The future of coeliac disease: immunology, environment and possibilities for new treatments.

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Malabsorption conditions
Study type	Observational invasive

Summary

ID

NL-OMON44841

Source
ToetsingOnline

Brief title
CDfuture

Condition

- Malabsorption conditions
- Autoimmune disorders

Synonym
Coeliac sprue, Gluten intolerance

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Coeliac disease, Environment, Immunology, T-cells

Outcome measures

Primary outcome

Definition of the disease associated T cell receptor repertoire in a large group of paediatric patients.

Determination of the functional characteristics of the disease associated T cells.

Correlation of the disease associated T cell receptor repertoire with disease onset and/or severity

Phenotypic and functional characterisation of the intraepithelial lymphocyte compartment in patients with and without CD.

Analysis of the cytokine mediated crosstalk between the lamina propria and epithelial compartments.

Secondary outcome

Ultimately we aim to develop novel diagnostics and preventive and therapeutic approaches for CD.

Study description

Background summary

As coeliac disease (CD) is a disease that is exclusively found in humans, the continuation of basic and translational research lines depends on the ongoing availability of patient derived materials from patients with and without CD. Such material can be obtained through routine diagnostic procedures, like venous blood sampling and the sampling of intestinal biopsies during diagnostic endoscopy under general anesthesia.

Recent results and technological developments offer novel opportunities to improve diagnostics and develop novel therapeutic approaches. For example, it has become clear that in patients with CD a biased T cell receptor repertoire is present that mediates the deleterious immune response to the dietary gluten proteins. The availability of novel tetramer reagents now allows a direct monitoring of the presence, abundance and functional characteristics of these T cells in peripheral blood and biopsy material of patients. This enables studies to determine if the occurrence of such cells coincides with disease onset and/or severity of associated symptoms. Moreover, we have novel insight into changes in the intraepithelial lymphocyte compartment that are associated with CD. We also have evidence that there is cytokine mediated crosstalk between the immune response in the lamina propria and epithelium which likely contributes to pathology. Therefore we wish to further characterize these interactions in functional terms in order to gain better insight into the involvement of innate immunity in CD pathology. These studies are further facilitated by the acquirement of the CyTOF mass cytometer, a new technological breakthrough allowing the simultaneous analysis of up to 34 cellular markers on a single cellular sample.
Ultimately we anticipate that these studies will be used to develop novel strategies to prevent or treat CD by elimination of disease causing cells by highly specific intervention targeting disease relevant cells without affecting immunity in general.

Study objective

The primary objective of CDfuture is to provide duodenal biopsies of patients with and without CD, and venous blood samples, to continue CD research as described above.

Study design

Case-control study

Study burden and risks

The extra biopsies and blood samples will be taken under general anesthesia during diagnostic endoscopy for medical reasons unrelated to this research protocol. This medical procedure in itself can cause stress and be a burden to the patient. The relevant medical and nursing protocols that are used in the LUMC describe among others guidelines to decrease stress, and increase safety. However, the extra biopsies and blood samples that are taken for the research described in this protocol cause no extra stress or burden since these materials will be sampled under general anesthesia.
There is a limited risk to taking biopsies during endoscopy to develop intra-intestinal or intramural hemorrhage, or even perforation. The risk is estimated to be < 1:10000. There is no additional risk in sampling an extra 10

ml of blood.
CD develops at a very young age. Most children that are diagnosed with CD in The Netherlands are below the age of 12 years. Therefore, in order to obtain enough biopsies for the research described in this protocol, it is necessary to include minors < 12 years of age in this study.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

All children that undergo diagnostic upper gastrointestinal endoscopy under general anesthesia for medical reasons in the Willem-Alexander Children*s Hospital of the LUMC are eligible for the study. Around 120 children undergo upper gastrointestinal endoscopy in the Department of Pediatrics of the LUMC each year. They will be divided in

- Cases: all children that are diagnosed with coeliac disease according to accepted criteria
- Controls: all children that are diagnosed with other conditions unrelated to coeliac disease
;Informed consent and suffiecient knowledge / understanding of the Dutch language are mandatory

Exclusion criteria

- No informed consent
- Insufficient knowledge / understanding of Dutch language
- Prior participation in protocol P06.140 or the present study if subject has undergone more than one endoscopy.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	14-07-2014
Enrollment:	400
Type:	Actual

Ethics review

Approved WMO

Date:	02-07-2014
Application type:	First submission

Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	31-08-2015
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	24-11-2015
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	28-04-2016
Application type:	Amendment
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	NL47320.058.14