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

Emergence

- No further transmission
- Continues transmission → Ceases/sporadic
- Continues transmission → Continues/endemic
Breaches in species barrier: emerging infections in humans

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

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

Russian influenza pandemic, 1889 - 1893

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

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


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

Alpha coronaviruses

Beta coronaviruses

Virus diversity

Animal reservoir

Intermediary host

CoV strain detected in humans

HCoV-NL63

HCoV-229E

HCoV-OC43

HCoV-HKU1

SARS-CoV

MERS-CoV

SARS-CoV-2

2003

2012

2019

Pandemic CoV
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


Number of cases

- Canada: 251 (43)
- United States: 29 (0)
- Colombia: 1 (0)
- United Kingdom: 4 (0)
- Ireland: 1 (0)
- France: 7 (1)
- Spain: 1 (0)
- Italy: 4 (0)
- Sweden: 5 (0)
- Germany: 9 (0)
- Switzerland: 1 (0)
- Romania: 1 (0)
- Russia: 1 (0)
- Mongolia: 9 (0)
- China: 5,327 (349)
- Russia: 1 (0)
- South Korea: 3 (0)
- Taiwan: 346 (37)
- Hong Kong: 1,755 (299)
- Macao: 1 (0)
- Philippines: 14 (2)
- Indonesia: 2 (0)
- Singapore: 238 (33)
- Malaysia: 5 (2)
- South Africa: 1 (1)
- Australia: 6 (0)
- New Zealand: 1 (0)
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.
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

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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, 48% 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.

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

Number of cases

- Outside Middle East
- Middle East

* Where the month of onset is unknown, the month of reporting has been used
** The data for April and May 2014 is incomplete

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

Source: ECDC
Nosocomial outbreak MERS Coronavirus, Korea, 2015

Source:: Ministry of Health South Korea
MERS Coronavirus: continued emergence to humans

Endemic in camels, Middle East, Africa – occasional human infection with amplification

Source: Killerbey::Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 26, No. 2, February 2020
Are we paying enough attention to infections in camels in sub-Saharan Africa?
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

Wild animal farming
Wild animal markets
Infection prevention and control healthcare and laboratories
Population understanding
Emergence of coronavirus

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

Could this emergence been prevented at the source?

- Animal Waste recycled
- Animal Feed
- Gelatin
- Tallow, animal fats
- Various extracts
- Salvage
- Butcher
- Slaughterhouse
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
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?

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)
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 monkeypox

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

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Japanese encephalitis

Symptoms:
- Headache
- Vomiting
- Fever
- Convulsions

- Mental status changes, neurologic symptoms, weakness, and movement disorders might develop over the next few days after the infection.
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 Mokdeka 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 Kow Bang 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 casual 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 identification was done in the United States," he says.
Nipah virus (emergence 1999): presumed transmission chain, Malaysia

- Fruit bat
- Domesticated swine
- Human
## Nipah virus outbreaks, humans, 1998 - 2008

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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
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

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

Community agriculture meeting