Hello. My name is John Patlan. I’m an Associate Professor in the Department of General Internal Medicine here at The University of Texas MD Anderson Cancer Center. And I’m going to be talking to you today about Oncologic Emergencies. Now, the field of oncologic emergencies really encompasses any emergency problem that could occur to a cancer patient. Obviously, it’s a very broad topic and we can’t cover everything.

So really, we --- what we will cover are the classical oncologic emergencies really which you see listed here: things that are directly related to the cancer or its treatment. So at the end of this lecture, you’ll be able to diagnose and treat the common structural emergencies, such as spinal cord compression or superior vena cava syndrome. You’ll be able to manage patients with neutropenic fever. And you’ll know how to treat metabolic emergencies, such as hypercalcemia and tumor lysis syndrome. And for your convenience the things that I think are the take-home lessons or most important points are italicized in red font on each slide.

Now oncologic emergencies traditionally are defined as any emergency problem which is due to the underlying malignancy or its treatment. For instance you see a picture there of a patient with a large brain mass with some edema and some midline shift. Assuming that’s a tumor, that’s an oncologic emergency. So traditionally the --- the oncologic emergencies are divided into structural problems, such as the patient that you see pictured there, infectious problems, hematologic problems, and metabolic problems. And we’ll --- we’ll talk about samples of each one of those.

Now in the real world, they don’t all break down so neatly. This is a pie chart to give you an idea of the relative frequency of the presenting problem or chief complaint of patients who visited the MD Anderson Emergency Room. Now this is old data. You see on the slide listed there, that’s about 10 years’ worth of data and there’s about 25,000. These days we see about 25,000 patients per year or so annually in the Emergency Center. But the problem distribution is about the same. So you see in the orange slice of the pie that the most common chief complaint for patients presenting to the MD Anderson Emergency Center is fever. And there’s a reason for that. Number one, because of the cancer or its treatment, many of our patients are at increased risk for infection and in the short term, at least, infection is actually the greatest health threat that they face. And the long run obviously is their malignancy. But in the short run, it’s infection. And most of the clinics here do a very good job of educating the patients that if they have fever or any other signs of infection, they should seek prompt medical attention.

So one caveat that you should keep in mind when you are evaluating a patient --- a cancer patient in the emergency room is that you should not always assume that the symptoms or whatever decompensation that they’re experiencing is
because of the cancer or its treatment. Cancer patients have all the same non- cancer-related problems that sim --- patients of similar ages and backgrounds experience. So for example, if a man with lung cancer comes into the Emergency Center and is complaining of chest pain or shortness of breath, don't assume that it's just tumor-related pain or something related to his cancer. You have to consider, could he be having an acute coronary syndrome? Could his shortness of breath be an exacerbation of congestive heart failure? Could he be having arrhythmias or could this be a COPD exacerbation? So just keep that in mind that our patients have all the same comorbid medical conditions that other patients have. The other very important consideration that you should remember when evaluating a cancer patient who presents to the Emergency Center is that many of the signs and symptoms that you have traditionally been taught to look for when you're evaluating any symptomatic complaint, those signs and symptoms may be blunted or masked in cancer patients. That can happen for a number of reasons. Steroids: many of our patients receive steroids as part of their treatment. Many of them are neutropenic and because of that, these signs and symptoms which are usually manifestations of inflammation may not be present or they may be minimally present. Also, because cancer happens with increased frequency as patient's age, many of our older patients also have sort of more subtle signs or symptoms of disease. So when I'm dealing with cancer patients and trying to train medical students, residents, or other trainees about how to evaluate these patients, I tell them that when you see patients --- cancer patients in the emergency room, you should have a high pretest probability of “badness,” whatever that is, whatever you think is going on. If a patient comes in complaining of new onset headaches and they're thrombocytopenic, consider subarachnoid or subdural bleeding. Whatever it is you think might be going on, lower your threshold for --- for doing a more extensive evaluation and not just dismissing that complaint because they don't present in the classic fashion for whatever it is that you think might be happening.

Now, like I mentioned, the oncologic emergencies are traditionally divided into a variety of categories: structural problems, fairly self-explanatory. That's compression, obstruction, invasion of some vital structure. That can be any --- any region of the body. The traditional things that are discussed in a lecture like this are spinal cord compression, which we will discuss; superior vena cava syndrome; brain metastasis with associated cerebral edema, a very common problem; as well as a number of other things that can happen which we won't discuss, such as bowel obstructions, bowel perforations, ureteral obstructions.

So the first case that we'll discuss is a structural problem. This is a 72-year-old man. He presents to the Emergency Center for evaluation. He has a background history of prostate cancer that was diagnosed about two years ago. At that time, he had localized disease. His Gleason score was 8. His PSA was fairly high at 20. He was treated with a radical prostatectomy and since that time, his PSA has been undetectable. He was last seen a few months ago.
So he says, you know, he’s been having worsening back pain, started four to six to eight weeks ago, sort of thoracic back pain in a girdle-like distribution, but recently it has gotten worse. It’s radiating down his left leg, so --- and the pain is most significant in the lumbar region. So you --- or the emergency room physician has performed an MRI of the lumbar spine. They do see some lesions that --- in the lumbar spine, L2, L3 vertebral bodies with some associated epidural disease that looks like metastasis. There’s some neural foraminal narrowing which could explain the --- the radiation down the leg. You are the oncologic consultant who is called to the emergency room.

And the emergency room doctor asks you what you should --- would like to do. So these are some options. As the initial step, you could say, well, let’s just give him some pain medication. We’ll discharge him. We’ll follow him up in the Oncology Clinic for his apparent new metastatic disease. You could say, well, why don’t you consult Radiation Oncology and have them do some --- some palliative radiation to these new vertebral metastases? Or, you could suggest to the emergency room physician, why don’t you go ahead and do a follow up MRI of the --- the complete spine; you need to visualize the cervical and thoracic spine as well. Or, you could say, well, he has new metastatic disease. He needs some --- He needs hormone treatment. We’ll go ahead and start an LHRH treatment to treat his cancer.

So the most appropriate initial step would probably be an MRI of the --- of the cervical and thoracic spine. You do need to visualize the thoracic spine. Now, all of those other steps would probably be appropriate at some point. But initially, you do need to visualize his thoracic spine, and --- and I’ll you why.

Let’s talk a little bit about spinal cord compression. It is the second most common neurologic complication of cancer after brain metastasis; very common. The most common malignancies that would --- that would present this way would be lung cancers, prostate cancer, breast cancer. On autopsy series of all patients with metastatic disease of any primary site, about 5% of them do have epidural disease whether it was clinically recognized during their life or not. So it’s a very common problem, about 18- to 20,000 cases of epidural spinal cord compression per year in cancer patients. And unfortunately, a significant percentage of these patients have permanent neurologic compromise at presentation. About --- More than half of them may no longer be able to walk. So that’s’ why it’s important.

