Clinical Ocular Grand Rounds Course # 40013

Instructor:
Blair Lonsberry OD FAAO

Section:
Systemic Disease

COPE Course ID:
38145 SD

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Qualified Credits:
1.00 credits – $39.00

COURSE DESCRIPTION:

Critical to clinicians is the ability to diagnose and manage unique and interesting presentations of typical ocular conditions, or to be able to diagnose a previously un–encountered condition. The following course will present patient cases with unique presentations of ocular conditions, including special testing. The course will focus on the ability of the clinician to analyze and interpret the unique case presentation and provide appropriate management and treatment options.

LEARNING OBJECTIVES:

- Assess a patient experiencing a vascular occlusion event incorporating the latest in diagnostic equipment, such as OCT, and how this technology helps in diagnosis and management
- Recognize the signs and symptoms of a patient experiencing a neurological complication and utilizing the appropriate diagnostic testing be able to educate the patient on any appropriate referrals, treatment/management and prognosis
- Assess a patient for potential hydroxychloroquine toxicity utilizing the latest screening criteria and what specifically to evaluate when utilizing the latest diagnostic equipment, such as OCT
Good afternoon. Welcome to Clinical Ocular Grand Rounds. My name is Blair Lonsberry, and I am a professor at Pacific University. Today’s lecture is going to focus on clinical grand rounds cases, so unique cases or conditions that you may have already seen before, as well as hopefully some new conditions, as well.

I am a paid consultant for: Alcon Pharmaceuticals, Bausch and Lomb, Carl Zeiss Meditec, Merck Pharmaceuticals, NiCox, SARcode.

What I want you to do is to grab a piece of paper and a pen, because I’m going to want you to do what is called a “Commitment to Change.” I want you to pick up three things from this presentation that you can incorporate into your practice to take care of patients better. Ultimately that is why we attend CE, so what I want you to do is just write numbers 1, 2 and 3 down, and hopefully you will gain three things that you can incorporate into your practice to take care of patients better.

To help you along, I want you to be interactive with me. In a presentation like this, it’s tough to interact with the other people viewing this presentation, but what I’m going to do is ask you questions during the presentation, and then I’m going to give you time to respond. After you’ve responded, I’ll put up a graph showing you the responses of about 100 optometrists who I’ve asked these questions to before. This graph will show you how you compare to those other doctors, and hopefully you will be on track with them.

**Case 1: Gonzalez**

Here is our first case. I have a 33 YO Hispanic female that presents with a painful, red right eye. It started a couple of days ago with deep, boring pain. She has tried Visine and, surprisingly enough, it hasn’t helped very much. She reports that she was “diagnosed” with rheumatoid arthritis (RA). Diagnosed is in quotes because we are not too sure how she was diagnosed, but she reports RA. She is taking Celebrex for her joint pain, and she reports that she occasionally gets a skin rash when she goes out in the sun. Her ocular history is unremarkable, and for her medical history, she reports that her mother has RA.

Her exam results are shown in Table 1. Figure 1 [Top] is not her eye, but is very similar to how her eye appeared. The pupils were PERRL-APD, and her other entrance skills were unremarkable with a blood pressure 130/85 mmHg RAS. On slit lamp, we saw a 2+ cell with mild flare, and pressures are 16 mmHg OU.

Take a look at the bottom picture of Figure 1. This is the patient’s fundus photo, and we can see that there are some cotton wool spots (CWS) present.

<table>
<thead>
<tr>
<th>Case 1 Entrance Skills</th>
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<tbody>
<tr>
<td><strong>VA:</strong> 20/30 OD, 20/20 OS</td>
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<tr>
<td><strong>Pupils:</strong> PERRL-APD</td>
<td></td>
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<td><strong>VF:</strong> FTFC OU</td>
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<td><strong>EOM's:</strong> FROM OU</td>
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<tr>
<td><strong>BP:</strong> 130/85 mmHg RAS</td>
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<tr>
<td><strong>SLE:</strong> See Fig 1 [Top] 2+ cells, mild flare</td>
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<td><strong>IOP's:</strong> 16, 16 mmHg</td>
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<td><strong>DFE:</strong> See Fig 1 [Bottom]</td>
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Question: What do you think is the underlying etiology of the CWS?

