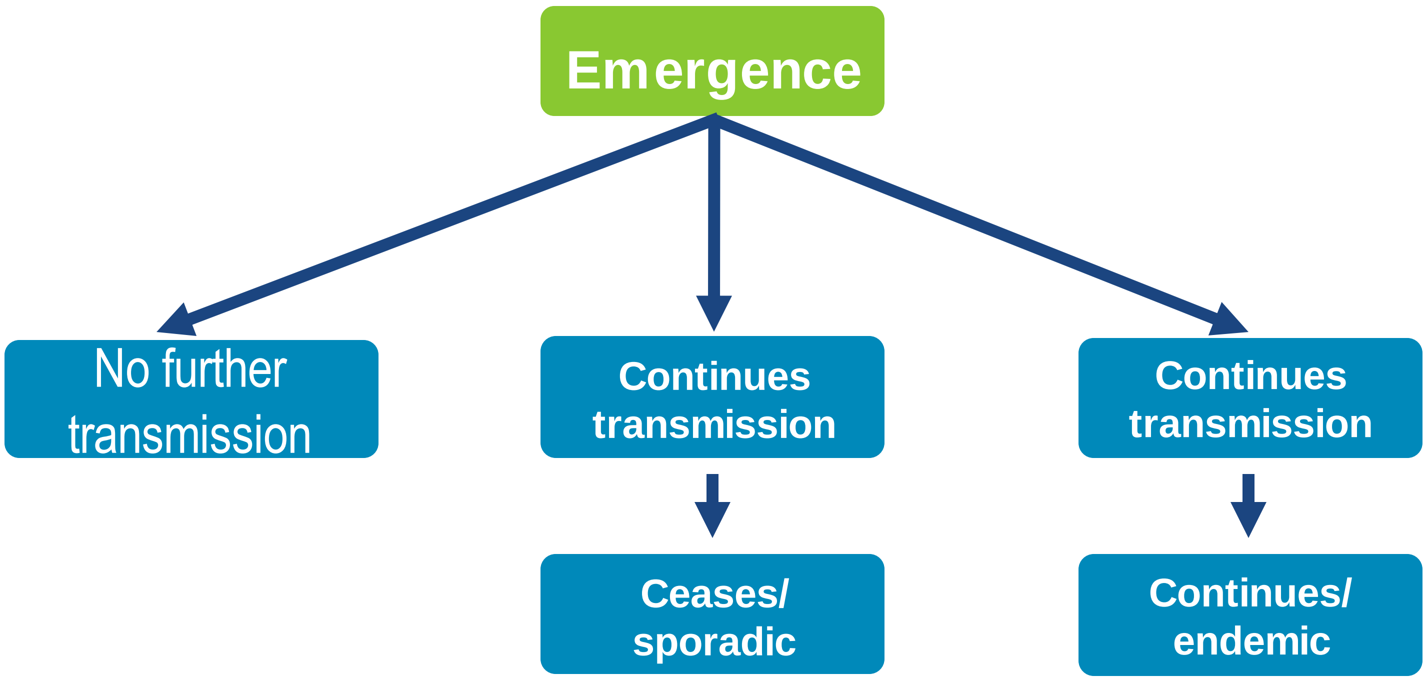
Infections at the human/animal interface: shifting the paradigm from rapid detection and response to prevention at the source

Potential transmission pathways, emerging infectious diseases



Breaches in species barrier: emerging infections in humans



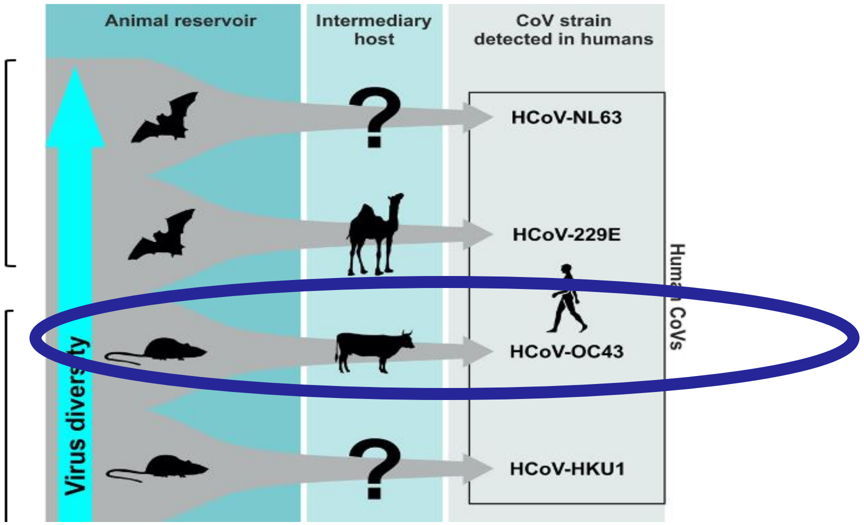




Infection	Animal linked to transmission	Year infection first reported
Ebola virus	Bats	1976
HIV-1	Primates	1981
E. coli O157:H7	Cattle	` 1982
Borrelia burgdorferi	Rodents	1982
HIV-2	Primate	1986
Hendra virus	Bats	1994
BSE/vCJD	Cattle	1996
Australian lyssavirus	Bats	1996
Influenza A (H5N1)	Chickens	1997
Nipah virus	Bats	1999
SARS coronavirus	Palm civets	2003
Zika virus	Monkey	2007
Influenza A (H1N1)	Swine	2009
MERS coronavirus	Bat/ Dromedary	2012
Influenza A (H7N9)	Poultry	2013
SARS coronavirus 2	Bats	2019

Human Coronavirus Infections

Alpha
coronaviruses



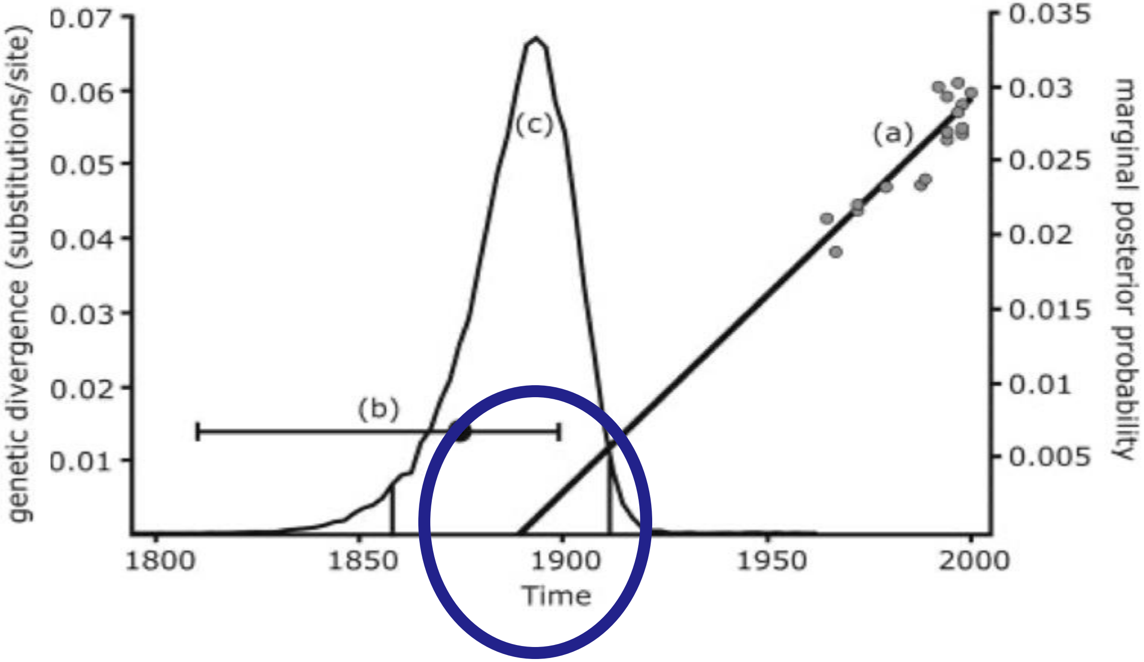
Seasonal CoVs:
Peak in the winter/ early spring
Mild disease/ upper respiratory tract
Elderly hit the most

Source:. Corman VM, Muth D, Niemeyer D, Drosten C. Hosts and Sources of Endemic Human Coronaviruses. *Adv Virus Res*. 2018;100:163–188.

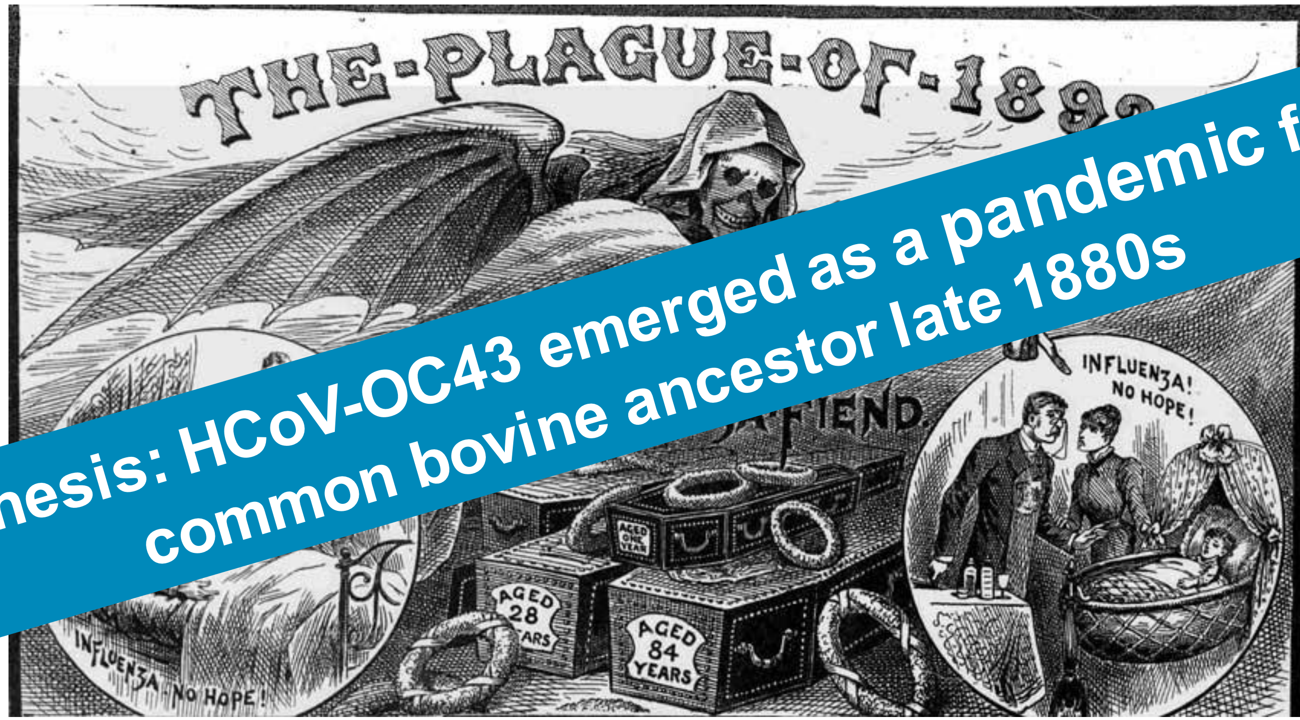
Molecular clock analysis of the spike gene sequences of BCoV and HCoV-OC43

Time of most recent common ancestor
a) Linear regression
b) Maximum likelihood
c) Bayesian coalescence

Vijgen L, et al. J Virol. 2005;79(3):1595-604.



