ARBOVIRAL RISKS TO BLOOD SAFETY IN AUSTRALIA

Clive Seed

Australian Red Cross Blood Service

ISBT TTD-WP meeting 26 June, 2015

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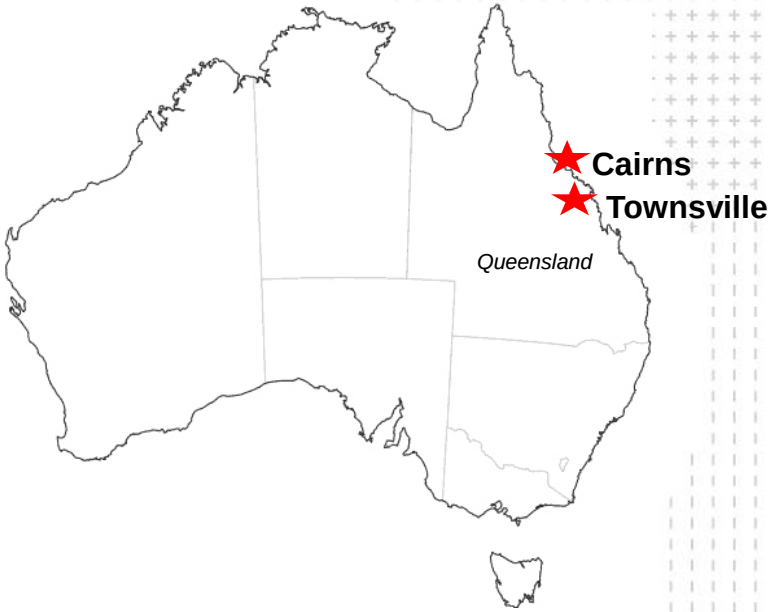
Transfusion significant arboviral threats

- **Dengue - epidemic**
- **Ross River virus - endemic/epidemic**
- West Nile virus Kunjin strain – endemic, low virulence/transmission
- ? Other endemic Australian arboviruses (Barmah Forest virus, Murray Valley encephalitis virus etc) - endemic/epidemic, low virulence/transmission
- ? chikingunya virus - occasional imported cases; vector present
- ? Zika virus - occasional imported cases; vector present

Dengue in Australia

- Seasonal outbreaks in NE Australia
  - Vary from <50 to >1,000 cases
- All four DENV types can occur
  - Occasionally together (last in 2009)

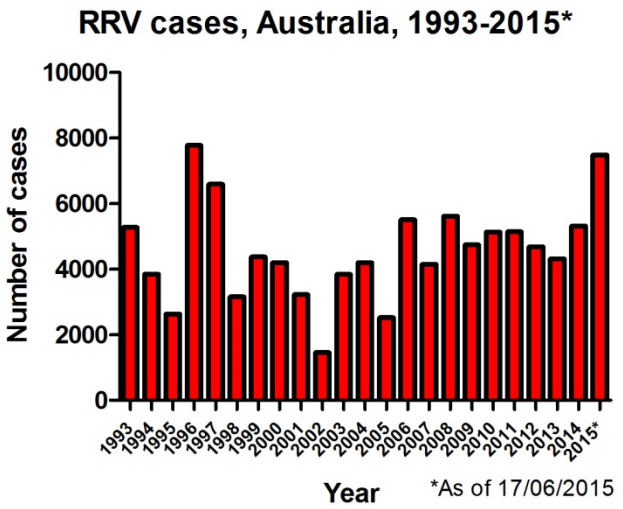


- Rapid public health response -> Very effective in minimising impact
- Transfusion risk
  - Implement supplementary donor questioning
    - Restriction to plasma for fractionation only for residence in or travel to outbreak area
  - Restrictions lifted 28 days after last case onset date

Faddy HM, Seed CR, Fryk JJ, et al.: Implications of dengue outbreaks for blood supply, Australia. Emerg Infect Dis. 2013;19: p. 787-789.

