So this is the last lecture. You know one of the things about the course and I’ve told a number of you 27 years ago when this started I got a call from Gerald Levy’s office who was the head of medicine and it was actually his secretary asking – they said Dr. Starz would you be willing to serve on the Update in Internal Medicine Committee and I was certainly honored. So in this last 27 years everybody else who has been on it has either left or died so that’s it, so I’m the last one. So but one of the things we try, I try to do and I hope you’ve all found that to be the case is we want to teach you something new and I want to teach you something useful, and I think those are very important.

And in thinking about this you know gout, and we’ll talk about gout, pseudogout and a couple of other aspects of crystals but what I wanted to start with though is something that I did not think much about before and that was crystals in disease. Think about in these lectures what you’ve heard. You know certainly we heard today about breast and the calcification within breast tissue, you know within atherosclerosis we saw those within the blood vessels, the heart valves we get calcium and it’s interesting those crystals are there and they, they don’t cause much in the way of an inflammatory reaction. Certainly in kidney stones and gallstones they can be very problematic. And what we are going to talk to you about today is crystals in the musculoskeletal system. And you know when we think about a crystal these are just these atoms, molecules that come together in this pattern that just repeats itself over and over. You know I was looking for crystal pictures. This is salt, this is Viagra, believe it or not that was a crystal.
So but okay so there are some principles you must take away, and one is this concept and I’ll show you about supersaturated. You know if you think about iced tea and you are putting sugar into iced tea to put sugar in you stir it and you can get more into solution, and then it starts to come out. And so when you stir it it goes into a supersaturated state and one characteristic of a supersaturated state is that the substances will come out much more easily. We have these inhibitor proteins in the body in different places and our knowledge about them is very marginal I must tell you because when we look at how crystals begin, look at kidney stones for example, the nidus of the calcium oxylate stones, the most common, is oftentimes uric acid right at the center of those kidney stones. Or if you get these molecules together and so the second concept that we want to talk to you about is the changes in that local environment actually make a difference, especially in these crystal induced problems.

So what is crystal induced arthritis? It is quite simply this inflammation that occurs in the synovial lining and in the fluid of joints in response to the presence of a number of crystals. These are the culprits. We are going to talk especially about gout monosodium urate, that happens to be the form that’s in the body, we tend to call it uric acid but this is, it’s a sodium salt. We look at the second is the calcium pyrophosphate dihydrate, I’m going to show you some cases that I think will be very helpful for you and that I believe will be important in your practice. Hydroxyapatite is a very interesting crystal and I’ll go over a little bit with you. It’s now become clear that osteoarthritis is not just a mechanical problem and there is definitely an inflammatory reaction occurring in these individuals and crystals are likely part of that process. And just to mention one other crystal that we
see sometimes if you ever happen to see it on a joint fluid it’s cholesterol crystals. We see these sometimes but they really do not evoke – cholesterol does not evoke an inflammatory reaction.

One last little slide about crystals to start. And if we look at this something that’s intrigued me greatly and I’ll show you some slides, one of which occurred when I was a fellow and that was why some of these – why crystals will evoke an inflammatory reaction. I must tell you we still don’t understand that well at all. Certainly this is this physical irregularity and there can be this negative surface charge on there, and so there can be a localized irritation in the – there is coating of these crystals, various protein coating that may play some role. Certainly crystals when they are deposited in tissues they cause mechanical damage. And in gout we’ll see that when the tophi become deposited in and around joints and it could really damage the joint structures. And but something that I find intriguing is these crystals can paradoxically reside in the tissues for years without causing any problems and this is a term that is frequently used and that’s crystal shedding. And I’ll show you at least some of the factors because when you are called to see a patient in the hospital who develops an acute gouty attack postoperatively or a woman in your office who has a swollen wrist due to pseudogout something has caused these crystals that have been deposited to shed, triggering this acute inflammation.

