It all starts with one little bite.....
Outline

• Insect borne disease and travel
  – Preventing insect bites
  – Overview of epidemiology, burden of disease and prevention
    • Dengue fever
    • Chikungunya
    • Japanese encephalitis
    • Yellow Fever
    • Malaria (separate presentation)
WORLD'S DEADLIEST ANIMALS
NUMBER OF PEOPLE KILLED BY ANIMALS PER YEAR

MOSQUITO
725,000

HUMAN
475,000

SNAKE

DOG (Rabies)

TSWESEFLY (Sporing Silwood)

ASSASSIN Bug (Roga Disease)

FRESHWATER SNAILS

ASCARIS ROUND WORM

TAPE WORM

CROCODILE

HIPPOPOTAMUS

LION

ELEPHANT

WOLF

SHARK

10

10

100

500

1K

2.5K

10K

25K

50K

SOURCES: WHO, crocodile-attack.net; Kasturiratne et al. [doi.org/10.1371/journal.pmed.0050218]; FAO [webcitation.org/6Dgp58sV0j]; Linnell et al. [webcitation.org/4ORl70B0U]; Packer et al. [doi.org/10.1638%2F0436497a1]; Alessandro De Maddalena. All calculations have wide error margins.
A few definitions..

• “Insect borne” disease
  - Any disease transmitted by an insect
    • Protozoa
    • Rickettsia
    • Viruses

• “Arbovirus”
  - **Arthropod borne virus**
  - Any virus transmitted by an insect (mosquito, tick, flea..)
    • Dengue fever virus
    • Chikunkunya
    • Zika virus
    • Ross River virus
    • West Nile virus
    • Japanese encephalitis virus

• “Flavivirus”
  - Viruses that belong to the family Flaviviridae
  - Most are insect borne
  - Includes
    • Dengue fever virus
    • Japanese encephalitis virus
    • Yellow fever virus
    • Zika virus
    • Tick borne encephalitis
    • West Nile virus
  - “Flavus” = Yellow
  - Responsible for spectrum of disease
Avoiding Insect borne disease

- **Behavioural**: Personal Protection Measures
- **Immuno-prophylaxis**
  - Japanese encephalitis
  - Yellow Fever
- **Chemo-prophylaxis**
  - Malaria
Scenario

• You see a family *(Mum, Dad, 11 year, 5 year and 18m old)* spending 3 weeks in rural forested areas of Laos where they will be at potential risk of both dengue fever and malaria.

• What advice are you going to give them regarding avoiding mosquito bites?
Avoiding Mosquito Bites: Behavioural

• How?
  – Avoid outliers
  – Use repellents
  – Use insecticide impregnated clothing and nets
  – Cover up with clothing
    • Light coloured
  – Minimise use of perfumes/soaps/body lotions
  – Avoid outdoor activities at peak biting times
  – Insect proof accommodation
  – Sleep under a bed net
  – Remove/reduce breeding sites
Insect Repellents

• “A chemical volatile substance that induces arthropods to move in the opposite direction”
  – DEET (N,N-Diethyl-3-Methylbenzamide)
  – Picaridin
  – Oil of Lemon Eucalyptus
  – Others
    • IR 3535
    • Other plant derived products
Insect Repellents: DEET

- Most studied
  - >50 years use
- Good safety profile
  - Children
  - Pregnant women
- **Rare** toxic reactions
  - Dermatitis
  - Allergic reaction
  - Neurologic side effects
  - Cardiovascular side effects
  - Encephalopathy in children (after inappropriate use)
- Can dissolve some synthetic materials

- Effective against
  - Mosquitoes
    - *Anopheles spp*
    - *Aedes spp*
    - *Culex spp*
  - Ticks
    - *Ixodes*

- Concentration
  - 20-25% may be minimum effective concentration
  - Length of effectiveness influenced by
    - Concentration
    - Carrier molecules
    - Sweating/swimming
  - Effect appears to plateau around 40-50% concentration


CDC Yellow Book
Insect Repellents: Picaridin/Icaridin

- Used since 1990s
  - Most studies using 20% concentration
  - 20% Picaridin non inferior to 20% DEET
- Does not damage plastics
- No recorded toxic reactions
  - Less likely to irritate skin

Reference: Lupi et al Trav Med Inf Dis 2013;11:374-411
Insect Repellents: Oil of Lemon Eucalyptus

• Recently approved by USA FDA and WHO
• Plant oil
• Evidence is as effective as DEET at 20% concentration
• “30% concentrations give ≈ 6 hrs cover”
Other Repellents

