Okay, so these are going to be the practical questions that I’m going to answer for you because you know and I think most of the speakers have done a great job of giving at least me information that I can use. So question number 1 is when should I order an ANA? Number 2 is does lime disease occur in Western Pennsylvania? Number 3 is does this patient with dry eyes have Sjögren’s syndrome? And number 4 is how long should I treat somebody with polymyalgia? Now those may seem like very divergent topics, and in some ways they are but I want to show you how actually they are very, very similar. And when we talk about this I want to just give you a perspective of how we as rheumatologists think. I think that’s helpful because if you compare us for example to the orthopedic surgeons, orthopedic surgeons are very mechanically oriented. They are carpenters and they look at the joint and if they are not good carpenters just like with a carpenter the door doesn’t work. You know that is how they think about diseases. We think about them differently. You know we look at this whole multisystem versus localized disease. I’m going to talk to you about disease mechanisms, it’s something you had – was touched on in many of the talks, this whole issue of correlating findings clinically with others, then with us as rheumatologists I’ll talk to you about this evolutionary course, a little tincture of time and then how we target our treatments.

So in order to understand this evolution I like history, and I just want to put this into perspective just to give you an understanding of why we are going to be talking about this today. If we take a look, a fact that is really pretty amazing to me is that it wasn’t until the 1880s that gout, rheumatoid arthritis and osteoarthritis were separated. Well those are tremendously different conditions and so when we think about them and we look at rheumatology we are the youngest of the disease organ system specialities. It was 1927, Mayo Clinic and NYU.
And we are going to be talking, I just put the diseases we are going to be considering today. Sjögren’s syndrome, Henry Sjögren described clinically this group of individuals who had dryness of their eyes and mouth and rheumatoid arthritis and exactly where it fit in was not very clear but there was a wonderful observation, a man named Klemperer in 1941 introduced the term collagen vascular disease. There was a great article in JAMA and he was the first pathologist to realize that there were similarities among these conditions, rheumatoid arthritis, lupus, scleroderma, myositis, the vasculitides and rheumatic fever. Think about that by the way, when was the last of rheumatic fever you saw? You haven’t seen one, and I’ll talk to you about that a little bit as we go through about the evolution of diseases.

But Klemperer recognized that there were similarities, there were abnormalities in what he called the collagenous connective tissues of the body. He realized that there were vascular abnormalities seen. Well it turns out that isn’t exactly right, the only collagen, the collagen disease is Ehlers-Danlos Syndrome, so these are not diseases of collagen per se. Scleroderma has an increased amount of collagen, and they are not vascular diseases directly per se. But it was a great concept to put these conditions together, they do have one thing in common is they have inflammation that they have an extended course.

If we go down there is really a remarkable occurrence in 1948 and that was Dr. Phillip Hench, he is the one holding the hand. He introduced steroids, he was at Pitt, he trained, he went to Pitt Medical School and won the Nobel Prize and that was a remarkable, a remarkable addition to our
armamentarium. We had really very little to treat diseases. It was thought actually it was a cure, but the problem was with these collagen vascular diseases, with these conditions we really just didn’t have a way of looking at them. We didn’t have a way to identify them. You know it was William Osler who we heard about before, he was the one who added the term disseminated to lupus erythematosus, it was thought to be a skin disease prior to Osler.

And it was in 1949 where Hargraves at the Mayo Clinic, a hematologist who was studying blood diseases in patients with lupus happened to leave a tube of the bone marrow in his pocket, and later that day he looked at it and saw some cells that I’ll talk to you about and that was the LE cell and that was, that and the rheumatoid factor came right around that time.

