

# INFECTIOUS DISEASES AND IMMUNOSUPPRESSION IN THE TROPICAL NORTH

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# NORTHERN TERRITORY NEWS



### WILDCATS

Sharpen their claws

### What's in the stars for 2007

Phone 8044 9500 Customer service

DARWIN, Saturday, January 21, 2006

\$1.60 (incl. GST)



### COURT BLITZ ON DRIVERS

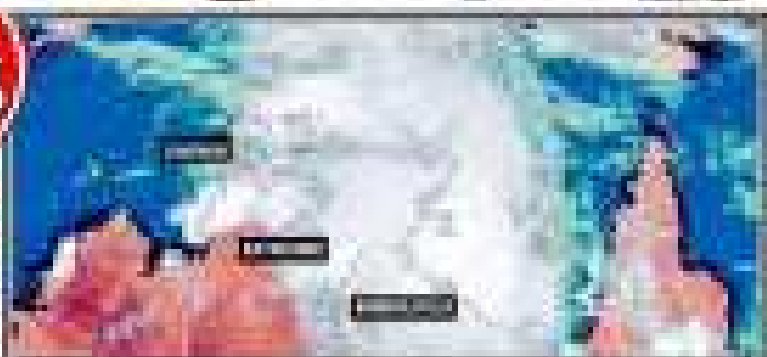
MORE FACE JAIL P-3



### BURYING LOVED ONES ON MOON

### Long arm of the jaws: Saltie chomps fugitive's head

# Croc bites man fleeing cops



### THE BIGGEST Illegal fishing is warned

### Cyclone tipped to form today: P3

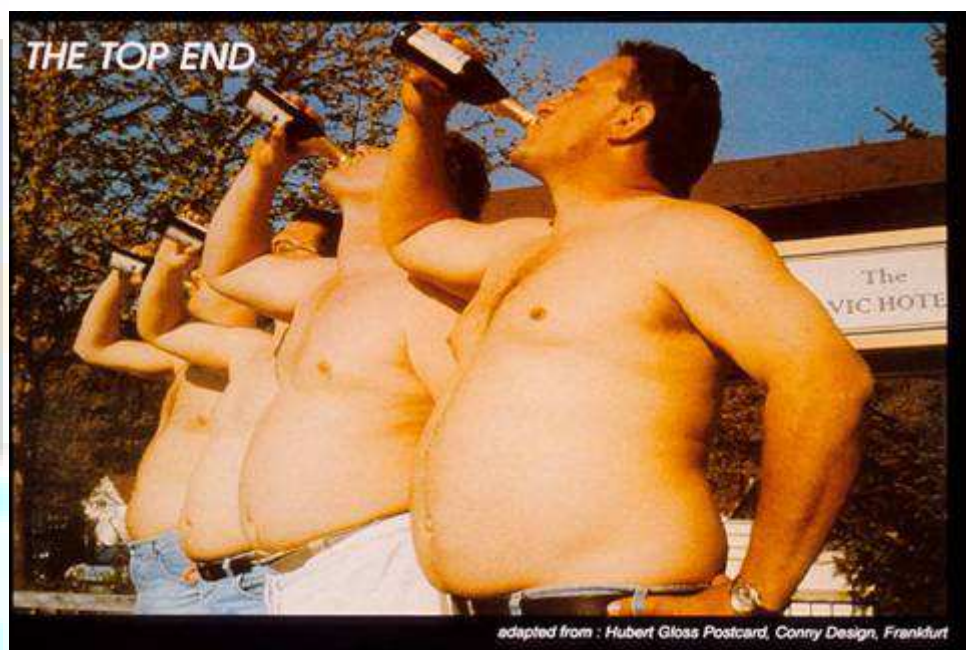
**Do you need financial assistance for a 'Business Plan'?**

Specialist in providing... assistance for business and... projects

# NORTHERN TERRITORY NEWS

# WET SEASON

## Survey reveals Territorians drunk six days a week



adapted from : Hubert Gloss Postcard, Conny Design, Frankfurt

# Outline

- Infectious complications in transplant patients in the Top End
- Specific issues
  - Bacterial Sepsis/infections
  - Melioidosis
  - Scabies
  - Strongyloides
  - Other infections

# Renal Transplantation

## **1984-2004**

- 134 allografts: 77 Indigenous
- Indigenous outcomes
  - 53% mortality
  - 71% of deaths attributable to infection, primarily bacterial