Russian influenza pandemic, 1889 - 1893



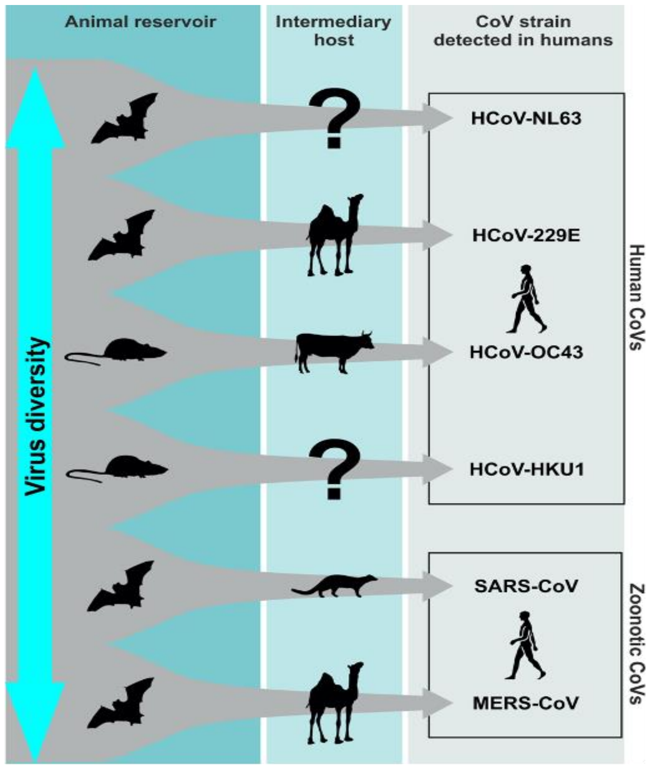
Hypothesis: HCoV-OC43 emerged as a pandemic from a common bovine ancestor late 1880s

- **1 million deaths worldwide**
- **Neurological symptoms (not consistent with influenza)**

Human Coronavirus Infections

Alpha coronaviruses

Beta coronaviruses



Seasonal CoVs:
Peak in the winter/ early spring
Mild disease/ upper respiratory tract
Elderly hit the most

2003

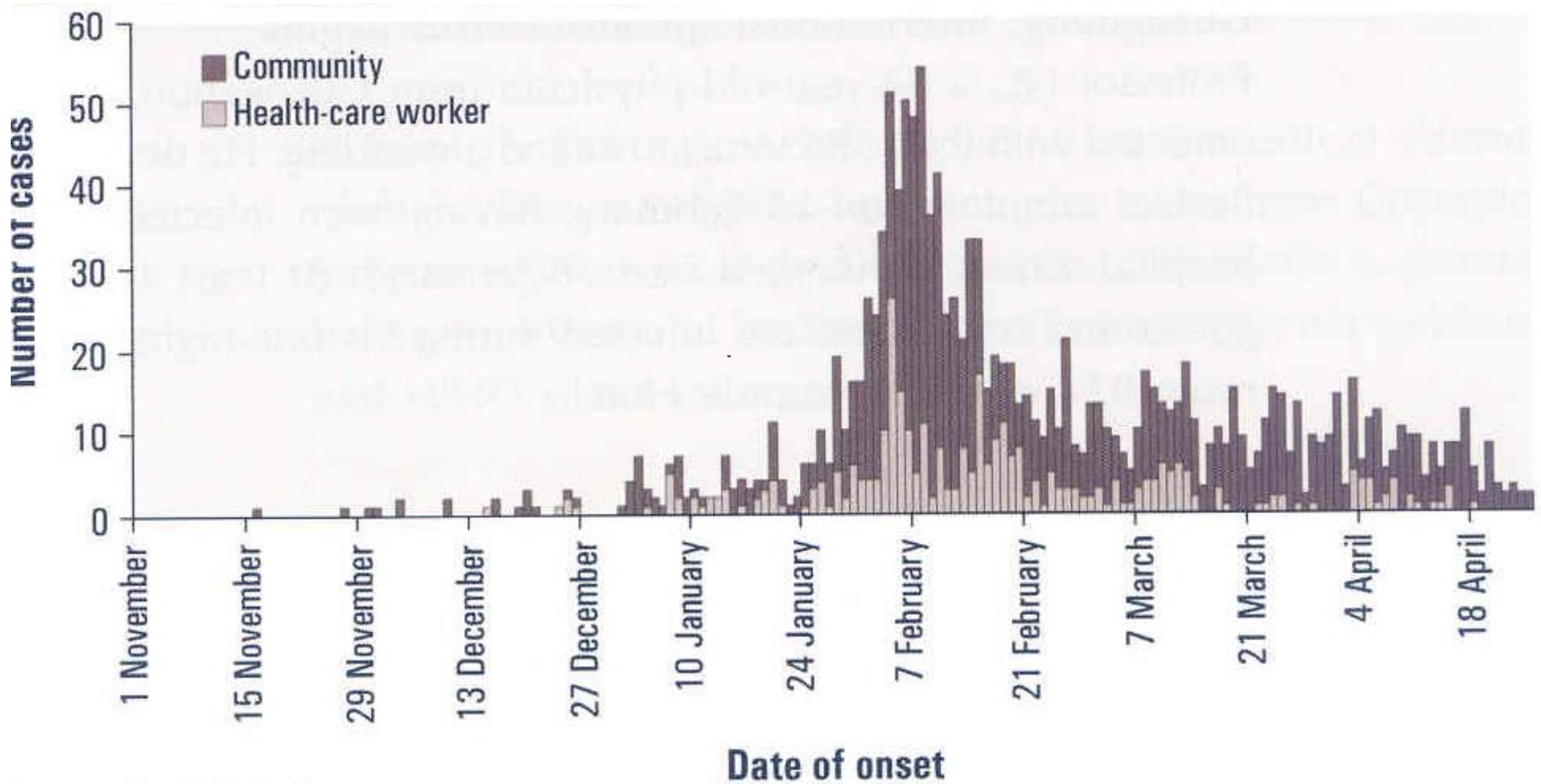
2012

SARS-CoV-2 **2019** Pandemic CoV

Source:. Corman VM, Muth D, Niemeyer D, Drosten C. Hosts and Sources of Endemic Human Coronaviruses. *Adv Virus Res*. 2018;100:163–188.

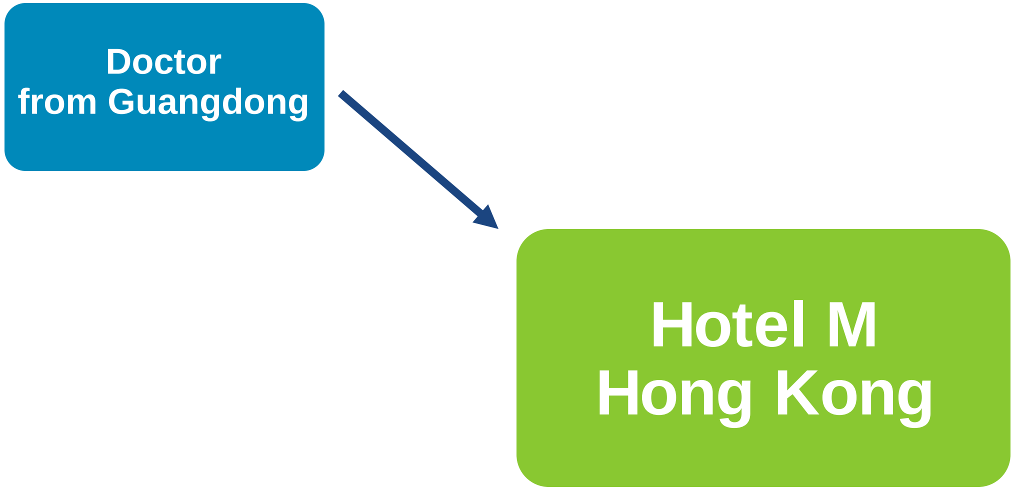
SARS CoV1: emergence 2002

SARS China, 2002 - 2003



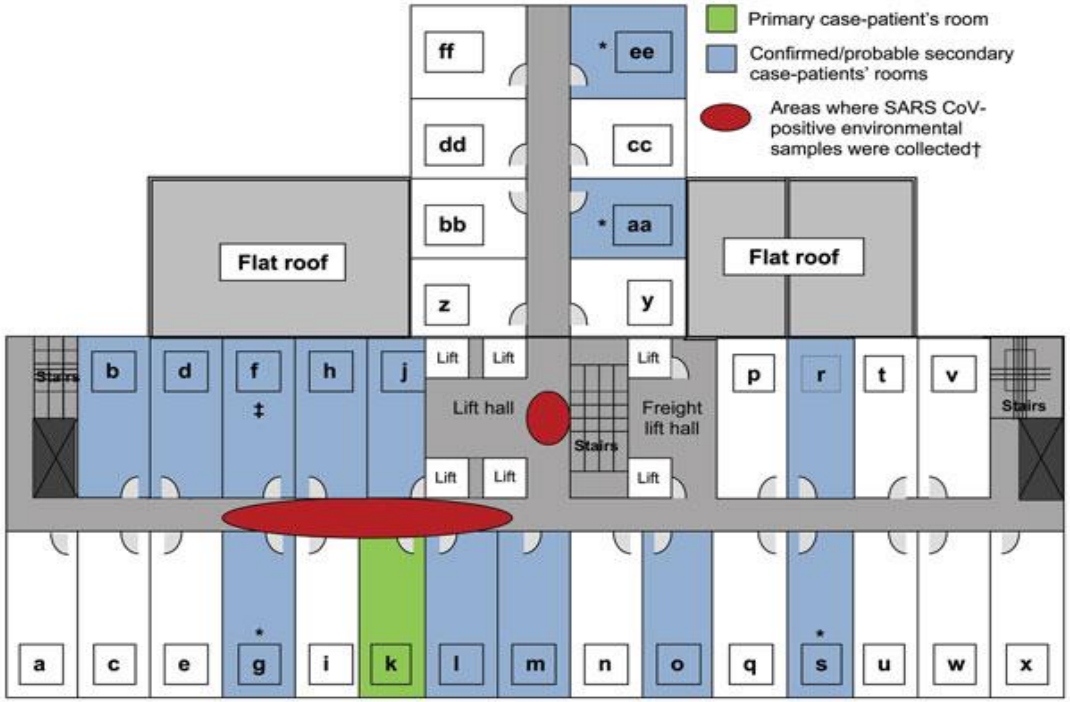
Source: Xu R-H et al[1]

