

Q Fever

What men and women on the land need to know

Dr. Stephen Graves

Director, Australian Rickettsial Reference Laboratory

Director, Division of Microbiology, Pathology North
(Hunter)

NSW Health Pathology, Newcastle, NSW



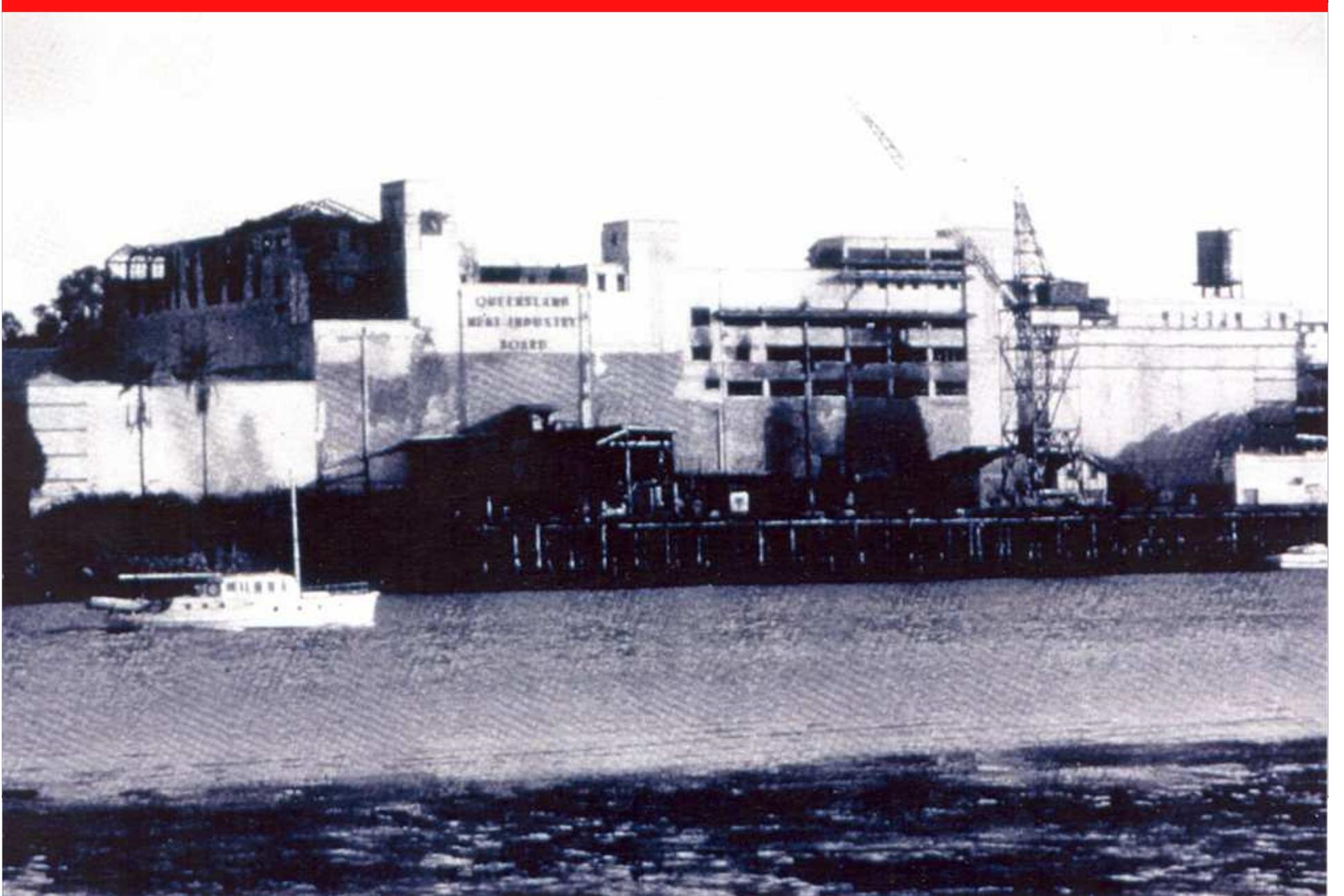
Q FEVER – Infection with *Coxiella burnetii*

