

Epizootic Lymphangitis

Pseudoglanders,
Pseudofarcy,
Equine Histoplasmosis,
Histoplasmosis Farciminosi,
African Farcy,
Equine Blastomycosis,
Equine Cryptococcosis

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- OIE Collaborating Centres:
- Diagnosis of Animal Disease and Vaccine Evaluation in the Americas
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Importance

Epizootic lymphangitis is a debilitating fungal disease seen mainly in equids. The most common form of this disease is an ulcerative, suppurative, spreading dermatitis and lymphangitis; however, other forms including pneumonia or ulcerative conjunctivitis also occur. Epizootic lymphangitis spreads most readily where large numbers of animals are assembled, and it was a serious problem during the early twentieth century when large numbers of horses were stabled together. This disease continues to be a significant concern in some countries such as Ethiopia, where the prevalence in carthorses is nearly 19%, and economic losses from this disease are high.

Etiology

Epizootic lymphangitis results from infection by a dimorphic fungus, *Histoplasma capsulatum* var. *farcimosum*. This organism has also been known as *Histoplasma farciminosum*, *Cryptococcus farciminosi*, *Zymonema farciminosum* and *Saccharomyces farciminosus*. *H. capsulatum* var. *farcimosum* exists as a yeast in animal tissues and a saprophytic mycelium in the environment.

Recent genetic evidence suggests that the isolates causing epizootic lymphangitis originated independently from different geographical clades of *Histoplasma capsulatum*. Based on this evidence, some authors question the existence of the variety *H. capsulatum* var. *farcimosum*, and consider epizootic lymphangitis to be a form of histoplasmosis, caused by *H. capsulatum*, that occurs in horses.

Species Affected

Epizootic lymphangitis mainly affects horses, donkeys and mules. *H. capsulatum* var. *farcimosum* has also been reported in camels, cattle and dogs, and experimental infections have been established in mice, guinea pigs and rabbits.

Geographic Distribution

Epizootic lymphangitis is more common in tropical and subtropical regions than in temperate zones. Currently, *H. capsulatum* var. *farcimosum* is endemic in some countries in the Mediterranean region, and in parts of Africa and Asia including India, Pakistan and Japan. Sporadic cases have been reported from other parts of the world.

Transmission

H. capsulatum var. *farcimosum* infects animals through wounds. Both the yeast form found in animals and the mycelial form in the environment can produce epizootic lymphangitis after experimental inoculation. The source of the organisms can be the skin lesions and nasal and ocular exudates of infected animals, or the soil. In its saprophytic mycelial phase, *H. capsulatum* var. *farcimosum* can survive for many months in warm, moist environments. This organism can also be spread on fomites such as grooming or harness equipment.

Biting flies in the genera *Musca* and *Stomoxys* are thought to spread the conjunctival form. Flies may also transmit the skin form mechanically when they feed on lesions and exudates. Ticks might be involved in transmission; in a recent study, tick bites appeared to be a predisposing factor for epizootic lymphangitis in mules. The pulmonary form, which is rare, probably develops when an animal inhales the organism.

Incubation Period

The incubation period is usually several weeks to 2 months. In a recent study, the incubation period was much longer in a horse inoculated with mycelial organisms than in a horse inoculated with the yeast form.

Clinical Signs

The most common form of epizootic lymphangitis affects the skin and lymphatics. It often occurs on the extremities, chest wall, face and neck, but can be seen wherever the organism is inoculated into a wound. The first symptom is a

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painless, freely moveable intradermal nodule, approximately 2 cm in diameter. This nodule enlarges and eventually bursts. In some cases, the lesions may be small and inconspicuous, and heal spontaneously. More often, the skin ulcers grow, with cycles of granulation and partial healing followed by new eruptions. The surrounding skin is edematous at first, and later becomes thickened, hard and variably painful. The skin over the nodules may be fixed to the underlying tissues. The regional lymph nodes can be enlarged, but fever is uncommon. The infection also spreads along the lymphatics, causing cord-like thickening and further skin involvement. These cycles of exacerbation and partial healing gradually resolve, leaving only a scar. The process usually takes about 2 to 3 months. Epizootic lymphangitis sometimes spreads to the underlying joints and results in severe arthritis. Occasionally, there may be ulcerative conjunctivitis, keratoconjunctivitis, a serous or purulent nasal discharge, or pneumonia. Extensive lesions can end in death; this usually occurs in areas where animals are in poor condition and veterinary care is limited.

