BLOOD CLOTS

IN CHILDREN

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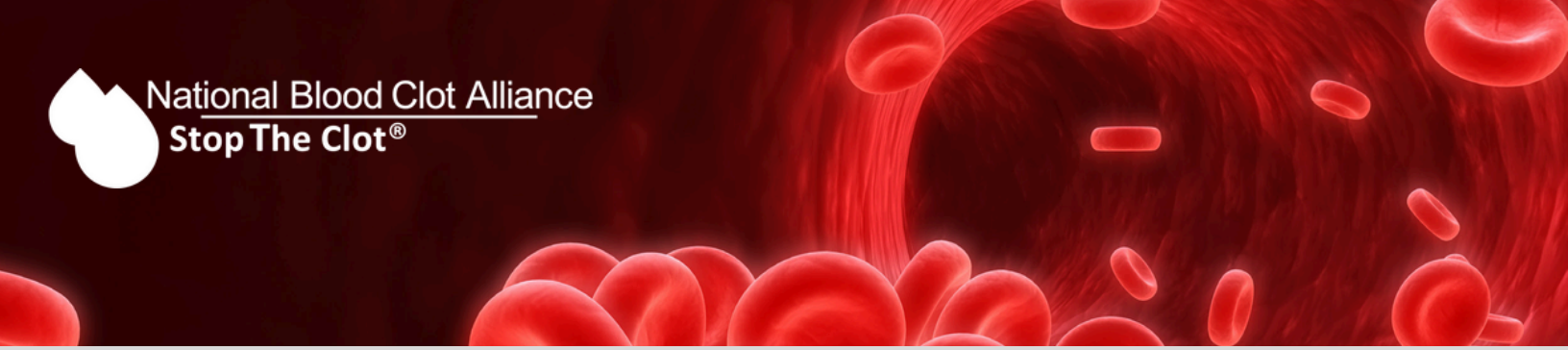

WHAT ARE "DVT," "PE," AND "VTE"? HOW COMMON ARE THEY IN CHILDREN?

Definitions:

- **Deep vein thrombosis or DVT:** A blood clot in your deep veins.
- **Pulmonary embolism or PE:** A blood clot in your lungs.
- **Venous thromboembolism or VTE:** The term that members of your health care team use to refer to both DVT and PE together.
- **Blood clot:** The way most people outside the medical field describe VTE.
- **Pediatric hematologist:** A type of doctor specially trained to treat children's blood disorders.

Blood clots can develop in the deep veins that carry blood back to the heart from your arms or legs. They can also develop in other deep veins, including those that carry blood back to the heart from your head and neck, or the organs in your abdomen (belly). This is called deep vein thrombosis, or "DVT."

Blood clots can also develop in the blood vessels of your lungs, or travel to your lungs from deep veins in your body, where they had originally formed. This is called pulmonary embolism, "PE."

DVT and PE can happen at any age. Although they happen more commonly in adults, they can also happen in children. About 1 in 10,000 children get DVT or PE, including as many as 1 in 200 hospitalized children.

This resource on blood clots in children is designed for use by patients under 21, their families, and their health care providers. In this resource, we review the causes, signs and symptoms, diagnosis, treatment, and long-term effects of DVT/PE.

We also explain the importance of a team approach for children with DVT/PE, and we recommend that this team should include a pediatric (child-focused) hematologist (blood doctor) who has experience in taking care of children who have DVT/PE. Although some of the information also applies to clots in large arteries, the focus is DVT/PE.

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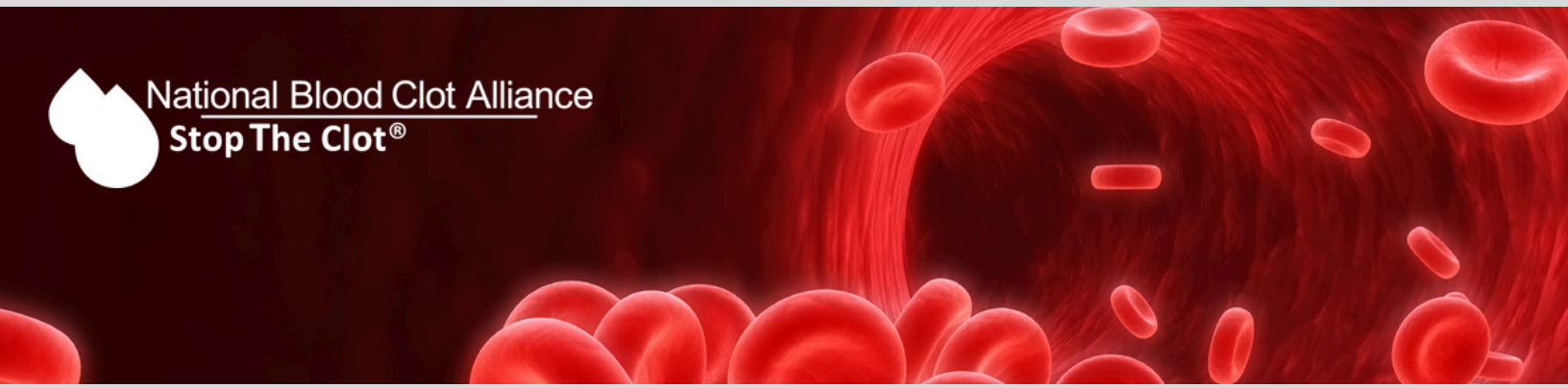


WHAT CAUSES DVT/PE IN CHILDREN?

Definitions:

- **Genetic thrombophilia:** Inherited clotting conditions that can increase a child's tendency to form blood clots.
- **Acute:** Sudden or short-term.
- **Chronic:** Long-term.

