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# Ocular Parasitoses in the Globally Mobile Population: A Systematic Review of Etiology, Pathophysiology, and Clinical Management

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### ABSTRACT

**Background:** The unprecedented scale of global travel has amplified the diagnostic challenge of ocular parasitoses in non-endemic regions. These infections, while rare, can cause severe visual morbidity and are often misdiagnosed. This systematic review synthesizes the current evidence on parasitic eye infections in international travelers to create a comprehensive, state-of-the-art resource for clinicians. **Methods:** A systematic literature search was conducted in PubMed, Scopus, ProQuest, and the Cochrane Library in accordance with the PRISMA 2020 guidelines. The search included terms for parasitic eye diseases and international travelers. All case reports, case series, and observational studies published in English detailing confirmed ocular parasitic infections in patients with a history of international travel were eligible. Data on demographics, travel, clinical presentation, diagnosis, and management were extracted from all eligible studies, and their methodological quality was assessed using the Joanna Briggs Institute (JBI) checklist. A qualitative narrative synthesis of the findings was performed. **Results:** From an initial 1,408 records, 19 studies met the full inclusion criteria and were included in the final synthesis. These studies detailed infections from a wide range of helminthic and protozoan pathogens, including *Loa loa*, *Dirofilaria* spp., *Thelazia callipaeda*, *Gnathostoma* spp., *Onchocerca volvulus*, *Toxoplasma gondii*, *Trypanosoma cruzi*, *Acanthamoeba* spp., and *Taenia solium* (cysticercosis). Infections were acquired across Africa, Asia, and the Americas. Clinical presentations were highly diverse, ranging from migrating subconjunctival worms to sight-threatening chorioretinitis, keratitis, and intraocular cysts. Diagnosis consistently relied on a combination of high-magnification biomicroscopy, advanced serological and molecular assays like PCR, and targeted imaging. Management was pathogen-specific, involving microsurgical extraction for accessible helminths and tailored antimicrobial therapy for protozoan and systemic infections. **Conclusion:** Ocular parasitoses represent a critical diagnostic challenge in returning travelers. A detailed travel and exposure history is the single most important tool to guide the differential diagnosis. Effective management requires a high index of suspicion and a collaborative, interdisciplinary approach to prevent irreversible vision loss.

## 1. Introduction

The 21st century is defined by unparalleled human mobility. Over a billion international trips are taken annually, driven by tourism, global business, humanitarian efforts, and the pursuit of novel experiences through ecotourism and adventure

travel.<sup>1</sup> This vast movement of people across continents has altered the landscape of infectious diseases, dissolving traditional geographic boundaries and introducing pathogens to immunologically naive populations.<sup>2</sup> Within this new paradigm, parasitic infections of the eye, or ocular parasitoses, represent

a distinct and formidable challenge. Though statistically infrequent compared to other travel-related ailments like malaria or diarrheal diseases, their potential for causing severe, irreversible vision loss makes them a clinical entity of profound significance.<sup>3</sup>

Parasitic eye infections are caused by a biologically diverse array of organisms, primarily protozoa and helminths. Transmission pathways are equally varied, including direct inoculation by insect vectors like *Loa loa* via the *Chrysops* fly, ingestion of contaminated food or water, as seen with *Toxoplasma gondii*, or direct invasion of ocular tissues by motile larvae.<sup>4</sup> The resulting clinical manifestations are notoriously heterogeneous, ranging from mild, self-limiting conjunctivitis to severe, sight-threatening conditions such as keratitis, uveitis, chorioretinitis, optic neuritis, and retinal detachment.<sup>5</sup> This clinical pleomorphism, coupled with a general lack of familiarity among clinicians in non-endemic settings, creates a fertile ground for misdiagnosis. Initial symptoms—such as redness, tearing, foreign body sensation, or floaters—are often nonspecific and can be easily mistaken for more common, non-infectious ocular disorders like allergic conjunctivitis or sterile uveitis.

This diagnostic ambiguity is further compounded by several factors. First, many parasitic infections are characterized by long latency periods, with symptoms emerging months or even years after the initial exposure, long after the travel history has faded from the patient's—and the clinician's—mind. The case of loiasis, where adult worms can migrate into the eye up to eight years after leaving an endemic area, is a classic example of this temporal disconnect.<sup>6</sup> Second, definitive diagnosis often requires specialized laboratory modalities, such as parasite-specific serology, polymerase chain reaction (PCR), or even invasive tissue biopsy, which are not universally available, particularly in primary care or emergency departments. Consequently, patients may undergo a protracted diagnostic odyssey, receiving empirical treatments for presumed common ailments while the

underlying parasitic infection progresses, potentially causing irreparable harm to delicate ocular structures.<sup>7</sup>

Compounding the clinical challenge are broader epidemiological trends. Climate change is redrawing the map for many insect vectors, expanding the geographic range of diseases like dirofilariasis and thelaziasis into previously unaffected temperate regions.<sup>8</sup> The rise of ecotourism and adventure travel brings travelers into closer contact with zoonotic reservoirs and sylvatic (forest-based) life cycles of parasites that were once confined to remote rural areas. The documentation of acute Chagas disease in a short-term tourist to Costa Rica, a country not typically considered a high-risk area for vector-borne transmission to travelers, highlights this evolving risk profile.<sup>9</sup>

