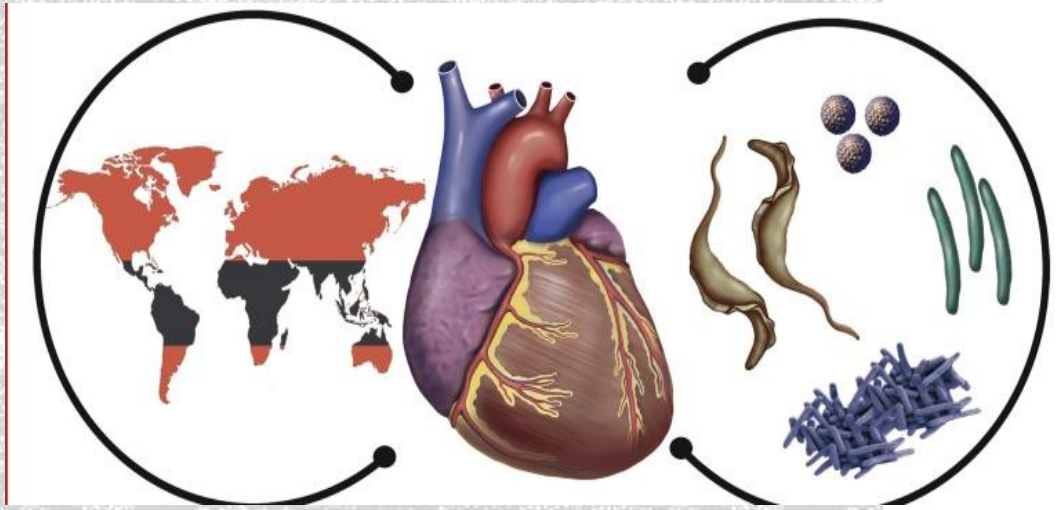
Block CVS-206

Cardiac Involvement with Parasitic Infections



Prepared by:

Dr: Nahed Ahmed Elossily

Professor of Medical Parasitology

Learning objectives

By the end of this lecture, students should be able to:

- ✓List parasites causing myocarditis and pericarditis.
- ✓Recall the infective and diagnostic stages of each parasite.
- ✓Demonstrate the pathological lesions in the heart caused by each parasite.
- ✓Explain host-parasite relationships (pathogenesis and main clinical presentations)
- ✓Describe laboratory diagnosis, imaging and pathological studies of the disease related to each parasite and recall treatment and prevention of them.

Parasites that directly affect the heart including:

A- Parasites causing carditis (myocarditis/ pancarditis):

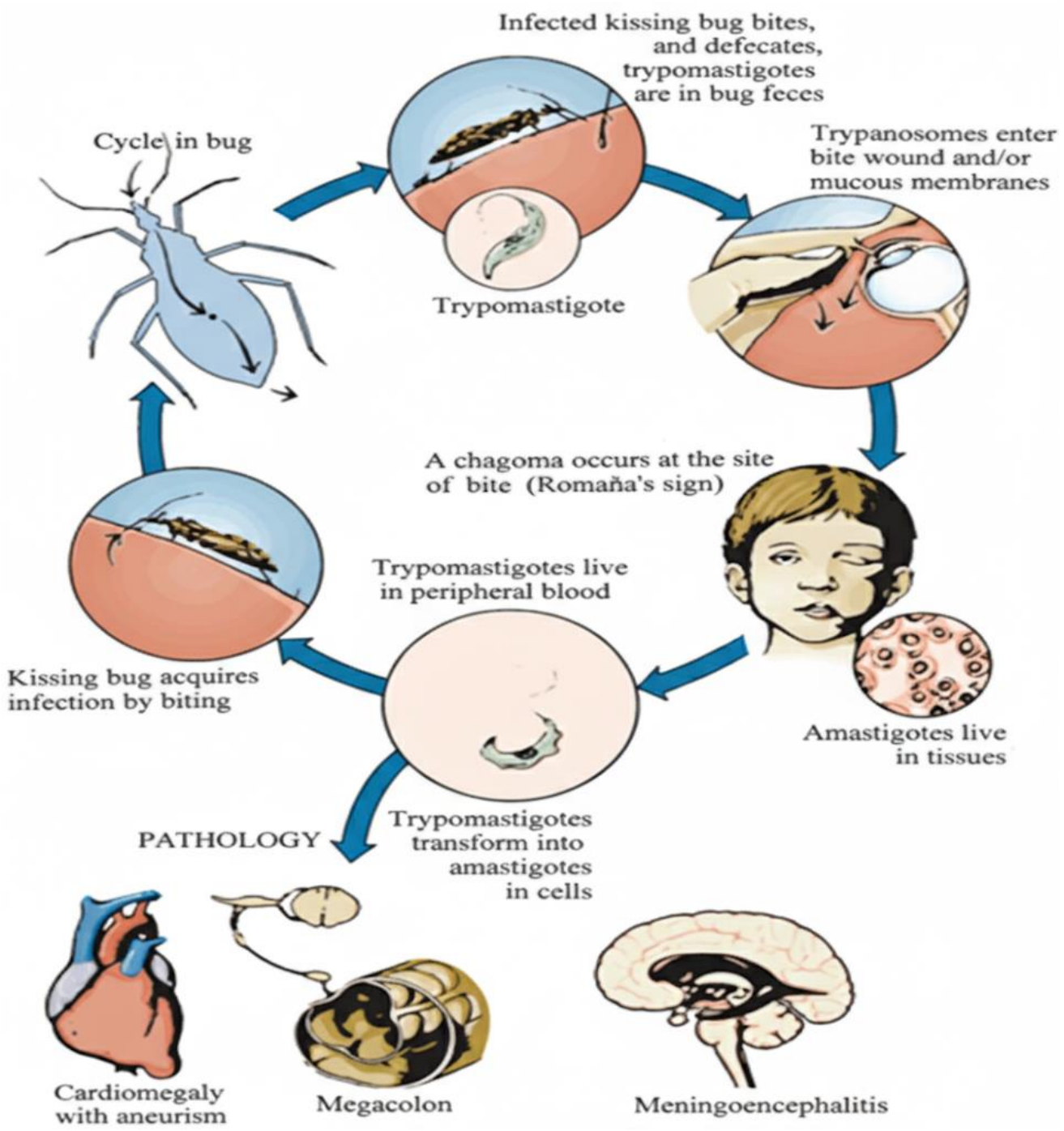
1. ***Trypanosoma cruzi*** (Chagas disease or American trypanosomiasis).
2. ***Toxoplasma gondii*** (toxoplasmosis)
3. ***Taenia solium*** (Cysticercosis).
4. ***Trichinella spiralis*** (Trichinosis)
5. ***Toxocara canis and T. cati*** (Severe cases of visceral larval migrans)

B- Parasites causing pericarditis:

1. ***Entamoeba histolytica*** (amoebic pericarditis).