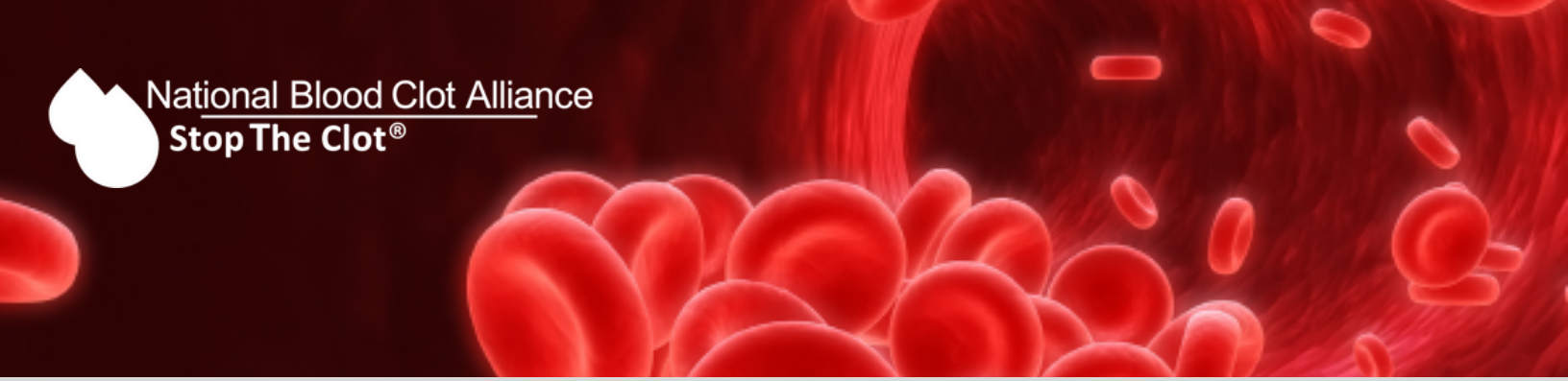
The following health issues can cause (or add to the risk of developing) DVT/PE in children:

- **Poor blood flow in the veins.** This may happen when children are confined to bed in the hospital. It can also occur in rare conditions where there is abnormal narrowing of a vein, including the iliac vein of the left leg (May-Thurner syndrome) or in the subclavian vein, near where the arm meets the chest (Paget-Schoetter syndrome, also known as venous thoracic outlet syndrome, or vTOS).

- **Damage to the inner lining of veins.** This can happen when a "central line" catheter, such as a "port" or "PICC," are inserted into a major vein. These long, flexible tubes are used when certain medications or fluids need to be given, but a standard IV catheter is not possible. It may also happen when certain medications, such as some chemotherapy drugs are given.

- **Inherited clotting conditions** (also known as "genetic thrombophilias"). One of the most common inherited conditions that increase the risk of DVT/PE is called factor V Leiden. This change in the gene for clotting factor V is present in approximately 5% of people who describe themselves as Caucasian. When a person has factor V Leiden for both copies of the factor V gene, it increases the risk of DVT/PE by about five times.

- **Other illnesses and certain medications.** A variety of recent or ongoing illnesses, such as infections, can activate the clotting system and make the blood more likely to clot. Birth control containing estrogen also increase the risk of DVT/PE, especially in patients who have a family history of DVT/PE that occurred before age 50 or who have other risk factors, especially factor V Leiden.



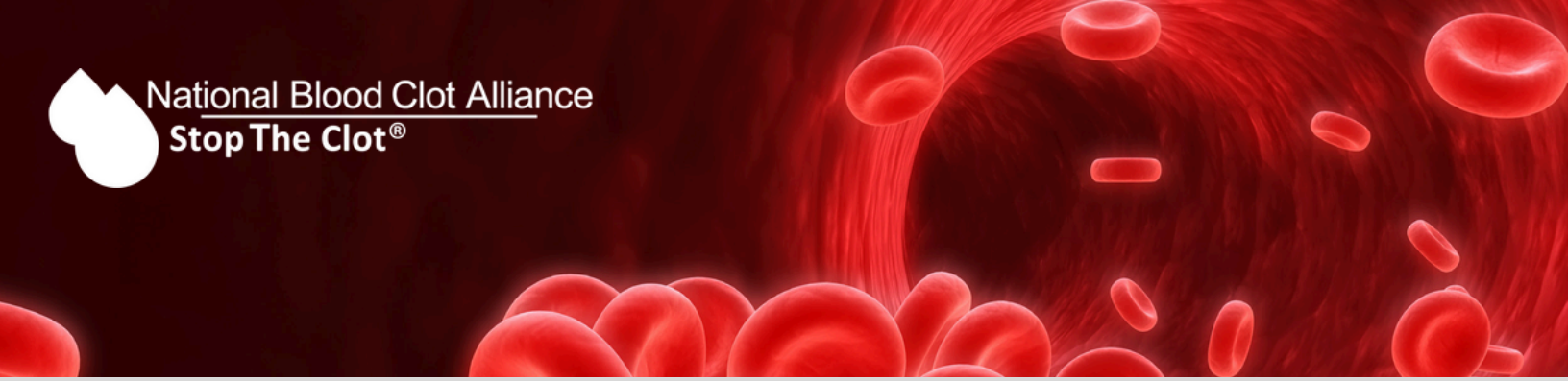
WHAT ARE THE SIGNS & SYMPTOMS OF DVT/PE IN CHILDREN?

DVT/PE in young people can happen in a variety of areas of the body. Signs and symptoms can depend on the location as well as on the amount of blockage of blood flow through the vein.

