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SYSTEMIC MYCOSES IN DOGS AND CATS

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ADVANCES IN MEDICINE now permit more effective control of certain bacterial and viral diseases, and mycotic infections are assuming greater importance. The reported prevalence of mycoses in man and animals in the Americas is the highest in the world and the known cases may represent only a fraction of the total. Animals may be exposed to fungi with mild or unnoticed response. The clinical disease is rare. The natural habitat of many pathogenic fungi is the soil (1) and the primary route of infection is by inhalation.

Emmons *et al* (16) in a survey of histoplasmosis extending over a period of eight years examined 4,664 animals of various species. Dogs and cats showed the highest incidence of the disease. Of 397 dogs examined 145 were infected, and of 449 cats 81 had *Histoplasma capsulatum* in their tissues. It is the most common cause of systemic mycosis in dogs in North America.

Between 1959 to 1962 specimens from 472 animals including 16 species, were examined at the U.S. Public Health Service Communicable Disease Centre, Kansas City, and 70 were found to have a mycotic infection. Of 70 positive cases, 42 were due to blastomycosis, 23 to histoplasmosis and the remaining five were due to other fungi (30).

The benign forms of histoplasmosis and blastomycosis are common (44). A total of 151 dogs were skin-tested with histoplasmin and blastomycin and of these 34 (23%) had a specific reaction to histoplasmin and seven (5%) had a specific reaction to blastomycin. In none of these dogs was *Histoplasma capsulatum* or *Blastomyces dermatitidis* demonstrated by cultural, histopathological or fluorescent antibody examinations. Porter *et al* (36) considered that only the fluorescent antibody technique and the cultural and histopathological examinations are reliable in identifying infections of blastomycosis and histoplasmosis.

Cases treated at the Ontario Veterinary College during the past five years included two cases of blastomycosis in dogs, six cases of histoplasmosis of which five were in dogs and one in a cat, and two cases of aspergillosis in dogs.

Species of fungi that are rarely if ever encountered as primary disease agents are not included in this review which covers only those fungi that are usually primary pathogens and that are most frequently encountered as disease agents.

Since Actinomyces and Nocardia are classified as bacteria they are not included in this review.

NORTH AMERICAN BLASTOMYCOSIS

North American blastomycosis is a chronic granulomatous and suppurative disease caused by *Blastomyces dermatitidis*. Blastomycosis is strictly American in distribution but the natural habitat of *B. dermatitidis* still remains unknown. It extends southward from Canada to Central America. No proof has been found to indicate that the disease is transmitted from animal to animal or from animal to man. Most cases originate as a respiratory infection and disseminate usually with pulmonary, osseous and cutaneous involvement. The dog appears to be more susceptible than other animals.

Although the upper airways are rarely affected, infection gains entrance to the body via the pulmonary tree and lung tissue. The bronchial and the mediastinal lymph nodes become infected. If untreated, the disease disseminates throughout the body to affect connective or osseous tissues. The skin may be affected causing fistulae and enlargement of local lymph nodes. Pulmonary signs are manifested by a chronic, nonproductive dry cough.

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The radiographic shadow of the lungs, in the early stages, is similar to that in pulmonary carcinoma or tuberculosis.

When the osseous system is involved, bone destruction similar to that seen in cases of bacterial osteomyelitis is characteristic. Infection of the bone usually is by the haematogenous route, but it may spread from an adjacent cutaneous lesion.

Grice *et al* (18) reported skeletal blastomycosis affecting mainly the long bones. The dog had respiratory involvement also. Radiographs of the lung revealed enlargement of the bronchial lymph nodes and irregular patchy areas of increased density. At necropsy *Blastomyces dermatitidis* was isolated. Badame and Peck (3) reported a case with a history of coughing. As the throat and the tonsils were inflamed and signs recurred in spite of treatment, a tonsillectomy was performed. After two years, the animal was presented again with increased temperature, anorexia and coughing. Lesions at post mortem were confined to the thorax and *Blastomyces dermatitidis* was present.

Cases have been reported which involved the eyes and the central nervous system.

Savage *et al* (43) reported a case of blastomycosis in a dog with a history of unilateral ophthalmitis and recurrent subcutaneous abscesses on the flank. There was also mild spasmodic coughing and marked loss of weight. As the dog did not respond to a wide range of therapy, euthanasia was performed. At post mortem examination, all visceral organs had yellowish grey nodules and *Blastomyces dermatitidis* was demonstrated.