- Many animal species are susceptible to Coxiellosis
 - Cattle
 - Sheep
 - Goats
 - Dogs
 - Cats
- Rural people are at the front line and at risk of infection

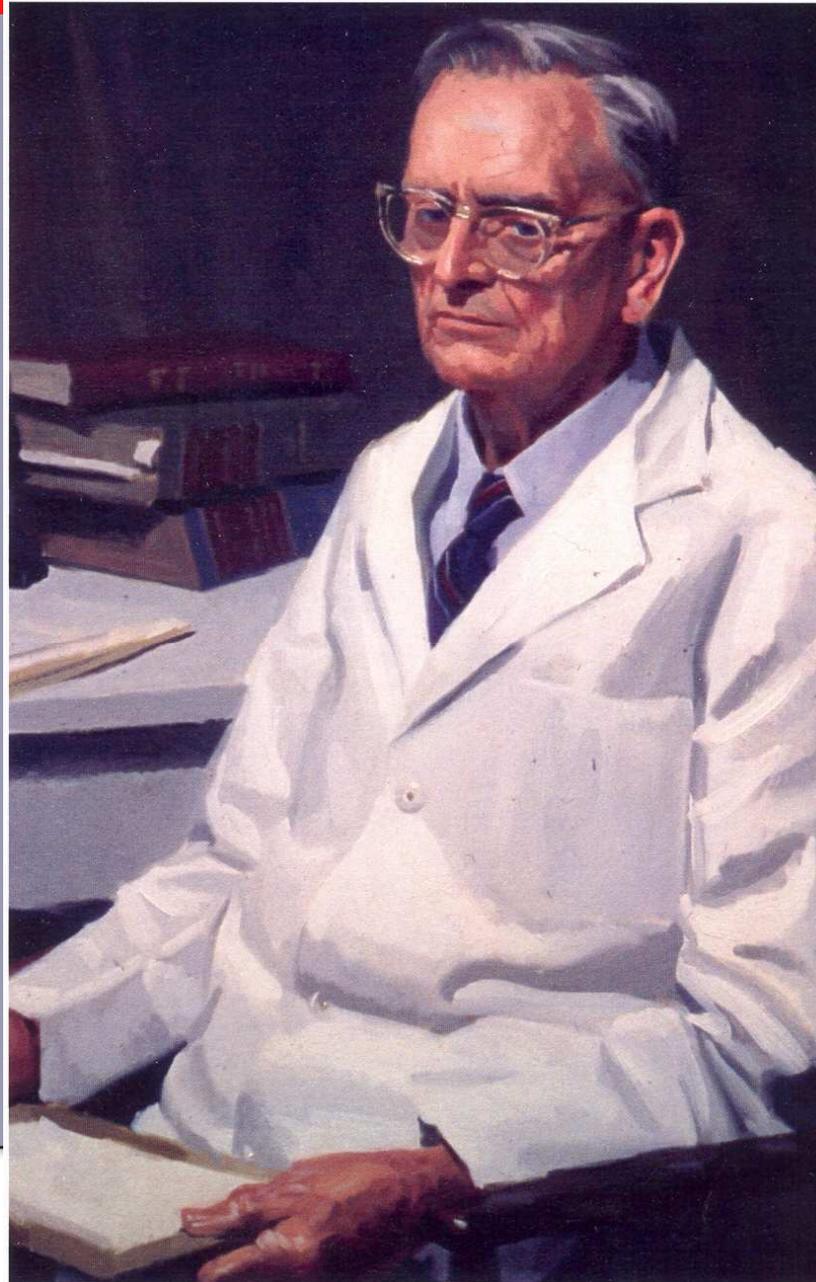
History of Q Fever

In Australia

- Unknown febrile illness (? query fever) in abattoir workers in Brisbane
- Derrick investigated disease
 - Derrick, E.H. (Ted) (1937) “*Q fever, a new fever entity: clinical feature, diagnosis and laboratory investigations*”. Med. J. Aust. 281 - 299



