What is a DVT and what is a PE?

DVT stands for deep vein thrombosis. “Thrombosis” is the doctorly word for, “clot,” and the deep veins are the larger veins of the legs and arms.

DVTs can disrupt the flow of blood from an extremity (arm or leg) causing swelling and pain. This is most commonly a leg, although it can happen in the arms, especially when there are larger IV lines in place (such as a PICC or PORT). However, the true danger of DVTs is their propensity to spread. Just as the spreading of cancer has a name (metastasis) the spreading of clot has a name—embolus.
Blood from the extremities flows into a big vein called the vena cava. As the diagram above shows, blood from the vena cava (including any clots it carries) travels to the right side of the heart, where it is then pumped out to the arteries of the lungs (pulmonary arteries). These vessels branch as they reach towards the edges of the lung and as they do so, they get smaller and smaller. When blood clots spread from the deep venous system to the lungs via this path, this is called a, “pulmonary embolus,” or “PE.” The clot will get lodged once it arrives in a vessel too small for its continued passage.
By blocking off the flow of blood to the lung, a PE deprives part of the lung of oxygen, causing it to die. This is very much like a heart attack, but in the lung. Once lung tissue dies, it cannot be regenerated and is thus lost forever. While this, “lung attack,” is going on, the most common symptoms are shortness of breath and chest pain. PEs can also cause the heart not to work well, and can even cause death.

Causes of DVT

There are many causes of DVT and sometimes more than one is at play. Among these are:

- Damage to the lining of a blood vessel (this lining is also known as, “vascular endothelium.” There are many cause for this type of damage including venous access lines like a PICC and the damage caused by a high-fat diet and lack of exercise)

- Stasis (including not moving around secondary to surgery or a long airplane trip)

- Surgery

- Inherited predispositions
Blood clots in Cancer: VTE and PE

by Dr. Weiss -

- Smoking
- Obesity
- Hormonal influences (pregnancy, hormone replacement therapy, birth control pills)
- Some medications
- Nephrotic kidney disease (the kind where protein is lost in the urine, including anti-clotting proteins)

The astute observer will note that I left off one of the most important causes of DVT and PE—cancers. One of the best studies to look at clots in cancer patients was published in 2009 by Wun and White in Cancer Investigations.

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<th>Regional stage</th>
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Table 2 from Wun and White, Cancer Invest, 2009: Comparison of the incidence of VTE based on initial cancer stage
Incidence rate of VTE in year after diagnosis of cancer (events/100 patients)

There are several important themes to this table that are echoed through similar studies. First, thrombosis (clotting) is very common in cancer. Second, more advanced cancers cause more clotting than more local cancers. Finally, lung cancer is one of the most prothrombotic.
Cancers. Also of note, the risk of clotting goes up, not down with chemo, even when the chemo works well to control the cancer.

Diagnosis—Physical Examination and Symptoms

The major symptoms of DVT are leg pain and swelling. In my opinion, almost any new leg swelling in a lung cancer patient should prompt evaluation for DVT, because it is so common and cause so many problems. Doctors often consider DVT more likely to be the cause of swelling if only one extremity is swollen. I agree with this, but note that I’ve diagnosed bilateral DVT in many lung cancer patients with swelling of both ankles.

When your doctor squeezes your ankles at physical examination, he/she is mostly looking for swelling. Another physical examination sign of DVT is a positive, “Homén’s sign.” In this test, the doctor bends your ankle towards your head—if this hurts, the sign is considered positive. While I do this test, it’s so-so in predicting for presence or absence of DVT.

Diagnosis—Medical Tests

Before getting to the tests that do work, I’ll get out of the way discussion of a blood test that I consider less useful in lung cancer patients, but worth mentioning because it is frequently done. D-Dimer is a blood test for clots. In non-cancer patients, a negative D-dimer is very predictive for absence of clot. However, lung cancer tends to elevate D-Dimer and so it’s really hard to find a lung cancer patient (even those without clots) with a negative D-Dimer.

So, let’s move on to good tests. The best test for DVT is an ultrasound of the legs. They’re called, “Doppler studies,” or, “LENIs” (lower extremity, non-invasive). The ultrastenographer places the ultrasound probe over the deep veins of the leg. Normal veins are easily compressible. However, clots are hard and if present, will cause the ultrastenographer to be unable to compress the vessel. In my hospital (and many others) if the test is negative, the ultrastenographer tells the patient. If it’s positive, the ultrastenographer sends the patient back to my office, and we address it together (more to come, in “treatment” below).

When a patient presents with shortness of breath, chest pain, or other symptoms that make the oncologist concerned for PE, we will test for it. The most commonly used test for PE is the CT angiogram, or CTA for short. In this test, CT contrast is rapidly administered so that it can light up the vessels of the lung. If any spot inside the vessels is dark instead of being lit up by the dye, this will be because clot is present. It looks like this:
The CTA is the preferred test for PE at most institutions. It is fast, easy, and readily available at any hour of the day or night. My favorite thing about the CTA is that it can also diagnose things other than PE because it images the whole lungs and heart. For example, if a patient with lung cancer comes to the ER with shortness of breath, a CTA might be ordered to evaluate for PE. Even if a PE isn’t present, the CTA might find compression of an airway by cancer, pleural effusion, pneumonia, or one of a myriad of other possible causes. However, CTA is not the right test for every patient. Its major limitation is the need for contrast dye, which can be a problem for patients with allergies or kidney problems. In this case, the doctor might order a V/Q scan. The, “V” stands for “ventilation” and the, “Q” for perfusion. When everything is working right, these should be matched—blood should flow maximally to places of maximal air exchange. With PE, these will be mismatched. Unfortunately, there are many other causes of V/Q mismatch and so back when this test was in common use, the most common answer was, “indeterminate” and resident physicians carried around cheat-sheets that combined pre-test probability of PE based on symptoms together with the test results to get a final probability of PE.

