Transmission Of Respiratory Tract microOrganisms In a School Environment

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

Summary

ID

NL-OMON56507

Source
ToetsingOnline

Brief title
The TORTOISE study

Condition

- Bacterial infectious disorders

Synonym
respiratory tract infections

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: ERC grant vanuit Europese Unie

Intervention

Keyword: immune respons, microbiome, Respiratory tract, transmission

Outcome measures

Primary outcome

Primary study parameter

To answer the primary objective we will record Spn carriage over time at a serotype level using qPCR. This will lead to a categorical variable with the following levels for each included serotype, per participant: never infected (no Spn detected during the sampling period), already colonized (Spn detected at the start of the sampling period), new colonization (Spn not detected at the start of the sampling period, but detected in the course of the sampling period) or re-colonization (same Spn serotype detected during sampling period with at least 3 samples in between not detecting Spn).

A transmission event will be defined as a SPn serotype that is observed in at least one child in the class and at a later timepoint also observed in one or more other children, as long as this is within 1 week of it being present in first child.

Secondary outcome

Secondary study parameters

Presence, transmission and/or introduction of common URT commensals/pathogens will be recorded and lead to categorical variables similar to the primary study parameter. Subtyping/sequencing will be performed where deemed relevant (rhinovirus, influenza virus etc.) to elude the source to the extent possible.

Local host immune response in response to colonization/infection of URT by pathogens and potential differences in response between different pathogens will be measured using tools as ELISA or multiplex technologies, such as Olink and Luminex. We will focus on innate and adaptive inflammatory markers. We will also measure antibodies against pathogens using tools as ELISA and antigen arrays.

The microbiome will be measured by 16S ribosomal RNA sequencing. Microbial products will be measured by tools like mass spectrometry.

Clinical symptoms of RTI*s will be recorded in categorical variables (yes/no).

To measure pollen (counts and species) and microbial presence in classroom environment via EDC and active air sampling (pollensniffer).

Other study parameters

Potentially relevant variables for colonization/infection, symptoms and host responses will be recorded in a questionnaire. This includes things like age and sex, history of respiratory infections, vaccination history, numbers and age of siblings, school/pre-school attendance, smoking status of parents, swimming pool visits. These will be used for exploratory purposes or as covariates in models.

Study description

Background summary

Respiratory tract infections impose a large burden of disease upon the world. Pneumonia remains the leading infectious cause of death in children under five worldwide. Known causative agents of pneumonia include, but are not limited to, SPn, Haemophilus influenzae (HI), Moraxella catarrhalis (MC) and viruses such as the Respiratory Syncytial Virus (RSV) and the influenza virus. These microorganisms are regularly found in the upper respiratory tract (URT) without causing severe disease. Colonization of the URT is thought to be important both for immune boosting and to provide competition for other potential harmful colonizers.

Study objective

This study aims to provide insights into the processes and key host immune and microbiota factors that determine the infection kinetics, transmission and development of immunity during such infections. Furthermore, this study will enable us to closely study the transmission of commonly found microorganisms in an environment that is prone to transmission within populations, the close quarters of school classes in which young children spend a large part of their time.

Primary Objective:
Describe classroom transmission- and colonization-rate of SPn in young children. This will be measured at a serotype-level as overall carriage rates are high.

Secondary Objectives:
a. To study transmission and colonization rates of other URT pathogens in a classroom setting.
b. To study nasal immune response in response to exposure, infection or colonization by URT microbes.
c. To describe the relationship between clinical symptoms of RTI*s, host immune responses, microbiome and URT pathogens.
d. Correlation of medical history with (rate of) transmission and colonization of respiratory pathogens and immune responses.
e. To measure pollen and bacterial presence (airobiome) in classroom environment via electrostatic dust fall collector and pollensniffer to differentiate between RTI and hay fever.
f. To describe the relation of URT pathogen colonization rate in young children and their teachers.

Study design

This is a prospective observational cohort study. Participants, children aged 4-7 years and their teachers, will be recruited from primary schools in North-Holland and/or South-Holland. Initially contact is made with primary schools by trained study personnel. If schools are willing to facilitate the study, contact is made with parents via the teachers, school-newsletters or directly through an information booth or other contact at the school. Parents and teachers will be informed about the study by trained study members through primary schools. Potential participants (or their parents) will have sufficient time (at least one week) to decide to take part and have the possibility to ask questions. Throughout the study the researchers will be available via telephone and e-mail.
Duration of the study for participants will be eight consecutive weeks during which we collect all samples. This period allows sufficient time to be able to precisely study transmission episodes and potential development of infection. Minimally-invasive nasal sampling will take place three times a week at the participating primary school, yielding 24 samples per participant. We have previously demonstrated that such minimally-invasive samples are an accurate tool to measure pneumococcal colonization in children. If participants are sick and cannot come to school, we will ask permission from them (in case of teachers) or their parents (in case of children) for a home visit, and will collect the SAM at home and complete a questionnaire related to the illness and potential treatment. We will sample in a period between school-holidays to have an uninterrupted study period. If there are children that join the class during the course of the study we will inform the parents and ask for informed consent to include these children as well. The children that start later will finish the sampling along with the rest of the class, and will thus provide less samples than the others.
We will also place an EDC in the classroom for the whole study period and collect weekly air samples by active sampling through a pollensniffer to measure environment particles. These devices are able to measure environmental microbes, potential human pathogens along with airborne pollen and give information on a collective *exposome* for the whole study period as well as weekly fluctuations based on seasonal differences. By doing so we may distinguish between hay-fever symptoms and RTIs. Along with the sampling, clinical symptoms will be observed and recorded by trained study personnel. In the first weeks of the study a baseline questionnaire will be completed by the parents.

Study burden and risks

Data will be collected through digital questionnaires, biological material by minimally invasive synthetic absorptive matrices (SAMs). Collection will take place on site (primary schools) by trained members of the study team three times a week for a period of eight weeks.
To engage children, we will include an educational component where children will learn from one of the clinical doctors involved in the study about micro-organisms in relation with health and disease Other than this, there is

no direct benefit for participants, we hope to elucidate the infection kinetics and transmission of microorganisms in primary school classrooms through this study, ultimately aiming to identify biomarkers for transmission of and invasive disease caused by pathogens. This might for example help with preventing unnecessary school closures in the future during respiratory infection dynamics. Risks involved for participants are minimal, as SAMs are minimally-invasive and well-tolerated by young children and adults. We will study young children because they are a significant risk-group for severe respiratory infections and spread microorganisms frequently due to close interaction with peers whilst being a main reservoir for respiratory pathogens.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Children (2-11 years)

Inclusion criteria

Children between the age of 4 and 7 years old or adult teacher attending the class

Exclusion criteria

Insufficient proficiency of parents in Dutch or English language

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	25-01-2024
Enrollment:	78
Type:	Actual

Ethics review

Approved WMO

Date:	05-01-2024
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	NL85480.058.23