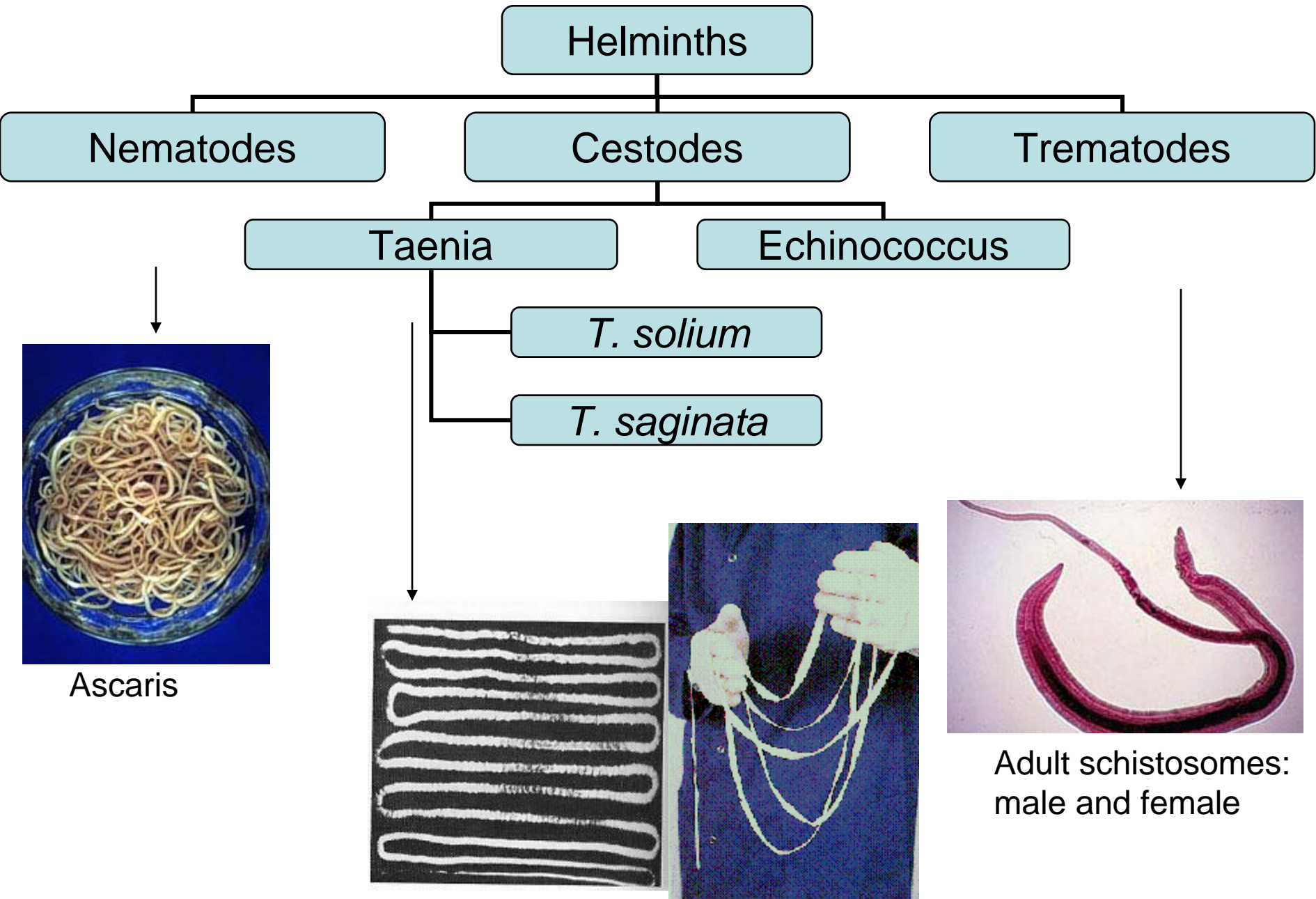


# **Ascaris, Pinworms, Trichinella**



# Nematodes in general...(review)

- Non-segmented round worms.
- Most are free living.
  - Only a small fraction are parasitic and affect humans.
- The most common are the Soil-Transmitted Helminths (STHs).
  - *Ascaris lumbricoides*
  - *Trichuris trichiura* (whipworm)
  - *Necator americanus*, *Ancylostoma duodenale* (hookworms)

# Nematodes in general...

- In developing countries children frequently harbor all three STHs.
  - Referred to as “the unholy trinity”
- These infections result in malnutrition, physical growth retardation, and deficits in cognitive and intellectual development.

# **World Health Assembly Initiative (2001)**

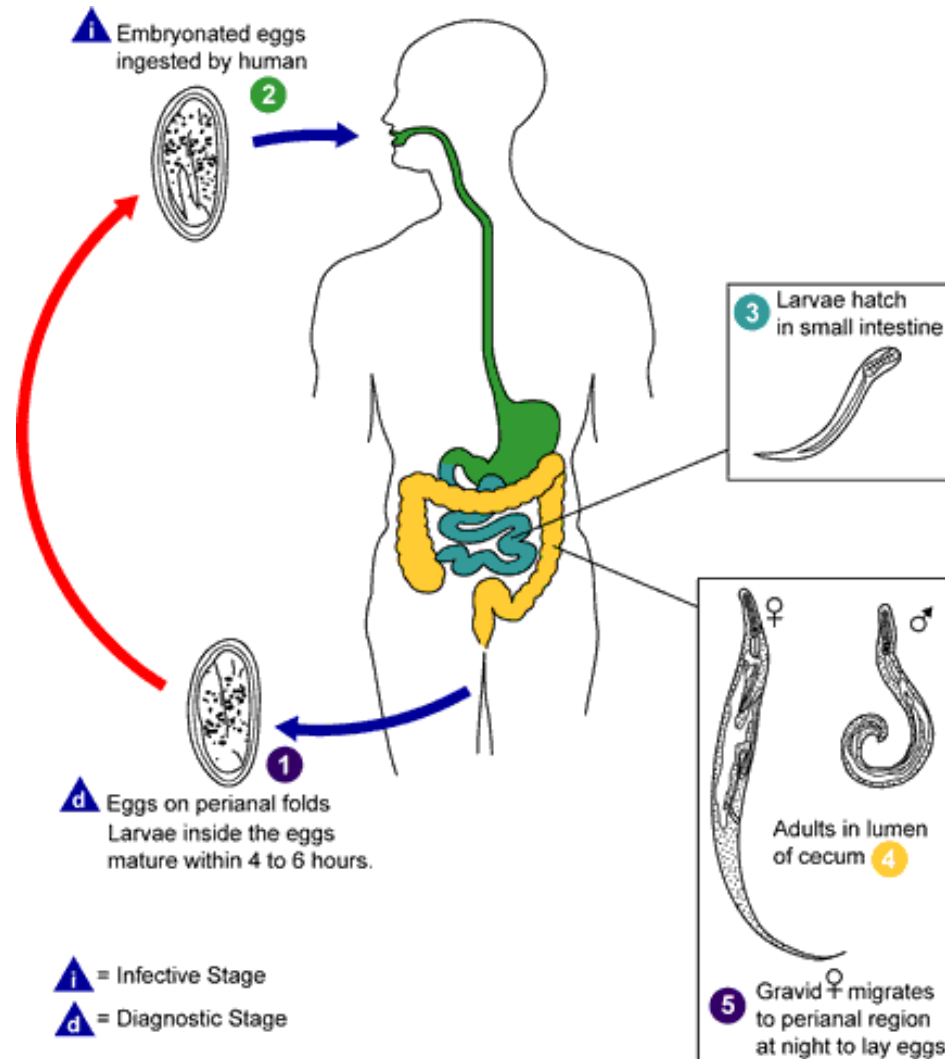
- Treat at least 75% of school-age children at risk for STH and Schistosome infections by 2010.**
- If carried out, this would become the largest health program ever attempted.**

***Enterobius vermicularis***  
**(Pinworms)**

**‘Tis better than riches  
To scratch when it itches.’**

**Anonymous**

# Lifecycle



# *Enterobius vermicularis*



**Male: 2-5 mm**



**Female: 8-13 mm**



# *Enterobius vermicularis* (*alae*)



# Definition

- Enterobiasis is a common infection of the intestinal tract caused by *Enterobius vermicularis*.
- Most infections are benign with anal pruritus as the only symptom.
- In more heavily infected patients (usually children) there may be loss of appetite, irritability, and insomnia.
- This infection is also referred to as oxyuriasis, pinworm infection, and threadworm or seatworm infection.

# Geographic Distribution

- **Enterobiasis is worldwide.**
  - More prevalent in temperate countries where bathing is less common.
  - Only infect humans
  - Most prevalent nematode infection of humans living in temperate climates.
- ***The Guinness Book of Records* claims that enterobiasis is the second most common infection (second only to the common cold).**
- **More than 291 million people are infected.**
- **Children are more commonly infected than adults, especially those living in crowded conditions.**

# Geographic Distribution

- **Prevalence in children in certain communities has been found to be as high as:**
  - **61% India**
  - **50% England**
  - **39% Thailand**
  - **37% Sweden**
  - **29% Denmark**

# Historical perspective...

- Dates back to Roman-occupied Egypt (30 BC- AD 395).
- Oldest known pinworm ova have been found in human coprolites dating back to 7800 BC from Danger Cave, Utah.
- Referenced in the writings of Hippocrates dating back to 430 BC.
- Ancient pinworm finds have occurred in a variety of archeological sites, the majority of them in the USA, with 2 from Chile, and one each from Peru, Mexico, Germany, Denmark, and Argentina, as well as one from a Han Dynasty mummy in China.



# Historical perspective...

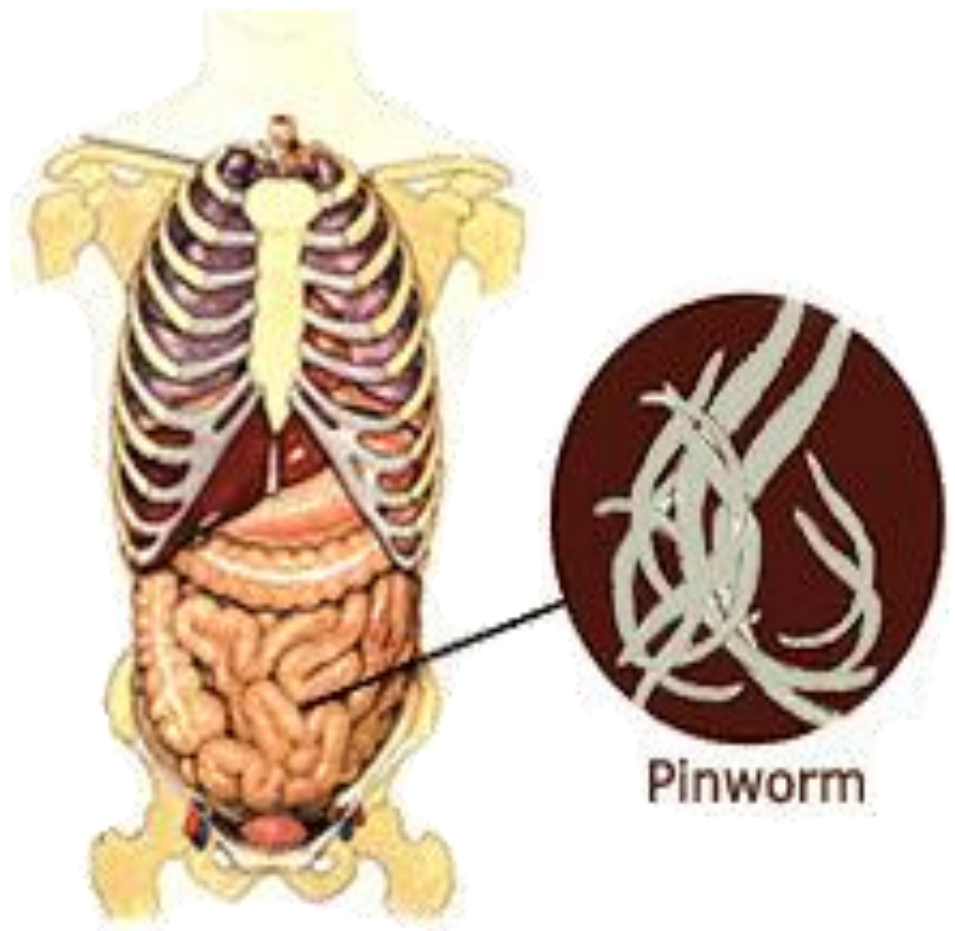
- Pinworm findings outside the New World have been scarce.
- Hypothesized to have arrived by land.
- One of the few helminths that could have arrived through this route.





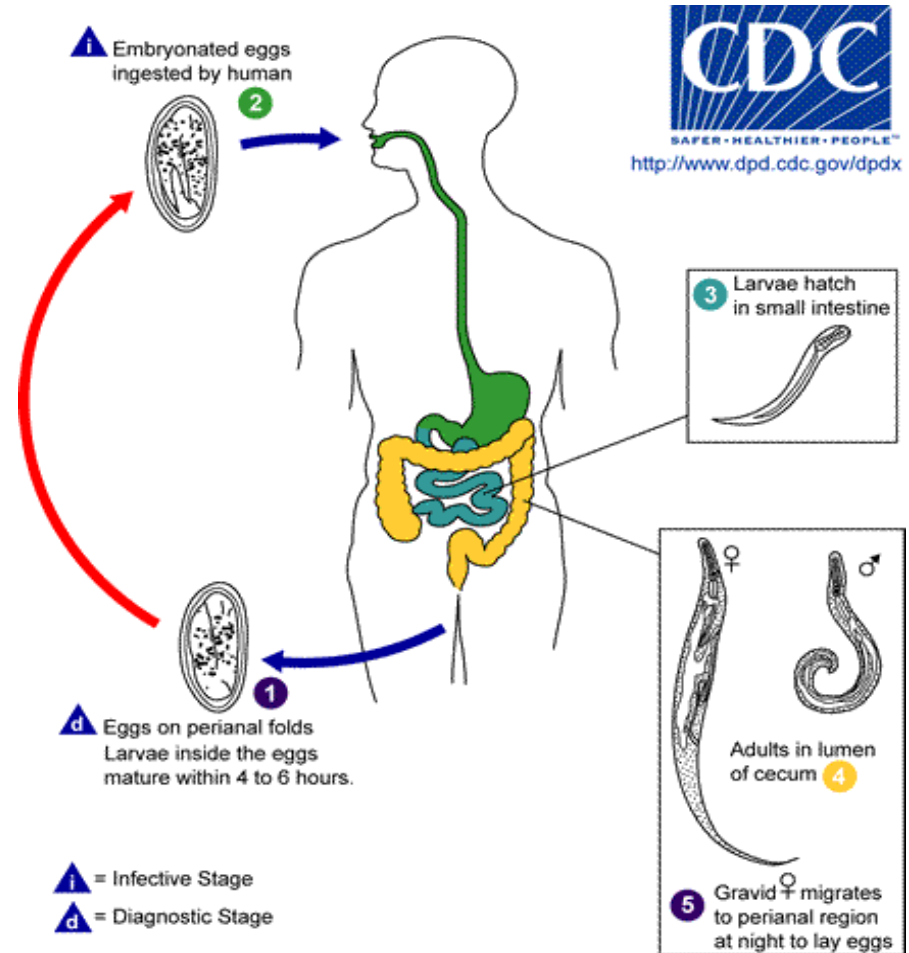
# Lifecycle

- Adults live in the lumen of the **transverse** and **descending** colon.
- Adults feed on *E. coli* and other bacteria found in formed stool.
- Embryonated eggs are swallowed and hatch into Second-stage larvae in the small intestine (L3 and L4 develop there too).
- Adults take up residence in the large intestine.