1. *Trypanosoma cruzi*
"Chagas disease"

Disease:	American trypanosomiasis "Chaga's disease"
Geog. distribution:	Central and South America.
Host	Man, especially infants and young children.
Reservoir host:	The most important reservoir hosts are armadillos.
Vector	Triatoma megista (Kissing bugs or cone-nose, winged-bugs).
Habitat:	Cells of the reticulo-endothelial system (liver, spleen, bone marrow, and lymph nodes), myocardium, smooth muscles, and nervous system)
Infective stage:	Metacyclic trypomastigotes
Diagnostic stage:	Trypomastigotes form in blood film and amastigote form in tissues
Mode of infection:	1. Biological transmission by the vector which is Triatoma megita. 2. Transplacental (Mother-to-child). 3. Blood transfusion and organ transplantation

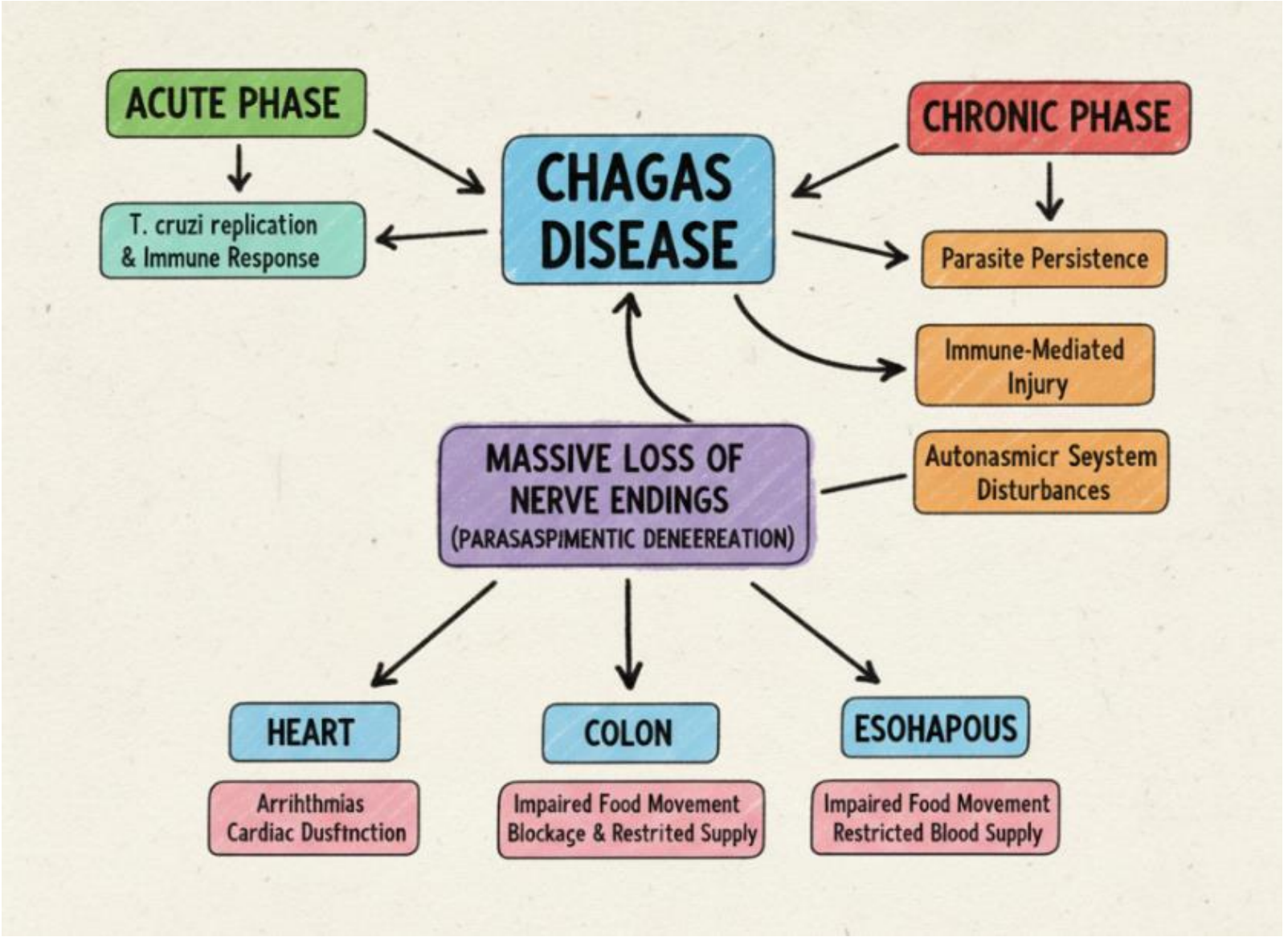

Infected kissing bug bites, and defecates, trypomastigotes are in bug feces
Cycle in bug
Trypomastigote
Trypanosomes enter bite wound and/or mucous membranes
A chagoma occurs at the site of bite (Romaña's sign)
Trypomastigotes live in peripheral blood
Amastigotes live in tissues
Kissing bug acquires infection by biting
PATHOLOGY
Trypomastigotes transform into amastigotes in cells
Cardiomegaly with aneurism
Megacolon
Meningoencephalitis

Pathophysiology:

The disease has two main stages:

1. **Acute phase of the disease**, signs and symptoms are due to the multiplication of T. cruzi and the immune system's response to it.

2. **Chronic phase:** caused by parasite persistence, immune-mediated injury and autonomic nervous system damage and micro vascular disturbances affecting mainly the heart, colon, and esophagus, chronic disease leads to a massive loss of nerve endings.


ACUTE PHASE
T. cruzi replication & Immune Response
CHAGAS DISEASE
CHRONIC PHASE
Parasite Persistence
Immune-Mediated Injury
Autonasmicr Seystem Disturbances
MASSIVE LOSS OF NERVE ENDINGS (PARASASPIMENTIC DENEEREATION)
HEART
Arrihthmias Cardiac Dusftnction
COLON
Impaired Food Movement Blockage & Restrited Supply
ESOHAPOUS
Impaired Food Movement Restricted Blood Supply

Clinical picture:
Chagas disease (acute and chronic)

Acute form: common in infants and young children.

1. **Chagoma:** primary cutaneous indurated lesion develops at the site of bite, parasite multiply inside macrophages.

2. **Romana's sign:** It is a unilateral swelling of the patient's eyelids associated with inflammation of the lacrimal gland and conjunctivitis. **It is a marker of acute Chagas disease.**

3. Invasion of the reticulo-endothelial cells causes generalized lymphadenopathy, splenomegaly and hepatomegaly.

4. Presence of anemia, continuous fever and severe headache.

5. In rare cases, infected individuals may develop acute myocarditis or acute meningoencephalitis which is life-threatening

Chronic form: common in adults

- The parasites are hidden in organs (the heart, digestive smooth muscles and nervous system), no parasites found in blood.

