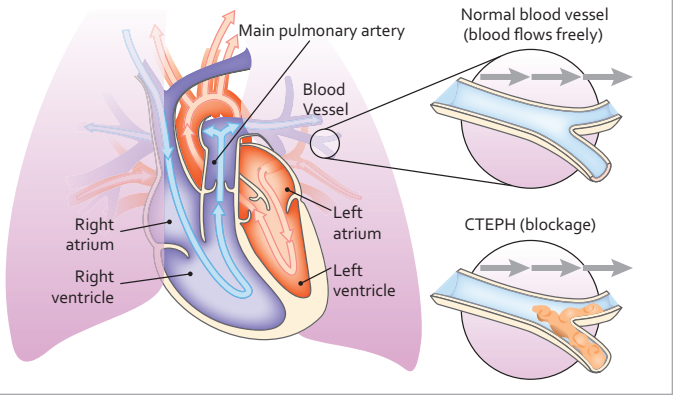
Chronic Thromboembolic Pulmonary Hypertension

Part 1

Chronic thromboembolic pulmonary hypertension (CTEPH) is a condition where there is elevated blood pressure in the pulmonary arteries caused by chronic blood clots (thromboembolic), which obstruct the free flow of blood through the lungs.



This is a special form of pulmonary hypertension that, unlike all the other forms, can potentially be cured with a surgical procedure. This is why it is extremely important that your health care provider makes sure that chronic blood clots are not the cause of your pulmonary hypertension.

What Is Pulmonary Hypertension?

To understand chronic thromboembolic pulmonary hypertension, let's start by briefly reviewing what pulmonary hypertension (PH) is (see ATS Patient Series on PH at www.thoracic.org/patients). After your blood has delivered oxygen to the tissues of your body, the blood needs to come back to the lungs to get more oxygen. It does this by returning the blood to the right side of the heart, which in turn pumps the blood into your lungs. The pressure that the right side of your heart is pumping against is called your pulmonary pressure. When this pressure is too high, it is called pulmonary hypertension. The high pulmonary pressure could be caused by several medical conditions.

What does chronic thromboembolic mean?

Thromboembolism is the medical term for blood clots. Forming blood clots is a normal defense mechanism of the body to prevent bleeding in the case of injury. However, sometimes blood clots form abnormally, typically in leg veins (so called deep venous thrombosis, or DVT), and then travel to clog the arteries in the lungs, so called pulmonary embolism (PE). With the help of blood thinners and the body's own internal clot dissolving mechanism, most pulmonary blood clots go away without any permanent damage. In a small number of people, pulmonary clots do not go away, and become scars that narrow the size of pulmonary vessels. These clots are called chronic thromboemboli, and are the cause of increased pulmonary pressure.

What Causes Chronic Thromboembolic Pulmonary Hypertension?

The exact cause of CTEPH is not known. One or more episodes of pulmonary embolism are the first step. Conditions that increase the chances of having blood clots include long periods of inactivity, major surgical procedures, cancer, pregnancy and the after pregnancy period, estrogen-containing oral contraceptives (birth control pills), obesity, and smoking, to name a few. Blood clots can also occur without any known cause. Conditions that seem to increase the chances of developing CTEPH include unexpected pulmonary embolism, a large PE, thyroid disease, cancer, surgical absence of the spleen, and infected pacemakers. The lupus anticoagulant/anti-phospholipid antibody syndrome is a blood coagulation disorder that is associated with CTEPH as well. CTEPH also presents without any underlying risk factor, even in people without a history of a previous blood clot in the legs or lungs. Because many patients with CTEPH have no history of PE or DVT, or do not know they had a PE, it can be overlooked or not suspected.

What are the Symptoms of Chronic Thromboembolic Pulmonary Hypertension?

The symptoms of CTEPH are quite similar to other types of PH (see ATS Patient Information Series handout on PH at www.thoracic.org/patients). There may be no signs or symptoms of CTEPH in its early stages. You might first notice that you

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become short of breath more easily. You might also notice you are more tired (fatigued) than usual. If you experience shortness of breath and/or fatigue several months after having a blood clot in the legs or lungs, your health care provider should look for CTEPH. Some patients also may feel "light headed" or even pass out. Swelling (edema) of your feet and ankles is common and may progress to swelling of your belly (ascites). Chest pain may also occur and can be mistaken for a heart attack. You may feel your heart racing or pounding (palpitations). The oxygen level in your blood may become very low, making your feet and/or fingers turn blue. Some people with CTEPH cough up blood.

