

Welcome to *Parasitic Diseases*

Fall 2006

Parasite

Any organism that takes metabolic advantage
of another organism

Viruses

Rickettsiae

bacteria

Fungi

Protozoa*

Helminths*

Nematodes - round worms

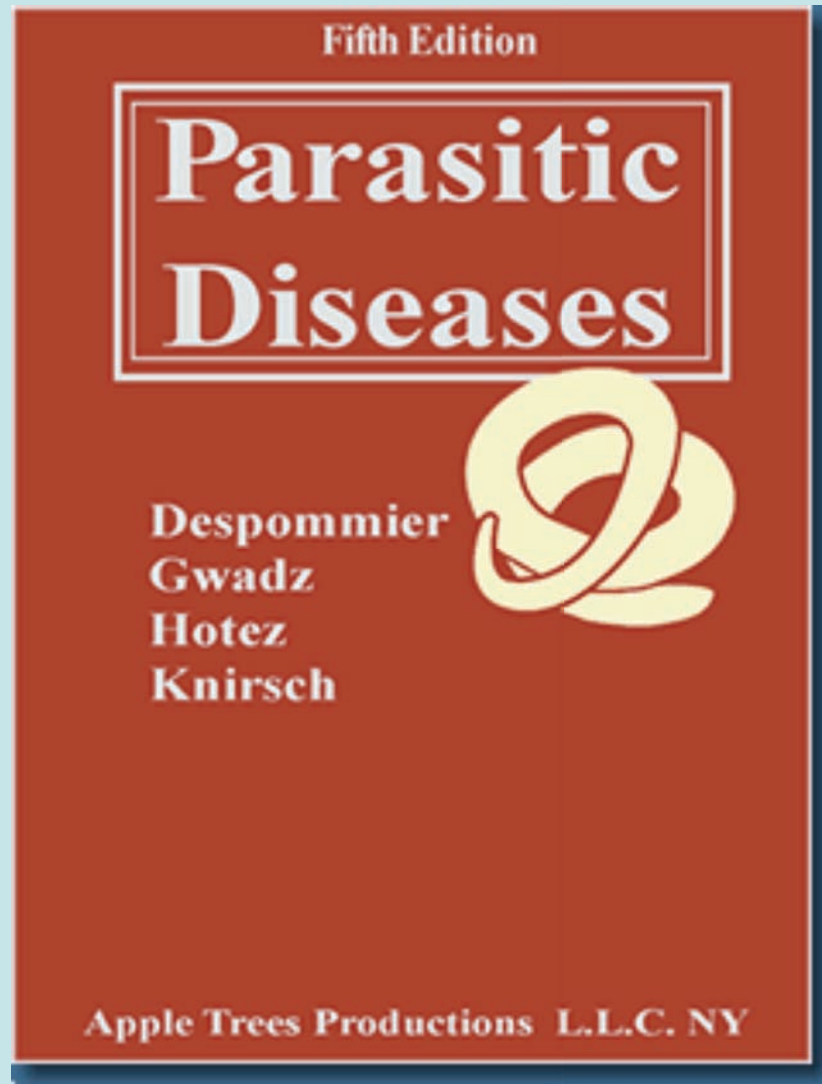
Cestodes - segmented flat worms

Trematodes - non-segmented flat worms

Arthropods* - six and eight-legged critters

* Covered in *Parasitic Diseases*

Required textbook:
Available at bookstore.
\$69.95



New England Journal Review of Parasitic Diseases 5th ed.

THE NEW ENGLAND JOURNAL OF MEDICINE

BOOK REVIEWS

PARASITIC DISEASES

Fifth edition. By Dickson D. Despommier, Robert W. Gwadz, Peter J. Hotez, and Charles A. Knirsch. 363 pp., illustrated. New York, Apple Trees Productions, 2005. \$69.95. ISBN 0-970027-7-7.

AS A MEDICAL EDUCATOR, I HAVE ALWAYS felt privileged to teach parasitology because it is fascinating — albeit the study of worms may be both fascinating and disgusting, the study of insects may be both fascinating and frightening, and the study of protozoa may be both fascinating and amazing. Teaching parasitology is fun, and when it is taught by a quintessential master such as Dickson D. Despommier — the Obi-Wan Kenobi of parasitology, as I have witnessed him to be in a classroom setting — it is pure magic for the students.

This book, written by Despommier and three of his colleagues, is concise, accurate, logical, and oriented toward the student — not the master. It begins with a short introduction to the world of eukaryotic parasites, followed by chapters on protozoa, worms, and insects, including vectors and organisms that do harm all by themselves. Next, a nicely philosophical chapter on the ecology of parasitic diseases makes it clear that we have evolved with these creatures and cannot simply eradicate them. This discussion is wholly consistent with a soon-to-be published report from an Institute of Medicine Forum on Microbial Threats meeting entitled “Ending the War Metaphor: The Future Agenda for Unraveling the Host-Microbe Relationship.”

The book's penultimate chapter, on travel medicine, offers just enough information to whet the appetite, but not enough to teach expertise; this raises the fear that students will practice without sufficient know-how when they travel to the tropics, where the risks are greater than their knowledge. This possibility is true of all areas of medicine, however, and it is experience based on knowledge that makes the clinician. The final chapter is a brief bonus on the pharmacology of antiparasitic drugs, including many new drugs that are still not available in the United States.

The appendixes are a nice touch. They include practical advice on diagnostic methods and the handling of infected specimens, a photographic atlas of parasites, and the August 2004 issue of *The Medical Letter*, which focuses on drugs for parasitic infections.

One of the things I have liked best about listening to Despommier's lessons about worms is the logical sequence in which he teaches life cycles. He adds the complexities one by one as the twists in the basic scheme are revealed, learned, and then easily recalled, along with all of the diagnostic and preventive implications for prevention. In this book, Despommier's hand is evident in the chapters on nematodes, although the chapter on hookworms must have been written by Peter J. Hotez, who knows everything about these blood-sucking worms and may one day soon introduce an effective and protective vaccine to prevent them — a first for a worm. Most of the chapters are concise, yet they include new molecular and cellular biologic insights into how these complex organisms work. There are a few editing blemishes, however; these include the use of the word “colony” for “colon” in the drawing of a pinworm's life cycle, and the reference to hepato-biliary ascariasis as HBA, which virtually nobody reading this book needs to know.

The chapters on insects include some striking and scary photographs, although the reader does not get a sense of the size of the animals themselves or of the lesions they cause. As in the rest of the book, these chapters contain brief and useful sections on pathogenesis, clinical disease, diagnosis, and treatment, including how to remove ticks and how to manage the bites of stinging insects.

I liked the chapters on protozoa the least, not because they lack up-to-date information, but because the presentation is too precise and fails to convey the wonder of these organisms in their dramatic and complex life cycles. These chapters also do not capture the near-certainty one should feel that it is quite impossible for many of these organisms to exist but for coevolution. Presumably because of cost containment, the colors of the

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THE NEW ENGLAND JOURNAL OF MEDICINE

PHAGES: THEIR ROLE IN BACTERIAL PATHOGENESIS AND BIOTECHNOLOGY

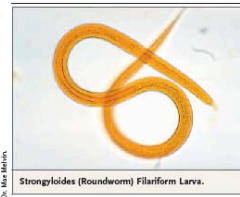
Edited by Matthew K. Waldor, David I. Friedman, and Sankar L. Adhya. 450 pp., illustrated. Washington, D.C., ASM Press, 2005. \$119.95. ISBN 1-55581-307-0.

“SIR, I AM ENTIRELY LYSED!” SHOUTED A technician in André Lwoff's laboratory at the Institut Pasteur in 1949, describing cells undergoing lysogenic induction. Phages (short for bacteriophages) are DNA or RNA viruses that infect only specific bacteria. Phages have colorful names, such as λ , T4, SopB Φ , Mu, Q β , P1, or Φ X174; they come in many shapes and sizes (e.g., tailed or nontailed, icosahedral, filamentous, and enveloped or nonenveloped); they have many different lifestyles (e.g., lytic or temperate); and they can carry genes that increase the pathogenesis of bacteria. They are among the most intensely studied viruses and are perhaps best understood in a molecular sense. This book is essentially a treatise on phages that in 22 chapters, prepared by 52 authors from six countries, describes our current knowledge of these unique viruses and their role in bacterial pathogenesis and biotechnology.

The book is divided into three interesting sections. In the first section, the authors review the history and biology of phages, their life cycles, and aspects of phage evolution and ecology, as well as phage lysis. The second section provides the reader with valuable information about the role of selected phages in the virulence of bacterial infections, such as the lambdaoid phages of salmonella and *Escherichia coli*, the tailed mycobacteriophages, phages of streptococci and staphylococci, the bacteriophages of vibrio and molluscs (myxoplasmids), and some of the more than 400 phages that have been isolated from listeria species.

In this section, the authors give the reader a clear understanding of how phages integrate their genetic material into the host genome and alter the virulence of bacteria. For example, the virulence of *Vibrio cholerae* is largely dependent on infection by the bacteriophage CTX Φ , in that the cholera toxin is encoded within the genome of this temperate and nonlytic filamentous phage and only strains of vibrio infected by CTX Φ are capable of causing epidemic disease. Another fascinating example includes the many toxins of staphylo-

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Dr. Max M. Martin



Strongyloides (Roundworm) Filariform Larva.

photographs are dull and do not look like the views under the microscope, although the images in appendix C are somewhat better.

I have some other minor complaints. For example, in the foreword, the term “DALY” is defined incorrectly as a “disease-associated lost year,” rather than as a “disability-adjusted life-year,” the correct definition that is used elsewhere in the text. The DALY, which adds the years of productive life lost because of premature death from a disease or condition to the years lived with a disability because of a disease or condition, has become an important measure of the burden of disease, so it is important to get it right, even in a foreword. Fortunately, few students will bother to read the foreword, although they should certainly read the pioneering work of its author, James Jensen, who with William Trager cultivated *Plasmodium falciparum* malaria in vitro — a true landmark in the history of modern malariaology.

I apologize for (excuse the expression) nitpicking, but I expected perfection from these authors, and they have simply proved to be human. Still, the book remains a gem for the current information it does include, in a field in which all too often the past is venerated and modern approaches are denigrated. Students should use it for these reasons, and they should keep it for their libraries, since they will want to refer to it in the future when they need to review the basics of parasitology.

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Helminths (Worms)

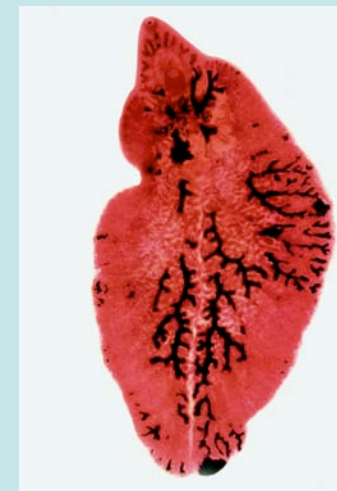
Nematodes - non-segmented
round worms



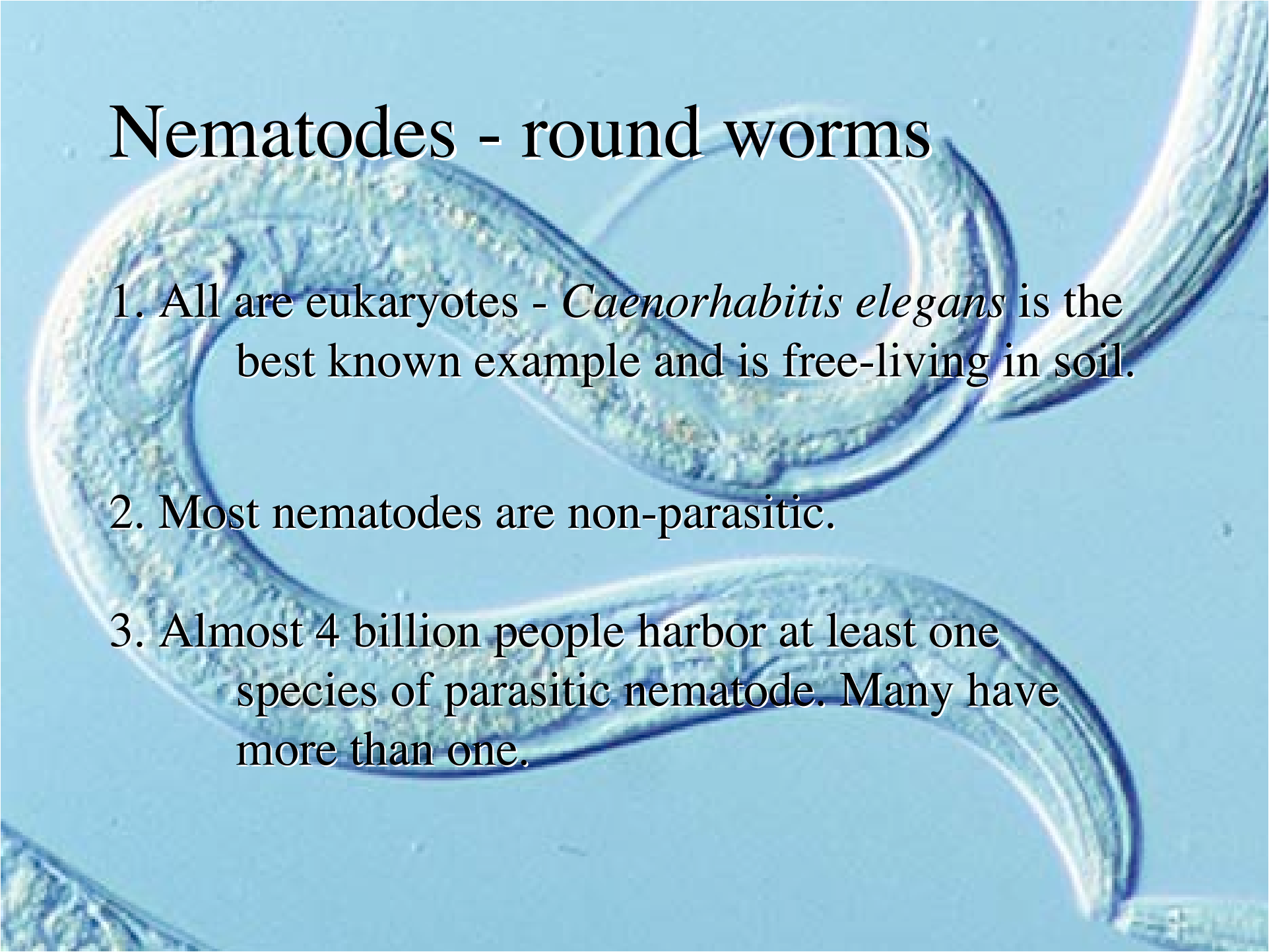
Cestodes - segmented flat worms



Trematodes - non-segmented
flat worms



Nematodes - round worms

The background of the slide is a microscopic image of several nematodes. The worms are translucent, showing internal structures like the gut and muscle layers. They are curved and overlapping, with some showing a distinct head region. The overall color palette is a light blue.

1. All are eukaryotes - *Caenorhabditis elegans* is the best known example and is free-living in soil.
2. Most nematodes are non-parasitic.
3. Almost 4 billion people harbor at least one species of parasitic nematode. Many have more than one.