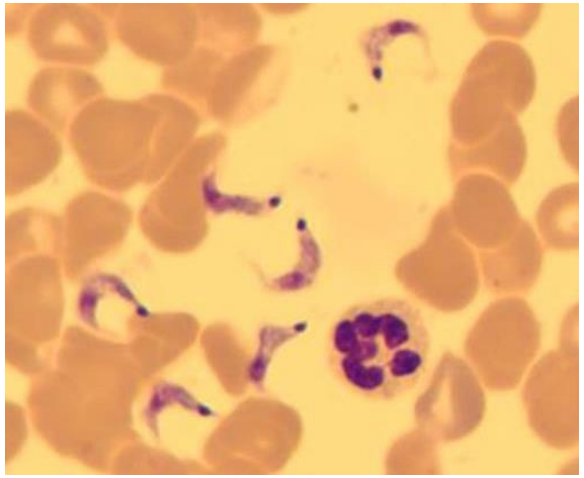
- Destruction of autonomic nerve ganglion in muscles of the heart and hollow organs resulting in mega organ disease
  - **Cardiomegaly.**
  - **Megaesophagus:** dilatation of the esophagus leading to dysphagia and chronic achalasia.
  - **Megacolon:** dilatation of the colon leading to constipation and patients with advanced disease can go for weeks between bowel movements

- **<u>Myocardial dysfunction</u>** is the most frequent consequence of chronic ***T. cruzi*** infection.
  - Fibrosis and cardiomyopathy can develop, resulting in congestive heart failure, clot formation and ventricular apical aneurysm.
  - **Dilated cardiomyopathy**, both ventricles become stretched and weakened and are unable to pump blood effectively.
  - **Arrhythmogenic cardiomyopathy,** characterized by atrial, ventricular arrhythmias as well as a wide variety of abnormalities of the conduction system. The most common ECG abnormalities are **right bundle branch block, atrioventricular blocks, and frequent premature ventricular contractions**

Diagnosis:

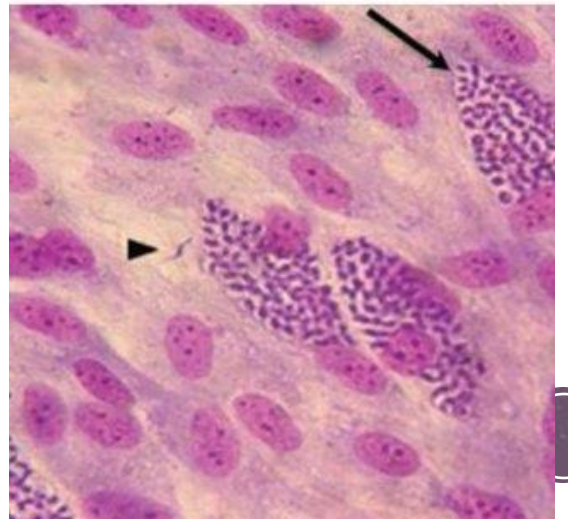
I. Clinical diagnosis: History (residence or traveling to endemic areas) and clinical picture.

II. Laboratory diagnosis:



1. **In acute cases**:

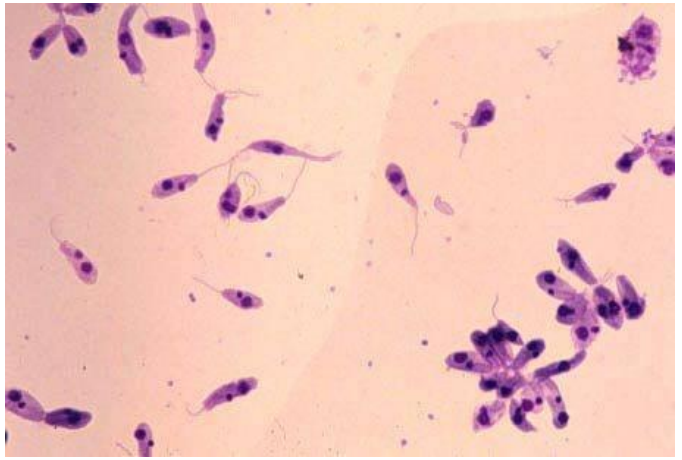
- Monomorphic trypomastigotes can be found by microscopic examination of thin blood smears and aspirates from chagoma, lymph node, bone marrow, and CSF



- Tissue sections from lymph nodes or heart for definitive diagnosis of acute stage Chagas disease (Amastigote form).

2. In light infections:

- **Xenodiagnosis:** Allow clean winged bug (bred in the laboratory and fed on plant juices) to feed on the blood of the suspected patient. After about 20-30 days the insect is dissected, and the rectum is examined for developmental stages as metacyclic trypanosomes.



- **Cultivation of the suspected blood on N.N.N.** medium (Novy-MacNeal-Nicolle Medium) and examined after (1-4 weeks) to show epimastigotes and trypomastigotes.

- **Inoculation in laboratory animals** (mice/ rats) to show monomorphic trypomastigotes.

3. In chronic cases: Serological tests are used to show immunoglobulins using complement fixation, indirect fluorescent antibody test or ELISA.

4. PCR-based methods are useful to diagnose acute, chronic and congenital Chagas disease as well as to monitor therapy.

III. ECG (Electrocardiography): To diagnose cardiomyopathy and arrhythmia.

IV. Imaging methods:

- Chest X ray to diagnose heart enlargement.
- Echocardiographic methods: To diagnose myocarditis and congestive heart failure.

