Rheum-Optometry: What the Eye Care Provider Needs to Know
Course # 40037

Instructor:

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Section:

Systemic Disease

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COURSE DESCRIPTION:

A review of common rheumatologic conditions and their relevance to practicing optometrists. Topics include: Rheumatoid arthritis, spondyloarthropathies, Lupus, Sjogren’s syndrome, and the vasculitis conditions.

LEARNING OBJECTIVES:

• Be able to conduct and order appropriate diagnostic testing for each condition
• Be able to recognize common systemic and ocular signs/symptoms of each condition
• Become knowledgeable in regards to the pathophysiology of systemic rheumatological conditions
• Be able to refer/co-manage these conditions with appropriate specialists
Usually in the classroom I teach six lectures related to rheumatology and today I’m condensing it into one. I hope by the end of this lecture that you will learn a little bit more about why rheumatology is pertinent to optometry. I am originally from San Jose, did my undergraduate work in San Diego, I went to Pacific University College of Optometry and did my residency at the Portland VA. In my spare time I like to do anything outdoors – backpacking, camping, snowshoeing, etc.

Today we are going to go over a couple of the important topics in rheumatology and how it relates to optometry. I have no financial disclosures here.

Just a quick overview: Rheumatology is the study of inflammation of the bones, joints, and connective tissues. A lot of these conditions are autoimmune diseases. Rheumatology also covers vasculitis, or inflammation of the blood vessels, as well. About 1/3 of patients who present for their primary care exam have a rheumatologic complaint or diagnosis, especially with the aging population. You may also hear the term collagen vascular disease, which essentially is interchangeable with rheumatology.

### Rheumatoid Arthritis

A quick background on the pathophysiology for rheumatoid arthritis (RA) and on most of the conditions today. The most common type of autoimmune arthritis is RA. About 1% of the US population has this condition. RA specifically targets the destruction of collagen. Collagen type 2 is very abundant in the joints, as well as in the eye. Table 2 lists different types of collagen and where they’re located, and you can see that quite a few of the different types are located in the eye. Type 2 is in the joints, as the hyaline and articular cartilage, as well as in the vitreous. These collagen types do tend to overlap, so if RA is affecting Type 2 collagen, it could also be affecting Type 1 or Type 3. What happens is that we get an immune response from the B cells and T cells, creating a response of the cytokines like tumor necrosis factor, interleukin, some macrophages, which also signal the matrix metalloproteinases (MMP’s) to increase in the body. As we know, MMP-9’s are found in the eye, so a lot of these patients will have dry eye conditions, conjunctivitis, uveitis, etc. and there is an overall degradation in the collagen, which can also affect the eye.
RA specifically is a bilateral, symmetric condition that affects the periphery. This means it doesn’t really affect the central portion of the body, it affects mainly the feet, knees, hands, and elbows. It is more common in Caucasian females. Again it’s an autoimmune condition and most females have a higher predilection for those. The age of onset varies somewhat here, depending on when the patient was diagnosed. A lot of the early symptoms are hard to diagnose because the patient has diffuse joint pain but without a laboratory finding or rheumatoid nodules, which tend to happen later in the condition. With rheumatoid nodules, patients will get these palpable nodes on their fingers, hands, elbows, etc. The nodules are not tender and can ulcerate in severe cases. About ¼ of patients get these nodules.

Symptoms are worse in the morning and made better with movements. Some older patients have joints and aching pain who may have been exercising or working in the garden may think “Oh, this pain is just because I’ve been working in the garden or exercising more lately.” The difference is that if you have mechanical pain, it gets worse as you use the joint, and better with rest. This is the exact opposite of RA pain, where the patient wakes up with pain that resides after use of the joints.

It’s important to diagnose RA early because a lot of the damage is done within the first year and also, many of the medications used take anywhere from 3-6 months to work, so the damage is already done before the patient’s medications have even started to work in cases of late diagnosis.

Another thing to note here is patients who have a hard time gripping things with their hands due to advanced arthritis, it’s hard for them to put in dry eye drops. Or other eye drops, such as if they have glaucoma, for example. You may want to come up with alternative methods, such as surgery, if they can’t put the drops in themselves.

RA is not HLA-B27 related. It is a different HLA gene. (The HLA family is a set of genes that code for protein.) Specifically, RA is HLA-DR4 or HLA-DRB4 related (found in 50-75% of RA patients). Smoking is another risk factor, essentially in all of these autoimmune conditions because it is pro-inflammatory.

Some testing you can do is to test for Rheumatoid Factor, which is found in 70% in patients who have RA, but it’s not very specific. 25-30% of normal patients can be Rheumatoid Factor positive without the condition. Then we run another test, the Anti-citrullinated protein antibody (ACPA) test, sometimes also called CCP, and if you run this test concurrent with Rheumatoid Factor tests, it can be 85-97% specific to RA.

