A European clinical database of patients with Wilson's disease

Information for parents of a child with Wilson's disease

Your child has recently been diagnosed as having Wilson's disease. A database of all newly diagnosed patients with Wilson's disease in Europe has been established. We are asking your permission to include your child's details in this database. Before you decide it is important for you to understand why the database has been set up and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

There is also an information sheet for children, and a leaflet called "Wilson's disease for younger people". We have a website called www.eurowilson.org which gives information about Wilson's and about this project.

Thank you for reading this. In the rest of this document Wilson's disease is called "WD".

What is the purpose of the study?

We already know a great deal about WD, but there is a need to find out more. Here are some of the questions we need to answer.

1. How common is it? The estimates we have vary from 1 in 30 000 to 1:100 000 people. We do not know whether this represents true variation in different populations, or under- or over-diagnosis.
2. Some patients with WD have mainly liver disease, some mainly neurological disease, and some have other clinical problems. We need to know exactly how many patients are in these different categories.
3. Sometimes diagnosis can be difficult. There are laboratory tests for WD, but sometimes they give unclear results. It can sometimes be difficult to distinguishing people with WD from people who are just carrying the gene. We need more information about which is the best test or combination of tests.
4. Since the gene for WD was discovered, it has become possible in some patients to make the diagnosis by studying DNA. Why not all patients? The reason is that there can be different mutations causing WD. In Eastern Europe we know that one particular mutation is most common, so this is very helpful in making the

diagnosis. But in other parts of Europe, there are many different mutations. We need to know what are the commonest mutations in different parts of Europe.

5. Do different mutations cause different sorts of problems with WD? There is some evidence that one particular mutation is more likely to cause neurological problems. But this cannot be the whole explanation for different sorts of clinical problems in WD, because people with exactly the same mutations may have different problems. So we need to look for other genes that may modify the effect of the WD mutation.
6. Which are the best drugs to treat WD? We now have a number of drugs, like penicillamine, trientine, zinc sulfate or acetate. The only way to decide which drug is best for which kind of disease is a randomised controlled clinical trial. Before we can even think about setting up a trial, we need to know exactly how many patients there are in each clinical category. That is what EuroWilson is all about – finding out how many patients there are.
7. Some patients with WD have such severe liver disease that a liver transplant is necessary. By carefully documenting these patients we hope to learn how to recognise them more quickly and to improve their treatment.
8. We need better information on the very long term outcome for patients treated for WD. EuroWilson is funded for 4 years, but we hope that we will be able to continue it after that so the progress of patients on the database can be recorded for many years.
9. When a diagnosis of WD has been made in a family, it is sometimes possible to identify younger brothers or sisters who have the genes for WD but have not yet developed any clinical problems. We need to decide how they should best be treated. First, we need to know how many such young people there are and what is currently happening to them in Europe.

Why has my child been chosen?

Because he or she has Wilson's disease and because we want to gather information about every patient diagnosed with Wilson's disease in the whole of Europe.

What will happen to us if we take part?

You will not have to take any action at all. There will not be any tests or hospital visits extra to those needed for his or her clinical care.

In this section we will explain what will happen if you do agree to take part.

Either your doctor, or another doctor in your country specialising in Wilson's disease, will enter data about your child's illness and tests into a computer. The computer is in Grenoble, France. The doctor who is entering the data has been supplied with a card with a password, and a card reader which fits into his or her computer. This card reader is able to encrypt data so that nobody else using the internet can gain access to it. Data will be anonymised so that the computer in Grenoble will not know your name or address. The data will be given a number, and only the doctor entering the data will know which number your child has been given.
The doctors who are looking after your child will have sent a blood sample to a genetics laboratory. There they will have looked to see whether he or she has mutations known to cause WD. This is part of making the diagnosis. We are asking

your permission for the laboratory to retain the sample securely, and to use any of the sample which is surplus to requirements for diagnosis, for the following purposes.

1. Improved methodology. The techniques which we have now for detecting mutations are much better than those we had a few years ago. We expect that there will be more technical advances in the future. Those new techniques need to be checked using real samples from patients. This means that a sample which has already been tested is checked again with new methods.
2. Quality control. All laboratories doing tests on patients samples need to be checked to make sure that their results are accurate and reliable. Mutation testing in WD is done by a small number of laboratories across Europe. It is planned to select samples from a small number of patients and ask all the laboratories to test them again, to make quite sure that all the laboratories accurately detect the mutations. Before any sample is used in this way, it is anonymised, so that your name does not go to the other laboratories. Your child or family will not get any direct benefit from this, and you are making a gift of the sample to the research team.
3. Modifier genes. We do not understand why different patients with exactly the same mutation may have quite different clinical problems, or similar problems with different severity. It is possible that other genes modify the effect of the Wilson's gene. In the future we may be able to test for other modifier genes. Although this research is not planned at present, it is likely that it will be done in the future. It will be necessary to link the mutations in your sample with an account of the clinical problems which you have had, but your name will not be used. The samples and the clinical accounts will be anonymised. Your child or family will not get any direct benefit from this, and you are making a gift of the sample to the research team.

By describing the use of surplus sample for these purposes as a gift, we mean

1. That you are voluntarily giving the sample for research, and
2. you are giving up any rights to information which may come from research on your child's sample

But your gift is conditional, and the conditions are

1. nothing will be done with the sample which is detrimental to your family's interests
2. it will not be possible to identify your family in any publication or report which arises from this research
3. there will be no commercial use of your child's sample, and none of the researchers will profit from research using your child's sample sample
4. You are only consenting to the uses specified above
5. A research project on modifier genes would be referred to a research ethics committeee for approval before it could go ahead.

