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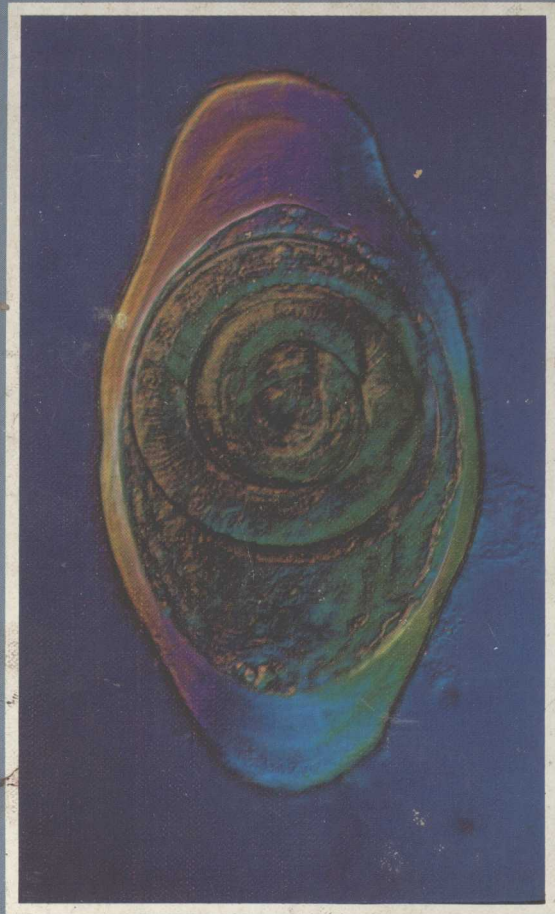

PARASITIC DISEASES

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Parasitic Diseases

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With 346 Illustrations Including
33 Parasite Life Cycle Drawings
and 4 Color Plates

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The illustration on the front cover is a differential interference contrast photomicrograph by Eric V. Gravé of the Nurse cell–parasite complex of *Trichinella spiralis.* The original photograph was awarded First Prize in the "Small World" competition (1976), sponsored by Nikon, Inc.

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To Joyce, Judy, Bruce, Bradley, and a friend

Foreword

Diseases caused by animal parasites remain, on a worldwide basis, among the principal causes of morbidity and mortality. This book gives the medical student—and the practitioner—the basic information about parasitic protozoa, worms, and anthropods and the diseases they cause that will enable the reader to recognize and manage them. One is impressed with the broad scope of the subject, the diversity of the parasitic modes of life, and how much there is yet unknown about the biology of parasitism. At the same time the book provides vignettes of the often fascinating historical background of our knowledge of animal parasites and glimpses of current research that is beginning to shape the future of parasitology.

William Trager, PH.D.
Professor Emeritus of Parasitology
The Rockefeller University
New York, New York

Preface

This book fills the need we have felt in teaching parasitic diseases to medical students. Many of the available texts are too detailed for what is inevitably an introductory course; others that do treat this subject with appropriate brevity are now out of date; still others lack documentation of references and thus fail to guide the readers to a broader understanding of this subject.

We have addressed ourselves to medical students, but they are not our sole target. Clinicians unfamiliar with the complexities of parasitic diseases need a guide to the diagnosis and management of these infections. We intend our book to serve this function as well.

In planning the organization of the book we followed a pedagogic format, instead of the traditional one according to evolutionary relationships, i.e., from the simplest to the most complex. This is the order in which we have taught this subject to medical students, and it has seemed most satisfactory. In general we have stressed the diseases and host response more than the organisms, and have provided diagnostic and therapeutic guidelines.

Although our book is targeted and has a mission, we hope that it nevertheless conveys the excitement of the subject matter. Parasitology is a fascinating science. It examines organisms superbly adapted to the environment through evolution of highly complex biological systems. In this respect the study of the life cycles may initiate in some readers an interest to pursue the subject of parasitology further as we were once inspired to do by our teachers, Harold W. Brown, William Trager, and George B. Craig, Jr. Many books and journals are available for such a purpose, and some of them are included in the references we cite.

