

A photograph of a golf course. In the foreground, a dark blue golf club head is on the left, and a white golf ball on a red tee is on the right. The background is a blurred green field with trees and a building in the distance.

# Golf, anyone?

Victoria Madigan  
Infectious Diseases Registrar  
Maroondah & Angliss Hospitals  
Eastern Health

# Background

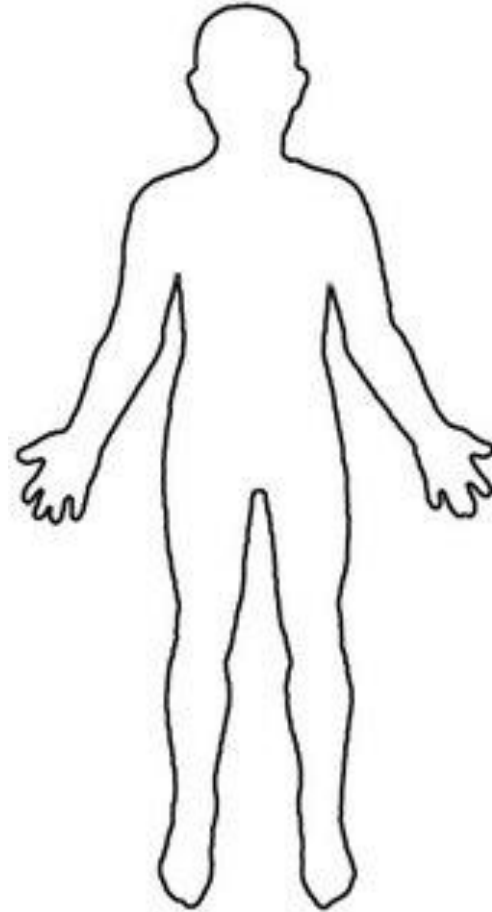
- 67yo man, born UK, migrated to Australia 24 years ago
- PHx:
  - Idiopathic cardiomyopathy
  - Atrial fibrillation
  - TURP (1999)
- Medications: warfarin, bisoprolol, perindopril
- Social Hx:
  - Married
  - Retired postal worker
  - Keen golfer, lives on a golf course in Cranbourne

# Presentation

- 5 days of fever, chills and rigors
- 3 days of headache – no meningism or focal neurological symptoms
- 2 days of jaundice

# Examination

- Looked unwell, clammy, **jaundiced**
- Alert, not confused
- HR 130, BP 134/103, **temp 38.4**
- No stigmata CLD, no metabolic flap
- No lymphadenopathy
- CVS & Resp: NAD, no murmurs
- Abdo: distended, soft & nontender
- No rash



# Initial Investigations

- FBE:
  - Hb 153
  - WCC 6.9 (lymph 0.80)
  - Platelets 55
- UEC:
  - Electrolytes normal
  - Creatinine: 126 (eGFR 50)
- CRP 317
- Blood cultures:
- Urine:
  - Microscopy & dipstick NAD
- LFTs:
  - Bilirubin: 125
  - ALP: 195
  - ALT: 203
  - GGT: 242
  - Albumin: 30 (total protein 59)
- INR 3.5 (warfarin)
- ECG: sinus tachycardia
- CXR: NAD
- US: fatty liver, nil else

# Initial Diagnosis and Management

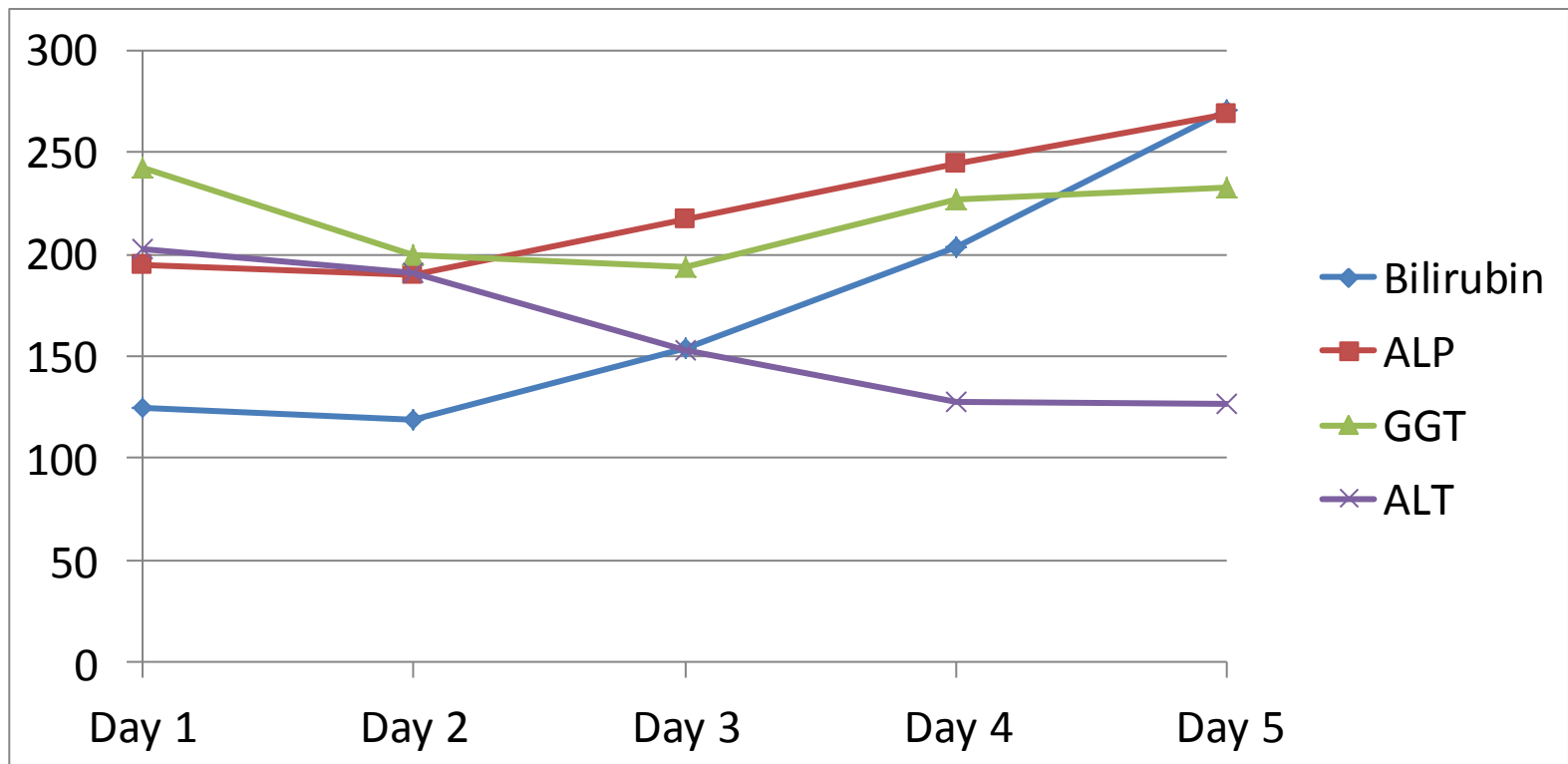
- Dx: ?viral hepatitis
- No antibiotics, supportive care

