

## Case Report: Conjunctival Infestation with *Thelazia gulosa*: A Novel Agent of Human Thelaziasis in the United States

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**Abstract.** We report a case of thelaziasis in a 26-year-old female, acquired in Oregon. A total of 14 worms were removed from the patient's left eye and were morphologically identified as being *Thelazia gulosa*. Until now, only two species of *Thelazia* have been implicated in causing human disease, *Thelazia callipaeda* in Asia and Europe and occasional reports of *Thelazia californiensis* from the United States of America. Here, we describe a third, previously unreported parasite of humans, *T. gulosa* (the cattle eyeworm) as an agent of human thelaziasis and the first reported case of human thelaziasis in North America in over two decades.

### INTRODUCTION

Thelaziasis is an ocular infection caused by nematodes of *Thelazia* spp., usually transmitted by flies that feed on lacrimal secretions. Although a common veterinary infection, human infection is considered to be a rare zoonotic event. Cases of human thelaziasis have been reported worldwide, predominantly in Europe and Asia.<sup>1</sup> Cases occur predominantly in rural communities with close proximity to animals and poor living standards. Thelaziasis mainly affects the elderly and children, who may be less able to keep flies away from their faces.<sup>2</sup> Most of the reported cases have been caused by *Thelazia callipaeda*, occurring in the old world, particularly in Japan.<sup>1</sup> *Thelazia callipaeda* has also rarely been reported infecting humans in China, Japan, India, Burma, Korea, Taiwan, Thailand, Indonesia, Russia, Italy, and France.<sup>3</sup> There have been 10 previously reported cases of human thelaziasis from the United States; nine from California and one in Utah, all were reported as *Thelazia californiensis*.<sup>4,5</sup> Other species of *Thelazia* are reported as infecting animals in the United States, these being, *Thelazia gulosa*, *Thelazia lacrymalis*, *Thelazia rhodesi*, and *Thelazia skrjabini*.<sup>3</sup>

### CASE REPORT

A 26-year-old avid outdoorswoman from Oregon reported left eye irritation accompanied by the sensation of a foreign object. The patient had, in previous weeks, been practicing horsemanship in Gold Beach, OR, a region where cattle farming occurs. The irritation worsened and on the eighth day of symptoms, the patient removed a small, translucent worm. She presented to a local physician who removed two additional worms. The worms were submitted to Northwest Pathology for analysis and identification where they were fixed in 10% buffered formalin and forwarded to the Centers for Disease Control and Prevention (CDC) Parasitic Diseases Reference Laboratory for identification. The following day, the patient presented to an optometrist where three additional worms were removed. The patient was arranged to see an infectious disease specialist who removed a partial worm,

which was also sent to the CDC. The patient was diagnosed with parasitic infiltration of the left periocular tissues and a secondary bilateral papillary reaction of the upper and lower palpebral conjunctivae. The patient was advised to undergo manual extraction rather than topical or systemic anti-helminthic therapy. Despite multiple washouts by ophthalmologists, no further worms were seen by providers; however, the patient continued to remove worms from her left eye. A total of 14 worms were removed from the patient's left eye over 20 days. Since this time, the patient has been without symptoms and no further worms have been observed.

### METHODS

A whole adult worm submitted to the CDC Parasitic Diseases Reference Laboratory Morphology Department was morphologically examined. The worm was preserved in 10% neutral buffered formalin, disallowing DNA extraction and molecular analysis. The worm was independently examined by microscopy by three experienced morphologists, followed by collation of their opinions to make a final identification. Further morphometric analysis was performed, in consultation with all major morphological references,<sup>3,6–8</sup> to confirm the species identification.

**Ethical approval.** Publication of this case report was granted institutional review board approval by the CDC center for global health office of the associate director for science, tracking number 2017-381.