- **DVT** (“deep vein thrombosis”) in the leg or arm usually causes painful swelling of the leg or arm, where a part of the leg or arm becomes noticeably larger than the same area on the opposite leg or arm.

- **PE** (“pulmonary embolism,” a blood clot in the arteries of the lung, which often has come from a blood clot that broke loose from a DVT of the leg or arm and traveled back to the heart and into the lungs) can cause shortness of breath and chest pain that worsens with deep breathing.

- **CSVT** (“cerebral sinovenous thrombosis,” a blood clot in the deep cerebral veins that bring blood toward the heart from the head) can cause severe or prolonged headaches. People who severe headaches caused by CSVT may also have blurred vision, and their headaches may feel worse after lying down for several hours.



HOW ARE DVT/PE DIAGNOSED IN CHILDREN?

Definitions:

- **Scan:** A way to take images (similar to pictures) of something inside the body, such as a blood clot.
- **Ultrasound:** A type of scan that uses a wand and sound waves to create an image of the veins blood flow through the veins. on a computer. At times during the procedure, the wand is pressed down gently on the area of the body that is located on top of the vein. The image shows blood flow through the veins.
- **Computed tomography (CT) venogram:** A type of "CAT" (or CT) scan of veins that is done after we inject dye through an IV. This scan gives us images of the veins and blood flow, and can be useful in areas that are difficult to image by ultrasound.
- **IV:** A small flexible tube placed in a vein, usually on the inside of the elbow
- **Magnetic resonance (MR) venogram:** A type of magnetic resonance imaging (MRI) scan that gives us images of the veins and blood flow. This scan can be useful in areas that are difficult to image by ultrasound.
- **CT pulmonary angiogram:** A type of scan that uses dye injected through an IV to take images of blood flow in the lung vessels. This scan is often used to diagnose a PE.
- **Ventilation-perfusion (V/Q) scan:** A type of scan that measures airflow and blood flow throughout the lungs.

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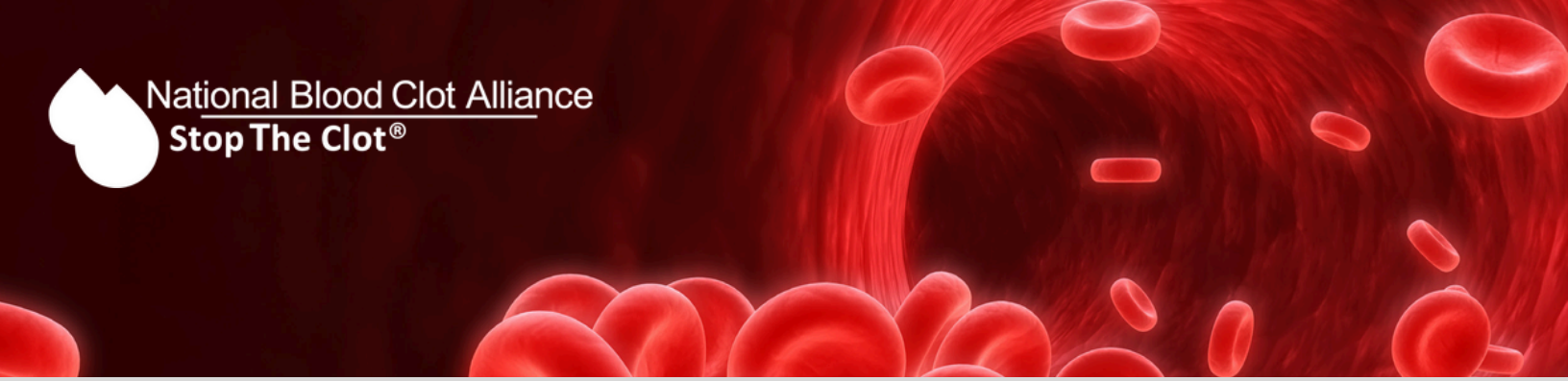

HOW ARE DVT/PE DIAGNOSED IN CHILDREN?

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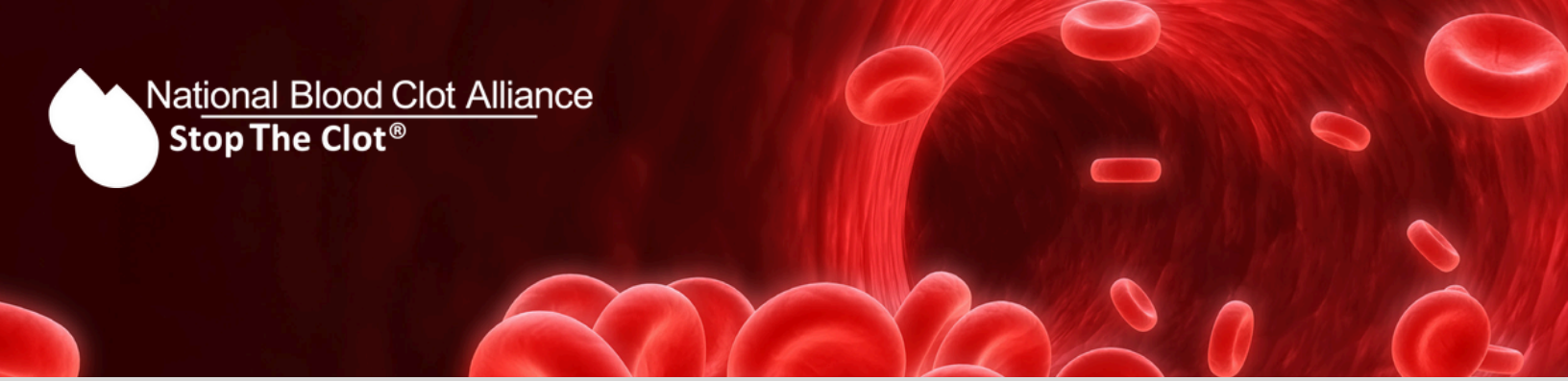
Doctors rely on scans to diagnose DVT/PE in children.