Dr Edward (Ted) Derrick



Differential diagnosis of this new disease (Q Fever)

- Typhus (*Rickettsia sp.*)
- Typhoid (*Salmonella typhi*)
- Leptospirosis (*Leptospira sp.*)

Microbe could be transmitted from humans to guinea pigs

Burnet showed it to be a probable rickettsia

History of Q Fever

In USA

Davis & Cox (1938)

Unknown microbial pathogen isolated from a tick
(Nine Mile Creek, Montana)

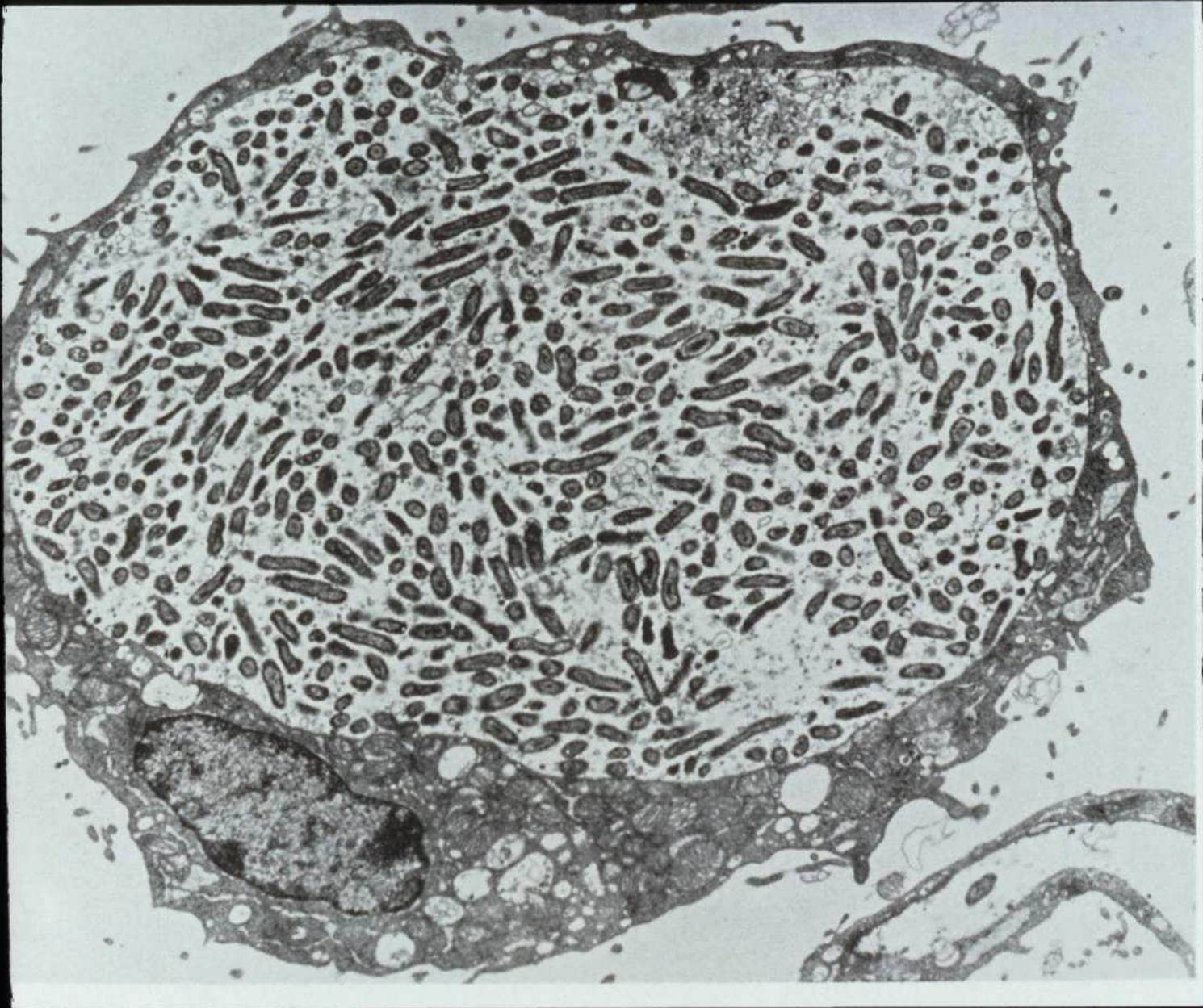
This became the 'Nine Mile' strain of *C. burnetii*

An accidental laboratory infection in the USA showed tick
microbe to be a human pathogen.

