



News Bulletin

Oktober 2012

‘Almost good is not good enough’

Professor Gerard Visser

Diabetes in heart development

Which genes play an important role in the development of the heart? And how does the interplay between environmental factors and genes affect proper heart development? To make a first start addressing these questions, the CHeartED consortium focusses on an important risk factor for congenital malformations: Diabetes of the mother during pregnancy. One of the most challenging parts of the project is to find sufficient children with a congenital heart disease born to a mother with diabetes. Quite a number of institutes

and hospitals in the United Kingdom, Norway and the Netherlands help to include patients. Professor Gerard Visser from the University Medical Center in Utrecht, is responsible for the recruitment in the Netherlands.

Dutch cohort

“In 1999 we started a unique cohort, that also is very useful for CHeartED,” Visser explains. “We asked all gynaecologists, internists, and diabetes nurse educators in the Netherlands to include all pregnant women with type 1 diabetes between April 1

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Gene- Environment
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1999 and April 1, 2000. All 118 Dutch hospitals participated. 323 women joined the cohort. They filled in questionnaires at inclusion (at around 10 weeks' gestation), at the end of the first trimester, and during the third trimester. Internists filled in a questionnaire including general characteristics, medical history, and diabetes related items; gynaecologists gave information about the outcome of pregnancy; and paediatricians filled in a questionnaire to collect information of the newborns. One year later 324 babies had been born. 29 of these babies had a congenital malformation, threefold more than you would expect in a random group of Dutch babies. 8 babies had cardiovascular malformations.”

Follow-up study

“We put a lot of effort in creating a good relationship with the mothers,” Visser continues. “And we asked them whether they would be willing to participate in future research. That formed a good basis for the follow-up study we started in 2007. The participation rate was very high. We collected data of 246 children, including growth data, blood pressure and heart function. 155 mothers agreed on additional blood sampling.”

Joining CHeartED

One of the goals of CHeartED is to search for genetic differences in the genome of persons with and without congenital heart disease born to a mother that had diabetes

during pregnancy. The Dutch cohort perfectly matched the needs of the project. Professor Antoon Moorman, project coordinator of CHeartED, knew about the cohort and asked Visser to join. Visser: “For us this was of course a great opportunity to get more data out of the cohort and to learn more about the influence of diabetes on genetic and epigenetic factors. Great advantage was that we already collected a lot of data and our good relationship with the mothers. However, not all mothers did like the idea that DNA of their child was being used for research. We could collect DNA samples of 125 children of which 3 had a heart disease.”

Complications by sugar

Besides the high chance of congenital malformations, diabetes during pregnancy also causes other serious complications. More babies are born too early, and more often by Caesarian section. This is partly caused by the large number of unborn children that grow disproportionately big and fat, because of the huge amounts of sugar they get via the placenta of their mother. The sugar is responsible for another complication. Since the children are not diabetic, they produce high levels of insulin to reduce the sugar that they get from their mother. Immediately after birth, this sugar supply stops while the insulin levels stay high. The insulin instructs the cells in the body to rapidly take up all glucose, resulting in an enormous sugar drop in the blood, which deprives the brain from sugar. This can cause serious brain damage and even death.

Tight control

“With very tight control of these pregnancies, we try to minimize the complications,” Visser explains. “In Utrecht we have an outpatient clinic especially for women with diabetes that have the wish to become pregnant. We motivate them to plan their pregnancies, help them to optimise the control of their blood sugar level and to start folic acid supplementation before conception.”



Despite tight control of the blood sugar level of the diabetic mother, the newborn is often abnormally big.

Frustrating

Visser: “Our very well controlled cohort contributed fantastically to our knowledge on complications, although the result of the study was quite frustrating: Despite a high frequency of planned pregnancies, resulting in good control of blood sugar levels (early) in pregnancy and adequate use of folic acid, complications were still increased in mother and child. Almost optimal control of blood sugar levels is apparently not good enough.”

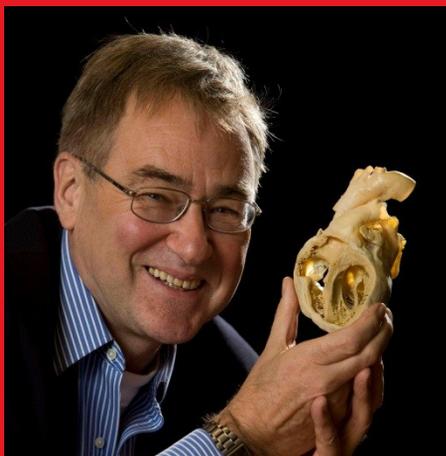
Challenge

“We are very curious whether the CHeartED consortium will find genetic changes in the genome caused by diabetes,” Visser concludes. “The heart develops very fast. In eight weeks it turns into its definitive fetal structure. Keeping blood sugar levels so constant that they do not intervene with proper development, seems to be an extreme challenge!”

Read more about the cohort in *BMJ* 2004;328:915

Announcement

‘Development of the heart’, a symposium on occasion of the retirement of professor Antoon Moorman.



Friday November 9, 2012; Amsterdam, the Netherlands

With lectures by:

Prof dr Richard Harvey (Sydney, Australia),
Prof dr Nadia Rosenthal (Monash, Australia)
Prof dr Robert Anderson (London, United Kingdom)
Prof dr Sir John Burn (Newcastle, United Kingdom)
Prof dr Margaret Buckingham (Paris, France)
Prof dr Roger Markwald (Charleston SC, USA)
Prof dr Christine Mummery (Leiden, The Netherlands)
Prof dr Vincent Christoffels (Amsterdam, The Netherlands)

Info: Maurice van den Hoff (m.j.vandenhoff@amc.uva.nl)
and Vincent Christoffels (v.m.christoffels@amc.uva.nl)

3rd Annual Meeting in Leuven, Belgium

November 22-23, 2012

Start of the meeting: 13.30 h on November 22

End of the meeting: 15.00 h on November 23

Hosts: Yves Moreau and Koen Devriendt

Participants will receive information about the location, the program, hotels in Leuven etc. by email.

Keep it simple!!!

Since the consortium covers very different disciplines, we ask all speakers to pay extra attention to their presentation: make sure that everyone in the room can understand what you are telling.



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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