## **2007- 2013**

- 44 allografts: 14 indigenous (4 in 2013),
- Mortality: 3 deaths (1 indigenous patient due to infection)

# Infectious Complications: Viral infections

Viral Infections	Non-Indigenous Patients		Indigenous Patients	
	n=30	%	n=14	%
CMV	7	23.3%	7	50.0%
Influenza (H1N1)	0	0.0%	2	14.3%
BK virus	7	23.3%	1	7.1%
HPV (warts)	1	3.3%	1	7.1%
VZV (shingles)	2	6.7%	0	0.0%
Rotavirus	1	3.3%	0	0.0%
HSV	0	0.0%	1	7.1%

# Bacterial Infections

	Non-Indigenous Patients		Indigenous Patients	
Bacterial Infections	n=30	%	n=14	%
UTI	9	30.0%	5	35.7%
Bacteraemia (UTI)	2	6.7%	0	0.0%
Pneumonia	0	0.0%	2	14.3%
SSTI	0	0.0%	2	14.3%
GIT (campylobacter)	0	0.0%	1	7.1%
Dental infection	1	3.3%	0	0.0%

# Fungal/Parasitic Infections

	Non-Indigenous Patients		Indigenous Patients	
Fungal/parasitic infections	n=30	%	n=14	%
Cryptosporidium	1	3.3%	1	7.1%
Scabies	0	0.0%	1	7.1%
Oropharyngeal candidiasis	1	3.3%	3	21.4%
Dermatophyte infection	0	0.0%	2	14.3%

# Liver Transplantation

- 16 current Liver transplant patients
  - 2 identify as indigenous
    - Transplanted 1992, 2002
  - 1 Indigenous patient from remote community
    - Transplanted 2001- deceased 2011
- Referrals last 12 months
  - 9 referrals, 4 transplanted, 2 patient declined, 2 listed
  - Moving interstate a significant barrier
  - No indigenous patients referred for chronic liver failure in recent years
- Infectious issues
  - Limited data
  - 1 case melioidosis (meningitis+ bacteraemia) 2012
    - Not on bactrim prophylaxis



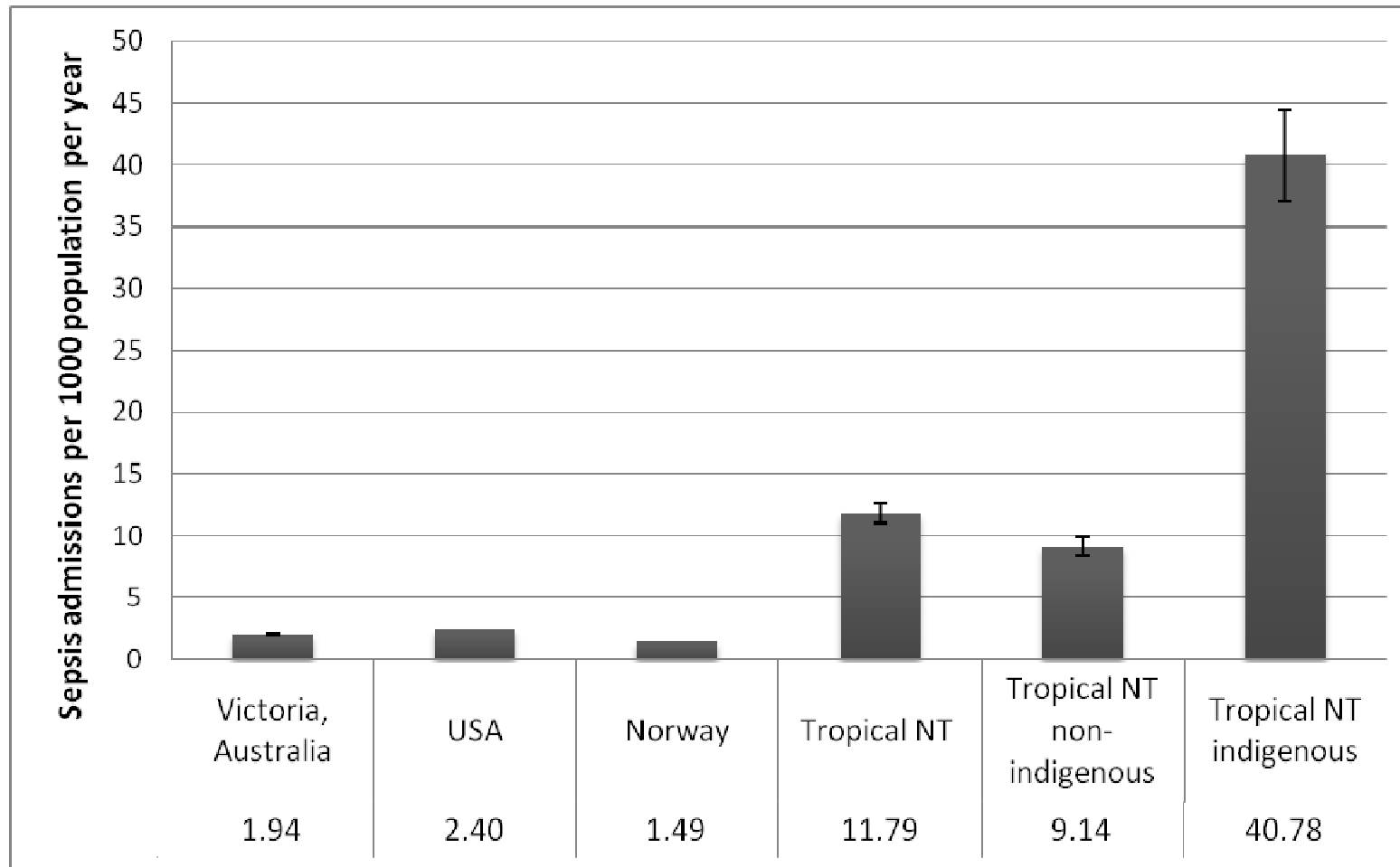
## Liver transplantation in Indigenous patient from remote community

