Author Affiliations: Departments of Ophthalmology (Dr Hatch), Medicine (Dr Bell), and Health Policy, Management, and Evaluation (Dr Bell), University of Toronto, Toronto, Department of Ophthalmology, Queen’s University and Hotel Dieu Hospital, Kingston (Drs E. de L. Campbell, El-Defrawy, and R. J. Campbell), and Institute for Clinical Evaluative Sciences, Kingston and Toronto (Drs Bell and R. J. Campbell), Ontario, Canada.

Correspondence: Dr R. J. Campbell, Department of Ophthalmology, Queen’s University, Hotel Dieu Hospital, 166 Brock St, Kingston, Ontario, Canada K7L 5G2 (rob.campbell@queensu.ca).

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**Novel Etiological Agent: Molecular Evidence for Trematode-Induced Anterior Uveitis in Children**

Histopathological analysis has provided support that trematode infections can cause a characteristic granulomatous anterior uveitis in children from South India. Southeast Asian populations are exposed to at least 70 species of foodborne and waterborne trematodes. The burden of disease and current distribution of the parasites within the population are largely unknown, however. Serologic testing is unreliable mainly because of cross-reactive antigens. Fecal egg identification likewise has limited utility because humans act as accidental hosts. Molecular diagnostic studies, in contrast, can identify individual species of trematodes involved in site-specific infections. In this study, we have applied polymerase chain reaction–based techniques to identify the trematode Procerovum varium as a cause of granulomatous anterior uveitis in children from South India.

**Report of a Case.** A 9-year-old boy from the village of Jagathapatinum in Tamil Nadu, India, came to the hospital with a 2-week history of left eye redness, which he said started after bathing in the village pond. There was no history of trauma. Visual acuity was 20/20 OU and intraocular pressures were normal bilaterally. Slitlamp examination of the left eye revealed a normal conjunctiva and cornea. A whitish granuloma was seen in the anterior chamber at the 6-o’clock position (**Figure 1A**). Fundus examination findings were normal. Systemic examination revealed a normal complete blood cell count and no evidence of tuberculosis, syphilis, or sarcoidosis. Stool and urine examination findings were unremarkable. Following informed consent, both aqueous fluid and the granuloma were aspirated using a 25-gauge needle under general anesthesia. The aqueous fluid was sent for cellular analysis, which revealed a predominance of eosinophils, consistent with our previously published work (Figure 1B).

Extraction of DNA from the granuloma was performed using a Qiagen polymerase chain reaction purification kit. Snails from the same village pond were collected for cercarial isolation in our laboratory (Figure 1C and D). The snails that released the cercarial larvae were sent to the Zoological Survey of India, Calcutta, India, where they were identified as Melanoides tuberculata. Real-time polymerase chain reaction was performed using the SYBR-Green assay on both the granuloma and cercarial DNA. A standard protocol was followed, using the universal forward primer AP101 (5’-AGAGCCGACGCAACTGTTGA-3’) and reverse primer AP101 (5’-TGGCAGTCCTAGCATCAGCC-3’). Nucleotide-free water was used as a negative control and Fasciola gigantica DNA was the positive control (**Figure 2**). The amplified DNA was loaded on a 2% agarose gel and found to be a 369–base pair fragment of the ribosomal DNA spanning the internal transcribed spacer 2 region. Bidirectional sequencing and
Basic Local Alignment Search Tool analysis were carried out using a standard protocol. Both the environmental cercaria and the granuloma revealed maximal similarity with *P. varium*—a trematode of the family Heterophyidae (Figure 2D).

**Comment.** Granulomatous uveitis has traditionally raised concern for tuberculosis infection among patients seen in regional hospitals of South India. Many South Indian children with granulomatous anterior uveitis have received antituberculosis treatment, which has proven ineffective. Notably, these patients typically describe a strong temporal association between the onset of symptoms and having bathed in regional ponds or waterways. Recently, our histopathological study of affected ocular tissues suggested the presence of a trematode infection, which we have now identified as *P. varium*. Snails act as the first intermediate host for this trematode in regional ponds, where they release cercarial larvae to infect the fish, which act as second intermediate hosts. Infected fish then transmit the trematode to birds. Fish-eating birds are the definitive hosts, while infected children become accidental hosts. Our data, together with the clustering of cases of granulomatous anterior uveitis in children from South Indian villages, suggest that trematode infection may be common in areas where fish and waterfowl infection is endemic.

**Author Affiliations:** Uveitis Service (Dr Rathinam) and Orbit and Ocular Prosthetics Services (Dr Usha), Aravind Eye Hospital and P. G. Institute of Ophthalmology, and Department of Microbiology, Aravind Medical Research Foundation (Mr Arya and Dr Prajna), Madurai, and Parasitology Laboratory, Department of Zoology, School of Life Sciences, North Eastern Hill University, Shillong (Dr Tandon), India.

**Correspondence:** Dr Rathinam, Uveitis Service, Aravind Eye Hospital and P. G. Institute of Ophthalmology, 1, Anna Nagar, Madurai, Tamil Nadu 625 020, India (rathinam@aravind.org).