The Australian and USA microbes were shown to be the
same and named after Cox and Burnet (*Coxiella burnetii*)

Coxiella burnetii

- A bacterium (hence infection treatable with antibiotics)
- Exists in 2 morphological forms
 - Large cell (intracellular replicating form)
 - Found in animals and patients
 - Small cell (survival, non-replication form)
 - Found in environment



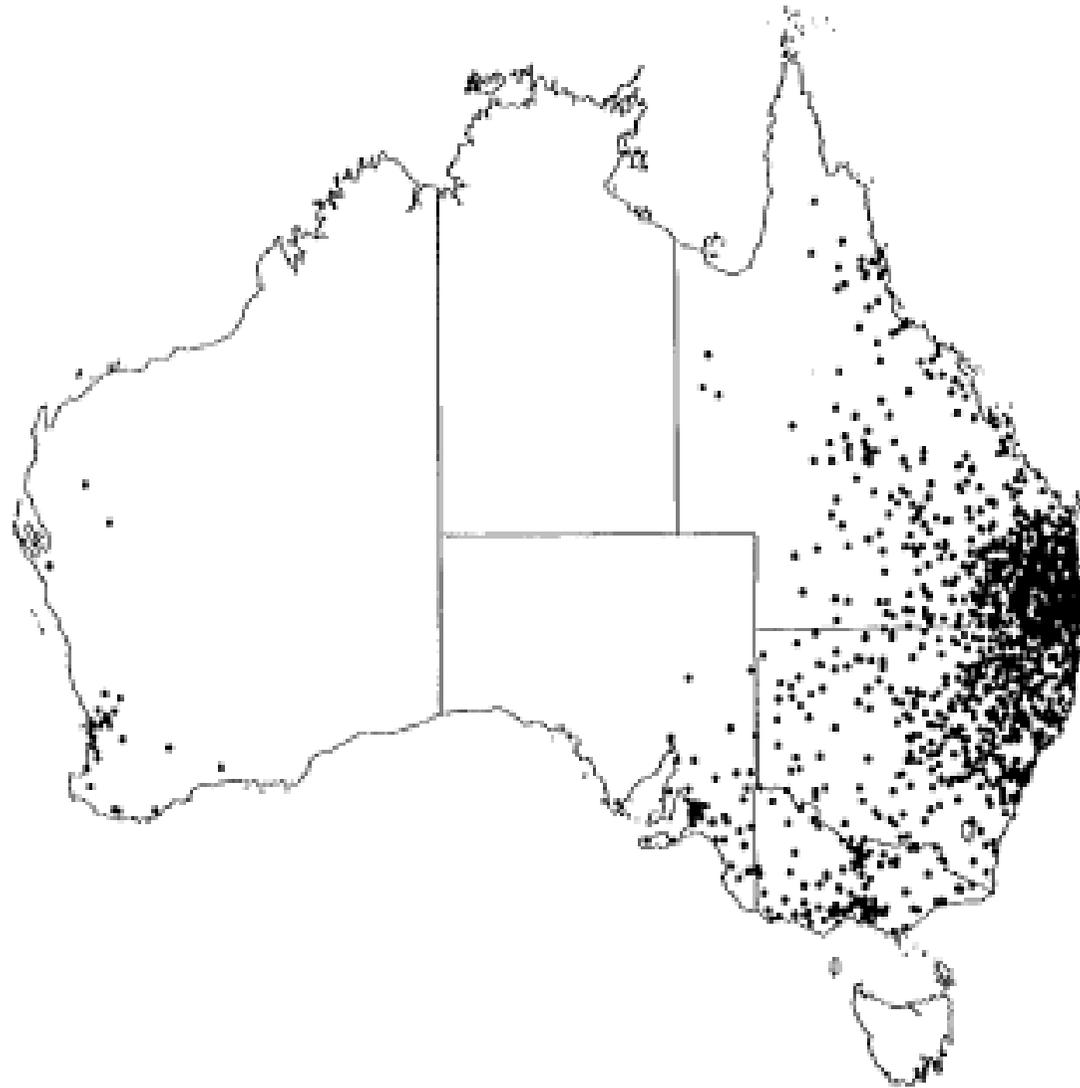
Coxiella burnetii

- Belongs to γ - subdivision of the Proteobacteria group
- *Legionella pneumophila*
 - (Legionnaires disease)
 - Is closest relative phylogenetically
- Obligate intracellular growth
 - Invertebrate cells (ticks)
 - Vertebrate cells
 - Sheep, cattle, goats, dogs, cats
 - Grows in vitro in cell culture
 - Grows in yolk sac of chicken embryos

Epidemiology of Q Fever

- Worldwide (except New Zealand and Tasmania)
- Queensland and NSW main foci, especially localities with high livestock concentrations or abattoirs
- In some parts of NSW 20% population is seropositive.

Incidence of Q Fever within Australia



Epidemiology of Q Fever

- Bush cycle involves ticks (several species, including the kangaroo tick, *Amblyomma triguttatum*)
- and macropods, bandicoots etc.
- Main occupational risk to humans
- cattle, sheep, goats
- Domestic animals (cats & dogs)
 - minor risk
- Most human infections are due to aerosol generation and inhalation of bacterium

Infected animals may be:

- a) Asymptomatic
- b) Asymptomatic but excreting low concentrations of *C. burnetii* in genital tract secretions, milk, urine and faeces.