- 28 year old indigenous man from remote community
- Presented with fulminant liver failure 2001
  - Budd Chiari +/- Hepatitis B
  - Liver transplant Adelaide
- Multiple issues post transplant
  - Poor medication adherence
    - Minimal immunosuppression
  - Insulin dependant diabetes mellitus
  - Pancreatitis
  - Neuropathy and neurogenic bladder
  - ETOH abuse
  - Multiple infectious complications...

# Infectious Complications

- Fournier's gangrene (VRE/ESBL)
- Pulmonary TB
- Osteomyelitis of Left malleolus
- Crusted Scabies
- Gangrenous diabetic foot infection
- Pyelonephritis → emphysematous kidney → nephrectomy
- Multiple complicated skin and soft tissue infection/ deep muscle abscess
- Gastro-enteritis
  
- Deceased 2011

# Incidence of sepsis at RDH



- Sepsis=7.46% of all admissions (cf. 1.1% in Victorian study)

Davis et al, MJA 2010

# Risk factors for Sepsis

## 2 Baseline characteristics of study subjects, by Indigenous status\*

Characteristic	Total (n = 1191)	Indigenous (n = 604)	Non-Indigenous (n = 587)	p†
Mean age in years (SD)	46.7 (17.4)	43.2 (14.4)	50.2 (19.2)	<0.001
Male	624 (52.4%)	261 (43.2%)	363 (61.8%)	<0.001
Remote-dwelling‡	288 (24.2%)	251 (41.6%)	37 (6.3%)	<0.001
Hazardous alcohol use§	339 (46.2%)	246 (62.0%)	93 (27.7%)	<0.001
Current smoking¶	413 (52.1%)	266 (66.5%)	147 (37.4%)	<0.001
Chronic renal disease**	140 (11.8%)	114 (18.9%)	26 (4.4%)	<0.001
Chronic liver disease**	111 (9.3%)	80 (13.2%)	31 (5.3%)	<0.001
Diabetes	285 (23.9%)	188 (31.1%)	97 (16.5%)	<0.001
Chronic lung disease**	159 (13.4%)	98 (16.2%)	61 (10.4%)	0.001
Immunosuppression††	50 (4.2%)	13 (2.2%)	37 (6.3%)	0.001
Malignancy	58 (4.9%)	17 (2.8%)	41 (6.9%)	0.002