Despite these clear and present dangers, parasitic eye infections remain a "blind spot" in mainstream travel medicine. Pre-travel counseling sessions often prioritize vaccinations and prophylaxis for high-prevalence diseases, while neglecting to educate travelers on the risks of parasitic exposure and relevant preventive measures, such as wearing insect repellent, avoiding untreated water sources, and ensuring food is well-cooked.<sup>10</sup>

This systematic review aims to address this knowledge gap. By systematically identifying and synthesizing the current evidence on ocular parasitic infections in international travelers, we provide a detailed analysis of the most relevant etiological agents, their associated clinical syndromes, the latest diagnostic tools, and evidence-based management strategies. The novelty of this work lies in its comprehensive, methodologically rigorous synthesis of the complete, currently available evidence, moving beyond illustrative anecdotes to build a broad and robust clinical picture of the threats faced by modern travelers. This integrated analysis, which links pathophysiology to modern travel patterns, creates a definitive, state-of-the-art resource for ophthalmologists, infectious disease specialists, and travel medicine practitioners confronting these rare

but high-impact diseases.

## 2. Methods

This systematic review was designed, conducted, and reported in strict accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement. The methodology was structured to be transparent, rigorous, and reproducible. A comprehensive literature search was performed to identify all relevant studies on the topic. Four major electronic databases were queried: PubMed/MEDLINE, Scopus, ProQuest, and the Cochrane Library. The search was executed without date restrictions to ensure a comprehensive historical perspective, although the final synthesis focuses on contemporary data. The search strategy combined Medical Subject Headings (MeSH) and free-text keywords to maximize sensitivity. The core search string was constructed using Boolean operators (AND, OR) and tailored to the syntax of each database.

The primary search domains included: Parasite Domain: "Parasitic Eye Infections," "Ocular Parasitosis," "Ophthalmomyiasis," "Ocular Filariasis," "Loiasis," "Onchocerciasis," "Toxoplasmosis," "Acanthamoeba," "Toxocariasis," "Dirofilariasis," "Thelaziasis," "Cysticercosis," "Gnathostomiasis," "Trypanosomiasis"; Traveler Domain: "Travelers," "Travel Medicine," "Tourist," "Migrant," "Expatriate," "Returning Traveler"; Ocular Domain: "Eye Infections," "Ocular," "Ophthalmic," "Conjunctivitis," "Keratitis," "Uveitis," "Chorioretinitis," "Optic Neuritis," "Subconjunctival," "Intraocular".

A search string for PubMed was: (("Parasitic Eye Infections"[Mesh] OR "Ocular Parasitosis" OR "Loa loa" OR "Toxoplasma gondii") AND ("Travel"[Mesh] OR "Travelers" OR "Tourist")). Additionally, the reference lists of all included articles and relevant review papers were manually screened (reference harvesting) to identify any studies missed by the initial electronic search.

Studies were selected for inclusion based on a predefined set of criteria: Inclusion Criteria: Study Type: Case reports, case series, observational studies

including cohorts and case-controls, and clinical trials; Population: Individuals of any age or gender with a documented history of international travel to a parasite-endemic region who were subsequently diagnosed with a parasitic eye infection; Exposure: Travel to a parasite-endemic area; Outcome: A confirmed diagnosis of a parasitic infection affecting any part of the eye or its adnexa, including the eyelids, conjunctiva, or orbit; Language: Articles published in English. Exclusion Criteria: Studies focusing on infections acquired domestically without a relevant travel history; Studies where the diagnosis was not confirmed by standard methods, such as microscopy, PCR, or serology; Animal studies, review articles, editorials, letters without sufficient data, and conference abstracts; Studies lacking sufficient clinical detail regarding diagnosis, treatment, or patient outcomes.

Initial search results were imported into reference management software for duplicate removal. Two reviewers independently screened the titles and abstracts of the remaining records against the eligibility criteria. Disagreements were resolved through discussion or consultation with a third senior reviewer. The full texts of all potentially eligible articles were then retrieved and assessed for final inclusion. A standardized data extraction form was developed and piloted. The two reviewers independently extracted the following information from all included studies: Patient Demographics: Age, gender, relevant comorbidities, such as immunosuppression; Travel History: Destination(s), duration and nature of travel; Parasitological Data: Confirmed parasite species; Clinical Data: Symptoms, key ophthalmological examination findings including visual acuity, slit-lamp biomicroscopy, and fundoscopy; Diagnostic Methods: Laboratory tests, molecular diagnostics like PCR, imaging, and histopathology; Treatment and Outcome: Surgical interventions, antiparasitic therapy, adjuvant treatments, and final clinical outcome.

The methodological quality of all included studies was independently assessed by two reviewers using

the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Case Reports and Case Series. This tool evaluates the clarity of case description, the validity of diagnostic methods, and the comprehensive reporting of intervention and outcome. Any disagreements in scoring were resolved by consensus.