- **✓ IR 3535**
  - Evidence as effective as DEET
- **But** not available in NZ

- **Citronella**
  - 1-2 hour protection max
- **NEEM**
  - Conflicting evidence
  - Concerns re toxicity

- **Other Essential Oils**
  - Thyme, Peppermint, Clove
    - Conflicting & limited efficacy
    - Volatile
    - Skin irritation

_Fradin et al. NEJM 2002;347(1):13-8
Lupi et al Trav Med Inf Dis 2013;11:374-411_
<table>
<thead>
<tr>
<th>PRODUCTS</th>
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<td>★</td>
<td>Oils of citronella, lemon grass, neem, eucalyptus, lavender</td>
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</table>
Lacking evidence

- Vitamin B
- Garlic
- Insect repellent bands
- Insect repellent discs/patches
- Coils
- Ultrasonic emitting devices
Insect Repellents: Practical Advice

• Use either DEET 20-40% or Picaridin 20-25%
  – Includes children and pregnant women
• Apply and re-apply according to manufacturer's recommendations
• Reapply more frequently if
  – Sweating
  – Swimming/washing
• Concomitant application of sunscreen may reduce efficacy of sunscreen
  – Apply sunscreen first, wait 30 minutes, then apply repellent
• Combination products may lead to over-application of repellent
  – Most authorities now advise using separate products
Insecticides: Permethrin

- Kills insect on contact
- Also act as repellent
- Permethrin most widely used and studied
- Insecticide impregnated bed nets have had a huge effect as part of the “Roll Back Malaria” project
  - Should be re-impregnated 6 monthly
- Can impregnate clothing, sleeping sheets/bag liners
  - Lasts at least 4-6 cold washes
  - Commercially pre-treated clothing may last 70 washes
Dengue

- Estimated about 50% of world’s population now living in endemic area*
  - Much of it in South/SEAsia*
- 30 fold increase in dengue cases in 50 yrs*
  - Why?*
    - Climatic changes
    - International travel
    - Unprecedented urbanisation
      - Slums, standing water, poor infrastructure, poor vector control

*Dr Annelies Wilder-Smith. Plenary session: Dengue 10th Asia Pacific Travel; Health Conference Ho Chi Min May 2014
Dengue in Travellers

- Risk to travellers determined by
  - Destination
  - Length of travel
  - Intensity of transmission

- High risk destinations
  - Geosentinel data*
    - South & S East Asia
    - Latin America
    - Caribbean
  - NZ data
    - 1997-2009 74.2% dengue acquired in the Pacific Islands**

Figure 8. Dengue fever notifications by year, 1997–2013

Dengue fever virus

- 4 serotypes DENV1-4
- *Aedes* mosquito
  - *A. aegypti*
  - *A. albopictus*
  - Day biting and urban dwelling
  - Infection with one
    - gives lifelong immunity to that type and short term immunity to all 4
    - May be a risk for more severe disease with future infections
- Incubation period
  - 3-14 days
Dengue fever virus

- Dengue fever
  - ≈ 75% asymptomatic
  - Fever, retro-orbital headache, myalgia, fatigue, rash and minor haemorrhagic manifestations

- Severe dengue
  - ≈ 5% develop severe haemorrhagic manifestations and/or fluid leakage
  - Typically occurs around day 4-6 of illness as fever defervesces
Current outbreaks:

http://www.healthmap.org/dengue/en

Map Layers:
- HealthMap Reports: Recent reports of local or imported dengue cases from official, newspaper, and other media sources.
- Source:
  - Country Level
  - Local Level
- Global Consensus Map (2013): Risk areas determined by consensus between sources including national surveillance systems, published literature, questionnaires, and formal and informal news reports.
- CDC Yellow Book Map (2012)
- CDC Yellow Book Map (2010)
- Endemic risk areas determined using data from Ministries of Health, International health organizations, journals, and knowledgeable experts.
- Source:
  - Endemic Area
Dengue fever: Prevention

• Behavioural: Avoiding mosquito bites
  – Day biting, urban dwelling
  – Stay indoors
    • A/C, screened
  – Cover up
  – Insect repellents
  – Permethrin impregnated clothing

• Currently no vaccine or chemoprophylaxis available
Dengue vaccines

• Promising control strategy
• Many being trialled but none yet licenced
  – Most advanced
    • Live chimeric based on YF vaccine
    • 3 doses over 6m
    • Most recent Phase 3 trial
      – 56% efficacy*
      – Limited use in travellers
  – *