- c) Aborting, with very high concentrations of *C. burnetii* in products of conception e.g. Dutch milking goats outbreak.

Q Fever in Humans

- Very low infectious dose (1 – 10 *C. burnetii*)
- Infection by respiratory route
- Only 50%, of infected persons develop symptoms
- The other 50% seroconvert, but remain asymptomatic

Q Fever in Humans – stages in disease

- Acute Q fever
- Latent Q fever
- Chronic Q fever
- Past Q fever (asymptomatic & immune)
- Post Q fever chronic fatigue syndrome

Q Fever in Humans

Acute Q fever

Symptoms 2 – 5 weeks after exposure
(depending on infecting dose)

- Fever
- Pneumonia
- Hepatitis
- Headache
- Muscle pain
- Severe fatigue

Disease is often misdiagnosed due to non-specific clinical symptoms e.g. “flu”

Q Fever in Humans

Acute Q fever

- ▶ Patients recover in 2 – 3 weeks (even without antibiotics)
- ▶ However in some cases microbe is still alive [latent Q fever] and relapse can occur later (chronic Q fever).
- ▶ In other cases microbe is killed entirely by patient's immune system

Chronic Q fever

- Months to years after acute Q fever
- Is due to relapse of original infection
- Occurs in ~ 5% of patients, especially if pre-existing abnormal cardiac valves.
- Endocarditis – high mortality
- Osteomyelitis
- Granulomatous hepatitis

Post Q Fever – Chronic Fatigue Syndrome

- In \approx 10% of patients with acute Q fever, especially if severe
- Fatigue lasts for years
- Pathogenesis not clear
 - Probably persisting antigens of microbe (not viable *C. burnetii*) and ongoing pro-inflammatory cytokine response by patient
- No known treatment
- No response to antibiotics

