

VENOUS THROMBOEMBOLISM

in Infants, Children, and Adolescents



INTRODUCTION

This leaflet was written for infants, children, and adolescents with venous thrombosis, and their parents/carers. This information should help you understand what venous thrombosis is, the problems it can cause and how it is treated.

WHAT IS VENOUS THROMBOSIS?

Venous thrombosis is when a blood clot occurs in a vein.

TYPES OF VENOUS THROMBOSIS

Most commonly, thrombosis affects a deep vein in the leg or arm – this is known as ‘**deep vein thrombosis**’ (DVT).

Often it can break off and travel through the body and block the arteries in the lungs, known as ‘**pulmonary embolism**’ (PE). The combination of thrombosis and embolism is known as venous thromboembolism or VTE.

Clots in the veins of the brain, are known as ‘**cerebral venous sinus thrombosis**’ (CVST). CVST may also be referred to as a type of stroke.

Less often thrombosis can affect the veins of other organs such as the kidney or liver.



VENOUS THROMBOEMBOLISM IN INFANTS, CHILDREN, AND ADOLESCENTS

Although venous thrombosis is far commoner in adults, it can happen in children.

A blood clot affects approximately

**1-5 CHILDREN
IN EVERY 100,000**

in the population each year.

The most common cause of a blood clot developing in a child is as a result of hospital treatment.

The number of clots being detected and treated in children has increased over the last 20 years for the following reasons:



The treatment for illnesses that cause a high-risk of thrombosis (such as congenital heart defects, cancer and prematurity) has improved and this has led to more children surviving with these conditions.



Doctors are more aware that children can have VTE.



The tests to diagnose VTE in children have improved.

WHAT ARE THE RISK FACTORS FOR VENOUS THROMBOEMBOLISM (VTE) IN INFANTS, CHILDREN, AND ADOLESCENTS

Risk factors include:

- A central venous line – this is a device inserted into a large, central vein that allows medicines to be administered. Examples include PICC lines, port-a-caths and tunnelled Hickman lines
- Cancer
- Congenital heart disease
- Prematurity
- Severe trauma
- Serious infection
- Surgery
- The combined (oestrogen and progesterone) oral contraceptive pill
- A congenital venous malformation – these are veins that have not developed in the typical way
- A chronic health condition e.g. nephrotic syndrome, inflammatory bowel disease, sickle cell disease or autoimmune disease
- Obesity



Most children who have experienced VTE have more than one risk factor and many have several risk factors. Children who have VTE are usually very unwell in hospital when the blood clot happens.

Occasionally, some children, usually adolescents, have a VTE that occurs without any warning. These children could be found to have an inherited problem with the way in which their blood clots (**'thrombophilia' or sticky blood**), making them more at risk of VTE. There may also be a history of VTE in other family members. These children are more at risk of having another blood clot in the future. Specialised testing including genetic tests might be suggested in some patients. If you know of other family members who have experienced VTE, it is helpful to share this with the medical team.

Line-associated thrombosis is a type of DVT in children with central venous lines. It is well known that central lines can develop clots in or around them. Children who need central lines have an underlying condition that will usually put them more at risk of blood clots too. The line is often very important for the treatment of the child's underlying health conditions and replacing it is not without risk. So provided the line is still functional it will often continue to be used if a DVT occurs and the thrombosis will be treated.



HOW IS VTE IN INFANTS, CHILDREN, AND ADOLESCENTS, DIAGNOSED?

Since VTE can affect children of all ages, the signs and symptoms may vary across different age groups. Given that thrombosis can recur, it is important for parents and carers to understand what signs to look out for in their child.

A **'deep vein thrombosis' (DVT)** can cause swelling and pain in the limb which may feel warm and tense or may often only cause pain. It is usually diagnosed using an ultrasound scan where a probe is placed over the limb to look for abnormal blood flow in the veins.

A **'pulmonary embolism' (PE)** can cause any of the following: slow or sudden onset of breathlessness; pains in the chest that are worse when taking a breath; coughing up blood; or sometimes collapse. It is usually diagnosed using computerised tomography after an injection of gadolinium which highlights blood flow (a CT pulmonary angiogram or CTPA) scan of the chest.