Figure 3 is a picture of Rheumatoid Factor. It is essentially an antibody that is recognized by another antibody, causing this inflammatory response, whereas the ACPA antibodies detect a modified protein. In this case, arginine...
has switched to citrulline abnormally, and the antibody recognizes this and starts an autoimmune inflammatory response.

Some ocular manifestations you might find with RA are listed in Table 4. I’ll point one thing out – uveitis is actually not that common with RA, it’s much more common in the other conditions we’ll talk about. You can get it, but it’s much more common to see dry eye with these patients. They can get Episcleritis or scleritis, Scleromalacia Perforans, which is a type of necrotizing scleritis without pain. Remember when we talked about those MMP’s that eat through the collagen and degrade the collagen, so you can see down into the inner layers (Fig 4) of the eye because of that inflammatory process. The patient can also get peripheral ulcerative keratitis (PUK) or stromal keratitis. These conditions happen near the limbus because the limbus is where the stem cells are created, so a lot of the inflammatory markers are in that area, as well. The affected areas can ulcerate and perforate, too. Some studies that I’ve read have said about 30% of patients who have scleritis have underlying RA.

Table 5 shows medications that are used for all of the conditions we are going to talk about today. As optometrists, we are very familiar with NSAIDs. With oral steroids, we need to be careful with some of the side effects of those. The great thing about the next group, the DMARDS, or disease-modifying anti-rheumatic drugs, is that they actually can prevent the progression of the disease while the first two only help with the patient’s symptoms and current inflammatory processes. Thus, you will probably want to know these medications, as patients on these likely have a rheumatological condition that could be the underlying cause of their dry eye, scleritis, etc.

Methotrexate and azathioprine are commonly used. Most of these are immunosuppressant agents, which means patients can have a secondary infection from them. There are also quite a few side effects from most of these medications. A lot of them were originally used as anti-cancer meds.

Sulfasalazine and hydroxychloroquine, which is important to know about as we will cover shortly. Cyclophosphamide and Cyclosporine have quite a few side effects, but they work very well in cases of severe RA. Of course, as optometrists, we know about cyclosporine because it is in Restasis, and it’s a T-cell inhibitor. Also, we have some newer medications which are very expensive and are administered as an injection; you’ve probably seen commercials for Humira or Enbrel, which are Tumor Necrosis Factor
alpha-blockers. We also have some newer biologics, as well. They work well, they are just more expensive and are not orally administered.

Most of us know about hydroxychloroquine toxicity. (Fig 5) It was originally used as an anti-malarial drug—it got into the parasite and changed the pH of their GI system, essentially killing the parasite. For us, it’s an anti-inflammatory medication. It does take a few months to work, again, so we want the patient to be diagnosed as early as possible so we can begin treatment. A lot of times, the doctors will start with an oral steroid and hydroxychloroquine or one of the DMARDs, taper the patient off of the steroid and keep them on the DMARD for longer once it becomes effective. Most patients, depending on their weight and age, are on 400 mg daily. Hydroxychloroquine binds to tissue, especially if there is a lot of pigment or melanin, which is why it likes the macula.

| Table 6 |
|-------------------|----------------------------------|
| **Indication**    | Anti-malaria drug                |
| **Mechanism of action** | Impairs cytokine response |
| **Time before effectiveness** | Takes 3-6 months for a response |
| **Dose**          | Dose: 200-400 mg daily           |
| **Side effects**  | Irreversible retinopathy in 1/2000, GI upset, nightmares, psychosis |

The main side effect we are concerned about is irreversible retinopathy. There are not that many other side effects that are devastating with this medication. Other drugs, like methotrexate, can cause severe kidney damage, liver failure, problems with infections, etc. Other side effects with hydroxychloroquine may include GI upset, and maybe nightmares and psychosis. Rheumatologists really like this medication as long as it’s not causing ocular problems. It’s also safe to use with pregnancy, too.

Rheumatoid arthritis and the other conditions we will talk about are not the only reason patients will be on hydroxychloroquine. I had a patient a few weeks ago who, when I looked at his list of systemic medications, I could not figure out why he was on hydroxychloroquine. The patient told me he was on the medication for CPD. I asked him, “Ok, what is that?” CPD is Calcium Pyrophosphate Deposition, basically pseudo-gout. Hydroxychloroquine is not used for gout itself, but it can be used for pseudo-gout.

I also recently had a patient who was about 12 years old and was on hydroxychloroquine. He had Lichen Planus, which is an autoimmune condition affecting the skin. He was bald, missing his eyebrows and some of his lashes.