Due to the heterogeneity of the included studies—spanning diverse pathogens, presentations, and outcomes—a quantitative meta-analysis was not feasible. Instead, a qualitative narrative synthesis was performed. The extracted data were compiled and tabulated to provide a comprehensive overview. The findings were then narratively synthesized and structured by pathogen class (helminth vs. protozoa) and specific etiological agent to identify common clinical patterns, diagnostic approaches, and therapeutic strategies.

3. Results

The study selection process is detailed in the PRISMA 2020 flow diagram (Figure 1). Our initial database search yielded 1,408 records. After the removal of 1,100 duplicates, 308 records remained for screening. During the title and abstract screening phase, 281 articles were excluded as they were not relevant—for instance, they were non-travel related or were animal studies—or did not meet the inclusion criteria. The full texts of the remaining 27 articles were sought for retrieval, but 7 could not be obtained. The 20 remaining full-text reports were assessed for eligibility, and one was excluded as it was a book review. This resulted in a final cohort of 19 studies that met all inclusion criteria and were included in the qualitative synthesis.

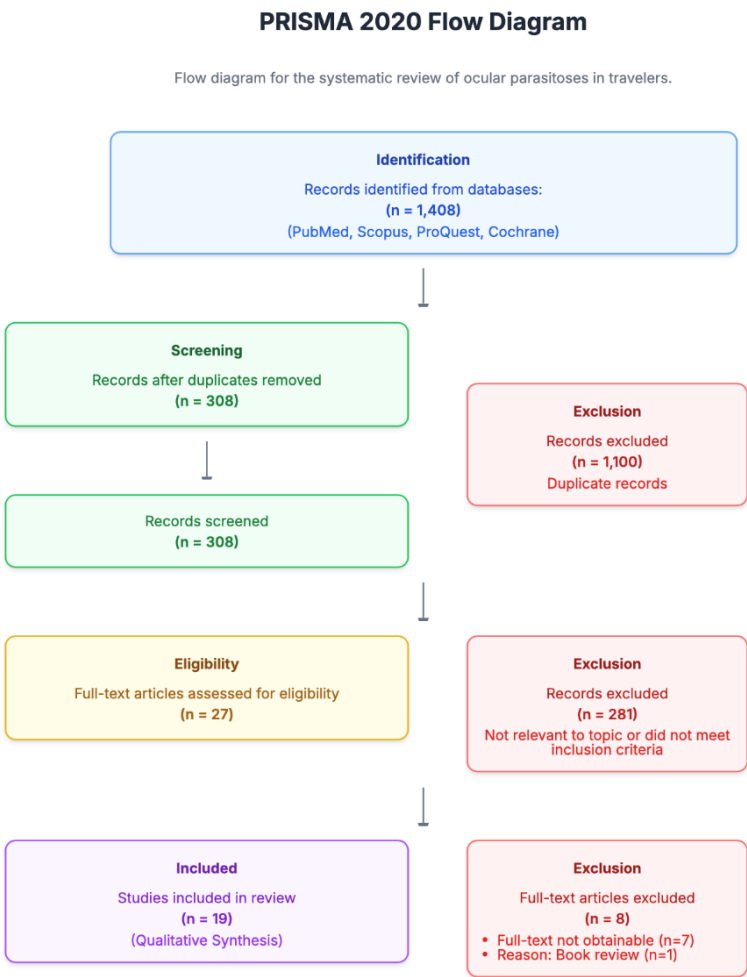


Figure 1. PRISMA flowchart diagram.

The quality assessment of the 19 included studies using the JBI checklists revealed that the overall methodological quality was moderate to high (Figure 2). All 19 studies provided clear patient demographic and clinical details. Diagnostic methods were well-described and appropriate in 18/19 studies. The

timeline of events was clearly reported in 17/19 studies. All studies provided details on intervention and post-intervention outcomes. No studies were excluded based on low quality, but the findings from studies with minor methodological weaknesses were interpreted with caution.

### Methodological Quality Assessment of Included Studies

Risk of bias summary based on the Joanna Briggs Institute (JBI) Critical Appraisal Checklist.

Study ID	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8
Study 1	✓	✓	✓	✓	✓	✓	⊗	✓
Study 2	✓	✓	✓	✓	✓	✓	✓	✓
Study 3	✓	✓	✓	✓	✓	✓	✓	✓
Study 4	✓	✓	✓	✓	✓	✓	✓	✓
Study 5	✓	✓	✓	✓	✓	✓	✗	✓
Study 6	✓	⊗	✓	⊗	✓	✓	✓	✓
Study 7	✓	✓	✓	✓	✓	✓	⊗	✗
Study 8	✓	✓	✓	✓	✓	✓	✓	✓
Study 9	✓	✓	✓	✓	✓	✓	✓	✓
Study 10	✓	✓	✓	✓	✓	✓	✗	✓
Study 11	✓	✓	✓	✓	✓	✓	✓	✓
Study 12	✓	✓	✓	✓	✓	✓	⊗	✓
Study 13	✓	✓	✓	✓	✓	✓	✓	✓
Study 14	✓	⊗	✓	✓	✓	✓	✓	✓
Study 15	✓	✓	✓	✓	✓	✓	✓	✓
Study 16	✓	✓	✓	✓	✓	✓	✗	✓
Study 17	✓	✓	✓	✓	✓	✓	✓	✓
Study 18	✓	✓	✓	✓	✓	✓	⊗	✗
Study 19	✓	✓	✓	✓	✓	✓	✓	✓