Another facet about these inflammatory arthritides is that they certainly – they occur spontaneously from whatever this whole process is. You have this acute phase reaction to it but then they stop and one factor about crystal induced arthritis is the intensity of the inflammation is tremendous. In fact
the two most painful inflammatory arthritides are crystal induced arthritis and septic arthritis, much more inflammatory than we see for example in rheumatoid arthritis or spondyloarthropathy or the like. So when these crystals start to initiate inflammation the last point, supersaturation, is important, the fact that they can be there in tissues without causing a problem, tophi don’t evoke inflammation usually. But then there is this very intense reaction.

Thomas Sydenham described I think something and it’s important, I’ll go through a few points. The patient goes to bed, gout attacks occur more common at night and he sleeps until about 2:00 o’clock in the morning when he’s awakened by pain in the first, in the great toe. Sometimes it’s the heel, calf of the leg or ankle. So a couple of points, gout attacks tend to occur at night, males are much more common, we’ll explain to why than females, and there is this tremendous predilection for the lower extremities. So you just don’t see somebody come with a swollen hand or shoulder or wrist from gout certainly as the initial attack almost ever. And so the pain begins and you can see again this chillness, fever is a reflection of the intensity. The pain is mild initially and then it gradually becomes more violent every hour. Now that’s very uncommon, we don’t see that in the arthritides, so that this reaction starts relatively abruptly and in fact it’s become so painful not to endure the weight of clothes or shaking of the room. Patients say that they can’t even put the bedsheets on. So that’s the classic example and that’s how it happens most of the time.

Just a little bit of history that I think is very interesting. Hippocrates and the ancient Greeks had this fascination for the humors circulating through the body, not a bad idea actually. And that they
would drop or flow into the joint causing the pain or inflammation. This is I think very interesting, if we take a look at Leeuwenhoek’s original microscope over here in the 1600s, he loved to look at anything and so one of his friends has draining tophaceous gout and these are actually the crystals, these are – he drew this picture. So we knew back then what the gouty crystals looked like. Garrod in the mid 1800s actually had a very crude test, a string test or the thread experiment in which he demonstrated that the uric acid was increased in the blood.

But something that has amazed me is that when was it determined that uric acid in the joint caused gout? Okay, so here is when it was, 1961. You must be kidding me. I mean what were people thinking of? In fact when I was a Fellow you know in the late – I finished in the mid-70s, that I remember asking Dr. Rodnan the head of Rheumatology, I am embarrassed – I asked him three times as to what did people think it was due to? And people didn’t know, they did not know that it was uric acid crystals. In fact Dan McCarty took and injected his own knee which was real smart, but and he got gout and that was how it was. So it’s an interesting point of we see what we are looking for. And I think hopefully today you’ve seen that there are so many facets of these diseases that we need to think about.

So looking at gout it is a very common problem. We can see that it occurs in you know over 8 million in our population, more men than women. I’m going to start just in – for the beginning of this I just – these are kind of the conclusion slides but I want to show you to build into that. I hate to end with the, you know the slides and then you think so where did all that come from? But not that
there is much here, but we want to show you about the effect. These are the new guidelines that just came out from the American College of Rheumatology and it says that you need to think a little bit about diet and lifestyle to manage the comorbidities that I’ll talk to you about. We are going to talk to you about the xanthene oxidase inhibitors, about Allopurinol the new one, Febuxostat, or how to use those. The one concept that we need to really understand that you must lower the uric acid to below 6, 6 or below really to get all of that material removed from the body.

A point that is very – I honestly almost monthly see this as an error, with uric acid lowering if – and we’ll talk to you about when you should do that, that you must start low and you must raise it up very gradually. The reason is changes in uric acid level either up or down are what precipitate the attacks of gout. The worst attack of gout I ever saw was someone – it actually as at the VA when I was a resident and had been treated with increasing - his acute attack was treated with increasing doses, actually 600 mg of Allopurinol and it unfortunately when you do that it really aggravates the problem. And we’ll talk about that, those last couple at the end here.

