



MEDICAL UNIVERSITY - PLEVEN
FACULTY OF MEDICINE

CENTER OF DISTANCE LEARNING

LECTURE № 3

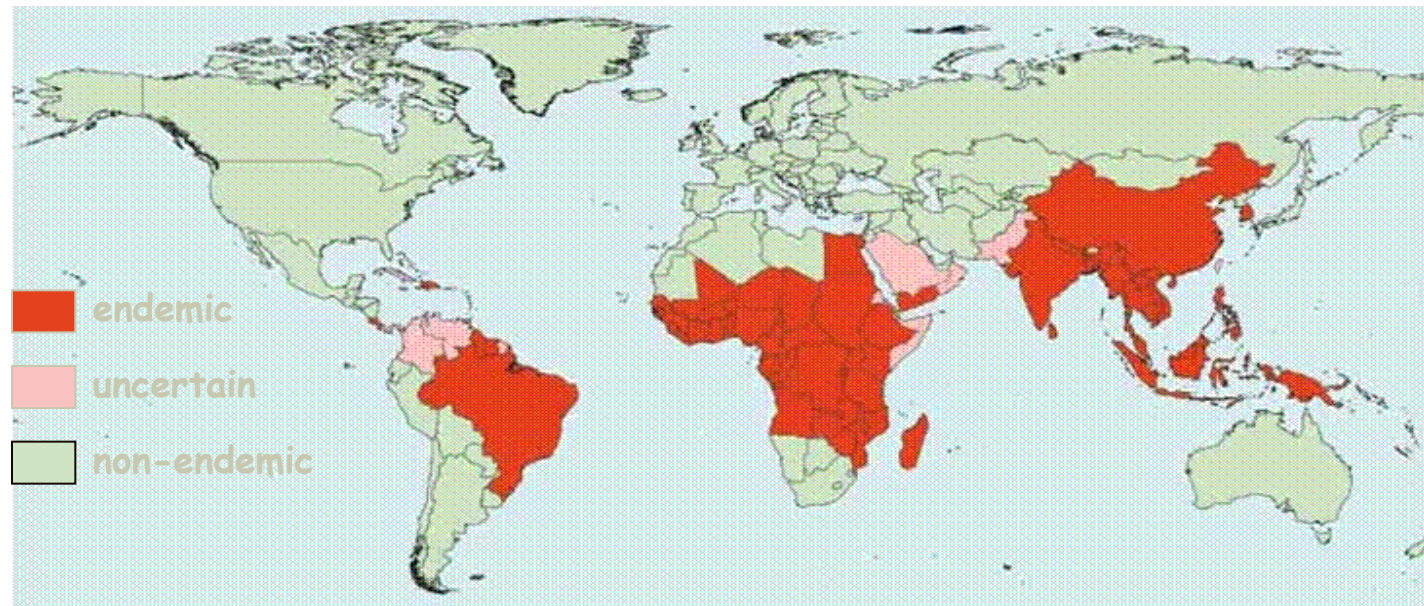
LYMPHATIC FILARIASIS
WUCHERERIASIS AND BRUG
FILARIASIS

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DEFINITION

Lymphatic filariases are transmissible endemic helminthiases, caused by nematodes of the family *Filariidae*. The adult parasites are found in lymph nodules and vessels, while larval forms (microfilariae) - in blood. Lymphatic filariases are caused by *Wuchereria bancrofti*, *Brugia malayi* and *Brugia timori*.

PREVALENCE AND IMPACT



Lymphatic filariases are seen in tropical and subtropical regions, particularly in Asia, Africa and some areas in the Middle East and South America.

The cases registered in countries with temperate climate are usually "imported" from endemic regions.

ETIOLOGY

Three species of lymphatic filarial worms, ***Wuchereria bancrofti***, ***Brugia malayi*** and ***Brugia timori***, cause lymphatic filariasis in humans.

Infection with ***W. bancrofti*** is called ***Wuchereriosis***, while ***Brug filariasis*** refers to infection by the other two species - ***Brugia malayi*** and ***Brugia timori***.

Wuchereriosis and ***Brug filariasis*** are helminthiases with a long incubation period and chronic course.

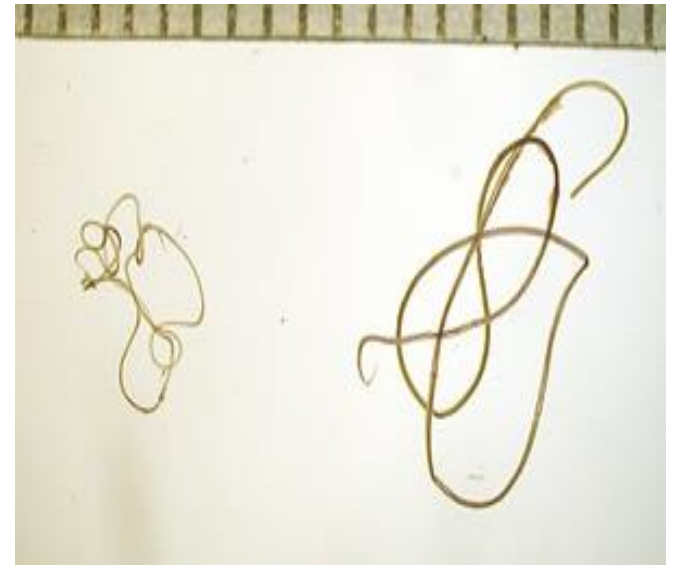
ETIOLOGY

The *W. bancrofti* male parasite is 40 mm long and 0.1 mm wide and the *B. malayi* is 22-23 mm long and 88 μm wide, with a ventrally curved tail.

