

Societal drivers of disease emergence - the consequences of human actions and activities

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Sixth World Conference of The Future of Science:

Viruses: the Invisible Enemy

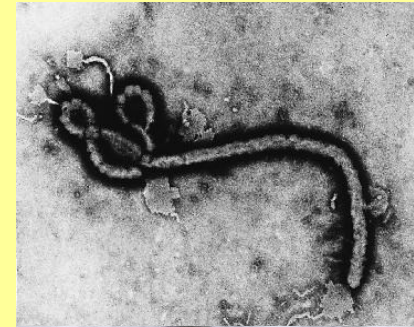
Venice, September 19-21, 2010

Plan of the presentation

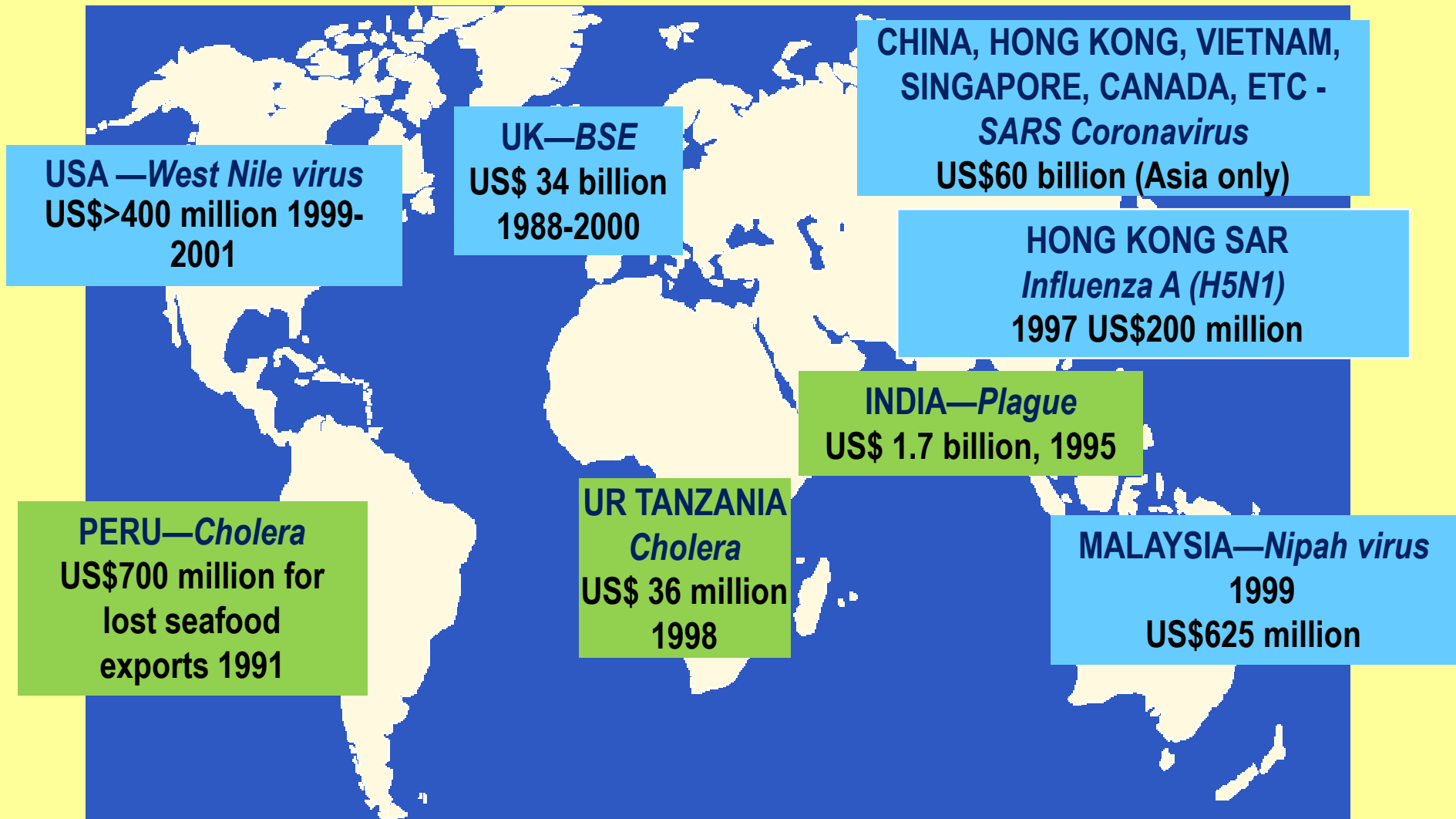
- First I will briefly discuss the major factors that affect the emergence of new, previously unknown viruses, or the resurgence of known viruses, and that promote their spread between countries and continents.
- The major part of the presentation will be a description of how these factors are associated with human actions and/or activities with respect to specific viruses – dengue, chikungunya, Murray Valley encephalitis, and Nipah viruses.
- I must also confess at the outset that I may be just a little parochial (Australian!) with some of the examples I've selected!

So, in the context of emerging/epidemic disease at the beginning of the 21st. Century:

- ❖ Emergence of new or newly recognised pathogens (e.g. Highly Pathogenic Avian Influenza [H5N1], swine influenza H1N1, SARS, Nipah, swine infections with Ebola-Reston)
- ❖ Resurgence of well characterised outbreak-prone diseases (e.g. dengue, measles, yellow fever, chikungunya - also cholera, TB, meningitis, shigellosis)
- ❖ Concern about accidental or deliberate release of a biological agent (e.g. smallpox, SARS, Ebola, anthrax, tularaemia, etc)
- ❖ The huge economic costs of infectious disease outbreaks (e.g. >US\$60 billion for SARS).
- ❖ **The reality is – we are vulnerable as a global community and need to understand the factors that presage virus emergence, epidemic activity and the mechanisms of virus spread, and only by understanding them can we mitigate or prevent their occurrence.**



Economic impact, selected infectious disease outbreaks, 1990–2004



Based on CDC, 2005

Factors Responsible for Emergence, Resurgence and Increased Spread of Infectious Diseases

(a) Human activities:

- **Changes in human demographics or behaviour:**
 - Population growth and migration; Urbanisation
 - War/civil conflict/bioterrorism;
 - Human behaviour - sexual behaviour/intravenous drug use
- **Changes in technology & industry:**
 - Globalisation of food supplies; Changes in processing; use of antibiotics as food supplements
 - New technologies; eg Organ/tissue transplantation;
- **Economic development and land use:**
 - Changes in agricultural practices; Intensive agriculture
 - Dam building; Increased irrigation
 - Deforestation/reforestation;
- **International travel & commerce:**
 - Worldwide movement of people and goods;
 - Transport of mosquitoes and other vectors, and establishment in new geographic areas.
- **Microbial adaptation and change:**
 - Microbial evolution;
 - Response to environmental selection.
- **Breakdown in public health:**
 - Reduction in prevention programmes;
 - Inadequate sanitation; inadequate vector control.

(b) Natural Occurrences:

- Climate
- Vertebrate host movement, such as migratory bird movements
- Natural disasters

Dengue viruses 1-4

- Examples of mosquito-borne Flaviviruses which have spread widely across tropical and sub-tropical areas of the world over the past 5-6 decades due to a several human activities/actions.
- They cause dengue fever, and occasionally in cases of secondary infection due to a different serological type, a severe disease known as dengue haemorrhagic fever (DHF), which can lead to the highly fatal dengue shock syndrome (DSS).
- Prior to the 1950s, dengue fever was a moderately common disease in tropical areas, but DHF/DSS was a rare complication.
- DHF was first described in 1887 in Charters Towers, Australia, but most cases prior to 1955 were reported from SE Asia.

Dengue Virus

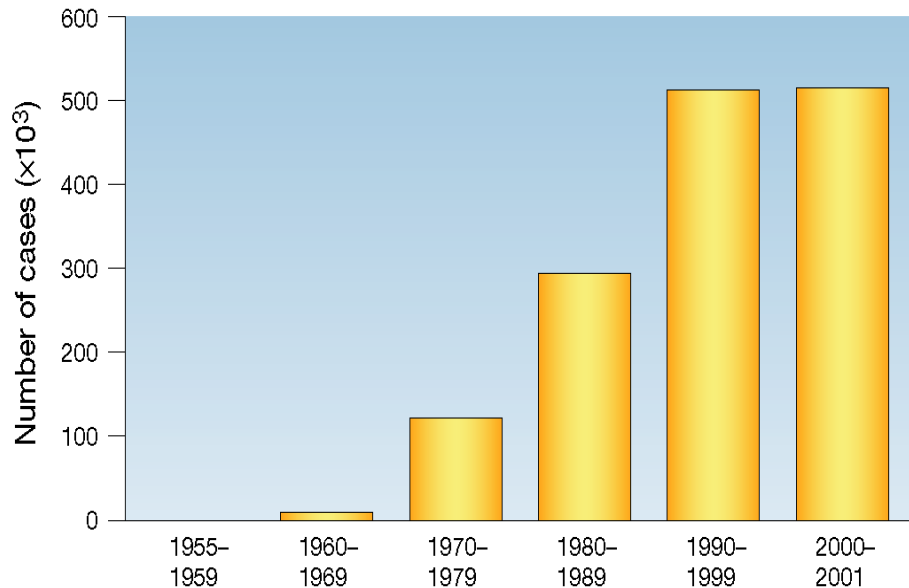
Dengue fever

- fever, retroorbital headache, myalgias, nausea, petechiae, acute illness lasts 3-7 days, convalescence may last weeks
- recently cases of encephalitis have been reported from a number of countries, including one Australian case.

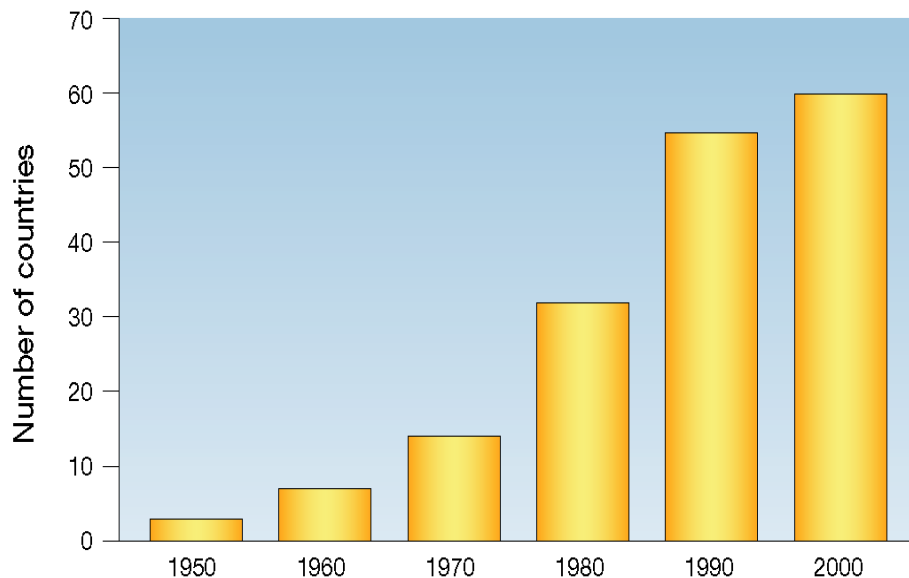
Dengue haemorrhagic fever/Dengue shock syndrome

- develop severe bleeding problems and possibly hypotension; due to antibody-mediated enhancement related to declining antibodies from prior infection by a different dengue serotype.

a Dengue/dengue hemorrhagic fever,
average annual number of cases reported to WHO, 1955–2001



b Countries in the world reporting DHF cases,
1950–2000 (cumulative)*



The major factors in dengue emergence:

- Population growth
- Urbanisation – crowded shanty towns, with uncleared garbage, poor sanitation and poor access to clean water.
- Modern, rapid international transportation.
- Establishment of vector(s) in new areas.

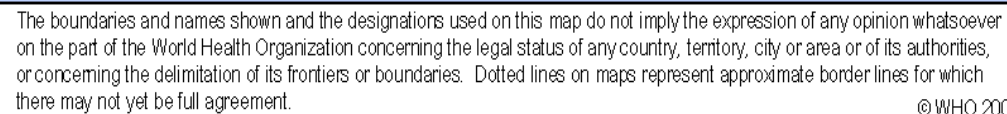
Mackenzie, Gubler & Petersen (2004) *Nature Med* 10(12): S98-S109

Global Dengue Disease Burden

	<u>Reported (1998)</u>	<u>Estimates</u>
No. Dengue cases/year	1.2 million	51 million
No. DHF/DSS cases/year	No data	400,000 [=0.8%]
No. deaths/year	3,500 [=0.3%]	15,000 [=0.03%]



WHO/CDS

[illegible]

Data Source: WHO
Map Production: Public Health Mapping and GIS
Communicable Diseases (CDS) World Health Organization

What precipitated the dengue viruses to emerge and spread?

Initially it was very much due to:

- Population increases; and
- Urbanisation – movement from rural areas to cities, resulting in rapid and uncontrolled urban growth



Science 1995;270:1125

Shanty town, Bangkok



What precipitated the dengue viruses to emerge and spread?

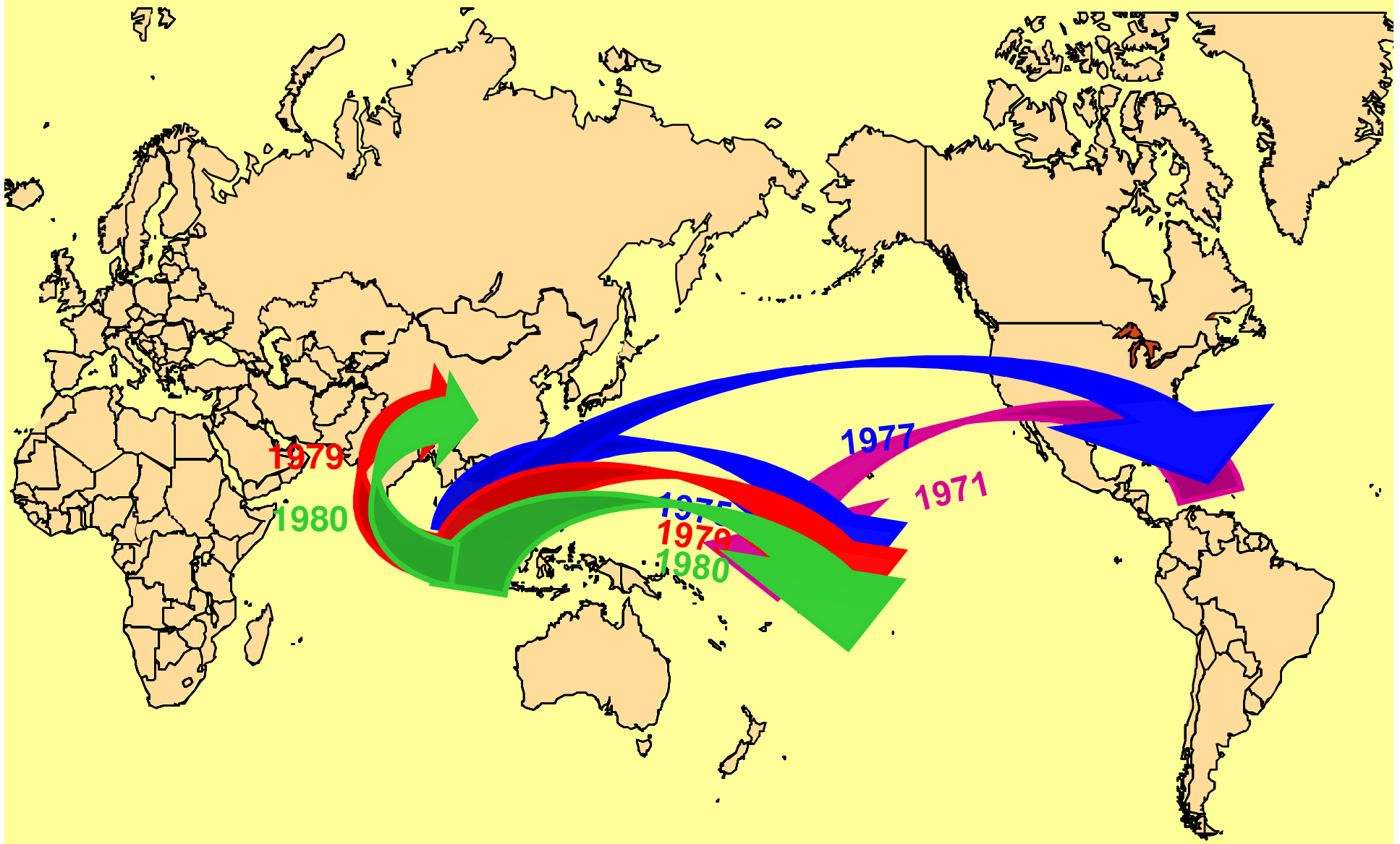
- Population increase
- Urbanisation – movement from rural areas to cities, resulting in rapid and uncontrolled urban growth
- Modern transportation – rapid intercontinental air travel, providing a means of spreading the virus around tropical and sub-tropical areas of the world through the movement of infected people and mosquitoes