When you think about gout for your own perspective it’s actually pretty straightforward and I would hope that when we finish this today that this is a disease you will own, it’s actually something that is common, but think about it in four stages. You can think about increased uric acid, we call it asymptomatic hyperuricemia. There are acute flares which we’ll talk to you about how to treat, pretty straightforward. This intercritical period meaning that after the acute flares my gosh the joints
go back to normal, and they absolutely do and then the few people who develop advanced gout, we’ll talk to you about how to predict who those are going to be and how you should treat them.

So what is hyperuricemia? Hyperuricemia is defined as the urate concentration, the uric acid concentration that exceeds the serum solubility. And that happens to be if you look at getting a test once it’s about 6.8 that means it’s above the serum solubility and that is the problem. The take home message for you when you think about uric acid, uric acid is a problem of solubility. When we look at uric acid over time, in the prepubescent period, this is age, this is the uric acid level, when we look at it both males and females uric acid in the prepubescent period about the same and then with puberty there is an increase in uric acid in both males and females with males however having a greater increase, in part related to muscle mass, in part related to estrogen effect on uric acid clearance by the kidney. That’s why when we see gout in women unless there is some renal insufficiency or some other cause it’s because it occurs in the postmenopausal period, because their uric acid goes up related to the decrease in estrogens which then decreases the amount of excretion of uric acid by the kidneys, so very straightforward.

So uric acid just for a – so what uric acid is just the final degradation product, that’s it. If nothing – you know you have the adenine and guanine which are very important, obviously DNA, RNA and the rest. That’s why by the way when you think about where do we see it in meat, red meats and fish and things such as that about where the purines come from, but these are all the important things that they do and but if it was not for kidney stones and gout we would really never even think about it.
Let’s take a look though, there are two sources of the purines. One is your endogenous biosynthesis. The reason we have that is because these are all so important in terms of our body, they are essential to our body of course, and the diet. So that’s – so we have two sources. The second is about excretion. So when we take a look about 600 mg a day of purines come from your diet and about 3 to 600 are synthesized. It’s in a balance, so the more we eat the less we make. And so it’s an interesting point just from this slide alone, if you go on a very strict purine restricted diet you can only decrease your uric acid you know by about a milligram percent, so because you have to have these purines and so you just if you decrease it in the diet you are going to get some increase in the synthesis.

And so what happens is they go into these purines, the DNA and RNA and cyclic AMP and all the rest, it’s metabolized and we have this pool of uric acid in the body. You know it’s 1200 mg, that’s it. And that’s in solution in our body and about a third of it is excreted by the intestine and the rest of it, two-thirds is by the kidney. And if we take a look then quite simply if we look at it going above the uric acid level of 6.8, now we all have that concept of the serum solubility, and so you have two basic possibilities. Either you increase the synthesis or you decrease the excretion. And here is the bottom line, most people have this problem because 90% of the difficulty is with underexcretion. Exactly why that is is not clear, and I’ll show you in the next slide a moment about this. There are various enzymes, there are various genes rather that control the renal tubular epithelium and their variations and we still don’t quite understand that. There is no question with kidney disease, diuretics, low dose aspirin is a big problem, by the way. If you take low dose aspirin because we are
competing – any small acid is competing with uric acid and as a result that your uric acid level goes up. So that is, you have individuals with heart disease on diuretics and low dose aspirin, that jacks up their uric acid.

It’s interesting with diabetic ketoacidosis it can go up. There is a correlation thought to be an effect on hypertension on the kidneys, but I must tell you back once McCarty realized that it was uric acid in the joints we got Allopurinol soon thereafter, I’m telling you there has been nothing done to look into these mechanisms further. We know about overproduction, diet and alcohol, we’ll talk to you about a little bit later, certainly myeloproliferative states as well.

