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Canine Blastomycosis: A Review of 47 Clinical Cases

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SUMMARY

In a limited retrospective survey, canine blastomycosis was found to be a disease affecting predominantly young, male dogs of the larger breeds. Clinical signs usually related to weight loss and to respiratory and ocular problems. The agar-gel immunodiffusion test was helpful in establishing a diagnosis. The diagnosis was confirmed by microscopic evaluation of aspiration or excision biopsies. Of 22 dogs treated with amphotericin B, 18 were clinically normal 6 months after initiation of therapy.

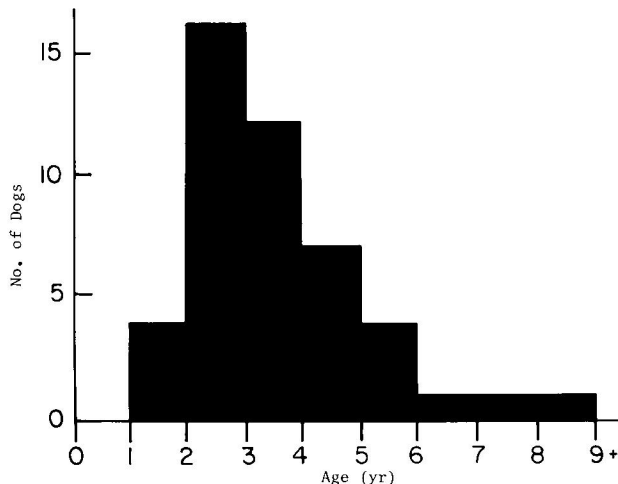


Fig 1—Age of 46 dogs with blastomycosis.

BLASTOMYCOSIS, a systemic fungal disease caused by *Blastomyces dermatitidis*, primarily affects dog and man.^{1,2} The disease is generally restricted to the Mississippi river and Ohio river basins and the central Atlantic states.^{1,3,4} The distribution of canine cases appears to parallel that of human cases. The greatest annual incidence of human cases, in numeric order, occurs in: Mississippi, Kentucky, Arkansas, North Carolina, and Tennessee.¹ The 47 cases in this study were seen at the Veterinary Teaching Hospital, University of Tennessee, from April 1977 through December 1979.

Case Review

Most dogs originated from Tennessee (41), but a few were from Kentucky (4), Virginia (1), and Alabama (1). Over 90% of the dogs were referred; therefore, they may have had more advanced disease than that commonly observed by the primary clinician.

Age, Sex, and Breed

The disease was found primarily in young dogs, with 2-year-old dogs most frequently affected (Fig 1). Males (34) accounted for 72% of blastomycosis

cases; females (13) were both spayed (4) and sexually intact (9). A variety of breeds were affected: German Shepherd Dog, 8; Doberman Pinscher, 7; mixed breed, 6; hound-type, 4; Labrador Retriever, 3; Irish Setter, 3; Cocker Spaniel, 2; Collie, 2; Golden Retriever, 2; English Setter, 2; and Old English Sheepdog, Beagle, Irish Wolfhound, Bulldog, Weimaraner, Siberian Husky, and Australian Shepherd Dog, 1 each. The breed was not recorded in 1 of the dogs.

A common characteristic was the large size of the dogs; none weighed <9 kg (20 lb). Nine (20%) weighed between 9 and 18.1 kg (20 to 40 lb), and 37 dogs (80%) weighed >18.1 kg (40 lb). The weight was not recorded in 1 of the dogs.

Clinical Signs

The initial problems were usually related to weight loss or to respiratory, ocular, skin, and musculoskeletal changes: weight loss (46%); respiratory problem, ie, cough, dyspnea, exercise intolerance (43%); ocular problem (37%); lameness (20%); dermatitis (20%); cellulitis (7%); testicular swelling (4%); regurgitation (4%); and seizures (2%).

