
بسم الله الرحمن الرحيم

Cutaneous Larva Migrans & Cutaneous Leishmaniasis

Dr Eman Albataineh

Larva migrans

Definition : It is an infection of human tissue by migrating larvae of non human nematodes. Rarely caused by larvae of human nematodes.

Larva migrans in man includes:

- Cutaneous larva migrans
- Visceral larva migrans.

Cutaneous larva migrans (Creeping eruption, Plumber's itch, Sand worm)

Mode of infection

1. Human infection is caused by penetration of the skin by animal hookworm's filariform larvae which are not adapted to man.
2. Infection occurs due to contact with contaminated soil (moist or sandy) with dog & cat excreta.
3. The larvae migrate in the superficial layers of the skin and not go beyond the basal layer of the skin and keep migrating in the epidermis without development and rarely reaching the circulation.
4. Hookworms are Ancylostoma caninum & Ancylostoma braziliense

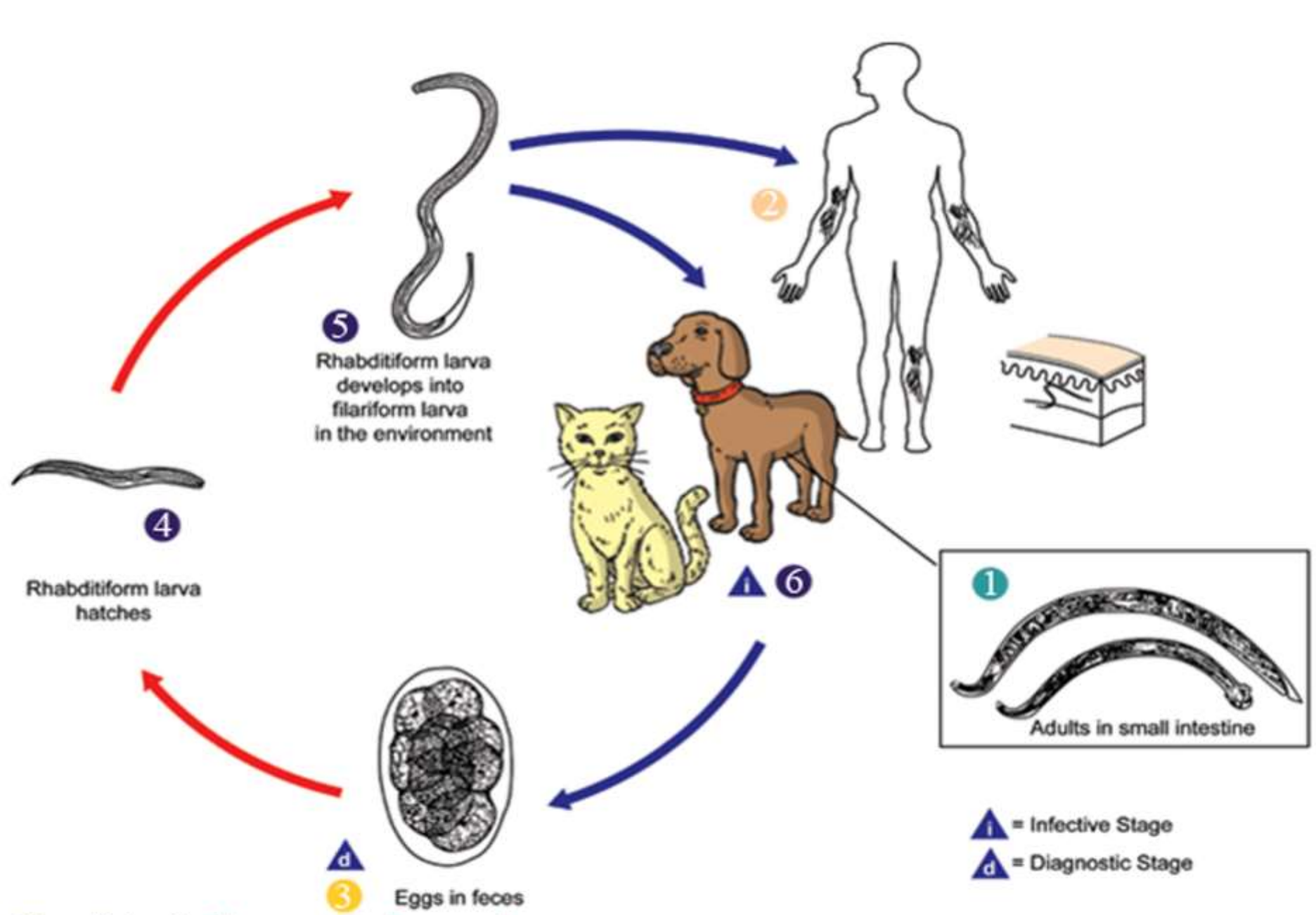


Fig. (24 - 1) Cutaneous larva migrans:-
Life cycle of *Ancylostoma caninum & Ancylostoma braziliense*

Pathogenesis and symptomatology

➢At the site of entry ➲ red itchy papule ➲ erythematous zigzag tunnel (1-2 mm) ➲ vesicles ➲ 2ry bacterial infection➲ sever irritation and pruritis.