- If a DVT is suspected in an arm or leg, an ultrasound is usually done.
- If a DVT is suspected in another part of a child's body other than the lungs, an ultrasound may be done or a different type of scan may be needed, such as a computed tomography (CT) venogram or magnetic resonance (MR) venogram.
- A catheter procedure with dye, called a conventional venogram, may be needed when abnormalities of the veins are suspected, such as May-Thurner syndrome or Paget-Schroetter syndrome.
- If a PE is suspected, a CT pulmonary angiogram is often used; sometimes, a ventilation-perfusion (V/Q) scan is done first.



HOW ARE DVT/PE TREATED IN CHILDREN?

Definitions:

- **Anticoagulants:** Medications used to prevent further blood clotting in the veins. Most people outside the medical field call them “blood thinners” or anti-clotting medication. They don’t “thin” the blood, they make it more difficult for your blood to clot. For this reason, the term “blood thinner” is not preferred, and is not used in this resource.

- **Heparin drip:** A type of anticoagulant or anti-clotting medication given as a continuous infusion through an IV (a flexible tube placed in a “superficial” (close to the surface) vein, usually in the arm. Heparin drip is only for short-term use when treating DVT/PE.

- **Low-molecular-weight heparin:** A type of anticoagulant given as an injection every 12 hours. An example of LMWH include enoxaparin (sold under the brand name Lovenox in the U.S.) Unlike heparin drip, LMWH can be used for both the initial DVT/PE treatment period and the rest of DVT/PE treatment.

- **Warfarin:** A type of anticoagulant or anti-clotting medication taken by mouth as a pill. Warfarin works by blocking the effect of vitamin K, which helps several of the “clotting factor” proteins in our blood to work properly. Warfarin (sold under the brand name Coumadin in the U.S.) requires regular blood draws to monitor its anti-clotting effect, which can be affected by many other medications and by foods that contain vitamin K. Warfarin also requires an initial period of treatment with heparin drip or LMWH at the same time as warfarin is being taken until the target levels of warfarin’s anti-clotting effect are reached.

- **INR test:** A blood test that measures anti-clotting effect of warfarin.

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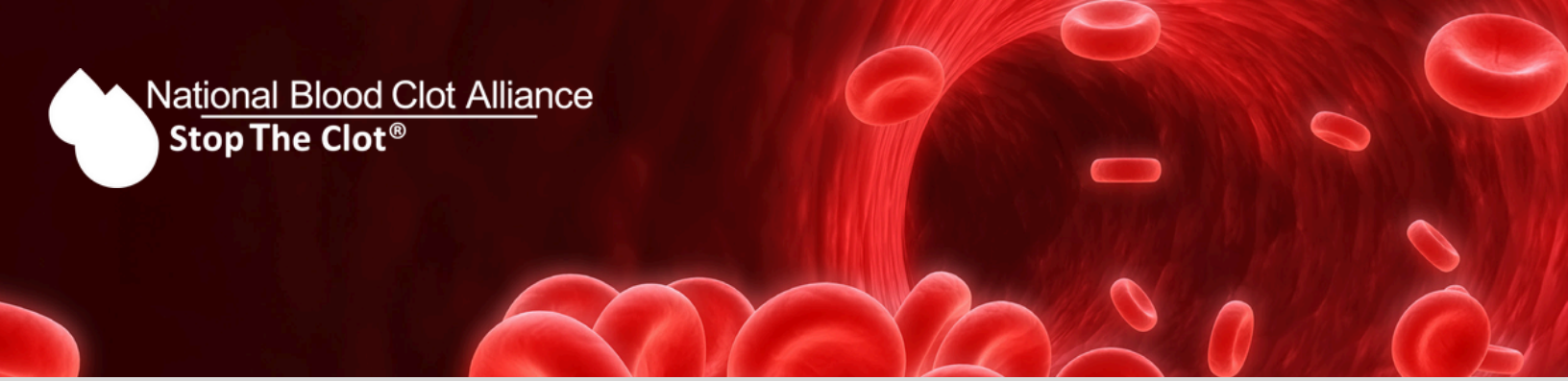

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HOW ARE DVT/PE TREATED IN CHILDREN?

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Definitions

- **Direct oral anticoagulant (DOAC):** A type of anticoagulant or anti-clotting medication taken by mouth as a pill or liquid. After initial treatment with heparin drip or LMWH, DOACs may be an option for many children for the rest of their DVT/PE treatment instead of LMWH or switching to warfarin. The anti-clotting effects of DOACs may be affected by some other medications, but fewer medications than warfarin. Also, unlike warfarin, anti-clotting effects of DOACs are not affected by foods.

- **Thrombolysis:** Clot-buster therapy. Thrombolysis can be given in a variety of ways. Most DVT/PE do not require this kind of treatment. In general, thrombolysis medications have a higher bleeding risk than anticoagulants. Because of this, their use is saved for special situations.

Treatment

When doctors diagnose your child with blood clots for the first time, they will usually treat them with anti-clotting medications, also known as anticoagulants or “blood thinners.”

Anti-clotting medications decrease the risk of a new DVT developing or an existing DVT getting larger. They also help prevent a DVT from breaking loose and traveling to the lungs and causing a PE, which can be life-threatening.