The *W. bancrofti* female parasite is 80-100 mm long and 0.24 - 0.3 mm wide, while the female *B. malayi* is 55 mm long and 160 μm wide, with a pointed tail.

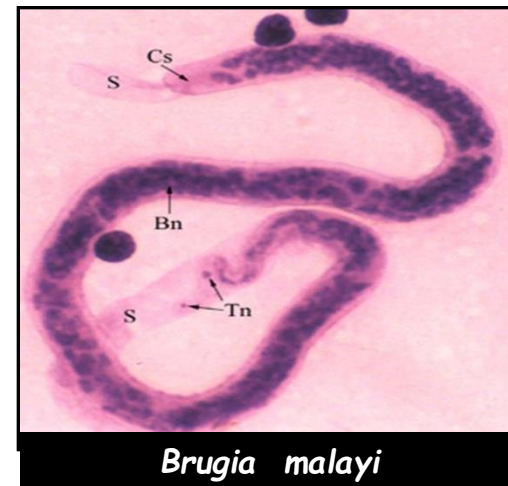
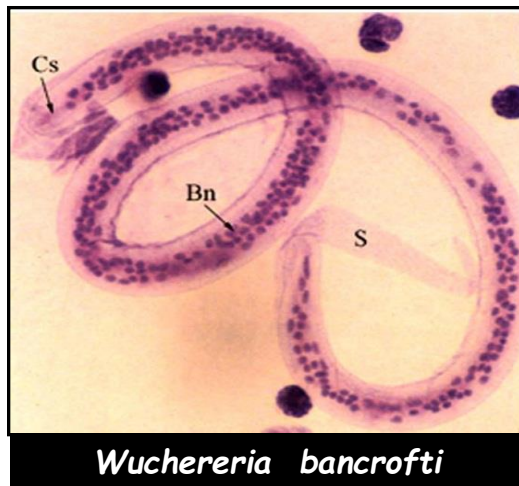
They are found in lymph vessels and nodes in different body regions.

The female parasites *produce microfilariae* (200-300 μm long), which circulate in blood.



ETIOLOGY

Microfilariae (127-320 μm long, 7-100 μm wide) are covered with an extra layer, and have a blunt front end and a pointed tail. When microfilariae are stained, multiple clusters of nuclei are seen in their central part. A specific diagnostic sign of *Wuchereria* is the column of nuclei that does not extend to the end of the parasite, while in the *Brugia* there is a terminal nucleus, located at a distance from the rest of the nuclei.



LIFE CYCLE

Lymphatic filariases are transmitted by mosquitoes.

These arthropods get infected through biting a human carrier of the disease.

In the mosquito they become invasive filariform larvae (third-stage larvae) for 1-2 weeks.

During the next bite, the larvae enter the site of the bite and infect the new host.

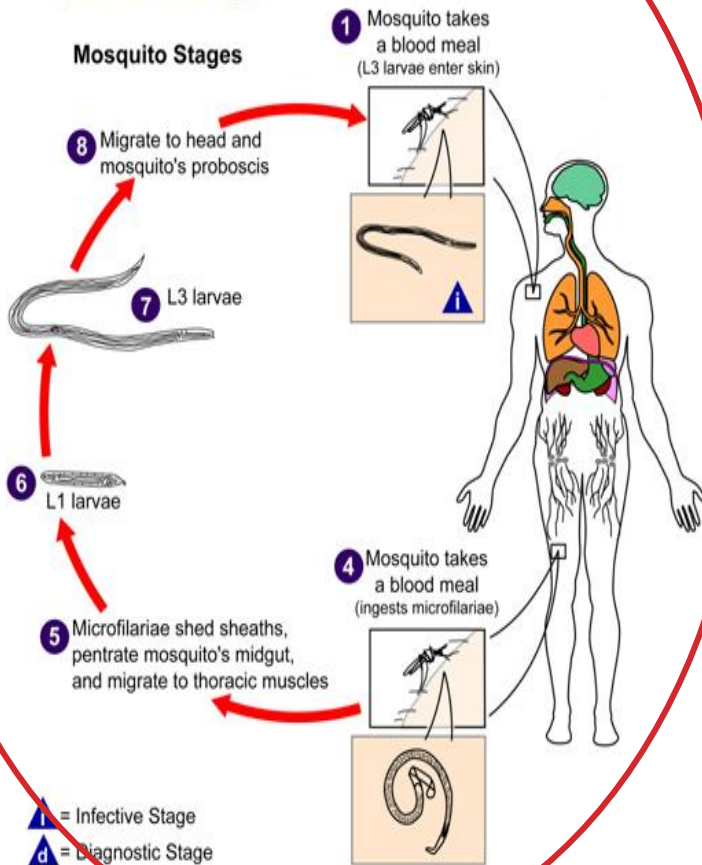
After a long-term migration in the body of the infected human individual, they reach specific locations, where they develop to become sexually mature parasites.