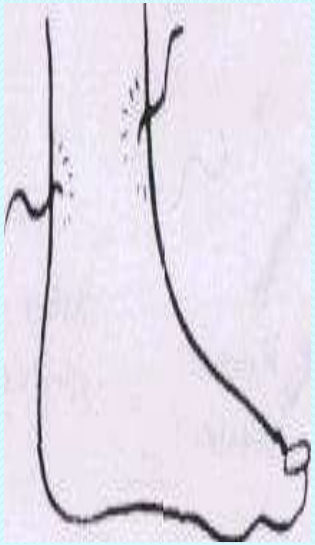
➢Larvae remain active, move **very slowly** in the epidermis layer only for several weeks or months till die.

Commonly affect the skin of feet, hands or buttocks and may advances to 1-2 cm / day.

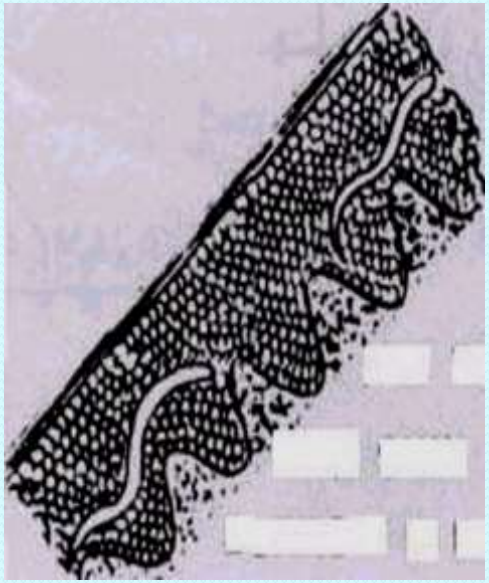
➢The skin lesion heals leaving linear white scars at the affected sites.

➢**Rarely** larvae reach the lung ➲ pulmonary symptoms, eosinophilia and pneumonitis.

CUTANEOUS LARVA MIGRANS



It penetrates the skin of man especially feet and legs



It fails to penetrate the skin fully

(not go beyond the epidermis)

Produce Zigzag tunnel

Laboratory diagnosis

- Skin biopsy for larval identification.
- No eosinophilia.

Treatment

- Antihistaminics.
- Antibiotics for 2^{ry}bacterial infection

Local freezing: Spray of skin by **ethyl chloride** (local freezing) or **carbon dioxide snow** which produce freezing of larvae till death➲ skin bleb ➲ larvae are lost with epidermal sloughs.

- Thiabendasole
- Ivermectin

Leishmaniasis classified into

Visceral Leishmaniasis (Kala azar)

Caused by

- *L. Donovani*
- *L. Infantum*
- ❖ *L. chagasi*

Cutaneous leishmaniasis

Caused by

- *L. tropica*.
- *L. major*.
- *L. aethiopica*.
- ❖ *L. mexicana*.

Mucocutaneous leishmaniasis

Caused by

- ❖ *L. braziliensis*.

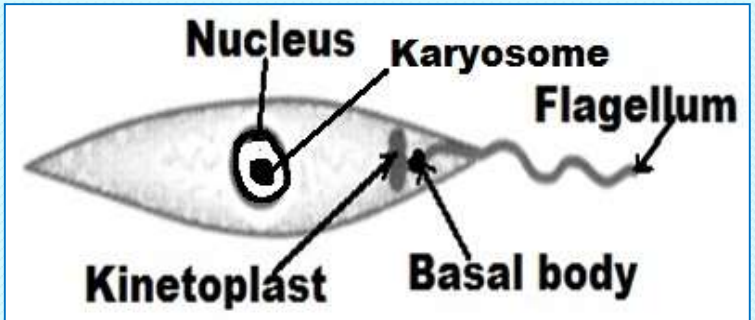
▪ Old World Leishmaniais

❖ New World Leishmaniasis

Old World Cutaneous Leishmaniasis

Morphological characters:

	1- Amastigote	2- Promastigote
Shape:	Oval	Fusiform or spindle
Kinetoplast:	Beside the nucleus	At the anterior end
Flagellum:	Absent	Present
Nucleus:	-Eccentric with central Karyosome	-Central with central Karyosome
Habitat:	-Intracellular (macrophage) -Tissue culture	-Midgut of the insect -Culture media



❖Mode of transmission

1- Bite of female sand fly (*Phlebotomus* species).

2- Direct contact with infected lesions.