How is Chronic Thromboembolic Pulmonary Hypertension Diagnosed?

If you experience any of the above symptoms and have a history of blood clots in the legs or lungs, your health care provider should suspect CTEPH. Even without a prior history of blood clots, these symptoms should trigger a suspicion for CTEPH if they remain unexplained after basic testing. Screening for CTEPH is mandatory for everybody with pulmonary hypertension.

There are two steps to the diagnosis of CTEPH: the evaluation of pulmonary pressure, and the diagnosis of chronic pulmonary clots as the reason for the elevated pulmonary pressure.

Your health care provider will usually order an ultrasound of your heart (echocardiogram). If the echocardiogram shows the pressure on the right side of your heart may be high, they may order a cardiac catheterization. During a cardiac catheterization, a rubber tube (catheter) is placed through a blood vessel into the chambers of your heart to measure the pressure in the right side of your heart. A cardiac catheterization is the best way to measure the blood pressure in the pulmonary artery.

Your health care provider will also order tests to look for chronic pulmonary clots. The screening test of choice for CTEPH is the ventilation-perfusion scan (VQ scan). During this test, radioactive material (radioisotopes) is injected to see how well air moves through the lungs and how well the blood circulates through the lungs. A normal result from a V/Q scan means you do not have CTEPH. If the VQ scan is abnormal, you will need additional X-ray testing requiring the use of intravenous dye to confirm the diagnosis. A computed tomography (CT) pulmonary angiography is a specialized type of CT scan that shows visual images of the pulmonary arteries and gives more details about the location and extent of pulmonary blood clots. You may also have a different type of pulmonary angiography, which is done similarly to a right heart catheterization, but allows for detailed visualization of blood flow and pulmonary arteries. This test can be performed at the same time as the cardiac catheterization.

Is There a Cure for Chronic Thromboembolic Pulmonary Hypertension?

Yes! The good news is, in most instances, CTEPH is curable with early diagnosis and surgery. This is why it is important to recognize this disease early, and to make sure that your health care provider orders a VQ scan to look for CTEPH if you have pulmonary hypertension or unexplained shortness of breath.

How is Chronic Thromboembolic Pulmonary Hypertension Treated?

A surgical procedure called pulmonary thromboendarterectomy (thrombow-end-arter-ectomee) (PTE, sometimes referred to as pulmonary endarterectomy, or PEA) is currently the recommended and only effective treatment for patients with CTEPH.

Although this is a cure for most people with CTEPH, some people are not good candidates for a variety of reasons. Whether you are a candidate for this treatment is determined by an expert CTEPH team. For people in whom surgery is not feasible, there are two treatment options: medical therapy to dilate pulmonary arteries, and/or a procedure called balloon pulmonary angioplasty (BPA).

Additional information about treatment of CTEPH will be provided in Part 2, Treatment of CTEPH.

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Reviewers: William Auger, MD; Marianna Sockrider MD, DrPH

Rx *Key Points*

- ✔ If you have a history of blood clots in the legs and/or lungs, and now are experiencing shortness of breath or fatigue, talk to your health care provider about CTEPH.
- ✔ If you have been diagnosed with pulmonary hypertension, make sure that your health care provider has excluded the possibility of CTEPH.
- ✔ The lung ventilation/perfusion scan (VQ scan) is the best test to look for CTEPH.
- ✔ If you have been diagnosed with CTEPH, talk to your health care provider about a referral to a specialized center. You may find CTEPH specialists at http://www.phassociation.org/CTEPH/DoctorDirectory.

