Immune response against Coxiella burnetii in Chronic Q-fever

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The principal goal of this study is to identify whether and how innate immune host factors predispose to the development of chronic Q-fever.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Bacterial infectious disorders
Study type	Observational invasive

Summary

ID

NL-OMON35955

Source
ToetsingOnline

Brief title
Immune response against Coxiella burnetii in Chronic Q-fever

Condition

- Bacterial infectious disorders
- Aneurysms and artery dissections

Synonym
chronic Q-fever, Coxiella burnetii infection

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: ZonMW

Intervention

Keyword: coxiella burnetii infection, host factors, immune response, Q-fever

Outcome measures

Primary outcome

1. Circulating cytokine profiles in serum of patients during different stages of the various clinical manifestations of Q-fever.

2. In-vitro recognition and signalling pathways, cytokine pattern, Th-cell differentiation and macrophage polarisation of peripheral blood immune cells and immune cells isolated from aneurismal aorta wall, after stimulation with C. burnetii components.

3. Immunohistochemical properties of immune cells in aorta specimens of (Coxiella-infected) AAA patients and mRNA analysis for genes encoding proteins involved in the recognition and signalling of C. burnetii.

4. Polymorphisms in innate and adaptive immune response genes that may be related to the susceptibility and/or the development of a clinical manifestation of Q-fever.

Secondary outcome

n.v.t.

Study description

Background summary

In the recent Q-fever outbreak in the Netherlands about 10.000 individuals have been exposed to Coxiella burnetii, the bacterium that causes Q-fever. In 2-5% of these individuals chronic disease develops, in which Coxiella burnetii persists at endovascular foci causing endocarditis or mycotic aorta aneurysm, or - in pregnant women - placentitis. Chronic infection with C. burnetii has a poor prognosis. It is currently unknown which host factors influence Q-fever susceptibility and the progression to chronic, life-threatening disease. We hypothesize that host factors in immune response against C. burnetii are important in development of chronic Q-fever.

Study objective

The principal goal of this study is to identify whether and how innate immune host factors predispose to the development of chronic Q-fever.

Study design

A case-control study will be performed in the Radboud University Nijmegen Medical Centre (RUN-MC). The duration of the study is 3 years. Patients and controls will be recruited from the RUN-MC and collaborating hospitals. We will use several approaches to investigate innate immune factors in Chronic Q-fever:

1. In sera from patients suffering from acute and chronic Q-fever, circulating cytokines belonging to the T helper (Th)1, Th2, Th17 and T regulatory cell types of response will be measured.

2. In-vitro experiments will be performed to determine the innate immune response to C. burnetii systemically of peripheral blood cells from patients.

3. The same experiments will be performed to determine the innate immune response to C. burnetii locally of immune cells in aneurismal aortic wall.

4. Genetic variations in the innate and adaptive immune response genes will be assessed in DNA samples of individuals displaying the complete spectrum of clinical manifestations.

Study burden and risks

Burden:
- For patients: collection of extra blood, if possible during regular blood sampling. This comprises a maximum of 1 heparin tube à 5 ml and 4 EDTA tubes à 10 ml and 1 serum tube à 3.5 ml.
- For controls: the same as for patients, but blood sampling for the purpose of this study only will be necessary in all cases.

- One specific group of newly diagnosed chronic Q-fever patients starting on treatment (n=10) (part 2ii) collection of extra blood repeatedly during regular blood sampling for follow up. This comprises 1 heparin tube à 5 mL at each 3 monthly control, plus 4 EDTA tubes à 10 mL at each 6 monthly control for a maximum duration of 2 years.

Risks:
- No risks other than local hematoma are related to venous puncture.
- No risks are involved in obtaining the surgical specimens in (Coxiella-infected) AAA or AOD patients. This will be rest material obtained during open surgery of the aortic wall.

Benefit:
There will be no benefits for the subjects enrolled in this study.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Elderly (65 years and older)

Inclusion criteria

Chronic Q-fever patients:
- Proven or probable chronic Q fever according to the recent consensus of the Dutch workgroup on Q-fever;Q-fever fatigue syndrome (QFS) patients:
- Laboratory-proven acute Q fever in the 3 years before presentation and/or positive serology fitting a past infection with Coxiella burnetii
- AND being severely fatigued, defined by scoring 35 or higher on the subscale fatigue severity of the CIS
- AND being fatigued for at least 6 months;Patients with past Q-fever infection without chronic infection or QFS
- A history of laboratory-proven acute Q-fever infection by either PCR on sera or serology fitting acute infection
- No chronic sequelae at least after 12 months of follow up;Healthy serologic negative volunteers:
- Negative Q-fever serology;Vascular patients with chronic Q-fever undergoing surgery for infected atherosclerotic aorta aneurysm (AAA) :
- Proven chronic Q-fever infection with infection of the vascular wall seen on CT, PET-CT or ultrasonography
- Necessity of resection;Vascular patients undergoing surgery, either with AAA or AOD
- For patients with uninfected AAA: An aneurysm of the aorta abdominalis for which resection with prosthetic replacement is necessary
- For patients with AOD: An obstructive defect in the aorta or iliacal artery for which resection with prosthetic replacement is necessary ;Seropositive individuals reporting no history of Q-fever
- Serology fitting past infection
- No reported history of acute Q-fever ;Seropositive individuals with a history of acute Q-fever
- A history of proven acute infection by either PCR on sera or serology fitting acute infection
- No chronic sequelae at least after 12 months of follow up;Seropositive individuals with QFS
- Laboratory-proven acute Q fever in the 3 years before presentation and/or positive serology fitting a past infection with Coxiella burnetii
- AND being severely fatigued, defined by scoring 35 or higher on the subscale fatigue severity of the CIS
- AND being fatigued for at least 6 months;Seropositive indivuals with chronic Q-fever
- Proven or probable chronic Q fever according to the recent consensus of the Dutch workgroup on Q-fever;Seronegative individuals (controls) living in the endemic area without a history of Q-fever
- Negative Q-fever serology
- Living in endemic area

Exclusion criteria

Age <18 years

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-08-2011
Enrollment:	990
Type:	Actual

Ethics review

Approved WMO Date:	19-07-2011
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	17-11-2011
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	24-01-2014
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	28-04-2015
Application type:	Amendment

Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	06-04-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	19-01-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL35784.091.11