Figure 6 is a patient I had recently whose visual field showed a central defect on a 10-2. The fundus exam was completely clean. So was the OCT, which you can see in Figure 7, and was verified by an ophthalmologist. This was actually the second time we’d seen this patient, and he had repeatable field defects. This patient was 65, positive for rheumatoid factor, positive for CCP antibodies, had RA with positive X-rays, and he had a cumulative dose of 1,600 grams of hydroxychloroquine. The ophthalmologist took this patient off of Plaquenil (hydroxychloroquine), told the rheumatologist, and now the patient is on Enbrel, doing well.
Figure 6: Visual fields and fundus exam of 65 YO patient positive for RA.

Figure 7: OCT of the above patient showing no maculopathy associated with Hydroxychloroquine
I had another patient who had the same thing – the fundus looked great, so did the OCT, and that ophthalmologist did not take the patient off of the hydroxychloroquine. The point is that we don’t always see all three – the bulls-eye pattern, the visual field defect, and the OCT. With the newer standards we no longer need to do color vision testing or Amsler grid testing.

**Spondyloarthritis**

Ankylosing spondylitis, along with the other spondyloarthropathies such as psoriatic arthritis, reactive arthritis, and enteropathic arthritis, are all HLA-B27 positive. They are rheumatoid factor negative. These are the ones that tend to have more of a uveitis presentation more commonly than rheumatoid arthritis. In addition, some of the literature I was researching says that up to 40% of patients who have recurrent anterior uveitis have ankylosing spondylitis or one of the spondyloarthropathies.

**Ankylosing Spondylitis**

In Ankylosing Spondylitis, we get unilateral, symmetric destruction of the spine and hips, shoulders, etc. Remember how RA was in the periphery? This affects the axial skeleton here. Most patients are young males and a lot of times they don’t like to admit that they have lower back and/or buttock pain, too. They think “I’m on the football team” or “I’m a construction worker” and “It’s just work-related.” But again, the symptoms are similar to RA, where the pain is worse when they wake up, or even when they are sleeping they can wake up with pain. This pain improves with movement.

Achilles tendinitis can occur, also, which is outside of the axial skeleton, but that’s because in RA you get an inflammation of the synovial joints whereas with Ankylosing Spondylitis, you get inflammation where the tendon or ligament attaches to the bone, which is why the Achilles tendon is affected in Ankylosing Spondylitis – there is not a lot of synovial fluid there for RA to affect.

Figure 8 is a picture of kyphosis. As Ankylosing Spondylitis progresses the patient starts to hunch over. Patients can also have pulmonary issues and heart issues. One thing as an optometrist you could do if you have an older patient like this is consider base down prism, because a lot of times the patient is facing down so much that it really helps bring up their line of sight.

Some testing that you can order as an optometrist if you have a patient with recurring anterior uveitis who maybe has symptoms of ankylosing spondylitis is an HLA-B27 test. This test is fairly specific for Ankylosing Spondylitis, or at least a spondyloarthropathy condition. I was looking into costs for this testing – it’s really good to know that...
you want to specifically order HLA-B27 because if you order a whole HLA panel of blood tests, it’s like $400-$500 dollars, but specifically HLA-B27 by itself is only $20 or $30. Again, these costs depend on the patient’s insurance – the insurance may cover the whole thing regardless.

These patients are also seronegative, remember, so you could also order a Rheumatoid Factor test if you are considering that the patient may have RA, but again, that test is not very specific. X-rays can be ordered, too. In Figure 9 we have what is called a ‘bamboo spine’, where the spine starts to fuse together at the spinal column. It also happens in the sacroiliac (SI) joint, which is in the pelvis. As a result, we get a narrowing of the space between the sacrum and the iliac joint.

The most common non-joint involving or non-articular manifestation is uveitis – 20-40% of patients have it. We also, again, get episcleritis and scleritis.

Treatment for ankylosing spondylitis, for most patients, is NSAIDs. These NSAIDs are used at an anti-inflammatory dose, which is higher than the over-the-counter dosing that would be used for just a headache. I’ll also add that HLA-B27 is more common in north and western Europe. It’s pretty rare for someone from south of the equator to be HLA-B27 positive.

**Psoriatic Arthritis**

Psoriatic Arthritis is also a spondyloarthropathy condition. About 1/3 of patients who have psoriasis, where they get a scaly, silvery rash on the body (Fig 10), can develop arthritis later on. I had a patient recently at the VA who had very severe psoriasis on his arms, face, etc. His chief complaint was dry eyes. I asked him if he had arthritis, and he said, “Yes, I definitely have it.” I asked him if he was HLA-B27 positive, and he didn’t know what I was talking about. Which was OK, because I was just curious.

Age of onset for psoriatic arthritis is middle-aged (30-50 years). It takes awhile to develop the arthritis, so it can be a later diagnosis. A lot of patients will get changes in their hands, what is known as dactylitis or sausage-feet (Fig 11 left). It happens on the toes and the hands, and is due to inflammation. You can also get nail dystrophy, or nail pitting (Fig 11 middle), where the nail separates from the bed, or you get what looks like punched-out holes in the nails. Uveitis (10-15%) is less commonly found with Psoriatic
Arthritis than with Ankylosing Spondylitis, but more than is found with RA. It’s pretty rare to have psoriasis alone and to get a uveitis without the arthritis component. Usually the patient will develop arthritis before uveitis.