Treatment

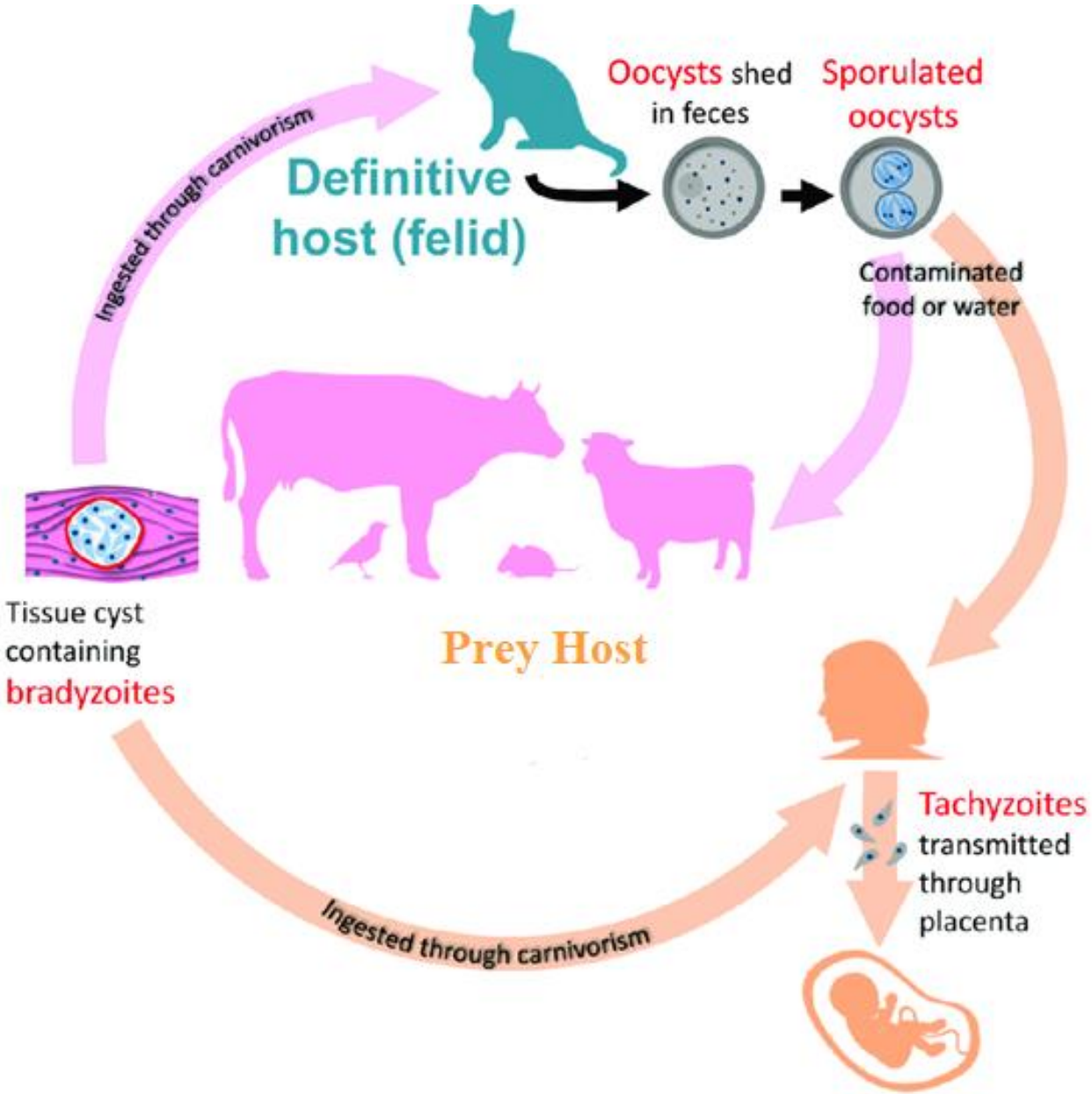
1. Early stage (acute stage): anti-parasitic drugs; benznidazole or nifurtimox
2. Late stage (chronic stage): Symptomatic treatment.
3. For chronic heart disease, antiarrhythmics drugs and pacemaker implantation for heart block are used.
4. Cardiac transplantation is an option.

Prevention and control

1. Treatment of infected patients
2. Destruction of reservoir hosts.
3. Eradication of vectors by dusting or spraying.
4. Screening of blood donors in endemic areas

2. *Toxoplasma gondii* "toxoplasmosis"

Disease	Toxoplasmosis
Geog. Dist.	cosmopolitan distribution
Definitive host:	The domestic cat (predator)
I.M. host:	All vertebrate hosts including humans serve as prey hosts.
Habitat	obligate intracellular parasites and are found in all nucleated cells
Mode of infection	1. Ingestion of sporulated oocysts in contaminated vegetables or water 2. Ingestion of tachyzoites or bradyzoites in cysts in undercooked meat or during handling infected raw meat. 3. Blood transfusion and organ transplant. 4. Congenital transmission
Infectious stages	the tachyzoites, the bradyzoites (in tissue cysts), and the sporozoites (in


Definitive host (felid)
Oocysts shed in feces
Sporulated oocysts
Contaminated food or water
Ingested through carnivorism
Tissue cyst containing bradyzoites
Prey Host
Tachyzoites transmitted through placenta
Ingested through carnivorism

Pathogenesis and clinical picture

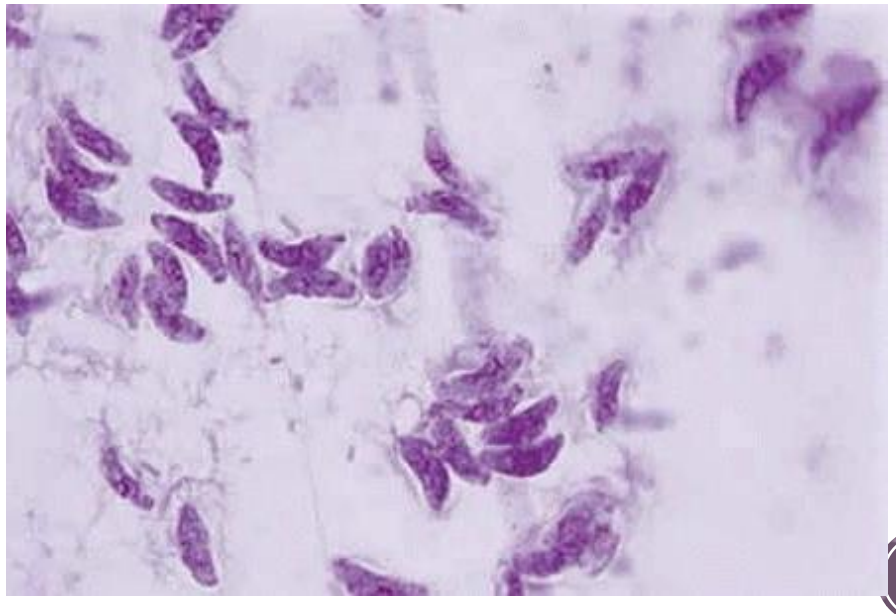
- ***Toxoplasma gondii*** multiplies intracellularly and spread to organs by the invasion of lymphatics and blood. Tissue cyst formation occurs within the first week of infection and is responsible for latent infection.
- **The clinical expression** of toxoplasmosis depends on the level of immunity in the human host.
  - **In immunocompetent patients**, acute toxoplasmosis is most often asymptomatic or gives flu- like symptoms. **Latent infection can persist for life.**
  - **Two categories are at high risk of severe infection**, the immunocompromised due to reactivation of a latent infection, and the pregnant women who receive their first exposure to ***T. gondii*** while pregnant; their fetuses are at particular risk.

