Imm-f@ct: Characterization of immune mechanisms in measles and other infectious diseases; role of specificities, functions, maintenance and fitness

Published: 20-01-2014
Last updated: 15-05-2024

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Hepatobiliary neoplasms malignant and unspecified
Study type	Observational invasive

Summary

ID

NL-OMON47081

Source
ToetsingOnline

Brief title
Imm-f@ct

Condition

- Hepatobiliary neoplasms malignant and unspecified

Synonym
Infectious diseases, pathogens

Research involving
Human

Sponsors and support

Primary sponsor: RIVM

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Cell Mediated Immunity, Humoral Immunity, Infectious diseases, Measles

Outcome measures

Primary outcome

Frequencies, functionality and specificity of biomarkers of specific B cell, T cell, and early immunity (antibody levels, avidity, functionality, memory B cells, plasma cells; cytokines, effector memory T cells, central memory T cells; cytokines, chemokines, innate immune cells).

Secondary outcome

Date of birth, gender; use of antibiotics last 3 months; chronic diseases; other disorders relevant for results of study; infectious diseases in past 5 years, including whether it was lab confirmed; presence or absence of clinical symptoms during the infectious disease under study; medication relevant for results of study; type of strain that caused the infectious disease under study; vaccination status.

Study description

Background summary

In addition to the presence of antibodies, cell mediated immunity (CMI) plays an important role in the protection against viruses and bacterial pathogens. In general, humoral immune responses prevent infection by killing the microorganism, whereas CMI prevents disease. Both responses are required for protection against infectious diseases.
CMI involves multiple T lymphocyte (T-cell) populations of the adaptive immune system, with unique antigen specificities and functions such as CD8+ cytotoxic T-cells and CD4+ helper T-cells, also involved in helping antibody production.

Both humoral and CMI mechanisms of the adaptive immune response can be acquired through natural infection or exposure to components of pathogens by vaccination. Not only direct effector mechanisms are then primed but also base levels of memory cells recalling specific antigens. These memory cells are there to rapidly and more effectively respond to renewed encounters with the pathogen, which is the mechanism behind vaccination. However, after an initial sharp rise of these responses post-encounter, a period of gradual waning follows. Studying characteristics of disease specific serological and CMI mechanisms in cases versus healthy controls in early and late phase after infection is important to unravel hallmarks of protection and waning immunity. In cases with a vaccination history, the type of humoral response may for example allow to distinguish between primary and secondary immune (vaccine) failure. These kinds of studies provide important information for future vaccination strategies and offer the opportunity to asses shared or unique immune responses after natural infection or vaccination, as well as to compare immune responses after infection with different viruses and pathogens.

Study objective

The main objective is to assess hallmarks of protective and waning immunity to vaccine preventable and non-preventable viral and bacterial diseases.in cases of various age groups and age-matched healthy controls. Secondary objectives are 1) to assess the proportion of cases that are due to primary or to secondary vaccine failure (in the case of measles and mumps), in order to determine if waning immunity is responsible for infection amongst those vaccinated and if additional steps need to be undertaken to prevent the risk of additional cases occurring amongst the vaccinated Dutch population; 2) to identify biomarkers of specific T-cell and B-cell responses for the evaluation of the breadth of the humoral and CMI response shortly and longer after infection; 3) to compare T-cell and B-cell responses after natural infection with vaccine-induced responses; 4) to relate magnitude, quality and dominance of pathogen specific T-cell responses to the quality of concomitant B-cell responses; 5) to compare T-cell and B-cell responses after natural infection between age-groups; 6) to compare the quality and quantity of humoral responses in serum and saliva; 7) to compare T-cell and B-cell responses after natural infection between different microorganisms; and 8) to assess the level of waning immunity over time, both within-host and cross-sectionally

Study design

Controlled observational, non-therapeutic trial

Study burden and risks

Per blood collection 8-80 ml heparinized blood will be collected, volume depends on age. The burden and risk is considered low. Blood collection might

be painful but only for a few seconds. Blood collection could result in a small bruise at the needle stick location, which will disappear within a few days. To reduce the burden, home visits will be performed.