We have been aided in our work by many colleagues and co-workers. We owe gratitude to them for their advice and criticism. Drs. Philip D'Alesandro, Martin Blechman, Thomas Brasitus, William Campbell, George Hillyer, Susanne Holmes-Giannini, Seymour Hutner, John Frame, Miklos Müller, Mike Schultz, William Trager, Jerry Vanderberg, and Ms. Joanne Csete were willing to review various parts of the text and to show us how to improve it. Any errors that it still contains can be attributed only to us. Dr. Benjamin Kean gave us free access to historical references. They were so fascinating that we wished we could devote more space to them. Fortunately, the book *Tropical Medicine and Parasitology: Classic Investigations* by Benjamin Kean, Kenneth Mott, and Adair Russell (Cornell University Press: Ithaca, New York, 1978) is available to those who want to broaden their knowledge of the history of parasitology. We also thank Drs. Robert Armstrong, Irene Cunningham, Gabriel Godman, Thomas Jones, Jay Lefkowitch, Donald Lindmark, David Meyers, Peter Schantz, Fred Schuster, Gerald Shad, Ralph Schlaeger, Roger Williams, Marianne

Wolff, Gregory Zalar, and Mr. John Ma, who supplied us with biological materials, which we used to produce various figures. Mrs. Terry Terrili and Ms. Patti Gilling committed many hours of their time to typing and correcting the text. Without their efforts, we would still be contending with the first draft of the manuscript. Ms. Marvick De Lima and Mr. Ronald Brier helped us with the organization of the technical work. The enormous help and encouragement given us by the publishers, especially Mr. Larry Carter, who nursed us along, and Ms. Berta Steiner and Mr. William Gabello, who directed the production, were invaluable to us.

Our labors are completed and the book must stand on its own. We dedicate it to our readers.

New York, New York and
Bethesda, Maryland
August 1982

Michael Katz
Dickson D. Despommier
Robert W. Gwadz

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I
The Nematodes

Introduction

Nematodes are nonsegmented roundworms belonging to the phylum Nematoda. The members of most species of nematodes are free living and inhabit soil and fresh and salt water, as well as other, more specialized habitats. The majority of parasitic nematodes have developed a highly specific biological dependence on a particular host and are incapable of survival in any other host. A few have succeeded in adapting to a variety of hosts.

Anatomy and Physiology

The typical nematode, both larva and adult, is surrounded by a flexible, durable outer coating, the cuticle, resistant to chemicals. It is a complex structure composed of a variety of layers, each of which has many components such as structural proteins, a small number of enzymes, and lipids. The cuticle of each species has a unique structure and composition. It not only protects the worm, but can also be involved in active transport of small molecules, including water, certain electrolytes, and some organic compounds.

All nematodes move by means of a muscular system. The muscle cells form an outer ring of tissue lying just beneath the cuticle and their origins and insertions are in the cuticular processes. In addition, there is some muscle tissue surrounding the buccal cavity and esophageal and subesophageal regions of the gut tract. These muscles are particularly important elements of the feeding apparatus in a wide variety of parasitic and free-living nematodes. Each muscle cell consists of filaments, mitochondria, and cytoplasmic processes that connect it with a single nerve fiber. The nervous system consists of a dorsal nerve ring or a series of ganglia that give rise to the peripheral nerves.

The digestive system of nematodes is divided into three major regions: oral (i.e., buccal) cavity and esophagus, midgut, and hindgut and anus. The oral cavity and hindgut are usually lined by epithelial cells extending from the cuticle; the midgut consists of columnar cells, complete with microvilli. The function of the midgut is the absorption of ingested nutrients, whereas the usually muscular esophagus serves to deliver food to the midgut.

In addition, a number of specialized exocrine glands open into the lumen of the digestive tract, usually in the region of the esophagus. These glands are thought to be largely concerned with digestion, but may, indeed, be related to other functions. For example, in hookworms the cephalic glands secrete an anticoagulant. In other instances, there are rows of cells, the stichocytes, that empty their products directly into the esophagus. These cells occupy a large portion of the body mass of trichinella and trichuris. The function of these cells is unknown.

The worms excrete solid and fluid wastes. Excretion of solid wastes takes place through the digestive tract. Fluids are excreted by means of the excretory system, consisting of two or more collecting tubes connected at one end to the ventral gland (a primitive kidney-like organ) and the excretory pore at the other.

Reproductive organs, particularly in the adult female, occupy a large portion of the body cavity. In the female, one or two ovaries lead to the vagina by way of a tubular oviduct and uterus. A seminal receptacle for storage of sperm is connected to the uterus. The male has a testis connected to the vas deferens, seminal vesicle, ejaculatory duct, and the cloaca. In addition, males of many species of nematodes have specialized structures to aid in transfer of sperm to the female during mating. Identification of the species of worm is often based on the morphology of these structures. Most nematodes lay eggs, but some are viviparous.