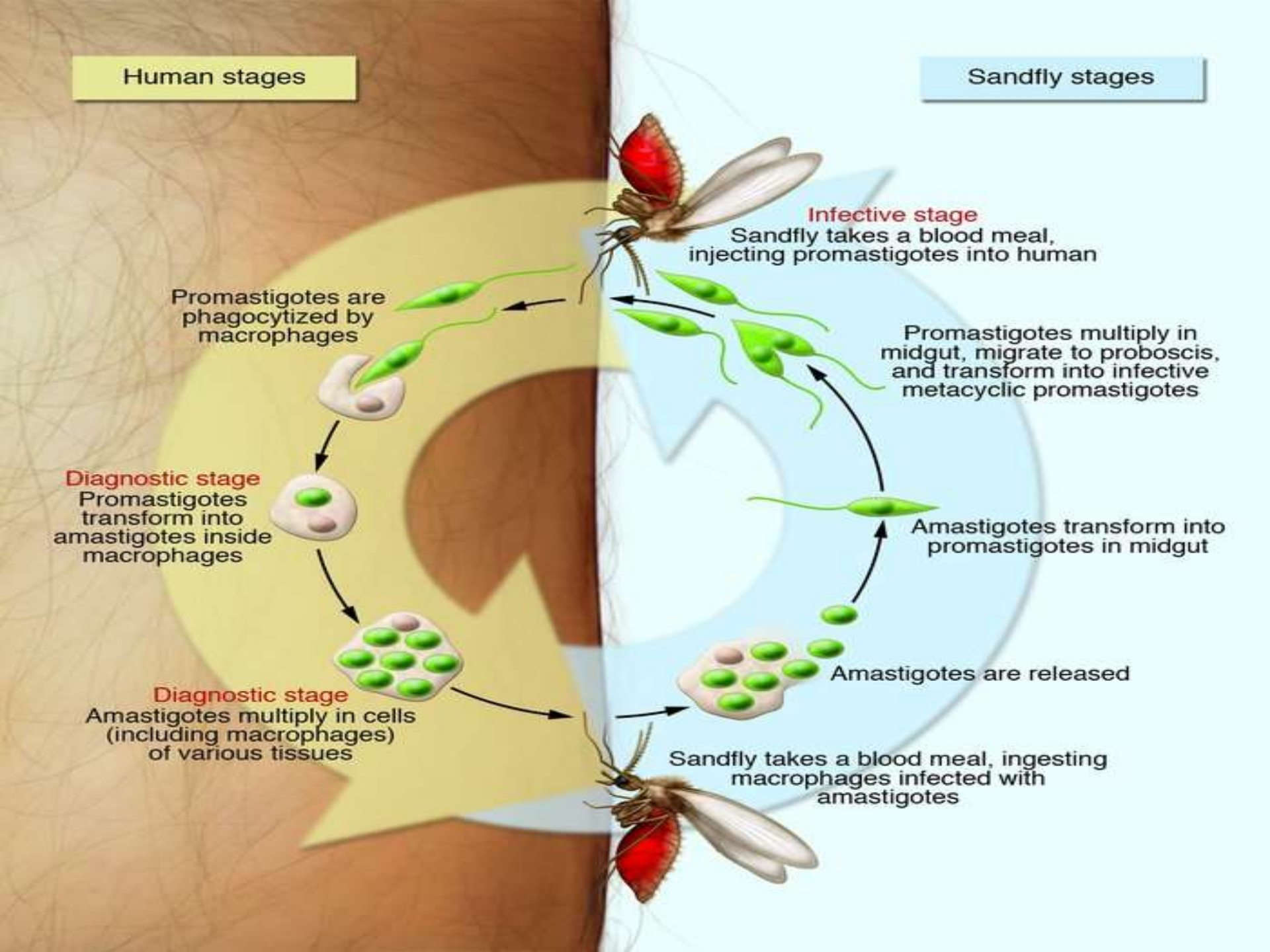
3- Mechanical transmission by blood sucking fly as *Stomoxys.*

D.H: Man

R.H: Dogs in *L. tropica.*
Rodents in *L. major & L. aethiopica*.

I.S: Metacyclic promastigotes in the mouth part of the female sand fly

Vector: Female sand fly (*Phlebotomus*)


Human stages
Sandfly stages
Infective stage
Sandfly takes a blood meal, injecting promastigotes into human
Promastigotes are phagocytized by macrophages
Promastigotes multiply in midgut, migrate to proboscis, and transform into infective metacyclic promastigotes
Diagnostic stage
Promastigotes transform into amastigotes inside macrophages
Amastigotes transform into promastigotes in midgut
Amastigotes are released
Diagnostic stage
Amastigotes multiply in cells (including macrophages) of various tissues
Sandfly takes a blood meal, ingesting macrophages infected with amastigotes

