

Lupus Society of Illinois
Moderator: Sonya Loynachan
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7:30 PM ET

Sonya Loynachan: Good evening everyone this is Sonya with the Lupus Society of Illinois. In just a few minutes, I will introduce our speaker for this evening, Dr. James Curran. I want to let everyone know that the lines will be muted during Dr. Curran's presentation. Once Dr. Curran's presentation is over, we will open the lines up for questions.

Dr. James Curran received his Bachelors of Science in Biology from Marquette University and his MD from the University of Illinois. After completing his residency at Bethesda Naval Hospital he completed his fellowship at the University of Chicago.

He was in the Navy and his career included Chief of Medicine at the US Naval Hospital in Naples and Chief of Rheumatology at Bethesda Naval Hospital. He's been at the University of Chicago since 1987.

Dr. Curran has had an interest in the diagnosis and natural history of late-onset rheumatoid arthritis. He published the initial 50 cases of the entity in Seminars of Arthritis & Rheumatism in 1992, defining the therapeutic requirements and clinical outcomes.

So please welcome, Dr. James Curran.

Dr. James Curran: Good evening. What I would like to do is generally talk about infectious considerations in lupus in a general format. Looking at risk factors for infection, medications that we use in systemic lupus that you may be familiar with. And the risk of infections to general health, and the imposition of other medical conditions on the assessment of lupus.

The first thing I'd like to talk about is a general consideration of a fever in a patient with lupus. The evaluation basically looks at specific organ systems. If you have a temperature, you may have a fever related to lupus. That is relatively low on the list of concerns.

What we do look at specifically are whether or not there are any bladder symptoms. Whether there's any urinary tract history or urinary tract infections. So we check a urine analysis and a urine culture. We would look at the sinuses, and the ear, nose, and throat evaluation because acute sinusitis can cause fevers in patients with systemic lupus. We look at the GI tract for any possible viral illnesses or in older patient's diverticulosis or diverticulitis. And importantly we look at the pulmonary system.

So if a patient presents with lupus, the first thing we are concerned about is an infectious ideology. So again we look at bladder symptoms, sinus issues, GI, and lung. And we do a careful assessment of each individual organ system. In the case of lung obviously a chest x-ray screening. Sinuses we can do a CT Scan or an x-rays of the sinus. We can do a urine culture. The GI tract is more clinical in terms of a physical examination.

In general, as you know systemic lupus is an autoimmune disease which is characterized by B-Cell over activity and immunoglobulin production. Patients with lupus in general

before any use of any immunosuppressive medications or cortical steroids have an increased risk of infections because of their immune dysfunction.

Looking specifically at medications that we use in systemic lupus, the biggest risk of an infection in SLE is our cortical steroids. If you compare Prednisone with Azathioprine, Cyclophosphamide, Hydroxychloroquine which is Plaquenil, or one of the newer medications such as CellCept. All studies have shown that the greatest risk is a patient on Prednisone on any dose.

In some individuals on Hydroxychloroquine it seems that Plaquenil offers some protection in terms of a decreased risk of infection. Specifically looking at medications one at a time Imuran Azathioprine has been used for steroid sparing and SLE. It's also been effective in hematologic or blood manifestations of lupus. It's used also in lupus nephritis.

The concern about Azathioprine is whether or not it can cause a decrease in white blood cell count which would set you up for risk of infections. More recently we have an enzyme study called TMPT, which stands for Trimethyl synthetase, which allows to determine whether or not a patient can metabolize the drug and whether or not they're at risk for a low white blood cell count. We check a TMPT synthetase level before we put patients on Azathioprine.

Hydroxychloroquine is a medication that probably decreases your risk of infection. It is the safest medication we use. We use it in mild lupus. It has recently been found to prevent pregnancy losses in patients with systemic lupus. So we even continue this medication in pregnancy. It is not known to increase risk of infections at all.

CellCept is a newer medication that is replacing Azathioprine in a lot of renal lupus patients. Again the increased risk of infection here. It's probably more related to the induction of low white blood cell counts.

Cyclophosphamide Cytoxan both orally and intravenously have been used for many years in lupus nephritis and lupus vasculitis. Its peak incidence of lowering your white blood cell count is 10 to 14 days after starting the medication. And there have obviously been increased risks of infection, other complications later on.

Two of the newer biologics, Benlysta and Rituxan, have an increased risk of viral infections usually later on during the course of therapeutics. It's not uncommon in lupus patients, as you know, to be on a combination of medications. For example, a patient with significant lupus arthritis or renal lupus may be on a combination of Imuran, Prednisone and Hydroxychloroquine.