Polymyalgia rheumatica was not even described before 1957, Barber described it. And like Henry Sjögren how did this happen? Well we were very dependent on our clinical findings and we just didn’t look at these conditions affectively pathophysiologically. The same is true with lyme disease, there were a group of women who brought their kids to Allen Steere who was a rheumatologist at Yale with the juvenile inflammatory arthritis and these unusual skin lesions. And he was the one who described lyme disease. Now it did not begin up there, lyme disease has been described well since the 1600s and we’ll talk to you a little bit about that, and we’ll talk to you about the last concept that I really want to make sure we think about and that is how to treat to target. The dilemma though is you have to know what the target is.
So I love titles and so that’s why I caught – and Dr. Holman who was head of Rheumatology at Sanford had an article in 1994 and it’s a very important article to me, it influenced my life. And I love titles as I say and it was thought barriers to understanding rheumatic diseases. What was the problem with understanding these diseases? And when we think of the thought barrier number 1 is about this single lesion causation. The classic example is this, you come in with a pharyngitis and we look over here, we see the streptococcus in there and so that that’s the single lesion. Now that’s a challenge because are these conditions a single lesion? And I’ll show you how actually they, they very likely may be but here is the challenge, and the challenge is this, and the challenge is that when we take a look at individuals and we have the individuals, we have if we look A is one group and then B, these people are genetically similar and when we take a look at the time to clinical manifestations what we see is that we have these environmental triggers and then when we look at them the question is how many triggers we have does it take to start the problem? You know I think when Larry Moreland talked to you about rheumatoid arthritis one of the unbelievable advances is that rheumatoid arthritis is a condition that if treated early we can stop it. If it goes on it develops a life of its own.

And when we think about this whole situation you know we have the second thought barrier is we use acute disease models to explain chronic diseases and that’s just not correct. You know if we look at whether it be an infection or a broken bone or removing a diseased organ like an appendicitis that just isn’t how rheumatic diseases behave. You know we just don’t have something where there is a pustule there and we take care of it. That acute model is not correct and if we look at the last is that we kind of study these in an isolated fashion. You know this is just a case of lupus going from
99 over here and all of the changes and blood studies or the clinical picture. Well I’ll tell you our clinical trials just look at very, very small periods of time, sort periods of time in these diseases. And really there the last good study of the natural course of rheumatoid arthritis was a study by Short in which he looked at rheumatoid arthritis over 25 years, and that was – it ended in the 1950s, so we have no studies that actually look at these diseases over long periods of time.

And then we – the whole other issue is confounding issues with these diseases. You know whether it be confounding environmental triggers, you know different drugs or whether – you know we heard about smoking, smoking is a big deal. And smoking is a big deal with rheumatoid arthritis and how they interact with the genetic influences. You know I thought a very important question was asked about prostate cancer, I mean how do we understand it? Well somehow I mean cancer is a genetic disease and these are in part genetic diseases, how do those factors, whatever exogenous factor comes into play how does that influence our gene because when we look at these diseases as I’ll show you we go from asymptomatic to severe. And we have all of these different manifestations, this course of the disease. I’ll tell you the bottom line is this, among all of us and we create the pathways that are being talked about, whether it be low back pain, you know the most important thing in low back pain is time, how long it’s been there. If it’s been there for a while it’s a problem. And so we need to be able to look where to make an intervention, and that really is a challenge.

So here it is, I finished my Fellowship, I’m walking out and Dr. Mickey Golomb said to me this statement, I must say my watch didn’t quite look like this, but he said to me, Terry he said don’t every forget, he said some diseases and he pointed to his watch you tell time on the watch your
watch like gout and the rest we see them very acutely, but others you tell time on the calendar. Now I’m as impatient as anybody else, and you know I see a lot of people every day and I want to get their problems solved, one of the difficulties with this disease category is the unpredictability, there are so many different variables involved here and when we take a look at these mechanism of disease you know we have all of these different mechanisms but these are the ones I want to talk to you about. Inflammation is something that we have to help you understand. And I’ll tell you think of all the diseases we have heard about and something that I don’t know when I, I mean obviously from what I do inflammation is important but it is – think about how we used to think about atherosclerotic heart disease? And think how we think of it now? It is an inflammatory lesion within that blood vessel wall. Why does it happen?

