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**Opportunistic Fungal infection**

 Opportunistic mycoses are fungal infections that do not normally cause disease in healthy host, but do cause disease in host with weakened immune defenses (immunocompromised). Weakened immune function may occur due to inherited immunodeficiency diseases, drugs that suppress the immune system (cancer chemotherapy, corticosteroids, drugs to prevent organ transplant rejection), radiation therapy, infections (e.g., HIV), cancer, diabetes, advanced age and malnutrition.

 Many compromised patients suffering from opportunistic fungal infections, and every year there are more and more such hosts and more fungal species involved. So, these infections are great challenge in diagnosis and in prevention.

**General features of opportunistic mycosis**

 The General features of opportunistic mycosis associated with:

1. **Causative agents: S**aprophyte in nature/found in normal flora
2. **Host:** Immunosupressed /other risk factors.

**Types of opportunistic mycosis:**

* **“Endogenous”** means that the fungus is a part of a normal animal flora. (***Candida* spp*).***
* **“Exogenous** means that the fungus does not normaly live in/on animal body, although it can transiently contaminate host body surfaces (especially respiratory tract).(***Cryptococcus neoformans, Aspergillus* spp., Zygomycetes)**

**Predisposing Factors of opportunistic mycosis:**

The main predisposing factors are associated with immunologic and non-immunologic factors.

**The immunologic factors includes :**

1-*Cancer* (esp. hematological malignancy, (Neutropenia ).

2-*Organ Transplantation* (bone marrow, liver, lung, kidney( Neutropenia, Impaired T cell function).

3-*Cellular Immune Dysfunction* (AIDS, lymphoma, Impaired T cell function).

**The non-immunologic factors includes :**

1-*Chemotherapy* (cytotoxic) - mucosal damage of GI, respiratory, GU tracts.

2-*Antibiotics* - Broad spectrum; loss of normal flora, esp. anaerobic.

3-*Invasive devices* - breach skin/mucosal defences, i.e. intravenous lines, urinary catheters, tracheostomies .

4-*Invasive procedures* - surgery, diagnostic biopsies.

**Transmission of Opportunistic Fungi.**

* *Candida*, *Trichosporon*, *Malassezia*
	+ - **ENDOGENOUS** : unique strain , colonization precedes infection, antibiotic suppression of normal flora, fungal overgrowth
		- **EXOGENOUS:** hand carriage health care worker
* *Aspergillus*, Zygomycetes, other filamentous fungi, *Cryptococcus*
	+ - **EXOGENOUS:** inhaled conidia, ventilation systems, construction, heliports, plants, environment, direct contact - dressings, arm boards, burns, wounds

**Cryptococcosis**

***Torulosis, European blastomycosis***

***Busse-Buschke’s disease***

Cryptococcosis is nearly always caused by *Cryptococcus neoformans*, an encapsulated yeast (Division Basidiomycota). Unlike most pathogenic fungi, this organism occurs in the yeast form both in the host and in the environment. *C. neoformans* is surrounded by a large capsule within its hosts and on some culture media. This capsule is important in its resistance to phagocytosis and in the identification of the organism. Strains differ in their virulence for animals and possibly humans, but the immune status of the host seems to be more important than the virulence of the strain. There are four serotypes - A, B, C and D - based on capsular antigens. There are three varieties: *Cryptococcus neoformans* var. *neoformans* comprises serotypes A and D. This organism is ubiquitous and causes most cases of cryptococcosis.

*Cryptococcus neoformans* var. *gattii* comprises serotypes B and C. This variety is less common in the environment than *C. neoformans* var *neoformans*. It has also been isolated from some cases of cryptococcosis in animals including cats, dogs, porpoises and llamas.

**Morbidity and Mortality: In Animals:**

Cases of cryptococcosis usually occur sporadically. Clinical cryptococcosis is reported most often in cats. It is particularly common in cats that are immunosuppressed by feline leukemia virus or feline immunodeficiency virus infections. Cryptococcosis may also be more common in immunosuppressed dogs. The prognosis is guarded, especially in cases with CNS disease. Untreated infections are fatal. Cryptococcal mastitis in cattle is usually associated with treatment of the mammary gland for another condition. Fungal mastitis is usually mild, but some infections can cause the death of the cow. Cattle rarely recover spontaneously from cryptococcal mastitis. Clinical cryptococcosis is very rare in birds, but the organism can be carried transiently in the intestinal tract. *C. neoformans* has been isolated from the feces of 26% of canaries, 18% of carrier pigeons, 2% of budgerigars and 1% of psittacine birds.