We look at these patients very closely. And if a patient develops a fever on these combinations of medications it's always significant. And always mandates early evaluation. Again, there are some patients with SLE who develop fevers and even swollen lymph nodes as a part of their disease, but that is always a diagnosis of exclusion. And we're always very urgently looking to see if there's any infection that's clouding the issue.

In terms of general health issues, we would urge patients with SLE to make sure their vaccinations are up to date. More recently that includes Tdap's because of the resurgence

of Bordetella pertussis at least in the Midwest. Influenza vaccine obviously in my estimation is indicated in all patients with systemic lupus.

This year we have a bit of a problem because the vaccine is probably only 23% effective in terms of full protection. I always encourage patients to have their pneumo vac's (ph) up to date. Originally it was every five to ten years, there's been some change in patients over age 65 when they should get this medication and how often.

One of the concerns and one of the caveats about vaccinations in lupus is that patients that are on immunosuppressive medications which includes medicines such as Prednisone, Azathioprine, CellCept and Cyclophosphamide cannot have live virus vaccinations. That for example includes Yellow Fever.

And a common question is the shingles vaccine which is a live attenuated virus. And the answer to that is if you're on immunosuppressive medications you can't take a live virus such as the shingles vaccine. You have to be off your immunosuppressive medication, then do the shingles vaccine.

Another issue has been the use of a drug such as Rituximab which may decrease your ability to mount a vaccine response to the vaccine or a protective response to the vaccine. This was studied. And it turns out if you have Rituxan and then I give you your flu vaccine after you've had the Rituxan, for your systemic lupus, your antibody response or safety protections from the vaccine is not as robust. So in individuals who are going to use this medication we make sure they're vaccinated prior to using a medicine such as Rituximab.

A third general issue is other medical conditions. It's not uncommon obviously with systemic lupus to have entities such as hypertension, diabetes, chronic bronchitis, asthma. It is important to make sure that other medical conditions are stable on SLE. And also to determine whether or not there's any medication interactions that can interfere with your immunosuppressive medication.

A couple of general comments. A question that was brought up is are there any guidelines as when to seek medical assistance? And again in a person that is on any medication that is immunosuppressive and even lupus in general I would urge the individual to seek medical attention if they develop a fever or any side effects of their medication. The first individual to be contacted is the primary care physician and possibly if that individual is unavailable the emergency medicine department.

Lupus is a chronic active condition which waxes and wanes. Our general goal in terms of therapeutics, is to induce a remission with a combination of medicines as such as the outlined Azathioprine, Prednisone or CellCept, Prednisone and Plaquenil. And then consolidate medications to the lowest dose of medication possible.

As long as you're on immunosuppressive medications you have an increased risk of an infection over time. There are some physicians that believe that a lot of the infectious process in lupus occur early in the disease. I have found clinically over the years that it is not uncommon for infectious issues such as viral infections to flare the disease. So you're at risk chronically over time.

In the flu season there is always a concern of how best to protect yourself from potential exposure. Obviously, hand washing, good general health, rest, and nutrition are the best safeguards. And as I pointed out flu shots are mandatory.

Renal lupus in patients who develop nephritic syndrome seem to have an increased risk of infection. And it is unclear why prolonged proteinuria and low albumin predispose to infections. But that really is an issue.

So at this point I would like to open up the question line to specific questions. Thank you.

Sonya Loynachan: The lines are open. If anyone has a question for Dr. Curran, please speak up.

Unidentified Participant: Hi. I actually had a question.

Sonya Loynachan: Sure, go ahead.

Unidentified Participant: Well, it was kind of difficult because I'm taking 25 milligrams of Prednisone now. And I actually just caught a respiratory infection, upper respiratory infection. So this was perfect timing for me. But I'm actually thinking of starting Benlysta soon. My insurance just approved it, but I'm just still kind of freaked out about it. And I just wanted to know your opinion about the -- I do know there's a high risk of infections with Benlysta as well. And if I were to get another upper respiratory infection or something else if I had to take antibiotics, and if it goes around the same time as my infusion then I'll have to put off the infusion.

Which also may make me more weak and tired. So it's just kind of like a Catch 22 it seems. So I just wanted your opinion on that.

Dr. James Curran: Okay, there's a number of really good points that I'll discuss. Number one, the corticosteroid dose of 25 milligrams a day depending upon what you're taking the corticosteroids for and how long you've been on it. Our goal is try to get or taper down as close as we can to 10 milligrams a day, and then reassess in terms of where we're going and what's happening.