So this is the mechanism of disease. Well, there can --- there can actually be several mechanisms of disease. Most commonly, patients have metastasis to the vertebral body. It may extend into the spinal canal so you have some compression of the epidural sac. Sometimes there is a vertebral metastasis and the vertebral body fractures. And there’s --- there’s a compression fracture with retropulsion of --- of bony fragments into the --- the canal. Sometimes, the tumor
can extend into the neural foramina. Or, occasionally you can have a direct tumor metastasis to --- to the cord itself.

Now, the point of this slide just --- is just to make the point that it's not just the mechanical compression like you see on the right-hand slide that's causing this --- this problem. There're a variety of factors that are going on here. There's venous obstruction. There's vasogenic edema. And so there's ischemia of the cord itself, which is a major contributor to the symptomatology and something that you can intervene in rapidly as we'll see.

So the clinical presentation of spinal cord compression could be very acute, for instance, if someone had a compression fracture with retropulsion of --- of bone into the spinal canal. Or, it can be subacute, kind of a gradual presentation over a period of several weeks to months. And the pain that's associated could be thoracic, could be lumbosacral, could be cervical. But the te --- But the important point here is that in patients who have spinal cord compression they --- they have disease at multiple levels in a significant percentage of the time. So that's why it's important to get visualization of the entire spine. So that you know that they -- - whether they do or do not have involvement at the thoracic or cervical level.

So clinically, they can have a range of presentations. At the --- At the very early stages, they could be essentially asymptomatic, but with radiologic findings, and I'll show you a picture of that, they could have some back pain without neurologic compromise. Or in a more advanced stage, they present with the neurologic deficits --- the classical neurologic deficits that you typically think of as a manifestation of spinal cord compression.

So this is a picture of a man who is essentially asymptomatic. I think you can see this is the MRI. These are the vertebral bodies. This dark area here in the middle is the spinal cord itself. I think you can --- can see --- see right here that the cord itself is being compressed. Interestingly, this gentleman was essentially asymptomatic. He had a little bit of back pain but not much and really, who doesn't have a little bit of back pain? And he had been out playing golf the week before. So he --- he was feeling fine. And this was a staging study done as part of his --- his initial evaluation and he had radiologic evidence of spinal cord compression.

When patients do have symptoms pain is by far the most common symptom. Almost all patients with spinal cord compression will have pain. It can be localized. It can be radicular. It can be dull. It can be constant. Trying to sort out back pain due to spinal cord compression versus ordinary, sort of garden variety back pain due to lumbosacral strain or any of the myriad causes of --- of nonmalignant back pain, this could be difficult. Some clues could be that the pain may be worse when the patients are sup --- supine. That's, for instance, different than you would --- you would see in someone who has a herniated disc, for instance, where the pain would typically be worse when they're upright.
Another clue might be if the pain is exacerbated by sudden movements or by valsalva where they may have some sort of electric shock sensation radiating down the affected area. Or if they describe the pain as sort of bilateral and band-like, which our patient in the case that we’ve discussed had sort of a girdle-like or band-like distribution of this pain. Those may be clues that this is more than ordinary back pain.

Now, as --- as their disease progresses, they may start to develop motor weakness. Now, initially, it may be fairly subtle. You may have to do some --- some directed testing to figure this out. Have them do heel-toe walking, for example, to detect more subtle weakness that the patient themselves may not even be aware of. As things progress, they may develop sensory loss, which you can detect through --- through physical exam. Even more advanced disease, they would have autonomic dysfunction, typically bowel and bladder incontinence, and then finally, complete paralysis of the lower extremities or --- or anywhere distal to the level of compression. So that’s --- that’s the general progression from asymptomatic to pain to motor weakness to more advanced neurologic compromise.

Now when you see someone that you think has spinal cord compression, as we said, they do need visualization of the entire spine. MRI is your --- your study of choice. If they can’t get an MRI for various reasons, they’ve got metal in place, they’ve got a pacemaker, something like that, you could consider doing a CT myelogram. But don’t rely just on plain films of the spine. They would show you if the patient had a compression fracture. But they would not be sufficient to rule out the many other causes of cord compression.

So as I said MRI is the preferred imaging mode. Here’s another picture to give you an example. This is a patient with --- you see the vertebral bodies here. And even those of us who are not radiologists can appreciate that at these levels indicated by the arrows the vertebral body looks different. It’s been replaced by - -- by tumor. You can see that there is some extension into the --- into the spinal canal and you can see the cord, which is labeled “C”, is being compressed at these two levels by the tumor. And again it also rein --- reinforces the point that this could be multilevel disease. So it’s important to visualize the entire spine.

So you do get an MRI of his thoracic and cervical spine. You see that he does have these blastic lesions that are causing compression at T5 and T12 like we just showed you. So the next step would be to consult Radiation Oncology, to administer corticosteroids, to consult Neurosurgery, go ahead and start him on hormonal treatment, or all of the above. So this is the most appropriate next step.

So the next step would be steroids. Now, if you said all of the above, really that’s true, you would be place --- doing all of these things, getting these things rolling. You would call the neurosurgeon for evaluation. You would consult Radiation
Oncology. You will, at some point, probably treat him with hormonal treatment for his underlying malignancy. But the most appropriate next step is steroids.

Like I mentioned, vasogenic edema is a big contributor to the neurologic problems that happen with spinal cord compression and steroids can start to reduce that edema and improve symptomatology and prevent complications very quickly. So the treatment is really urgent once the diagnosis is established or even if the diagnosis suspected. It’s best administered before there is neurologic damage. The main predictor of post-treatment neurologic function is the level of neurologic function before treatment. So if patients are able to walk into the hospital, they'll probably be able to walk out of the hospital. Now you're more likely to be able to reverse neurologic deficits if the compression has occurred gradually. Radiation when it's initiated, can shrink tumor within several days. But if patients have an acute onset of symptoms, for instance, you think that they have compression fracture with bony fragments compressing the cord, steroids are not going to fix that. Radiation is not going to fix that. They may require surgery.

Well, like I said, a rapid radiologic diagnosis and initiation of treatment is necessary for patients who have suspected spinal cord compression. Steroids should be given first. The dosing, there’s no randomized controlled trial to give us idealized dosing. But a standard dosing regimen would be 10 mg of dexamethasone as a loading dose and then scheduled doses of 4 mg or so every 6 hours which, like as I mentioned, will reduce the edema which is the underlying cause of neurologic damage for most patients.