# Further investigations

- Serology
  - Hepatitis A IgM, Hepatitis B sAg, Hepatitis C antibody all **negative**
  - HIV serology **negative**
  - CMV IgG positive, IgM **negative**
  - EBV IgG & IgM (VCA) both **positive**
- Blood cultures (4 sets over 4 days)
  - All **negative**

# Progress: D2-5

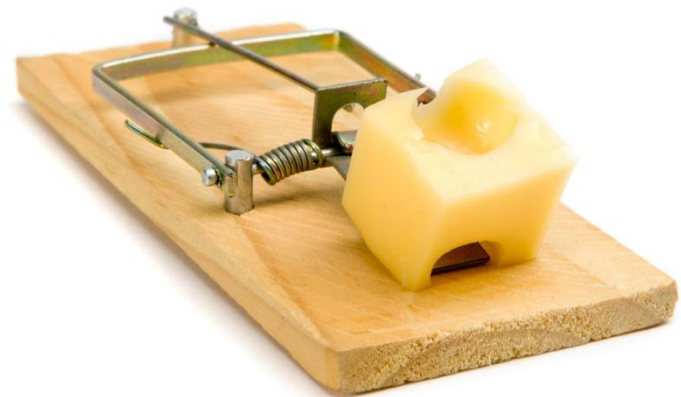
- Remained febrile, rigors, unwell
- Provisional Dx acute EBV - no antibiotics given
- LFTs continued to worsen



# D5 referred to Infectious Diseases...

Further history obtained:

- Recent trip to Yarrawonga
  - Played golf with friends
  - Arrived 3 days before onset of illness
  - Became unwell on last day of trip
- **Recent flooding in area**
- **Mouse plague, many traps**



# Infectious Diseases Opinion

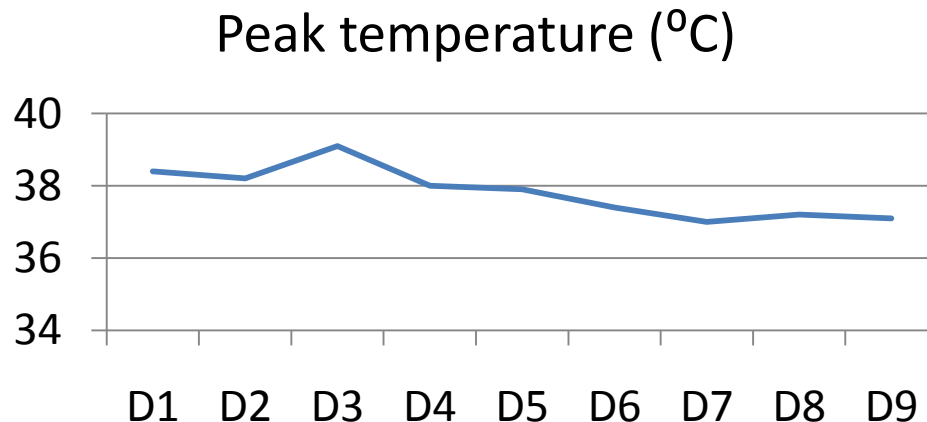
- Differential Diagnosis:
  - Biliary sepsis
  - Zoonosis
  - Viral hepatitis unlikely
- EBV IgM probable cross-reaction
- Piperacillin/tazobactam and doxycycline recommended
- Further investigations suggested...

# Further serology suggested

- Leptospirosis
- Rickettsia
- Q fever
- Ross River, Barmah Forest
- Flavivirus
- Legionella serology and urinary Ag
- EBV Nuclear Antigen IgG

# Progress: D6-9

- Medical Unit decided NOT to give antibiotics
- Began to improve from D6 of admission:
  - Afebrile
  - LFTs improving
- Discharged home D9...



## Progress: D10

- Leptospirosis serology reported positive (*Leptospira interrogans* IgM EIA)
- Medical Unit arranged patient readmission and commenced benzylpenicillin
- ID review:
  - Well and afebrile
  - Changed to oral doxycycline and discharged home