# Lifecycle

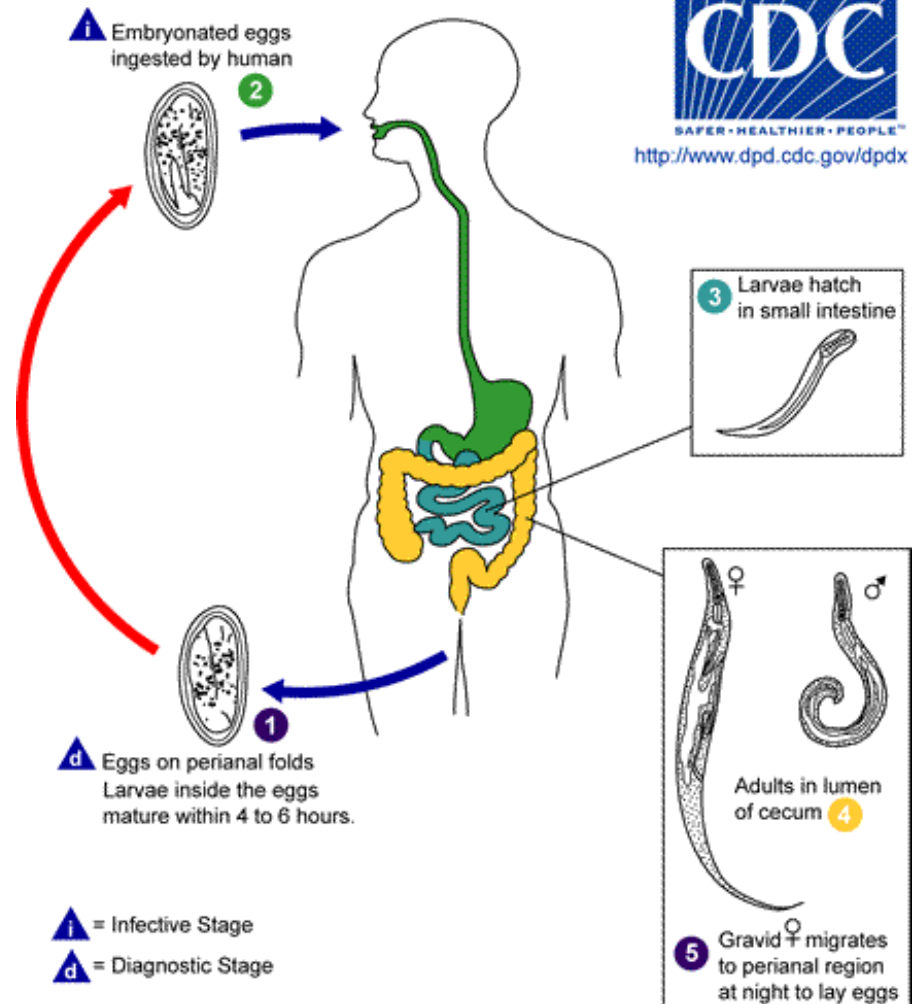
- Entire process lasts 4-6 weeks.
- Alternatively (*i.e.*, if not swallowed) eggs can hatch at the site of deposition and crawl back up through the anus.
- Retrograde infection
  - Vaginal infections.





# Lifecycle

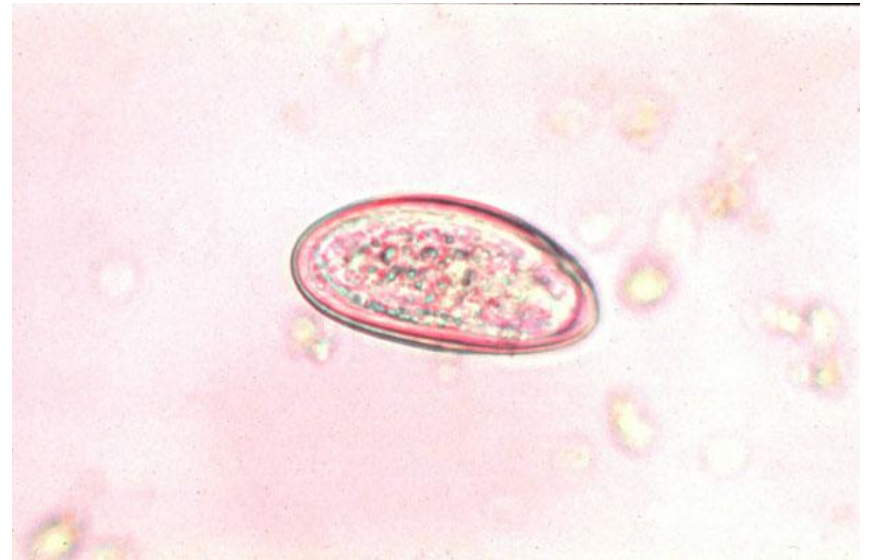
- 6 weeks after mating the female can produce between 5000-17,000 eggs.
- The female migrates to and through the anus and dies after oviposition.
- Eggs become infective after 6 h.





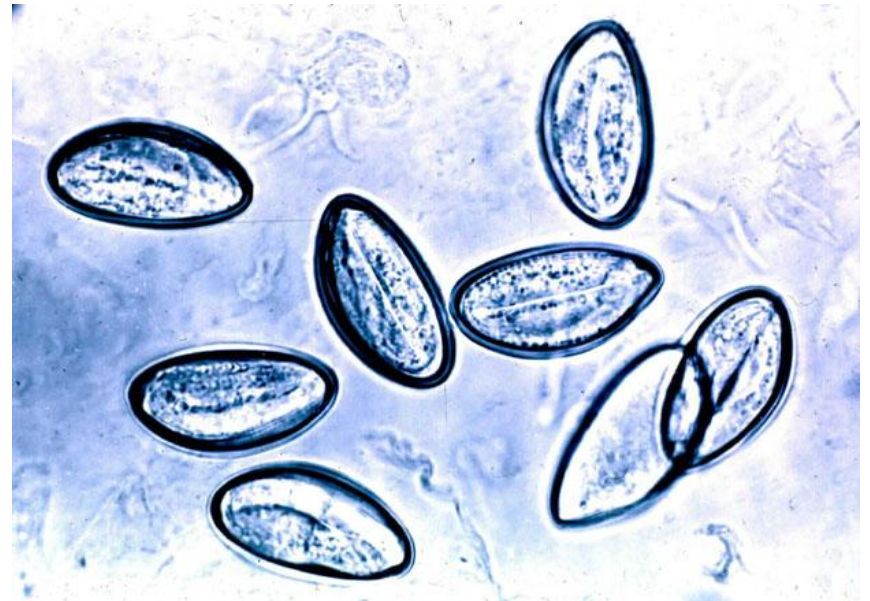
# Enterobius eggs

- **50-60  $\mu\text{m}$  by 20-30  $\mu\text{m}$**
- **Colorless, asymmetrical, and flattened on one side.**
- **Egg shell has 2 layers and is smooth and thick.**
- **The outer albuminous layer is sticky and this is the portion that causes intense anal itching.**
- **This ultimately results in egg spreading.**



# Enterobius eggs

- Eggs can survive up to two weeks.
- Resistant to commercial disinfectants.



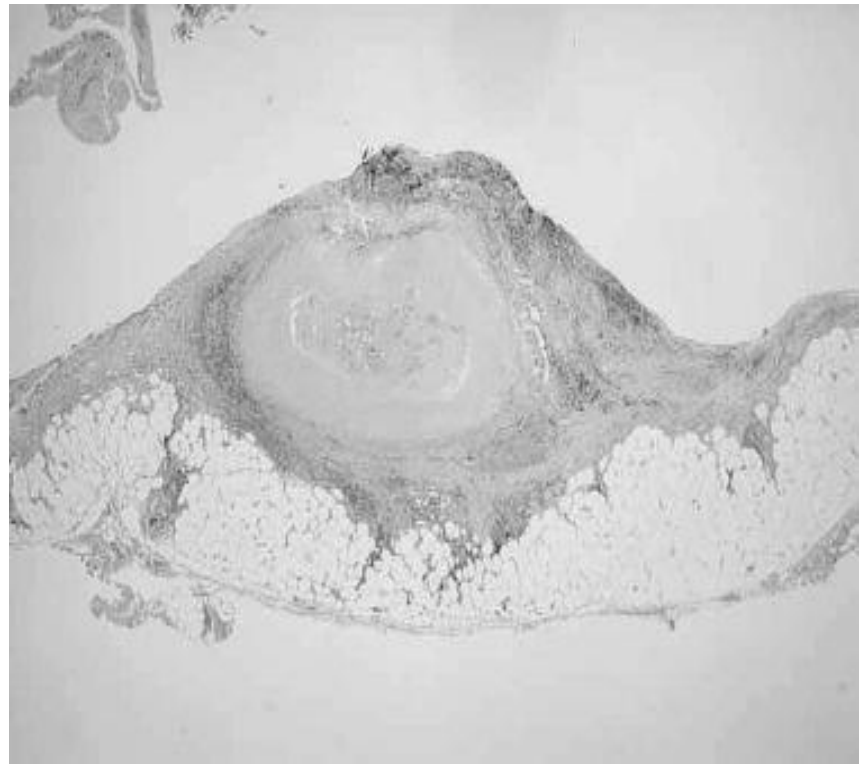
**Pinworm tape**

# Symptoms of Infection

- Most individuals are symptom free.
- Itching of perianal area.
- Aberrant infection leads to vaginal itching/discharge.
- Abdominal pain may be documented if patients co-infected with *Dientamoeba fragilis* ('piggy-backed' infection).
- Susceptibility to infection decreases with age.

# Pathology

- **Enterobius infections seldom causes serious lesions.**
- **Rarely worms cause petichial hemorrhage of cecum, appendix, and lower ilium from penetration.**
- **Deeper invasion causes a granulomatous reaction.**
- **Appendicitis????**



**Granulomatous reaction to  
*E. vermicularis* ovum.  
Thomson, J.C. *J. Obstet.  
Gynaecol. Res.* 30:90-95. 2004.**

# Diagnosis/Treatment



- Egg identification or adult worms.
- Ova rarely in feces and are best collected from perianal skin by using the sticky side of cellulose tape applied to skin.
- **TREATMENT:** Mebendazole (100 mg single dose) is drug of choice. Piperazine hexahydrate (50-75 mg/kg daily for 7 days and pyrantel pamoate (10 mg/kg single dose) are less effective

# Prevention and Control

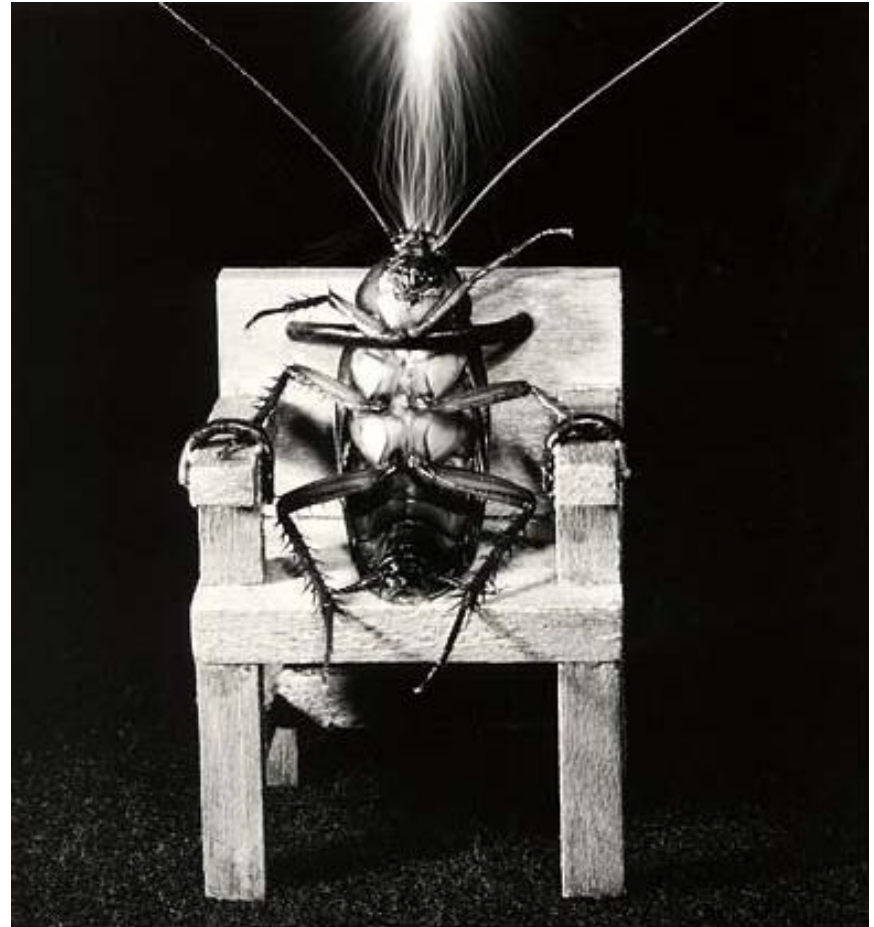
- **None.**
- **No predilections on the basis of sex, race, or socioeconomic class.**



# The cockroach as a host for *Trichinella* and *Enterobius vermicularis*: implications for public health.

- Known carriers of bacteria and fungi that produce disease in humans.
- Link between pathogenic helminths and cockroaches has not been explored.
- **Study showed that there are naturally occurring infection of cockroaches with *Trichinella* and *Enterobius*.**
- Reservoirs for nematodes.

Chan O.T., Lee E.K, Hardman J.M., Navin J.J. *Hawaii Med. J.* 63:74-77. 2004.



# Trichinellosis

**Trichinosis, n.** The pig's reply to proponents of porcophagy.

**Ambrose Bierce (1842-1914?), *Devil's Dictionary***

**Despite their reputation, pigs are clean and wallow in mud to protect themselves from the sun's heat and from lice and other parasites.**

**Grolier Multimedia Encyclopedia (1996)**

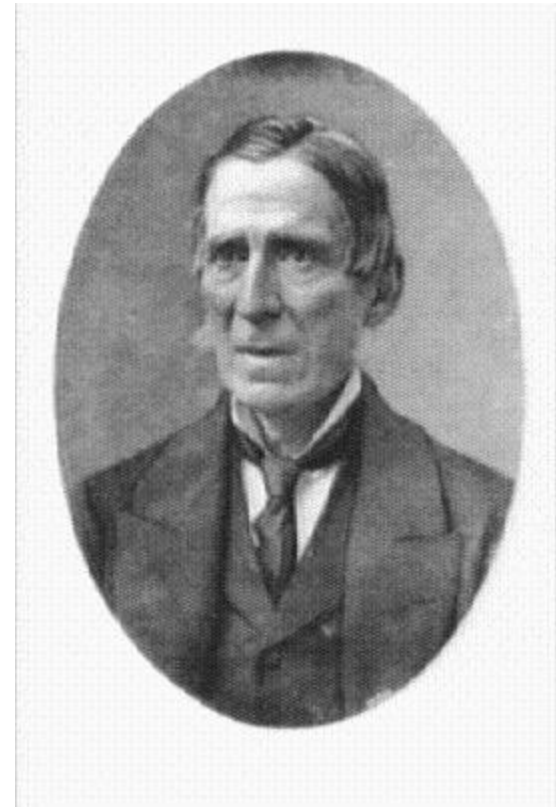


# Trichinellosis

- Trichinellosis (or trichinosis) is caused by *Trichinella spiralis* (superfamily **Trichuroidea**).
  - *T. murrelli*, *T. paupae*, *T. pseudospirallis*,  
*T. britovi*, *T. nelsoni*, *T. zimbabwensis*.
- Other medically significant members of this superfamily include *Trichuris truichiura* (whipworm), *Capillaria hepatica*, *C. philippinensis*, and *C. aerophila*.