\* Data are number (%) unless stated otherwise. † P values compare Indigenous with non-Indigenous subjects. ‡ Remote-dwelling was defined according to the Accessibility / Remoteness Index of Australia.<sup>18</sup> § Hazardous alcohol use was defined as ethanol ingestion of > 40 g/day for a man or > 20 g/day for a woman.<sup>19</sup> The denominator for hazardous alcohol use was 733 (Indigenous, 397; non-Indigenous, 336) due to missing data. ¶ The denominator for current smoking was 793 (Indigenous, 400; non-Indigenous, 393) due to missing data. \*\* Definitions for chronic renal, liver and lung disease are those used in the revised Charlson Comorbidity Index.<sup>20</sup> †† Immunosuppression was defined as HIV infection with CD4 counts of < 200 or use of any of the following medications within the past 3 months: prednisolone > 0.5 mg/kg per day (or the equivalent) for more than 14 days; immunosuppressive drugs used for bone marrow or solid organ transplantation or cancer chemotherapy.

Indigenous patients:  
• Increased rates severe sepsis

• 27.8% vs 18.1%

• ICU admission:

• 20.1% vs 11.9%

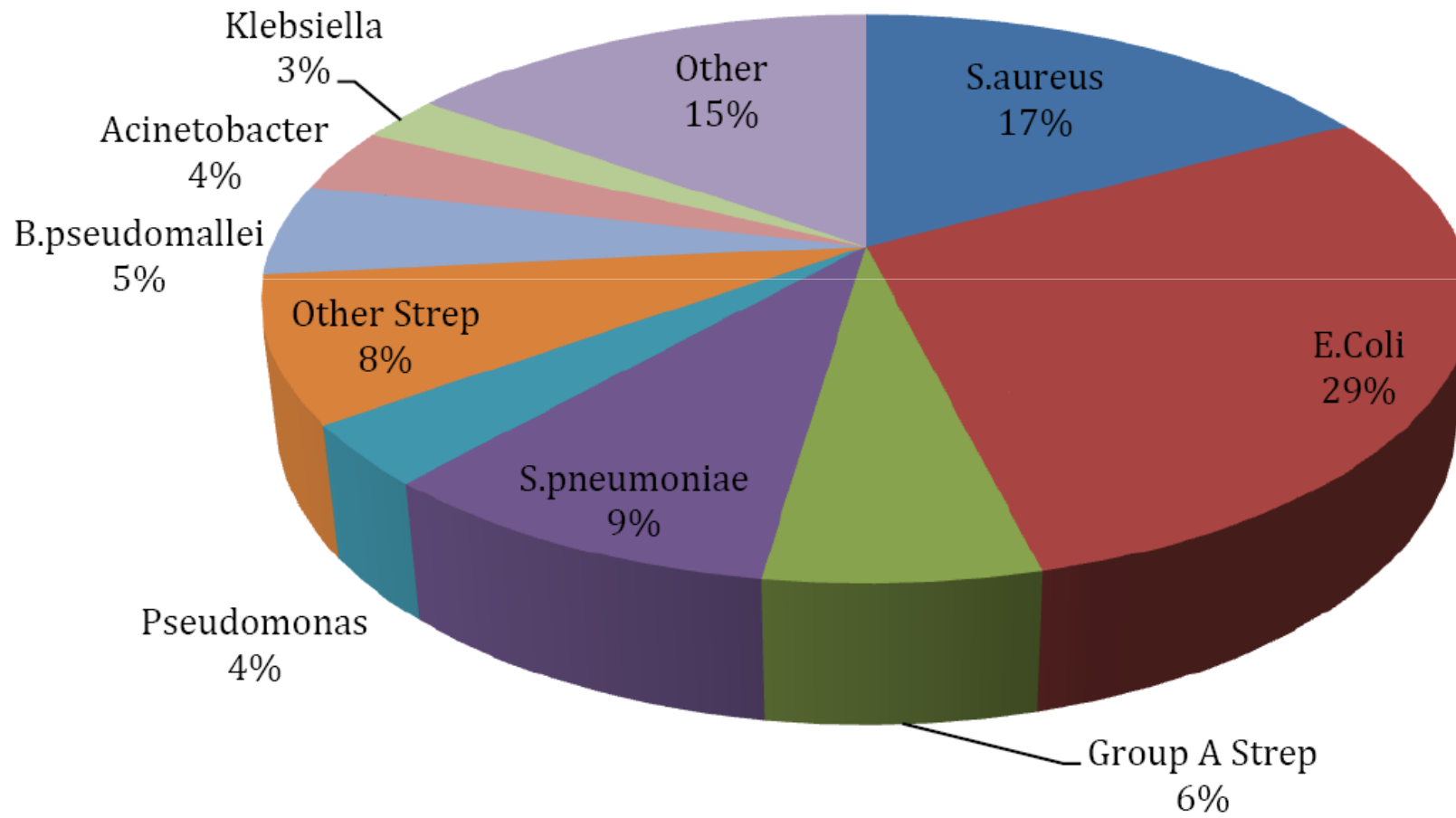
Overall mortality

• 5.4%

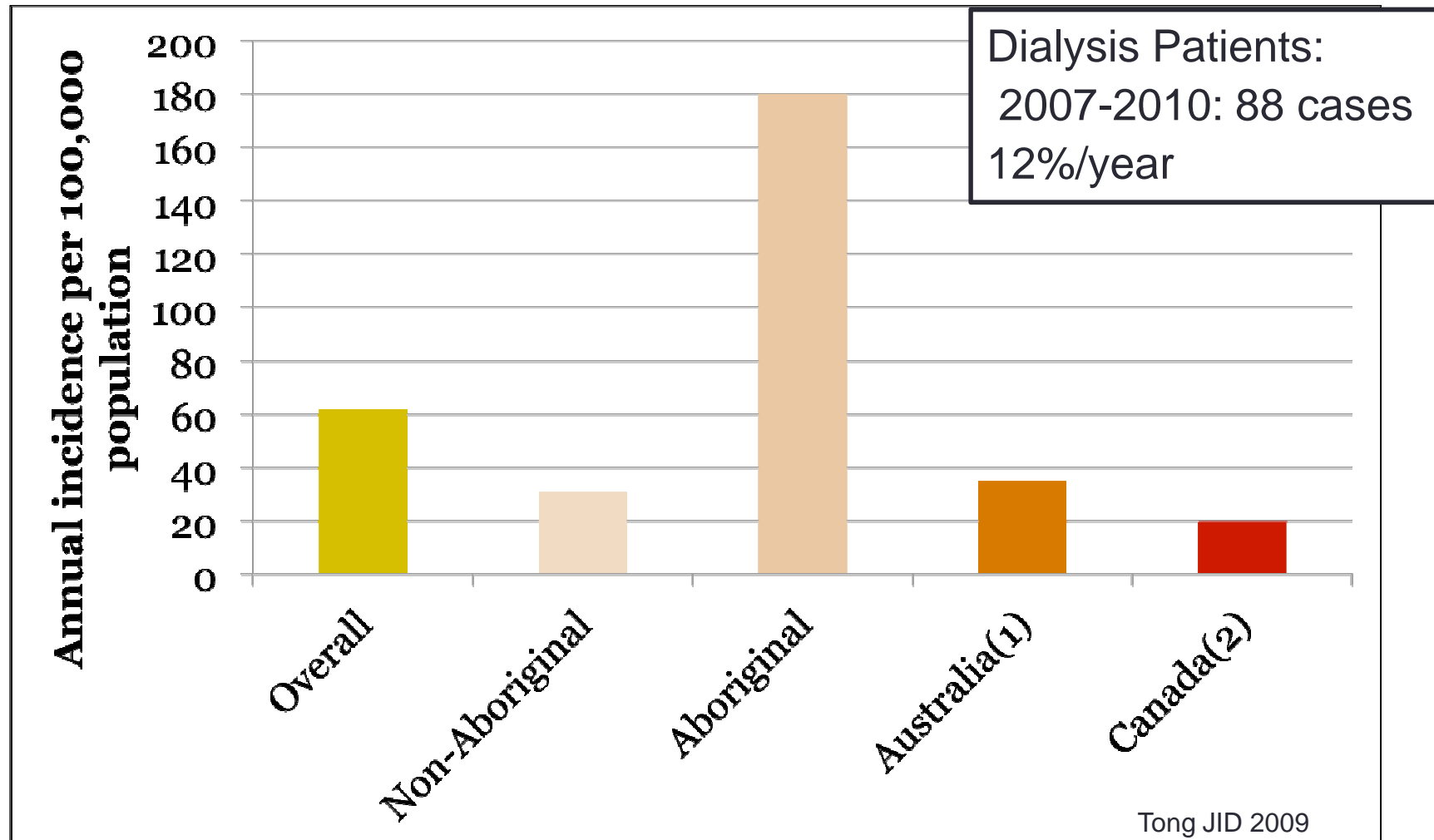
• No difference

Indigenous/non-indig

## PRESTO - Causative organisms bacteraemic patients (n=193)



# *S. aureus* bacteraemia: Top End



# Diabetic foot infections

- Potential barrier to transplantation

12 month audit at RDH:

- Total numbers: 195 admissions in 161 patients
  - 22 (13.6%) patients on Haemodialysis (25 admissions)
  - ≈15% of dialysis population
- 94 (58%) patients had CKD stage 2 or greater

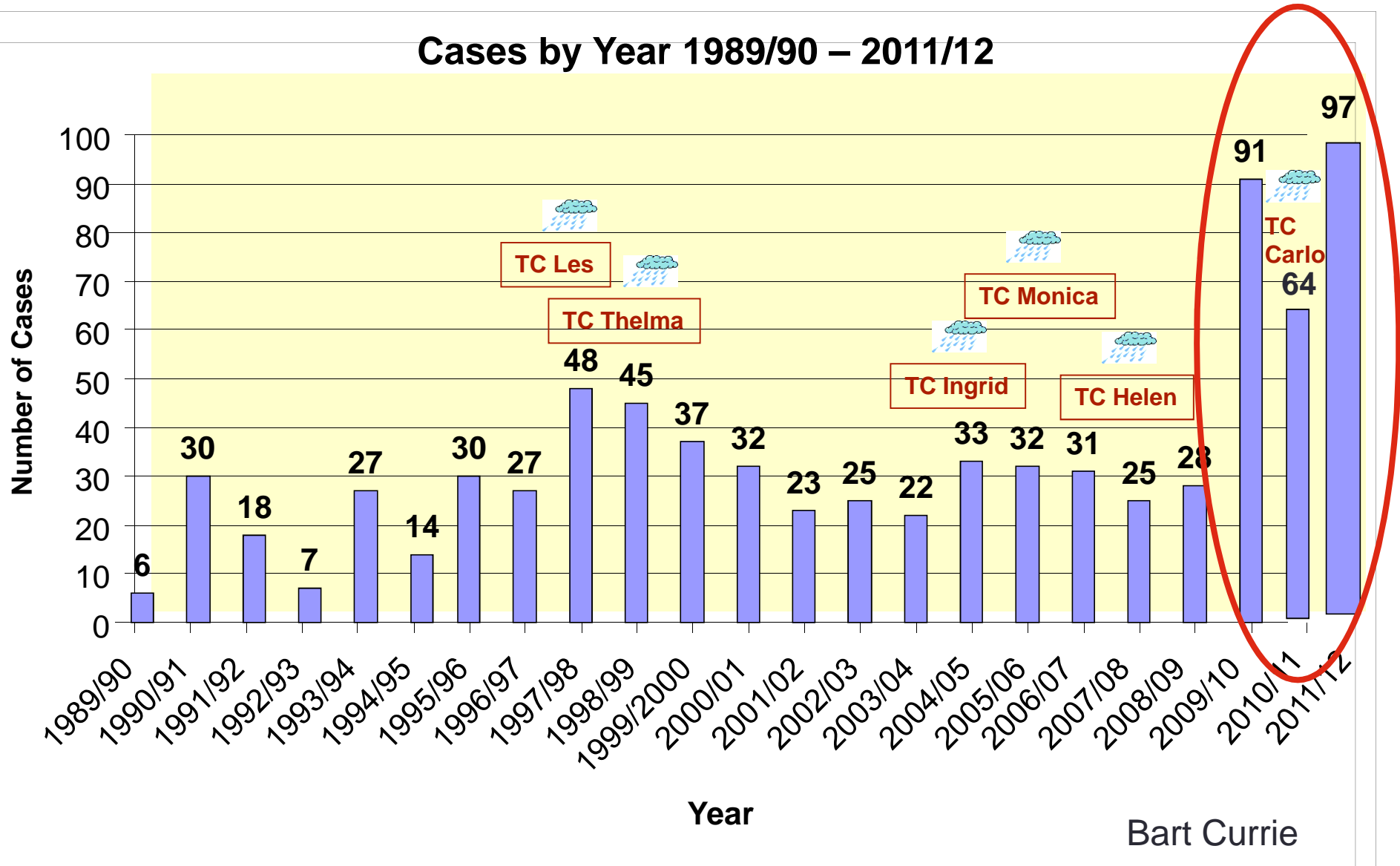
# Melioidosis

- Infection with *Burkholderia pseudomallei*
- Environmental bacterium – in soil and surface water in endemic areas
- Strong association with rainfall and environmental damage
- Acquisition:
  - percutaneous, inhalation, ingestion
- Darwin prospective melioidosis study
  - 820 cases – 24 years
  - 109 deaths (13%)

