

The treatment of thyrotoxicosis (an overactive thyroid gland) in young people

Parent / Guardian information Sheet

We would like to invite you / your child to take part in a research study that is trying to find out the best way of treating young people with an overactive thyroid gland. Before you decide 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 carefully and ask us if there is anything that is not clear or if you would like more information. Thank you for reading this.

What is the purpose of the study?

A young person with an overactive thyroid gland (thyrotoxicosis) produces too much thyroid hormone. This can damage health in the long term and so it is important to treat this condition. The young person is usually treated with the drug carbimazole to reduce the amount of thyroid hormone produced. Children and adolescents are given this drug for approximately 2 to 3 years. It is then stopped because we know that in some people the gland will no longer be overactive. There are, however, two possible ways to use the drug carbimazole:

Treatment 1

The 'block and replace' approach where thyroid hormone production by the thyroid gland is stopped completely. Thyroxine is then added in a normal replacement dose. The young person therefore takes two medicines (carbimazole and thyroxine).

Treatment 2

The 'dose titration' approach where a smaller dose of carbimazole is used so that thyroid hormone production by the thyroid gland is reduced to normal but not blocked completely. The young person therefore only takes one drug (carbimazole).

Both of these approaches are used in the United Kingdom and the aim of this study is to find out which is best.

How long will the study last ?

The study will last for a total of 6 years although your child will only be closely monitored for the first 4. The first 3 years will involve treatment with medication (either the 'block and replace' or 'dose titration' approach) and the fourth year will be a period of monitoring to see whether the thyroid gland becomes overactive again when the medication has been stopped. We will also contact your child's doctors after 2 more years to find out whether anything has changed.

Why has my child been chosen?

You/your child has been chosen because they have an overactive thyroid gland (thyrotoxicosis). We intend to recruit a total of around 130 patients from centres in the United Kingdom as part of this study.

Does my child have to take part ?

It is up to you/your child to decide whether or not to take part. If you decide to take part you will be given this information sheet to keep and be asked to sign consent forms, one of which you will also keep. 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.

What will happen if my child takes part ?

If you / your child agrees to take part then they will be randomly allocated to one of the two treatments ('block and replace' or 'dose titration') described above. The choice of treatment 1 or 2 is made by a computer that has no information about the individual – hence it is made by chance.

Your child will then be treated for 3 years at which point the medication will be stopped. We will then see whether or not the thyroid gland becomes overactive again during the fourth year of the study and then after six years. The study will not involve more blood tests

(venepunctures) than would occur if your child did not take part in the study. Most young people taking part will also have a wrist X-ray (bone age) to look at bone maturity and an ultrasound scan soon after they have been diagnosed with thyrotoxicosis and some will also have an isotope scan of the thyroid gland. An ultrasound scan involves placing a probe against the neck and an isotope scan involves injecting a special dye into a vein to look at how the thyroid gland is working. All are tests that are commonly requested by doctors looking after young people with thyrotoxicosis not taking part in a study. We also hope to be able to arrange for a wrist X-ray and ultrasound scan at the end of the third and fourth years of the study. Finally, we would also like to take a blood sample from your child and from you so that we can study the genes that are involved in people getting thyroid problems in the first place- as outlined on the next page.

What are the drugs being tested?

The main drug that is being used in this study is called carbimazole. Occasionally a similar drug called propylthiouracil is used. Both of these medicines have been used in the United Kingdom for many years and they are the only two drugs that can be used to reduce thyroid hormone levels in the young person with an overactive thyroid gland in the longer term. The dose of carbimazole or propylthiouracil used depends on the size of the young person but will be lower in the 'dose titration' group (treatment 2).

For those people treated with the 'block and replace' approach (treatment 1) a second medication, thyroxine, will be used. This is the same as the thyroxine made by the body except that it is produced artificially. The dose of thyroxine used depends on the size of the young person.

Are there lifestyle restrictions ?

There are no lifestyle restrictions whilst taking part in this study although your child will need to take the medication regularly.

What are the alternative treatments ?

The only other treatment options in the young person with an overactive thyroid gland are surgery or radio-iodine. Surgery involves removing overactive thyroid tissue although the person can only be operated on when the thyroid hormone levels have been reduced to normal. Radioiodine involves taking a dose of radioactive iodine to destroy the thyroid gland. Most paediatric doctors do not recommend surgery or radio-iodine as an initial treatment in the young person with an overactive thyroid gland although both are used in the young person who still has thyrotoxicosis despite a course of antithyroid drug treatment.

What are the side effects of treatment ?

Carbimazole and propylthiouracil can cause relatively minor side-effects such as a rash. However there is one very important side-effect of carbimazole and propylthiouracil that you need to be aware of which is that these drugs can reduce the number of white cells in the blood stream that fight infection. Any person on these medicines should therefore stop them if they have signs of an infection (especially a sore throat) until the white cell count has been checked and is found to be normal. It is important to seek medical advice as soon as possible in these circumstances so that the white count is checked the very same day. The number to use for emergency use if this is the case is as follows:

Phone number for emergency use

What are the disadvantages and advantages of taking part ?

