

Overview of Mosquito borne diseases

Dr Candice Holland

Infectious diseases physician, Public Health Registrar

West Moreton Health

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Acknowledgement of Traditional Owners

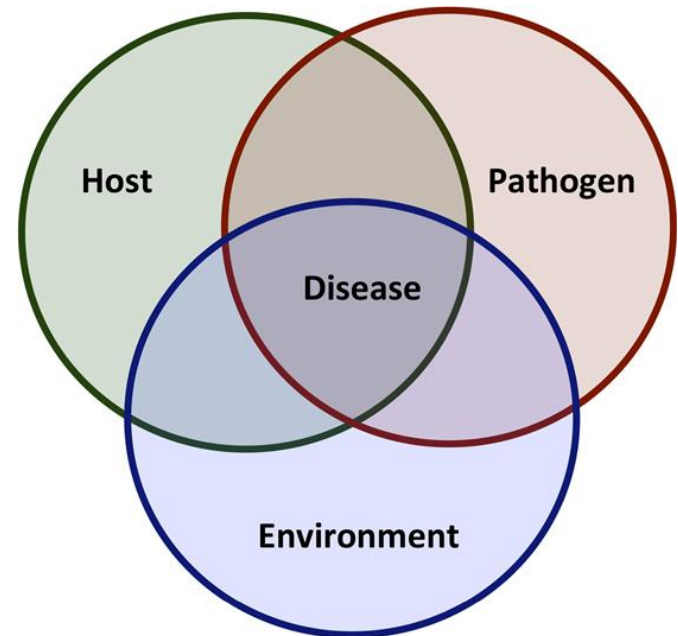
I would like to acknowledge and pay my respects to the Jagera (jag-er-a), Yuggera (yug-er-a) and Ugarapul (U-ga-ra-pul) Peoples, the Traditional Owners and Custodians of the land on which we are meeting today and recognise their continuing connection to land, waters and community.

I would like to pay my respects to elders' past, present and emerging.



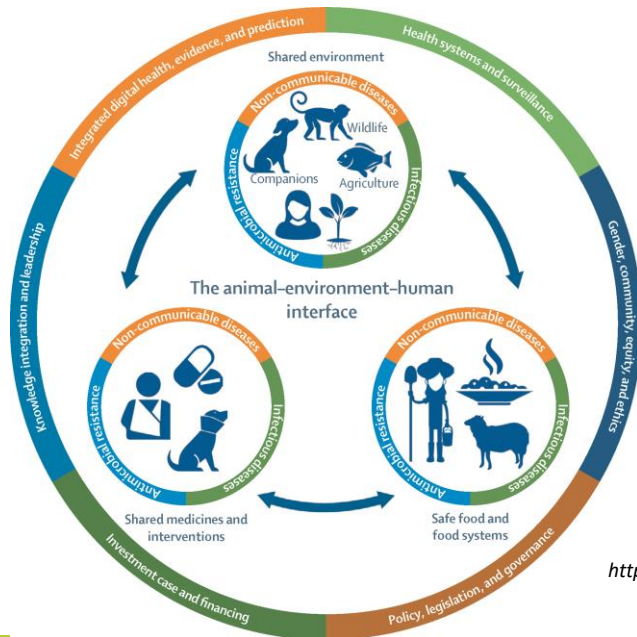
Overview

- Key concepts / definitions
- Classification
- Epidemiology
- Mosquito-borne diseases in focus:
 - JEV
 - Dengue
 - Malaria
- Disease prevention and control strategies



One Health

- One Health is a collaborative, multisectoral, and transdisciplinary approach — working at the local, regional, national, and global levels — with the goal of achieving optimal health outcomes recognizing the interconnection between people, animals, plants, and their shared environment. (CDC)

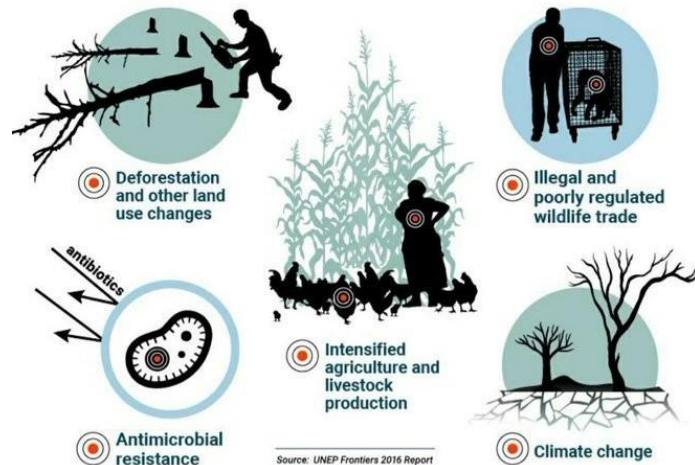


<https://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2820%2931027-8/fulltext>

Zoonosis

- Any disease or infection that is naturally transmissible from non-human vertebrate animals to humans. Transmission can be direct, indirect, vector-borne, food- or waterborne.

What factors are increasing zoonosis emergence? (Diseases transmitted from animals to humans)



#COVID19

UN
environment
programme

<https://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2820%2931027-8/fulltext>

Definitions

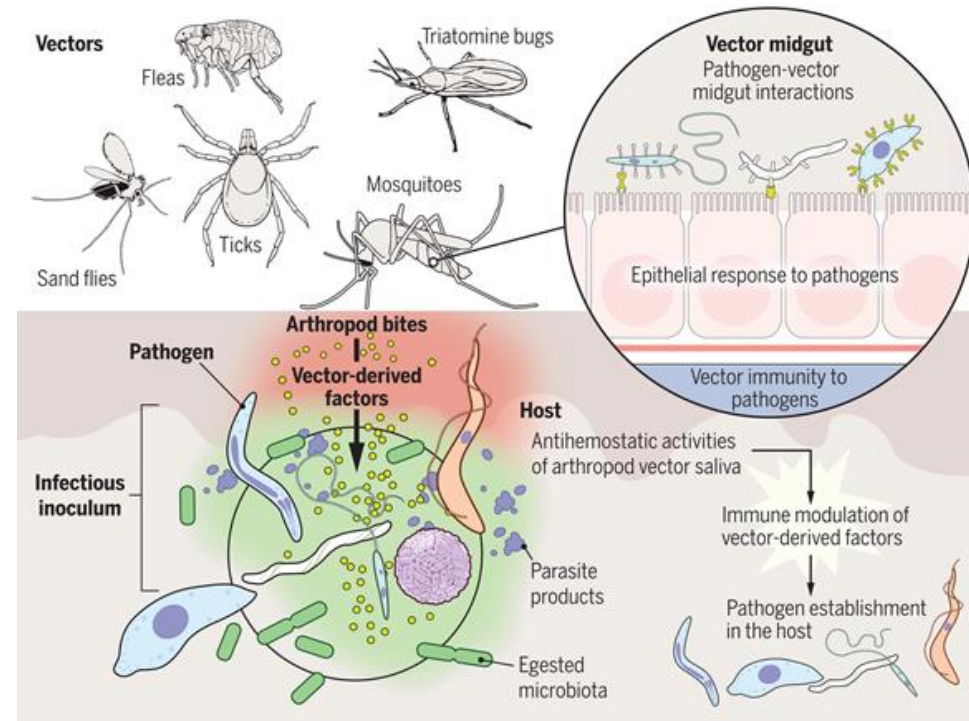
Vector-borne disease:

- Illnesses caused by parasites, bacteria or viruses that are transmitted from between hosts through the bite of an arthropod vector.