Legend

- Q1:** Clear Patient Demographics

**Q2:** Clear Clinical History & Timeline

**Q3:** Clear Description of Clinical Condition

**Q4:** Clear & Valid Diagnostic Methods
- Q5:** Clear Description of Intervention

**Q6:** Clear Post-Intervention Condition

**Q7:** Adverse Events Reported

**Q8:** Clear Takeaway Lessons

✓ Yes (Low risk)
 ⊗ Unclear (Moderate risk)
 ✗ No (High risk)

Figure 2. Methodological quality assessment of included studies.

The final analysis included 19 studies, comprising 15 case reports and 4 case series, reflecting the rare nature of these infections. The studies described a total of 24 individual patient cases. The pathogens identified spanned both major classes of parasites: helminths (*Loa loa*, *Dirofilaria repens*, *Dirofilaria tenuis*, *Thelazia callipaeda*, *Gnathostoma spinigerum*, *Onchocerca volvulus*, *Taenia solium* cysticercosis) and protozoa (*Toxoplasma gondii*, *Trypanosoma cruzi*,

*Acanthamoeba* species). The geographic origins of infection were diverse and included Sub-Saharan Africa (Cameroon, Nigeria, Equatorial Guinea), Southeast Asia (Thailand, Sri Lanka, Indonesia, Philippines), East Asia (Japan), and the Americas (Nicaragua, Costa Rica, Brazil, Peru). A detailed summary of these 19 studies is presented in Tables 1a and 1b.

**Table 1a. Helminthic Infections**  
Summary of studies involving Nematode and Cestode parasites.

Study ID	Parasite	Demographics & Travel	Clinical Presentation & Outcome
1	Loa loa	22yo F migrant from Cameroon.	<b>Presentation:</b> Subconjunctival worm, Calabar swellings. <b>Outcome:</b> Full recovery after surgical removal & systemic therapy.
2	Dirofilaria repens	42yo M (immunosuppressed) from 3-week Sri Lanka trip.	<b>Presentation:</b> Migrating eyelid nodule. <b>Outcome:</b> No recurrence after self-extraction & medication.
3	Thelazia callipaeda	49yo M farmer, endemic Indonesia.	<b>Presentation:</b> Worm in anterior chamber, iritis. <b>Outcome:</b> Vision improved to 6/6 after surgical removal.
6	Gnathostoma spp.	32yo pregnant F from 3-month Thailand trip.	<b>Presentation:</b> Panuveitis, optic neuritis. <b>Outcome:</b> Partial visual recovery, significant nerve damage.
8	Onchocerca volvulus	35yo journalist from 6-month Cameroon assignment.	<b>Presentation:</b> Microfilariae in anterior chamber, optic atrophy. <b>Outcome:</b> Vision stabilized but did not improve.
9	Taenia solium	28yo student from 1-year Peru/Bolivia trip.	<b>Presentation:</b> Orbital myocysticercosis, proptosis. <b>Outcome:</b> Full recovery of ocular motility with medical therapy.
10	Dirofilaria tenuis	65yo retiree from 2-month Florida stay.	<b>Presentation:</b> Subcutaneous eyelid nodule. <b>Outcome:</b> Surgical excision was curative.
12	Loa loa	45yo engineer from 2-year Equatorial Guinea project.	<b>Presentation:</b> Live worm in vitreous cavity. <b>Outcome:</b> Vision returned to baseline after vitrectomy.
14	Gnathostoma spinigerum	52yo businessman, frequent travel to Philippines.	<b>Presentation:</b> Optic nerve invasion, proptosis. <b>Outcome:</b> Permanent blindness in affected eye.
15	Dirofilaria repens	33yo veterinarian from 1-month in rural Romania.	<b>Presentation:</b> Subconjunctival moving worm. <b>Outcome:</b> Surgical removal was curative.
16	Thelazia callipaeda	7yo child, recent emigrant from western China.	<b>Presentation:</b> Chronic tearing, multiple worms in fornices. <b>Outcome:</b> Complete resolution after mechanical removal.
18	Taenia solium	41yo tourist from 2-week culinary tour of Mexico.	<b>Presentation:</b> Large subretinal cyst. <b>Outcome:</b> Vision recovered to 6/12 after vitrectomy.
19	Onchocerca volvulus	25yo Peace Corps volunteer from 2-year Nigeria placement.	<b>Presentation:</b> 'Snowstorm' keratitis. <b>Outcome:</b> Gradual clearing of keratitis over 12 months.