Geohelminths

Enterobius vermicularis (Pinworm)

Trichuris trichiura (Whipworm)

Ascaris lumbricoides (Giant intestinal worm)

Toxocara canis and *T. cati* (Visceral larva migrans)

Hookworms

Ancylostoma duodenale

Necator americanus

Strongyloides stercoralis (Cochin China diarrhea)



Disability-Adjusted Life Years - DALY (WHO)

Disease / Parasite	Population at risk (millions)	No. of endemic countries	No. of infected (millions)	Estimated deaths (humans × 1000)	DALYs female	DALYs male	Total DALYs
Malaria	2 000	90	300–500	1 080	182.3	17.5	357.3
Leishmaniasis	350	82	12	41	12	8.6	20.6
Lymphatic filariasis	750	65	119	No direct mortality	5.6	2.9	7.5
Guinea worm disease	140	18	c. 0.12	No direct mortality			
Onchocerciasis	122	34	17.6	No direct mortality	3.7	2.7	6.4
African trypanosomiasis	50	36	0.02–0.30	50	9	8.8	17.8
Chagas disease	90	19	16	21	14.8	12.6	27.4
Schistosomiasis	500–600	74	200	11	29.9	15.4	45.3
<i>Ascaris</i> infection			1 000		53.8	51.4	105.2
<i>Trichuris</i> infection			900		32.2	30.9	63.1
Hookworm infection			500		5.8	5.6	11.4
<i>Entamoeba</i> infection			500	40–100			
Giardiasis			200				
Taeniasis	40		15				
Neurocystocercosis			50	50			
Food-borne trematodes			500				
Fascioliasis	180.25	8	2.39				
Clonorchiasis	289.26	6	7				
Opisthorchiasis	63.60	5	10.30				
Paragonimiasis	194.80	5	20.60				
Other intestinal flukes		6	1.28m				

Anatomic Site In The Host

Alimentary tract	197 species
Cavities, organs, and tissues	107 species
Circulatory system	21 species
Skin and tissues	56 species

Helminths that routinely infect humans

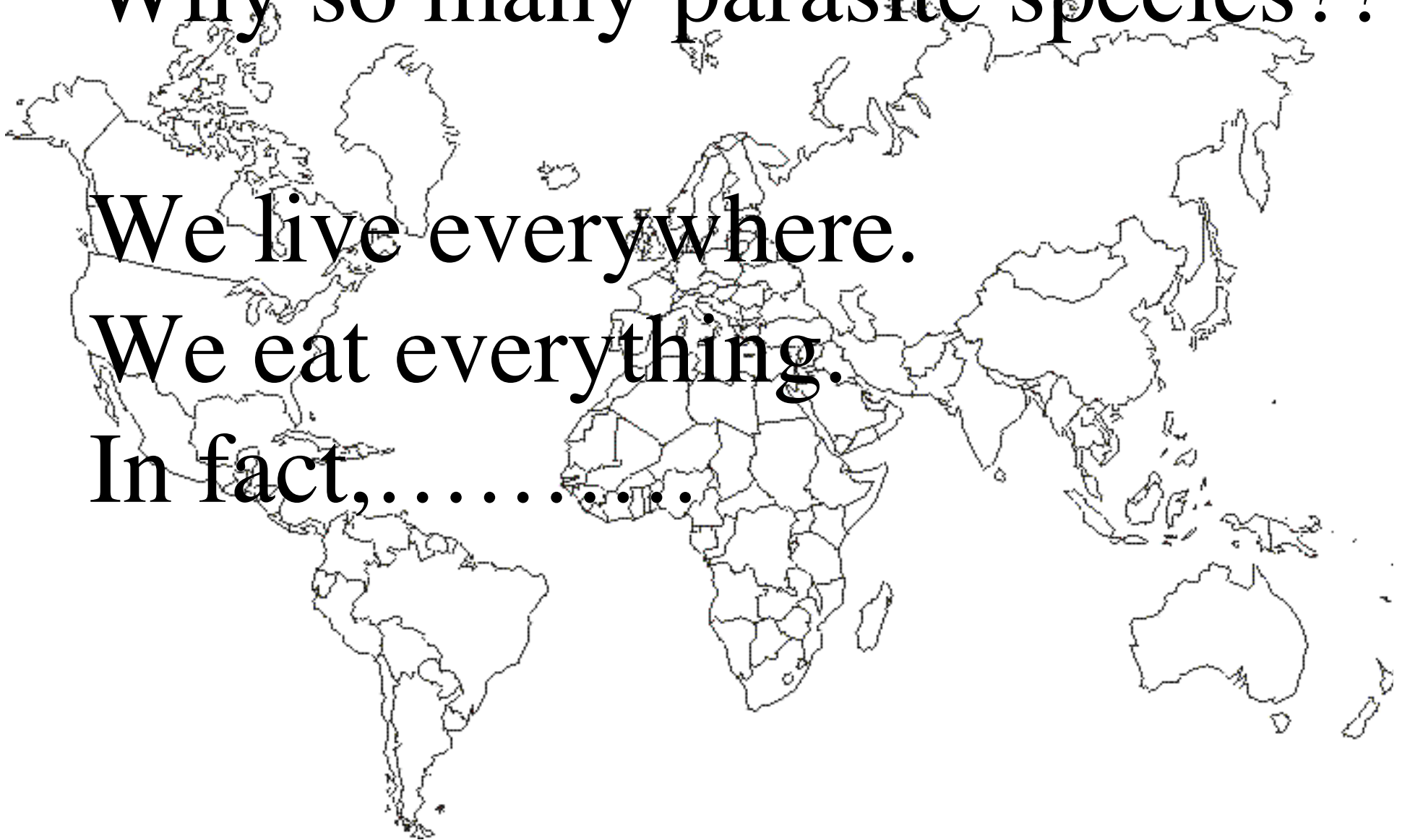
Acanthocephala	7 species
Nematoda	138 species
Nematomorpha	24 species
Platyhelminthes	173 species
Digenea	113 species
Eucestoda	57 species
Turbellaria	3 species
TOTAL	342 species

Why so many parasite species??

We live everywhere.

We eat everything.

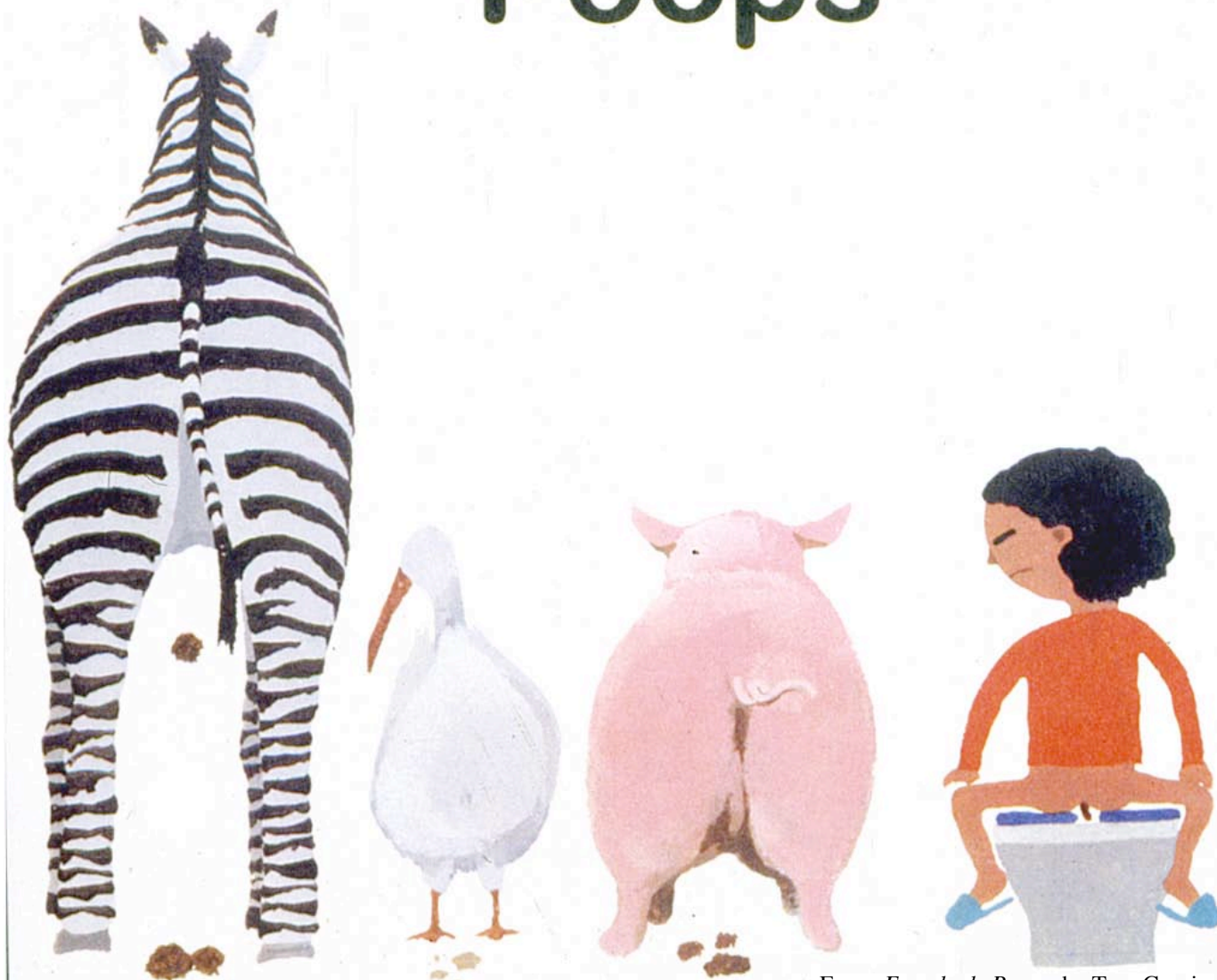
In fact,.....



All living things eat, so



Everyone Poops



From: *Everybody Poops*, by Taro Gomi.
Kane/Miller Book Publisher, New York

Night Soil



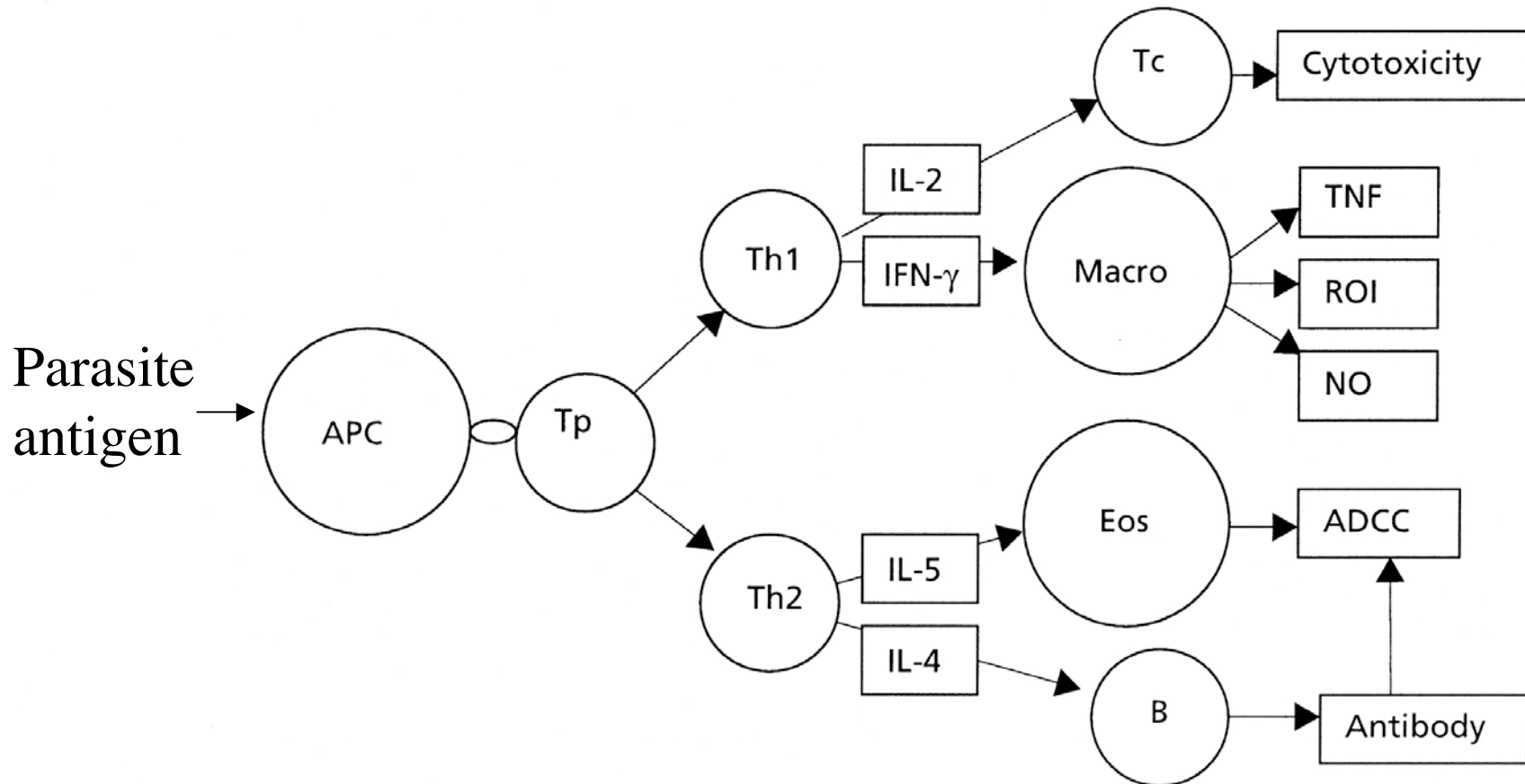
What will it be today?



Reality Check



Immunity and Parasitism



Worm infections elicit Th2 protective immune responses.
Protozoan infections elicit Th1 protective immune responses.