Arbovirus:

- Any of a group of viruses transmitted by mosquitoes, ticks or other arthropods

Arthropod vectors are ectothermic, thus particularly sensitive to climatic factors

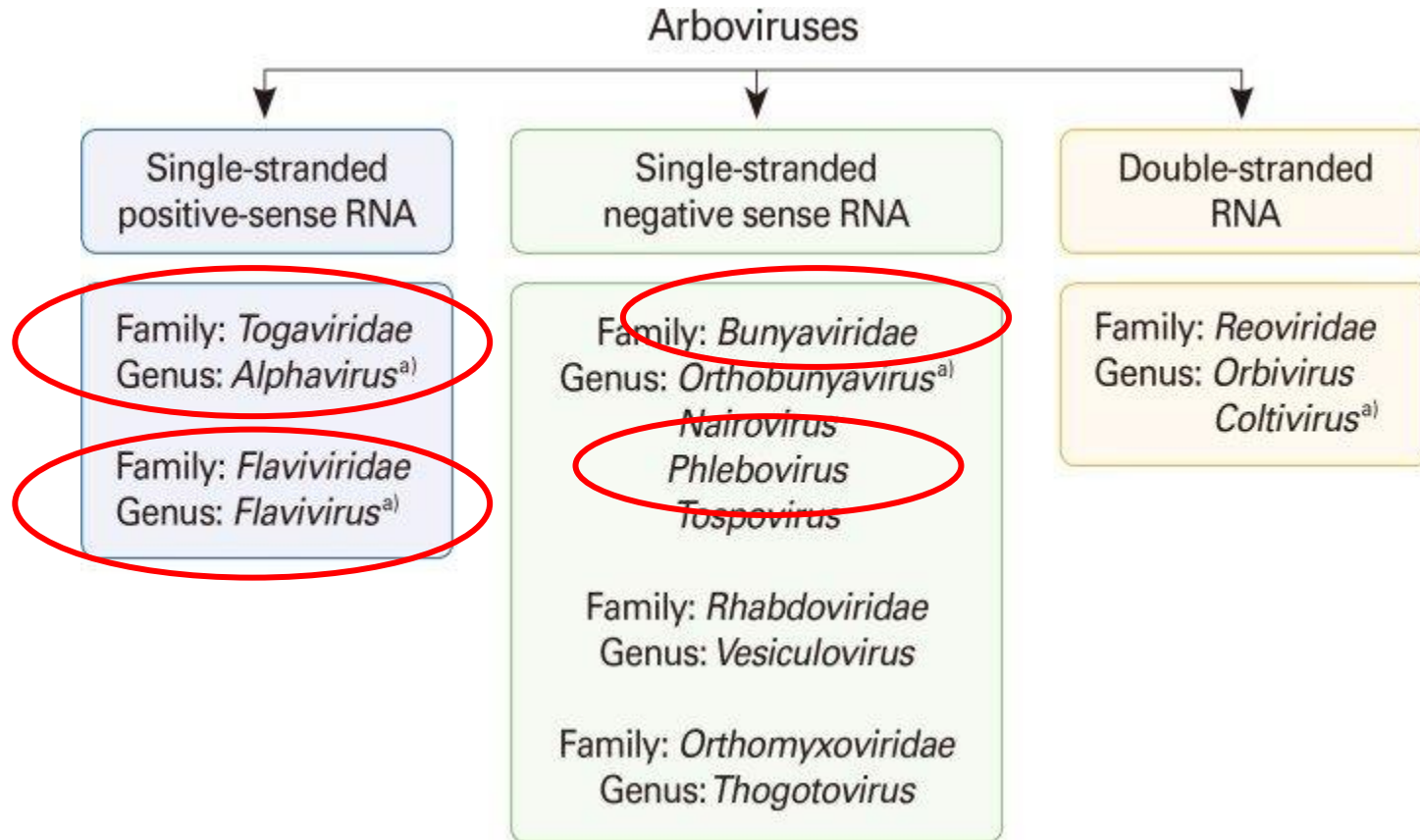


<https://www.science.org/doi/10.1126/science.abc2757>

Vector	Disease caused	Type of pathogen
Mosquito	<i>Aedes</i>	Chikungunya
		Dengue
		Lymphatic filariasis
		Ross River fever (<i>also transmitted by Culex sp.</i>)
		Yellow Fever
		Zika
	<i>Anopheles</i>	Lymphatic filariasis
		Malaria
	<i>Culex</i>	Japanese encephalitis
		Lymphatic filariasis
		West Nile fever (Kunjin)
Aquatic snails	Schistosomiasis (bilharziasis)	Parasite
Blackflies	Onchocerciasis (river blindness)	Parasite
Fleas	Plague (transmitted from rats to humans)	Bacteria
	Tungiasis	Ectoparasite
Lice	Typhus	Bacteria
	Louse-borne relapsing fever	Bacteria
Sandflies	Leishmaniasis	Parasite
	Sandfly fever (phlebotomus fever)	Virus
Ticks	Crimean-Congo haemorrhagic fever	Virus
	Lyme disease	Bacteria
	Relapsing fever (borreliosis)	Bacteria
	Rickettsial diseases (eg: spotted fever and Q fever)	Bacteria
	Tick-borne encephalitis	Virus
	Tularaemia	Bacteria
Triatome bugs	Chagas disease (American trypanosomiasis)	Parasite
Tsetse flies	Sleeping sickness (African trypanosomiasis)	Parasite

<https://www.who.int/news-room/fact-sheets/detail/vector-borne-diseases>

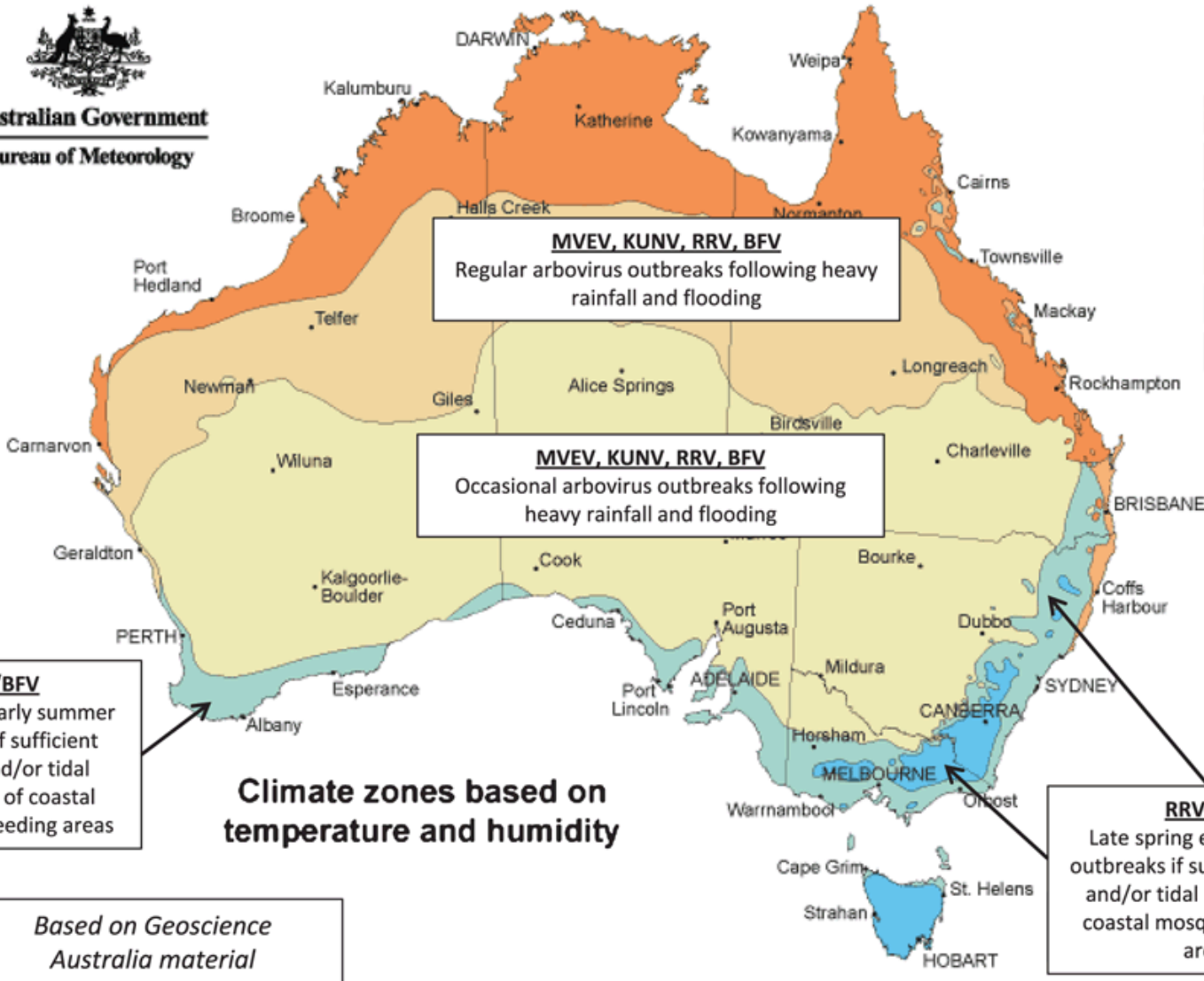
Arbovirus classification



https://www.researchgate.net/figure/Classification-of-arboviruses-Arboviruses-are-included-in-six-different-taxonomic-virus_fig1_259743924