A **'cerebral venous sinus thrombosis' (CVST)** can cause: severe headache; fits; vomiting; weakness or numbness of an arm or leg, excessive drowsiness; or long pauses in breathing (apnoeas). It is usually diagnosed using a CT or MRI scan of the head.

Thrombosis in the kidney or liver may cause pain in the tummy and/or abnormal blood test results. It can be diagnosed using an ultrasound scan or a CT/MRI scan of the abdomen.

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How is VTE in children treated?

VTE is treated using ‘**anticoagulants**’ which are drugs that prevent clots from getting any bigger and stop new blood clots from forming. The clots themselves are usually partly or fully dissolved by the body but these medicines work to prevent things getting worse in the meantime. They may also be called ‘blood thinners’.

Anticoagulants come in different forms with different names and slightly different modes of action. Some are infused via a device into the bloodstream (intravenous or IV), some are injected under the skin (subcutaneous or subcut), and some are taken orally (liquid or tablet).

The initial treatment either an oral (tablet) anticoagulant, or a form of heparin. Heparin is a type of anticoagulant given as an infusion or an injection under the skin for the full course of treatment. Babies are usually treated with low molecular weight heparin injections whereas older children and adolescents are more likely to be treated with oral anticoagulants. This is because less research has been done into using oral anticoagulants in babies, but this may change in the future.

Heparin infusion

Children who are very unwell or who have a high risk of bleeding, for example because they have had recent surgery, may be started on a heparin infusion. This is given through a very small needle or tube placed into a vein and is monitored by frequent blood tests. Due to the monitoring required, these children are usually in an intensive care or high dependency ward setting.



Low molecular weight heparin injections

Low molecular weight heparins are used in children and include dalteparin, enoxaparin, and tinzaparin.

- Low molecular weight heparins are given by injection just under the skin (subcutaneous injection) usually twice a day.
- When a child goes home from hospital a parent may be trained to give the injections or it may be necessary for a community nurse to visit the home to give the injections
- Blood tests are required to check that the right dose of heparin is being given. The blood test, called an anti-Xa level, may be taken before the injection and/or 3-4 hours after an injection.
- An anti-Xa level assesses the activity of heparin in the blood. If the level is not within the ‘target range’ the dose of the medicine must be adjusted. If the level is too low, the heparin is not having enough of an effect and the dose should be increased. If the level is too high, the medicine is having too much of an effect and the dose needs to be reduced.
- If the blood test is performed more than 4 hours after the dose is given, it is not a reliable measure of how well the heparin is working. The test should be rescheduled to 3-4 hours after the next dose. If this is during the night it can usually wait until the next day. You can speak with the medical team if you are worried or unsure.
- At the beginning of treatment blood tests may be needed every few days to check the levels. Once the levels are stable, the blood tests can be reduced in frequency. Every child is different, and it can sometimes take weeks to achieve stable levels.
- It can be helpful to keep a record of your child’s levels, any dose changes, and when the next blood test is required (see table at the end of this leaflet).
- It is important when administering this medicine to always check you are giving the correct dose in both **MILLILITRES** and **UNITS**. Millilitres represent the volume of liquid you are giving. The dose within that volume can vary depending on the concentration it has been prepared as. The actual dose of the medicine is reflected in the number of **UNITS**. Always check both.

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Direct Oral Anticoagulants (DOACs)

DOACs have been used in adults for many years but only more recently have trials demonstrated they are just as effective and safe at treating VTE in children. They are taken orally up to three times per day depending on the weight of your child. You will be instructed exactly how often your child should take the medicine by the doctor or pharmacist. Blood test monitoring is not usually required when taking a DOAC.

The largest trial of anticoagulant treatment ever done in children is the EINSTEIN-Jr phase 3 study, and the EINSTEIN-Jr DVT study. These were published in 2019. The results from both of these showed that children with VTE who were treated with rivaroxaban had a low risk of having another clot and a low risk of bleeding, when compared to standard anticoagulants. The children taking rivaroxaban in the trial had the added benefit of fewer hospital visits for blood tests.

The EINSTEIN-Jr CVT sub-study compared rivaroxaban with standard anticoagulants (heparin and warfarin) in children with cerebral venous thrombosis. The children treated with rivaroxaban had a similarly low risk of clot recurrence and a low risk of clinically relevant bleeding, when compared with standard anticoagulants.

