Unravelling the measles paradox: a disease associated with both immune suppression and immune activation

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Unravelling the *measles paradox* by in-depth characterization of the immune repertoire before and after natural measles or measles vaccination.

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

Summary

ID

NL-OMON56923

Source
ToetsingOnline

Brief title
MISIA

Condition

- Viral infectious disorders

Synonym
airborne disease, measles virus

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: ZonMw

Intervention

Keyword: immunity, measles

Outcome measures

Primary outcome

The main study parameter is the immune repertoire before and after measles.

Secondary outcome

The secondary parameters in this study are:

Comparison of humoral responses to various pathogens and the change over time in samples taken before and up until 3 years after measles in comparison to vaccination. This will also be compared 10 years after infection or vaccination

Profiling of peripheral cytokines and the change over time in samples taken before and up until 3 years after measles in comparison to vaccination or participants that remain uninfected. This will also be compared 10 years after infection or vaccination.

Quantifying cellular responses by flow cytometry after antigenic stimulation with a wide range of bacterial and viral pathogens and change over time in samples taken before and up until 3 years after measles, in comparison to vaccination, or participants that remain uninfected. This will also be compared 10 years after infection or vaccination.

Comparison of measles-specific immunity 10 years after infection or vaccination.

Correlation of above parameters to disease severity.

Study description

Background summary

Measles is caused by measles virus (MeV). The disease is associated with lymphopenia and immune suppression, which is an important cause of measles-associated morbidity and mortality. Measles immune suppression can last several years, whereas measles lymphopenia is usually resolved within two weeks. At the same time, measles induces lifelong immunity. This apparent contradiction, known as the *measles paradox*, was partially solved when we demonstrated that MeV infects and depletes pre-existing memory cells, thereby causing *immune amnesia*. This model is supported by observations in animal models and clinical studies. However, several questions remain to be addressed.

Study objective

Unravelling the *measles paradox* by in-depth characterization of the immune repertoire before and after natural measles or measles vaccination.

Study design

Observational cohort study. We will perform phenotyping and functional analyses of T- and B-cell (sub)populations in blood from individuals before and after measles or measles vaccination to assess changes in the composition of the immune repertoire.

Study burden and risks

This study is an observational cohort study in young adults that involves the collection of clinical specimens before and after natural measles or measles vaccination. A maximum of 50ml blood, a nose brush, and a nasosorption will be obtained in 6 study visits. Negligible risks are associated with participation. Participants will be informed of their measles immune status and advised to be vaccinated if seronegative, with protection from measles in an upcoming outbreak as potential benefit.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Cohort A (18-25 years)
- No known history of measles or vaccination
- Decided to take MMR vaccination before the upcoming measles outbreak

Cohort B (18-25 years)
- No known history of measles or vaccination (seronegative confirmed)
- Contracted measles during the upcoming outbreak

Cohort C (18-25 years)
- No known history of measles or vaccination (seronegative confirmed)

Cohort D (18-25 years)
- Experienced measles during the 2013 outbreak

Cohort E (18-25 years)
- Received second dose of measles vaccines ±10 years ago

Exclusion criteria

1. Diagnosed chronic disease
2. Immune suppression (due to medication or underlying disease)
3. Additionally for subjects recruited to Cohort A:
-pregnant women or women planning to get pregnant in less than one month after the start of the
study. This is a precaution; the MMR vaccine is not recommended for pregnant women.
-People who have had a severe allergic reaction (e.g., anaphylaxis) after a previous vaccination.

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):	01-06-2024
Enrollment:	300
Type:	Anticipated

Ethics review

Approved WMO

Date:	19-07-2024
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL86804.078.24