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

For cases entering the study at time point 1:
In order to be eligible to enter the study at time point 1, the following criteria must be met:
* A case has a symptomatic viral/bacterial infection that is laboratory confirmed, and the time point of inclusion is within 3 months after diagnosis (*acute phase*)

* Willing to adhere to the protocol and perform all planned visits and sample collections
* Having given written informed consent themselves and/or through parents or legal representatives ;For cases first entering the study at time point 2:
In order to be eligible to enter the study at time point 2, the following criteria must be met:
* A case has had a symptomatic viral/bacterial infection that is laboratory confirmed, and the time point of inclusion is around 9 months (± 1 month) after diagnosis or a case has had a symptomatic Bordetella pertussis infection that is laboratory confirmed and the time point of inclusion is around 12 months (± 1 month)
* A case does not enter the Periscope pertussis group
* Is willing to adhere to the protocol and perform all further planned visits and sample collections
* Has given written informed consent him/herself and/or through parents or legal representatives ;For cases first entering the study at time point 3:
In order to be eligible to enter the study at time point 3, the following criteria must be met:
* A case has had a symptomatic viral/bacterial infection that is laboratory confirmed, and the time point of inclusion is around 18 months (± 2 months) after diagnosis
* A case does not enter the Periscope pertussis group
* Is willing to adhere to the protocol and perform the further planned visit and sample collection
* Has given written informed consent him/herself and/or through parents or legal representatives ;For cases first entering the study at time point 4:
In order to be eligible to enter the study at time point 4, the following criteria must be met:
* A case has had a viral/bacterial infection that is laboratory confirmed, and the time point of inclusion is around 36 months (± 3 months) after diagnosis
* A case does not enter the Periscope pertussis group
* Is willing to adhere to the protocol
* Has given written informed consent him/herself and/or through parents or legal representatives ;For age-matched controls:
* Negative clinical history and absence of a serological response against at least one of the panel of pathogens of interest for this study in the past 12 months.
* Having given written informed consent themselves and/or through parents or legal representatives
* Having been vaccinated, if applicable according to birth cohort, against measles, Bordetella pertussis, Streptococcus pneumoniae and/or mumps

Exclusion criteria

* Be or have been under immunosuppressive medical treatment, like cytostatics and prednisolons that might interfere with the results of the study, within the previous 3 months. In exemption to this criterion, short-term (*15 days), systemic immunosuppressive medication is permitted in case this medication is used to treat infections;
* Have any known primary or secondary immunodeficiency;
* Have a bleeding disorder or be under treatment with anticoagulants. In case of use of anti-coagulants, adult volunteers can be included if no spontaneous bleedings occurred in the month prior to venipuncture, if the dose of medication is stable (no changes in the month

prior to venipuncture) and/or INR testing is performed at * 2 times a month, and if the INR value is below 3.5 (based on the information provided by the volunteer).;A control is not eligible when he/she reports to
* Have developed clinical symptoms of a virus or pathogen infection in the very short period of time between the identification as a control and the date of the home visit.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	29-05-2014
Enrollment:	840
Type:	Actual

Ethics review

Approved WMO Date:	20-01-2014
Application type:	First submission
Review commission:	METC Noord-Holland (Alkmaar)
Approved WMO Date:	12-06-2014
Application type:	Amendment
Review commission:	METC Noord-Holland (Alkmaar)
Approved WMO	

Date:	04-09-2014
Application type:	Amendment
Review commission:	METC Noord-Holland (Alkmaar)
Approved WMO Date:	30-09-2015
Application type:	Amendment
Review commission:	METC Noord-Holland (Alkmaar)
Approved WMO Date:	22-02-2018
Application type:	Amendment
Review commission:	METC Noord-Holland (Alkmaar)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 22598
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL46795.094.13
OMON	NL-OMON22598

Study results

Date completed:	15-12-2021
Results posted:	05-04-2022
Actual enrolment:	419

Summary results

Trial is onging in other countries

First publication
21-03-2021