Vitamin K Antagonist (VKA)

The most common Vitamin K antagonists used are warfarin, or sometimes acenocoumarol. Both have been used reliably in children with a VTE for many years. They are anticoagulants taken in a tablet form.

Both warfarin and acenocoumarol are medicines which require frequent blood monitoring, and their anticoagulant effect is altered by changes in diet, other illness and other medicines. Antagonists have mostly been replaced by direct oral anticoagulants (DOACs), however they are still used in some children, for example in certain cardiac conditions such as mechanical heart valves. They have the benefit of being readily reversible, which is a necessity for some children. If your child is prescribed warfarin or another Vitamin K Antagonist, you will receive separate information on monitoring.

Warfarin has mostly been replaced by direct oral anticoagulants however it is still used in some children, for example in certain cardiac conditions such as

metallic heart valves. It has the benefit of being readily reversible, which is a necessity for some children. If your child is prescribed warfarin, you will receive separate information on warfarin monitoring.

Administering anticoagulants

Your team will want to ensure you are set up for success when administering medicines at home. Too much or too little of an anticoagulant can have serious consequences. Although rare, errors can happen particularly when the dose is being adjusted very frequently. It is important to always check your prescriptions and that you have been given the correct dose before administering the anticoagulant.

How long does an infant, child or adolescent with VTE need an anticoagulant for?

This will vary depending on the cause and the child's medical history.

For a deep vein thrombosis (DVT) or pulmonary embolism (PE), anticoagulants are usually continued for 3 months when the thrombosis has been 'provoked', meaning that there was a recognised reason for it happening.

Line-associated thrombosis may only need 6 weeks of treatment if the clot resolves within this time. A repeat scan will be done at 6 weeks and if the clot is still present the treatment will be continued for three months in total.

Anticoagulants are usually continued for six months for cerebral venous sinus thrombosis.

Anticoagulants are likely to be continued for 6-12 months or longer when the thrombosis was 'unprovoked', meaning that there was no particular reason for it happening.

In some children the risk of further clots developing may remain, and so stopping the anticoagulant can be too risky. In these children it may be necessary to continue the anticoagulant long-term. The reason for this is that usually there is an abnormality making the blood more likely to clot (such as '**thrombophilia**'), a congenital abnormality of the veins, or a long-term disease that increases the risk of VTE.

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What are the side effects of anticoagulant treatment in infants, children, and adolescents?

A child who is taking an anticoagulant may bruise more easily than normal and may bleed for a little bit longer from minor cuts and grazes. This is usually not serious, but you should seek medical attention if your child experiences:

- Nosebleeds lasting longer than 10 minutes, not responding to applying pressure
- Persistent bleeding from a cut or graze, not responding to applying continuous pressure
- Blood in the urine
- Blood in the stool or dark stool
- Heavy periods

The major side effect of anticoagulant treatment is serious bleeding. Intracranial bleeding is bleeding in or around the brain. This can cause disability or death but is extremely rare and would usually only occur if there was a significant head injury. Symptoms of intracranial bleeding include headache, drowsiness, change in behaviour, vomiting or fits.

IT IS IMPORTANT that anyone who looks after a child on anticoagulant treatment should be aware of the potential for bleeding and should know who to contact in an emergency. This includes relatives, nursery staff and school teachers. It may be helpful to give them a copy of this leaflet.

Some parents arrange for their child to wear a medical alert bracelet or necklace that provides information about their medical condition and anticoagulant treatment just in case something happens when there is no one around who knows about this.

Can children still do physical activities or sports when they are on an anticoagulant?

It is important for children who have had a VTE to remain active since activity can reduce their risk of having another blood clot. However, the risk of bleeding into the brain when a child is on anticoagulants means that there are some restrictions:

- Boxing, rugby and martial arts have a high risk of head injury so **MUST** be avoided;
- A helmet should always be worn when riding a bike or a skateboard;
- There are many other sports that children can enjoy and take part in such as, running, swimming, cycling, dance, tennis. Although a helmet might need to be worn if there is a risk of falling and injuring the head.
- It is important for the sports teacher to know about the child being on anticoagulant treatment.

What can be the occasional consequences that occur in a child who has had a VTE?