You know you heard about the – in looking at adding the CRP now you know what CRP, C-reactive protein, that happens to be a reaction against the C, the carbohydrate, R you know that’s – it’s against the C-reactive area of a pneumococcus, the capsular region. And it’s a very nonspecific reaction that just represents inflammation, because when we look at this it’s a very complex biological response and it’s our body response to harmful stimuli. And we have these classic symptoms we see, but remember about the immune system. I’m going to show you a couple of slides, and about those slides that show how we recruit our immune system into this and that immune system is important because that is to try to get away, get these injured – injurious stimuli especially infections. Remember our immune system is setup, it is setup primarily to fight off infections. So it recognizes quite simply the different organisms out there, it represents you know the structures of the cell surface primarily, and it recognizes this and makes a reaction. The problem
is when that inflammation is not shut off, and I don’t care whether it’s in your joints or your bowel or wherever it is not good because that results in damage. And you know we think about you know having some injury such as this, this is pretty simple. And I put this in just because you know you have a thorn prick and you have this reaction. The problem is we don’t know with most of these conditions what the thorn is, and why is it? Is it like with Allen Steere you know we just didn’t understand that the ticks with the Borrelia Burgdorferi organism and that is it. We will learn what the organisms are, and we are going to learn them and I don’t think it’s anything new, it’s not like Aids, it’s not like some new organism comes here.

Here is an interesting fact though, there is not a case of rheumatoid arthritis before the 1600s, that’s it. They’ve identified all the other kinds of arthritis but – and it’s just like the fact that we don’t see rheumatic fever now. You know I think what we are seeing is that these changes in the environment in terms of these environmental pathogens and you know as I say that certainly is the case. You’ve seen slides like this, but this slide shows us when there is this injury up here we then get into this very, very complex situation and we have all of these mediators. What’s so unbelievable we can now target them. You know the TNF drugs and the rest that is amazing to be able to target and it makes a lot of difference. The problem is that that immune response has tremendous variability, not only as to how it responds to a specific stimulus but in because of our genetic variations. And then we bring into play all of these other parts of the system and so then it becomes quite challenging. The bottom line message is chronic inflammation is an essential element to many of the diseases we take care of, so we need to think about it and we need to think about whether it be in the arthritis type categories or for with any of these others. We need to think that that’s the mechanism that we
are really focusing on because when we look at RA as Larry was talking to you about, when it goes from here over to here you know we don’t see this too much anymore, at all anymore. But this is the synovium and this is the damage the synovium actually as he said, like a low grade malignancy eroding into the bone right there. Now we need to stop it, the sooner we stop it the better.

All right, so with that background I want to talk to you and show you kind of how we think about you know four different areas, ANAs, Sjögren’s syndrome, polymyalgia rheumatica and lyme disease. There is a lot of similarity in there and I want to give you some take home messages.

So ANAs, just think about them, they are antibodies directed against certain macromolecular components of the normal cell nucleus. What is amazing about ANAs is as opposed to carbohydrates and proteins which we can – our body relatively easily makes antibodies against them. You know if we look at the antistreptococcal antibodies and all the rest, those are pretty easy. But we don’t make antibodies well against nuclear material. So what is it, what is it that causes those to be made? And I’ll show you about them because one fact is that you know many of us make a small amount of them and so what does it mean when we have these antibodies? And when we take a look and go back to Hargraves Mayo Clinic in his coat. He looked at the bone marrow and found this cell, it’s a polymorphine nuclear cell that has this glop of stuff in there. Well it happened to be that he had it in his coat and it was actually on the inner part of his coat so it was warmed up a little bit and that is a DNA histone released because there was some breakdown of the cells and it had an anti-DNA histone antibody, an antinuclear antibody. Now this was a revelation of being able to diagnose lupus, to be able to look at the spectrum of this disease, to identify people with a test.
And so after that it was certainly quickly determined that it was an antibody that caused that reaction and so now we went from there to a situation in which we had an identification of the different components because we make a lot of different kinds of antinuclear antibodies, they are directed against various macromolecular components. So if you take that thought and just remember that we’ll show you how to remember about this.