For most children, the risk of a new DVT developing, a DVT growing, or a DVT breaking loose and causing a PE is highest during the first several weeks after their DVT/PE was first diagnosed, or first developed. The length of time of increased risk for more clots or PE is what blood doctors (called “hematologists”) consider when they determine how long a child with DVT/PE should stay on anti-clotting medications. (More information on the topic of length of treatment is provided later.)

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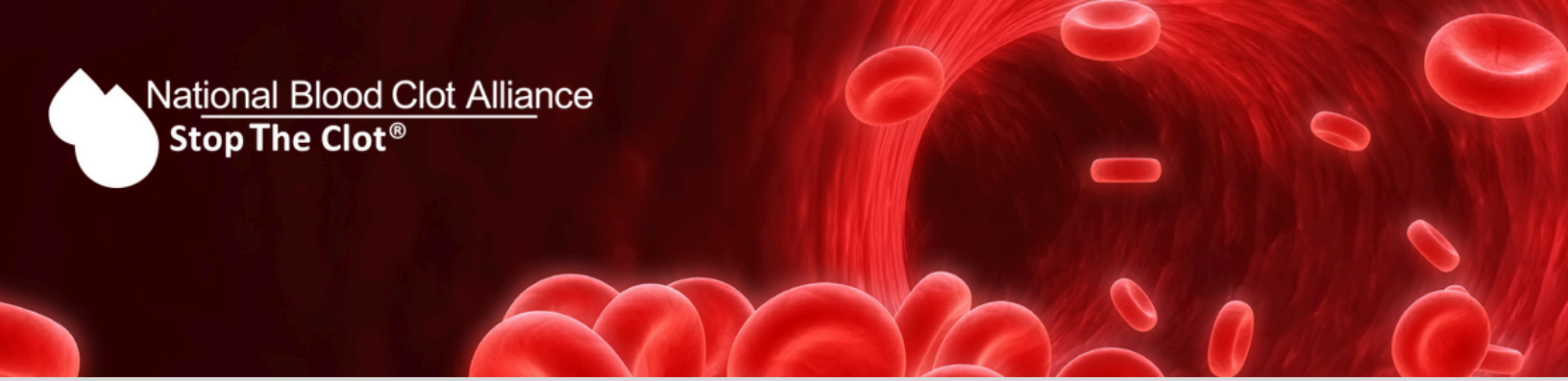

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HOW ARE DVT/PE TREATED IN CHILDREN?

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Anti-clotting medications are not proven to "get rid of" DVT/PE. Doctors and scientists do not yet fully understand the factors that lead blood clots to resolve over time.

One factor may include how well a child's own blood chemistry works to breaks down a DVT/PE, which may also be affected by the types of other illnesses that the child may have, and how severe those other illnesses are at the time that the DVT/PE is being treated.

Doctors usually start to treat children's blood clots with anti-clotting medications while in the hospital. Most often, they either start children on a heparin drip through an IV, or with low-molecular-weight heparin (LMWH) injections about every 12 hours. After several days, they either continue LMWH or switch the anti-clotting medication to an oral (pill or liquid) option.

Before 2021, the main anti-clotting medication available to children as a pill was warfarin (known under the brand name Coumadin in the U.S.).

Diet and other medicines can affect warfarin's ability to control a child's blood clotting. Because of this, warfarin requires weekly to monthly blood tests to check clotting levels in a child's blood. We call this an international normalized ratio or INR test. The INR test requires a blood sample drawn from a vein, usually on the inside of the elbow.

Some other medicines, but not diet, can affect the effect of DOACs on blood clotting. Although DOACs may be a treatment option for many children with blood clots, LMWH or warfarin may be recommended by a child's hematologist.

For example, if a child has a type of antibody in the blood called an "antiphospholipid antibody" (tested at the time that the DVT/PE is diagnosed), LMWH may be recommended instead of a DOAC. Teenagers, children with autoimmune conditions, recent infections, and whose DVT/PE seemed to develop without any triggering factors or events may be at risk for having these antiphospholipid antibodies.

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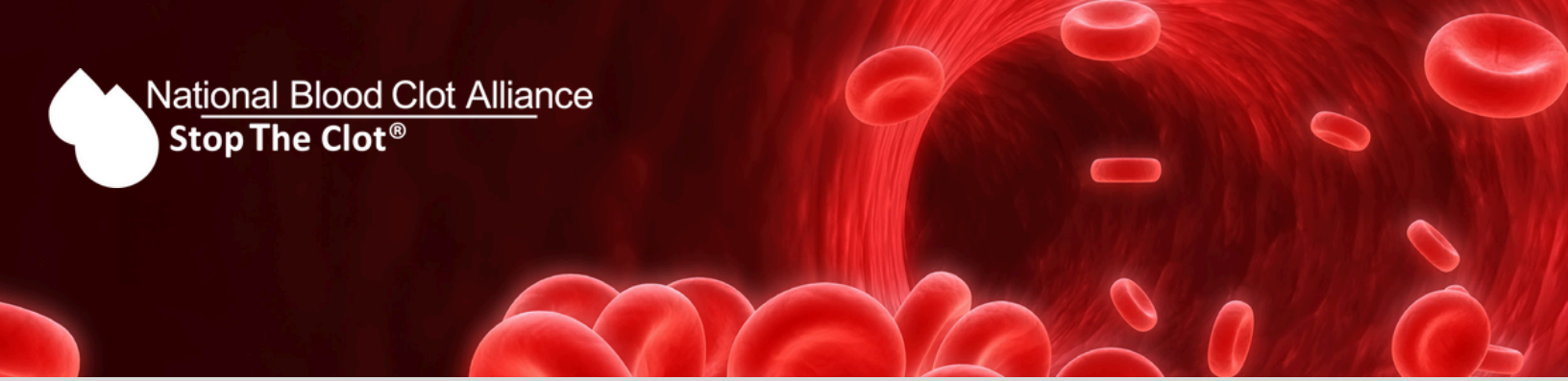

HOW ARE DVT/PE TREATED IN CHILDREN?