LIFE CYCLE IN THE MOSQUITO

Filariasis

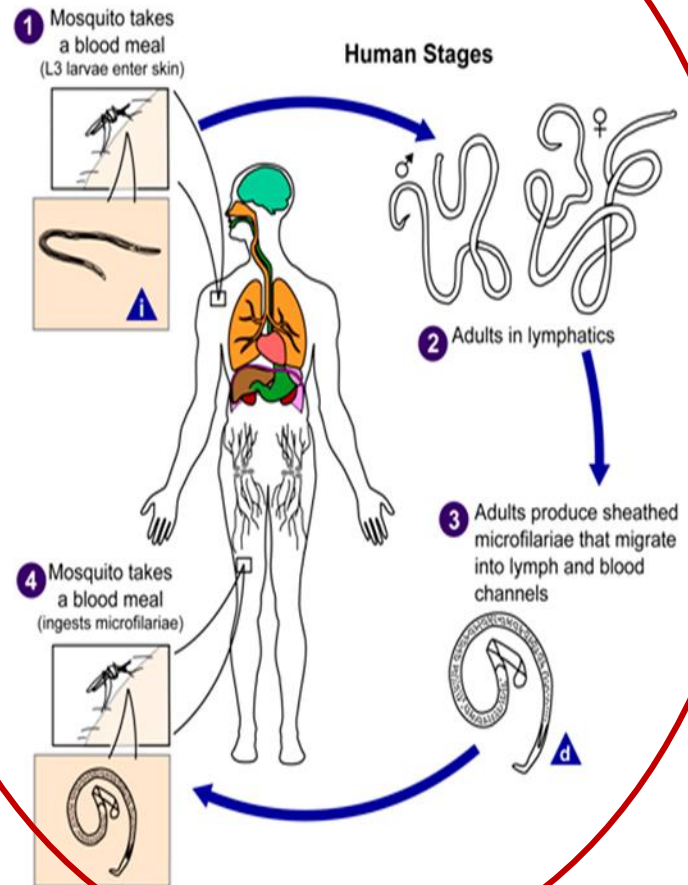
(*Wuchereria bancrofti*)

Mosquito Stages



LIFE CYCLE IN THE HUMAN

Human Stages



MIGRATION OF THE MICROFILARIAE

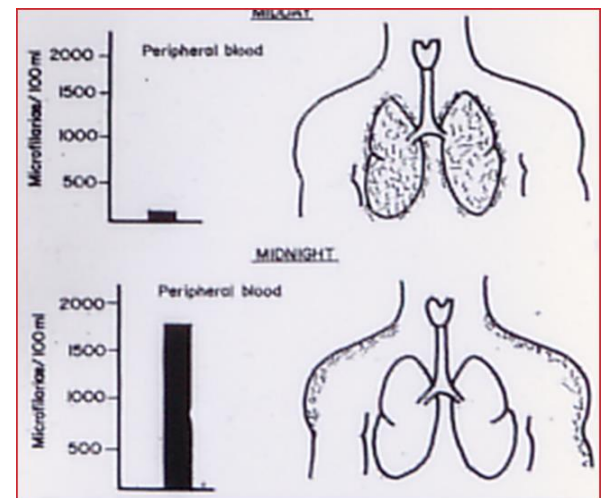
The microfilariae parasitize in the circulatory system, migrating from deeper to peripheral blood vessels on a 24-hour basis.

Depending on the type of migration, there are two strains: **periodic** and **sub-periodic**.

The **periodic strain** has a peak of concentration of microfilariae in peripheral blood during a specific time of day or night (in meantime, the microfilariae are in the pulmonary blood vessels).

The microfilariae of the **sub-periodic strain** are found in peripheral blood all 24 hours, but their concentration is higher in daytime or night.

Wuchereria bancrofti has a **periodic strain with a night peak** of concentration of microfilariae and **sub-periodic strains with a daytime peak**. There are two strains of **Brugia malayi** as well: **periodic and sub-periodic**, but the peak for both strains is during **the night**.



PATHOGENESIS AND PATHOLOGY

- The metabolite products of larval and adult parasites cause sensitization and the development of local and general allergic reactions.
- The gathering of sexually mature filariae in the lymph vessels slows down the lymph flow, and lymphostasis occurs resulting in varicose dilatation of the vessels and enlargement of lymph nodes.
- The lymphostasis is a blocking of the vascular lumen as a result from the cell reaction in the vascular walls and proliferation of the endothelium, where transudation occurs in the tissues (lymphedema), which leads to cellular proliferation of connective tissue and elephantiasis.

CLINICAL PRESENTATION

In endemic countries, many individuals are diagnosed with microfilaremia and without clinical symptoms and pathological changes.

The **incubation period** is long, varying from 5 to 15 months.

The **early stage** is characterized by allergic reactions, urticariae, conjunctivitis, focal edemata (scrotum, upper and lower limbs), eosinophilia. In some cases funiculitis, epididymitis and orchitis are seen.

CLINICAL PRESENTATION

The **chronic stage** occurs 2 to 7 years later, and symptoms are related to the damages of the lymphatic system.

Lymph vessels and nodes of the lower extremities and the organs of the genitourinary system are the ones most commonly affected.

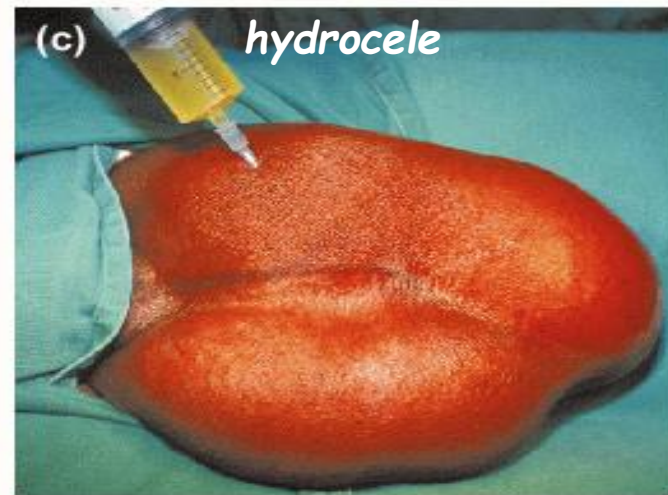
The strains of *Wuchereria pacifica* affect predominantly to the upper limbs and upper parts of the body.