Results of Physical Examination

The dogs were commonly but not consistently emaciated. Dyspnea and harsh bronchovesicular sounds were usually evident in dogs with respira-

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June 1, 1981

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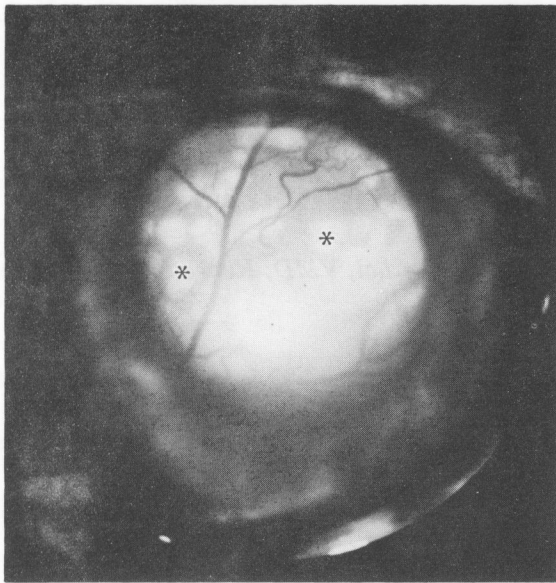


Fig 2—Sensory retina and its blood vessels visible through pupil. Asterisks show 2 of several subsensory retinal granulomas; notice that retinal vessels cross over those that are in the same area.

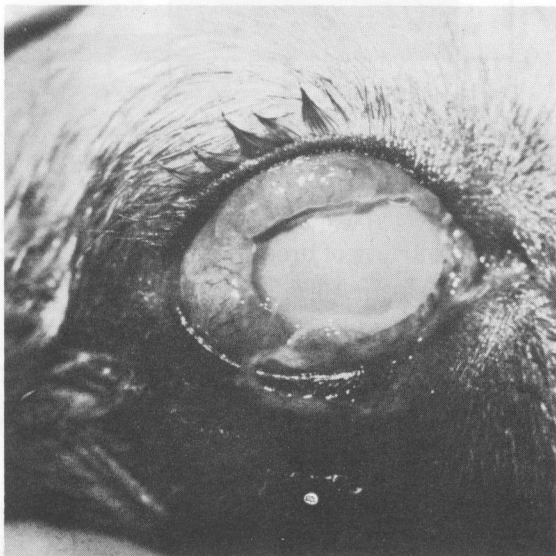


Fig 3—Marked chemosis of the conjunctiva and dense corneal edema. The globe is larger than normal.

tory disease. Fever was found in 45% of the cases, with a temperature range of 39.4 C to 40.7 C (103.0 F to 105.3 F). Skin lesions of ulcerative or granulomatous type were common. Lymphadenopathy was commonly noted. Testicular and prostatic enlargements were relatively uncommon.

Signs compatible with the ocular form of blastomycosis were evident in 41% of the cases. The history included epiphora, ocular redness and pain, opacification of the cornea or lens, swelling of the eye, and blindness. Clinical findings included corneal edema, iridocyclitis, inflammatory cataract, granulomatous-appearing chorioretinitis, retinal separation with granuloma-like subsensory retinal

TABLE 1—Results of Blood Counts in 38 Cases of Blastomycosis

	Distribution of values (% of cases), according to selected ranges*			
	28-32(16)	33-36(21)	37-50†(63)	...
PCV (%)				
Total WBC (cells/mm ³)	6,000-17,000†(34)	17,000-30,000(53)	30,000-40,000 (8)	>40,000 (5)
Total neutrophils (cells/mm ³)	3,000-11,500†(24)	11,500-20,000(55)	20,000-30,000 (13)	>30,000 (8)
Nonsegmented neutrophils (cells/mm ³)	0- 300†(21)	300- 1,500(37)	1,500- 3,000 (24)	>3,000(18)
Lymphocytes (cells/mm ³)	<500 (21)	500- 1,000(18)	1,000- 4,800†(58)	>4,800 (3)
Monocytes (cells/mm ³)	150- 1,350†(53)	1,350- 3,000(42)	>3,000 (5)	...