Benlysta as a medication, it's interesting. They had a debate about Benlysta at this most rheumatology meeting in Boston. And the general feeling was that in a third of the patients it's not effective. In a third of a patients there are side effects or reasons not to continue it. And in a third of the patients the response is good.

The response is going to take time. It is not a rapidly active medication. It takes probably four to six months to be fully effective. So it is more of an add-on medication for SLE. An add-on to your primary therapeutic modalities. And then if you respond slowly tapering your other medications on.

So in a third of the patients it's wonderful. A third of the patients have difficulty tolerating it. And a third of the patients it doesn't particularly work. One other thing about Benlysta is it seems to work better in Caucasians rather than African-American populations. And it also seems to be more effective in patients who have high titer Antibodies. If they have high titer or double stranded of DNA antibodies or high titer Smith antibodies those are the people that statistically respond the best.

Unidentified Participant: Okay, thanks so much.

Unidentified Participant: I have a question. And that is that I have SLE lupus. And when I'm really active the rash is all over the arms and shoulders, and neck, and other areas. When the rash leave, where the rash was turns brown. So I'm kind of spotty all over. In some areas underneath the skin are lumps. So I'd like to know if the -- if I can use something to lighten the brown spots up to make me feel a little more confident. And those lumps that's under the skin, how major of a concern should I be with them?

Dr. James Curran: What medicine have you tried to use for the skin rash in lupus?

Unidentified Participant: They have me to use -- I use something for my face and something for the skin. The face is Protopic ointment.

Dr. James Curran: Okay.

Unidentified Participant: And for the other part of my body is Tram --

Dr. James Curran: Triamcinolone?

Unidentified Participant: Yes.

Dr. James Curran: Okay. One of the things that has been helpful in lupus skin disease. So what you're describing is probably a lupus skin rash which is not discoid lupus. Because discoid lupus gives you scarring and diffused hypopigmentation. What you're describing is a rash that flares when the disease does. And when the rash dissipates you're left an area of hyperpigmentation which we call post-inflammatory hyperpigmentation. Meaning as the rash subsides it stimulates skin pigment to darken.

That eventually over time will dissipate. It takes time for that to happen, but it usually does. Discoid lupus will leave you with a central area that is white, very white with kind of a reddish rim around it. And that is a more scarring condition. People get that in their scalp.

The drug that seems to work well for skin disease especially peripheral skin disease is Hydroxychloroquine which is Plaquenil. And the standard dosage of that medicine is 200 milligrams twice a day. There are some people who don't respond to Plaquenil. And occasionally we add another antimalarial drug called Atabrine to it. But those two medications are effective in lupus.

Obviously, higher doses of corticosteroids will work in most people. But the problem with that of course is the effects of higher doses of corticosteroids on your blood pressure, your blood sugar, your bones, your skin in general. And of course as I pointed out corticosteroids are probably the single biggest risk of infection in lupus patients.

As far as the nodules under the skin, there's something called panniculitis which is inflammation of the fatty tissue below the surface of the skin. And that may be what you're talking about. Or there may be a little bit of scarring or inflammation in the dermis below the surface of the skin that gives you that nodular consistency. In general, that is not anything to worry about. And it should respond to the standard care for systemic lupus.

Unidentified Participant: Okay, one other thing that has recently started happening to me is three of my fingers, two fingers on the left which is my thumb and my index finger, and my index finger on the right hand. They turn brown. The fingernails come off not all the way at the bottom. There's still a little bit of attachment. The fingernail is just not there and there's a little skin or something there. I've showed it to a couple of doctors, but I still haven't gotten anywhere with that.

Dr. James Curran: Is there any problem with the circulation to your hands? Are your fingers cold? Do you have Raynaud's Phenomenon in other words?

Unidentified Participant: Every now and then my color of my fingernails is different or reddish like at the very tips they get very sensitive. But other than that, no.

Dr. James Curran: Have you had any problem with skin ulcers or breakdown of the skin? Have you had any sores or ulcers on your fingertips?

Unidentified Participant: I did on the fingertips, but it went away. But I had some fingertips, yes I've had.

Dr. James Curran: Well, one thing we look for in lupus and other connective tissue disease is the occurrence of small little blood clots or thrombi associated with what we call the antiphospholipid lipid or anti-cardiolipin antibodies.