Global aviation network

Hufnagel L et al. PNAS 2004;101:15124-15129



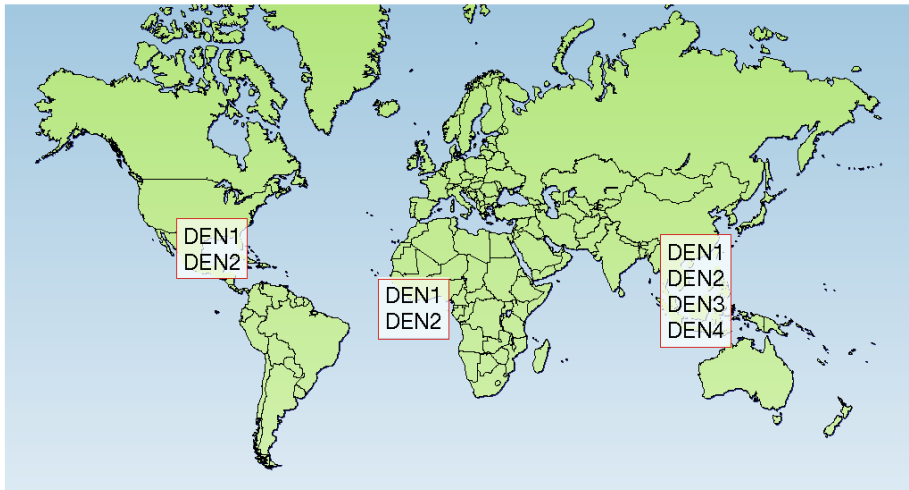
Global Movement of Dengue (1971-1980)



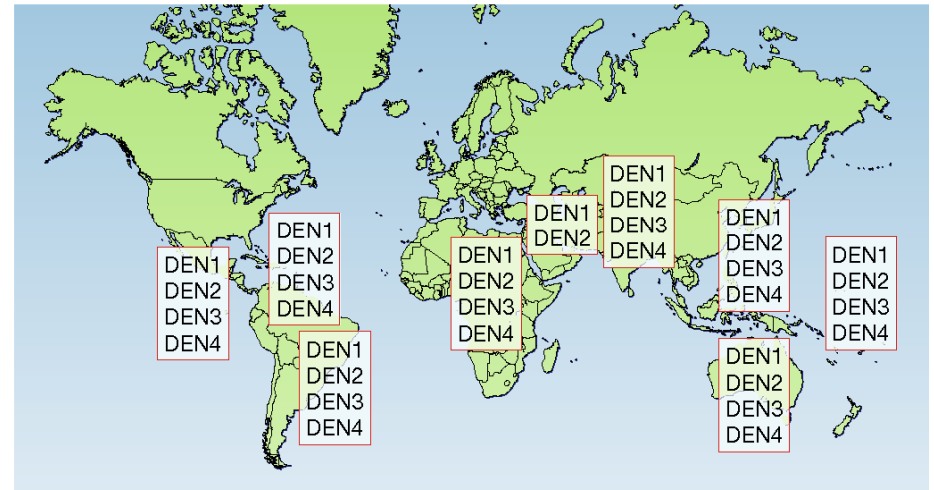
DENV – 1; DENV – 2; DENV – 3; DENV – 4

Gubler, 2010

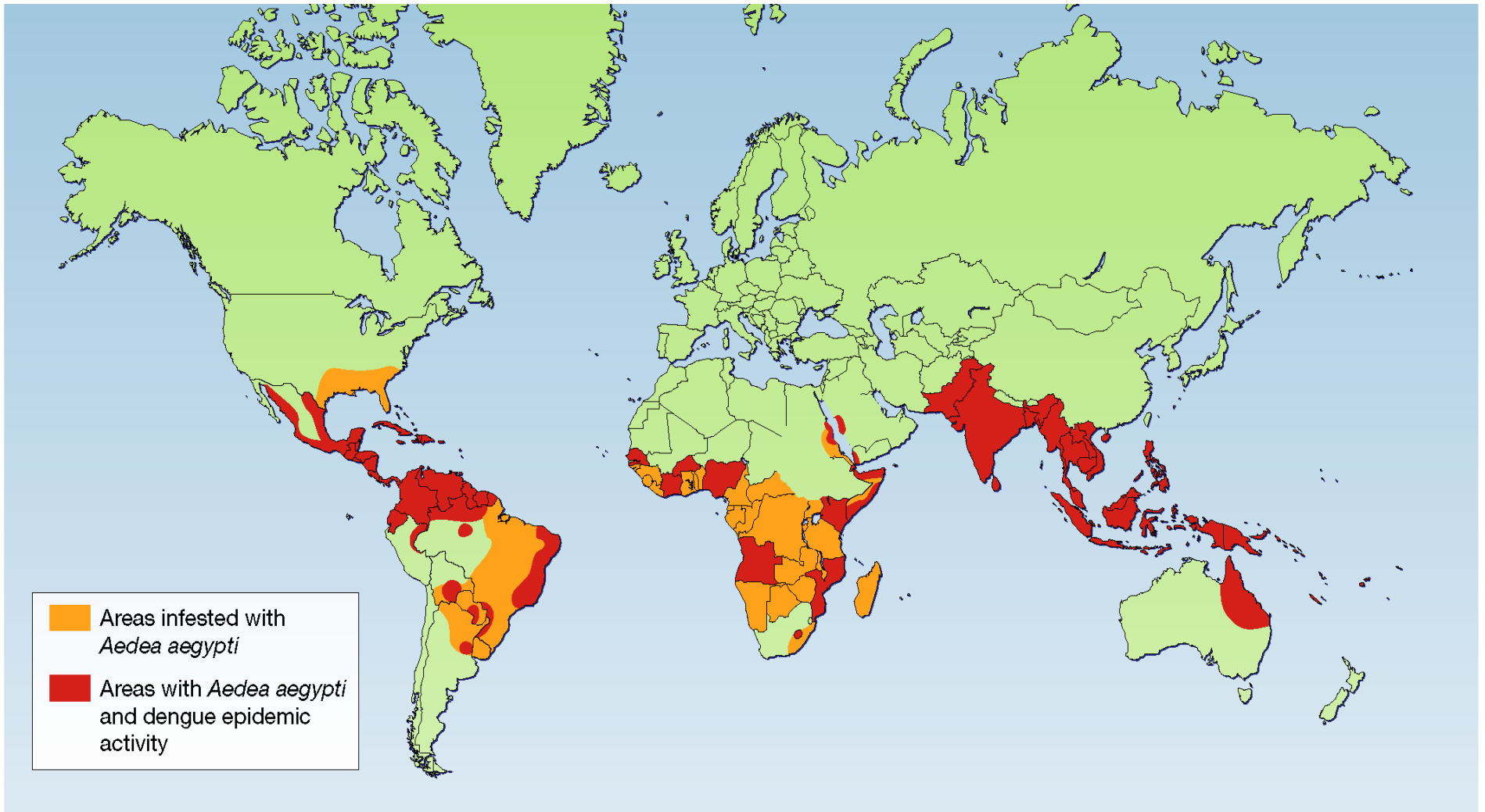
Global distribution of dengue virus serotypes, 1970



Global distribution of dengue virus serotypes, 2004



Areas infested with *Aedes aegypti*, and with dengue epidemic activity - 2005



Mackenzie, Gubler & Petersen (2004) *Nature Med* 10(12): S98-S109

What precipitated the dengue viruses to emerge and spread?

- Population increase
- Urbanisation – movement from rural areas to cities, resulting in rapid and uncontrolled urban growth
- Modern transportation – rapid intercontinental air travel, providing a means of spreading the virus around tropical and sub-tropical areas of the world through the movement of infected people and mosquitoes
- Increased trade assisting spread of vectors
- Establishment of vectors in new geographic locations

The major vectors:

Aedes aegypti: the major vector of dengue



Aedes albopictus: an important secondary vector of dengue



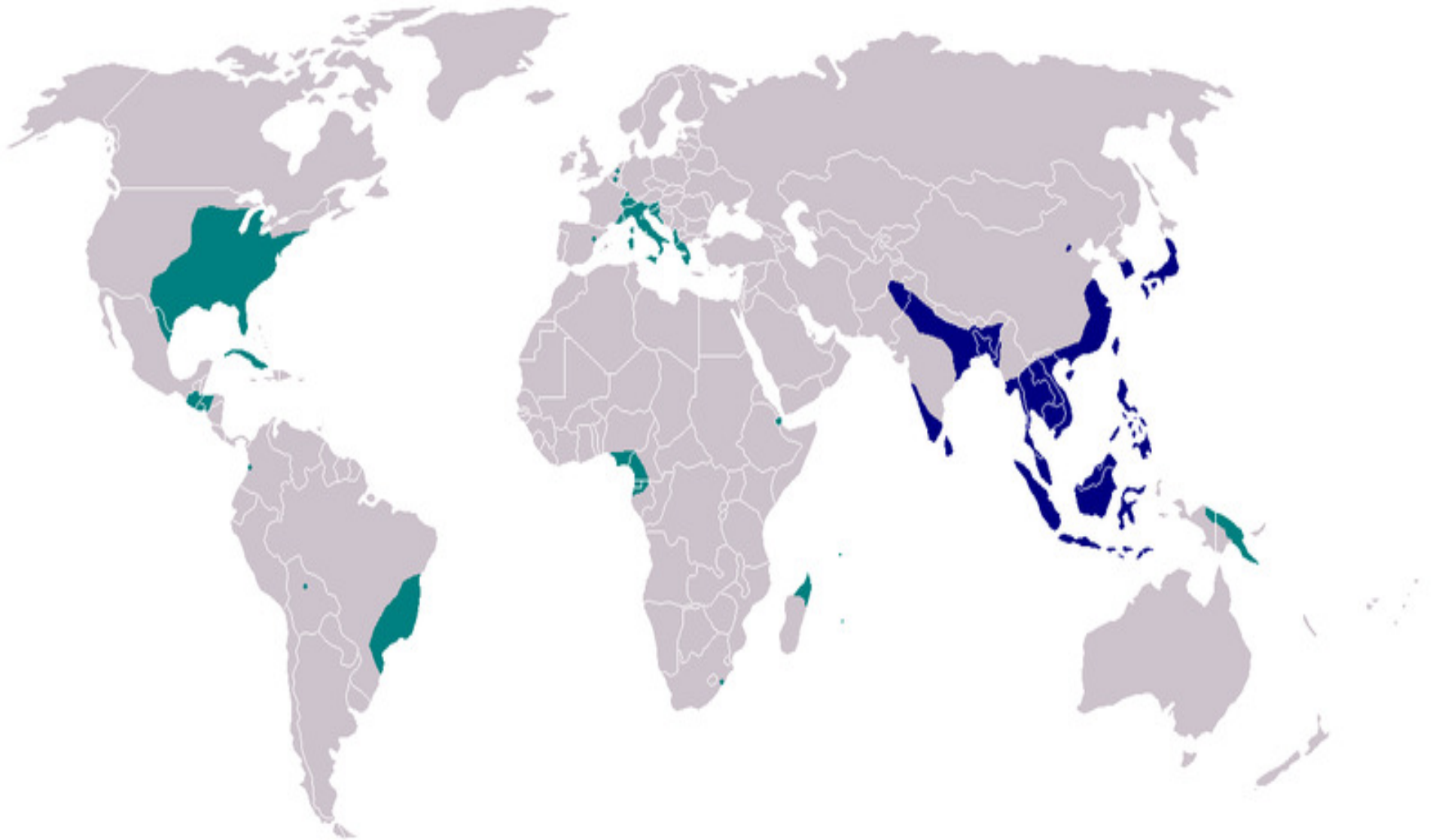
Global spread of *Aedes aegypti* and *Ae. albopictus* on vessels and aircraft



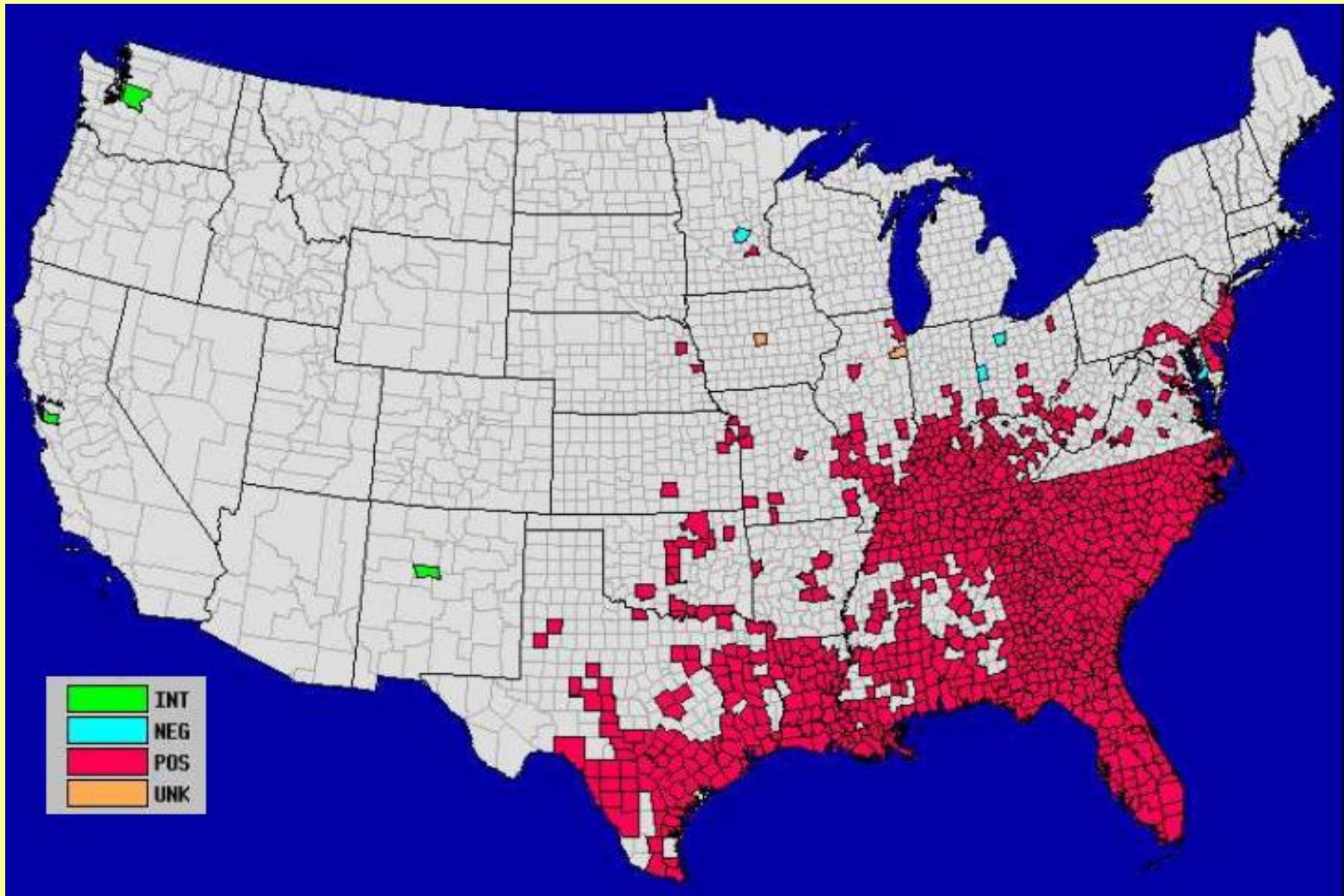
Countries /areas at risk of dengue transmission, 2005



Distribution of *Aedes albopictus* as at 2007



Aedes albopictus in the United States, 2000



Trouble ahead??

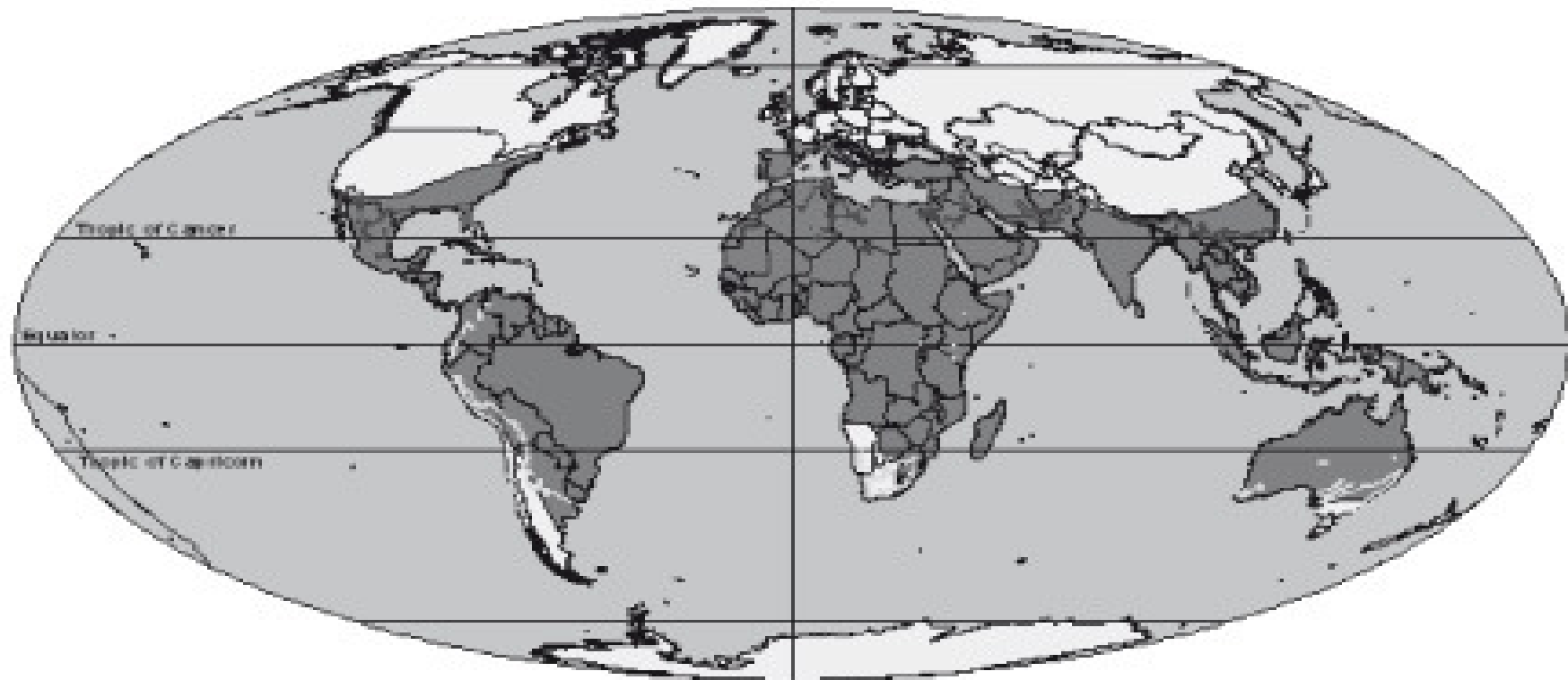
- 2.5 billion people at risk of dengue world-wide
- In the Americas, 50-fold increase in reported cases of DHF (1989-1993 compared to 1984-1988)*
- Widespread abundance of *Aedes aegypti* in at-risk areas
- Increasing spread of both *Ae. aegypti* and *Ae. albopictus*.