Treatment involves UV light, which is anti-inflammatory. UVA or UVB light can be used. Any of the medications that we’ve talked about (listed again in Table 7) except hydroxychloroquine will work. Hydroxychloroquine can actually advance the flare-ups of psoriasis, so you don’t want to use that one. But any of the others can be used. It’s important to also avoid oral steroids, as well, as they can cause a flare-up much like hydroxychloroquine does.

**Reactive Arthritis**

Reactive Arthritis used to be called Reiter’s Syndrome, and it went by the mnemonic “Can’t see, can’t pee, can’t dance with me.” Meaning they get conjunctivitis or uveitis, urethritis (pain upon urination), and arthritis, as well. They’ve gone away from that for a couple of reasons – they are trying to not name things after people anymore but to move towards a more universal name. Also, apparently Reiter was convicted of WWII crimes, so they didn’t want to name the condition after him anymore. However, it kind of goes under the same thing. You can get eye inflammation, chlamydia or urethritis, and then joint pain. If Reactive Arthritis comes from an STD, it is usually Chlamydia. If it’s from GI upset, it’s usually salmonella, E-coli or dysentery. Some kind of infection will cause a reaction in the body leading to inflammation and arthritis in other parts of the body. Usually the symptoms of arthritis don’t occur until up to 4 weeks later, so sometimes patients delay coming in, and it’s hard to diagnose them because the bacteria has already left their body, in the case of dysentery, etc.

Reactive Arthritis usually happens in young men, ages 15-40 years old. Later on in life they can get the same symptoms without the initial infection. Thus, if they were infected, and they get Reactive Arthritis, then later on in life, they can get the arthritic component again.

The main component that we will see in the eye in a Reactive Arthritis patient is conjunctivitis – not necessarily uveitis, but it can happen. You may ask patients if they have a recurrent conjunctivitis, we ask about Chlamydia, which is a very common reason for getting a reactive arthritis.
Testing can be problematic, depending on how long ago the patient had the infection. You can do a stool sample, a swab or urine analysis for Chlamydia. A lot of these patients are also HLA-B27 positive. Figure 13 shows another skin manifestation. Patients can get rashes on the palms of their hands or the soles of their feet.

Treatment is antibiotics if the patient has a current infection, and a lot of times they will treat prophylactically, too. NSAIDs and/or corticosteroids and DMARDs are also used, as well. I’ve had two friends with Reactive Arthritis, both young males. One was my husband’s friend who was in the Peace Corps in China and acquired Amoebic Dysentery and got Reactive Arthritis from it. He said he couldn’t get out of bed. He was trying to hug his girlfriend and he just couldn’t move. They found out it was from rats getting into his food in China. In the US, it might be more Chlamydia-related.

**Enteropathic Arthritis**

The last of the spondyloarthritic conditions is Enteropathic Arthritis. This is arthritis related to Crohn’s Disease or Ulcerative Colitis, and the other inflammatory bowel conditions. Symptoms here include diarrhea, GI upset and joint pain which can be similar to Reactive Arthritis, though a lot of times these patients already know that they have Crohn’s or Ulcerative Colitis. You can do a colonoscopy or a biopsy of the colon here, rather than a stool sample.

Ocular manifestations include uveitis in about 5% of these patients, which can be anterior as well as posterior uveitis involvement. Also, like in the other conditions, we can get conjunctivitis, episcleritis, scleritis and PUK.

Testing involves colonoscopy or biopsy to help with diagnosis, as I’ve covered before.

Treatment is the same. Antibiotics can help if they have a concurrent infection. You want to be careful with any NSAIDs used, as those can cause GI upset and these patients already have GI upset from their underlying diagnosis.

### Table 8

<table>
<thead>
<tr>
<th>Treatment</th>
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<tr>
<td>DMARDs</td>
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<tr>
<td>Steroids</td>
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<td>Antibiotics</td>
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**Systemic Lupus Erythematosus (SLE)**

Switching gears a little to Lupus, which is really called Systemic Lupus Erythematosus (SLE) because it can affect any part of the body. We think of it as affecting the skin, but it can involve the kidneys, lungs, and people can die from it. It is most common in women of childbearing age, so young women. Figure 14 is Seal, which while he doesn’t fit the demographics, he has Discoid Lupus. This means that he has skin findings of Lupus, but not systemic findings. It also causes more scarring, which you can see on his face here. This is more common on young, African-American females.

It can also be caused by medications, being medication-induced Lupus. Minocycline and some of the tetracyclines can do this, as well as some of the DMARDs. There are a bunch of medications that can cause it, but you want to be careful with these, as logic would say that we treat this with some of the
DMARDs, but they can actually make it worse. Drug-induced Lupus can go away once the patient stops the medication.

