# All creatures great and small

This article describes the clinical legacy of a holiday for a man and his grandson. It highlights the difficulties with diagnosis of a febrile illness and reminds general practitioners of a common multisystem and potentially serious infection.

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**Case study – Mr ID**

Mr ID, 56 years of age, attended the emergency department of a district hospital complaining of several days of fever, headache, vomiting, photophobia, lethargy, itchy rash, and generalised aches and pains. He had previously been well but had past diagnoses of depression, glucose intolerance, and possible scleroderma. A splenectomy had been performed for trauma. He is a nonsmoker, drinks no alcohol, lives with his wife in town, and is unemployed. His only medications are sertraline and glucosamine. He has not travelled overseas but spent 2 weeks on his brother's beef cattle property on the New South Wales northern tablelands a fortnight earlier, accompanied by his 11 year old grandson, who was also now experiencing fevers, rash, lethargy, headache, and limb aches.

**Examination revealed a fever of 38.4°C, photophobia, oxygen saturations in the mid 90s, and right upper quadrant abdominal tenderness. A subtle pink papular rash was present on his trunk. Tachycardia and neck stiffness were absent, as were abnormal chest or neurological signs.**

## Investigations

Pathology investigations are outlined in *Table 1*; liver function results shown represent the worst, recorded several days after admission. Chest X-ray was unremarkable on presentation. Serology for hepatitis A, B, C, toxoplasmosis, and recent cytomegalovirus and Epstein-Barr virus were negative. Tests for possible zoonoses, *Brucella*, *Leptospira* and Q fever, were requested. Abdominal ultrasound revealed changes consistent with fatty liver. Urinalysis was normal on admission but microscopic haematuria developed over the next 2 days, accompanied by a rise in serum creatinine to 147 mcmol/L. At that time Mr ID also developed a slight dry cough, dyspnoea, a further fall in oxygen saturations, and basal lung crepitations; the chest X-ray appearance became consistent with mild left heart failure.

Initial therapy was for sepsis, source unknown, using intravenous flucloxacillin and gentamicin. With deteriorating hepatic, pulmonary and renal function, oral doxycycline (to cover Q fever and leptospirosis) and intravenous ceftriaxone (for broader antibacterial cover) were included, resulting in improvement within 48 hours. Serology for Q fever, leptospirosis and brucellosis were reported as negative. Mr ID improved slowly, sufficiently to be discharged 1 week later. After a further week, repeat Q fever tests revealed positive phase 2 serology for both Mr ID and his grandson.

## Discussion

It is probable that Mr ID and his grandson acquired Q fever via a farm dog that was contaminated with blood after eating a bovine placenta and with dust after mauling the carcass of a dead cow. No-one else on the farm reported any illness.

*Coxiella burnetii* (*Figure 1*) is a small intracellular bacterium (coccobacillus).[1] It causes Q fever, an infection most commonly contracted from cattle and sheep, transferred to one another via ticks. It can however be transmitted from dogs, cats, other mammals and birds.[2] The bacteria concentrate in the uterus, placenta and mammary glands of infected female mammals. The organisms are very resistant to drying, and last up to months in dried faeces, milk and carcasses. Aerosolised *C. burnetii* in contaminated soil is highly contagious over large distances, with reports of entire villages being infected by flocks of infected sheep being driven

| Table 1. Mr ID's investigation results | |
|---|---|
| Full blood examination (FBE) | WCC 7.9x10$^9$/L with mild lymphopaenia (NR 4–11) |
| Cerebrospinal fluid (CSF) | Clear, no blood cells or organisms, no growth |
| C-reactive protein (CRP) | 380 mg/L (NR <5) |
| Bilirubin | 71 mcmol/L (NR 2–20) |
| Alanine amino transferase (ALT) | 294 U/L (NR 5–40) |
| Gamma glutamyl transferase (GGT) | 531 U/L (NR 15–73) |
| Albumin | 24 g/L (NR 35–50) |
| Midstream urine (MSU) | No growth on culture |
| Blood | No growth on culture |

past. Infection of individuals more than 18 km from the source has occurred. As little as one organism can cause a clinical infection.[3] The infection may be contracted by inhalation, ingestion, and possibly sexually. The incubation period is 3–30 days.

Cattle, sheep and goats are the major source of human infection. People are at risk if they are in contact with animals, particularly cattle, sheep, goats and kangaroos, whether feral or domestic. Q fever is an occupational hazard for people working with these animals, particularly abattoir workers. New recruits to these occupations are especially at risk as they may not have developed immunity through previous exposure. Nonimmune visitors to contaminated environments may also become infected (*Table 2*).