Deep vein thrombosis can cause long-term problems with swelling, pain, and skin changes of the affected limb. This is known as '**post-thrombotic syndrome**' and it occurs in around 25% of children with DVT. It is usually mild but may mean that the child has to wear a tight stocking to help drain the blood from the limb and relieve the symptoms. Some children may be suitable for a surgical procedure much later on, such as stent insertion, to relieve the symptoms. This is generally considered when the child is older and well grown and is assessed case-by-case by a team of specialists.

Pulmonary embolism can increase pressure in the blood vessels of the lungs causing breathlessness on exertion. This is called pulmonary hypertension. It is a very rare complication in children.

Cerebral venous sinus thrombosis can cause neurological problems including fits, headaches and persisting weakness or numbness. If these occur please talk with your healthcare professional.

A thrombosis in a kidney can cause high blood pressure or reduced kidney function.

A thrombosis in the liver can cause enlargement of the spleen. In some cases, this can cause low blood counts and bleeding from vessels in the stomach and around the gullet.

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Coordination of care

Different hospital teams lead on the management of venous thrombosis depending on the cause and how unwell your child is. In more serious cases, your child may spend time initially in intensive care or on an inpatient ward. Ward based care can take place in your local hospital or in a hospital providing specialist care.

Usually there is a haematologist who understands and works with all of the teams. If you are unsure who is leading your child's care, speak to the medical team and ask who is your child's consultant.

Eventually, the treatment will continue at home, and you will be followed up by your local hospital team and sometimes a specialist team too. Your child's medical team will know where the most appropriate place is for your child to be managed.

Often specialist teams will give advice to your local hospital team about how to manage your child's thrombosis. Blood tests and reviews will often take place at your local hospital and the local team will liaise with the specialists who may advise changes. If you are unsure who is leading on your child's care, speak to the medical team for clarification.

Before you leave hospital, find out who your child's consultant is, which specialties are following them up and who to contact if you have a question or need advice. There is more information about this at the end of the leaflet.

What follow-up is required?

Venous thrombosis (not including CVST) with a clear cause and treatment duration does not require any follow-up unless your child develops new symptoms or problems arise.

Follow-up practices will differ, but children with CVST will generally be followed-up to monitor or manage any problems that may arise from the blood clot.

Children with CVST will generally be followed up by Neurology to monitor for or manage any neurological problems that may arise from the thrombosis.

For unprovoked thrombosis, i.e. clots with no clear cause, your child will need to be investigated and followed-up by the Haematology team. Children with unprovoked thrombosis are at an increased risk of having further blood clots in the future and may have an underlying problem with how their blood clots. Some

children with provoked thrombosis will also be followed up by Haematology if they have had complications.

What happens at the end of treatment?

In most cases, where an anticoagulant duration has been decided and there are no new symptoms, there is no need to repeat a scan at the end of the treatment. Many parents are keen to know whether the clot has fully resolved before stopping anticoagulants. However, this underpins how anticoagulants work. We know however that in quite a few people who have had a blood clot, there will be some residual clot, but it will not cause any further or continuing problems, and so if a scan shows some residual clot is present, it does not mean anticoagulation is still required.

Further Support

Supporting a child through a VTE can be very stressful and worrying for parents and carers. There is support available. Speak to your local and specialist hospital teams if you have questions or concerns. There is also more information and support on the Thrombosis UK website (see below). If as a parent, you are struggling with anxiety or poor mental health, you can access more support through your GP or health visitor. If your child is struggling with poor mental health, speak to your medical team who can arrange more support for them.

Who to contact if you need help

In case of an emergency – dial 999

If you are concerned your child is more unwell, call 111 or attend your local emergency department

If you need general advice, contact your local hospital. Each hospital will have different arrangements, there may be a specialist nurse you can contact, or you may be given your consultant's secretary's details. Find out who you should contact if you need help before you go home. You can record these details below:

Who to contact:

Contact details

ANTI-XA LEVEL RESULTS

Target range

Date of blood test	Anti-Xa level	New dose	Next check due

Find out more about thrombosis on the **FREE** 'Let's Talk Clots' information app.



Links to support groups
Thrombosis UK (www.thrombosisuk.org)
Email: admin@thrombosisuk.org