* Organization of American States,
Human Health in the Americas, 1996

FIGURE 1

Historical distribution of *Aedes aegypti*

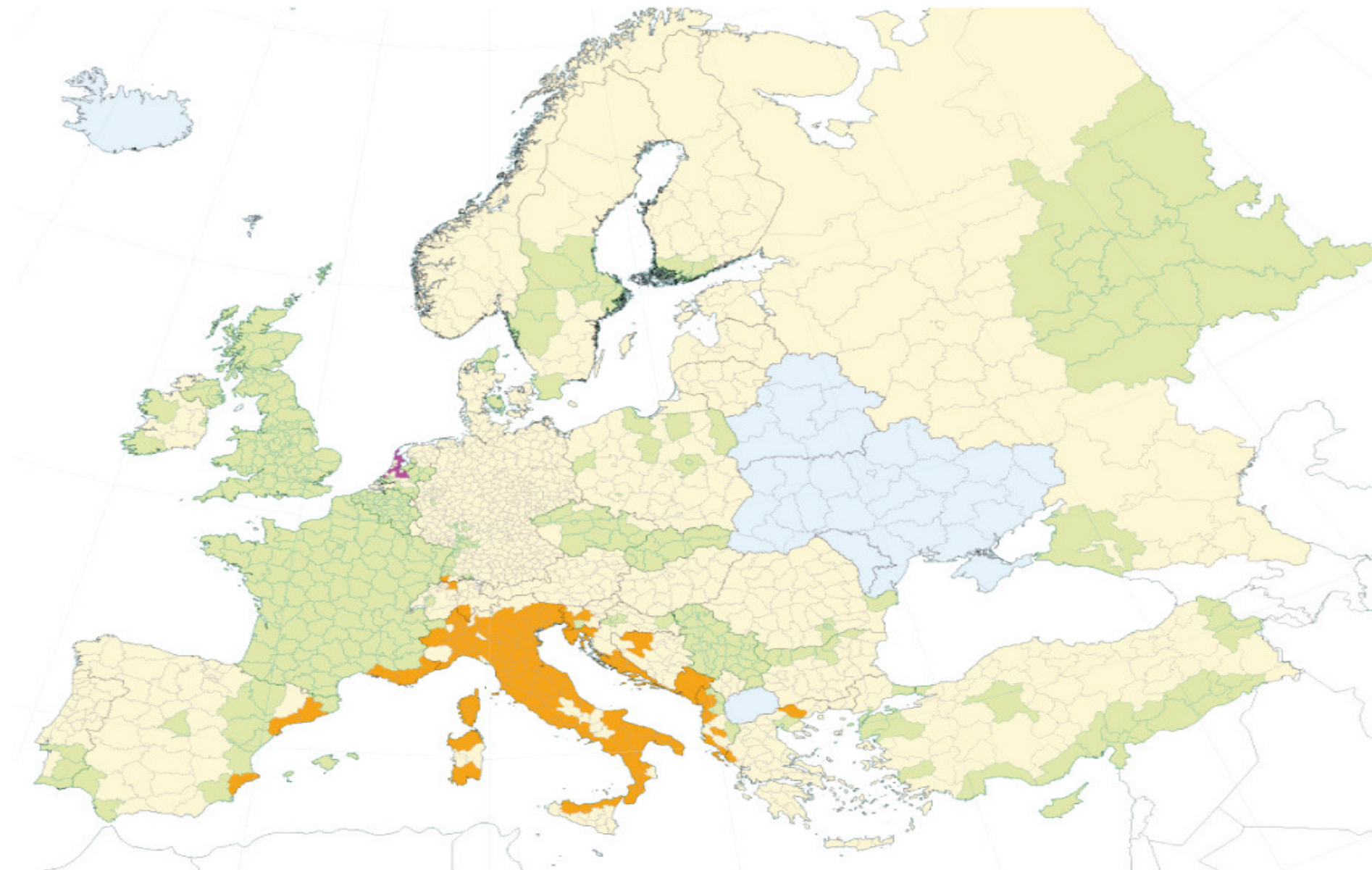
P.Reiter (2010).Euro Surveill.15(10)



Dark grey areas: maximum range distribution of *Ae. aegypti*, black lines: January 10°C isotherm in the northern hemisphere; mid grey lines: the July 10°C isotherm in the southern hemisphere. The distribution limit broadly fits the 10°C isotherm in the southern hemisphere, but far less so in the northern hemisphere. Source: adapted from a map published by Christophers [9].

FIGURE 2

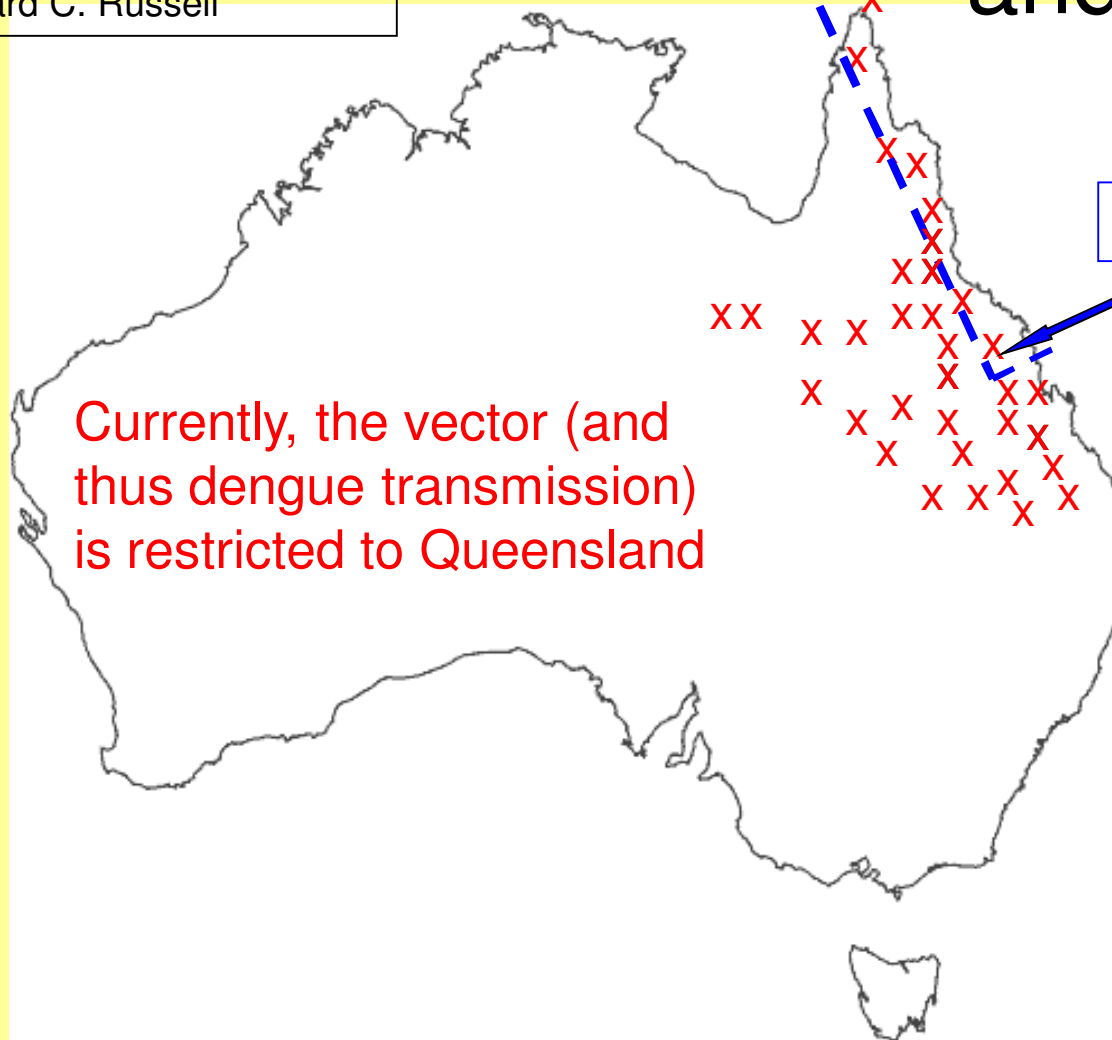
Current (2009) distribution of *Aedes albopictus* in Europe by administrative unit



Orange: overwintering expanding populations; purple: populations only observed indoors (in glass houses); green: not detected in past 5 years; pale yellow: no recent data on mosquito fauna; blue: no information on any mosquito studies; white: not included in this study. Source: [10].

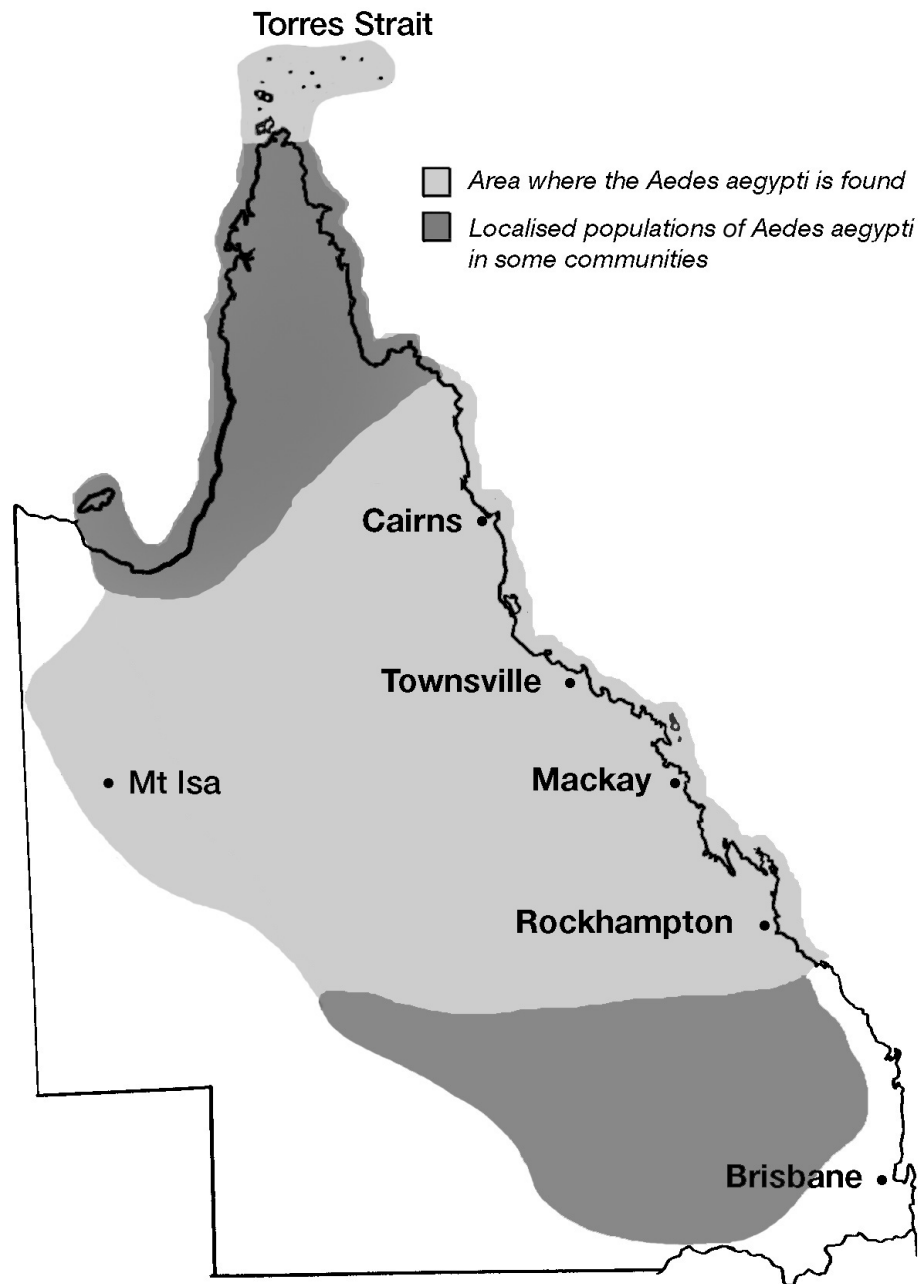
Current distribution of *Aedes aegypti* and dengue

Compiled from various sources
by Richard C. Russell



Charters Towers

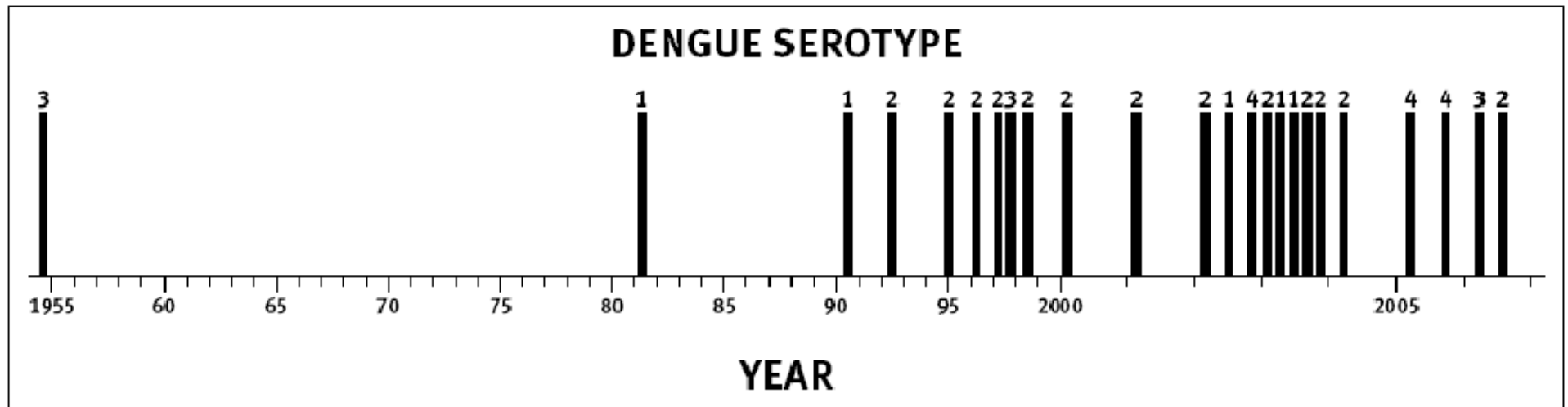
Currently, the vector (and
thus dengue transmission)
is restricted to Queensland



Dengue in Australia

- All Australian cases are imported from infected travellers arriving in dengue-receptive areas of north Queensland;
- A significant number of importations are recognised each year, and of these, several result in subsequent epidemic activity.

Dengue outbreaks north Queensland (Cairns, Townsville and Charters Towers)



Australian Quarantine Ports and their Mosquito Vector Introduction Risk

Risk Category

- 1 (High)
- 2
- 3
- 4
- 5 (Low)



AQIS First Ports

Seaports - 62

Airports - 16

Chikungunya virus:

- Spread by international travel
- Spread and establishment of vector species in new geographic environments

Chikungunya virus – its origins

- First isolated in Tanzania in 1953 during a suspected dengue outbreak.
- An Alphavirus in the Semliki Forest sero-complex, and it exists as a single sero-group and three genetic lineages/phylogroups.
- Found widely across sub-Saharan Africa and southern and south-eastern Asia.
- Causes a disease almost identical to dengue fever, and very occasionally can also cause a severe haemorrhagic fever, but it is very rarely fatal.
- Monkeys are believed to be the main reservoir hosts, but humans become reservoir hosts during outbreaks.
- *Aedes aegypti*, and more recently, *Ae. albopictus*, are the major mosquito vectors.