Pathogenesis & Symptomatology

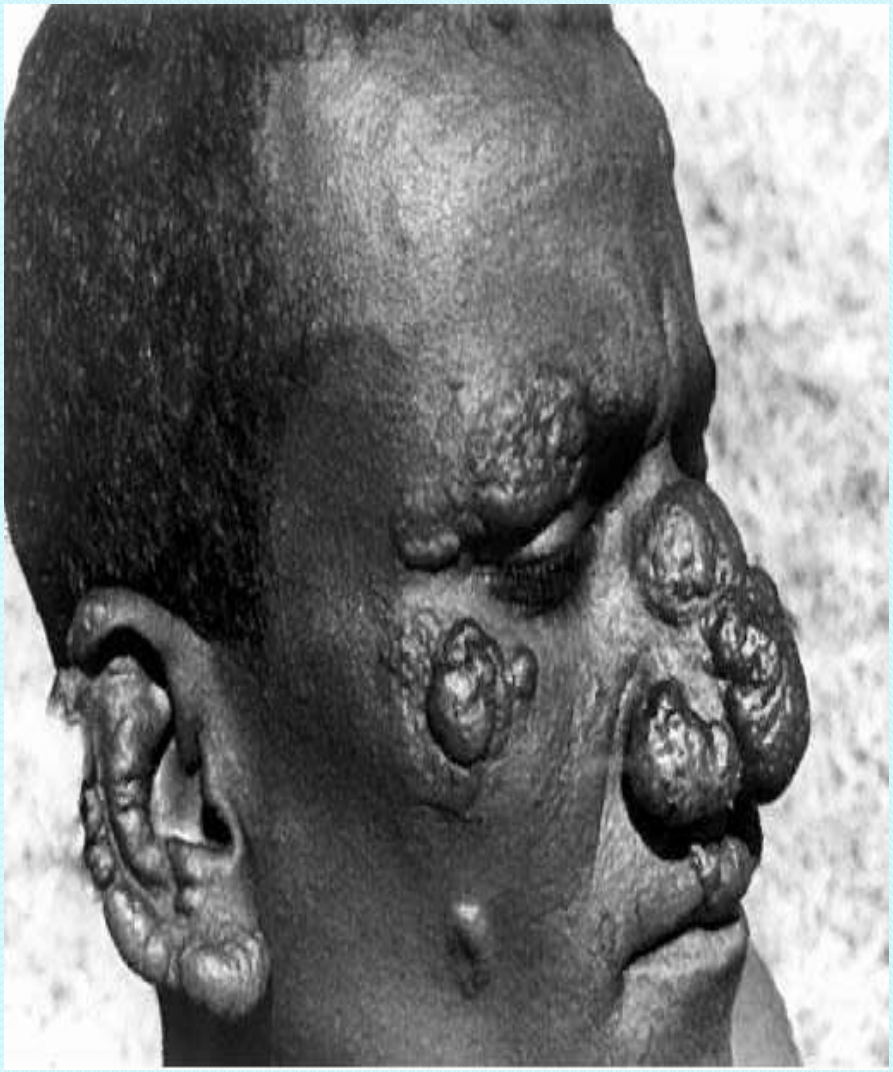
1- Old World Cutaneous Leishmaniasis

	L. tropica (Dry or urban CL)	*L. major* (Wet or rural CL)	*L. aethiopica* (lepromatous lesions)
Geog.Dist:	Middle East, Asia ,Africa in big cites (urban areas)	Middle East, Asia, Africa in villages (rural areas)	East Africa (Ethiopia & Kenya)
Pathog. & CLinical	Oriental sore (Baghdad boil or Delhi boil) -Localized nodules at the bite site ➡ necrosis ➡ painless ulcer é sharp edges & raised indurated margin. -2nd bacterial infection is common.	The same as *L. tropica* Except the followings: (in the next slide)	Diffuse Cutaneous Leishmaniasis -Thickening of skin, papules & multiple nodules like lepromatous leprosy

L. tropica (Dry or urban CL)	*L. major* (Wet or rural CL)	*L. aethiopica* (lepromatous lesion)
-Has chronic course if untreated.	- Has an acute course.	-Usually affects immuno-compromised patients.
-Has long Inc.Period (2-12 ms)	-Short Inc.Period(2-6 ws).	-No mucosal infection or ulceration
-Scanty exudate & slow healing (12 ms).	-Serous exudate & rapid healing (3-6 ms).	
-The ulcer mainly on the face & limbs.	-Usually on the lower limbs.	-Mainly on face & limbs
-Single or multiple ulcers.	- Multiple ulcers.	-Usually multiple nodules
-Heals spontaneously after 1-2 years giving depigmented disfiguring scars.	-Heals spontaneously living large disfiguring scars.	-No spontaneous healing & can be relapse.
-Gives solid immunity to *L. tropica* only.	-Gives immunity against both *L. major* & *L. tropica*	-No solid immunity

Oriental sore

Leishmania aethiopica



New world cutaneous leishmaniasis (American leishmaniasis)

New World Cutaneous Leishmaniasis

Leishmania mexicana

Chiclero ulcer or bay sore

New World Mucocutaneous Leishmaniasis

Leishmania braziliensis

Mucocutaneous Leishmaniasis (Espundia)

Chiclero ulcer	Espundia
Caused by *L. mexicana*	**Caused by *L. braziliensis***
-A small single nodule at the site of sand fly bite ➲ ulcerates. -Usually on the face & ear pinna ➲ heals within 6 months. -Ear lesion causes destruction of the catilage of the ear pinna. -Seen in chicleros who live in forests & collect gum from chicle trees.	-Primary skin lesion: Nodule in exposed regions ➲ ulcerates. - The ulcer with raised indurated margin ➲ heals in scar in months. -Secondary metastatic lesion: The parasite migrates from the primary site to blood & lymph to mucocutaneous junctions. -Sites: nasal septum, lips, palate nasopharynx & larynx. -Deformity & 2nd bacterial infection. - Death from septicaemia and bronchopneumonia.