### RESULTS

The worms submitted to the CDC were female and had acquired a degree of opacity in the formalin preservative (Figure 1). Minor shrinkage had occurred in the formalin fixative, one worm measured 11-mm long by 320  $\mu$ m at the widest point. The anterior sharply tapered toward a deep, cup-shaped buccal cavity (width 35  $\mu$ m, depth 25  $\mu$ m). No lips were observed at the buccal cavity. The prominent esophagus met the intestinal junction 470  $\mu$ m posterior to the anterior-most portion of the cephalic region of the worm (the anterior opening of the buccal cavity). The width of the widest point of the esophageal bulb was 180  $\mu$ m. Oval, thin-shelled, spirurid-type eggs were observed within the ovaries. The vulva opened 20  $\mu$ m anterior to the esophago-intestinal junction and 450  $\mu$ m from the anterior-most portion of the cephalic region of the

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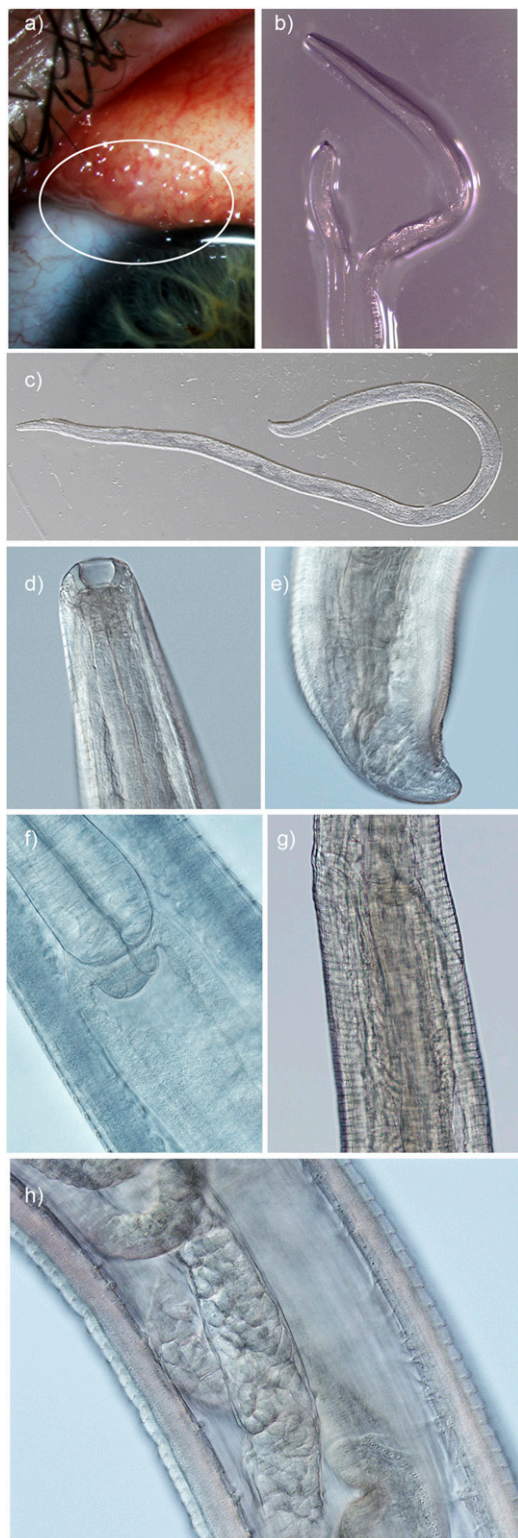


FIGURE 1. *Thelazia gulosa* (A) in situ on the surface of the patient's conjunctiva (circle); (B) adult female immediately after removal from the eye. Morphological identifying features of adult female worm submitted for analysis; (C) whole adult female ( $\times 40$  magnification, cleared); (D) deep buccal cavity; (E) tail with nonprotruding anal opening and postanal papilla; (F) esophageal-intestinal junction; (G) nonprotruding vulval opening slightly anterior and to the left of the esophageal-intestinal junction; and (H) mid body with prominent cuticular striations, intestinal tube, and ovaries containing spirurid eggs ( $\times 200$  magnification, cleared).