In immunocompromised persons, the heart is the second most commonly affected organ after the brain:

- Cardiac involvement includes myocarditis, constrictive pericarditis, pericardial effusion, associated with arrhythmias, and congestive heart failure.
- ***Toxoplasma gondii***-associated myocarditis can also occur in transplant patients. Toxoplasmosis is the most commonly reported parasitic disease occurring after heart transplantation and may simulate organ rejection.

Diagnosis:

1. **Clinical picture**
2. **Serological tests;** as ELISA (most commonly used), immunofluorescence assay (IFA) and Sabin-Feldman dye test (specific) to detect antibodies against ***T. gondii***.
3. **Biopsy and immunohistochemistry** for antigen detection.
4. **Isolation of *Toxoplasma*** trophozoites from suspected infected tissues followed by intra-peritoneal inoculation to laboratory mice.
5. **PCR** for detection of parasite DNA.



Treatment: Combination of pyrimethamine and sulphadiazine is the drug of choice.

Control:

1. Daily cleaning of cat litter boxes and proper disposal of feces.
2. Washing of hands after handling raw meat and before eating.
3. Rodents should be controlled.
4. Raw meat should not be fed to cats.

3. Visceral larva migrans (VLM)

Definition: It is a condition produced by the invasion of the human tissues (heart) by the larvae of ascarids of dogs and cats (***Toxocara canis and Toxocara cati***). Most cases of visceral larva migrans occur in children.

Pathogenesis: The larvae migrate through viscera (liver, lung and heart) and form granulomatous lesions.

Clinical picture:

- Symptoms and duration of illness depend on the site and severity of infection.
- In severe toxocariasis, myocarditis, cardiac pseudo-tumour and cardiac tamponade.

Diagnosis:

- Serology for antibody detection using ELISA.
- CBC shows High eosinophilia.
- Hyper-gammaglobulinemia with raised IgM and IgG levels.

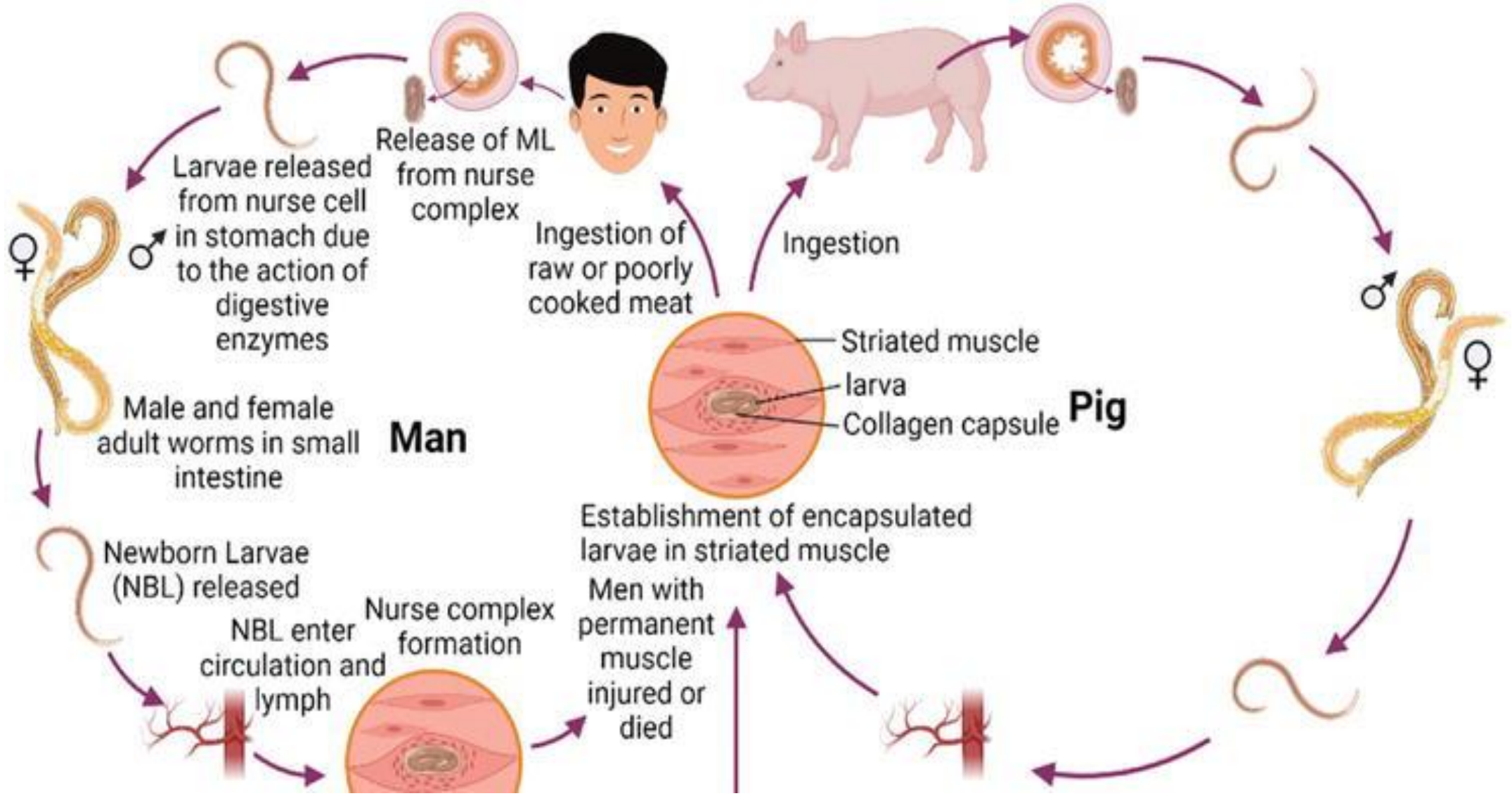
Treatment: Diethylcarbamazine or Thiabendazole.