*The data are in columns, but the columnar arrangement does not imply that any entry in one column is necessarily related to another entry in that column. †Normal range.¹⁵

exudates (Fig 2), and panophthalmitis. In almost all cases of panophthalmitis, increased intraocular pressure and buphthalmos (Fig 3) were found. These latter cases were usually referred by the practitioner because of glaucoma unresponsive to medical therapy. Dogs with glaucoma or extensive retinal separation were blind.

Laboratory Findings

Of the 47 case records, 38 included blood counts (Table 1). The most consistent change in the blood counts was mild to moderate neutrophilia with a left shift. Mild anemia, lymphopenia, and monocytosis were also frequent findings. Serum chemical profiles were generally normal. Hypercalcemia was noted in 3 of the cases (calcium, 12.5, 13.9, and 13.9 mg/dl). In 1 case, the high calcium concentration decreased after amphotericin B (AMB) treatment. The possibility of bone demineralization was considered to account for hypercalcemia, but no precipitating cause (eg, bone lesions) was evident.

Radiographic Findings

The most commonly observed radiographic lesions were in the lungs. Generalized interstitial lung disease was evident in most of the cases, with the predominant interstitial pattern being that of small, poorly margined nodules, some of which appeared to coalesce (Fig 4). The interstitial changes were often accompanied by other changes such as those of bronchial or alveolar disease, creating a mixed pattern (Fig 5). Pleural effusion and pneumomediastinum were seen on rare occasion. Bone involvement was evident in approximately 1/4 of the cases, 2/3 of which had solitary bone lesions. There was a tendency for the bone lesions to be situated near the ends of the tubular bones. The lesions tended to be osteolytic, with some reactive-type bone proliferation (Fig 6 and 7). Periosteal reactions were present in about half of the involved cases.⁵

Distribution of Lesions

The following organs were affected, as determined by physical, radiographic, cytologic, and necropsy evaluations: lung, 85%; peripheral lymph

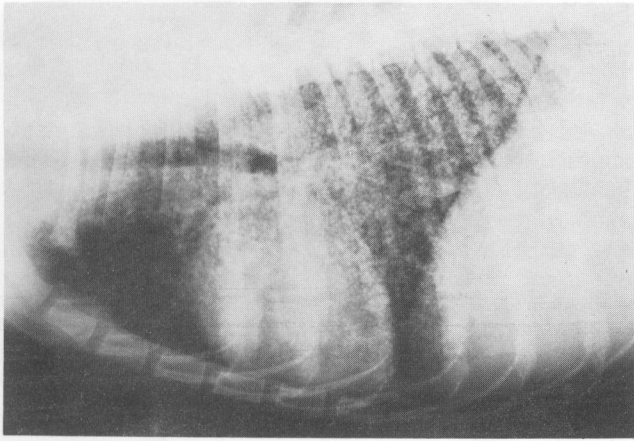


Fig 4—Lateral radiographic view of thorax, showing the generalized, miliary, interstitial nodule pattern frequently seen in blastomycosis.

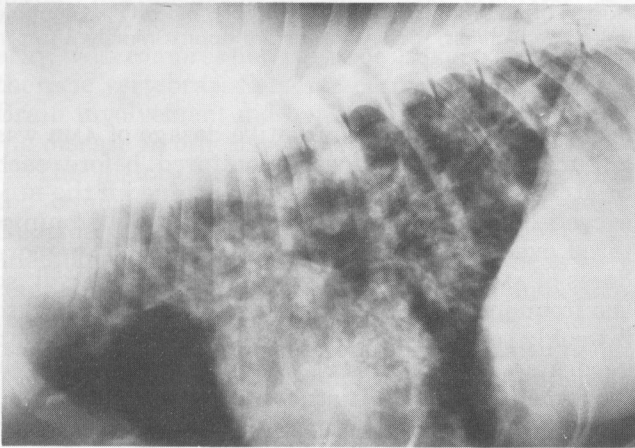


Fig 5—Lateral radiographic view of thorax, showing the bronchointerstitial lung pattern occasionally seen in blastomycosis.

nodes, 59%; eye, 41%; skin, 26%; bone, 24%; subcutaneous tissues, 13%; testes, 7%; prostate gland, 4%; brain, 4%; and nasal cavity, 2%. Though blastomycosis is usually a multisystem disease, 4 of the dogs had solitary lung, eye, bone, or subcutaneous tissue involvement.