# Outcome

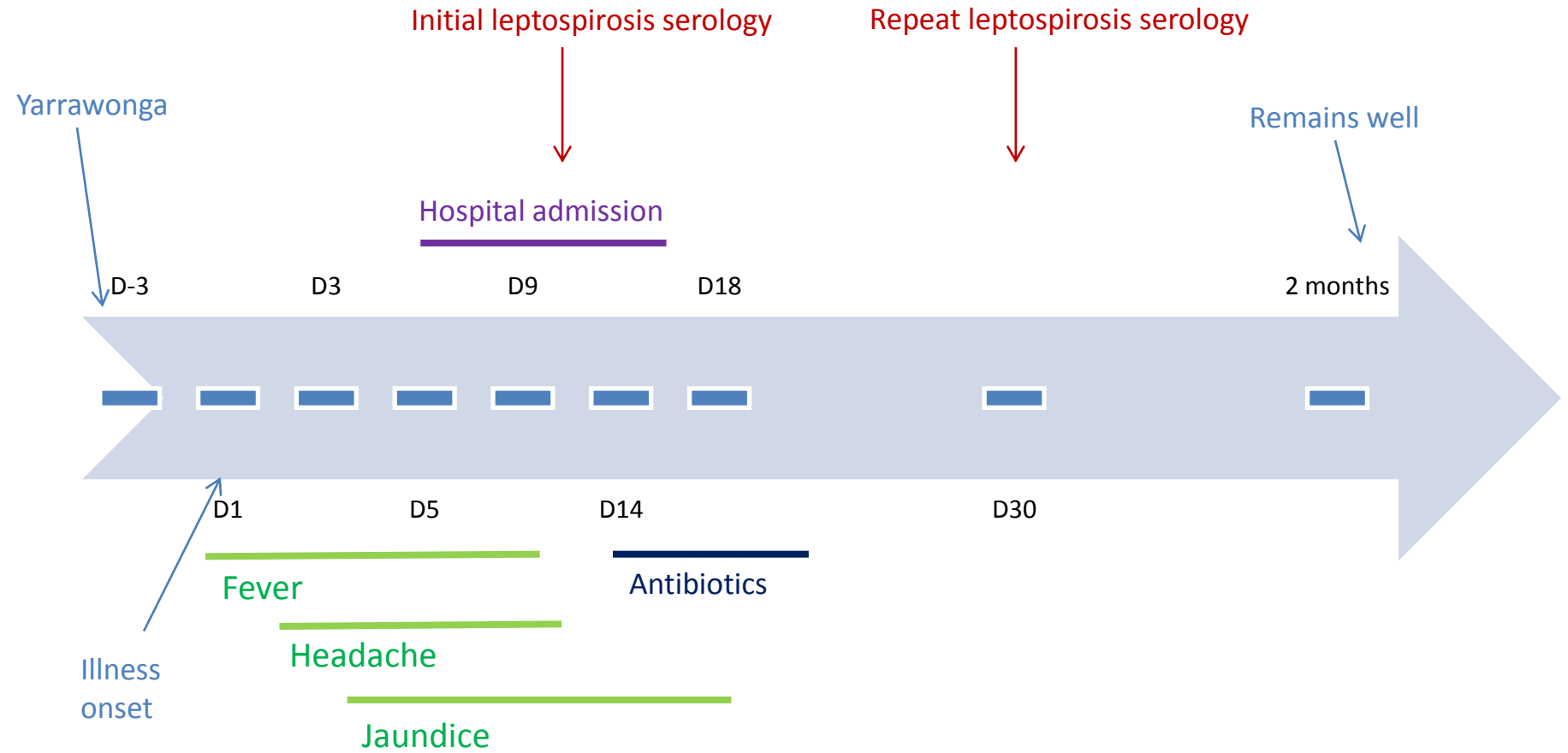
- Full clinical recovery
  - Repeat serology performed at day 30 after illness onset
  - LFTs returned to normal
  - Last contact 2 months after illness – well
  - About to head overseas on holiday

# Leptospirosis Serology

- *Leptospira interrogans* IgM (EIA) positive (day 11)
- Microscopic Agglutination Test:

Serovar	Day 11 Titre	Day 30 Titre
Australis	<50	<50
Canicola	50	50
Copenhageni	400	<50
Grippityphosa	<50	<50
Hardjo	800	200
<b>Arborea</b>	<b>200</b>	<b>3200</b>
Pomona	<50	<50
Tarassovi	<50	<50
Zanonii	<50	<50

# Timeline of events



# Summary

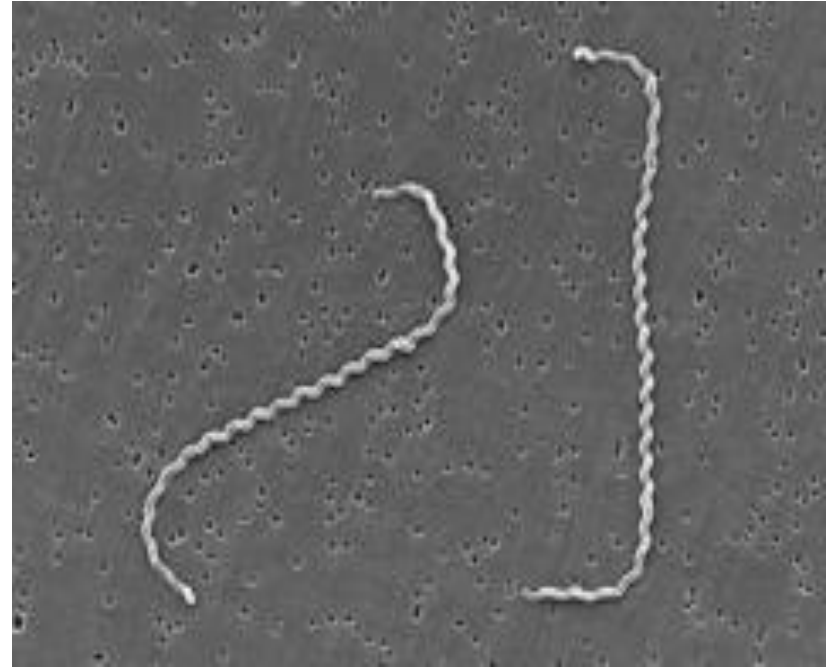
- 67yo man from metropolitan Melbourne with leptospirosis
- Likely acquired in Yarrawonga on golfing trip
- Recent flooding and mouse plague

# Outline

- Clinical features and management
- **Epidemiology**
- **Diagnosis**

# Leptospirosis

- Spirochete
- 20 species described
  - Pathogenic
    - e.g. L. interrogans*
  - Saprophytic
    - e.g. L. biflexa*
  - Indeterminate
- > 280 serovars
- Genotypic and serological classifications



# Clinical features

- Incubation period 2-26 days
- asymptomatic ↔ Weil's Syndrome
- Biphasic pattern
- Features:
  - Fever – 52-99%
  - Myalgia – 40-100%
  - Headache – 55-98%
  - Conjunctival suffusion - 28-99%
  - Jaundice – 0-95%
  - Cough – 20-57%
  - Diarrhoea – 11-53%
  - Rash <10%
  - Acute renal failure – 13-40%
- Certain serovars associated with more severe disease
  - Copenhageni
  - Ictohaemorrhagae