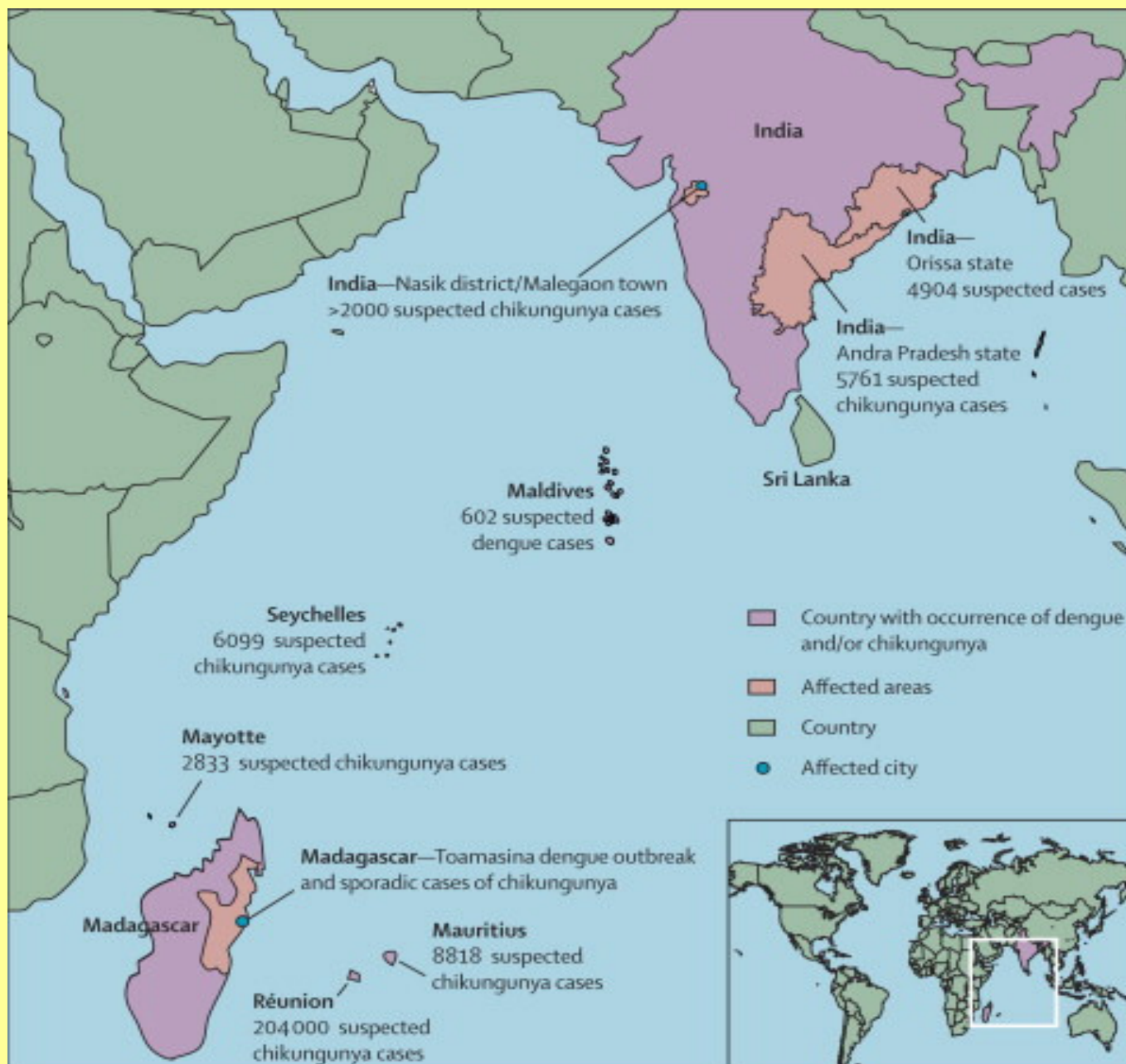
Approximate Global Distribution of Chikungunya Virus, by Country, 2010*



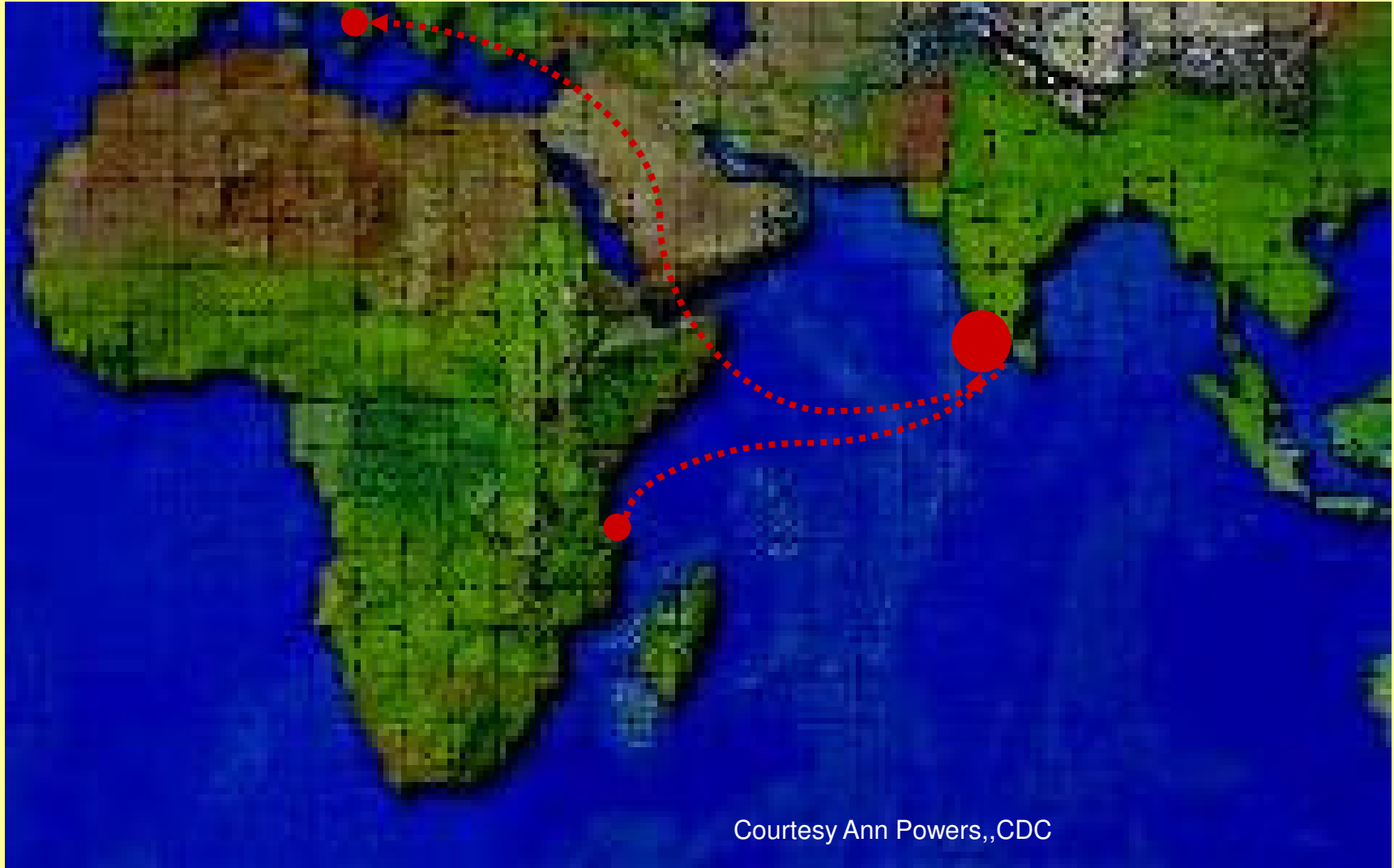
*Modified from: Powers AM, Logue CH. Changing patterns of chikungunya virus: re-emergence of a zoonotic arbovirus. *J Gen Virol*. Sep 2007;88(Pt 9):2363-2377.

CDC

Chikungunya in the South-West Indian Ocean: 2005-07



Movement of Chikungunya to Italy



Courtesy Ann Powers,,CDC

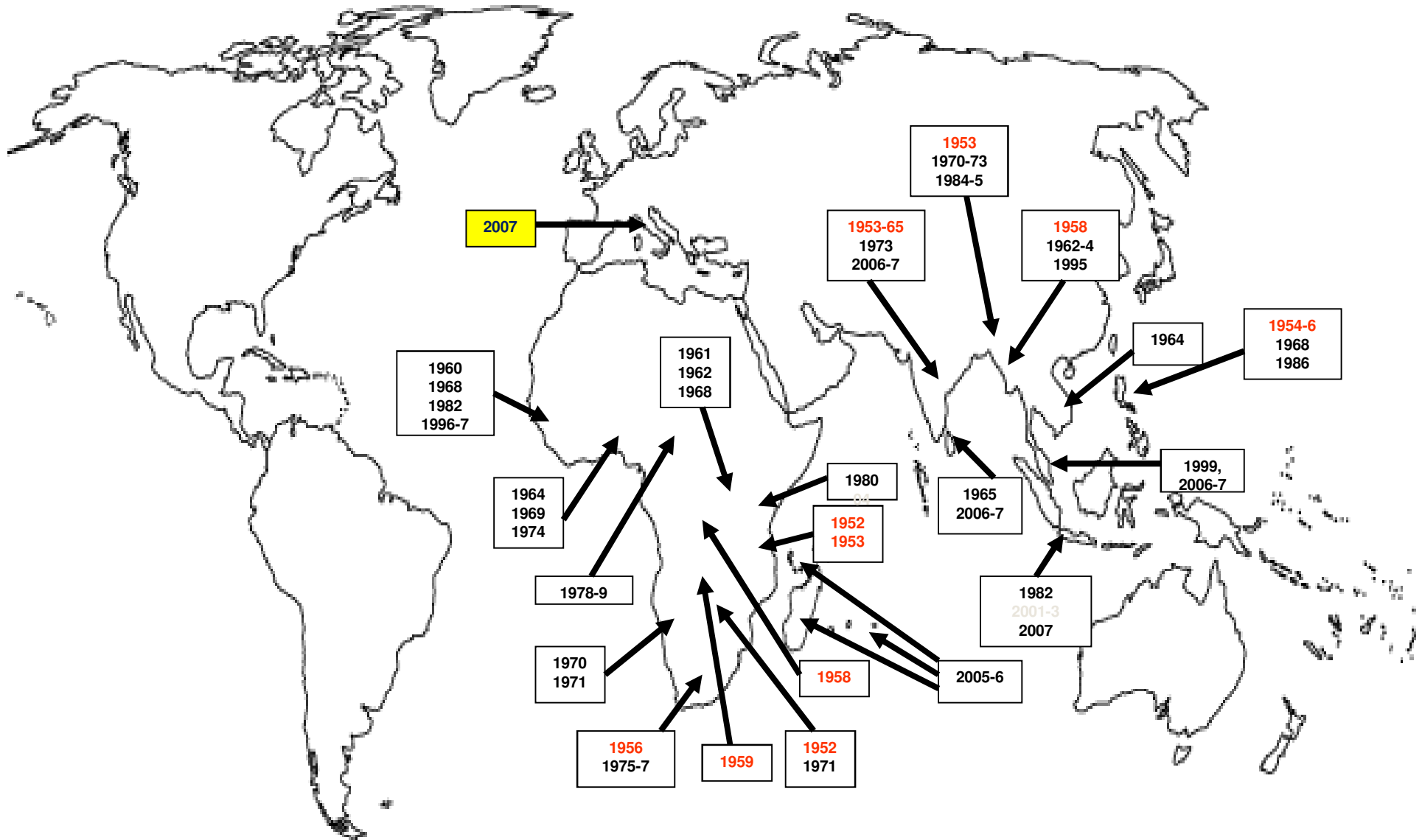
Chikungunya Outbreak in Italy, 2007

Made possible by the establishment of *Aedes albopictus*



334 suspected cases, 204 lab confirmed. Outbreak initiated by travel from Kerala, India. Cases also in Rimini and Ravenna

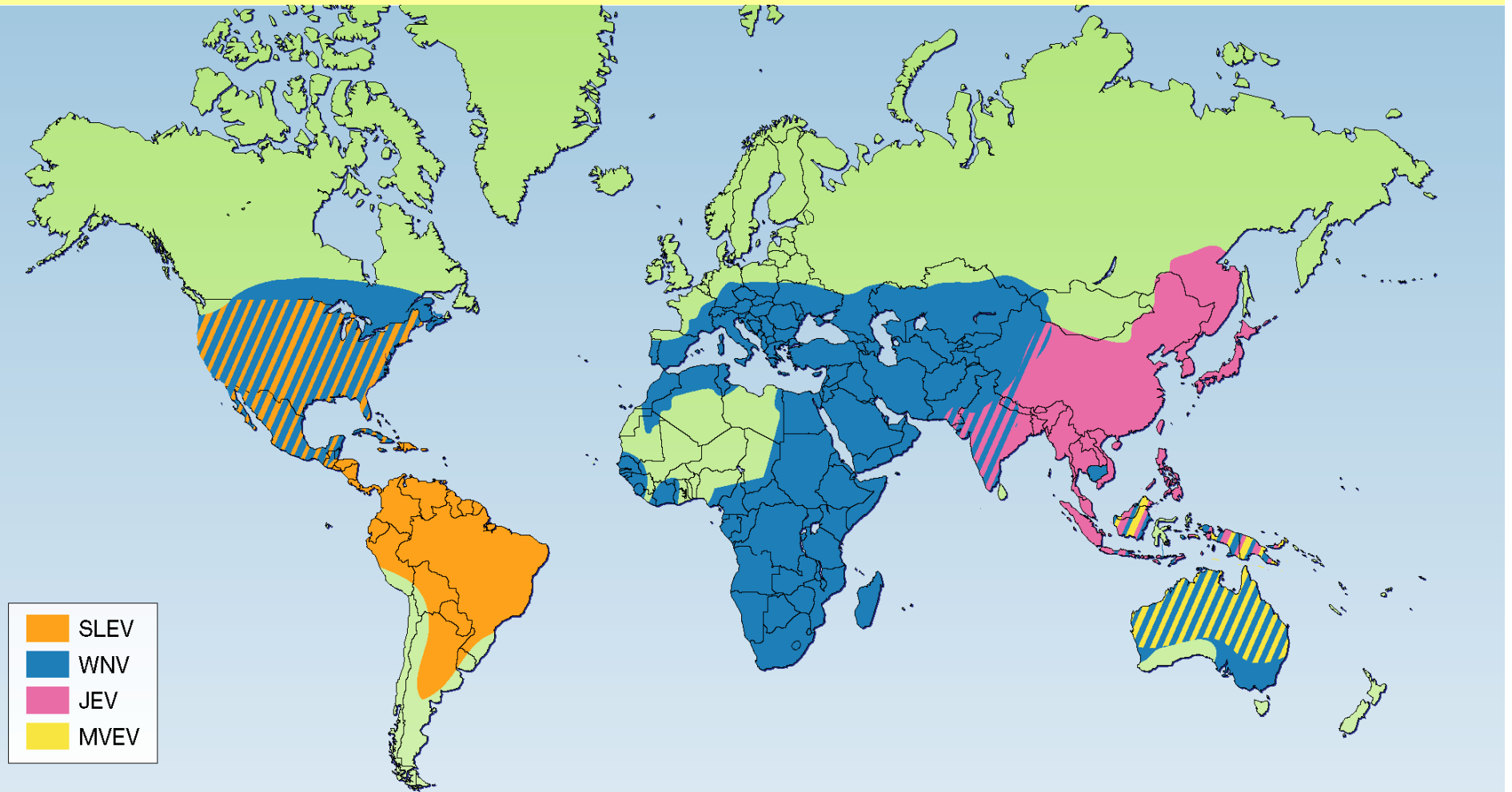
All reported Chikungunya Outbreaks – By Year 1952-2007



Murray Valley encephalitis (MVE) virus:
the major encephalogenic flavivirus of Australia, Papua
New Guinea, and eastern Indonesia

- The effect of changes in land use
- Building of Dams
- Irrigated agriculture

Japanese encephalitis serological group



Mackenzie, Gubler & Petersen (2004) *Nature Med* 10(12): S98-S109

MVEV: isolation and ecology

- A member of the Japanese encephalitis sero-complex of Flaviviruses;
- First isolated from human infections in 1951;
- Endemic to northern Australia in the tropical monsoonal belt;
- Natural transmission cycles between ardeid birds (herons) and *Culex* sp. mosquitoes.
- Most cases occur towards the end of the wet (monsoonal) season.