# Discovery

- **Discovered by Richard Owen & James Page (right).**
- **First to describe the larva of *Trichinella* in a human diaphragm in 1835.**
- **Life cycle of *T. spiralis* not described until 1860.**



# Historical Perspective

- Trichinella has been identified in the intercostal muscles of mummified Egyptians (1200 B.C.).
- Major cause of political and economic disputes between the pork industries and governments of U.S. and the European nations, who considered U.S. pork unsafe in the late 1800s.



**A nineteenth century Danish cartoon showing the arrest of trichina worm by police. *New York: Plenum Press, 1983.***

# Historical Perspective

- **Early outbreaks in Germany (1860-1880) had mortality rates of up to 30%.**
- **Outbreaks in the Arctic in the late nineteenth and early twentieth centuries hindered exploration.**
- **In 1897, the occupants of an ill-fated hydrogen balloon expedition in the Arctic died, not from exposure, but from acute trichinellosis acquired from eating uncooked bear meat.**
- **Incidence in the U.S. has declined significantly (100 cases/year).**

# Trichinellosis Definition

- Diseases caused by *Trichinella spp.*
- *T. spiralis* and *T. murrelli* cause the majority of the human cases.
- The domestic pig is the main reservoir for *T. spiralis*.
- *Trichinella spp.* Infect a broad-spectrum of mammalian hosts.
- One of the world's most widely-distributed group of nematode infections.
- Other species can infect humans (e.g., *T. pseudospiralis*, *T. paupae*, *T. nativa*, and *T. britovi*).
- **UNIQUE** in that this group of nematodes live a part of their lives as intracellular parasites.



# Reservoirs for *Trichinella* spp.

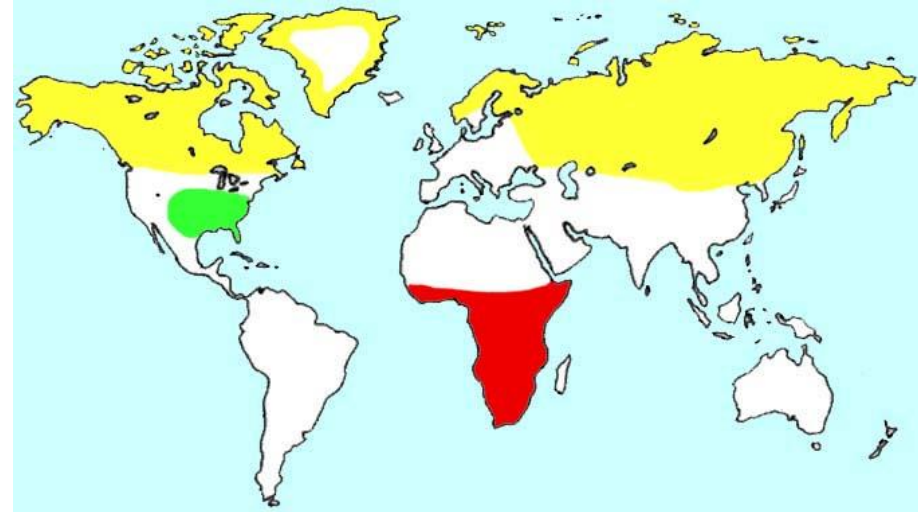




# Geographic Distribution



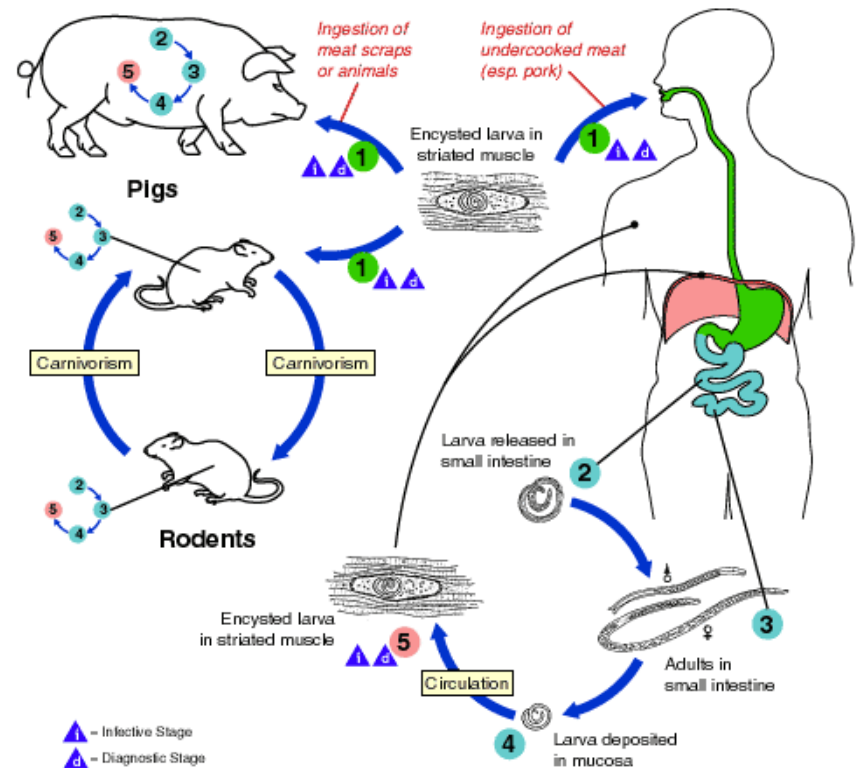
**Green=** *T. spiralis* (most common member of the genus).



**Yellow=** *T. nativa* (carnivores)  
**Red=** *T. nelsoni*  
(Hyaenidae/Felidae)  
**Green=** *T. murrelli* (carnivores)

# Life Cycle

- 1. Ingestion of meat containing cysts (**Nurse cell-larva complex**).
- 2. Pepsin induces larvae to be released, invade the small bowel mucosa where they develop into adults.



# Life Cycle-Nurse Cell

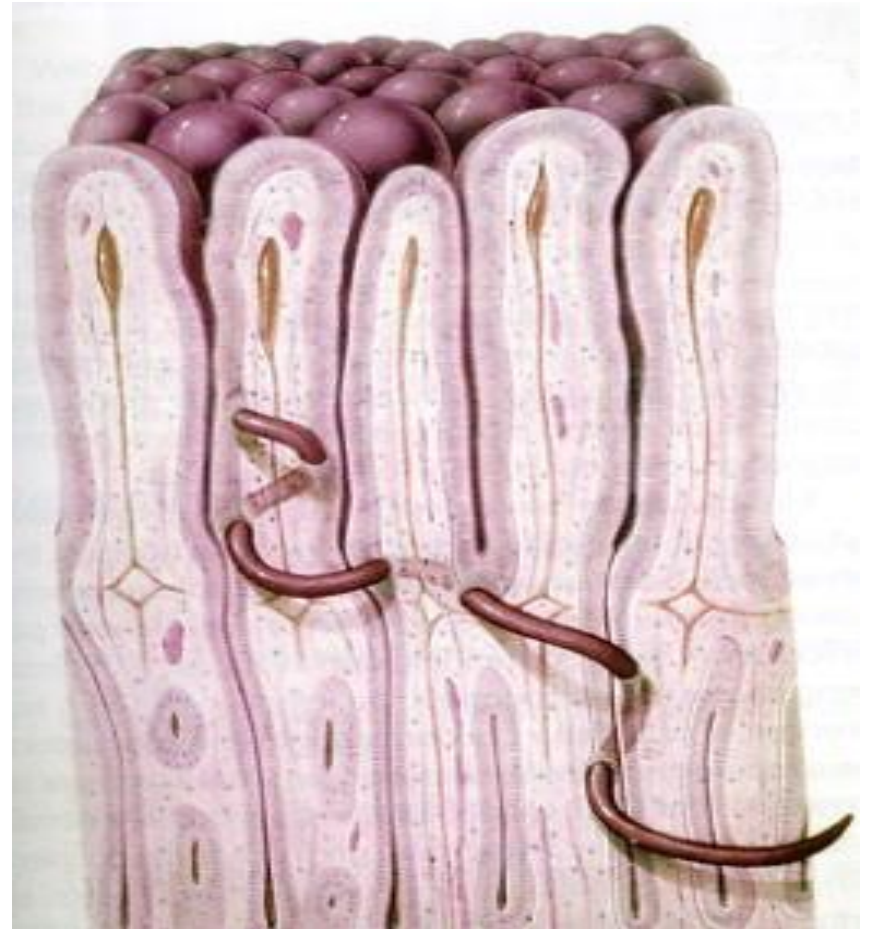


# Life Cycle-Newborn Larvae



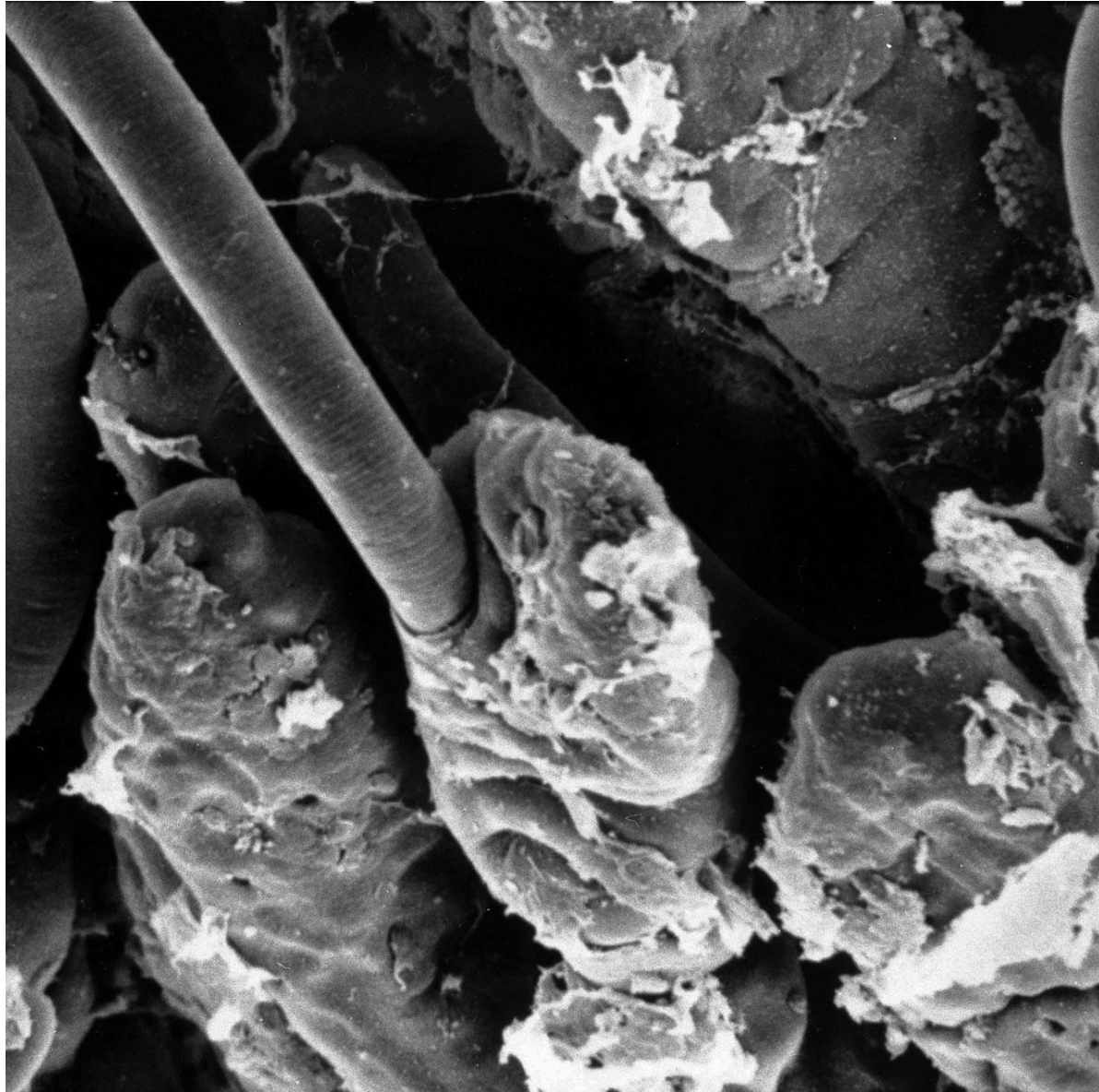
# Life Cycle

- The immature parasites penetrate the columnar epithelium at the base of the villus.
- They live within a row of these cells, and are considered **intra-multi-cellular** organisms.

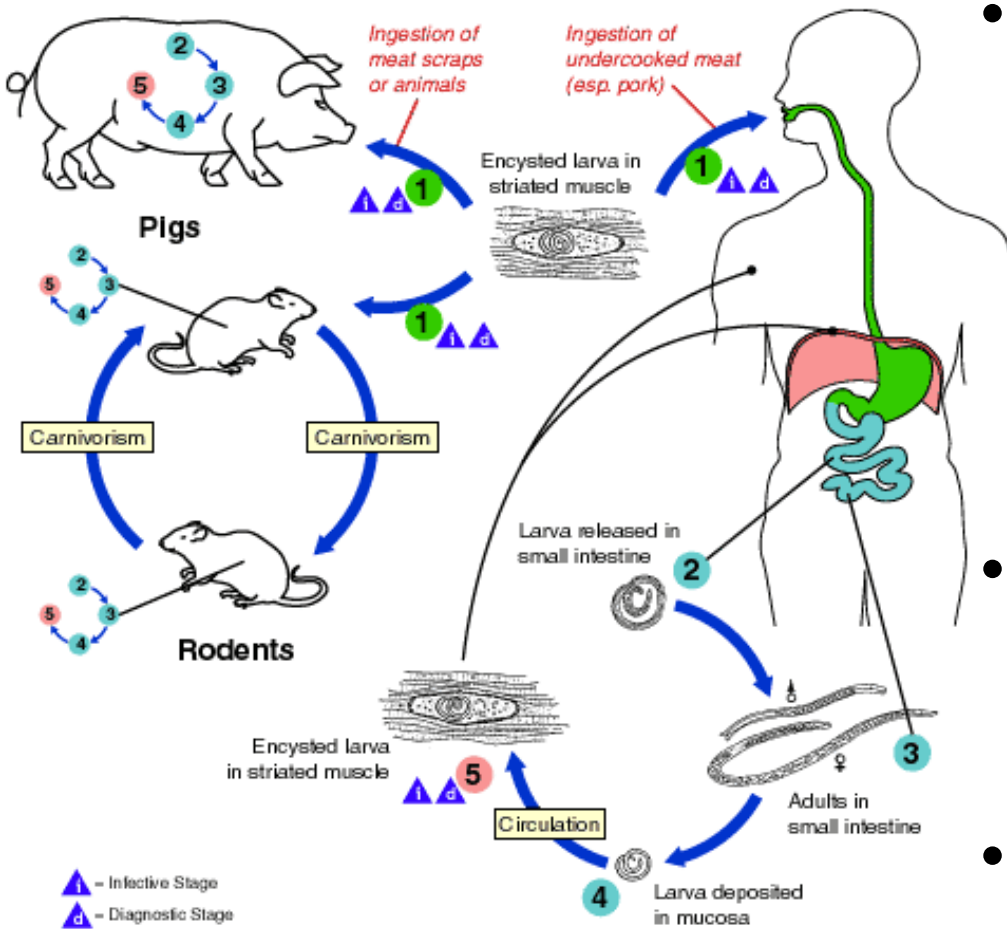




# Life Cycle-L1 Entering Cells

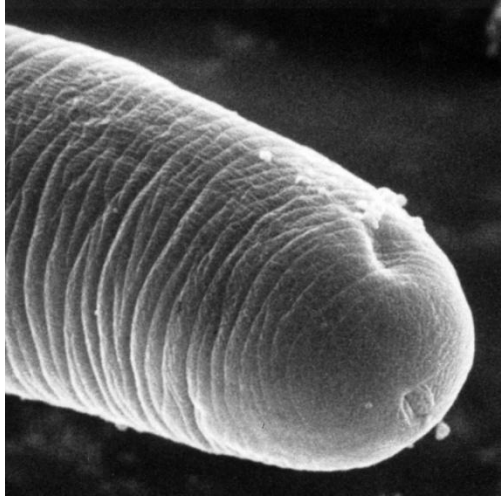


# Life Cycle



- Larvae molt four times in rapid succession over a **30-hour** period, developing into adults (4 weeks).
- Patency occurs within five days after mating.
- Adult females produce newborn larvae.