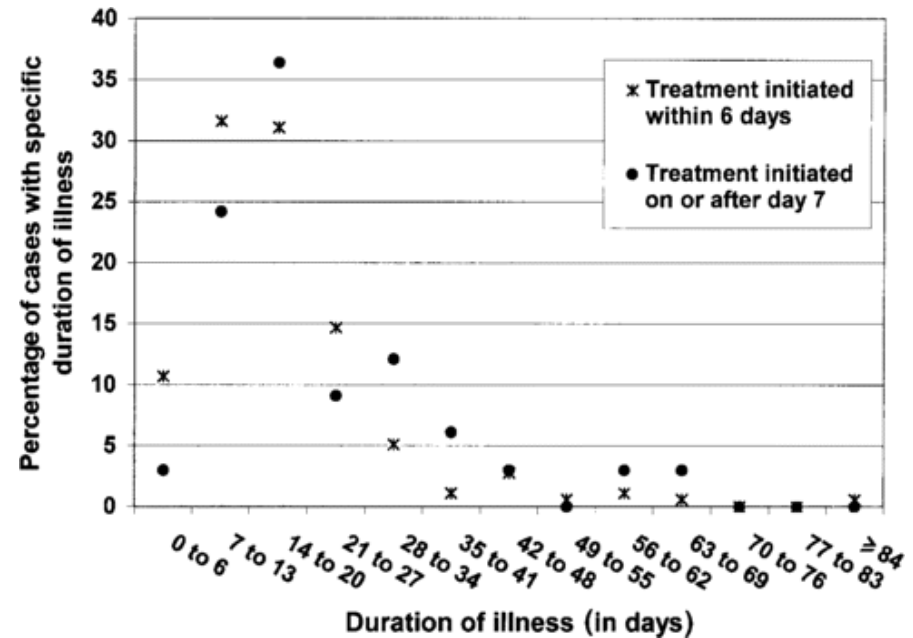


Lancet Inf Dis (2011) 11: 152

- Levett, P. Clin Micro Rev (2001), 14: 296
- Katz, AR. CID (2001) 33: 1834
- Slack, AT. Epidemiol. Infect (2006), 134: 1217

# Management

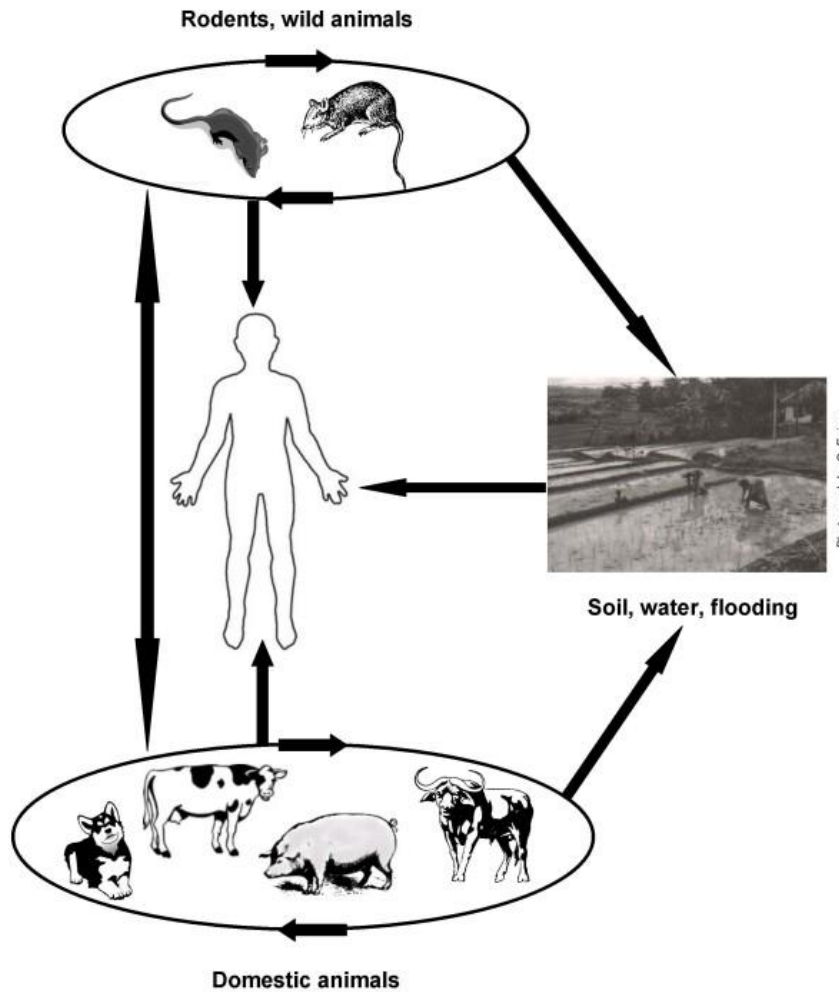
Duration of Illness vs Timing of Antibiotic Commencement (Katz, CID 2001)



- Mild cases - nil
- Severe infection:
  - IV penicillin
  - Doxycycline
  - Ceftriaxone
  - Quinolones
  - Azithromycin
- Earlier antibiotic treatment reduces severity and duration of illness

- Hartskeerl RA. (2011) Clin Micro Infect 17: 494  
- Katz, AR. CID (2001), 33: 1834  
- Suputtamongkol, Y. CID (2004), 39: 1417

# Transmission

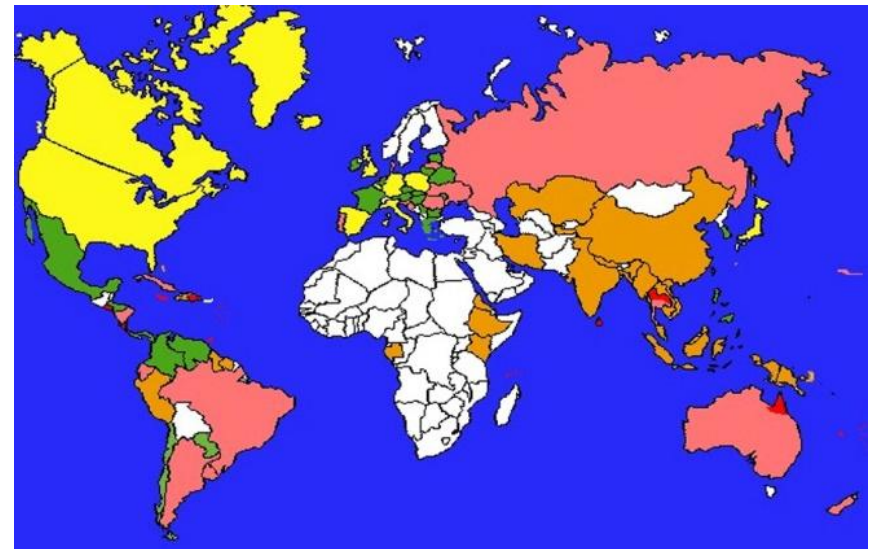


# Epidemiology

- Worldwide distribution with distinct epidemiological patterns:
  - Temperate regions: sporadic
  - Tropical regions: endemic
- Recent trends:
  - Increase in urbanized setting
  - Outbreaks due to major flooding events
  - Increase in recreational exposure
- Countries with high annual incidence (no./million):

