

How Do Infectious Diseases Clinicians Manage Patients with Suspected Ocular Tuberculosis? Results of an Emerging Infections Network Survey

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Introduction

- Ocular tuberculosis (Otb) is considered an uncommon TB presentation and infrequently reported in low TB incidence regions.
- Otb most commonly manifests as granulomatous uveitis and can occur with/without concurrent pulmonary/ extra-pulmonary TB (1,2).
- The incidence of Otb is unknown. Ocular findings are reported in 1.4% to 15% with pulmonary/extrapulmonary TB in some series (3,4)
- The diagnosis of Otb, especially granulomatous uveitis, has received increasing attention from ophthalmologists, many now include IGRAs in evaluation of uveitis of unknown etiology (5)
- Some ID physicians (IDPs) report increased referrals for suspected Otb, predominantly TB uveitis
- Some states, including Michigan and Oregon, report large increases in Otb as a proportion of their extrapulmonary TB cases (6,7).
- We wished to determine how IDPs approach suspected ocular tuberculosis/TB uveitis, including the diagnosis, management and reporting of this syndrome

Specific Aims of This Study

- To determine if IDPs are seeing increased referrals for suspected or confirmed Otb and what the specific indications for referral are
- To determine how IDPs approach the diagnosis, management and treatment patients with suspected Otb
- To understand the impact of TB specific risk factors on IDPs' approach patients with suspected Otb referred for positive IGRA results
- To understand how IDPs interact with public health departments when treating cases of presumed but not microbiologically confirmed Otb

Methods

- The Infectious Diseases Society of America Emerging Infections Network (IDSA EIN) is a provider-based emerging infections sentinel network of primarily North American IDPs
- The IDSA EIN regularly disseminates topic based surveys to its members.
- EIN staff and two US IDPs with extensive TB experience collaborated to create a 9- question multiple choice/open comment survey addressing various components of the study aims above
- The confidential, web-based survey was disseminated to 1379 IDPs with an adult practice from February 19 through March 14, 2019. No incentives for participation were provided
- Results were analyzed with SAS v9.4. To assess non-response bias, geographic and practice patterns of responders and non-responders were compared
- Open comments were systematically reviewed, coded for relevant themes and grouped into categories

Results

Respondent Characteristics

- 754 of 1379 surveyed (55%) responded
- Geographic Distribution of responders (absolute #) Years of Practice, Employment and Hospital Type are shown Respondents more likely to:
 - Have ≥ 25 years of ID Experience (p=0.002)
 - Work for the Federal Government (p=.03)
 - Work in a VA/Federal Hospital (p=.04)

Region:		# of Respondents
New England		56
Mid Atlantic		116
East North Central		110
West North Central		85
South Atlantic		134
East South Central		35
West South Central		55
Mountain		30
Pacific		129
Puerto Rico		0
Canada		4

Years Since ID Fellowship:		# of Respondents
< 5 years		147
5 -14		254
15-24		129
≥ 25		223