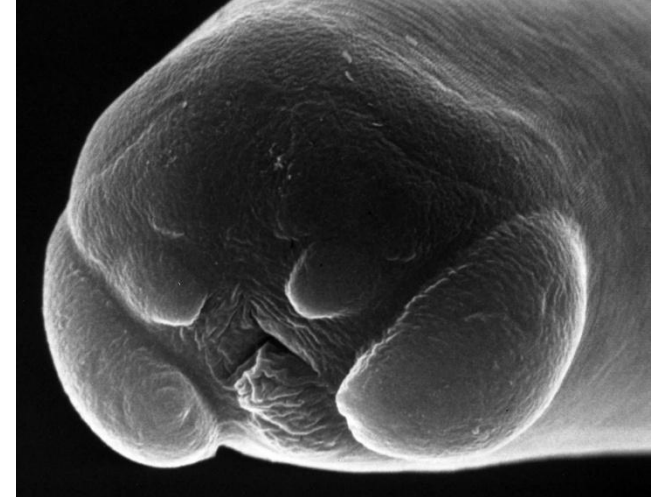
# Male Worm Development



6 h



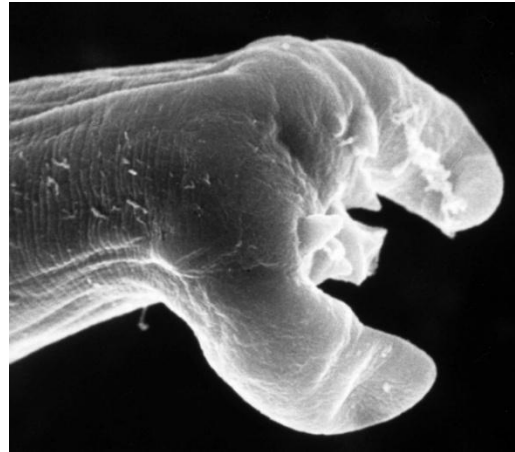
13 h



17 h



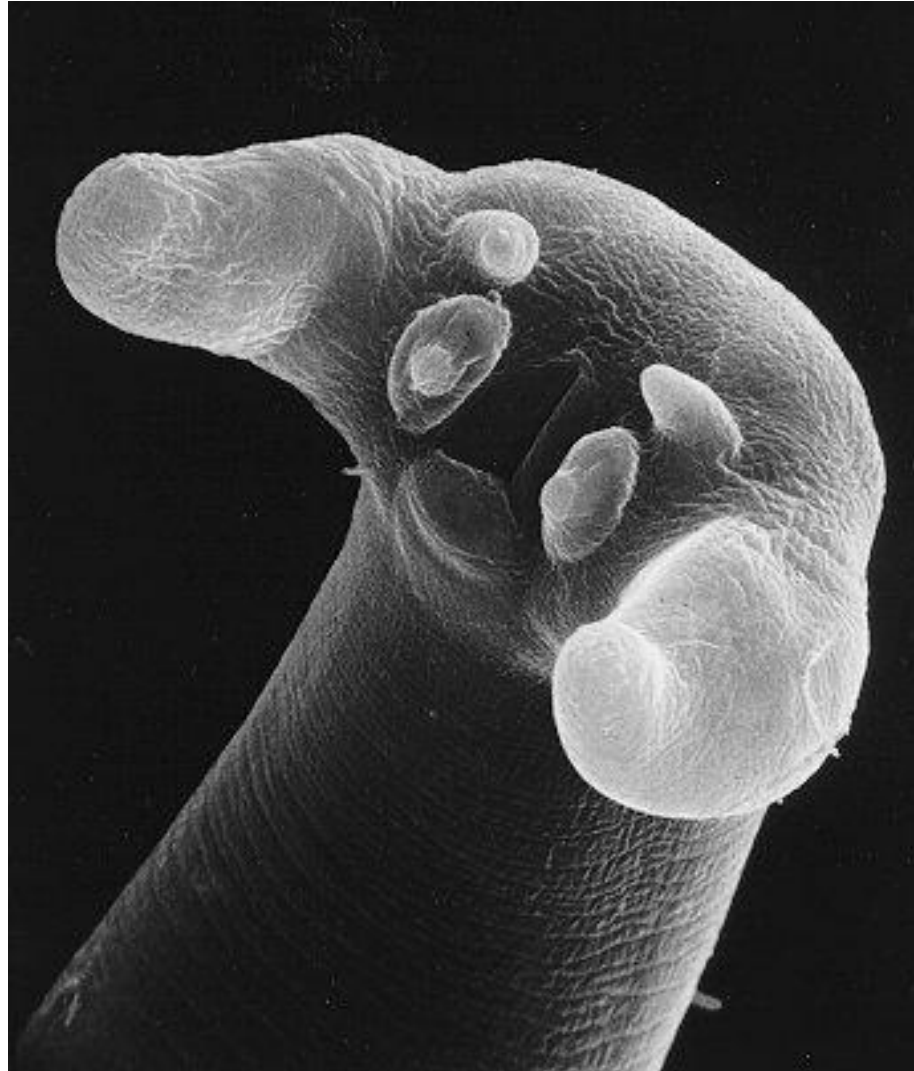
24 h



Adult



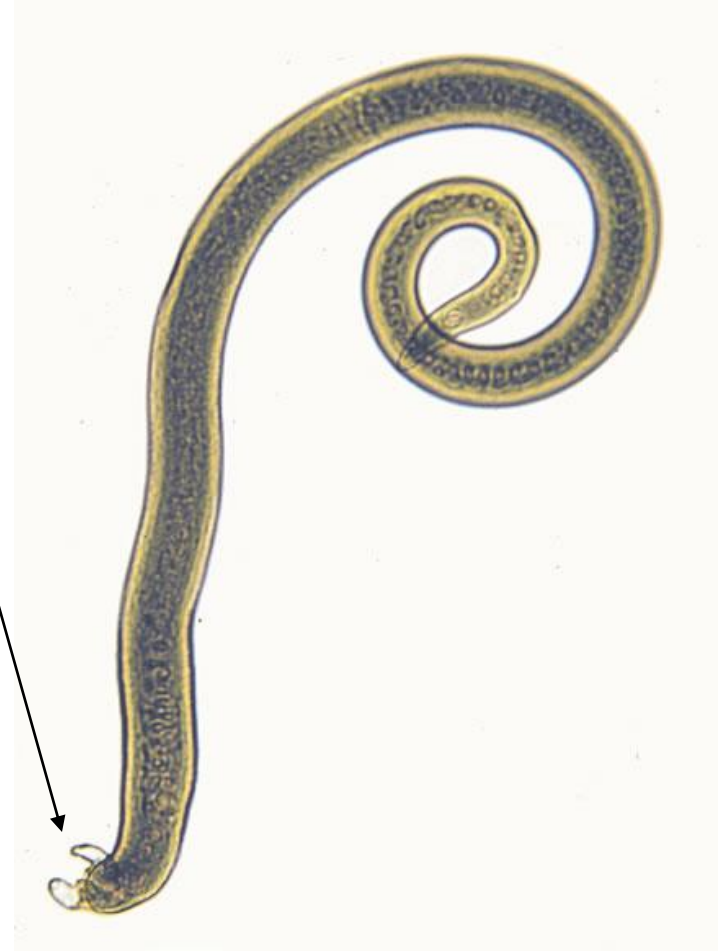
# ***Trichinella* spp. Claspers**



# Life Cycle



**Female: 3 mm**



**Male: 1.5 mm**

**Full-formed larvae in uterus  
--Viviparous**

# Life Cycle-Female and Offspring



Each female can produce up to 500 larvae.



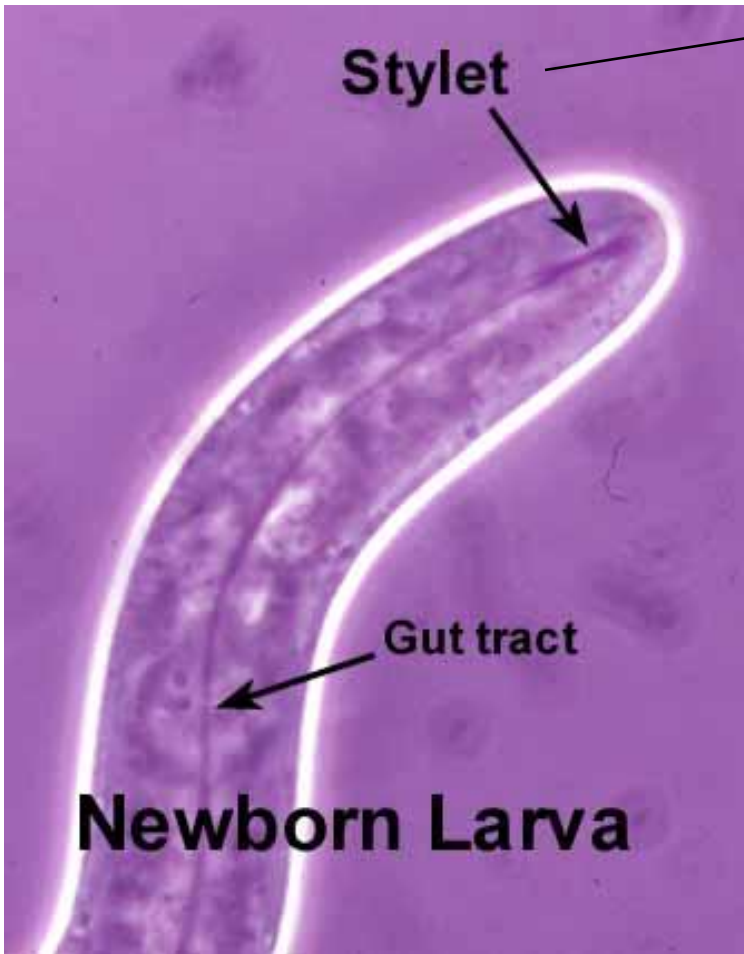


# Life Cycle

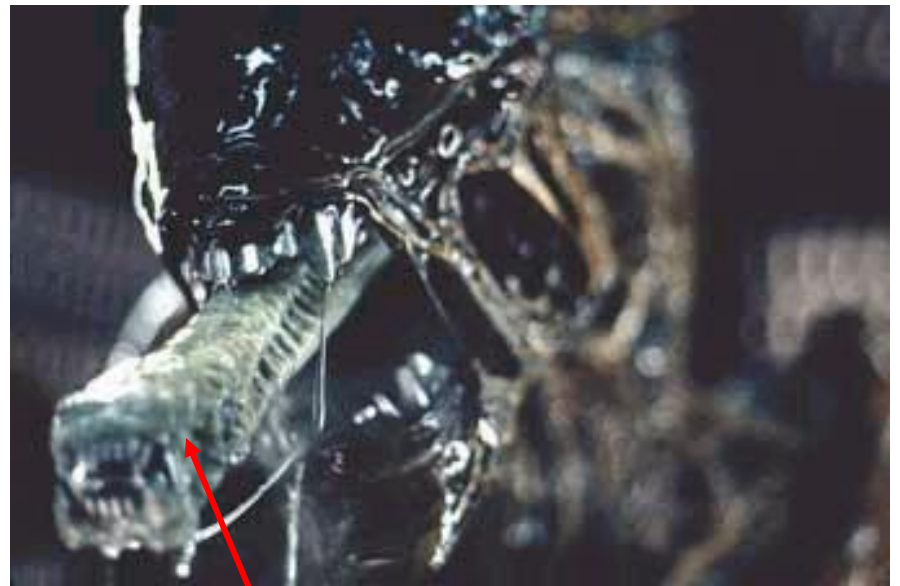
- **Newborn larvae are 0.08 mm in length.**
- **The adult female will produce offspring as long as host immunity (acquired) does not develop.**
- **Newborn larvae are the only stage of the parasite that possesses a sword-like stylet, located in its oral cavity.**



# Stylet



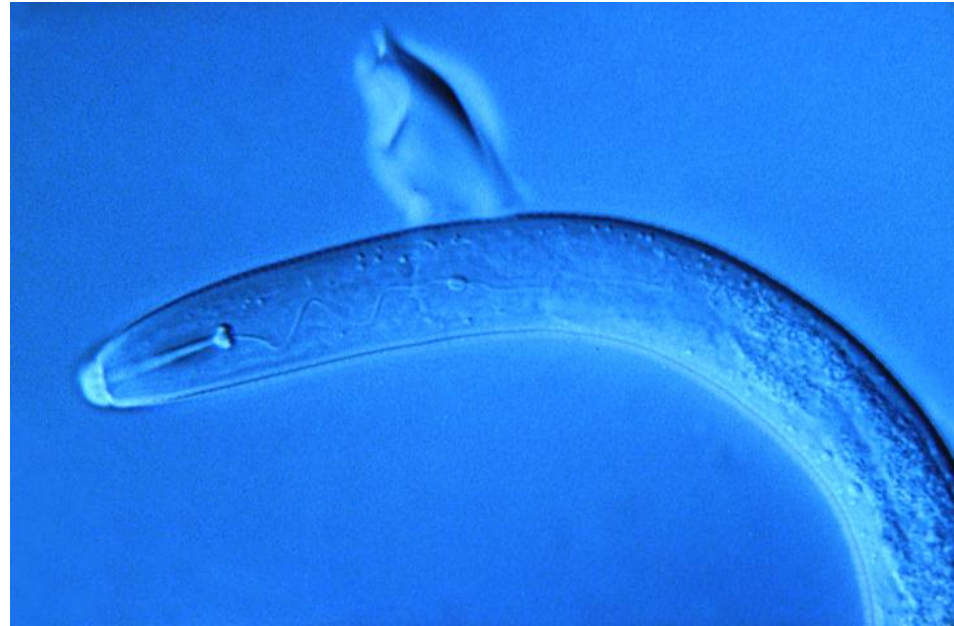
Used for creating an entry hole  
In potential host cells.



Stylet?