Zika Virus

- Flavivirus closely related to Dengue fever virus
- Recent concerns regarding links to neurological adverse events especially microcephaly in babies born to women infected while pregnant
Zika Virus (ZIKV)-History

- **1947**: First identified in Africa in macaque monkey from Zika Forest
- **1954**: First human case recorded (Nigeria)
- **1954-2007**: Sporadic cases/local outbreaks in Africa and Asia
  - Largely benign disease
- **2007**: Outbreak in Yap (Micronesia)
  - Although 73% of population infected, largely mild disease
- **2012-2014**: Spread across Pacific: French Polynesia, New Caledonia, Cook Islands, Vanuatu, Solomon Islands, Easter Island..
  - In French Polynesia outbreak, first reports of spike in Guillain-Barre Syndrome
- **2015/16**: South & Central America and Caribbean
  - Reports of spike in microcephaly and other foetal/neonatal abnormalities
  - Reports of spike in Guillain-Barre Syndrome & other neurological sequelae
- **Feb 1st 2016**: WHO declares PHEIC (Public Health Emergency of International Concern)
Countries and territories showing historical time-line of Zika virus spread (1947 - 2016)

http://www.who.int/emergencies/zika-virus/zika_timeline.pdf?ua=1
Zika Virus (ZIKV)-History

• Why is the clinical picture changing?
  – Is the virus evolving?
  – Are the populations now being infected reacting differently?
  – Are there environmental or other co-factors?
  – Have the more severe outcomes always been there, but not noted?
How the Zika Virus Enters the Human Population

The virus originates with nonhuman primates in tropical rainforests but can infect humans. Warm, urban environments with standing pools of water attract mosquitoes, and can lead to the virus's spread.

**SYLVATIC CYCLE**
- Chimpanzees
- Monkeys
- Baboons
- Mosquitoes (Ae. africanus, Ae. lusitaniae)

**URBAN CYCLE**
- Mosquitoes (Ae. aegypti, Ae. albopictus)
- Human Population

It appears that Zika can be transmitted through sexual intercourse, blood transfusion, and in utero.

Sources: CDC, PLOS, Reuters  Credits: David Foster, Laurie Gussert, Doug Halsey, Gabriella Meltes
ZIKV-Modes of Transmission*

• **Bite from infected mosquito**
• **Sexual contact via infected semen** (Case reports of ZIKV RNA isolation and infection of sexual partners)
• **Transplacental**
• **Perinatal, breast feeding, saliva** (ZIKV RNA detected but absolute proof of infection lacking)
• **Blood transfusions, haemodialysis, organ transplantation** (Based on experience with other flaviviruses)
ZIKV-Clinical Characteristics

• Usually mild, self limiting
• Based on Yap outbreak
  – ≈ 80% asymptomatic
• Typically
  – Fever
  – Headache
  – Rash
  – Arthralgia & Myalgia
  – Conjunctivitis
ZIKV-Diagnosis

• Nil pathognomonic clinical, biochemical or radiological features, so reliant on laboratory confirmation

• BUT
  – Reverse-transcriptase PCR (RT-PCR) can detect ZIKV in blood during the first 1 week of illness and in urine up to 4 weeks. Has been used to detect ZIKV in amniotic fluid, but clinical significance not currently known.
  – Serology is less reliable due to potential cross reaction with antibodies against other similar viruses (including dengue). This makes it difficult to differentiate Zika virus infection using antibody testing alone.

• NZ MOH Guidelines: “For this reason, Zika virus serology is not recommended at this time as part of the algorithm for assessing pregnant women with a history of travel to areas with active Zika virus transmission. If Zika serology is being requested a discussion with a microbiologist needs to occur prior to testing.”
ZIKV & Guillain-Barre Syndrome

• French Polynesia Case Control study
  – Rate of GB Syndrome
    • 0.24 per 1000 ZIKV infections
  – Comparison
    • Background rate: 1 to 4 per 100,000 person years
    • Post Campylobacter: 0.25-0.65 per 1000 infections
  – In current outbreaks Brazil, El Salvador, Colombia & Venezuela have all reported increase in number of GB cases
    • But could be due to enhanced surveillance/reporting
ZIKV and Congenital Zika Syndrome

- Assumed transplacental and sexual transmission of ZIKV have been reported
- Congenital ZIKV infection associated with microcephaly & other anomalies
- Oct 2015: Brazil reported unusual increase in number of cases of neonates with microcephaly in NE Brazil
  - 20 fold increase on previous reported cases
  - Coincided with ZIKV epidemic
- Nov 2015: French Polynesia also reported unusual increase in foetal and neonatal CNS malformations
ZIKV-Infected countries