Control:

1. Periodic examination of dogs and cats and treatment of infected animals.
2. Personal hygiene.
3. Avoid playing of children in gardens where dogs or cats may have defecated

4. *Trichinella spiralis*

Disease	Trichnillosis
Geog. distribution	Worldwide, It is common in pork eating countries.
Host	✓ Rats and pigs are natural hosts. Man is an accidental host. ✓ The same animal and man act as final and intermediate host.
Habitat	✓ Adult male and female inhabit the small intestine. ✓ Larvae are encysted in the muscles of the same host especially active ones as muscles of tongue, deltoid, diaphragm and muscles of mastication.
Infective stage	Encysted larvae in muscle
Mode of infection	Man is infected by ingestion of raw or undercooked pork meat containing infective (viable) encysted larvae.
Diagnostic stage	Encysted larvae in muscle


Release of ML from nurse complex
Larvae released from nurse cell in stomach due to the action of digestive enzymes
Ingestion of raw or poorly cooked meat
Ingestion
Striated muscle
larva
Collagen capsule
Pig
Male and female adult worms in small intestine
Man
Establishment of encapsulated larvae in striated muscle
Newborn Larvae (NBL) released
Nurse complex formation
NBL enter circulation and lymph
Men with permanent muscle injured or died

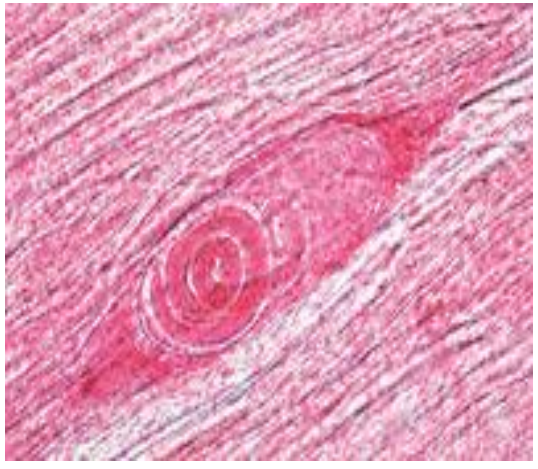
Clinical picture and pathogenesis

- migrating larvae of *Trichinella spiralis* cause local inflammatory response producing Eosinophilic myocarditis

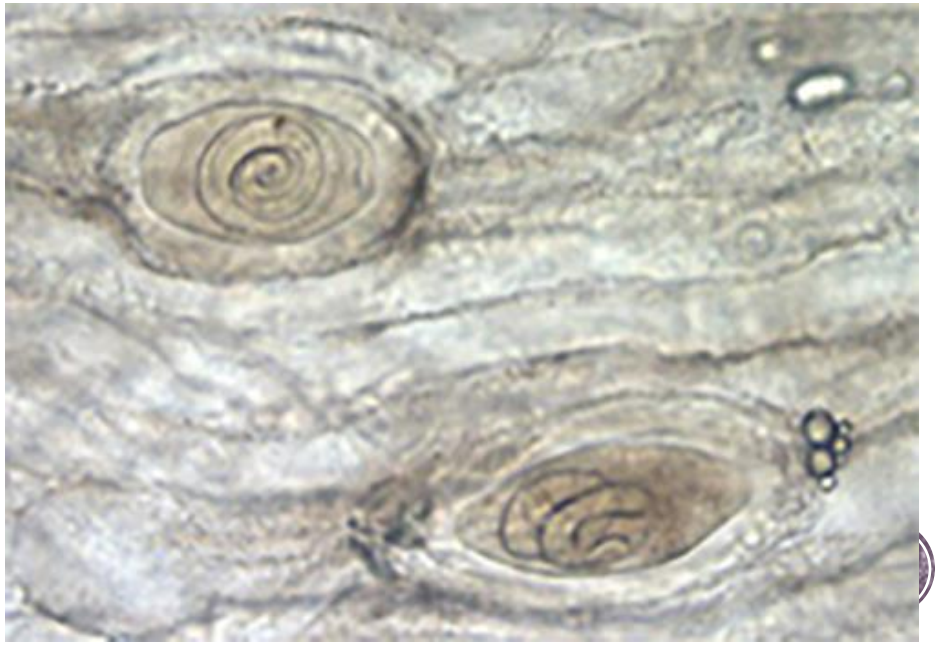
- Myocarditis manifested by chest pain simulating acute myocardial infarction and may be complicated by arrythmias and congestive heart failure

Diagnosis:

1. The clinical suspicion of trichinellosis is based on suggestive history associated with the typical clinical presentation and the
2. CBC shows high eosinophilia.
3. Serology is done for antibody detection using ELISA.
4. Muscle biopsy to detect larvae in muscles is a confirmatory test.



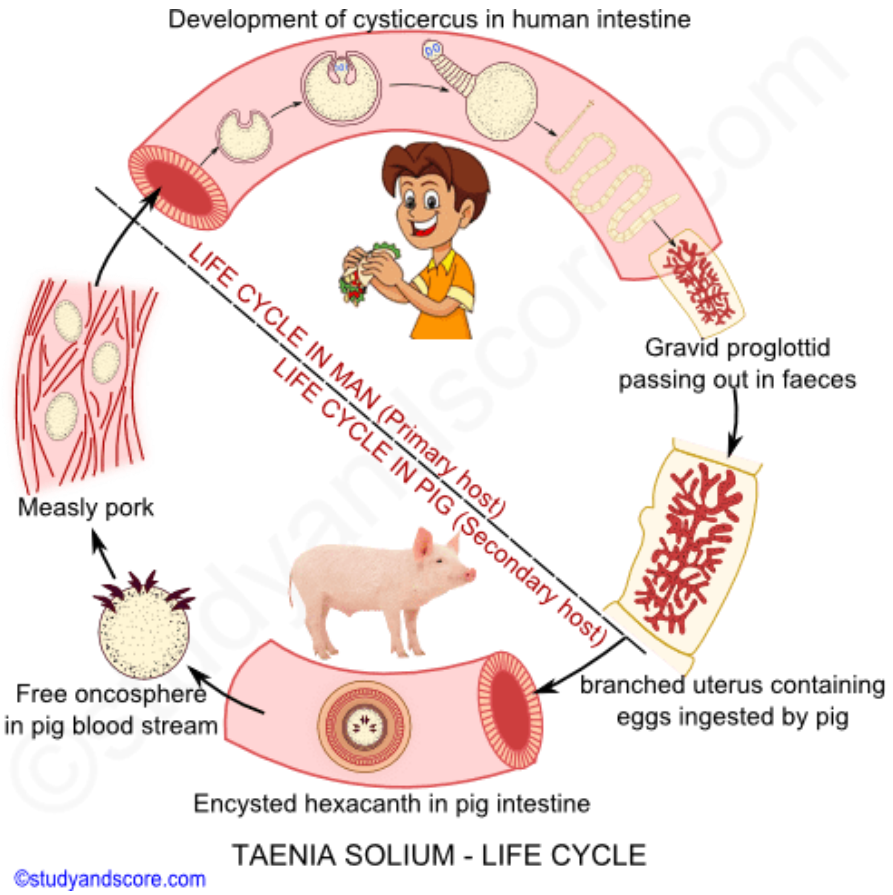
Treatment: A combination of anti-parasitic (mebendazole or albendazole) and corticosteroids