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5. Rajamohan M, Srikanth K, Raghuraman V, Srinivasan R, Nelson Jesudason...
**Eales Disease Associated With Serpiginous Choroiditis**

Eales disease is an idiopathic, usually bilateral, inflammatory, retinal vascular occlusive disorder. Serpiginous choroiditis is an idiopathic, usually bilateral, recurrent acute progressive inflammation of the inner choroid and retinal pigment epithelium. To our knowledge, we describe the first case of Eales disease followed by serpiginous choroiditis.

**Report of a Case.** A 49-year-old immunocompetent white man had gradual vision loss in his left eye. Visual acuity was 20/20 OD and 20/100 OS. Anterior segment examination of the left eye demonstrated small, white, central keratic precipitates but no cells or flare. Fundus examination revealed left temporal retinal vascular occlusive disease, arteriolar and venous sheathing, and peripheral retinal ischemia with neovascularization (Figure, A). The right eye was normal. Complete blood cell count, thrombophilia screen, antinuclear antibody, syphilis serology, and QuantiFERON results were normal. An anterior chamber paracentesis was negative for herpes simplex virus, varicella-zoster virus, and cytomegalovirus by polymerase chain reaction. Chest radiograph and tuberculin skin testing results were normal. Eales disease was diagnosed, scatter laser photocoagulation was applied to areas of ischemic retina, and systemic corticosteroids (60 mg/d) and mycophenolate mofetil (1.5 g/d) were prescribed.

After 9 months, slowly progressive lobular peripapillary choroiditis (Figure, B), peripheral temporal retinal vascular occlusive disease with vitritis, and keratic precipitates developed in the right eye (Figure, C). Visual acuity remained 20/20. On fluorescein angiography, the area of peripapillary choroiditis revealed hyperfluorescent transmission defect and periphlebitis. Retinal neovascularization was detected at the edge of the capillary closure temporally. Bilateral Eales disease and right serpiginous choroiditis were diagnosed and the ischemic areas were photocoagulated. During the following 7 years, the capillary closure and retinal neovascularization progressed bilaterally, with development of cataract, rubecotic glaucoma, cystoid macular edema, and progressive serpiginous choroiditis with vitritis in the right eye (Figure, D-F). For this reason, bilateral intravitreal bevacizumab and triamcinolone injections and right intravitreal dexamethasone implants (Ozurdex), peribulbar triamcinolone injections, phacoemulsification with intraocular lens implantation, and pars plana vitrectomy were performed. Polymerase chain reaction results from the vitreous for *Mycobacterium tuberculosis*, herpes simplex virus, and varicella-zoster virus were negative.

**Comment.** Although tuberculous infection and/or hypersensitivity has been associated with both Eales disease and serpiginous choroiditis, the evidence remains inconclusive. *M tuberculosis* has been detected by polymerase chain reaction from vitreous biopsies in patients with Eales disease, but the same biopsies were negative for mycobacterial cultures. In patients with systemic tuberculosis, the development of Eales disease is uncommon. A positive QuantiFERON result was detected in 11 of 21 patients with serpiginous-like choroiditis. Choroidal tuberculous lesions mimicking serpiginous choroiditis have been described and named tubercular serpiginous-like choroiditis. Previous authors believe that tubercular serpiginous-like choroiditis may be distinguishable from classic serpiginous choroiditis by the presence of vitritis and smaller, multifocal lesions in the fundus of patients from tuberculosis endemic regions.

To our knowledge, the coexistence of Eales disease and serpiginous choroiditis has been reported only once before, in a 35-year-old Pakistani man with bilateral amniogtic choriotreitis followed by unilateral Eales disease. Mantoux skin test results were positive with no active tuberculosis infection. Although an association between serpiginous choroiditis and retinal periphlebitis and/or vein occlusions was previously reported, testing for tuberculosis in these cases was either not performed or had negative results. Furthermore, in our patient, the area of Eales disease was distinct from the peripapillary serpiginous choroiditis.

Our patient does not fit into either category of serpiginous disease previously described. Unlike patients with tubercular serpiginous-like choroiditis, he had a solitary, peripapillary lesion and negative results on extensive investigation for tuberculosis; unlike patients with classic serpiginous choroiditis, he exhibited bilateral intraocular inflammation with vitritis in the right eye and keratic precipitates in both eyes. Because it is improbable that these 2 rare conditions would coexist, it is possible that Eales disease and serpiginous choroiditis represent manifestations of the same underlying inflammatory disease.

**Author Affiliations:** Vitreous-Retina-Macula Consultants of New York and LuEsther T. Mertz Retinal Research Center, Manhattan Eye, Ear, and Throat Institute (Drs Fung, Yzer, and Yannuzzi) and Department of Ophthalmology, Columbia University (Drs Yzer and Yannuzzi), New York; and Fondazione per la Macula Onlus (Dr Nicolò) and Department of Neuroscience, Ophthalmology, and Genetics, University of Genova (Drs Nicolò and Traverso), Genova, Italy.

**Correspondence:** Dr Massimo Nicolò, Clinica Oculistica, Di. N.O.G.Mi, Università di Genova, Viale Benedetto XV, n.5 16132 Genova, Italy (massimo.nicolò@unige.it).

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