1. *Enterobius vermicularis* (Linnaeus 1758)

Enterobius vermicularis, commonly known as pinworm, is one of the most widely prevalent parasitic nematodes of man, affecting mainly children below the age of 12 years. It has no host other than man.

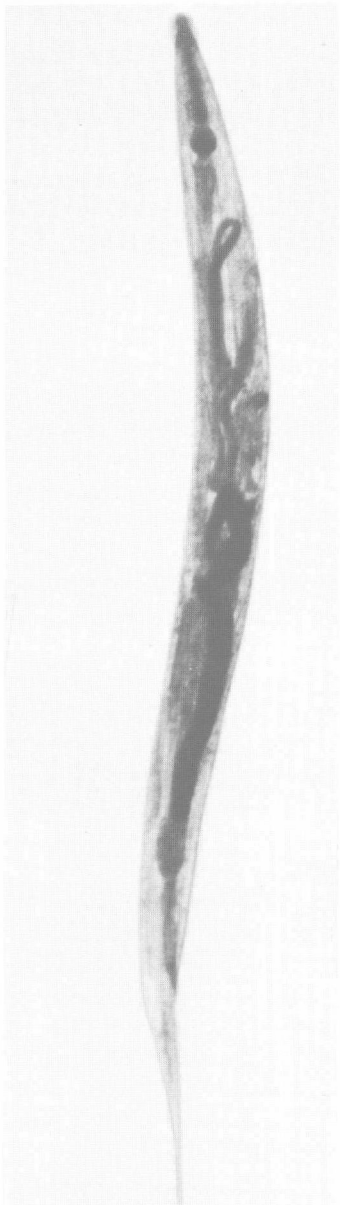


Figure 1.1. Adult female *Enterobius vermicularis.* The tail is pointed or pin-shaped, hence the common name "pinworm." ×20.

Historical Information

Early medical writings describe a worm infection that resembled in all respects infection with *E. vermicularis,* a name assigned to it by Linnaeus in 1758. Johann Bremser in 1824 distinguished this worm from the other Oxyurids and Ascarids and provided an accurate classification of it.[1]

Life Cycle

The adult pinworms live freely in the lumen of the transverse and descending colon and the rectum. The female worm (Fig. 1.1) measures 8–13 mm in length and 0.3–0.6 mm in width. The male (Fig. 1.2) is smaller, measuring 2–5 mm by 0.2 mm. The distal end of the male contains a single copulatory spicule and is quite curved, a characteristic permitting ready morphological differentiation from the female.

Although the biochemical and physiological requirements of the adult pinworms are not known, it is presumed that they utilize fecal matter as the source of their nutrients.

The adult worms copulate, and each female produces approximately 10,000 fertilized, nonembryonated eggs. At night, presumably spurred by the drop in the body temperature of the host, the female migrates through the anus onto the perianal skin, where she experiences a prolapse of the uterus, expels all the eggs, and dies. This expulsion can be so intense that the eggs, which are quite light, become airborne and are distributed throughout the surrounding environment. More