The mainstay of clot treatment, both DVT and PE, are blood thinners. The body has complicated chemical cascades that remodel clots by simultaneously breaking down clots while rebuilding them. Blood thinners work by blocking some part of the rebuilding part, shifting the balance towards breaking down. Perhaps the most commonly used blood thinner in the US for lung cancer patients is lovenox. Lovenox is given as a shot twice a day. The need for
self-injection and high cost are the major disadvantages of lovenox and related drugs such as arixtra. Their advantages are data for superior efficacy in cancer patients, and drug levels that are easy to get right without the need for a lot of blood tests. Lovenox can be used both in the hospital and at home, at the same doses.

The major alternative to lovenox is the blood-thinner pill Coumadin (warfarin). The major advantages of Coumadin are that it is cheap and that it is oral. However, I must be honest that while it is in common use both in the US and the rest of the world, it is one of my least favorite medicines. Coumadin has a lot of food and drug interactions. If you change your meds, your diet, or even look at your pills the wrong way, Coumadin drug levels will be off. When levels are low, the risk of clotting increases and when they are too high the risk of bleeding increases. Therefore, to use Coumadin correctly, blood tests (the test is called INR or PT) should be done very frequently. Finally, in the first few days it is started, Coumadin is actually pro-coagulant, and so must be used together with another blood thinner like lovenox or a heparin drip.

A new class of drugs have been developed called, “direct thrombin inhibitors” or DTIs. The only one FDA approved in the US is dagibatran. It is not yet indicated for DVT/PE, but I look forward to the day when it is—I’d love to be able to offer my patients a pill to thin their blood whose levels are always right. I’ve been actively trying to encourage the manufacturers of these pills to study them further in lung cancer patients—let’s keep our fingers crossed!

I also recommend compression stockings to patients who have had a DVT. They can reduce the incidence of complications after a DVT (called post-thrombotic syndrome).

Finally, there are two less commonly used therapies that I’d at least like to mention. The first is an IVC filter. The IVC is the big vein that carries blood from the lower part of the body back to the heart. The idea of the filter is that it will catch any clots that try to travel (embolize) to the lung. This device makes a huge amount of common sense, but isn’t nearly as good as it sounds. In fact, IVC filters are very controversial. They can be great for stopping a DVT from turning into a PE if there’s some reason that you can’t use blood thinners, like right after major surgery or trauma or if the platelet count is super low. And, they work well for a few months. However, after that time, especially in patients already prone to clots like lung cancer patients, they actually increase the risk of new DVTs. I occasionally use them when in a bind, but feel that they are generally used too much. I also feel that when placed, most of them should be removed after the tough situation has passed, typically within a few months. The second less-common therapy is thrombolysis. These are clot-busting drugs. Their best use is with the worst life-threatening PEs—the ones that cause the heart to have trouble pumping well. While these drugs work great to break up clots, their major problem is that they cause bleeding—bad bleeding. One newer use of these drugs is to use fancy catheters to deliver smaller doses of the drug right to the site of the clot (“catheter-directed thrombolysis). I’ve used this some in patients whose clots don’t improve on a blood thinner alone and have had some good results, but do not consider it the standard therapy for the average patient.

Every blood thinner increases the risk of bleeding. Therefore, it is wise for the oncologist to monitor platelet counts carefully while on chemo. As a patient, it is wise for you to consider
wearing an alert bracelet that you are taking a blood thinner. If you should have any trauma like a car accident, it will be important for anyone caring for you to know that you are on a blood thinner.

A final word must be made regarding duration of anticoagulation. The minimum anticoagulation period after a clot for a lung cancer patient is 3 months. However, in my opinion (and, forgive me, I’m very opinionated because I’ve spent a lot of time thinking about clots in lung cancer patients) the optimal duration for a patient with metastatic lung cancer is life-long. The reasons is that the cause of the clot never goes away—while metastatic disease can sometimes be controlled for a long time, the cancer is still there in the body secreting its pro-inflammatory chemicals and the patient may still need chemo, which increases the risk further. While I do worry about bleeding in my patients on anticoagulation, I worry more about clotting. The reason is simple—if a patient bleeds, I can replace the blood. However, I cannot replace tissue that dies because of lack of blood flow, and the incidence of death from clots is very real. Lifelong anticoagulation is not right for every patient with lung cancer and a DVT or PE. However, for the motivate patient who isn’t super bothered by the shots, and has no contraindication, I think that lifelong anticoagulation is the best thing to do.

Prevention

It makes great sense to try low doses of blood thinners in lung cancer patients who have never had a clot and it is has been tried. So far, there’s no great evidence that this is the right thing to do. So, as a patient, I recommend keeping mobile, keeping hydrated, and watching out for leg swelling. And, as I was pretty frank about above, I believe that the best prevention against a new clot in a patient who has already had one is lifelong, full-dose anticoagulation, ideally with lovenox or a similar agent.

For More Information

For more information about clots, I recommend http://www.clotconnect.org/. I know and work with the people running the site, have reviewed it, and think that it’s great.