4. Cysticercosis

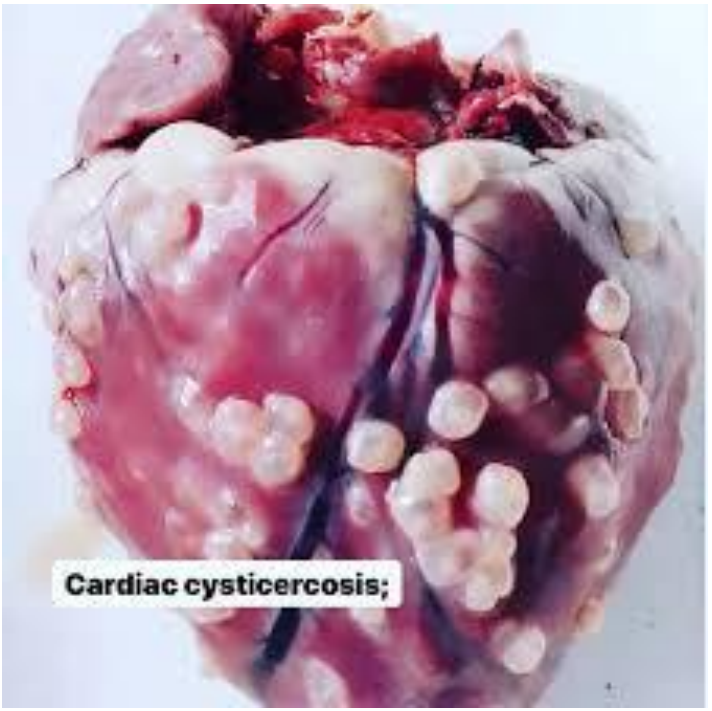
- **Definition:** It is the invasion of human tissues by the larval stage of ***Taenia solium*** (***Cysticercus cellulosae***). Man acts as a blind intermediate host.
- **Geographical distribution:** Worldwide
- **Mode of infection:**

  1. Ingestion of raw vegetables or water contaminated by infected feces containing eggs of ***Taenia solium***.
  2. Autoinfection.



Pathogenesis and signs:

- Cysts have been observed in the heart as incidental findings at autopsy or during cardiac surgery for unrelated causes.
  - The degeneration of cysts in the myocardium may result in **granuloma formation and fibrosis**.
  - This may result in **arrhythmia and conduction abnormalities. Pericardial effusions** may occur.



Diagnosis:

1. Clinical diagnosis.
2. **Direct methods:** Usually post-operative microscopic examination of biopsy specimens to demonstrate the cysticerci.

3. Imaging techniques: Echocardiography, CT and MRI may demonstrate the cysts which are multiple and randomly distributed in the subpericardium, subendocardium and myocardium.

4. Serology to detect antibodies in serum using ELISA, IHT and IFT.

5. Blood picture: Show high eosinophilia.

Treatment:

1. In man praziquantel and albendazole are of some value as possible alternatives to surgery.
2. Steroids are essential to relieve the intense local inflammatory reactions of the antigenic material produced by dead larvae.

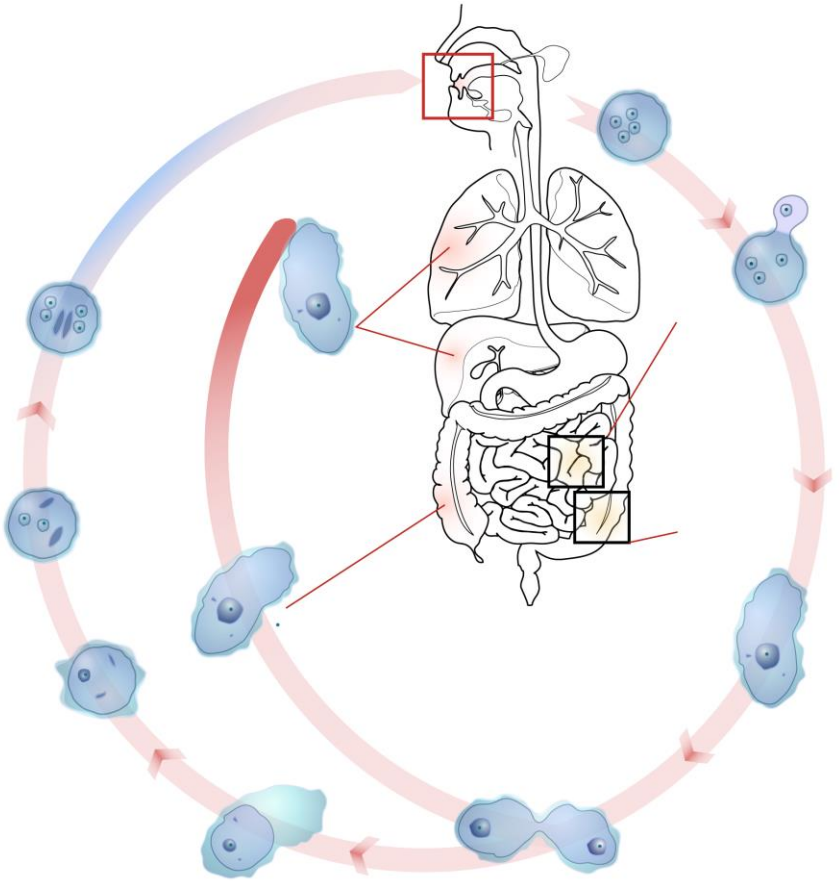
Control:

1. Proper treatment of infected patients with ***T. solium*** (avoid vomiting).
2. Avoid using human manure as fertilizer.
3. Personal hygiene and periodic examination of food handlers.

6. Entamoeba histolytica
"Amoebic pericarditis"

Habitat: The parasite lives in the mucosa and submucosa of the large intestine (intestinal amoebiasis). It may reach the liver, lung and brain causing amoebic abscesses (extra intestinal amoebiasis).

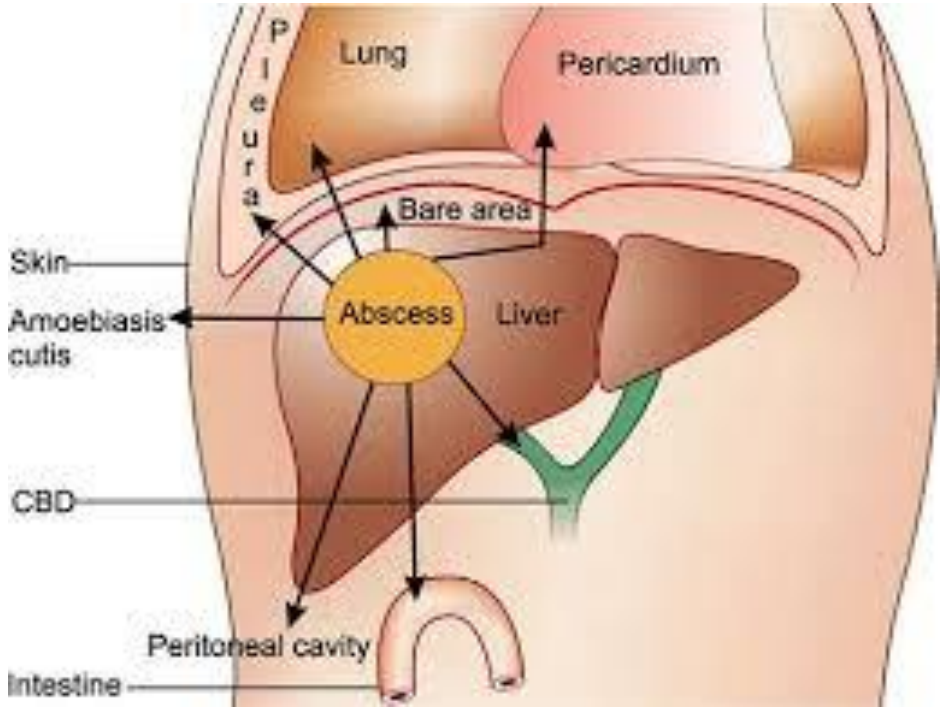
Transmission: Faeco-oral route. Persons get infected by ingestion of the **quadrinucleated cyst** contaminating fingers, food, and water and by flies.