Cytokines and Immunity to Parasites

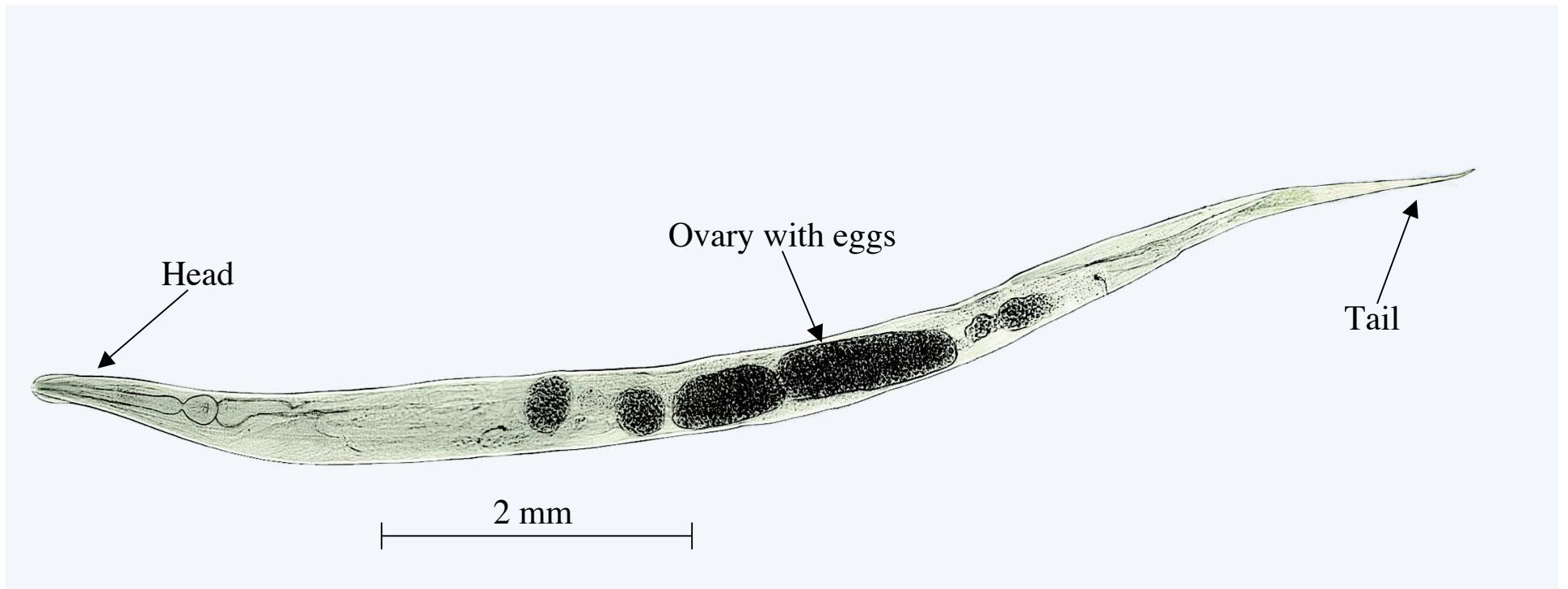
Th1 cytokines	Th2 cytokines	Pro-inflammatory cytokines	Counter-inflammatory cytokines	Cytokines that can lead to pathology (e.g. increased vascular permeability, tissue damage, circulatory collapse, multi-organ failure etc.)
IFN- γ *	IL-4*	IL-12	IL-4	IL-1
IL-2	IL-5*	IL-15	IL-10	IL-6
IL-3	IL-3	IL-18	TGF- β	IL-8
TNF- α	IL-13	IFN- γ		IL-12
TNF- β	IL-6			TNF- α
GM-CSF	IL-10			MIF
	TGF- β			

*most important in immune expulsion of protozoa and worms

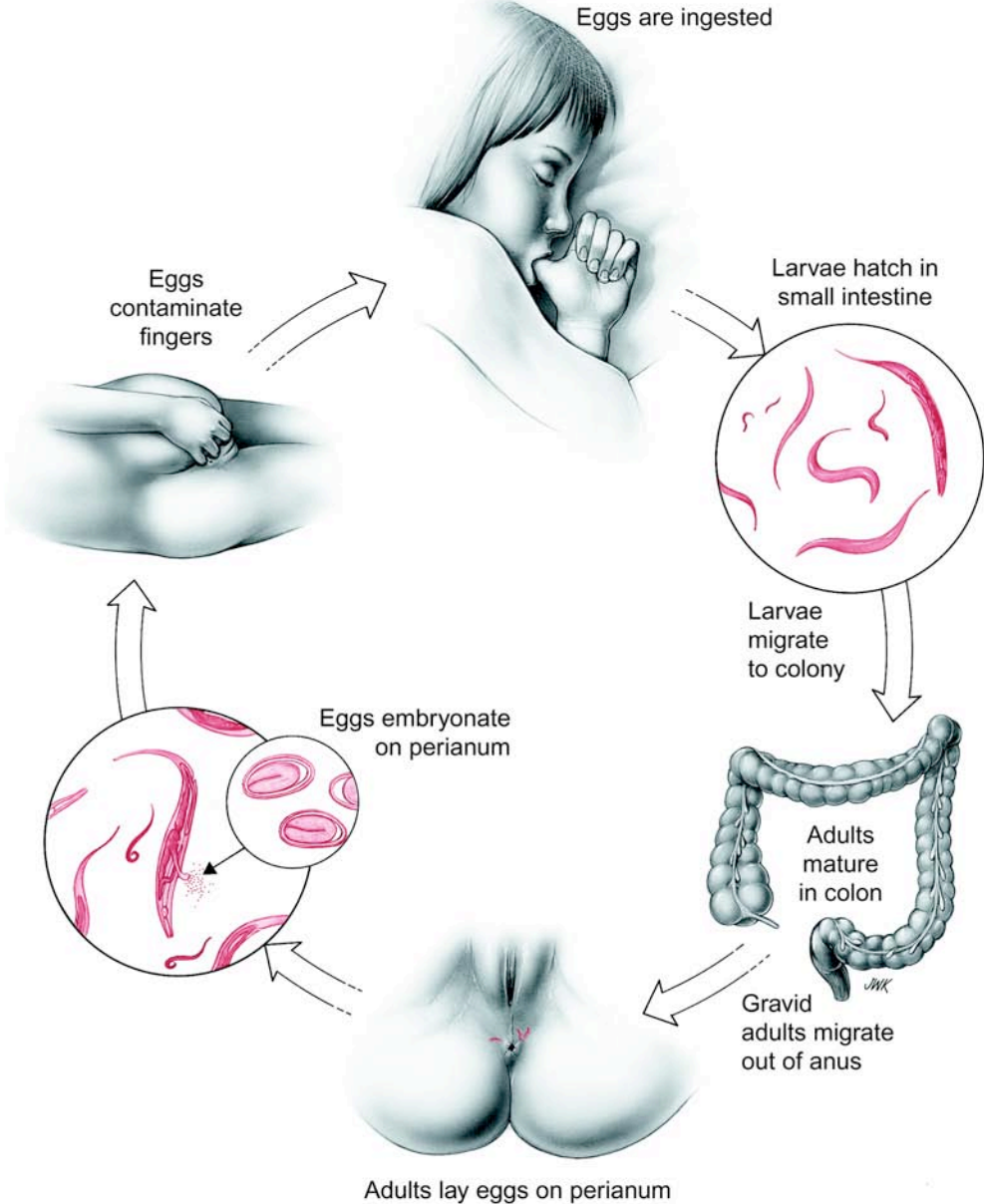
Helminths: Nematoda

Enterobius vermicularis
(Pinworm)

Adult Female *Enterobius vermicularis*



Enterobius vermicularis



Heavy Infection of *Enterobius vermicularis*



Photo: Martin Weber, MD, Children's Hospital; Hannover Medical School; Hannover, Germany

Eggs of *Enterobius vermicularis*



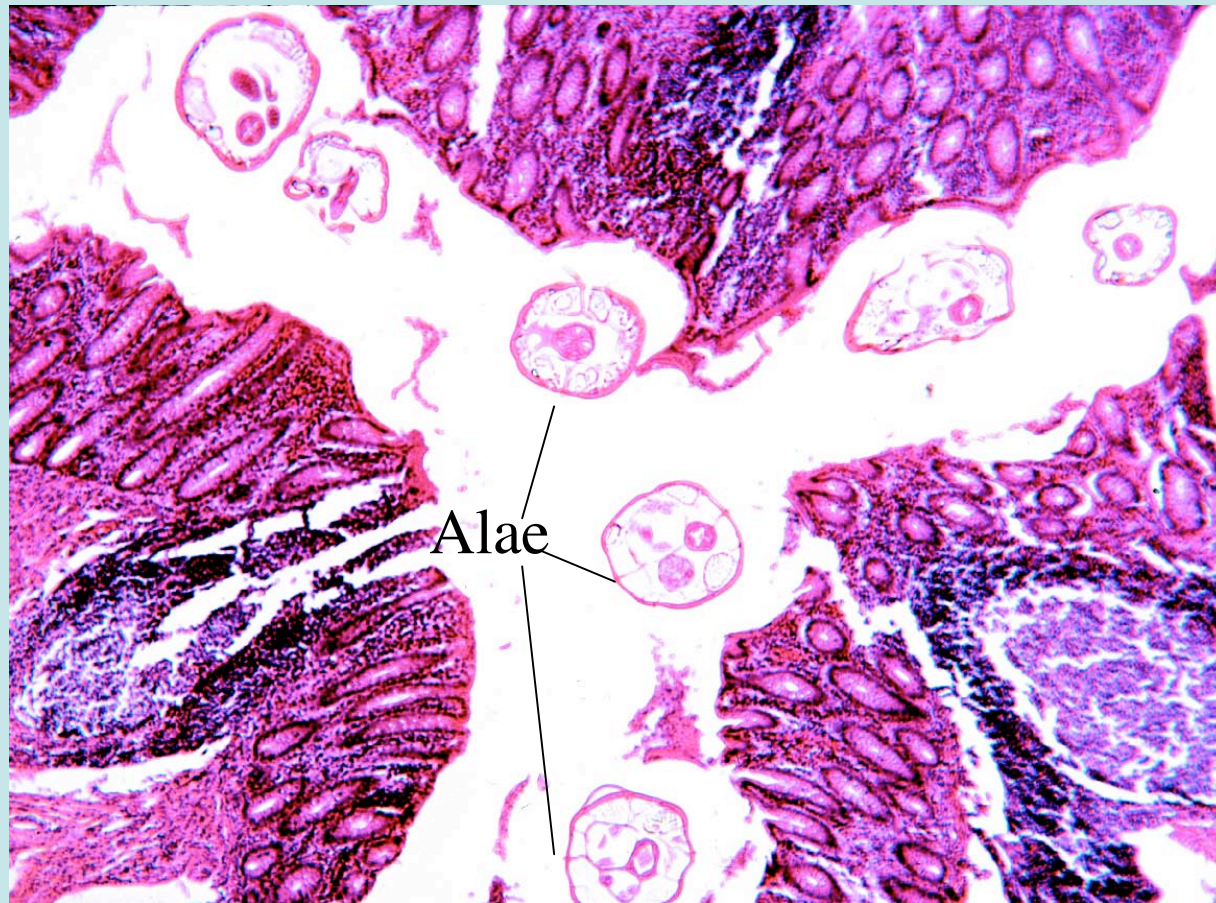
Unembryonated



Larva

Embryonated

Enterobius vermicularis in appendix



Clinical Disease:

None

Diagnosis:

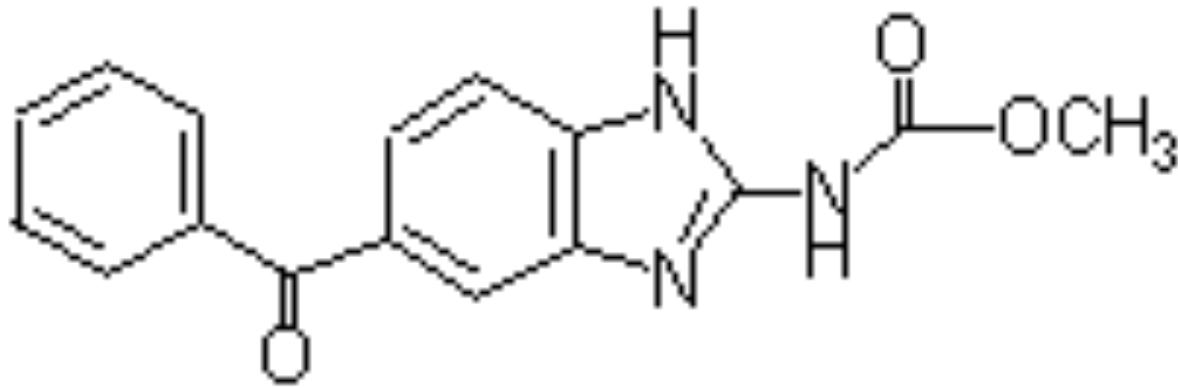
Eggs found on microscopic examination of clear sticky tape.



larva

Drug of Choice:

Mebendazole



Mode of Action:

De-polymerizes all species of invertebrate tubulins; not vertebrate tubulins.

Prevention and Control:

Prevention is difficult among children, especially those attending day care facilities and lower grades in school. We “out-grow” our pinworm infections once we reach puberty.

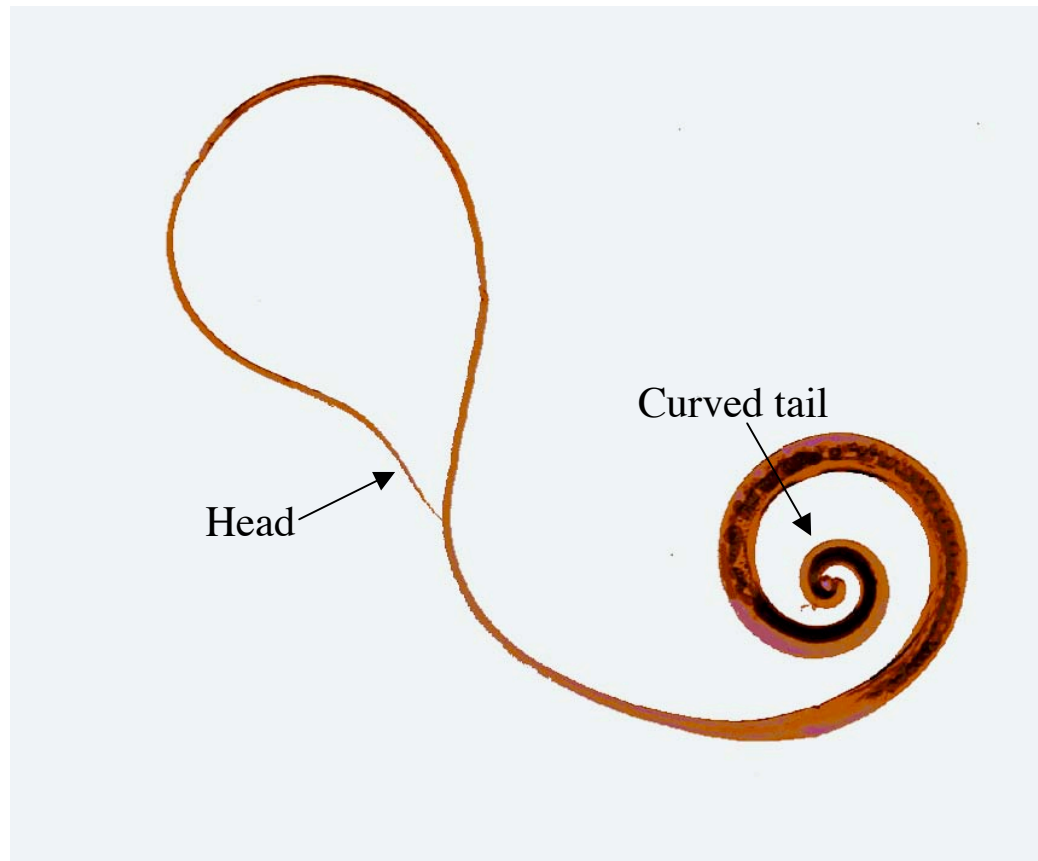
Helminths:
Nematoda

Trichuris trichiura
(Whipworm)