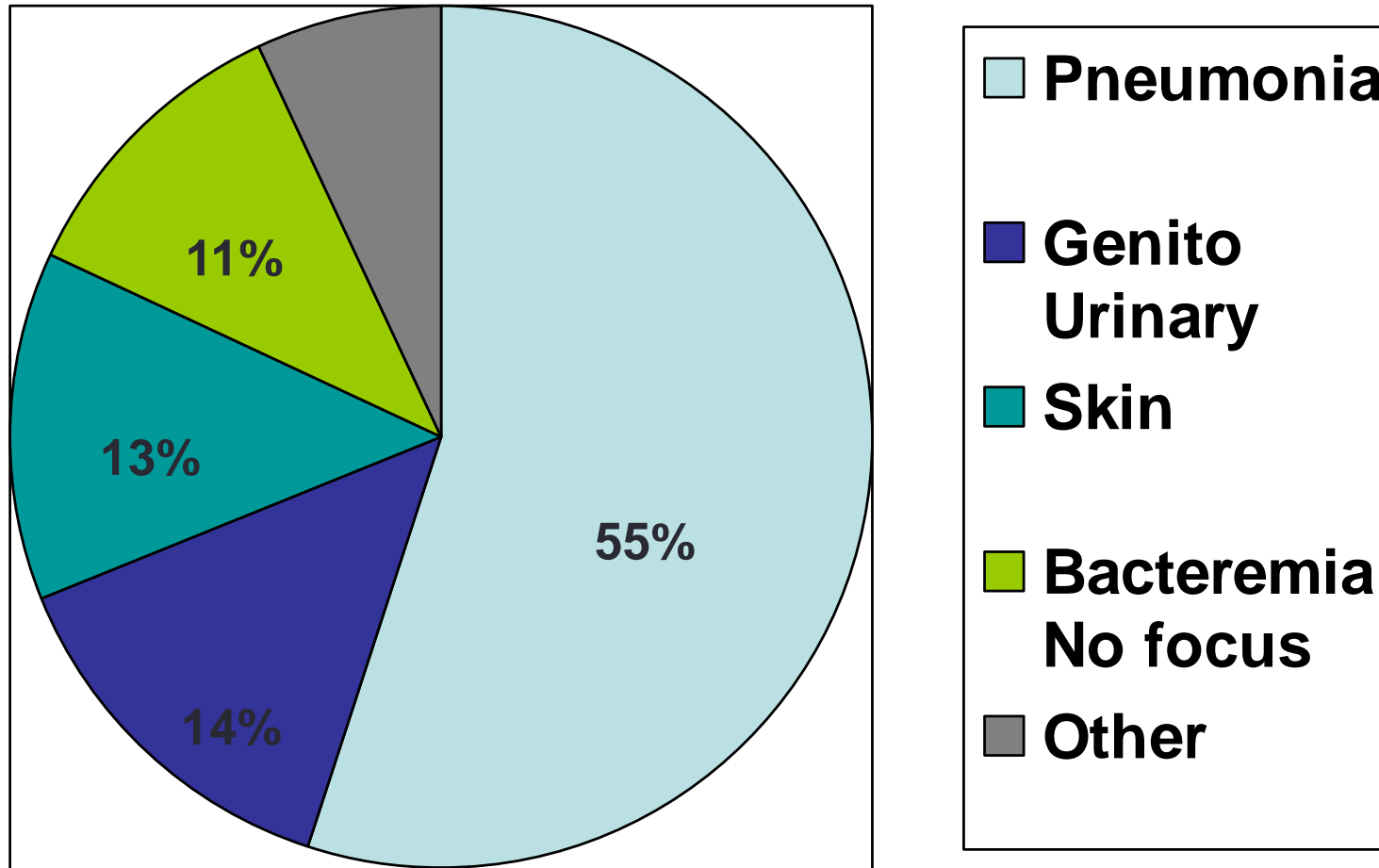




# 23 years of the Darwin Prospective Melioidosis Study



## Melioidosis Clinical Presentations



- 55% Blood culture positive

- 22% Septic Shock
  - 50-90% mortality

Bart Currie

# Risk Factors for Melioidosis

Risk factor	Patients		Deaths	
	n	% of total	n	% who died
Diabetes	213	39%	33	15%
Hazardous alcohol use	211	39%	33	16%
Chronic lung disease	140	26%	27	19%
Chronic renal disease	65	12%	13	20%
Rheumatic heart disease and/or congestive cardiac failure	39	7%	9	23%
Malignancy	31	6%	8	26%
Immunosuppressive therapy and other immunosuppression	31	6%	6	20%
Kava use	27	5%	4	15%
Other <sup>2</sup>	6	1%	2	33%
No risk factors	106	20%	23	2% <sup>6</sup>

# Melioidosis and Renal Patients

- 5 cases in renal transplant patients in Australia
- Dialysis patients
  - 27/785 cases in prospective study
  - RR 38.4 (95% CI 25.7-57.5) compared to non-dialysis
  - Increased presentation of bacteraemia with no focus
    - 37% vs 11%  $p < 0.001$
    - Mortality 11% vs 13% non-dialysis patients (NS)
- Bactrim prophylaxis continued in all Indigenous renal transplant patients

# Scabies

- Ectoparasite: *Sarcoptes Scabiei*
- Common in Remote communities
  - Monthly prevalence in children <15: 13.5%
- Immunosuppressed patients at risk of crusted scabies
  - Cell mediated immunity important
  - High mite burden and skin crusting
  - Associated high rates bacterial sepsis and mortality



Andrews et al, Plos NTD 2009  
Roberts et al. Journal of Infection, 2005

# Crusted Scabies: RDH 1991-2000

**Table 1** Demographics of people with crusted scabies

Demographic features and death rates	
Number of cases	78
Mean age	43
Year of presentation (range)	1991-2000
High mite count confirmed	71%
Definite immunosuppressive risk factor	26%
Possible immunosuppressive risk factor	60%
Indigenous	97%
Annual death rate prior to 1997 <sup>a</sup>	4.3%
Annual death rate from 1997	1.6%