What these antibodies do is induce areas of thrombosis or clots in small vessels which can make the digits sore and tender. Can cause color change, and can cause skin ulcerations. So looking at your blood to see if you have any of these factors would be reasonable given how you describe it.

So they do a blood test for what we call phospholipid antibodies in people who have sores on their finger, skin ulcerations. Which is a little bit different than somebody with Raynaud's Phenomenon where those people have a tricolor change from blue to white to red. And they have cool fingers, and they can get sores or skin breakdown because of tissue damage.

Unidentified Participant: Okay. All right.

Unidentified Participant: Hello, can I ask a question?

Dr. James Curran: Yes. Go ahead.

Unidentified Participant: Yes. Yes, doctor, I have SLE. And I am experiencing pains in both legs. The lower legs, the upper legs, even my joints. Sometimes I can't walk. I have a difficult time walking. And I'm falling a lot. I am taking Plaquenil. But I'm trying to work part time so I can continue to work because I want to work. It's good for my mental health. What would you suggest I do, and say to my rheumatologist?

Dr. James Curran: When you say falling, is that because of balance issue, or is it because of weakness in your extremities?

Unidentified Participant: Weakness in my extremities.

Dr. James Curran: Okay, do you have problems for example raising your foot up? We call it foot drop. Do you have trouble with stumbling or climbing stairs?

Unidentified Participant: Sometimes I do, yes.

Dr. James Curran: Well, there's a couple things. One of the nice things about being a rheumatologist is the fact that basically you're a general internal medicine doctor because there are a number of -- lupus is a PAN (ph) system disease and it involves basically all the organ systems. So the thought would be when you have problems with weakness in your lower extremities and it's relatively symmetric. And you have falls and stumbling the differential is number one do you have a peripheral neuropathy, what we call a mononeuritis multiplex which is a single branch of the nerve causing weakness in one leg or the other.

Or do you have a neuropathic process which starts at your feet and moves up. You can get a mononeuritis multiplex or a single nerve involvement with lupus vascular disease. You can get a peripheral neuropathy from lupus because it involves the peripheral nervous system.

I always look at somebody when they have weakness and I can't find anything directly going on in terms of looking for circulation and numbness or paresthesias or numbness and tingling. I always look at the lumbar spine. Because people with degenerative disc disease, people with disc herniations, spinal stenosis will present with weakness and gait problems. Difficulty with walking and heaviness with prolonged walking. So the differential becomes vascular claudication, meaning a problem with my circulation. I don't get enough blood flow to my extremities and they get weak when I use them.

Neuroclaudication means that I have problems with pinched nerves arising from arthritis in my lower back. So those are two big things. Lupus itself can call muscle weakness, myalgias and myositis. It can cause as I said peripheral neuropathies and something that's called mononeuritis which means one nerve on one leg is affected more than the other.

So that's the general differential you look at in terms of somebody with lupus. You look for vascular issues. You look for blood clots and thrombosis with the phospholipids. You look at your peripheral nervous system with nerve conduction velocities and EMGs. And if there's any hints that there's involvement of the spine, I usually look at an MRI, a CT of the lower back. And that kind of covers all bases. And I just do it sequentially looking for evidence of active lupus. Looking for manifestations of lupus in other organ systems.

If those are lacking, I look for neuromuscular problems in terms of is that a pinched nerve or a peripheral neuropathy and taking that approach. So something is giving you an issue and the question is whether it's related to lupus or something else in your general medical health.

Unidentified Participant: Okay, thank you doctor.

Unidentified Participant: I have a question. Hello?

Dr. James Curran: Yes.

Unidentified Participant: Hi. So this is with regards to the shingles vaccine.

Dr. James Curran: Yes.

Unidentified Participant: I had shingles five years ago, and of course I'm on Plaquenil, Prednisone, and CellCept. Is it recommended -- I have not gotten my shingles vaccine yet. But because I am on those is it or can it be recommended that I get off of the immunosuppressants so I can get the shot like in a few days or --

Dr. James Curran: Yes, that's an excellent question. Yes, it's a live virus. And the general feeling we see that question is raised a lot with people on biologics like Humira for rheumatoid arthritis or Enbrel. And the answer basically is anything that is an immunosuppressant if you give somebody a live virus there is a risk that the live virus can disseminate, and can spread and give you systemic illness.

So the shingles vaccine is relatively congregated (ph) in people on immunosuppressant medicine. Plaquenil is not an immunosuppressant medicine, and you're not required to stop it. It's unclear what the dose of Prednisone is, and people go back and forth. But CellCept, Imuran, and Cyclophosphamide are considered immunosuppressive medications. And you would increase your risk of dissemination of a live virus like shingles.