Lymphangitis, lymphadenitis, varicose widening of the vessels are most commonly seen.

The disease is usually characterized by repeated attacks of lymphadenitis, accompanied by high fever.

CLINICAL PRESENTATION

The blocking of lymph vessels, followed by ruptures (spontaneous or traumatic) results in lymphorrhagia (lymph escape from the damaged vessel) in various organs.



CLINICAL PRESENTATION

In 95% of the cases, the lower limbs are affected, one or both, or in combination with damage in the scrotal area or the hands.



CLINICAL PRESENTATION

The knee, foot, mammary glands, vulva, etc. may be affected.



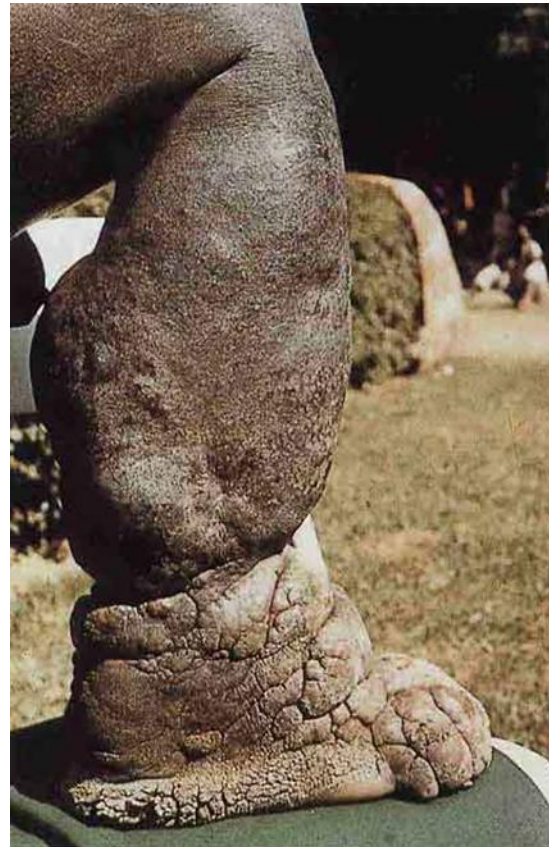
CLINICAL PRESENTATION

In brug filariasis, the lower limbs are predominantly involved. The organ affected is usually enlarged, shapeless, with dry atrophic skin. Eczematization and trophic ulcers are common.



CLINICAL PRESENTATION

The scrotum affected may become a mass of 20-30 kg, and mammary glands may hang to and below knee level. The late clinical manifestations of the disease are irreversible.



CLINICAL PRESENTATION



DIAGNOSIS

The diagnosis is complex and based on epidemiological and parasitological data.

Materials for investigation - blood and lymph samples.

In cases the invasion is by **the periodic strain** of *Wuchereria bancrofti*, blood samples **must be collected after 10 p.m.**, while in the cases the invasion suspected is by **the sub-periodic strain**, samples can be **collected during the day**.

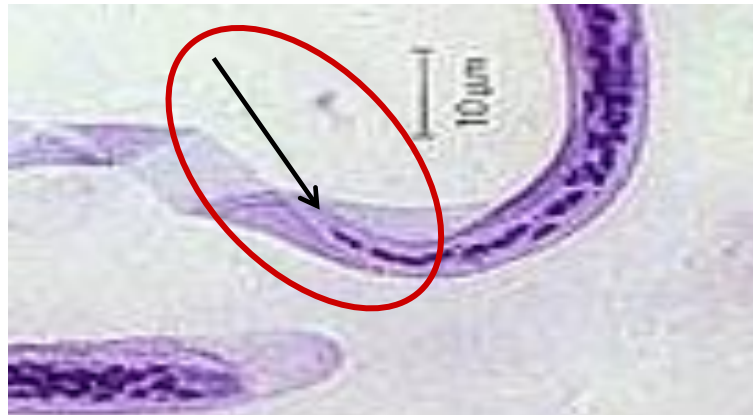
DIAGNOSIS

Methods of investigation

Microscopic methods:

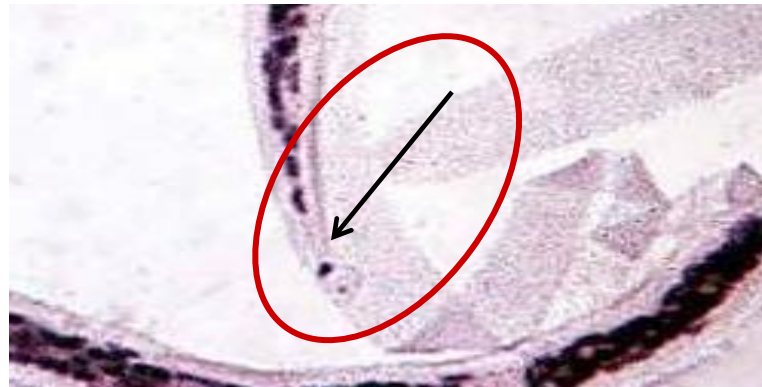
-native preparation from a blood drop. Moving microfilariae can be seen.

- a thick blood smear **stained by Romanowsky-Giemsa or with hematoxillin-eosin.** The types of microfilariae are recognized by the specific arrangement of the nuclei and the presence of an additional layer covering the body of the parasite.



Wuchereria bancrofti

Wuchereria bancrofti there is a column of nuclei that does not extend to the end of the parasite.



Brugia malayi

Brugia malayi there is an end nucleus, located at a distance from the rest of the nuclei.