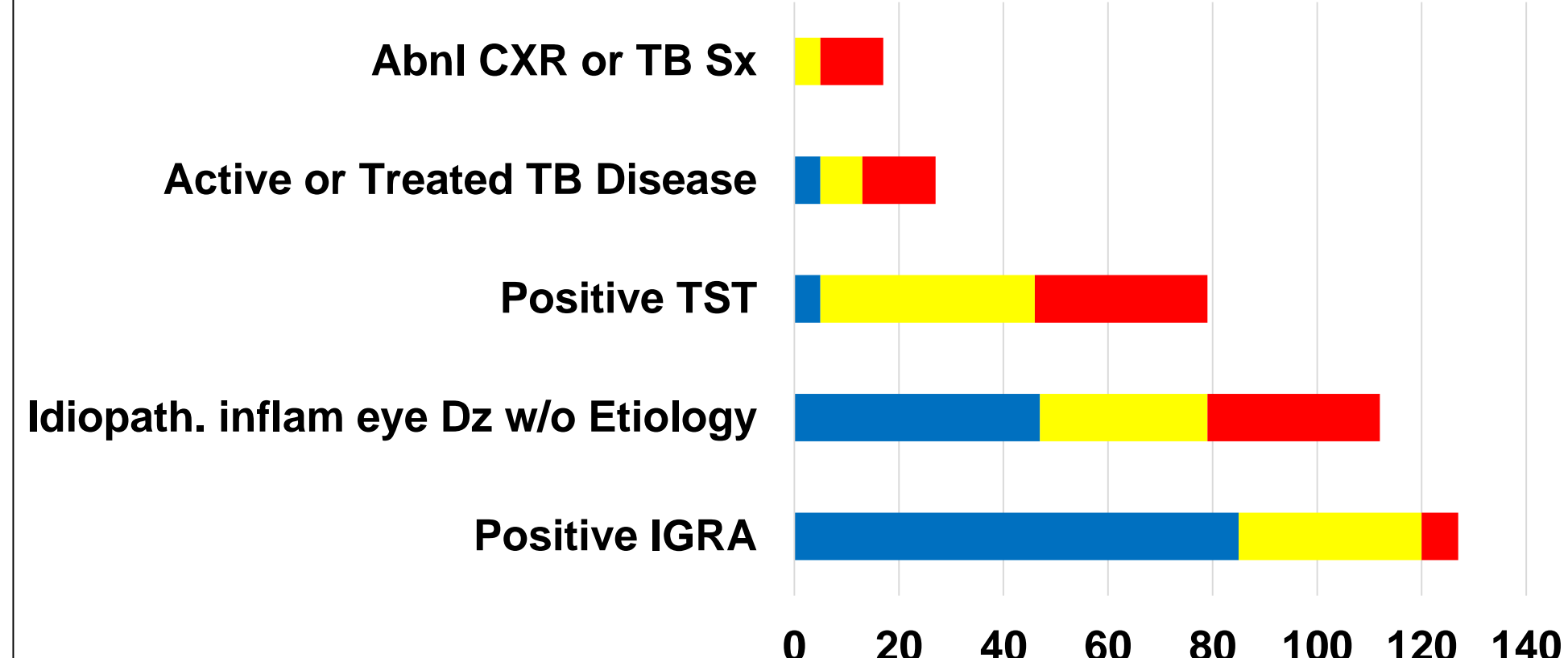
Employment:		# of Respondents
Hospital/clinic		263
Private/group practice		195
University/medical center		247
VA, military, other Federal		49

Primary Hospital Type:		# of Respondents
Community		200
Non-University Teaching		185
University		279
VA Hospital or DOD		54
City/ county		37

