Q-fever Fatigue Syndrome (QFS) - a relation with upper respiratory tract infections?

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To see whether C. burnetii is able to induce epigenetic changes in monocytes, resulting in a more distinct pro-inflammatory response to re-stimulation with viral particles, to see whether these changes are present in circulating monocytes of QFS...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON42875

Source
ToetsingOnline

Brief title
QFS - Upper respiratory tract infections

Condition

- Other condition
- Bacterial infectious disorders

Synonym
Chronic Fatigue, Q fever Fatigue Syndrome

Health condition

Chronische vermoeidheid

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: Stichting Q-support (via de overheid)

Intervention

Keyword: Q fever, Q fever Fatigue Syndrome, upper respiratory tract infections epigenetics

Outcome measures

Primary outcome

1. Cytokine concentrations of monocytes (from healthy blood donors) that were

trained with C. burnetii and re-stimulated with several viral particles, and of

monocytes, from QFS patients, that were stimulated with several viral particles.

2. Histone modifications surrounding the promoter regions of set cytokines,

after training with C. burnetii in healthy blood donors and in QFS patients.

Secondary outcome

3. Outcomes of SIP and CIS questionnaires on limitations and fatigue, related

to cytokine concentrations and histone modifications.

4. Clinical description of complaints / symptoms of QFS patients.

Study description

Background summary

Up to 20% of patients that are diagnosed with acute Q fever will develop Q fever fatigue syndrome (QFS), a state of prolonged fatigue that often coincides with muscle ache, painful joints, headache, memory loss, loss of concentration, and frequently recurring upper respiratory tract infections. The latter is an interesting phenomenon that might be explained by the concept of trained immunity. The theory behind trained immunity is that myeloid innate immune cells can be epigenetically reprogrammed by (infectious) stimuli, making their response to a second (infectious) stimulus more pro-inflammatory. Since Coxiella burnetii is known to reside and divide in monocytes and macrophages,

it is likely that this bacterium is able to reprogram the epigenetic makeup of these cells and induce trained immunity. Secondary stimuli such as viral respiratory tract infections could then induce a more distinct pro-inflammatory reaction, giving the patient the sensation of more frequently recurring and more severe upper respiratory tract infections. We would like to investigate this theory through in vitro and ex vivo models.

Study objective

To see whether C. burnetii is able to induce epigenetic changes in monocytes, resulting in a more distinct pro-inflammatory response to re-stimulation with viral particles, to see whether these changes are present in circulating monocytes of QFS patients and to see whether these changes can be reversed with epigenetic drugs.

Study design

this experimental case control study will be performed at the Radboudumc, Nijmegen. The duration of the study is 1 year. In total, 10-15 QFS-patients and 10-15 healthy controls will be recruited. The study will consist of three modalities:

1. In vitro training experiments with C. burnetii, re-stimulating with several viral particles.
- Measure monocyte cytokine concentrations upon re-stimulation with viral particles and measure histone modification surrounding the promoter regions of these cytokines.
2. Investigate the presence of set histone modifications in an ex vivo model of QFS patients that experience frequent upper respiratory tract infections since their acute Q-fever infection.
3. Investigate whether these histone modifications can be reversed with epigenetic drugs in ex vivo models of QFS patients that experience frequent upper respiratory tract infections since their acute Q-fever infection.

Study burden and risks

Burden:
- Collection of 7 tubes of EDTA blood (10ml) and for healthy controls 1 serum tube (3.5mL).

Risks:
- No risks other than a local hematoma related to a single venous puncture.

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

QFS patients (n = 10 - 15)
- Meet the LCI guideline on QFS criteria for QFS
- Age >= 18
- Self report of frequent upper respiratory tract infections on outpatient clinic (>= 3 upper respiratory tract infections a year).;Healthy individuals (n = 10-15)
- Age >= 18

Exclusion criteria

QFS patients (n = 10 - 15)
- No use of immune suppressive medication in the past 3 months;Healthy individuals (n =

10-15)
- No past Q-fever infection (serology)
- No chronic Q-fever
- No Q-fever vaccination
- No use of immune suppressive medication in the past 3 months

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:	Recruitment stopped
Start date (anticipated):	30-05-2017
Enrollment:	30
Type:	Actual

Ethics review

Approved WMO

Date:	04-04-2017
Application type:	First submission
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	NL60241.091.16