Simon and Helper (46) described two cases of blastomycosis with ocular involvement. Both dogs had uveitis followed by glaucoma and panophthalmitis. Histological examination of lesions revealed *Blastomyces dermatitidis*. In both dogs there were numerous granulomata in the lungs.

Riser (38) diagnosed six cases over a fifteen year period. Three of these were pulmonary, two cutaneous, and one case involved bone. The latter was diagnosed as an osteomyelitis or malignant bone neoplasm in a metatarsal bone of a dog. At necropsy blastomycotic lesions were found throughout the body. A generalized infection in a ten-month-old male Labrador was described by Kurtz and Sharpnack (24).

In the past five years, two cases of canine blastomycosis have been diagnosed in the hospital of the Ontario Veterinary College. The first occurred in a two-year-old Beagle. Blastomycosis had caused lobular pneumonia, ascites, hepatomegaly, cellulitis of all paws and osteomyelitis of a number of phalanges.

The second case occurred recently in an 18-month-old male Weimaraner with a history of low grade fever, lameness and cutaneous nodules. However, the most significant lesion was a necrotic orchitis which also affected the skin of the scrotum. An aspirate from the testicles revealed an infection with *Blastomyces dermatitidis*. The dog was castrated and at the same time a radical scrotectomy was performed. Following surgery the dog was treated with amphotericin B. The cutaneous nodules regressed and no new one has appeared.

Sheldon (45) reported pulmonary blastomycosis in a cat with respiratory distress. At necropsy there were lesions in the lungs and in the mediastinal and bronchial lymph nodes. Four cases in Siamese cats were described by Jasmin, Carrol and Baucom (23).

Diagnosis

The causative agent of blastomycosis, *Blastomyces dermatitidis*, can be recovered from biopsies and pus.

Using wet mount and potassium hydroxide the specimen should be examined for thick walled yeast cells (8μ to 15μ) with buds which have a broad flat area of attachment. Confirmation of identity requires growth of both phases of the organism and demonstration of pathogenicity for mice. The blastomycin skin test and the complement fixation test for blastomycosis have not been found reliable for the diagnosis of blastomycosis. The tissue form may be obtained *in vitro* by incubating at 37°C blood agar plates inoculated with clinical material. The mycelial phase develops well on Sabouraud dextrose agar incubated at 22°C.

In positive cases, typical histopathological findings in the lungs include granulomatous lesions containing neutrophils, lymphocytes and monocytes. The organism *Blastomyces dermatitidis* can be identified easily when the Bower stain is used on the tissue section.

Histoplasmosis

The disease is caused by the diphasic fungus *Histoplasma capsulatum*. The organism occurs throughout the world (1). On this continent it is endemic in the Mississippi basin in the United States. In Canada it occurs in southwest and eastern Ontario, the Ottawa river valley, metropolitan Montreal, in the St. Lawrence river valley, and to a lesser extent, in the central and eastern part of the United States and Canada.

Histoplasma growing in soil under trees

which shelter starlings and other birds is probably the most frequent source of urban exposure (13). In the country, the fungus appears to be most frequently associated with decayed or composted chicken manure (53). More recently the organism has been found in several species of bats (15). Infection is usually by inhalation of the saprophytic phase of the spores and the most common primary site of histoplasmosis is the respiratory system. Ibach, Larsh and Furcolow (22) isolated *Histoplasma capsulatum* from the air.

The disease occurs usually in a mild or asymtomatic form, but in a small percentage of cases, it may occur in disseminated forms.

In the benign type, the lungs are involved primarily and generally there is no evidence of illness, although radiographs may reveal pulmonary nodules. Even in mild self-limited histoplasmosis in which all signs are limited to the pulmonary lesions, the predilection of *Histoplasma capsulatum* for the reticuloendothelial system and the isolation of *Histoplasma capsulatum* from urine indicate that the disease actually is disseminated. In systemic histoplasmosis the spleen, liver and adrenals frequently are enlarged and the animal has a concurrent ascites and anaemia. Lesions in disseminated histoplasmosis may occur in any part of the body, but chiefly in those organs or tissues which are rich in reticuloendothelial cells. Involvement of the intestines in the disseminated form is attended by an intractable bloody diarrhoea. Lesions are confined to the mucosa and the mesenteric lymph nodes in these cases.