I just want to show you for a moment about how indirect immunofluorescence works because it’s important when you are interpreting a test. This is the way we detect these. And I’ll show you on the next slide and because these antibodies they you know you have a tissue and they will bind to that tissue at the particular sites. And so we look at the amount and we look at where they are attached, and so the amount it’s just you titer the blood, you know a 1 to 40 is diluting the blood 1 to 40. Obviously the detection of them in the higher dilutions means that more are there of the antibodies. So remember one thing, 1 to 320, actually 1 to 640 is kind of a cutoff, I mean below those the clinical significance is pretty marginal and so when we look at it here is how indirect immunofluorescence works, it’s very simple. You have a tissue, and you know they used to use mouse liver, there are all kinds of different and you take a section of it. And so when you section the tissue you expose those nuclear antigens, you put the patient’s serra on there and if there are antibodies directed against exposed antigens they will attach. So how do we pick them up? Well there is another anti-human antibody that you have fluorescein attached to it and that being the case that you will see a pattern and that’s it. Now this is – I remember going through this, this tortures you, this is my rheumatology board knowing all of the different patterns. You don’t have to know
all of those. But the reason why I left this in though was look at all of the different kinds of antinuclear antibody possibilities there are, but these are the ones we deal with primarily.

So you are going to get back and you order an ANA, we’ll talk about who you order in a moment, but you get back an ANA and there are going to be one of four patterns, homogeneous, speckled, nucleolar or peripheral. Now homogeneous is the most common and this just means that there is this anti-DNA DNA histone antibody in there and this is what we see in lupus, we see it, but you see it in other diseases. Like we see it, as Larry said to you, in rheumatoid arthritis. Why are some people with rheumatoid arthritis clinically relatively the same disease but they have this – they have a rheumatoid factor or a CCP. And what does ANAs mean in lupus? And that’s hard to say exactly what that means.

Speckled is very interesting because this pattern, and we see it certainly also in patients with lupus but we see it in Sjögren’s, we see it in this overlap of the connective tissue. MCDD is an overlap of myositis, lupus and scleroderma. Now we don’t see it very often but you have all of those different features; and again Larry when he brought out that with rheumatoid arthritis we see individuals who have this whole variety. Nucleolar is very uncommon, this is against the nucleoli, but this is very suggestive of scleroderma.

And then lastly the peripheral is pretty specific for an anti-double stranded DNA. So that’s – that’s not to torment you with more than you want to know, but it just shows you that’s what the patterns mean to us. And so but remember healthy normal people can have antinuclear antibodies. And so
you know 20% have a little bit, 5% can have 1 to 160, as I said to you going up to the 640 is usually increasing age our immune systems change as we get older. And there are also gender differences. It appears that estrogens have some influence on that because if we look at increasing age we have increasing frequency of ANAs and women have more than do men.

Here is an important point though, remember if somebody’s relative had lupus they have a much greater chance, but they don’t necessarily have a likelihood of having a disorder again depending on the titer. Remember these ANAs are certainly not specific, and so you know that’s why we really need to look at these clinical features that the patients have. And again these slides are – you have – I just wanted to show you that you know the sensitivity you know of you know how many – how good they are at picking up the disease and how specific that is to ruling out other diseases you know there are lots of issues within these. So as everybody has emphasized in their lectures, we go look at the patients and make sure. But honestly with lupus just to take away the bottom line with lupus is the ANA is almost always posited higher than 1 to 640, there are some patterns if you have the double stranded DNA, that’s the peripheral pattern that we see. The SM pattern, SM by the way stands for Smith, that was the woman who it was first found in. And that happens to be again that’s a speckled pattern. And by the way people with lupus they make multiple different antinuclear antibodies. They don’t just make one of them. So that does give you that idea.

This though I find to be intriguing and Larry showed you a little bit on rheumatoid arthritis but having auto antibodies before the onset of lupus and there is a large pool of serra that exists out there in the military and that’s where all these studies come from. And it turned out that in this 130
patients with lupus 88% had at least one auto antibody you know up to 9 years before the diagnosis. And that’s intriguing, and so as I had showed you before in terms of this thought barrier what was the stimulus that started the process? And you know that’s what we really have to think about. It certainly seems that there has got to be some infection and whether – it’s hard to believe that there are going to be conditions like Legionella you know that in 1978 when they had the Legionnaires’ Convention the reason why it wasn’t described it just wasn’t easily grown on culture. And so but it’s not a new disease. I just don’t think that it’s going to be a new virus or a new something, the real question is how do you know given the genetic situation how does that predispose some individuals and then there is some stimulus. And remember it’s interesting about this is that the higher the titer was very important, and we could see all these different types of auto antibodies. You know the antidouble stranded DNA really does have more of a correlation with renal disease for example, and so but it just wasn’t that, it was all of these other ones. Look at this whole dilemma when you order a coagulation profile and you get antiphospholipid antibodies, whoa, you know that’s a problem because most of those people are just not going to have any difficulties.