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In some severe cases of DVT/PE, doctors may recommend clot-buster therapy – called “thrombolysis” – in the first few days or weeks of blood clot treatment. Due to bleeding risks and other risks that are related to clot-buster medications and procedures, it is not recommended in most children.

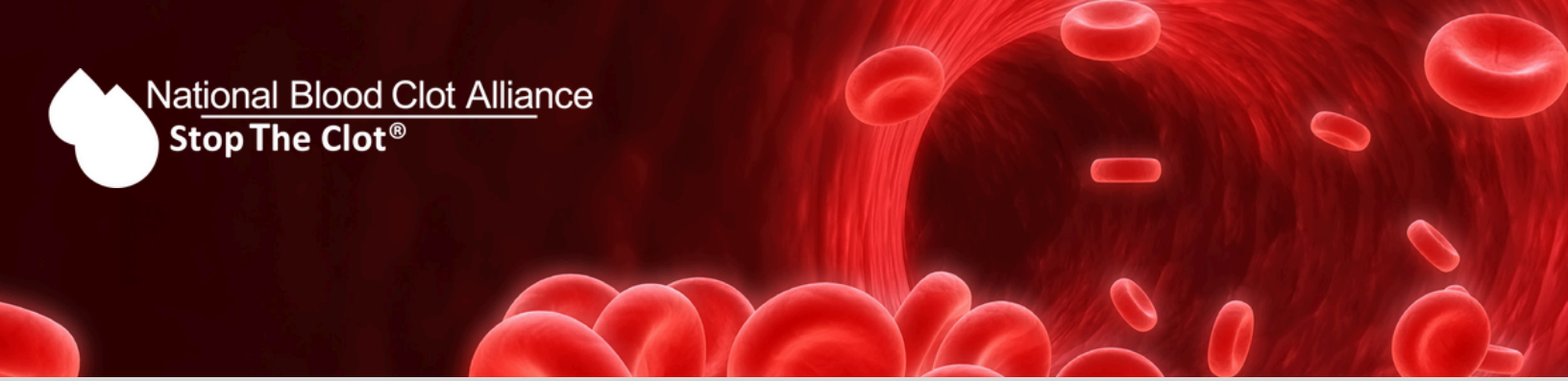
Unlike anti-clotting medications, clot-buster therapy removes or breaks up your child’s blood clot. If a child undergoes clot-busting treatment, anti-clotting medications are needed afterward to prevent new blood clots from forming.

In addition to selecting the treatment for a child’s DVT/PE, hematologists also try to identify the risk factors that may have contributed to their DVT/PE. Reducing or eliminating those contributing risk factors also helps to prevent a DVT from growing or new DVTs/PEs from developing. For example:

- Doctors prescribe antibiotics to treat severe bacterial infections that may have contributed to the development of a child’s DVT/PE.

- If a teenager is taking birth control pills that contain estrogen, doctors will stop or switch that medication since receiving extra estrogen contributes to the development of a DVT/PE.

- If a child’s DVT occurred near a catheter that is in a deep vein (“central venous catheter” or “central line”), the central line will usually be removed as soon as it is no longer needed.



WHAT SHOULD PARENTS LOOK FOR WHEN THEIR CHILDREN TAKE MEDICATIONS FOR BLOOD CLOTS?

When a child takes anti-clotting medications, it lowers the risk of new DVT/PE. However, it does not lower this risk to zero. Parents whose child was recently diagnosed should look for new signs and symptoms of DVT/PE, and for signs and symptoms that of the DVT/PE getting worse. Signs and symptoms of DVT/PE are reviewed in an earlier section of this resource.

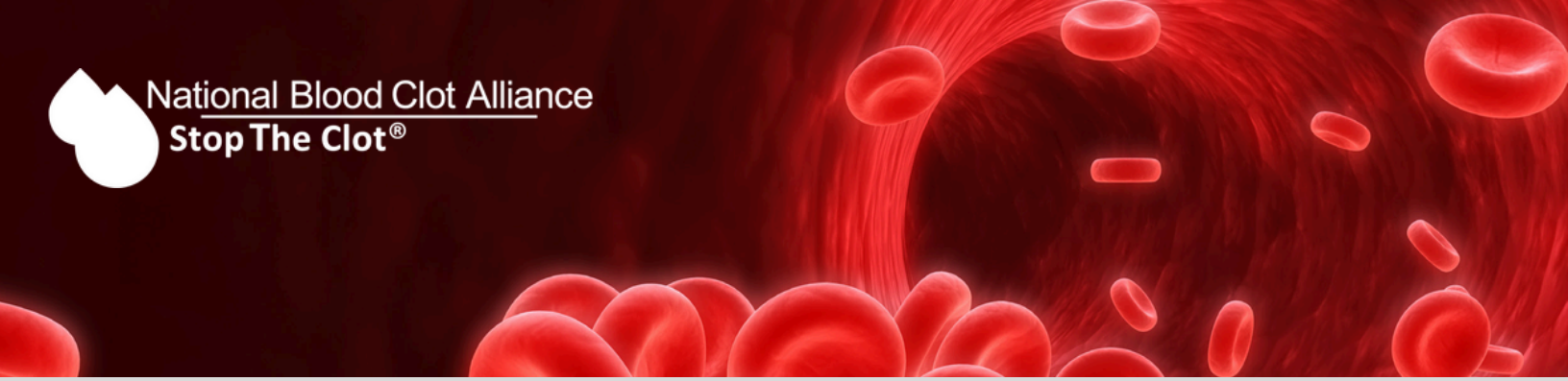
Parents whose child is on treatment with anti-clotting medications also need to look for signs of bleeding. They should also make a plan with their child's doctor about what to if their child starts bleeding while taking anti-clotting medications.