Occasionally a generalized lymphadenopathic form is seen. In these cases all palpable lymph nodes are enlarged and there is an accompanying anaemia and persistent pyrexia.

Rhoades *et al* (39) reported a case presented with a history of recurrent diarrhoea over a six month period in a two-year-old Chihuahua. Necropsy findings included an irregularly thickened intestine with focal ulceration and haemorrhage. The liver and lung contained scattered grayish white foci. The mediastinal, mesenteric and ileocoecal lymph nodes were enlarged. The cellular reaction was granulomatous in nature and consisted essentially of hyperplasia of the reticuloendothelial cells and infiltration of mononuclear cells. *Histoplasma capsulatum* was isolated from lesions in the liver, spleen, lungs and lymph nodes but not from the segments of intestines.

A similar case in a two-and-one-half-year-old Dalmatian was described by Ditchfield and Fischer (11). According to these workers, enteritis appears to be an important feature of histoplasmosis in the dog and culture of the feces from dogs with persistent diarrhoea is recommended.

Five dogs and one cat referred to the teaching hospital of the Ontario Veterinary College had chronic coughs, varying degrees of dyspnea, persistently high temperatures and fatigued easily. Radiographically nodular densities were observed with an associated pneumonia. Two recent cases were treated with amphotericin B. One continued to lose weight and was eventually destroyed, but the other when last observed appeared to have recovered (20). The one case seen in a cat occurred in a six-year-old Siamese which had been suffering from a cough for a year. It was treated with amphotericin B and when discharged was making good progress.

Disseminated histoplasmosis may occur when benign cases do not heal spontaneously. In the lungs, the disseminated form gives rise to pulmonary cavitation. In these roentgen aspects as in others, histoplasmosis closely resembles tuberculosis.

The disease does not appear to be as common in the cat. Akum (2) described infection of a six-month-old cat which had signs of weight loss, progressive cachexia, hypochromic anaemia, excessive nasal secretion and coughing. Necropsy of this kitten revealed a disseminated focal necrosis of the liver, splenomegaly, miliary granulomata of the lungs, ulcerative gastritis and a catarrhal enteritis. In some patients the pulmonary lesions resolve entirely, but in others evidence of past infection persists in the form of calcification or scarring.

Diagnosis

The most positive approach to diagnosis is by means of biopsies of lymph nodes and organs. Hoff and Fogle (20) reported the isolation of the yeast phase from sputum obtained during the bronchoscopic examination of a dog with the pulmonary form of the disease. This examination also revealed nodular areas at the bifurcation of the trachea. Though skin tests and complement fixation tests are not satisfactory they serve as valuable adjuncts to diagnosis (7).

According to Beamer (4), bistoplasmin is an ineffective diagnostic agent in dogs. Similar observations were reported by Okudaira *et al* (33), while Cole *et al* (9) reported that of 27 infected dogs tested all had positive reactions except one with acute disease.

Lesions should be removed for histology and culture when allergic and serologic tests follow to assist in diagnosis. Wet mounts and potassium hydroxide mounts are of no value.

Impressions of tissue, stained with Giemsa and/or the Periodic-Acid-Schiff (PAS) stains and examined under oil immersion for intracellular yeast, should be used in direct microscopic examinations.

Histoplasma capsulatum may be found in the cytoplasm of mononuclear and occasionally polymorphonuclear cells in the form of small round or oval yeast-like cells one to four microns in diameter. Some organisms may be found free in the tissue also.

Confirmation of identity requires recovery of the filamentous form on Sabouraud dextrose agar incubated at 25°C and observations of tuberculate chlamydospores and the yeast phase in tissue. Brain heart infusion blood agar media with and without antibiotics have been recommended for growth of the tissue phase. Inoculation of mice with the material from a lesion is also recommended since one to ten yeast cells are infective for a mouse (40).

Cryptococcosis

The disease is caused by *Cryptococcus neoformans*. The distribution of the organism and the disease is world-wide. Virulent strains of *C. neoformans* are found often in bird droppings, especially those of pigeons, and at the present time this is the most common source of this pathogenic fungus (14, 49). Transmission from host to host has not been demonstrated.