So the take home messages here you – and I think all of us here are pretty good at this, make sure we look at this clinical evaluation. You know you’ve got to have people who have inflammatory polyarthritis. A little interesting thing if you’ve got inflammatory polyarthritis and Reynaud’s phenomenon, boy that segregates much more to lupus than rheumatoid arthritis for example. But you know you just have to take a look at those clinical manifestations of the disease because ANA testing has really a very low specificity and a positive predictive value, it’s just not good you know as a screening test. It should not be used in that way because you know you can see ANA positivity
in you know in other connective tissue diseases certainly. And we can see them like in autoimmune hepatitis, that’s another situation. So if you think about it, injuring cells probably is what is responsible for exposing the antigens and I’m going to show you how that is probably true in some of these other conditions we are going to talk about.

Okay, so remember that there are some more you know that are specific you know, but let me just suggest to you, this is not something that – it is really challenging even for us as rheumatologists, so it’s okay to get a screening test but before ordering a lot of the other anti-DNAs, SMRMPs etc. I think you know unless you feel very comfortable about that I think I would consider rheumatologic consultation. Because you know you just have to correlate these with the clinical symptoms and some of them are pretty challenging.

Okay, so let’s look now at Sjögren’s syndrome. Sjögren’s syndrome has always intrigued me because you know this is an American College of Rheumatology slide, bit parotid enlargement. You know I’ve seen a couple of people like that, but I’ll tell you, a lot of people have dry eyes and dry mouth. And Sjögren’s syndrome is something that’s very intriguing because it happens to be a situation in which there is inflammation occurring within glandular tissue. So take this message away you know just we accept that atherosclerosis for goodness occurs in blood vessel walls, so Sjögren’s occurs in glandular tissues. And kind of the message is that inflammation will – I mean inflammation is inflammation no matter where in the body within a range, and it somehow localizes for reasons that we are not totally clear of in these particular systems, organ systems. And so it’s an xerogram because we see it not only in the eyes as here, the eyes but we could see it as here as a
primary condition but we can also see it associated with other rheumatic diseases. Now everybody with RA doesn’t – we used to do lip biopsies which patients weren’t real wild about having you know in patients, and a lot of people with – the reason we don’t do them is that they are not very helpful. But it is interesting that those who have primary without other connective tissue disease really have much more sicca, dry eyes, dry eye symptomatology. Again this tremendous female to male predominance, and it tends to occur in older decades of life, again reflecting changes in our immune system over that time.

Another point that I want to show you about which all of us have to do, and these guidelines like we see, like the low back pain, you know it has to be in the electronic record, we’ve got to put these guidelines in there. It was like Larry showed you, even we as rheumatologists I’m sure can – that it’s hard for us to remember all of the number points and the rest of how that – and so all of them should be in there because I’ll show you the ones for Sjögren’s, they are actually pretty useful and that’s why you know we don’t know exactly how often it occurs because when we think of this dry eye you know we’ve got these different glands, the lacrimal glands, other ones that you know that cause our eye to have appropriate moisture within it. But I’m telling you, you have all of these different problems of you know Sjögren’s I don’t know, I don’t think it’s that common, but I tell you all of us see and certainly with aging I think hormones play a tremendous role you know when we get to be estrogen deficient and the rest.

So we need to have these criteria, and so you have ocular symptoms, dryness of the eyes, you know this is the Schirmer’s test, people are real happy to stick a piece of you know paper in their eye, you
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know that doesn’t – you know that’s not great so we don’t tend to do that. This is a sialogram so we don’t tend to do that. You know that shows abnormalities there. We don’t biopsy them. So essentially, so people have dryness of their eyes or mouth. If they have them get these tests. As I’ll talk to you about the SSA, Sjögren’s syndrome A, Sjögren’s syndrome B, those falls into the antinuclear antibody categories. If you have dry eyes or dry mouth you really should get them, they are not perfect but they do help you.