- European CDC

- USA CDC
European CDC


<table>
<thead>
<tr>
<th>Countries</th>
<th>Last case since 3 months</th>
</tr>
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<tbody>
<tr>
<td>American Samoa</td>
<td>Widespread transmission</td>
</tr>
<tr>
<td>Anguilla</td>
<td>Sporadic transmission</td>
</tr>
<tr>
<td>Argentina</td>
<td>Widespread transmission</td>
</tr>
<tr>
<td>Aruba</td>
<td>Widespread transmission</td>
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<tr>
<td>Barbados</td>
<td>Widespread transmission</td>
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<tr>
<td>Belize</td>
<td>Widespread transmission</td>
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<tr>
<td>Bolivia</td>
<td>Widespread transmission</td>
</tr>
<tr>
<td>Bonaire</td>
<td>Sporadic transmission</td>
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<tr>
<td>Brazil</td>
<td>Widespread transmission</td>
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<tr>
<td>Cape Verde</td>
<td>Widespread transmission</td>
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<tr>
<td>Colombia</td>
<td>Widespread transmission</td>
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<tr>
<td>Costa Rica</td>
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<td>Curacao</td>
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<tr>
<td>Dominica</td>
<td>Widespread transmission</td>
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<tr>
<td>Dominican Republic</td>
<td>Widespread transmission</td>
</tr>
<tr>
<td>Ecuador</td>
<td>Widespread transmission</td>
</tr>
</tbody>
</table>
Zika virus

Zika virus infection is a mild febrile viral illness transmitted by mosquitoes. The mosquitoes that are able to transmit Zika virus are not normally found in New Zealand.

This information is intended for health professionals. For general information and advice about Zika virus, see Zika virus in Your Health.

The following information on Zika virus infection is provided as it is an emerging disease.

On this page:
- Latest updates
- About Zika virus
- Zika virus and pregnancy
- Sexual transmission of Zika virus
- Symptoms of Zika virus infection
- Further information
- Laboratory testing

Downloads
- Interim guidance information for LMCs, GPs and other health professionals dealing with Zika virus in pregnancy (4 July 2016) (docx, 212 KB)
- Interim guidance information for LMCs, GPs and other health professionals dealing with Zika virus in pregnancy (4 July 2016) (pdf, 443 KB)

Related websites
- Zika virus infection complicated by Guillain-Barre syndrome: Eurosurveillance
- Zika virus outside Africa: Centers for Disease Control and Prevention
- Fact sheet for health professionals: European Centre for Disease Prevention and Control
ZIKV-Information/Guidelines

• NZ Ministry of Health

• Australian Department of Health

• USA CDC

• European CDC

• WHO
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<tr>
<th></th>
<th>Female Currently Pregnant</th>
<th>Female Not pregnant Recently travelled Zika area</th>
<th>Male Recently travelled Zika area Partner pregnant</th>
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<td>Abstain/Condoms 8 weeks</td>
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<td>Abstain/Condoms for 6 months</td>
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<td>Abstain/Condoms 4 weeks</td>
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<td>USA CDC</td>
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<td>Abstain/Condoms No time frame “Discuss with Dr”</td>
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<td>Abstain/Condoms duration of pregnancy</td>
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Zika: Prevention

• Behavioural: Avoiding mosquito bites
  – Day biting, urban dwelling
  – Stay indoors
    • A/C, screened
  – Cover up
  – Insect repellents
  – Permethrin impregnated clothing

• Currently no vaccine or chemoprophylaxis available
Chikungunya*

- Alpha virus
- Discovered in 1950s
  - Africa
  - Asia
- Re-emerged in 2004
  - Indian Ocean
  - S E Asia
  - Caribbean
  - Pacific
- 1 confirmed case in NZ in 2013
  - Likely under diagnosed
Chikungunya*

- *Aedes* mosquito
  - *A aegypti*
  - *A albopictus*
  - Day biting and urban dwelling
- Incubation period
  - 2-12 days
- Up to 30% may be asymptomatic
- Typical symptoms
  - Fever, joint pain and stiffness, +/- rash, fatigue, myalgia, nausea/vomiting
  - Complications are rare, except some evidence ongoing arthralgia
Countries and territories where chikungunya cases have been reported*  
(as of July 1, 2014)