**Transmission:**

*C. neoformans* grows naturally in the environment. *C. neoformans* var *neoformans* is ubiquitous in the soil, where it grows as a saprophyte. It is common in old pigeon nests and around pigeon droppings; the bird droppings appear to create a favorable environment for its growth. It can also be isolated from numerous environmental sources including vegetables and fruit, house dust, air conditioners, air and sawdust. It can survive for months to years outside the host. *C. neoformans* var *gattii* is found in bark and plant debris under eucalyptus trees (the river red gum tree Eucalyptus *camaldulensis* and the forest red gum tree, *E. tereticornis*). It is also found in the air around these trees, particularly when they bloom in late spring. It is not associated with pigeon droppings. Recently, *C. neoformans* var *gattii* was isolated from trees and soil on Vancouver Island in British Columbia .

Transmission seems to be mainly by inhalation, but *C. neoformans* can also enter the body through the skin. Infections seem to be acquired mainly from the environment. Cryptococcosis can also result from the reactivation of a latent infection. Cryptococcal mastitis in cattle is usually associated with the treatment of the mammary gland for another condition. The organism may be introduced into the teat in contaminated syringes, cannulas or antibiotic preparations. It can also enter the mammary gland if the teat ends are not adequately cleaned before treatment. Cryptococcosis does not seem to be very contagious. There are no reports of transmission from mammalian animals to other animals or to humans. However, in one recent case, an immunosuppressed human probably acquired *C. neoformans* from the feces of an asymptomatic pet bird.

 **Disease in Animals:**

Clinical cryptococcosis is most often found in cats. Outbreaks of cryptococcal mastitis and pneumonia have been described in cattle. Clinical cases have also been reported in dogs, ferrets, guinea pigs, horses, sheep, goats, pigs, llamas, foxes, mink, cheetahs, gazelles, koalas, wallabies, porpoises, non-human primates and other animals. *C. neoformans* can be isolated from asymptomatic mammals. *C. neoformans* can be found in the feces of birds including canaries, budgerigars, psittacine birds, chickens, sparrows, starlings, skylarks, pigeons and turtledoves. The presence of this organism in the feces can be due to a transient asymptomatic intestinal infection, or to the inoculation of the feces with organisms carried on the beaks or feet. Clinical infections in birds are very rare.

**Clinical Signs: Cats and Dogs:**

In cats, disease may be seen in a single organ system or many. Upper respiratory disease (unilateral or bilateral chronic rhinitis or sinusitis) is the most common form of cryptococcosis in cats. The symptoms may include sneezing, snoring or snorting, dyspnea, or a mucopurulent or serosanguineous nasal discharge. Polyp-like masses may protrude from one or both nostrils. Pulmonary symptoms are uncommon. *C. neoformans* can cause skin lesions, particularly on the face. Typically, there are one or more firm, nodular, cutaneous or subcutaneous swellings on the head, particularly the bridge of the nose, side of the face, upper lip or nostril. Some lesions may ulcerate. There is little or no pruritus. Fluctuant or firm papules and nodules may also occur on other parts of the body; generalized skin disease suggests disseminated cryptococcosis. Central nervous system (CNS) disease, due either to a focal mass lesion or diffuse neurologic disease, is also common. Neurologic signs may be mild or severe, and can include a change in temperament, depression, disorientation, ataxia, paresis or paralysis, seizures, circling, abnormal pupillary responses, anisocoria and blindness. *C. neoformans* can also invade other organs and less common presentations, including osteomyelitis, may be seen.

The gross lesions may appear either as granulomas or as gelatinous masses with minimal inflammation. In cats, lesions can occur in any organ system. Often, there is a viscous exudate in the nasal passages and sinuses, and/or small gelatinous nodules scattered on the viscera of the abdominal and thoracic cavities. In cases with CNS involvement, the meninges may be congested and thickened. They sometimes have a cloudy, gelatinous appearance, and they may be covered by a scant mucoid exudate. Abscesses may be found in the brain or spinal cord. Ocular lesions including chorioretinitis or panophthalmitis can also be seen.

