

12.18.2025 Ocular TB Webinar Chat Q&A

TIMING OF EXPECTED RESPONSE TO TREATMENT; WHAT TO DO IF WORSE (STOP?)

When will the patients see improvement after medication started?

Kevin Winthrop: Eye conditions might get worse in the first 2 months of treatment.

That hasn't been my experience (though I have much less experience with this than Dr. Winthrop! But I have the same question... I tend to make a decision at the 2-month mark to determine if I should change them from suspected ocular TB to clinical cases. **What if they are not better? Or if they are worse... is it because uveitis can wax and wane?** (I assume perhaps other affected areas might also wax and wane)

What percentage of cases do we see improvement in vision/ocular findings? What time frame should we expect to see improvement? If we don't see improvement, when do we consider stopping treatment?

Kevin Winthrop: Treat for 2 months, look then for improvement. Sometimes you see improvement starting around 1 month. Sometimes it worsens before it improves. Sometimes you see IRIS-like phenomena even around the 2-month mark. But generally, you see improvement 1-2 months after, and make a judgment at 2 months to decide whether you should treat more.

WAXING/WANING SYMPTOMS; RELAPSE? IRIS? IMMUNE REACTION? PULMONARY TB?

Have you seen patients with intermittent eye symptoms, either short-term (month-year) or long-term (even many years), that you think could be caused by TB?

Second Question: Is TB uveitis ever relapsing? I have several patients on treatment right now who have a several-year history of waxing and waning symptoms; they seem to respond to steroids. Then somebody checks an IGRA and all of a sudden, it is considered ocular TB!

Re: second question. Same here. I have no way of proving it is *not TB, so I am treating for TB and assessing for improvement, which is not always easy. If they are tolerating it well and are either stable or improving, I continue them as a clinical case. I want to give them the best opportunity to be cured of TB if they have it; all fine as long as I don't harm them.

I consider the waxing and waning of symptoms and findings, despite adequate TB treatment, to be like a paradoxical or IRIS reaction. The TB is eradicated, but the immune system finds something to react to.

When would you consider repeating TB treatment in a patient who has recurrent inflammatory ocular findings after completing HRZE?

(HRZE – isoniazid, rifampin, pyrazinamide, and ethambutol)

Kevin Winthrop: Almost never. I've done it once because the ophthalmologist felt so strongly about it, and they were from a country with high rates of MDR.

How many of these cases presented with pulmonary TB or TB in other parts of the body?

Kevin Winthrop: Hard to know on relapse rates, given "relapse" can be just sterile inflammation. Patients can often have uveitis flares months and years after treatment that are not associated with current active disease.

Kevin Winthrop: Definitely see patients that sometimes have wax/wane course (multiple uveitis flares) over the course of several years before ocular TB is diagnosed. Also, should underscore the importance of looking in chest (CXR) and exam to see if disease elsewhere outside the eye (5-10% of time there is active lung or other disease).

Third Question: If a patient has already had a response to steroids, does that make TB less likely? Since there is a large immune component to this disease, I can see how steroids may make it a little better, but if symptoms resolve completely with steroids, do we need to treat?

Kevin Winthrop: Question is for how long. If they get better with steroids and they successfully taper off and stay quiet, then who knows? It might not be TB. The problem is, sometimes it is presumably a very low level of infection or even just the presence of some bacilli part or an immune reaction to prior bacilli being present. It still might be worth clearing out a bacillary reservoir that might just spill into the eye via the bloodstream from time to time. There are no good answers here, but I've had patients who have been on/off steroids for several years, and it is only after treating the TB that this cycles stops. (and sometimes it doesn't stop!)

Is it theoretically possible for active pulmonary TB to be transmitted through ocular mucus membranes that have been disrupted by surgery?

Kevin Winthrop: No.

Is there a similar retinal pathology seen with ocular TB and syphilis of the eye?

How does this differ from patients with ocular issues from syphilis? Should we ask to see the scans from the ID doctors?

Kevin Winthrop: Yes. Can be similar, so one should work the patient up for both. Diagnosis of syphilis also difficult, but based on blood tests and sometimes CSF.

STANDARD TREATMENT (HRZE)? PARTICULARLY EMB? QUESTION RE: RIF?

What are your thoughts on including Ethambutol (EMB) in the TB regimen, given the risk of worsening optic neuritis/difficulty monitoring ocular symptoms?

**Do you use standard RIPE regimen? (RIPE – rifampin, isoniazid, pyrazinamide, and ethambutol)
No concerns with use of ethambutol?**

Do you typically use Ethambutol for your ocular cases? Some of our ID physicians are very conflicted about using EMB.

[John Szumowski, MD] EMB also hard in older patients with preexisting nonTB eye disease.