<sup>a</sup> Rates of death directly attributable to crusted scabies are shown before and after the routine use of ivermectin during 1996. This difference is significant  $p=0.02$ , Fisher Exact test.

Immunosuppressive risk factor	Frequency
Heavy ethanol use	17
Past leprosy	13
Heavy kava use	8
Type 2 diabetes mellitus <sup>a</sup>	8
Malnutrition	5
Hepatic cirrhosis	5
Renal transplant immunosuppression <sup>a</sup>	4
Systemic lupus erythematosus <sup>a</sup>	3
Chronic hepatitis B infection	3
Renal dialysis <sup>a</sup>	2
Hypothyroidism	2
Mixed connective tissue disease <sup>a</sup>	2
Syphilis	2
Behcet's disease <sup>a</sup>	1
Scleroderma <sup>a</sup>	1
Chronic Myelogenous Leukemia <sup>a</sup>	1
Chronic petrol inhalation	1
Sturge-Weber Syndrome <sup>a</sup>	1
HTLV-I infection	3
HIV infection	0
No risk factor identified	33 (42%) <sup>b</sup>

Some patients had more than one risk factor.

# *Strongyloides Stercoralis*



- Nematode (roundworm)
- Endemic in most remote communities of Top End of NT, especially East Arnhem
- Asymptomatic/mild symptoms in most immunocompetent patients
- Risk of dissemination with immunosuppression
  - 0-2 cases/year seen at RDH, high mortality
  - Presents with fever, abdominal pain, pulmonary infiltrates and sepsis
- Treatment with ivermectin
- Screening with serology, eosinophil count and stool M/C/S
- Empiric treatment of high risk immunosuppressed pts

# Other Infectious Diseases

- Hepatitis B
  - HbsAg +ve: estimated prevalence 8% in remote Indigenous communities
  - HbcAb +ve: 63% in one study in remote community
- Tuberculosis
  - NT incidence 2-5 times higher than other states
  - Local transmission in some remote communities
- Less common Bacterial infections: Nocardia
  - 1997-2010: 44 cases, 16% 30 day mortality
- Fungal infections: Cryptococcus

O'Sullivan, 2004; Carroll 2010  
Barry 2009; Whiting 2011



**QUESTIONS?**