1. Hypertension
2. Diabetes
3. Rheumatoid Arthritis
4. None of the above

(Scroll down to view correct answer)

Let's see how you compared:

Correct Answer: 4  
Correct: 62.16%  Incorrect: 37.84%  Cumulative: 60.138%
The majority of the people who responded to this question (about 100 doctors) chose answer 4: None of the above. If you are thinking CWS and chose either 1 or 2, hypertension or diabetes, respectively, I would agree with you that I would tend to think vascular changes first. But if we look at the photo, if you are expecting either hypertensive retinopathy or diabetic retinopathy, I would expect microaneurysms, A/V crossings, 90 degree crossings, nicking, or some other indication that the patient has either hypertensive retinopathy or diabetic retinopathy. We are usually not going to default to CWS without going through those other changes, first. Some autoimmune diseases can result in CWS, but RA is not one of them.

Table 2 shows us the common etiologies for CWS. Agreeably, vascular causes are probably the most common. However, if you look under the autoimmune diseases, Lupus is one of those conditions that can result in CWS. RA is not a common one.

Question: All of the following demographic data is “typical” of a patient diagnosed with rheumatoid arthritis except?

1. Average age of onset between 35-50
2. Predominantly female
3. Positive family history
4. Predominantly African-American/Hispanic

(Scroll down for answer)
The correct answer is 4. Patients with RA do have an average age of onset between 35 & 50. They are predominantly female with a very strong family history. However, RA is predominantly Caucasian patients, not African-American or Hispanic. Thus, thinking back to our patient, she was 30 years old when she was diagnosed, and is currently 33. She does have a family history of RA and is female, but is Hispanic, not Caucasian. So we were thinking, “Let’s order some lab tests to figure out what’s really going on with her.”

Question: Which of the following would NOT be indicated in diagnosing this patient?

1. ANA
2. Anti-DNA antibodies
3. RPR
4. Rheumatoid factor (RF)
5. Complement C4 levels
6. Joint x-rays

(Scroll down for answer.)
The correct answer is 3. This group of 100 doctors didn’t do so well on lab tests. Hopefully you did better. If you look at this group of tests, if you think about how the disease process works, and that really helps you figure out what’s going on with our patient.

If we’re thinking the two major diagnostic conditions are either RA, which she feels that she has, or Lupus (SLE). When we think about RA, which joints are primarily affected first? That’s usually the fingers and the toes, then it moves towards the trunk. We do have a screening test for RA, which is RF, or Rheumatoid factor. It’s not a great screening test, more than 50% of patients with early RA will actually test negative to RF, though if you have high titers of RF, it’s usually a strong indicator that RF is there. Diagnostic for RA is the joint x-rays.

When we start thinking about Lupus, Lupus attacks the DNA of your cells. There is no cell in your body that is not fair game for Lupus to attack. Thus, the first tests that we tend to do for Lupus is ANA, or anti-nuclear antibodies. This is looking for destruction of cell material releasing that nuclear material. We are looking for antibodies to that nuclear material. ANA is about 99% sensitive for Lupus, so it picks up pretty much everybody. In addition to that, it also picks up patients who will test positive for ANA because they have RA, or Scleroderma, or any number of other autoimmune diseases. Thus, even though it’s a good screener test, it is not diagnostic for Lupus. The next test that is going to be run if they test positive for ANA is anti-DNA antibodies. These antibodies are specific for Lupus, and if a patient tests positive for anti-DNA antibodies, it’s pretty much conclusive that it’s Lupus. Why don’t we just use that test right off the bat? Unfortunately, it has a very low sensitivity, so it doesn’t pick up everybody who has the condition.

The other test we have on there is Complement C4 levels. The Complement System is our immune cascade in our body. If you have an autoimmune disease, your immune system is kicked on all the time, so what ends up happening is that those Complement C4 levels get chewed up. Because the immune system is kicked on all the time, we have low levels of C4. Low levels of C4, in addition to anti-DNA antibodies is pretty much 100% conclusive for Lupus.

And our number 6 answer is joint x-rays, which we are going to use to diagnose patients with RA.
Question: Thinking back to that lesion from Figure 1 [Top], what is the “nodular” lesion on the patient’s left eye?

1. Pinguecula
2. Episcleritis
3. Scleritis
4. Scleromalacia perforans

(Scroll down for answer)
The correct answer is 3. A pinguecula is not likely to give you that deep, boring pain with an anterior chamber reaction. Episcleritis is not going to do that, either. Scleromalacia perforans is diagnostic for patients who have longstanding RA, usually about 20 years or more of RA. First of all, our patient doesn’t have RA, and even if she did, she hasn’t had it long enough to be diagnosed with scleromalacia perforans. Our correct answer is scleritis.

