Q Herpen II, Post outbreak screening in a Q fever high incidence area for late consequences of Q fever including chronic Q Fever.

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

Summary

ID

NL-OMON38602

Source
ToetsingOnline

Brief title
Q Herpen II

Condition

- Bacterial infectious disorders

Synonym
Q fever

Research involving
Human

Sponsors and support

Primary sponsor: GGD Hart voor Brabant

Source(s) of monetary or material Support: Ministerie van Volksgezondheid, Welzijn en Sport (VWS),Ministerie van VWS

Intervention

Keyword: chronic Q fever, high incidence, Q fever, screening

Outcome measures

Primary outcome

1. IgG phase I antibody titre as measured with IFA (seroprevalence of C.burnetii)

2. Presence (or not) of *possible* chronic Q fever* with a safety margin for those with a risk factor (see comment below).

3. Presence (or not) of severe fatigue/other morbidity of those that have or have not been infected with C. burnetii

*There is no international consensus on the definition of chronic Q fever (Wielders et al 2013) and different IFA antibody titre cut-off point are applied. "Possible" chronic Q fever is defined by the Dutch Q fever Consensus Group as an IFA antibody titre against IgG phase I of C. burnetii >=1:1024 (Wegdam-Blans et al. 2012). The diagnosis *possible* or *proven* chronic Q fever can only be made after referral to a Q fever centre as this requires PCR test results, and a specialist medical assessment of clinical symptoms, risk factors and diagnostic imaging results, in addition to the IFA titre. In this study (as in other current studies) we apply a safety margin for those with a known risk factor with an IgG phase I >= 1:512 (one IFA titration step lower).

Secondary outcome

1. Height of cytokine response to C. burnetii as measured by IFNg test

2. Health status as measured by scores in NCSI and EQ-5D

Other study parameters:

Characteristics of participants, including age, sex, ses, comorbidity, and proximity to putative source(s) (farms). Information on these variables will be related to the outcome measures described under the primary and secundary study parameters.

Study description

Background summary

Between 2007 and 2010 the province of Noord Brabant, the Netherlands experienced the largest Q fever outbreak described in the world. The number of notified cases (acute symptomatic cases) according to the national notification records, exceeds 4.000. Chronic Q fever and Q fever fatigue syndrome (QFS) are serious sequels of acute infection documented among notified cases. However, the large majority of people with an acute Coxiella burnetii (C. burnetii) infection present no symptoms or only mild illness, for which they seek no medical care. The risk for chronic infection in this group is unknown but patients diagnosed with chronic Q fever in the Netherlands often lack a history of acute illness. Therefore it is possible that chronic infections remains undetected until serious illness occurs.

The village of Herpen in Noord Brabant experienced the first large Q fever outbreak in the Netherlands. An earlier study in this village in 2007, just after the first outbreak, found that 16.5% (73/443) of participants had - unbeknownst to them - recently been infected with C.burnetii.

General practitioners (GP*s) and Q-uestion (patient organisation of people that have been infected with Q fever) repeatedly expressed their concern that Q fever infected individuals (even though their initial infection was asymptomatic) might suffer chronic Q fever or other morbidity caused by Q fever. If this is indeed the case or not can only be established through further research. These groups were instrumental in requesting further research and were from an early stage involved in the conception of this study idea and

fundraising.

In the present Q-Herpen II study this village (population 2.820) will serve as a sample population for the Q fever stricken population in Brabant. Screening the adult population in this village with a high Q fever incidence regardless of their Q fever status- will enable us to identify patients with possible chronic Q fever or other Q fever related morbidity. These participants are unaware that they are at risk as their past Q fever infection was asymptomatic /undiagnosed.

Study objective

This study will provide a robust estimate of the prevalence of C. Burnetii exposure and possible chronic Q fever among asymptomatic participants. This is important in order to assess whether population screening in a high incidence area is useful and should be expanded to other areas. Furthermore these study data will establish whether asymptomatic/mild C.burnetii infection has an effect on the health status and fatique status as measured with the NCSI (Nijmegen Clinical screening instrument) a standardised instrument for the health status (includuing the fatigue status) and the EQ-5D (a standardised instrument for use as a measure of health outcome http://www.euroqol.org/)

Another objective is to provide clarity where uncerntainty reigns. Hopefully this thorough study will put worries and concerns to rest.

An adequate diagnosis, even after 6 years, will result in referral to a specialist centre and, if needed, treatment and monitoring.

Study design

A cross sectional population-based study among the adult inhabitants (18 and older) of a Q fever high incidence area. The sample high incidence area is the village of Herpen (postal code 5373; total population 2.820) in the municipality Oss. Based on data of the municipal administration all approximately 2.200 inhabitants - age 18 and older - will be posted a questionnaire on awareness of their Q fever status, Q fever testing history, underlying disease, risk factors, and health status (NCSI and EQ5D). Participants receive a laboratory form for one venipuncture for 2 test tubes (10 ml) (tests IFA and IFNg=Q-Detect) together with an invitation with an proposed day and time for blood drawing at a location in the village.The GGD (Municipal Health Service) will offer six blood drawing opportunities over a period of one week.
For those that were unable to participate during the first round a second and last opportunity will be offered 3-5 weeks later with two blood drawing sessions. Tests are offered free of charche.

An adequate diagnosis, even after 6 years, will result in referral to a specialist centre and, if needed, treatment and monitoring. Furthermore we will compare the Health Status (including the fatigue status using the NCSI (Nijmegen Clinical screening instrument) and EQ-5D (a standardised instrument for use as a measure of health outcome http://www.euroqol.org/) for the of participants in this sample.

Data are analysed in SPSS and corrected for confounders, age, sex, SES, underlying disease, smoking etc.

Study burden and risks

The burden for participation consists of;
1. Filling out a questionnaire (10 to 35 minutes- after testing) (sent by post) on the participant*s awareness of his/her Q fever status, Q fever testing history, underlying disease, risk factors, and health status.
2. Donation of two blood samples (6 and 4 ml respectively) during one venipuncture, during one visit to a convenient location in the village.
The venipuncture will be executed by trained staff and poses a minimal burden and no significant risks.

Benefits
Patients with an IFA suggestive of possible Q fever will require further examination. Since not all patients with a high IFA have proven chronic Q fever this may cause psychological discomfort due to uncertainty of the final diagnosis. A high/low IFA value in combination with a low or high IFNg response, will aid the diagnosis *possible* Q fever.
The benefit for participants is that those with an asymptomatic chronic infection are identified and referred to a specialist centre.

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

Resides in the postal code area 5373 and
is 18 years of age or older and
of sound mind and judgement

Exclusion criteria

Living outside postal code area 5373 or
younger than 18 years of age or
not of sound mind and judgement

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-02-2014
Enrollment:	2200
Type:	Actual

Ethics review

Approved WMO

Date:	19-11-2013
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	NL45224.041.13