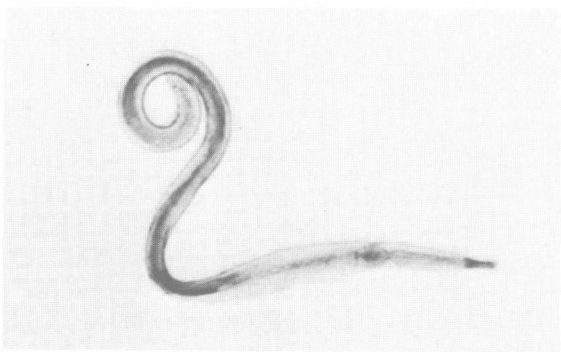
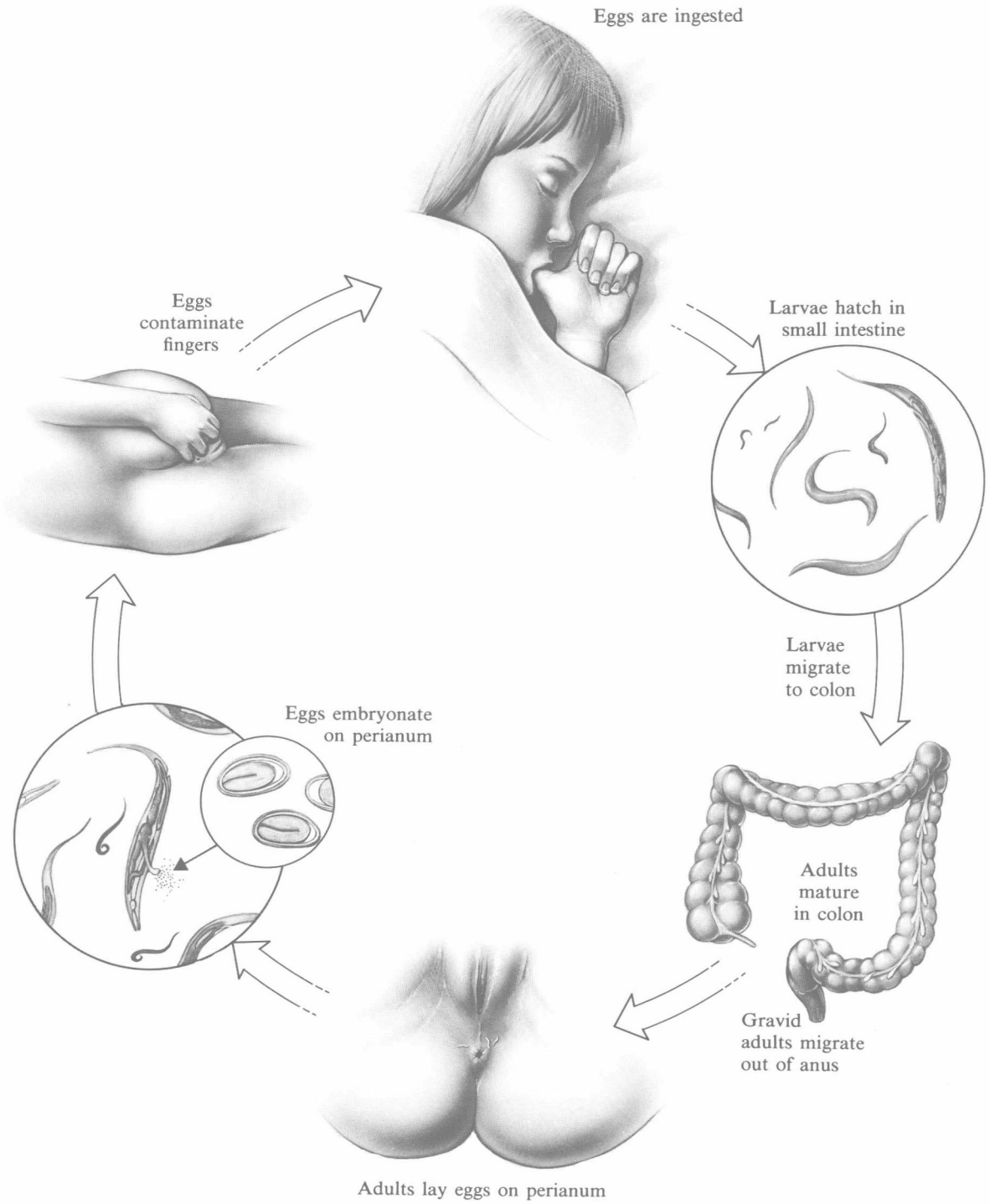


Figure 1.2. Diminutive male *Enterobius vermicularis.* ×20.

Enterobius vermicularis



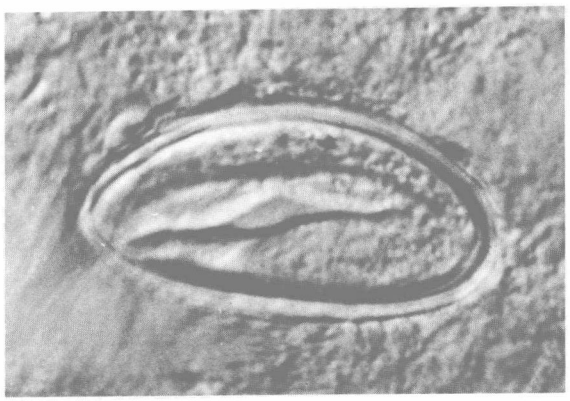


Figure 1.3. Embryonated egg of *Enterobius vermicularis* containing an infective larva. ×1000.

often, however, they remain at the site of deposition. The eggs embryonate (Fig. 1.3) and become infective within 6 h of being laid.

