DIAGNOSTIC SLIDE SESSION CASE 10

B.K. Kleinschmidt-DeMasters, MD

Disclosures:

I am not a trainee

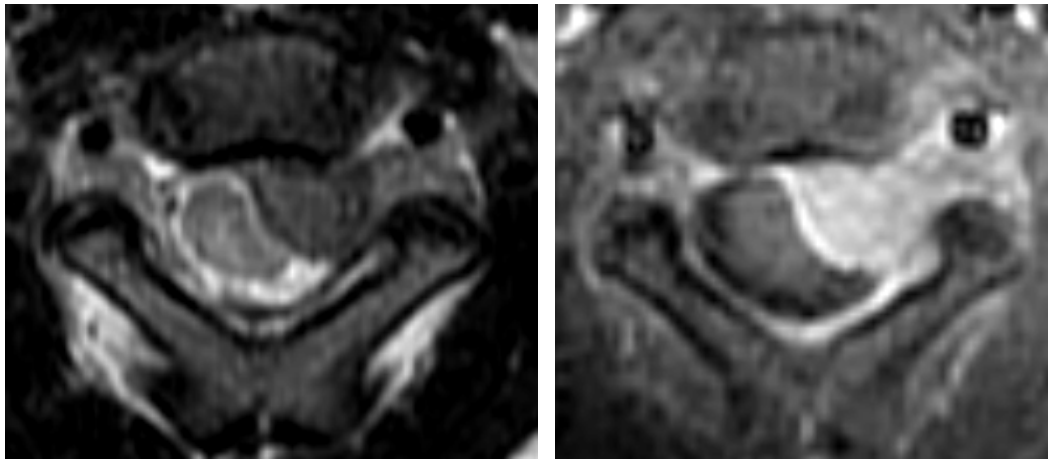
Caterina made me do this…

CASE 2016-10: :

- The patient is a 5-year-old girl with Down syndrome, obstructive sleep apnea, and an AV canal defect present at birth (now repaired). She had complaints of headaches and progressively worsening neck pain over 2 or 3 months. She then began to have severe arm pains that lead to imaging, which demonstrated an avidly enhancing, extradural soft tissue mass centered within the left anterolateral aspect of the C2-C3 spinal canal, extending through and remodeling the left C2-C3 neural foramen.

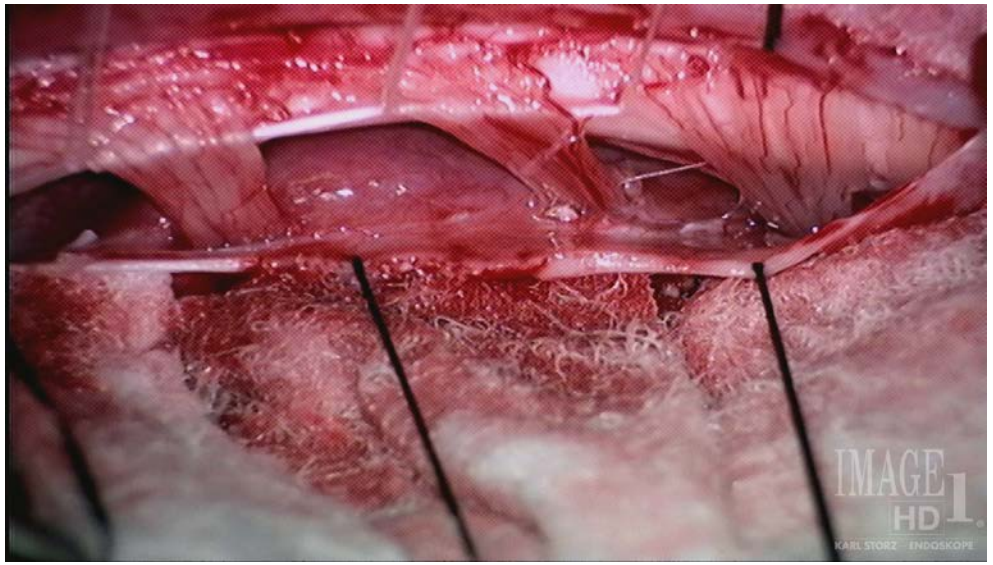
CASE 2016-10: :

- Primary consideration included a nerve sheath tumor, such as a schwannoma or neurofibroma, or meningioma, though it would have been highly unusual in a patient of this age.