Epidemiology

- Vector-borne diseases account for >17% all infectious diseases, cause >700 000 deaths annually globally
- Largest burden is due to Malaria (219M cases, 400 000 deaths per year)
- Dengue most prevalent viral infection (96M symptomatic cases, 40,000 deaths per year)
- In Queensland – Ross River virus and Barmah Forest virus endemic, contribute the largest annual disease burden
- Emergence of Japanese encephalitis virus (JEV) across Eastern/Southern Australia in 2022



Steps of an outbreak investigation

- **Confirm outbreak and diagnosis**
- **Case definition and identification**
- **Descriptive data collection and analysis**
- **Develop hypothesis**
- **Analytical studies to test hypotheses**
- **Special studies**
- **Implementation of control measures**
- **Communication, including outbreak report**

WHO/CSR



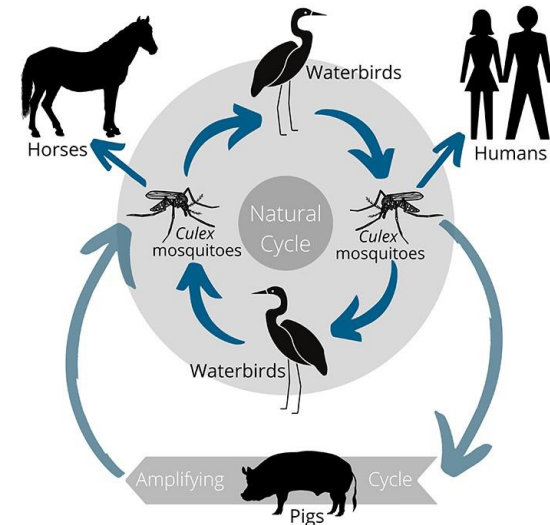


Japanese encephalitis virus

<https://www.health.qld.gov.au/news-events/news/what-is-mosquito-borne-japanese-encephalitis>

What is JEV?

- Mosquito borne disease (MBD) – *Culex* spp.
- Flaviviridae
 - ss+RNA, enveloped
- Waterbirds are natural reservoir
- People and horses are ‘dead-end hosts’
- Pigs and some types of wild birds are ‘amplifying hosts’

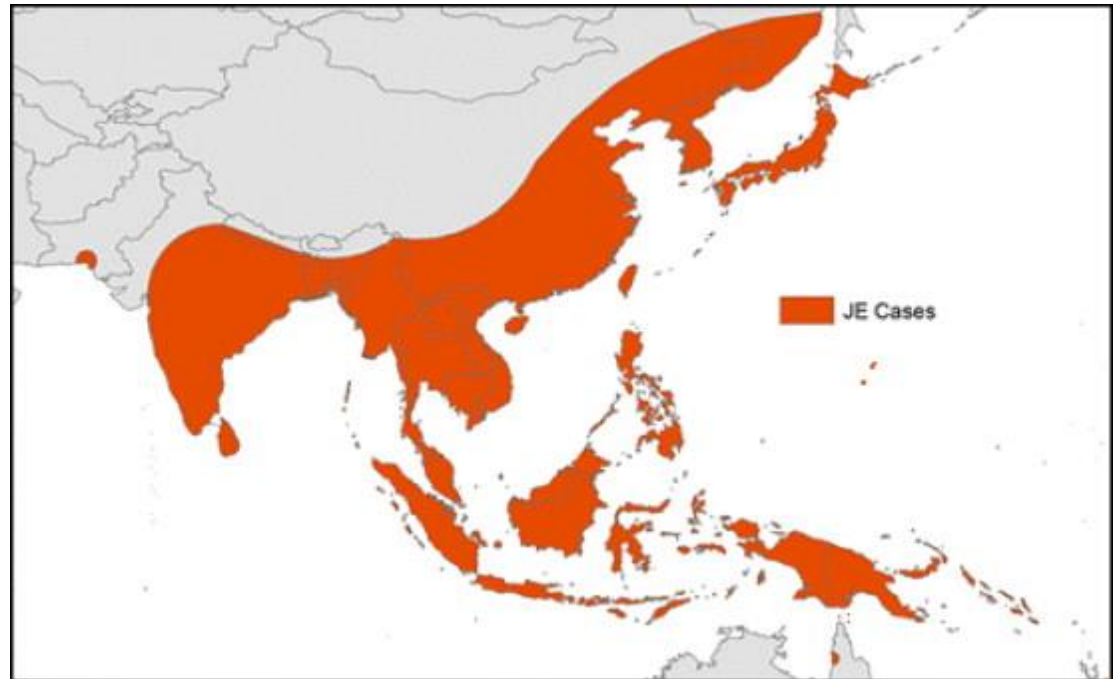


<https://www.environment.act.gov.au/parks-conservation/plants-and-animals/biosecurity/biosecurity-alerts/japanese-encephalitis-virus>

Epidemiology: Distribution prior to 2022

Australia:

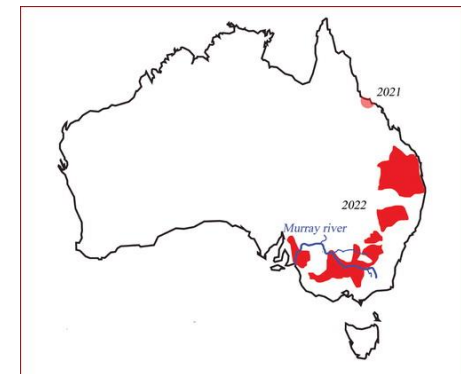
- Three sporadic cases + animal detections in outer Torres Strait Islands and remote Cape York in 1990s
- Tiwi Islands 02/2021
- Imported cases in travellers from endemic areas



<https://www.sciencedirect.com/science/article/abs/pii/S0168706906160103>

Emergence in Mainland Australia

- 28 February 2022:
 - Concurrent detections in piggeries down the East Coast in 4 jurisdictions
 - Concern re: cluster of unwell persons in SA
- 03 March 2022:
 - First human JE case notified in QLD
- Now 45 confirmed or probable cases, 7 deaths
 - 5 in QLD



<https://www.magonlinelibrary.com/doi/10.12968/live.2022.27.4.186>

Clinical features

- Approximately 99% of JE cases have either no or mild or symptoms, like fever and headache.
- Encephalitis is rare
 - cause neck stiffness, disorientation, tremors, convulsions, paralysis, coma, permanent neurological complications, or death
- Incubation period 5-15 days
- Children under 5 and older people are at a higher risk of developing severe illness
- Treatment is supportive

Testing

- CSF – JEV IgM (preferred sample)
 - May be taken too early in the illness for IgM to be present at a diagnostic titre.
 - One 1995 study only 75% of CSF samples taken on days 3-4 of the illness were positive; whereas more than 95% of those taken beyond day 10 of illness were positive.
- JEV PCR – blood or CSF
 - Short viraemia limits the usefulness of PCR
- Flavivirus serology (specify “JEV” on request)
 - Two specimens at least 14 days apart, sens increases from ~75% IgM at day 4 to most pos at day 7-10