# Larvae

- Larvae then enter the lamina propria and penetrate into either the mesenteric lymphatics or into the bloodstream.
- Most enter the general circulation and become distributed throughout the body.
- Larvae leave circulation and enter cells.
- Larvae die after entering host cells unless they are muscle cells.
- **NO TROPISM.**

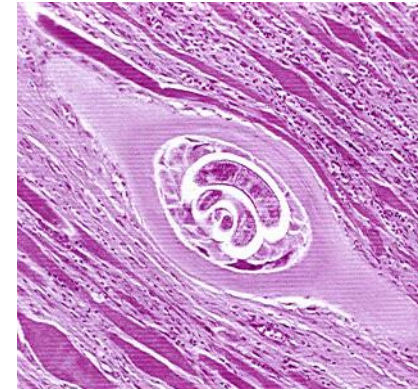
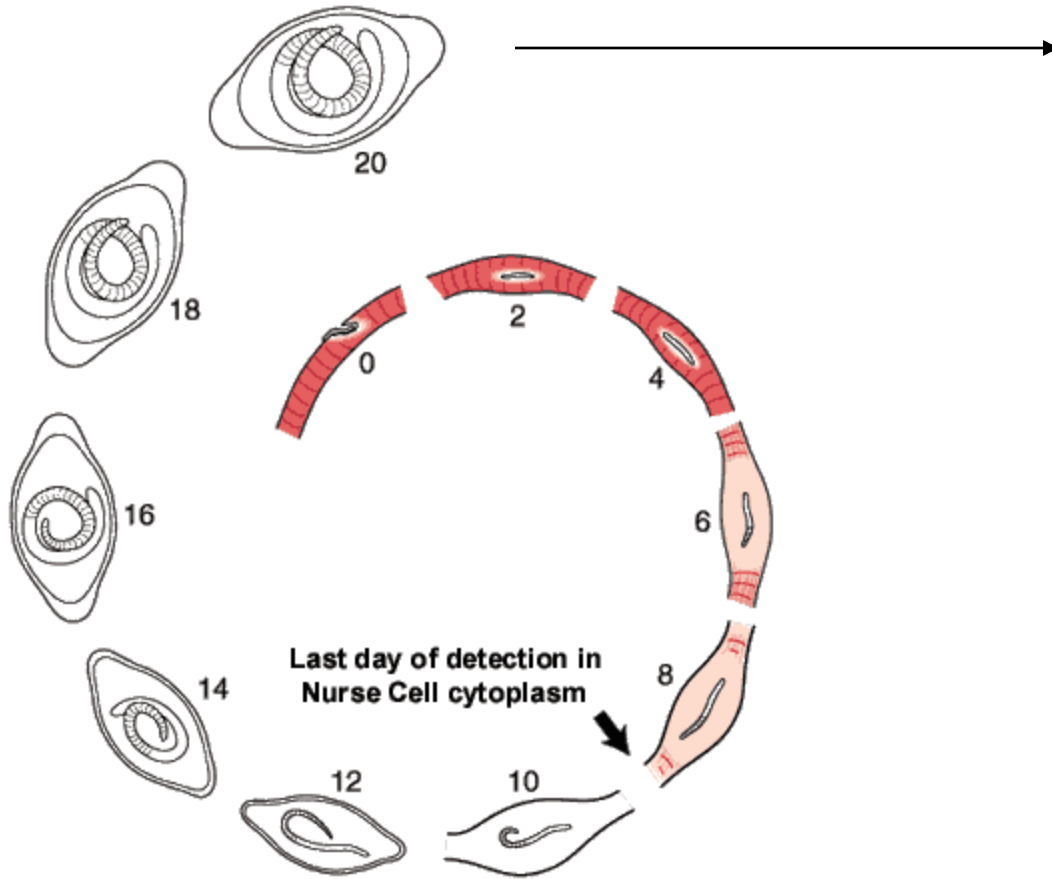




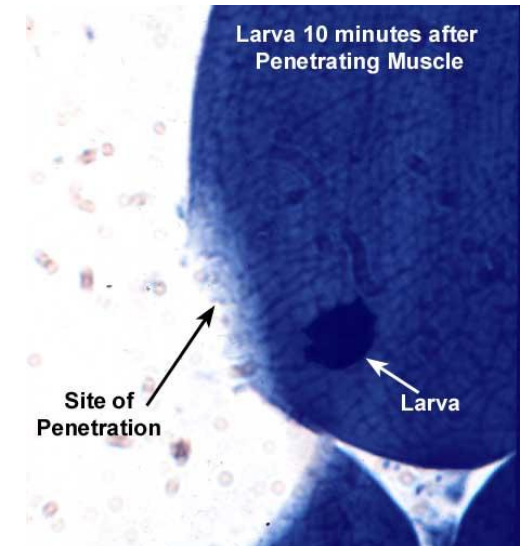
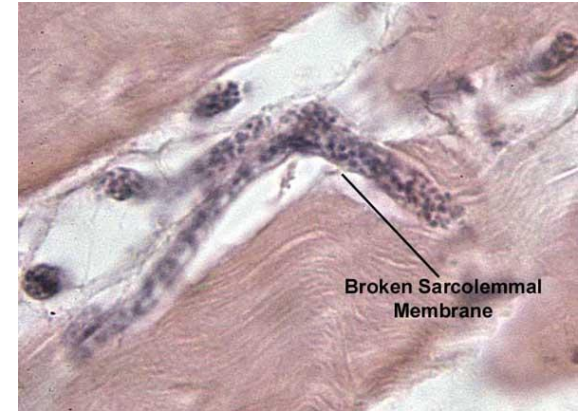
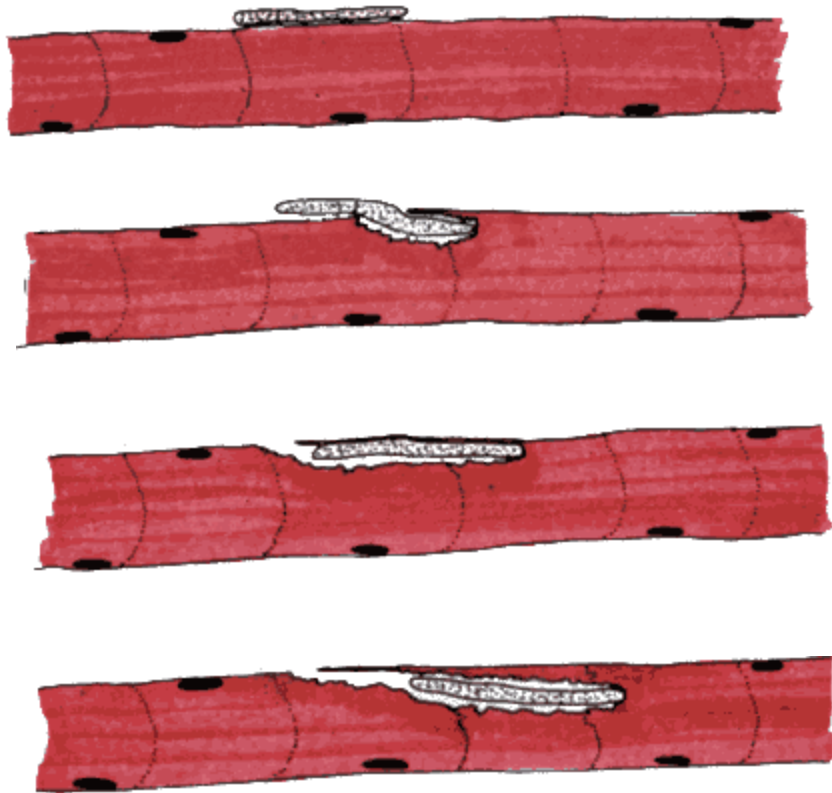
# Nurse cell formation

- Larvae entering muscle cells not only remain inside them but they induce a remarkable series of changes to this cell type.
- Transforms muscle cell into a factory that supports the growth and development of the larva.
- This process is termed Nurse-cell formation.
- The net result is that the host cell switches from an aerobic to anaerobic metabolism.
- *T. spiralis* is infective by day 14 (continues to grow up to day 20).