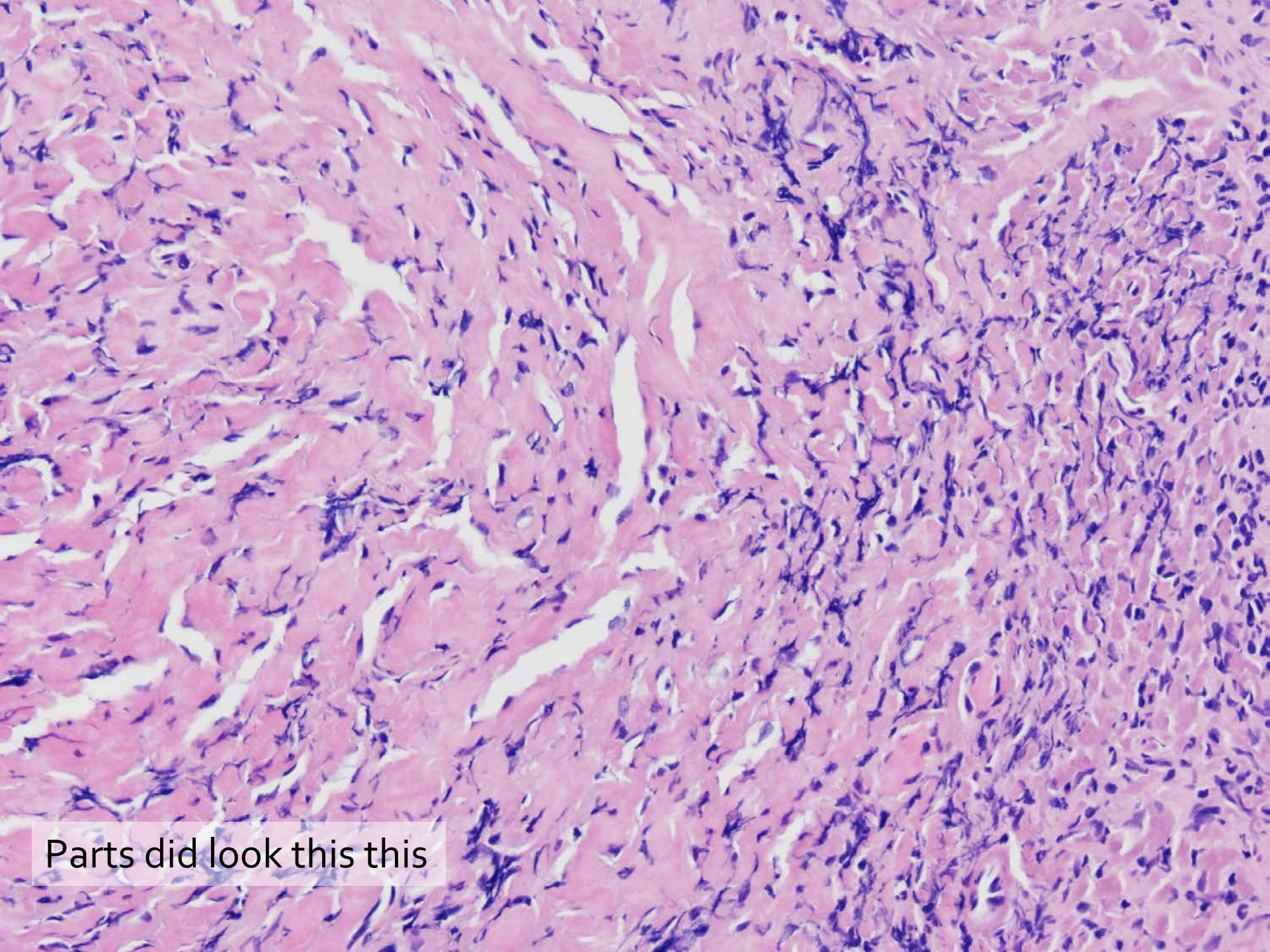


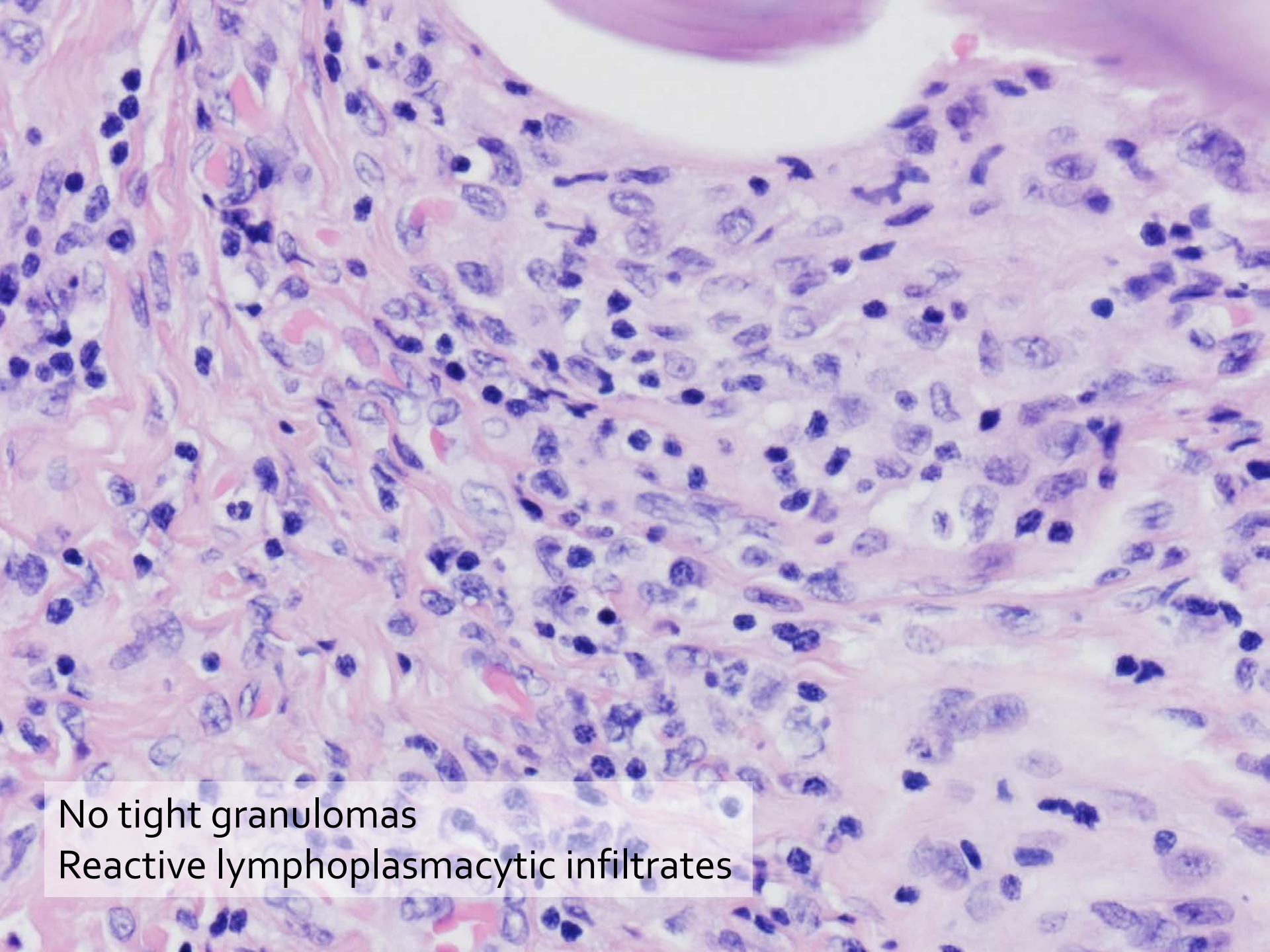
CASE 2016-10: :

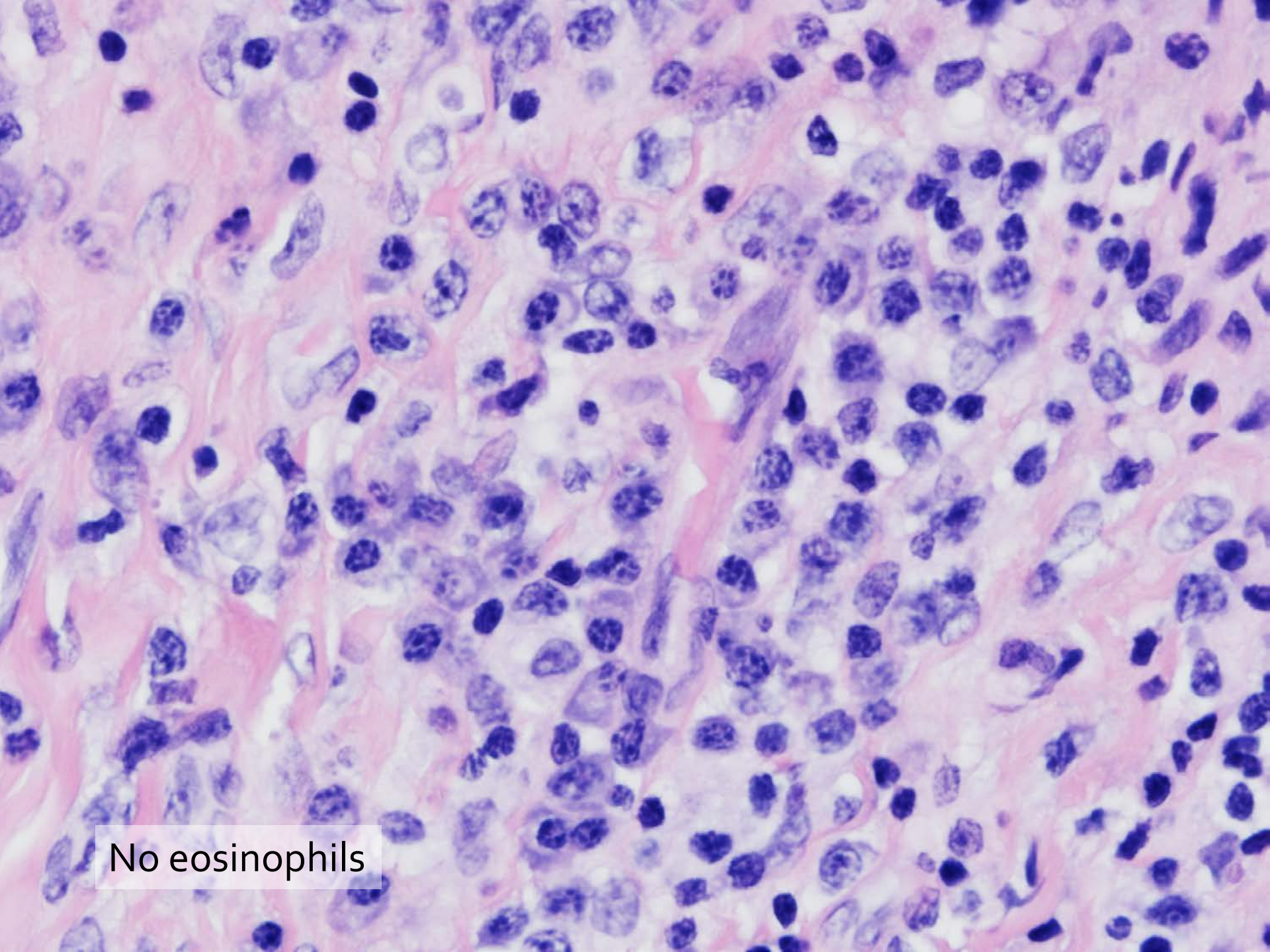
- A cervical osteoplastic laminectomy and microsurgical radical subtotal resection of tumor was performed. Somatosensory and motor evoked potentials were diminished on the left side at the outside of the case, but they gradually improved, as the case proceeded. The tumor was densely adherent to dura, and not at all adherent to the spinal cord. The left cervical nerve roots 2, 3, and 4 could easily be separated from the tumor and were left largely intact.

