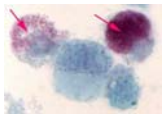
Coxiella burnetii, and Q fever

(in humans)

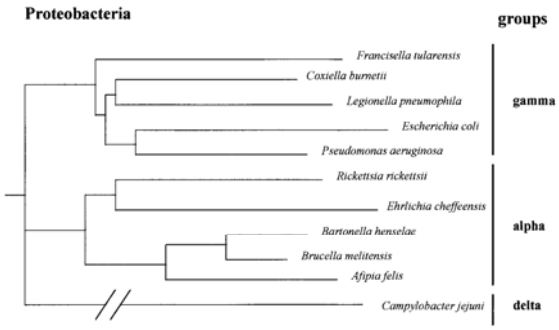
Bacteriology

- «Gram negative», not-stained with Gram
- Gimenez staining



- 0.2-0.4 mm wide, 0.4-1 mm long
- initially mis-classified in the *Rickettsiales* order (strict intracellular, tick-borne)

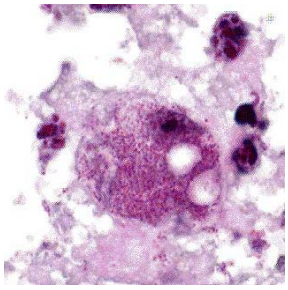
Bacteriology



Facultative versus obligate

Legionella pneumophila

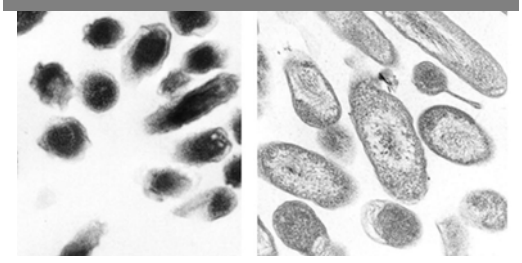
Coxiella burnetii



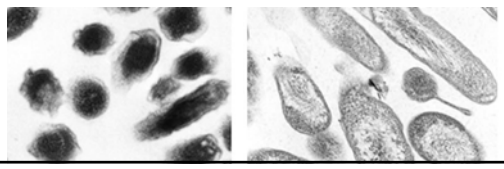
Developmental stages

small cell variant (SCV): resistant stage
large cell variant (LCV): replicative stage, larger

SCV **LCV**



SCVs	LCVs
0.2–0.5 μm	⩾1.0 μm
Rod shaped	Pleomorphic
Condensed chromatin	Dispersed chromatin
Low metabolic activity *in vitro*	High metabolic activity *in vitro*
Infrequent replication	Active replication
Infects cultured cells	Infects cultured cells
Stable in environment	Mechanically fragile

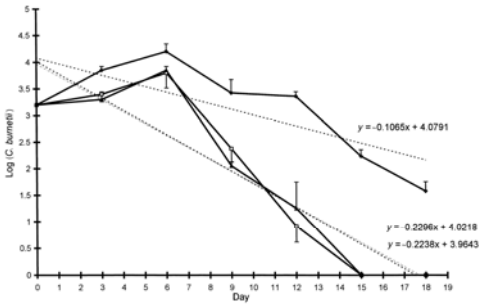


SCV: resistance +++

Coxiella burnetii **may survive:**
- **40 months in milk at room temperature**
- **2 years at - 20°C**
- **7 to 9 months at 20°C**
- **to high variation of pH**
- **30 minutes at 60°C**
- **to dessiccation**
- **to various biocides**

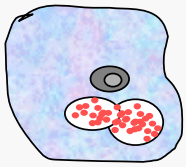
➡ **Bioterrorism agent**

Coxiella may survive in *Acanthamoeba* during more than 16 days …

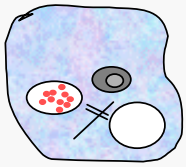


La Scola *et al.* CMI 2001

Adaptation to macrophages



Coxiella burnetii**: survive to acidic pH of the lysosome**



Legionella pneumophila**: prevent the fusion of phagosome & lysosome**

Genome of *Coxiella burnetii*

- 1.995.275 bp
- Different from strain to strain
- phase of reductive evolution with gene decay/gene loss

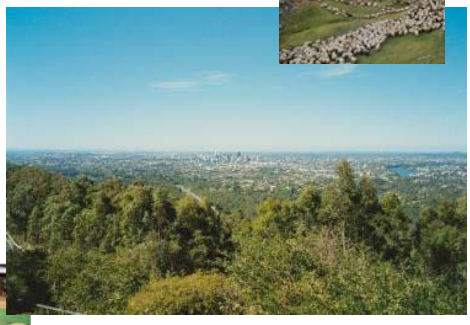
4 types of plasmids have been identified corresponding to 4 genotypes associated :
- to different types of lipopolysaccharidiques,
- to different growth kinetics, and potentially
- to different pathogenic potential (?)

Reshadri R, Paulsen IT, Eisen JA, Read TD, Nelson KE, Nelson WC, Ward NL, Tettelin H, Davidsen TM, Beanan MJ, Deboy RT, Daugherty SC, Brinkac LM, Madupu R, Dodson RJ, Khouri HM, Lee KH, Carty HA, Scanlan D, Heinzen RA, Thompson HA, Samuel JE, Fraser CM, Heidelberg JF. Complete genome sequence of the Q-fever pathogen *Coxiella burnetii*.