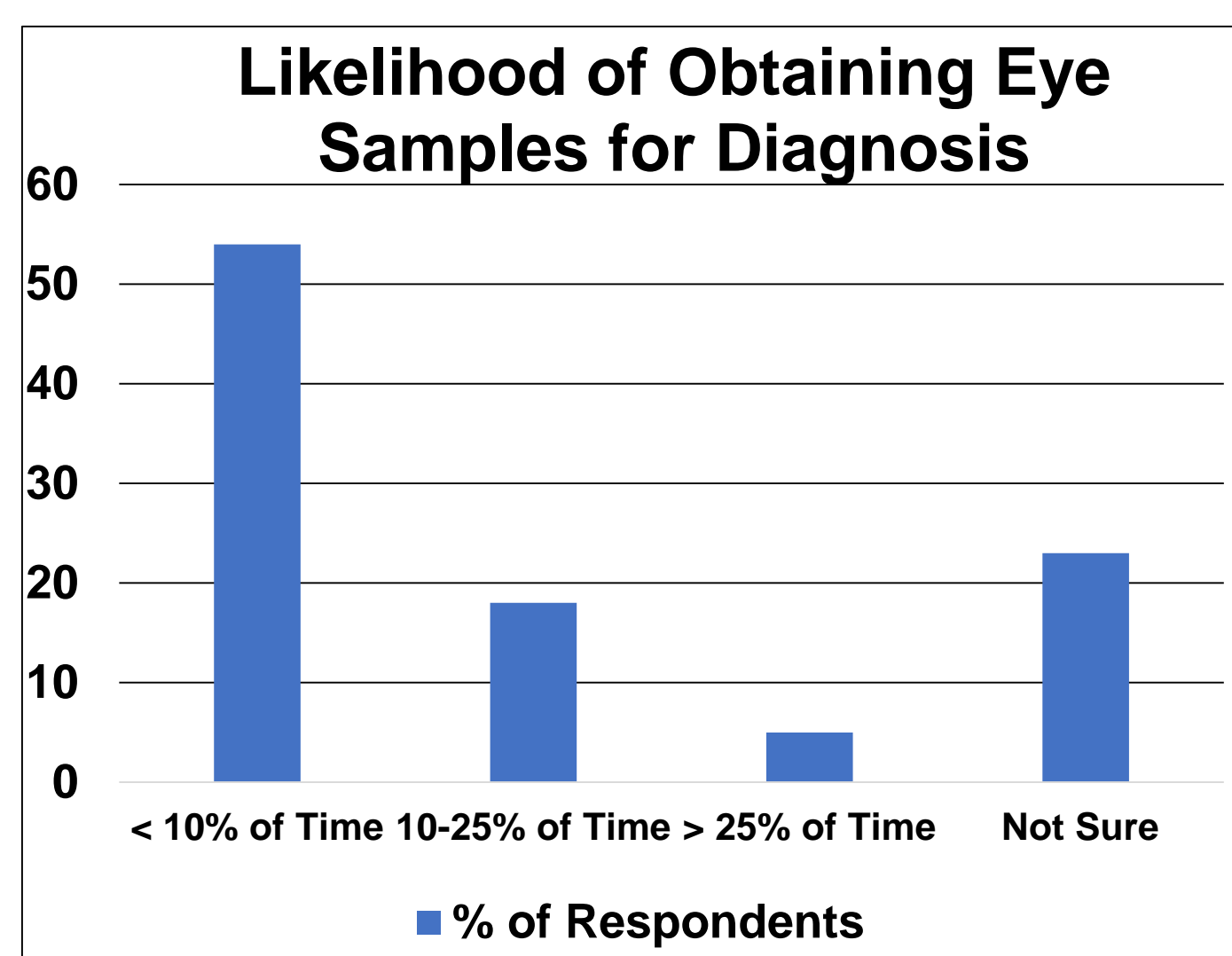
Otb Referral Patterns

- 613 (81%) had seen no referrals for Otb in the past 3 years
- 101 (13%) saw 1 to 3, 28 (4%) saw 4 to 6, and 12 (2%) saw > 6 referrals for Otb in the past 3 years
- 35% who saw Otb referrals reported increasing referrals for "possible" Otb based on positive TST or IGRA but only 14% saw increased referrals for "probable or confirmed" Otb.
- Few reported decreased Otb referrals over this time
- The most common reason for referral was uveitis with a positive IGRA, though many referrals were also for idiopathic uveitis without any tuberculosis testing. Few referrals were for eye findings in patients with known or suspected extraocular TB disease or TB related symptoms

Most Common Reasons for Referral (Ranked as #1,2 or 3)