Ross River virus (RRV)

- Alphavirus (*Togaviridae*)
  - Same antigenic family as CHIKV
- Most common arboviral disease in Australia
  - ~5,000 cases notified annually



- Endemic throughout coastal regions of northern and central Australia; epidemic throughout rest Australia
- Causes non-fatal epidemic polyarthritis or RRV disease
  - Asymptomatic/mild infections in 50-75% of cases
- Incubation period 2-21 days – average 7-9 days

RRV - transfusion transmission risk

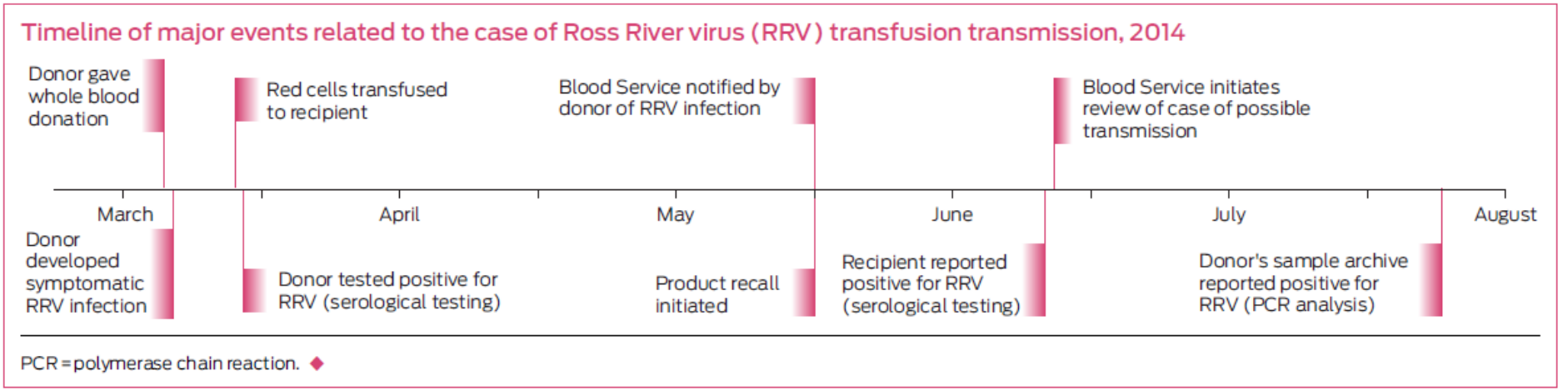
- Virus first isolated in early 1970's – TT-RRV suggested in mid 1990's
- Asymptomatic viraemia (mouse model) - typically 5, but up to 9 days[1]
- Potential TT-RRV risk estimated:
  - For 2004 outbreak in Cairns -> ~1 in 13,000 [1]
  - After increased rainfall -> ~1 in 7,333 [2]

  } Similar to DENV TT-risk for contiguous outbreak

- Maintain close watching brief

1. **Shang G, Seed CR, Gahan ME, et al.: Duration of Ross River viraemia in a mouse model-implications for transfusion transmission. Vox Sang. 2012;102: p. 185-192.**
2. **Faddy H, Dunford M, Seed C, et al.: Seroprevalence of Antibodies to Ross River and Barmah Forest Viruses: Possible Implications for Blood Transfusion Safety After Extreme Weather Events. Ecohealth 2014. (Epub ahead of print).**

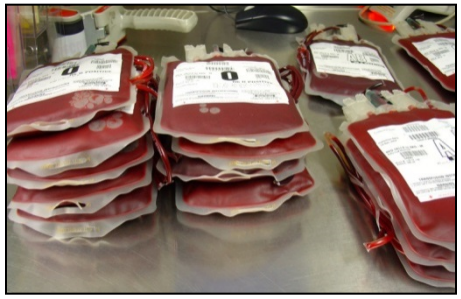
First probable case of TT-RRV



Hoad VC, Speers DJ, Keller AJ, Seed CR et al.: First reported case of transfusion-transmitted Ross River virus infection. Med J Aust. 2015;202: p. 267-270.