Healthcare Provider's Contact Number:

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Resources:

Pulmonary Hypertension Association
http://www.phassociation.org/CTEPH

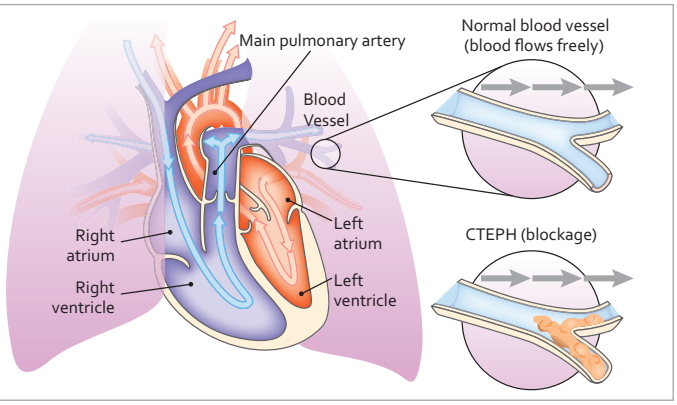
Pulmonary Hypertension Association Europe
http://www.phaeurope.org/dissease-information/what-is-cteph/

American Thoracic Society
http://www.thoracic.org/patients

Chronic Thromboembolic Pulmonary Hypertension

Part 2

Chronic thromboembolic pulmonary hypertension (CTEPH) is a condition where there is elevated blood pressure in the pulmonary arteries caused by chronic blood clots (thromboembolic), which obstruct the free flow of blood through the lungs.



This is a special form of pulmonary hypertension that, unlike all the other forms, can potentially be cured with a surgical procedure. This fact sheet will review treatment of CTEPH. For more information about the diagnosis of CTEPH, see ATS Patient Information Series piece *Chronic Thromboembolic Pulmonary Hypertension (CTEPH)* at www.thoracic.org/patients.

What are the treatment options for CTEPH?

Left untreated, CTEPH is a deadly condition. Fortunately, it is perhaps the most treatable form of pulmonary hypertension, and for some people even cure is possible. The treatment of choice for CTEPH is a surgical procedure called pulmonary thromboendarterectomy [thrombo-endar-ter--ek-tomy] (or PTE for short, sometimes referred to as pulmonary endarterectomy, or PEA). This procedure has a proven track record of positive results over several decades, and it offers a definitive cure for many people with CTEPH. This is why, as soon as the diagnosis of CTEPH is made, you should be evaluated at a medical center with experience and expertise in performing PTE surgery.

After this evaluation, some people are deemed to not be good candidates for surgery. For people in whom surgery is not possible or indicated, there are two other treatment options: medications to dilate small pulmonary arteries, and/or a procedure called balloon pulmonary angioplasty (BPA).

How do doctors determine who is a good candidate for PTE surgery?

Doctors look at three main factors to decide who is a good candidate for this procedure. The first one is whether or not the chronic blood clots are located in big enough arteries, so that they can be reached by the surgical instruments. The second question is whether or not the high pulmonary blood pressure is likely accounted for by the amount of pulmonary clots present.

And finally, a person has to be otherwise strong enough to be able to get through and survive a big operation. If the answer to these three questions is yes, then PTE surgery is a good idea. The main challenge however, is that these decisions are complex, largely based on expert opinion, and shaped by the team's experience and expertise. This is why this determination needs to be made at an expert center. Importantly, older age and obesity do not routinely represent absolute barriers for this procedure.

How is PTE surgery done?

This operation is done through a chest wall incision; this is the same type of incision used for heart bypass surgery. Then, doctors stop the heart, drain the blood from the heart and lung arteries, and cool the person's body to about 60 degrees, which prevents brain damage. The surgeon then peels off the scar clot tissue lining and plugging the pulmonary (lung) arteries. Performing a PTE requires a dedicated team and a highly skilled surgeon.

What is the recovery like after PTE surgery?

The usual hospital stay is 10-14 days. Some people notice immediate and dramatic improvements in their breathing function and comfort, while for others it may be a more gradual process. You will be able to gradually resume your usual activities over the following 4-6 weeks. Pulmonary rehabilitation with supervised exercise is often helpful. You may need extra oxygen for some time after surgery. You will be given blood thinner medication, which you will need to keep taking for the rest of your life. By 3-6 months after successful PTE surgery, most people are able to resume normal or near normal levels of activity and lead normal productive lives. Your healthcare providers will want to see you frequently to check for improvements in exercise capacity and pulmonary pressures, as well as for potential complications. You will have follow-up tests

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such as the 6-minute walk test, echocardiography, ventilation–perfusion scan and right heart catheterization during the first 3-6 months after surgery. These tests can be done at the PTE center or with your local pulmonary hypertension doctor. For more information on pulmonary rehabilitation, see ATS Patient Information series piece at www.thoracic.org/patients.