In dogs, both cutaneous infections and infections that disseminate to internal organs have been reported.

Post Mortem Lesions [Click to view images](#)

At necropsy, areas of the skin and subcutaneous tissue are thickened, and the skin may be fused to the underlying tissues. The regional lymph nodes may be enlarged and inflamed. Nodules in the skin have a thick, fibrous capsule and the affected lymphatic vessels are usually thickened or distended. Both nodules and lymphatics contain purulent exudates. In some cases, the lesions may extend to the underlying joints, resulting in arthritis, peri-arthritis or periostitis. Multiple, small, gray-white nodules or ulcers with raised borders and granulating bases may be apparent on the nasal mucosa, and lesions may be found on the conjunctiva and cornea. The lungs, spleen, liver, testes and other internal organs may also contain nodules and abscesses.

Morbidity and Mortality

Epizootic lymphangitis is more common in the tropics and subtropics than in temperate areas. Warm, moist conditions allow the organism to survive in the soil for months. The incidence of this disease is much higher when large numbers of animals are gathered together than when populations are less dense. The prevalence can be high in some areas. In Ethiopia, nearly 19% of the carthorses in warm, humid areas are affected, and the overall prevalence was 21% among mules in two towns. Death is uncommon if an animal is in good condition and receives good care, but animals with extensive lesions may die.

Diagnosis

Clinical

The symptoms are highly suggestive in cases with skin lesions. Epizootic lymphangitis should be suspected in horses, mules or donkeys with skin nodules or ulcers that follow a pattern of partial healing followed by renewed eruption. This disease must be differentiated by laboratory tests from other conditions such as glanders.

Differential diagnosis

The differential diagnosis includes the skin form of glanders (farcy), strangles, ulcerative lymphangitis, sporotrichosis, cryptococcosis, sarcoids and cutaneous lymphosarcoma. Epizootic lymphangitis also resembles histoplasmosis, which is caused by *Histoplasma capsulatum* var. *capsulatum*.

Laboratory tests

Epizootic lymphangitis can be diagnosed by detecting *H. capsulatum* var. *farcinosum* in lesions. Histopathology or the direct examination of smears from exudates is helpful in diagnosis. In established lesions, the organisms may be numerous. Tissue sections can be stained with hematoxylin and eosin, periodic acid-Schiff or Gomori methenamine-silver staining. In a Gram-stained preparation, *H. capsulatum* is a Gram-positive, pleomorphic, ovoid to globose structure that is approximately 2–5 µm in diameter. Organisms are found extracellularly or in macrophages, and can be seen singly or in groups. Each yeast is often surrounded by a capsule, which does not stain and appears as a halo. An immunofluorescent technique to demonstrate *H. capsulatum* has also been developed. Electron microscopy may be used on skin biopsy samples.

H. capsulatum var. *farcinosum* can be cultured on a variety of fungal media including mycobiologic agar, enriched Sabouraud's dextrose agar with 2.5% glycerol, brain-heart infusion agar with 10% horse blood, and pleuropneumonia-like organism (PPLo) nutrient agar with 2% dextrose and 2.5% glycerol (pH 7.8). This organism grows as a mycelium at cooler temperatures. These colonies grow slowly and develop in approximately 2 to 8 weeks at 26°C. They are dry, granular, wrinkled and grayish-white, becoming brown as they age. Aerial forms are rare. On microscopic examination, the hyphae are hyaline, septate, branched, pleomorphic and Gram stain variable. A variety of conidia including chlamydospores, arthroconidia and blastoconidia may be found, but *H. capsulatum* var. *farcinosum* does not produce the large, round, double-walled macroconidia often seen in *H. capsulatum* var. *capsulatum* cultures. Isolation may fail in up to half of the cases.

