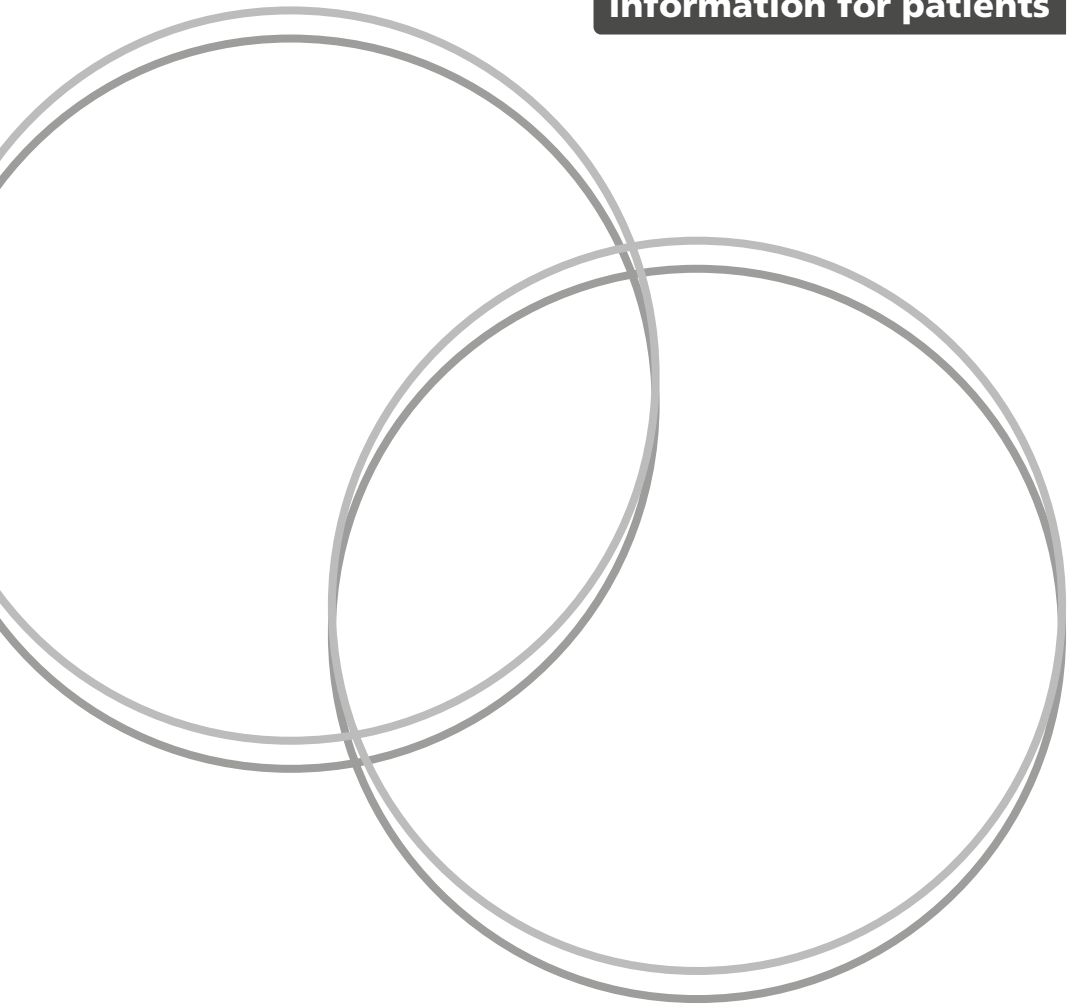
Oxford University Hospitals
NHS Foundation Trust

Thrombotic Thrombocytopenic Purpura (TTP)

Information for patients



You have been diagnosed with thrombotic thrombocytopenic purpura (TTP). This leaflet aims to give you information about this condition.

What is thrombotic thrombocytopenic purpura (TTP)?

Thrombotic Thrombocytopenic Purpura (TTP) is a rare blood disorder, with 100 to 150 new cases every year in the United Kingdom. It is more common in women than men. It can affect people of all ages, and the average age at diagnosis is 40 years. TTP occurs when lots of small blood clots form in the blood vessels throughout the body. These clots may form in any part of the body including the brain, heart and kidneys.

TTP episodes are serious and life-threatening

TTP is considered a medical emergency. Without treatment, 90-100% of people will die from TTP. Once treatment has started the risk of death is low, as treated TTP has a survival rate of greater than 90 in 100. Treatment must be started as soon as possible when TTP is suspected.

What causes TTP?