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



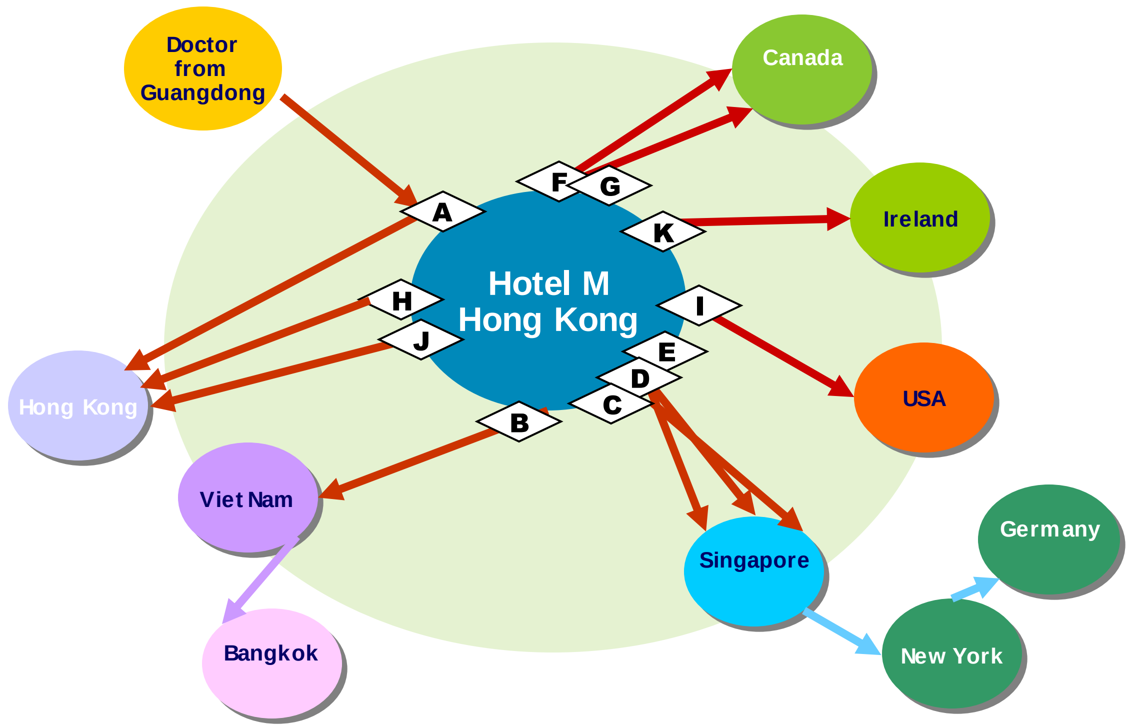
Source: CDC/WHO

SARS: Hotel M, Hong Kong, 21 February, 2003



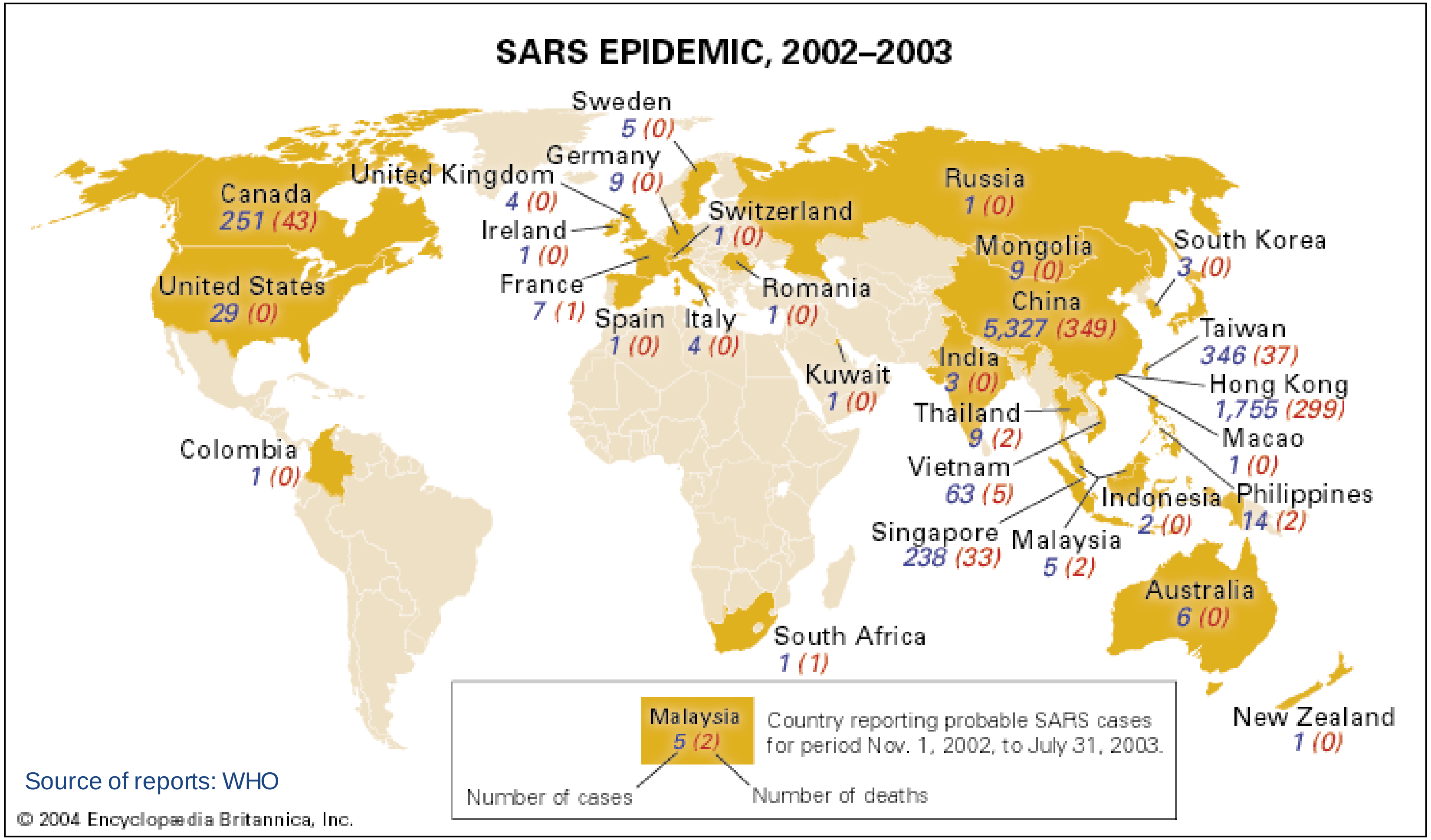
Source: CDC/WHO

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



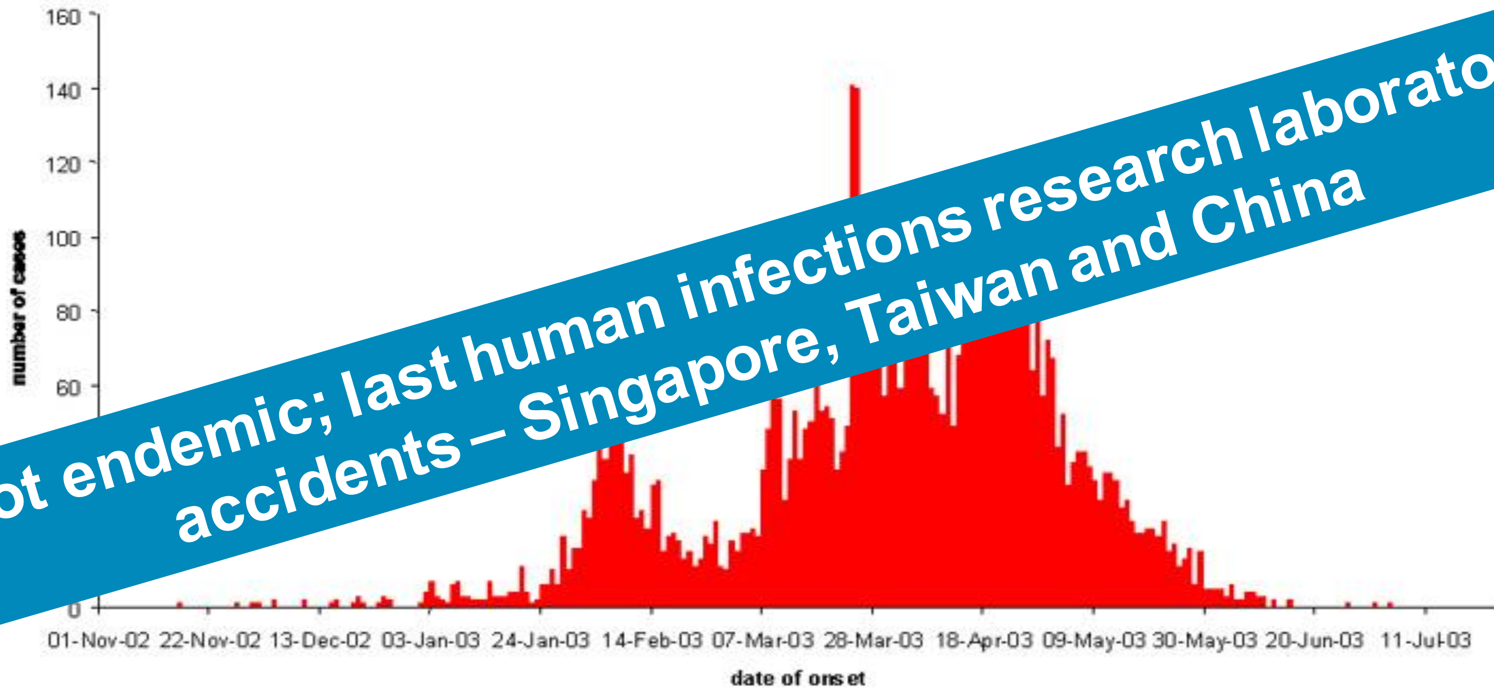
Source: CDC/WHO

SARS 2002-2003: worldwide spread



Source of reports: WHO

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



Not endemic; last human infections research laboratory accidents – Singapore, Taiwan and China

*This graph does not include 2,527 probable cases of SARS (2,521 from Beijing, China), for whom no dates of onset are currently available.

SARS, nosocomial transmission, Singapore 2003

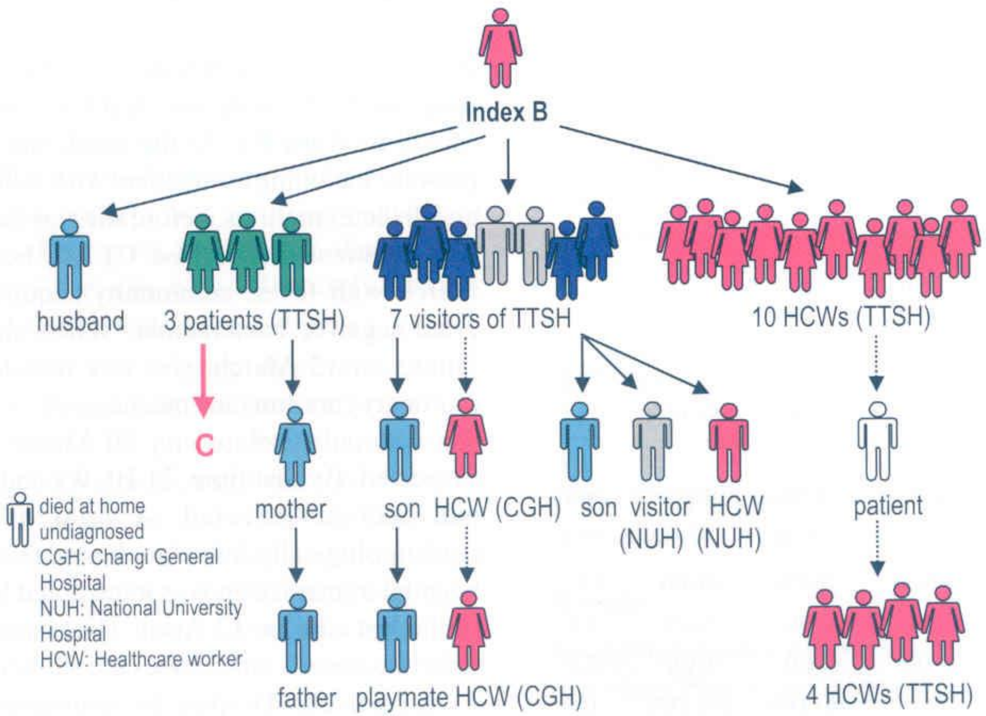


Fig. 2. Chain of transmission of index case B (healthcare worker), Tan Tock Seng Hospital (TTSH).