Cases of cryptococcosis have been diagnosed more often in cats than in dogs. *C. neoformans* infection in dogs and cats probably occurs through inhalation followed by haematogenous spread from the lungs. This organism produces diffuse granulomatous meningitis and focal granulomas in the brain, nasal passages and lungs, but it may involve any part of the body, including the orbit.

The demonstration of pulmonary lesions in all forms of cryptococcosis strongly suggests the probability that cryptococcosis begins as a pulmonary disease. In most cases, the pulmonary lesion heals by encapsulation of the lesion. In the active pulmonary cryptococcosis low grade fever, weight loss and cough may occur. If the disease is untreated it is invariably fatal but it may run a chronic course as long as three months.

Although systemic mycotic infections in cats are rare, cryptococcosis is the one most likely to occur. Since the first report of *C. neoformans* in a domestic cat in the United States by Holzworth (21), cases have been recorded in the United States, Japan, Britain, Australia and New Zealand. The most common sites of lesions were the lungs, the central nervous system and facial regions, especially the nasal, oral and retropharyngeal areas. A stubborn diarrhoea was the only sign in a cat reported by Yamamato *et al* (52).

Trautwein and Nielsen (50) described two cases of cryptococcosis in cats. In the first case, a six-year-old female cat was intermittently sick and had shown progressive weight loss, anorexia and temperature of 104°F. At necropsy there were granulomatous lesions in the lungs and severe degenerative changes in the liver and kidneys; stained tissues of lungs, liver and spleen revealed *Cryptococcus neoformans*. In the other case (a 12-year-old cat) the authors observed a swelling in the frontal region of the head and lesions on the eyelids. Olander *et al* (34) reported dermal cryptococcosis in a cat in which the lesion was a swelling on the bridge of the nose. This was surgically excised without recurrence. Okoshi and Hasegawa (32) described disseminated cryptococcosis in a two-year-old female cat. Lesions were observed in the brain, trachea, lung, spleen and kidney.

Campbell *et al* (8) reported cryptococcosis in a domestic cat with a granuloma in the subcutaneous tissue of the left temporal region. Kurtz and Finco (25) described systemic cryptococcosis in a dog with bilateral intraocular nonsuppurative granulomas in the retina and choroid. Granulomas were present in and around both optic nerves. Cryptococcal infection of the choroid, retina and optic nerves in dogs has been reported previously by Rubin and Craig (41). In these cases, there were granulomas in the brain. Wagner, Pick and Krigman (51) diagnosed cryptococcosis in a dog with symptoms of meningoencephalitis and otitis. Although the lungs represent the usual site of a primary lesion and the meningeal lesions are seen frequently, any organ or tissue of the body is subject to invasion (47). Dermal cryptococcosis usually is associated with a systemic infection and probably is preceded by a respiratory infection. Cryptococcal meningitis may resemble tubercular meningitis. Cryptococcosis must be differentiated from other infections and malignant disease of the lungs by demonstration of the fungus.

Diagnosis

Sputum, spinal fluid, urine or other body fluids are used as specimens. A loopful of the specimen or preferably of sediment from a centrifugal specimen is placed on a slide and mixed with a small drop of India ink, covered with a cover slip and examined under the microscope. The size of Cryptococcus (4 to

20 μ in diameter) permits its detection in unstained preparations particularly as the mucoid capsule is demonstrated as a halo between the spherical cell of Cryptococcus and the India ink particles. Stained smears are of little value in demonstrating the organism.

Cryptococcus neoformans grows on most bacteriological media containing 1–2% sugar. It is recommended that an enriched medium such as brain, heart infusion agar be included. Since *C. neoformans* is sensitive to cycloheximide, media should not contain this antibiotic. Colonies may appear within 48 hours but may take ten to fourteen days. They are soft and creamy in texture and are composed of yeast-like budding cells.

The most satisfactory methods for demonstrating *C. neoformans* in tissue are the PAS or Myer's mucicarmine stain. With the latter stain, budding cells and capsular material stain a brilliant carmine-red and tissues are stained yellow.

Since circulating antibodies cannot be detected with sufficient frequency and dependability in cryptococcosis, diagnosis of the disease by serologic methods has no application. Mice are susceptible to experimental infection and may be used in the diagnosis.