– Seychelles:	432
– Trinidad & Tobago:	120
– Barbados:	100
– Sri Lanka:	54
– Thailand:	49
– New Zealand:	26
– <b>Australia:</b>	<b>9</b>

Global Annual Incidence of Human Leptospirosis (Pappas, IJID 2008)



■ >50/million ■ 5-50/million ■ 1-5/million ■ <1/million ■ probable high □ no data

- WHO, Wkly Epidemiol Rec (1999) 74: 237
- Pappas, G. IJID (2008) 12: 351
- Ko, AL. Lancet (1999) 354: 820
- Baranton, G. Int J Infect Dis (2006) 10: 162

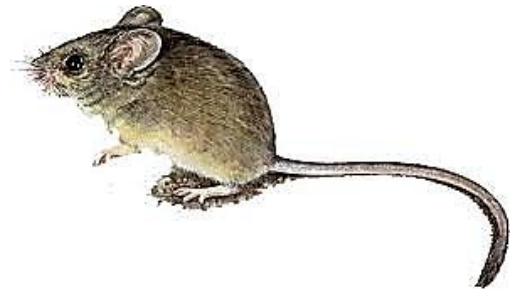
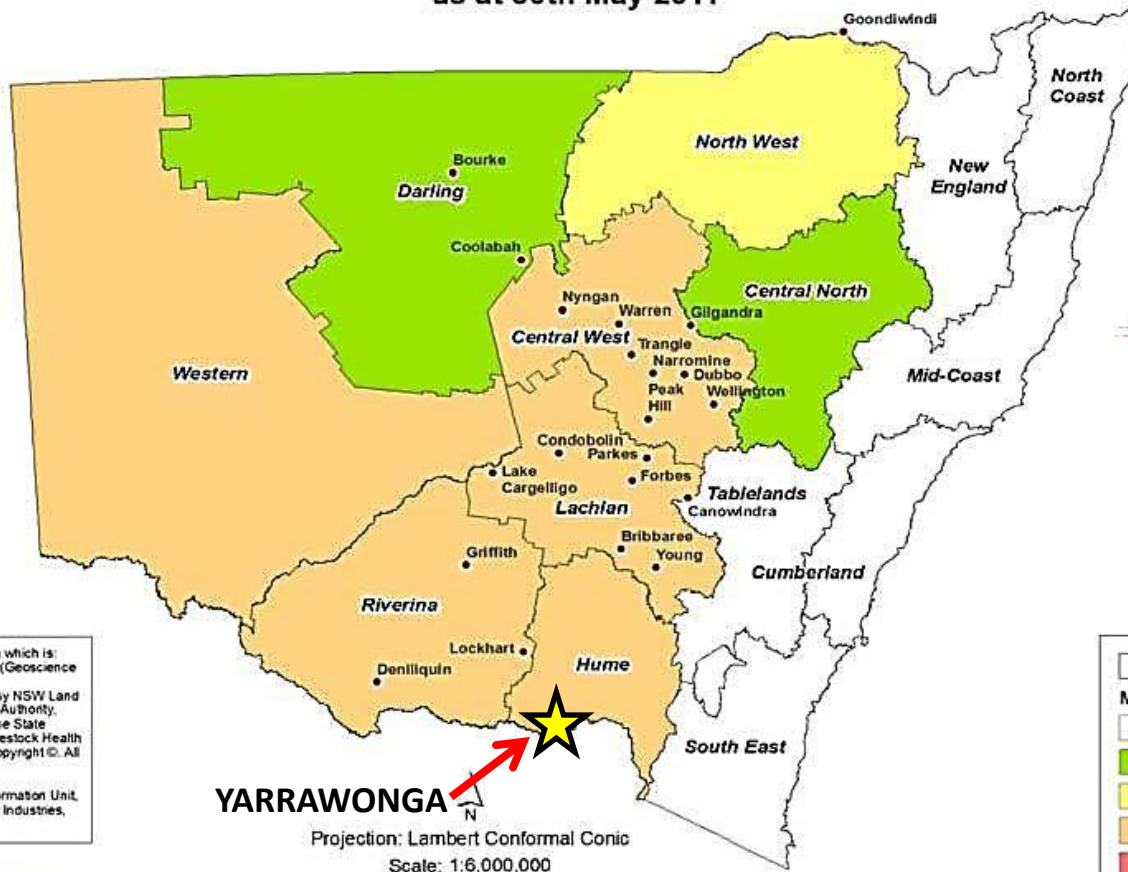
# Leptospirosis in Australia

- First recognized in cane-cutters in Ingham, QLD, 1933
- Nationally: 100-150 cases per year
- Endemic in far north Queensland
  - 70-80% of national cases
  - Risk factors: Banana industry, livestock workers, recreational activities
  - serovars Zanoni, Australis, Hardjo, Pomona, Arborea
- Sporadic cases in temperate regions
  - Risk factors: Livestock and agricultural workers
  - serovars Hardjo and Pomona predominate

- Department Health & Ageing. NNDSS website  
- Slack, AT, Epidemiol. Infect. (2006), 134: 1217  
- Victoriano, AF. BMC Infect Dis (2009), 9: 147