Chiclero ulcer

Espundia

Laboratory diagnosis

Direct

1-Scraping the edge of the ulcer or aspiration by a needle (not the base as contains pus and necrotic tissues) and examined by :-

- Direct smear stained by Giemsa or leishman.
- Culture on NNN medium (amastigotes changes into promastigotes).

2- Biopsy from the edge of the ulcer and examined by direct smear.

Indirect

1-Immunodiagnosis:

- Leishmanin Int.Derm test (Montenegro test): Not a specific test. It is +ve with cutaneous and mucocutaneous leishmaniasis but negative in diffuse cutaneous leishmaniasis.

2- PCR: A reliable diagnostic test. than routine smear and culture and it used also for species differentiation.

Treatment

1) Local

- Cryosurgery, curettage or local application of heat to raise the intra- lesional temperature to 37- 43 ° C for 12 hours as amastigote do not grow above 33 ° C.
- Surgical excision of the lesion.

2) Chemotherapy

- **Non-ulcerated lesion**: Intra- lesional injection of pentavalent antimony compounds.
- **Ulcerated lesion:** Should be treated with systemic pentavalent antimony compounds (ex. Pentostam).
- **Alternative drugs to pentostam:** Amphotericin B, imidazoles or Allopurinol.
- **Antibiotics** for secondary bacterial infection of lesions.

TRICHINELLA SPIRALIS A NEMATODE

INTRODUCTION

- ***Trichinella spiralis***, tissue **nematode**,is the causative agent of **trichinosis**.
- Trichinella (trichos: hair, ella: suffix for diminutive, spiralis refer to the ***spirally coiled*** appearance of larvae in muscles)
- The common name is **Trichina Worm**.

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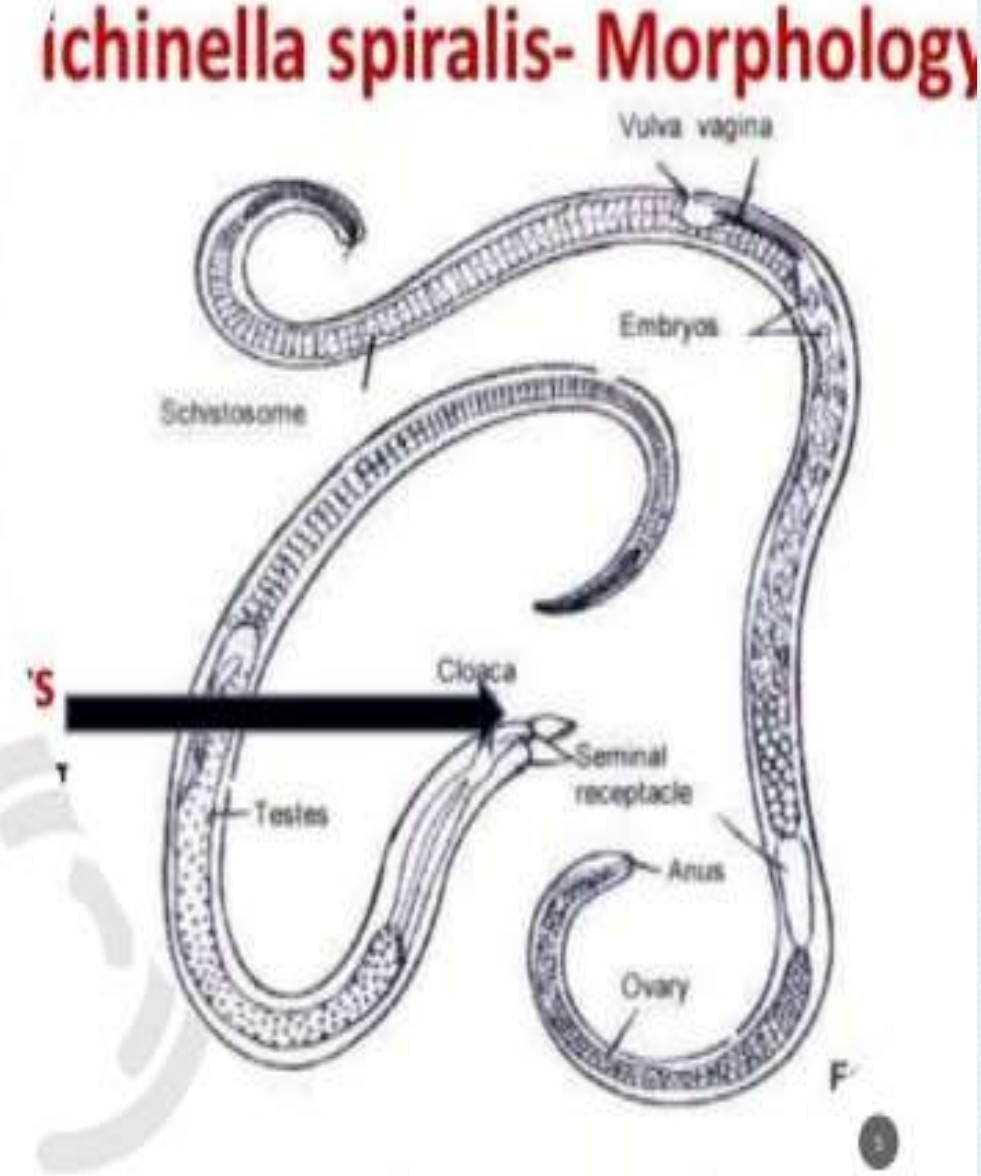
HABITAT