Candidiasis

The reports regarding candidiasis in dogs and cats are scanty and frequently unsatisfactory. Candida species in dogs are often associated with chronic otitis externa and occasionally with skin lesions and mucous membranes. *Candida albicans* is the most common species isolated from man and animals. Candidiasis is often associated with long continued therapy with broad spectrum antibiotics or some other predisposing factors. Since these fungi are opportunists, the clinician should search carefully for other causes.

Diagnosis

Species of Candida are present in the normal oral cavity, upper respiratory passages and intestinal tract. The isolation of the organism in culture is of doubtful significance. In general the diagnosis of candidiasis rests upon laboratory studies and clinical interpretation.

The presence of a large number of organisms in a fresh specimen may have some diagnostic significance. Masses of budding cells and fragments of mycelium may be demonstrated. *C. albicans* is readily isolated on most bacteriological media. Ability to produce chlamydospores on cornical agar plus 1% Tween 80 and ability to ferment certain sugars are important criteria in the identification of *Candida albicans*.

Aspergillosis

Aspergillosis includes any infection caused by an *Aspergillus* species. *Aspergillus fumigatus*, the most virulent and most versatile of the aspergilli, is the usual etiologic agent of pulmonary aspergillosis. It may also invade the orbit and paranasal sinuses. Strains of the *A. flavus-oryzae* group are second in importance to *A. fumigatus* in the etiology of pulmonary aspergillosis.

Cases of aspergillosis are more frequent in birds, particularly water birds, than in mammals. The most important aspect of mammalian aspergillosis is in connection with mycotic abortion in cattle and sheep.

The aspergilli may also contribute to allergic types of respiratory troubles such as pneumonitis and asthma especially in young animals.

Pulmonary aspergillosis although most often secondary to some other disease such as cancer, bronchiectasis, lymphoma and leukemia may occur in the absence of other demonstrable diseases. Sporadic cases of aspergillosis are due to inhalation of spores which are present in some environments. Aspergillus usually causes nodular pneumonic lesions with alveolar exudate. Dissemination to other organs may occur. The most common locations are brain, kidney and myocardium. Sauter, Steele and Henry (42) reported pulmonary aspergillosis in two cats that exhibited general malaise, pyrexia and nasobronchial distress. At necropsy hyphae were seen in nodules found in the lungs. Aspergillosis in the nasal cavity of dogs was reported by Malicka (28) and Otto (35).

Two cases of aspergillosis seen at the clinic of the Ontario Veterinary College in the last five years occurred in dogs, a German Shepherd and a German Shorthaired Pointer.

The first dog was admitted suffering from a chronic nasal discharge. Soon after admission it collapsed in convulsions and was acutely ill for about five days. Following recovery the frontal sinus was opened surgically, flushed and drained. Radiographs had revealed a loss of turbinate structure plus an increased density of the nasal cavity and the maxillary and frontal sinuses. After the operation the dog was treated with amphotericin B and seemed to make a good recovery. However, three months later it again suffered a number of convulsions. Further radiographs revealed a slight increase in the density of the sinuses. At that time the animal, a trained guard dog, showed a marked alteration in temperament,

although his reflexes remained normal. The dog's intellectual ability was impaired. He ignored commands and did not respond to his environment. The damage to his cerebral cortex caused symptoms similar to those seen in man following a frontal lobectomy. Although the dog was destroyed it was not made available for necropsy.

The second dog had a unilateral chronic nasal discharge. The frontal sinus on this dog was also opened and the area was flushed and curetted. This dog was also suffering from a chronic nephritis and hence the administration of amphotericin B was contraindicated. When the owner reported to the clinic three months later, euthanasia was being considered due to the dog's continuing loss of weight and a return of the nasal discharge.

Diagnosis

A diagnosis of aspergillosis can be made only after repeated demonstration of hyphal fragments in pathological material and isolation of the fungus in culture media. If the conidiophores of *A. fumigatus* are sufficiently distinctive a specific identification of the fungus *Aspergillus fumigatus* as well as other *Aspergillus species* are readily cultured on Sabouraud dextrose agar. *Aspergillus fumigatus* will grow at the temperature of 37°C and above. Histological examination of early infection will reveal *Aspergillus fumigatus* penetrating the walls of bronchi and extending to the surrounding parenchyma as an acute necrotizing pyogenic pneumonitis. In routine examinations of the lungs of animals dead from other causes, colonies of *Aspergillus fumigatus* may be found in bronchi which exhibit little or no evidence of inflammatory reaction.