Question: What is the mainstay treatment for a patient diagnosed with a non-necrotizing scleritis?

1. Oral NSAID
2. Topical NSAID
3. Topical steroids
4. Topical vasoconstrictors

(Scroll down for answer.)

The correct answer is actually 1. I see this split an awful lot – I see many ODs wanting to prescribe topical steroids. Topical steroids can be used, but they cannot be used in and of themselves. Our mainstay is really oral NSAIDs, such as Indomethacin 50 mg TID. If the oral NSAIDs are not successful, we will move to oral steroids, and if those don’t work, we will move on to immunosuppressants.
If you think back to our patient’s case history, what medication is she already taking? She is taking Celebrex, which is a prescription NSAID. Why is this not working for our patient? It’s not working because our patient does not have RA – she has Lupus. The NSAIDs weren’t strong enough to take care of the scleritis.

When we had our patient sent off for diagnostic testing, she was actually diagnosed with Lupus. It was found not only that she had the scleritis, but she also had additional changes going on in her body, she had two or three other organs that were starting to be affected. When the rheumatologist consulted with her, they actually bypassed the next step, which is typically oral steroids, and put our patient on immunosuppressive agents. They felt that she had a sight-threatening condition, and already had damage to her systemic organs so they were very concerned for her, and thus moved straight into immunosuppressive agents.

In addition, they took the patient off of Celebrex, which she was using as management for her joint pain, and put her on Plaquenil, or hydroxychloroquine, 400 mg QD. Plaquenil is an extremely good medication for increasing mobility and function in patients. That is what it is primarily used for; it increases their mobility and gets them moving around and so ultimately, patients are put on Plaquenil to manage pain and increase mobility.

**Plaquenil**

Let’s talk a little bit about Plaquenil. In March 2011, the screening guidelines for Plaquenil changed, and I think it’s important that you know those new guidelines, so I’m going to go through them with you in a moment.

A little bit about hydroxychloroquine: It’s more common and less toxic than chloroquine. The typical dosage for patients on Plaquenil is 200-400 mg QD at night. The onset of action is 2-4 months. It has a very mild DMARD effect. (DMARD stands for disease modifying anti-rheumatic drug) DMARDS slow down joint destruction and are the primary medications for patients with RA. This group of medications include your biologicals such as TNFalpha-blockers such as Enbrel, Humira, Remicade. The other major ones are anti-DNA medications such as methotrexate. These are considered the primary medications because they slow down joint destruction. Remember when we talked about diagnosis of patients with RA, the diagnostic test is joint x-rays. When patients are being managed for the condition, they have successive x-rays that are done and ultimately, when they are on medications, will show that they are slowing down the joint destruction. Again, Plaquenil has a very mild DMARD effect, so it is not considered a primary medication for patients with RA. It’s really good for increasing mobility and function, and it will slow down joint destruction somewhat.

Plaquenil loves pigmented tissue. Thus, any tissue in the body, it loves to accumulate in that tissue. The ones that we, as eye doctors, get concerned about is, of course, the retina. Plaquenil has a toxic effect on the RPE and photoreceptors, and can lead to not only rod and cone loss, but ultimately atrophy in that paracentral zone.

It has a really slow excretion rate from the body. We used to think that it accumulated in the adipose tissue, but ultimately what it does is it loves to stay in the body. There have been reports of patients having continued damage from Plaquenil even 2-5 years after the medication has been stopped. It’s one of those medications that we want to monitor carefully for our patients because, even after they stop it, they can have continued changes for several years.
Question: Which of the following depicts a retina undergoing hydroxychloroquine (Plaquenil) toxicity?

(Scroll down for answer)

Correct Answer: 4
Correct: 94.44%  Incorrect: 5.56%
Cumulative: 60.138%
The correct answer is 4. Quickly looking through these conditions, I think you would agree that looks like AMD – drusen, potentially confluent in this case. Our next one is a macular hole. Number 3 is Ocular Histoplasmosis Syndrome, we are actually calling it OHS now instead of POHS – after 100 years, it is not ‘Presumed’ anymore. Our triad for diagnosing a patient with OHS is parapapillary atrophy, punched-out lesions, and the third one is macular involvement, specifically the development of a sub-retinal neovascular membrane. There is a break in Bruchs membrane, choroidal vessels come through, and result in the scar that you can see over the macula.

