Sinus and cerebral vein clots are uncommon. They can lead to severe headaches, confusion, and stroke-like symptoms. They may lead to bleeding into the surrounding brain tissues. The clot can be triggered by infections of the ear, face, or neck, by estrogen use and pregnancy, and can be caused by inherited and acquired clotting disorders.

The diagnosis is, unfortunately, sometimes initially missed by health care professionals, as a plain CT or MRI of the head can be normal. It takes special MRI or CT scans (called MR venogram or CT venogram) to make the diagnosis.

Blood thinners (heparins) are typically initially given, even if there is already bleeding into the brain at the site of the clot. Subsequently, warfarin is given for varying lengths of time, depending on the trigger of the clot: for 3-6 months if there was a clear temporary trigger (infection, estrogens), 6-12 months if the clot was unexplained and no strong clotting disorder has been found, long-term, if a strong clotting disorder is present.

A Consensus Statement published for health care professionals on February, 2011 (reference 1 at the end of this document) contains information and recommendations on diagnosis and treatment.
Normally, blood is transported through arteries into the brain, where it delivers oxygen and nutrients. Once the blood has done its job, it collects into small veins (=cerebral veins) that drain into large veins, called sinus veins. The sinus veins lead to the jugular veins in the neck, which carry the blood back to the heart (see image below).

For clarification: These sinus veins have nothing in common (except for the name “sinus”) with the sinuses of the face on both sides of the nose and above the eyes which can get infected, leading to sinusitis.
Thrombosis Terms
A blood clot in the veins that drain the blood from the brain is called a sinus or cerebral vein thrombosis (see image below). Other names also in use are:

- Cerebral venous thrombosis (CVT)
- Cerebral vein thrombosis
- Cerebral venous and sinus thrombosis,
- Cerebral venous sinus thrombosis (CVST)
- Cerebral sinovenous thrombosis (CSVT)
- Cerebral vein and dural sinus thrombosis
- Sinus and cerebral vein thrombosis

How common is it?
Sinus and cerebral vein thrombosis is an uncommon type of clot. Only about 1,500 people in the U.S. are diagnosed with it per year (compared to nearly a million people every year with deep vein thrombosis and pulmonary embolism, and 150,000 to 300,000 people with strokes).
**Why do symptoms occur?**

The obstruction of the blood flow from a clot in these veins leads to a back up of blood and increasing blood pressure in the blood vessels just before the obstruction (see previous image). This is like water in front of a dam. The increased pressure leads to swelling of part of the brain, which results in headaches; the pressure can damage the brain tissue, leading to stroke-like symptoms. The increased pressure can also lead to rupture of the blood vessel and bleeding into the brain (see image below).

In medical terms this is called “cerebral hemorrhage”. It is like water in a reservoir overflowing into the surroundings or like a ruptured dam. This is referred to as “venous hemorrhagic infarction” or “venous hemorrhagic stroke”. It can lead to further damage of brain tissue. About one-third of patients with sinus and cerebral vein thrombosis have such bleeding.
Symptoms

Symptoms from sinus and cerebral vein clots depend on the location and extension of the clot and vary from patient to patient. The most common symptom is a severe headache, often the worst headache that a patient has ever had. It can be of sudden onset, develop over a few hours, or a few days. Nausea and vomiting may occur, as may blurred vision. A variety of other neurological symptoms can occur: seizures, speech impairment, one-sided numbness and/or weakness of an arm, a leg, or both, confusion, a decreased level of alertness. Symptoms may be exactly what people think of as occurring in a stroke. A very extensive blood clot may lead to loss of consciousness and death.

Who develops it? What are the causes?