Symptoms – overall, the patient is not feeling well. In a lot of these autoimmune conditions, the patient feels weak, they can have weight loss and a fever. The most common symptom or sign is not facial, but rather, it’s joint pain. About 90% of patients with SLE get joint pain.

SLE causes a Malar, or butterfly, rash as pictured in Figure 15. The rash can extend up onto the forehead, as well. It usually spares the naso-labial folds, which is good as a differential for other conditions. It causes hair loss (alopecia) a lot of times – so if you have a young woman of childbearing age with hair loss, consider SLE. When hair grows back, they call it “Lupus hair,” because it’s kind of a wispy, coarse hair, and a lot of women don’t like that.

Symptoms are exacerbated by UV light and they come and go, so the patient won’t always have the rash. It may be subtle and hard to see under makeup, too, like in ocular rosacea. It can, again, affect any organ, such as the kidneys, and in that case they call it Lupus-nephritis. It can cause CNS involvement – in this case, you’ll have a young woman with seizures or difficulty walking, memory loss, and other similar things you wouldn’t expect in a young person. It can also affect the lungs and the heart.

There is a wide variety of things we may see in the eye. Up to 1/3 of patients have some kind of ocular manifestation. Dry eye syndrome, just like with the other conditions, is the most common here. You can get episcleritis, scleritis, conjunctivitis, as well as optic neuritis. With optic neuritis we tend to think MS, but some testing will help and an MRI hopefully can differentiate the two. We can get cranial neuropathies, double vision, and in the back of the eye we can get cotton wool spots, retinal exudates, hemorrhages, etc. These are patients you would want to do some extra blood testing on if they didn’t have an underlying cause for what you’re seeing in the back of the eye. They can, rarely, also have uveitis, but it’s less common than with the spondyloarthropathy conditions.

A great test to do for this is ANA, or anti-nuclear antibody. It’s present in up to 95% of these patients. ANA can also be found in Sjogren’s patients, but Sjogren’s Syndrome is often times caused by a secondary condition, which can be Lupus. Thus, ANA is fairly specific to Lupus or possibly Sjogren’s. If you want to get even more specific, you can test for Anti-double-stranded DNA antibodies (Anti-dsDNA AB) and anti-snip antibodies (Anti-sm AB), which are specific to SLE.

Sometimes there can be overlapping symptoms between Lupus and RA, in which case, they call it Rupus – they’re not really sure which one it is.
Treatment is to avoid anything that causes the skin condition – sunlight, for example. Stress, which includes pregnancy. Again, these are young females, and they want them to be treated for their Lupus for 6 months to 1 year before they get pregnant, because you can get Neonatal Lupus, which causes fetal heart block and babies can get very sick and die. But, if they are monitored well, patients can still get pregnant. Again, they are at risk for more infections, so they need to have all of their flu shots and hepatitis shots.

Patients with Lupus have a 2-5x higher risk of death than the normal population, so reducing cardiovascular risk factors, whether with medication or with lifestyle, is important. It’s important to avoid any of the medications which can cause Lupus is also critical. They can use NSAIDs or DMARDs, as long as that specific medication is not one that causes Lupus. The drug of choice here is hydroxychloroquine. These patients can use steroids until the hydroxychloroquine kicks in. You can have a patient on hydroxychloroquine for this reason.

**Sjögren’s Syndrome**

In talking about Sjogren’s Syndrome, we all know that this can cause dry eyes and dry mouth, as well as vaginal dryness. It’s basically an autoimmune condition against the lacrimal and salivary glands. Most commonly found in females (12:1) who are middle aged. A lot of times the ocular manifestations that we see, other than dry eyes, come because Sjogren’s can be secondary to RA or Lupus, or even a vasculitis condition.

For testing, the diagnostic test is a biopsy of the salivary gland or the lip. You can do ANA testing, though Lupus is fairly highly specific for that, as well. Patients here have a high percentage of Rheumatoid Factor positive testing, and that’s because, many times, Sjogren’s is secondary to RA. Specific antibody testing you can do for Sjogren’s are: Anti-Ro/SSA or Anti-La/SSB antibody tests. You can also do any of the dry eye tests that we routinely do in clinic: TBUT, Schirmer’s, etc. Now, we can also do the Sjo test (Fig 16) in-office and bill for it. The Sjo test checks for some of the classic biomarkers we were just talking about, including SSA and SSB. It also tests for some of the Rheumatoid Factors, depending on which antibody they are connected to. ANA is tested for, as well.