Diagnostic Procedures

Diagnosis of blastomycosis should be made by cytologic, histologic, and cultural methods. Direct microscopic visualization of the organism was an inexpensive and highly accurate method of diagnosis. The diagnosis was confirmed microscopically in 36 cases. In 8 cases, the diagnosis was made from a combination of physical, radiographic, and serologic findings. In 3 cases, the owners elected to have the dogs euthanatized after physical examination; therefore, only necropsy was done. The diagnosis of blastomycosis was established by: aspiration of lymph node or subcutaneous tissue or by skin impression (52%); radiography and serology—not confirmed histologically (18%); biopsy of bone, lymph node, or subcutaneous tissue (9%); eye

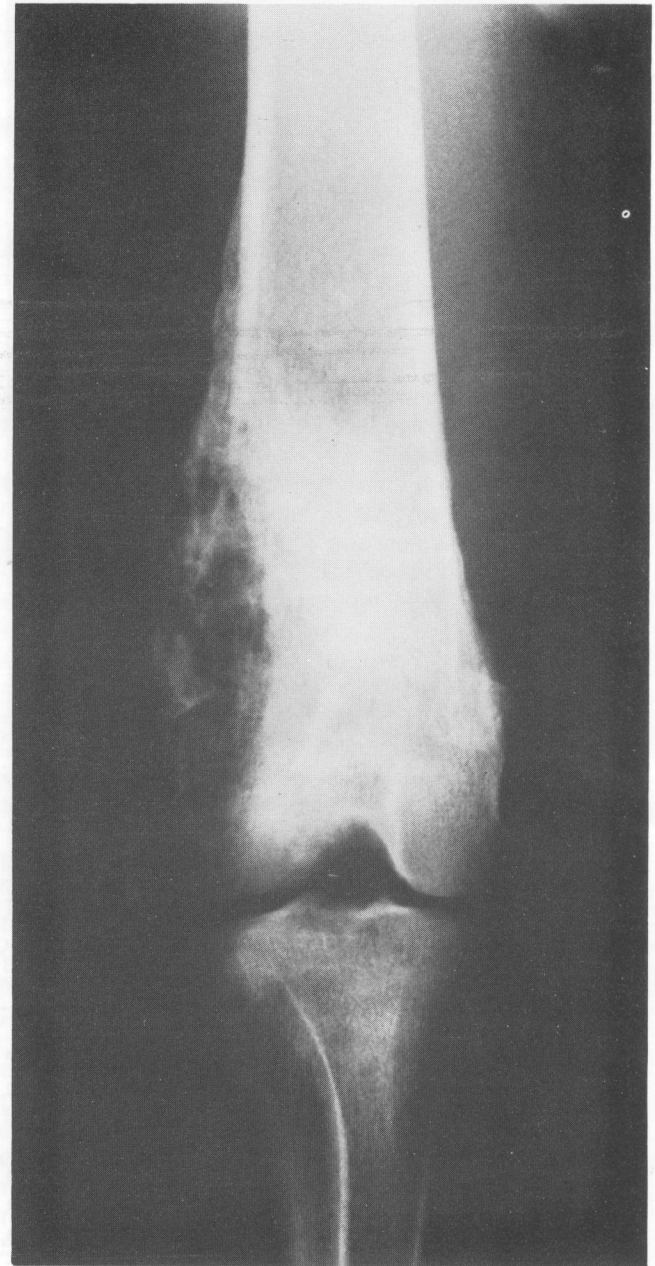


Fig 6—Craniocaudal view of stifle, showing an irregular periosteal reaction, cortical bone lysis, and increased medullary bone density in a case of blastomycosis. (Courtesy of Dr. R. E. Roberts and *Veterinary Radiology*.⁵)

aspirate (7%); enucleation and histopathology (7%); tracheal wash (5%); and urinalysis (2%).