- Adult worms: live deeply buried in mucosa of small intestine (duodenum or jejenum)
- Encysted larvae : present in the **striated** muscles of these hosts.
- There are no free living stages.

MORPHOLOGY

Adult worm

- It is a small white worm just visible to naked eye.
- It is one of the **smallest nematodes** infecting humans.
- The anterior half of the body is **thin and pointed**, well-adapted for burrowing into the mucosal epithelium.



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Male VS Female

- Size: 1.5mm*0.04mm
- **Half** the length of female.
- Presence of **claspers**, a pair of pear shaped clasping papillae, used to hold female during mating.
- The male worm dies soon after fertilizing female,

- Size: 3mm*0.06 mm
- **Twice** the length of male.
- Female worm is **viviparous** and discharges larva instead of eggs.
- Female dies after 4 weeks to 4 months (the time required for discharging the larva)

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LARVAE

- The larva becomes encysted in striated muscle fiber.
- The larva in the cyst is coiled and thus called ***spiralis.***

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CYST

- It is the tissue reaction around the encapsulated larvae.
- It develops preferentially in active muscles like diaphragm, jaw muscles, biceps ,neck, lower back, which are relatively poor in **glycogen** and **hypoxic** environment.
- More abundant near the site if attachment of **muscles to tendons and bones** and lie **longitudinally** in muscle fibres.

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LIFE CYCLE

- It is a parasite with direct life cycle, completes life cycle in a host.
- **Optimum** host: **PIG** (favourable or principle)
- **Alternate** host: **MAN** (other than principle host)
- Man is the **dead-end** of the parasite, as the cysts in human muscles are unlikely to be eaten by another host.
- **Infective form**: Encysted larva found in muscles.
- **MOT**: Man acquires infection by raw uncooked pork or inadequately processed sausages or other meat products containing viable larvae.

CONTINUED....

Meat eaten without adequate cooking

↓

Cysts are digested by the gastric guice and viable larvae are released (excystation) in the stomach, duodenum and jejenum.

↓

Larva immediately penetrate the mucosal epithelium.

↓

They moult **four times** and develop into adults (2nd day of infection).

↓

They become sexually mature (within 6 days)

LIFE CYCLE

Male dies after fertilizing the female but the fertilized female start releasing motile larva by 6th day of infection

↓

Larva continue to discharge during the lifespan (4 week to 4 months)