Enzootic transmission

VECTOR



Culex annulirostris



Murray Valley encephalitis cases 1951-1971

Australian Quarantine Ports and their Mosquito Vector Introduction Risk



1951	45	NSW, VIC, SA
1956	3	VIC
1969	1	WA
1971	2	QLD, NSW

AQIS First Ports

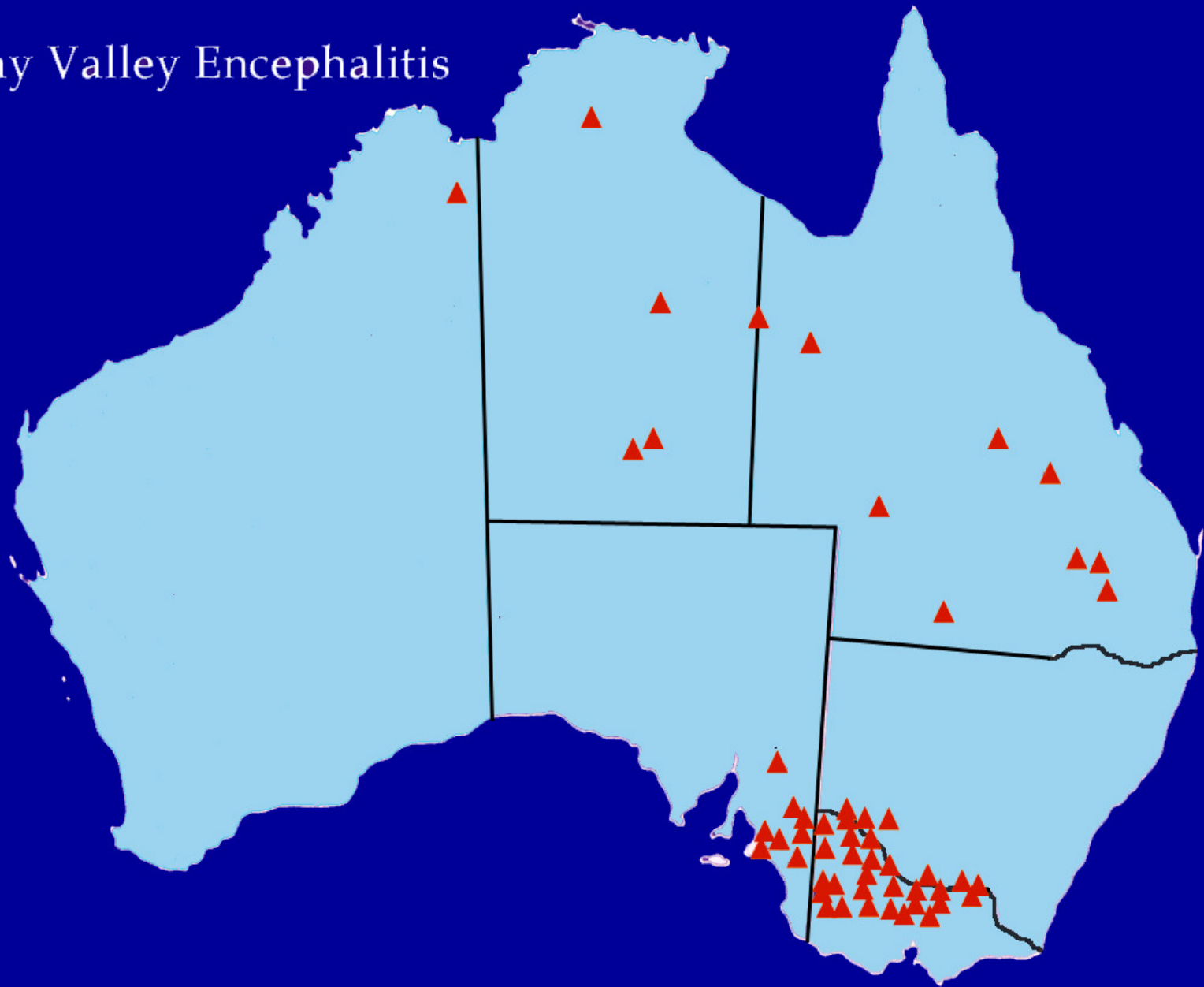
Seaports - 62

Airports - 16

Murray Valley encephalitis cases 1951-1974

1951	45	NSW, VIC, SA
1956	3	VIC
1969	1	WA
1971	2	QLD, NSW
1974	58	NSW, VIC, SA (44 cases) NT(5 cases), WA (1 case), QLD (8 cases).

Murray Valley Encephalitis



Location of 1974 cases

Murray Valley encephalitis cases 1951-2006

1951	45	NSW, VIC, SA
1956	3	VIC
1969	1	WA
1971	2	QLD, NSW
1974	58	NSW, VIC, SA (44 cases) NT(5 cases), WA (1 case), QLD (8 cases).
1978-2006	>80	WA (40 cases), NT (19 cases), Qld (5 cases), NSW (1 case)

Thus a major shift from epidemic cases in southern states of Australia to endemic cases in northern states

MVEV: Ecology in northern Australia

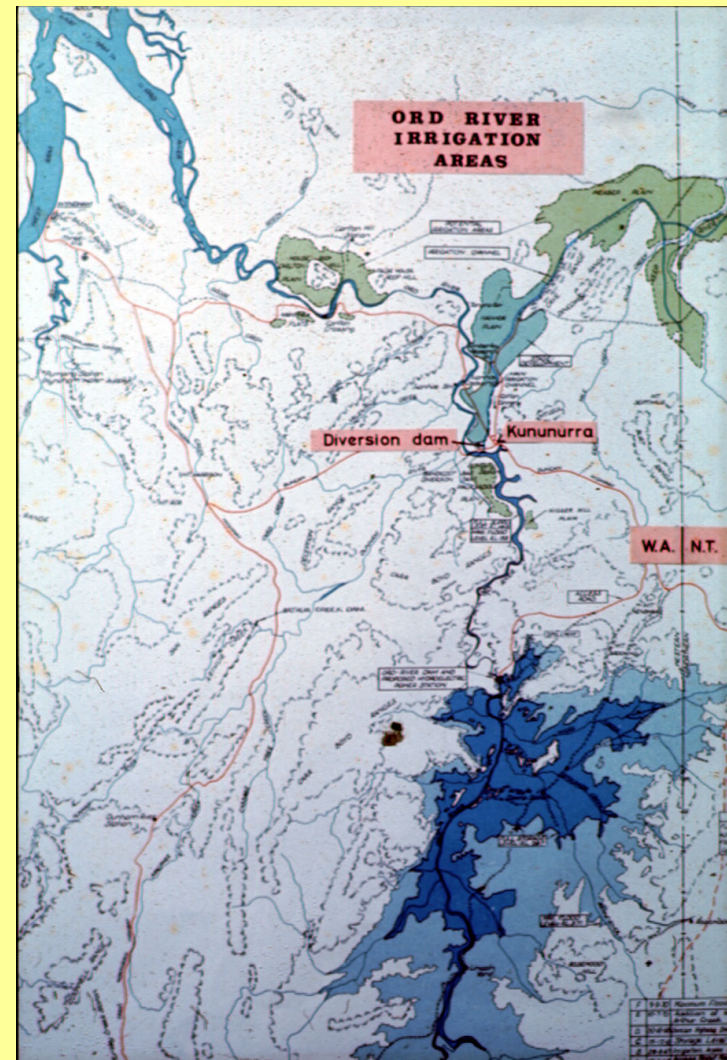
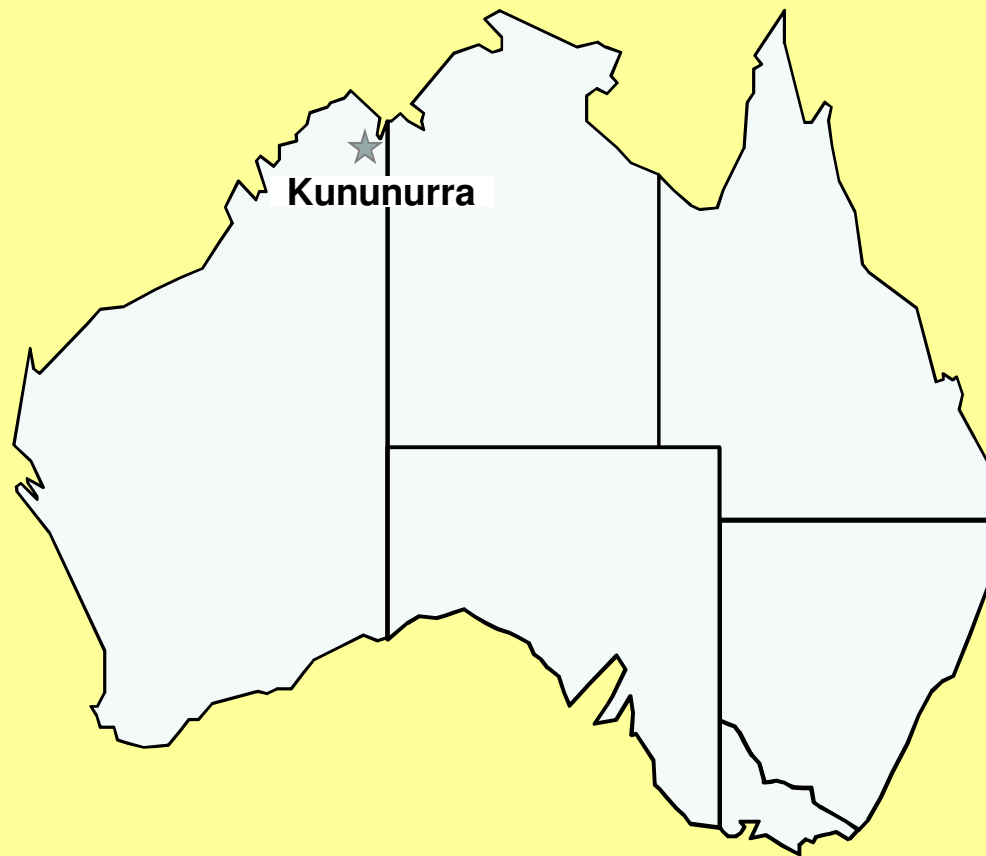
- The monsoonal summer weather patterns in northern Australia result in massive river flows and flooding over wide areas – some rivers having a flood plain up to 20 km wide – but then rapidly drying up in the dry season and often retracting to become a series of unconnected oxbow lakes.
- The river flows may be exceptional (eg. every 10 seconds, the equivalent amount of water in Sydney Harbour flows down the Fitzroy River at Fitzroy Crossing when in flood).
- Thus virus activity and transmission was relatively short-lived, and restricted to late in the wet season and shortly thereafter.



MVEV ecology in northern Australia (cont.)

- *Early 1970s, a major change in land use in the tropical north-east which had a profound effect on the surrounding ecology – the development of 14,000 hectares of irrigated tropical agriculture instead of very sparse cattle grazing.*
- This was made possible by damming the Ord River to establish Lake Argyle, and constructing a second diversion dam as a source of water for irrigation, resulting in profound changes to the local ecosystem, with huge increases in aquatic birds numbers and in *Culex* sp. mosquitoes.
- This has resulted in the potential for year-round transmission of MVEV, rather than being restricted to the monsoonal wet season, and to the establishment of intense local transmission cycles.
- As some competent *Aedes* vectors lay desiccation-resistant eggs, there has been a gradual and expanding 'seeding' of MVEV widely across northern Australia. Thus there has been a very significant increase in cases of encephalitis since 1974.

