Borrelia-induced inhibition of antigen presentation: a novel escape mechanism from the host defense system.

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To further study the mechanisms responsible for the Borrelia induced inhibition of antigen presentation and the impaired immuneresponse in Lyme disease pat¡ents, we would like to assess the immunological changes that occur in patients with a...

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

Summary

ID

NL-OMON54756

Source
ToetsingOnline

Brief title
LymEscape

Condition

- Bacterial infectious disorders

Synonym
Lyme borreliosis, Lyme disease

Research involving
Human

Sponsors and support

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

Intervention

Keyword: antigen presentation, Borrelia burgdorferi, innate and adaptive immune system

Outcome measures

Primary outcome

To assess immunological changes in patients with acute, early Lyme borreliosis.

The main parameters and endpoints are immunological determinants such as the

expression of antigen presentation markers (e.g.

CD74, HLA-DR, HLA-DM) and the adaptive immune response by measuring cytokine

production.

Secondary outcome

1) To determine the role and mechanism of antigen presentation inhibition in

the development of acute, early Borrelia infection and

disseminated Lyme disease in patients.

2) To assess thê impact of immunological changes on acute, localized, early and

late disseminated Lyme borreliosis.

3) To study the effect of Borrelia-induced antigen presentation inhibition on

the adaptive immune response.

4) To evaluate which changes in confirmed patients are still existent several

months after diagnosis and/or treatment.

Study description

Background summary

One olthe major clinical needs for Lyme disease is a robust diagnostic assay to identify Lyme disease in patients. Pathogenomic

signs such as the development of an erythema migrans (EM) are currently used to diagnose patients with Lyme disease, however,
these signs don't develop in all patients. Standard serological tests (ELISA and Western blot) for diagnosing Lyme disease have
limitations, such as a low sensitivity in acute, early infection, and lgG positivity for years after infection. Current data suggest the
presence of an impaired or weak immune response toward B. burgdorferi sensu lato. ln vitro and ex vivo data demonstrate that
Borrelia bacteria strongly downregulate genes and proteins involved in antigen presentation. Antigen presentation by monocytes,
macrophages and DCs was inhibited, interfering with crucial steps for optimal T-cell and B-cell response, towards Borrelia bacteria
and/or Borrelia antigens. Providing a possible explanation for why Lyme disease patients do not develop an effective immune
response and thus leading to survival of the Borrelia spirochetes.

Study objective

To further study the mechanisms responsible for the Borrelia induced inhibition of antigen presentation and the impaired immune
response in Lyme disease pat¡ents, we would like to assess the immunological changes that occur in patients with a specifîc focus
on Borrelia-induced inhibition of antigen presentation innate immune cells, their communication with and effects on the development
of an adaptive immune response.

Study design

This is a prospective cohort study with a three- till twelve month follow-up, depending on the early findings, and a total duration of 1
year.

Study burden and risks

Minimal, there is a small chance of developing a hematoma or vasovagal reaction at blood withdrawal. The participants will fill out
questionnaires at each measurement point. There is no direct benefit for participating in the 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

Patients with acute localized infection:
- Patients must be 18 years or older;
- Must have a confirmed erythema migrans (EM) with a diameter of more than or 5 cm that has been present for
less than a week, the diagnosis being confirmed by the treating physician after inclusion;
- Have not yet started treatment for the lyme borreliosis (LB) at the moment of inclusion or at most one week prior
to the moment of inclusion;
- Do not have signs or symptoms at inclusion attributed to a previous episode of Lyme borreliosis;
- If the patient has presented with EM's or Lyme borreliosis related symptoms before inclusion, but no longer have,
this will be recorded in their patient file/through the questionnaire.
Patients with disseminated or post-treatment lyme borreliosis syndrome (PTLBS):
- Patients must be 18 years or older;
- Must have a conflrmed diagnosis of Lyme borreliosis, with clinical and laboratory criteria largely based on the

case definitions of ESGBOR and published by Stanek et al.;
- Must have started treatment at most 1 week before inclusion.
Healthy controls:
- Patients must be 18 years or older;
- Patients must have bacterial skin/soft tissue infections (e.g. erysipelas, cellulitis) and they must have a confirmed
diagnosis according to the leading guidelines.
Cross-reactive controls:
- Patients must be 18 years or older;
- Patients must be diagnosed with either erysipelas or cellulitis

Exclusion criteria

Patients with acute and localized LB or disseminated LB/PTLBS:
- Suffering from other tick-borne or infectious diseases;
- Suffering from severe immunological deficiencies that result in consistent immunosuppression;
- The use of immunosuppressive medication before, during and/or after infection;
- The use of immunomodulating medication including > 7,5 mg prednisone daily, methotrexate, biologicals;
- Unable to give informed consent or do not have a thorough command of the Dutch language.
Healthy controls:
- Unable to give informed consent or do not have a thorough command of the Dutch language;
- Suffering from other tick-borne or infectious diseases, HIV seropositivity if known, active syphilis or leptospirosis,
an active infection with EBV/CMV;
- Suffering from auto-immune disease if known
- The use of immunosuppressive medication before, during and after Borrelia infection occurred;
- The use of immunomodulating medication including > 7,5 mg prednisone daily, methotrexate, biologicals;
- Severe immunological deficiencies that result in consistent immunosuppression.
- Known (severe) immunodeficiencies, hematologic malignancies in the medical history or chemotherapy in the
last year;
- Current LB with typical symptoms;
- Other co-morbidities such as auto-immune diseases, severe acute and chronic infections.
Cross-reactive controls:
- Unable to give informed consent or do not have a thorough command of the Dutch language;
- Suffering from other tick-borne diseases;
- The use of immunomodulating medication including > 7,5 mg prednisone daily,

methotrexate, biologicals,
consistent immunosuppression;
- Other co-morbidities.

Study design

Design

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

Primary purpose: Diagnostic

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-06-2023
Enrollment:	120
Type:	Anticipated

Ethics review

Approved WMO Date:	23-03-2020
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	22-05-2023
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	NL69332.091.19