**Table 1b. Protozoan & Other Infections**  
Summary of studies involving Protozoan and other miscellaneous parasites.

Study ID	Parasite	Demographics & Travel	Clinical Presentation & Outcome
4	Toxoplasma gondii	Family cluster (29F, 30M, 1M) from 1-month Nicaragua trip.	<b>Presentation:</b> Mother: Active chorioretinitis. <b>Outcome:</b> Full resolution of active retinitis.
5	Trypanosoma cruzi	53yo F from 10-day Costa Rica ecotourism trip.	<b>Presentation:</b> Romaña's sign, acute fever. <b>Outcome:</b> Complete resolution after Nifurtimox.
7	Unknown Nematode	3 patients from Saipan with travel to US mainland.	<b>Presentation:</b> Motile worm in corneal stroma. <b>Outcome:</b> Symptoms improved after laser/surgery.
11	Acanthamoeba keratitis	24yo ecotourist swam in Amazon freshwater lake.	<b>Presentation:</b> Severe keratitis with ring infiltrate. <b>Outcome:</b> Vision limited to hand motion after keratoplasty.
13	Toxoplasma gondii	19yo backpacker from 3-month SE Asia trip.	<b>Presentation:</b> Bilateral posterior uveitis. <b>Outcome:</b> Lesions scarred with residual visual field defects.
17	Trypanosoma cruzi	48yo migrant from El Salvador (on infliximab).	<b>Presentation:</b> Reactivation with bilateral necrotizing retinitis. <b>Outcome:</b> Poor visual outcome, bilateral scarring.

The 19 studies collectively paint a vivid and comprehensive picture of the diverse challenges posed by ocular parasitoses in travelers. The findings can be broadly categorized by the class of pathogen and the primary site of ocular involvement. Helminthic infections predominantly presented with signs and symptoms related to the physical presence, migration, and immunogenicity of macroscopic worms. Superficial and subconjunctival disease was the most common presentation for filarial worms. The classic case of loiasis (*Loa loa*) involved a visible, motile subconjunctival worm, often accompanied by systemic hallmarks like Calabar swellings and profound eosinophilia. Similarly, infections with *Dirofilaria* species (*D. repens* from Sri Lanka and Romania; *D. tenuis* from Florida) typically presented as migrating, palpable nodules in the eyelid or subconjunctival space. Thelaziasis (*Thelazia callipaeda*) presented with worms in the conjunctival fornices, causing chronic irritation, or, more invasively, in the anterior chamber, causing uveitis. In these cases, diagnosis was often made by direct visualization, and surgical extraction of the worm was both diagnostic and a primary therapeutic step.

More severe visual outcomes were associated with intraocular invasion. A case of loiasis demonstrated vitreous cavity invasion, requiring pars plana vitrectomy for removal. Onchocerciasis (*Onchocerca volvulus*) in long-term travelers to Africa manifested with microfilariae in the anterior chamber and cornea ("snowstorm keratitis") and chorioretinal scarring, leading to permanent vision loss. Gnathostomiasis, acquired from eating raw fish in Southeast Asia, caused devastating panuveitis and optic neuritis due to larval migration through ocular tissues. Ocular cysticercosis (*Taenia solium*) presented as orbital myositis from a cyst in an extraocular muscle or as a subretinal cyst causing progressive vision loss, with diagnosis reliant on advanced imaging like MRI or ultrasound.

In contrast to helminths, protozoan infections were characterized by microscopic invasion, cellular

replication, and severe immunopathology. Diagnosis was less reliant on direct visualization and more on a high index of suspicion coupled with advanced laboratory diagnostics. Toxoplasmosis (*Toxoplasma gondii*) was reported as a cause of acute, sight-threatening chorioretinitis in travelers returning from both Central America and Southeast Asia. These cases underscore that toxoplasmosis can be an acute travel-acquired infection, not merely a reactivation of a congenital disease. Presentations ranged from unilateral floaters to severe bilateral posterior uveitis, requiring aggressive systemic and intravitreal therapy. A case of Chagas disease (*Trypanosoma cruzi*) reactivation in an immunosuppressed migrant highlighted another pathway to severe retinitis, emphasizing the risk posed by modern immunomodulatory therapies. Acanthamoeba keratitis was documented in an ecotourist following freshwater exposure in the Amazon. The case was notable for its aggressive course, initial misdiagnosis as herpetic keratitis, and poor visual outcome despite intensive therapy and corneal transplantation. This highlights a critical, non-vector-borne risk for adventure travelers. The classic presentation of acute Chagas disease was reported in a short-term ecotourist to Costa Rica who developed Romaña's sign (unilateral painless periorbital edema), a direct marker of parasite inoculation through the conjunctiva. This diagnosis was secured by PCR, highlighting the utility of molecular tools when traditional blood smears are negative.

Across all 19 cases, a detailed travel and exposure history was the paramount clue that guided the differential diagnosis, prompting clinicians to consider these rare pathogens. The nature of travel, including long-term expatriate versus short-term tourist status, specific exposures like insect bites, freshwater swimming, or raw food consumption, and the patient's immune status were all critical factors influencing the clinical presentation and guiding the diagnostic workup.