*Does not include countries or territories where only imported cases have been documented. This map is updated weekly if there are new countries or territories that report local chikungunya virus transmission.

http://www.cdc.gov/chikungunya/geo/index.html
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<tr>
<th>AFRICA</th>
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Chikungunya: Prevention

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  – Permethrin impregnated clothing

• Currently no vaccine or chemoprophylaxis available
Tableau 1 – Tableaux cliniques comparatifs Dengue, Chikungunya et Zika*

<table>
<thead>
<tr>
<th>Symptômes</th>
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<td>Hémorragies</td>
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* Adapté de Halstead SB et al. Am J Trop Med Hyg, 1 et de la plaquette du Yap State Department of Health Services 2

http://www.tahiti-infos.com/L-epidemie-de-zika-en-Polynesie-va-permettre-de-mieux-connaitre-ce-virus_a90116.html
Japanese encephalitis

• Flavivirus
• Vector
  – *Culex spp*
  – Night biting, rural
• Distribution: South/South east Asia and Asia/Pacific rim
• 5-15 day incubation period
• Fever, headache and general malaise
• Encephalitis causing hemiparesis, acute flaccid paralysis, convulsions, coma and death (or permanent neurological sequelae)
Japanese encephalitis: distribution
Japanese encephalitis: Life Cycle

Mosquito bites a bird & picks up the JE virus

Infected mosquito bites animals & passes the JE virus

Virus multiplies inside body cells

Infected mosquito bites a bird & passes on the virus

Mosquito bites infected animal & pick up the JE virus

Infected mosquito bites humans & non-host animals who are unable to pass on the virus
Japanese encephalitis: the disease

- Likely the bulk of infection (99%) asymptomatic or mild
- In endemic countries is predominantly a disease of children
  - Neurological sequelae
- Of those that present with acute disease, it is often quoted that approximately 30% die, 30% survive and 30% left with permanent neurological disease*
Japanese encephalitis: Risk to travellers

• **CDC 1993***
  – *CDC Recommendations of Advisory Committee on Immunization Practices (ACIP) 1993*
  • USA 1981-1993 11 cases (ie approx. 1 per year in USA). During same period 13 cases in non-USA travellers
  • Crude risk estimate of **<1 per million** travellers to endemic areas per year
  • Risk of rural travellers assumed to be same as that to local residents and crude estimate of 1 per 5000 per month of stay or 1 per 20,000 per week of stay.

• **UK and Swiss Travellers 2009***
  • 1978-2008 40 published case reports in travellers
  • Likely under-reported and would not capture disease occurring during travel
  • 99% travelled to endemic countries without vaccination
  • Of 17 million European travellers going to endemic countries during that time, 42% (7.1 million) travelled during transmission season
  • Risk incidence calculated as **1.3 cases per 7.1 million** “at risk” European travellers
Japanese encephalitis: Risk to travellers

• Reported Cases 1992-2008*
  • Anecdotal reporting of 21 cases
  • Suggesting increase in absolute numbers
    (as travel to endemic areas increases)
  – Half were short-term visitors
  – Several contracted the disease outside the “official” transmission seasons
• 13 fatal or permanent neurological sequelae
• Certainly an under-estimate of cases
• For Swedish travellers to Thailand calculated risk one 1 per 400,000 per trip
  (regardless of length of type of stay)
JE: Prevention

- Behavioural: Avoiding mosquito bites
  - Night biting, rural
  - Sleep in A/C or screened accommodation
  - Cover up
  - Insect repellents
  - Permethrin impregnated clothing

- Immunoprophylaxis: Vaccination
Yellow Fever

• Flavivirus
• Vector
  – *A aegypti (urban)*
  – *Haemagogus spp.*
• Incubation
  – 3-6 days
• Many infections likely asymptomatic
• The disease
  – Acute phase: 3-4 days
    • Fever
    • General malaise/myalgia/headache/anorexia
  – About 15% deteriorate in following 24 hrs:
    • Fever reappears
    • Jaundice
    • Abdominal pain
    • Bleeding (mouth, eyes, GI tract)
    • Deteriorating renal function.
    • ≈ 50% CFR
Yellow Fever: Prevention

• Behavioural: Avoiding mosquito bites
  – Day biting
    • Sylvatic/Forest
    • Intermediate
    • Urban
  – Cover up
  – Insect repellents
  – Permethrin impregnated clothing

• Immunoprophylaxis: Vaccination
Yellow Fever Vaccination: Indications

• Recommended
  – Personal Protection

• Required
  – Public Health measure