DIFFERENTIAL DIAGNOSIS

Diagnoses like:

- bacterial lymphangitis;
- septicemia;
- malaria;
- tuberculosis;
- onchocercosis;
- lymphoma;
- hydrocele and chyluria of a different origin;
- elephantiasis nostras (with bacterial etiology).

TREATMENT

Etiological therapy.

Treatment aims to eliminate the two forms of the parasite (larvae and sexually mature forms).

The drug used is **Diethylcarbamazine** (tabl. 50 mg, 100 mg), daily dose of 6 mg/kg b.w. for 12 days several times a day, per os (for invasions caused by ***W. bancrofti***), and 3-6 mg/kg b.w. a day (for invasions caused by ***B. malayi*** and ***B. timori***).

Pathogenetic therapy - antihistamine drugs.

EPIDEMIOLOGY

Source of infection. The source of infection in *Wuchereriasis* is an infected human. In *Brug filariasis*, apart from infected humans, monkeys, cats, dogs and other animals can be definitive hosts.

Mechanisms, factors and routes of transmission.

Lymphatic filariases is transmitted by mosquitoes of the genera *Anopheles, Culex, Aedes, Mansonia* for *W. bancrofti* and *Mansonia, Anopheles* and *Aedes* - for *B. malayi*.

Susceptibility and immunity. Susceptibility is universal.

PREVENTION

Preventive measures include:

- ✓ early diagnosis and treatment of parasitized individuals;
- ✓ systematic mass chemotherapy (in case that over 5% of the population is parasitized);
- ✓ health education concerning protection from mosquito bites;
- ✓ extermination of mosquitoes and larvae using insecticides.

ANCYLOSTOMIASIS

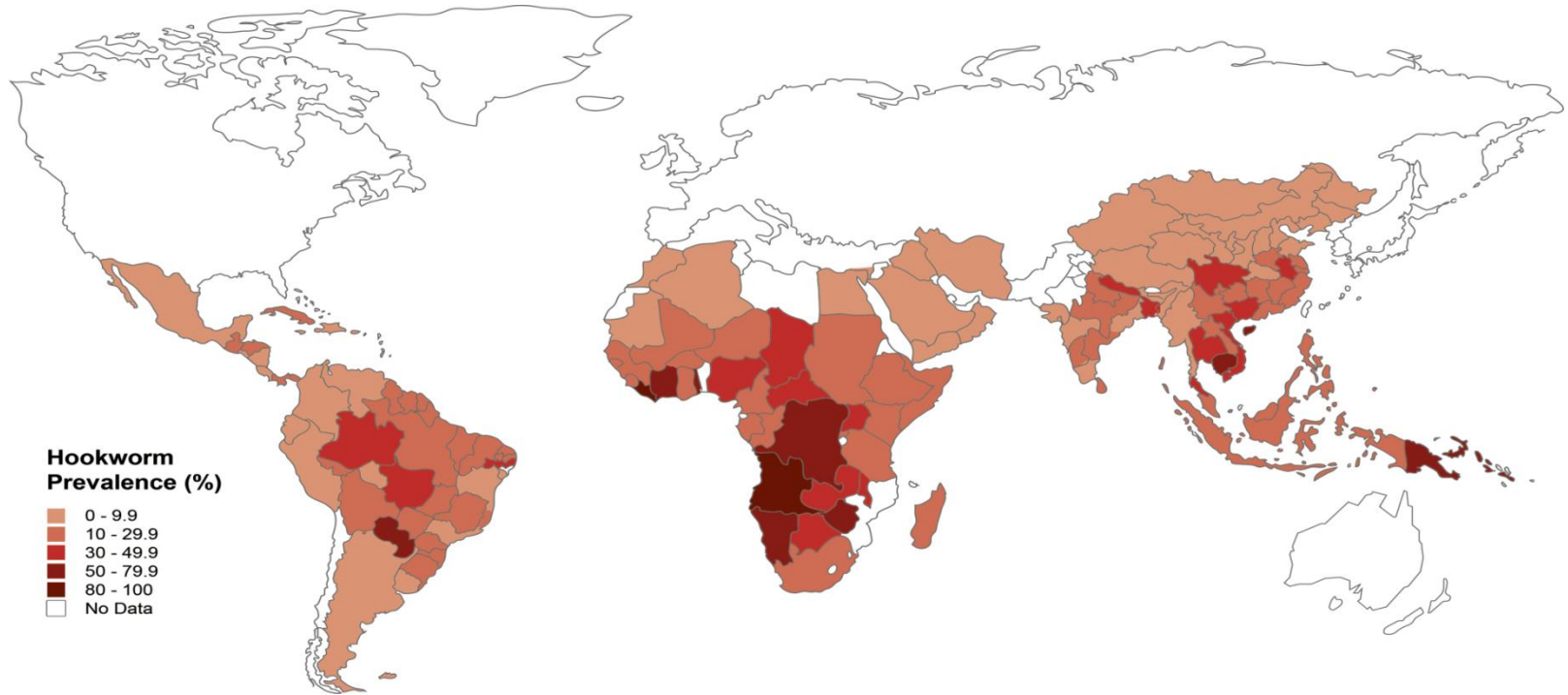
(HUMAN HOOKWORM DISEASE)

DEFINITION

Ancylostomiasis (human hookworm infection) is a chronic parasitosis that is characterized by allergic reactions and symptoms of duodenojejunitis at the onset. Later, progressive iron deficiency anemia develops.

It's caused by two types of nematodes: ***Ancylostoma duodenale*** and ***Necator americanus***.

DISTRIBUTION



Ancylostomiasis is widely spread in all countries with tropical and subtropical climate. They are also seen in some countries with a moderate climate, where humidity and temperature provide favorable conditions for the development of the larvae in the soil.