What are the potential complications of PTE surgery?

Like with any other major operation, not surviving the procedure is the most serious potential outcome. Currently, in experienced centers, risk of death after PTE surgery is under 5%. Immediately after surgery, fluid build-up in the lungs and bleeding are the most important complications. Pulmonary pressures can remain elevated after surgery. Even if pulmonary pressures return to normal immediately after surgery, they can increase again several months or years later. The CTEPH team will assess how likely these complications are for you, and factor this into the decision to offer surgery.

What is the role of medications in CTEPH?

Everyone who has CTEPH needs to be on a blood thinner for life. This remains true even after successful PTE surgery. Warfarin (brand name -Coumadin) continues to be the preferred blood thinner, as health care providers have decades of successful experience using this blood thinner in people with CTEPH. Whether or not the newer blood thinners available are as effective and safe is not clear at the moment. There is no current blood thinner that addresses the scar clot tissue or the pulmonary pressure elevation. Blood thinners only prevent new blood clots from forming.

Treating this type of pulmonary hypertension with medications is only indicated if you have been properly evaluated by an expert CTEPH center and deemed not to be a good candidate for pulmonary thromboendarterectomy. Currently, there is one FDA approved pill for this indication called riociguat. This medication can also be used if you are left with pulmonary hypertension after PTE surgery. Under these circumstances, this medication is known to improve symptoms and relief pressure elevation in the lungs. Your healthcare provider may also choose to use other medications instead of or in addition to those approved for other forms of pulmonary hypertension.

What is balloon pulmonary angioplasty (BPA)?

In general, angioplasty is a catheter-based procedure well established in its use for treating blocked vessels in the heart and brain. Its application in the lungs is called balloon pulmonary angioplasty (BPA). A rubber tube (catheter) is placed through a blood vessel into the pulmonary arteries. Inflatable balloons are then used to open up blocked vessels. Today, several centers in Japan and increasingly in the USA and Europe are using modern equipment and techniques for this procedure with good results. While BPA is far less invasive than thromboendarterectomy and patients are awake during the procedure, the arteries in the lung are fragile and vulnerable to puncturing (perforation). Moreover, to minimize the risks, BPA must be performed in two to five separate sessions—a process some people might find difficult. BPA is currently indicated only for people in whom PTE surgery is not indicated or not possible.

What is the best treatment option for me?

This is a very difficult decision that requires careful consideration. The stakes are really high. If surgery is feasible, this is clearly the treatment of choice, as it offers the highest likelihood of significant short-term and long-term improvements, even cure in many cases. If surgery is not indicated, medical therapy and/or balloon pulmonary angioplasty are now reasonable treatment options for you. The choice needs to be made after evaluation at an expert CTEPH center with the ability to perform all of these three treatment options. You should not be treated with medicines or BPA in lieu of a surgical evaluation.

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Rx Key Points

- ✔ The best treatment for pulmonary hypertension due to chronic blood clots (CTEPH) is a surgical procedure called pulmonary thromboendarterectomy (PTE, also called pulmonary endarterectomy or PEA).
- ✔ When surgery is not feasible, medications and/or a procedure called balloon pulmonary angioplasty (BPA) are alternative treatment options.
- ✔ If you have been diagnosed with CTEPH, make sure that you are evaluated at a medical center with experience and expertise in CTEPH, and able to offer all three currently available treatment options.

Healthcare Provider's Contact Number:

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Resources:

Pulmonary Hypertension Association
http://www.phassociation.org/CTEPH

PHA Europe (European Pulmonary Hypertension Association)
http://www.phaeurope.org/dissease-information/what-is-cteph/

American Heart Association (AHA)
http://www.heart.org/HEARTORG/

American Lung Association
http://www.lungusa.org

American Thoracic Society (ATS)
http://www.thoracic.org/patients

National Organization of Rare Diseases (NORD)
https://rarediseases.org/organizations/nihoffice-of-rare-disease-research/