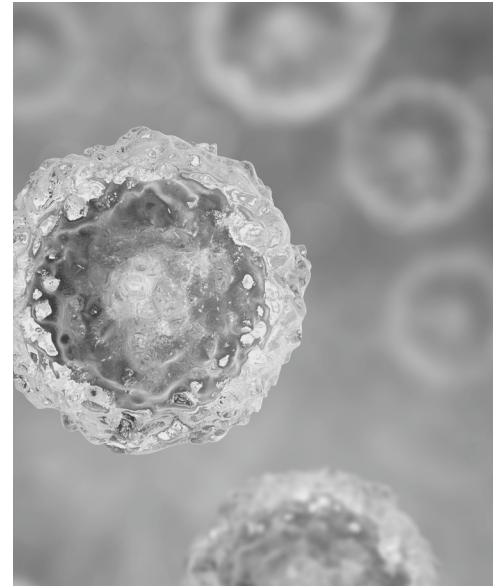


An Adult Patient's Guide to Understanding Veno-Occlusive Disease (VOD) of the Liver

A possible complication following
hematopoietic stem-cell transplantation



Know the risk factors and the signs and symptoms
to watch for and discuss with the transplant team



VOD is a disease that can sometimes occur in patients who have received stem-cell transplant. The transplant team will be monitoring for VOD to help ensure that it is quickly identified if it begins to develop.

This brochure will help you understand what VOD is and what signs and symptoms you should look for.

You will also learn about the factors that could put you at increased risk for VOD and what information you should share with the transplant team.

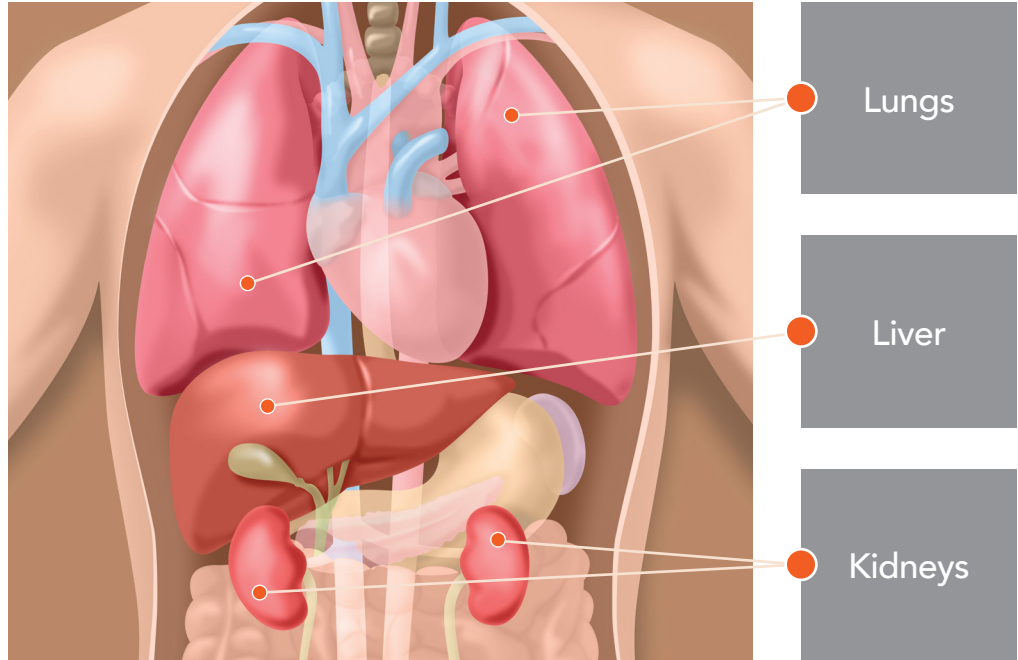
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What is VOD?

Hepatic veno-occlusive disease (VOD) is a complication that affects the liver and can occur following stem-cell transplant. VOD may also be referred to as sinusoidal obstruction syndrome, or SOS, by the transplant team.



VOD begins in the liver and can quickly affect other vital organs, most notably the kidneys and lungs. Understanding the signs and symptoms, as well as how to recognize them, can help ensure treatment begins as soon as possible, if appropriate.

When VOD is identified, it requires immediate medical attention, as it can rapidly worsen.

What causes VOD?

VOD is thought to be caused by certain treatments given to prepare the bone marrow for stem-cell transplant. Treatments given to prepare the bone marrow for stem-cell transplant are called conditioning regimens and may include chemotherapy or radiation.

These treatments can damage cells in the liver, leading to a blockage that can reduce blood flow in the liver. This can cause changes throughout the body.



KEY TERMS

Liver: The liver has many functions, including removing waste from blood before it goes to the rest of the body. It is located in the abdomen on the right side, just below the rib cage. "Hepatic" refers to the liver.

Abdomen: The area of the body below the chest and above the pelvis. The abdomen contains most of the major organs.

