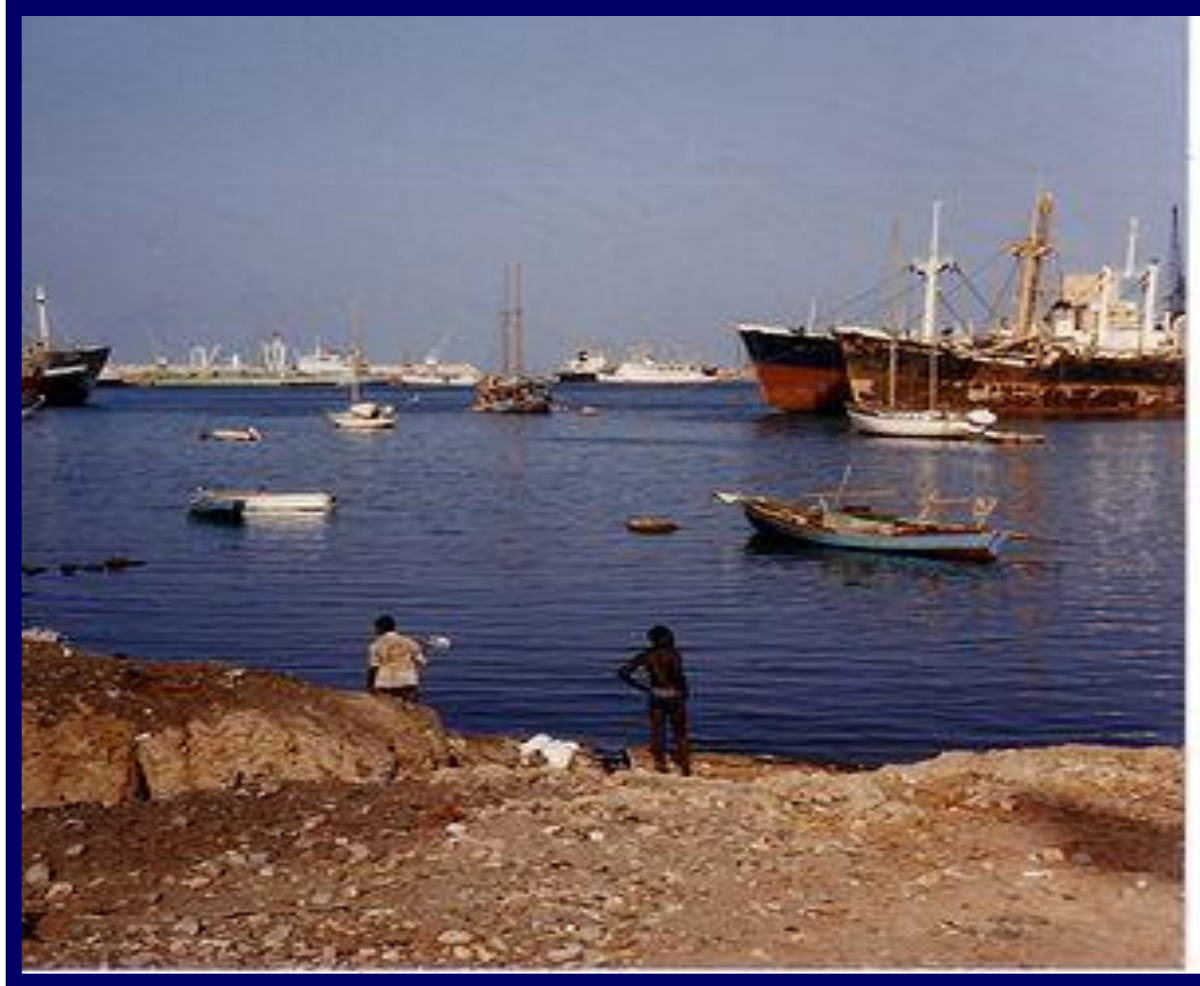
El Nino-associated flooding, East Africa, 1998



Rift Valley Fever, human infection, Sudan, 1998



Animal husbandry and trade, Sudan



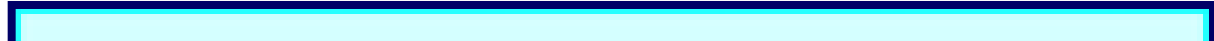
Clandestine livestock trade routes, Sudan and Arabian peninsula



**Rift Valley Fever outbreak,
animals and humans,
2000**

Source: WHO

So in summary..... when you think of pandemics,



and how to assess and manage the risks



....think of animals and Swiss cheese

What's the risk?

Nipah transmission by Bats in Bangladesh.wmv