Now radiation treatment will be part of most patients' treatment. But like I said, it takes several days at a minimum to have its effects. Most patients will be sufficiently treated with radiation treatment …

… but surgery may be needed for some patients if, for instance, they have such extensive disease that their spine is unstable or if if the patients don’t have a cancer diagnosis yet. If this is the presenting phase of their illness they may need surgery may be beneficial to at least stabilize their spine and give you a tissue diagnosis. Now, if patients have been previously irradiated, they may not be a candidate for further irradiation. Surgery may be the treatment of choice. Or if they have very rapid neurologic dysfunction, as I mentioned then then they may require surgical treatment rather than waiting for radiation.

Now, you will see in many references chemotherapy listed as a treatment option for epidural spinal cord compression and that’s true for some very chemosensitive tumors, small cell lung cancer, many lymphomas, germ cell tumors, etc. But in real life, this is not going to be the sole treatment. Almost all patients will be treated with steroids and/or radiation prior to or in addition to receiving chemotherapy.
Now, the prognosis, as I mentioned, really depends upon the neurologic status at the time of diagnosis. If they walked into your hospital, they probably will walk out. If they were weak but not completely paralyzed a significant portion will regain locomotion. If they are completely paralyzed by the time they present, then unfortunately very few patients will be able to walk out of your hospital. Now one of the take-home lessons I want you to remember is that for most patients the pain symptom precedes the onset of neurologic deficits by several weeks. There’s a reference there of a European study, and in this study, they --- they looked at patients who did have proven spinal cord compression. And they went back and asked them about when their pain symptoms started. And they did find that, on average, these patients had new or worsening back pain about 6 weeks or so before they ultimately developed neurologic compromise and then were diagnosed with spinal cord compression. Now you can think of that as good news and bad news. The bad news is it took us 6 weeks to figure that out in these cancer patients. The good news is you have time to figure this out in most patients who --- cancer patients who present with new or worsening back pain. So if you have somebody, you think they’re a high-risk patient, they have a --- they have a cancer diagnosis, it’s a cancer that likes to metastasize to bone and they present with new or worsening back pain, consider doing an MRI. Now if they have new --- back pain, but no neurologic deficits, it’s not an emergency. You don’t have to send them to the emergency room to get the MRI. If you can get it within 24 to 48 hours that should be sufficient. If they have neurologic deficits it is an emergency. Send them to the emergency center to --- to get initiated with treatment and --- and undergo the evaluation like we’ve just discussed.

Next case: another structural problem. This is a 65-year-old man. He’s a smoker. He does not have a cancer diagnosis. He comes to the emergency center, however, complaining of two weeks of gradually worsening shortness of breath. When he’s examined in the emergency center it is noted that he has some facial fullness, some --- some rubor, erythema. He’s got marked edema of his upper extremity but no lower extremity edema, interestingly. His lungs are clear and he has no cardiac rub on exam.

So a CT scan of his chest is obtained and you can see on this contrast study the --- the radiocontrast is --- is the bright areas. This is the aorta. This little sliver right here is the superior vena cava. And you see the reason that it is so slit-like is that it’s being compressed by this large mass.

So he clearly has superior vena cava syndrome. So he doesn’t have a diagnosis yet. We don’t know why this is happening. So the most common cause of superior vena cava syndrome in this man or in any patient would be, A) Small cell lung cancer; B) A syphilitic aortic aneurysm; C) Squamous cell lung cancer or any other non-small cell lung cancer, D) Lymphoma; or, E) Thrombosis due to his central venous catheter.
The answer really is C) squamous cell or any other non-small cell lung cancer. Now the other cancers that we list, those are thoracic malignancies as well but among the lung cancers, --- [speaker meant to say] --- non-small cell is about 80/85% of --- of lung cancers so it’s just the most common.

So as we said, for --- for malignant causes, it --- it is a thoracic problem so it is a manifestation of thoracic malignancies, lung cancers being very common, non-small cell being the most common kind of lung cancer, then small cell. Lymphomas can also present this way. Any other thoracic malignancy can also present this way but is less common, breast cancers, germ cells tumors. Then not all patients with superior vena cava syndrome do have malignancies. There are nonmalignant causes. In another era these were more common, tuberculosis; radiation fibrosis. Syphilitic aneurysms used to be a fairly common cause but we just don’t see that very much anymore. Now the problem with superior vena cava syndrome is that for many, if not most patients who have this problem, this is the presenting feature of their illness. They do not yet have a known or established cancer diagnosis. And that is a problem as --- as you shall see.

So on exam, it’s actually not very hard to figure this out. You’ll see --- typically see very extended jugular veins because of the vena cava compression. Frequently, the patients have edema and erythema of the face, shoulder and arms. They have these very prominent superficial venous collaterals of the chest wall. And so you have to try to figure out, is this superior vena cava compression? Is this heart failure tamponade, some other cause of pulmonary hypertension? An imaging study would usually establish diagnosis like --- like I showed you.

So once you --- you’ve got this diagnosis, once you --- you’ve figured out that your patient really does have superior vena cava compression. But as in this case, the patient doesn’t have a diagnosis yet, doesn’t have a cancer diagnosis, what is the most important next step in management? Should you call an urgent radiation consult to shrink the tumor, relieve the compression? Should you consult interventional radiology to place a superior vena cava stent? Should you pursue a biopsy or some other attempt to establish a tissue diagnosis? Or should you go ahead and intubate this patient for airway progression --- airway protection?

The answer really is [to] obtain a tissue diagnosis.

Superior vena cava syndrome is traditionally presented in the oncologic emergencies lecture, but truth be told, it’s not really an emergency problem in most cases. It is an urgent problem, it does require some urgent attention. But it is not usually an immediately life-threatening problem. Just by the --- the presentation, if you see, for instance, a patient with venous collaterals over their chest wall, that did not happen overnight. That took weeks to develop. So this is
typically a subacute development and presentation. Now in the past, this was viewed as a more emergent problem. We used to be more worried about doing procedures --- interventional procedures on these patients but we --- we feel more comfortable about it these days. And it’s important for you to establish a tissue diagnosis because in many cases, this could be a curable condition.

So what’s happening here is that you’ve got some mass lesion that’s causing some obstruction of venous drainage of the --- compressing the vena cava, obstructing venous drainage from the head and the upper extremities. This typically happens because you have external compression of the vena cava by tumor. There can be direct invasion of the vena cava by tumor. Or, there can be intraluminal thrombosis, or some combination of all of the above. Now as I mentioned, because this is a thoracic problem, this is a --- a manifestation of thoracic malignancies, typically in lung cancers, lymphomas are almost all cases. But like I mentioned before, about 60% of the patients who have this problem do not yet have a tissue diagnosis.