Children taking anti-clotting medications may experience some of these side-effects:

- Small cuts on the skin may ooze longer than they did before.
- Nosebleeds can occur more frequently or last longer.
- Bruises in areas of injury can occur more easily and grow larger.
- Teenage girls may have heavier periods.

Parents should seek prompt medical attention for their child with DVT/PE if:

- The child has new signs or symptoms of a DVT/PE (see prior section on signs and symptoms of DVT/PE).
- The signs and symptoms of the child's DVT/PE get worse.
- The child bleeds often, or for a long time.
- The child becomes pale or tired after bleeding has occurred.
- The child develops any other issues that the doctor has discussed with the parents as needing prompt medical attention.

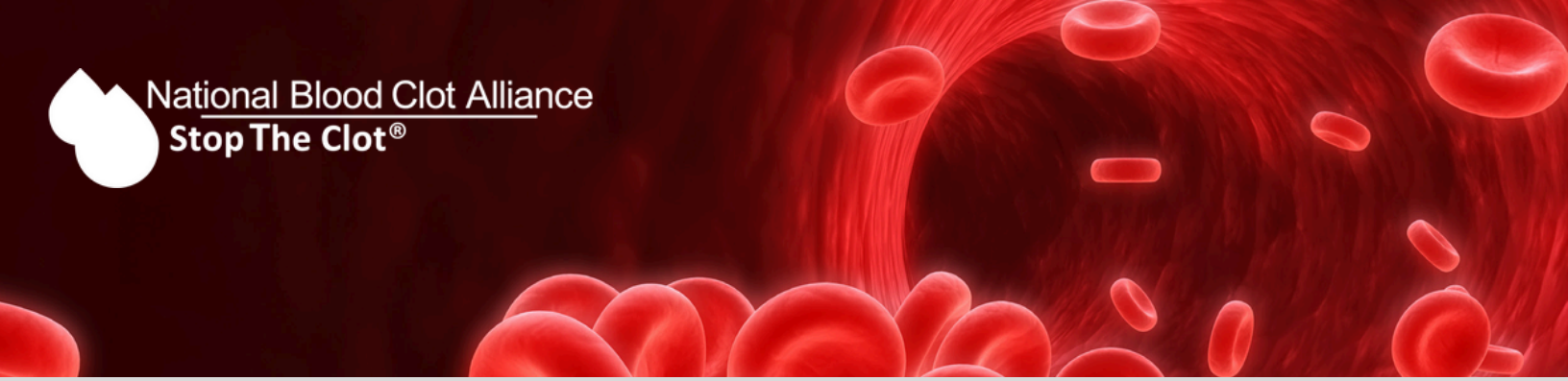


HOW LONG DO CHILDREN NEED TO REMAIN ON ANTI-CLOTTING MEDICATIONS?

For many children who have developed DVT/PE with contributing factors identified (in other words, whose DVT/PE did not occur “out of the blue”), the length of treatment with anti-clotting medications can be as short as six weeks, especially if the contributing factors are no longer present, or much less significant, by that time. This was shown in a recent multi-national research study called Kids-DOTT, funded by the U.S. National Institutes of Health.

However, for children whose DVT/PE have no contributing factors identified, or who have had another DVT/PE in the past, or who for other reasons do not fit the features of children who participated in Kids-DOTT, the length of treatment with anti-clotting medications is typically three months.

For children whose DVT/PE had no contributing factors identified, or who have strong and long-lasting risk factors for developing new DVT/PE, or who have had multiple prior DVTs/PEs, the length of treatment may be six to 12 months or even life-long.



WHAT ARE THE POSSIBLE LONG-TERM EFFECTS OF DVT/PE IN CHILDREN?

Potential long-term effects of DVT/PE depend on the parts of the body or organs involved. For example:

- After a child has a leg or arm DVT, the clotted vein can be damaged by the increased pressure so that they no longer work as well in bringing blood back toward the heart. This condition – known as “chronic venous insufficiency” or “post-thrombotic syndrome (PTS)” – develops in about 25% of patients.
    - Children with PTS can have swelling, pain, aching, heaviness, itching, tingling, color changes, rash or sores on the skin of their arm or leg where they had the DVT.
    - For most children, PTS symptoms are mild, and mainly occur after standing or exercising.
    - PTS symptoms are usually improved by elevating the arm or leg and using custom-fit graduated compression stockings (GCS) that are prescribed by your child’s doctor.
- After a PE, children can develop long-term breathing problems from pulmonary hypertension. This results from increased pressure in the pulmonary artery, which brings blood from the heart to the lungs. Other times, long-term breathing problems can occur from areas of lung damage (known as pulmonary infarction) due to blockage in blood flow.
- If a CSVT has caused bleeding or infarction (damage to the brain tissue) due to increased pressure in the vessels of the brain, a child can have long-term neurological difficulties, such as weakness of one side of the body or face. Children can also develop chronic headaches if there is increased pressure in the brain from chronic blockage in the drainage of blood back to the heart.
- If the increased pressure affects the optic nerve, it can cause blurred vision and long-term vision damage. Procedures can be done to prevent vision damage.