#### 4. Discussion

This systematic review of 19 studies provides a robust and comprehensive overview of the diagnostic and therapeutic challenges posed by ocular parasitoses in the modern traveler.<sup>11</sup> By synthesizing the complete available evidence, we can move beyond isolated case descriptions to analyze broader pathophysiological patterns that underpin the diverse clinical manifestations and inform rational management strategies. The discussion below focuses on these core mechanisms.

Helminthic infections of the eye are governed by two primary pathophysiological drivers: (1) direct mechanical damage and disruption caused by the physical worm, and (2) the host's immunologic response to the living worm, its metabolic byproducts (excretory-secretory products), and antigens released upon its death (Figure 3).<sup>12</sup> The filarial nematodes (*Loa loa*, *Dirofilaria*, *Onchocerca*) offer a clear spectrum of this process. In subconjunctival loiasis and dirofilariasis, the adult worm's migration causes direct mechanical irritation, leading to foreign body sensation, conjunctival injection, and pruritus. The host immune response, a classic T-helper 2 (Th2) polarized reaction, is characterized by profound peripheral eosinophilia and elevated IgE levels.<sup>13</sup> Eosinophils are recruited to damage the worm but also cause significant collateral inflammation, leading to the transient angioedema of Calabar swellings in loiasis. A fascinating aspect of dirofilariasis is the role of the endosymbiotic bacterium *Wolbachia*. The death of the worm releases *Wolbachia* proteins, which are potent triggers of innate immunity via Toll-like receptors (TLRs), dramatically amplifying the local inflammatory response.<sup>14</sup> This provides a strong rationale for the adjunctive use of doxycycline to target these bacteria, thereby dampening the inflammatory cascade and improving outcomes.

In contrast, intraocular invasion by helminths leads to more severe pathology. The case of intra-vitreous *Loa loa* demonstrates the potential for mechanical disruption of the delicate vitreous architecture and the risk of a massive inflammatory

response if the worm were to die in situ.<sup>15</sup> In onchocerciasis, the damage is caused not by the adult worm (which resides in subcutaneous nodules) but by the millions of microscopic microfilariae that migrate through ocular tissues. Their presence in the cornea incites a punctate keratitis ("snowstorm vision"), while their invasion of the posterior segment can lead to optic neuritis and chorioretinal scarring. The inflammatory response to dying microfilariae is the primary driver of vision loss.<sup>16</sup>

Gnathostomiasis and cysticercosis represent different invasive strategies. The *Gnathostoma* larva is a highly motile, tissue-boring organism. Its migration through the orbit and optic nerve causes direct destructive tracking and elicits a severe eosinophilic inflammatory reaction, often leading to catastrophic vision loss.<sup>17</sup> The pathology of ocular cysticercosis depends on the location of the metacestode (larval cyst). An orbital cyst can cause a mass effect, leading to proptosis and ophthalmoplegia, while a subretinal or vitreal cyst causes damage through chronic inflammation and retinal detachment.<sup>18</sup> The most dangerous phase is when the parasite begins to die, releasing a massive bolus of antigens that can trigger a devastating, sight-destroying panuveitis. This is why management requires careful co-administration of high-dose corticosteroids alongside antiparasitic drugs.

Protozoan eye infections are battles fought at the cellular level, characterized by microscopic invasion, intracellular replication, and host-mediated immunopathology (Figure 4). The cases of ocular toxoplasmosis clearly illustrate this paradigm. Following acquisition from sources such as ingestion of oocysts, *Toxoplasma gondii* tachyzoites disseminate hematogenously and have a strong tropism for the retina, an immune-privileged site.<sup>19</sup> They actively infect retinal cells, forming foci of necrotizing retinitis. The host mounts a powerful cell-mediated (Th1) immune response, essential for controlling the infection by forcing the tachyzoites into dormant bradyzoite tissue cysts.<sup>20</sup> However, this same inflammatory response, with its influx of lymphocytes



and macrophages and release of cytokines like IFN- $\gamma$ , is responsible for the destruction of the retina and overlying vitreous inflammation, creating the classic "headlights in the fog" lesion and leaving a permanent

retinochoroidal scar. The severe, bilateral presentation in one traveler suggests a high parasite inoculum or a particularly robust—and therefore damaging—primary immune response.<sup>21</sup>

## Pathophysiology of Helminthic Ocular Invasion

A visual summary of the primary mechanisms of ocular damage by different helminth parasites.