Kununurra and the Ord River Irrigation Area





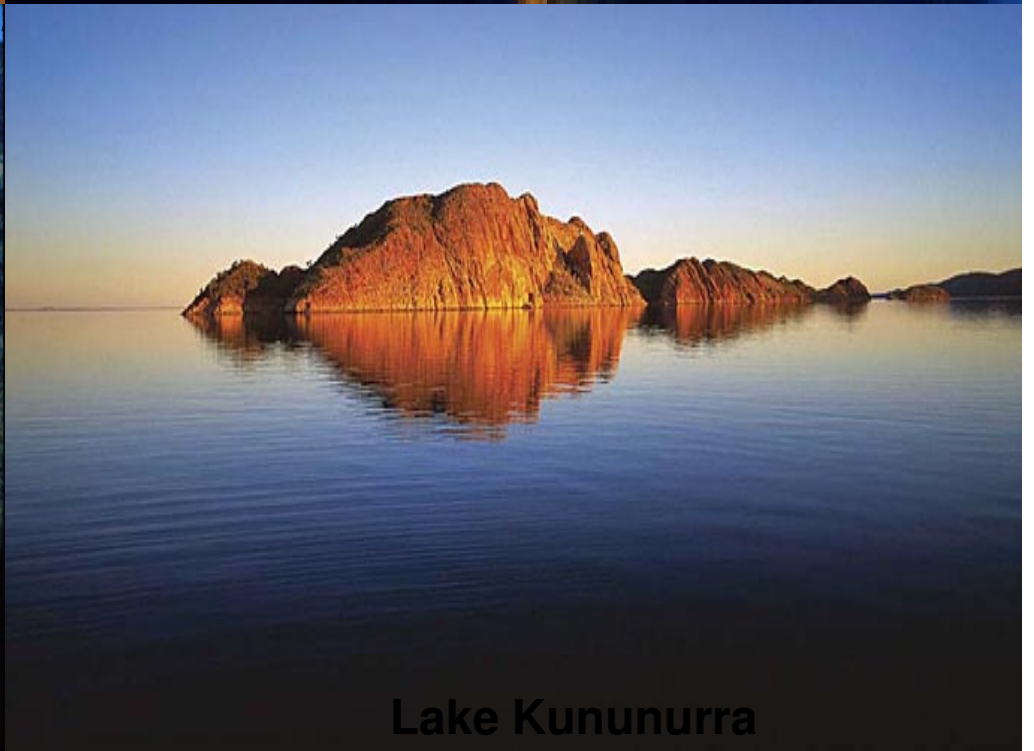
Lake Argyle from space



Lake Argyle



Diversion dam



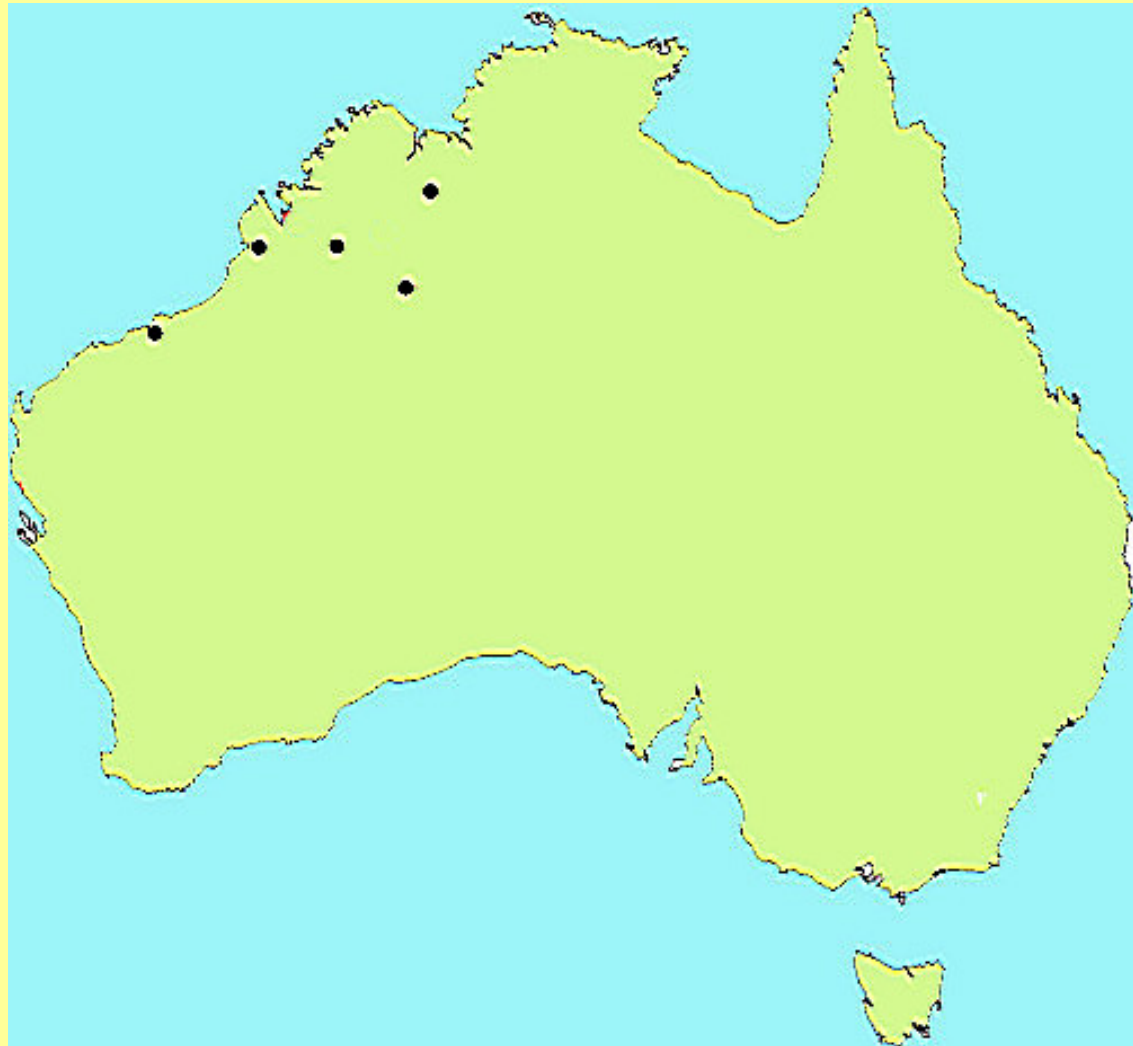
Lake Kununurra

Irrigated Agriculture and Flocks of Magpie Geese, Kununurra



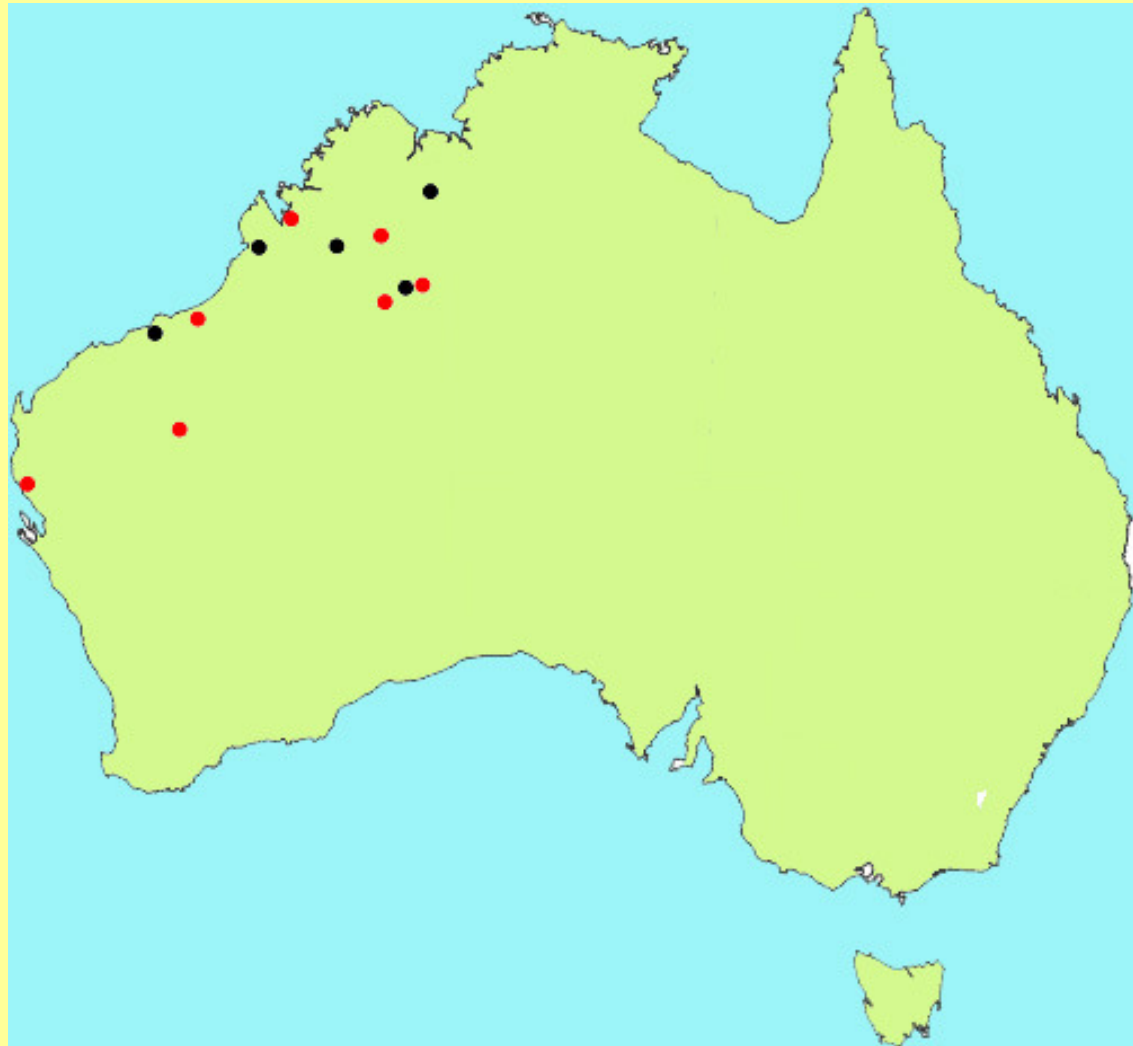
Location of MVE cases: 1978-2006

- 1978-1979



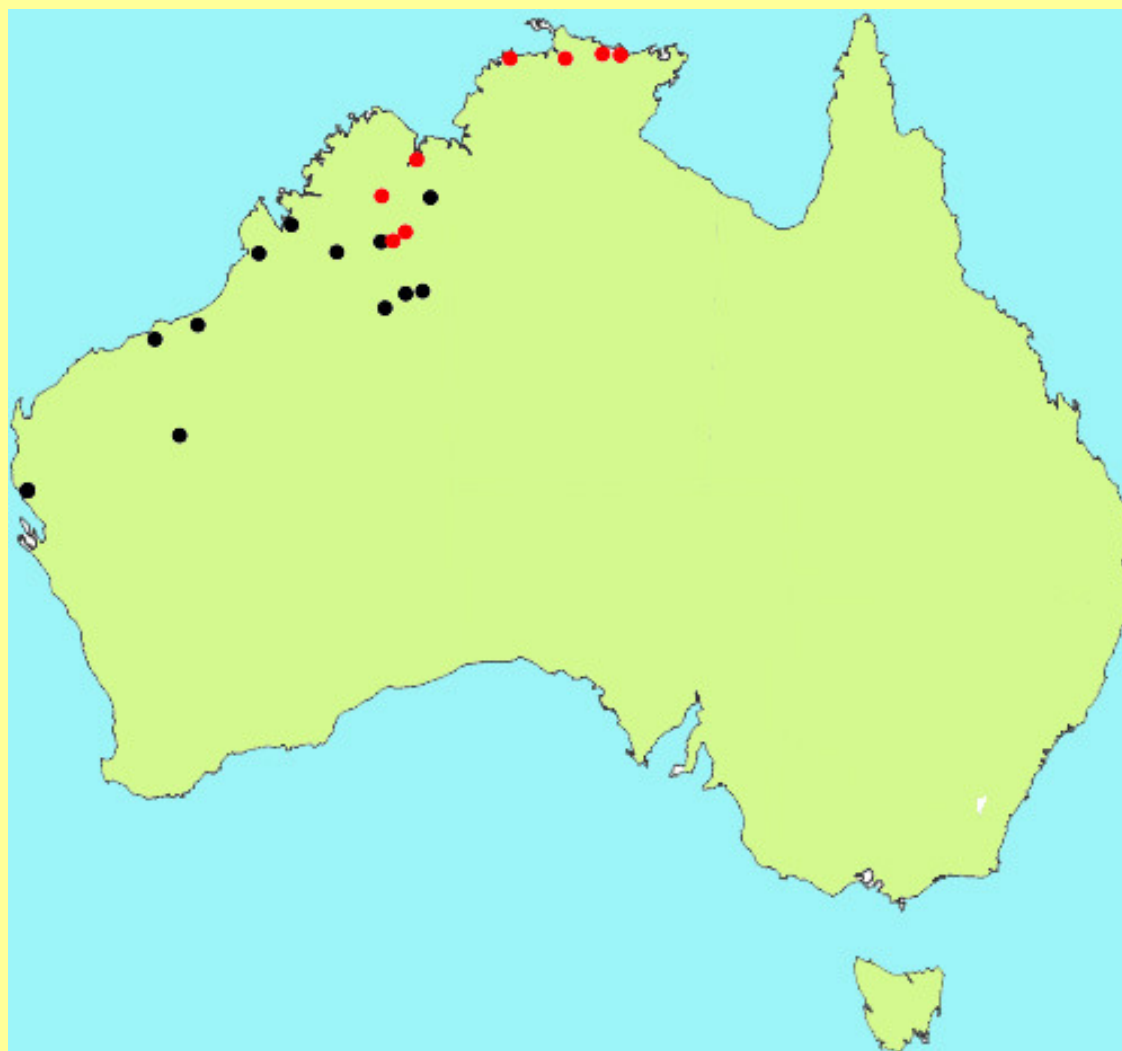
Location of MVE cases: 1978-2006

- 1978-1979
- 1981



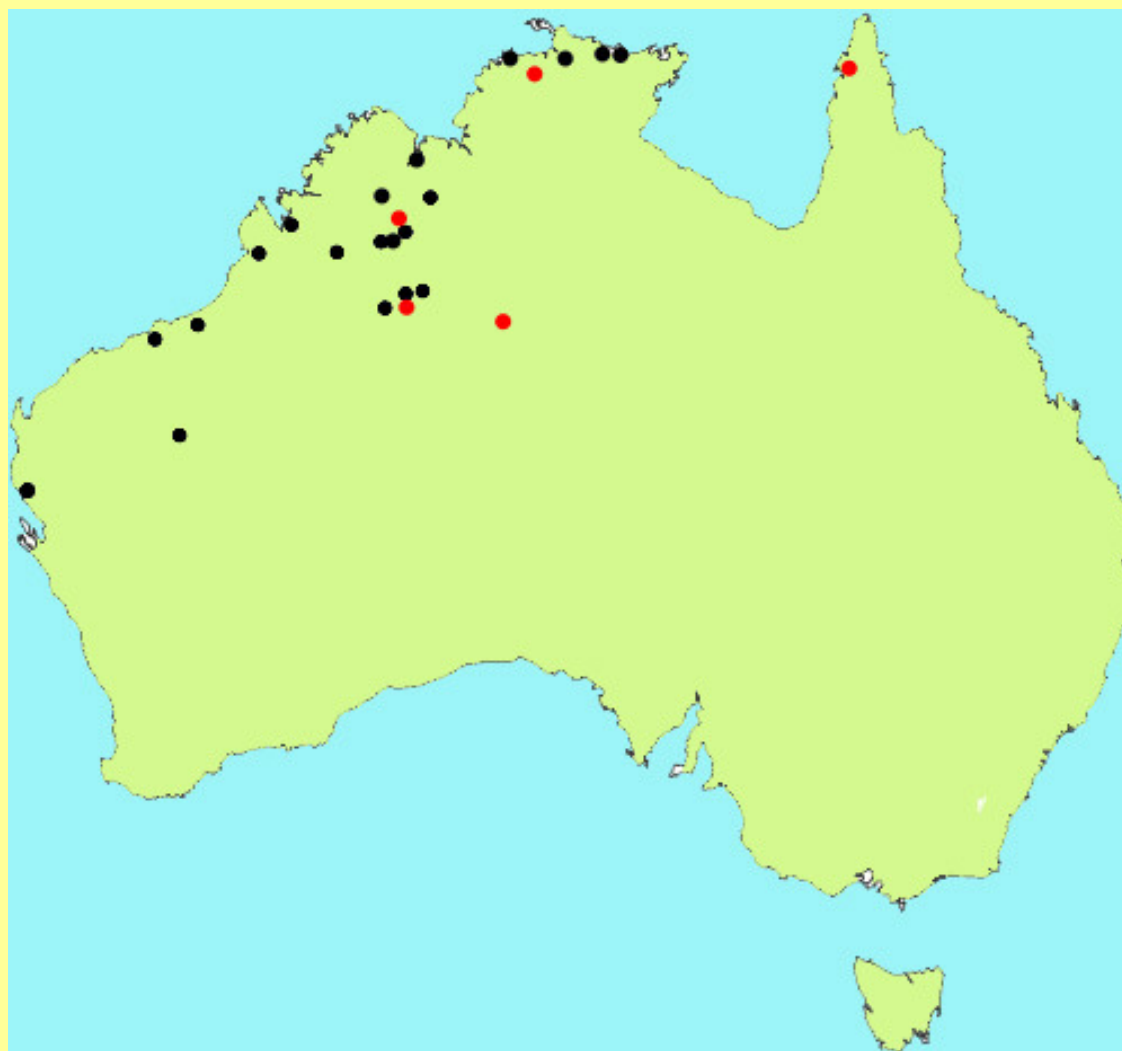
Location of MVE cases: 1978-2006

- 1978-1979
- 1981
- 1984-1989



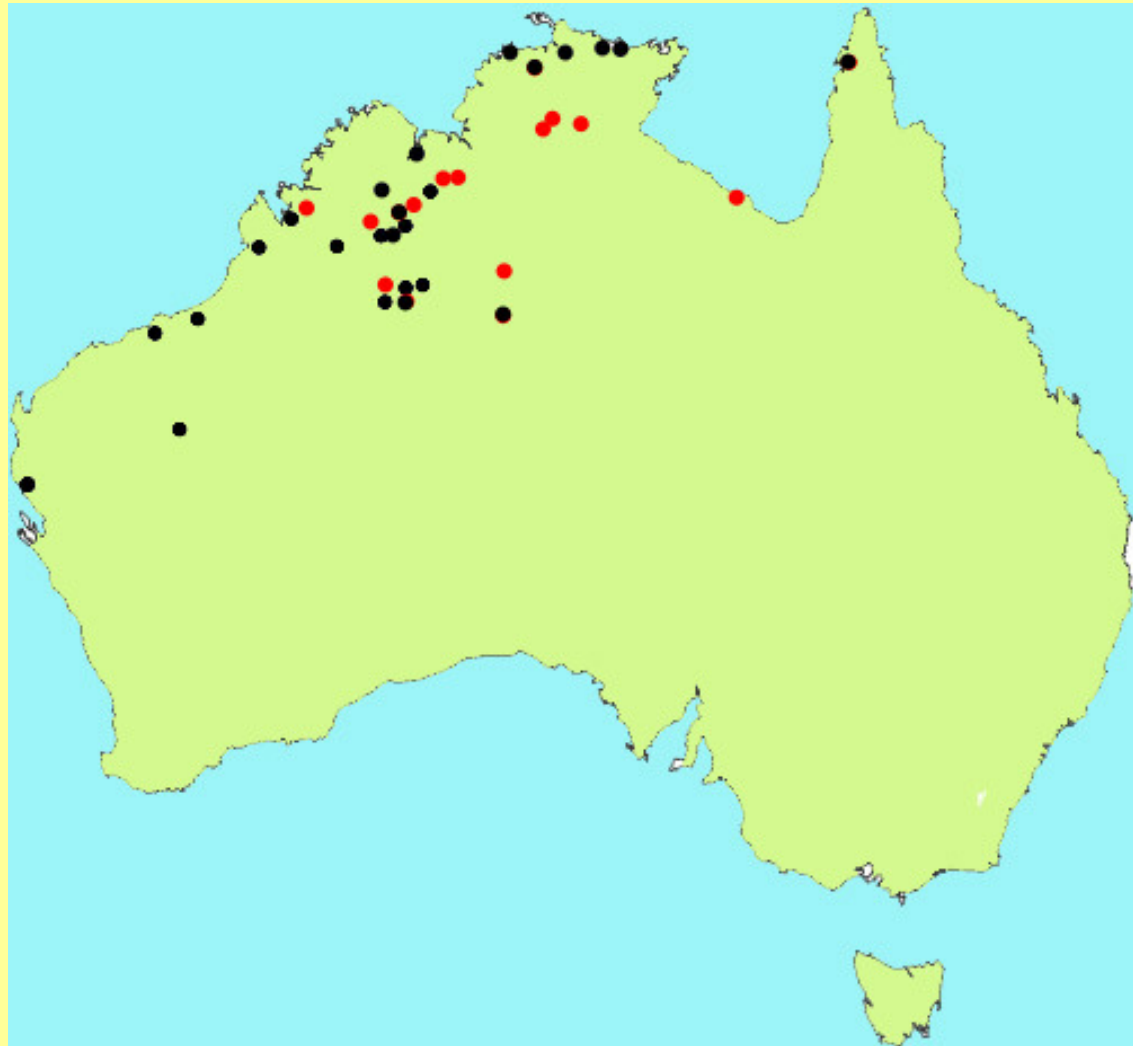
Location of MVE cases: 1978-2006

- 1978-1979
- 1981
- 1984-1989
- 1990-1991



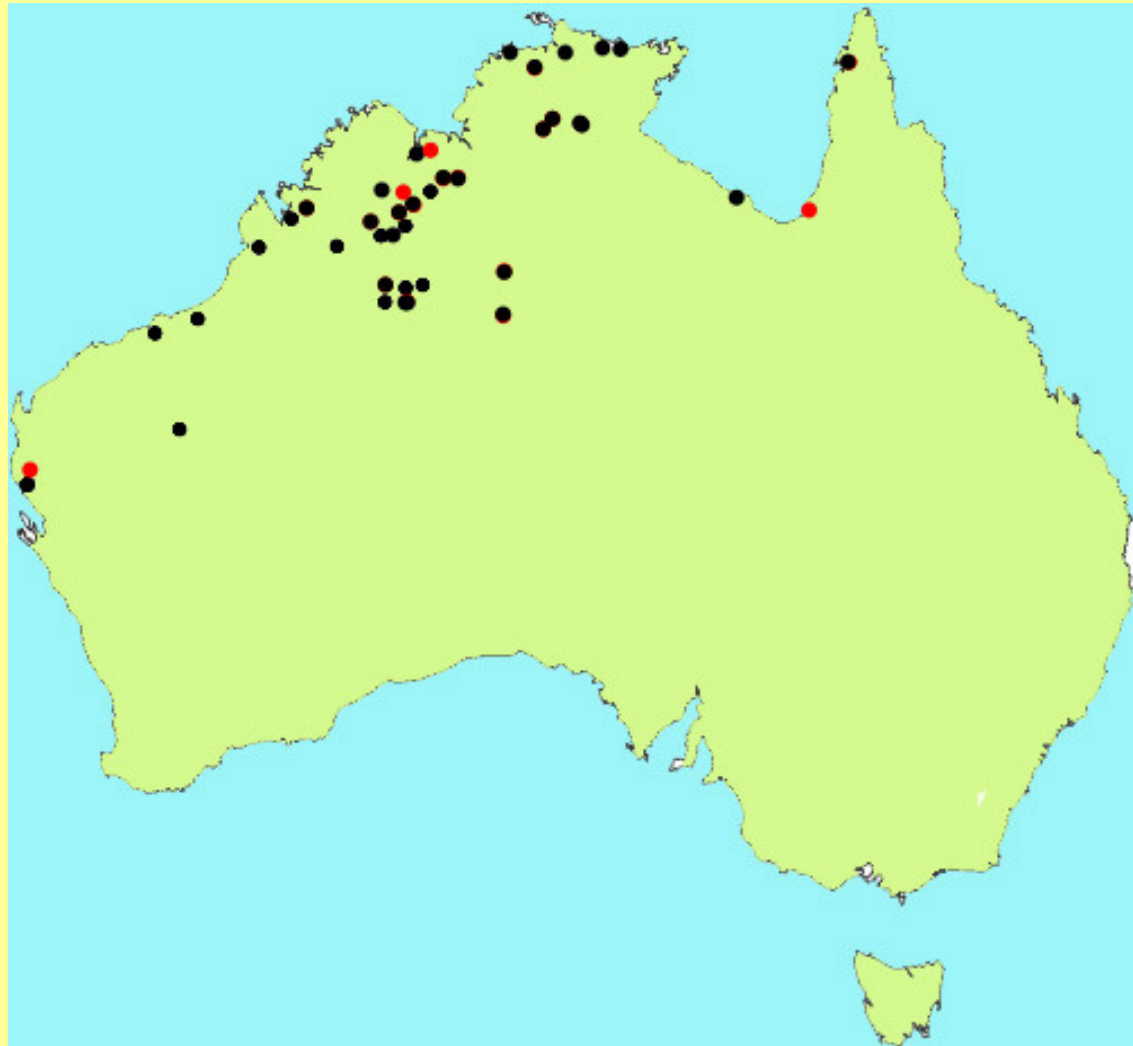
Location of MVE cases: 1978-2006

- 1978-1979
- 1981
- 1984-1989
- 1990-1991
- 1993-1994



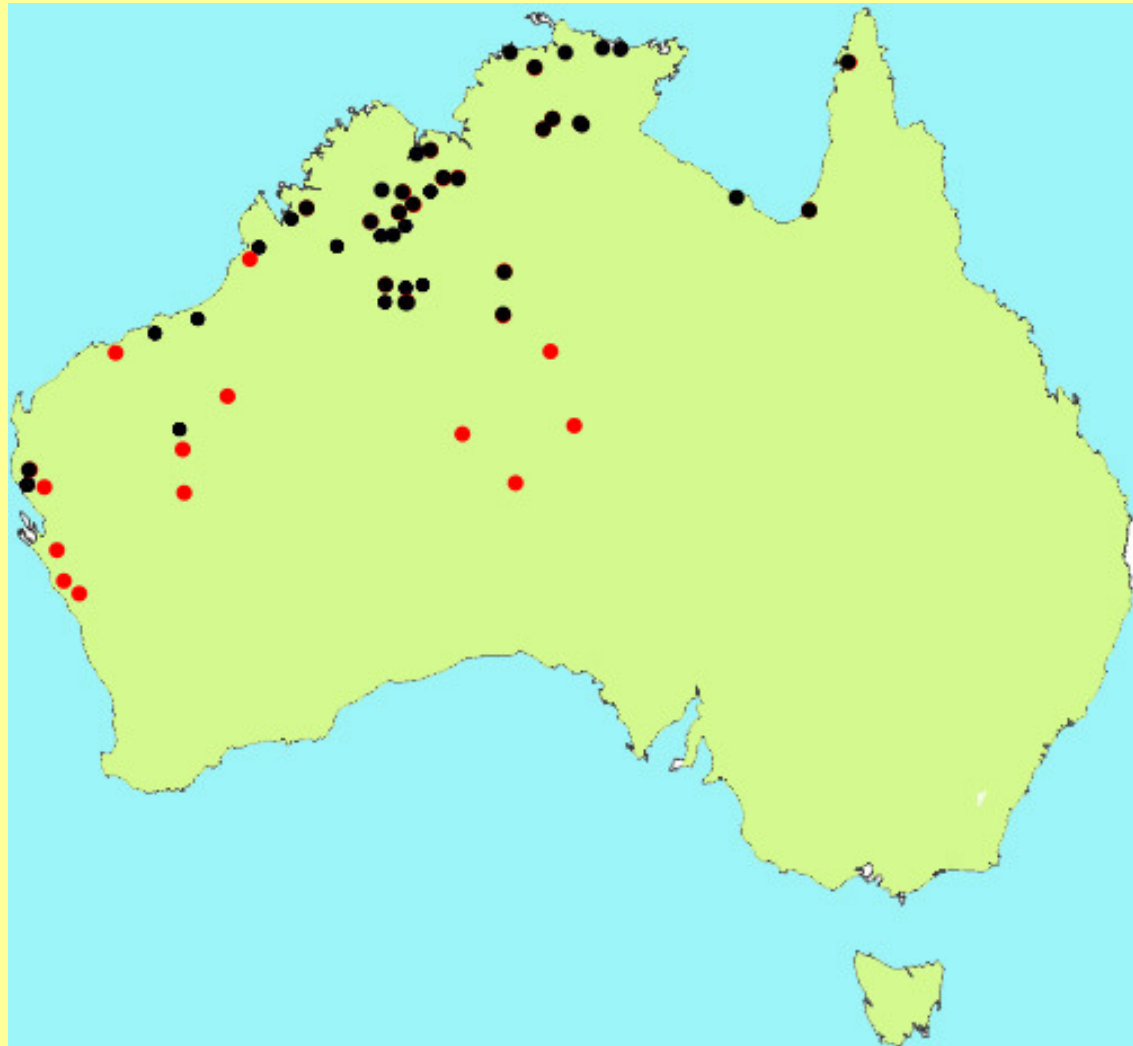
Location of MVE cases: 1978-2006

- 1978-1979
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- 1993-1994
- 1997-1998



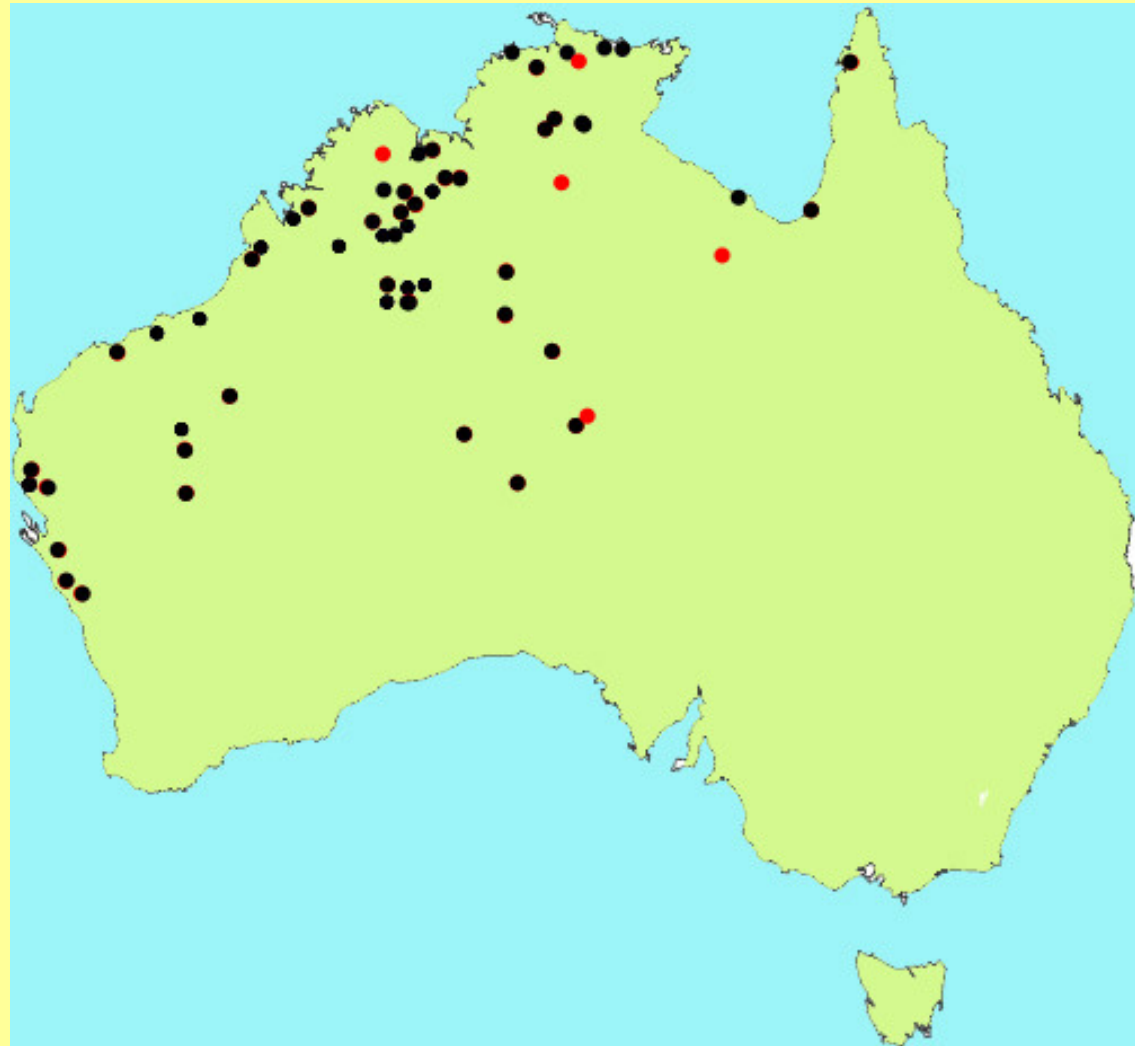
Location of MVE cases: 1978-2006

- 1978-1979
- 1981
- 1984-1989
- 1990-1991