Most dogs have severe disseminated disease. Neurologic disease is the most common form in dogs and resembles the disease in cats. Ocular lesions are also common and may include granulomatous chorioretinitis and optic neuritis. Disease can also occur in other organs, but cryptococcosis rarely affects the nasal cavity in dogs.

**Clinical Signs: Other Animals**

Outbreaks of cryptococcal mastitis occur in cows. The symptoms may include anorexia, decreased milk production, and enlargement of the supramammary lymph nodes. The affected quarters are usually swollen and firm. The milk may be viscid, mucoid and grayish-white, or it may be watery with flakes. Pulmonary disease and mastitis have been described in sheep and goats. Syndromes that have been reported in horses include meningoencephalitis, pulmonary disease, upper respiratory disease affecting the frontal sinuses and paraorbital area, and abortions. Obstructive growths in the nasal cavities are the most common presentation. Cryptococcosis is very rare in birds; mycotic rhinitis and sinusitis have been described. However, the organism can be found in their feces especially in pigeons.

 **Diagnosis in animals:**

Cryptococcosis is usually diagnosed by detecting *C. neoformans* in biopsies, impression smears, aspirates, or swabs of nasal secretions or skin exudates. In cases of CNS disease, *C. neoformans* may be found in the cerebrospinal fluid (CSF). *C. neoformans* can sometimes be found in clinical samples by direct observation. This organism is an encapsulated 4 to 6 mm, round to oval yeast. It is surrounded by a halo-like capsule that stains strongly with Mayer’s mucicarmine. In an India ink preparation, yeast cells surrounded by a clear halo (the capsule) may be seen; unless budding is observed, the organisms can be confused with fat droplets or other artifacts. *C. neoformans* can be identified in the tissues by immunofluorescence. A definitive diagnosis can be obtained by culture. Although *C. neoformans* grows on most media, growth is best on fungal media such as Sabaraud’s dextrose agar without cycloheximide. A latex agglutination test or ELISA can detect *C. neoformans* capsular antigens in blood, CSF or urine. Serology may be useful in some cases; however, large amounts of capsular antigen in the circulation appear to tie up antibodies. Cats with clinical disease seldom have positive titers. Serologic tests used in cats include complement fixation, immunodiffusion, indirect immunofluorescence and tube agglutination.

 **Treatment in Animals:**

Cryptococcosis can be treated with amphotericin B, flucytosine, itraconazole and fluconazole. Amphotericin B and flucytosine are often used in combination. A combination of ketoconazole and itraconazole has been effective in some experimentally infected cats, including animals with neurologic disease

**Prevention and Control**

Prevention of **environmental exposure** is difficult, as *C. neoformans* is ubiquitous in the environment. Avoidance and/ or environmental control of pigeon droppings may be beneficial in preventing disease due to *C. neoformans* var *neoformans*. Removal of pigeon droppings should be preceded by chemical decontamination or wetting with water or oil to decrease aerosolization. Pigeon droppings can remain infectious for up to 2 years. *C. neoformans* var *gattii* infections are mainly associated with exposure to eucalyptus trees, particularly during the period when they bloom (November to February). Avoidance of these trees may reduce the risk of exposure but other sources of *C. neoformans* var *gattii* also seem to exist.

**Pet birds** can carry *C. neoformans* var *neoformans* asymptomatically in the intestinal tract. The organisms are found mainly in the feces and can be aerosolized by sweeping, cleaning the cage and similar activities. Animals that may be sources of *C. neoformans* should be treated with caution, particularly by people who are immunosuppressed. Although no cases of mammal-to-human transmission have been reported, people handling animals with cryptococcosis should also use appropriate precautions and wear protective clothing such as gloves and a mask. Cages and litter boxes should also be decontaminated regularly. Fluconazole has been used for prophylaxis in AIDS patients.

**Cryptococcal mastitis in cattle** is usually associated with the treatment of the mammary gland for another condition. Care should be taken not to contaminate syringes, cannulas or antibiotic preparations with *C. neoformans* from soil or other sources. The teat ends should also be adequately prepared before treatment.