ETIOLOGY

Ancylostomiasis is caused by two types of nematodes (hook worms): ***Ancylostoma duodenale*** (A. duodenale) and ***Necator americanus*** (N. americanus), which belong to the family *Ancylostomatidae*.

A. duodenale causes ***Ancylostomiasis***, and ***N. americanus*** - ***Necatoriasis***.

The adult parasites are found living in the small intestines of humans, predominantly in the jejunum, more rarely - in the duodenum and sometimes in the ileum.

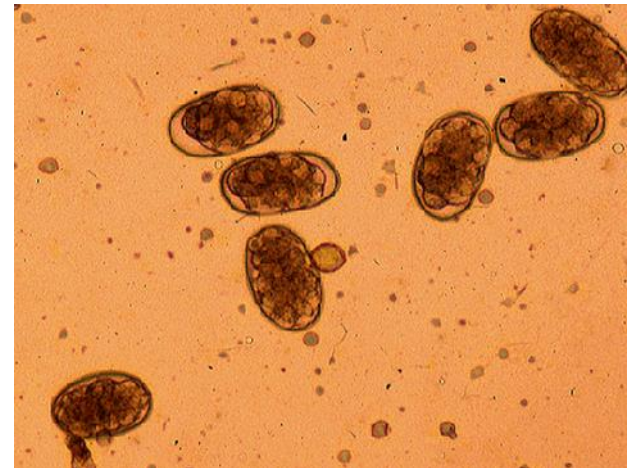
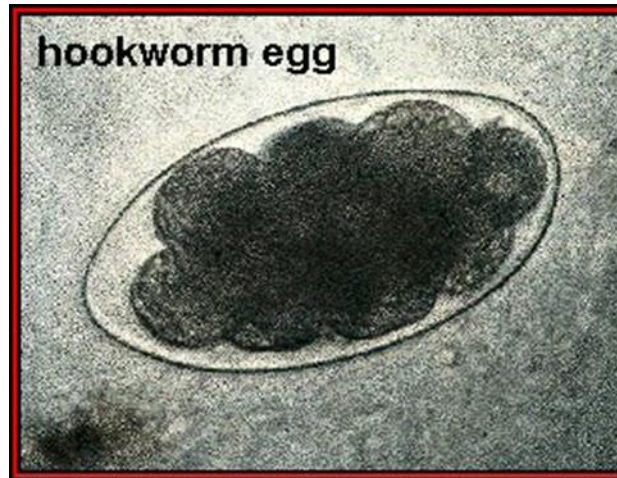
ETIOLOGY

- ✓ *Ancylostoma duodenale* parasites are small and cylindrical in shape. They are pinkish-white or greyish-white.
- ✓ The anterior end of the parasites is slightly narrowed and slightly curved, as their name "hook worms" imply.
- ✓ The male ancylostomas are 8-11 mm long and 0.4 mm wide. The females are longer: 10-13 mm, and are 0.6 mm wide.



ETIOLOGY

A female produces 25 000 - 30 000 eggs, which are oval or ellipsoid (65 μm long and 40 μm wide), which are colourless and enveloped in a transparent chitin shell. Usually, each egg contains four blastomeres. The life span of *A. duodenale* is 4-5 years.



ETIOLOGY

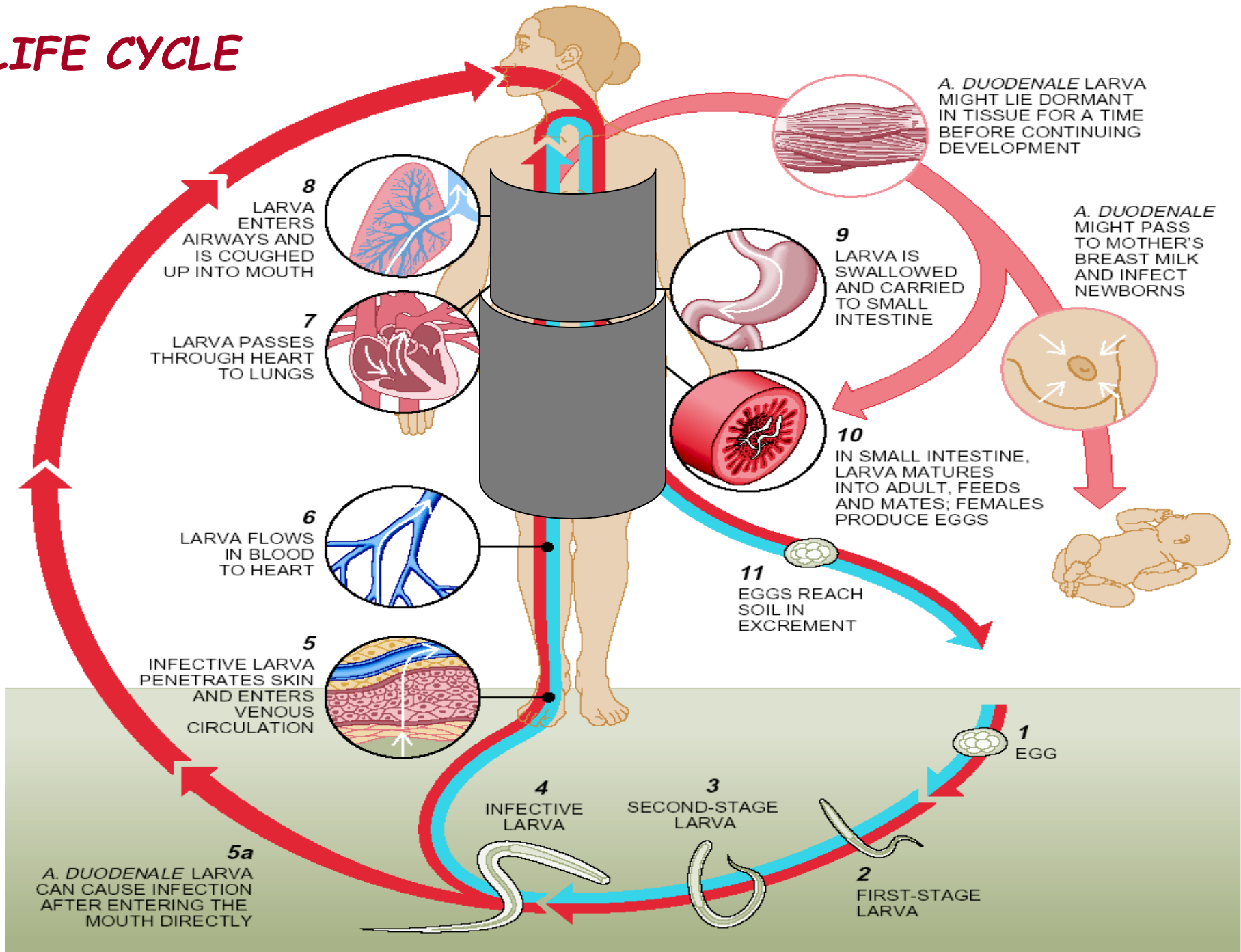
- ✓ *Necator americanus* is smaller and thinner than *A. duodenale*. The males are 7-9 mm long, and 0.3 mm wide. The females are 9-11 mm long and 0.4 mm wide.
- ✓ They have two dorsal and two ventral cutting plates around the small buccal capsule.
- ✓ A female can produce about 9 000 eggs a day. The eggs are slightly larger - 64-76 μm long and 36-40 μm wide, and usually contain 8 blastomeres.
- ✓ The typical life span of *N. americanus* is 10-15 years.