Kevin Winthrop: Yes. Standard RIPE unless they have optic nerve disease or involvement. Some folks with glaucoma underlying have some optic nerve disease already, so we might avoid. But generally ok to use. If you can't monitor color vision due to poor vision, then you can avoid it (since you will have hard time monitoring during therapy).

[John Szumowski, MD] I have sometimes used Fluroquinolones (FQ) instead of EMB though has its own issues with tolerability.

[participant] In our two current ocular cases, we have not used Ethambutol due to the potential visual changes. In one case, we used moxi (moxifloxacin (MOX)) in its place for the intensive phase.

Kevin Winthrop: Yes. Ok to use Levaquin. I sometimes also swap it in if I can't use EMB.

Do you continue EMB beyond two months (because of concern for Isoniazid (INH) resistance with no culture result)?

Kevin Winthrop: Typically, we treat for 2 months and then judge clinical improvement. If improved, we assume we are treating the right thing and we drop to INH/RIF (rifampin) and treat for a total of 6-12 months depending on where disease is in the eye (as I mentioned). If no better at 2 months, then might give it more time. Another 1-2 months. Somethings IRIS at 2 months and things have not improved or are slightly worse. So sometimes I give it a bit more time.

Do you avoid use of rifamycin in treatment among patients with intraocular lens implants r/t concern for discoloration?

Kevin Winthrop: No. No concern.

How might history of glaucoma affect TB regimen choice?

Kevin Winthrop: If they have optic nerve disease from their glaucoma already, then I'd leave off the EMB.

DR-TB REGIMEN OR IF DRUG INTOLERANT

[participant] Empiric treatment is relatively doable unless side effects come up—MGMT thoughts at that point: stop treatment and/or change to other second-line drugs. Probably depends on your level of certainty the eye symptoms are truly from TB.

What is the most effective treatment for ocular TB in multi-drug (RIPE) resistant patients?

Kevin Winthrop: Usually (95%) you don't have susceptibility or any epi data that would tell you they have MDR. If you do have that info, then there is no data of course, but could pursue BPaLM or other MDR regimen based on susceptibility information. Also---you can sometimes use topical ABX (e.g., compounded amikacin drops) to add to a regimen if resistance is present. (BPaLM – bedaquiline, pretomanid, linezolid, and moxifloxacin)

BORDERLINE IGRA/NO RISK FACTORS; DO YOU TREAT (OR TREAT SHORTER/DIFFERENTLY)?

What we see often is patient with uveitis, no risk factors for TB and IGRA positive, but close to the cut off. Repeat testing again close to cut off or negative. Are you treating most of these cases?

Last question: we are getting a LOT of referrals for low-risk patients with positive IGRA and minimal findings; ophthalmologists don't understand how hard it is to get patients to finish a course. If it is a questionable case with no serious findings, **what do you think about treating shorter course since it is a paucibacillary disease?**

[participant] We use three-times weekly regimen, for paucibacillary form of TB.

Kevin Winthrop: With regards to questions of low-risk patients with low positive IGRA with uveitis. Think it depends on several factors—where is the uveitis (anterior versus posterior, choroiditis, etc.). Certain presentations increase the likelihood. Was everything else ruled out (e.g., syphilis)? How has it behaved the last few years? Has it responded to steroids or other immunosuppressives, and now it is back despite that therapy? Must consider these and risk factors to make. Decision...

SPUTUM COLLECTION AND ROLE OF CXR IN OCULAR TB DX

Dr. Winthrop, what are your thoughts on collecting sputum to R/O pulmonary involvement? We have a provider that often does not want to do this d/t eye pressure.

[John Szumowski, MD & participants] Seems unnecessary to avoid unless already high intraocular pressures

Kevin Winthrop: I would not collect sputum unless the CXR has suggestion of active TB. If not, they will not produce worthy sputum likely. There is no contraindication to trying (not going to be problem for eye pressure), but just not worth doing unless CXR abnormal.

Lisa True: Appreciate clinical rationale, CDC guidelines do recommend sputum collection for all persons presumed to have TB (including extrapulmonary).

https://www.cdc.gov/tb/media/Core_Curriculum_TB_eBook.pdf

Do they isolate the patient until completing 5 RIPE doses, since they don't evaluate?

Kevin Winthrop: No.

I might have missed it, but what are **thoughts on treating for ocular TB if they have a normal CXR/chest CT?** BTS Clinical Statement on ocular TB relies heavily on identifying evidence of old or active TB on chest imaging.

Kevin Winthrop: Yes. Decision re: ocular TB is not influenced by CXR/CT. But one should be done to rule out concomitant active pulmonary TB.

TESTING FOR SYPHILIS (AND OTHER TESTS FOR DDX OF UVEITIS)

Would it be best practice to test for Syphilis regardless of risk factors just to rule it out?