TTP stands for **Thrombotic Thrombocytopenic Purpura**

- **Thrombotic (T)**: clots in the blood vessels
- **Thrombocytopenic (T)**: low platelets (small cells in the blood important for normal blood clotting)
- **Purpura (P)**: bleeding into the skin forming spots or bruising caused by low platelets

TTP is caused by lack of an important enzyme in the blood called ADAMTS13 which normally breaks down a very large protein involved in blood clotting called Von Willebrand Factor.

People with TTP do not have enough ADAMTS13, so long sticky strings of Von Willebrand Factor form in their blood. Platelets (small cells in the blood important for normal blood clotting) stick to the Von Willebrand Factor. This leads to lots of small blood clots forming in the blood.

There are two types of TTP:

- **Immune-mediated TTP**: this is caused when a persons immune system starts to produce antibodies, a protein that mistakenly attacks the ADAMTS13 enzyme and stops it from working properly. You may hear this described as an autoimmune condition. In some cases, immune-mediated TTP may be triggered by other health conditions such as systemic lupus erythematosus, cancer, HIV, infections or pregnancy. It may also be triggered by some medications such as chemotherapies and contraceptive pills containing oestrogen. Immune-mediated TTP cannot be passed on to children or other family members. You cannot ‘catch’ TTP from someone else who has it.
- **Congenital (inherited) TTP**: this is much less common than immune-mediated TTP and is a condition where a genetic change means the body is not able to make ADAMTS13.

Diagnosing TTP

People with TTP experience many different symptoms including flu-like illness, fever, tiredness, headache, confusion, bruises or dots on the skin (petechiae), anxiety, chest pain, dark coloured urine, yellow colour of the skin and eyes, stomach upset, disturbed vision, and stroke-like symptoms.

Blood tests may show low numbers of platelets (thrombocytopenia) and damage to red blood cells (red cell fragments). TTP is confirmed by finding very low levels of ADAMTS13 in the blood.

Treating TTP

A number of different treatments are available for managing TTP. The type of treatment you receive will depend on the severity of your symptoms and other aspects of your health and whether you have immune-mediated or congenital TTP.

TTP is a medical emergency and treatment **must** be started as soon as possible. People with TTP are usually treated with a combination of plasma exchange and medicines: steroids, rituximab and caplacizumab.

The information below describes these treatments and some of their side effects. It is likely that you had some or all of these treatments at the time you were admitted to hospital. Please talk to your haematology consultant or nurse specialist if you have any questions about your treatment.

Plasma exchange

Plasma is the fluid part of the blood which carries all your cells, antibodies, nutrients and clotting factors.

Plasma exchange treats TTP by removing a person's plasma along with the antibodies that have caused TTP. The plasma that is removed is replaced with donor plasma with normal levels of ADAMTS13.

What happens during plasma exchange?

People are usually awake in bed during the procedure. Blood is taken out of a large vein either from a person's arm or from a special intravenous tube, placed in a large vein at the top of the leg or side of the neck. The blood is fed into a machine and spun very quickly so that the different parts of blood get separated into layers. The separated blood cells are returned with the replacement plasma. The person's own plasma will travel up to a collection bag and be discarded.

How long will it take?

Each plasma exchange can take 2 to 3 hours and you will usually have a blood test before and after the procedure.

Who will perform the procedure?

Your plasma exchange will be performed by a specially trained Nurse Practitioner. Please feel free to ask them any questions.

What are the main side effects of plasma exchange?

During plasma exchange we use an anticoagulant (blood thinner) to stop your blood from clotting whilst in the machine. It may cause low calcium levels, leading to tingling in your hands or face. This can be easily treated by the nurses giving you calcium in the vein or with calcium tablets which you chew. People can sometimes also get reactions to the replacement donated plasma even though we use the safest products possible. We can treat most reactions easily with medications.

Steroids

Most people are prescribed steroids such as methylprednisolone to treat their TTP. These drugs work by dampening down your immune response and reducing antibody levels in your bloodstream to slow down ADAMTS13 breakdown. Steroids are a good treatment for TTP and most people only need a short course (3 days) of treatment.

Side-effects of steroids

Steroids normally cause few problems if they are given for a short period of time.

People who have longer courses of steroids often feel hungrier when taking steroids and may put on weight. If you need repeated courses of treatment or have to take them for a long time, you may have other side effects. Since steroids weaken your immune system, this can increase your risk of bacterial and viral infections. Steroids can also cause thinning of the bones (osteoporosis), stomach ulcers and high blood sugar levels (diabetes). They can change your facial appearance and cause thinning and bruising of the skin. These side effects usually reverse when the steroids are stopped. Your doctor may also prescribe you medications to prevent stomach ulcers and bone thinning if you are taking steroids for a long time.