LIFE CYCLE

The eggs develop in the soil.

- ✓ When the conditions are good the eggs mature quickly and 12 to 24 hours later, rhabditiform larvae are hatched.
- ✓ A rhabditiform larva grows fast and elongates to become filariform larva, capable of invading the human organism.
- ✓ On direct contact of a human individual with contaminated soil, larvae capable of invasion reach the subcutaneous layer through the hair follicles, pores or skin lesions.
- ✓ The larvae then penetrate into lymph vessels and venules, and via the blood stream and the heart, reach the lungs. There the larvae move up to the bronchi, trachea, larynx and pharynx, and are swallowed, to move down to the duodenum and jejunum and finally settle there.
- ✓ It is here that they copulate and start producing eggs that are to be excreted with the feces.

LIFE CYCLE



PATHOGENESIS

- ✓ Filariform larvae enter the human body through intact skin and mucosae.
- ✓ The severity of the disease depends on the number of parasites and the general health of the host.
- ✓ The main pathogenic mechanisms in ancylostomiasis include:
 - mechanic trauma;
 - toxicoallergic action;
 - chronic blood loss ;
 - malabsorption syndrome.
- ✓ As a result, microcytic, hypochromic iron-deficiency anemia develops during the chronic stage.

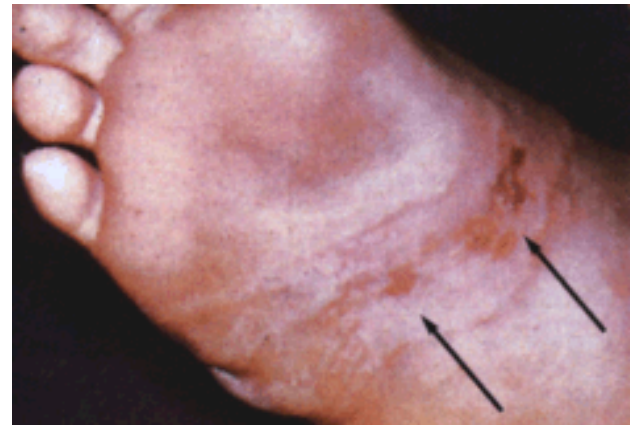
CLINICAL PRESENTATION

When the invasion is less intensive, the course is latent and the parasitosis may be diagnosed only by detection of eggs of the parasite in the stool. In the rest of the cases, the clinical course of ancylostomiasis has three stages:

- stage of skin penetration;
- stage of lung migration;
- stage of intestinal localization.

STAGE OF SKIN PENETRATION

At the moment of penetration of larvae, there is a feeling of a pin-prick, and local allergic dermatitis develops. This is accompanied by itching and scratching.



