Leukocyte dynamics in ageing: in vivo labelling of dividing leukocytes using deuterated water

Published: 29-03-2011
Last updated: 02-05-2024

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON38081

Source
ToetsingOnline

Brief title
Leukocyte dynamics in ageing

Condition

- Other condition
- Immunodeficiency syndromes

Synonym
lymphopenia; immune cell loss

Health condition

immunologische veroudering

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: NWO

Intervention

Keyword: (cell) population dynamics, aging, leukocytes, stable isotope labeling

Outcome measures

Primary outcome

The main parameter of the study is the amount of deuterium (label) that the different leukocyte populations have incorporated in their DNA by cell division at a given time. For this purpose blood withdrawals are done both in the period during which participants drink 2H2O (uplabelling phase) and in the period after stopping with 2H2O intake (downlabelling phase). Data obtained during uplabelling and downlabelling phases can be interpreted by mathematical models that describe the dynamics of leukocyte populations.

Secondary outcome

With the obtained materials several in vitro immunological test will be performed, including determination of blood- and plasma levels and analysis of cell phenotypes and cell numbers within subpopulations.

Study description

Background summary

Ageing of the immune system plays an important role in the development of various age-related health problems among elderly, e.g. increased susceptibility to infections and reduced vaccine efficiency. During ageing dramatic changes take place in the immune system: the number of total and naive lymphocytes declines and important shifts between subpopulations take place. To

explain what is causing these changes we want to quantify how the dynamics of leukocytes (expressed in terms of production rate and lifespan) change as people age. Quantitative insights in these dynamics will facilitate the tackling of the problems of immune and vaccine failure in elderly. Moreover the availability of reference values of healthy dynamics will allow for a fair comparison of patients with healthy controls of matching age.

Study objective

In this study we want to apply heavy water labelling to investigate how ageing affects the dynamics of different leukocyte populations.
The main objectives of this study are:
(A) to get more insight in the dynamics of an ageing immune system, in order to improve our understanding of what is causing immune-related health problems in the elderly.
(B) to obtain reference values for leukocyte dynamics in healthy young and healthy older individuals, in order to
(i) get more insight in how these dynamics change in various patient populations (compared to healthy individuals of matched age);
(ii) investigate how certain pathological situations can lead to premature ageing of the immune system.

Study design

The study concerns longitudinal observational research with invasive acts. It is composed of temporary consumption of deuterated (heavy) water (2H2O) and prospective blood withdrawals and urine sampling for laboratory research. Blood is drawn 7 times in the period during which participants drink heavy water (uplabelling phase) and 8 times in the period that follows (downlabelling phase). From the blood samples various leukocyte populations will be sorted after which in the DNA of these samples deuterium enrichment can be quantified using gas chromatography and mass spectrometry (GC-MS). Frequent sampling of urine makes it possible to correct, per time point, for the intake of deuterium by an individual.

Study burden and risks

The frequent blood- and urine sampling and associated hospital visits make the burden of this study substantial. In addition, the questionnaires can be considered an incursion on one's privacy. There is no direct advantage of participation. The necessary amounts of heavy water are not harmful. The total volume of withdrawn blood falls within the limits applied by Sanquin Bloedbank. Safety of heavy water for human consumption is reaffirmed with a test. Participation hence comes with burden, but is safe.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

5 healthy young individuals; 20-25 years of age
10 healthy older individuals; at least 60 years of age

Exclusion criteria

(i) Infection with human immunodeficiency virus (HIV), hepatitis B virus (HBV), or hepatitis C virus (HCV);
(ii) Other severe infections, e.g. malaria, infectious mononucleosis, a sexually transmitted disease (STD);
(iii) Hayfever or allergy;
(iv) Asthma or COPD;

(v) Diabetes;
(vi) Auto-immune disease, e.g. rheumatoid arthritis;
(vii) Heart problems, or a history of heart problems;
(viii) Kidney problemns, or a history of kidney problems;
(ix) Chest pain or shortage of breath, in rest or during exercise;
(x) Body weight of less than 50 kg;
(xi) Use of medication, with the exception of (a) analgesics when taken less frequent than weekly (paracetamol, ibuprofen, aspirin) (b) contraceptives;
(xii) History of cancer;
(xiii) Pregnancy or parent's wish in the coming year;
(xiv) Excessive alcohol consumption;
(xv) Drug use;
(xvi) Changing and unsafe sexual contacts;
(xvii) Sexual contact with an individual infected with HIV or another STD within the last 12 months;
(xviii) Extreme sensitivity to car-sickness and/or sea-sickness

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	12-08-2011
Enrollment:	15
Type:	Actual

Ethics review

Approved WMO

Date:	29-03-2011
Application type:	First submission

Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	06-06-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	30-03-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	NL30762.041.10