Public Health measures

- Surveillance – animals, humans, mosquitoes
- Clinician alerts
- Public messaging – self protective measures and reduce mosquito breeding sites
- Vaccines
 - Imojev: live attenuated, single dose primary course, 9m.o +
 - JEspect – inactivated, 2 dose primary course, safe in pregnancy/immunocompromise

Dengue fever

A potentially lethal disease that affects 50 million people a year

- ▶ Four distinct but related viruses cause dengue
- ▶ Recovery from one gives lifelong immunity to that strain, but not to the other three



- ▶ Good evidence that further infection by different virus strains can lead to **dengue hemorrhagic fever (DHF)** - a lethal complication of dengue
- ▶ **2.5 percent** of DHF cases are **fatal**. With intensive supportive therapy, rate can drop to 1 percent but **untreated it is as high as 20 percent**

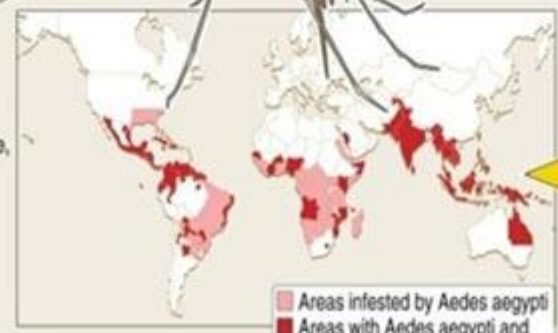
Symptoms

- Fever
- Vomiting
- Muscle pain
- Disintegration of blood vessels leading to heavy bleeding

- Transmitted to humans through bites of female ***Aedes aegypti*** mosquitoes

- Mosquito acquires virus from **feeding on infected person's blood** - incubates virus for 8 - 10 days
- Virus circulates in blood of humans for two to seven days

- Found in tropical and sub-tropical areas worldwide, predominantly in urban and semi-urban areas



Southeast Asia and Western Pacific the most seriously affected

Source: WHO/CDC/Stanford/

230908 AFP

Dengue virus

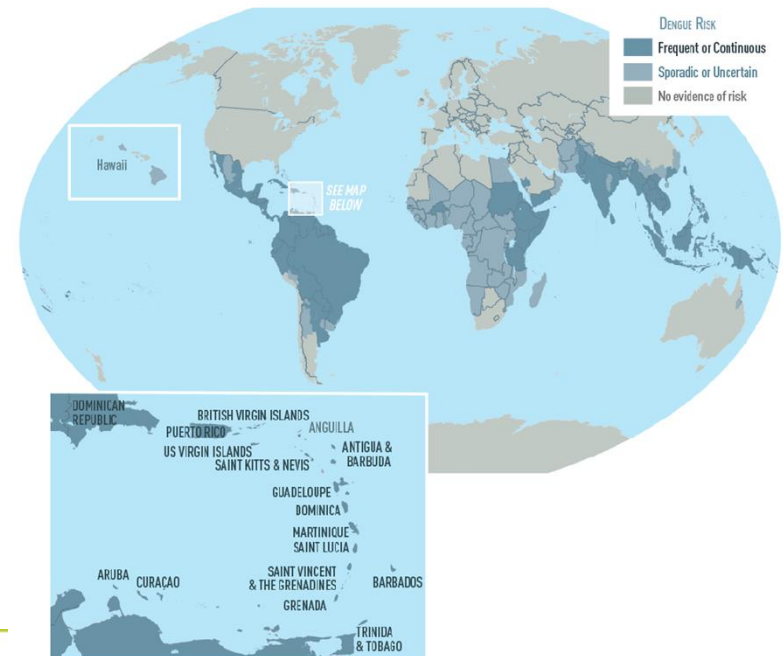
<https://douglas.qld.gov.au/business/environmental-health/dengue-fever-facts/>

What is dengue virus?

- Flavivirus
 - 4 distinct, but closely related serotypes (DENV-1 to -4)
- Humans are the reservoir (monkeys in Africa)
- Leading cause of serious illness and death in some Asian and Latin American countries
- Transmitted by *Aedes aegypti*
 - urban mosquito, tropics and subtropics. Confined to QLD in Aus
 - Prefers man-made containers, indoor, sheltered resting sites.
 - Day biting
- Secondarily *Aedes albopictus*
 - Peri-domestic, pesty day-biting mosquito
 - Man-made + naturally occurring breeding sites
 - Aggressive coloniser, confined to Torres Strait in Aus

Global Epidemiology

- Most rapidly spreading mosquito-borne virus in the world – 30-fold increase over the past 50 years
- 100-400M infections annually in over 100 endemic countries
Widespread throughout tropics
- Spatial variations
 - Due to transmission drivers as above
- Significant economic burden
 - Direct – health care costs
 - Indirect – loss of productivity



<https://www.cdc.gov/dengue/areaswithrisk/around-the-world.html/>

Drivers of dengue transmission

- Ecological factors
 - Vector species and abundance
 - Climate change via interaction with biotic and abiotic factors
 - Rainfall
 - Temperature
 - Relative humidity
 - Extreme events
 - Vertical transmission in mosquito
 - Cryptic and subterranean breeding sites

Drivers of dengue transmission

- Socio-demographic factors
 - Housing structure
 - Urbanisation
 - Population growth
 - Movement (people and goods)
 - Proximity to endemic areas
 - Water storage containers
 - Degree of urbanisation



Courtesy Dr Gulam Khandaker, Central Queensland Public Health Unit

Epidemiology in Queensland

- 3rd most common mosquito-borne virus after RRV and BFV
- Epidemics in North QLD predominantly from imported cases
- Not endemic in recent decades
- First noted 1873, epidemics date back to 1879
- Decrease in dengue incidence in late 1950s to early 1980s but increased since then

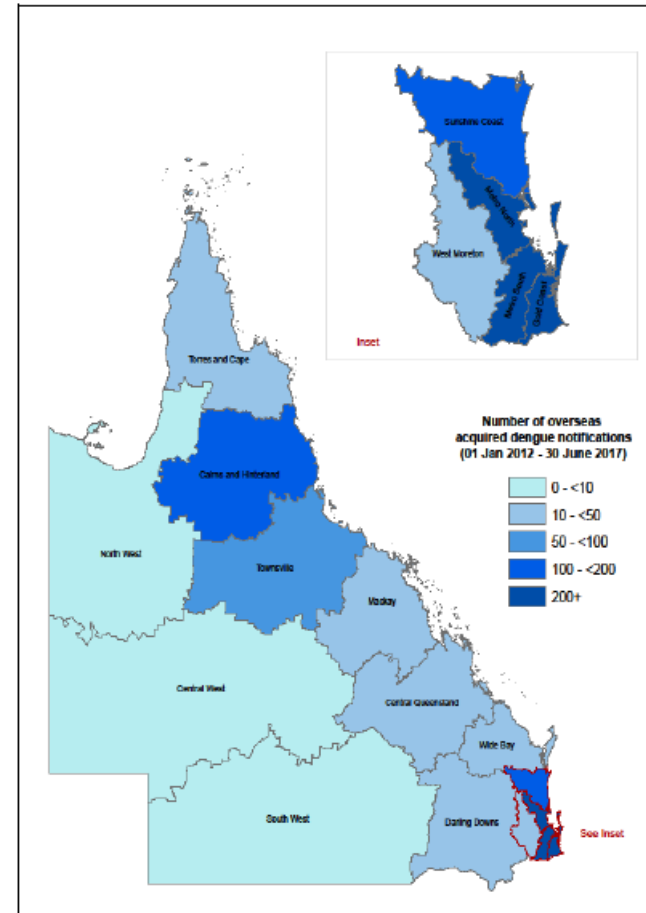


Figure 7: Number of overseas acquired dengue notifications by HHS area, Queensland, 01 July 2012 – 30 June 2017