Conversion to the yeast form can be demonstrated at 35–37°C by subculturing the mycelium into brain-heart infusion agar containing 5% horse blood, or by growing the organism in Pine's medium in 5% CO₂. The yeast phase forms colonies that are flat, raised, wrinkled, white to

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grayish brown, and pasty. Complete conversion occurs only after repeated serial transfers to fresh media. Animal inoculation into immunosuppressed mice or other laboratory animals has also been used for diagnosis.

Antibodies can usually be found in animals with clinical signs. Serological tests include fluorescent antibody tests, enzyme-linked immunosorbent assays (ELISA) and passive hemagglutination. Skin hypersensitivity tests can be used to detect cell-mediated immune responses.

Samples to collect

Before collecting or sending any samples from animals with a suspected foreign animal disease, the proper authorities should be contacted. Samples should only be sent under secure conditions and to authorized laboratories to prevent the spread of the disease. Rare human infections with *H. capsulatum* var *farciminosum* have been reported, and precautions should be taken to prevent zoonotic disease.

Samples should be collected from unruptured nodules for culture. These samples should be placed in a liquid nutrient medium that contains antibacterials. They should be kept refrigerated and sent to the laboratory on wet ice as soon as possible. Air-dried smears from exudates should be prepared on glass slides and fixed immediately for direct examination. Samples of lesions that include both viable and nonviable tissue should be collected in 10% neutral buffered formalin for histopathology. Serum samples should also be submitted for serology.

Recommended actions if epizootic lymphangitis is suspected

Notification of authorities

Epizootic lymphangitis must be reported to state or federal authorities immediately upon diagnosis or suspicion of the disease.

Federal Area Veterinarians in Charge (AVIC):

https://www.aphis.usda.gov/aphis/ourfocus/animalhealth/contact-us/CT_Vet_Acred_Asst_DD

State Animal Health Officials (SAHOs):

http://www.usaha.org/upload/Federal%20and%20State%20Health/StateAnimalHealthOfficials_rev.pdf

Control

Epizootic lymphangitis can be controlled or eradicated by quarantines and the euthanasia of infected animals. Screening may help identify cases. Infected premises and equipment must be thoroughly cleaned and disinfected. *H. capsulatum* can be inactivated by 1% sodium hypochlorite, glutaraldehyde, formaldehyde and phenolic disinfectants. Its susceptibility to 70% ethanol is questionable. This organism is also destroyed by moist

heat of 121°C for at least 15 minutes. Bedding should be burned. Organisms in the soil may survive for long periods.

In endemic areas, good cleaning and disinfection can help prevent *H. capsulatum* var *farciminosum* from spreading between animals. Care should be taken to prevent transmission on grooming equipment or harnesses. Early cases may be treated with sodium or potassium iodide, but the lesions may later recur. Amphotericin B has also been used, but it is more expensive. In some cases, nodules may be drained and packed with iodine, or excised surgically. Vaccines are not widely available; however, live and inactivated vaccines have been used in some endemic regions. Published reports suggest that some of these vaccines may be promising.

Public Health

Rare human infections by *Histoplasma capsulatum* var. *farciminosum* have been reported.

Internet Resources

The Merck Veterinary Manual

<http://www.merckvetmanual.com/mvm/index.jsp>

United States Animal Health Association. Foreign Animal Diseases

http://www.aphis.usda.gov/emergency_response/downloads/nahems/fad.pdf

World Organization for Animal Health (OIE)

<http://www.oie.int>

OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals

<http://www.oie.int/international-standard-setting/terrestrial-manual/access-online/>

OIE Terrestrial Animal Health Code

<http://www.oie.int/international-standard-setting/terrestrial-code/access-online/>

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