The embryonated eggs are swallowed and hatch into the second-stage larvae once they reach the small intestine. Development to the third and fourth stages also occurs there. Finally, the adult worms take up residence in the large intestine. The entire cycle is completed within 4–6 weeks after the original ingestion of the egg. Alternatively, the eggs have been known to hatch on the skin at the site of the original deposition and the second-stage larvae then crawl back through the anus into the rectum and eventually the colon, where they develop into reproducing adults.

In women and girls, the larvae that hatch on the skin near the anus occasionally crawl into the vagina instead of the rectum, and there establish an aberrant infection. Even less frequently, gravid female worms make their way into the fallopian tubes. Other reported aberrant infections have included pelvic peritonitis[2] and ovarian infection.[3]

Pathogenesis

The migratory phase of the pinworm is restricted to the gastrointestinal tract and thus the host does not experience any systemic reactions. The parasite does evoke a minor inflammatory response in the intestine that may be associated with a low-grade eosinophilia, but it has not been definitively documented.

The pruritis that some patients develop results from an allergic response to the worm proteins. Whether pinworm infection causes secondary problems, such as appendicitis or pelvic inflammatory disease, is moot. Pinworms have been found in these organs at autopsy with no evidence of an inflammatory reaction.

Although there are no comparable studies in man, there is experimental evidence that immune status of the host does affect the infection. The mouse pinworm *Syphacia oblevata* reaches much larger numbers in nude (athymic) mice than it does in the same mice into which subcutaneous implant of thymic tissue from syngeneic donors was introduced.[4]

In man susceptibility to pinworm infection decreases with age, but the reasons for this are not clear and it remains to be determined whether this difference in susceptibility is immunologic.

Clinical Disease

The majority of infected individuals are free of symptoms. Those few who are symptomatic experience an intense itching of the perianal area; women with vaginal infection develop vaginal itching and, sometimes, serious discharge.

Although enuresis has been attributed to infection with pinworm, no causal relationship has been established.[5] Gnashing of teeth and sleep disturbances have not been definitely related to the pinworm, either, although there are myths that they are.

Diagnosis

The infection is best detected by the examination of a transparent plastic adhesive tape previously applied to the perianal region. This tape, subsequently cleared with xylol, or another suitable solvent, and attached to a glass slide, is examined microscopically at the ×100 magnification for the presence of the eggs (Fig. 1.4). The eggs can be readily detected. They are not usually found in the feces and therefore examination of a stool specimen is useless.

There are no serological tests and no known specific reactions that help to make an indirect diagnosis. Although low-grade eosinophilia has been reported in some cases, this relatively nonspecific finding is not helpful in the diagnosis.

Adult pinworms can be readily identified when they are seen on histological sections (Fig. 1.5) because of bilateral cuticular ridges known as alae, which are not present in any other intestinal nematode of man.

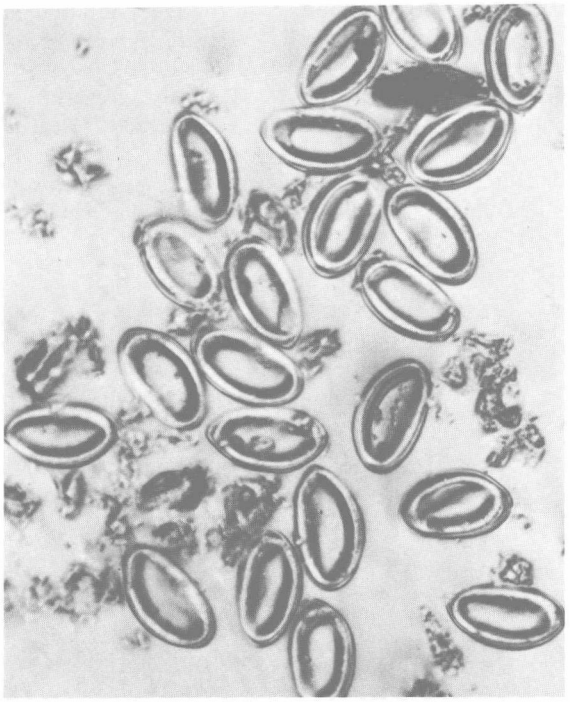


Figure 1.4. Eggs of *Enterobius vermicularis* as seen attached to a transparent cellophane adhesive test tape. ×240.