So what you’ll do for them is that you’ll try to facilitate venous drainage by doing head elevation, giving them oxygen as needed for --- for shortness of breath. Diuretics may help with --- by reducing some edema. You can give them steroids. Ideally this would be administered after your tissue diagnosis especially if lymphoma is --- is a consideration --- is a diagnostic consideration in that pre-diagnosis or pre-biopsy steroids can start to degrade the tissue and make it difficult for the pathologist to establish a lymphoma diagnosis. Now if patients have very severe symptoms, stenting of the superior vena cava can relieve symptoms. But really the definitive treatment is going to be the treatment of the underlying treatment, whether that’s chemotherapy, radiation treatment, or some combination of that.

Like we mentioned, though, tissue diagnosis is usually necessary in most of these patients. And it will be necessary before you choose the optimal treatment --- or the optimal cancer treatment. Since this is not an em --- a true emergency in most cases, you don’t really need to do pre-biopsy radiation treatment. And if - -- if pre-biopsy radiation is done, it can also obscure the histology and make it harder to give you a definitive tissue diagnosis. And there are some questions about the efficacy of radiation to re-establish patency of the superior vena cava --- patency of the superior vena cava although patients typically do experience symptomatic relief after radiation.

Now this is a picture just to show you what stenting looks like. This is a patient undergoing a --- an interventional radiology procedure. You see a catheter being threaded into the superior vena cava here. You see the --- the cava being outlined with the radiocontrast dye. And you see there’s this intraluminal filling defect. That’s obviously tumor or something within the lumen that --- that’s compressing or obstructing flow and sort of a trickle flow more distally. So you
see that once the stent is deployed, you have good visualization of the vena cava and good venous flow there.

So the prognosis really depends upon the underlying malignancy. Unless the patients are very, very advanced and they’ve got some tracheal obstruction or edema, this is usually not an immediately life-threatening problem. You have time to work on these people to try to get them a diagnosis.

Next structural problem we’ll talk about is unfortunately a very common problem and that’s cerebral metastasis with associated cerebral edema. It can be sometimes challenging to diagnosis. Patients can present with just about any neurologic symptom: headaches, focal neurologic symptoms, seizures, occasionally sometimes just idiopathic nausea and vomiting. I have seen patients, for instance, in the MD Anderson Emergency Center who presented with just persistent nausea and vomiting, no clear cause for it. This is not immediately post-chemotherapy. They’re not hypercalcemic. They’re not taking narcotics or any other medication that should cause this. So if somebody has that, don’t have a good explanation, if they have a cancer which could cause cerebral metastasis, consider doing an imaging of the brain. So really what’s happening here, they have a brain metastasis. The tumor has produced vasogenic edema and you’ll need to get some imaging to try to figure that out. And you will initiate corticosteroids to reduce edema and relieve their symptoms which can work very quickly.

So this is an example of a patient who does have brain metastasis. Let’s say this patient comes in complaining of headaches. You get an MRI of the brain. There are unenhanced images here. I think even those of us who are not radiologists can appreciate that there is some difference between this side and this side. This side looks like it’s got some edema. You see some edema here, maybe a little there but when you give them the gadolinium enhancement, you do see these spots light up and this unfortunately is multifocal brain metastasis.

So once you’ve diagnosed this problem please initiate corticosteroids. They will reduce the edema and improve the symptoms very, very rapidly. It’s very impressive. We typically give dexamethasone as the steroid of choice because it does not have mineralocorticoid activity. And you don’t want to give anything that has mineralocorticoid activity because you don’t want to raise their blood pressure because they may already have increased intracranial pressure. Typically a typical dosing would be 10 mg bolus followed by a divided dose throughout the day, 4 mg, 4 times a day, something like that.

Now, for patients who do have brain metastasis, they probably are going to be on corticosteroids for some extended period of time. So just be aware of the complications of corticosteroid therapy. Make sure that they have GI prophylaxis to prevent stress ulcers. Be aware looking for hyperglycemia and manage that if
it occurs. Also be aware of the --- of the lesser known side effects of corticosteroids. Some patients experience mental status --- mental status changes just from the steroids maybe not because of the brain metastasis. And if they’re on corticosteroids for a long period of time, weeks or longer, they can start to develop steroid myopathy. They will have a risk --- increased risk for infection, for opportunistic pathogens, such as a pneumocystis. So you do try to reduce the dosing as you can to the lowest possible dose to control their edema and minimize these kinds of side effects.

The prognosis for cerebral metastasis --- patients with cerebral metastasis unfortunately is not very good. If patients are receiving supportive care only and just getting steroids for symptomatic relief, survival is --- is measured in a period of weeks. If they are going to get active cancer treatment then they are generally divided into favorable prognosis or poor prognosis and those factors that --- that determine that really are patients' age, their overall performance status and, very importantly, what is the likelihood that their oncologist is going to be able to get control of their systemic disease. So if they fall into the favorable prognosis category then they have a reasonable prognosis, six to seven months. If it’s poor prognosis, because of these things are not good, then again, survival is measured in a period of a few weeks.

Now, we are going to move on to infectious problems. Like I mentioned in --- early in the talk infection is a very common problem among cancer patients either because of the cancer itself for patients with hematologic malignancies, for example, or because of the can --- the treatment that we’re giving them. If we’re giving them chemotherapy and they’re immunosuppressed, or steroids or whatever, infection in the short term is the most immediate threat to their health and their life. We see the whole range of infectious complications that --- that you can see here at MD Anderson and in any --- any cancer hospital. These are some of the common infectious problems that we see: patients who have fever and neutropenia; patients who have infected central venous catheters; patients who have pneumonias, for instance, post-obstructive pneumonias in patients with --- with bronchial lesions; patients who have biliary obstruction and second --- and cholangitis because of that; and on and on. You know, the list is --- is endless. But really we --- we’ll focus on some of the common things that you really will need to know about.

So the next case is an infectious problem. This is a 55-year-old woman. She has breast cancer. She underwent adjuvant chemotherapy. She comes into the Emergency Center because she’s been febrile at home. She had a temperature of 102° and she was instructed by her clinic that if you have any fever, to please come to the Emergency Center to be evaluated. But by the time she gets here she’s --- her temperature is lower. It’s 99.6. She’s a little tachycardic, heart rate is 114. She is normotensive. She really aside from the fever has no other symptoms and her physical exam is normal. So you do some basic evaluation. You draw a CBC. You do note that her white blood cell count is low, 0.1. Her
hemoglobin is low, but not critically low. Plat --- Hemoglobin is 9.4. Platelets are also a little bit low, but really not seriously low.

