



News Bulletin September 2011

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The second CHeartED Annual Meeting,
the Medical Birth Registry of Norway and
two dissertations**

Annual Meeting

On May 18-19 2011 CHeartED organized its 2nd Annual Meeting in Bergen, Norway. 32 consortium members joined the successful meeting. Sharing knowledge, discussing scientific hurdles, or just a little chatting during dinner, it certainly strengthened the collaboration within the consortium.

As the project itself, the agenda covered a wide range of scientific issues: From basic genetic research on heart development, studies on genes involved in congenital heart defects, experimental studies on the effects of maternal hyperglycemia on cardiovascular heart disease to the informatics aspects of genetic research.

Recruiting patients

Professor Lorentz Irgens was the host of the meeting. His group plays an important role in patient sample collection for workpackage 1 of the CHeartED project. Together with professor Judith Goodship from Newcastle, he recruits samples of children with cardiovascular malformations that have a mother that had diabetes when she was pregnant. Diabetes increases the risk of congenital heart defects. Workpackage 1 searches for interactions between genes and environment - like diet or medication - that influence this risk. This knowledge could help to prevent the development of congenital heart defects.

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**Gene- Environment
Interactions
in Heart Development**

www.CHeartED.eu





The second CHeartED Annual meeting was organized in Bergen, in the largest wooden building of the country, the building where the Medical Birth Registry of Norway (MBRN) is located. Today Norway is one out of five countries to have a national medical birth registry, as explained in a nice information booklet. The registry records all births in Norway and was established in order to prevent perinatal health problems. The immediate background was the numerous birth defects caused by the sleeping medicine Thalidomide in the 1960s. A main objective of the MBRN was then, as now, to identify new trends in birth defects as early as possible by means of epidemiological surveillance. The other main objective is epidemiological research on health problems originating in pregnancy or neonatally. The MBRN was the world's first national medical birth registry. Since it was established in 1967 it has developed greatly and today represents one of the world's most comprehensive medical birth registers, collaborating to an increasing extent in international research.

The Medical Birth Registry of Norway

Although cardiovascular malformations are the commonest birth defects, the number of children born with a cardiovascular malformation is quite small. Finding in this group those children of which the mother had diabetes during pregnancy is a real challenge. But not in Norway: 'We have a Medical Birth Registry (MBRN) that is very helpful finding these children', Irgens explains. 'With 2.5 million births registered since 1967, the MBRN forms a unique resource. The registry records all births and contains also data of the mothers. Since registration is compulsory, we have a nice set of data which we can use for the CHeartED project. Of course, the files for analysis are made anonymous.'

Participation disappointing

The group of Irgens searched in the registry for children born from a diabetic mother in the period from 1999 till 2008. Each year approximately 60,000 children were born of which about 500 had a mother that was

diabetic during pregnancy. Over these years 88 children with a diabetic mother were born with cardiovascular malformations. Their mothers were all contacted and invited to participate in the CHeartED research project. For yet unknown reasons, the participation rate is disappointing: so far, only 38 mothers gave their consent and saliva samples have been collected from 23 children.

As a control group, 251 diabetic mothers of a child without cardiovascular heart disease were randomly selected. 74 of them responded positively. In total, samples have been collected from 68 children who do not have cardiovascular malformations (13 of them are siblings of children that do have a malformation).

In the United Kingdom, Goodship and her collaborators encounter the same recruiting problems. They managed to get approval to recruit in ten hospitals. Samples have now been collected from 25 children with cardiac defects and 171 controls who do not have a cardiac defect.

Preventive efforts successful

The Medical Birth Registry has shown to be very useful for epidemiological surveillance. Professor Rolv Skjærven, chief statistician of the Bergen group, presented the results of his analysis during a guest lecture. He gave inside in the successes of the preventive efforts that have been undertaken to reduce the problems caused by diabetes during pregnancy. Since 1967, the risk of stillbirth, especially at the end of pregnancy, and the risk of a baby with cardiac defects is greatly reduced.