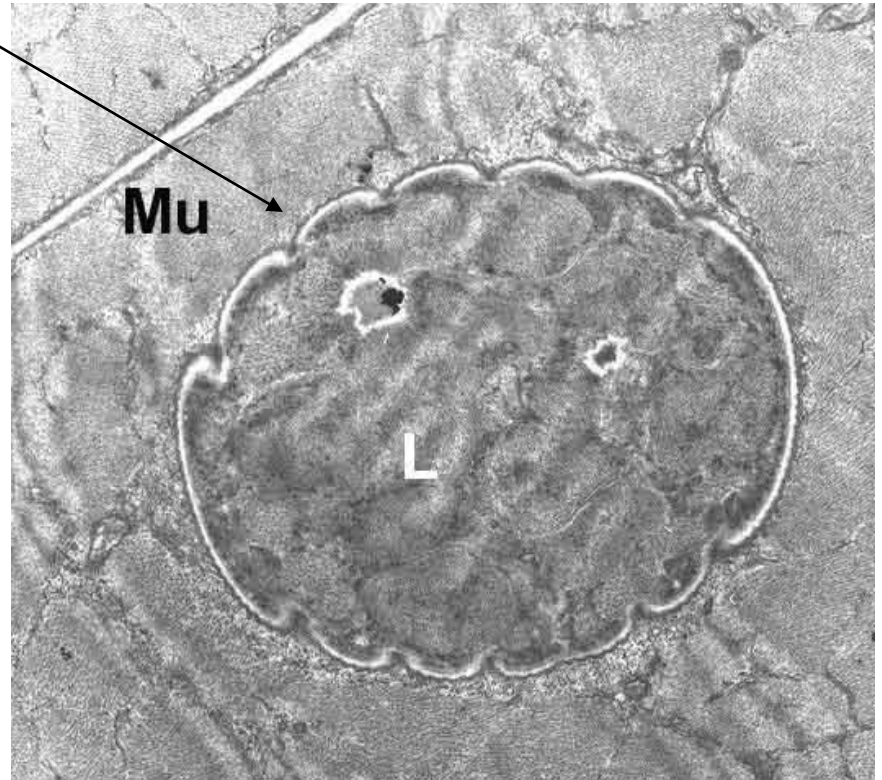
# Nurse cell formation



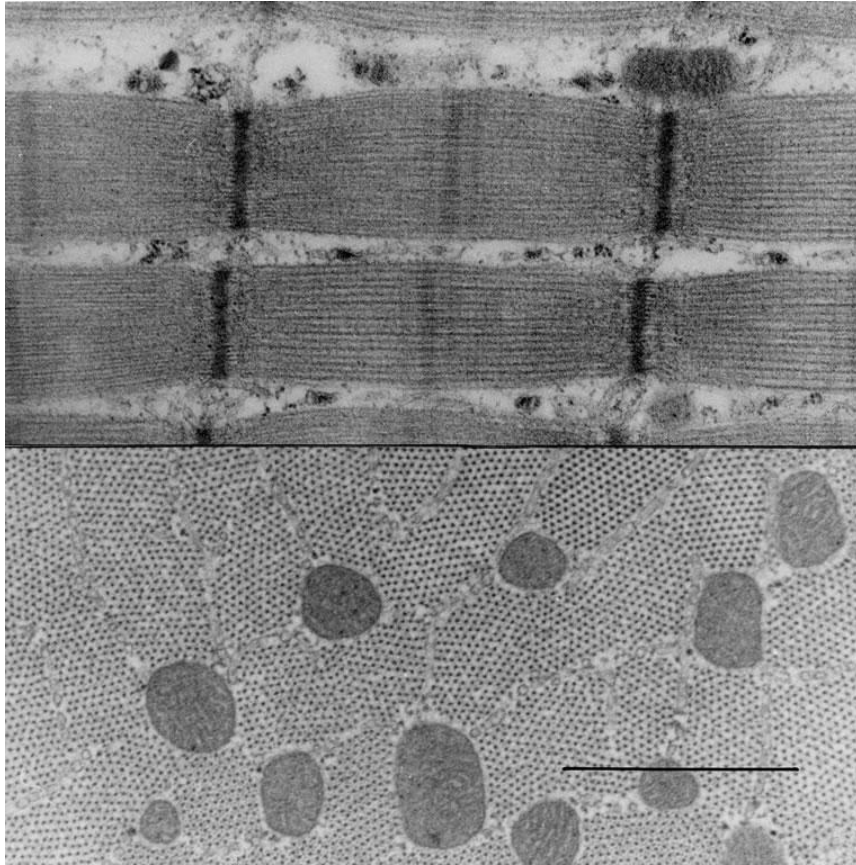
# Muscle Cell Penetration



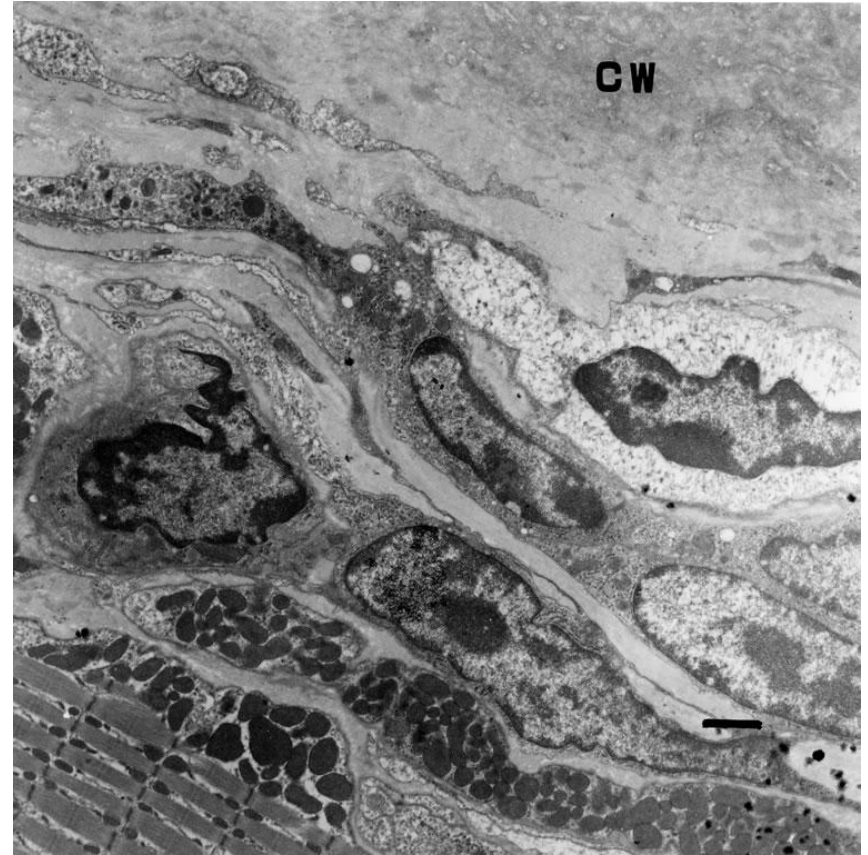
# Muscle Cell Penetration



# Muscle-Nurse Cell Development



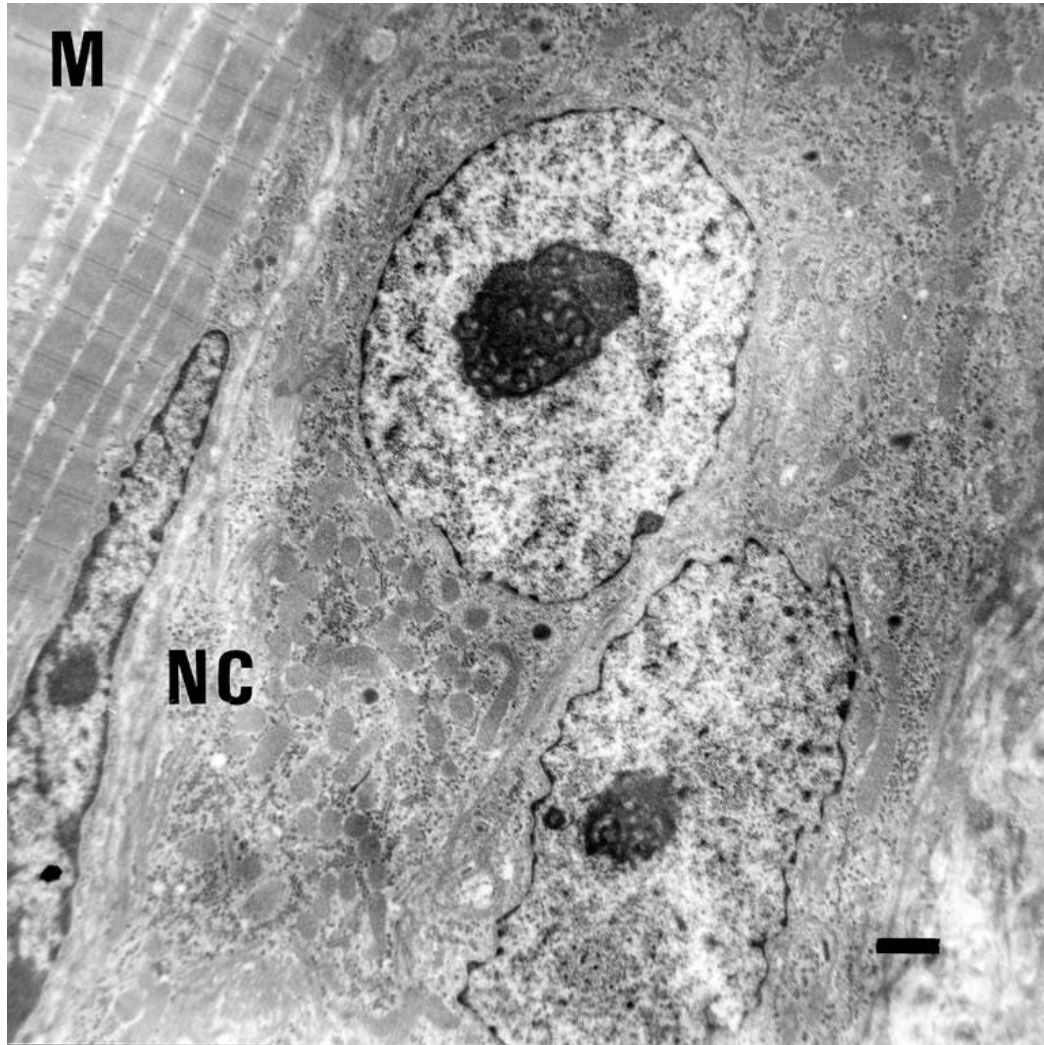
**Normal Muscle**

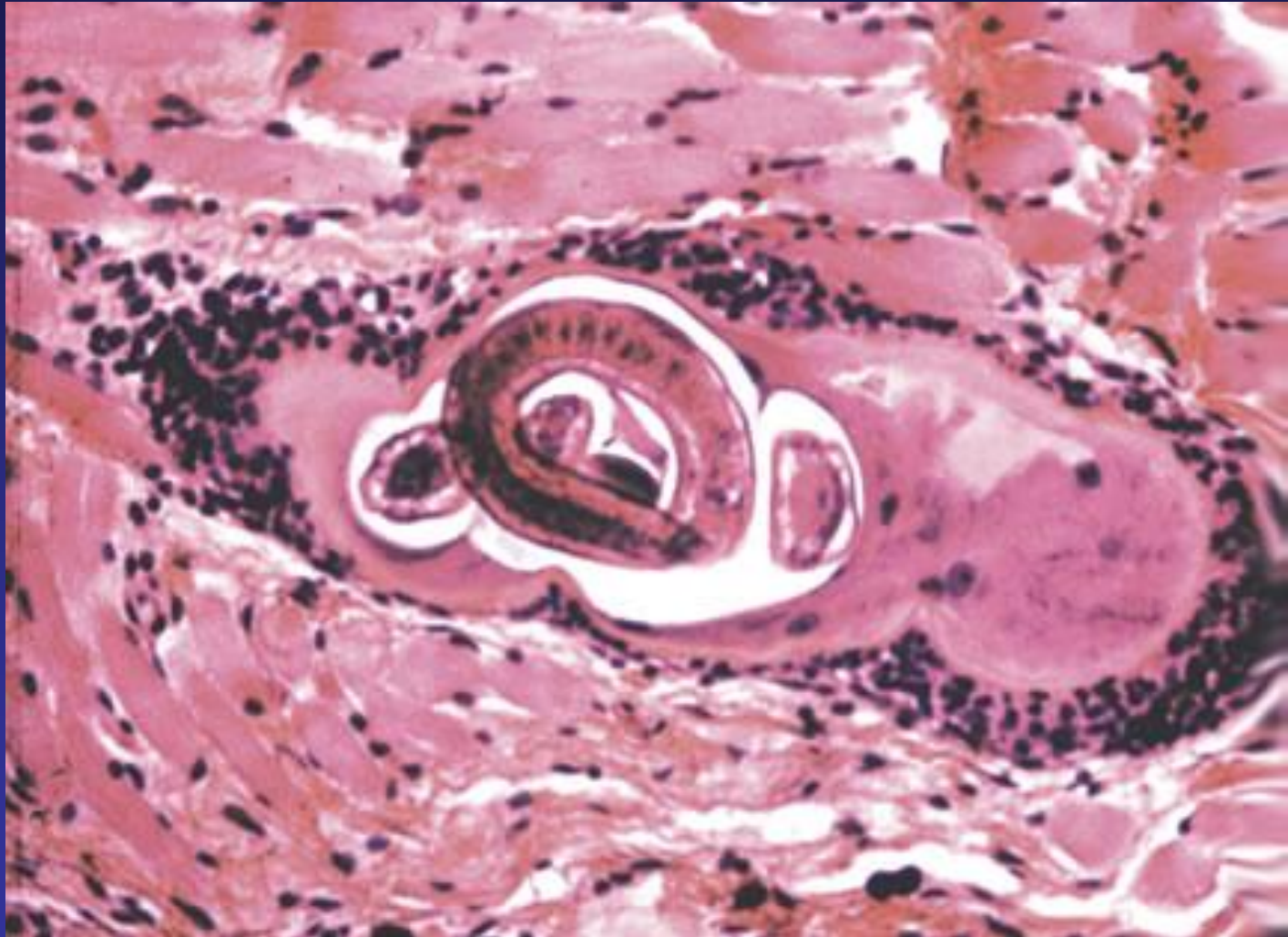


**Infected Muscle**



# Muscle-Nurse Cell Development

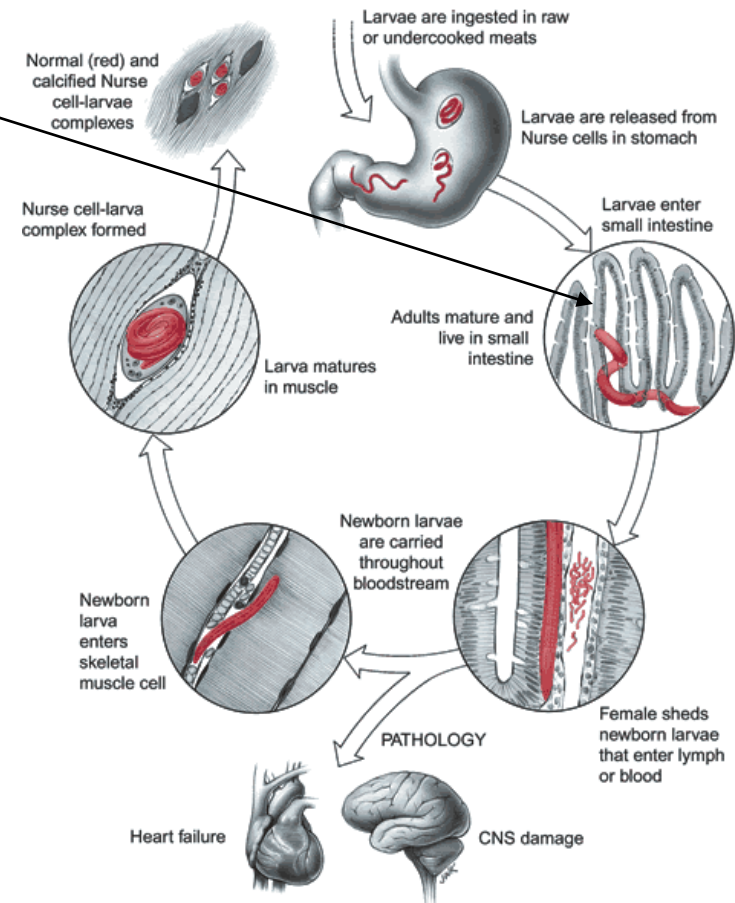






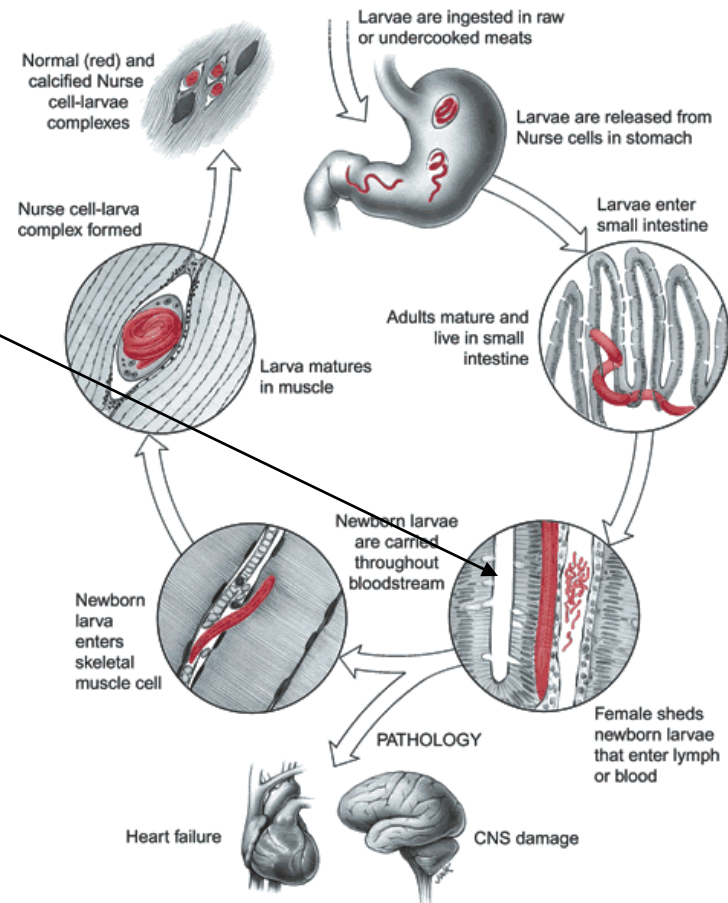
# Pathogenesis

- In the enteral (intestinal) phase (L1-4), immature/mature adults developing worms can damage columnar epithelium.
- Local inflammation



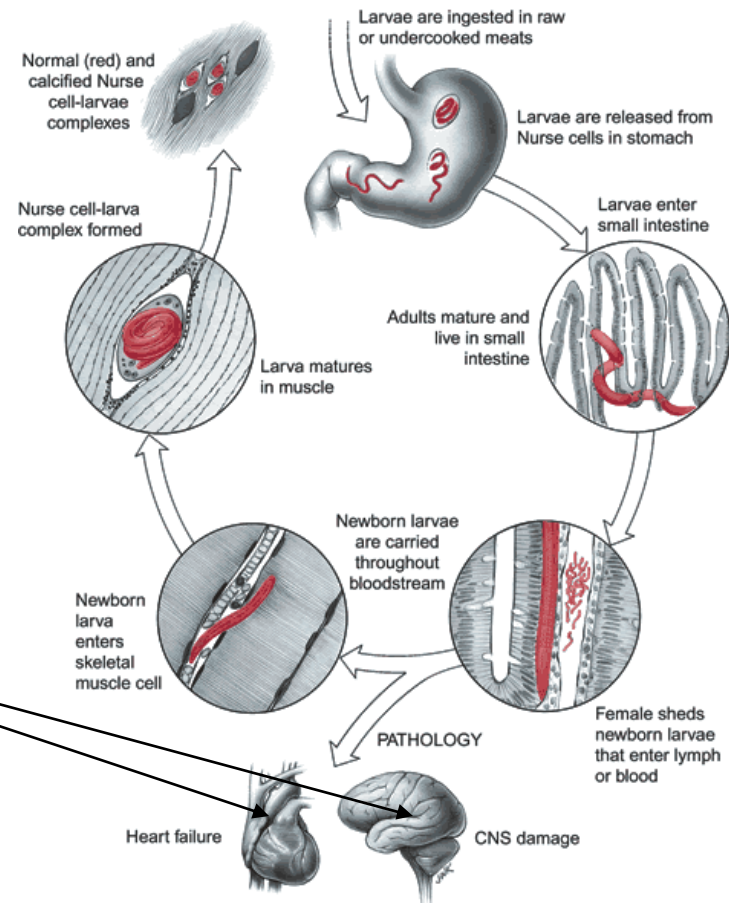
# Pathogenesis

- When larva penetrate lymphatics or circulation, bacteremia due to enteric flora may result and death as a result of sepsis has been reported.



# Pathogenesis

- Parenteral phase causes the pathological consequences.
- **Dose-dependant.**
- **Attributable directly to the migrating newborns as they RANDOMLY penetrate cells.**



# Clinical Disease

- **Disease presentation varies over time.**
- **Severity is dose-dependent.**
- **First few days: gastroenteritis associated with diarrhea, abdominal pain, and vomiting (abates within 10 days).**
- **Confused with food poisoning.**

# Clinical Disease

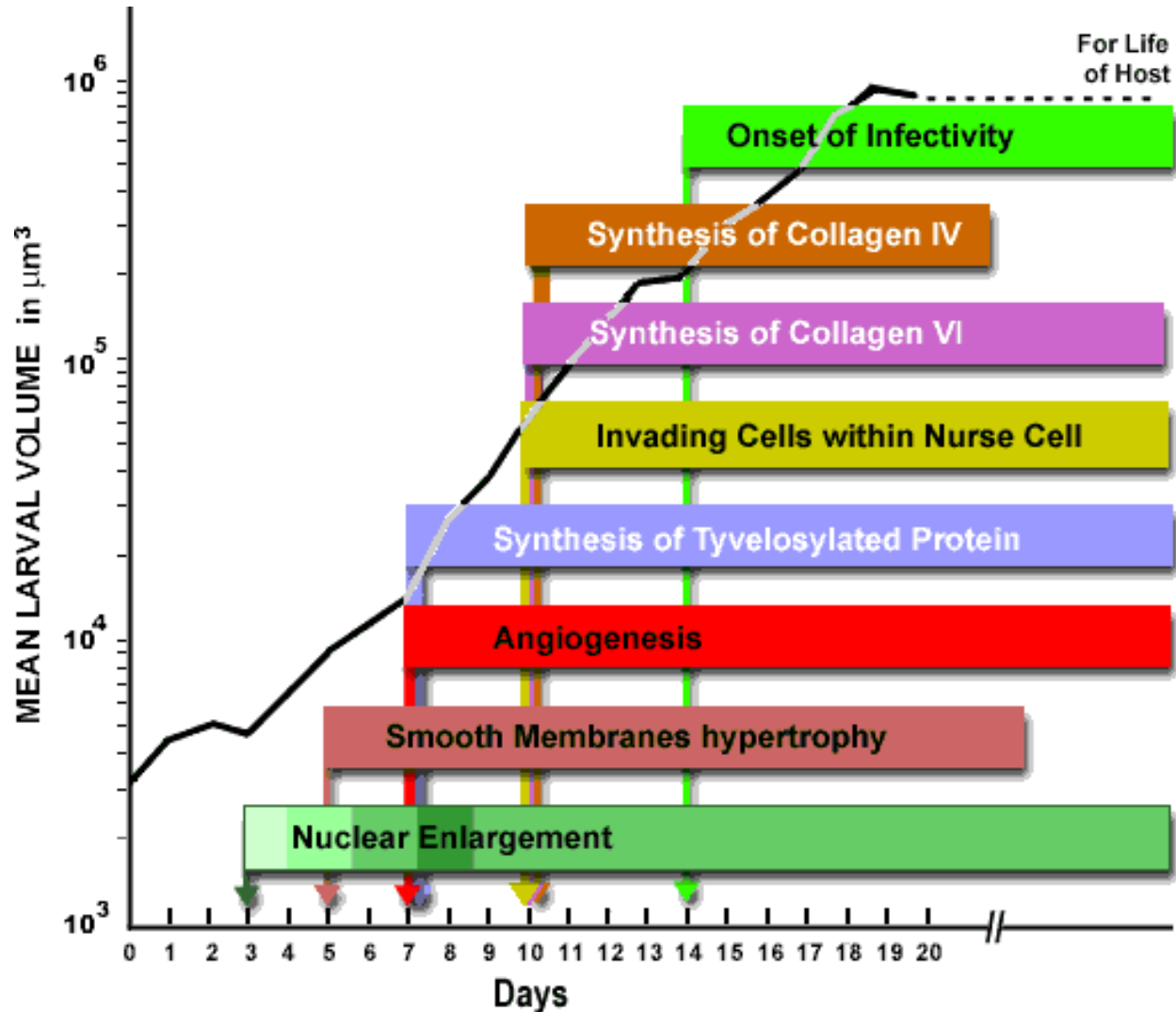
- **Parenteral phase associated with fever and myalgia, bilateral periorbital edema, and petechial hemorrhages.**
- **Eosinophilia**
- **Fever**
- **Weakening of muscles.**
- **Headaches**
- **Shortness of breath.**
- **Elevated WBCs.**