So you at the point are the emergency room physician. You have to make a treatment plan and disposition. So the patient had a fever at home, 102°. And they are leukopenic here in the emergency center but clinically stable. Should you reassure the patient and send her home, tell her just follow-up in oncology clinic? Should you obtain cultures and send her home with symptomatic treatment, say, here, take some Tylenol, if anything shows up in the cultures, we'll give you a call? Should you obtain cultures, send her home with antibiotics and say, please follow up within the next 24 to 48 hours in the clinic? Or, should you go ahead and admit her to the hospital for intravenous antibiotics?

Okay, really this is kind of a trick question because there really are two correct answers here and it really sort of depends upon the setting in which you were practicing and --- and I'll explain that.

Let me go back. So in general, however, D is always going to be a correct answer. It is always reasonable to admit patients to the hospital for intravenous antibiotics if they have fever and neutropenia no matter what setting you're in. In certain settings, C will be a --- a correct answer as well, and I'll explain that.

So when patients have fever and neutropenia this requires some definition because your body temperature and your neutrophil count are both physiologic variables that exist on a continuum. So we have to sort of set a --- a sort of an arbitrary cutoff as to what we're going to call a fever and what we're going to call neutropenia. Because once we say that we have fever and neutropenia that is going to trigger a response from us and we don't want to be treating everybody who has a little bit of a temperature elevation or who has a slightly low white blood cell count because they don't have the same risk profile. So this is the Infectious Disease Society of America definition of fever and neutropenia. Fever is defined as any temperature greater than 38.3°C, which is 101.3°Fahrenheit, or any sustained temperature greater than 38°C for more than an hour. Okay? And neutropenia is defined as an absolute neutrophil count less than 500, or if it's less than 1,000 when you see them but you believe they're --- they're going to bottom out at less than 500. Now the neutrophil count is important because their risk for infection increases with the severity and duration of the neutropenia. Some patients will be barely neutropenic. Their neutrophil count is, say, 900. And so their risk for infection is much lower than somebody who is walking around with a neutrophil count of zero.

Now when patients have fever and neutropenia, we'll go looking for infection. Unfortunately, most --- well, fortunately or unfortunately, depending on your perspective, most of the time we don't find anything. Most of the time we will obtain cultures, chest x-ray, we'll do all the standard evaluation yet everything is negative. So an infectious source is identified in only the minority of cases,
maybe 25% of cases or so. And when a source is identified, mostly commonly it’s only an isolated positive blood culture. Now in years past, this was typically gram negatives. And just --- just so you know, most of the bacteria that --- that we’ll recover are really for the patient’s own flora. You will see patients --- cancer patients who are getting treatment walking around with masks or being very careful about being around anybody who’s sick. But really it’s not other people who are the risk to them. It is their own flora, their mouth flora, their skin flora, their gut flora. That if they’re going to develop a serious bacterial infection it’s usually from their own flora. Now in years past, this was mainly gram negatives from the gut. That the spectrum of bacteremia has changed, however, and recently it’s --- it’s usually gram positives. There’s a reason for that. The main reasons are, number one, we use a lot more central venous catheters these days than we used to and that’s --- those are typically gram positive infections --- when they’re --- when they’re infected. And also, we do a much better job of prophylaxing against gram negative bacteremia because, as you probably know, patients are much more likely to die, to crash and burn more quickly from gram negative sepsis from --- than gram positive sepsis.

So when you are the physician or --- or provider who is evaluating a patient who has fever and who has neutropenia, you will do a thorough history and physical. You’ll ask for any kind of localizing symptoms, infection, respiratory symptoms, urinary symptoms, abdominal pain, any kind of gastrointestinal symptoms. You do a physical exam. Look for any oral mucositis. If they have significant mucositis that could be a route for infection from for --- from the oral flora. Do a good head-to-toe exam looking for areas of cellulitis or soft tissue infection or any kind of abscess. Traditionally you should always looks in the perianal area to look for a perirectal abscess but people --- people are always instructed, please do not perform a digital rectal exam on a patient who is known to be neutropenic because you can introduce bacteria through performing that exam. Now I will tell you, when patients really do have a perirectal abscess, this is usually not a subtle presentation. You only have to ask, do you have a lot of pain and swelling down there? They will tell you if they have a perirectal abscess. So it’s not like --- you don’t really have to do a --- a vigorous digital rectal exam to find some subtle finding. Now if they do have a central venous catheter, please inspect that catheter for any signs --- localized signs of infection, such as erythema or discharge at the --- the exit site. Now for all patients who are coming in with fever and neutropenia you will need to do a --- a thorough evaluation for infection regardless of their symptoms. You need to get blood cultures. If they have a central venous catheter, culture from the catheter site as well as from a peripheral site to help figure out if it’s the catheter that could be the source. Do a urinalysis and culture even they don’t have urinary symptoms. Do a chest x-ray even if they don’t have urinary symptoms. As we mentioned early in the talk patients who have neutropenia may lack the ability to mount the kind of inflammatory response that would produce the symptoms that you’re typically looking for.
So if they have any known infectious source or any suspected infectious source, you’d --- you’d direct your treatment in that direction. But you’re going to start empiric antibiotics even if there is no clear source of infection. Now in another era this was not always the practice. In the sixties and early seventies this was not standard practice and at that time infection caused about 75 --- 75% of the mortality of patients who were getting chemotherapy and that’s because we would cause profound immunosuppression. And we would culture them up and then treat infections as they showed up. But by that time many of them would get very sick, end up in the ICU and dying. So we figured out a long time ago that when patients have fever and neutropenia don’t wait until you have a proven infection. Start empiric antibiotics up front until you figure out whether they really do or do not have some serious bacterial infection. Now because gram negatives are more virulent than gram positives everybody will get gram negative broad spectrum coverage including anti-pseudomonal coverage. You don’t typically add vancomycin or any other gram positive agent unless you have reason to think that the patient has a gram positive infection. For instance if they had severe oral mucositis, the oral flora are typically gram positives. If they are hypotension and they look septic then you will add gram positive coverage to this gram negative coverage or if they tell you a story that sounds suspicious for a catheter infection. A good story for catheter infection might be, for instance, you know, doc, every time my wife flushes the catheter at home, 15 minutes later I get these shaking chills and that’s when I spike a fever. Okay, that’s a good story for an infected catheter.

Now, this is a busy slide. I don’t actually expect you to --- to read or remember this slide. I’m only showing you this slide to show you the point that there are two arms here. In patients who have fever and neutropenia there is a high-risk category and a low-risk category. High-risk, you admit them and do all the evaluation that we just described including intravenous antibiotics. Low-risk, I want to point out, oral antibiotics are an option.