<table>
<thead>
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<th>Treatment</th>
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<tr>
<td><strong>Artificial tears, Restasis, punctal plugs, ointment</strong></td>
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<td><strong>Saliva replacement</strong></td>
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<tr>
<td><strong>NSAIDs, DMARDs</strong></td>
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<td><strong>Corticosteroids</strong></td>
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<tr>
<td><strong>Pilocarpine</strong></td>
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<tr>
<td><strong>Avoid: Caffeine, juice, sucrose</strong></td>
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<tr>
<td><strong>Recommend: sugar-free gum, routine dental care</strong></td>
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Table 11

Treatment includes treating the dry eye with our arsenal of treatments, including Restasis, which we said was a T-cell inhibitor. It can also be used orally, as well. Saliva replacement, any of the medications that treat SLE or RA, if that’s their underlying condition. Oral Pilocarpine, not topical, is a parasympathomimetic, so it can induce salivation. Avoid anything that can cause dryness of the mouth: no caffeine, no alcohol, etc. They also need to avoid anything sugary, because these patients can get cavities very easily as they don’t have that saliva running through their mouth. We can recommend that they chew sugar-free gum and hard candies, and that they see their dentist often.

**Vasculitis Conditions**
The last part we are going to talk about is the vasculitis conditions (Table 12). There is a whole host of them, but the ones that you will see most commonly are Giant Cell Arteritis, Wegener’s Granulomatosis now called GPA (Granulomatosis with Polyangitis), and Behcet’s Disease.

A quick overview of the pathology of vasculitis. When blood vessels become inflamed, the diameter of the lumen shrinks, so the blood doesn’t flow quite as readily. You can also get an outpouching, or an aneurysm, which is what we are most concerned about.

**Giant Cell Arteritis**

Giant Cell Arteritis (GCA) they say the number one risk factor for is age. It is rare in patients under 50, but really, the patient is 70 or 80 years old. It’s a little more common in Caucasian women (women 2:1, Caucasians > African-Americans), is associated with smoking as so many conditions are. As we talked about, there is an increased risk of an aneurysm that bursts. There is a higher prevalence of GCA in patients who already have an underlying auto-immune condition or vasculitis, which makes sense. I found it interesting that it hasn’t been established that hypertension, diabetes, or high cholesterol are risk factors, so it’s actually controversial at the moment as to whether those conditions are actually risk factors for GCA. I would probably still ask about those as I am asking the patient if they are a smoker, as well.

If a patient comes to your office, what they’ll complain about is a new, severe headache. It’s usually very painful and on one side only. They have tenderness of their scalp, so when they brush their hair in the morning, it’s painful. They have jaw claudication; when they move their jaw it’s painful. They can also have arm claudication, because essentially the blood vessels are narrowing so you’re not getting enough oxygen to some parts of the body. If you feel around where their temporal artery is, it can be inflamed, engorged, and have a reduced pulse, as well.

The patients will tell you that recently they lost vision for a short period of time in that eye – it went totally black. Or they might have not noticed, and now their vision is really blurry and they have this really bad headache. Overall, they are just not going to be feeling well. They’ve recently lost weight, are tired, they have a fever. The older patient may assume that some of these symptoms just come with age, so they are not feeling well, they have some joint pain, but what brings them in are their eye findings – blurry vision, or they’re concerned because they’ve recently lost their vision and, oh, by the way, their headache is getting worse, too.

In about 1/3 of patients, their vision can be less than 20/200. Some journals I read said up to 20% are no light perception with very severe vision loss. They will complain of a short period of transient vision loss. When you look in the back of the eye, they can either have a swollen nerve, or if it’s been awhile and they never came in with the original symptoms, they can have a pale optic nerve. You’ll notice an APD.
The patient can have double vision because when the carotid artery comes up, it bifurcates going up towards the eye and down towards the jaw for the claudication. The blood vessels also supply the nerves that innervate the extra-ocular muscles, which is why the patient can get double vision. The external carotid artery comes up temporally, which is why the patient gets temporal arteritis.

Up to 10% of patients will have CRAO. So, if you have a patient who is older and has a CRAO, you definitely want to do the testing and make sure they don’t also have GCA.

On these patients you also want to do a same-day visual field. It can also help you differentiate if the patient has an NAION, which will give you an altitudinal defect. Temporal arteritis can present in a lot of different ways, but sometimes it gives a total defect. Sometimes it can be an arcuate scotoma. Sometimes, it can even show up in the other eye, depending on where the defects in the blood vessels are. The patient can also have posterior optic neuropathy, where you won’t see any of it, but their vision is very poor.

Lab testing includes Erythrocyte Sedimentation Rate (ESR) is going to be really high – sometimes over 100 mm/hour. Their C-reactive Protein (CRP) levels will also be high. These two tests are very helpful to diagnose, but sometimes if the tests aren’t severely elevated, some patients, especially when they are older, naturally have elevated inflammatory markers because they already have arthritis, or they’ve had an infection recently.

The diagnostic test is a temporal artery biopsy, as seen in Fig 17. It’s important that the surgeon take out at least 2 centimeters, because in the temporal artery you can have skip lesions, so if you don’t take out a large enough chunk, you won’t have those giant cells that stain when they do testing.