# Clinical Disease

- Larvae penetrating muscle tissues can result in cardiovascular involvement.
- Invasion of the diaphragm and the accessory muscles result in dyspnea.
- Neuro-trichinellosis

# Summary of Infection





# Diagnosis/Treatment

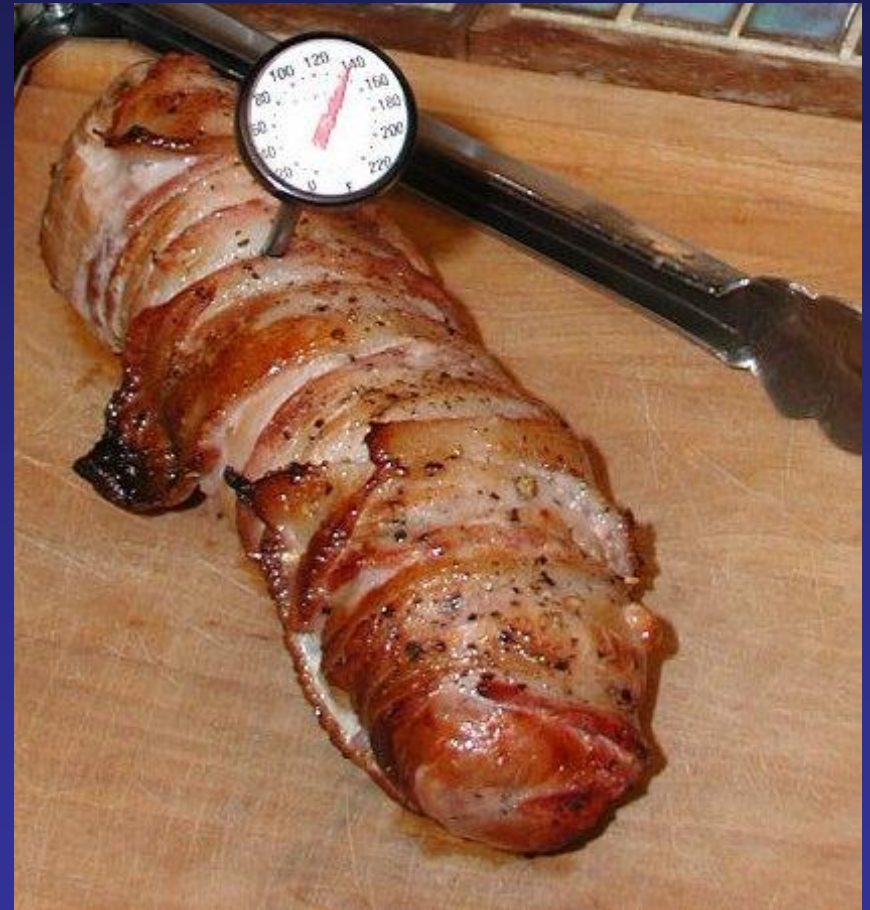
- Definitive diagnosis depends upon finding the Nurse-cell parasite.
- Detection of *Trichinella*-specific DNA (by PCR).
- No specific anti-helminthic drug
  - Mebendazole give early during infection may reduce the number of larvae that might lead to further clinical complications.
  - Corticosteroids
- Myopathic phase is treated in conjunction with antipyretics and analgesics.

# Prevention & Control

- **Outbreaks of trichinellosis in the U.S. have been rare over the last 10 years.**
- **Associated with the ingestion of undercooked meats from game animals and NOT from commercial sources.**
- **This represents a shift in the epidemiology of outbreaks compared to 20-30 years ago (*i.e.*, contaminated pork).**

# Prevention & Control

- **Cooking meat thoroughly at 58.5 C for 10 min or freezing at -20 C for three days.**
- **Meat inspection is nonexistent in the U.S. with respect to trichinella.**

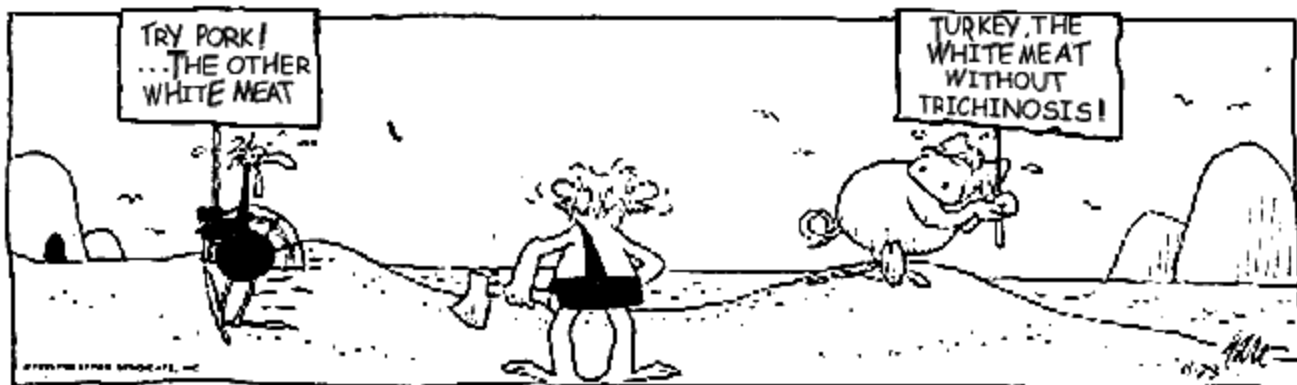


# Prevention and Control-Suitability of Freezing

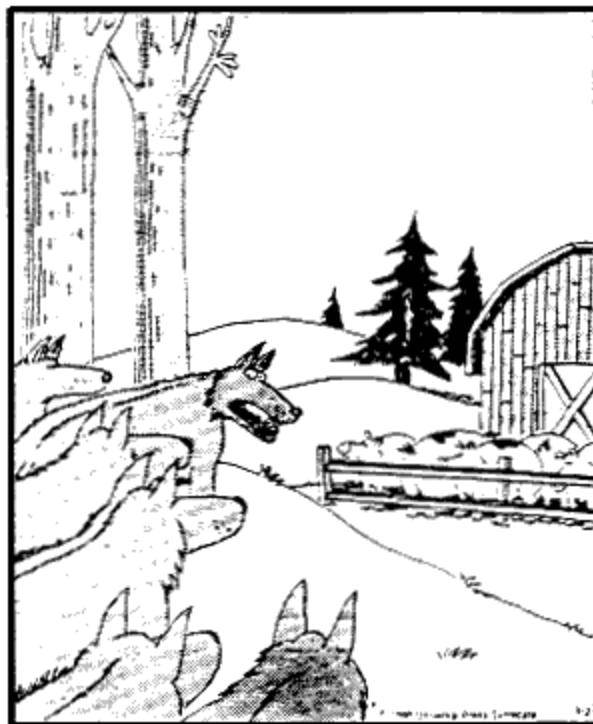
Origin of infected pork	Age of larvae	Temperature °C	Week/s of freezing	Infectivity of larvae after thawing	Reference
Naturally infected wild boar	unknown	-20	3	yes	9
Naturally infected wild boar	unknown	-20	4	no	9
Experimentally infected pigs	5-10 weeks	-18	1 - 4	no	10
Experimentally infected pigs	5-10 weeks	-5	1 - 4	yes	10
Experimentally infected wild boar	5 - 10 weeks	-18	1 - 4	no	10
Experimentally infected wild boar	5 - 10 weeks	-5	1 - 4	yes	10
Naturally infected pigs	unknown	-18	1	no	a
Naturally infected wild boar	unknown	-35	1	yes	11

B. C.

BY JOHNNY HART



**THE FAR SIDE**



"I say we do it . . . and trichinosis be damned!"

# *Ascaris lumbricoides*

*A little, wretched,  
despicable creature; a  
worm, a mere nothing,  
and less than nothing;  
a vile insect that has  
risen up in contempt  
against the majesty of  
Heaven and earth.*

**Jonathan Edwards  
(1703-1758)**





# Ascariasis

- **A general term for the disease caused by parasitic roundworms of the genus *Ascaris*.**
- ***Ascaris lumbricoides* parasitizes humans.**
- ***A. suum*, a natural parasite of pigs, may also infect humans (Koino, 1922).**

# *Ascaris lumbricoides*

- One of the largest nematodes to infect humans (up to 30 cm).
- The most severe consequences of *Ascaris* infection occur in children.
- The suggestion has been made that human infection arose in association with pig domestication, possibly first in China.

# **Geographic distribution & Epidemiology**

- ***A. lumbricoides* is present in temperate and sub-tropical zones; highest prevalence in tropical, rural situations where sanitation is poor.**
- **Some regions of Africa 95% of the population infected.**
- **Central and South America, some areas have a 45% incidence.**

# Geographic distribution & Epidemiology

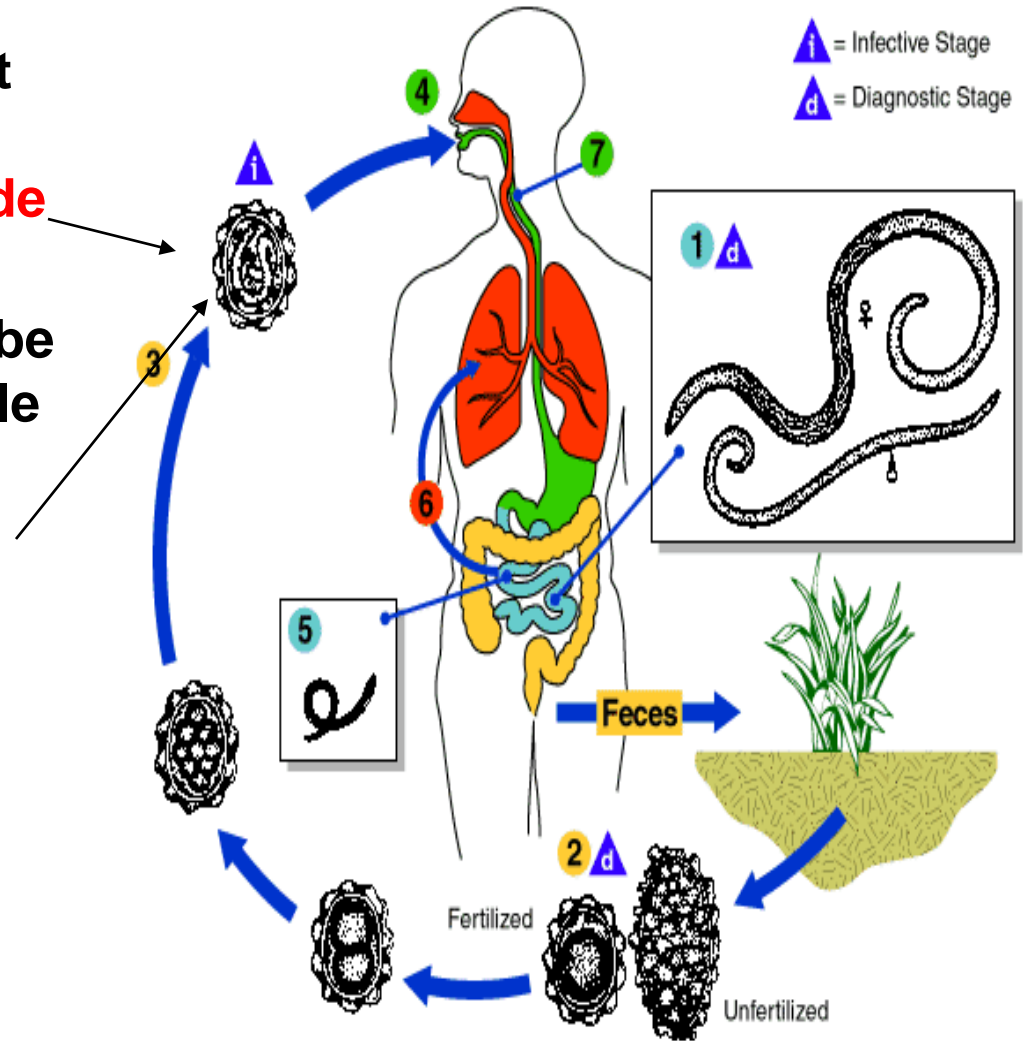
- **About 1/3 of the world's population infected.**
  - Estimated 1.22 billion people infected (800 million in Asia alone).
- **Eggs of *A. lumbricoides* vary greatly in their survival times in soil e.g., they may survive 6 years in cooler soil but only a few hours in warmer, tropical soils.**
  - Survive in sub-arctic regions
  - Recovered from all sorts of environmental surfaces e.g., paper currency.
- **In Saudi Arabia, the eggs die so rapidly that it causes a 'break' in transmission.**

# Ascariasis: 4 main clinical syndromes

- **First**, larvae migrating through lung cause eosinophilic pneumonitis (Löeffler's syndrome).
- **Second**, adult worms in the intestine may cause abdominal discomfort, acute epigastric pain, diarrhea, and debilitation.
- **Third**, an entanglement of adult worms may on occasion, obstruct the small intestine.
- **Fourth**, migration of adult worms into the ampulla of Vater, into the pancreatic ducts or into the biliary ducts, may cause sudden and life-threatening complications.

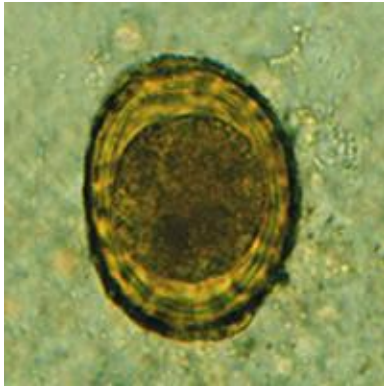
# Life Cycle: Soil to Small Intestine

- Eggs can survive in moist environments for up to 2 months-6years (**ascaroside lipoprotein**).
- Embryonated eggs must be swallowed for the life cycle to continue.
- L1-L3 develop inside the egg.

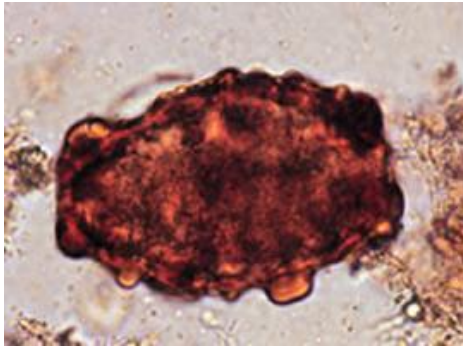




# Egg Development



A.