Now this is the --- the guidelines from the Infectious Disease Society of America just I --- I point this out just to --- to make the point that these days outpatient management of low-risk patients with neutropenic fever is acceptable with several caveats. So first we have to define them as low-risk. What is low-risk? Low-risk means solid tumor patients, no patient with hematologic malignancies, and patients who don’t look sick. They’re not hypotensive and septic-looking in the emergency center. They don’t have major organ system failure. They don’t have horrible mucositis so they’ll be able to tolerate oral intake including your oral antibiotics. And social factors, meaning they are reliable patients, they can be relied upon to take their medicines and to follow up as directed. There are various oral antibiotic regimens that are used. The most commonly used would be ciprofloxacin with amoxicillin/clavulanate. And there’re a lot of data these days to show that the outcomes for low-risk patients who are treated as an outpatient using this kind of regimen is the same as low-risk inpatients. So it’s much more convenient for patients as long as you can follow them closely in the
outpatient setting and they are reliable patients and they qualify as low-risk, you can manage them as outpatients.

Next, we're going to move on to hematologic problems. In the cancer center, we see the whole range of hematologic problems from very high counts of various cell lines to very low counts. So if you have very high white blood cell count called hyperleukocytosis, you could have leukostasis, which we'll discuss. A very common problem is thrombocytopenia with bleeding complications. Of course, intracranial bleeding would one of the most devastating. We see lots of patients with anemia. A commonly discussed problem would be disseminated intravascular coagulation which you can see as a manifestation of acute promyelocytic leukemia. And of course, there're lots of transfusion reactions. So what really we're going to focus our discussion on hyperleukocytosis.

So this is not a very common problem. It is seen in patients with acute leukemia. Typically with patients with acute myeloid leukemia more so than with acute lymphoblastic leukemia, more common in these subtypes listed here. One of the things you should be aware of is in patients who present with acute leukemia, their white blood cell counts can rise very rapidly. So over a period of a day, two days, their count can double. Now these --- these white blood cell counts that are contributors are very --- are the white blood cells that are contributing to these very high counts are these leukemic blasts. They are not normal white blood cells. They are less deformable than mature myeloid cells. They are less able to kind of squeeze through capillary beds. They can cause these little plugs in the microcirculation, cause local hypoxemia, trigger cytokine release with a whole bunch of inflammatory manifestations. Now theoretically, this problem, which is a microcirculatory problem could be aggrivated by red blood cell transfusion because that increases the viscosity of blood but we --- we'll talk more about that in a second.

So because this is a micro --- a problem in the microcirculation, it the symptoms are --- where you would think of that microcirculatory symptoms would occur. So if you have congestion in your pulmonary circulation, you have pulmonary symptoms. Or if you have CNS microcirculatory problems, you have CNS symptoms. So typically, patients have headaches, mental status changes, can have visual changes, can have retinopathy. Most of them will have some pulmonary symptoms, cough, shortness of breath, hypoxemia. Most of these patients are febrile with or without any proven infection. Sometimes it's just the massive inflammatory responses being triggered. And this is a very serious condition. If patients present in this way, they have a very high seven-day mortality.

So really, the --- the treatment of their very high white blood cell count is to reduce the high white blood cell count. If you are an emergency room provider who's seeing patients in the community hospital, for instance, and you don't have access to an oncologist or you're trying to transfer them to a referral center, you
can try to stabilize them if you think they --- you’re going have to hold on to them for a period of time, with high-dose oral hydroxyurea. If they’re admitted to the hospital, they can be --- receive induction chemotherapy. Or if they qualify and if --- if this kind of treatment is available, they can undergo leukopheresis, which is similar --- what you can think of like plasmaphoresis in which their blood is removed through a catheter, circulated through a machine, and the --- and the machine redu --- reduces --- removes the high white blood cell count, reduces their counts. You also provide supportive care. Everything that you would think would be necessary. If they need --- If they’re anemic, if they need transfusion, give them transfusion, but do it slowly, for the reason we mentioned above. Make sure they’re adequately hydrated. Make sure they have supplemental oxygen as needed and antibiotics for any suspected infections.

All right. So metabolic problems. We see a lot of metabolic problems here. The two things that we’ll talk about are hypercalcemia, which is very common, hyperuricemia or tumor lysis syndrome, which is fortunately less common. Things we won’t talk about are hyponatremia, which is probably the most common metabolic disturbance in any hospital, but commonly presents in cancer patients sometimes as paraneoplastic syndrome of inappropriate ADH. Hyperkalemia, which can happen for a number of reasons.

So our next case is a metabolic problem. This is a new patient to your --- your hospital. He is an 18-year-old man recently found to have a mediastinal mass which was biopsied and found to be a Burkitt’s lymphoma. He began chemotherapy three days ago. At that time, his creatinine was normal and now he presents to the emergency center complaining of weakness, lethargy, says his urine output is diminished. And on his baseline labs that you perform in the emergency center, you see that he is now hyperkalemic. He is hypocalcemic. His BUN is normal, but his creatinine is markedly elevated compared to the baseline a few days ago. His uric acid is elevated and his phosphorus is also elevated. You get an EKG and you see some peaked T waves.

So what is your initial management? Should you consult the nephrology service for urgent hemodialysis? Should you administer calcium, glucose, insulin and pol – sodium polystyrene in the emergency center? Should you give him aggressive hydration, try to improve his creatinine? Should you start him on allopurinol for the hyperuricemia that you’ve noticed? Should you give him rasburicase also for hyperuricemia?

So really, the most appropriate initial management in the emergency center is the calcium, glucose, insulin and sodium polystyrene, which is the treatment for hyperkalemia.

So as we mentioned, I’m going to go back here. In this case, this man was hyperkalemic and he has EKG changes related to his hyperkalemia. So this is
immediately this --- this is an emergency problem and potentially immediately life-threatening. He can develop a malignant ventricular arrhythmia.

So you have to treat the hyperkalemia urgently with this kind of treatment. So calcium, glucose and insulin, and then the sodium/potassium exchange resin which you will administer orally.

So he has tumor lysis syndrome. So tumor lysis syndrome is a group of metabolic derangements that occurs when you have a very high tumor burden and rapid cell turnover. So Burkitt's, for instance, typically a very bulky cancer, and he got chemotherapy so essentially what you're having is cell death of all of these tumor cells and they're releasing their intracellular contents. And so the intracellular contents, for instance, phosphorus is typically intracellular, so see hyperphosphatemia. Potassium is typically intracellular so you can see hyperkalemia or as a manifestation of renal failure as well. Uric acid will be elevated and that's because you have release of DNA and the purine. Purines are metabolized to uric acids. You'll see hyperuricemia. And because the phosphorus is elevated, you can get precipitation of calcium-phosphorus product and so you get secondary hypocalcemia. And because of the hyperuricemia, the uric acid crystals can start to crystallize in the renal tubules and we can develop acute renal failure. So this is the syndrome of things that you'll see typically running together.