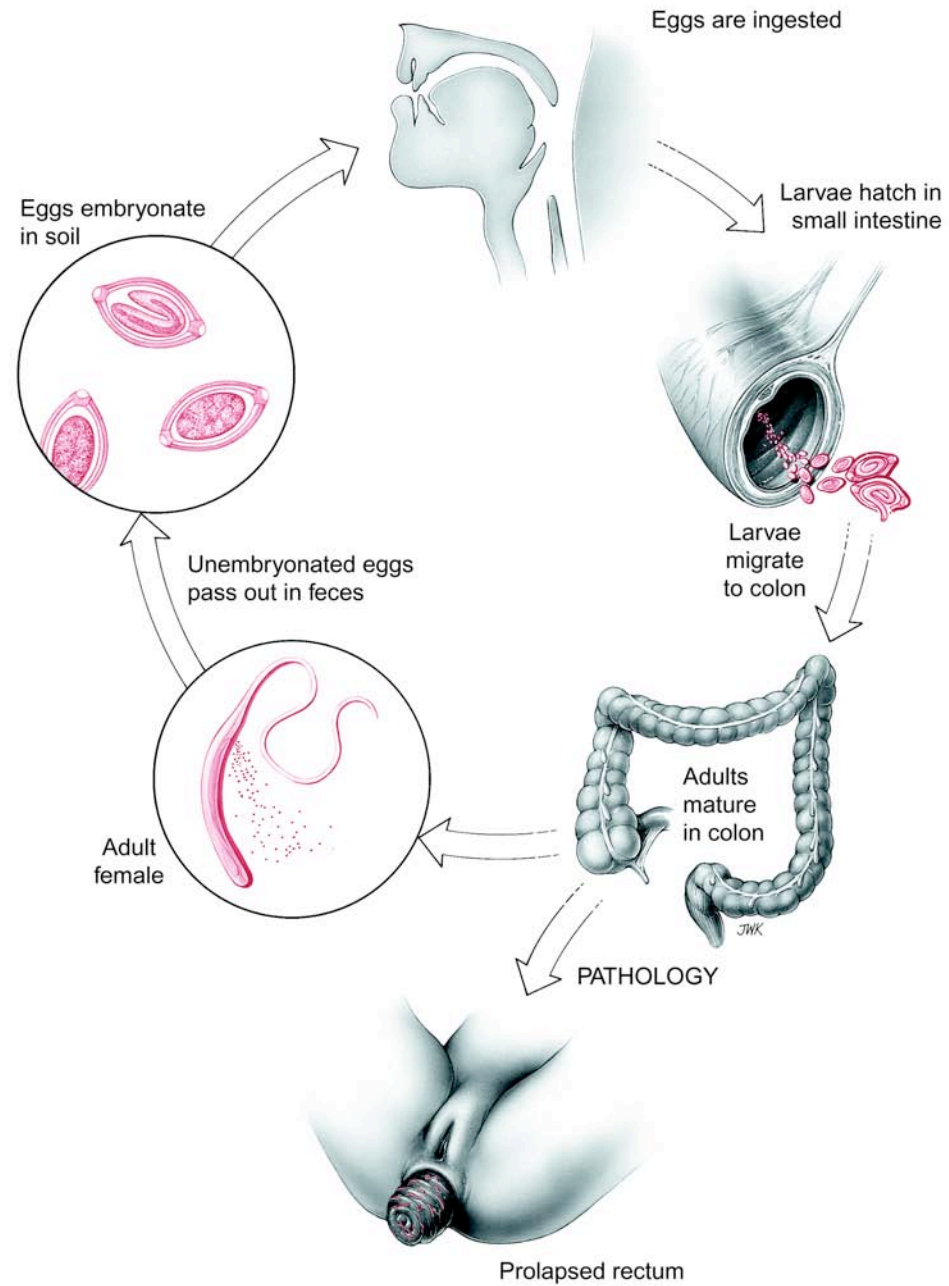
Female adult *Trichuris trichiura*



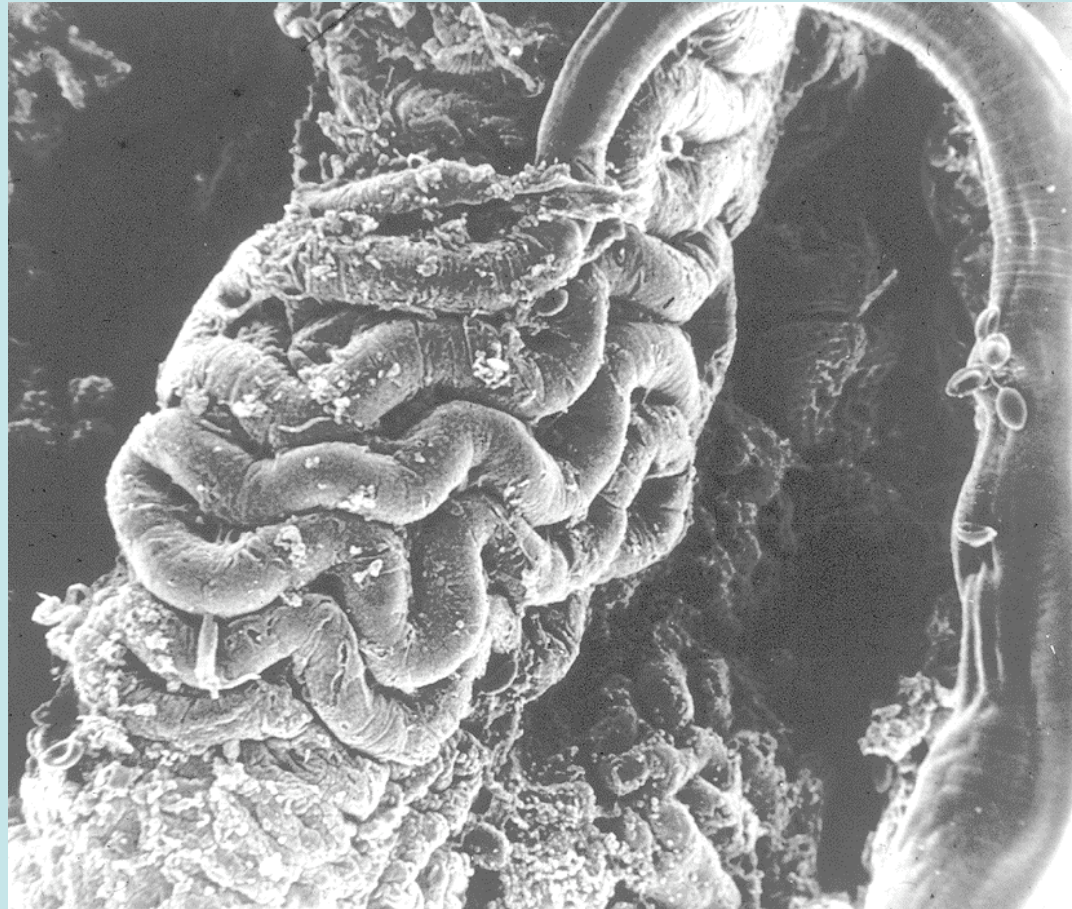
Adult male *Trichuris trichiura*



Trichuris trichiura



Adult *Trichuris muris* in situ (SEM)



Pathogenesis:

Trichuris spp. secrete a pore-forming protein that may play a role in anemia and diarrhea.

Adult worms ***do not*** feed directly on blood or other host tissues. Mechanism of anemia still unknown.

Prolapsed rectum with adult
Trichuris trichiura



Clinical Disease:

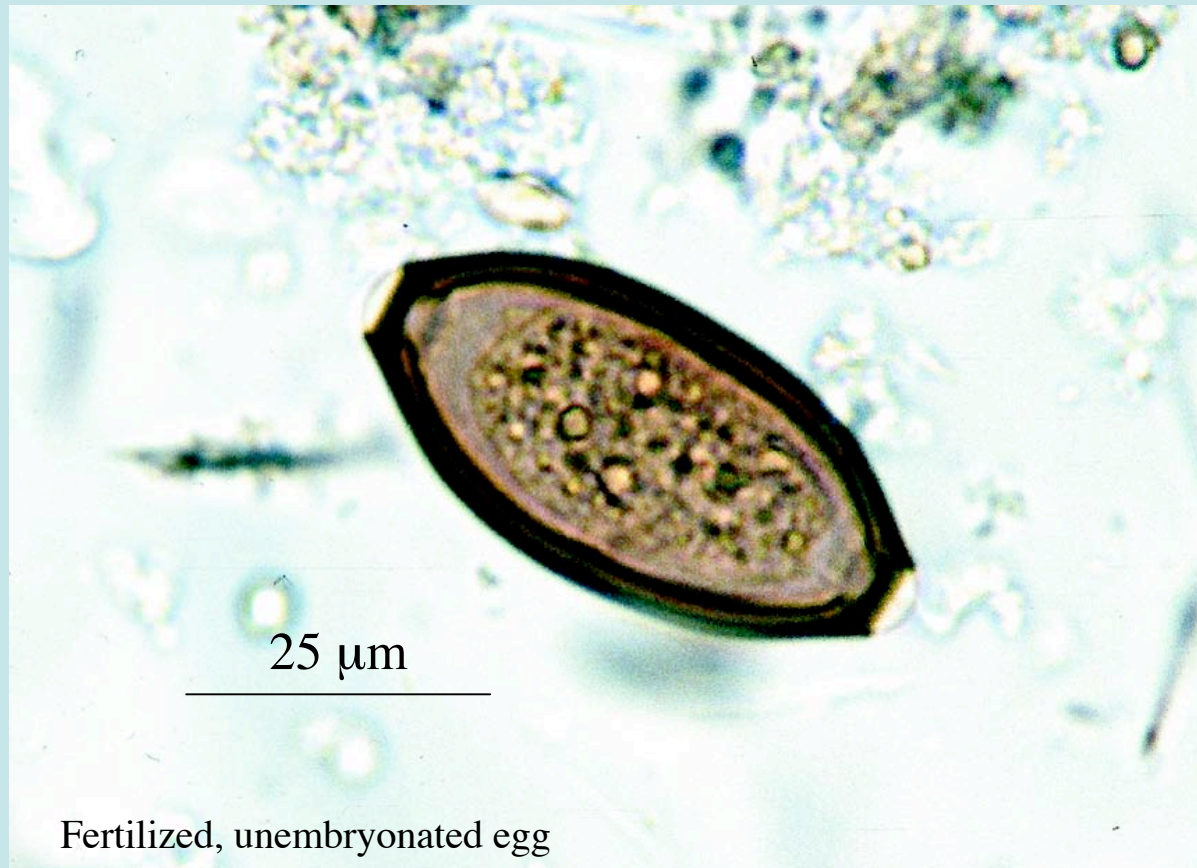
1. Diarrhea

2. Anemia

3. Malnutrition (protein calorie deficiency?)

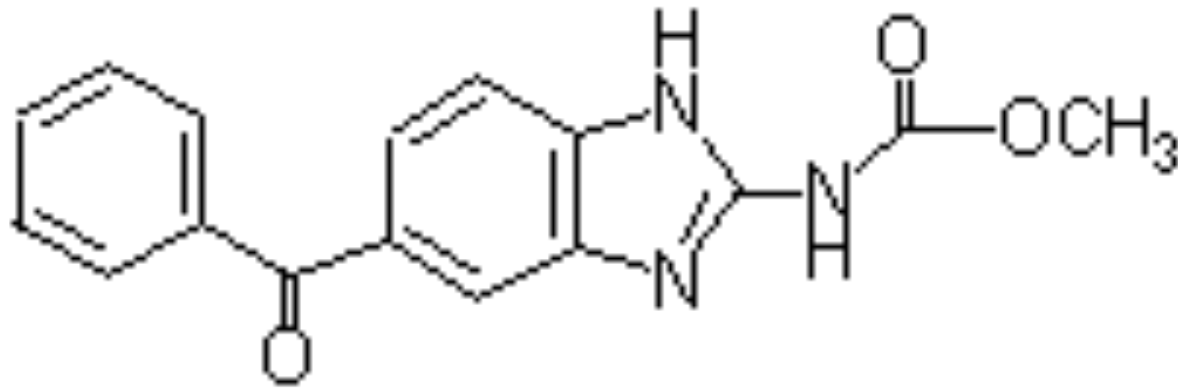
Diagnosis:

Microscopic examination of feces for eggs



Drug of choice:

Mebendazole



Mode of Action:

De-polymerizes invertebrate microtubules, only

Prevention and Control:

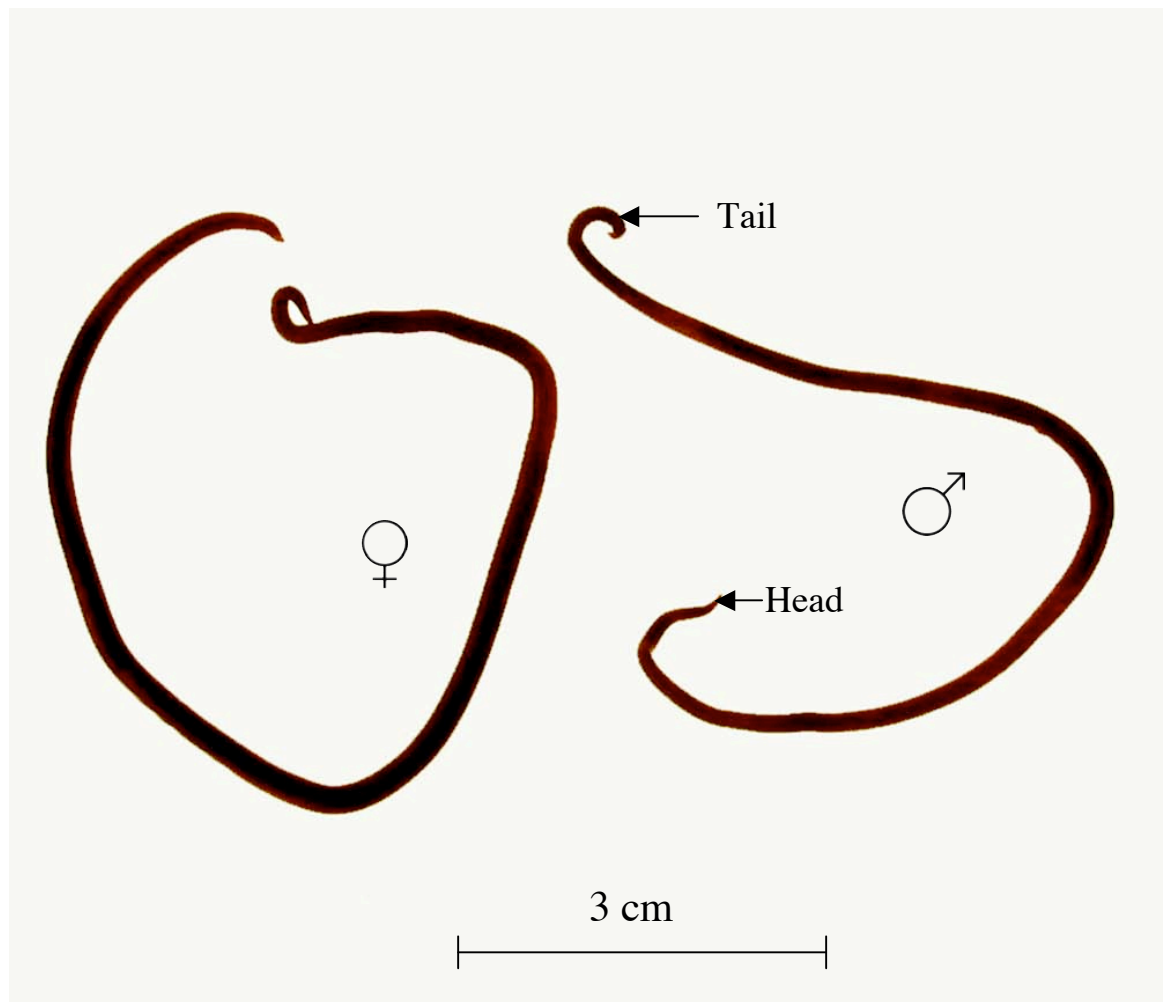
Sanitary disposal of feces



Helminths: Nematoda

Ascaris lumbricoides
(Giant intestinal worm)