So and when we look at these SSA I mean these are a little bit – this is a different part that we are looking at in terms of that antibody and we actually have a lot of knowledge of where that’s directed but how they are involved in the pathophysiology is not clear. But they occur commonly in you know with Sjögren’s. So you should order both the SSA and if you have that they do have some, especially SSA has the correlation with extraglandular features. But what is so interesting is if the mother has – you know if a mother has SSA positivity their child can have neonatal lupus and they can have congenital heart block at birth because that antibody reacts against the conducting system. Think about rheumatic fever, you know so we are looking at – you know you don’t want to have antibodies directed against, so that again puts that into a situation somehow where you – where in these glands, we have this inflammation going on and we have these antibodies and if they attach to certain parts of our body they can really do lots of damage.

SSB antibodies you know should also be checked for, but and if you happen to have both of them it tends to be more severe disease. What Larry says is correct though, we just don’t understand pathophysiologically. And when we look at the etiology you know there is no question about it, we
can take a look at our – the major histocompatibility complex on the 6th human chromosome, I mean that’s you know you get HLAB27 that’s where you know we are looking a the 6th human chromosome and that happens to be where that’s all regulated and so you know there is something about this immune regulation occurring there and then we get these, somehow these triggers. And something appears to damage the cells, and once those cells get damaged antigens are exposed and the inflammatory reaction has started like this, and these are the foci of it. But look at this, the rest of the gland is pretty normal, and that’s interesting of what’s going on there and it’s been looked at and we don’t know exactly because you know you can individual lobules get destroyed, but these patients retain a fair amount of normal tissue. And I tell you that because try to have them focus with dry eyes and dry mouth upon the fact that you know all you need is a little extra amount of fluid there in the eye or the mouth. That’s why I use with dry eyes you know have them use the liquid – the Tears frequently. And it just drys – it helps them enormously in that.

And you know one of the other things that is so interesting it’s just not that, the inflammatory cytokines they also have other effects. And like for example they impair acetylcholine release, they interfere with the neural stimulation of glandular secretion, so it’s really an interesting situation. So those neural mediators are pretty big deals in terms of the whole situation. Do remember one thing with Sjögren’s syndrome, and if you have people with primary Sjögren’s I mean they can develop other connective tissue diseases but this is what we worry about, these lymphomas. And I mentioned to you about SSA and heart block. So we are almost done.
So you are starting to see how you can think about these relatively divergent situations. PMR is a very interesting disease, and PMR is not rheumatoid arthritis because PMR is this inflammatory disease that occurs in people over 50 and it just does not occur in younger individuals. We can see somewhere around 15 to 20% of RA presenting with shoulder problems, but I’ll tell you very quickly they develop peripheral joint involvement. And it’s a common problem and it tends to be you know with its peak in the 70s, more among whites, northern Europeans and women. And again this appears to be a situation where you have this genetic susceptibility, some environmental factors, I’ll show you it does something, and we’ll show you what it does.

And so when we take a look these – you have a patient come into your office and they’ve got shoulder and hip girdle stiffness, and I’ll tell you what’s so remarkable about this disease it comes on pretty quickly. RA is very insidious in its onset, just people don’t know the day it began. Some people actually wake up with this in the morning and we see although there is no diagnostic tests, we don’t have a rheumatoid factor or ANA or whatever but this clinical presentation, this and some people have more shoulder involvement, some people have more hip girdle involvement, a lot of people have both and it begins there. It’s a dilemma I’ll tell you when they start having some peripheral joint involvement. It really worries me that you know that there may be rheumatoid arthritis there.

Our treatments aren’t terribly – they are different in the sense that we use much more steroids on this than we do with RA. And you know and remember one other thing, this fever, malaise, low grade fever you know there is a systemic reaction that these patients are having. And but it’s not - the
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problem is it’s myalgia but it’s not there because this is inflammation at the synovium and bursa and this just shows you, you know these are some studies that just – the inflammation is right in there. It’s not a muscle disease. And it doesn’t cause weakness. Remember polymyositis causes weakness, it doesn’t have much pain and so but the really the challenge is what’s the relationship between polymyalgia and giant cell arteritis? And I tell you this is you know it’s a real challenge.