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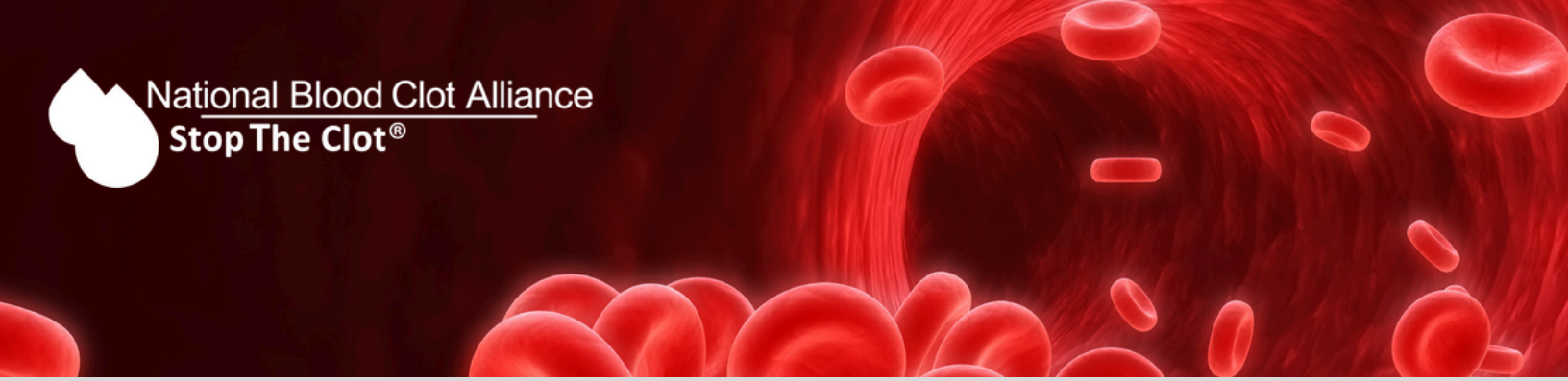

WHAT ARE THE POSSIBLE LONG-TERM EFFECTS OF DVT/PE IN CHILDREN?

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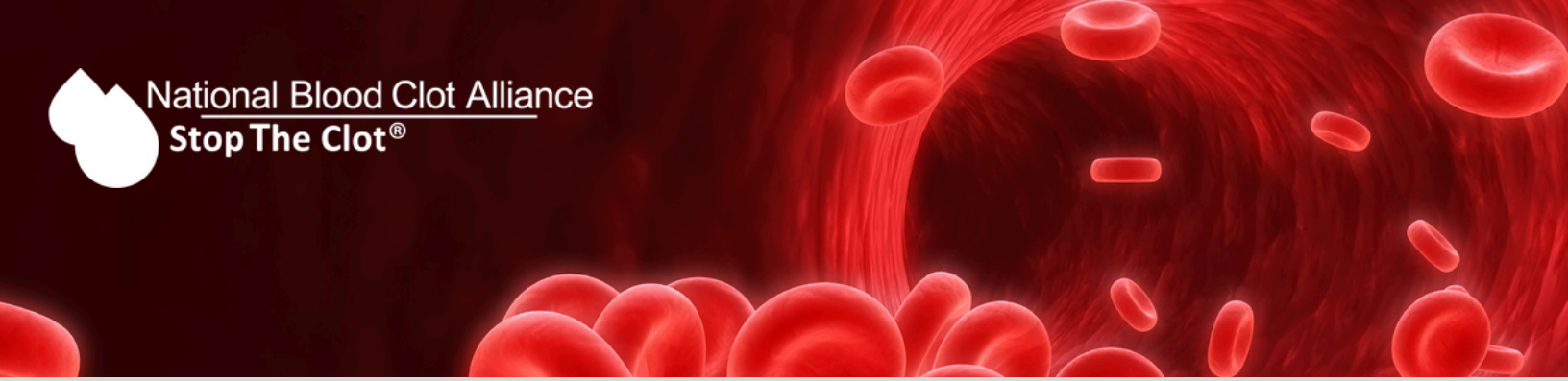
- Children with DVT of the kidney veins (known as renal vein thrombosis) can develop high blood pressure.

- Children with DVT of the liver veins (known as hepatic vein thrombosis) or the portal vein (portal vein thrombosis) can result in spleen enlargement, which can cause low blood cell counts. Hepatic and portal vein thrombosis can cause bleeding in the stomach or esophagus from increased pressure in the veins that return blood to the heart from these areas. (Note: The portal vein drains blood from the intestines, spleen and other organs into the liver).



HOW CAN DVT/PE BE PREVENTED IN CHILDREN?

For prevention of DVT/PE in children, doctors usually prescribe less intense dosing of anti-clotting medication than is used for treatment of DVT/PE in adults.

In children who were born with a certain type of heart condition, recent research suggests that DOACs may be useful for preventing DVT/PE and blood clots in the arteries.

Other steps that can be taken to help prevent DVT/PE from occurring include:

- Staying well-hydrated and drinking plenty of fluids that have very little sugar or caffeine. (Dehydration increases the risk of DVT/PE.)

- Not smoking or vaping. Smoking damages the inner lining of blood vessels and increase the risk of DVT/PE as well as clots in the arteries.

- Not taking estrogen, such as birth control pills, especially if the child is known to have factor V Leiden or family members who developed DVT/PE at younger than 50 years old.

- Putting a plan in place with the child's hematologist for how to prevent DVT/PE in a child who has a personal or strong family history of DVT/PE or genetic risk factor during situations in which a child's risk of DVT/PE is increased. These situations include hospitalizations and after certain surgeries. This plan may involve using anti-clotting medication for a short period of time, at a less intense dosing than is used for treating DVT/PE, until the child is back to their usual state of health.