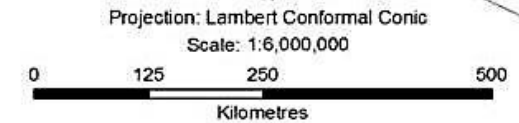
# Mouse plague Southern NSW 2011

Mouse Activity  
as at 30th May 2011



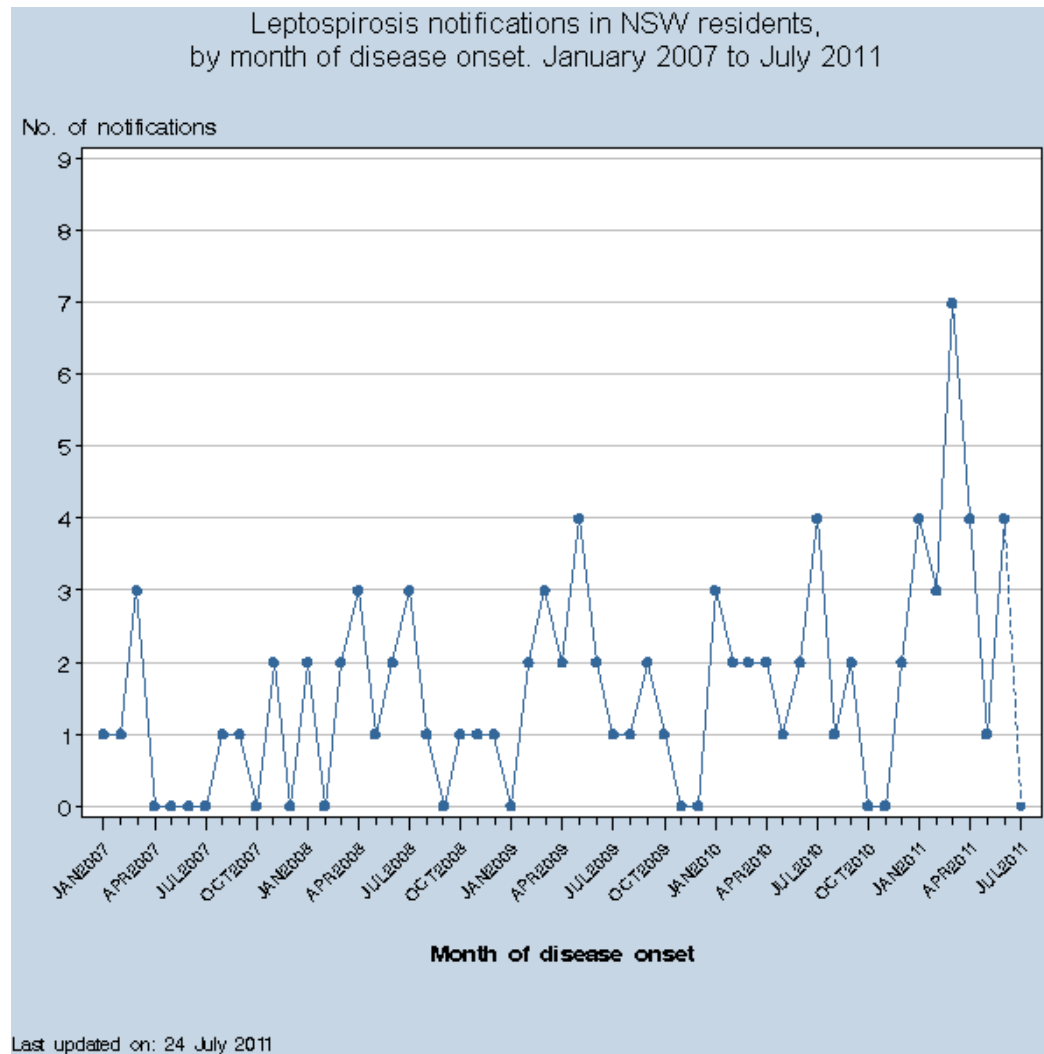
This map incorporates data which is © Commonwealth of Australia (Geoscience Australia) 2008.  
LHP district boundaries courtesy NSW Land and Property Management Authority, Bathurst, Australia, and the State Management Council of the Livestock Health and Pest Authorities. Crown Copyright ©. All rights reserved.  
Produced by the Resource Information Unit, NSW Department of Primary Industries, May 2011.

**YARRAWONGA**



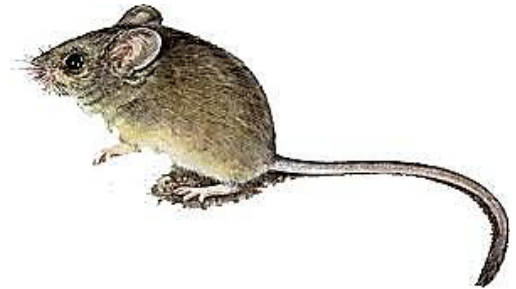
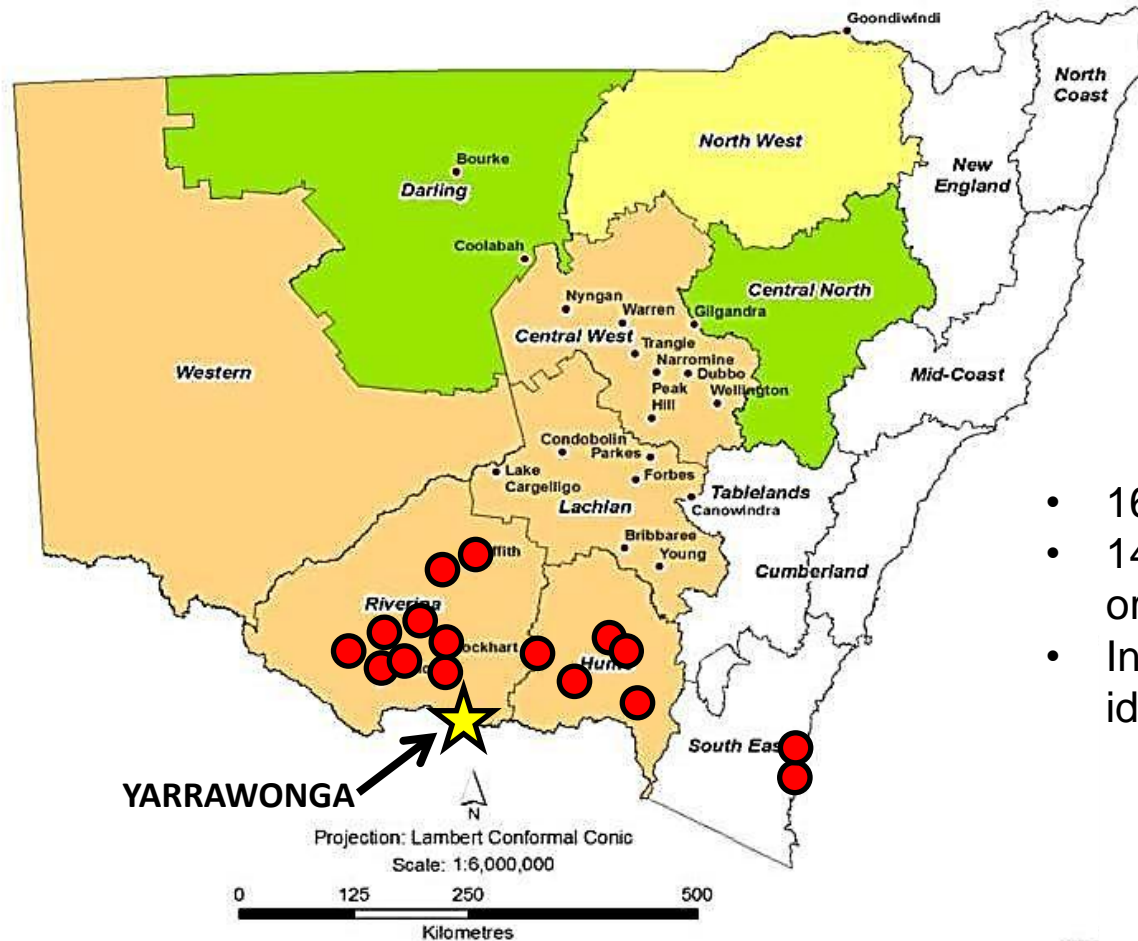
	LHP Districts
<b>Mouse Activity</b>	
	Nil/Not reported
	Low
	Medium
	High
	Severe
	Activity hotspots