Treatment

Of the available drugs, pyrantel pamoate,[6] in a single dose, or mebendazole,[7,8] also in a single dose, is the best therapy. Neither piperazine citrate nor pyrvinium pamoate, drugs used until recently, has any place in the treatment of this parasite.

In treating the patient, one must remember that neither drug kills the eggs. Therefore, "blind" retreatment of the patient is recomended 2 or 3 weeks after the original therapy. This will destroy worms that have hatched from eggs ingested after the first treatment.

Prevention and Control

The probability of infection and reinfection is exceedingly high because of the ready transmissibility of the pinworm. Compounding the problem is the fact that the eggs can survive for several days under conditions of high humidity and intermediate to low temperatures.

The groups showing highest prevalence of infection are school children and institutionalized individuals. There are no differences in predilection on the basis of sex, race, or socioeconomic class.

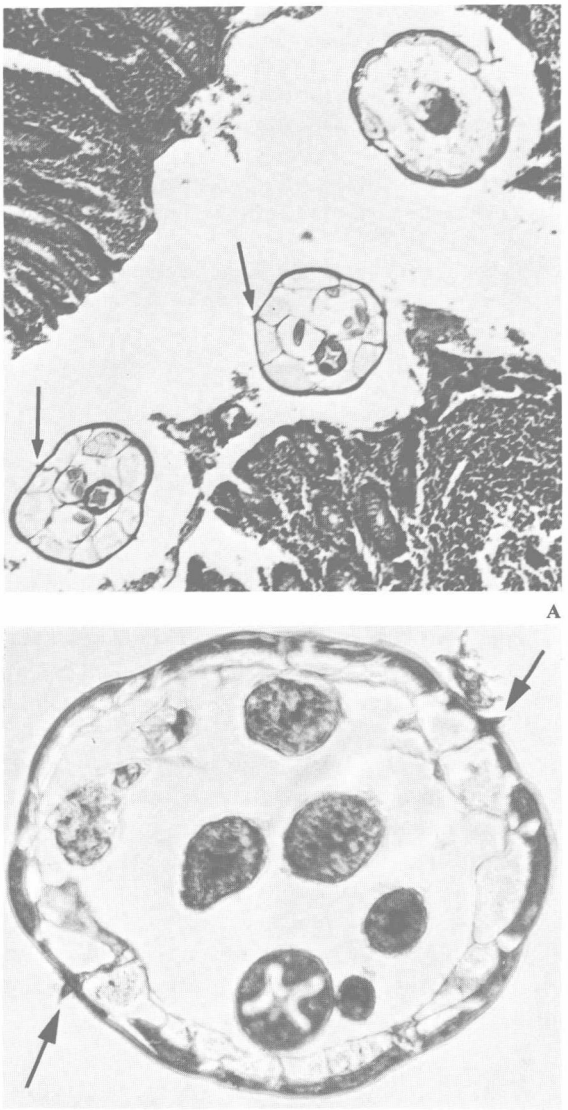


Figure 1.5. A and **B.** Cross-sections of adult *Enterobius vermicularis.* Note characteristic cuticular projections, called alae (*arrows*), which help to identify this nematode in histological sections. **A,** ×90; **B,** ×270.

No effective means for prevention are currently available. Pinworm infection should not be considered per se as evidence of poor hygiene. Any exaggerated attempts to eradicate the infection in the household should be discouraged by a rational discussion to allay anxiety.

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2. *Trichuris trichiura* (Linnaeus 1771)

Trichuris trichiura, popularly known as whipworm because of its characteristic shape, is distributed throughout the world in the same areas where ascaris and hookworm are found. It is estimated that there are at present some 500 million infections.

There are no reservoir hosts for *T. trichiura,* but other species of trichuris are found in a wide range of mammals (e.g., *T. vulpis* in the dog; *T. muris* in the mouse; and *T. suis* in the pig). Host specificity is the rule, but one case of *T. vulpis* in a child has been reported.

Although trichuris infections are usually not serious clinically, overwhelming infections leading to death have been reported in children.