Mosquito Borne Diseases in Queensland 1 July 2012 – 30 June 2017. Queensland Health, Communicable Diseases Branch. 2018:
https://www.health.qld.gov.au/_data/assets/pdf_file/0020/712253/mbd-report-annual.pdf

Table 4: Notifications of dengue in Queensland, 1 July 2012 to 30 June 2017, by local or overseas acquisition (changes made to table)

Place of acquisition	2012/13	2013/14	2014/15	2015/16	2016/17	Total (%)
Queensland	207	203	70	33	18	531 (28.0)
Overseas	215	259	207	364	315	1360 (71.8)
Not available	0	1	0	1	2	4 (0.2)
Total (%)	422 (22.3)	463 (24.4)	277 (14.6)	398 (21.0)	335 (17.7)	1895

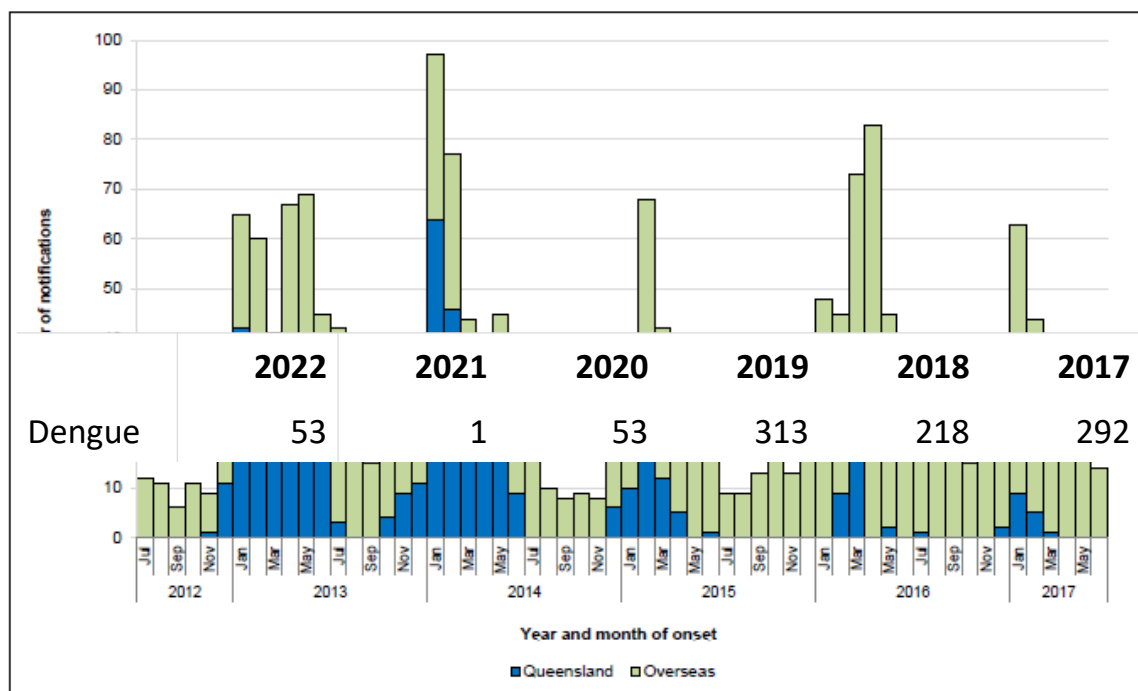


Figure 5: Notifications of dengue in Queensland with onset from 1 July 2012 to 30 June 2017, by month, year and place of acquisition

Locally acquired cases

- Outbreaks triggered by imported viraemic cases entering dengue receptive area
- 28% of notified cases 2012 – 2017
- 77% in Cairns and Hinterland HHS, 17% Townsville HHS
- Decreasing over time, most likely due to the implementation of *Wolbachia* in previously dengue-prone centres of Cairns and Townsville

Overseas acquisition of QLD reported cases

- Imported cases predominantly notified in large population centres in SE and North QLD
- In 2018: Oceania (40%) and SE Asia (43%)
 - Most common countries Thailand (17%) and Samoa (30%)
- Imports dependent on:
 - Season in country of acquisition
 - Travel activity
 - Virus circulation in areas of travel
 - Risk of exposure

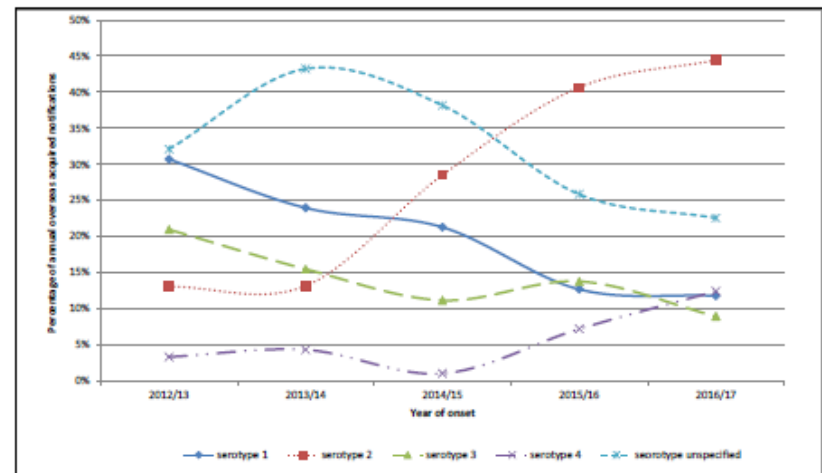


Figure 8: Notifications of overseas acquired dengue 1 July 2012 to 30 June 2017, by year and serotype.

Mosquito Borne Diseases in Queensland 1 July 2012 – 30 June 2017. Queensland Health, Communicable Diseases Branch. 2018:

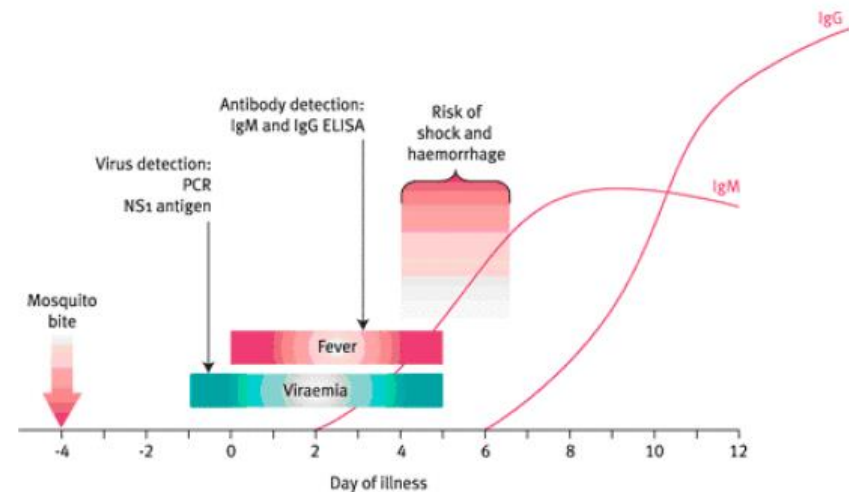
https://www.health.qld.gov.au/_data/assets/pdf_file/0020/712253/mbd-report-annual.pdf

Clinical features

- Incubation period 4-10 days
- Majority of cases asymptomatic or mildly symptomatic
- Occ. Severe flu-like illness, lasting 2-7 days
 - Severe headache, pain behind eyes, myalgia/arthralgia, nausea/vomiting, lymphadenopathy, rash
- Severe dengue
 - Caused with secondary infection with different serotypes
 - Severe plasma leakage, shock, ARDS, haemorrhagic shock, hepatic failure, encephalitis
- Treatment is supportive

Dengue Case Surveillance

- Early diagnosis is vital for rapid control measures
- Dengue is notifiable under PHA 2005
- FSS is arbovirus reference lab for QLD
- Detection is via direct methods – PCR, NS1 antigen in bloods, and indirect methods – serology (issues with cross-reactivity)



Queensland Dengue Management Plan 2015-2020. Queensland Health, Communicable Diseases Branch. 2015:
https://www.health.qld.gov.au/_data/assets/pdf_file/0022/444433/dengue-mgt-plan.pdf

Public Health Management of Dengue

- Vector surveillance
- Timely detection, reporting and management of cases
- Control to prevent local transmission
- Reduce spread of vectors into novel geographic locations
- Support adoption of protective behaviours by the public
- Novel/research initiatives – *Wolbachia*, vaccine development

Advertisement

There are some simple steps you can take to defend yourself and your family against dengue fever.