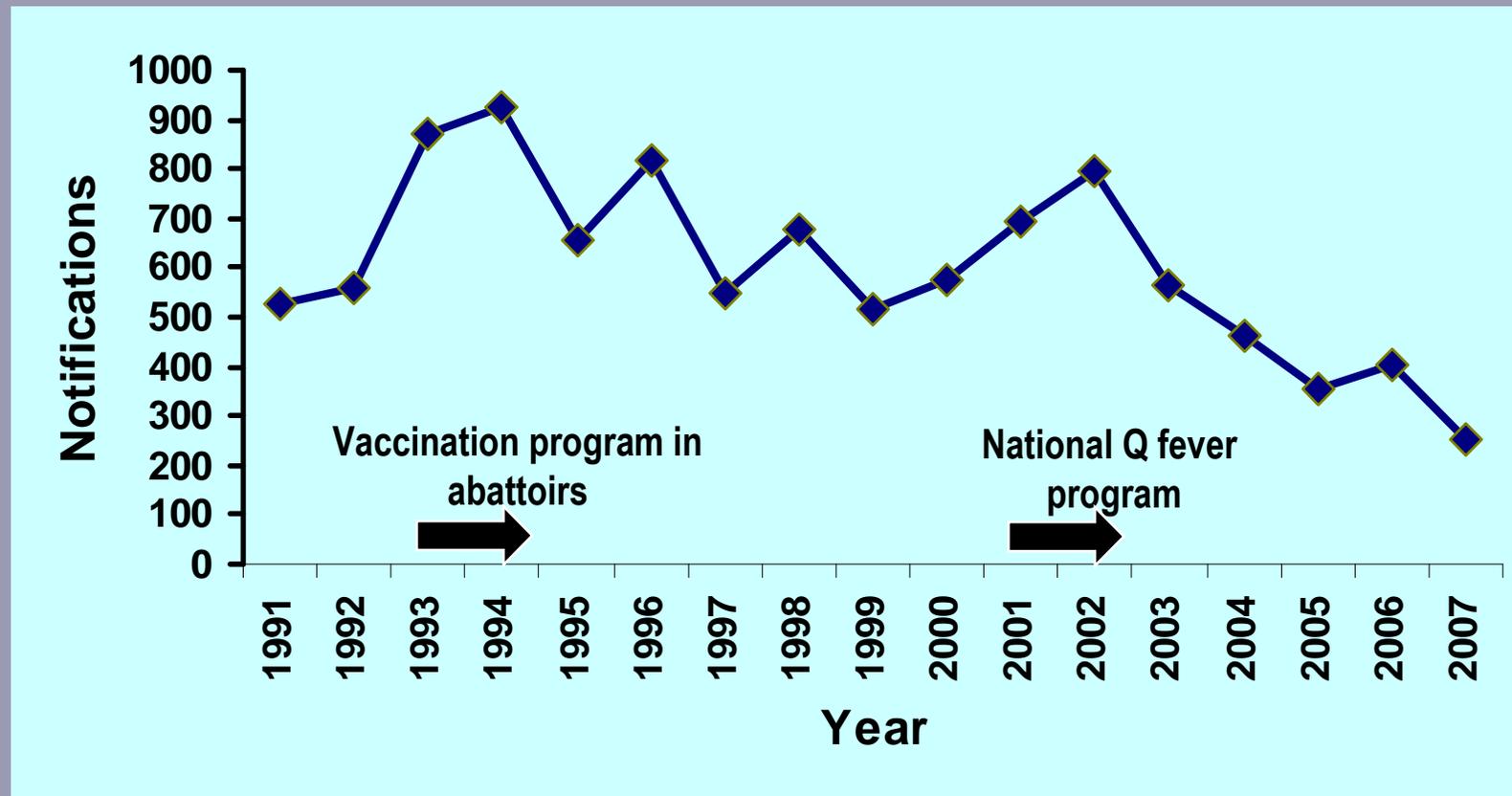
Human Q Fever Vaccine (“QVAX”)

- Only available in Australia
- Developed by Marmion & Ormsbee
- Produced by “CSL Biotherapies”, Melbourne
- Formalin-killed phase 1 whole cell
- Henzerling strain (Italy)
- Grown in embryonated yolk sac