So that's kind of where that stands. You'd have to stop your immunosuppressant medication. And the next question is, how long? Because a drug like CellCept and Imuran if you stop it today there's still going to be a prolonged immunosuppressive effect in the system. Probably a month or two, but again that's unclear.

So I just tell people in general if you aren't on these medications, it's recommended. If you've had shingles in the past there's no guarantee that you won't get it again. I've had people with recurrent disease or recurrent shingles over time. Fortunately, they're working on a vaccine now that is a killed virus. And when that is available we should be able to give that to everybody.

Unidentified Participant: So it's pretty much dependent on how active my lupus is right now? To see if my doctor would be comfortable with getting me off of those?

Dr. James Curran: Yes, the standard question is the CellCept. I mean the hang up is probably the CellCept. And the answer would be as long as you're on CellCept I wouldn't give anybody a live virus.

Unidentified Participant: Okay, thank you.

Unidentified Participant: I have a question.

Dr. James Curran: Yes.

Unidentified Participant: Can you have an infection without having a fever, but just having swollen lymph nodes?

Dr. James Curran: Yes, you can. A lot of the fungal or atypical tuberculosis, mycobacteria tuberculosis, those kinds of infections can smolder along for quite awhile before you get a fever. You can have lymphadenopathy which is swollen lymph nodes with these more indolent infections. Now that's obviously one of the concerns is using immunosuppressant medicine in someone who is PPD positive or TB positive. That's been studied a lot in rheumatoid in the biologics.

And we check for tuberculosis and try to avoid fungal exposure in those individuals. If that happens, you have to stop the biologic and then treat the infection. So what you're saying can you have a cult (ph) infection without a raging fever, yes.

If you're on corticosteroids, steroids in general suppress the febrile response which makes it difficult. So in my mind if a person has 100 degree temperature on 30 of Prednisone that's like somebody else not on steroids having 104 degree fever. So you're febrile and inflammatory response on corticosteroids is blunted. Which is why it's difficult in these individuals.

Where you'd normally say, "Gee, you only have 100 degree temperature, that's not a big deal." Yes, it is. If you're on Prednisone it's a big deal. Your temperature would be much higher off of it.

So to answer your question you can have low-grade infections. And if you're on higher doses of corticosteroids you can suppress the febrile response that you would normally get if you're not on these medications, on this medication.

Unidentified Participant: Okay, thank you.

Unidentified Participant: I had a question.

Dr. James Curran: Yes, ma'am?

Unidentified Participant: My mom she has lupus and she's had it for a couple years now. And she's taking Methotrex (ph) for her rheumatoid arthritis which was caused by the lupus. And she's also taking Prednisone. Now she takes 15 milligrams of Prednisone combined with the Methotrex which is taken once a week. And it's at 20 milligrams. And she mainly takes it because of her hands and inflammation that it's causing her.

Now it's not really helping her. Would you recommend a higher dosage of Methotrex? Because I know that you said that Prednisone is really bad and I don't know what I should be doing in regards to this.

Dr. James Curran: How old is she?

Unidentified Participant: She just turned 60 years old

Dr. James Curran: Okay, and she's being treated for the predominant symptom of her lupus which is joints.

Unidentified Participant: Mm-hmm.

Dr. James Curran: Which is an inflammatory arthritis. Does she have erosions or damage to her joints yet?

Unidentified Participant: Not yet. And I'm kind of afraid that that's going to happen.

Dr. James Curran: Okay. In systemic lupus there are some people that have lupus rheumatoid overlaps. We call them rheum-a-lup's (ph). They actually have both diseases. They have erosive rheumatoid arthritis, and they have serology and other features of SLE. In general, we treat the most dominant feature of the disease.

One of the reasons Methotrexate is kind of tricky to use and especially in higher doses is that the side effects of Methotrexate are low platelet count and low white count. And one of the features of blood manifestations of lupus is low white count and low platelet count. So for me I'm a little dicey about using that medicine because the side effects are difficult to sort out from a lupus flare.

For a specific arthritis, it's a good medication. A dose of 20 milligrams of Methotrexate is an adequate dose. That's on the high side, 20 to 25 milligrams a week is usually the maximum dose. And we usually end up giving that by injection because it's easier to tolerate.