Tip it
Tip out any water that's pooled in things like pot plant bases, plastic containers and tarpaulins.

Store it
Store anything that can hold water in a dry place or undercover. Including tyres, gardening equipment, toys, buckets, trailers or boats.

Throw it
Throw out any rubbish lying around your yard like leaves in gutters, old palm fronds and unused containers or tyres.

Check around your yard every week. Stop the mosquito breeding and...

DEFEND AGAINST DENGUE

For more information on dengue fever visit the website:
www.health.qld.gov.au/dengue

Authorised by the Queensland Government, George Street, Brisbane.

<http://www.mackay.health.qld.gov.au/dengue-fever-case-confirmed-bowen/>

Dengue outbreak Rockhampton 2019

- Outbreak of dengue 2 in Rockhampton from May 2019
- First outbreak in the area for many decades
 - 71 y.o. male with illness onset from 05/05/2019. PCR Positive for DENV 2
 - Exposure period – 23/04/2019 – 2/05/2019, No travel overseas or to FNQ
 - Viraemic period 4/05/2019 - 17/05/2019

'Full outbreak response': First Rockhampton dengue fever case in decades

By Toby Crockett and Stuart Layt
May 24, 2019 – 12:22pm

f t e A A

Leave a comment

TODAY'S TOP STORIES

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Police shoot man dead after disturbance in Brisbane's south
1 hour ago
- CRICKET**
Mack Horton refuses to share podium with Sun Yang after Chinese swimmer wins
1 hour ago
- TRUMP'S WHITE HOUSE**
'Apologise to America', Trump tells Democratic congresswomen
1 hour ago

The central Queensland city of Rockhampton has its first confirmed dengue fever case in almost 30 years, prompting a "full outbreak response", according to Queensland Health.

Council officers and health officials will doorknock the patient's neighbours on Friday to warn them.

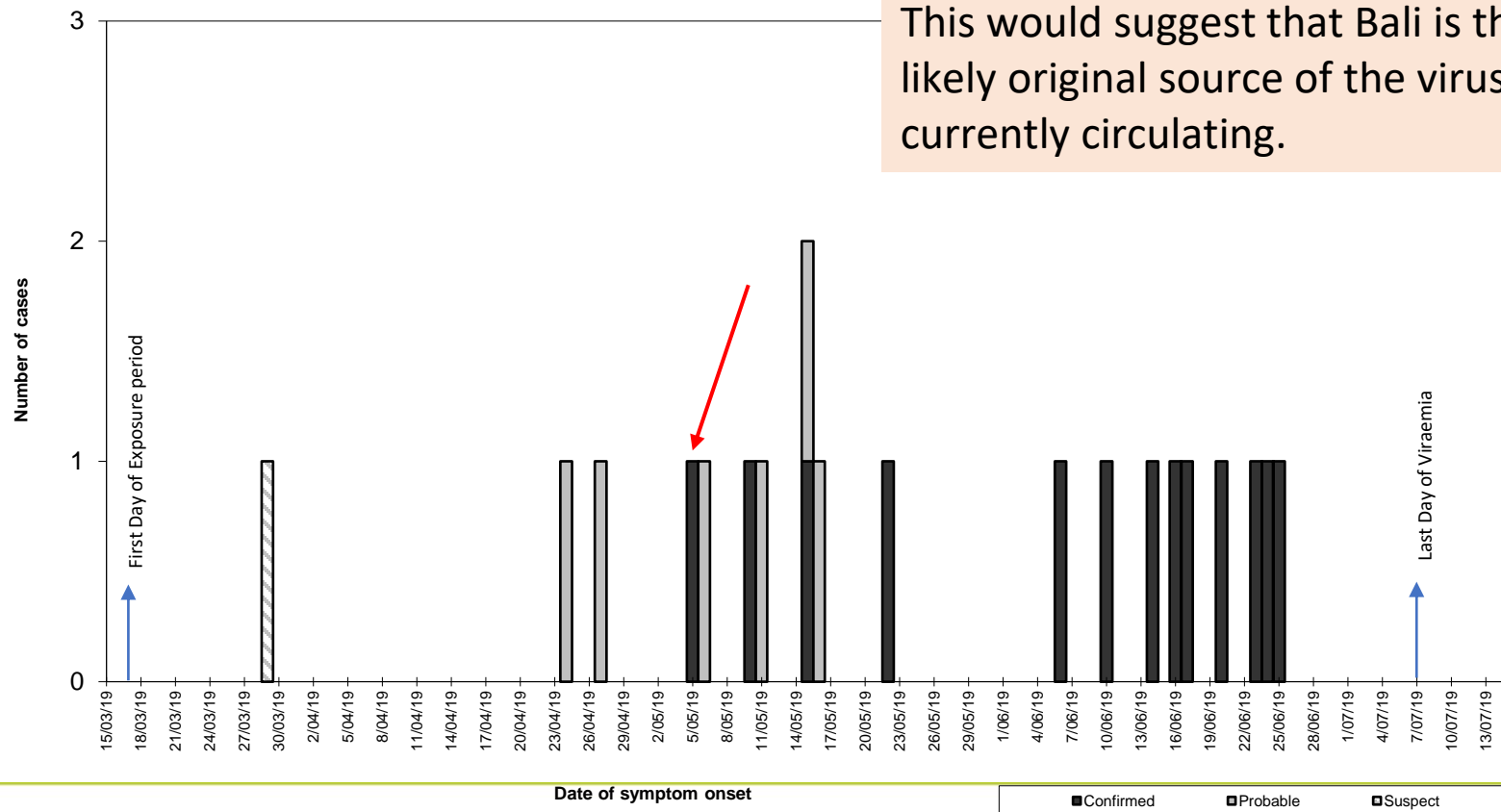


<https://www.abc.net.au/news/2019-05-24/first-locally-acquired-case-of-dengue-fever-in-central-qld/11144996>

Dengue outbreak Rockhampton 2019

- IMT formed 23/5/19
- Media release
- Public Health Alert for GPs/ED and local residents
- Working together with Rockhampton Regional Council
- ARCBS kept up to date
- Set traps at case residence
- Door knock immediate surrounding area + vector control
- Follow up any resident with symptoms and/or recent travel history from the immediate surrounding area

Dengue outbreak Rockhampton 2019



Dengue outbreak Rockhampton 2019

- Total 20 cases (13 confirmed, 7 probable)
- No significant complications
- > 600 properties inspected and sprayed – *Aedes Aegypti* found at significant number of those properties
- Media and public engagement +++



Outcomes of outbreak

- Declaring Rockhampton as a Dengue-receptive area
- Ongoing surveillance and control activities are important
- Increasing CQPHU's capacity in mosquito surveillance and control activities (e.g. staff training)
- Preparedness – commitment from the council/targeted program (e.g. modification of environment, junk collection, ongoing surveillance and education)