What are the signs and symptoms of VOD?

General signs and symptoms of VOD include:



Pain and tenderness in the abdomen, especially on the upper right side, due to swelling of the liver, known as hepatomegaly



Rapid weight gain compared to weight when the transplant treatment was started



Bloating of the abdomen due to fluid buildup, known as ascites



Yellowing of the skin, known as jaundice

The signs and symptoms listed above are not official diagnostic criteria for VOD. The transplant team will officially diagnose VOD if it occurs.

Other signs of VOD that may be identified by certain lab values include:



Elevated bilirubin



Low platelet levels requiring multiple platelet transfusions



Elevated liver function tests, most commonly the liver enzymes

When do the signs and symptoms of VOD typically occur?

21 days

Because of the treatments given to prepare the bone marrow for stem-cell transplant, signs and symptoms of VOD most often occur within the first 21 days following stem-cell transplant.

Monitor for signs and symptoms

VOD can still occur after 21 days following stem-cell transplant, so it is important to continue to monitor for signs and symptoms even after discharge from the hospital and contact your doctor if any occur.

How are the early symptoms of VOD managed?

- Management of early symptoms, such as buildup of fluid, is an important part of the supportive care of VOD.
- Reducing the amount of fluid that has collected in the abdomen and other parts of the body is one of the main goals.
- Medications known as diuretics are given to encourage the passing of urine. Diuretics are sometimes called water pills.
- The amount of fluids given within a day is reduced.

Be sure to talk to the transplant team about any signs or symptoms that appear after transplant. Many of these signs and symptoms can result from other conditions. The transplant team will help determine whether it is VOD or something different.

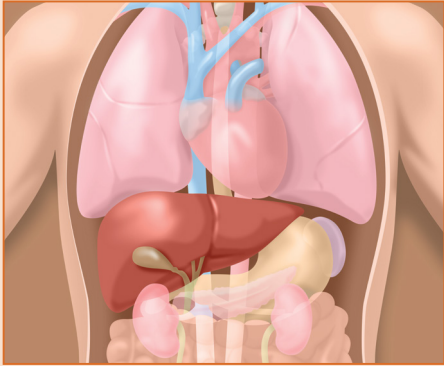
KEY TERMS

Bilirubin: A substance formed from the normal breakdown of red blood cells in the liver and removed from the body through the digestive system. If the liver is not functioning properly, bilirubin may build up in the blood and cause yellowing of the skin (jaundice).

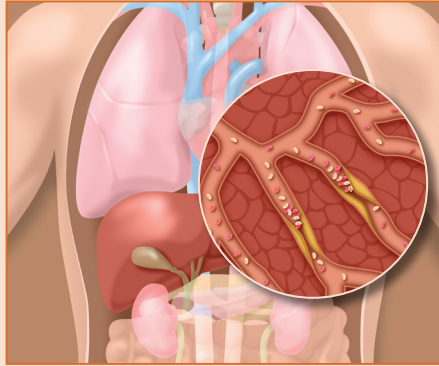
Platelet: A type of blood cell that helps the blood to clot to stop bleeding.

Liver enzymes: Proteins in the liver that help speed up chemical reactions. When the liver is injured, liver enzymes are increased in the blood.

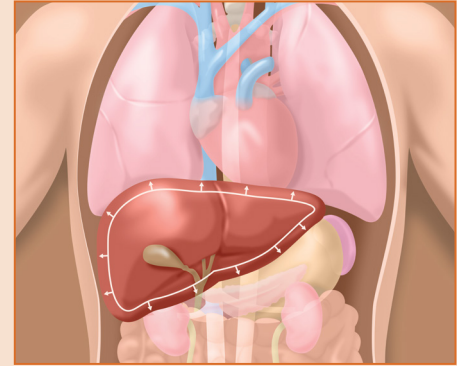
What effect does VOD have on the body?



The main function of the liver is to filter harmful substances, called toxins, and other waste products from the blood before it goes to the rest of the body.

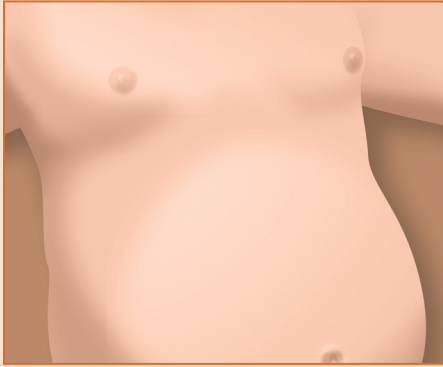


As VOD develops, the blood vessels that transport blood through the liver become narrow. This causes reduced blood flow, and these vessels may become completely blocked.



When there is reduced blood flow, fluid builds up inside the liver, causing it to swell. This condition is known as hepatomegaly, and it often leads to pain and tenderness in and around the right side of the abdomen, below the rib cage.