SARS-like coronavirus antibody in civet cats, Guangdong Province, China

Volume 10, Number 12—December 2004

Dispatch

Antibodies to SARS-Coronavirus in Civets

Changchun Tu*[1], Gary Crameri†[1], Xiangang Kong‡, Jinding Chen§, Yanwei Sun¶, Meng Yu†, Hua Xiang*, Xianzhu Xia*, Shengwang Liu‡, Yunwen Hu§, Yedong Yu¶, Bryan T. Eaton†, Hua Xuan*✉, and Lin-Fa Wang†

Author affiliations: *Changchun University of Agriculture and Animal Sciences, Changchun, China; †CSIRO Livestock Industries, Geelong, Australia; ‡Harbin Veterinary Research Institute, Harbin, China; §South China Agriculture University, Guangzhou; China; ¶Guangdong Provincial Veterinary Station of Epidemic Prevention and Supervision, Guangzhou, China

Cite This Article

Abstract

Using three different assays, we examined 103 serum samples collected from different civet farms and a market in China in June 2003 and January 2004. While civets on farms were largely free from SARS-CoV infection, ≈80% of the animals from one animal market in Guangzhou contained significant levels of antibody to SARS-CoV, which suggests no widespread infection among civets resident on farms, and the infection of civets in the market might be associated with trading activities under the conditions of overcrowding and mixing of various animal species.

Source: Tu C, Crameri G, Kong X, Chen J, Sun Y, Yu M, et al. Antibodies to SARS-Coronavirus in Civets. Emerg Infect Dis. 2004;10(12):2244-2248. https://doi.org/10.3201/eid1012.040520

SARS-like coronavirus antibody, wet markets, Guangdong Province

> MMWR Morb Mortal Wkly Rep. 2003 Oct 17;52(41):986-7.

Prevalence of IgG antibody to SARS-associated coronavirus in animal traders--Guangdong Province, China, 2003

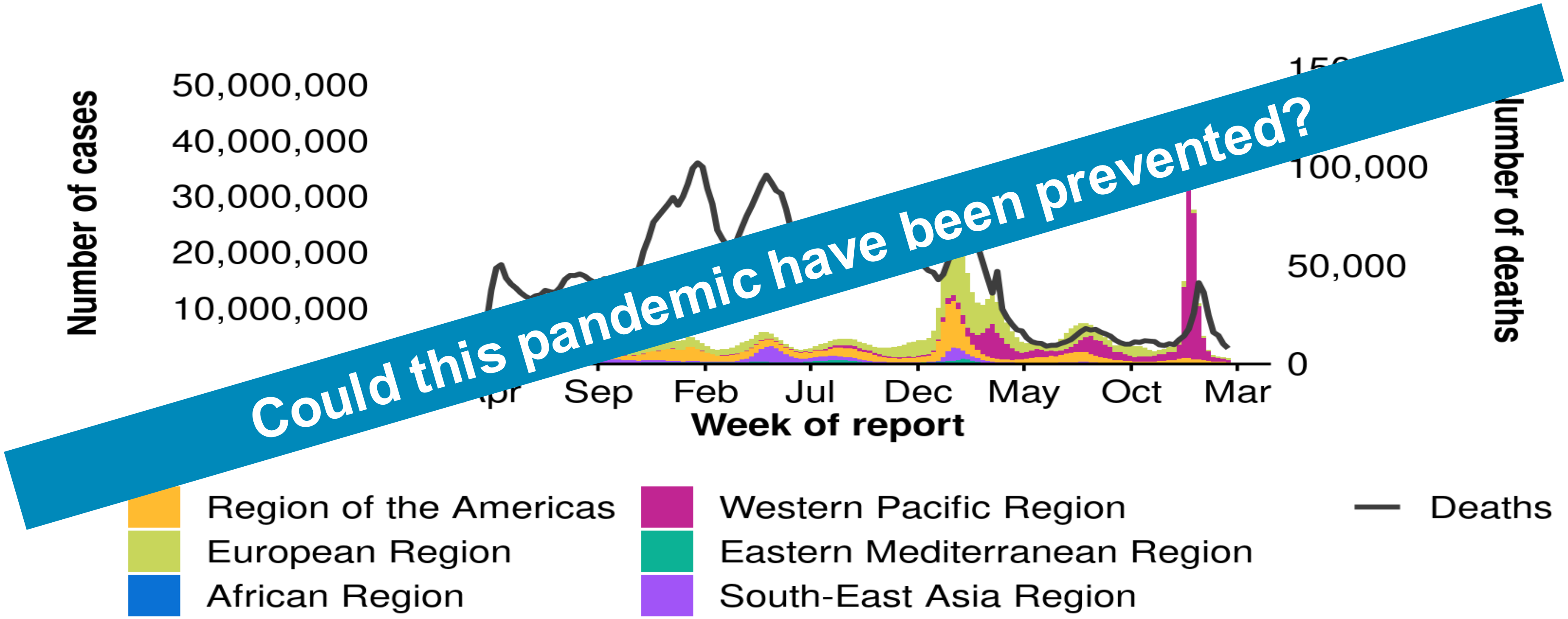
Centers for Disease Control and Prevention (CDC)

PMID: 14561956
Free article

Abstract

Severe acute respiratory syndrome (SARS) was identified in 2003 as an infectious disease caused by the SARS-associated coronavirus (SARS-CoV), a member of the coronavirus family not observed previously in humans. Because its sequence data differ from that of known human coronaviruses, SARS-CoV is suspected to have crossed the species barrier between an animal host and humans. The SARS outbreak began in China's Guangdong Province, where approximately 1,500 probable cases were identified during November 2002-June 2003. Detection of SARS-like coronavirus has been reported previously in masked palm civets (sometimes called civet cats) and a raccoon dog for sale in a live animal market in Shenzhen municipality. This report summarizes results of an investigation conducted by public health authorities in Guangdong Province, which compared the seroprevalence of SARS-CoV IgG antibody in animal traders (i.e., workers in live animal markets) with that of persons in control groups. The results indicated that 13% of the animal traders, none of whom had SARS diagnosed, had IgG antibody to SARS-CoV, compared with 1%-3% of persons in three control groups. Although the results provide indirect support for the hypothesis of an animal origin for SARS, they also underscore the need for detailed patient histories and more focused animal studies to confirm an animal origin for SARS.

Reported COVID-19: weekly cases and deaths (2020-2023)



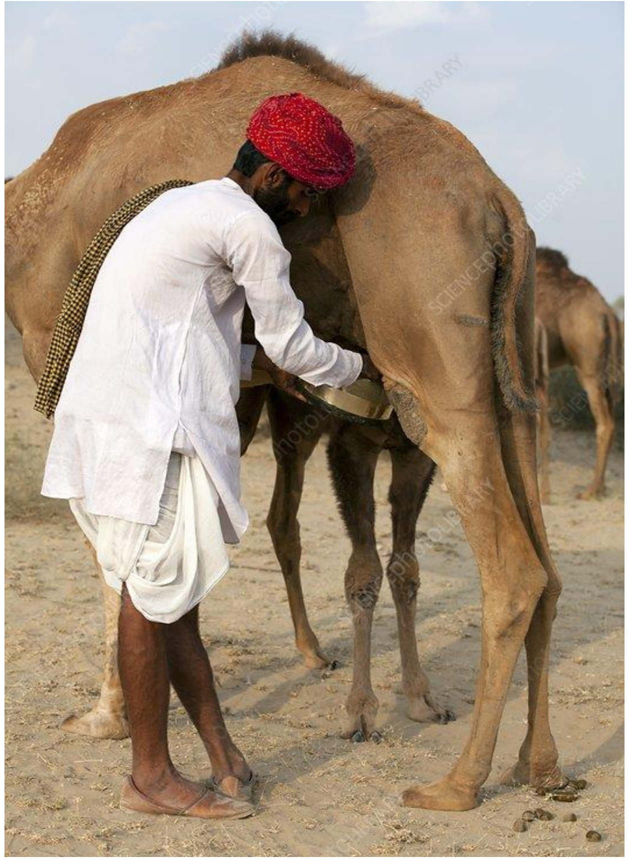
** Data are incomplete for the current week. Cases depicted by bars; deaths depicted by line.*

Source: WHO

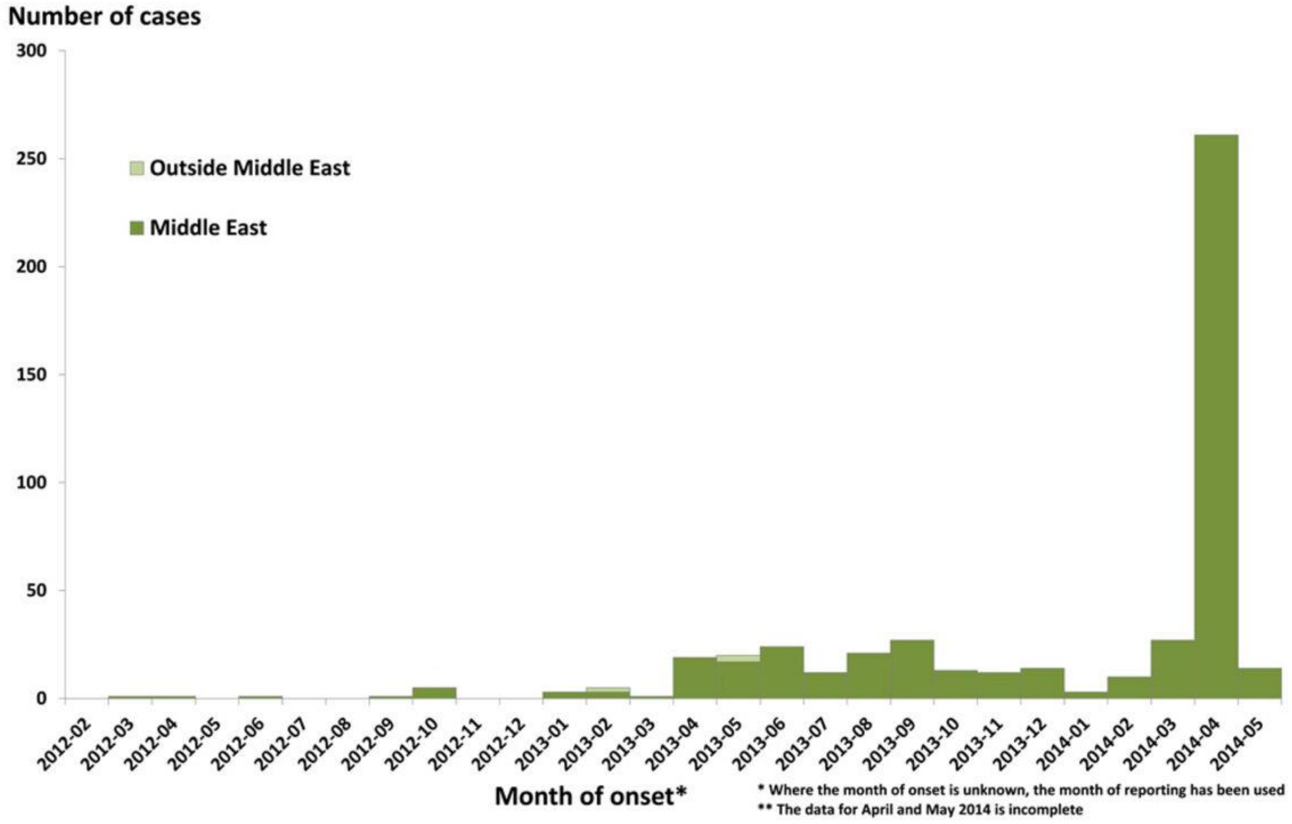
Translation of research findings into action