Hookworm in a Human
Foot

STAGE OF SKIN PENETRATION

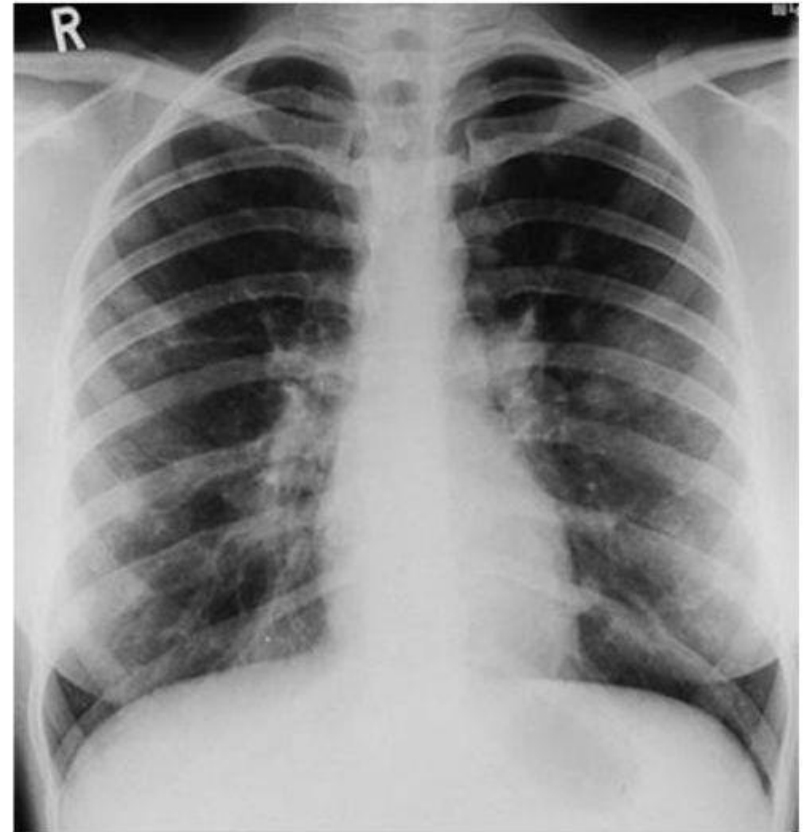


Hookworms are transmitted to humans by penetration of the skin

STAGE OF LUNG MIGRATION

- ✓ About a week after the invasion, there occurs a spastic cough, expectoration, dyspnea, low fever, headache and insomnia.
- ✓ X-ray reveals Loeffler's eosinophilic infiltrations, and blood cells count shows marked eosinophilia as high as 50 - 80%.
- ✓ The symptoms heal in 1 to 2 weeks.

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STAGE OF INTESTINAL LOCALIZATION

During this stage, two periods are clinically distinguished: acute invasion and chronic invasion.

ACUTE INTESTINAL INVASION

- ✓ It is characterized by general fatigue, nausea, vomiting, meteorism, abdominal pain that worsens after meals, bulimia or lack of appetite, diarrhoeal stools (5-10 times for 24 hours), without admixtures or with small quantities of mucus.
- ✓ Blood tests prove eosinophilia and leukocytosis.
- ✓ This period lasts 2 weeks to 2 months.

STAGE OF INTESTINAL LOCALIZATION

CHRONIC INTESTINAL INVASION

- ✓ Manifestations of iron-deficiency anemia dominate over the dyspepsia.
- ✓ Clinical findings include easy fatigue, dizziness, weight loss, pallor and decreased skin turgor. The face is puffy, eyelids are swollen, hair is dry and fragile. Feet and ankles are edematous.
- ✓ Hemoglobin and red blood cell count (RBC) are markedly lower. The anemia is characterized by iron-deficiency, with hypochromia and microcytosis.
- ✓ Severe forms are accompanied by cachexia, marked by aplastic anemia, and the outcome may be fatal.

DIAGNOSIS

- **MATERIALS INVESTIGATED** include stool, duodenal juice, blood serum.
- **METHODS OF INVESTIGATION**
 1. **Macroscopic method.** Sexually mature parasites may be detected in stools or duodenal juice.
 2. **Microscopic methods:**
 - helminthovoscopy of native stool smear to detect eggs;
 - concentration methods: sedimentation and flotation to detect eggs;
 - larvoscopy by the method of Berman and Harada-Mori;
 3. **Immunological methods** - ELISA and RIF.

DIFFERENTIAL DIAGNOSIS

It includes:

- ascariasis and strongyloidiasis;
- pneumonias of various etiology;
- bacterial intestinal infections;
- other intestinal helminthoses;
- alimentary dyspepsia;
- Ulcers;
- iron-deficiency anemia in other conditions;
- anemias with other etiology;
- kidney diseases, etc.

ETIOLOGICAL TREATMENT

The following drugs are used for specific etiological therapy:

Albendazole (Zentel) tabl. 200 mg and 400 mg;

It is applied in a single dose of 200 mg in children under 2 years old, and 400 mg in adults and children over 2 years old. It is contraindicated in pregnancy.

Mebendazol (Vermox) - tabl. 100 mg; suspension 30 ml (100 mg in 5 ml). 100 mg, twice a day for three successive days is prescribed.

The course of treatment is repeated after 3-4 weeks.

ETIOLOGICAL TREATMENT

Levamisol (Decaris) - tabl. 50 mg; 150 mg; syrup (40 mg in 5 ml).

It is applied once in a dose of 2.5 mg/kg b.w. in the evening. In case of severe invasion, the treatment is repeated in 7 days. The drug is not recommendable in lactating and pregnant women.

Pyrantel pamoat (Combantrin) - tabl 125 mg and 250 mg; suspension 15 ml (250 mg in 5 ml). The drug is applied once, at a dose of 10 mg/kg b.w. but no more than 1 g.

EPIDEMIOLOGY

SOURCES OF INFECTION

The source of infection are infected human individuals who excrete eggs of the parasite with the stools.

MECHANISMS, FACTORS AND ROUTES OF TRANSMISSION

- ✓ The basic route of transmission of ancylostomiasis is through direct physical contact.
- ✓ Another mechanism of transmission is alimentary.

SUSCEPTIBILITY is universal.

PREVENTION AND CONTROL

In endemic regions, prevention can include:

1. Extermination of adult parasites: active screening and treatment of invaded and ill individuals.
2. Extermination of larvae: prevent soil and water contamination with larvae by sanitation systems.
3. Personal prophylaxis: wearing shoes and gloves when walking in moist soil and grass; complete rinsing of fruit and vegetables that are consumed without heat processing.

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