The acute symptoms of Q fever are variable and nonspecific. Often patients present with a flu-like illness with fever, sweats, severe headache, muscle and joint aches, and rash. Pneumonia, characterised by cough and nonspecific X-ray changes is common, as is hepatitis with hepatomegaly and abnormal liver function tests. Glomerulonephritis and myocarditis are uncommon but well documented acute syndromes. A chronic form of Q fever can occur, sometimes years later or in the absence of an acute infection. The chronic form is usually due to an endocarditis developing in predisposed individuals.

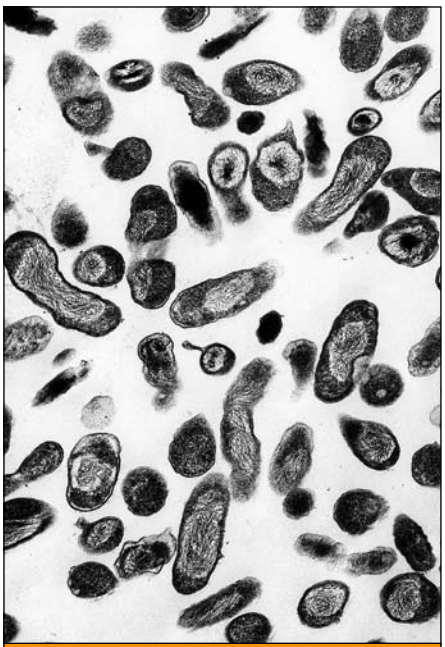

Figure 1. *Coxiella burnetii*

| Table 2. Risk groups for Q fever |
|---|
| • Meat processor (abattoir) workers |
| • Visitors to high risk environments such as meat processing plants (eg. electricians, mechanics, telephone engineers, school groups) |
| • Sheep shearers |
| • Farmers |
| • Station owners |
| • Farm and station hands |
| • Wool classers |
| • Livestock buyers and auctioneers |
| • Livestock transporters |
| • Pelt and hide processors |
| • Veterinary workers |

Mr ID's illness was typical in the range of organ systems involved, in the need to wait weeks for 'convalescent' serology to confirm diagnosis, and in the several days taken for a response to appropriate antibiotics. His positive phase 2 Q fever immunofluorescence is characteristic of an acute infection; phase 1 is associated with the chronic form. As a follow up, transoesophageal echocardiogram after a prolonged course of antibiotics is normal, and the likelihood of Mr ID developing a chronic infection is extremely low.

His grandson experienced marked lethargy but became less ill than his grandfather and did not require hospital admission. This is common; 70% of children with Q fever infection remain asymptomatic.[2]

Human-to-human transmission of *C. burnetii* is rare[4] – isolation of cases is unnecessary – and many infected individuals remain asymptomatic or respond to common antibiotics. Despite this, Q fever is considered a potential agent for bioterrorism given the qualities of durable bacteria, high infection rates over long distances, varied routes of infection, multi-organ effects, difficulty with clinical diagnosis, and delays in both laboratory diagnosis and response to appropriate treatments.

## Q fever vaccine

Q fever vaccine, Qvax, is highly effective in preventing the disease. However, vaccination of those already exposed to Q fever can result in severe reaction, therefore a skin test is required before vaccination to assess previous exposure. The Q fever vaccine has been in short supply and the future of vaccine supplies was in doubt after CSL Limited announced in late 2005 that it would cease production of the vaccine on economic grounds. There is no other manufacturer of Q fever vaccine worldwide.

In November 2006 the Australian Commonwealth Government announced funding to vaccine manufacturer CSL Limited to build a specialised manufacturing facility at which CSL will manufacture the vaccine and provide screening tests under a 10 year contract to the government. Stocks of the vaccine will remain in short supply until the new facility is operational (probably 2008–

2009). Rationing of current stocks by CSL will continue until that time to those at highest risk – abattoir workers and those visiting abattoirs.

### Resources

- Australian Government Department of Health and Ageing. Immunise Australia Program. Q fever vaccine. Available at: www.health.gov.au/internet/immunise/publishing.nsf/Content/q-fever-qa#how
- Australian Q fever register. Available at www.qfever.org
- CSL Q fever and vaccination information. Available at www.csl.com.au/QFever.asp.

Conflict of interest: none declared.

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### References

1. Parker NR, Barralet JH, Bell AM. Q fever. Lancet 2006;367:679–88.
2. Walker DH, Raoult D, Dumler JS, Marrie T. Rickettsial diseases. In: Braunwald E, Fauci AS, Kasper D, et al, editors. Harrison's principles of internal medicine. 16th edn. New York: McGraw Hill, 2005;Ch 158.
3. Maurin M, Raoult D. Q fever. Clin Microbiol Rev 1999;12:518–53.
4. Kagawa FK, Wehner JH, Mohindra V. Q fever as a biological weapon. Semin Respir Infect 2003;18:183–95.

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