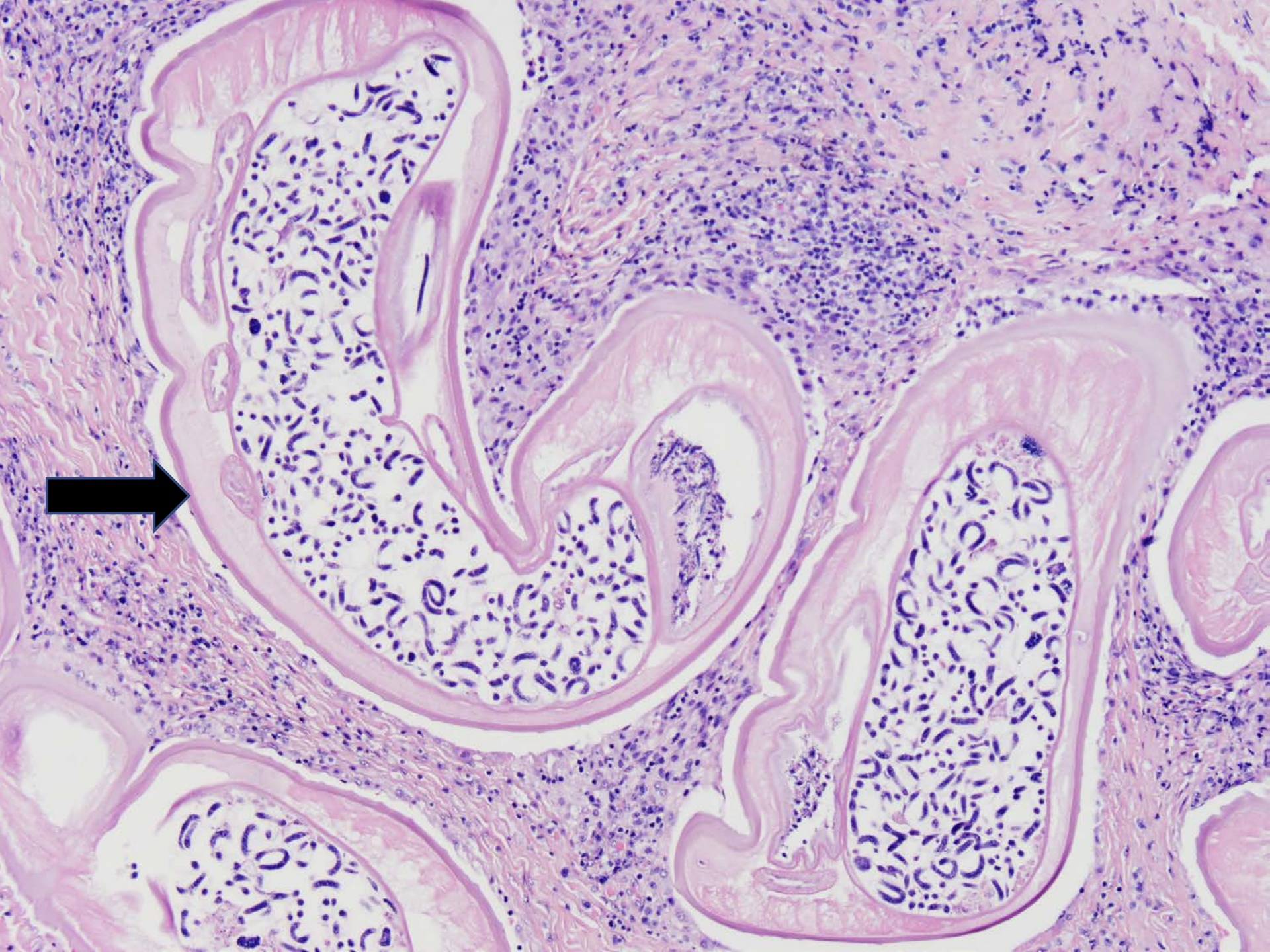


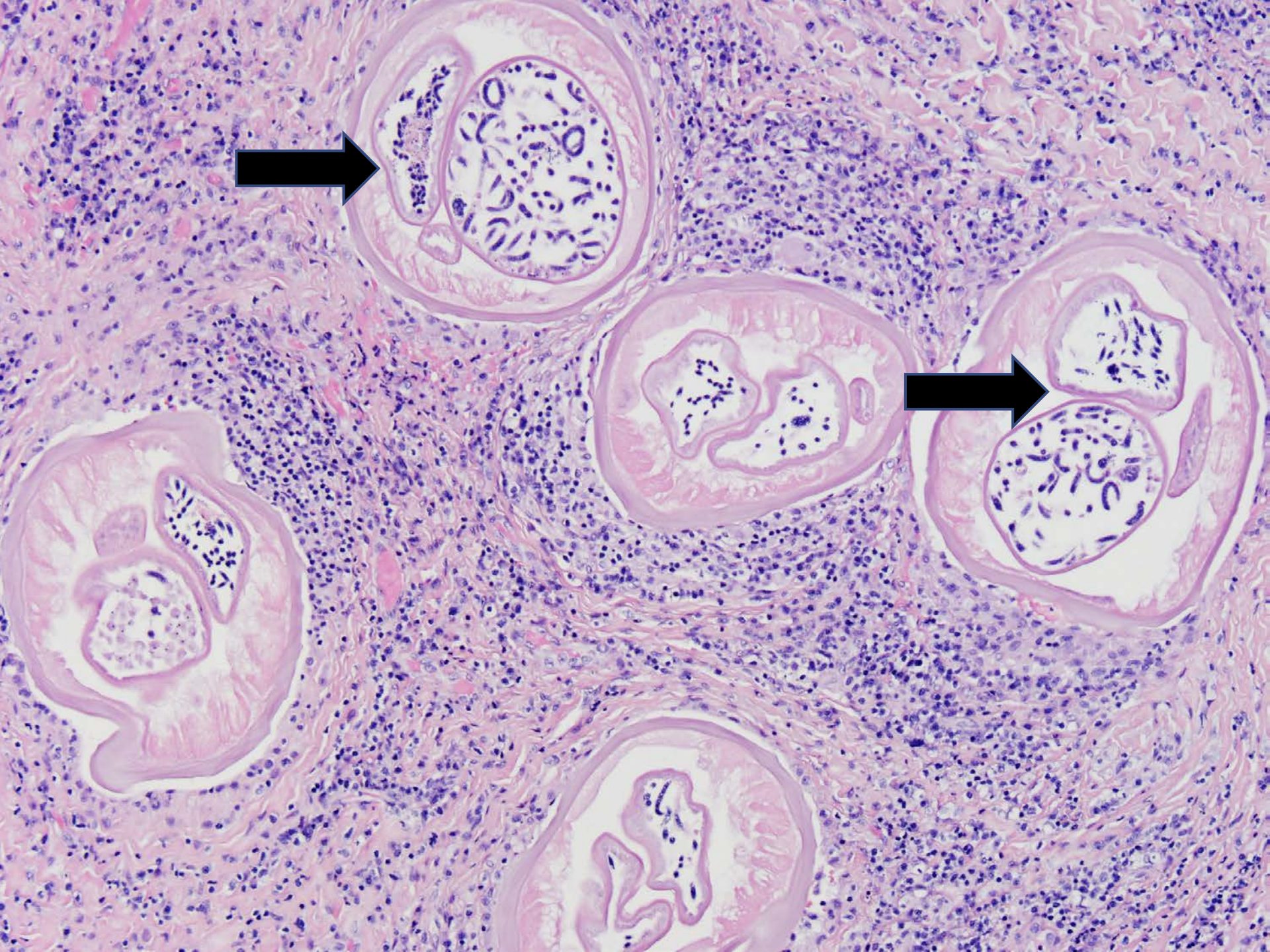
- Preliminary frozen section diagnosis at the outside pediatric hospital was "consistent with fibrous meningioma".

