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

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

Summary

ID

NL-OMON33432

Source
ToetsingOnline

Brief title
Leukocyte dynamics in health and disease

Condition

- Other condition
- Immunodeficiency syndromes

Synonym
lymphopenia; immune cell loss

Health condition

lymfopenie ten gevolge van stamceltransplantatie

Research involving
Human

Sponsors and support

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

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

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

Study description

Background summary

During the last decades, our knowledge of the immune system has been strongly improved. Still, large controversies exist as to how long the most important cells of the immune live, how fast they proliferate, and how fast they are produced in the thymus and bone marrow, under normal, healthy conditions. Lack of insight in a healthy situation hampers our understanding of how leukocyte

dynamics are changed when the immune system is disturbed, as is the case in HIV-1 infection or following hematopoietic stem cell transplantation. Thanks to the combination of the recently developed stable isotope labelling technique and mathematical modelling it is now possible to study leukocyte dynamics in vivo, under physiological circumstances.

Study objective

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)). Knowledge in these basic parameters is essential if we want to get more insight in (i) how HIV-1 infection influences leukocyte dynamics, (ii) how the immune system reconstitutes in HSCT-patients, (iii) what the contribution of thymus output is in the maintenance of the T cell pool, and (iv) how ageing influences leukocyte dynamics. Hopefully, a better understanding of the dynamic basis of such disturbances will also lead to better perspectives in the development or improvement of therapeutic interventions.

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 physical 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. To restrict personal burden, these visits will, where feasible, coincide with regular control visits (HSCT patients, HIV-patients), and within the group of healthy individuals over 60 years the blood withdrawals (except the first one) will be carried out at the old people's home instead of the UMC Utrecht . Blood withdrawals can on rare occasions lead to subcutaneous hematomas.

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 confirmed with an HIV-test
b. healthy, 60 years or older, HIV-negative confirmed with an HIV-test
c. healthy, 18 years or older, complete thymus removed at young age because of heart

surgery, HIV-negative confirmed with an HIV-test
d. stem cell transplantation patiënt, 18 years or older, treated for lymphoma with an autologous HSCT, HIV-negative confirmed with an HIV-test
e. 18 years or older, HIV-1-infected, untreated before and during the study

Exclusion criteria

Participants will be asked to answer a questionnaire which informs us about their health status. Exclusion criteria for each group separately:
a. (i) heart- and/or kidney problems, (ii) immunologic disorder (iii) diabetes, (iv) blood transfusion within the last 6 months, (v) hormone therapy within the last 6 months, (vi) transplantation, (vii) vaccination within the last 4 weeks, (viii) infection and/or fever within the last 4 weeks, (ix) surgery within the last 4 weeks, (x) severe allergy, (xi) for women: pregnancy or parent's wish in the coming year (xii) excessive alcoholic consumption or excessive drug use
b. (i) heart- and/or kidney problems, (ii) immunologic disorder (iii) diabetes, (iv) blood transfusion within the last 6 months, (v) hormone therapy within the last 6 months, (vi) transplantation, (vii) vaccination within the last 4 weeks, (viii) infection and/or fever within the last 4 weeks, (ix) surgery within the last 4 weeks, (x) severe allergy, (xi) excessive alcoholic consumption or excessive drug use
c. (i) heart- and/or kidney problems, (ii) diabetes, (iii) blood transfusion within the last 6 months, (iv) hormone therapy within the last 6 months, (v) transplantation, (vi) vaccination within the last 4 weeks, (vii) infection and/or fever within the last 4 weeks, (viii) surgery within the last 4 weeks, (ix) severe allergy, (x) for women: pregnancy or parent's wish in the coming year (xii) excessive alcoholic consumption or excessive drug use
d. (i) transplantation-related complications, (ii) severe infections (iii) heart- and/or kidney problems, (iv) diabetes, (v) hormone therapy within the last 6 months, (vi) vaccination within the last 4 weeks, (vii) severe allergy, (viii) for women: pregnancy or parent's wish in the coming year (ix) excessive alcoholic consumption or excessive drug use
e. (i) treatment with antiretroviral therapy or expectancy of treatment in the coming year (ii) heart- and/or kidney problems, (iii) diabetes, (iv) blood transfusion within the last 6 months, (v) hormone therapy within the last 6 months, (vi) transplantation, (vii) vaccination within the last 4 weeks, (viii) surgery within the last 4 weeks, (ix) severe allergy, (x) for women: pregnancy or parent's wish in the coming year (xi) excessive alcoholic consumption or excessive drug use

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:	29-09-2009
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	NL28972.041.09