- China response: forbid sale of live wild animals
- One health response:
  - Clean up wild animal farming and markets
  - Educate live animal market handlers
  - Educate population
  - Develop and use veterinary vaccines
  - Stronger infection and control in healthcare facilities and laboratories

MERS Coronavirus: emergence 2012

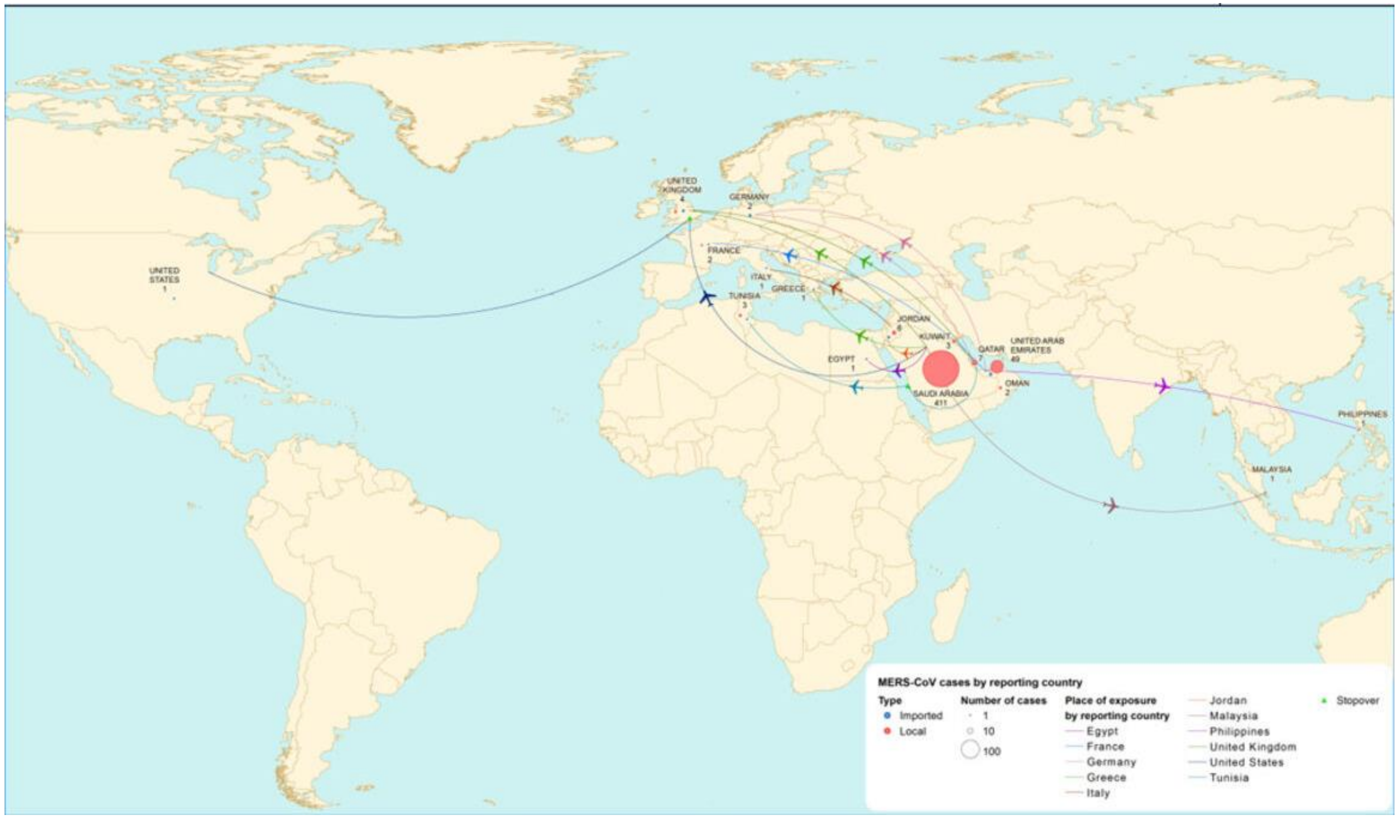


MERS CoV, initial reported cases, 2012 - 2014



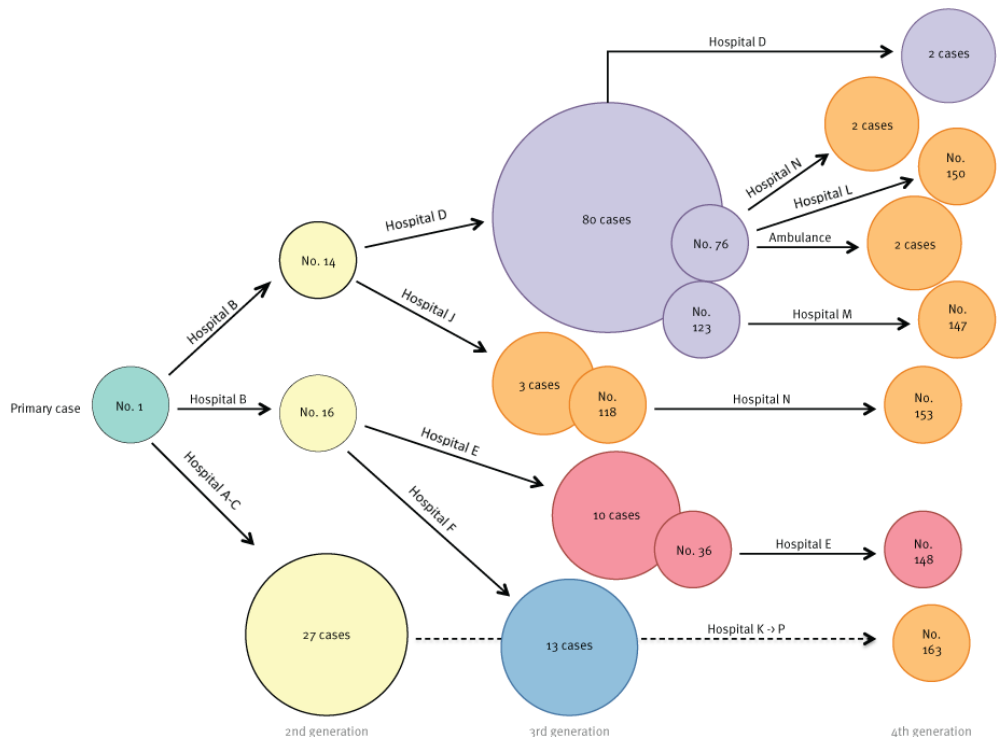
Source: ECDC

Initial international spread, MERS Coronavirus, ECDC, 2012 - 2014



Source: ECDC

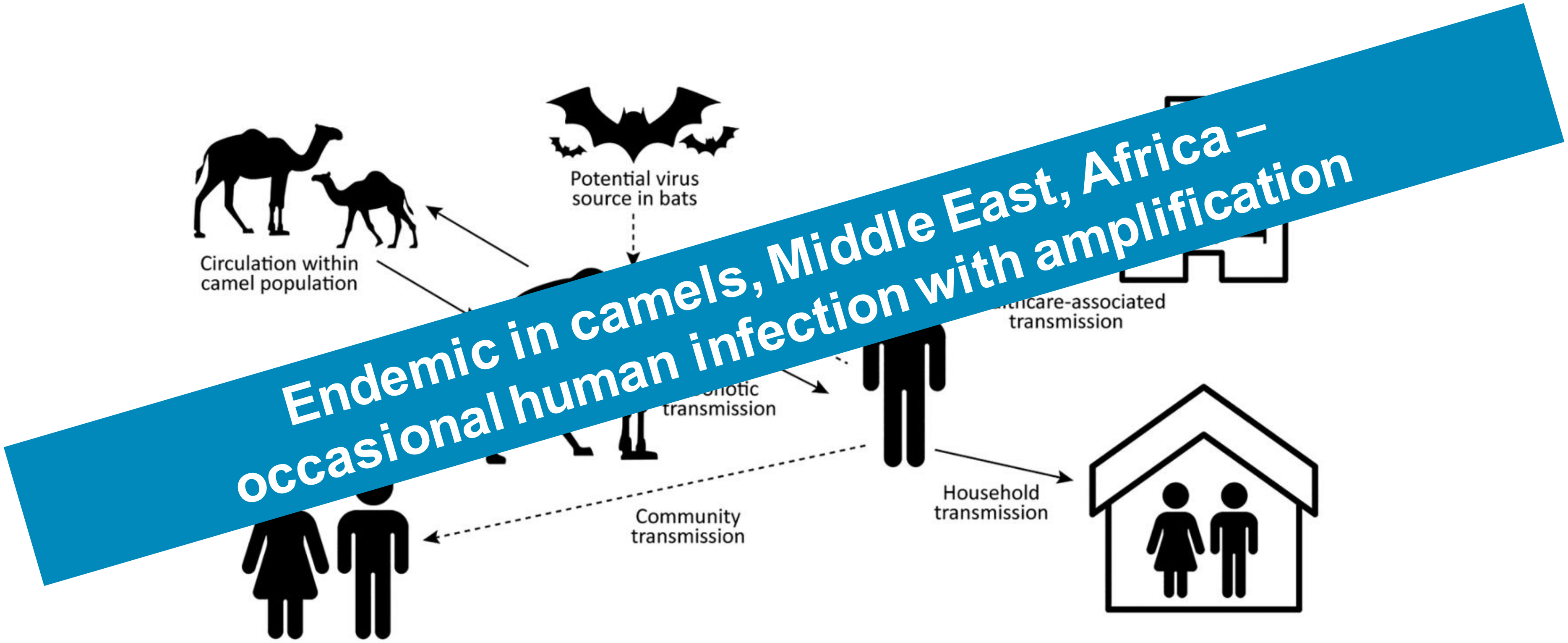
Nosocomial outbreak MERS Coronavirus, Korea, 2015



MERS-CoV: Middle East respiratory syndrome coronavirus.