There was an autopsy study done in Sweden, and they do autopsies on everybody and it turned out that almost 2% of individuals over 70 had asymptomatic areas of giant cell arteritis in their aorta. That’s nice. So it really is. And so I think this happens. And I’ll show you where it happens in a second because when we take a look at this they do occur together, but I can give you a take home message, it doesn’t happen often. Okay, we used to do temporal artery biopsies in everybody with PMR, and you don’t need to do that because the studies don’t suggest that this clinically that they have a problem. But there is no question if you have pure PMR you know you can see it and 4% is what the studies are.

And here it is, it turns out that if you look at the internal elastic lamina all right, you know with giant cell arteritis it doesn’t occur inside the vault and the reason it doesn’t is because when your arteries penetrate the vault you start losing your internal elastic lamina, and that’s one argument. And if you take a look at this you can actually find these giant cell occurring right at that internal elastic lamina. And so that’s it. Somehow that antigenic material has been exposed. This is a different type of reaction, giant cells are coming, it means that we just can’t process that in the same way. This isn’t an antibody related disease. But it’s interesting that these – this is – PMR is self-limited. And it goes
away, RA doesn’t go away. Once it gets going for a while it just – it’s hard to stop and these people and so you need enough Prednisone, at least 20, I tend to start out with 35 and then you slowly taper them by 5 mg every 2 weeks down to about 10 mg then we go down by 1 mg because if you go too fast it comes right back again. And you know it’s amazing, and non-steroidals do work but they don’t work until it’s been reset. And so you know this is said the average length of the disease, I think if you treat people effectively there are few people that we have to use other agents like Methotrexate with. And remember it is interesting, there is this suggestion that the fact is that they may have a little bit elevated bachelor disease and that’s why we don’t like using steroids particularly for atherosclerosis. Remember one other thing about aneurisms you know these patients may have an increased frequency of aneurisms because of inflammation. This is the differential, I’m telling you that the – you don’t see bilateral rotator cuff tendonitis, there are very few. Most people who come in with bilateral shoulder and add hip girdle to it they’ve got PMR.

All right our last little topic is lyme disease. You know it’s a tremendous – it’s an unbelievable disease this tick, the Ixodes, it used to be called dammini scapularis, that’s the tick. So this is where it occurs. Okay, why does it occur here? And you know there are cases reported at least described apparently in the 1600s, you can go back there. And it turned out that back in the colonial days there was huge deforestation of all this area, okay when they were doing farms and all the rest. Remember Johnny Appleseed started here. Why did you need apples? Well you had to have apples because they just cut down all the trees and as part of your – in order to get the land claim you had to plant some apple trees, that was part of the deal. And so but and it was argued that there were just clusters
left of trees and so this is why – who knows? I’m telling you, fortunately it has stayed pretty much in that area.

Does it occur elsewhere? Well you know how do you know? I took this picture, this is the guy who goes out and collects the ticks, okay. You know Tom Mixer I think is his name, and so he goes out in the woods, collects the ticks and so if you look this previous slide was where you see lyme disease, this looks at the ticks. You can see it’s in the place, it’s really here and here is the big place. And why that’s the case is just not clear.

Does it occur in – these are the records from the CDC, okay. This is 2002 to ’06, these are confirmed cases, the question, it said that there are 25,000 cases in the United States, and it’s thought that there may be as many as 300,000; but I’m telling you if you look at here versus there is a lot in eastern Pennsylvania, okay. And Chester County, all the rest, it doesn’t occur here too often, if it did I think I’d see it, but I don’t know. So and you know unfortunately as I’ll show you so this is the tick, Borrelia Burgdorferi, Burgdorferi was the guy who actually was able to isolate the organism, and it’s from the bite of ticks. But just to give you a couple of facts so that – so that you know. So it’s the tick is the Ixodes Scapularis, so it’s on deer but the other reservoir are these little rodents, you know rats, mice and things such as that, and so that’s – I have a picture, I’ll show you. They can – and these little things are small, because it’s the nymphs that are the key. And so people actually don’t oftentimes see them. And they can be anywhere, and they’ve got to be attached for a while because they are eating. You know they have one meal you know as a nymph and you know and so they eat for a couple of days. And so it’s said that they have to be on there for 36 to 48 hours before
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that you know the bacterium is up in their pharynx. And so that’s what it has said. Most are by these immature ticks, actually it’s female you know for some reason more than male ticks. These are little teeny things, and it’s during the cooler months of the year. All right those are the facts.