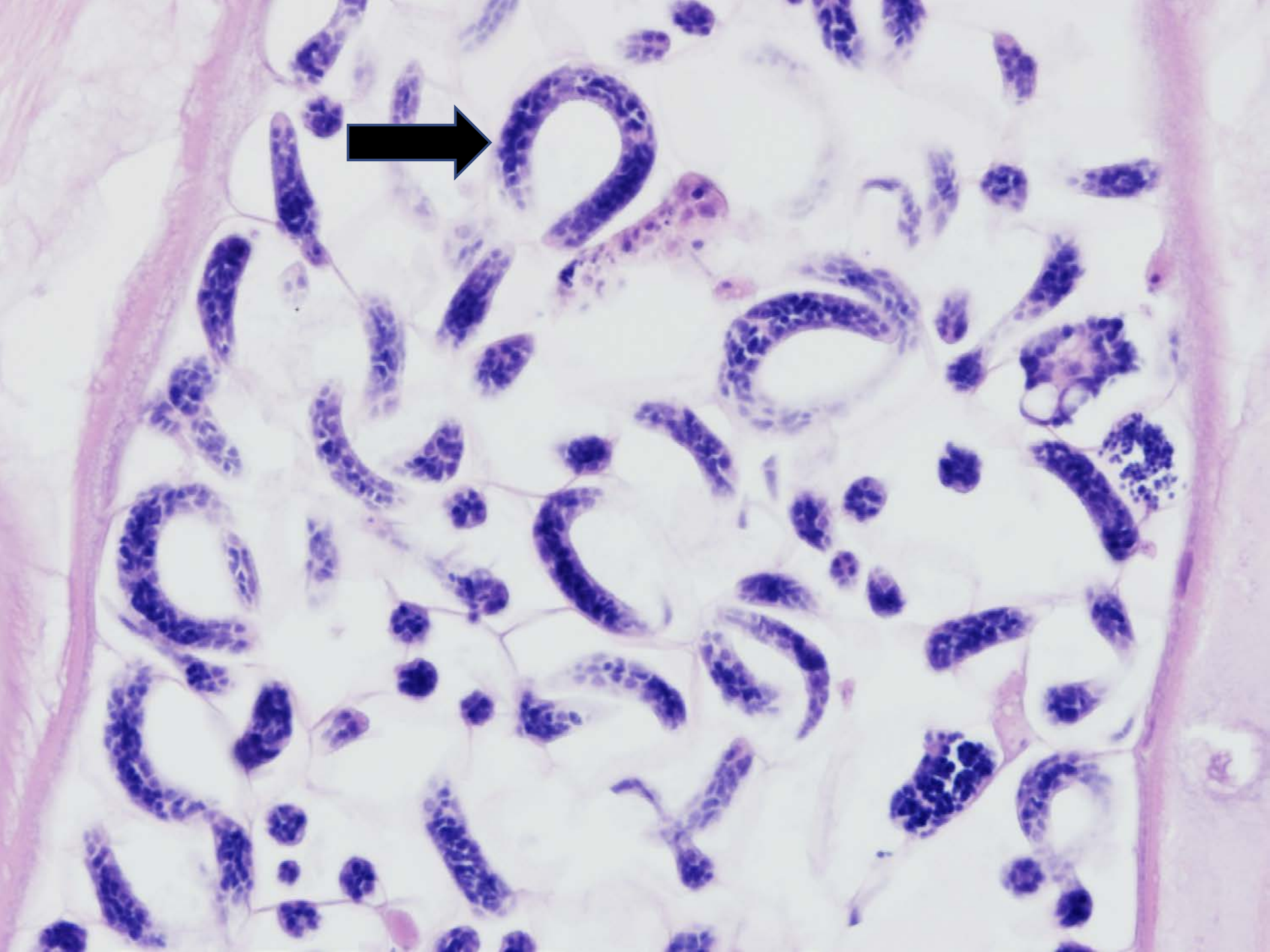

Parts did look this this


No tight granulomas
Reactive lymphoplasmacytic infiltrates

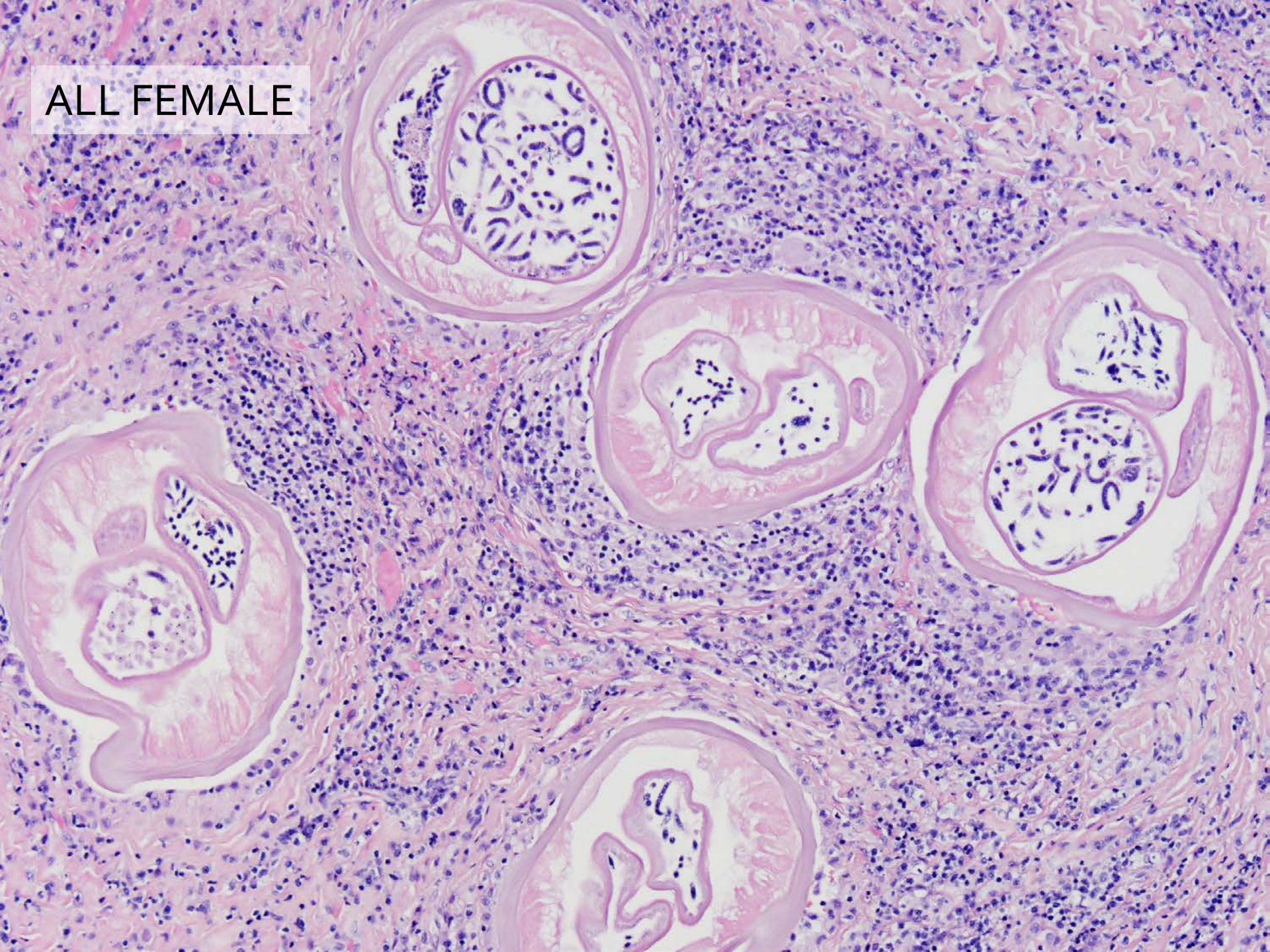

No eosinophils

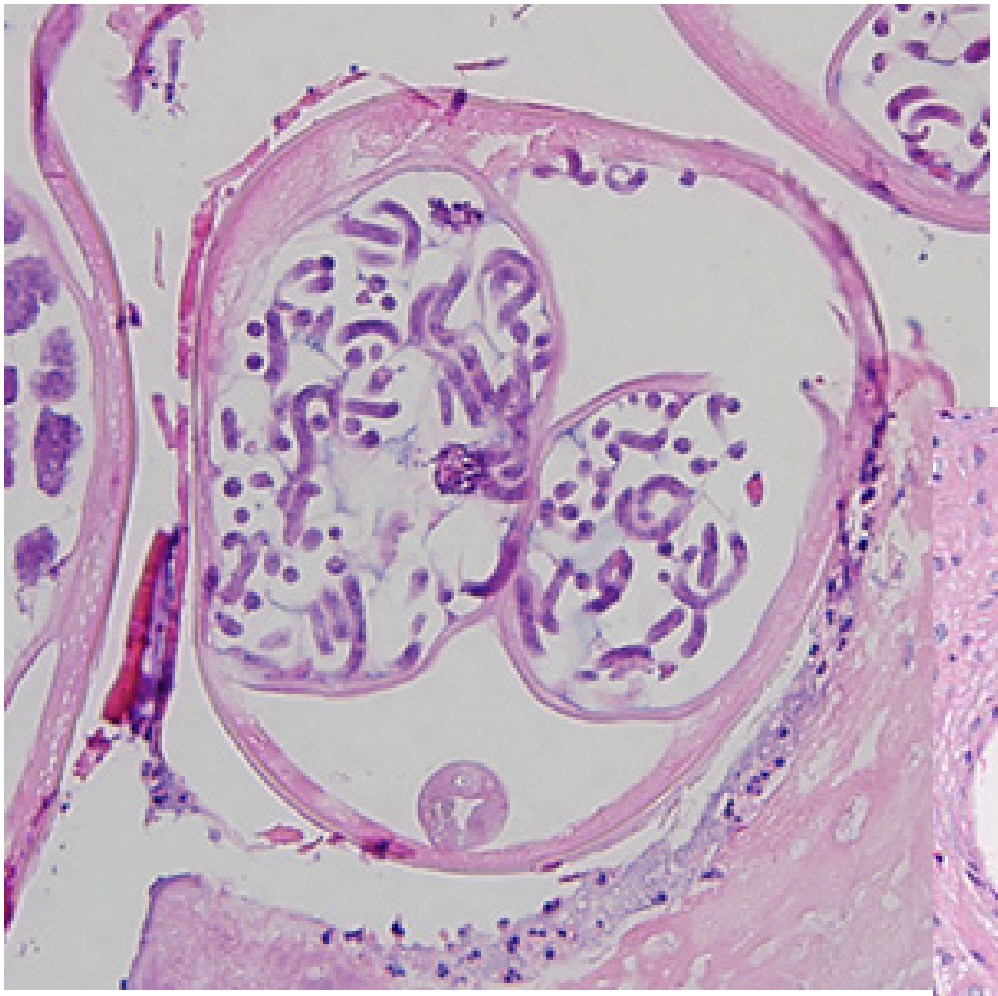




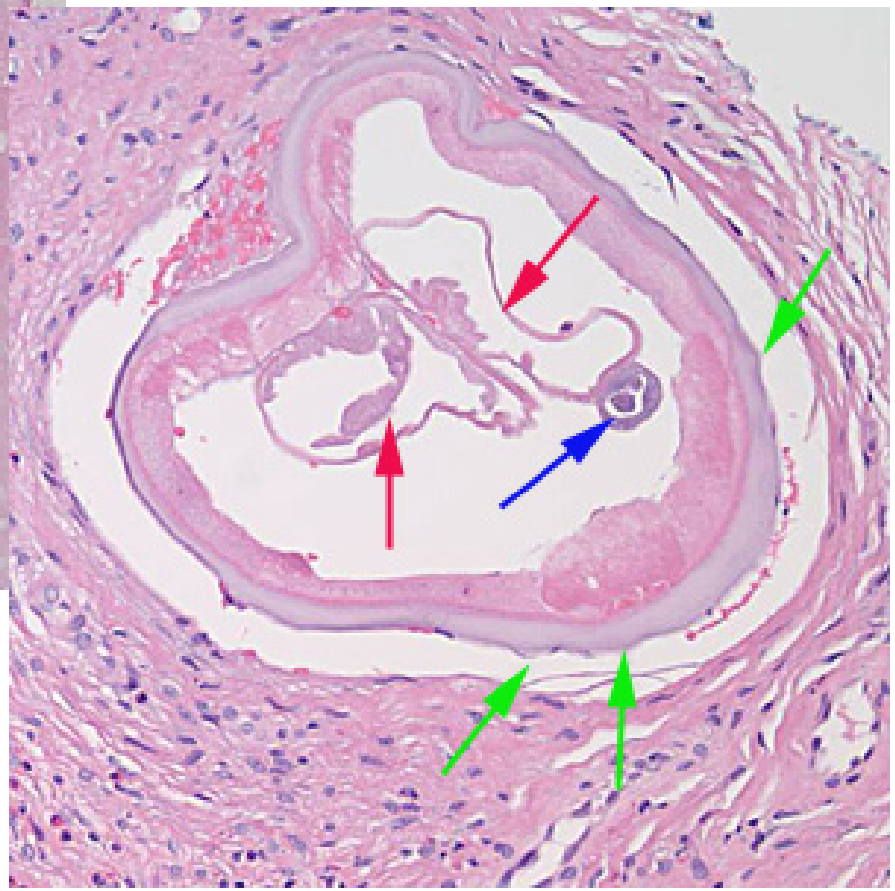


DISCUSSION


ALL FEMALE



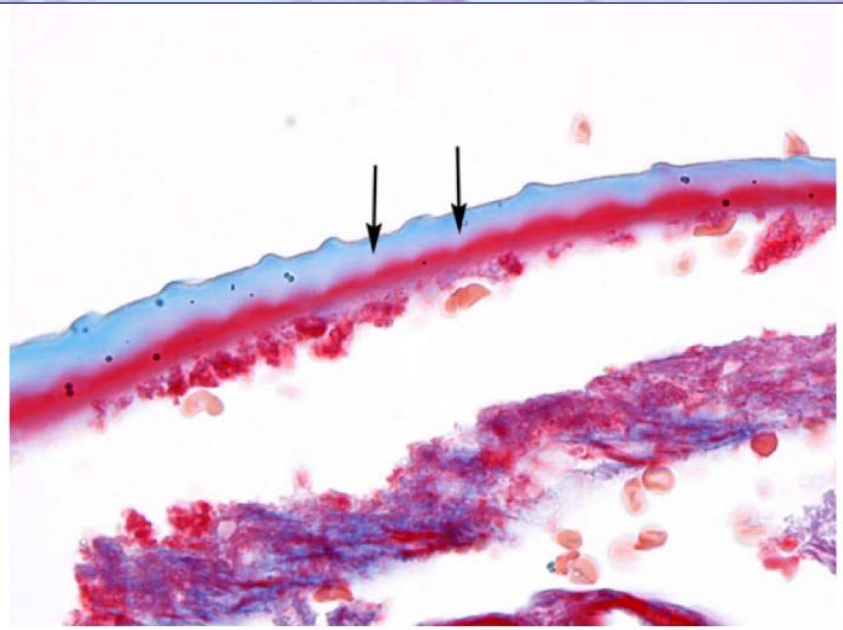
Uterus red arrow
Intestine blue arrow
Cuticular nodules
green arrows