One thing just to follow-up kind on what David showed you about the kidney though, it’s interesting, uric acid is filtered, it’s reabsorbed, rescreted again and but only about 10% of the filtered load actually gets excreted. And so we can – we take a look at that whole situation. There is no question that the bottom line message though that you want to take away is that about 90% of people are under-excreters, they just do not get rid of it. A lot of the question if you have a little bit more acid urine you will not be able to dissolve because you know the PK of the uric acid, just it’s not very soluble, and so that, it’s thought that these people put out a little bit more acidy urine.

Okay, so some practical information. If we take a look at this whole situation there is no question as you increase your uric acid level, as you increase your uric acid level the chance of having gout is increased. But take away two points from this. Number 1 is that no everybody with high uric acid levels are going to get gout. In fact the majority of people don’t get gout. But if you start getting in
to the 9s and 10s, I’m telling you those are the people who not only develop grout they are the ones who develop kidney stones, they develop tophi, they develop joint damage. So just from this piece of information alone it gives you some idea of who probably should be treated. The second point that is not necessarily obvious until it’s mentioned, and that is you don’t have to have a uric acid level above 7 to have gout. And why is that? Because the serum solubility is not 6.8 for everybody, it’s probably less, it is less for some people. And so that’s – so take away those messages. The higher your uric acid the more likely you are to develop gout, kidney stones and tophi, but you can still have gout. You don’t usually have gout if your uric acid is 4 or 5. But certainly we see it all the time.

Just a little bit about these risk factors, because of renal function it’s thought with increasing age, now you understand about this estrogen effect on the kidneys so that men are higher than – diuretics are big. We don’t use much of those – diuretics and low dose aspirin, this whole issue of the purines and the like, it is no question about that with meat and seafood and the rest you can, but remember when you take in more purines you are going to decrease endogenous biosynthesis, so the effect of it. What is interesting though is fructose, and if we look at the – if you look at that uric acid level and if you check a patient’s uric acid level today and compare it to 10 years ago if they are not on diuretics or low dose aspirin the biggest factor that influences change is whether they put on weight. As your body weight goes up your uric acid level goes up. And certainly there is no question about it, this fructose as well.
CRYSTAL INDUCED ARTHRITIS: NEW UNDERSTANDING OF OLD DISEASE, TERENCE W. STARZ, MD

You know back when Allopurinol came out it was argued that uric acid like cholesterol was a risk factor for heart disease. And you know that has been a controversy, and because there are these associations with the metabolic syndrome, obesity, renal insufficiency, hypertension, heart failure and so but that’s a real question as to which causes what. As to whether uric acid per se causes these problems to be worse is very problematic. These in and of themselves are not indications to put people on uric acid lowering treatment. This is the big thing, emphasize to people their – the biggest things are number 1 is their weight and number 2 is their alcohol consumption, especially beer as I’ll show you.

Okay, so let’s go through and let’s talk about it. So we’ve got asymptomatic hyperuricemia, pretty straightforward here. This is an acute attack of gout. Look at the redness here of the – and here are the classic joints, first MTP and the ankle, mid-foot, knee. My favorite slide is the devil gout biting into the first MTP joint. So now you’ve got it, the characteristics of the acute attack, abrupt, it’s a very intense reaction, the swelling, erythema, pain, you get the rest. The acute attack though honestly it stops in 3 to 10 days, I mean it’s amazing of how it does with that intensity of inflammation. The majority, 90% of initial attacks are one joint only, tremendous lower extremity predilection, 50% are in the great toe. So when I was a Fellow you know Dr. Rodnan, he loved history, actually some of those slides are from his, the invitation to the gout was the thing.. And so he would have us as Fellows, people would go into the Clinical Research Unit and he loved to, to reproduce what had occurred in the past. And back in England the Aldermen in fact there is a term an Aldermanic Feast, and he would get – bring these people in and the only people who could come
in were actually the people usually of not great means, and so he would be feeding these people pigeon and port wine and everything else, and they would have – and so this is a slide from that. And you can see their uric acid level would fluctuate. You put alcohol in there and it goes up even higher, especially beer because beer, there are two things when alcohol is metabolized it’s through a small acid which will compete with uric acid but also guanosine is in beer, it’s a purine and so and I’ll tell you in this slide I like it because it shows you that you – up here it comes back down and it’s this change in uric acid. And of course we had to go as Fellows right in the middle of the night always to go see the patient, which was real nice. I put this slide only in to show you gosh, I mean this is the compilation, this is the world I live in now. I’m going to the American College of Rheumatology next week and this is what we will be dealing with all week of looking at the – all of these mechanisms. I’m telling you, we still don’t understand about how this occurs in terms of the situation. But this is gout and this I just put this in to show you, acute attack and this is after over 10 days, and that’s what happens.