Okay, so we have the rodents and you know we have this, that’s where they – and unfortunately that’s why when we are out in the woods because you have the deer and the rodents out there and so and the ticks are on the ground. You know they don’t stay on – it happens to be this is where – these are the – you know they bite them as well. And when they bite them, this is – you know this is the thing, this is what they look like, so it’s not very big. And this is what happens, that the burrowing in there and this is when it’s bloated up with – after it’s taken in the blood.

You can remember there are 3 stages, this is the one we are really thinking about, this erythema migrans I’ll show you about, and you can see a little of this stuff in the beginning early phase, the disseminated phase, because it’s essentially a bite and then it disseminates, it goes through your body. It is a spirochete, it’s like syphilis, treponema palatum, that’s why it was so hard to culture in looking at it. And so you get this rash, the rash is called erythema migrans, I’ll show you, you can with this 3 to 30 days after the bite. So if you see somebody and they’ve got the bite and you take it right out it’s likely they are not going to have it. You can give them one dose of Tetracyclline then and you know that probably doesn’t do anything but you know if you wanted to do – some people start developing these general symptoms you know and then we see this rash. But the rash only occurs, it only occurs in somewhere 70 to 80%, so people can have lyme disease. So if you are in an epidemic area, that’s why it creates a dilemma for us, this isn’t an epidemic area so people come in
and they’ve got this chills or fever, aching, you know if I was in New Jersey or whatever I’d think much more about lyme.

And we’ll show you about this rash. Okay this is the classic rash, you can see the little thing here with the bulls eye and the clearing. This is said to be the most common, you know this with more spreading, I’m sorry this is the most common here. It just—it doesn’t, it looks like a rash right there. So you’ve got to be in the endemic area indices.

What if you don’t treat it? Well you know if you don’t treat it it really can spread and so you know treating as you’ll see it’s 10 days of Tetracycline, you can use Amoxicillin, you know there’s nothing wrong with doing that. And these can—oh the Bell’s palsy headaches just because of the dissemination. And that’s what is so interesting about diseases. So if we look at lupus we look at Sjögren’s syndrome or whatever, inflammation occurring localizing in certain places depending on that organism. I mean how does it know to go to the facial nerve? You know how is it to know? But most of these symptoms resolve without treatment. But you know treatment is nothing.

So what about the test? It’s a two-tiered test and this is it. And so you don’t order both of them, there is an ELISA, an enzyme, and essentially this is not unlike the indirect immunofluorescence, it’s just you use an enzyme instead of the fluorescence. The problem is it’s not great, it can miss about—it’s only positive in about 65% of people. And so but the question is—most people are going to get better, you can treat them anyway and you can keep it from occurring so you know that’s the dilemma.
There is another test that we can use and you know and we – you know the ELISA tests they are pretty sensitive but they are not great and they are certainly not – because remember this Borrelia organism oh my gosh you can make – there are lots of different antigenic areas where you can make antibodies against. And remember this, you can make antibodies against bacteria in your mouth that cross react with it, that’s one of the problems. So that’s why you use this Western blot, the problem is it’s much more expensive and but these look at all the different antigens. The treatment is in there, it’s Doxycycline, you know you give 100 mg twice daily for 10 days, that’s it. And so you know one of the problems is these chronic lyme, I have to deal with this about you know – and as to whether it occurs – you know think about EB virus and CMV and stuff like that, I mean when people are infected with things they can have a systemic reaction, and that really is the challenge about it for all of us.

All right so what do we do? So now you see how I think about diseases, hopefully you know I wasn’t trying to be overwhelming I just wanted to show you kind of a potpourri of looking at things like ANAs. I mean you know that’s our body makes antibodies. Looking at inflammation, you know seeing in Sjögren’s syndrome I find it’s intriguing it occurs there in glandular tissue, taking a look at something like PMR, you know that’s – although we have muscle symptoms that’s occurring there, very treatable in terms of that whole situation. And then lyme disease which is intriguing.