- 1993-1994
- 1997-1998
- 2000



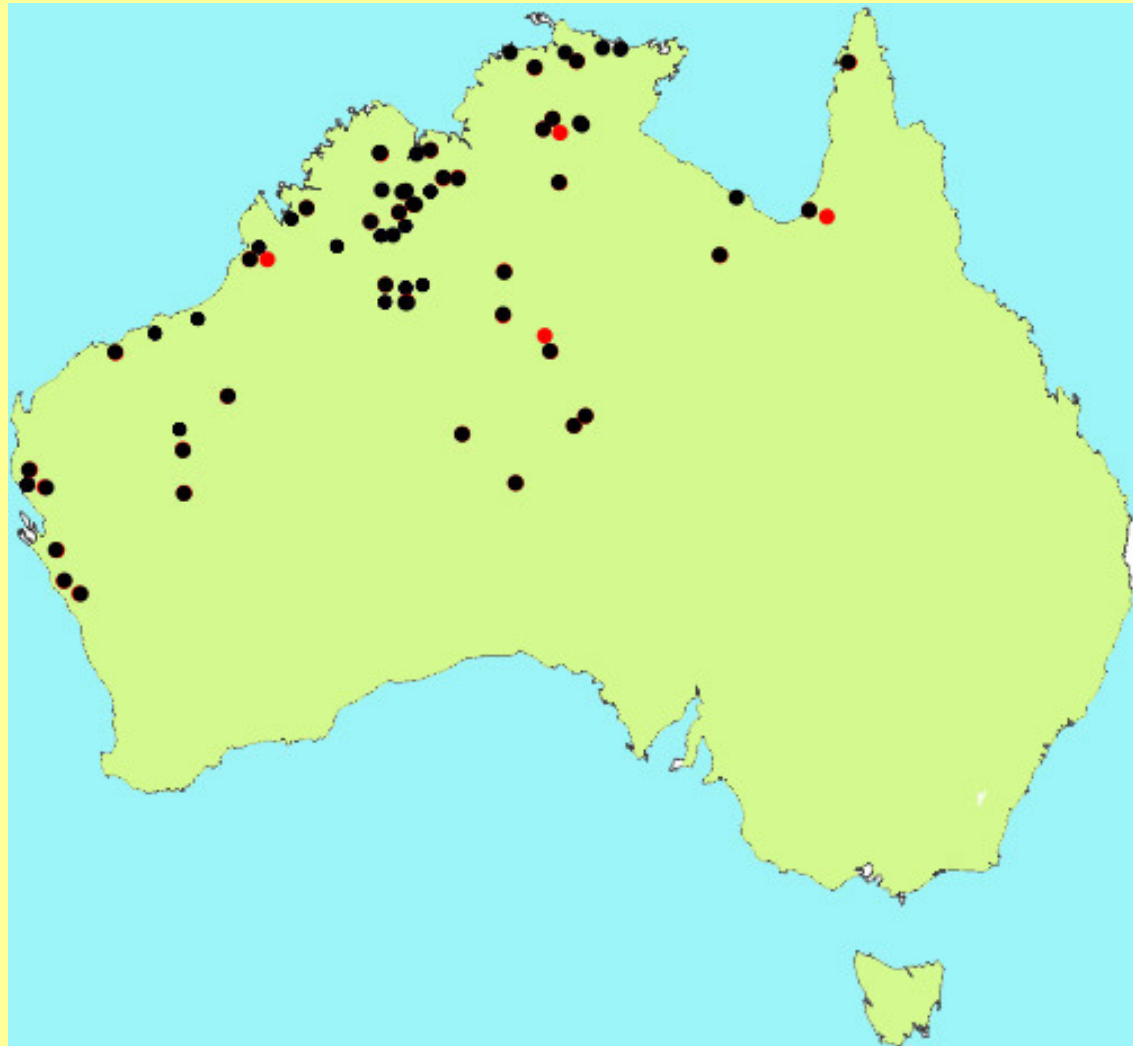
Location of MVE cases: 1978-2006

- 1978-1979
- 1981
- 1984-1989
- 1990-1991
- 1993-1994
- 1997-1998
- 2000
- 2001-2002

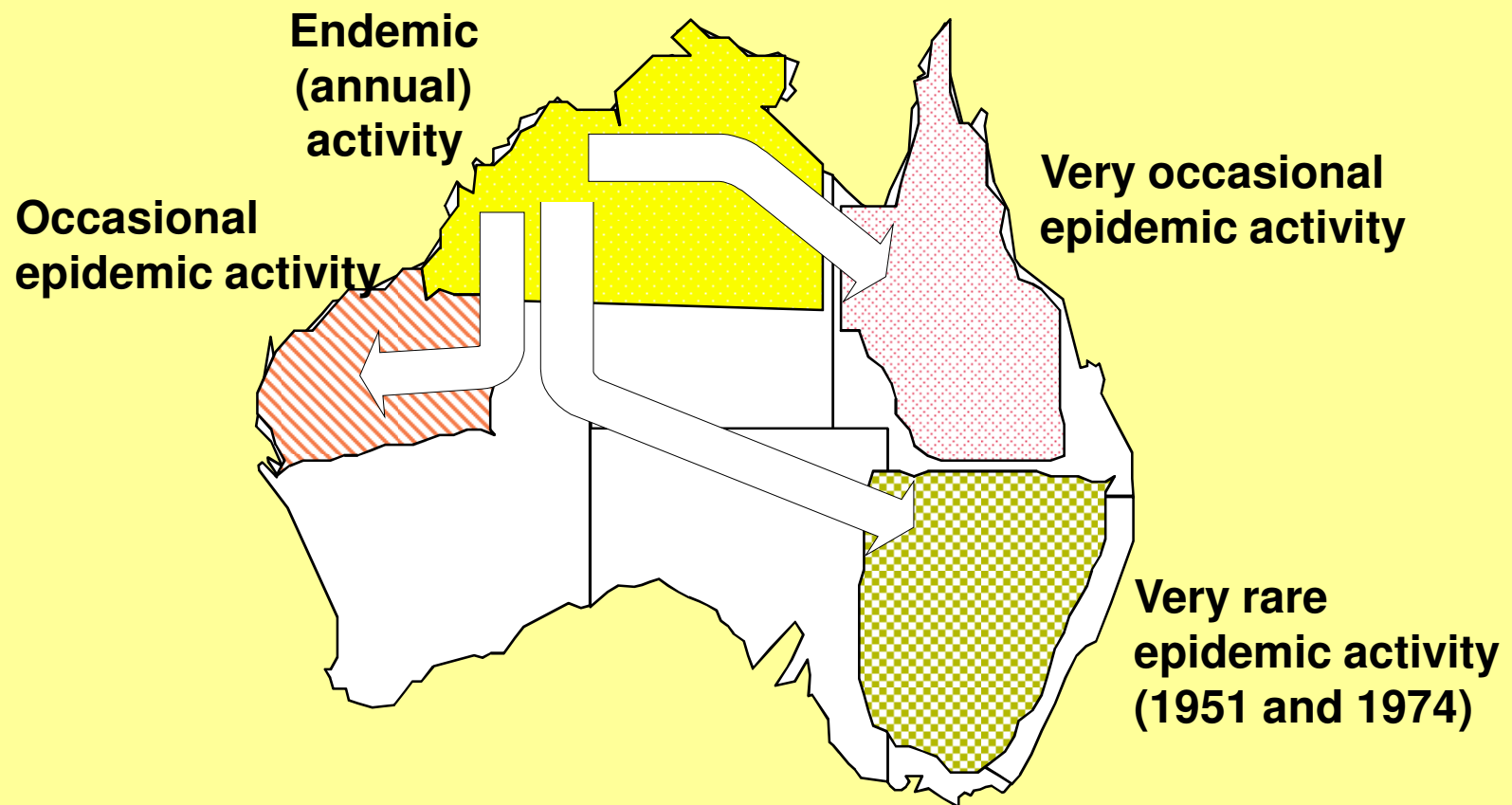


Location of MVE cases: 1978-2006

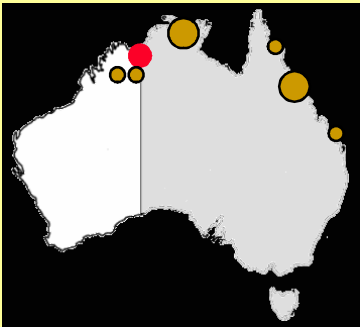
- 1978-1979
- 1981
- 1984-1989
- 1990-1991
- 1993-1994
- 1997-1998
- 2000
- 2001-2002
- 2004-2006



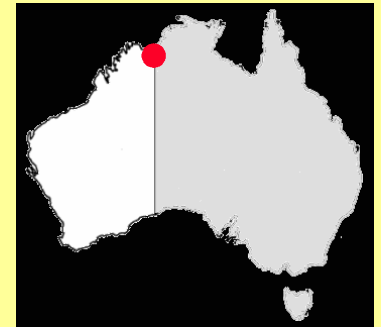
Spread of MVE from the Kimberley via vagrant waterbirds and desiccation-resistant mosquito eggs



Culex gelidus



Aedes vexans



MVEV:Summary

- Thus the effect of the changes to the ecology of the north-west of Australia brought about by the damming of the Ord River and developing the irrigation area have had a major affect on the incidence and geographic spread of MVEV (and West Nile virus/Kunjin strain).
- It has also placed the south-east of Australia at greater risk of incursions of MVEV and outbreaks of encephalitis through the movement of birds and mosquitoes following rare, heavy rainfall events in central Australia.