- RBC recipient - symptoms consistent with RRV
  - IgM detected
  - Haemagglutination inhibition (HI) positive

Imputability and risk assessment



- Imputability - probable case
  - No molecular matching BUT RNA positive donation transfused to recipient who later developed symptoms consistent with RRV
  - No other RRV notifications in recipient's public health unit
  - Recipient had no recollection of mosquito bites & spent majority time indoors

- EREEID* risk framework
  - Escalate from 'yellow' to 'red' status
  - Notify regulator (TGA) & conduct risk assessment

** Emerging, Re-emerging & Emerged Infectious Disease*

Risk analysis

- Risk Analysis (Western Australia [residence of case], Jan – Mar 2014)
  - Blood Service model: 1 in 26,177 (7,729 to 103,628)
  - EUFRAT: 1 in 14,943 (5,094 to 48,593)

  [predicted issue of 1 (0.3-2.9) infectious donation (WA, Jan-Mar 2014), or 11 (4-39) annually, Australia-wide]

- <u>Key risk considerations</u>
  - Transmission risk from transfusion very minor when compared to ~5,000 vectorial notifications annually
  - High proportion of asymptomatic infections
  - Clinical illness generally mild and self-limiting
    - No mortality
  - Scope and continuity of RRV outbreaks

Risk management options

1. Enhanced donor education/post-donation illness reporting

Recommended

2. Geographically based fresh component restrictions during high transmission periods (as per the current strategy for local dengue outbreaks)

Not recommended – donor/product sufficiency concern

3. RRV donor testing

No licensed blood screening tests available

4. Pathogen reduction for clinical plasma and platelets (assuming future licensing of PRT)

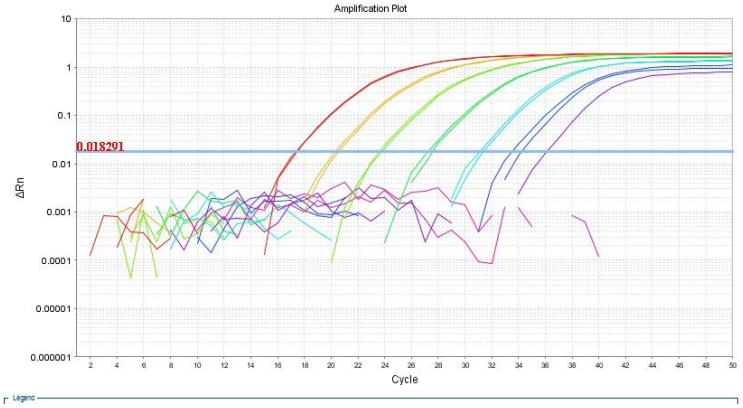
Not currently available

Research - RRV

- Risk is proportional to rate of RRV viraemia among donors – unknown

AIM: Determine rate of RRV RNA carriage among Australian donors

- Samples (n=7,500) from high-risk areas, during higher risk seasons
- RT-PCR (based on pathology laboratory methods)
  - MS2 phage (extraction and amplification control)
  - QIAsymphony (automated RNA extraction and RT-PCR plate set-up)
  - TaqMan chemistry; StepOnePlus Real-Time PCR System



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Conclusions

- Australia has a number of arboviral threats to blood safety
- Of these dengue, WNV proven TT and now strong evidence for RRV
- Dengue TT risk effectively minimised by rigorous public health response and activating supplementary donor measures during local outbreaks
- RRV TT recently confirmed
  - Very low risk compared to vectorial transmission given 5,000+cases per year
  - Contrasting dengue - lacks severe clinical consequences for recipients
  - Scope and size of outbreaks precludes geographical deferral strategy
- RRV risk management – enhanced post-donation symptom reporting messaging (under development)

Acknowledgements

Australian Red Cross Blood Service

- Dr Veronica Hoad
- Dr Anthony Keller
- Dr Helen Faddy

Australian governments fund the Australian Red Cross Blood Service to provide blood, blood products and services to the Australian community