In thinking about other conditions that can result in the development of a neovascular net, I would like you to think of 4 other conditions. The development of wet, or exudative, AMD, is the number one cause of a neovascular net developing. Histoplasmosis is our 2nd cause. Then thinking about conditions such as lacquer cracks, which can develop with degenerative myopia, can show up anywhere on the fundus. Potentially if they go through the macular area, they can result in a significant decrease in vision. If we think about lacquer cracks that go through the macular area, they can result in a significant decrease in vision. If we think about lacquer cracks that radiate out from the optic nerve, those are called angioid streaks. For the top five causes for the development of angioid streaks, remember the mnemonic PEPSI (not Coke, Pepsi): Pseudoxanthoma Elasticum, Ehlers Danlos, Piagets, Sickle Cell, and Idiopathic. Our 5th potential cause of a neovascular net is trauma – any time there is a break in tissue, which can happen in trauma, you need to consider the possibility. To review, the top 5 conditions which can give you a neovascular net are: AMD, histoplasmosis, lacquer cracks, angioid streaks, and trauma.

Our 4th picture here is the bullseye maculopathy, which is the classic association with bull’s-eye maculopathy.

**Question:** Which OCT goes with a patient undergoing hydroxychloroquine toxicity?
The correct answer is 3. Quickly looking through these images, Image #1 is associated with a patient undergoing the ocular histoplasmosis syndrome and the development of a net. You can see a break in Bruch's and the development of a net that is forming. In picture #2, we have the development of a macular hole. Picture #3 has RPE atrophy just outside of the macular area, which is consistent with hydroxychloroquine toxicity. I’m going to go through this picture a little bit more closely with you in just a minute. Our 4th picture is the drusen picture, associated with the AMD patient.

Toxicity of Plaquenil can lead not only to the bulls-eye maculopathy that we saw with the previous pictures, but also you can get changes to the cornea, as well. You can get things like a whorl keratopathy that can form. Early stages of the maculopathy are often seen as mild stippling changes, and it’s thought that they were originally reversible, but now we are finding that they are not reversible. If you are seeing any fundus changes, it is probably relatively late in the process. The classic bulls-eye maculopathy is seen in later stages, and this is an irreversible damage to the retina. Even if you discontinue the medications, you are not going to have any improvement to the retina or to the visual function of that tissue.

Again, the classic pictures that we tend to look for is this bulls-eye maculopathy (Fig 2 Top) and the development of whorl keratopathy (Fig 2 Bottom) on the cornea. If you have a patient who has a whorl keratopathy, but is on no medications, what condition do they have? Fabry’s Disease. Optometrists pick up Fabry’s Disease probably earlier than most other healthcare professionals. Why? This keratopathy shows up relatively early in the disease process, so if you’re doing a slit lamp exam and see this keratopathy in a young patient on no medications, you need to eliminate Fabry’s Disease as a possibility. This is an alpha-galactosidase A deficiency, and this material is found throughout the patient’s entire body. This certainly increases their mortality rate, so we want to diagnose this early because there are medications with which to treat the patient.
The original screening guidelines for Plaquenil came out in 2002. They were revised in March 2011. In the original screening guidelines there was not a lot of prevalence data that was out there. Under the new guidelines, we are seeing that Plaquenil toxicity is probably a bit more prevalent than we thought it was. I don’t want you to remember a ton of numbers through this presentation, but one number that I want you to remember is 1%. That’s your patient’s overall risk of developing toxicity from taking Plaquenil. 1%, for patients who exceed 5 years of exposure to Plaquenil. That’s a really low number of patients out of the millions of patients who are taking this medication. I think patients really need to know this number. They are being seen by their rheumatologist who tells them, “I’m going to put you on this medication, but you need to be screened before you take the medication, then you need to be screened every year with visual fields and other testing, and you have the potential to go blind or lose vision from this.” That is particularly scary for patients, and I think we need to reassure them that this is a relatively safe medication, and that their overall risk is 1%. That’s important for you to let the patient know. Tell them that you are going to screen them very carefully, but their overall risk of developing damage is only 1%.

**Question:** Under the old guidelines, all of these tests were acceptable screening tests. Under the new screening guidelines for hydroxychloroquine retinopathy, which of the following is still considered an acceptable screening test?