# Increase in notifications in NSW March-May 2011



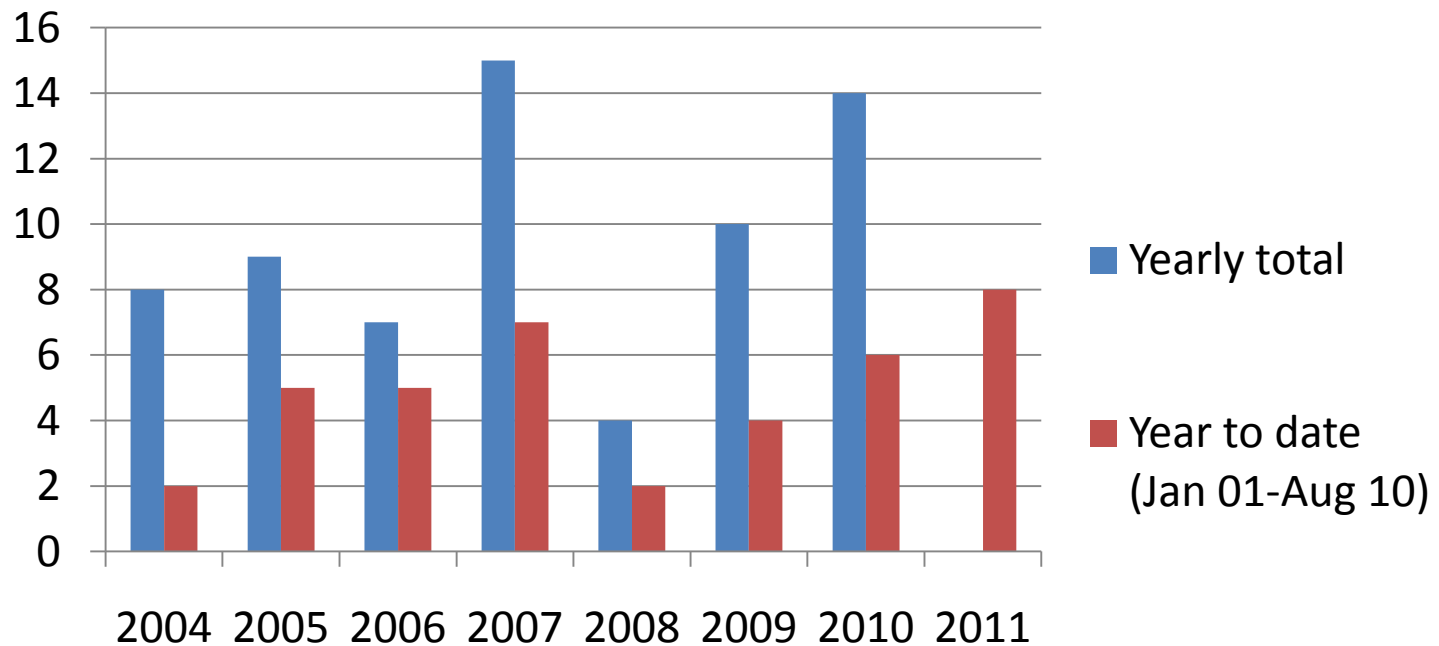
NSW Health Department,  
Public Health Division,  
available from:  
<http://www.health.nsw.gov.au/data/diseases/leptospirosis.asp>