Adult *Ascaris lumbricoides*

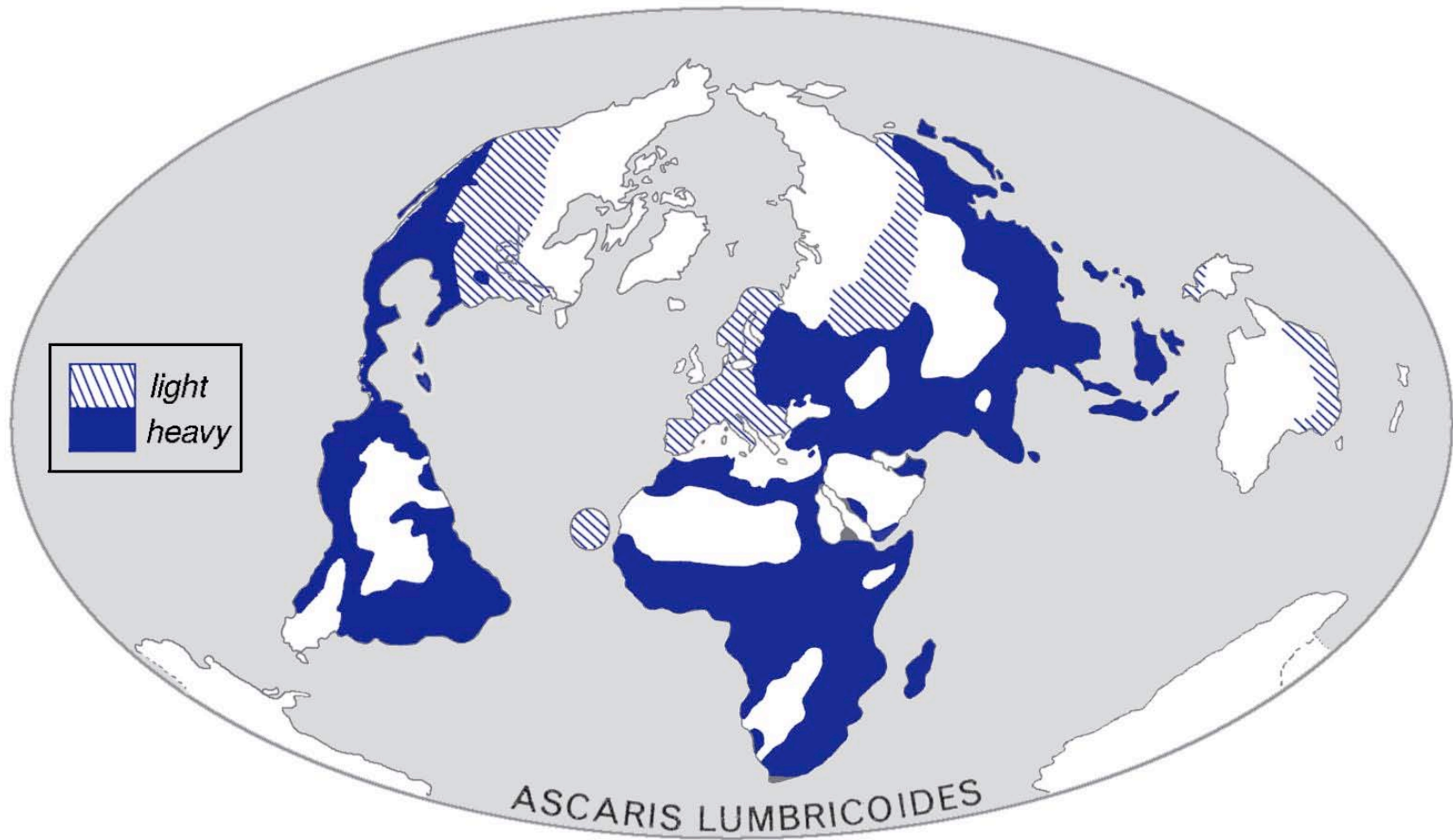




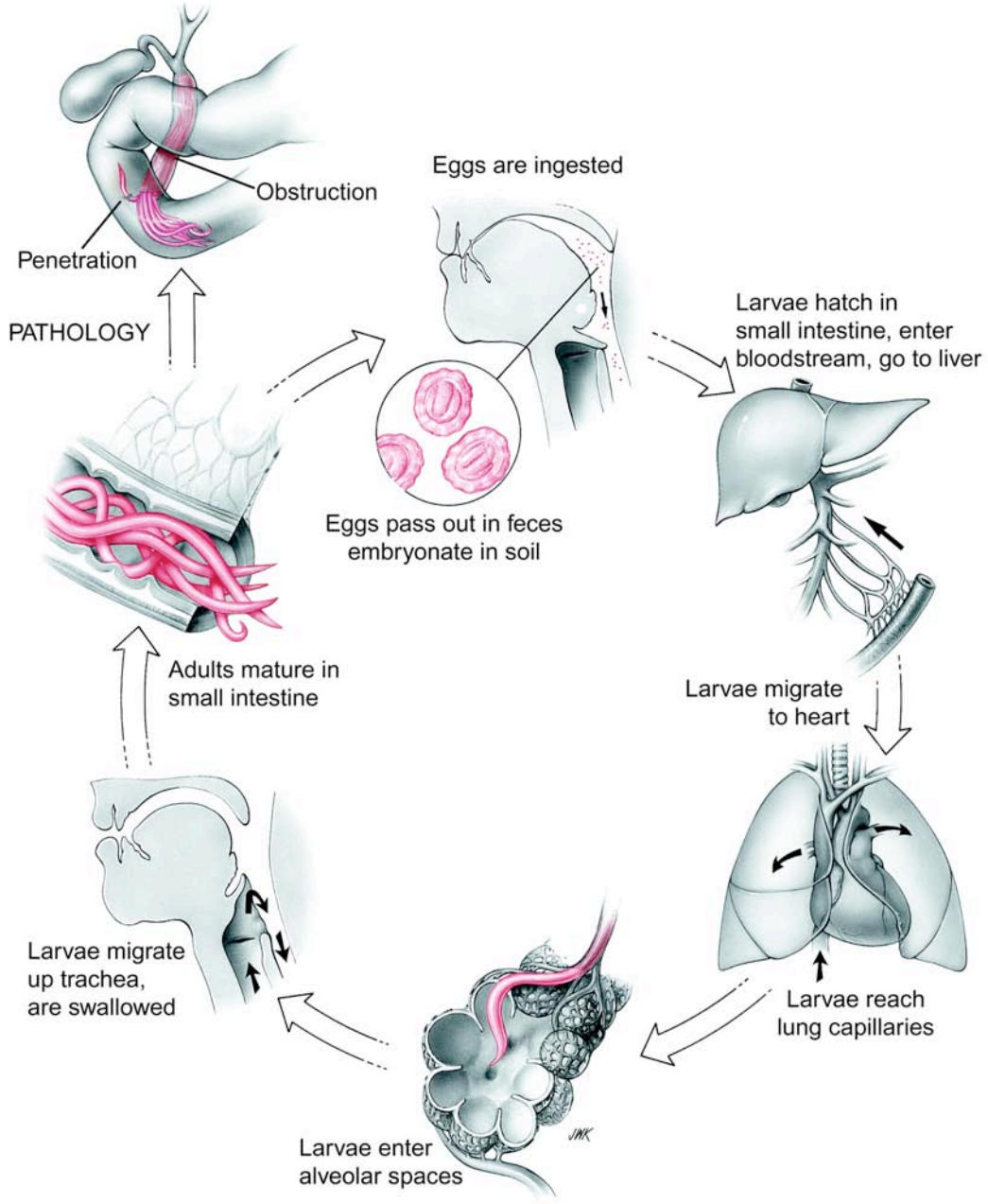
“Jar-O-Worms”

Collected from one rural village in Bangladesh in a single day!





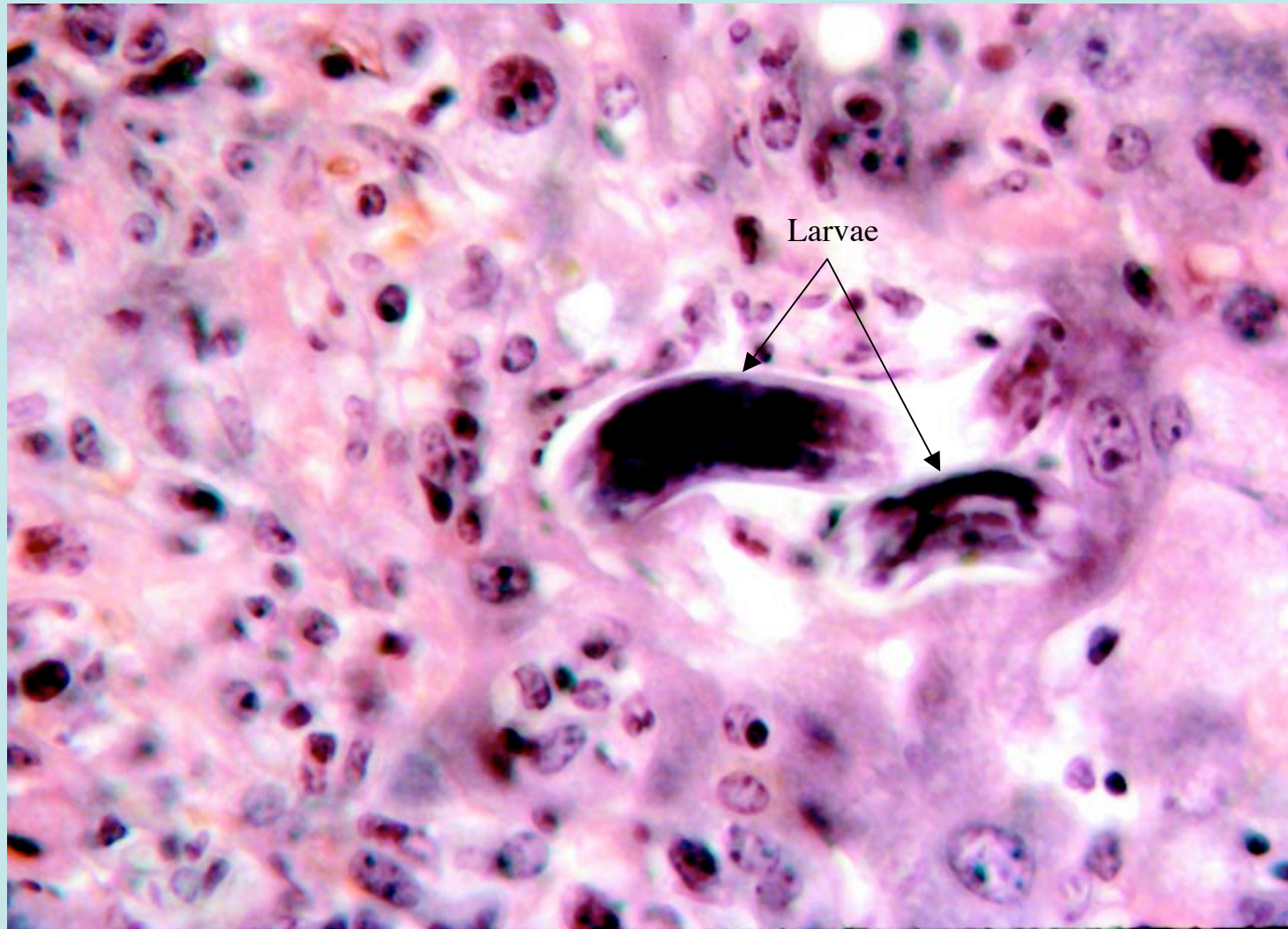
Ascaris lumbricoides



Cross section of adult *Ascaris lumbricoides*



Larvae of *Ascaris lumbricoides* in liver



Larva of *Ascaris lumbricoides* in lung



Pathogenesis:

1. “Verminous” pneumonia, lung tissue damage due to migratory larvae.
2. Bowel obstruction - too many adult worms.
3. Parasite secretes trypsin inhibitor, prevents host from digesting proteins.
4. Aberrant migration of “irritated” adult worms to:
 - a. Ampulla of Vater
 - b. Common duct
 - c. Liver
 - d. Pharynx
 - e. Peritoneum

Clinical Disease:

1. Light infections are asymptomatic as long as the adult worms do not migrate.

2. Heavy infection leads to:
 - a. protein calorie malnutrition - “failure to thrive” syndrome.
 - b. bowel obstruction.
 - c. aberrant migratory events.

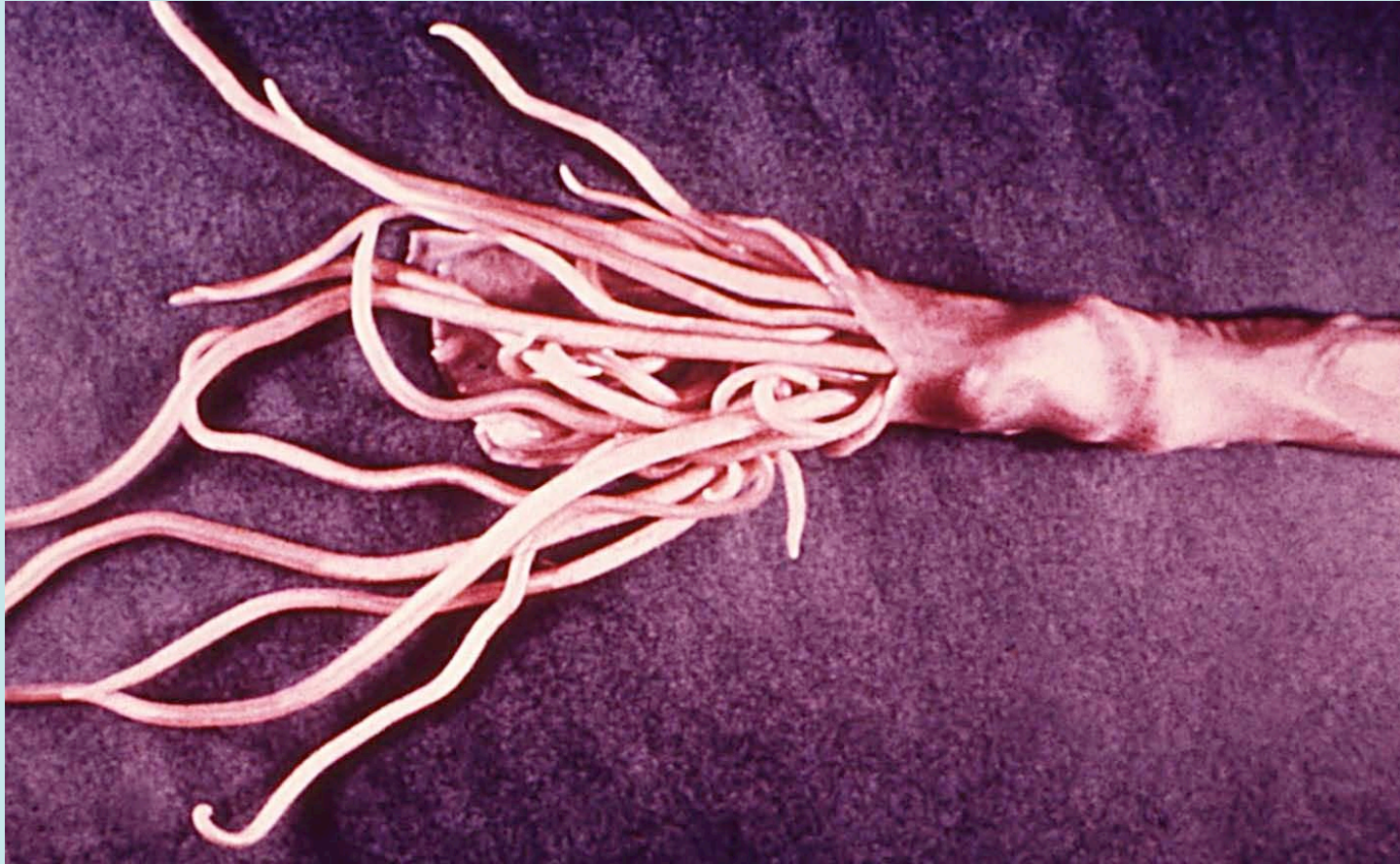
Child with heavy *Ascaris lumbricoides* infection