1. Amsler grid
2. 10-2 visual field
3. Time domain OCT (i.e. Stratus)
4. Color Vision Testing
5. 1, 2, & 3
6. All of the above are still acceptable screening tests

*(Scroll down for answer)*
The correct answer is 2. Amsler grid is no longer considered an acceptable screening test. It is not equivalent to a 10-2 visual field. Your 10-2 visual field is the only acceptable test from this group. OCT is now a part of the screening guidelines, but it is not time domain, it is spectral domain that needs to be used. Color vision can still be done, but it’s not considered an acceptable screening test anymore.

To the right is a snippet from the new screening guidelines, and you can see here that newer objective tests are more sensitive than visual fields. When they took a look at how many pieces of equipment are out there compared to visual fields, there are many more visual field machines in the field than there are these very specialized pieces of equipment, so under the new guidelines, it is now recommended that along with a 10-2 visual field, one of these other three objective tests needs to be done. Those are our new screening guidelines: a 10-2 visual field in addition to either a multifocal ERG, Fundus autofluorescence, or an SD-OCT.

Of course, everyone in their practice has a multifocal ERG, correct? Yeah, not so much. I’m not too sure I could even find a mfERG in Portland, anymore. It’s one of the few tests that gives you both a subjective and objective component, but its availability is very low. Most people are going to default to either an SD-OCT or FAF.

With your 10-2 visual fields, that is white-on-white. You don’t have to change the stimulus color. The recommendation is that the patient have their first baseline field within their first year of taking the medication. Most rheumatologists will send the patient in prior to them starting the medication, but ultimately we just need to do it within their first year of taking the medications.

Really, there won’t be much damage until five years out, as this is a cumulative dose of 1000g. You will still screen the patient every year, but then when we reach that five year time period, you will look for any changes
in that 10-2 visual field. If you find a patient that presents with a new defect in that 10-2 visual field, you need to repeat that visual field within the next couple of weeks to see if that is a repeatable visual field defect. What you can’t do is just attribute it to the patient being tired that day, or otherwise skip over that spot. What has happened is that doctors have done that, only to find out later that was the first change related to the toxicity, and it was skipped over. Then the next time the patient came back, that defect was larger. Any changes on that 10-2 from the baseline, that field needs to be repeated within the first couple of weeks. If it’s a repeatable visual field defect, then what needs to happen is that needs to be reported to the rheumatologist or their primary care physician.

I would strongly recommend that you don’t say that the patient will come off of the medication. Ultimately, patients may stay on the medication even though they have the visual field defects. Why? Because Plaquenil is very good for increasing mobility and function in patients. If they come off of that medication, the alternatives are things like steroids, which we know have lots of complications. My warning to you is to not tell the patient they will come off of the medication, but rather that you are going to report this to their physician, then the physician, rheumatologist and patient will discuss it. I actually got caught on that once, telling the patient that they were going to go off of the medication, and they did not. Refer the patient back to their rheumatologist to make that decision.

The typical visual field defects that we tend to see in patients with Plaquenil toxicity are paracentral scotomas. (Fig 3)

With our new guidelines of SD-OCT, what we are going to look for is changes to the PIL (photoreceptor integrity line). That is really an artifact that we see on the SD-OCT, a junction between the inner and outer photoreceptor segments that I will show you momentarily. The other area we are going to look for is thinning in the outer nuclear layer. In FAF, which we primarily use in AMD nowadays, what we will see is if we have damage to the RPE cells secondary to Plaquenil, lipofuscin gets produced, which results in an increase in fluorescence. More fluorescence indicates that there is more damage. Ultimately we will see that when there is atrophy to a tissue, there is no fluorescence. With FAF, an increase of fluorescence indicates damage to the RPE cells. The mf-ERG in a patient with Plaquenil toxicity results in a paracentral depression on the ERG in early maculopathy.