The other thing that I thought was interesting, I was wondering “Why can they just take out a large chunk of the temporal artery? They can’t just take out a chunk of the internal carotid and go biopsy it.” However, there are a lot of anastomoses that happen in the upper skull, so other places can still be innervated and perfused if you remove the temporal artery.

A test you can do in-office is to test the pulse between the two sides of the patient’s temporal artery. In GCA, one will be reduced while the other one is normal.

This is an emergency! You want the patient seen the same day by ophthalmology. They can lose vision in the other eye within just a couple of hours, depending on how long they’ve had the condition. You can start these patients on oral steroids. If you don’t want to put them on really high doses you can go...
with a lower dose, and then once they’ve had a positive biopsy, the ophthalmologist will put them on a higher dose. They may need to be on IV medications, as well.

This is a really slow taper. Some patients are on a low dose of oral steroids for the rest of their lives. Others are on a taper over a couple of years. Sometimes, concurrently the patient will have a low dose of oral steroids as well as methotrexate or another of the DMARDs. They are on low dose aspirin as well to prevent stroke and myocardial infarction. We talked about them possibly being on methotrexate or cyclophosphamide in addition to the oral steroids.

**Granulomatosis with Polyangitis**

You might be familiar with the term Wegener’s Granulomatosis, but now it’s called GPA – Granulomatosis with Polyangitis. It’s a small vessel disease, so now instead of affecting the large vessels, we see the small vessels such as those in the lungs or on the skin affected. Typically the lower appendages have these purpura (Fig 18) or rashes that are elevated. They can have joint involvement, difficulty breathing, and kidney involvement, as well.

<table>
<thead>
<tr>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rhinorrhea, sinusitis, hearing loss (90%)</strong></td>
</tr>
<tr>
<td>Hemoptysis</td>
</tr>
<tr>
<td>Oral ulcers</td>
</tr>
<tr>
<td>Saddle-nose deformity</td>
</tr>
<tr>
<td><strong>Cough, painful breathing</strong></td>
</tr>
<tr>
<td>Hematuria</td>
</tr>
<tr>
<td>Joint pain</td>
</tr>
<tr>
<td><strong>Fatigue, malaise, weight loss</strong></td>
</tr>
</tbody>
</table>

It’s found in older patients, typically equally in males and females. A lot of patients used to die, but now that we can diagnose it earlier and treat the patient, there’s not that many fatalities. (80% die within 2 years if not treated.)

A lot of the symptoms of GPA affect the ears, nose and throat. Patients can get a runny nose or a bloody nose, a sinus infection, and a lot of them get otitis media, causing hearing loss. They also get oral ulcers. Not in all cases, but in quite a few they get a saddle-nose deformity, which you would want to use to differentiate from some of the other systemic conditions. Coughing and painful breathing because, as I’ve talked about before, GPA can affect the lungs. Also, as mentioned before, joint pain.

The patient in Fig 19 has some pretty bad chemosis going on in the eye. There are some serious eye findings that come along with GPA in up to 50% of patients. Severe proptosis with diplopia, uveitis posteriorly as well as anteriorly, scleritis, and episcleritis. They can get a nasolacrimal duct obstruction, which can lead to excessive tearing. They can have hemorrhages in the back of the eye or cotton wool spots.

You may have heard of Churg-Strauss Syndrome, which is kind of in the same family of small vessel vasculitis conditions, but again it’s not called Churg-Strauss, it now has another name, just like GPA has been renamed.

![Figure 18: Purpura on the legs of a patient with Granulomatosis with Polyangitis](Image)

![Figure 19](Image)
Testing for GPA involves X-rays of the chest where you can see the inflammation on the lung, and it can also be seen on a CT scan – the bronchiole destruction and inflammation. You can also do a renal biopsy and urinalysis.

Lab tests for when you suspect a vasculitis include ANCA, or anti-neutrophil cytoplasmic antibody. Quite a high percentage of patients with GPA are positive (82-94%). Most are PR3-ANCA positive or C-ANCA positive, which is a good way to distinguish between this and Churg-Strauss diagnosis. C-ANCA stands for cytoplasmic ANCA and PR3-ANCA is perinuclear ANCA.

The treatment for GPA is the same as we’ve been talking about this whole course – immune-suppressants. Methotrexate, prednisolone, cyclophosphamide and rituximab.

**Behcet’s Disease**

The last condition we are going to cover today is Behcet’s Disease. It’s a vasculitis that affects the large blood vessels, the small blood vessels, vessels of basically any size. Traditionally it’s quoted as “oral and genital ulcers with recurrent iritis.” A lot of times we think it’s more common in males, but it’s actually equally common in both males and females, it’s just that males get a more severe form of it. It happens usually in East Asian and Mediterraneans along the Silk Road (Fig 20). These patients are young.