The older you get the more you decrease your clearance of Methotrexate. So if I give you 20, you're actually getting 22.5 or 23 milligrams because with age you're granting (ph) clearance, or your clearance. Not granting clearance. Your clearance of the drug decreases with age.

The other concern in systemic lupus is renal disease. Methotrexate is cleared by the kidneys. You have to have an intact renal function 100 percent to excrete the medication or it builds up in your body.

So for those reasons if there's severe arthritis if that's all you're treating, fine. But if you're requiring corticosteroids and Methotrexate in combination for what sounds like active lupus. We usually switch off to a drug like Imuran. Azathioprine which is Imuran was FDA approved 25 years ago for rheumatoid arthritis. It was approved just before Methotrexate. It's effective in both systemic lupus and for rheumatoid arthritis. It takes a little bit longer to work than Methotrexate, but it's effective. Azathioprine/Imuran is also effective in lupus, lupus nephritis, blood manifestations of lupus, brain manifestations of lupus.

So I would consider the combination of Plaquenil, Imuran, and Prednisone and tapering down the dose of corticosteroids. And managing or trying to manage the arthritis with Imuran because it's an effective anti-arthritis drug. Interestingly, Selseb (ph) the other drug that's used a lot in lupus these days is not effective in joint symptoms. It was studied in rheumatoid arthritis and found to be ineffective.

So I usually use in a person who has a lot of joint problems a combination of Imuran and Plaquenil which have both been used in RA and taper the corticosteroids. And also the Imuran and Plaquenil will be helpful in treating lupus in general.

Unidentified Participant: Okay. Thank you.

Dr. James Curran: You're welcome.

Unidentified Participant: Hello?

Dr. James Curran: Hello?

Unidentified Participant: Hi, I have a question.

Dr. James Curran: Sure.

Unidentified Participant: My lupus seems to effect -- I have CREST.

Dr. James Curran: Okay.

Unidentified Participant: But I seem to have lately mostly lung issues. I finished nine months of TB. God only knows where I got it. I haven't been anywhere. Now I have ILD, interstitial lung disease. And all these doctors that I see: the cardiologist, the TB doc, the pulmonologist, now a critical care pulmonologist. They all have different things -- doctors that they want me to see, specialists, or procedures. And I don't know who to listen to. I mean one wants me to go to Northwestern. One wants me to go to University of Chicago. Another to Loyola because they can't do anything for me out here in the northwest suburbs.

Dr. James Curran: Okay, so do you have CREST or is it Lupus or a combination?

Unidentified Participant: Both.

Dr. James Curran: Both.

Unidentified Participant: Both.

Dr. James Curran: Okay, down where I hang out we see lots of interstitial lung disease, tons and tons. The specialty or one of the specialties I work in is inflammatory muscle disease and interstitial lung disease. Now CREST or CREST variance scleroderma usually if it's by itself is characterized by finger changes, Raynaud's Phenomena, a bad esophagus, and no interstitial lung disease. So that interstitial lung disease is not really part of CREST.

Lupus can give you interstitial lung --

Unidentified Participant: (inaudible). Sorry.

Dr. James Curran: I'm sorry. Go ahead.

Unidentified Participant: The interstitial lung disease is more recent. In fact, I'm on oxygen now since Labor Day.

Dr. James Curran: Well, CREST usually doesn't do that. Lupus can, Children's (ph) can, rheumatoid can, all of our other connective tissues diseases can give you interstitial lung disease. And in general there are two types, and I didn't make up these names, the pulmonologists did. One is called UIP, the other is NSIP. USIP (ph) means usual interstitial pneumonitis and it is a more scaring and fibrotic process which is difficult to treat. Capital NSIP, which is non-specific interstitial pneumonitis is inflammatory, and responds better to combinations of medications such as CellCept and Prednisone, Azathioprine and Prednisone. Those combinations work well in NSIP.

So what you do depends upon what your CT of your chest shows what the predominate lung disease you have is. There are some people that feel that NSIP will transfer to UIP and when you have complete fibrosis your response to medications isn't particularly good.

In terms of how you work that up, you do a CT Scan of the chest. You do pulmonary functions with the diffusing capacity, and you do 2D echo cardiogram to kind of establish a baseline. You treat aggressively the lung disease because that is the determining factor in terms of how your lungs are doing.

So that becomes the predominate feature. The muscle disease, myositis, arthritis, rash, all that becomes secondary to the lung involvement. And everybody focuses on that immediately. And the UFC they've got a big interstitial lung disease clinic that we deal with. Where the pulmonary department has an ILD clinic. But it sounds like you have an overlap connective tissue disease with lupus as one part of it and CREST as another part of it. Does that answer your question?