↓

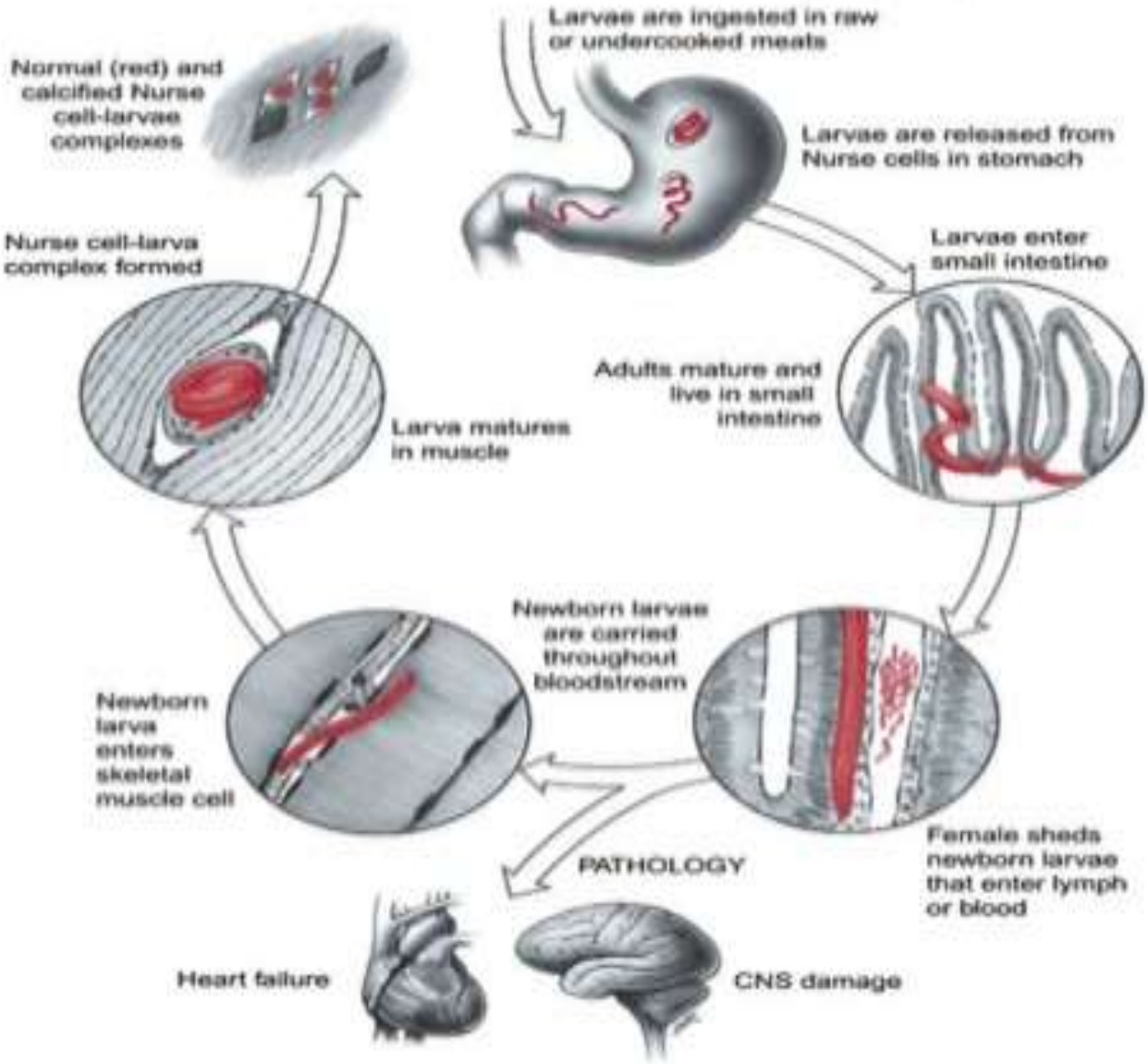
Larva enter intestinal lymphatics or mesenteric venules and are transported in caiculation to various parts.

↓

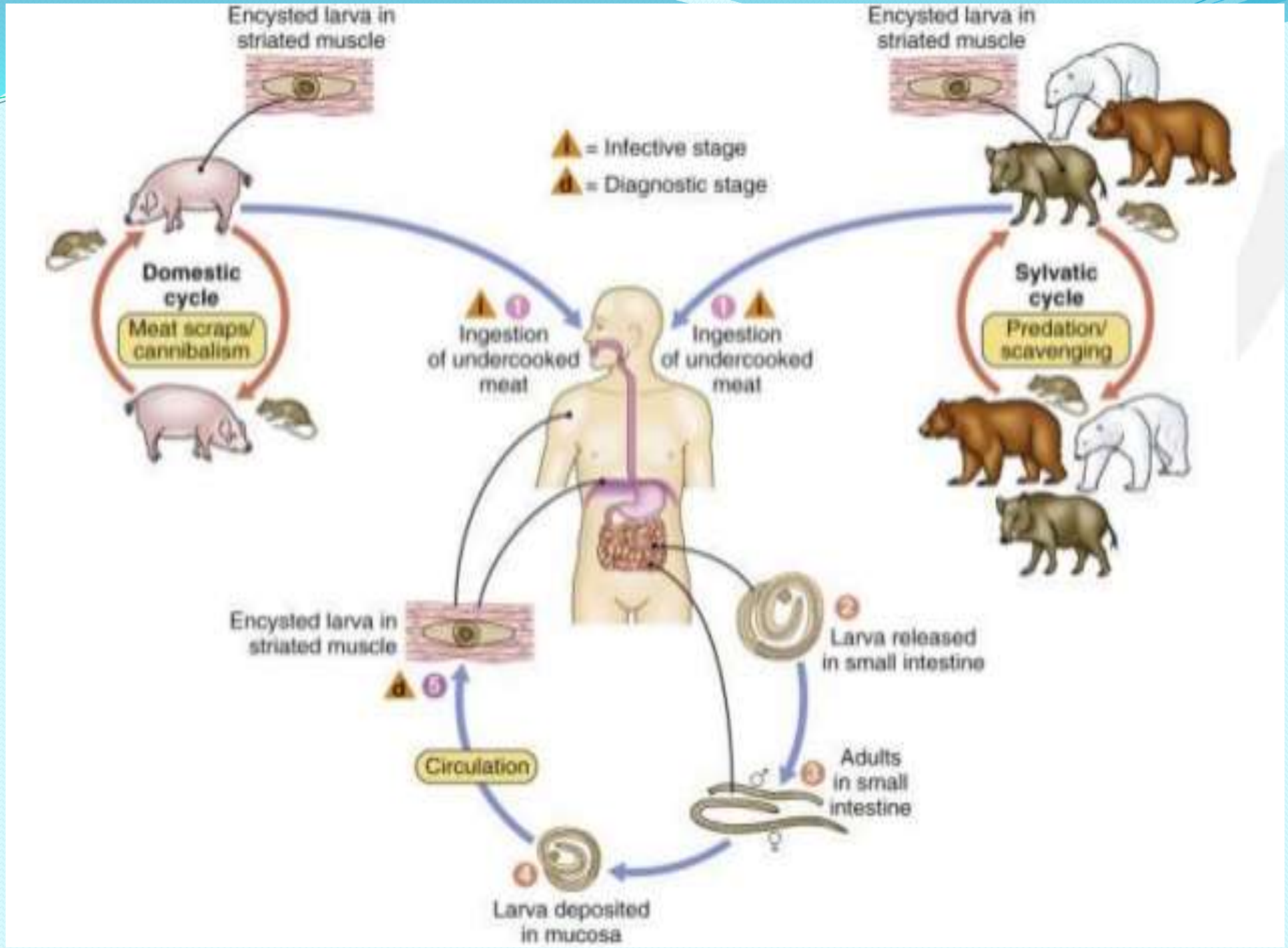
They get deposited in muscles (2nd week), CNS, and other sites. The larva dies in other sites except skeletal muscles, where it grows and develops (3-4 week)