[John Szumowski, MD & participants] Testing for syphilis should absolutely be done; it's much easier to treat; there's a lot of syphilis out there.

Kevin Winthrop: Agree with syphilis. Most uveitis patients will have a syphilis screen, IGRA, Toxo titer, Ace level (for sarcoidosis).

Agree with testing for toxo, syphilis etc. but it can get tricky when patient has a positive toxo IgG and a positive IGRA with panuveitis for instance. **What do we treat for? How can you differentiate between toxo uveitis and TB?**

[John Szumowski, MD & participant] You really need an ophthalmologist who has TB experience and interest in TB eye disease. Harder and harder in the US.

Kevin Winthrop: Agree. Toxo often has very characteristic lesions that are distinct and make it easier to recognize. IgG titers that increase over a few weeks or a positive IgM obviously point one toward toxo.

Kevin, **are there studies of patients with macular inflammation or epiretinal membranes without eye granulomas or TB symptoms and clear CXR and skin test who might still have extrapulmonary TB?** There are many people with macular pucker and no obvious cause for the condition according to ophthalmologists. Some are monocular, not always binocular condition.

Kevin Winthrop: Not aware of any. Not sure, I would think TB would cause macular pucker.

QUESTIONS FOR KRISTI

Strange question- is active or disseminated TB common in returning Peace Corps volunteers?

Kristi Mathieson: I was the only one in my cohort to test positive. I think it depends on your sector and exposure. I was in the health sector and worked directly with a hospital. There are other environmental and educational volunteers who likely have less exposure.

Kristi.....what should they have done differently for you to have better understood the importance of DOT?

***Kristi Mathieson:** I think had I started my treatment on DOT, I would have been more likely to have been on board, but it felt like I was all of a sudden not being trusted, as I was given medication to take on my own and then transferred to a new provider who started the DOT.*

Kristi, did your eyes improve after TB treatment?

***Kristi Mathieson:** My vision actually improved in the one eye! I cannot say if that was due to the steroid drops, TB Drugs, or if it was merely coincidental!*

OTHER COMMENTS/QUESTIONS

Some good news is that with recent RVCT revisions we can now distinguish eye as disease site in TB surveillance data ('Eye and eye appendages'); helpful for future data reviews.

***Kevin Winthrop:** Good news on the RVCT. I didn't realize they broke apart eye from the ear. That's great. Thanks*

We struggle with providers giving a "clinical diagnosis" that would be considered countable for RVCT purposes, unsure if others have this situation?

***Ann Scarpita:** CDC Clinical Case Definition: A case that meets **all** of the following criteria:*

- a positive tuberculin skin test result or positive interferon-gamma release assay for *Mycobacterium tuberculosis*;
- other signs and symptoms compatible with tuberculosis (TB) (e.g., abnormal chest radiograph, abnormal chest computerized tomography scan or other chest imaging study, or clinical evidence of current disease);
- treatment with ≥ 2 anti-TB medications; and
- a completed diagnostic evaluation.

Because of that rarity, ocular TB cases often hinge on meeting the clinical surveillance criteria (positive IGRA/TST + compatible signs/symptoms + treatment + evaluation). However, identifying what counts as "signs/symptoms" in ocular disease (e.g., uveitis) must still be documented in a way that meets surveillance criteria.

*Note: The software for TB surveillance developed by CDC includes a calculated variable called VERCRIT, for which one of the values is "Provider Diagnosis." "Provider Diagnosis" is selected when the user chooses to override a "Suspected" (corresponding to a "possible" case as described in these recommendations) default value in the case verification screen as "Verified by Provider Diagnosis." Thus, "Provider Diagnosis" is not a component of the case definition for TB in the current "Tuberculosis Case Definition for Public Health Surveillance" (Appendix A). CDC's national morbidity reports have traditionally included all TB cases that are considered verified by the reporting areas, **without a requirement that cases meet the published case definition.***

[John Szumowski, MD]: interesting to consider >6 month treatment, have not usually done that.

[Janice Louie, MD]: John S, would be interesting what is relapse rate for 6 month duration in a low incidence setting. A review of CNS TB to see if there is a high frequency of prior ocular TB treated for

standard 6 months might help answer this question. Felicia Chow has done a review of SF cases and almost all did not have prior history of TB treatment for any site- might be difficult to determine in US given low numbers.

[John Szumowski, MD]: yeah, I think you would have to look outside the US

@Kevin Winthrop Macular edema manifested in a patient shortly after intense coughing episode secondary to URI (not known to be TB). It resolved for the most part but later edema manifested in the other eye and has not resolved. Patient history of corneal surgeries AK & RK.

Kevin Winthrop: Macular edema is from leaky vessels. Would be odd to be associated with TB, unless it is TB retinal vasculitis—rare, but can happen.