worm. The pattern of the cuticle at the vulval opening was not uniform and the vulval opening did not protrude. There were approximately 5.5 distinct transverse cuticular striations in each  $10 \mu\text{m}$  of the cuticle at the widest point of the worm. These striations were rounded rather than serrated in appearance. The width at the anal opening was  $100 \mu\text{m}$ . There was no protrusion of the anal opening, a unilateral postcloacal tapering and two postanal papillae were observed on the bluntly rounded tail. After analysis of the observed anatomical features and consultation with references describing the morphology of species of *Thelazia* reported from humans and animals,<sup>3,6-8</sup> the worms were identified as belonging to the species *T. gulosa*, a cattle eyeworm. Several morphological features were used to differentiate this isolate from other *Thelazia* spp., including the two species previously recorded infecting humans, these are listed in Table 1. Features differentiating this isolate from other species found in North America and the two species previously identified as infecting humans were the following: the distance of the vulval opening from the anterior cephalic region that the vulval opening had no distinct features and was at the same level as the esophago-intestinal junction; possession of a deep and cup-like buccal cavity, rounded, tightly spaced, and relatively discrete cuticular ridges; a nonprotruding anus with unilateral tapering postanally and the presence of two postanal phasmids.

#### DISCUSSION

*Thelazia gulosa*: phylum Nematoda, order Spirurida, family Thelaziidae, and genus *Thelazia* are parasites affecting the conjunctiva of the definitive host, where they are ovoviparous. In North America, *T. gulosa* is distributed throughout the northern states of the United States and southern Canada.<sup>3,9</sup> The intermediate host, *Musca autumnalis* (face flies) ingests L1 larvae passed in the definitive host lachrymal secretions.<sup>3,10</sup> These larvae develop within the abdomen of the fly, then migrate to the hemocoel, where development to L3 larva requires a minimum of 9 days at  $27^\circ\text{C}$ .<sup>11</sup> The L3 larvae migrate to the mouthparts and are inoculated into the conjunctiva of a new host with feeding.<sup>3,10</sup> The L3 larvae then develop into the adult stage in the conjunctival sac and prebulbar tear film. This patient's outdoor pastimes of riding horses and fishing during the summer months likely allowed exposure to vector face flies, and she may have delayed brushing away of these flies from her face. All recorded cases of human thelaziasis have been reported during the summer months.<sup>3</sup>

*Thelazia gulosa* is widely distributed throughout North America and Europe, Central Asia, and Australia, where it is commonly a parasite of cattle.<sup>3</sup> The vector fly in North America, *M. autumnalis*, was introduced from the Palearctic region immediately after World War II and has spread across the continent, including the state of Oregon, since that time.<sup>11</sup> This fly also transmits another cattle eyeworm, *T. skrjabini*, in North America.<sup>3</sup> The prevalence of *Thelazia* spp. larva in face flies captured in Massachusetts, Iowa, and Alberta during the summer months varying between 1% and 37%, with an average of 2.5–4.2 larva per infected fly.<sup>11</sup> Vector flies of *T. gulosa* in other regions of the world include *M. autumnalis*, *Musca larvipara*, and *Musca osiris* in Europe,<sup>12</sup> *Musca amica* in the Russian Far East, *Musca vitripennis* in Crimea, and possibly also *M. larvipara* in Ukraine.<sup>9</sup> *Musca domestica* has been suggested as a vector, but this remains controversial.<sup>13</sup>

TABLE 1  
Differentiating morphological features, geographic distribution, and known hosts of female *Thelazia* spp.<sup>3,6-8,14</sup>