Malaria

Malaria – the global burden

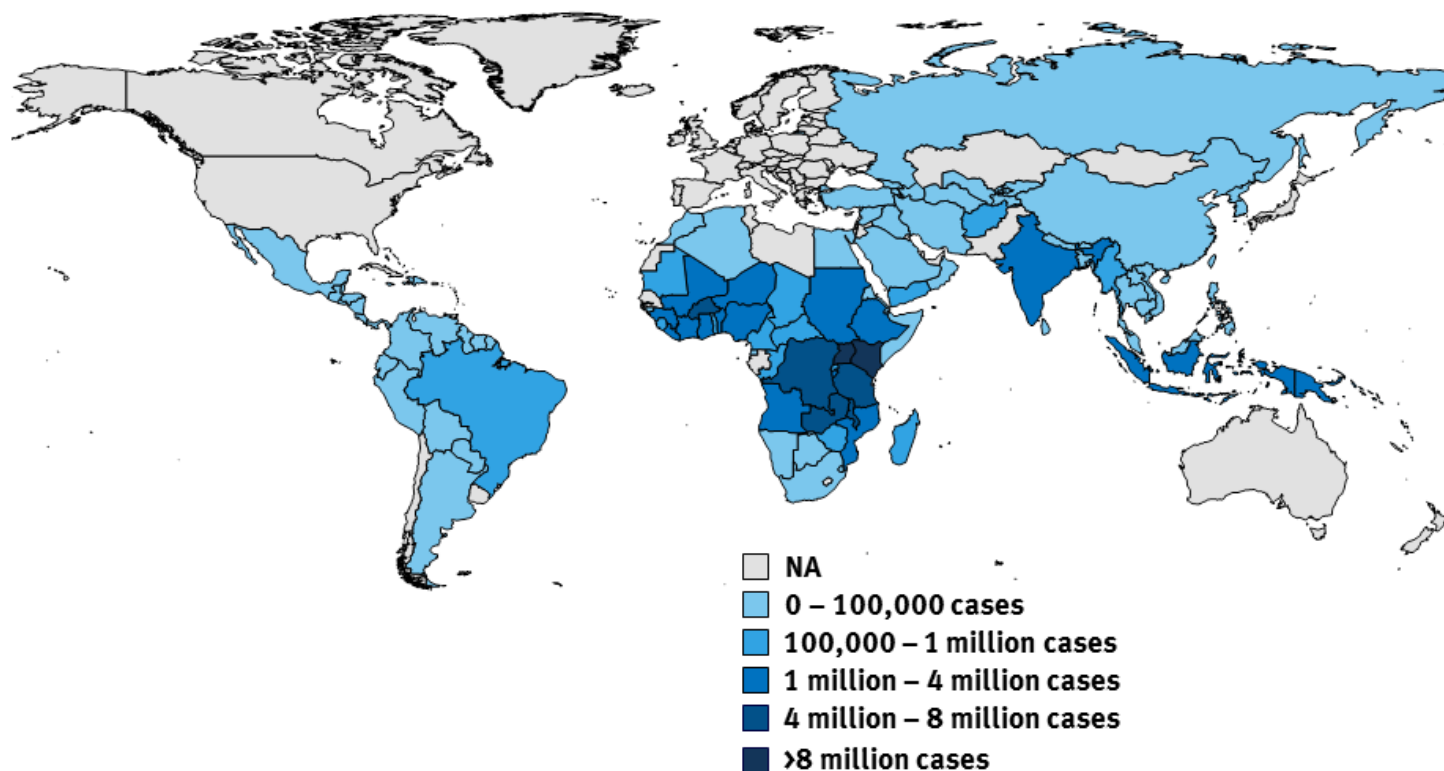
- One of the major tropical diseases of interest to WHO and other such organisations
- In 2013:
 - Estimated 198 million cases worldwide
 - Approx. 584 000 deaths, mostly African children
- It is preventable and treatable

Malaria – the global burden

- Some good news
 - Mortality rates have fallen globally by ~47% since 2000, and by ~54% in Africa
 - Predominantly by distribution insecticide treated mosquito nets and effective combination treatments

Distribution

Reported Malaria Cases, 2011



SOURCE: Kaiser Family Foundation, www.GlobalHealthFacts.org, based on WHO, World Malaria Report 2012; December 2012.

Distribution

- Largely tropical
- Developing countries
- Most cases and deaths in sub-Saharan Africa
- Australia declared Malaria free in 1981
 - Still ~600-800 cases annually
 - Mainly imported by travellers

Blood Parasites

- *Plasmodium* spp.:
 - Plasmodium falciparum
 - Plasmodium vivax
 - Plasmodium malariae
 - Plasmodium ovale

- Plasmodium knowlesi

Transmission

- Anopheles mosquito
 - 25 of 400 species are good vectors
 - ie long-lived, robust, preferentially bite humans

Transmission

- Stable transmission
 - Constant, year round
 - Intense transmission, mortality highest in early childhood and most adult infections asymptomatic
- Unstable transmission
 - Low, erratic, focal
 - Full protective immunity not acquired therefore symptomatic at all ages
 - Large epidemics with substantial mortality when changes in environmental, social or economic conditions (often armed conflict)

Who is particularly at risk?

- Young children in stable areas, not yet immune
- Pregnant women in 1st and 2nd pregnancies
- HIV infected persons
- International travellers from non-endemic areas
- Immigrants returning home

Biology and Life Cycle

- Asexual cycle
 - 48 hrs for *P. falciparum*, *P. vivax* and *P. ovale* (tertian fever),
 - 72hrs for *P. malariae* (quartan fever).
 - 24hr for knowlesi
- **Incubation** period 12-14 days
- Parasite densities $\sim 50/\mu\text{L}$ at time of symptoms and detectability by microscopy and diagnostic tests

Biology and Life Cycle

- Parasites attach to erythrocytes via ligand-receptor interactions which are unique to different species
- Disease caused by red cell parasitisation and red cell destruction + host immune response
- Meiosis only occurs in mosquito

Recurrent or persistent malaria

- Blood stage can persist if untreated
- Intrahepatic forms can remain dormant as hypnozoites in *P.vivax* and *P.ovale* infections causing relapsing disease

Changes to the human genome

- Sickle cell disease
- HbC and HbE
- Ovalocytosis
- Thalassaemias
- G6PD deficiency
- Mechanisms: reduced parasite growth at low oxygen tension, reduced cyto-adherence, parasite densities and invasion and multiplication

Immune response

- Not completely understood
- Both innate and specific immune arms, humoral and cellular immunity
- Protect from illness but not infection

Clinical features

- Initially non-specific
- Fever
- Nausea, vomiting
- Orthostatic hypotension
- Fatigue
- Muscle aches
- Abdominal pain
- The eighth great mimic!

Clinical features

- Examination findings
 - Fever
 - Anaemia
 - Hepatosplenomegaly
 - Jaundice
 - Respiratory distress: APO, acidosis

Clinical Features

- Severe malaria
 - P.falciparum cause adhesive proteins to be expressed on erythrocyte surface allowing adherence to vessel walls and each other
 - Leads to sequestration in organs (brain, placenta)

Clinical Features

- Severe malaria
 - Severe anaemia
 - ALOC
 - Jaundice
 - >2% RBCs parasitised
 - Metabolic acidosis
 - AKI
 - ARDS
- Warrants immediate IV antimalarial therapy

Complications

- Cerebral malaria
 - Extensive microvascular obstruction of capillaries and venules, impaired perfusion
 - Intact BBB and little inflammation
 - ↑ ICP secondary to ↑ cerebral blood volume

Complications

- Cerebral malaria
 - 3-15% children who survive cerebral malaria have residual neurological deficits
 - Hemiplegia
 - Cerebral palsy
 - Cortical blindness
 - Deafness
 - Impaired cognition, language and learning
 - Epilepsy

Complications

- Pulmonary Oedema/ ARDS
 - ↑pulmonary capillary permeability, particularly on commencement therapy
 - Pathogenesis not fully understood
 - Therapy is careful fluid balance management, avoidance rapid infusion large boluses
 - Mortality >80% or >50% if mechanical ventilation avail.