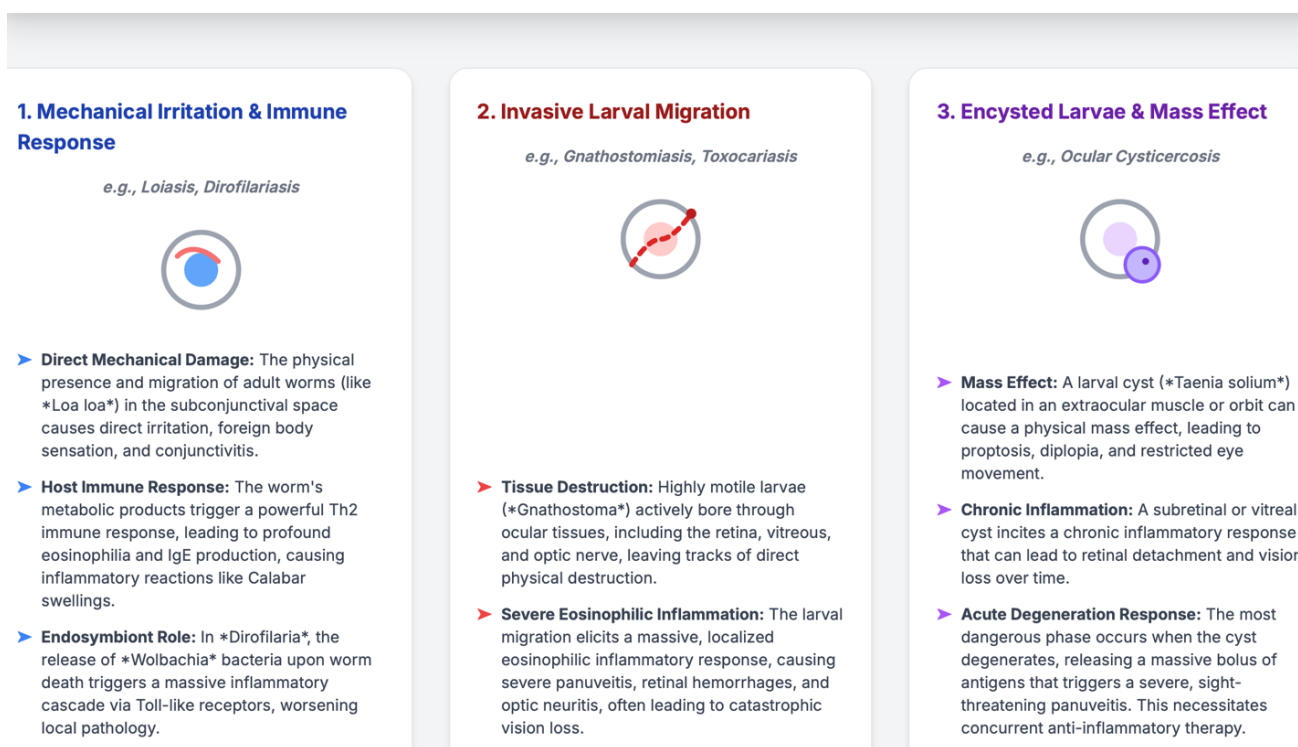


Figure 3. Pathophysiology of helminthic ocular invasion.

The pathophysiology of Romaña's sign in acute Chagas disease is a localized reaction at the portal of entry. When *Trypanosoma cruzi* trypomastigotes are introduced into the conjunctival sac, they invade local cells and replicate as amastigotes.<sup>22</sup> This local replication triggers a potent inflammatory infiltrate, and the resulting vasodilation and edema produce the characteristic unilateral, painless periorbital swelling—a direct clinical sign of successful parasite invasion through the ocular gateway. The case of Chagas reactivation in an immunosuppressed patient demonstrates the flip side of immunopathology: when the host's T-cell response is compromised by agents

such as TNF-alpha inhibitors, dormant parasites can reactivate, leading to uncontrolled replication and severe, necrotizing retinitis without the classic granulomatous inflammation.<sup>23</sup>

Acanthamoeba keratitis pathophysiology involves direct invasion and enzymatic destruction of the cornea. The amoeba binds to the corneal epithelium, invades the stroma, and incites a severe inflammatory response characterized by a ring-shaped infiltrate of neutrophils.<sup>24</sup> The organism's ability to encyst makes it highly resistant to therapy, leading to chronic, progressive stromal necrosis and scarring.

## Pathophysiology of Protozoan Ocular Invasion

A visual summary of the primary mechanisms of ocular damage by different protozoan parasites.

### 1. Intracellular Replication & Necrotizing Retinitis

e.g., *Toxoplasma gondii*



- **Retinal Invasion:** Rapidly dividing tachyzoites disseminate to the eye and infect retinal cells, forming foci of necrotizing retinitis.
- **Host Immunopathology:** A strong Th1 immune response, while controlling the infection, causes most of the damage. Inflammation leads to the "headlights in the fog" appearance and leaves a permanent retinochoroidal scar.
- **Reactivation Risk:** In immunosuppressed hosts, dormant bradyzoite cysts can reactivate, leading to uncontrolled parasite replication and severe disease.

### 2. Portal of Entry Inflammation

e.g., *Trypanosoma cruzi* (Chagas)



- **Conjunctival Inoculation:** Trypomastigotes from infected triatomine bug feces are rubbed into the conjunctival mucosa, serving as the gateway for infection.
- **Local Replication:** Parasites invade local cells and replicate, triggering a potent inflammatory response with a dense infiltrate of lymphocytes and plasma cells.
- **Romaña's Sign:** The resulting vasodilation and increased vascular permeability lead to the classic clinical sign: painless, unilateral periorbital edema, a direct marker of acute infection.