So as I mentioned, there'll be hyperuricemia. You may if you're sufficiently motivated, be able to visualize the uric acid crystals on urinalysis. They look like these little diamond or barrel-shaped yellow-brown crystals on a spun urine. You'll see typically, they'll have renal failure with rising creatinine. They are typically oliguric or may even be anuric.

Now, the uric acid, the phosphorus, all these laboratory measures that we've talked about, these are all things that also exist on a physiologic continuum, so you have to set a cutoff when you're going to call tumor lysis syndrome. So this is the standard definition developed by Cairo and Bishop. So a patient is said to have laboratory tumor lysis syndrome if they have any two of the following: uric acid greater than 8; potassium greater than 6; phosphorus greater than 4.5; calcium less than 7. Now, they're said to have clinical tumor lysis syndrome if they have laboratory tumor lysis plus something else like a rising creatinine greater than 1.5 times the upper limit of normal. Or they have arrhythmias which is usually secondary to their --- these metabolic disturbances such as the hyperkalemia or possibly hypocalcemia; seizures, which can be due to hypocalcemia. Then they have clinical tumor lysis syndrome.

Now like we mentioned, this is common --- most common in patients who have poorly differentiated lymphomas, bulky tumors such as Burkitt's, sometimes patients who have leukemias. It's usually a post-treatment phenomenon, which makes sense in that you've given them chemotherapy, the cancer cells are dying
and they’re releasing their intracellular contents like we mentioned. It can occur spontaneously, however. For instance, in Burkitt’s, that’s sort of a classic presentation of Burkitt’s. And as we mentioned you have this hyperuricemia, the uric acid is crystallizing in the acidic urine starting to obstruct the renal tubules which causes the renal failure. Now if you recall your --- your physiology background, you --- you’ll remember that normal urine is acidic. So uric acid will start to crystallize in --- in anybody’s urine assuming your kidneys are functioning --- were functioning normally. Now tumor lysis syndrome has also been described in a variety of other tumors but much less commonly.

So when patients are being treated for cancer we do try to risk stratify them into very high-risk patients, intermediate risk patient, low-risk. So high-risk would be people with Burkitt’s like I mentioned, people with ALL with very high white blood cell counts, people with AML, also with high white blood cell counts. Intermediate risk patients would be patients with the aggressive lymphomas besides Burkitt’s such as diffuse large B cell lymphoma or ALL or AML with lower white blood cell counts. And then low-risk patients would be people with solid tumors or some of the indolent lymphomas like a follicular lymphoma, for instance.

So the best treatment for --- for tumor lysis really is to prevent it in the first place. So because this is a post-treatment phenomenon, in most cases, we make every effort to try to prevent it from occurring. So for the at-risk patients typically before treatment they’ll be initiated on allopurinol. Allopurinol you remember from pharmacology, is a xanthine oxidase inhibitor and it --- it reduces the production of uric acid. Another agent that is available is a recombinant uricase enzyme called --- an example is rasburicase. This is typically only done for very high-risk patients, mainly for cost reasons. Another standard treatment for --- for prevention is to make sure that patients are --- are hydrated. So typically they’re hooked up to an IV fluid bag and given continuous intravenous fluids to try to maintain a urine output, at least 2, 2.5 liters per day. That’s just to try to flush out the uric acid crystals before --- or uric acid before it has a change to crystallize in the tubules. And sometimes for --- before treatment, you can alkalinize the urine. You can give sodium bicarbonate in their --- their bag of fluids to try to keep the urine pH above 7. And again the idea is to try to prevent the crystallization of the uric acid in the renal tubules. It’s unclear whether hydration alone --- or hydration with bicarbonate is any better than --- than hydration alone but it’s commonly done. You’ll see it done. But just know that sometimes the --- the urinary al --- urinary alkalinization can give you other electrolyte problems.

Now, that was prevention. After tumor lysis has occurred then it’s --- it’s harder to -- to deal with. You will try to wash out these obstructing uric acid crystals. So do try to give them fluids as you can, keeping a close eye on their volume status. So you may have to give them fluids and loop diuretics to try to facilitate diuresis. Sometimes in high-risk patients, we use the recombinant uricase, rasburicase, like I mentioned, which will catalyze uric acid which is insoluble into water soluble
allantoin so that can be excreted. Now sodium bicarbonate is not helpful at this stage to try to alkalinize the urine and will usually buy you more metabolic complications. So please try to avoid it at this stage. And then if all else fails, some patients will will require nephrology consultation for hemodialysis until they recover. And most patients will recover at least to some degree. But the take-home lesson here is the best treatment of tumor lysis is to prevent it through the methods that we described before.

Now just to to refresh your memory about the way that these agents work, allopurinol which is given as a preventive agent, inhibits the enzyme called xanthine oxidase. So these are these are the elements from the DNA which is being metabolized. Adenosine goes on this pathway to hypoxanthine and then to uric acid. Guanosine goes to xanthine and then to uric acid. So if you inhibit the enzyme at these steps then you prevent the formation of uric acid. These are more water soluble than than uric acid.

Rasburicase works through a different mechanism so, here again here is allopurinol inhibiting these steps in this this pathway to uric acid formation. What rasburicase or this this uricase or any uricase enzyme will do is take the uric acid that already exists and then catalyze the reaction to form allantoin which is water soluble and can be excreted in the urine. So this will lower the existing uric acid then. But as as I mentioned, this is really only given as treatment or for prophylaxis for high-risk patients mainly because of cost because it’s very, very expensive, sometimes in the $4,000 per day range. So if you don’t have to use it your hospital will probably prefer if you don’t use it.

Next case: sixty-eight-year-old woman, multiple myeloma. She’s being treated. She comes into the Emergency Room. She complains of anorexia, generalized weakness, constipation, just feeling fatigued, sleepy, sleeping a lot, up to 16 hours per day. Also having worsening nausea, vomiting. You do your baseline laboratory evaluation in the emergency center and you find that she is hypercalcemic. Her calcium is 14. This actually probably should be even higher if you correct for the relatively albumin there. And she has an elevated BUN and creatinine which is higher than her baseline.

So she looks like she has hypercalcemia and that probably her symptoms are related to hypercalcemia. So the most appropriate initial management would be: A) Urgent chemotherapy of the myeloma which you presume is the cause of the underlying --- is the underlying cause of her problem. B) Consult nephrology for renal renal consult for urgent dialysis since she has some renal dysfunction. C) Aggressive hydration. D) Subcutaneous calcitonin to try to lower the the calcium. E) An intravenous bisphosphonate of your choosing; or, F) You can combine C, D, and E into into one package.