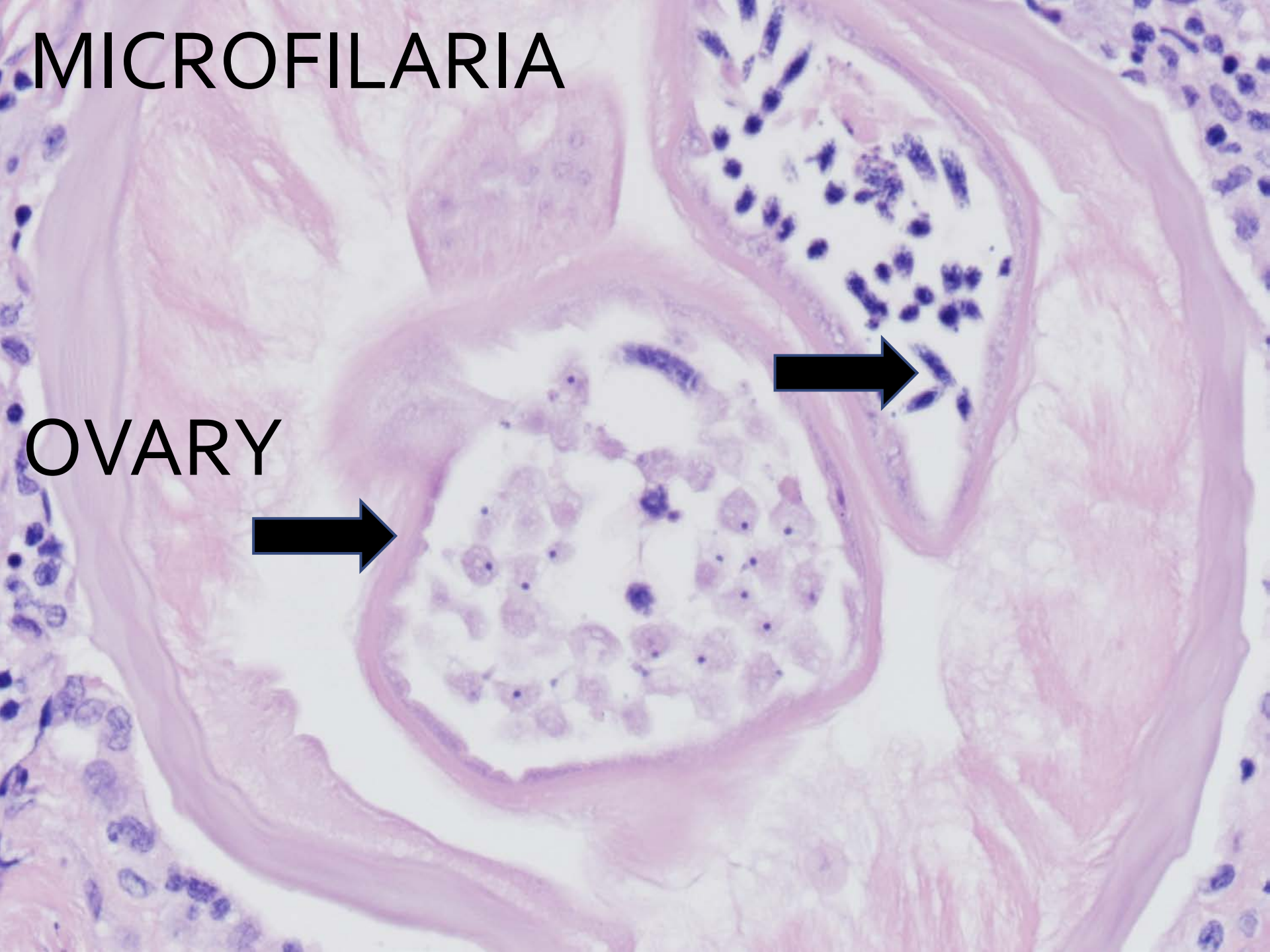
GRAVID FEMALE WITH TWO-CHAMBERED UTERUS

http://www.cdc.gov/dpdx/onchocerciasis/gallery.html#adults.

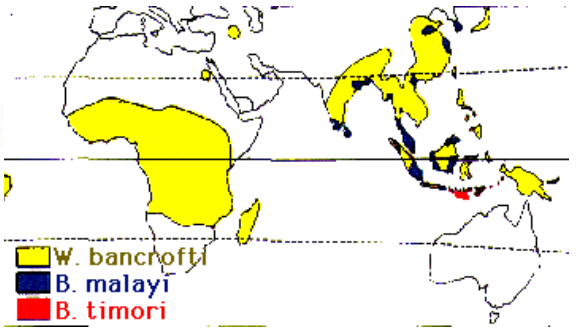
CUTICLE



CID 2016:62 (15 March) • Cantey et al


MICROFILARIA
OVARY

Species which are primarily responsible for human filarial infections are *Wuchereria bancrofti, Brugia malayi, Onchocerca volvulus*



Wuchereria bancrofti and Malayan filariasis (*B. malayi*) cause elephantiasis

Most elephantiasis worldwide caused by *Wuchereria bancrofti*.
In Asia, *Brugia malayi* and *Brugia timori*

Onchocerca volvulus

-transmitted through repeated bites by blackflies of the genus *Simulium*

-Infection leads to visual impairment or blindness, skin disease, including nodules under the skin or debilitating itching.

-Worldwide onchocerciasis is second only to trachoma as an infectious cause of blindness

-called *River Blindness* because the blackfly that transmits the infection lives and breeds near fast-flowing streams and rivers and infection can result in blindness

Fig. 18.2. Subcutaneous nodule due to onchocerciasis.

Handbook of Clinical Neurology, Vol. 114 (3rd series)

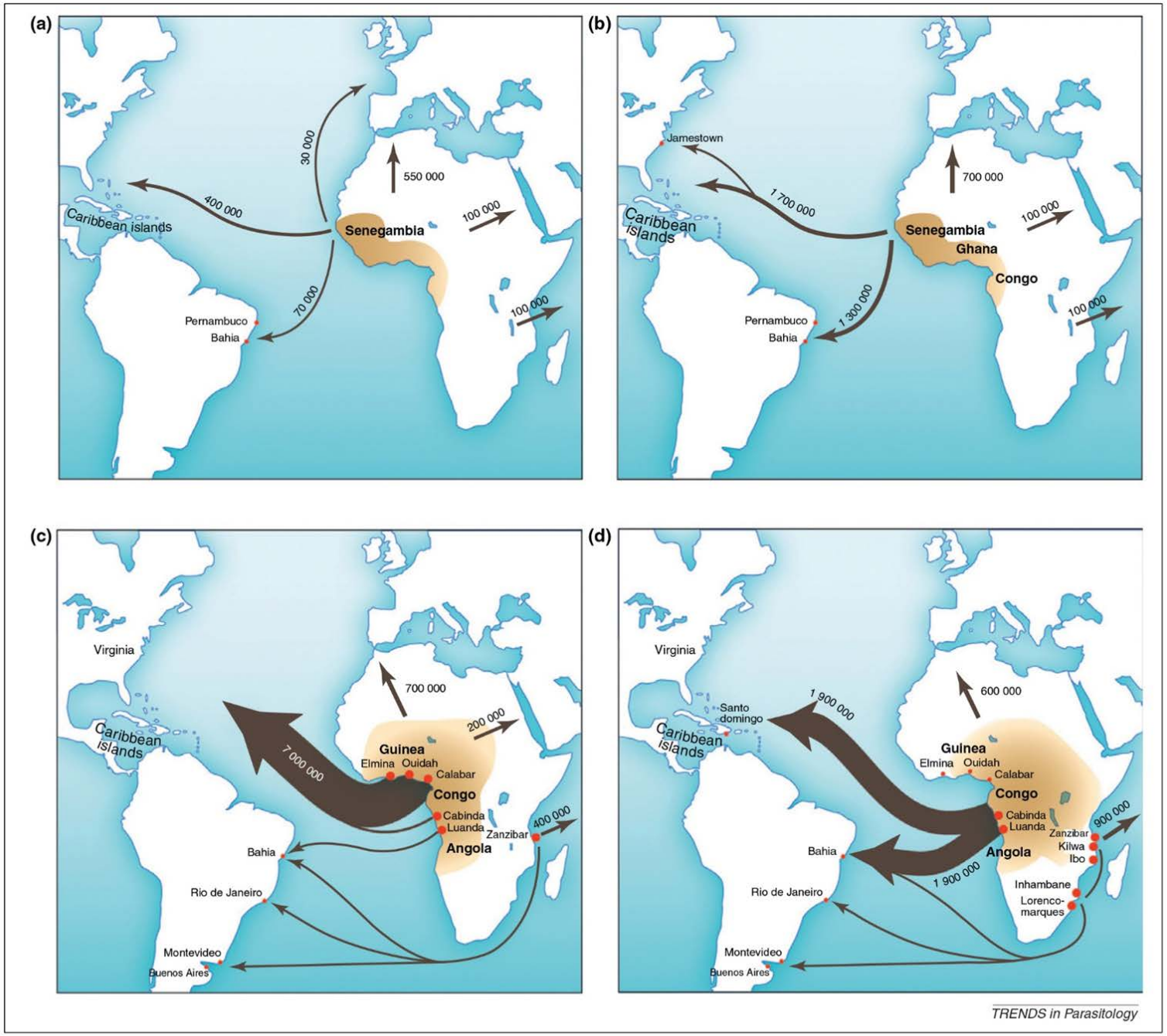


Figure 1. Trend in direction and numbers of African slaves transported over time. **(a)** 15th–16th century. **(b)** 17th century. **(c)** 18th century. **(d)** 19th century. Data source: UNESCO.

Review

Cell PRESS

The onchocerciasis chronicle: from the beginning to the end?

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The year 2012 marks the 25th anniversary of the donation of ivermectin to fight onchocerciasis and the projected date for elimination of transmission of the disease in the Americas. This review looks at the history of onchocerciasis, from its discovery through to 2025, by which time it is projected that the disease will have been eliminated as a public health problem, except in a handful of sub-Saharan countries, where it should be well on the way towards elimination.