ECO TOURISM PROJECT
ANIMALS
AND BIRDS
KEEP OUT

Global Threat of Epidemic Vector-Borne Infectious Diseases

- **Movement of Pathogens and Vectors via Modern Transportation**
- **Lack of Effective Laboratory-based Surveillance**
- **Lack of Public Health Infrastructure to Prevent & control Vector-borne and Zoonotic Diseases, great need for additional:**
 - Trained personnel**
 - Laboratory capacity**
 - Tools (vaccines, drugs, insecticides, etc)**
 - Understanding disease ecology**
- **Political Will**
 - Economic support**

Henipaviruses:

- Effects of deforestation
- Changes in land use
- Intensive agricultural practices (Nipah virus)

There have been new viruses from fruit bats

✓ 1994 – Hendra virus (Australia)

1996 – Australian bat
lyssavirus (Australia)

1997 – Menangle virus
(Australia)

✓ 1999 – Nipah virus (Malaysia)

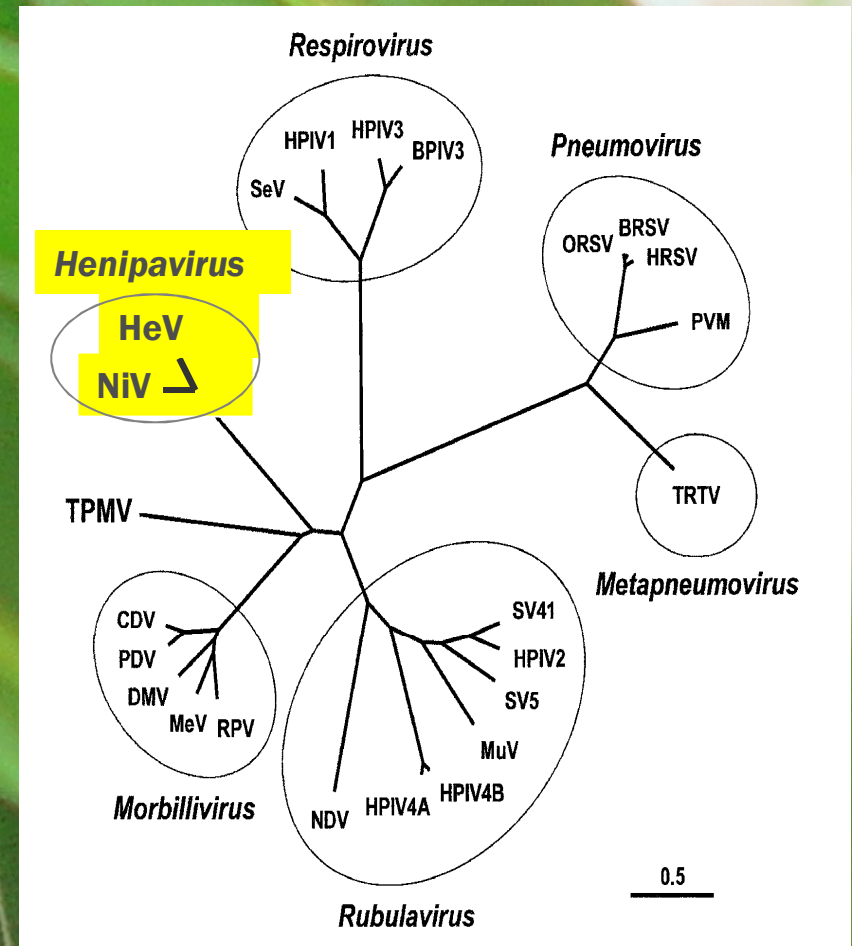
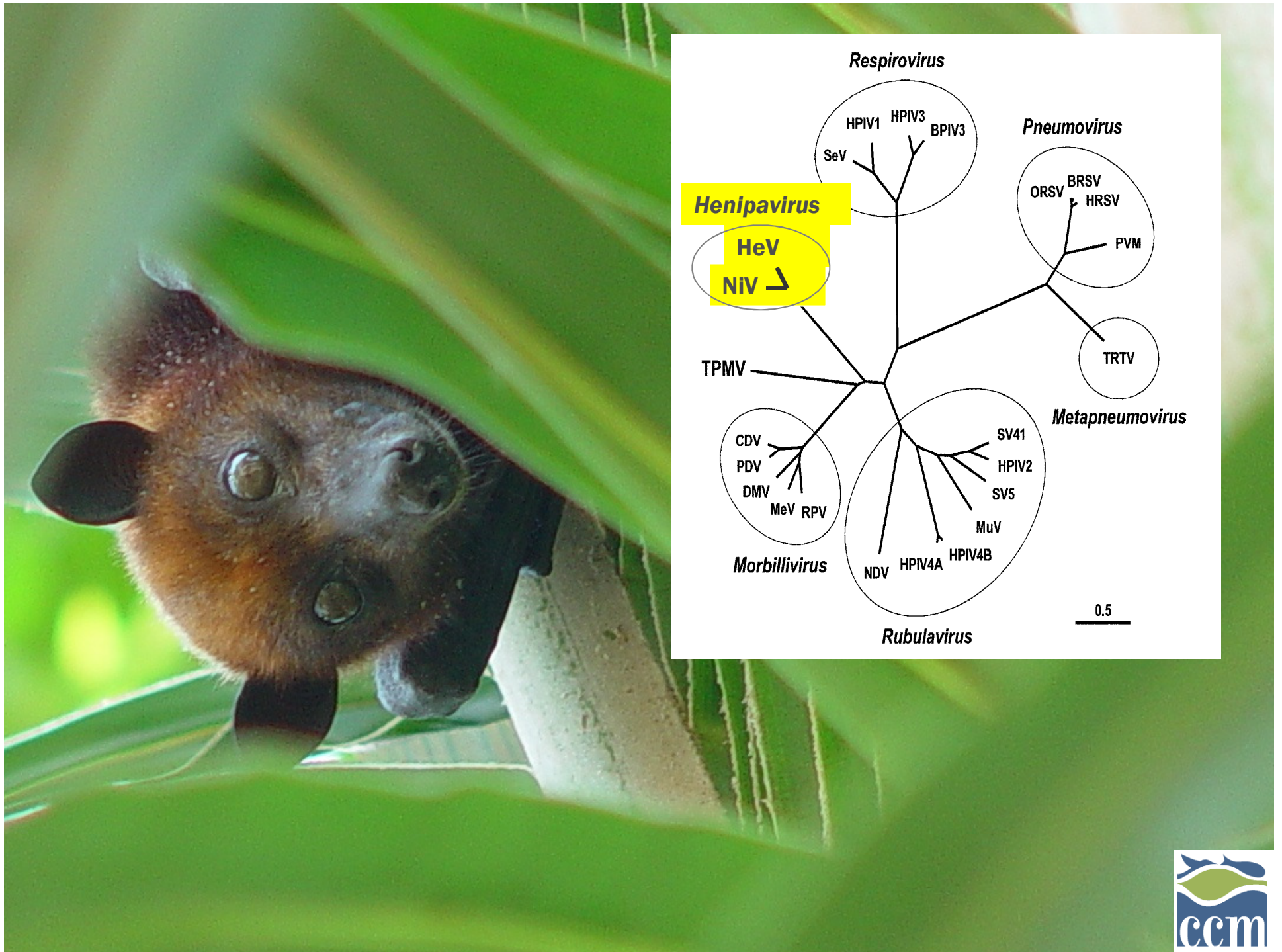
2000 – Tioman virus
(Malaysia)

2007 - Melaka virus
(Malaysia)



Henipaviruses

- Henipaviruses represent a novel genus in the Paramyxovirus family;
- Hendra virus first emerged in 1994 in Brisbane, Queensland, as a severe acute respiratory disease of race horses and humans with a high case fatality rate. Some cases were later shown to present with neurological features.
- Nipah virus emerged in Malaysia in 1999 as a severe disease of pigs and humans with both respiratory and neurological syndromes, and also displaying a high fatality rate.
- The natural reservoir host of both viruses was found to be fruit bats (flying foxes) in the genus *Pteropus*.



Hendra, Brisbane, Queensland, September 1994:
“first” outbreak in 21 horses
2 human cases with one fatality



Image ©2009 Sinclair Knight Merz & Fugro

©2009 MapData Sciences Pty Ltd, PSMA

©2009 Google

History of Hendra Virus Outbreaks

- **September 1994:** “first” outbreak in 21 horses and 2 human cases with one fatality in **Hendra**, Brisbane, Queensland
- **October 1995:** Retrospective diagnosis of HeV infection in dead two horses in **Mackay**, Queensland with one human fatality from severe encephalitis 13 months after exposure
- **Since 1999**, eleven focal, spatially & temporally unrelated outbreaks: - all confined along the east coast of Australia
 - ten in Queensland
 - one in New South Wales
- **Since Hendra discovery**, five outbreaks involved human cases
 - seven humans affected with four fatalities

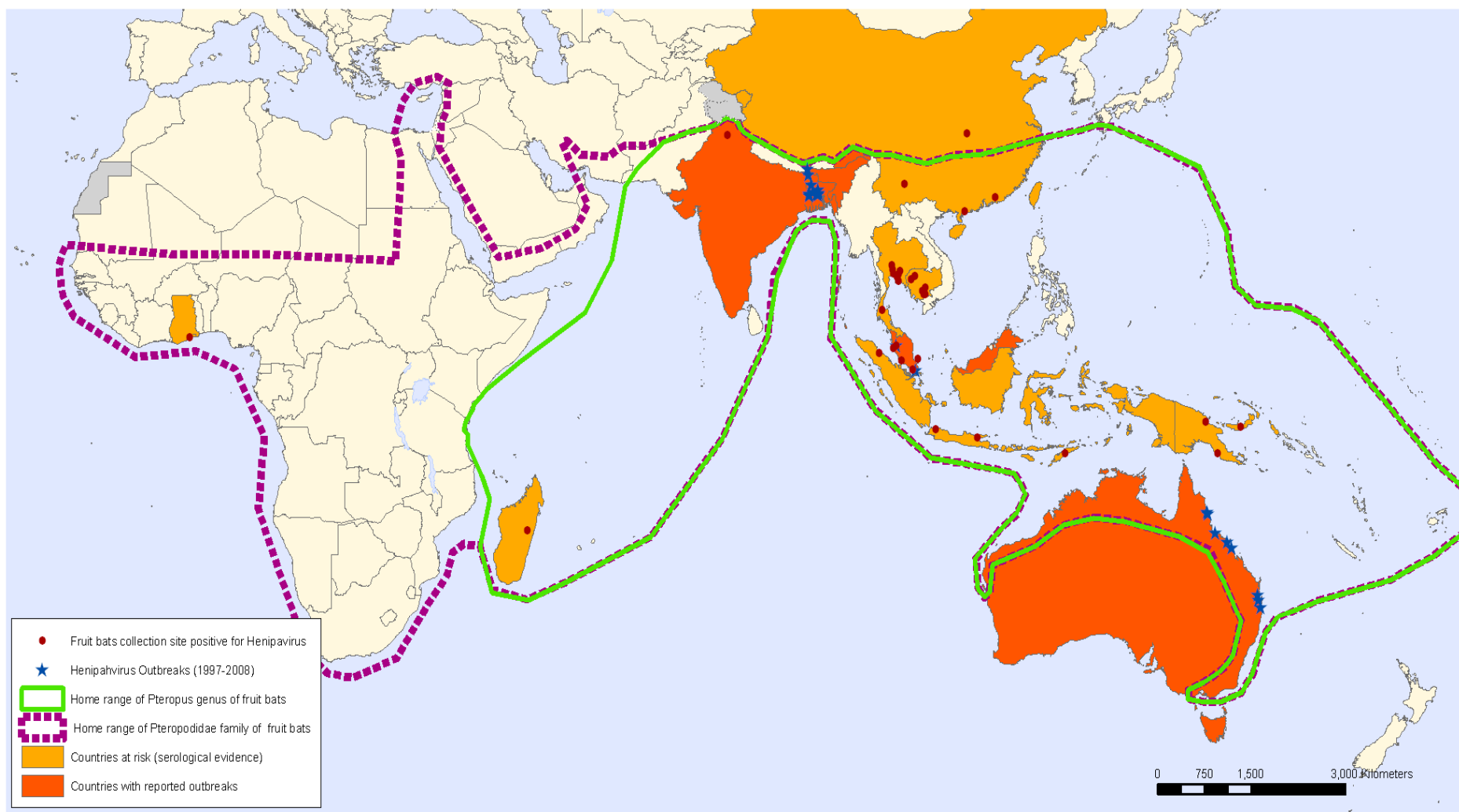
Kampung Sungai Nipah, Perak State, in Malaysia
1998-1999: first outbreak of Nipah among pig farmers
265 cases including 105 deaths.



History of Nipah Virus Outbreaks

- **1998-1999:** first outbreak of fatal encephalitis among pig farmers in Kampung Sungai Nipah, Perak State, in Peninsular Malaysia with 40% fatality (Cases similar to Japanese encephalitis) Malaysia 1999 outbreak cost 625 million USD
- **1999:** small outbreak in Singapore following importation of sick pigs from Malaysia
- **Since 2001,** 11 outbreaks have occurred in India and Bangladesh
 - Nine in Bangladesh (Kushtia, Faridpur, Manikgonj, Meherpur, Naogaon, Rajbari, Tangail and Thakurgaon districts)
 - Two in West Bengal of India (Siliguri and Nadia)
- **Since Nipah discovery,** 477 human cases including 248 deaths

Geographic distribution of Henipavirus outbreaks and fruit bats of Pteropodidae Family



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.

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



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How did these Henipaviruses emerge?

Hendra virus (HeV)

- HeV is believed to have emerged because fruit bats have become much more urbanised as they seek new sources of food (nectar or fruit).
- The natural food sources for these animals is the nectar of trees in forest settings, but these have been destroyed with increasing land clearance for agriculture.
- All human infections with HeV have been acquired through intermediate hosts, horses, and the potential for this interaction with horses is due largely to the peri-urban/urban locations of fruit bats 'camps'.
- Horses become infected by grazing on pastures contaminated with bat 'spats', urine, and possibly birthing fluids.
- It is essential that veterinarians are aware of the need to use personal protective equipment when dealing with sick horses.

How did the Henipaviruses emerge?

Nipah virus (NiV)

- The emergence of NiV is believed to be similar to that of HeV, but other factors are also undoubtedly important .
- Thus more intensive agricultural practices have played an important role in the genesis of NiV emergence. Larger pig farms and increased numbers of farms in peri-urban environments have been a consequence of economic development in Malaysia. In addition, many farms had a secondary product – fruit, with fruit trees often assisting in providing shade for the pig pens.
- Bats eat the fruit, and urinate, spit their masticated spats and drop fruit contaminated with saliva into the pig pens.
- Thus control can be achieved simply by ensuring fruit trees do not encroach or overhang the pig enclosures.

Nipah Virus Outbreaks: Malaysia, Singapore, Bangladesh and India

Dates	Location	No. cases	No. deaths	CFR(%)
Sep1998-Apr 1999	Malaysia; Singapore	265 11	105 1	40 9
Feb 2001	Siliguri, W. Bengal, India	66	45	68
Apr–May 2001	Meherpur, Bangladesh	13	9	69
Jan 2003	Naogaon, Bangladesh	12	8	67
Jan-Apr 2004	Goaland, Bangladesh	29	22	76
	Faridpur, Bangladesh	36	27	75
Jan-Mar 2005	Tangail, Bangladesh	12	11	92
Mar-Apr 2007	Kushtia, Bangladesh	19	5	26
	Nadia, W. Bengal, India	5	5	100
Feb-Mar 2008	Manikganj and Rajbari, Bangladesh	18	8	44

Nipah virus: Differences between the Malaysian outbreak and subsequent outbreaks in Bangladesh and India

- In Malaysia, pigs were the spill-over hosts – all human cases were acquired from pigs; in Bangladesh and India, there are no spill-over hosts – virus acquired most frequently from drinking palm juice contaminated by bat saliva or urine.
- In Malaysia, no human-to-human transmission; in Bangladesh and India, human-to-human transmission has been documented, including nosocomial transmission in hospital settings (mechanism/route of transmission is unknown).
- In Malaysia, the CFR was about 40%; in Bangladesh and India, the CFR has been about 80%.

Nipah in Bangladesh and India

Of international concern:

- The CFR of Nipah infection in India and Bangladesh is higher than in Malaysia.
- Good evidence of human-to-human transmission in Bangladesh and India, with at least 8 cycles of transmission, and nosocomial infections in hospital settings in Siliguri, West Bengal, and in Fardipur, Bangladesh.
- The mechanism of transmission remains to be determined.
- No evidence of pigs as intermediate hosts, and little direct evidence of bats in Siliguri or in Bangladesh in 2007 – thus source of virus remains to be determined in many instances.
- Does this indicate future pandemic potential??



Conclusions

- I hope I have shown in these few examples that our future security with respect to infectious diseases depends largely on our understanding of how diseases emerge, resurge and spread.
- There are many ways we can reduce or mitigate epidemic activity and spread – eg: reduction in urban shanty towns, reduction in mosquito breeding along the edges of dams, use of residual insecticides in aircraft, improved sanitation at ports and airports, education of general practitioners to take travel histories of patients presenting with fever, rash and/or myalgia, attract more science students into virology and entomology, improved environmental planning, increased political will and funding, etc
- Forewarned with this knowledge, we have also to understand that we are, in a sense, our 'own worst enemies' – that we are responsible for many of the conditions and actions that lead to an increased incidence and spread of many of 'our invisible enemies'.