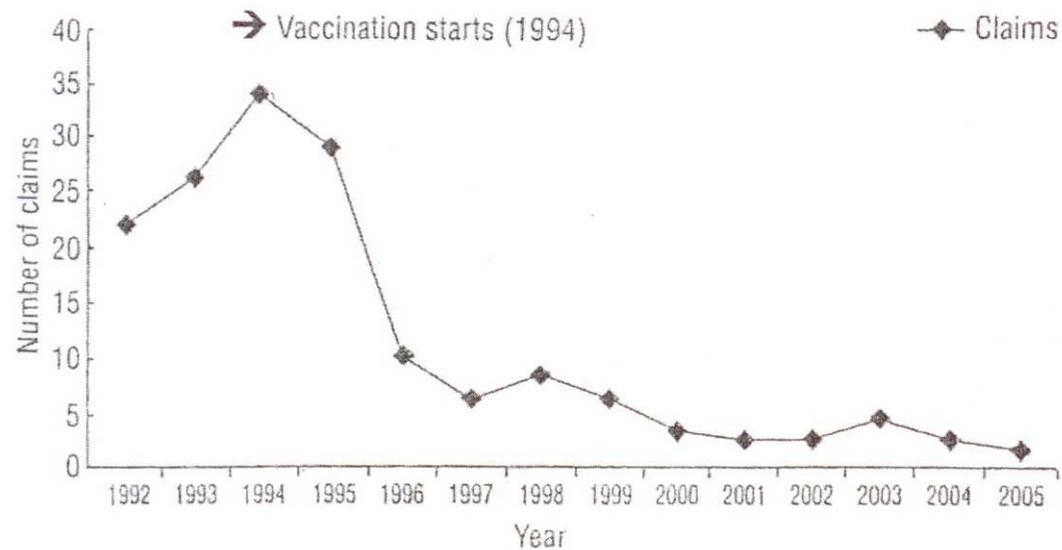
Q Fever Vaccine (continued)

- Licensed for use in 1989 (22 years experience now)
- Tested in abattoir workers and shown to be extremely effective
- Pre-screening of vaccinees needed to exclude those already exposed (already immune ?) to *C. burnetii*
 - Antibody blood test
 - Intradermal skin test of T-lymphocytes (read at day 7)

Falling Q Fever incidence



1 Control of abattoir-associated Q fever in a major Queensland abattoir complex



Claims per annum for compensation for clinically and laboratory-proven, occupationally acquired Q fever. (Data supplied by and reproduced with permission of Australian Meat Holdings, Queensland.)

Q Fever Vaccine (continued)

- Vaccine consists of 20 μ g (0.5ml) given subcutaneously, once; no boosters
- Patient immune by 2 weeks
- No post- vaccination blood tests needed
- Side effects:
 - 1/500 mild injection site reactions
 - 1/10,000 severe reactions
 - granuloma
 - abscess
 - myalgia
 - arthralgia
 - lymphadenopathy

Diagnosis of Q Fever (in humans)

Acute disease

Week 1

Nucleic acid amplification (PCR) to detect DNA of *Coxiella burnetii* in leucocytes of peripheral blood

Test available in reference labs

Week 2

PCR and/or serology

Week 3

Serology only

Antibodies to *C. burnetii* now present and detected by several assays (micro-immunofluorescence is gold standard). DNA has disappeared.

Diagnosis of Q Fever (in animals)

- More difficult than in humans
- Clinically, increased abortion rate
- Serology; complement fixation test (all species)
- enzyme immunoassay for cattle
- PCR laboratory test to detect *C. burnetii* DNA in aborted material
- Histopathology (granulomas) and specific stains

Infection Control against Q Fever

- Vaccination
- Limit aerosol risk e.g. surgical masks
- Dispose of all surgical and aborted materials safely
- Disinfect surfaces after operative procedures (70% ethanol)
- [avoid tick bites]

Take Home Messages

1. Q Fever is present in many animal species in Australia.
2. Q Fever in animals manifests as abortion, during which very large numbers of *C. burnetii* are excreted into the environment
3. Viable “spores” are spread by wind
4. Rural people are at increased risk of Q Fever and should consider “QVAX” vaccination