

New Methods of Detecting Fetal Chromosome Abnormalities EACH Study (Incorporating Rapid Study)

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We are inviting many of the women who attend our Fetal Medicine Unit to take part in a research study. Before you decide whether or not to take part it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. One of our team will go through the information sheet with you and answer any questions you may have.

What is the purpose of the study?

The aim of this study is to evaluate new methods of fetal chromosome testing. Our genes are made up of building blocks called DNA which are located on structures called chromosomes. All our cells contain 46 chromosomes (23 inherited from each parent). Our genes act as instructions for passing on inherited characteristics such as eye colour and height from parent to child. They also provide the instructions for the baby's development. As a result, changes in baby's genes can lead to problems in development.

If a problem is found on a pregnancy scan, 1 in 4 of these babies will have a chromosomal abnormality. In some cases the baby has part or all of a chromosome missing while in others there is part or a whole extra chromosome. Down's syndrome is an example of a chromosome abnormality where the baby has a whole extra chromosome.

In order to diagnose a chromosome abnormality it is necessary to examine a sample of the baby's cells. These are obtained by amniocentesis or chorion villus sampling (CVS). In either case the sample of cells is initially examined for common major chromosome abnormalities (for example Down's syndrome). The result of this initial (rapid) test is available within 72 hours. In addition a more detailed test called karyotyping is performed. This test is offered as part of your normal standard care, and examines all of the baby's chromosomes. The result of this longer test is usually available within 14 days. However, if only a small part of a chromosome has been gained or lost, karyotyping cannot detect this. As these gains or losses can contain several important genes they can have a major effect on the baby's development. In this study we are using a new method of examining the DNA in our chromosomes - array comparative genomic hybridisation (or array CGH for short). The array test has the potential to detect around 5 to 10% more significant gains or losses of genetic material which are too small to be detected by karyotyping. Some of these gains or losses reflect normal variation and have no implications for a baby's development, but others have been found to be responsible for some physical and/or developmental problems in children. As some of these changes may be inherited from a parent we will ask to take a sample of your blood and, if possible, your partner's blood so that, if we find a change in your baby's DNA, we can check to see whether it has been inherited from a parent (and so is less likely to cause problems for the baby's development).

The aim of this study is to find out how much more information about the baby is provided when we use the array test, rather than the standard karyotyping test. The study will also determine how quickly array test results can be obtained and will help inform the NHS whether array CGH should replace karyotyping for the detection of fetal chromosome abnormalities.

Another new method of detecting some fetal chromosomal abnormalities is to examine maternal blood. We now know that when you are pregnant the baby's DNA can be found in your blood. Using new tests we are able to identify the baby's sex, blood group and possibly some genetic and chromosomal abnormalities such as Down's syndrome. In order to get the

greatest benefit from the samples collected in this study we propose, in addition to the array CGH study, to use your blood sample for another research study called RAPID which may help develop these additional new tests which, ultimately, may allow the diagnosis of some genetic and chromosomal abnormalities without the need for amniocentesis or CVS.

Why have I been chosen?

We are inviting all women who have decided to have an amniocentesis or CVS after a problem in their baby was seen on scan to take part in the study.

Do I have to take part?

It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and asked to sign a consent form. If you decide to take part you are free to withdraw at any time without giving a reason. If you do not feel able to take part it will not in any way affect the care you or your family receives.

What will happen to me if I take part?

If you agree to take part we will ask you to donate a blood sample. Where possible we would also like to take a sample of blood from your partner. We will use the sample taken at your CVS or amniocentesis to perform the array test, but only if there is enough material left after performing the routine karyotyping test. We will not take any additional amniotic fluid or chorionic villi.

If the initial test, which is available within 72 hours or the CVS or amniocentesis, shows a major chromosomal abnormality we will not perform the array CGH test. We would still use your blood sample to see if we could have detected the abnormality in the baby's DNA in your blood as part of the RAPID study.

We will also seek permission to ask your doctor, or check your hospital notes, to confirm the outcome of your pregnancy. With your agreement we may contact you when your baby is around 2 years old to arrange a follow-up to find out how he/she is developing. A small number of women will also be asked if they are prepared to participate in an in-depth interview with a researcher about their experience – more information will be provided to those women interested in taking part.

Will my taking part in this study be kept confidential?

Yes. We will follow ethical and legal practice and all information will be handled in confidence. Any information you give us will only be used by the research team in the course of the research. Any samples and data stored will be stored securely.

What are the possible benefits of taking part?

The results of the routine karyotype test will be available to you. If this shows a major chromosomal abnormality not detected on the initial (rapid) test then the implications of the result and your pregnancy options will be discussed with you by a specialist doctor. If the karyotype test is normal and the array CGH test is normal we will not inform you of the array result.

Very occasionally, despite a normal result on the initial (rapid) and karyotype tests, the array test will detect a loss or gain of genetic material from one of the baby's chromosomes. In this case the laboratory will perform an array test on your blood and whenever possible the baby's father's blood. If the same finding is present in one of the parents (as is often the case) then we can assume that the loss or gain of genetic material in the baby has been inherited from the parent and is very unlikely to explain the scan findings. However, if the loss or gain of genetic material is not present in a parent and particularly if it involves a number of important genes, we will report this finding to your doctor as it may account for the scan problems and could have important implications for the baby's development. In this case a specialist doctor will discuss with you what the array result might mean for your baby and your pregnancy options. However some of the genetic variations detected by the array test cannot be accurately interpreted at the current time. Therefore only changes which we can interpret clearly on the basis of the available medical literature will be reported.