Aspiration Biopsy

Aspiration of infected tissues (subcutaneous masses and lymph nodes) was performed by means of a 12-ml syringe and 20-gauge needle. In dogs with nonfunctional eyes, aspirates were taken from the eye, with the dog under anesthesia. The globe was grasped at the dorsal limbus with fixation forceps while the eyelids were held open. A 2.5-cm, 20-gauge needle on a 2.5-ml syringe was placed against the bulbar conjunctiva, 6–8 mm from the limbus. At

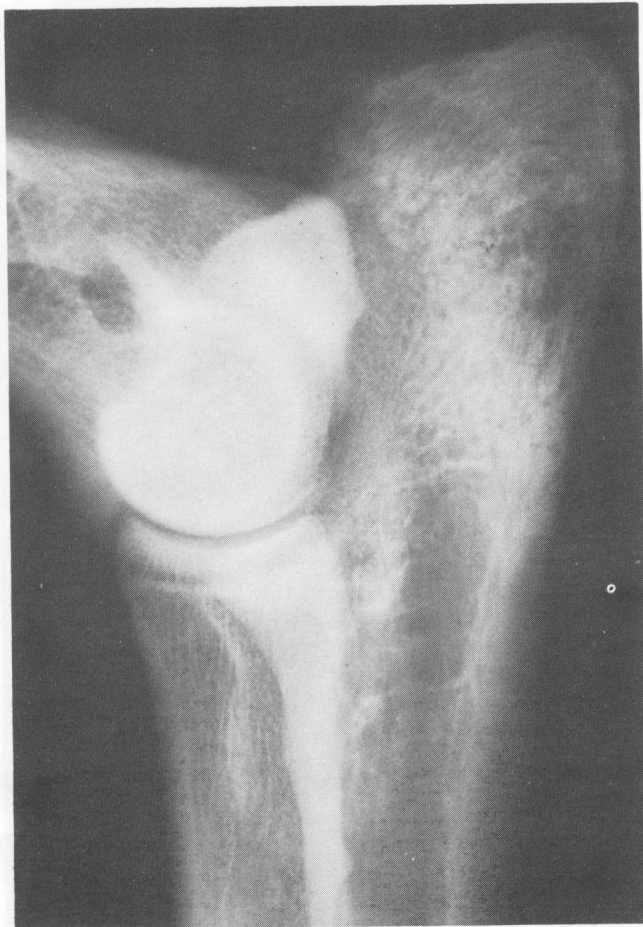


Fig 7—Lateral radiographic view of elbow, showing irregular bone lysis and bone production in the proximal end of the *B dermatitidis*-infected ulna.

about 45 degrees to a tangent to the globe, gentle pressure was used to insert the needle 1.0–1.5 cm into the globe. Suction was used to draw off 0.5–1.0 ml of fluid, which was usually purulent and viscid. Small amounts of aspirated material were placed on glass slides, gently smeared, and stained with Wright's stain. Organisms were usually plentiful in enlarged lymph nodes and areas of cellulitis, resulting in a high percentage of diagnoses. In all instances of ocular aspiration, free or intracellular organisms morphologically compatible with *B dermatitidis* were seen (Fig 8). Aspiration biopsy was not necessary in skin lesions because impression smears usually revealed the organisms.

Serologic Findings

In a series of 35 histologically confirmed cases of blastomycosis, 32 were positive serologically, using the agar-gel immunodiffusion technique. The results of testing correlated well with clinical disease.