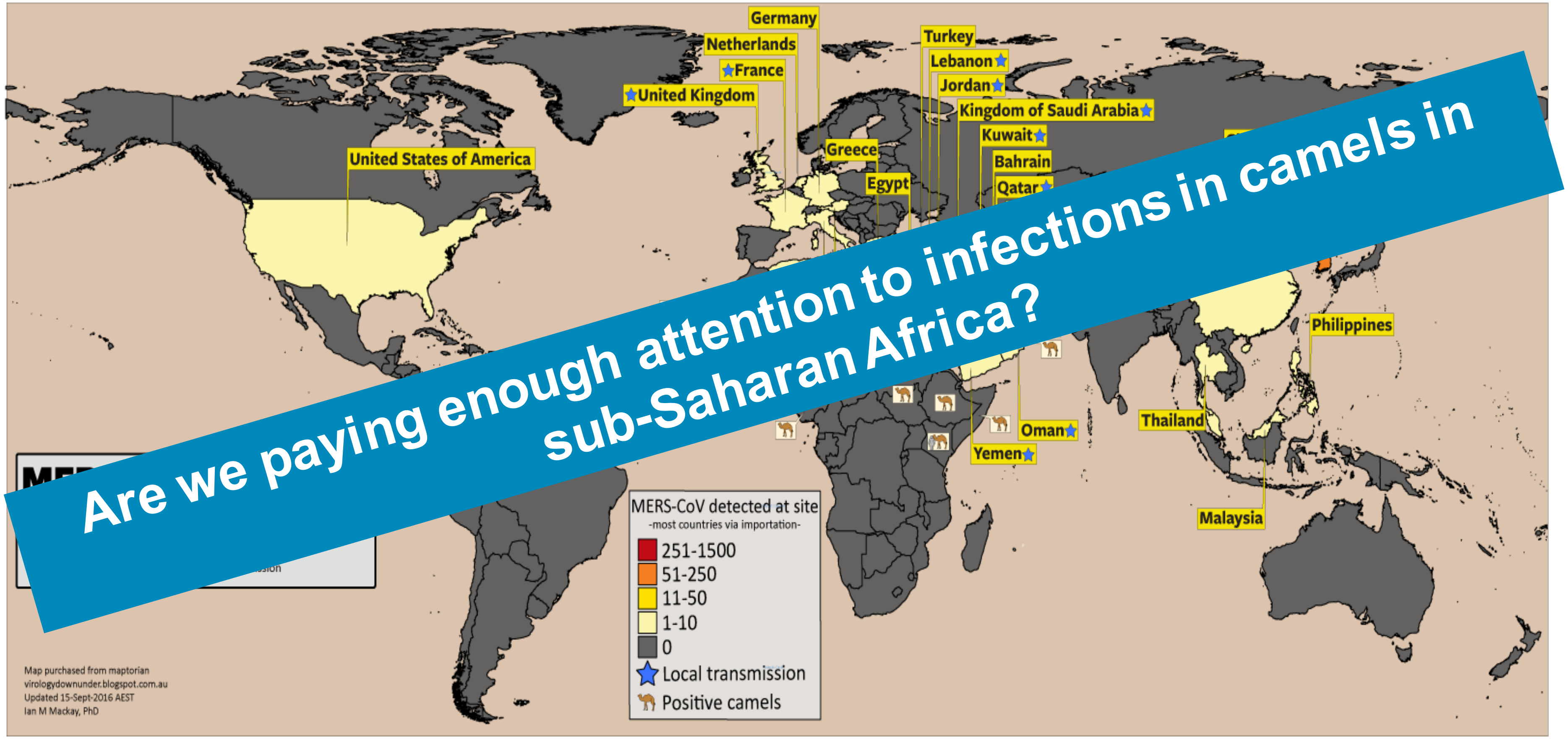
Source:: Ministry of Health South Korea

MERS Coronavirus: continued emergence to humans



Source: Killerbey::Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 26, No. 2, February 2020

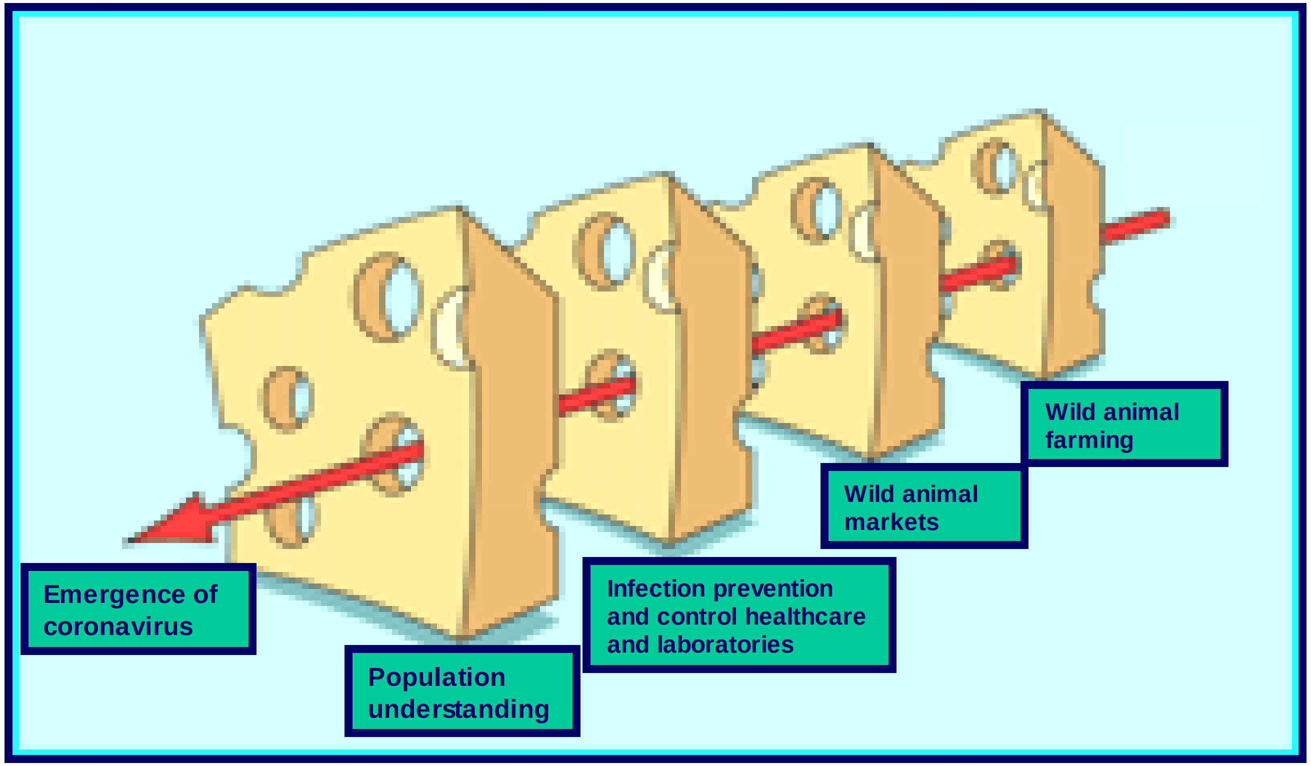
MERS Coronavirus worldwide, September 2016



Outbreaks and pandemics at the human/animal interface

- Humans are often the sentinel population for infections in animals
- Outbreaks cause human sickness and death
- Outbreaks cost economies and each sector including animal and human health
- The extent of economic burden in the animal health sector depends on whether emergence is one time, or periodic and leads to culling

Swiss cheese analysis:
shifting the paradigm to prevention at the source



James Reason: BMJ 2000;320:768-770

- Current paradigm: rapid detection and response

Bovine spongiform encephalopathy

Culling cattle with Bovine Spongiform Encephalopathy, UK, 1990s

Human prion-associated disease

Kuru

Creutzfeldt-Jakob Disease

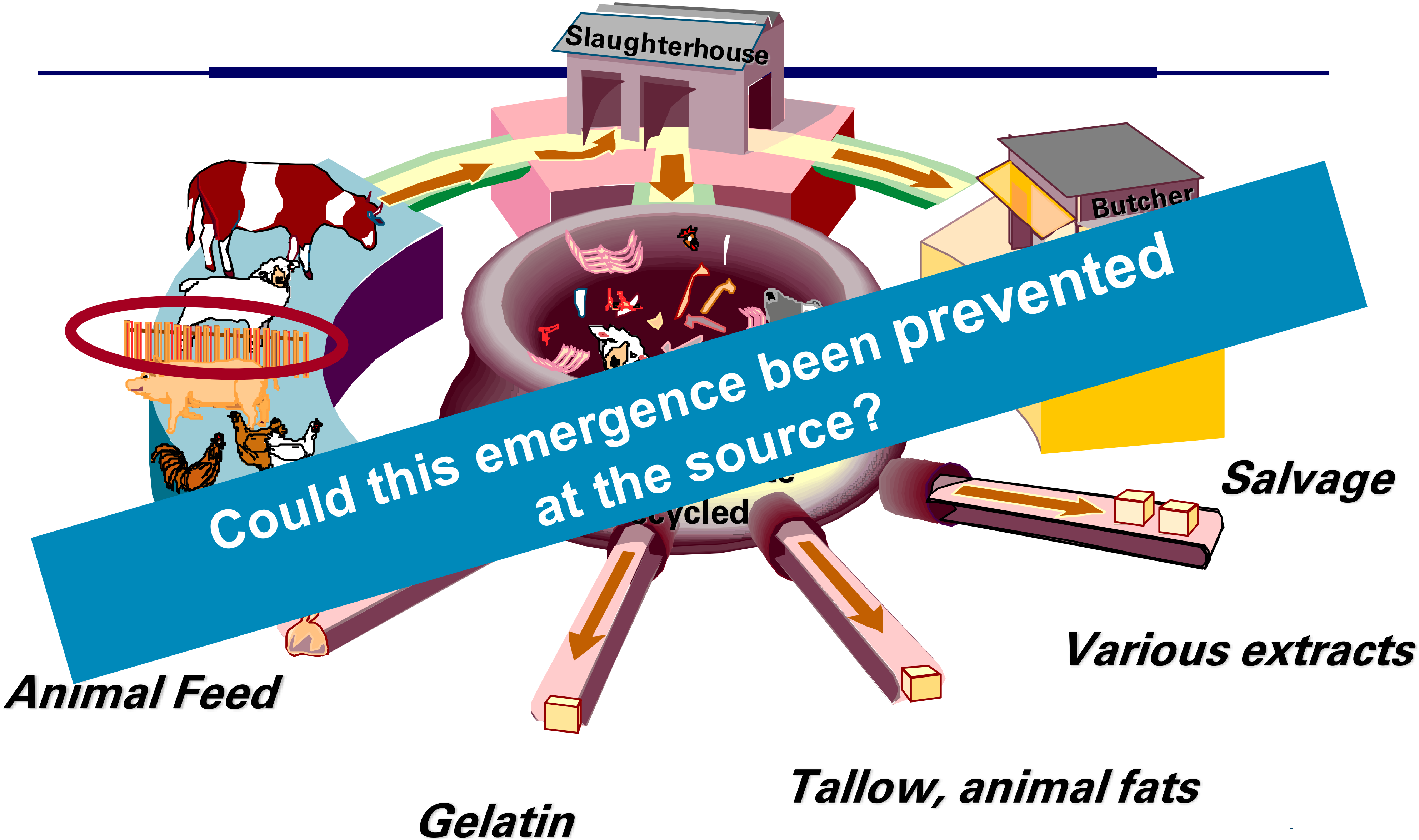
BSE: precautionary measures

BSE in humans:
variant Creutzfeldt-Jakob Disease (v-CJD)

- Age: 29 (16-52)
- Symptoms: psychiatric symptoms early stage
- Duration: 24 months (9.5-38) to death

first identified 1995/1996

The great recycling, late 1980s



Certification of smallpox eradication,1980

Fenner F et al.. Smallpox and its Eradication. World Health Organization

Human monkeypox 1970: identification of a new infection in humans

World Health Organization photo library

Human monkeypox 1958 – 1979: Congo basin clade (Clade I)*

First identified: captive (laboratory) monkeys, 1958, Copenhagen

Case investigations 1970 – 1979:

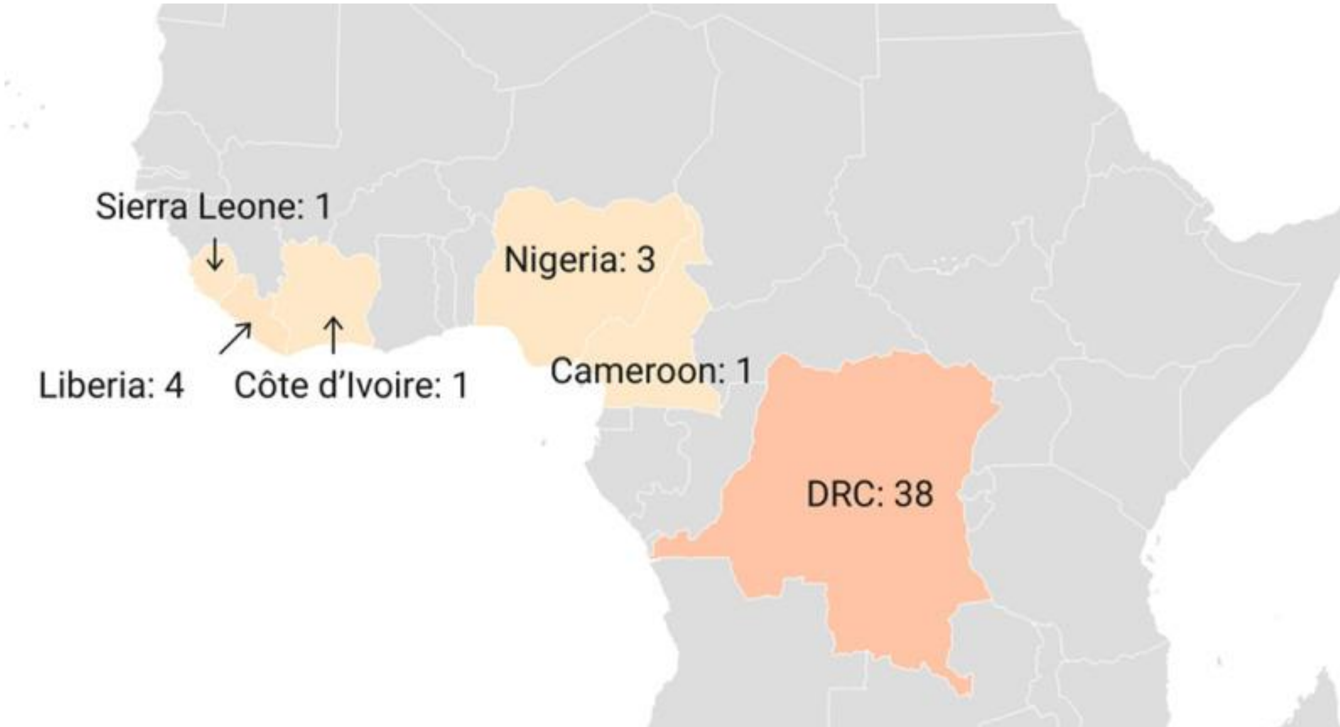
- sporadic West and Central Africa (n=48)
- 72% of cases animal contact
- 3 generations transmission maximum, occurred in 8% of outbreaks
- case fatality 10%, some facial scarring
- primary cases rare over 15 years of age
- most secondary/tertiary infections in unvaccinated parent or sibling
- Smallpox vaccination protected against infection

- Question: will human monkeypox fill the epidemiological niche left by smallpox as smallpox vaccination coverage decreases?

* Likely Clade I

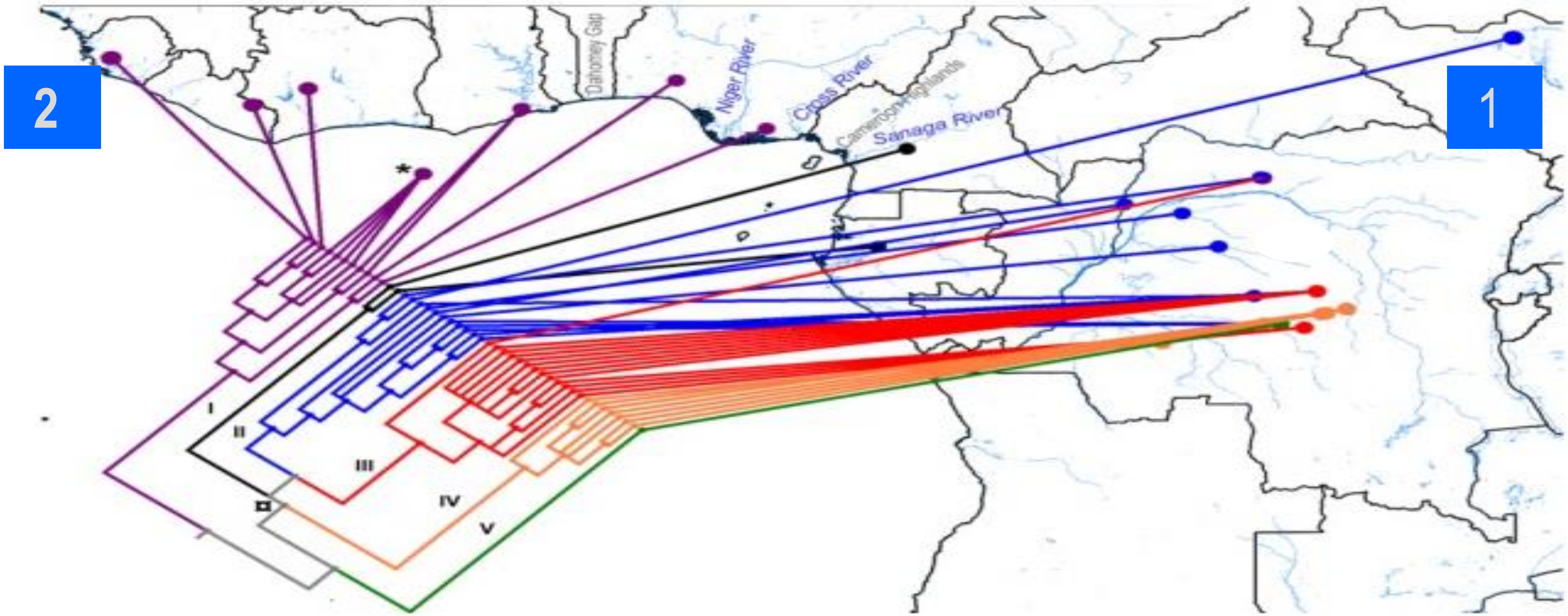
Jezek Z, Grab B, Szczeniowski M, Paluku KM, Mutombo M. Clinico-epidemiological features of monkeypox patients with an animal or human source of infection. *Bull World Health Organ.* 1988;66(4):459–464.

Confirmed, probable and/or possible human monkeypox cases 1970-1979



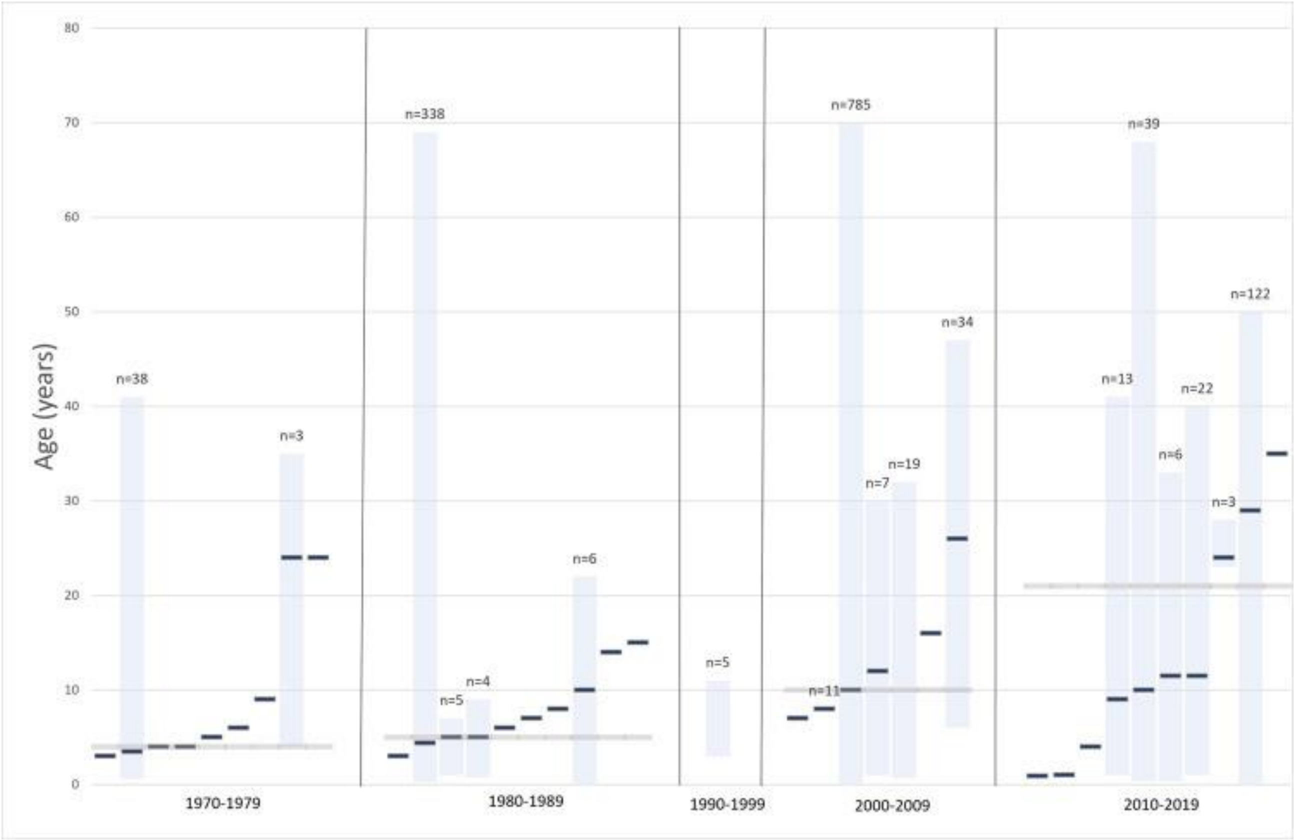
The changing epidemiology of human monkeypox—A potential threat? A systematic review - PMC (nih.gov)

Human monkeypox, clades 1 and 2



Viruses 7(4):2168-2184
DOI:10.3390/v7042168

Age of human monkeypox infections by year, 1970 – 2019 (horizontal lines represent weighted median)



The changing epidemiology of human monkeypox—A potential threat? A systematic review - PMC (nih.gov)

Confirmed, probable and/or possible human monkeypox cases 2010-2019

The changing epidemiology of human monkeypox—A potential threat? A systematic review - PMC (nih.gov)

Human monkeypox (Mpox), 2022

2022 Monkeypox Outbreak Global Map

Data as of 06 Dec 2022 5:00 PM EDT

View: ◉ CASES ○ DEATHS

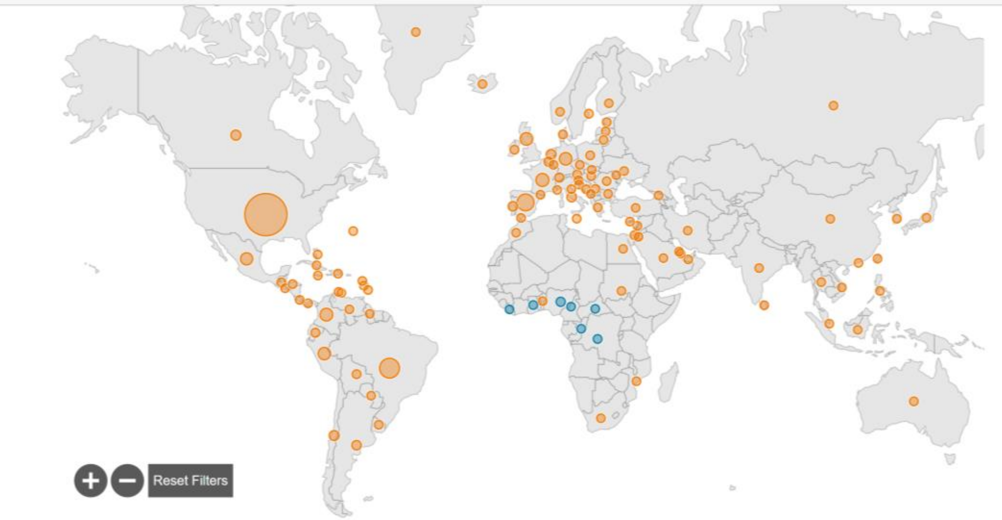
< 2022 U.S. Monkeypox Outbreak

Confirmed Cases

82,147 Total Cases	**81,174** in locations that have not historically reported monkeypox	**973** in locations that have historically reported monk