Diagnostics



Management Issues

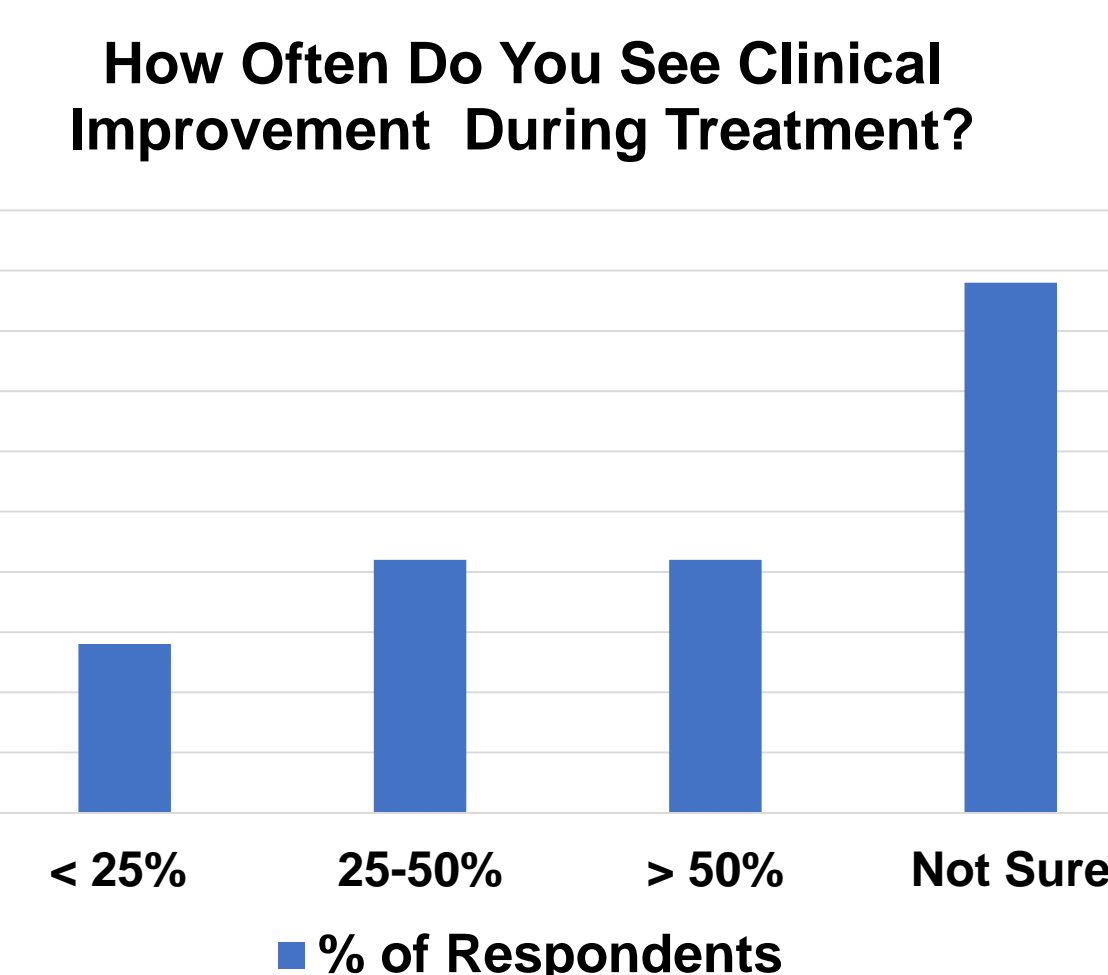
Management of Granulomatous uveitis with Positive IGRA With /Without TB risk factors

- Respondents much more likely to treat as Otb with/without additional sampling if from TB endemic area or other TB risk factors (79% vs 29%, p $\leq .01$)
- More likely to treat as Otb if ophthalmologist had high clinical suspicion (91% vs 60%, p $\leq .01$)
- More likely to treat as Otb if CXR abnormal (78% vs 53%, p $\leq .01$)