I put this slide in to show you this is cellulitis, and that’s what you have to think about. I mean you almost never get a septic arthritis of your ankle or your first MTP unless there is some trauma to the area. But think about cellulitis right down in those areas, that would be – and I’ll tell you cellulitis is usually not nearly as painful as gout. So these are the common places, tremendous lower extremity. What you get thought recurrent attacks you can get multiple joints and you can see the upper extremities. This you have t know, and that is that as we look, as we get older especially in older women who have DIP osteoarthritis and they are on diuretics you will see these tophi here in their
distal intervallic geo joints, and I’m telling you I see a fair number of people with this as a problem. So do understand that because you can see the classic gouty lesions right there in the finger.

So let’s look at the mysteries of why we get this deposition. Well it turns out that when you look at the distal parts of your extremities, the low temperature, the lower temperatures in your feet is why it’s thought that it occurs, but I’m telling you there is no good explanation as to why it’s your first MTP joint. Certainly injury can precipitate it. One reason at night is you get a little dehydrated, you dehydrate your joints a little bit so we may concentrate the fluid. But that’s it, that’s the best we can do as to why it occurs. The binges, remember that picture of the slide I just showed you, fluctuation in uric acid level, so that’s one of the things that certainly can do it.

These common, these are very useful and to go over these just a little bit, so you have the acute attack, and this is exactly how it is, maximum intensity usually in the 6 to 12 hours, but this is highly suggestive. Now what about looking at crystals? I’ll show you them in a minute. I can get fluid out of the first MTP joints and people are real happy when they’ve got this intense inflammation, you stick a needle in there. You don’t really – that’s it, that’s what causes gout. We usually do not aspirate that joint. We said about this uric acid, the 6.8, now you’ve got the number but remember there is certainly a third of cases are below that as a number. You know and so if you do get the fluid you certainly should take a look at it. We’ll show you with the whole situation.
And this is what the crystals look like. Look at them, they are the same as you know the original Leeuwenhoek and his microscope, he showed them. And it has to be phagocytized within a white cell, and that’s it. We have all types of different polarizing lights in the first order red compensator, you don’t need those. You can see – actually you can see them without a compensator. You know this is how you get that fluid out of there. We used to – but I show you this slide to remind you, one other thing Dr. Rodnan had us do is we had to aspirate the first MTP joints on asymptomatic individuals with hyperuricemia. Okay, they were happy too about that. So you can get fluid out and it turned out that 30% of them had uric acid crystals that you could see but never had gout. So they are there, as to what happens.

I just put this in, it’s in your handout and it – I thought it was really a very good thing and you already know all this stuff. You make somebody who is a male, who this and you see those characteristics right in there, this is, this is just as good as aspirating the joint and all the rest. So you’ve got the thing right now. So you see somebody they’ve got lower extremity rapid onset like that, and that’s the case.

So what about progression, okay, and that’s the one problem is that if this uric acid depending on if it stays up like that it really can progress causing the renal damage, tophi, sometimes joint damage and sometimes you can actually damage the kidneys and certainly kidney stones. This is the classic example, see this right here. This isn’t what rheumatoid arthritis looks like, this is a tophus sitting right in here. And this called an overhanging margin. And in rheumatoid arthritis we just erode that
right away, and so these are tophi sitting here within – in the joints. And this is what they look like in the elbow. If you look at them, by the way, they are kind of a little yellowish. Rheumatoid nodules aren’t yellowish, and here is what – see how there’s a little yellowish color in there, why these two places are very unclear and that’s what the tophaceous material look like.