Historical Information

Linnaeus, in 1771, classified this organism as a nematode, then called "Teretes." In 1740, Morgagni[1] described the location of *T. trichiura* in the caecum and transverse colon. This description in 1761 was followed by an accurate report by Roederer[2] of the external morphology of *T. trichiura.* Roederer's report was accompanied by drawings that are considered accurate by current standards.

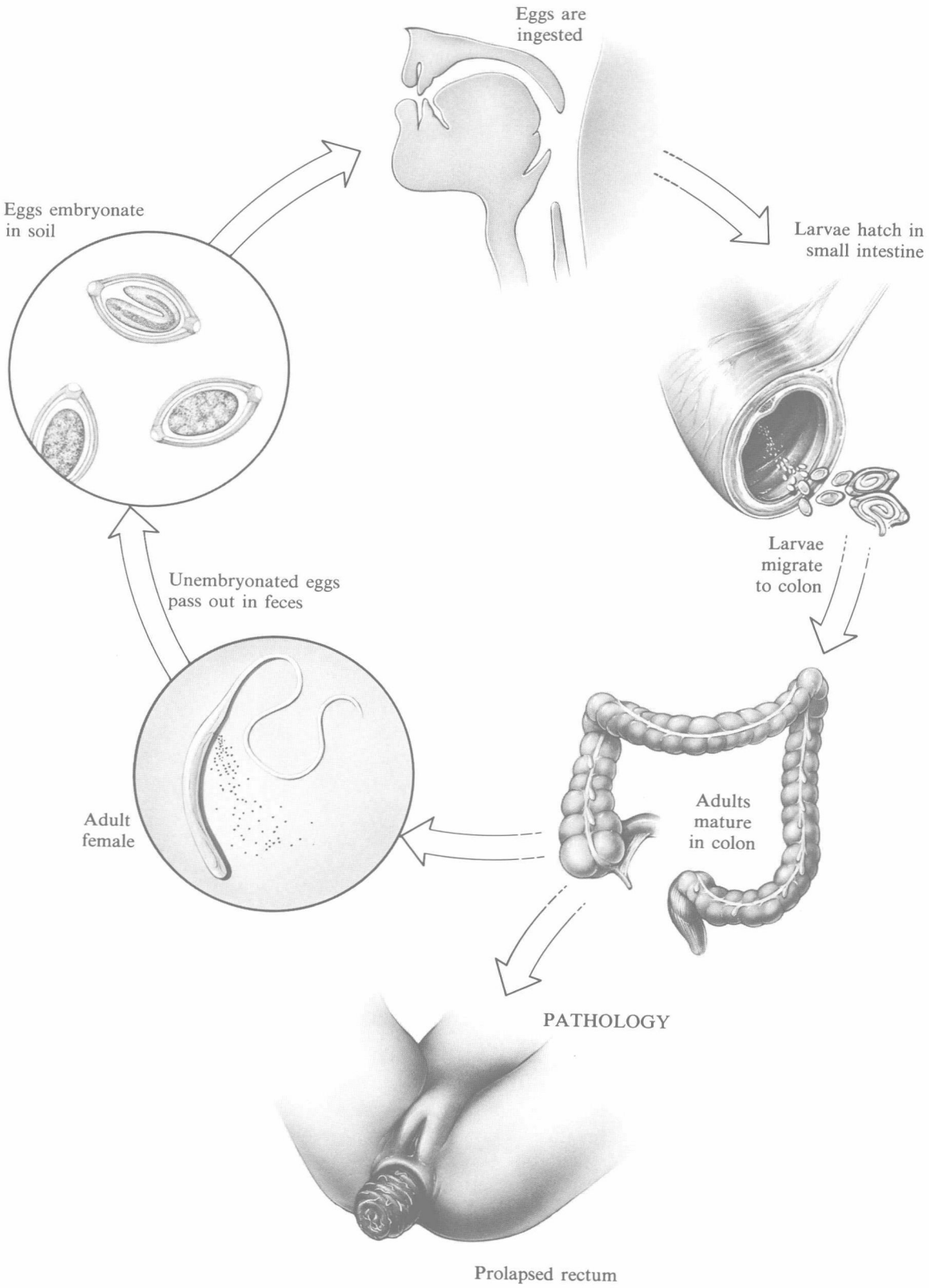
Human infection with trichuris has been identified in coprolites of prehistoric man.