Proc Natl Acad Sci U S A. 2003 29;100(9):5455-60.

Let's go to Brisbane



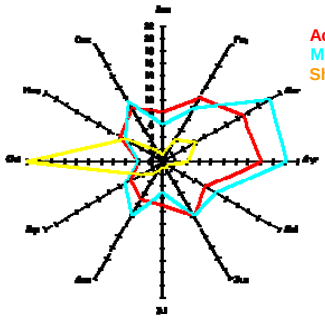



- **Brisbane, 1937**
- **Bagnes (Switzerland) 1983: 415 cases**
- **Briançon (France) - juin 1996 :**
  29 cas exposition à l'abattoir
- **Drôme – 2000 :**
  10 cases: goats
- **Chamonix – juin 2003:**
  92 cas certains: sheep

Q fever

- **Zoonose**
- Sheep / goats / bovines
- **Aerosols** (wind)
  - Placental infection with abortion
  - Chronically excreted in milk, feces, …

Wind



Tissot-Dupont H, Torres S, Nezri M, Raoult D. Hyperendemic focus of Q fever related to sheep and wind. Am J Epidemiol. 1999 Jul 1;150(1):67-74

Clinical presentation

- **60% asymptomatic**

- **40% sympomatic**
  - **38% flu-like disease**
  - **2% hospitalised**
    - **1.8% acute Q fever: - fever**
      - headache
      - atypical pneumonia
      - hepatitis
    - **0.2% chronic Q fever**

Evolution

- Incubation: 2 to 3 weeks
- Acute Q fever last for 2 to 14 days, with a spontaneous healing in most cases
- **Chronic form especially if valvulopathy, anevrysm ou valvular prosthesis, or immunosuppression**
- Pregnancy :
  - risk of miscarriage (1st trimester)
  - risk of preterm delivery

Chronic Q fever

	No. of Identified Cases	
	(n = 313)	%
Endocarditis	229	73
Vascular infection	25	8
Pregnancy (mothers and babies)	20	6
Chronic hepatitis	8	3
Osteoarticular infection	7	2
Chronic pericarditis	3	1
Adenopathies	1	<1
Splenic pseudotumor	1	<1
Lung pseudotumor	1	<1
Chronic neuropathy	1	<1
No identified foci	6	2

Raoult 2000

Determinants of the outcome of *Coxiella* infection

1. Mode of infection (digestive route vs aerosols)
2. Inoculum (dose)
3. Virulence (strain)
4. Cytokines (balance)
5. Host factors:

   Pregnancy, immunosuppr., valvular anomaly

Antigenic variations

Similar to smooth-rough variation in *Enterobacteriaceae*

Phase 1

natural phase,

smooth LPS, highly infectious

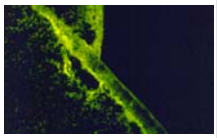
Phase 2

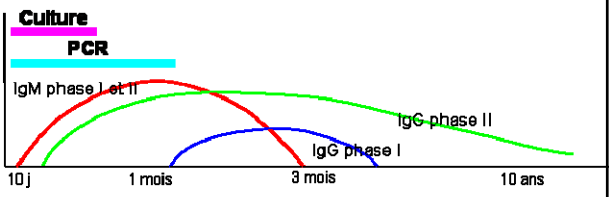
obtained in vitro (cell culture, eggs)

rough - truncated LPS,

sugar composition is different

Diagnostic: serology



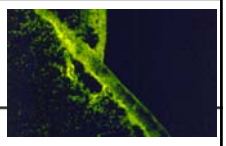


Phase 2
Acute Q fever

Phase 1

Unité des Rickettsies / IFR 48 website

Diagnostic: serology



Phase II antibody titer		Phase I antibody titer (IgG)	
IgG	IgM		
≤100			No active Q fever
≥200	≥50		Acute Q fever
		≥1:800	Chronic Q fever
		≥1:1,600	Chronic Q fever

Phase 1: natural, **Phase 2** in vitro (cell culture)

Tissot-Dupont H. Clin Diagn Lab Immunol. 1994 Mar;1(2):189-96

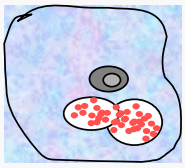
PCR home-made in Lausanne

- Excellente specificity: no false positive among 200 samples blindy tested
- Retrospective analysis of 300 cases with an atypical pneumonia : 1 single positive sputum
- Sensitivity of 89% on valve samples [received from D. Raoult (Marseille)]
- Amplification of DNA of *C. burnetii* in the serum

Treatment of chronic form

- **Importance of replicative niche:**

low pH → add hydroxycloroquine



***Coxiella burnetii*: survive to acidic pH of the lysosome**

Raoult et al. 1999

Conclusions

- **Zoonotic infection**
- **Severe chronic disease**
- **Poorly studied pathogenesis (except the immunopathogenesis)**
- **Important and useful to better understand the biology of this strict intracullar bacteria**