B.

- **A. Fertilized egg, still at the unicellular stage.**
  - Found in stool at this stage.
  - Full larva development requires 18 days of favorable conditions.
- **B. Unfertilized egg.**

# Egg Development

- **A. Egg containing larva.**
  - Infective if ingested.
  
- **B. Larva hatching from and egg.**
  - 0.2-0.3 mm long.
  - 0.014 mm wide.



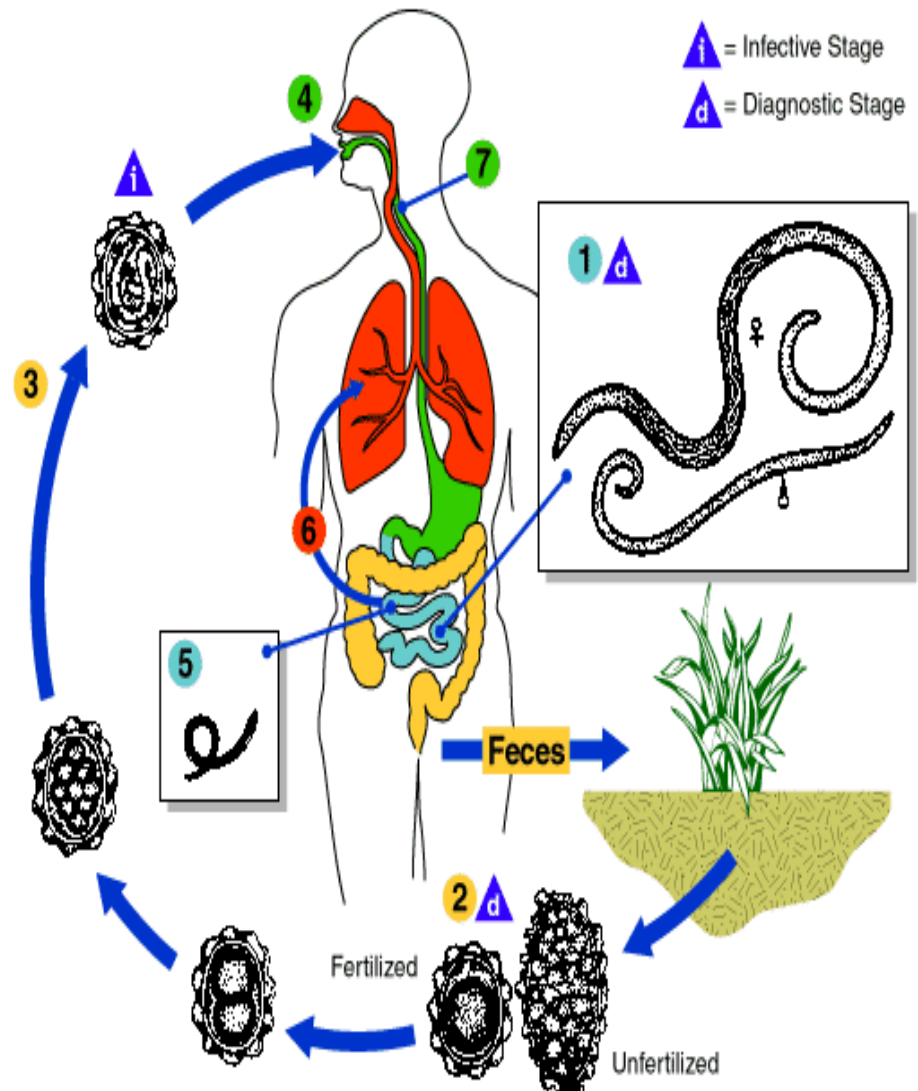
**A.**



**B.**

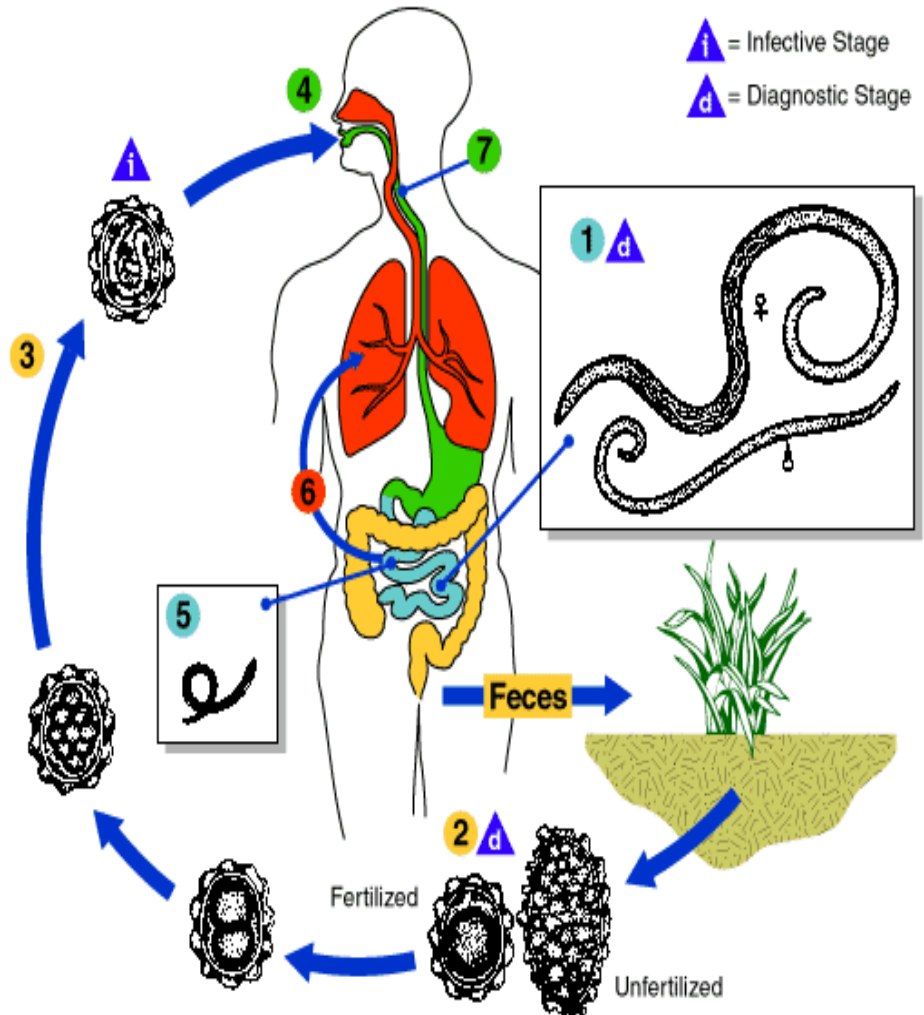
# Life Cycle

- In the host, the 2<sup>nd</sup> stage larva are stimulated to hatch by a combination of alkaline conditions in the small intestine and bile salts.
- These conditions induce the larva to produce a proteolytic enzyme, facilitating its exit from the egg. **Filiariform larvae**.
- The infectious process is accompanied by a dramatic shift in *Ascaris*' metabolism from **aerobic** to **anaerobic**.



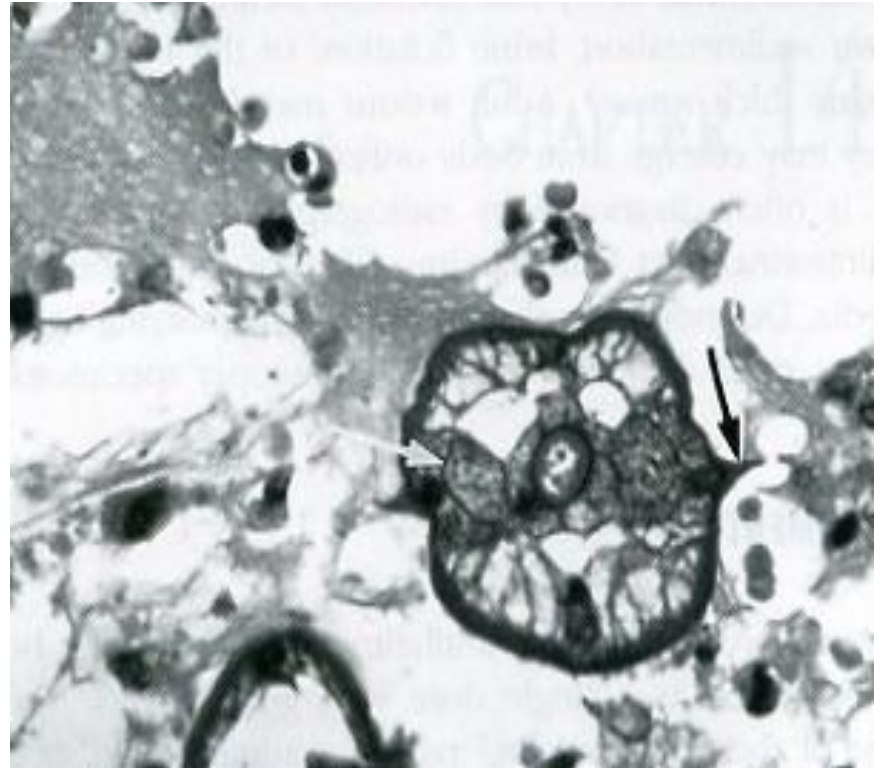
# Life Cycle

- The immature parasite, now in the intestinal lumen, enters the lamina propria, penetrates a capillary, and is carried by the portal circulation to the liver.
- In the liver, the worm feeds on parenchymal tissue and grows.
- Migrates via bloodstream to the heart and into the pulmonary circulation.
- **Intestines to lungs: 3 days.**



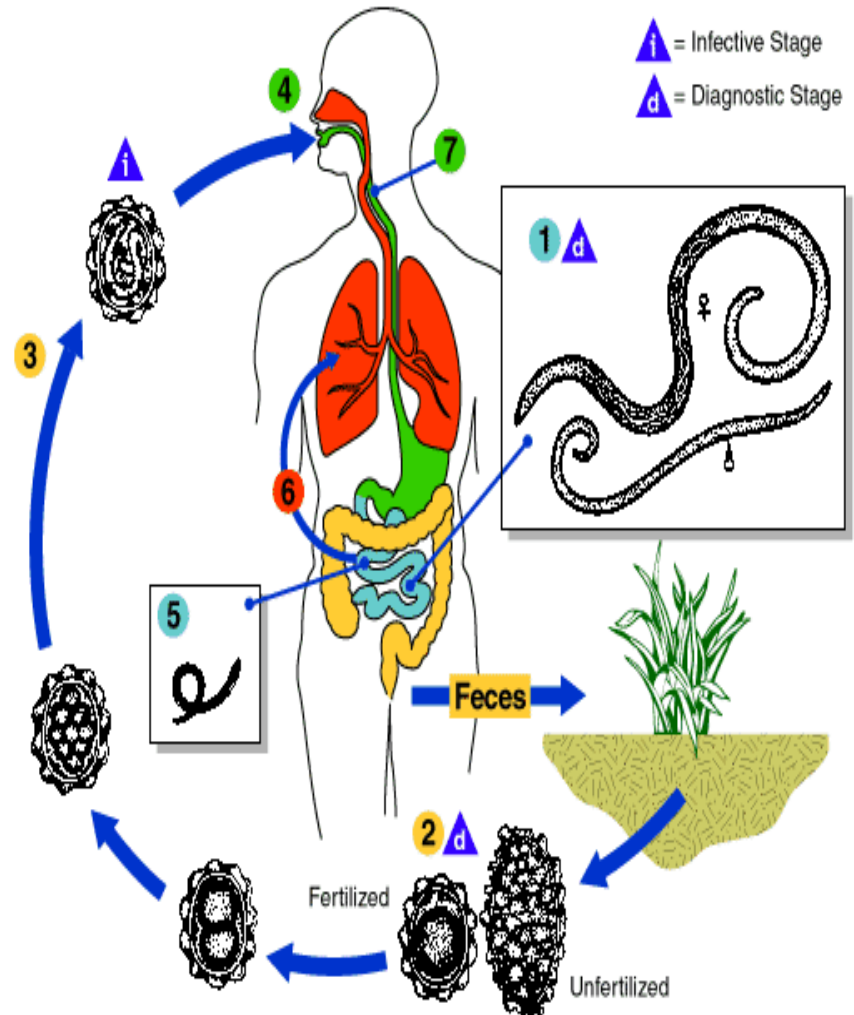
# Lung Stage

- The larva molt twice and grow in the alveolar capillary.
- The worm receives a **thigmotactic** signal.
- Breaks into the alveolar spaces causing 'verminous' pneumonia.



# Life Cycle

- The larva migrate up the bronchi into the trachea and across the epiglottis; swallowed, finally reaching the small intestine again!!
- After 2 more molts the worms grow and mature to adulthood in 6 weeks.
- All adult worms mate.
- Occupy the lumen of the upper small intestine.
- Live on predigested food.
- Maintain themselves in the lumen by assuming an S-shape.
- **Egg to adult: 8-12 weeks.**





# Adult Stage



- **Worms covered by thick cuticle**
- **Adult female can produce 176,000-350,000 eggs/day.**
- **25 million eggs/lifetime**
- **Adults can live for 1 year in the intestine then expelled (20 months maximum).**

# Male/Female Ascarids



- **Male (15-31 cm) smaller than the female (22-35 cm).**
- **Male tail-end contains two curved spicules each measuring 2 mm long can protrude from the cloaca.**



# Clinical Disease: Migratory Phase

- Intensity of the systemic response is dose-dependent.
- High infection dose lead to pneumonitis, enlargement of the liver.
  - Löeffler's type; elevated IgE; anti-ABA1
  - Migration through lungs can be accompanied by fever, chills, dyspnea, paroxysmal cough, lassitude, malaise, body aches, and pneumonia, cyanosis, sensation of pressure.
  - Different from TB and viral pneumonia...how?

# Clinical Disease: Intestinal Phase



Appendix to Cecum.

- In large numbers can cause obstruction.
- Penetrate the intestine, obstruct the biliary tract.
- 10,000 deaths annually in developing countries.
- HPA or hepatobiliary and pancreatic ascariasis
- Ectopic migration caused by...



Cut surface of the liver showing many *A. lumbricoides* in dilated bile ducts





# Ascariasis



- Child with distended abdomen due to large bolus of *A. lumbricoides* adult worms.
- Adult Ascaris recovered from child in above photo after treatment with mebendazole.
- Ascaris-infected children develop **malabsorption** of fat, protein and vitamin A, lactose intolerance from damaged mucosa, impaired intestinal permeability, and anorexia.
- Deaths are rare (0.62%).



# Diagnosis/Treatment

- Cannot be specifically diagnosed on the basis of signs or symptoms during the migratory or intestinal phases of infection.
- HPA difficult to diagnose by radiographic techniques.
- Identification of **eggs in stool** is the most definitive form of diagnosis.
- Albendazole, mebendazole.
- Piperazine citrate used in cases of intestinal obstruction.

# Prevention and Control

- Transmission from soil to humans depends not only on egg survival but on socioeconomic factors too.
- **Contamination of soil by human feces and crowded living are the most important factors in promoting infection.**
- An agricultural environment, illiteracy, and poor sanitation also promote high rates of infection.
- **Infection most common among school and preschool children.**
- Infection is acquired from fecal contamination of food, toys, fingers, inhalation of dust and contaminated vegetables, fruits, and drinking water.

# Prevention and Control

- **Primarily hygiene and education.**
- **Ascaris eggs are destroyed by exposure to direct sunlight for 12-hours.**
- **Die when exposed to temperatures in excess of 40 C.**
- **Exposure to cold does not affect eggs.**
- **Eggs also resistant to many commonly used chemical disinfectants.**
- **Thrive in treated sewage for months to years.**