Coccidiodomycosis

This disease which is caused by *Coccidioides immitis* occurs frequently in animals in areas in which the infection is endemic. Most cases of coccidioidomycosis occur in the desert areas of Arizona, New Mexico, California and Texas (27). The results of several years observations by Reed and Converse (37) established a pattern of high infectivity during the warm dry, dusty season of the year and a reduced rate of infection in the cool winter and spring months when rains normally fall in that region. Coccidioidomycosis is a primary respiratory infection, which in a majority of cases is benign and nonprogressive. A small percentage of the infections disseminate from the lung and may produce lesions in the skin, subcutaneous tissues, bones, joints and visceral organs. In dogs there is a remarkable breed predisposition, Boxers being particularly susceptible. The lesions of coccidioidomycosis are granulomatous.

Recently Brodey *et al* (6) reported disseminated coccidioidomycosis in a dog in Philadelphia. The initial diagnosis was osteomyelitis. Coccidioidal spherules were found in bronchial washings. At necropsy, fungus was found in the lungs, bronchial lymph nodes, liver, humerus and tibia. In two previous reports of coccidioidomycosis in dogs, the bones mainly have been infected (10, 19).

Diagnosis

Diagnosis depends upon the laboratory demonstration of the fungus in pathological specimens, or sections of tissue and its isolation in culture. A histological diagnosis of coccidioidomycosis cannot be made without the demonstration of the specific fungus. Usually in active lesions spherules with endospores can be demonstrated in the hematoxylin-eosin stained tissues thereby enabling the pathologist to make a positive diagnosis without special stains. In tissues or body fluids *C. immitis* exists in the form of spherical bodies commonly called spherules. Mature spherules which range from five to 200 microns in diameter are recognized in wet unstained preparations by their thick refractile walls and the presence of endospores. The endospores range from two to five microns in diameter. If structures are found suggestive of *C. immitis* the identification should be confirmed by animal inoculation. A pathological specimen treated with penicillin and chloramphenicol may be injected intraperitoneally into guinea pigs or mice.

The serological tests are sufficiently specific to be of great diagnostic value, particularly precipitin and complement fixation tests.

Sporotrichosis

Sporotrichosis affects domestic animals and man but has been recorded more frequently in horses than in other animals. The causative agent, *Sporotrichum schenckii*, is a saprophyte of the soil and of plants. Primary infection probably occurs through a wound. The principal endemic area is the Mississippi Valley, although the disease has been reported in most parts of the world.

The commonest type of sporotrichosis follows the subcutaneous implantation of spores in penetrating wounds caused by a thorn or splinter. A small ulcerated lesion may develop at the site of injury and remain localized.

The lesion fails to heal and does not respond to topical therapy. The lymph nodes which drain the area of the primary lesion become swollen and suppurate.

Diagnosis

Direct examination of pus is of little value in laboratory diagnosis since it is difficult to find the organism. In tissues *S. schenckii* appears in the form of small oval yeast-like budding cells often described as cigar shaped.

Cultures should be made if sporotrichosis is suspected. Scrapings from skin lesions or swabs from ulcers may provide good culture material. *Sporotrichum schenckii* is dimorphic, but because bacterial contamination is often heavy it is advisable to culture the first mycelial phase on Sabouraud cycloheximide chloramphenicol agar. After obtaining *S. schenkii* in the mycelial phase it is essential to demonstrate the tissue form. If conversion cannot be obtained on artificial media such as brain heart infusion agar with or without blood, animal inoculation may be necessary. A suspension of the mycelial culture in physiological saline is inoculated intraperitoneally or intratesticularly into several mice. After a period of two or three weeks, orchitis is produced. Gram-stained smears of the pus will reveal the characteristic oval budding cells. Routine methods for serological tests are not available.

Histopathological methods have little practical application since it is difficult to detect the organism in tissues, even when sections are stained by selective fungus stains. (For a fuller description of the method used for the identification of fungi, the reader is referred to the Laboratory Manual of Medical Mycology by Ajello *et al* 1963. U. S. Public Health Service Publication).

Treatment

Although amphotericin B is the most effective antifungal antibiotic presently available, relapses may occur. Evans and Baker (17) give the list of fungus infections against which amphotericin B has been tested experimentally and clinically. Their experiments suggest that amphotericin B has also a strong antifungal action against *Aspergillus fumigatus*. It is effective against a number of deep seated fungi (29, 31). The drug is contraindicated if initial doses elicit a hypersensitivity reaction unless the disease process is likely to be fatal if left untreated.