So after the attack it goes back to being asymptomatic and you have – but the problem is once you start getting the attacks they frequently start occurring in more frequent times. And so what happens when you think about the goals of management, so you’ve got to look at how to – so just divide it, acute attacks and the long term, and obviously we want to control pain, inflammation and then the question is here that we’ll address. So number one you want to take this point away, the earlier you treat them the better. The longer the attack goes on the harder they are to treat. And I’m telling you because of the intensity, and so that’s why we treat them very aggressively early, we need to think about how to protect further flares and then we’ll talk about how to, to actually lower the uric acid. I’ll tell you the two big things right here are weight loss and reduced alcohol consumption, that’s it. Gout, bad gout is one of the things that will actually keep people from drinking. To tell you the absolute bottom line on alcohol though it’s beer is the biggest because of this guanosine in beer. Spirits are next. Wine has less of an effect on it, I’m not sure why that – again it’s been very poorly studied. You know there is this argument that, by the way that milk products decrease your uric acid level by mechanisms that are not clear as does vitamin C thought to be related to renal effects.
And so when we take a look at this whole situation how do you stop an acute attack? It’s pretty straightforward. You have one of three approaches. Nonsteroidals, the classic one that we used in the past was – actually the classic one was Phenylbutazone, which we don’t – you know Butazolidin, my God that caused aplastic anemia. But so we – Indocin, I like Indocin but the trouble is Indocin is really not well tolerated. So we tend to use Naprosyn, but you have to use 1,000, 1,500 mg. And you treat them and so it works. The second is Colchicine, but Colchicine is not antiinflammatory, it stabilizes the lysosomal membranes and so if you don’t treat them early with Colchicine and with Colchicine you give them you know 2 of the .6 mg tablets and then you repeat it an hour. And it does work. And then corticosteroids, we use a lot of these in the hospitals and what we like about them is that you can either give them by mouth, you give intravenously if you need to, if somebody’s NPO you can give them IM, you can give them interarticularly.Injecting a joint is really a very effective way of doing it. People used to use ACTH, I don’t – none of us have used ACTH in years, just to stimulate.

This slide is just important though because once you start developing the attack unless you can get the weight down or unless you decrease alcohol intake you know people are going to start to have recurrent attacks. And so who do you lower their uric acid? And these are the criteria. If people are starting to have two or more attacks a year is one thing; if they have joint damage here remember now the higher your, once your uric acid starts going above 9 you know that can certainly be a problem. If you have to be on diuretics, certainly if you’ve had kidney stones right there and you know that’s what is important because what you want to do is you want to lower somebody’s uric
acid if – essentially if they’ve got some tissue damage, kidney stones or if they are really having these frequent attacks then what you want to do is get the uric acid level to below 6. You want to get it down in that range because it’s now out of the supersaturated state, it will come out of – the uric acid will come out of the stores.

But remember one thing is that when you treat individuals and you lower their uric acid what are you doing? Well we inhibit this enzyme, xanthine oxidase, you know and that’s okay. So we have these purines and the difference between hypoxanthine and xanthine which levels are increased by the way, they happen to be much more soluble than uric acid. That’s it. That’s the mystery. So if you look at them, what you are doing is just decreasing this and increasing the amount of hypoxanthine and xanthine, that’s essentially what happens.

We have two inhibitors, the one we use the most, the time-tested id Allopurinol. Allopurinol is metabolized to Oxypurinol which is the active form, it lasts 24 hours so you only have to use it once a day. The new one is Febuxostat which is Uloric and they are both good, it’s another xanthine oxidase, non-purine xanthine oxidase. It is more expensive and the question is is it more effective? This is the problem with these, as I explained to you before, when you are doing this our goal is to get it to 6 or less, to do it and there is no question when you do it all of them manifestations, believe me the tophi go away, the gout stops, that’s it. But one of the problems is that you have to protect as you are lowering the uric acid, that’s why we use prophylaxis. While somebody is lowering their uric acid and what you do, the first mistake that you don’t ever want to make is don’t start during the
acute attack, wait for 2 to 4 weeks, start with 100 mg, increase it every 3 weeks by 100 mg up to about 300 mg a day.