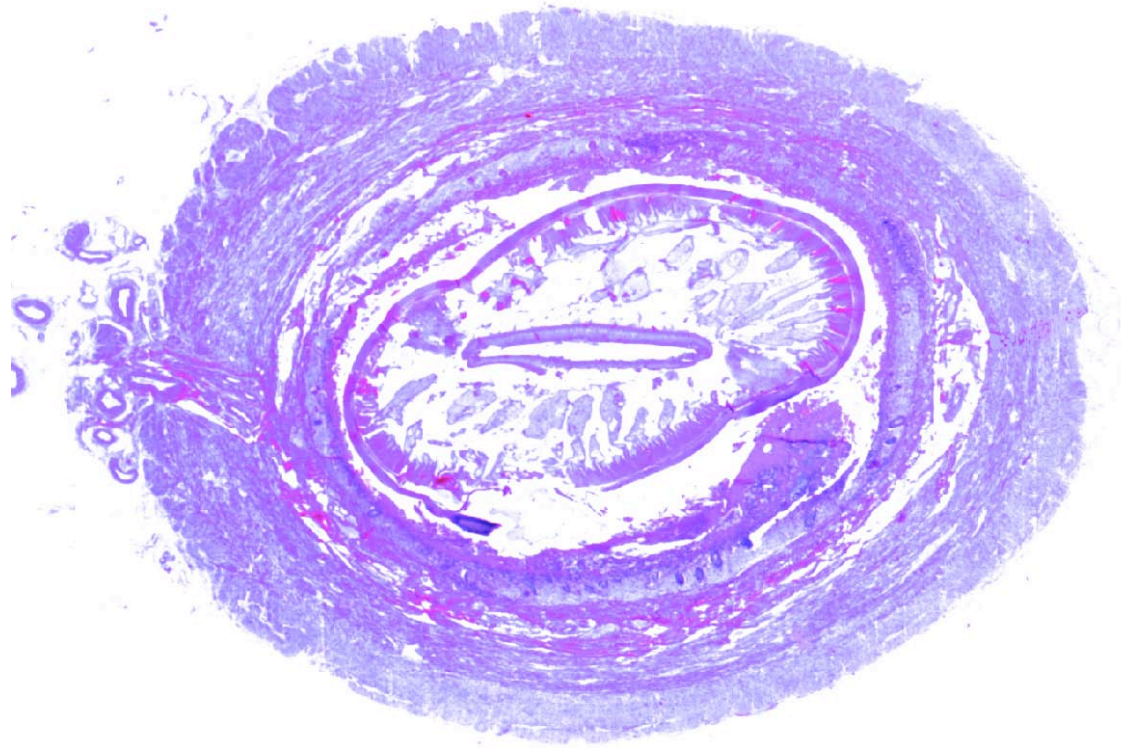
Infant with heavy *Ascaris* infection



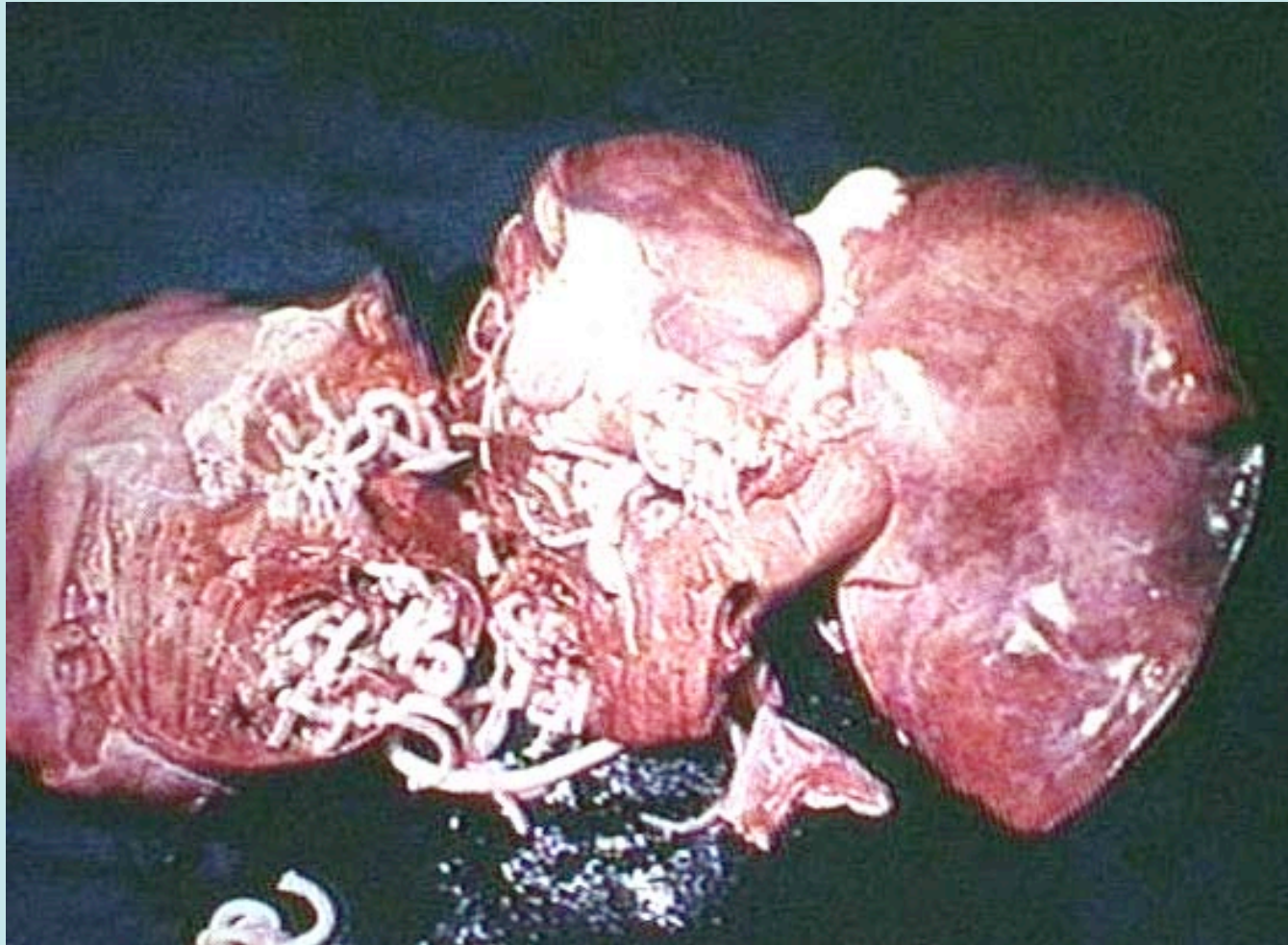
Bolus of *Ascaris lumbricoides* in small intestine



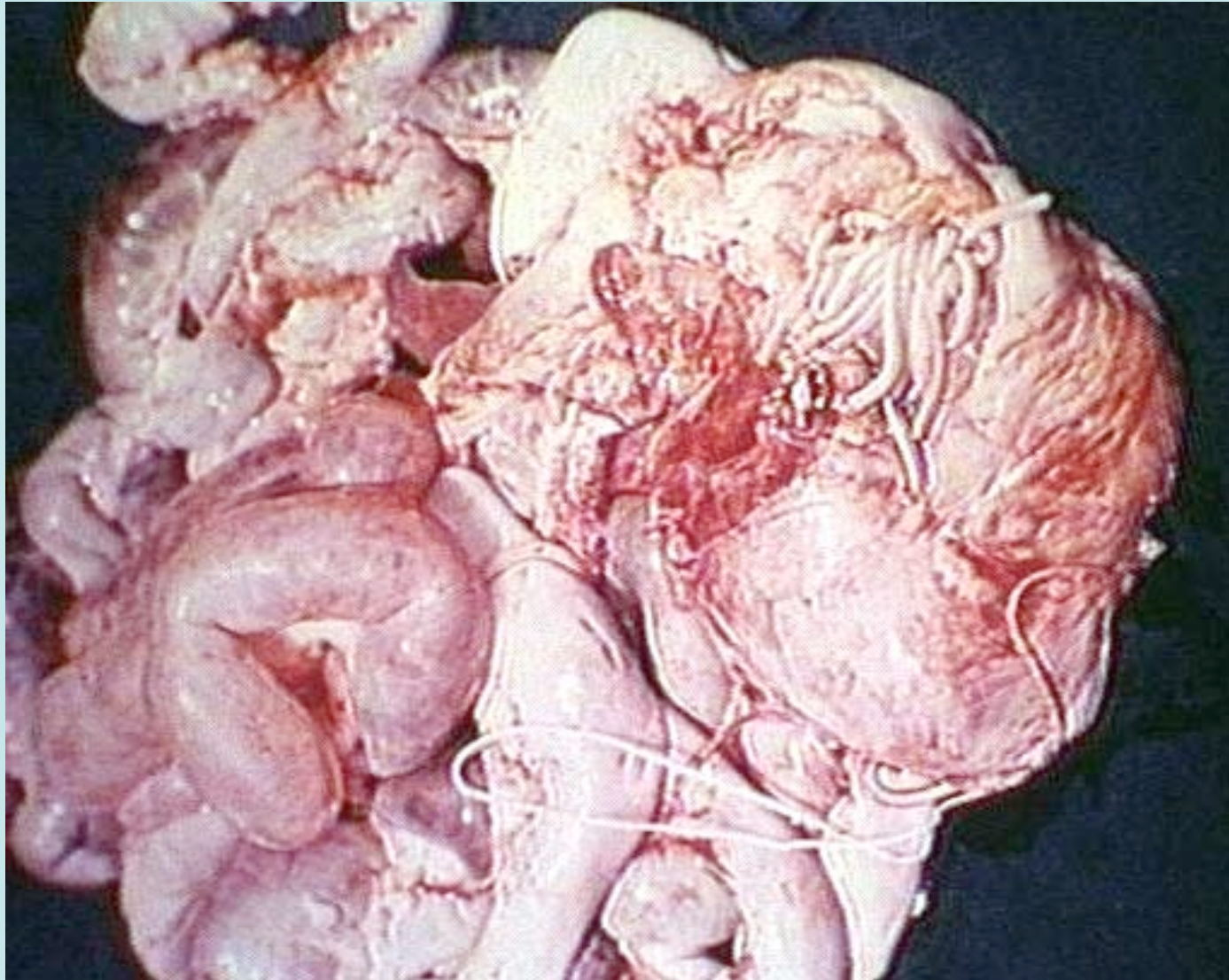
Ascaris lumbricoides adult in appendix



Ascaris adults in liver (fatal case)

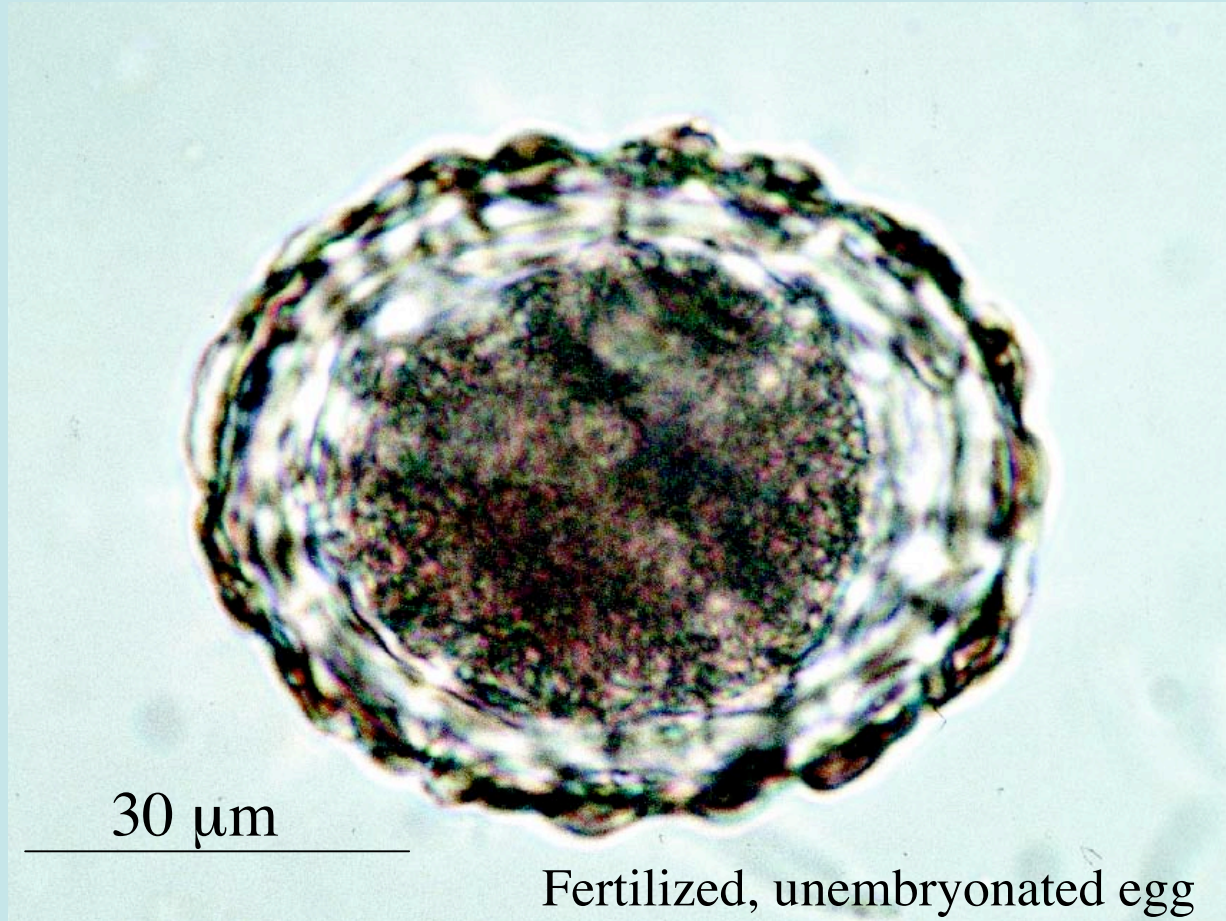


Bolus of *Ascaris lumbricoides* (fatal case)