It is very important that you do not stop taking steroids without advice from your doctor, as your body starts to rely on them. They need to be cut down slowly to so that your body has time to adjust, otherwise you experience weakness and fatigue. If you are worried about possible side effects, please discuss your treatment with your doctor before making any changes to your medication.

Rituximab

Like steroids, rituximab dampens down the immune response and stops ADAMTS13 from being broken down. It is an antibody (developed by a medicines company) that affects your white blood cells. It is not made from donated human blood.

Rituximab is given as an infusion through a drip (a small tube into a vein in your arm) once a week for four weeks. It takes 2 to 4 hours for the dose to be given. This will be started while you are an inpatient. If further treatments are needed when you leave hospital, these will be given on the Haematology Day Treatment unit, Churchill Hospital.

What are the advantages of rituximab?

For people newly diagnosed with TTP, rituximab reduces the risk of TTP coming back. For people who have previously had TTP and whose ADAMTS13 falls (a subclinical relapse), rituximab improves the ADAMTS13 in 95 in 100 of cases.

What are the risks of rituximab?

Most people who are treated with rituximab for TTP have no side effects. The most common problem is a short-term reaction to the infusion (such as a fast heart rate or breathlessness), but you will be monitored closely while it is given.

Although rituximab works by stopping white blood cells from making antibodies, you are not likely to have any problems with infections. Before receiving rituximab, you must also be screened for hepatitis B (a viral infection), as rituximab can make this infection more serious.

Caplacizumab

Caplacizumab works by stopping platelets from sticking to Von Willebrand Factor. This reduces the risk of small blood clots forming in vital organs. Caplacizumab is a medicine that is injected into a vein for the first dose and injected under the skin for doses after that. If you are given caplacizumab then it will be given every day after plasma exchange and will continue as an outpatient for several weeks after the last plasma exchange. Your doctor may recommend a longer or short course depending on your blood results.

What are the advantages of caplacizumab?

In clinical trials, people treated with caplacizumab were in hospital for 3 days less on average than those who were not. People treated with caplacizumab were less likely to have another episode of TTP within 30 days of stopping plasma exchange and a low risk of death

What are the risks of caplacizumab?

Caplacizumab can cause bleeding, which may be severe in 1 in 100 people. Examples include nose or gum bleeding, stomach or intestinal bleeding, or heavy menstrual bleeding.

If you are having surgery or any invasive procedures, for example a dental extraction, let your team know as the procedure may need to be delayed or caplacizumab may need to be stopped.

Supportive medicines

As well as the treatments above, you will also be given medicines to help protect you from side effects from treatment. You will be given a medicine to protect the lining of your stomach (lansoprazole or omeprazole). You will be given folic acid to help your body make more red blood cells. When your platelet count recovers, you will be given a heparin injection (dalteparin) to prevent blood clots.

Other immunosuppressant medications

A range of other medications that suppress the immune system can also be used to treat TTP.

Some examples of these are:

- azathioprine
- mycophenolate
- ciclosporin
- obinutuzumab.

These medications work in slightly different ways, but all reduce the number of white blood cells in your body. Like steroids, these medicines increase your chance of getting infections. If you need any of these drugs, your doctor will talk to you about the risks and benefits.

Going home after TTP

You will be discharged home when your platelet count is within normal limits. You will be given an outpatient appointment to be seen in the TTP clinic the following week.

It might take some time to recover. You will feel very tired, even though you are recovering. You may feel less able to return back to your normal routine and it should be done gradually, with plenty of rest. You may also need further help and support at home during your recovery, a TTP specialist nurse will discuss with you a recovery plan prior to your discharge from the hospital and accept offers of help from friends and family.

Consider going back to work part-time or a phased-return if possible. We are able to provide certificates and letters for your employer. Your GP will be informed of your condition and any treatments that you have received. We will work with your local hospital if you live some distance from the Churchill Hospital.

Everyone is different, but patients can sometimes feel overwhelmed by their experience in hospital. If you feel that you would benefit from seeing a psychologist, we will arrange this for you through one of our TTP clinics.

Can TTP come back again?

TTP is a life-long condition. Between one third and one half of people who have TTP once will have TTP again. This is called a relapse. If you are going to relapse, this is most likely to happen within the first two years of diagnosis. You will be monitored life-long in the TTP clinic after you leave hospital. We can spot early signs of TTP returning on blood tests. We aim to always detect TTP coming back early so we can give treatment to stop it fully coming back.

