EVALUATION OF THE USE OF VACCINES AGAINST EPIDEMIC FLU AND THE PRESENCE OF CROSSREACTIVE T CELL RESPONSES AGAINST POTENTIALLY PANDEMIC INFLUENZA VIRUSES IN CHILDREN

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

Summary

ID

NL-OMON32610

Source
ToetsingOnline

Brief title
CTL immunity against influenza in children

Condition

- Viral infectious disorders

Synonym
crossreactive T-cell responses, Influenza

Research involving

Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: CTL, Influenza, Vaccination

Outcome measures

Primary outcome

Comparison of CTL immunity in two different groups of children:

Main study parameters/endpoints:

The main study parameter will be the number of virus specific -CD8+ T cells in the peripheral blood of children of the two study groups. Data for this parameter can be obtained after collecting a single blood sample of 5 millilitres.

Secondary outcome

Seroincidence of influenza in children with CF

Study description

Background summary

SUMMARY
Rationale: Currently an ongoing outbreak of human infection with Novel Swine-Origin Influenza A (H1N1) Virus has resulted in an influenza pandemic. Until June 11th almost 30,000 people were infected with the virus of whom 144 died [5]. Excess morbidity and mortality is feared, especially in high risk groups.

Cytoxic T lymphocytes (CTLs) play an important role in the control of virus infections, including those caused by influenza viruses. In mice, mortality caused by influenza viruses infection was reduced and more efficient viral clearance was shown upon adoptive transfer of virus specific T cells [6]. In humans, the level of influenza virus-specific CTL activity correlated with the rate of viral clearance upon experimental infection [7]. In case of an influenza pandemic caused by influenza viruses of a novel subtype, antibodies provoked by vaccination with the common used vaccines will not be able to protect against infection. However, CTLs provoked by natural infection, might be able to protect against severe disease symptoms, because they are able to recognize more conserved epitopes of the influenza A virus (cross protection) [8]. Of special interest is the notion that especially younger individuals are infected with influenza and for H5N1 viruses it is known that younger individuals have a higher risk of fatal outcome of infection than older individuals [4, 9]. Almost all people will be infected by influenza viruses before the age of 3 years. In a number of countries, including the USA, Finland and Austria, annual vaccination of all healthy children 6 to 59 months of age is recommended since 2007 [10]. These children may not become infected with the epidemic influenza A strains and do not develop a virus specific CTL response and therefore might be at higher risk of severe disease and mortality in case of an infection with a highly divergent influenza stain. Children with cystic fibrosis are at high risk for serious infection and vaccinated annually. This group allows us to check whether differences in immunity can be found between influenza vaccinated children and children that are not. Clearly vaccination is advantageous to children with well described risk factors for serious influenza infection. It should be noted that this study is not designed to discourage vaccination in these groups. However, may be the use of live attenuated vaccines should be preferred rather than the use of inactivated subunit vaccines. . The reason for this is that live attenuated vaccines do cause a mild infection and thus expose most viral proteins to the host*s immune system inducing cell-mediated immunity.

The aim of this study is to evaluate the presence and activity of cross protective CTLs and antibodies in these children and compare these data with data from children of the same age that are not vaccinated annually. The outcome of this study can possibly be used for the development of optimal vaccination strategies for influenza in both healthy children and children at risk for serious complications..

Study objective

The hypothesis of this study is that children that are vaccinated since birth will have significant less or no cross protective CTLs compared to children that have not been vaccinated since birth.
Objective: Determination of the effect of annual vaccination on the development of cross-reactive T cell immunity during childhood.

Study design

Study design: Comparison of CTL immunity in two different groups of children.

Study burden and risks

Nature and extent of the burden and risks associated with participation, benefit and group relatedness:
The burden associated with participation in this study is that one extra blood sample of 5 ml will be collected. Since only one blood sample will be taken from the study subjects, the burden is considered limited and the risks associated with this procedure negligible. In addition 5 ml of blood will be used obtained from children enrolled in the MIMIC study.

This study can only be performed in children. Currently, no cohort composed of adult patients can be identified that has been vaccinated throughout life from birth on. In addition occasionally the viral vaccination strain does not correspond with its seasonal counterpart, thus providing only limited protection and subsequently allows for infection. In conclusion, in time all adults will eventually develop T cell immunity against influenza viruses due to natural infection. Therefore, only in children there is an opportunity to investigate the effect of vaccination on the development of virus-specific T cell immunity.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

- Age: children between 3-8 years old
- Vaccinated against influenza on an annual basis (CF-patients): group 1
- Not vaccinated against influenza: group 2

Exclusion criteria

-Immune deficient children (e.g. due to haematological, genetic disorders or iatrogenic)
- Children that chronically receive immunosuppressive medications
- Children with diabetes

Study design

Design

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

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-11-2009
Enrollment:	90

Type:	Actual

Medical products/devices used

Registration:	No

Ethics review

Approved WMO Date:	04-11-2009
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	NL29399.078.09