The toxicity from Allopurinol is not very great. You know you get a skin rash occasionally, the problem with it is though that you can as you are lowering uric acid, so we use either Colchicine .6 mg a day or a nonsteroidal like Naprosyn 500 mg once a day to stop it. If in fact they can’t tolerate one of those two agents really I don’t have anybody on Probenecid, there is a new agent out that is a uric acid, it’s – we look at it, it’s a pegylated antibody against uricase. And I’ll tell you it will really lower it down, the problem is it’s you know we are looking at $50,000 a year and it’s a very expensive treatment. So it’s something that we really don’t use except in extreme situations.

And so the goal is here with gout quite simply is it’s a disease that we all should really own, it’s a disease that has 4 stages, elevated uric acid, the 6.8 is what you want to remember. People will get the acute flares, in part related to the level but certainly you can have a normal level. You get the intercritical phases and we really do have these treatments and they are very straightforward, nonsteroidal, Colchicine or steroids. If somebody is having recurrent attacks 2 or more a year we should think about it.

I want to show you just in the last minute just to let you know because these calcium pyrophosphate dihydrate, these are conditions you’ll see all the time. And this is where you get another crystal, and it occurs with aging but you know the real key with it is that if you look, here are these cases that
you are going to see. You’ll see a 78 year old female with an onset of right wrist swelling and pain, all right. You’ll see an 86 year old man with the acute onset of swelling in his left knee. Then you’ll see an interesting case of a 52 year old man who has osteoarthritis in very unusual places, you know like his MCPs and wrists. This is what pseudogout looks like, here is a hot swollen wrist. I’m telling you that’s it. And you get an x-ray and you’ve got this calcification right here in this triangular ligament cartilage region. And you see somebody like an older person who comes in with a swollen wrist, that’s it, they’ve pseudogout. You can inject them, treat them with steroids, treat them with an N-SAID and they’ll go away.

This is what these crystals look like, these are calcium pyrophosphate crystals. Now again it’s hard to get fluid out of there but it’s not hard to get fluid out of this. The other clinical situation you’ll see is an older person, an older male or female and they come in, look, here is calcium right there. And they come in with an acute arthritis.

This, you need to know this. Remember we had – why do we want to do hemochromatosis, because it’s a common problem. You see somebody come in and you know they’ve got a suntan in the middle of winter or they have cirrhosis or diabetes and the rest and it’s very interesting, the arthritis with them is that they have these hooklike osteophytes and they also develop chondrocalcinosis. So that’s another thing.
And the one last condition that we leave you with today is this hydroxyapatite disease. This is a – you know hydroxyapatite is bone, but it can cause probably when we look at osteoarthritis these crystals, you are going to start hearing more and more about them being responsible, and these may be targets for treating osteoarthritis. But you’ll see a 48 year old man who comes in with a hot shoulder, or an older woman with a problem with her shoulder. And see this right here, this is hydroxyapatite. And this is a calcific tendonitis, I see them all the time. And these people respond to nonsteroidals or a tapering course of Prednisone or an injection and it goes right away. And actually those can reabsorb. But a very interesting situation is you’ll see these and think about you have an older individual, especially a woman who develops a significant amount of arthropathy of their shoulders, and this is a destructive arthropathy right here and look at all this calcification, this is hydroxyapatite. So again that’s just another crystal and that’s what it says.

All right, so there is gout to leave you. And this is actually what we want everybody’s toe to look like. I showed you this before and this is it for the end of the thing. Mr. Osborne, may I be excused, my brain is full. Okay, give us all your feedback for next year. We look forward and thank you, guys, really, thanks everybody for coming. Really what a great time.