Unidentified Participant: I also have pulmonary hypertension.

Dr. James Curran: The pulmonary hypertension it can be either primary, which doesn't sound like it, or a secondary which is related to scar tissue from the interstitial lung disease. CREST patients with CREST have a clear chest x-rays, and develop pulmonary hypertension related to CREST and it's vascular. It has nothing to do with interstitial lung disease.

Patients with lupus and scleroderma and rheumatoid will develop pulmonary hypertension because of scar tissue in the lung. And the name of the game there is to prevent further scaring in the lung to keep the pulmonary hypertension from getting worse.

Unidentified Participant: Okay. That's good. I think I know where to go now or have the --

Dr. James Curran: Okay.

Unidentified Participant: -- (inaudible) treated. Thank you.

Unidentified Participant: I have a question.

Dr. James Curran: Yes, ma'am.

Unidentified Participant: I have diffused nephritis. I had my second kidney biopsy recently and this time around apparently I have CREST since (ph).

Dr. James Curran: (inaudible)

Unidentified Participant: Yes, but nomenclature is normal. My kidney function has always been normal. I was initially diagnosed with Class 4/5 lupus nephritis five years ago. My doctor, and we haven't pursued this, but his recommendation is to go with Cyclophosphamide but I'm a little bit leery of that because of the possible side effects and me wanting to have more children. My question is do you know of any studies that supports the effectiveness of another treatment like Rituxan or anything else other than Cyclophosphamide?

Dr. James Curran: Well, it depends upon who you are in terms of what your race is. It depends upon how old you are in terms of child bearing and Cytoxan. Patients in their early 20's can get Cyclophosphamide and have no real problems with fertility. Patients in their late 20's and early 30's are more likely even with trying to protect the ovaries with having problems with Cytoxan induced ovarian failure. So a lot of that is age related.

I'm old enough that I was around at Bethesda when the NIH was doing the original Cytoxan studies in lupus nephritis Class 4 and nephritis about 25, 30 years ago. And basically they used high dose Cyclophosphamide, a gram roughly a month times six months. And then every three months or 18 months. And it was effective, but not curative in some people.

So you treat them and then have to retreat them again. And of course everybody's concerned about Cytoxan side effects. So that has led to two pathways. One is the Euro-Lupus protocol where the Cytoxan dose is much lower. It's like 500 milligrams every month or so. A lower dose for a shorter period of time. And then a switch to a drug called CellCept and CellCept maintenance. That is compared to CellCept alone in lupus nephritis.

And in certain populations CellCept is as effective as Cyclophosphamide in lupus nephritis. So we're talking about a dose of CellCept of approximately 1500 milligrams twice a day.

Unidentified Participant: That's what I'm on now.

Dr. James Curran: The original lupus studies with Cytoxan used Azathioprine as a maintenance medication. So these days if you're African-American you're not really going to respond that well to Cytoxan. So they use CellCept primarily. It works better than the Euro-Lupus protocol.

Unidentified Participant: I'm Asian.

Dr. James Curran: Well, okay.

Unidentified Participant: If that matters.

Dr. James Curran: Yes, and so your choices are the Euro-Lupus Cytoxan protocol which is low-dose Cytoxan with CellCept maintenance. Or trying CellCept as primary therapy. And we've had people all over the lot (ph). I've had good results with CellCept in lupus nephritis.

Everybody's concerned about the side effects of Cytoxan. The dose of Cytoxan in the Euro-Lupus protocol is much less. And it is as effective as similar to CellCept. Both these drugs you can't get pregnant on. Both of them are class D or whatever. They cause problems with birth defects so you can't use them.

Rituxan is interesting. Rituxan probably is as effective in certain subsets of patients with systemic lupus, but it has not been approved for overall care. So depending on what kind of lupus you have and what's involved some people respond to Rituxan. Right now it doesn't have the FDA approval for a lupus nephritis. So your choices probably are the Euro-Lupus protocol or CellCept. And a lot of people would opt for the CellCept. It depends upon obviously what your kidney function is now.

If your kidney function is normal and you have no significant proteinuria (ph), CellCept is probably reasonable treatment because of the fact that you've got some time. If a patient has severe lupus nephritis and has a creatinine (ph) of 2.5 and acute renal failure most people would use the Cytoxan protocol. So it kind of depends upon where you're at. And nobody these days for the most part uses the old NIH protocol Cytoxan unless the individual has vasculitis.