We envisage that the results of the study will enable us to develop more effective prenatal tests for rare chromosomal conditions as well as Down's syndrome.

What are the possible disadvantages and risks of taking part?

The only additional sample to be collected is a blood sample. This will be carried out by someone who is skilled in taking blood. Some people may experience bruising at the site which will resolve over a few days. If the karyotype or array CGH test suggests an abnormality, there may be some distress caused by the need to contact the baby's father (if he was not present at the initial consultation).

What will happen if I don't want to continue in the study?

You are free to withdraw at anytime. If you withdraw from the study we will not access any further samples and will destroy any of your samples that were collected for the study.

What will happen to any samples I give?

Any unused DNA extracted from the baby's amniocentesis or CVS sample and your blood samples will be stored as part of a Research Tissue Bank. The samples will be coded and no personal data (name and address) will be stored with the sample. The DNA samples will only be used in research studies designed to develop these new methods of diagnosing chromosomal abnormalities.

What will happen to the results of the research study?

The results from our project will be published as research papers in medical journals. No data will be published that will allow individuals to be identified.

Where can I get further information or discuss any problems?

Please contact a member of the research team at Royal Victoria Infirmary on 0191 282 0362 to discuss any questions or worries about the study. If the problems are not resolved or if you wish to speak to someone independent of the study please contact the Patient Advisory Liaison Services (PALS) if you have any concerns regarding the care you have received, or as an initial point of contact if you have a complaint. Please telephone **0800 320 202**, you can also visit PALS by asking at any hospital reception.

Who is organising and funding the research?

This research is organised by the Fetal Medicine Unit Research Teams at Newcastle upon Tyne Hospitals NHS Trust and Great Ormond Street Hospital for Children NHS Trust funded by the National Institute for Health Research.

Who has reviewed the study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by the Newcastle and North Tyneside 2 National Research Ethics Committee. The RAPID Study has also been reviewed, and was given favourable opinion by the University College London Hospitals Research Ethics Committee.

Thank you for taking the time to read this information leaflet.

Glossary

Genes

Genetics is the branch of science that deals with how you inherit your physical and behavioural characteristics. The genetic information that controls these characteristics, such as the colour of your hair and eyes, is located in genes which are found in chromosomes. Our genes are made up of building blocks called DNA.

Chromosomes

Each cell in the body contains 23 pairs of chromosomes. These carry the genes that you inherit from your parents. In this way you can inherit a health condition or disease, or a tendency to develop a particular condition. One in each pair is inherited from each parent, so with one exception, there are two copies of each gene in each cell.

DNA

Deoxyribonucleic acid (DNA) is the long molecule that stores genetic information. DNA is made of two strands coiled together, each one a mirror image of the other. Because of this, it can be divided easily when a cell divides and the genetic code is passed on exactly. However, sometimes part of the DNA can become altered and result in small changes that could be responsible for developmental anomalies.

Amniocentesis

Amniocentesis is a test carried out during pregnancy which involves using a fine needle to remove a small amount of the amniotic fluid around your unborn baby. Amniocentesis is used to detect chromosomal abnormalities such as Down's syndrome as well as certain other genetic conditions. Amniocentesis is known as a diagnostic test because it gives you a diagnosis. For example it tells you that your baby does or does not have Down's syndrome. Amniocentesis is carried out after 15 weeks of pregnancy. One in every 100 women (1%) who have an amniocentesis will miscarry.¹

Chorion Villus Sampling

Chorionic villus sampling (CVS) is a test carried out during pregnancy which involves using a fine needle to remove a small amount of the placenta (afterbirth). CVS is used to detect chromosomal abnormalities such as Down's syndrome as well as certain other genetic conditions. CVS is known as a diagnostic test because it gives you a diagnosis. For example it tells you that your baby does or does not have Down's syndrome. CVS is usually carried out between the 11th and 14th week of your pregnancy. One or two in every 100 women (1-2%) who have a CVS will miscarry.¹

Karyotyping

Karyotyping looks at the cells taken during amniocentesis or CVS under a powerful microscope. This allows the person who is carrying out the test to examine the chromosomes directly. By counting the chromosomes and by checking their shape, it may be possible to detect changes that could be responsible for genetic abnormalities.

Array CGH

Array CGH (comparative genomic hybridization) examines DNA from cells taken during amniocentesis or CVS. It is used to detect very small gains or losses of genetic material which are too small to be detected by karyotyping. These gains or losses deletions or insertions can be responsible for genetic abnormalities leading to physical and/or developmental problems in children..

¹ More information on amniocentesis and CVS can be found in a leaflet called 'Amniocentesis – information for parents' or Chorionic villus sampling (CVS) – information for parents'. These are available here:
[http://fetalanomaly.screening.nhs.uk/publicationsand leaflets.](http://fetalanomaly.screening.nhs.uk/publicationsand%20leaflets)