Can science, human ingenuity and teamwork conquer onchocerciasis?

subsistence farming population of the continent. It is also called river blindness because the blood-feeding flies that transmit the ultimately blinding disease inhabit lush, fertile land alongside the rivers in which they breed. Onchocerciasis was first scientifically observed almost 140 years ago, despite it having been around for centuries. Subsequently, scientists recognised that humans develop the disease after being bitten by vector blackflies of the genus *Simulium* (Box 1) that were carrying infective larvae of a filarial threadworm parasite, *Onchocerca volvulus* (Box 2). Some 13 million km^2 of the earth became covered by the disease, with infection rates varying considerably

Am. J. Trop. Med. Hyg., 93(6), 2015, pp. 1295–1304
doi:10.4269/ajtmh.15-0364

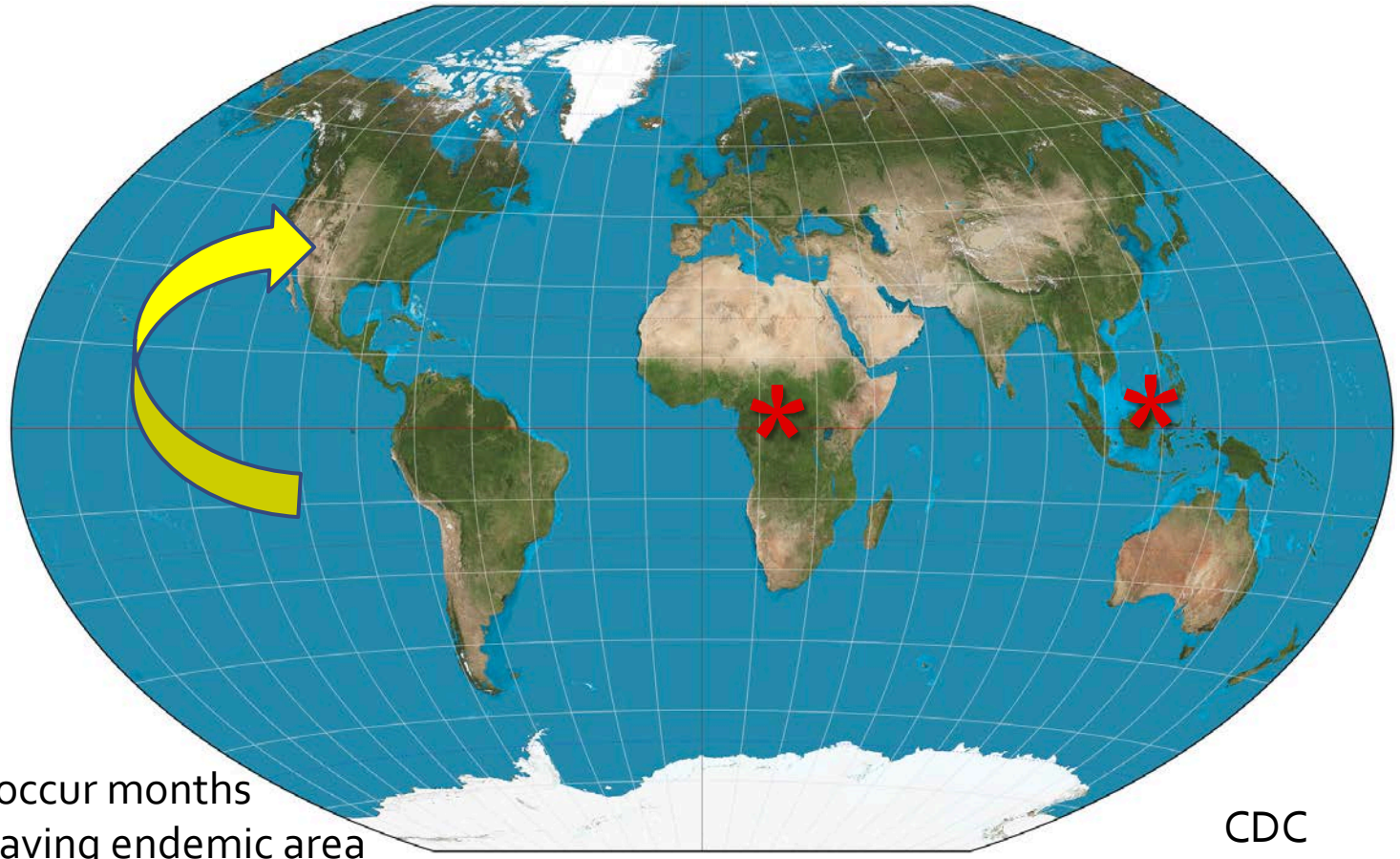
One Hundred Years After Its Discovery in Guatemala by Rodolfo Robles, *Onchocerca volvulus* Transmission Has Been Eliminated from the Central Endemic Zone

Frank Richards Jr.,* Nidia Rizzo, Carlos Enrique Diaz Espinoza, Zoraida Morales Monroy, Carol Guillermina Crovella Valdez, Renata Mendizabal de Cabrera, Oscar de Leon, Guillermo Zea-Flores, Mauricio Sauerbrey, Alba Lucia Morales, Dalila Rios, Thomas R. Unnasch, Hassan K. Hassan, Robert Klein, Mark Eberhard, Ed Cupp, and Alfredo Domínguez

River Blindness Elimination Program, The Carter Center, Atlanta, Georgia; Centro de Estudios en Salud of the Universidad del Valle de Guatemala (UVG), Guatemala City, Guatemala; Ministerio de Salud Pública y Asistencia Social, Guatemala City, Guatemala; Onchocerciasis Elimination Program for the Americas (OEPA), The Carter Center, Guatemala City, Guatemala; Global Health Infectious Disease Program, Department of Global Health, University of South Florida, Tampa, Florida; Division of Parasitic Diseases and Malaria, Centers for Disease Control and Prevention, Atlanta, Georgia; Department of Entomology and Plant Pathology, Auburn University, Auburn, Alabama

Abstract. We report the elimination of *Onchocerca volvulus* transmission from the Central Endemic Zone (CEZ) of onchocerciasis in Guatemala, the largest focus of this disease in the Americas and the first to be discovered in this hemisphere by Rodolfo Robles Valverde in 1915. Mass drug administration (MDA) with ivermectin was launched in 1988, with semiannual MDA coverage reaching at least 85% of the eligible population in > 95% of treatment rounds during the 12-year period, 2000–2011. Serial parasitological testing to monitor MDA impact in sentinel villages showed a decrease in microfilaria skin prevalence from 70% to 0%, and polymerase chain reaction (PCR)-based entomological assessments of the principal vector *Simulium ochraceum* s.l. showed transmission interruption by 2007. These assessments, together with a 2010 serological survey in children 9–69 months of age that showed Ov16 IgG4 antibody prevalence to be < 0.1%, meeting World Health Organization (WHO) guidelines for stopping MDA, and treatment was halted after 2011. After 3 years an entomological assessment showed no evidence of vector infection or recrudescence of transmission. In 2015, 100 years after the discovery of its presence, the Ministry of Health of Guatemala declared onchocerciasis transmission as having been eliminated from the CEZ.

-Onchocerciasis VOLVULUS is not acquired in United States.
-Occasional cases found in immigrants or travelers from endemic areas: however, symptomatic onchocerciasis usually requires heavy infestations and repeated exposure to the vector fly
-Short-term travelers at little or no risk of disease
-Pruritus, dermatitis, and eosinophilia may occur in travelers who stay longer than 3 months in endemic areas of Africa



-Symptoms may occur months to years after leaving endemic area

CDC

http://www.cdc.gov/dpdx/onchocerciasis/gallery.html#adults.

A perfect match….

Am. J. Trop. Med. Hyg., 88(3), 2013, pp. 601–605
doi:10.4269/ajtmh.12-0733

Case Report: Zoonotic *Onchocerca lupi* Infection in a 22-Month-Old Child in Arizona: First Report in the United States and a Review of the Literature

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Division of Parasitic Diseases and Malaria, Centers for Disease Control and Prevention, Atlanta, Georgia; Department of Pediatrics, Pathology and Neurosurgery, Maricopa Medical Center, District Medical Group, University of Arizona, Phoenix, Arizona

Abstract. A 22-month-old girl presented with neck pain and stiffness and magnetic resonance imaging showed an extradural mass extending from C2 through the C4 level with moderate to severe compression of the cord. A left unilateral C2–C4 laminectomy was performed revealing an extradural rubbery tumor; a small biopsy was obtained. Examination of stained tissue revealed the presence of a parasitic worm that was identified as a gravid female *Onchocerca lupi*. A magnetic resonance imaging at 7 weeks follow-up showed a significantly decreased size of the enhancing lesion and the patient's symptoms gradually resolved. This is the first report of zoonotic *O. lupi* in the United States. The parasite has been reported in dogs and cats in the western United States, and from people in four cases reported from Europe. A great deal more needs to be learned, including full host range and geographic distribution, before we fully understand *O. lupi* infections in animals and man.