The majority of young people with an overactive thyroid gland in the UK are already treated with anti-thyroid drugs using one of the two treatment approaches described above (block and replace or dose titration). What this study will do is work out which is best. There will therefore be no direct benefit to you / your child although it will help us to establish which is the best treatment for young people with an overactive thyroid gland in future.

What if new information becomes available ?

Sometimes during the course of a research project, new information becomes available about the treatment/drug that is being studied. If this happens your doctor will tell you about it and discuss this with you. You will then be able to withdraw or continue in the study. On receiving new information your doctor might also consider it to be in your child's best interests to withdraw them from the study. He/she will explain the reasons for this.

What do genetic studies involve?

We would also like to take a sample of blood from you (and from your child at the time of routine blood tests) that will be used to find out which genes make us more likely to get thyroid problems and other autoimmune disorders. The blood samples taken will be stored for a maximum of 10 years before being destroyed (by incineration). The results of the genetic studies will not influence the treatment of your child. You can agree for your child to take part in the study of antithyroid drug medication whilst not donating the sample of blood for the genetic studies. Any other studies on stored blood samples must be passed by an Ethics Committee.

What happens when the research study stops ?

When the research study stops (after 6 years) your child may be off all medicine or may have relapsed and be back on anti-thyroid drugs. It is also possible that if your child has relapsed before the end of the study (in the final year) and that you will have decided to treat the overactive thyroid gland with surgery or radio-iodine. You will obviously have had plenty of opportunity to talk to your doctor about this.

What if something goes wrong ?

In the unlikely event that your child is harmed by taking part in the research project there are no special compensation arrangements. If you are harmed due to someone's negligence then you may have grounds for a legal action but you may have to pay for it. Regardless of this, 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.

Will my taking part in this study be kept confidential ?

All information that is collected about you during the course of the research will be kept strictly confidential. Any information about you which leaves the hospital will have your name and address removed so that you cannot be recognised from it. Your GP and your child's GP will be informed if you take part in the study.

What will happen to the results of the research study ?

The results are likely to be available in 5 to 7 years time and will be described at medical meetings and published in medical journals.

Who is organising the research ?

This study has been designed by the clinical trials unit of the British Society for Paediatric Endocrinology and Diabetes.

If you have any questions regarding this study, please contact your child's paediatrician or the study co-ordinator who is

Dr Tim Cheetham Senior Lecturer in Paediatric Endocrinology, Royal Victoria Infirmary, Newcastle-upon-Tyne, UK. Telephone 0191 233 6161 bleep 2333

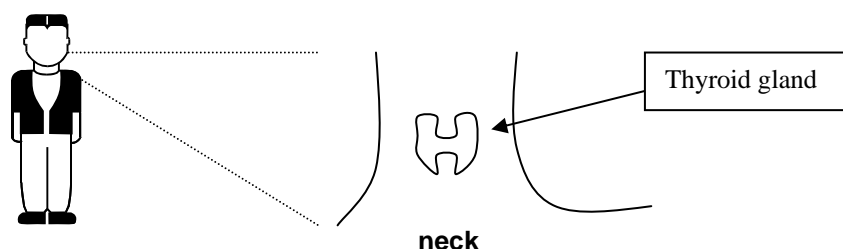
The treatment of thyrotoxicosis (an overactive thyroid gland) in young people

Patient / young person information sheet (12 – 16)

We would like to invite you to take part in a research study that is trying to find out the best way of treating young people with an overactive thyroid gland. Before you decide it is important for you to understand why the research is being done and what it will involve. Please ask us if there is anything that is not clear. Thank you for reading this.

What is thyrotoxicosis ?

Your parents and doctors have found that you have a condition called thyrotoxicosis. This means that your thyroid gland is overactive – in other words it makes too much thyroid hormone. The thyroid gland is in the neck (see the picture below) and sometimes this can get bigger than normal in people with this condition.



Too much thyroid hormone can make you feel unwell. Sometimes young people with thyrotoxicosis feel very unwell and other times they just feel a little bit different to normal. We know that it is best to treat this problem because it makes the person feel better and helps to keep them to grow and develop normally in the long term.

What is the purpose of the study?

A young person with an overactive thyroid gland (thyrotoxicosis) is usually given a medicine called carbimazole to reduce the amount of thyroid hormone produced. They are usually given the medicine for 2 to 3 years. It is then stopped because we know that in some people the gland will no longer be overactive. There are two ways to use the drug carbimazole:

Treatment 1

'Block and replace' where thyroid hormone production by the thyroid gland is stopped completely. Thyroxine is then added in an amount normal replacement dose. The person therefore takes two drugs (carbimazole and thyroxine) during the 2 to 3 year treatment period.

Treatment 2

The 'dose titration' approach where a smaller dose of carbimazole is used so that thyroid hormone production by the thyroid gland is reduced to normal but not blocked completely. The person therefore only takes one drug (carbimazole).

Doctors use both approaches and this study is designed to find out which is best.

How long will the study last?