Symptoms include recurrent ulcers of the mouth – not just one, it’s multiple that come and go. They are painful. They get skin lesions, mainly on the lower part of the body, just like GPA. They can also have central nervous system involvement, such as seizures, memory loss, and difficulty walking. Ocular manifestations are found in 2/3 of patients. (Fig 22)

Uveitis is the most common ocular manifestation of Behcet’s Disease, and they will usually get a concurrent hypopion. They can get vasculitis, periphlebitis, neovascularization of the disc, optic neuritis as well. Vascular occlusions such as BRVO are common, as well.
Testing that we can do includes a Pathergy test, where we prick the patient’s skin with a needle and see if a little pustule forms. Or you can do a CBC tests. There is no specific ANCA test for Behcet’s, a lot of it is diagnosed based on physical signs and symptoms.

Treatment involves the autoimmune medications we’ve talked about (see Table 16), along with Colchicine. Colchicine is usually used for gout, but it’s a microtubule inhibitor also used for Behcet’s Disease.

**Clinical Case**

I just wanted to share a quick case that I had recently. I didn’t actually see the patient myself directly, but it was a colleague of mine next door at the VA. This patient was 65, he came in because his left eye was “seeing through grease.” His vision was 20/25 OD and 20/50 OS. Before dilating he had a 3+ anterior chamber reaction and a small APD. His pressures were 21 OD and 34 OS. Some granulomatous KP’s were noted on his cornea, as well. Figure 23 shows what we found in the back of the eye.

Table 17

<table>
<thead>
<tr>
<th>Labs</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>RPR</td>
<td>Non-reactive</td>
</tr>
<tr>
<td>FTA-ABS</td>
<td>Non-reactive</td>
</tr>
<tr>
<td>Toxo AB</td>
<td>72.9 IU/ml (0-6 norm)</td>
</tr>
<tr>
<td></td>
<td>12.5 AU/ml (0-8 norm)</td>
</tr>
<tr>
<td>ACE</td>
<td>66 U/L (14-82)</td>
</tr>
<tr>
<td>CBC</td>
<td>WNL</td>
</tr>
<tr>
<td>Quantiferon-gold</td>
<td>Positive</td>
</tr>
<tr>
<td>P-ANCA, C-ANCA</td>
<td>WNL</td>
</tr>
<tr>
<td>Chem-7</td>
<td>ALT, AST elevated</td>
</tr>
<tr>
<td></td>
<td>Creatinine low</td>
</tr>
<tr>
<td></td>
<td>Glucose high</td>
</tr>
<tr>
<td>Chest X-ray</td>
<td>WNL</td>
</tr>
</tbody>
</table>
we talked about. A Chem-7 lab and a chest X-ray were also done.

Some interesting things came up. First of all, the Quantiferon-gold test was positive, but the chest X-ray was negative, so it could be a false positive – maybe the patient was previously exposed to TB. Now he is working with infectious disease to figure out why he tested this way, and I believe they are re-testing him at Casey Eye Institute. At the time of this lecture, this patient was seen only last week, so I don’t currently have any additional information.

Table 18 a and b

<table>
<thead>
<tr>
<th>Lab test</th>
<th>Lab tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBC</td>
<td>ANA</td>
</tr>
<tr>
<td>VDRL or RPR</td>
<td>RF</td>
</tr>
<tr>
<td>FTA-ABS</td>
<td>ACE</td>
</tr>
<tr>
<td>PPD/Quantifieron Gold</td>
<td>ANCA</td>
</tr>
<tr>
<td>Chest X-ray</td>
<td>HIV</td>
</tr>
<tr>
<td>HLA-B27</td>
<td>Lyme titer</td>
</tr>
<tr>
<td>ESR</td>
<td>Herpes titer</td>
</tr>
<tr>
<td></td>
<td>Toxo antibodies</td>
</tr>
<tr>
<td></td>
<td>Urinalysis</td>
</tr>
</tbody>
</table>

The patient’s Toxo antibodies were also very high. 6 is the norm, and our patient was at 72. The second antibody test they did for toxo was also very high (12.5 with a norm of 8).

When he was seen again with ophthalmology his pressures were 20 and 43. They diagnosed him with hypertensive panuveitis with chorioretinitis. They were considering putting the patient on triple-therapy for TB, but he’s getting a fluorescein angiography and a couple other special tests at Casey.

I just included Tables 18 a and b in here in case you could use them as a reference in clinic, if you are ever wondering, “Which labs should I order? There’s so many.” You could maybe check off if you don’t need to do any rheumatoid testing, or use these as a general workup, depending exactly on how the patient presents. This may be easier to use rather than remembering everything we talked about today.

Thank you very much for your time and attention. Please feel free to contact me with any questions.

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References

5. UpToDate; 2015 UpToDate, Inc