Sinus and cerebral vein thrombosis may occur in newborns or adults. It can be due to (a) temporary risk factors, and (b) permanent (inherited) ones. In newborns, the most common cause for the clot is an infection. Infection of the inner ear (otitis), the bone behind the ear (mastoiditis), the mouth, face or neck and sinusitis can be triggers. Birth control pill, patch and ring, estrogen replacement therapy, pregnancy and postpartum state, and certain medications (tamoxifen, chemotherapy) also increase the risk, as may cancer. Acquired clotting disorders (antiphospholipid antibodies) or inherited ones (factor V Leiden, prothrombin 20210 mutation, deficiency of protein C, S and antithrombin) are other risk factors. Sometimes, no obvious cause is identified, in spite of an extensive laboratory work-up.

Diagnosis and Treatment

How is it diagnosed?

Sinus and cerebral vein thrombosis is easily missed if the correct imaging X-ray study is not done. The appropriate test to do is an MRI venogram (=MRV) or CT venogram (=CTV). If available, the MRV is slightly preferred over CTV. The usual routine CT or MRI, as are often done for evaluation of stroke or bleeds into the head, are often normal. Also, a plain X-ray of the head or skull is not helpful.
The health care professional who evaluates the patient with severe headache or neurological symptoms needs to think about sinus and cerebral vein thrombosis, otherwise the diagnosis is easily missed. The health care professional should have an increased level of suspicion that a patient may have a sinus or cerebral vein thrombosis if the patient has (a) the worst headache ever, (b) risk factors for blood clots, such as being on estrogens or progestin contraceptives, being pregnant or having delivered in the preceding 3 months, (c) a personal or family history of blood clots or (d) a known clotting disorder (thrombophilia).

**Clotting disorder work-up**

In unexplained sinus and cerebral vein thrombosis, work-up for a clotting disorder is appropriate, to look for a strong clotting disorder, that may influence the length of treatment with “blood thinners” (discussed below). An appropriate laboratory work-up in the patient with an unprovoked sinus and cerebral vein thrombosis includes a CBC (=complete blood count), and tests for factor V Leiden, prothrombin 20210 mutation, protein C, S and antithrombin deficiency, and antiphospholipid antibodies (lupus anticoagulant, anticardiolipin antibodies, anti-beta-2-glycoprotein-I antibodies).

**How is it treated?**

Patients with an acute clot are admitted to the hospital. If symptoms are severe, patients will be admitted to a stroke or intensive care unit. The immediate treatment consists of giving “blood thinners” (= anticoagulants). In the first few days these are either heparin into the veins (= intravenously), or injections of low molecular weight heparin (Enoxaparin, Dalteparin, Tinazparin, Lovenox®, Framin®, Innohep®) under the skin (= subcutaneously). The purpose of giving “blood thinners” is to prevent the existing clot(s) from getting bigger and new clots from forming. The body’s own clot-dissolving system then slowly, over weeks and months, works on dissolving the existing clots.
Clot busters (=fibrinolytic drugs) are typically not given, as they may increase the risk of bleeding into the brain. Radiological or surgical procedures with catheters to break up and extract the clot (thrombectomy; endovascular therapy) are done only in severe cases and in patients who get worse despite adequate “blood thinning” therapy. If a patient has bleeding into the brain due to the clot, the routine “blood thinners” are typically still given to prevent new clots from forming. However, the physicians have to pay very close attention that the bleed does not get worse.

Once the patient has been stable for a few days, an oral blood thinner (warfarin; Coumadin®, Jantoven®) is started. The injectable and the oral “blood thinner” need to overlap for at least 5 days AND until the INR is above 2.0. (INR= International Normalized Ratio; this is the measure of how “thin” the blood is and how much warfarin the patient needs to take). The typical target INR is 2.0-3.0. A key question is how long a patient needs to be on warfarin. Solid treatment guidelines have recently been published (see reference 1 at the end).