The study will last for a total of 6 years. The first 3 years will involve treatment with medication (treatment 1 or 2) and the fourth year will involve monitoring you when the

medication has been stopped. We will also contact your child's doctors after 2 more years to find out whether anything has changed.

Why have I been chosen?

You have been chosen because you have an overactive thyroid gland (thyrotoxicosis). We want to involve a total of 130 young people with thyrotoxicosis from centres around the United Kingdom in this study.

Do I have to take part ?

It is up to you and your parents to decide whether or not to take part. If you decide to take part you will be given this information sheet to keep and be asked to sign consent forms, one of which you will also keep. If you decide to take part you are still free to withdraw at any time and without giving a reason.

What will happen if I take part ?

If you agree to take part then you will be given one of the two treatments ('block and replace' or 'dose titration') described above. You will be treated for 3 years and then the medication will be stopped. We will then see whether or not the thyroid gland becomes overactive again in the fourth year of the study. The choice of treatment is made by a computer – hence it is made by chance. The study will not involve any extra blood tests (venepunctures) than would happen if you didn't take part.

Most young people taking part in this study will also have a wrist X-ray and an ultrasound scan soon after they have been diagnosed with thyrotoxicosis and some will also have an isotope scan of the thyroid gland. All are tests that are often requested by doctors looking after young people with an overactive thyroid. An ultrasound scan involves placing a probe against the neck and an isotope scan involves injecting a special dye into a vein to look at how the thyroid gland is working. The injection into the vein will be given after anaesthetic cream or spray has been used so that it does not hurt. We hope to arrange for a wrist X-ray and an ultrasound scan at the end of the third and fourth years of the study as well. Finally, we would like to take a sample of blood to work out which genes are involved in young people getting thyroid problems in the first place. This blood sample can be taken at the same time as one of the routine blood tests.

What are the drugs being tested?

The main drug that is being used in this study is called carbimazole. Occasionally a similar drug called propylthiouracil will be used. Both of these medicines have been used in the UK for many years and they are the only two drugs that can be used to reduce thyroid hormone levels in the longer term. The dose of carbimazole or propylthiouracil used depends on your size but will be lower in the 'dose titration' group (treatment 2). For those young people treated with the 'block and replace' approach (treatment 1) a second medication, thyroxine, will be used. This is the same as the thyroxine made by the body except that it is produced artificially.

What are the alternative treatments ?

The only other way to treat the young person with an overactive thyroid gland is with surgery or radio-iodine. Surgery involves removing the overactive thyroid tissue and radioiodine involves taking a dose of radioactive iodine to destroy the thyroid gland. Most doctors do not recommend surgery or radio-iodine as a first treatment in the young person with an overactive thyroid gland although both are used in the young person who still has thyrotoxicosis despite a course of the antithyroid medicine.

What are the side effects of treatment ?

Carbimazole and propylthiouracil can cause minor side-effects such as a rash. However there is one very important side-effect of carbimazole and propylthiouracil that you need to be aware of which is that these drugs can reduce the number of white cells in the blood stream that fight infection. Any person on these medicines should therefore stop them if they have signs of an infection (especially a sore throat) until the white cell count has been checked and is normal. You must therefore tell your parents, carers or doctors straightaway if you feel unwell.

What are the disadvantages and advantages of taking part ?

Most young people with an overactive thyroid gland are already treated with anti-thyroid drugs using one of the two approaches described above (block and replace or dose titration). What this study will do is work out which is best. There will therefore be no direct benefit to you but it will help us find out which is best for young people in future. There are no restrictions in terms of what you can do whilst taking part in this study although you will need to take the medicines regularly.

What if new information becomes available ?

Sometimes during the course of a study new information becomes available about the treatment that is being studied. If this happens your doctor will tell you about it and discuss this with you. You will then be able to withdraw or continue in the study.

What do the genetic (gene) studies involve?

The genetic studies are to try and work out why people get thyroid and other similar problems in the first place. This will not involve another blood test because this will be taken at the same time as other samples. The blood samples taken will be stored for a maximum of 10 years before being destroyed (by burning them). You can agree to take part in the study of the two treatments whilst not donating the sample of blood for the genetic studies.

What happens when the research study stops?

When the research study stops you may be well off all medicines or may have had to go back onto anti-thyroid drugs. It is also possible that gland over-activity returned before the end of the study (in the final year) and that you / your parents have decided to treat the overactive thyroid gland with surgery or radio-iodine. You will have plenty of opportunity to talk to your parents or carers and doctor about this.

Will my taking part in this study be kept confidential ?

Information about you that is collected during the course of the research will be kept strictly confidential. Any information about you which leaves the hospital will have your name and address removed so that you cannot be recognised from it.

What will happen to the results of the research study ?

The initial results are likely to be available in 5 to 7 years time and will be described at medical meetings and published in medical journals.

Who is organising the research ?

This study has been designed by a group of doctors from the clinical trials unit of the British Society for Paediatric Endocrinology and Diabetes.

If you have any questions about the study then please talk to your parents or your doctor.