# Leptospirosis in Southern NSW Feb-June 2011



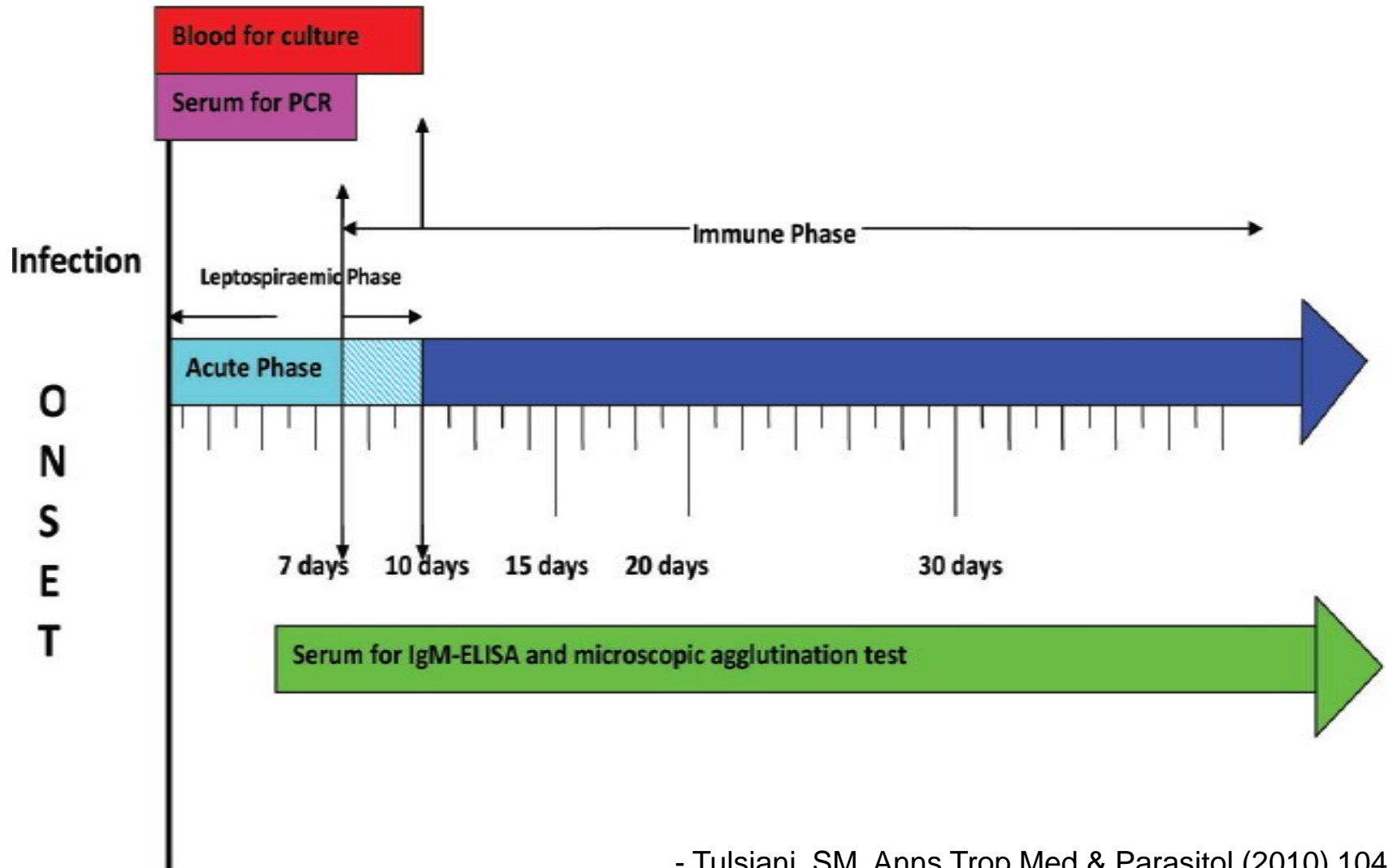
- 16 cases
- 14/16 (88%) reported direct or indirect exposure to mice
- In 9/16 cases serovar identified
  - 8 Arborea
  - 1 Hardjo

# Leptospirosis in Victoria 2004-2011



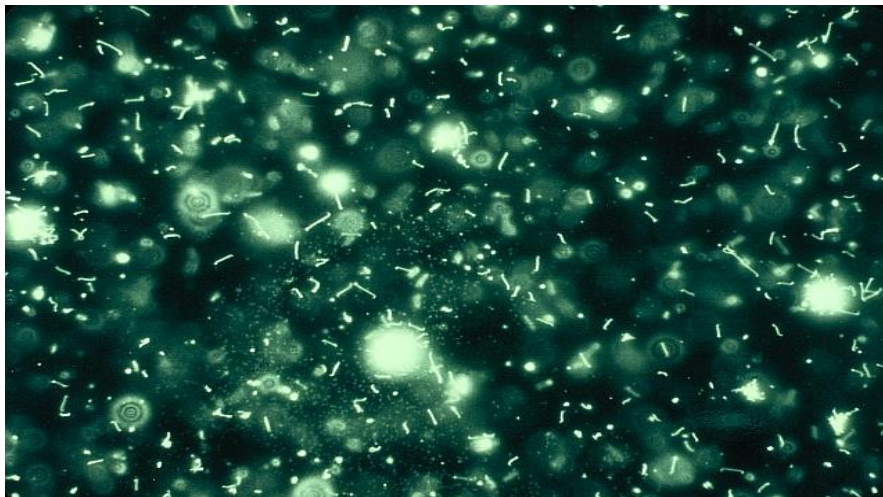
- Usual trends:
  - Serovar Hardjo predominates
  - Majority of cases from Barwon-South Western & Gippsland
  - Increased cases in spring/summer

# Leptospirosis: diagnosis



# Microscopic Agglutination Test

- Current gold standard
- Expertise required to interpret results and maintain large panels of antigens
- Knowledge of local strains important
- Requires paired testing to identify infecting serovar



- WHO Guidelines. WHO (2003)
- Smythe, L. Am J Trop Med (2009) 81: 695
- Chappel, RJ. J Clin Micro (2006) 42: 5484
- Levett, PN. CID (2003) 36: 447

# Leptospirosis PCR

- Available from WHO/FAO/OIE Collaborating Centre for Reference and Research on Leptospirosis, Western Pacific Region (Brisbane)
- Targets 16S rRNA region
- Sensitivity 56% Specificity 90%
- Higher sensitivity if performed in first 5 days, no antibiotics given
  - Correlates well with positive blood cultures

- Thaipadungpanit, J. PLoS One (2011) 6:e16236

- Slack, A. Diagnost Micro & Infect Dis (2007) 57: 361

# Summary

- 67yo man from Melbourne with Leptospirosis
- Acquired in Yarrawonga
- 16 other cases in nearby Southern NSW since Feb 2011
- Expect an increased number of cases in 2011

# Acknowledgements

- Prof Ben Adler, Leptospira Laboratory, Monash University
- Scott Craig, WHO/FAO/OIE Collaborating Centre for Reference and Research on Leptospirosis, Brisbane
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- Fiona Devenish, Eastern Health Pathology
- Dr Catherine Marshall & Dr Uma Devi, Eastern Health