Differentiating morphological features of adult female <i>Thelazia</i> spp. nematodes										
<i>Thelazia</i> species	Length of adult female (mm)	Diameter at widest point (µm)	Distance of vulval opening from anterior cephalic region (µm)	Position of vulval opening relative to esophago-intestinal junction	Morphological features of vulval opening	Morphological features of buccal cavity	Morphology of cuticular ridges in midsection	Morphological features of female posterior	Reported geographic range	Reported hosts
<i>Thelazia bubalis</i>	6.5-7.8	250	900	ND	ND	ND	ND	-	India	Water buffalo
<i>Thelazia californiensis</i>	12-18.8	330-420	700-1,000	Posterior	No distinctive features	Deep and cup like	Rounded, moderately prominent, and widely spaced	Anus protrudes, two phasmids protrude from tip of tail, and no unilateral tapering	USA and Brazil	Humans, canines, felines, bears, deer, and sheep
<i>Thelazia callipaeda</i>	10.7-18.5	290-510	520-710	Anterior	Short flap at opening	Wide and cup like	Serrated, very prominent, and tightly spaced	Anus protrudes, two phasmids protrude from tip of tail, and no unilateral tapering	Europe, Asia, and India	Humans, monkeys, canines, felines, and rabbits
<i>Thelazia ershowi</i>	5.0-8.7	188-207	395-489	ND	ND	ND	ND	ND	Former Union of Soviet Socialist Republics	Pig
<i>Thelazia gulosa</i>	8.0-11.5	350-460	460-610	Same level	No distinctive features	Deep and cup like	Rounded, very prominent, and widely spaced	Anus does not protrude, two postanal phasmids, and unilateral tapering postanally	North America, Europe, former USSR, and Australia	Human, Cattle
<i>Thelazia lacrymalis</i>	10.5-12.5	279-289	493-593	Posterior	No distinctive features	Deep and cup like	Rounded, not prominent, and tightly spaced	Anus does not protrude, two postanal phasmids, and unilateral tapering postanally	North America, South America, Europe, Asia, and North Africa	Buffalo, camel, dog, and equine species
<i>Thelazia leesei</i>	14-21	400	425-440	Same level	ND	ND	ND	ND	Europe, India, Central Asia, and Africa	Camels
<i>Thelazia rhodesi</i>	12.5-20.5	300-500	505-536	Posterior	Cuticular pattern differs, vulva protrudes	Deep and cup like	Serrated, very prominent, and widely spaced	Anus protrudes, one phasmid protrudes from tip of tail, and unilateral tapering postanally	North America, Europe, United Kingdom, Asia, Ghana, Zambia, Afghanistan, and Japan	Cattle, buffalo, zebu, bison horses, sheep, and goats
<i>Thelazia skrjabini</i>	11-19	178-378	410-710	Posterior	Protrudes	Short and indistinct	Rounded, scarcely visible, and widely spaced	Anus protrudes, two postanal phasmids and rounded with no unilateral tapering	North America, Europe, former USSR, India, and Australia	Cattle, buffalo, and horses

ND = no data.

The most common clinical findings are mild conjunctival inflammation, foreign body sensation, follicular hypertrophy of the conjunctiva, and excessive lacrimation. Occasionally, the worms migrate across the surface of the eye and cause corneal scarring, opacity, and blindness.<sup>3</sup> Because the localization of *Thelazia* infestation is confined to the conjunctiva and removal of worms with a cotton swab or forceps is sufficient. The clinical signs usually resolve quickly after the removal of the parasites.<sup>3</sup> Immediate postremoval irrigation with Lugol's iodine or 2–3% boric acid may be considered.<sup>3</sup> Injection of 2 mL levamisole into the conjunctival sac or administration of 5 mg/kg orally or parenterally has been used in the treatment of *T. californiensis* infection<sup>3</sup> before the availability of ivermectin. A subcutaneous dose of 2.2 mg/kg of ivermectin has been used to cure human infections in Asia and Europe.<sup>3</sup>

Previously, only two *Thelazia* spp. have been implicated as causing human thelaziasis worldwide, these being *T. californiensis* (in the western United States) and *T. callipaeda* (in Europe and Asia).<sup>2,3</sup> In this report, we add a third species, *T. gulosa*, an endemic eyeworm of cattle in North America, Europe, Central Asia, and Australia as a novel agent of human thelaziasis in the United States of America.

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