Therapy

Twenty-seven dogs were treated with AMB according to the following protocol. Initially, 0.5 mg of AMB/kg of body weight was given IV in 500 ml of a 5% dextrose, followed by a dosage of 1 mg/kg

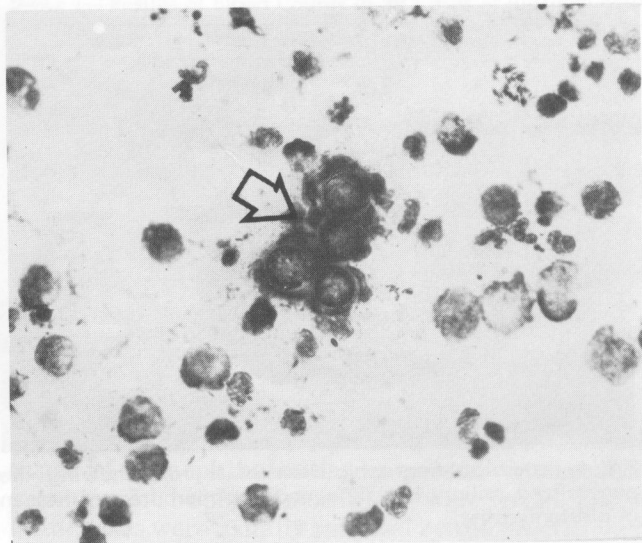


Fig 8—Smear from subsensory retinal aspirate, showing a cluster of 4 organisms (arrow) morphologically compatible with *B dermatitidis*; the organisms are approximately 8 μ m in diameter. Wright's stain; \times 400.

every other day. The cumulative dosage of AMB was 8.5 mg/kg. The BUN was monitored before each treatment, and therapy was discontinued if the BUN exceeded 50 mg/dl. The AMB infusion was administered over a 6- to 8-hour period. After 5 or more doses of AMB, most dogs had a BUN of >50 mg/dl, so the frequency of AMB administration was reduced to biweekly or weekly intervals as renal function permitted. The results of therapy were: normal at 6–29 months after initiation of therapy, 15; normal at 2–6 months after initiation of therapy, 5; died during therapy (at days 1, 3, 3, and 7), 4; and relapsed after treatment (at 3, 7, and 7 months), retreated, and well, 3. One dog with unilateral panophthalmitis and glaucoma was treated by enucleation without AMB therapy and is normal 27 months after surgery. The deaths occurring during therapy were due to respiratory failure (3 cases) and meningoencephalitis (1 case). Thirteen dogs were euthanized at the owners' request because of economic considerations or irreversible blindness.

Discussion

In our study, blastomycosis was a disease occurring predominantly in young, male dogs. The dogs were most frequently affected at 2 years of age, with a few dogs older than 5 years of age. The highest occurrence at 2 years was consistent with that in other studies.^{1,6} Male dogs accounted for 72% of our series, which was consistent with a male rate of 67% previously reported.⁶ The reason for this sexual bias has not been determined; however, a similar incidence in man has been noted in that 89% of the patients studied were male.¹

Blastomycosis was diagnosed in a variety of breeds, with German Shepherd Dogs and Doberman Pinschers most frequently involved. Statistical studies were not done, but the high frequency of occurrence in these breeds may reflect their popu-

larity. Dogs under 9 kg (20 lb) were not infected, and 80% of the involved dogs weighed more than 18 kg (40 lb). The histories in these cases did not identify whether the dogs were primarily indoor or outdoor dogs. Large breeds of dogs appeared to be at increased risk for infection. In our area, large breeds of dogs are often housed outdoors. An increased probability of exposure to *Blastomyces* sp in dogs maintained outdoors may have accounted for the increased occurrence of blastomycosis in large breeds of dogs. In an earlier study,⁶ the Beagle was the breed with the highest incidence of blastomycosis.

In our study, blastomycosis affected a number of body systems in a variety of ways. In enzootic areas, lymphadenopathy, dyspnea, cough, uveitis, ulcerative or granulomatous dermatitis, and lameness warranted consideration of blastomycosis. Less commonly, cellulitis, orchitis, and prostatitis also were found. Regurgitation of solid food occurred secondarily to massive tracheobronchial lymphadenopathy, with compression of the esophagus against the thoracic vertebrae. Seizures occurred uncommonly. Brain involvement did not occur without fulminating disease in other systems.

The history and physical examination alerted the clinician to the possibility of blastomycosis. Neutrophilia, lymphopenia, monocytosis, and slight anemia were common findings. These changes were compatible with any inflammatory or infectious condition. Monocytosis was not a consistent finding. Serum chemical analyses were helpful in ruling out other conditions but were not helpful in establishing a diagnosis of blastomycosis.