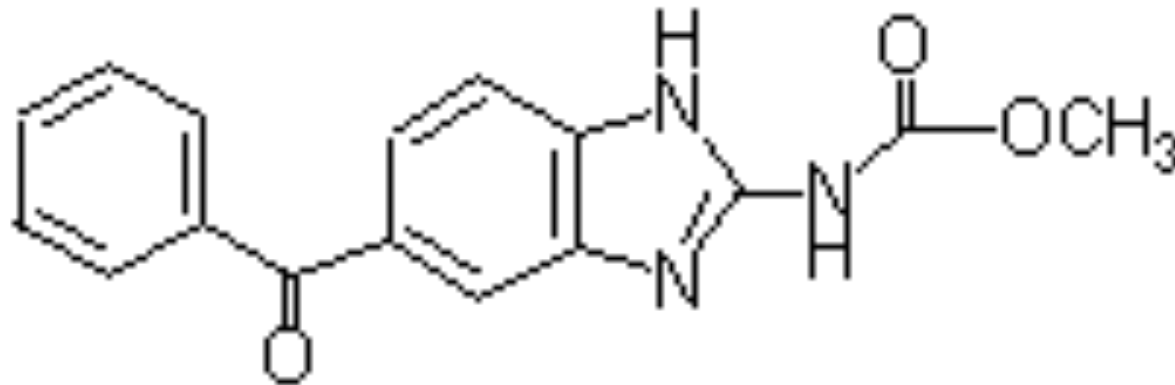
Diagnosis:

Microscopic examination of feces for eggs



Drug of choice:

Mebendazole

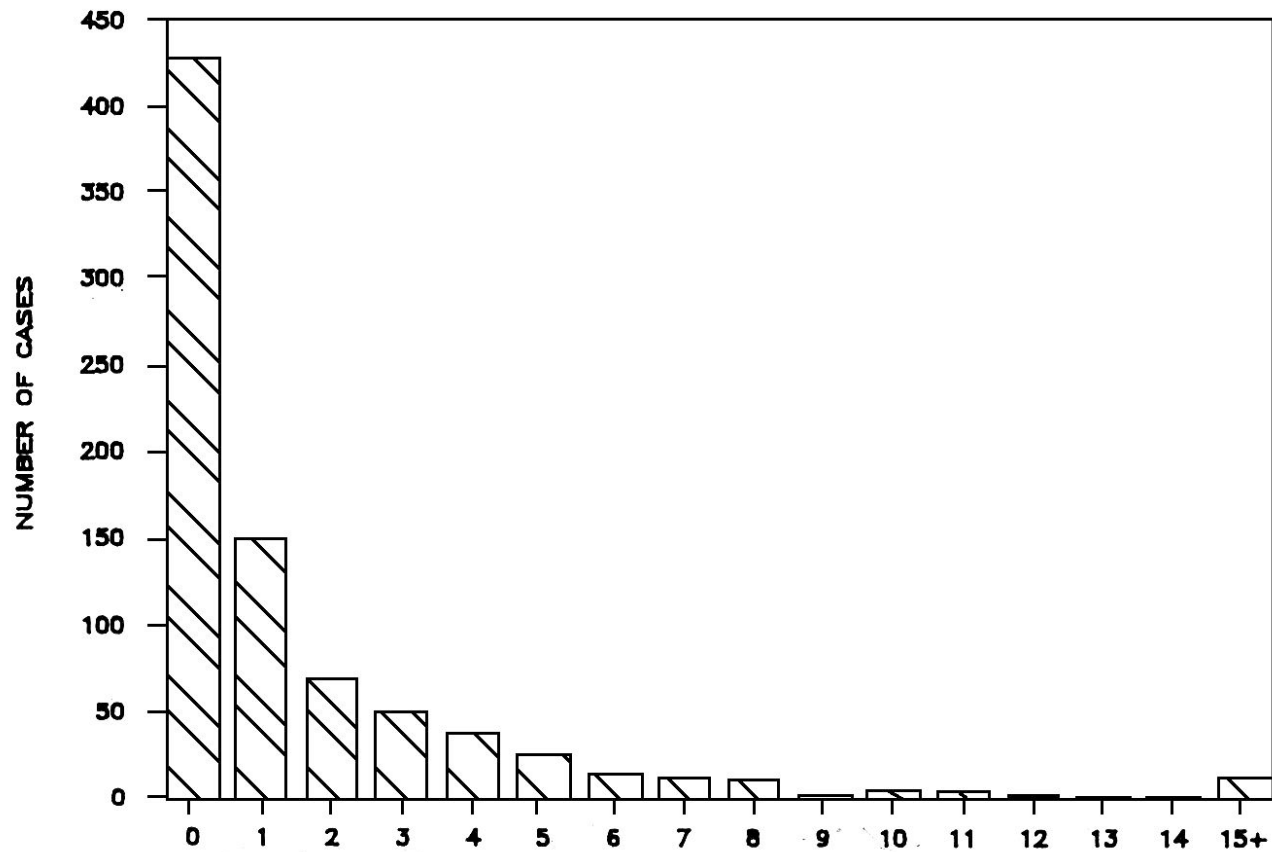


Mode of Action:

De-polymerizes invertebrate microtubules, only

Medical Ecology

ASCARIS : KOREA



Prevention and Control:

Sanitary disposal of feces



Helminths: Nematoda

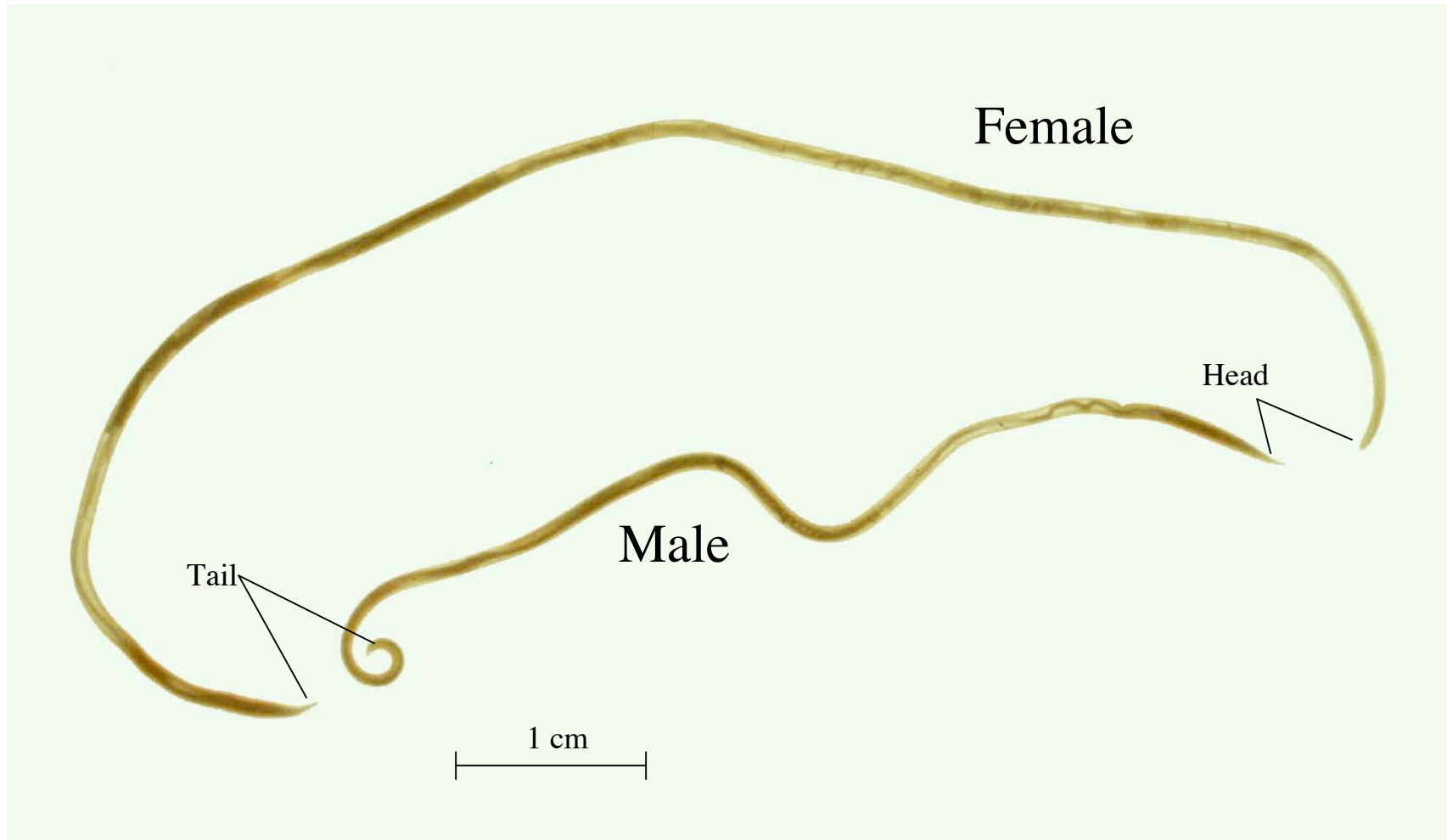


Toxocara canis

Toxocara cati

Visceral and ocular larva migrans

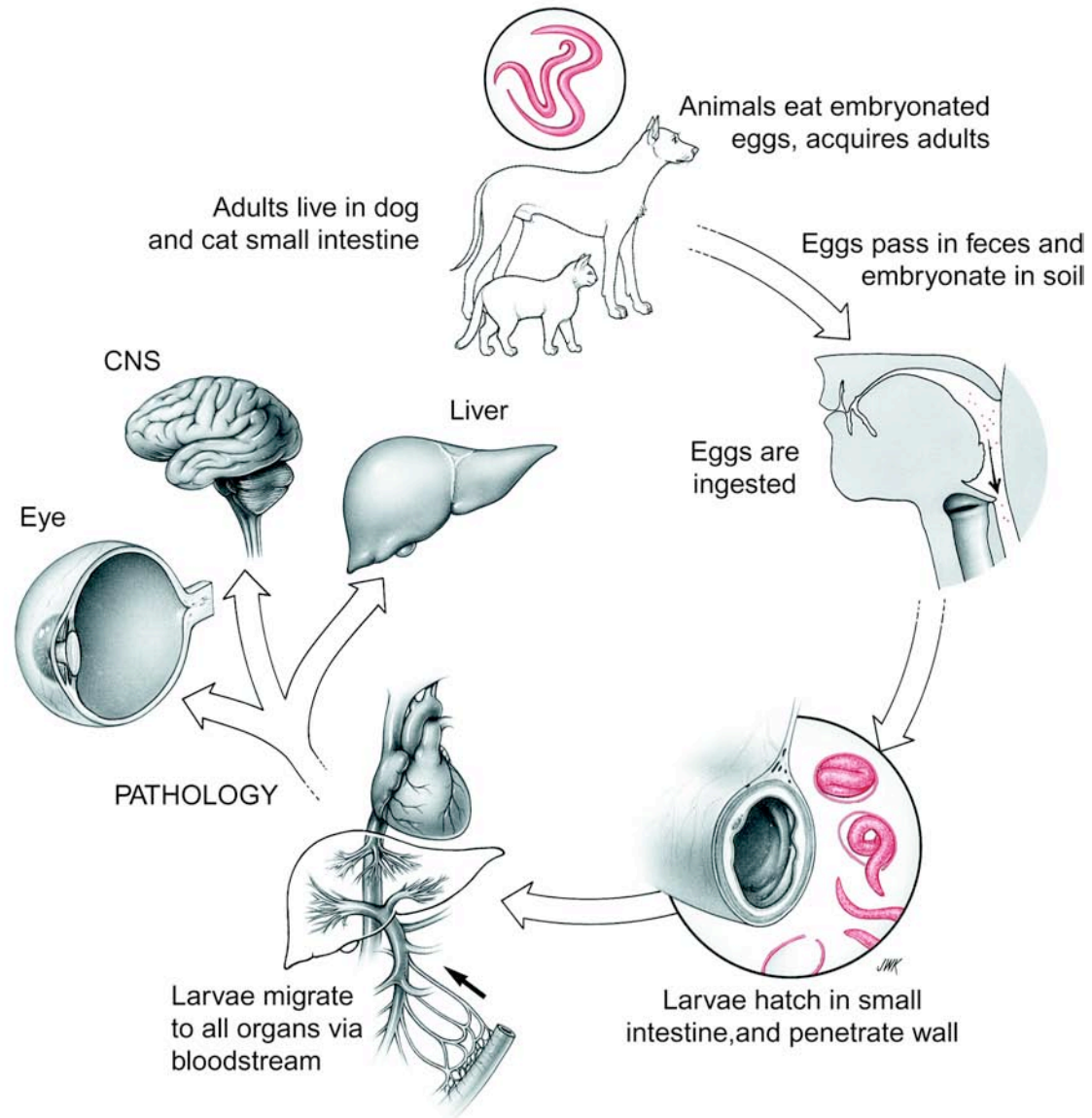
Adult *Toxocara canis*



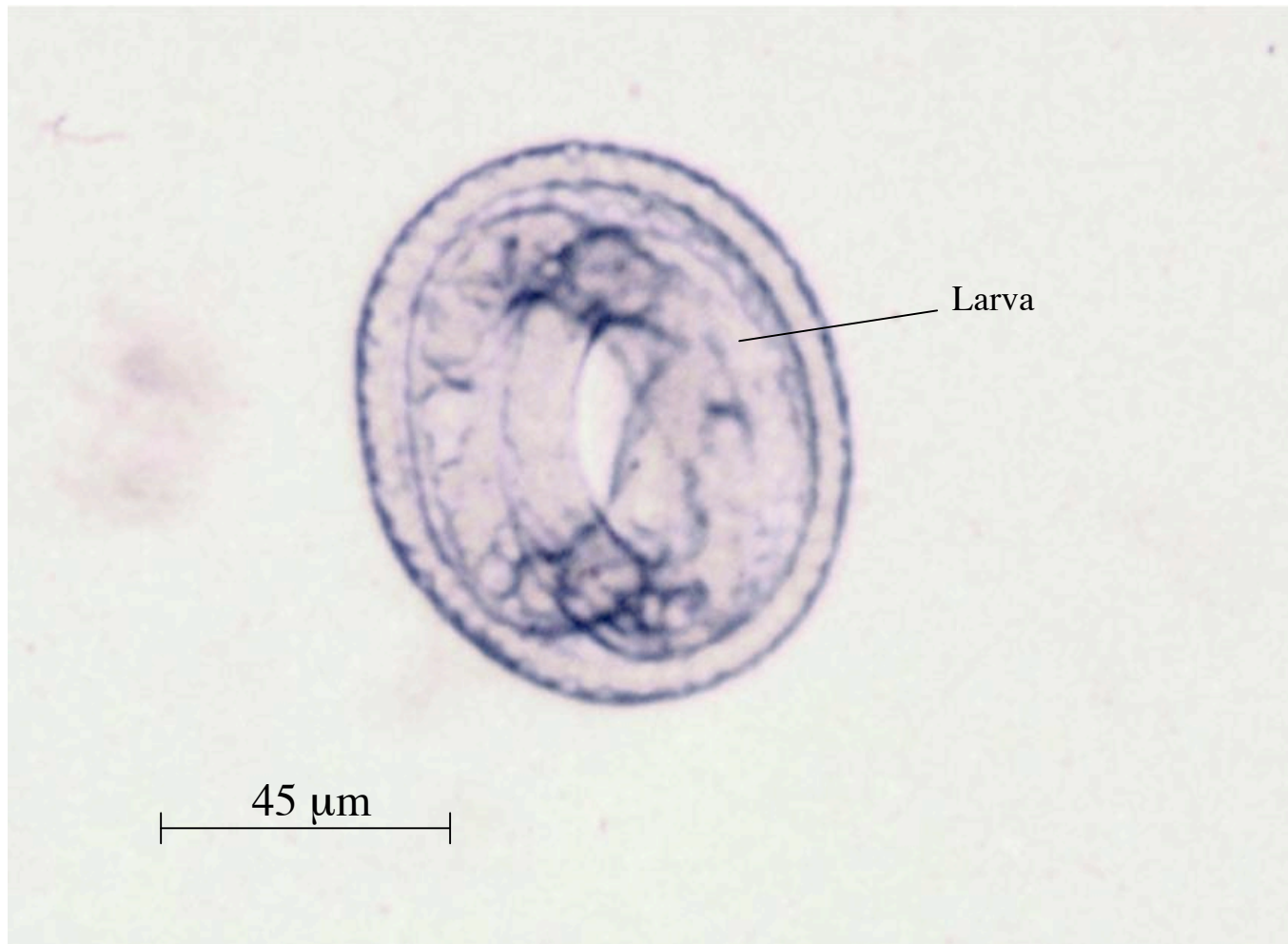
Street scene in Paro, Bhutan



Toxocara canis and *Toxocara cati*



Embryonated egg of *Toxocara canis*



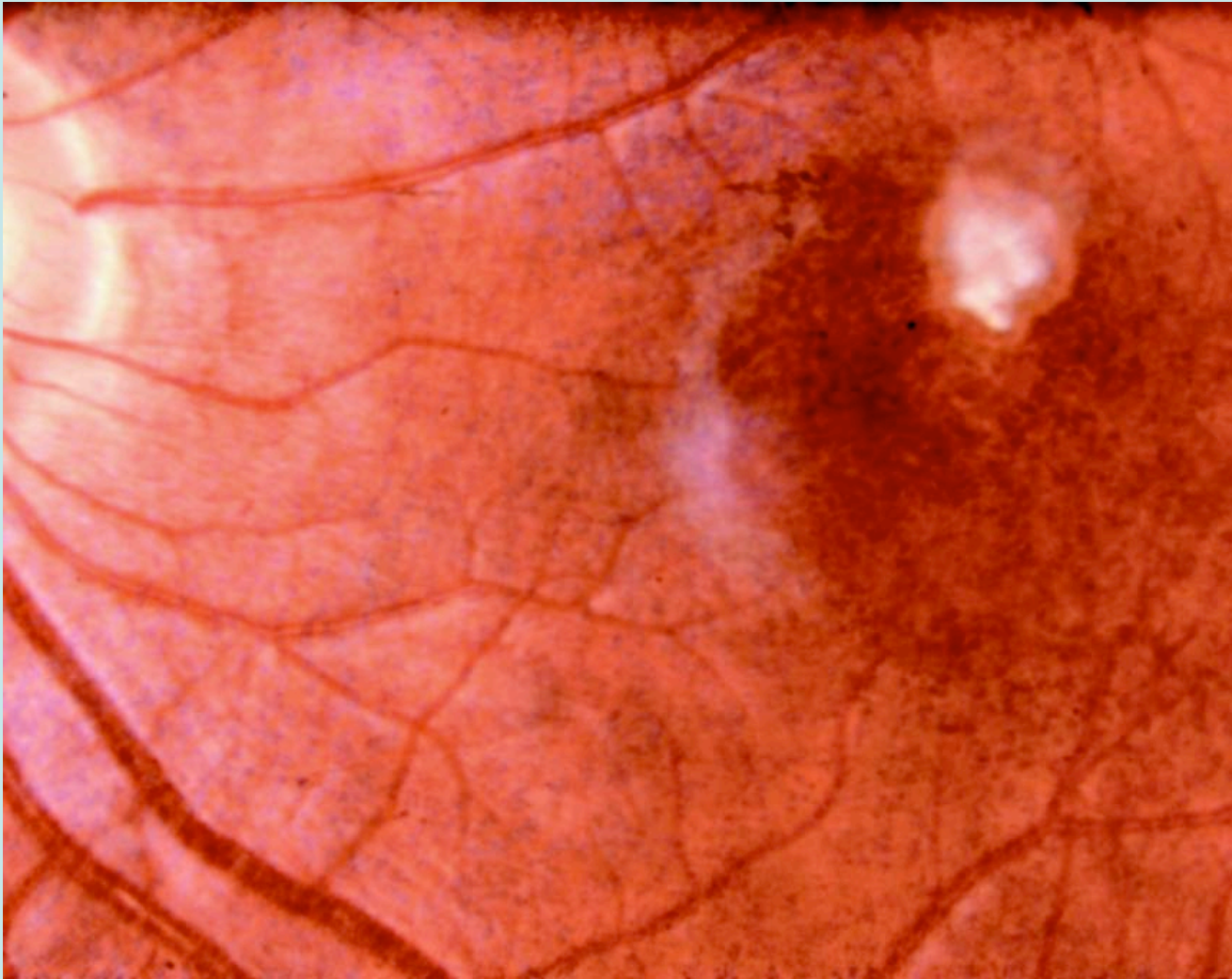
Pathogenesis:

Tissue damage (systemic) due to migratory
3rd stage larva

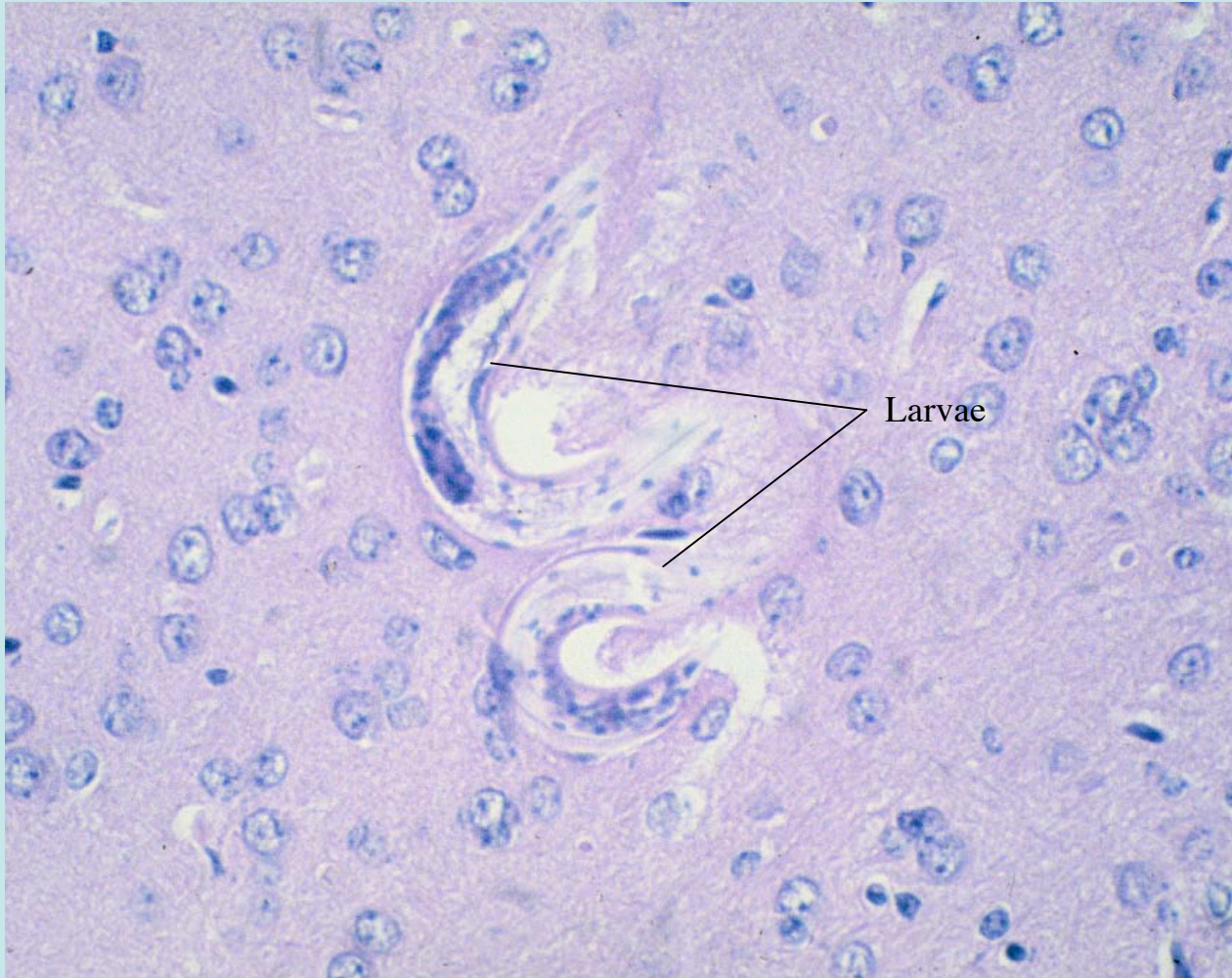
Clinical Disease:

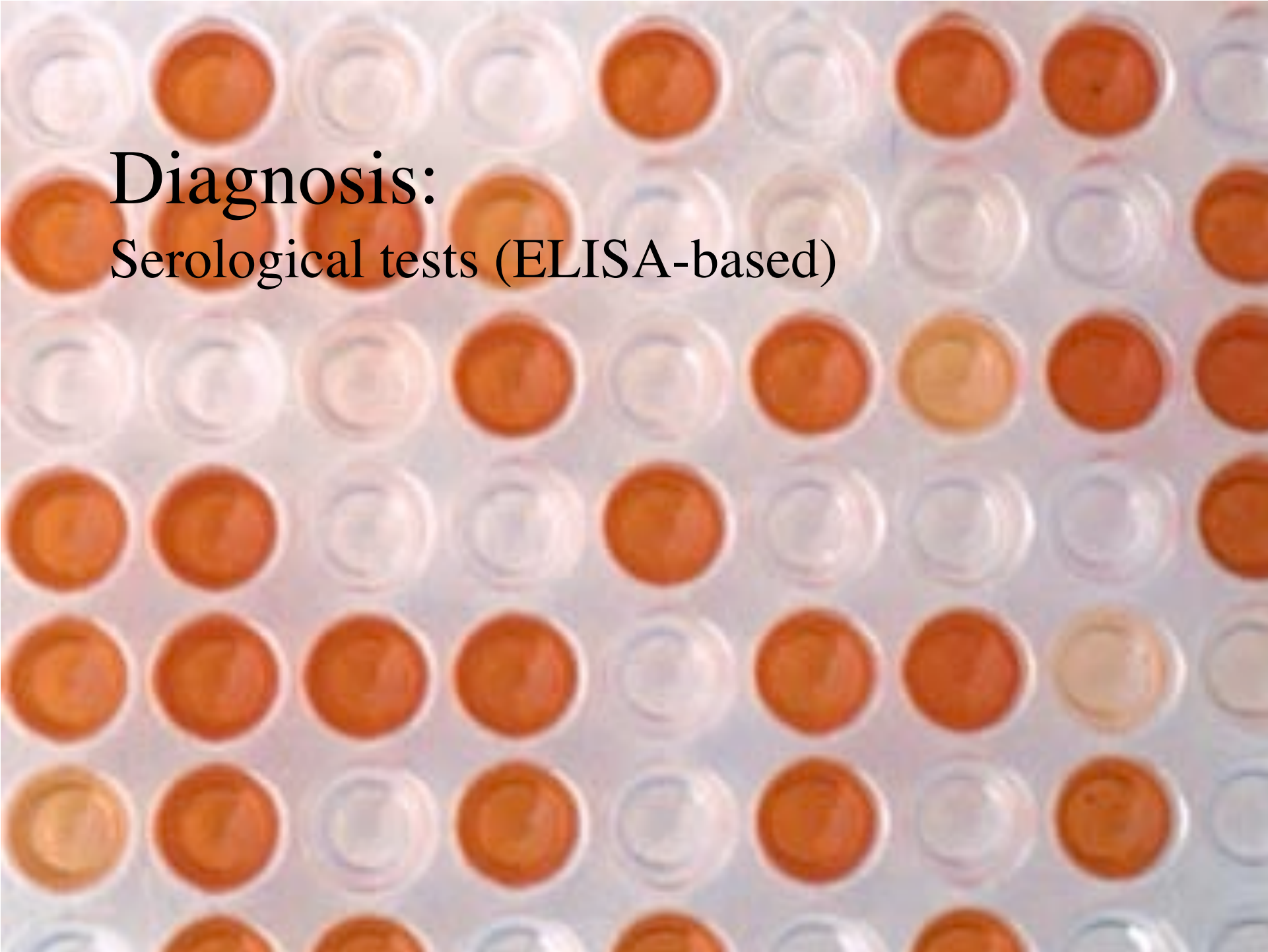
1. Fever
2. Loss of visual acuity
3. Blindness
4. Learning disabilities

Granuloma in retina due to *Toxocara canis*



Larvae of *Toxocara canis* in mouse brain

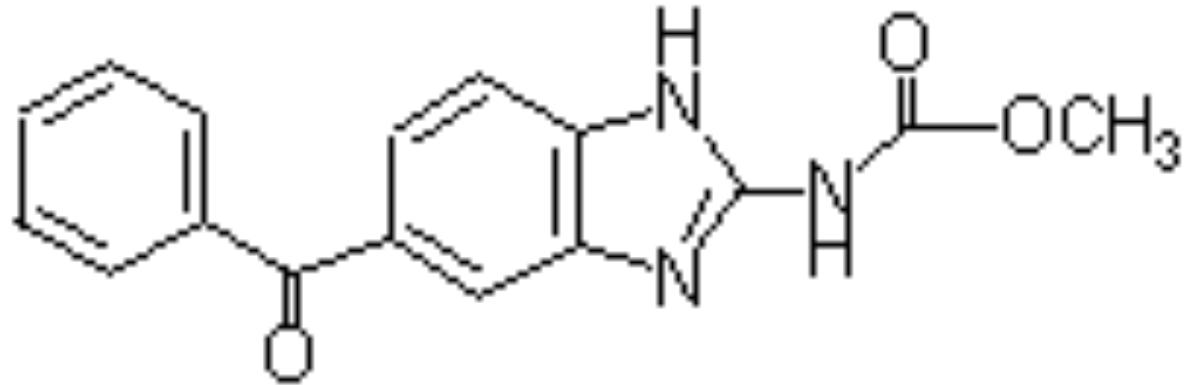




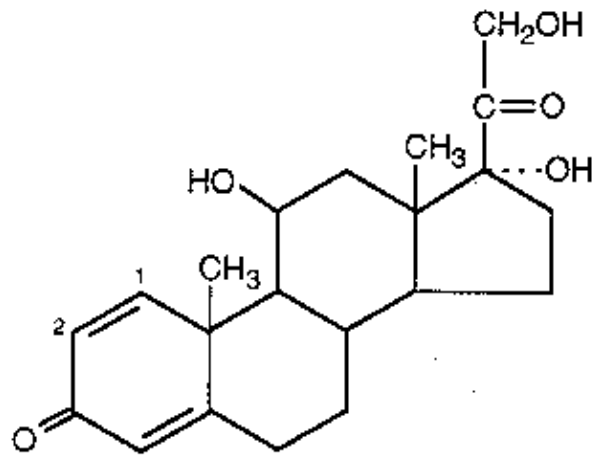
Diagnosis:
Serological tests (ELISA-based)

Drugs of choice:

Mebendazole



Steroids



Prednisolone

Prevention and Control:

Sanitary disposal of dog and cat feces



Not practical



Pooper-scooper



Potty-trained cat!

Prevention and Control (cont'd):

2. Periodically de-worm pets.
3. Cover public sand boxes at night.