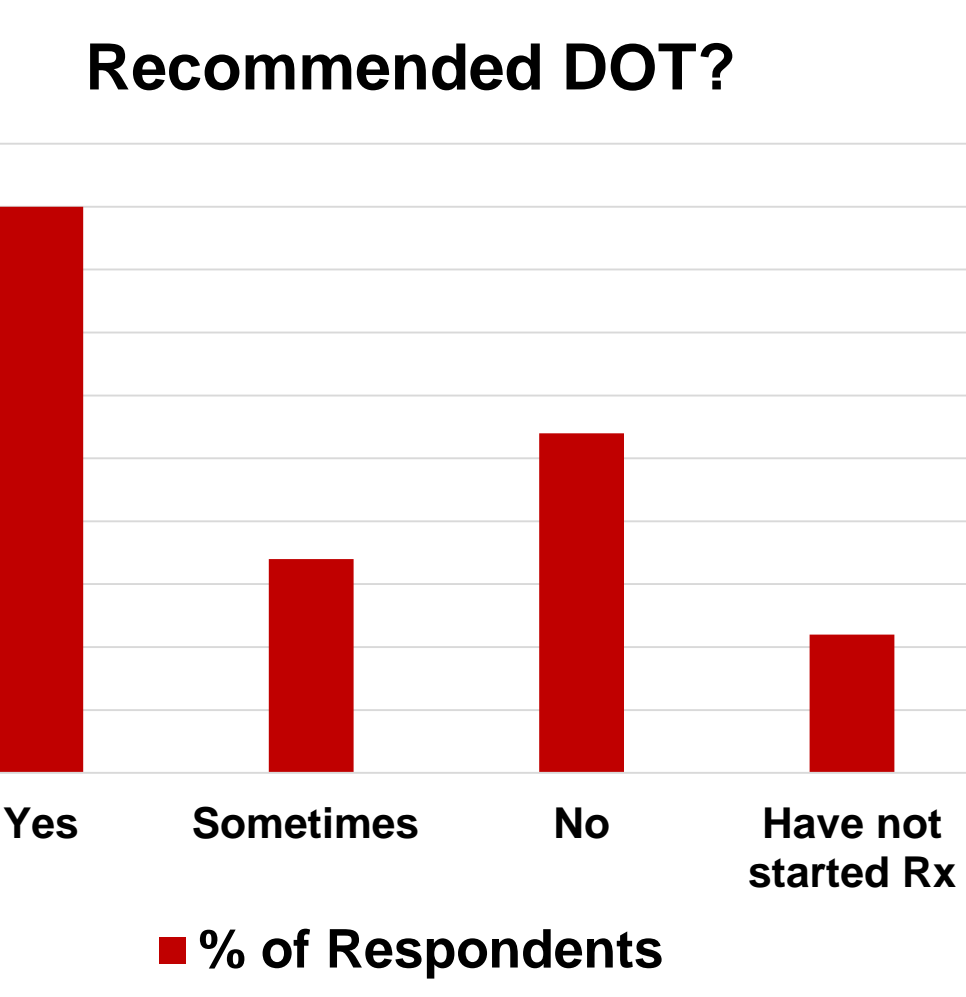
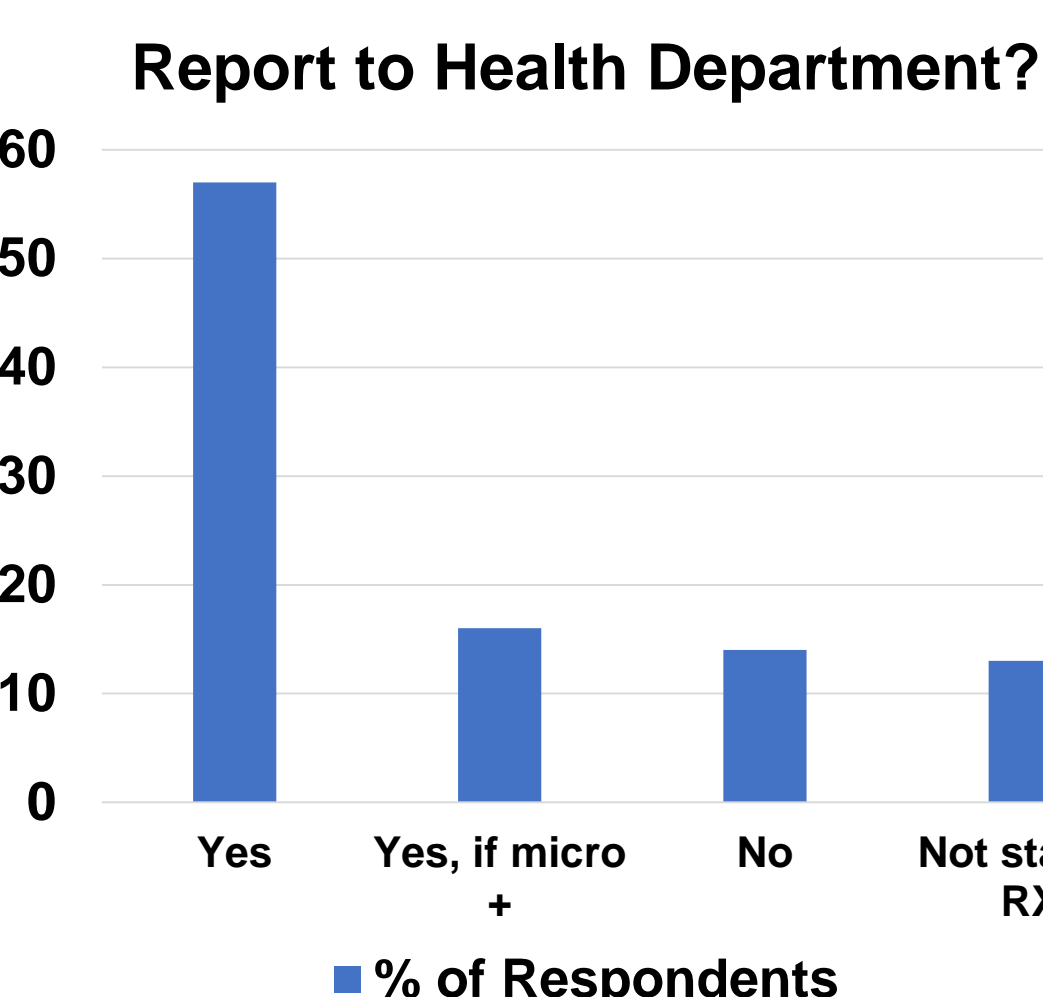
	Case A (-) Risk Factors N=138	Case B (+) Risk Factors N=136
Treat for LTBI	32(23%)	6 (4%)
Request eye sampling for PCR + Culture, Treat TB Disease only if (+)	54 (39%)	16 (12%)
Request eye sampling for PCR + culture, but treat TB Disease regardless	25 (18%)	59 (44%)
Treat for TB Disease without sampling	15 (11%)	48 (35%)
Other	12 (9%)	7 (5%)