The successful treatment of deep mycotic infection is very much dependent upon an accurate diagnosis. Many deep bacterial infections are clinically indistinguishable from mycotic disease. Only after the organism has been observed histopathologically, or cultured from a biopsy, or pus, should treatment be instituted with the antifungal antibiotic. Because prolonged treatment is necessary, potentially dangerous side effects may be seen. Unless it is absolutely essential, corticosteroid and antibacterial antibiotics should not be administered during the course of treatment.

Amphotericin B invariably causes some degree of renal damage and it is important that before treatment, the blood urea nitrogen (BUN) be ascertained and a microscopic urinalysis be carried out. Renal damage is confirmed by the presence of granular and hyaline casts and sometimes by microhaematuria. A BUN concentration in excess of 75 mg/100ml indicates that the treatment should be temporarily suspended. A recommended dosage scale is 0.25 increasing to 1.0 mg/kg body weight given in a 5% dextrose in water solution at a concentration not greater than 0.2 mg/ml of solution. The drug[1] is administered intravenously on alternative days until a total dose of 10 mg/kg has been given. However, if the effect of renal dysfunction is appreciable the individual dosage at each treatment should be halved and administered only twice a week. Failure to observe these precautions will result in permanent renal damage. Provided that the dosage is modified in the light of the evidence of an elevated BUN and an unfavourable urinalysis, the renal dysfunction is usually reversible at the termination of treatment.

Other signs of toxicity include normocytic normochromic anaemia and rarely, thrombocytopenia, hepatotoxicity and fever. Hypokalemia also occurs and may require correction by oral or parenteral potassium therapy. A pharmacological guide to the clinical use of amphotericin is given by Bindschandler and Bennett (5).

Epidemiology

The mycoses already discussed are not contagious and infection in man and animals follows inhalation or traumatic implantation of the fungi from their normal saprophytic habitats. It is already established that under unusual circumstances of abnormal susceptibility of the patient these fungi become parasitic.

All of the fungi under discussion are exogenous parasites, since they are not nor-

[1]Amphotericin B, Fungizone intravenous. E. R. Squibb & Sons.

mally harboured by man and animals. They are known to exist, or in the case of *Blastomyces dermatitidis*, are presumed to occur in nature as free-living saprophytes.

Ecological studies directed toward *C. immitis*, *C. neoformans*, and *H. capsulatum* have been quite fruitful. *Cryptococcus neoformans* flourishes in bird droppings, especially that of pigeons (14). Staib (48) has shown that this association may be governed by the presence of creatinine, which is utilized as a nitrogen source by *C. neoformans* but not by competing microorganisms. Natural infections of birds by *C. neoformans* have not been demonstrated, although pigeons injected by the intracerebral route develop meningitis and systemic infections (26). *Histoplasma capsulatum* has a predilection for bat and bird habitats, but the basis for this association has yet to be determined. Campbell (7) has suggested that bats might not only be involved in the transmission of *H. capsulatum* but be also the source of the infection. *Blastomyces dermatitidis* presents one of the greatest ecological challenges. Its natural habitat remains unknown.

Recognition of the saprophytic nature of the fungi which cause mycoses, their predilection for specific types of enriched soil or organic debris and the ecological relationships which some of them bear to specific animals or birds are essential to an understanding of the epidemiology of mycoses.

Summary

This review includes discussion of common systemic mycoses in dogs and cats. Cases reported in the literature and those treated at the Ontario Veterinary College teaching hospital are discussed.

A guide to the clinical use of amphotericin B, the antibiotic used against fungi causing deep mycoses, and a brief discussion on the epidemiology of systemic mycoses are also included.

Résumé

Cet article contient une revue des mycoses systémiques courantes du chien et du chat. Les auteurs commentent des cas rapportés dans la littérature ainsi que ceux qu'ils ont traités à l'hôpital d'enseignement du Collège vétérinaire de l'Ontario. Ils y ajoutent un guide sur l'emploi en clinique de l'amphotéricine B, cet antibiotique utilisé contre les champignons causant des infections en profondeur, et un bref commentaire sur l'épidémiologie des mycoses systémiques.

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