↓

Within 20 days, larva become encysted in muscle cells. A muscle containing ***T.spiralis*** is called **nurse cell.** Encysted larva lies parallel to the muscle fibres.Encysted larva can survive for months and years. In man , the life cycle ends here.


Larvae are ingested in raw or undercooked meats
Larvae are released from Nurse cells in stomach
Larvae enter small intestine
Adults mature and live in small intestine
Female sheds newborn larvae that enter lymph or blood
Newborn larvae are carried throughout bloodstream
Newborn larva enters skeletal muscle cell
Larva matures in muscle
Nurse cell-larva complex formed
Normal (red) and calcified Nurse cell-larvae complexes
PATHOLOGY
Heart failure
CNS damage

Contoso


Encysted larva in striated muscle
Encysted larva in striated muscle
= Infective stage
= Diagnostic stage
Domestic cycle
Meat scraps/ cannibalism
Sylvatic cycle
Predation/ scavenging
Ingestion of undercooked meat
Ingestion of undercooked meat
Encysted larva in striated muscle
Larva released in small intestine
Circulation
Adults in small intestine
Larva deposited in mucosa

	Stage of intestinal invasion First stage	Stage of muscle invasion Second stage	Stage of encystation Final stage
Pathology	This stage begins with ingestion of raw pork containing larva and ends with invading the intestine and developing into adult.	This stage begins when new infective larvae released from adult female and ends with deposition of the larvae in muscles. Myositis and basophilic degeneration of muscles.	This stage occurs only in striated muscles. The infective larvae become encysted in this stage.
Clinical Features	Malaise, Nausea, Vomiting, Diarrhoea, Abdominal cramps. Onset within 2-30 hours of ingestion of infective food.	Fever, Myalgia, periorbital edema, weakness of affected muscle, myocarditis (if heart muscle is involved), encephalitis (if CNS is involved).Eosinophilia is a constant feature.Onset within 1-4 weeks after infections.	

DIAGNOSIS

- **DIRECT**
- **Muscle biopsy**: Detection of larvae in muscle tissue.Deltoid, biceps, gastrocnemius, or pectoralis are usually selected for biopsy.
- **Stool Test**: detection of adult worms during the diarrhoeic stage
- **Xenodiagnosis**: Biopsy bits are fed to laboratory taits, which are killed in a month or so,later. The larvae can be demonstrated more easily in the muscled of such infected rats.
- **INDIRECT**
- **History**: History of eating of raw or uncooked pork 2 weeks earlier
- **Blood examination**: Eosinophilia, raised creatine phosphokinase.
- **Serology**: Detection of antibody by ELISA, Bentonite flocculation test, Latex fixation test,

- **Radiological**: Calcified cysts can be seen on X-ray.
- **Molecular**: PCR
- **Bachman intradermal test**: It uses 1:5,000 or 1:10,000 dilution of larval antigen. An erythematous wheal appears in positive cases within 15-20 minutes. The test remains positive for years after infection.

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TREATMENT

- **Mild cases**
  - Supportive treatment like bedrest, analgesics and antipyretics.
- **Moderate cases**
  - Albendazole (400 mg BID for 8 days) or
  - Mebendazole (200-400 mg TID for 3 days, then 400 mg TID for 8 days)
- **Severe Cases**
  - Add glucocorticoids like prednisolone to albendazole or mebendazole.

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PROPHYLAXIS (Prevention)

- Proper cooking of pork and other meat likely to be infected.
- The most effective methods is to stop the practice of feeding pigs with raw garbage.
- Extermination of rats from pig farms- the spread of infection.
- Smoking, salting, or drying the meat doesnot destroy the infective stage. Prolonged freezing decontaminates the meat.


ThankYou