Unidentified Participant: Okay, thank you.

Dr. James Curran: You're welcome.

Sonya Loynachan: And do we have any other questions?

Unidentified Participant: No.

Dr. James Curran: Hello?

Unidentified Participant: No, well let me ask one other question. I have a vascular necrosis of the hips and the shoulders. And is it possible to get AVN in the pelvis bone or lower back also?

Dr. James Curran: Well, you can get avascular necrosis pretty much anywhere in your body. I've had people with lupus who -- first of all avascular and necrosis has several causes. One of the most famous causes is a brief course of high dose Prednisone. I've had people who were treated for asthma in childhood with high doses for a week or two develop avascular necrosis as an adult or become symptomatic as an adult.

Lupus itself can be a cause of avascular necrosis if it's associated with Antiphospholipid (ph) Antibody Syndrome. So that's also a cause. The common locations of avascular necrosis are the hips, the shoulders, I've seen it in the ankles and feet. I've seen it on both sides of the knee joint, the tibia and the distal femur. I've seen it in the wrists.

So to answer your question, you can probably get aseptic necrosis in just about any set of bones in the body. Again the common most (ph) locations I've enumerated, but I've seen it pretty much everywhere.

Unidentified Participant: Okay. Do you recommend shoulder --

Dr. James Curran: Well, let me just --

Unidentified Participant: Oh, go ahead.

Dr. James Curran: Go ahead. I'm sorry. Excuse me, go ahead.

Unidentified Participant: Do you recommend shoulder replacement at all?

Dr. James Curran: Okay, they've come up with new shoulder surgeries. It's called a reverse shoulder. They put it backwards. They used to put the stem in the femur, and now they put the stem up higher in the shoulder. It's become highly effective. It's become the method of choice for most shoulder surgeries depending upon anatomy.

But to directly answer your question, the indication for shoulder surgery is always intractable pain. Pain is the indication that you're looking for. You're not ever going to get your full range of motion back with a shoulder replacement because the joint is just too complex. But you should get nice pain relief, and some function in the shoulder. But you're never going to get your full shoulder motion back.

So the newest prosthesis that they have on the market seems to be quite successful. I've had four patients that have had that surgery, and it's been effective in all of them.

Unidentified Participant: Okay, thank you.

Dr. James Curran: If there are no other questions, I was handed a list of four questions that were forwarded earlier in the day. And one of the questions, are there any specific actions or guidelines

lupus patients should follow for best protection and/or prevention of an infection and complications?

That kind of is a difficult question. And just basically harkens back to general health. Making sure your vaccinations and flu shots and pneumonia vacs (ph) are up to date. If you're not on immunosuppressive medications, I would recommend the shingles vaccine. I would get the Tdap vaccine if you've not had it because again of the recurrence of Bordetella pertussis. And that's basically what you would do.

The second question, is to prepare for an initial evaluation what health and personal information would be most helpful to medical personal to ensure fastest, safe, best treatment and recovery? Basically, when I see a patient for the first time for SLE or for evaluation of a connective tissue disease I'm very interested in the family history.

I want to know your entire past medical history. You may not think it's important that you had a joint infection or a joint infusion 20 years ago, or that you once upon a time had diphtheria, etcetera. All those things in a person with connective tissue disease are relevant.

The family history, any past medical history, any current medications, any current problems. Any medication allergies. In order to be effective as a rheumatologist you have to be an effective internist. You have to look at the entire patient. You have to look at their entire medical history. You have to gauge your treatment based upon what you find in the individual.

Treatment of lupus is an individual process. Yes, we have a variety of medications that we can use but it's an individual. There's no cookbook for treating this disease. It depends upon what you present, and what other organ systems you have that are involved.

The third question is with whom should treatment be initiated for a suspected organ-assisted involvement? I tell my patients who I have on immunosuppressives if they have a problem I need to hear about it. Because I'm the one that's been managing their immunosuppressive medications. I know what their allergies are.

I consider any fever or bronchitis or a sinus infection significant in a patient on immunosuppressive medication. And I'm much more inclined to treat aggressively with antibiotics in that individual than someone who does not have those problems.

Any other questions?

Sonya Loynachan: Since we don't have any more questions, we'll go ahead and wrap up the call. Thank you very much, Dr. Curran for presenting. You gave a lot of useful information.

Sonya Loynachan: We will have a transcript of this teleconference. It will be posted on our website within the next few weeks. Thank you!