Pathogenesis:

- **Amebic pericarditis** is a **rare** but serious complication of liver abscess or pleuropulmonary abscess when it ruptures into the pericardium.

Cardiac tamponade: sudden onset of compression of the heart by an accumulation of fluid in the pericardial sac and even perforation can occur, but typically the course is more insidious and involves substernal chest pain as well as congestive heart failure



Sources:

1. Kaplan USMLE Step1 Lecture Notes Immunology and Microbiology 2021.

2. First aid for USMLE step 1. Student to student guide 2019. Pages: 158-160.

3. Oxford handbook of Medical Sciences 2011. Pages: 810, 819

4. Garcia, Lynne Shore, and David A Bruckner. Diagnostic Medical Parasitology. New York: Elsevier, 2016. Pages: 79, 156, 157, 177

Do you have any Questions?


TEST
ASSESSMENTS
QUIZ

Case 1:

A 25-year-old journalist had recently returned to Egypt from a vacation in Brazil. She developed fever, anorexia and shortness of breath. On examination, she had upper and lower eyelid edema in the right eye with conjunctivitis. ECG showed non-specific abnormalities suggestive of right bundle branch block. Microscopic examination of blood sample revealed a few flagellated spindle-shaped protozoan parasites (some assuming an S shape) with undulating membranes. The characteristic parasite is shown in the figure.

Questions:

1. **What is your suggestive diagnosis?**

a. Acute chagas disease.
b. Chronic chagas disease.
c. acute sleeping sickness.
d. Chronic sleeping sickness.

Acute chagas disease

2. Which blood protozoan parasite is causing the infection?

a. *Trypanosoma brucei gambiense*

b. *Trypanosoma brucei gambiense*

c. *Trypanosoma cruzi*

d. *Toxoplasma gondii*

Answer:

- The patient has **American trypanosomiasis, or Chagas'** disease.
- This infection is caused by ***Trypanosoma cruzi.***

3. How is this infection transmitted ?

a. By Tsetse flies transmitting metacycilic trypanosomes.

b. By *Triatoma megista* transmitting amastigote form.

c. By *Triatoma megista* transmitting metacycilic trypanosomes.

d. By sand fly transmitting the promastigote form.

Answer:

- BY Triatoma megista, Contaminative with stool, posterior station development, cyclo-propagative type.
- Contamination of the bite by reduviid bug which defecate during the process of feeding .The insect deposits infective feces containing, metacycilic trypanosomes near or at the bite site.

5. What is the name of the lesion that may develop at the site of inoculation of the parasite?

a. Chancer
b. Calabar swelling.
c. Onchocercoma.
d. Chagoma

6. What is the name given to the unilateral edema of the eye in this disease?

a. Romana's sign.
b. Winterbottom's sign.
c. River blindness.
d. Keratitis

8. Which complications may occur?

a. Hematemesis
b. Hemoptysis
c. Congestive heart failure
d. Mega-colon
e. Mega-esophagus

Answer:

Complications as;

- Progressive congestive heart failure may develop.
- Megaesophagus and megacolon.

9. How is this infection treated?

a. By giving nifurtimox
b. By giving benznidazole
c. By giving flagyle
d. By giving corticosteroid

Answer:

- **Most drugs have proven to be ineffective in treating Chagas' disease.**

- **Acute Chagas' disease may be treated with nifurtimox, or benznidazole.**

10. Mention the infective and diagnostic stages of this parasite.

Answer:

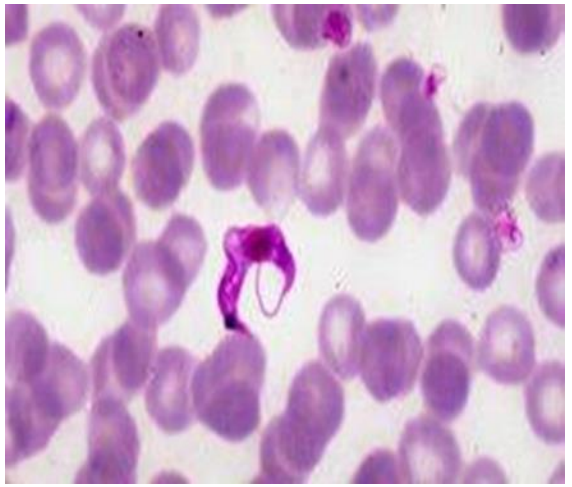
Infective stage: metacyclic trypomastigotes

Diagnostic stages: Monomorphic trypanomastigote and amastigote

11. Which methods are available to diagnose this infection?

Answer:

1. The monomorphic trypomastigotes of *T. cruzi* are usually visible in thick or thin blood smears stained with Giemsa stain in patients with acute Chagas' disease. They are not visible during the chronic phase of illness.



2. Antibody detection by serological methods is most useful in the diagnosis of chronic disease.

- Serological methods available include the complement fixation assay, the indirect hemagglutination assay, IFA, and ELISA,. These methods are also useful to screen blood donors in endemic areas, such as South American countries.

3. PCR methods are more sensitive and specific than traditional tests and are useful to diagnose acute and chronic Chagas' disease as well as to monitor therapy.

4. Xenodiagnosis is a technique whereby uninfected reduviid bugs bred in the laboratory are fed on the patient's blood. If parasites are present in the patient's blood, they multiply in the insect gut and may be recovered from the gut contents about 4weeks later.

5. *T. cruzi* may also be cultured in NNN media.

12. Mention the methods to prevent and control these cases?

Answer:

1. Treatment of infected patient
2. Destruction of reservoir hosts.
3. Eradication of vector by, dusting or spraying.
4. Screening of blood donors in endemic areas