Serological diagnostic of Q fever

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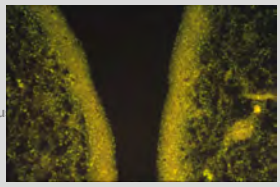


Coxiella burnetii phase 1 et 2

- Phase variations (phase 1 – 2). The natural bacteria is described as *C. burnetii* phase 1. It is protected by a layer of low antigenic lipo-polysaccharides. The highly antigenic *C. burnetii* phase 2 is artificially produce by multiple passages in cultures with modification of the lipo-polysaccharides surface (truncated LPS).
- This phase 2 antigen is very useful for early diagnostic of Q fever.
- Quality of serology depends on quality of *C. burnetii* phase 1 and 2 antigens

Acute Q fever

1. Latency period 2-3 weeks
2. Abrupt appearance of symptoms with fever >38.5, myalgia, headache and asthenia
3. The disease resolves spontaneously with a prolonged period of convalescence. Doxycycline treatment shorten the symptoms but the convalescence period.
4. Early antibiotic treatment does not seem to cut development of antibodies (seroconversion, as far as we know).

Chronic Q fever

Slow course of the infection

- Endocarditis (negative culture)
- Infection of vascular endothelium (heart valves, aneurism, vascular prosthesis…)
- Granulomatous hepatitis
- Matrix – placenta

Symptoms: malaise, intermittent fever, night sudation…

Diagnostic tools for acute and chronic Q fever

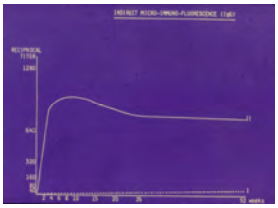
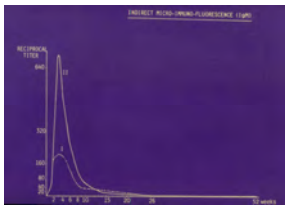
- Serology (MIF, ELISA, CF): *C. burnetii* phase 1 and 2 (IgG and IgM antibodies are detectable within the first week of disease). Serology is essential for the diagnostic of chronic Q fever (IgG, IgM and IgA).
- Culture (labo P3) + IF
- PCR on serum or plasma: acute Q fever (positive before emergence of IgG)
- PCR on serum ou plasma: chronic Q fever
- PCR on aortic valves or biopsies

Serology : acute Q fever

- IF IgM: appears 4-10 days to *C. burnetii* phase 1, or phase 2 or both

Dupuis et al , JCM 1985, 22:484-7

- IF IgG: appears 3-5 days after IgM to *C. burnetii* phase 2 only
- Quick rise of antibodies IgG and IgM (3-5 days interval allows to detect IgG seroconversion or increasing titers)
- By the 3rd week IgM decrease
- IgG to *C. burnetii* phase 1 may appear within 3-4 weeks

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Serology : Past Q fever

- 1 year after the acute episode 95% of people still had IgG antibodies to *C. burnetii* (by IFA).
  - 2 years 91%
  - 6 years 82%
  - 10 years 69% of people were still positive.

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Serology: acute Q fever

- Examples:

	Cb1/Cb 2		Cb1/Cb 2	PCR	Diagn.
IgG	<20/320	IgM	80/160	neg	acute Qf?
1 week later					
IgG	<20/5'120	IgM	160/640	neg	
IgG	<20/<20	IgM	<20/80	++	acute Qf
3 days later					
IgG	<20/40	IgM	<20/640	neg	
IgG	80/640	IgM	80/40		past Inf.
IgG	<20/<20	IgM	<20/640	neg	ac. Qf ?
2 weeks later					
IgG	<20/<20	IgM	<20/640	neg	no Qf

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Serology: chronic Q fever

- Elevated IgG to *C. burnetii* phase 1 and 2 (≥1/2560 and usually phase 1 > phase 2)
- IgA to *C. burnetii* phase 1
- IgM may be detected
- PCR positive (on first serum sample)

Example:

	Cb1/Cb 2		Cb1/Cb 2		Cb1/Cb 2	PCR
IgG	40'960/20'480	IgM	80/160	IgA	320/40	pos

PCR *Coxiella burnetii*

- PCR publication Tillburg J.H.C. et al JCM 2010,48:3923-7
- Sequences target the transposase gene of the *C. burnetii* IS1111a insertion element.
- The multicopy IS1111a insertion element is present in 20 to 100 copies in the genome of *C. burnetii*
- High sensitivity of this PCR assay

PCR *C. burnetii on serum samples*

- Acute Q fever 20/22 cases of sero-conversion (old samples)
- 6/6 new cases

Global sensitivity 92.8%

- Chronic Q fever 21/22 cases (old samples)
- 4/4 new cases

Global sensitivity 96.2%

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Conclusion

- Serology and immunofluorescence in particular, is the method of choice for the diagnosis of acute and chronic Q fever.
- PCR is an additionnal method useful for both acute and chronic stages of Q fever (serum, plasma, biopsy).

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