- If the clot was associated with a transient risk factor, such as an infection or trauma, a period of 3-6 months is typically sufficient.
- If strong risk factors suggesting a high risk of recurrent clot are present, long-term warfarin is often chosen. Strong clotting disorders are: antiphospholipid antibody syndrome, deficiency of protein C, S or antithrombin; 2 abnormal genes for factor V Leiden (=homozygous); two abnormal genes for the prothrombin mutation (=homozygous); one abnormal gene for each of these mutations (double heterozygous).
- In all other patients with unprovoked clot, a treatment period of 6–12 months is often chosen. This includes patients who only have one abnormal gene for factor V Leiden (i.e. who are heterozygous) or have one abnormal gene for the prothrombin 20210 mutation (i.e. are heterozygous).
The risk of another sinus or cerebral vein thrombosis, once a patient has stopped warfarin, is relatively low in the person whose first clot was unprovoked and in whom no strong clotting disorder is present: only approximately 1.5% of patients (one out of 70) will develop another sinus or cerebral vein thrombosis per year [reference 2 at the end]. However, patients are also at increased risk to develop other vein clots, mostly deep vein thrombosis (DVT) of the legs and pulmonary embolism (PE) – about 1 in 25 patients will develop such a clot per year [reference 2]. Thus, patients who stop warfarin need to know the symptoms of DVT and PE and be on the lookout for them, to seek medical attention early if such symptoms occur.

Finding leftover clots (scar tissue, recanalized clots) after a few months of treatment with “blood thinners” typically does NOT influence the decision how long to treat with “blood thinners”. Therefore, repeating brain imaging studies (MRV or CTV) on a regular basis is not needed, as it does not change management. However, once a decision is made to stop warfarin, a baseline imaging study (MRV or CTV) should be done. The purpose of this is to have a baseline or reference study, in case new symptoms come up in the future. If one has a baseline study for comparison, it is easier to tell new clot from old/previous clot. In approximately 80% of patients the clots partially or completely dissolve and the veins become patent again, but 20% of patients will have chronic occlusion of their sinus or cerebral vein(s) that was/were occluded. Clinically this does not seem to matter and there is no correlation between chronic symptoms and the degree of vessel patency. This is another reason why routine follow-up MRV or CTV Xray studies are not needed.

What complications may arise?

In the acute setting some patients with extensive clot or associated bleed may die. However, the majority of patients recover completely: Almost 80% of patients fully recover, but it may take several weeks or months to get back to normal. Headaches, and seizures may persist for some time. Minor disability (concentration or memory problems) occurs in 6% of patients (1 of 17 people). Fourteen percent (1 of 7 people) will have a poor outcome, with major neurological deficits.
What else do I need to know?

If you have had a sinus and/or cerebral vein thrombosis make sure you understand:

- What your risk factors were to have developed the clot and whether you have had an appropriate laboratory work-up to look for a clotting disorder;
- How long you should be on warfarin. Make sure your health care professional is aware of the published management consensus statement (Listed as Reference 1 at the end of this document)—you may want to print it out and provide it to him/her;
- That you should avoid estrogen therapy or progestin pill or injections in the future; that the Mirena® IUD is probably safe;
- That it is o.k. for most women to become pregnant in the future, if they want to. However, “blood thinner” therapy should be considered during pregnancy and for several weeks (6-12 weeks) after delivery;
- That you are at somewhat increased risk for other blood clots, i.e. deep vein thrombosis (DVT) and pulmonary embolism (PE) and should, therefore (1) modify your DVT and PE risk factors (normalize weight, stop smoking, be physically active), (2) know the symptoms of DVT and PE, and (3) get good DVT prophylaxis in future risk situations (major surgery, hospitalization, pregnancy).

Anything my family needs to know?

Your siblings, children and parents are possibly at slightly higher risk for blood clots, because you had a clot. However, no screening of them is needed (MRV or CTV scan, blood work), unless you were found to have a strong inherited clotting disorder. In that case it might be appropriate to consider testing them for the same clotting disorder. However, individualized decisions on testing need to made, as this is a complex issue.
References and Guidelines


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