Radiography played a major role in the diagnostic process. The respiratory tract was involved in most (85%) of the cases. Lung changes were strongly suggestive of a mycotic disease. Lytic bone changes (24% of the cases) also were suggestive of blastomycosis. The characteristic ocular changes were supportive of a diagnosis of blastomycosis.

Confirmation of a diagnosis of blastomycosis was easily and reliably done by aspiration biopsy or by examination of impression smears. The organisms were usually plentiful in infected tissues, frequently resulting in diagnosis from these procedures. Aspiration of bone lesions was not very productive; therefore, open biopsy of these lesions was done to confirm the diagnosis. In ocular involvement, eye lesions were aspirated or a diagnosis was made histologically after enucleation of a nonfunctional, painful eye. Organisms were occasionally found on microscopic examination of tracheal wash material, but recovery of organisms was not consistent. Tracheal wash was rarely done because examination of lymph node aspirate or skin impression smears confirmed the diagnosis. In cases with urogenital involvement, organisms were found on urinalysis or from a prostatic aspirate. When direct visualization of the organism was not possible, a diagnosis was made from physical and radiographic findings combined with a positive serologic test (agar-gel immunodiffusion). The agar-gel immunodiffusion test has

a sensitivity and specificity of over 90% in canine blastomycosis,⁷ and a positive reaction is strongly supportive of a diagnosis of blastomycosis.

Systemic blastomycosis, as seen in this study, is usually a fulminating, progressive disease that requires therapy. Various regimens of treatment with AMB have been advocated, using 0.1 to 0.5 mg/kg per dose at various intervals until a cumulative dosage of 7 to 25 mg/kg is achieved.^{8,9} Results of AMB therapy in canine blastomycosis have not been reported. The regimen in our study involved more AMB per dose (1 mg/kg) than previously recommended. Administration by slow IV drip was done in an attempt to reduce the likelihood of renal toxicosis. Nephrotoxicosis was a frequent complication of therapy, requiring prolongation of the interval between treatments to a week or longer. Therapy was discontinued if the BUN concentration increased above 50 mg/dl but was resumed when it decreased below 50 mg/dl. The BUN concentration remained elevated for months in certain dogs, but eventually returned to normal values. The long-term response to this regimen of therapy was good, with 15 of 22 dogs free of signs and detectable disease 6 months or more after initiation of therapy. The 3 dogs requiring retreatment were complicated by the renal compromise persisting from the initial therapy.

Four dogs died during treatment. One dog with brain lesions was moribund at the time of admission. The other 3 dogs were severely dyspneic when admitted and died of respiratory failure. All deaths occurred during the 1st week of therapy; dogs surviving the initial week justified a more favorable prognosis.

In an early report¹⁰ on canine blastomycosis, euthanasia of infected animals was suggested for public health reasons, but recently it has been stated that there is no public health significance to canine blastomycosis.^{2,11} Thirty percent of the dogs in this series were euthanatized at the owners' request because of economic considerations or blindness but not because of public health fears or extent of disease.

Transmission of blastomycosis from dog to man has not been reported; however, a common environmental source of the infection was suspected when both dog and man in the same household were infected.^{2,11,12} The dogs in one study¹¹ developed the disease first and were considered good sentinels for detecting human exposure. *Blastomyces* sp does not appear to be widely distributed in nature but is found at selected sites.¹³ Attempts at culturing *Blastomyces* sp from areas housing infected dogs have been generally unsuccessful, except for a case involving a tobacco barn.¹³ One human case of blastomycosis was attributed to inhalation of organisms in infected-pigeon manure used in gardening.¹⁴ The source of infection in blastomycosis has been rarely identified. Kaplan, in a review of the epidemiology of mycotic disease, stated that "there is no justification for isolating a patient affected by these systemic mycoses or for euthanatizing an infected animal for

the sole purpose of protecting contacts."² Veterinarians are not justified in euthanatizing dogs with blastomycosis for public health reasons.

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