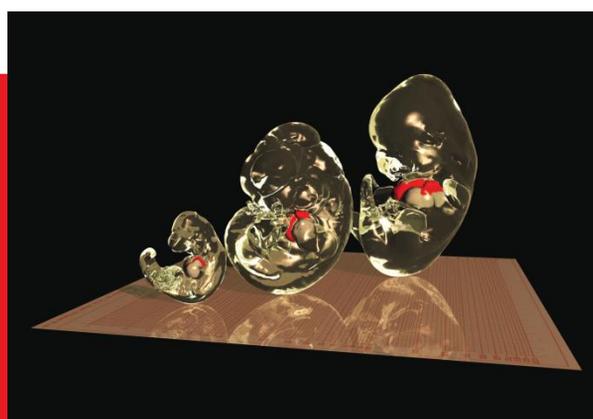
Other good news from professor Skjærven: Nowadays, newborn babies of diabetic mothers have the same chance to survive as babies of non-diabetic mothers. However, his analyses also indicate that women that have diabetes before their first pregnancy have reduced fertility for a second pregnancy and even more reduced for a third. In the next generation reduced fertility was observed in both sons and daughters. Daughters also had excess risk of developing all types of diabetes.

The first CHeartED dissertations

The CHeartED consortium is very proud that recently two of her PhD students successfully defended their thesis: Bouke de Boer of the Amsterdam Medical Center and Jeroen Breckpot of the Catholic University of Leuven. Congratulations!

Bouke de Boer received his doctors degree on July 7. He studied gene expression patterns in the mouse embryo to get a better understanding of heart development. In mice, the heart develops in a few days from a linear primitive tube into a complex heart with four chambers. To gain insight into the morphological changes a computer program was developed to automatically find cross sections in a reference model. To delineate heart compartments, De Boer collected the expression patterns of 12 genes and mapped them to one reference heart. With this atlas he revealed 18 domains with unique gene expression profiles. In addition he described the morphology and growth of the embryonic mouse heart and showed that cells in different compartments can have very diverse lengths of their cell cycle. With his work on the 3D gene expression atlas of embryonic heart development, De Boer contributed to workpackage 3.

Jeroen Breckpot defended his thesis on September 6. His project contributed to workpackage 4 and focussed on the



Cover photo of Bouke de Boer's thesis: 'Morphology, growth and patterning of the developing heart. Methods and applications'.

development of the CHD Wiki, the portal where all clinical and molecular data on Cardiovascular Heart Diseases can be integrated. Using this database, Breckpot identified novel genes involved in cardiovascular heart disease. In addition he discusses the use of array comparative genomic hybridization as a diagnostic tool and introduces an algorithm for the interpretation of copy number variants in patients with cardiovascular heart disease. Interesting are the differences he observed in copy number profiles in monozygotic twins of which only one has a congenital heart defect.

In the next News Bulletin, De Boer and Breckpot will tell more about their contribution to the CHeartED project.



The CHeartED consortium at the 2nd Annual Meeting on May 18-19 in Bergen, Norway

Look at www.CHeartED.eu for more photos

General remarks for CHeartED consortium

Website

- We ask you to check the information on the website. If you have any adjustments, please notify the dissemination manager.
- Visit the open-access CHDwiki via the CHeartED website. The Wiki contains lots of information about genetic and environmental knowledge on heart development. We invite you to take a look at the website and actively help to enlarge the database.

Dissemination

- To keep all consortium members informed, we ask the beneficiaries to announce CHeartED related meetings, courses, workshops etc. on the website.
- To share publications related to CHeartED with all consortium members, please upload all publications on the website.

To upload events or publications yourself, you have to login first. You may also ask the dissemination manager.

Do not forget to mention EU support in all publications, courses, workshops etc. as follows:

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Contact:

Coordinator: Prof. dr. Antoon Moorman
tel: +31-(0)20-5664928 or 5664647
e-mail: A.F.Moorman@amc.uva.nl

Project manager: R. van der Gaag, PhD
tel: +31-20-566 4927
e-mail: r.vandergaag@amc.uva.nl

Dissemination manager:

Nanna Claij, PhD
tel: +31-70-3155635
e-mail: n.claij@hartstichting.nl