Let’s look at these images again. Figure 4 [Top] shows a normal Outer Nuclear Layer, and a normal PIL (Photoreceptor Integrity Layer) line. Figure 4 [Middle] shows mild maculopathy, with paracentral scotomas. We still have a foveal peak on the ERG, and still have a PIL line on the OCT underneath the foveal area, though paracentrally it’s gone. Then, in advanced (Figure 5) maculopathy, we have central and paracentral scotomas in the visual fields, flattened foveal peak in the ERG, and the only remnant of the PIL line is right under the fovea. Now we are getting atrophy paracentrally, which results in beams from the OCT penetrating down into the choroid. It’s really important that you know what you’re looking for on your OCTs. When you do a baseline visual field and OCT’s, what you’re looking for is change over time.
Figure 4 [Top] A normal OCT (time domain and spectral domain) as well as a normal mf-ERG. [Bottom] Moderate maculopathy, showing a thinned ONL with PIL still intact on the OCT. ERG shows a normal foveal peak but with flattening paracentrally.


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PIL=PR Integrity Line

Under the new guidelines, Table 3 shows the risks for retinopathy. It’s duration of use – this is a cumulative dose. Patients who have been taking the medications for more than 5 years are at higher risk for toxicity.

A cumulative dose of 1000 g. Remember, this is a cumulative dose, not a successive dose. This means a patient can have taken this medication 10 years previously, and has now started it up again, that 10 years previously incorporates into their cumulative dose.

A daily dose of more than 400 mg/day puts them at higher risk. Most patients we see today aren’t on a daily dose higher than 400 mg. If anything, the body size that is taken into consideration are our patients who are very tiny may actually be put on less than 200 mg.

### Table 3

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<thead>
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<td>Age</td>
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Figure 5: Advanced maculopathy showing RPE atrophy paracentrally and a remnant PIL underneath the fovea on the OCT, a flattened foveal peak on the ERG, and dense paracentral and central defects on the 10-2 visual field.

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Age: elderly. The report doesn’t really give an age. If you are one of my interns, you may consider me as elderly. I’ll let you decide for yourself what elderly is – I think it’s probably 65 and above.
Any systemic disease that results in kidney and liver damage decreases the body’s ability to process that medication out, which results in increased toxicity levels.

Ocular disease: this is the other thing I want you to remember. Do you think that their PCP or rheumatologist knows that the patient has drusen? Probably not. What can happen is that some of these retinal conditions can actually mask some of the toxicity that is going on. Remember that looking at the fundus is not considered part of the screening criterion, it’s really the visual fields and the OCT. But we have had patients who have been monitored for drusen secondary to AMD, and we found out that they were taking Plaquinil and those drusen were masking the changes that were happening on the retina. In addition to that, if we have any conditions that result in compromise to the macula, those could result in increased toxicity just because there’s already damage to the tissue. If your patient ends up having any changes to the retina, I think those should be reported back to the rheumatologist and the patient’s PCP.

Older literature on Plaquinil really focused on the daily dose/kg of patient weight. Now the new literature focuses on the cumulative dose, so you want your screening of them to be within the 1st year of taking the medication, and then really nothing until 5 years out. You’re still going to screen them every year, but your risk of them developing toxicity is nothing until 5 years out.

**Case 2**

We have a 48 YO white female who presents for her diabetic exam. She was referred by her PCP about 2 weeks ago. When she was supposed to come in for that visit, she had fallen that day, and was unable to come to her appointment. She has now been rescheduled as an emergent patient because she’s noticing that she has decreased vision in her right eye, which has been getting worse over the past several weeks. She has had diabetes for about a year & a half. Her control is 120 to 240 on her sugar levels. Her last A1c is 9.1.

**Question:** What does an A1c of 9.1 roughly convert to in plasma glucose?

1. 170
2. 2191
3. 213
4. 243
5. 274

*(For answer, scroll to next page.)*
The correct answer is 3 – it converts to about 213. Why this is important for us is because we want to know the patient’s last blood sugar, we want to know their range, and their A1c value as an average of their sugar levels over a 3 month time period. It doesn’t really tell us the fluctuation on a daily basis. In addition to that, we know that most patients will lie if they are given the chance to, and patients with diabetes may say “My blood sugar never goes over 150.” Well, if the last A1c was 9.1, we know that converts to 213. So a rough way to guestimate what an A1c converts to is to take that 9.1, make it 91, and multiply it by 2.2, or the equivalent of converting from kg to lbs. That will give you a rough estimate of what your patient’s sugar levels are. It works very well on A1c’s of 6-8, above 8, you will be slightly underestimating, but it will give you a rough estimate.

Question: At what blood plasma glucose level will patients begin to show symptoms of sweating, pallor, confusion, ataxia (“drunkenness”)?