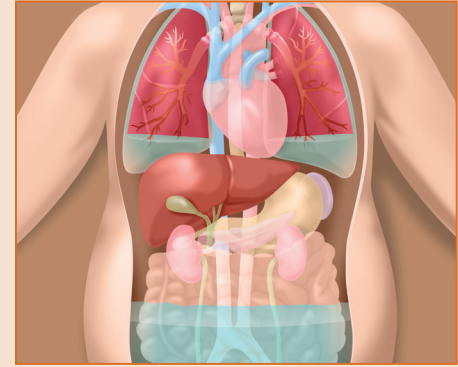
VOD can quickly start to affect the function of some of the most important organs in the body.



The reduced blood flow also leads to high pressure in the veins that carry blood to the liver. As a result, fluids can leak from the liver and build up in the abdomen. This swelling is known as ascites.



As liver damage worsens, the function of other organs, such as the kidneys and lungs, can be affected. The kidneys may hold excess water and salt, causing the arms and legs to swell.



Fluid buildup in the abdomen and lungs can make it harder to breathe.

VOD with multi-organ dysfunction describes VOD that affects other organs in the body in addition to the liver, such as the kidneys (renal system) or lungs (pulmonary system). When multi-organ dysfunction occurs, it may become life-threatening. It is important to let the transplant team know if you notice any signs or symptoms.



What factors put a patient at risk for VOD?

While VOD can occur in any patient receiving stem-cell transplant, there are factors that may increase the risk of developing VOD. These include some current or prior conditions, such as cancers or noncancerous blood disorders; certain patient characteristics; and previously received medications or treatments. If you have any of the factors listed, it does not mean you will develop VOD, but you may be more likely to.



Current/prior conditions

- Advanced disease: beyond second complete remission or relapsed/refractory disease
- Preexisting liver conditions
- Metabolic syndrome
- Thalassemia, a blood disorder



Patient characteristics

- Older age



Medications/treatments

- Allogeneic stem-cell transplant (stem-cell transplant with cells from another person)
- Second stem-cell transplant
- Unrelated stem-cell donor (stem-cell transplant from a donor that is not related to the patient)
- Current or previous use of drugs that damage the liver, including those used to prepare the bone marrow for stem-cell transplant
- Female taking the hormone norethindrone, a form of birth control



KEY TERMS

Preexisting liver conditions: These may increase the chances of developing VOD and include cirrhosis (scarring of the liver), hepatitis (an inflammation impacting the liver), and hepatic steatosis (fatty liver disease).

Metabolic syndrome: A group of conditions that includes high blood pressure, high blood sugar, excess fat in the abdominal area, and abnormal cholesterol, which are associated with an increased risk of heart disease, stroke, and type 2 diabetes.

Drugs that may damage the liver: Some of these are cyclophosphamide, busulfan, gemtuzumab ozogamicin or inotuzumab ozogamicin, tacrolimus, and sirolimus.

How does the transplant team monitor for VOD?

During the first 21 days after stem-cell transplant, the team will closely monitor for any signs of VOD.^{732,29}

VOD is a clinical diagnosis, meaning there is no one specific test to determine if VOD is present. A VOD diagnosis is based on a number of laboratory tests and physical assessments performed by the transplant team. They will monitor closely for signs and symptoms and any test results that point to possible VOD.

What exams and tests help diagnose VOD?

Following transplant, the team will perform a number of physical exams and will monitor liver and kidney function with blood tests. In addition to blood work, the physician may conduct imaging, such as an X-ray, CT (computed tomography) scan (also called CAT scan), or ultrasound to help confirm suspected signs and symptoms associated with VOD. In rare situations, a liver biopsy may also be performed to help diagnose VOD and determine the severity of liver damage.

What will the transplant team be monitoring and looking for?

- Sudden weight gain
- Liver function
- Kidney function
- Lung function
- Pain, tenderness, and/or bloating of the abdomen due to swelling of the liver
- Possible yellowing of the skin (jaundice)
- Fluid buildup, seen as swelling of the arms and/or legs

Because VOD can still occur at any time after stem-cell transplant, the team will continue to monitor for signs and symptoms beyond 21 days after the transplant.

What should I watch for to tell the transplant team?

The transplant team will be monitoring closely, but it is important to alert the team if any of the following signs and symptoms start to occur, as VOD can rapidly progress to become a serious and life-threatening condition.



Abnormal weight gain, which can occur rapidly



Shortness of breath or difficulty breathing



Bloating of the abdomen



Yellowing of the skin



Discomfort or pain in the abdomen



Urinating less often



KEY TERMS

Ultrasound: A probe is gently moved over the skin to provide a view of structures within the abdomen. A Doppler ultrasound is a special type of ultrasound that may be performed to show blood flow in the liver.

Liver biopsy: In this procedure, a small piece of liver tissue is removed so it can be examined under a microscope.

Following discharge from the hospital, it is important to continue watching for signs and symptoms of VOD and contact the transplant team immediately if any start to occur, even beyond 21 days after transplant.



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