Do we have to take part?

It is up to you and your child to decide whether or not to allow your child's details to be included in the database. . If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take

part you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive. If you do ask to withdraw, you will be asked if we may retain a minimum of coded data (your child's age, gender, and clinical category) because this will help us to know how many patients there are in total, but your wishes in this matter will be respected.

It is also up to you to decide whether or not to allow research to be carried out on your DNA sample.

Will our taking part in this study be kept confidential?

All information which is collected during the course of the research will be kept strictly confidential. Any information which is entered onto the database will have the name and address removed so that you cannot be recognised from it.

Your own GP will be notified of your participation in the database unless you say you do not want this.

If you agree to taking part in this study, then coded information about your case may be passed to researchers in countries that do not have the same protections as in the UK.

What sort of data will be collected?

These are the categories of data which will be collected, and the reasons for collecting them.

Data	Reason for collecting data
Age	WD is different in children from WD in adults
Gender	We do not know if there is a difference in severity between meles and females
Clinical problems at time of diagnosis	Some WD patients initially have liver problems, some have neurological problems, some have other problems. Within those groups there are some different kinds of problem. We need to know how many are in each category, so that we can design trials of different treatments which are best for each category.
Laboratory tests at the time of diagnosis	This is so that the research team can check that the diagnosis of WD is certain
Mutations	This is so that we can find out if particular mutations are associated with particular kinds of clinical problems, or better or worse response to treatment
Treatment given	We need to know which treatments are being used in different across Europe
Clinical problems at yearly intervals after diagnosis	This will tell us how different groups of patients are responding to the treatment they have been given
Laboratory tests after diagnosis	Looking at the results of tests will also tell us how well you are responding to your treatment

How long will data be kept?

This project is funded for 4 years. We hope that after that there be more funding to continue the database and to set up clinical trials of different treatments. WD is a lifelong condition which will need treatment indefinitely. It is important that we study how well patients progress over many years. So we are asking permission to retain your child's anonymised details in the database for so long as we are able to maintain the database securely.

I f we are not able to find funding to continue the database after 4 years then the records will be destroyed.

How long will my DNA sample be kept if I give permission for you to retain it?

It will be kept for 4 years as part of this project. We hope that after that there be more funding to continue the research, and so we ask permission to retain the samples for as long as there is funding.

Will it be used for any of the following purposes?

- Commercial research No
- Research into diseases other than WD No
- Any forensic purpose No

Can I consent to just a part of the study?

Yes, you can. For example, you may consent to your child being in the database but not want to consent to research on the DNA sample. If you do not wish all your child's details to be in the database we will ask if you will allow us just to record minimal anonymised facts for the purposes of counting patients.

Are there any direct benefits to us of taking part in this research?

No. This research will be of benefit to future patients with WD who will have better treatment,

What are the possible disadvantages and risks of taking part?

We do not believe there are any risks at all.

Where can I find more information about WD?

There is a web-site, www.eurowilson.org

What if new information becomes available?

If additional information about WD becomes available during the course of the research it will be posted on the website.

What if something goes wrong?

If you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms should be available to you.

What will happen to the results of the research study?

Results from this study will be published in papers published in the medical literature. Reports of the progress of the study, and of any papers published, will appear on the website, www.eurowilson.org. You will not be identified in any report or publication.

Who is organising and funding the research?

This project is funded by the European Union. It is called a "Coordination Action", because doctors from 15 different centres have come together to form a consortium to do this research. It is led by the University of Sheffield. The names of the centres and the doctors participating are all on the web-site.

The doctors conducting the research are not being paid for conducting this research, but their expenses for attending meetings of the consortium are met.

Who has reviewed the study?

The Trent Multi-Centre Research Ethics Committee, REC reference number 04/MRE04/65

Contact for Further Information

Further information can be obtained from

The doctor who is treating your WD, or

Dr Anil Dhawan
Consultant Paediatric Hepatologist
Kings College Hospital
Denmark Hill
London SE5 9RS
Tel 020 7346 3214
Fax 020 7346 3564

Professor Stuart Tanner
Sheffield Children's Hospital
Western Bank
Sheffield S10 2TH
Tel 0114 271 7303
Fax 0114 275 5364

Or the website at www.eurowilson.org

Thank you very much for agreeing for take part in this study. This is a copy of the information sheet for you to keep. You will also be able to keep a signed consent form.

UNIVERSITY OF SHEFFIELD

www.eurowilson.org

CONSENT FORM FOR PARENT

Title of Project: Wilson Disease: Creating a European Clinical Database and designing randomised controlled clinical trials.

Name of Researcher: Professor Stuart Tanner, University of Sheffield, Tel 0114 271 7303

	Please initial box
1. I confirm that I have read and understand the information sheet dated ..... (version .....) for the above study and have had the opportunity to ask questions.	
2. I understand that our participation is voluntary and that we are free to withdraw at any time, without giving any reason, without my child's medical care or legal rights being affected	
3. I agree to data from my child's notes being included in a European database, on the understanding that his/her name and other information by which our family might be identified is withheld.	
4. I understand that genetic material from my child's blood sample can be used to help make the diagnosis of Wilson's disease, and I give permission for any surplus sample to be used as in the information sheet.	
5. Please tell my child's GP that we have consented to be in this database	
6. I agree to that coded data about my child relating to this study may be sent to countries that do not have data protection laws similar to those in the UK.	

Name of patient	Signature	Date
Name of Person taking consent	Signature	Date
Researcher	Signature	Date

1 copy for patient; 1 for researcher; 1 to be kept with hospital notes