# Coxiella burnetti – Q fever

## **1. Overview & Taxonomy**

* Small, pleomorphic, **Gram-negative coccobacillus**.
* **Obligate intracellular** (replicates in acidic phagolysosomes of host cells, esp. macrophages).
* Two morphologic variants:
  + **Small Cell Variant (SCV)** — metabolically inactive, environmentally resistant; survives months–years in dust, wool, milk.
  + **Large Cell Variant (LCV)** — metabolically active.
* **Non-motile**, no flagella.
* **Antigenic phases** (LPS variation):
  + **Phase I** — smooth LPS, virulent, found in nature.
  + **Phase II** — rough LPS, avirulent, seen after in vitro passage.
* **Reservoirs**: sheep, goats, cattle (primary); also cats, dogs, wild mammals, birds, ticks.
* **Transmission**:
  + Aerosolised particles from birth products, urine, faeces, milk.
  + Raw milk ingestion possible (less common).
  + Very low infectious dose (~1 organism).
  + Rare human-to-human spread.
* **Epidemiology**: Worldwide; UK notifiable disease.

## **2. Laboratory Microbiology**

### **A) Safety**

* **Hazard Group 3** — highly infectious via aerosols. All culture or manipulation in **BSL-3** containment.

### **B) Growth & Culture**

* No growth on routine bacteriological media.
* Requires **eukaryotic host cells**: embryonated eggs, cell lines (e.g., Vero, L929, HeLa), or lab animals.
* Culture performed only in reference labs (never routine).

### **C) Staining**

* Gram stain: faint Gram-negative coccobacilli (often not seen).
* **Gimenez stain**: organisms stain red against green background.
* **Stamp stain** (modified Ziehl-Neelsen): organisms stain red.
* **Immunohistochemistry (IHC)**: detects antigen in tissue (valve, liver) — useful in culture-negative IE.

### **D) Molecular Diagnostics**

* PCR is **first-line in early acute infection** (before seroconversion).
* Best specimens:
  + EDTA blood or serum in early acute (<2 wks).
  + Tissue from valves, vascular grafts, aneurysms, liver biopsy in chronic disease.
* Limitations:
  + Sensitivity declines after 2 weeks in acute infection or after antibiotics.

### **E) Serology (IFA = reference standard)**

* Measures IgG/IgM to Phase I and II antigens.
* **Acute Q fever**:
  + High **Phase II** IgG ± IgM; Phase I low or absent early.
* **Chronic Q fever**:
  + High **Phase I** IgG (≥1:800; lab-specific cut-off), often high Phase II IgG too.
* Paired sera (2–3 weeks apart) may be needed — early samples can be negative.
* Cross-reactions: occasional low-level with *Legionella*, *Bartonella*, *Chlamydophila*.

### **G) Antimicrobial Susceptibility Testing**

* Not routine — obligate intracellular nature prevents standard MIC testing.

## **3. Clinical Syndromes**

### **A) Acute Q Fever**

* Incubation: ~2–3 weeks.
* Presentations:
  + Asymptomatic (≈50%).
  + Abrupt **flu-like illness**: fever, sweats, headache, myalgia.
  + **Atypical pneumonia**: non-productive cough, patchy infiltrates.
  + **Hepatitis**: fever, hepatomegaly, raised transaminases ± jaundice.
* Complications: meningoencephalitis, myocarditis, pericarditis.

### **B) Chronic Q Fever**

* Occurs in <5% of infections; months–years after acute phase.
* Risk factors: pregnancy, immunosuppression, valvular/vascular abnormalities, prosthetic valves/grafts.
* Most common form: **culture-negative endocarditis**.
* Others: infected aneurysm, vascular graft infection, chronic hepatitis, osteomyelitis.
* High mortality untreated.

### **C) Q Fever in Pregnancy**

* Higher maternal and fetal risks: miscarriage, stillbirth, preterm delivery.
* Chronic infection risk increased.

## **4. Diagnosis – Practical Summary**

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| **Scenario** | **Best test(s)** |
| Early acute (<14 d) | PCR on EDTA blood ± serum |
| Acute (>14 d) | Serology (rise in Phase II IgG/IgM) |
| Chronic Q fever | Serology: high Phase I IgG ≥1:800 ± PCR on tissue |
| BCNIE / vascular | Coxiella + Bartonella serology; PCR on valve if available |

## **5. Treatment**

### **A) Acute Q Fever**

* Adults: **Doxycycline 100 mg bd × 14 days** (7 days may suffice for uncomplicated pneumonia; use 14 days if hepatitis).
* Pregnancy: **Co-trimoxazole 160/800 mg bd** until delivery (stop ~32–36 wks to avoid folate antagonism).

### **B) Chronic Q Fever (IE/vascular infection)**

* **Doxycycline 100 mg bd + Hydroxychloroquine 200 mg tds**
  + Duration: ≥18 mo (native valve), ≥24 mo (prosthetic/graft).
  + Monitor HCQ levels (target 0.8–1.2 µg/ml) and retinal toxicity.
  + Follow Phase I IgG titres — falling titres suggest cure.
* If HCQ contraindicated: doxycycline + fluoroquinolone (less effective).

### **C) Post-Exposure Prophylaxis**

* For high-risk exposures (e.g., pregnant lab worker): **Doxycycline 100 mg daily × 5–7 days** within 8–12 days post-exposure.

## **6. Prevention & Control**

* No UK-licensed human vaccine (Q-Vax in Australia; whole-cell inactivated; requires pre-vaccine screening).
* Animal control: manage birthing products, pasteurise milk, vaccinate animals in endemic areas.
* Lab: strict BSL-3 containment for culture/high-risk specimens.

## **7. Exam Pearls**

* Always request **Coxiella + Bartonella serology** in BCNIE.
* Chronic Q fever = **high Phase I IgG** — a **major Duke-ISCVID criterion** for IE.
* PCR from blood is **early-phase only**; tissue PCR preferred in chronic disease.
* Pregnancy: treat until delivery even if asymptomatic (to reduce fetal loss).
* Phase I vs Phase II serology differentiation is a favourite exam question.
* Extremely infectious: single organism can cause disease; lab safety is critical.