Leukocyte dynamics in health and disease: in vivo labelling of dividing leukocytes using deuterated water

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Objective of this study is to determine the turnover of leukocyte populations in health (young, old) and how this compares to situations in which the immune system is disturbed ((HIV-1 infection, HSCT, thymectomy).

Ethical review	Not approved
Status	Will not start
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON33161

Source
ToetsingOnline

Brief title
Leukocyte dynamics in health and disease

Condition

- Other condition
- Immunodeficiency syndromes

Synonym
lymphopenia; immune cell loss

Health condition

lymfopenie t.g.v. stamceltransplantatie

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: ZonMW; Landsteiner Stichting voor Bloedtransfusie Research

Intervention

Keyword: (cell) population dynamics, leukocytes, stable isotope labelling

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 (delabelling phase). Data obtained during uplabelling and delabelling phases can be interpreted by mathematical models that describe the dynamics of leukocyte populations.

Secondary outcome

n.a.

Study description

Background summary

Large controversies exist as to how long immune cells live, how fast they are produced, and how fast they die in a healthy individual. Lack of insight in a healthy situation hampers research focused on how leukocyte dynamics are changed when the immune system is disturbed, as is the case in HIV-1 infection or hematopoietic stem cell transplantation. A recently developed technique named stable isotope labelling has made it possible to study cell dynamics in vivo, under physiological circumstances. In this study we intend to give the label "deuterium" to individuals as heavy water, to determine the turnover

parameters of diverse leukocyte populations in health (young adults, healthy seniors of 60 years and older, healthy individuals that had their thymus removed at young age), and compare these to situations that disturb the immune system (HIV-1 infection, hematopoietic stem cell transplantation (HSCT)). A better insight in these basic parameters is essential if we want to answer more concrete questions, like whether in HIV-infection chronic immune activation or a homeostatic response to CD4 T cell depletion is responsible for the increased CD4 T cell turnover, and whether in lymphopenic HSCT-patients an active homeostatic response is triggered or not. Eventually, a better understanding of the dynamic basis of such disturbances will help in the development or improvement of therapeutic interventions.

Study objective

Objective of this study is to determine the turnover of leukocyte populations in health (young, old) and how this compares to situations in which the immune system is disturbed ((HIV-1 infection, HSCT, thymectomy).

Study design

The study entails an open observational study, consisting of temporary consumption of stable-isotope-labelled (deuterated, or heavy) water (2H2O), and prospective blood and urine sampling for laboratory tests. Blood withdrawals are done maximally 7 times during the period that heavy water is taken (uplabelling phase), and maximally 7 or 8 times in the period thereafter (delabelling phase). From the blood samples several cell populations will be sorted, after which the deuterium enrichment in DNA isolated from these populations can be determined by a combination of gas chromatography and mass spectometry (GC-MS). Frequent sampling of urine permits the correction of label intake by an individual at a given time point.

Study burden and risks

The burden for participants of this study is minimal. Intake of small amounts of 2H2O as described in this study is not harmful and the daily intake during the uplabelling phase can take place at home. Only the initial bolus of 2H2O of 10 ml per kg of body weight, which is given in little doses at the day care, can possibly cause some dizziness or nausea. Blood withdrawals take place maximally 7 times in the period during which 2H2O is taken (uplabelling phase) and 7 times in the period after stopping 2H2O intake (delabelling phase). If necessary and possible, an 15th blood withdrawal will be done at least a year after stopping 2H2O intake. Hence, participants will visit the UMC Utrecht 14 to 15 times. Where feasible, these visits will coincide with regular control visits (HSCT patients, HIV-patients). Blood withdrawals can on rare occasions lead to subcutaneous hematomas. An exception to the UMC visits are the healthy individuals of 60 years and older: all blood withdrawals except the first one

will be carried out at the old people's home instead of the UMC Utrecht.

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

a. healthy, 20-30 years of age, HIV-negative
b. healthy, 60 years or older, HIV-negative
c. healthy, 18 years or older, complete thymus removed at young age because of heart surgery
d. stem cell transplantation patiënt, 18 years or older, treated for hematological malignancies with an autologous HSCT, HIV-negative
e. 18 years or older, untreated HIV-1-infection

Exclusion criteria

a, b, c. do not suffer from immunological disorders and show no obvious symptoms of infections
d. do not suffer from graft-versus-host-disease or severe (viral) infections
e. do not receive antiviral therapy

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	60
Type:	Anticipated

Ethics review

Not approved

Date:	23-06-2009
Application type:	First submission
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	NL27614.041.09