Q-fever in the Netherlands
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notified cases of Q fever in NL, 2007-2009
Netherlands 2009: largest outbreak of Q fever ever
What is Q-fever?

An infectious disease of animals and a zoonosis of humans, world wide.

Causative agent: *Coxiella burnetii* (‘Query-fever’)
- a small, intracellular bacterium,
- spores, able to survive 40 months in environment

Reservoir: rodents, birds, farming animals, cats, dogs, insects (ticks)

Sheep, goats and cattle = main reservoir for human infection.
- excretion via dung, urine, milk, saliva, etc. placental tissue = highly infectious
- dried excreta: air-borne spread of spores from stables, wool, farming land.

Infection of humans via:
- Inhalation of spores (most frequent)
- Consumption of contaminated food (rare)
- Tick bite (incidental)
Symptoms of Q-fever

**Humans:**

50-60% asymptomatic infection

20% flu-like: head ache, fever, nauseous, muscle pain.

20% serious disease: persisting fever, chest pain, severe head ache, diarrhoea, vomiting, **often:** atypical pneumonia.

rare: hepatitis, pericarditis, meningo-encephalitis

3-5%? chronic infection (endocarditis): 1-11% *

• Increased risk if: pregnant; cor vitium; vascular disease.
• Pregnant women: abortion, premature birth.

**Ruminants:**

asymptomatic, abortion, premature birth
Diagnosis and treatment

first 2 weeks of disease: PCR on Cb DNA in serum
week 3 and later: serology (IgM, IgG; phase 2 and 1)

doxycycline 1 dd 200 mg, 14 days
the origin of Q fever in NL:

3 years of air borne spread of *Coxiella burnetii* spores from infected dairy goat farms
an example:

42 hospitalised patients in the surrounding area

De geitenmelkerij in het Zuid-Limburgse Voerendaal. (foto: Chris Keulen)

"Voerendaal is ziek van de geitenboerderij", NRC 11 december 2009.
1 report of transfusion transmitted Q fever in 1977
Q fever: policy of Sanquin Blood Transfusion Service

- Dutch Health Counsil (Gezondheidsraad): 'Q fever is not a threat to the safety of blood'.

in 2009 Sanquin decided to:

- study silent/incubating Coxiella infection among blood donors

- develop a Coxiella screeningstest based on PCR
  (started on March 15th 2010: routine screening of donations from high risk areas by PCR)
Q fever study by Sanquin

Samples:
- serum sample from all donations by consenting donors, collected at 6 collection stations, in the area most affected by Q fever in the two previous years. (November 2009: ~25,000 frozen samples)

a) November 2009: selection of 1000 'hottest' samples: PCR

b) 559/1000: serial (follow-up) samples available: serology in progress

Assays:
- real time PCR targeting insertion element IS1111 (transposase, 7-120 copies per genome); see Schneeberger et al., Clin. Vaccine Imm. 2010; 17(2): 286-290.

- serology: IgG and IgM, against phase 1 and 2 antigens, using both ELISA (Serion) and IFA (Focus, Cypress, CA).
Legenda

- inzamelcentrum met Q-monitoring
- inzamelcentrum zonder Q-monitoring

Q-koorts incidentie (aangegeven gevallen):
- 1 / week
- 2-5 / week
- 5-10 / week
- >10 / week
part 1: *C. burnetii* PCR on 1000 at risk donations:

6 reactive samples
(weak signals, high Ct values):
<table>
<thead>
<tr>
<th>donor</th>
<th>date</th>
<th>PCR Ct</th>
<th>IFA titles</th>
<th>Conclusion</th>
</tr>
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<tbody>
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<td>1 donor A (Landerd)</td>
<td>26-5-2009</td>
<td>35.0</td>
<td>&lt; 1:32 (4x)</td>
<td>early infection</td>
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<td>fase 1 IgG 1:32</td>
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<td>fase 1 IgM 1:256</td>
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<td>fase 2 IgG 1:512</td>
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<td>fase 2 IgM 1:256</td>
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<tr>
<td>2 donor B (Bernheze)</td>
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<td>fase 1 IgG 1:512</td>
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<td>fase 2 IgG 1:512</td>
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<td>fase 2 IgM &lt; 1:32</td>
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<td>11-9-2009</td>
<td>negative</td>
<td>fase 1 IgG 1:128</td>
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<td>fase 2 IgM &lt; 1:32</td>
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<td>4 donor D (Bernheze)</td>
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<td></td>
<td>10-12-2009</td>
<td>negative</td>
<td>&lt; 1:32 (4x)</td>
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Q study by Sanquin

part 1: *C. burnetii* PCR on 1000 at risk donations:

- non-infectious Q DNA fragments present in blood?

- transfusion of fresh PCR+ donation into Q-negative mice

- 2 of the 3 PCR+ donations have been used:
  1 recipient has been tested by ELISA and IFA: IgG +++, IgM borderline (T=10m)
part 2: *C. burnetii* serology on 559 series of samples:

in progress.
last sample of each series tested by IgG phase 2 Serion ELISA:
444 series tested:
  387/444 = neg
  57/444 = pos in last sample;
  13/50 = neg in first sample
(to be confirmed by IFA)

→ high seroprevalence (13%) and high seroconversion rate (3%)

→ specificity: random donors from North Holland province: 92/92 = neg
part 3: look back (by dr. Marian van Kraaij):

- 8 donors notified their blood bank: (lab confirmed) Q fever within 3 weeks after donation (mean 13, range 5-22 days)

- PCR on repository samples of last donation:
  1/8 PCR positive (recipient: terminal patient, not tested)

- 6 recipients (PCR- donors):
  2/6 positive IgG serology:
    1x known with diagnosed Q fever before transfusion
    1x persisting IgG, no clinical signs, living in endemic area
Q fever and Dutch blood donors: *summary and questions*

- 2 possible cases of transfusion transmitted Coxiella infection.
  - specific IgG in 2 recipients:
    - 1x PCR positive donor (study)
    - 1x PCR negative donor (look-back) who reported Q fever after donation

- High seroprevalence and seroconversion rate among local donors.

- DNA-aemia = infectious bacteraemia?

- Risk of breathing in Brabant overshadows the risk of transfusion?

- Is the sensitivity of screening test (PCR) sufficient?

2010:
- screening of at-risk donations since March 15th: negative
- no increase (yet) of notification or clinical cases
Sanquin

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JBZ, RIVM, St.AH

Peter Schneeberger
Mirjam Hermans
Wim van der Hoek
Frederika Dijkstra
Erik van Hannen
Blood collection in East Brabant

in affected area in 2008, during 6 months:
38,420 full blood donations and 21,410 other donations