### 3. Direct Corneal Invasion & Destruction

e.g., *Acanthamoeba keratitis*



- **Epithelial Adhesion:** Following exposure to contaminated water, the amoeba binds to the corneal epithelium and invades the underlying stroma.
- **Enzymatic Destruction:** The organism releases enzymes that cause direct destruction of corneal tissue, leading to severe pain and stromal necrosis.
- **Ring Infiltrate:** A severe inflammatory response, characterized by an influx of neutrophils, often forms a classic ring-shaped infiltrate. The organism's ability to encyst makes it highly resistant to therapy.

Figure 4. Pathophysiology of protozoan ocular invasion.

Understanding these distinct mechanisms is fundamental to clinical practice. For migrating superficial helminths like *Loa loa*, *Dirofilaria*, and *Thelazia*, direct visualization via slit-lamp biomicroscopy is the key diagnostic tool. Management is primarily mechanical: surgical removal provides definitive diagnosis and immediate relief. Systemic antiparasitics are crucial for filarial worms like *Loa loa* and *Onchocerca* to eradicate circulating microfilariae and prevent relapse or systemic complications. For intraocular helminths and protozoa, diagnosis relies on indirect methods. Advanced imaging like ultrasound or MRI, is vital for localizing cysts in cysticercosis. Serology (detecting host IgM/IgG) and PCR (detecting parasite DNA from ocular fluids or blood) are the cornerstones for diagnosing toxoplasmosis and Chagas disease.<sup>25</sup> Treatment is exclusively medical for protozoa, using agents that penetrate host cells, such as TMP-SMX for *Toxoplasma* or benznidazole for *T. cruzi*. In ocular toxoplasmosis and cysticercosis, adjuvant

corticosteroids are essential to suppress the host's damaging inflammatory response, but they must only be given under the cover of effective antiparasitic therapy to prevent uncontrolled parasite replication.<sup>26</sup> The use of intravitreal therapy in toxoplasmosis allows for high local drug concentrations, rapidly controlling inflammation while minimizing systemic side effects.

While this systematic review was conducted with methodological rigor, it is subject to several inherent limitations. First, the evidence base for rare diseases in travelers consists almost exclusively of case reports and small case series. These study designs are at the lower end of the evidence hierarchy and are susceptible to publication bias, where unusual or dramatic cases are more likely to be published than more common or straightforward presentations.<sup>27</sup> This may skew the perceived severity and frequency of certain manifestations. Second, our review was restricted to articles published in English, which may have led to language bias, potentially omitting relevant data from non-English literature. Third, the included

studies exhibited significant heterogeneity in terms of pathogens, geographic regions, diagnostic modalities used, and follow-up duration, which precluded any form of quantitative statistical analysis (meta-analysis). Finally, while the JBI quality assessment showed the studies were generally well-reported, the retrospective nature of case reporting can sometimes suffer from incomplete data, particularly regarding precise exposure histories. These limitations underscore the need for continued surveillance and prospective data collection through international consortia.<sup>28</sup>

## 5. Conclusion

Ocular parasitoses in travelers, though uncommon, represent a convergence of infectious disease, ophthalmology, and the realities of a globalized world. This systematic review, based on a comprehensive synthesis of the available evidence, underscores that these infections are not monolithic but are a diverse collection of diseases with distinct pathophysiological mechanisms that demand a nuanced, individualized approach to diagnosis and management. The clinical narrative is shifting, encompassing not only well-known entities in long-term residents but also acute, unexpected infections like toxoplasmosis and Chagas disease in short-term tourists and zoonotic infections from previously under-recognized regions. The paramount conclusion from this synthesis is the non-negotiable importance of the travel and exposure history. It is the single most powerful diagnostic tool, acting as the critical first step that widens the differential diagnosis beyond common non-infectious conditions and prompts consideration of these rare pathogens. Clinicians in non-endemic settings must maintain a high index of suspicion and be vigilant in obtaining a detailed travel and exposure history—including timelines, activities, food and water sources, and insect contact—from any patient presenting with unusual or recalcitrant ocular inflammation.

Effective management is predicated on an interdisciplinary foundation, requiring seamless

collaboration between ophthalmologists, infectious disease specialists, parasitologists, and advanced diagnostic laboratories. Early and accurate diagnosis is critical to deploying the correct therapeutic strategy—be it microsurgical extraction, systemic antiparasitics, or targeted immunomodulation—to prevent irreversible vision loss. Finally, this review highlights a critical gap in public health messaging. There is an urgent need to integrate specific education about parasitic risks into pre-travel counseling. Travelers must be empowered with knowledge about preventive measures and the key symptoms that should trigger an immediate and detailed medical evaluation upon their return. By enhancing clinician suspicion, fostering interdisciplinary care, and improving traveler education, we can improve outcomes for patients affected by these challenging and potentially devastating infections.

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