Onchocerca lupi

Originally described in a wolf in the Caucasus region of the Republic of Georgia, common in dogs in Europe

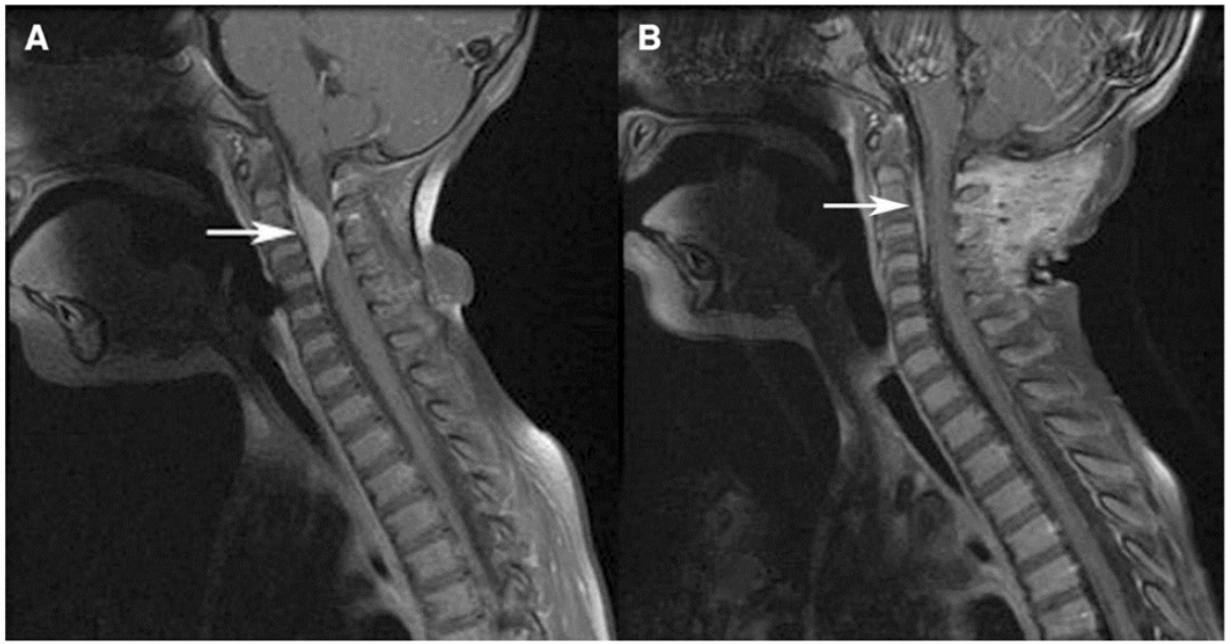


FIGURE 1. T1 post-contrast magnetic resonance (MR) images of the neck with fat saturation of patient with zoonotic *Onchocerca* infection. (**A**) Image pre-biopsy showing a soft tissue mass (arrow) in the cervical central canal extending from C2 through the C4 level. (**B**) Image 7 weeks post biopsy showing significant reduction in the soft tissue mass (arrow) in the cervical central canal extending from C2 through the C4 level.

Am. J. Trop. Med. Hyg., 88(3), 2013, pp. 601–605

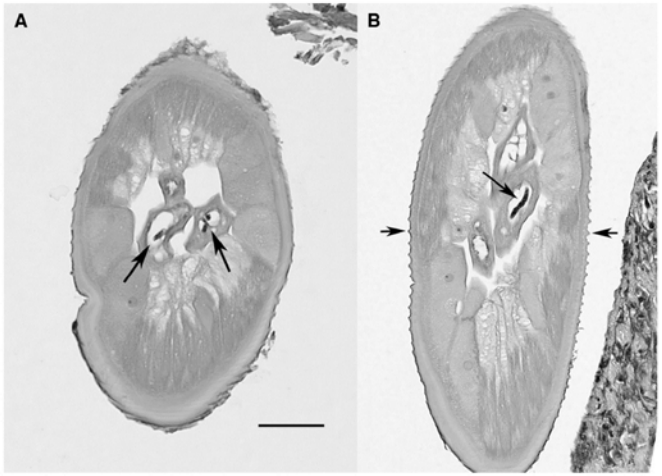


FIGURE 2. Tissue sections of female *Onchocerca lupi*, hematoxylin and eosin stain. (**A**) Cross-section illustrating the morphology of the worm, including the detail of the muscle cells and large lateral chords, and the presence of microfilariae *in utero* (arrows). Scale bar = 50 μm. (**B**) Tangential section in which the same morphologic features are evident, including the presence of a microfilaria *in utero* (large arrow), and illustrating the distinctive cuticular ridges (small arrows). Scale bar same as in (**A**).

Am. J. Trop. Med. Hyg., 88(3), 2013, pp. 601–605

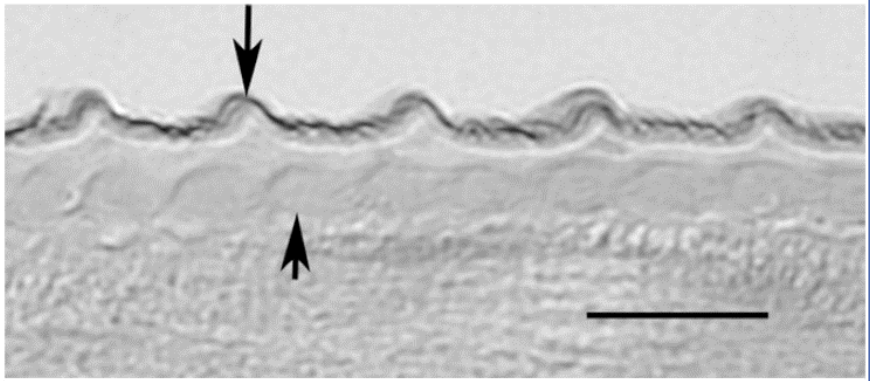


FIGURE 3. Longitudinal section of female *Onchocerca lupi* at higher magnification illustrating the multilayered cuticle with external circular ridges (long arrow) and inner striae (short arrow). Scale bar = 10 μm.

Am. J. Trop. Med. Hyg., 88(3), 2013, pp. 601–605

Follow up on this child

- Postoperative day 18 lumbar puncture negative for microfilariae
- Ophthalmic examination negative
- Patient started on ivermectin + doxycycline
- Did well

Filaria IgG4 Antibody 0.29

REFERENCE RANGE: <1.50

INTERPRETIVE CRITERIA:

<1.50 NEGATIVE
1.50-3.00 EQUIVOCAL
>3.00 POSITIVE

"This assay detects Filaria IgG4 associated with infections caused by the major filarial parasites, including Dirofilaria immitis, Wuchereria brancrofti, Brugia malayi, and Onchocerca volvulus. Detection of IgG4 subclass antibody offers enhanced specificity without sacrifice of sensitivity. Chronic filarial infections manifesting as elephantiasis may not show a significant IgG4 response, and cannot be ruled out by this assay. Equivocal results may represent cross-reactive antibodies induced by infection with other nematodes."

CDC agreed with Onchocerca lupi…

Clinical Infectious Diseases

INVITED ARTICLE

EMERGING INFECTIONS: James M. Hughes and Mary E. Wilson, Section Editors

The Emergence of Zoonotic *Onchocerca lupi* Infection in the United States – A Case-Series

Paul T. Cantey,[1] Jessica Weeks,[2] Morven Edwards,[3] Suchitra Rao,[4] G. Amin Ostovar,[5] Walter Dehority,[6] Maria Alzona,[7] Sara Swoboda,[2] Brooke Christiaens,[8] Wassim Ballan,[8] John Hartley,[8] Andrew Terranella,[2] Jill Weatherhead,[3] James J. Dunn,[3] Douglas P. Marx,[3] M. John Hicks,[3] Ronald A. Rauch,[3] Christiana Smith,[4] Megan K. Dishop,[9] Michael H. Handler,[4] Roy W. R. Dudley,[10] Kote Chundu,[5] Dan Hobohm,[5] Iman Feiz-Erfan,[5] Joseph Hakes,[11] Ryan S. Berry,[6] Shelly Stepensaski,[12] Benjamin Greenfield,[6] Laura Shroeder,[13] Henry Bishop,[1] Marcos de Almeida,[1] Blaine Mathison,[1] and Mark Eberhard[1]

[1]Division of Parasitic Diseases and Malaria, Centers for Disease Control and Prevention, Atlanta, Georgia; [2]Indian Health Service – Navajo Area, Window Rock, Arizona; [3]Baylor College of Medicine, Houston, Texas; [4]Children's Hospital Colorado, University of Colorado School of Medicine, Aurora; [5]Maricopa Medical Center, District Medical Group, University of Arizona, Phoenix; [6]University of New Mexico Health Sciences Center, Albuquerque; [7]Clin-Path Associates, Tempe, and [8]Phoenix Children's Hospital, Arizona; [9]Children's Hospitals and Clinics of Minnesota, Minneapolis; [10]Montreal Children's Hospital, McGill University, Montreal, Canada; [11]San Juan Regional Medical Group, Farmington, New Mexico; [12]Division of Dermatopathology, Pathology Associates of Albuquerque, New Mexico; and [13]North Phoenix Infectious Diseases, Arizona

This case-series describes the 6 human infections with *Onchocerca lupi*, a parasite known to infect cats and dogs, that have been identified in the United States since 2013. Unlike cases reported outside the country, the American patients have not had subconjunctival nodules but have manifested more invasive disease (eg, spinal, orbital, and subdermal nodules). Diagnosis remains challenging in the absence of a serologic test. Treatment should be guided by what is done for *Onchocerca volvulus* as there are no data for *O. lupi*. Available evidence suggests that there may be transmission in southwestern United States, but the risk of transmission to humans is not known. Research is needed to better define the burden of disease in the United States and develop appropriately-targeted prevention strategies.

Keywords. *Onchocerca lupi*; emerging infectious diseases; zoonotic infection.