Complications

- AKI
 - ATN type picture likely secondary to impaired microcirculatory flow
 - Early haemodialysis/haemofiltration
- Jaundice
 - Haemolysis, hepatocyte injury, cholestasis
 - Chronic Hep B coinfection common and predisposes to severe malaria

Interaction with other infections

- Invasive bacterial infections
 - Translocation gut bacteria across enteric epithelia
 - Functional exhaustion PMNs
 - Haemolysis induced dysfunction haem-oxygenase 1 induction
- Misdiagnosis severe infections in children with incidental parasitaemia
- Acceleration HIV transmission and progression, more severe malaria in HIV infected patients

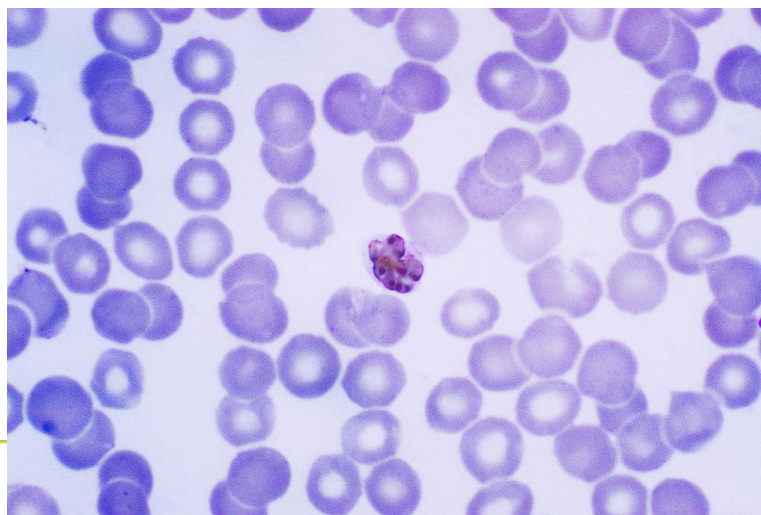
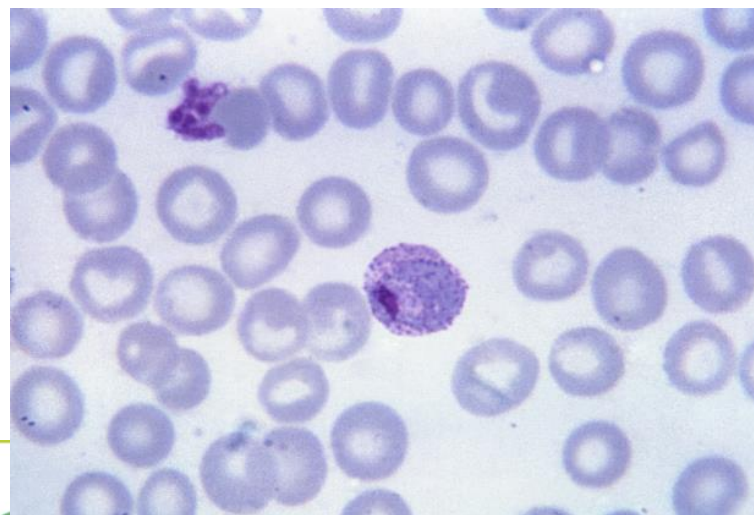
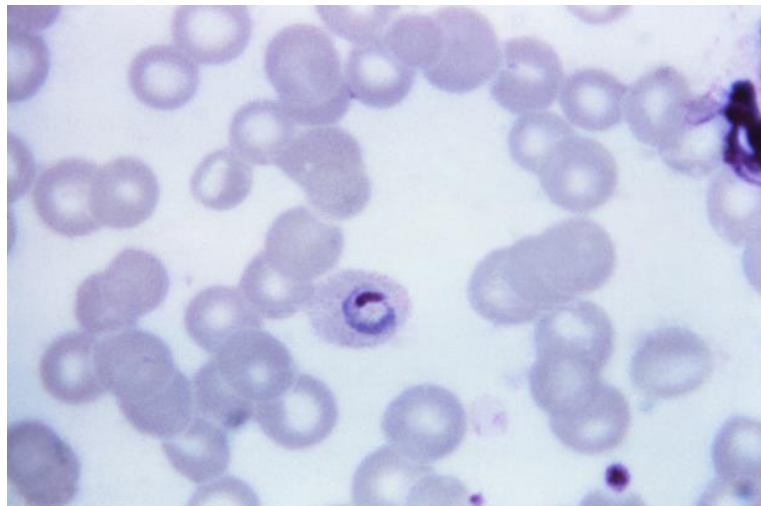
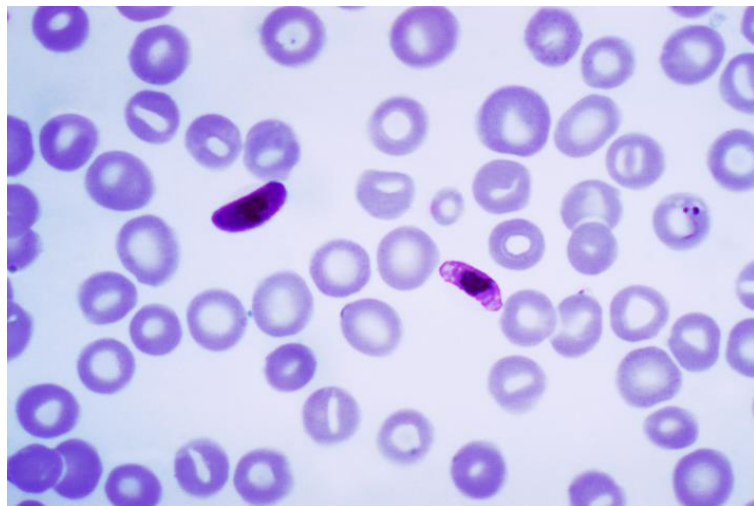
Malaria in pregnancy

- LBW
- High infant mortality
- Foetal distress
- Premature labour and stillbirth
- ↑ frequency more severe malaria in mother
- 5% congenital malaria

Diagnosis

- Thick and thin films
- Rapid diagnostic tests

Thick and thin films



Rapid diagnostic tests

- PfHRP2
 - Can be quantitative in serum for estimation sequestered biomass
- Pan-malaria species specific LDH
- Aldolase ag in fingerprick

Prevention

- Vector control
 - Pyrethroid treated mosquito nets (some resistant mosquitoes)
 - Indoor insecticide spray
- Chemoprevention and chemoprophylaxis
 - Never 100%
- Vaccination
 - RTS,S subunit antiparasite protein

Chemoprophylaxis

- Atovaquone-proguanil (once daily)
 - Inhibitor parasite mitochondrial fx, pyrimidine biosynthesis + DHFRi
 - Renally cleared, pregnancy cat. B2
 - SE's GI upset, allergy, pancytopenia, hepatitis
- Doxycycline (once daily)
- Mefloquine (once weekly)
 - may form toxic complexes with free haem that damage membranes and interact with other plasmodial components
 - Pregnancy B3
 - SE's GI upset, neuropsych, prolonged QT, interaction with quinine

Treatment

- Severe malaria – parenteral therapy
 - IV artesunate
 - Mechanism not fully understood, ?inhibit DNA replication and transmission
 - Well tolerated, cardiotoxicity at high doses, drug fever, BM suppression, delayed haemolysis
 - Superior to quinine
 - IV quinine
 - Many SE's: rash, fever, hepatitis, hypoglycaemia, haemolysis in G6PD defic., visual effects

Treatment

- Uncomplicated malaria
 - Artemether-lumefantrine
 - Inhibits conversion haem – haemazoin + impairs nucleic acid and protein synthesis
 - Pregnancy category D
 - SE's reported often similar to malaria symptoms
 - Atovaquone-proguanil
 - Quinine + doxycycline or clindamycin

Supportive management

- Early haemofiltration/HD
- Regular BSL monitoring \pm dextrose infusion
- Monitor parasite count and hct Q6-12H, transfusion support
- Careful fluid balance
- Treat co-infections
- Combination therapy as soon as possible

References

- Who.int
- CDC
- ECDC
- QH communicable disease control guidelines

Thank you