Locations with cases

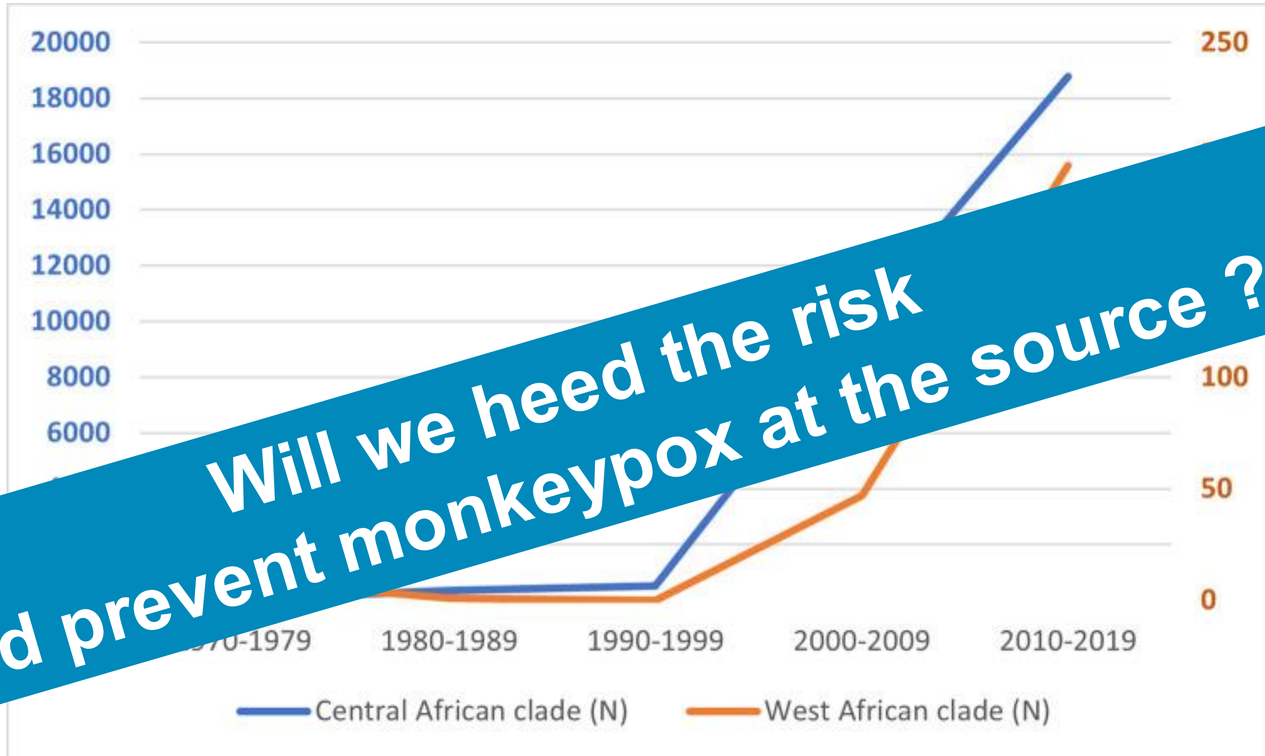
110 Total	**103** Has not historically reported monkeypox	**7** Has historically reported monkeypox



Legend

● Has not historically reported monkeypox ● Has historically reported monkeypox

Suspect and confirmed human monkeypox infections, 1970-2019



Will we heed the risk and prevent monkeypox at the source ?

[The changing epidemiology of human monkeypox—A potential threat? A systematic review - PMC (nih.gov)]

Infections at the human/animal interface

- To shift the paradigm from rapid detection and response to prevention at the source:
  - Identify and block the risks/think of Swiss Cheese
  - Learn from the past and translate to the future
  - Work together in the human, animal and environmental sectors

- **A shift to prevention at the source can be made with understanding of risk factors, innovation and working across sectors**

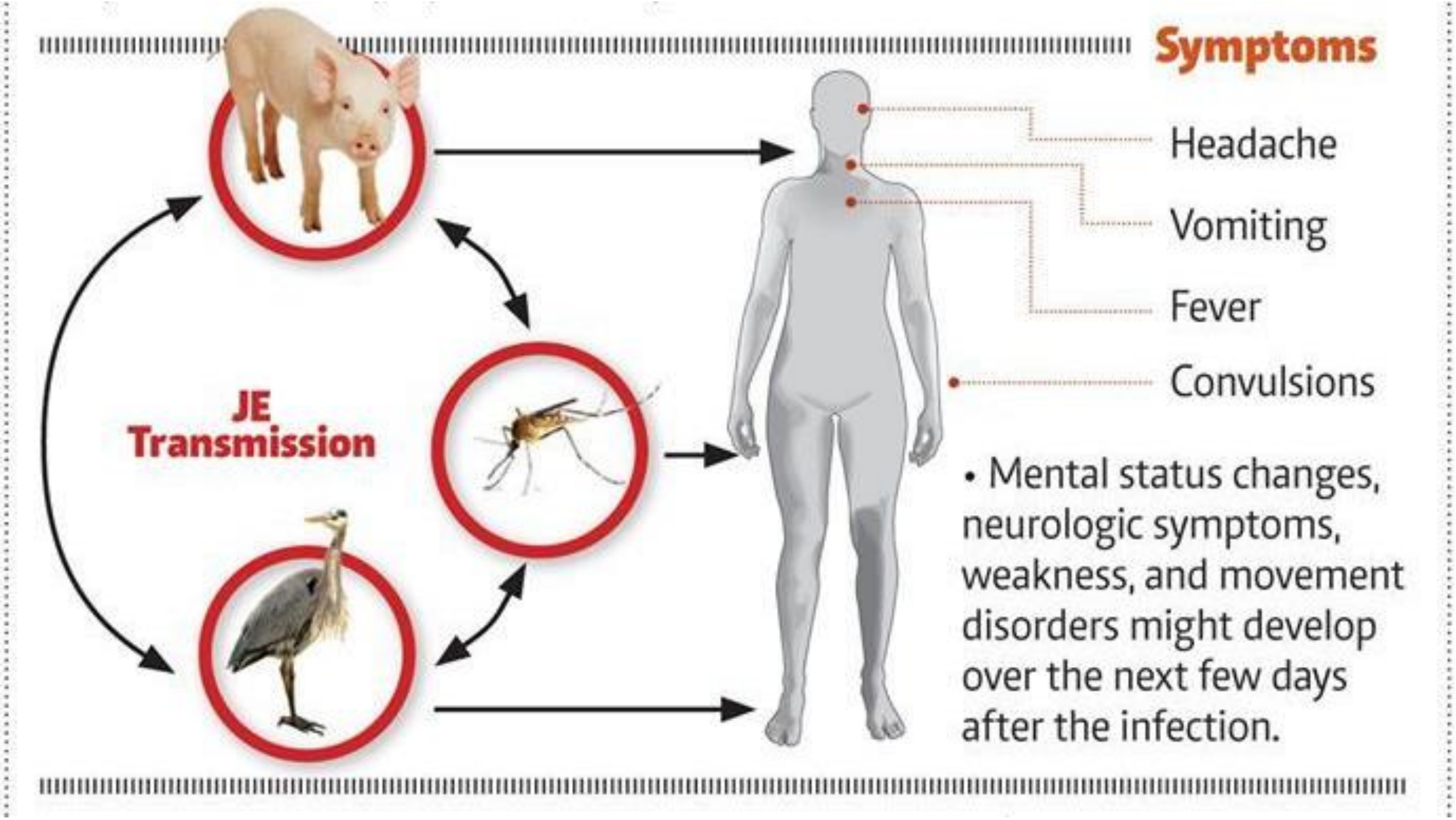
Encephalitis among pig famers, Malaysia, 1998-1999

Source: Chua KB, Journal of Clinical Virology, April 2003

Encephalitis outbreaks, humans, 1998 - 1999

Dates	Location	No. cases	No. deaths	CFR(%)
1998-1999	Malaysia;	265	105	40
1999	Singapore	11	1	9

Japanese encephalitis



Discovery of Nipah virus, paramyxovirus, Malaysia,1998

Discovery of Nipah virus a major breakthrough

IT WAS service to the country and he wasn't looking for fame or recognition. But Dr Tan Chong Tin who led the Nipah encephalitis investigation team from Universiti Malaya gained global acknowledgement for his work in discovering a new virus.

And last year, the team was recognised nationally when they were awarded joint recipients of the Merdeka Award in the health, science and technology category.

"We feel honoured to have contributed to the discovery. As human beings, it does feel good to have affirmation of our work – but we don't look for it," says Dr Tan humbly.

He also credits the actual discovery of the virus to Dr Chua Kaw Bing and says that "accepting the award was another way of recognising his discovery."

When asked how he feels about his team's accomplishment, he says it was a good piece of scientific work.

"It is widely recognised but more importantly, it made a difference to many people's lives. It also created real knowledge – not just locally, but internationally as well," he says, adding that their discovery had a great impact when there was an outbreak of the Nipah virus in Bangladesh and India.

However, he adds that there is another dimension apart from the recognition of the work done.

"This kind of award is quite timely as the country needs to recognise good scientific work. There is a need to put science and research in a higher hierarchy in our local values. This sort of emphasis will augur well for the future of our society and for professionalism in general."

Describing the early days of the outbreak, he says when the first cases surfaced in Ipoh, the health authorities thought it was Japanese encephalitis (JE) and health measures were taken accordingly.

However, it was not until cases appeared in Seremban three months later and patients were referred to the University Malaya Medical Centre (UMMC) that it came to their attention. But the realisation that the virus was completely unknown was not a *eureka* moment.

"Actually, the discovery of the disease was a gradual thing. Within the first three to four days, we knew that there was something about the virus that was different from JE. The evidence came cumulatively, and as more came in, we did tests to confirm it.

"We gradually began to feel more comfortable with it as evidence told us we were on the right track.

"Final confirmation came within 10 to 12 days and final identificatioin was done in the United States," he says.

Proud team: Dr Tan (far right) and Dr Chua (second from right) together with other members of the Nipah encephalitis investigation team from Universiti Malaya's Faculty of

Nipah virus (emergence 1999): presumed transmission chain, Malaysia

Fruit bat

Domesticated swine

Human

Nipah virus outbreaks, humans, 1998 - 2008

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

Changing Nipah virus epidemiology: Bangladesh and India 2001 - 2008

- ✓ Human-to-human transmission first suspected 2001, hospitalised patients, India
- ✓ Human to human transmission suspected again in 2003, 2005, and 2007, Bangladesh in close family members and hospitalised patients
  - no cases could be linked to direct pig exposure
  - known that fruit bats carried Nipah virus
  - one potential exposure to bat guano: palm sap collector

Palm sap collector, Bangladesh

Preventing Nipah Virus emergence: hypothesis generation

Fruit bat

Bat guano palm sap

Palm sap ready to drink

Assessing the risk/testing the hypothesis

The risk is plausible through the food chain

Courtesy: Dr Shovon Shazzad, Dr Salah Uddin Khan, and Dr Steve Luby, ICCDR,B and Stanford University.

Nipah virus transmission from bats to humans from date palm sap, December 2010 – March 2014

- 15 clusters Nipah infection identified by hospital surveillance
- 3 clusters investigated: 14 cases, 8 of whom died
  - 8 drank fermented palm sap regularly
  - 6 provided care to infected patient in home or hospital

Source: Islam MS et al, EID Volume 22:4, April 2016

Precautionary measure: community understanding of importance to cover the collection containers

Community agriculture meeting