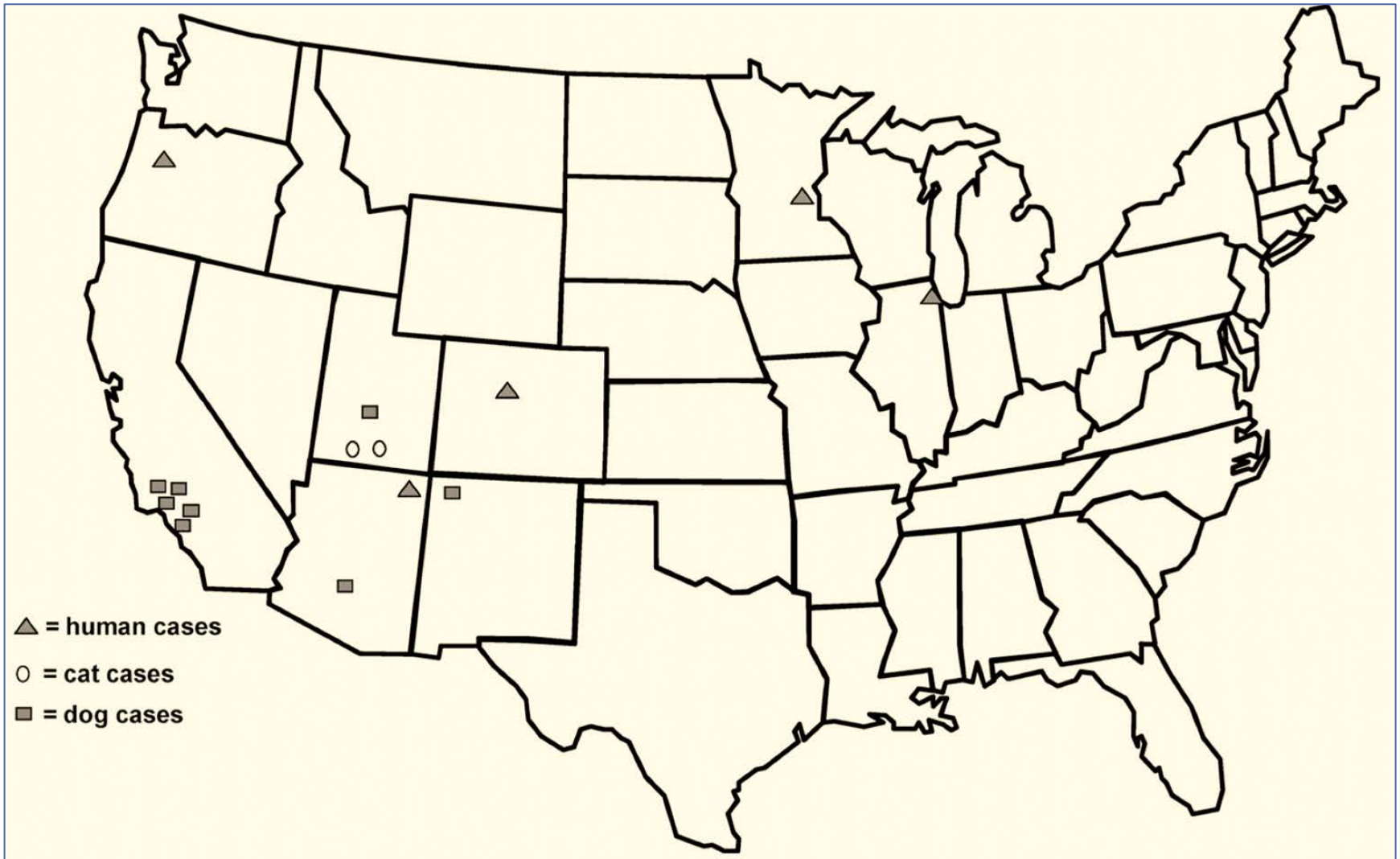


FIGURE 4. Map of the United States illustrating the approximate location where the 15 unusual cases of onchocerciasis have been reported in humans, dogs, and cats.

Am. J. Trop. Med. Hyg., 88(3), 2013, pp. 601–605

TABLE 1

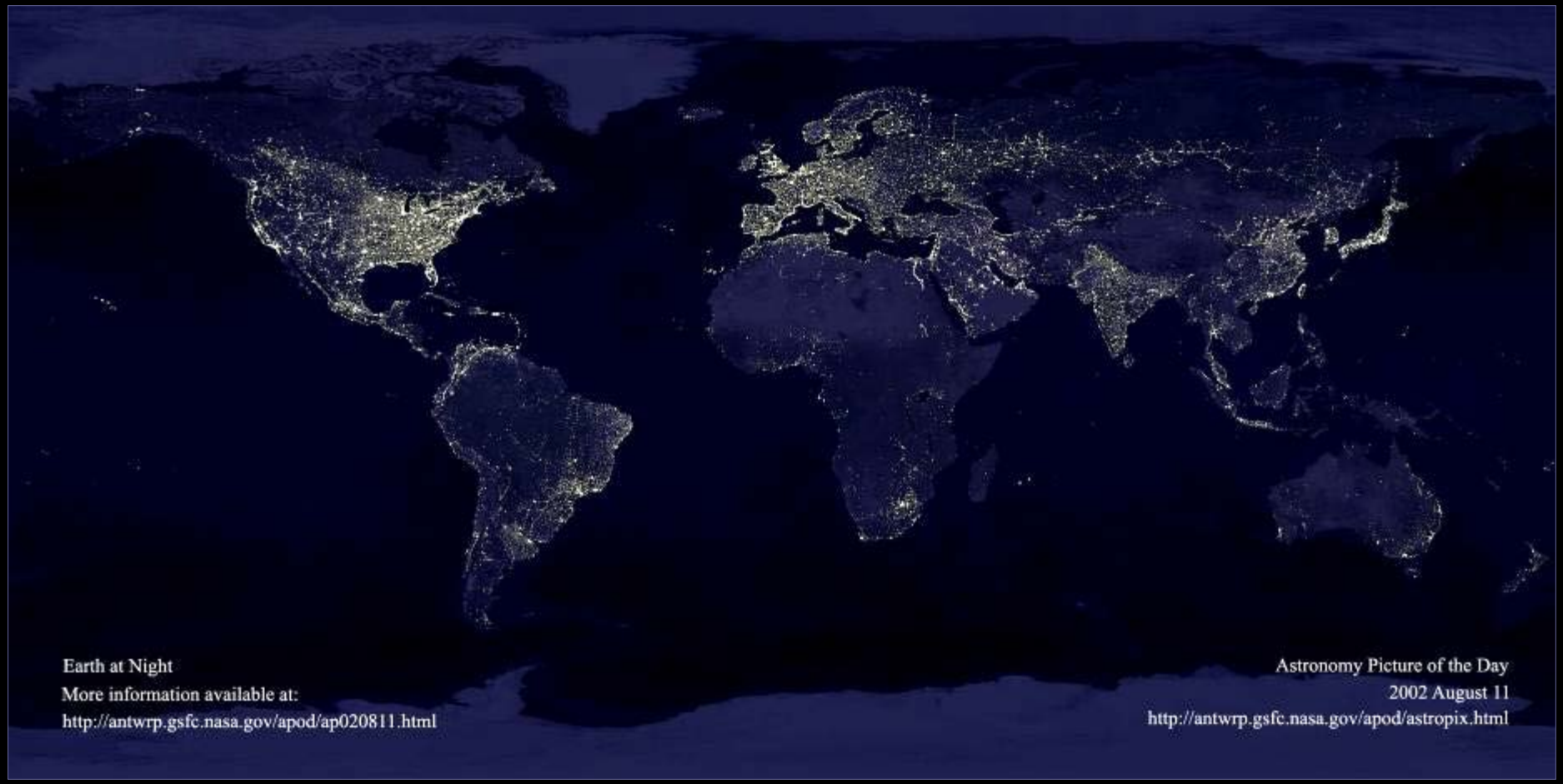
Summary of zoonotic onchocerciasis cases

Case	Patient		Lesion	Parasite		Reference
	Age/sex	location		Sex	species	
1	15 F	USSR	Eye muscle tendon	F	*O. gutturosa/cervicalis*	2
2	25 M	Switzerland	Knee	F	*O. gutturosa/cervicalis*	3
3	48 F	Illinois, USA	Wrist	F	*O. gutturosa/cervicalis*	4
4	43 F	Ontario, Canada	Wrist	F	*O. gutturosa/cervicalis*	5
5	2 F	Japan	Sole of foot	F	*O. dewittei japonica**	6
6	57 F	Japan	Wrist	F	*O. dewittei japonica**	7
7	52 F	Colorado, USA	Ant. Chamber	F	*O. gutturosa/cervicalis*	8
8	52 F	Japan	Head	M	*O. dewittei japonica*	9
9	16 M	Albania	Subconjunctiva	F	*O. lupi*	10
10	50 F	Minnesota, USA	Shoulder	F	*O. gutturosa*	11
11	58 F	Japan	Hand	F	*O. dewittei japonica*	12
12	69 F	Japan	Neck	F	*O. dewittei japonica*	13
13	65 M	Hungary	Ant. Chamber	F	*O.* sp. (larva)	14
14	59 F	Austria	Head	F	*O. jakutensis*	15
15	12 F	Kuwait	Abdomen	F	*O.* sp.	16
16	70 M	Japan	Knee	F	*O. dewittei japonica*	17
17	18 F	Turkey	Subconjunctiva	F	*O. lupi*	18
18	26 M	Turkey	Subconjunctiva	F	*O. lupi*	19
19	8	Tunisia	Subconjunctiva	F	*O. lupi*	20
20	56 M	Oregon, USA	Ant. Chamber	F	*O.* sp. (larva)	21
21	2 F	Arizona, USA	Neck	F	*O. lupi*	Present case

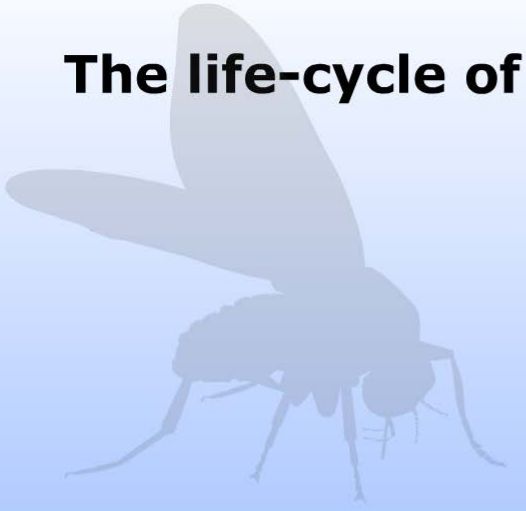
*Subsequent study of these cases has resulted in modification of the original species diagnosis.
F = female; M = male. For case 18, the sex was not given.

Am. J. Trop. Med. Hyg., 88(3), 2013, pp. 601–605

EMERGENCE OF ZOONOTIC *ONCHOCERCA LUPI* INFECTION IN THE UNITED STATES


Earth at Night
More information available at:
http://antwrp.gsfc.nasa.gov/apod/ap020811.html
Astronomy Picture of the Day
2002 August 11
http://antwrp.gsfc.nasa.gov/apod/astropix.html

The life-cycle of onchocerciasis in humans



http://www.who.int/tdr/publications/documents/onchocerciasis-life-cycle.swf