1. 100
2. 70
3. 50
4. 25

(For answer, scroll down to next page)
The correct answer is 3. Below 70, patients will be hypoglycemic. Below 50, they are going to start having the symptoms that go with it. This is something that we are going to have to watch with our patients. If our patients have diabetes and the start to look like they are not paying attention anymore, they start to get white or maybe start to sweat, we need to make sure that we are checking their sugar levels, because at less than 50, they will start to present with those symptoms. We don’t want them to pass out, because it will be very difficult for us to get sugar into them at this point.

Diabetes is diagnosed with a fasting blood sugar of greater than 126 or an A1c value of greater than or equal to 6.5.

Question: What percent of patients who have diabetes have their blood sugar, blood pressure, and lipids in the “target zone”?

1. 7%
2. 15%
3. 22%
4. 27%

(Scroll to the next page for answer.)
The correct answer is 1. 7%. 7% of patients will have control of all 3 in their target zones. I tell patients this statistic. I ask them that exact question, and I get varying responses from 15 to 50%. It’s 7%, which is just an indication that it’s very difficult to manage this condition. If your patients happen to be Hispanic or Black, the value is actually less than that – closer to 4 or 5%.

Back to our patient. She presents with CF vision in her right eye, and 20/40 in her left. APD in the right eye. Her pressures are 16 mmHg OU. Figure 6 are not her nerves, but are very similar to how her nerves appeared.

Question: Based on the optic nerve appearance, what would you “diagnose” this patient as having?

1. Ischemic optic neuropathy
2. Optic neuritis
3. Papilledema
4. Swollen optic nerve heads
5. Optic nerve head drusen

(Scroll to next page for answer.)
I really think that there are 2 correct answers in this case, those being 3 and 4. Papilledema, by definition is raised intracranial pressure that is resulting in swollen and optic nerve heads. I don’t know what state you are seeing this in, but I am not aware of any state that allows us to do spinal taps. Ultimately, all that you know is that your patient has swollen optic nerve heads. However, when you are coding this, there is no ICD9 code for ‘swollen optic nerve head’ so we have to code this patient as ‘Papilledema, unspecified.’ Ultimately, you only know that the patient has swollen optic nerves. Your Ischemic Optic Neuropathy is not likely going to show up bilaterally. The same thing with optic neuritis – 70% of optic neuritis’ are unilateral in presentation. The only one that is going to be bilateral in presentation is the optic nerve head drusen, but you are not likely going to go to finger count vision, have all these other changes going on, just from optic nerve head drusen.

When I entered the exam room, I noticed that the patient’s arm was twitching. As we moved that arm out of position, that twitch actually increased. I asked her how long that had been going on, and she said about the last 2-3 weeks. I said, “Is that about the same time you fell?” She said yes. I asked if she got headaches, and she said she got the worst pounding headaches that wake her up at night.

I contacted her PCP. Unfortunately she is uninsured so it took us a little while to get her an MRI. I contacted the PCP on a Wednesday, and we couldn’t get her in to the MRI until Friday.

Figure 7 shows what was found. This figure is not her actual MRI scan, but is very similar to how her MRI looked. She was diagnosed with a condition called a craniopharyngioma. These are pretty rare tumors, but they show up in the same area that a pituitary tumor does. Ultimately all the problems that she was having, her diabetes, peripheral neuropathy (the patient was in a walker), the arm twitch, everything she was experiencing was coming from this tumor. She was estranged from her family, but her mother visited her in the hospital and said, interestingly.

Figure 7: MRI very similar to our patient’s MRI.
Source: http://neurosurgery.ucla.edu/images/Pituitary%20Program/Craniopharyngioma/Cranio_Sag_Preop_fullylabeled.jpg
enough, “You’ve had two uncles die from the same thing.” Thus, it’s very important to know case history at this point.

Craniopharyngiomas are slow-growing tumors of epithelial-squamous origin that arise from remnants of the craniopharyngeal duct. They are a benign tumor with malignant side effects. In other words, these tumors show up in areas that result in significant changes in the patient’s health. The patient’s diabetes and all of the other neurological stuff was coming from this tumor. The patient was sent for emergency surgery. The neurosurgeon actually contacted me and said that this was the largest tumor he’d ever removed from anyone’s brain – it was actually tangerine-sized. She said that if we had not found the tumor and referred the patient out, the patient likely would have been dead within the week. Thus, I think that this is a very important case for us to show that ultimately yes, we save vision, but we also save people’s lives, as well.