Okay, again, here there’s really kind of two correct answers. Probably the the most correct answer is C) aggressive hydration. Again in real life probably you
are going to do D and E as well, but the initial management really is hydration. And the reason we'll go into in just a second.

So hypercalcemia is a very common problem. Maybe 10 or 20% of all cancer patients in a variety of cancer types: breast cancers, lung cancers, myelomas very commonly, and it can happen through a variety of mechanisms. Typically you have increased bone reabsorption. If you remember most of the overall majority of calcium in your body is locked up in your bones. Very little calcium is circulating free in your bloodstream. So if you start to have increased bone reabsorption then you'll have to start you'll have increased circulating calcium which causes the symptoms. So this can happen through a variety of mechanisms. Very commonly it's a paraneoplastic syndrome. Many tumors will secrete a --- a protein called parathyroid hormone-related protein. So essentially it mimics the action of parathyroid hormone and causes the hypercalcemia. Or, sometimes you have osteolytic metastasis and just release of calcium from those regions of bone that have been destroyed. Some tumors will produce hypervitaminosis D and will produce hypercalcemia through this mechanism and there are a variety of other cytokines that can also contribute to hypercalcemia.

So when you see hypercalcemia, usually hypercalcemia is encountered in two different scenarios. Most patients who have symptomatic hypercalcemia where it's very, very high, and they can have the kind of symptoms as seen in our patient anorexia, nausea, constipation, somnolence, mental status changes. This is almost always because of malignancy and those patients are going to require hospitalization. Now a more common presentation of hypercalcemia is actually the asymptomatic patient where it's discovered on the routine lab draw. Usually these patients do not have an underlying malignancy. Usually those patients have hyperparathyroidism and can be evaluated and managed as an outpatient.

Now the symptoms of hypercalcemia are kind of nonspecific, at least early on, generalized weakness, lethargy, fatigue, nausea, vomiting, constipation, anorexia. Now truth be told, almost all patients at a cancer center complain of generalized weakness, lethargy, fatigue, nausea, constipation, anorexia. I mean that's not very specific. But as the hypercalcemia progresses their symptoms can worsen. They can start to develop mental status changes. Sometimes they're just very somnolent. Sometimes they're confused. Sometimes they may look demented. They can be very sedated, sleeping 16, 18, 20 hours a day. They can see things that aren't there. They can be --- They can look like they're psychotic to you. Now the hypercalcemia produces polyuria and polydipsia. So virtually all patients who present to you with symptomatic hypercalcemia like the patient in this scenario are going to be very significantly dehydrated and volume depleted. So that's why the most appropriate initial step that we said in this case is going to be hydration. They need hydration, hydration, hydration to try to restore their volume status. Even just the hydration alone will lower the serum calcium to some degree because the calcium is --- is hemoconcentrated because
their --- their dehydrated sta --- state. It will also start to facilitate kaliuresis or --- or elimination of the --- the calcium through --- through their kidneys. So just hydration alone is going --- is going to help you quickly. Now another manifestation that you may list --- you may say listed in some references is hypertension. And hypercalcemia certainly cause hypertension and cas --- can cause shortened QT intervals and even arrhythmias, although in real life that’s a very rare manifestation. So really these things on the top: weakness, GI symptoms, mental status changes; these are the primary symptoms that you’re going to look for in patients who have hypercalcemia.

Now the treatment, like I said, is that you want to increase their urinary calcium excretion. Isotonic saline and lots of it, for the reasons that we mentioned. So try to hydrate them up and try to give them a brisk urine output, maybe 100, 150 cc per hour. This is one of the few indications where you --- you may also want to give saline and diuretics at the same time. Loop diuretics such as furosemide will also facilitate kaliuresis --- I’m sorry, kaliuresis. One downside of --- of diuretics, however, is that diuretics will give you other electrolyte losses such as hypomagnesemia, hypokalemia, so you’ll have to replace those other electrolyte losses. So fluids plus or minus diuretics, that will start to lower your calcium quickly. So it’s --- it’s a quick treatment. Unfortunately, it’s not a very potent treatment.

What you really want to do is you want to turn off the problem at the source, and like I mentioned, the main problem here is that in almost all patients, you have increased bone reabsorption so you need to turn off that process. You really have two options here. One is bisphosphonates, such as zoledronic acid, which is probably the most commonly used these days. An older agent is pamidronate. They both work, they’re both effective. The main reason that zoledronic acid is favored these days really is just for --- for ease of --- of administration. It’s a quick infusion, 15 minutes com --- compared to, say, 24 hours versus pamidronate. Now, this is a very potent treatment and it will definitely get your calcium under control and it will last for several weeks. Unfortunately, it’s not a quick treatment. So it typically takes three, four, maybe seven days before you have your peak --- peak effects of bisphosphonates but it will last for several weeks typically. One caution you have to do to --- to be aware of for patients rec --- receiving bisphosphonates is that you have to reduce the dose in renal insufficiency and if patients are going to be receiving bisphosphonates chronically, as many patients with hypercalcemia and malignancy will be, then it can be associated with osteonecrosis of the jaw. So be aware of any kind of new dental complaints that they may have.

Now so, we talked about let me go back --- we talked about saline with or without diuretics, which we said was quick but not potent.

We talked about bisphosphonates, which we said were potent but not quick. And so here you have something which is in between. Calcitonin, it’s something that
you can administer subcutaneously. It will have a fairly effect, start working within a few hours, not quite as potent as zoledronic acid or the bisphosphonates but it will start to lower your calcium more effectively than saline alone. Unfortunately, it does not last very long. Typically you start to develop tachyphylaxis or resistance to the action of the medication within, say, 48 hours or so. So this is sort of an intermediate step. And so on the first slide, when we talked about the options, we said all of the above. This is one of the all of the above. You can --- You can do all of these things together.

Now we talked about a variety of oncologic emergencies. As I mentioned there’s no way that anyone can cover in any one lecture all of the emergency problems that one might encounter in a cancer patient but the clinical pearls that I do want you to remember when you see any patients --- any cancer patients who present to the emergency center or with emergency problem is that, first of all, any new symptoms or decompensation may not be due to the cancer or its treatment. Please remember to consider their non-cancer medical problems. The other thing I want you to remember is that the typical signs and symptoms of disease that you’re typically taught to look for – for an acute abdomen, for a pneumonia, for whatever, they may be blunted or masked in cancer patients so have a lower pretest probability of “badness” or whatever it is that you think could be the worse thing that this could be. And --- And a lower threshold for initiating the necessary diagnostic steps to --- to figure out whether it’s a CT scan or whatever you need to do. So I thank you for your attention and we welcome your feedback.