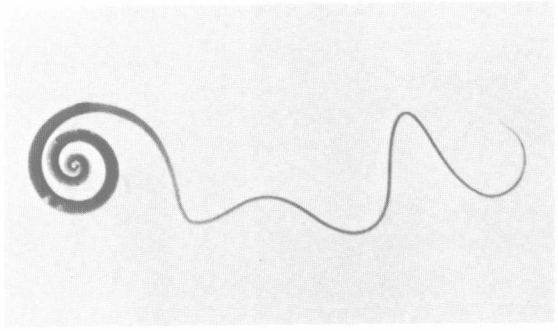
Life Cycle

The adult worms (Figs. 2.1, 2.2A and B) live in the transverse and descending colon. The anterior

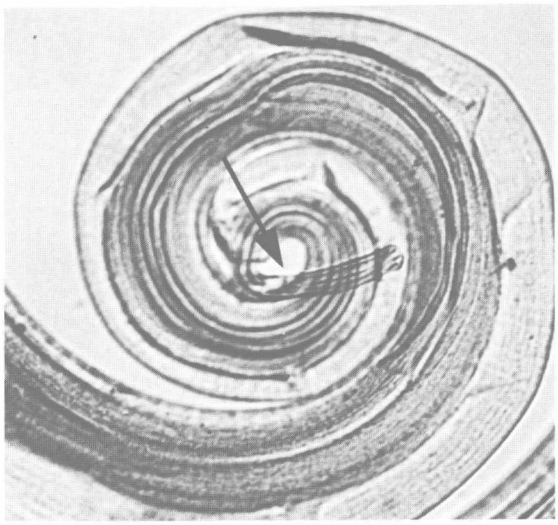
Figure 2.1. Adult female *Trichuris trichiura.* ×5.

Trichuris trichiura





A



B

Figure 2.2. A. Adult male *Trichuris trichiura.* **B.** Enlarged view of male *Trichuris trichiura* showing the copulatory spicules (*arrows*). **A,** ×5; **B,** ×36.

narrow portion of their bodies is embedded within the columnar epithelium (Fig. 2.3); the posterior end protrudes into the lumen.

Nothing is known about the nutritional requirements of the adult worms, but experimental evidence on related species suggests that they do not ingest blood.[3]

The worms mature in the large intestine, mate, and lay eggs. Females produce 3000–5000 eggs per day,[4] and live 1.5–2 years.[5] Fertilized eggs (Fig. 2.4), deposited in the soil with feces, are undeveloped and must embryonate before becoming infectious. For this they require a favorable environment. Such external factors as high humidity, sandy or loamy soil, and a warm temperature (i.e., 20°–30°C) favor embryonation, which, under optimal conditions, takes place within 18–25 days.[6]

Infection is acquired by swallowing the embryonated egg. The larva hatches in the small intestine, penetrates the columnar epithelium, and comes to lie just above the lamina propria. Four molts later, the immature adult emerges and is passively carried to the large intestine. The time required for a new infection to become patent (i.e., for mature worms to begin laying eggs passed into the feces) is about 90 days after ingestion of the egg.

Pathogenesis

The mechanism by which trichuris causes diarrhea remains unknown, although a number of theories have been suggested. These include intoxication with various products of metabolism of the worm and direct mechanical damage to the intestinal mucosa.

Clinical Disease

Only heavily infected patients develop clinical disease, which presents as chronic diarrhea, characterized by mucous stools, and associated with tenesmus. If the diarrhea is protracted, the patient may develop rectal prolapse, more likely to occur in small children. Many individuals infected with trichuris —symptomatic, or not—tend to be malnourished and anemic. Nevertheless, no direct causal relationships have ever been established between trichuris infection and malnutrition and anemia. In view of the fact that trichuris is widely prevalent and that in the area where it is found there is a high frequency of anemia, malnutrition, and infection, the correlation may not be causal. In an experimental animal study using labeled erythrocytes, no evidence of intestinal loss of blood due to trichuris was demonstrated.[3] Severe diarrhea in association with trichuris infection is not necessarily attributable to trichuris; other causes for it must be sought (see Diagnosis).

Diagnosis

Identification of the characteristic eggs of trichuris (Fig. 2.4) in the stool establishes the diagnosis of infection. Presence of Charcot-Leyden crystals (see Figs. 25.8A and B) strongly suggests that there is colitis due to trichuris and therefore implies in the particular patient a causal relationship between this organism and diarrhea. In any case, search for pathogenic protozoa such as *Entamoeba*