Treatment and Response to Therapy

- 94% would initiate treatment with RIPE (84%) or RIP (10%)
- 59% would treat for 6-9 months regardless of clinical response
- But 29% would stop therapy at 2 or 4 months if no response
- Expected likelihood of improvement varied widely among respondents; 44% were uncertain whether improvement occurred



Public Health Notification and DOT



Discussion

- Many IDPs do not see referrals for Otb but of the ~20% of who do, ~1/3 report increased referrals for possible Otb, mainly for idiopathic uveitis and positive IGRA.
- There is considerable variation in management of possible Otb.
- Decision by IDP's to treat patients with uveitis and (+) IGRA for Otb is heavily influenced by TB risk factors. Significantly more IDPs would treat for Otb if foreign born or other TB risks.
- Without TB risks, IDPs would more likely treat only if positive eye culture or PCR, but also think these specimens are rarely obtained. Treatment decisions are also influenced by ophthalmologists' impressions and having CXR abnormalities.
- There is heterogeneity among IDPs in treatment duration and expectation of response to therapy. Most give RIPE or RIP for 6-9 months regardless of response, but 29% would stop earlier if no clinical response. However, many are also unsure as to whether to expect a response during treatment
- The open comments noted difficulty in assessing responses in patients concurrently receiving topical or systemic steroids.
- Uveitis specialists have a growing interest in TB uveitis management and have performed similar surveys on how ophthalmologists approach this condition, and have initiated multicenter observational studies to help answer some of the same questions we that we have posed to IDPs (8,9,10)
- Improved collaboration with referring ophthalmologists including better familiarity with emerging ophthalmology literature on treatment response of Otb, as well as better understanding role for diagnostic testing are necessary to improve management of this emerging syndrome.
- Not all patients treated for suspected Otb are reported to public health agencies, likely contributing to the lack recognition of this emerging problem

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