Follow up appointments

Your follow up will be in the TTP clinic at the Churchill hospital or at the Oxford Haemophilia and Thrombosis Centre, Nuffield Orthopaedic Hospital. Appointments may be face to face, by telephone or video.

You will be seen in the TTP clinic after you leave hospital. This will be:

- Every week for the first 4 weeks after you leave hospital
- Every two to four weeks for the following 3 months
- Every three months for the next 12 months
- Every three to six months after that.

At your TTP clinic appointment, we will talk about:

- Any problems that you still have after TTP
- Psychological support
- Pregnancy (if relevant to you)
- Research studies
- Anything else you want to ask or tell us about.

Blood tests

Each time you come to the TTP clinic, we will take a blood sample to check your platelet count and ADAMTS13 activity. If the ADAMTS13 activity level falls, this can be an early sign that TTP may come back. This usually happens long before the platelet count falls. We will see you more often in clinic if your ADAMTS13 activity falls.

If your ADAMTS13 activity falls very low, we will arrange to give you more treatment to stop you getting TTP again. This will usually be treatment with rituximab once a week for 4 weeks as an outpatient. You would have this treatment on the haematology day treatment unit at the Churchill Hospital.

Sometimes people who have had TTP feel like their symptoms are coming back. If this happens, please call **Haematology Triage at the Churchill Hospital urgently on 01865 572192** and we can arrange for you to have blood tests.

Research and clinical trials

You may be asked to take part in a research trial or study following your TTP diagnosis. Your doctor or a research nurse may discuss taking part in the UK TTP registry with you during your inpatient stay or in an outpatient follow-up clinic once you are discharged from hospital. The UK TTP registry is important to help improve our understanding of TTP. Although it may not benefit you directly, information is collected anonymously including blood results to help improve TTP care and treatment. You may also be asked to take part in other studies related to TTP.

Psychological support and neuropsychological testing

TTP can affect both mood and brain function or cognition, for example, how you think or remember.

Neurological and neuropsychological symptoms are common after a TTP diagnosis and affect approximately 50 in 100 people.

You may commonly experience low mood or depression, anxiety, and post-traumatic stress or issues with your memory or concentration, which can present in many ways.

They may happen early after diagnosis or several weeks or months later, and can be temporary or, occasionally, last longer. It is important that you discuss it with your doctor or specialist nurse anytime you experience any of these symptoms as support is available.

You may be referred to a clinical psychologist for a baseline assessment following your initial TTP diagnosis. The psychologist is experienced in talking to people with TTP and has a good understanding of the impact it can have on your health and mental wellbeing. You may or may not choose to continue regular follow-up with the psychologist.

You may also be referred to a neuropsychology specialist who can test your memory and cognitive function and can help you to improve it.

Dos and Don'ts with TTP

DO ask questions about your treatment.

DO check with us before you travel abroad. You may need specialised insurance.

DO speak to your consultant haematologist if you are considering starting a family.

DO contact us if you develop any new health problems or planning to start a new medication.

DON'T wait if you have new symptoms you think might be related to TTP. Get in touch with your specialist nurse or doctor.

How to contact us

Please discuss any areas of concern with your doctor in clinic.

For questions about your appointment, please contact:

Service Coordinator
Telephone: **01865 235184** or **01865 235185**
Service Email: orh-tr.clinicalhaematology@nhs.net

TTP Specialist Nurse
Working hours: Monday - Thursday 8am-6pm
Telephone: **01865 235154**
Work mobile: **07920 861380**
Email: immuno-haem.nurse@ouh.nhs.uk

For Emergencies

If you think your TTP symptoms are returning, please call:

Haematology Triage at the Churchill Hospital urgently on 01865 572192 and we will arrange for you to have a blood test.

This number is a 24 hour help line and you will speak to a nurse who can discuss your symptoms with a TTP doctor. Please call this number outside of working hours, after 5pm and during weekends.

Further information

The TTP network is a good source of information and support:
www.ttpnetwork.org.uk

Further Information

Please speak to the department where you are being seen if you would like an interpreter. You will find their contact details on your appointment letter. Please also ask them if you would like this information leaflet in another format, such as:

- easy read
- large print
- braille
- audio
- electronically
- in another language.

We have tried to make this information meet your needs. If it does not meet your individual needs or situation, please speak to your healthcare team. They will be happy to help.

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