*Figure 8: Bi-temporal field loss*

A craniopharyngioma results in bi-temporal field loss (Fig 8), which is very similar to what is going to show up with a pituitary tumor. It shows up in about the same area, but can be much more progressive than a pituitary tumor.

Our patient is unfortunately not doing very well. They had a hard time managing her intracranial pressure, so she was ultimately sent in for surgery to install a shunt. Then, unfortunately, she developed an infection. She is still no light perception (NLP) in her right eye and has about 20/40 in the left eye, retaining the temporal hemianopia OS.

**Case 3**

Let’s move on to our next case. I have a 65 YO Caucasian patient who presents with sudden onset loss/blurring of vision in the right eye. The patient has had hypertension for the last 15 years and is taking a “water pill.” VA’s are 20/60 OD, 20/25 OS. Pupils were PERRL with no APD, with an inferior visual field defect noted in the right eye, left eye was clear.

**Question:** What I want you to do for me now is pick the fundus that goes along with this patient.

1. ![Fundus Image 1](image1.png)
2. ![Fundus Image 2](image2.png)
3. ![Fundus Image 3](image3.png)
4. ![Fundus Image 4](image4.png)

(Scroll down for answer)
The correct answer is 3. The majority of doctors polled got this correct. If you take a look at these images, #1 is a CRAO, with the classic cherry-red macula with a whitening around it. Remember with central retinal artery occlusions, that cherry-red macula only lasts for the first couple of days. Eventually the retina is going to re-perfuse and can look perfectly normal, but the patient is not going to have any vision.

The 2nd image is a central retinal vein occlusion (CRVO). The 3rd image, our correct answer, is a BRVO, or branch retinal vein occlusion. #4 is actually a pre-retinal hemorrhage. If you have a pre-retinal heme, what do you instantly think about your patient? You should think that they have proliferative diabetic retinopathy. Why that is is that there are no naturally-occurring blood vessels in that pre-retinal space. If there are no naturally-occurring blood vessels in that space, then how did the blood get there? Ultimately, from new blood vessel growth. Thus, you don’t need to see the blood vessels under the blood to know that they are there. Ultimately if you see a pre-retinal or vitreal heme, and the patient does not have a history of trauma, you need to think of PDR.

With vision loss without pain, one of the things we think about is vascular problems, such as diabetes and diabetic retinopathy. Things we want to look for: changes in vision – typically myopic, microaneurysms, dot & blot hemes, cotton wool spots, neovascularization. I think it’s very important in our patients with diabetes that you go in and actively look for issues. You cannot just use the force and wait for things to jump out at you – what you really want to do is go in and actively look for these different conditions. I guarantee you that if you are not specifically looking for IRMA, you are likely going to miss it.

Question: Which of the following would you recommend for a patient who has diabetic macular edema and a VA of 20/40?

1. Monitor for 1 month
2. Refer for focal laser treatment
3. Refer for intraocular kenalog injection
4. Refer for intraocular anti-VEGF injection
I put that all answers are correct, in this case, with the majority of the doctors polled going with answer #4, which is referring for anti-VEGF, and I think that is really what is now the standard of care. You can certainly monitor for a month, but the patient already has decreased vision and we know from the criterion for diabetic macular edema that VA is not a part of that. Focal laser treatment was the standard of care until a few years ago, but we know that patients tend to have a subtle decrease of vision after that procedure. Kenalog is primarily not used anymore in the treatment of diabetic macular edema, but anti-VEGF is.

What happens with VEGF is that you get not only changes with new blood vessel growth, but it also increases permeability. One thing that I want you to remember is the original name for VEGF, which is Vascular Endothelial Growth Factor, and Vascular Endothelial Permeability Factor. It does increase permeability of tissues, in addition to promoting new blood vessel growth. What we see in Figure 9 is that diabetes results in hypoxic or metabolic changes, which results in VEGF production, which results in increased permeability and also new blood vessel growth. Thus, it is an increase in VEGF that results in not only the diabetic macular edema, but the new vessel growth, as well.

In August of 2012, the FDA approved Lucentis for the treatment of diabetic macular edema. From the two clinical studies (involving 759 patients treated and followed for 3 years), they found that upwards of half of the patients treated monthly with Lucentis had up to 3 lines improvement in vision over the placebo. Now, the standard of care is injection of anti-VEGF, primarily Lucentis. *(Course continues in Part 2)*