Ixodes: exploration of a cell mediated immunity test for the early detection of Borrelia infection

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

Summary

ID

NL-OMON47121

Source
ToetsingOnline

Brief title
Ixodes: catching Borrelia early on

Condition

- Bacterial infectious disorders

Synonym
borreliosis, Lyme Disease

Research involving
Human

Sponsors and support

Primary sponsor: Innatoss Laboratories BV
Source(s) of monetary or material Support: Innatoss Laboratories

Intervention

Keyword: Biomarkers, Borrelia, Lyme Disease

Outcome measures

Primary outcome

* Measure cytokine production induced by recombinant Borrelia antigens using a whole-blood CMI-based test

* Classify participants in an infected and not-infected group based on erythema migrans and/or seroconversion after 12 weeks

* Determine the percentage of infected subjects that is identified at 4 weeks by serology or the CMI-test or both.

Secondary outcome

* Measure increases in addtional cytokines induced by Borrelia antigens using a whole-blood CMI-based test

* Determine whether a combination of 2 or 3 biomarkers may be better in predicting the likelihood of developing disease symptoms.

* Determine the variation in cytokine concentrations in unstimulated samples, antigen-stimulated samples and positive controls using the Mesoscale Discovery Technology and specifically developed ELISA tests.

* Determine an appropriate cut-off that differentiates infected and non-infected subject.

Study description

Background summary

Laboratory tests for Borrelia infection are diverse. They are subject to discussions on interpretation and diagnostic value. Discussions in the Netherlands ended in a CBO guideline published in 2013. This guideline does not provide a solution for diagnosis of Lyme in an early stage, with the exception of a clinical diagnosis based on development of a (strictly defined) Erythema migrans (EM). Many infected people do not develop a characteristic EM. It is therefore important to identify and develop alternative methods for diagnosis of Lyme disease that are highly sensitive and sufficiently specific. In this study a cell mediated immunity test will be investigated for this purpose.

Study objective

The objective of the study is to develop a whole blood cell-mediated immunity test for Borrelia infection and investigate whether such a test can detect Borrelia infections more reliably than the currently used antibody tests in the early stage of infection.

Study design

Subjects with a tick-bite in the previous 10 days will be recruited and tested for Borrelia infection using standard serological tests and a cell-mediated immunity test. Tests will be repeated 4 and 12 weeks after the tick-bite. Prior infections will become apparent during the first measurement.
The difference in antibodies and cytokines between 1, 4 and 12 weeks will be determined for each subject. At the same time clinical symptoms will be reported using questionnaires.
At the end of the study the total number of infections will be determined. This will allow calculation of the percentage of infections identified by serology, CMI test or both.
Having sufficient infected and non-infected subjects will allow the generation of a classification model, that will subsequently be used to predict the infection status of subjects that only developed less characteristic symptoms.

Study burden and risks

Risks
The risks associated with standard blood drawing by a professional are negligible.
Risks associated with testing for Lyme Disease are that a healthy subject may be positive in the Lyme test indicating present or past exposure to Borrelia. Considering the fact that there is a high background infection rate in the Netherlands, this does not require specific actions, provided that the subject is symptom-free and there is no indication for a recent infection. If a recent infection is suspected based on seroconversion the GP will be informed. Discovered in an early stage, Lyme disease can be effectively be treated with antibiotics.

Benefits
The advantage of participation is that any subject testing positive for early Lyme disease will be able to get treatment fast. His/her GP will be informed in order to decide on medical follow-up. Considering the consequence of lack of treatment, it is not possible to participate without consent on this point.
This will be registered in the informed consent form.

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

- 18 years or older
- a tick-bite in the previous 10 days and attachment of the tick for > 16 hours, or
- an erythema migrans (EM) observed in past two weeks with a documented tick-bite or evidence of tick-bite in the center of the EM

- controls: subjects without tick bite after 1 Jan 2015

Exclusion criteria

< 18 years of age
Infectious diseases that are transmissable by blood
Not fulfilling the inclusioncriteria

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):	09-06-2015
Enrollment:	770
Type:	Actual

Ethics review

Approved WMO Date:	13-05-2015
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	27-01-2016

Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	05-10-2016
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	07-05-2018
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)

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	NL51306.028.15

Study results

Date completed:	31-12-2018
Actual enrolment:	671