Immunity to pertussis transmission and disease among household contacts of infected children.

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Whooping cough is very contagious. Earlier research shows that family members of a child with whooping cough are often also infected with the pertussis bacterium. However, not everyone who is infected with the bacterium develops symptoms. In this...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Bacterial infectious disorders
Study type	Observational invasive

Summary

ID

NL-OMON48617

Source
ToetsingOnline

Brief title
PITA-study

Condition

- Bacterial infectious disorders

Synonym
whooping cough

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: Het is een project dat is gefinancierd door Innovative Medicines Initiative 2 (IMI-2) Joint Undertaking;project nummer 115910

Intervention

Keyword: Bordetella pertussis, family study., household contacts, immune response, vaccination, whooping cough

Outcome measures

Primary outcome

The primary objective of this study is to identify differences in immunological biomarkers at inclusion (T1) between confirmed infection (asymptomatic) and confirmed pertussis (symptomatic) in cases.

We will measure immunological biomarkers in blood and in mucosal samples of household contacts at inclusion (T1) as well as changes in immunological biomarkers from T1 to T2 (=2 months after T1). As the primary objective, we will investigate differences in PT antibody responses at T1 and T2 between confirmed pertussis and confirmed infection (asymptomatic) cases (see highlighted rows in Table .

Primary endpoint. PT-IgG and PT-IgA geometric mean concentrations at T1 and T2

Secondary outcome

The secondary objectives of this study are to compare other immunological biomarkers measured in blood and mucosal samples at inclusion (T1), as well as changes in immunological biomarkers between T1, TS and T2 in relation to the case definitions described above. These include: comparison of mucosal and serum antibody responses, including functional antibody responses, and T and B cell responses in confirmed pertussis (symptomatic) and confirmed infection (asymptomatic) cases.

Secondary endpoints:

1. Serum IgG and IgA GMC titers against other pertussis antigens (including

Prn, FHA and Fim) at T1, T2 and TS

2. Mucosal IgG and IgA GMC titers against pertussis antigens (including PT,

Prn, FHA and Fim) at T1, T2 and TS

3. Frequency of pertussis-antigen specific memory B cells and their ratio*s at

T1 and T2

4. Pertussis antigen-specific T cell responses and their ratio*s at T1 and T2.

5. Pertussis-specific T and B cell responses at TS.

6. Assessment of functional pertussis-specific antibody levels in serum and

mucosal samples at all time points

Study description

Background summary

Whooping cough (or pertussis) is a respiratory infection that is often accompanied by severe cough attacks. Almost all children in the Netherlands are vaccinated against whooping cough. Whooping cough vaccination prevents serious disease due to whooping cough but does not always prevent infection. As a result, whooping cough is still common in the Netherlands. Young children in particular are at risk of developing whooping cough because they have not yet been (fully) vaccinated. This can also lead to hospitalization.

Study objective

Whooping cough is very contagious. Earlier research shows that family members of a child with whooping cough are often also infected with the pertussis bacterium. However, not everyone who is infected with the bacterium develops symptoms. In this study we want to study why this is the case. To do this, we want to investigate immunity against the perussis bacterium in the blood and nose-throat of family members of a child with whooping cough. With this knowledge we hope to develop better vaccines to control whooping cough. This knowledge will also contribute to the further optimization of the National

Immunization Program of RIVM.

Study design

Home visit and measurements:
For this study we will visit the family at home at least twice. The first home visit will take place as soon as possible. The second home visit takes place 2 months later. If a family member develops pertussis-related symptoms after the first visit, a third home visit will take place.

The following will take place during the home visit:
* filling in a questionnaire about possible complaints, medical/vaccination history and medication (± 15 minutes).
* blood collection (venapuncture). A maximum of 4 tubes of blood (40 ml total) are collected from adults. For children the volume depends on the age:
Age Volume (mL)
0-11 months 4 ml
1-2 yr 6 ml
2-6 yr 7.5 ml
7-10 yr 16 ml
11-15 yr 26 ml
16-19 yr 36 ml

* nasal-throat swabs and nasal fluid will be collected. For family members over 16 years of age we will also gently scrape along the inside of the nose to collect tissue.

The family will be called every week for 2 months. During this phone call we will ask questions about whooping cough symptoms of participating family members. This phone call will take approximately 10 minutes.

(Cough) complaints after the first home visit
It is possible that a participant does not have whooping cough complaints at the first home visit, but that these develop at a later timepoint. If this is the case, we ask you to contact us directly by telephone. We will then organise a home visit to take blood and nose-throat samples. We will then test whether this person is infected with the whooping cough bacterium. The result of this will be communicated to this person and to the general practitioner / specialist.

Study burden and risks

Holding an arm when taking a blood sample may feel uncomfortable and the puncture of the
needle may be a bit painful and a bruise may occur. In children, an anesthetic cream will be used so that the puncture will hardly be felt. The collection of

material from the throat/nose can cause sneezing and watery eyes. This is of a temporary nature and there are no major risks associated with participation.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

Child < 16 years old with a PCR-proven infection with Bordetella pertussis and minimal 2 asymptomatic household contacts.

Exclusion criteria

Households:
* With a pregnant contact (>34 weeks of gestation)
* With a contact younger than 6 months old or unvaccinated child.
* With a contact with significant disorders, including immunodeficiency, cancer, oral steroid therapy or any other medical conditions
* With risk contacts for which antibiotic prophylaxis is recommended for the whole household.
* In which it is not possible to organize visit T1 within 5 days.
Incapacitated Household contacts will be excluded.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	125
Type:	Anticipated

Ethics review

Approved WMO Date:	25-09-2019
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	24-12-2019
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	NL65912.091.19
Other	wordt aangevraagd