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Ocular lesions of blastomycosis in the dog

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SUMMARY

Twenty-one dogs with ocular disease and blastomycosis were studied clinically. The most common ocular lesion was uveitis. Other findings included retinal separation, panophthalmitis, and glaucoma. The results of the study indicated that when uveitis is found in dogs in central United States, east of the Mississippi River, blastomycosis should be a diagnostic consideration. When the uveitis was associated with lung, lymph node, skin, bone, or testicular lesions, the likelihood of blastomycosis was greater.

BLASTOMYCOSIS is characterized by pyogranulomatous inflammation and may be expressed as a localized lesion or it may become disseminated to involve multiple organ systems. Lung, skin, bone, lymph node, testicle, and eye appear to be the tissues most susceptible to colonization by the causative organism.¹⁻³

In 2 reports on large numbers of natural cases of blastomycosis, the eye was involved to some degree in 22%–41% of dogs.^{3,4} Most reports describing ocular blastomycosis in detail are case reports dealing with animals having advanced disease.⁵⁻¹¹ The following is a report of the early and late clinical ocular changes seen in 21 dogs that had confirmed blastomycosis.

Materials and Methods

Patients selected for this study included 21 dogs admitted for ocular and other complaints and in which blastomycosis was later diagnosed (Table 1). Eighteen of the animals came from Tennessee and 1 each came from Illinois, Kentucky, and Virginia. Seventeen of the dogs had been included in a report dealing predominantly with nonocular aspects of blastomycosis.⁴

Clinical studies relating to the eye included direct and indirect ophthalmoscopy and biomicroscopy. In some cases,

diagnostic modalities included ocular fundus fluorescein angiography and cavernous sinus venography.

The diagnosis of blastomycosis was made by examination of one or more of the following: agar gel immunodiffusion reactions, aspirates or smears from lymph nodes and other areas, and aspirates from the space created when there was separation of sensory retina from retinal epithelium (subretinal space) (Table 1). The latter procedure has been described in detail.⁴ In 15 cases, when ocular tissue became available for histologic examination, the presence of organisms within these tissues was confirmed.

Identification of the causative organism usually was based on morphologic features. In smears of histologic sections, *Blastomyces dermatitidis* was round to ovoid and 5–15 μ m in diameter. It had a thick, refractile cell wall which enclosed granular cytoplasm with at least 1 nucleus; budding forms occasionally were seen (Fig 1). Ocular aspirates from 3 dogs (12, 13, and 16 in Table 1) were cultured at 25 C on Sabouraud agar. Within 3 weeks, all produced fungal colonies composed of slender segmented mycelia bearing single oval conidia and thus were considered compatible with the mold form of *B dermatitidis* (Fig 2).¹²

Some of the patients received IV amphotericin B as treatment.⁴

Clinical Findings

Table 1 lists clinical information for the cases studied. Most of the dogs were young males; all had access to the outdoors.

In 20 of the cases, the client was aware of the dog's ocular problems. All but 2 of the dogs had evidence of dissemination of infection, including pneumonia and lymphadenopathy. In many cases, however, the client or referring veterinarian was unaware of any but the ocular changes. The most common ocular problem that prompted the client to seek veterinary assistance was a reddened, sensitive eye—usually diagnosed and treated as conjunctivitis. Such patients were later referred because they did not respond as expected to medication. Many of the ocular lesions had progressed to panophthalmitis and glaucoma and had failed to respond to appropriate therapeutic regimens.

The initial ocular signs in most dogs were referable to anterior uveitis: blepharospasm, photophobia, epiphora, conjunctival hyperemia, miosis, and a variable degree of aqueous flare. Affected eyes were sensitive to the dog and softer than normal, as judged

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A-463

TABLE 1—Tabulation of 21 cases of canine blastomycosis with ocular involvement

Case No.	Breed	Age (yr)	Sex	Original ocular complaint	Ocular diagnoses at admission*	Nonocular abnormalities	Method of diagnosis	Treatment, final disposition
1	Great Dane	7	M	"Runny" eyes	Anterior uveitis, right eye	Pneumonia, dermatitis, orchitis	Smear from foot lesion, histology	None, euthanized
2	Doberman Pinscher	1	M	Red, painful left eye	Keratitis, uveitis, each eye; retinitis, optic neuritis, right eye	Pneumonia, lymphadenopathy	Smear from skin lesion, tracheal wash, serology, histology	IV amphotericin B, euthanized
3	Labrador Retriever	1	M	Red, painful eyes	Keratitis, uveitis, retinal separation, each eye	Pneumonia, lymphadenopathy, osteomyelitis	Lymph node aspirates, serology	IV amphotericin B, alive
4	German Shepherd Dog	1	M	Enlarged left eye	Choroiditis, retinitis, retinal separation, right eye; panophthalmitis, glaucoma, left eye	Pneumonia, lymphadenopathy, orchitis, dermatitis, prostatitis	Smear from skin lesion and prostate secretion, lymph node aspirate, serology	IV amphotericin B, alive
5	Mongrel	3	F	None	Papilledema, each eye; iridocyclitis, left eye	Pneumonia, dermatitis	Smear from skin lesion, serology	IV amphotericin B, alive
6	Mongrel	1	M	Red, painful eyes	Keratitis, uveitis, retinal separation, retinal hemorrhage, each eye	Pneumonia, lymphadenopathy	Subretinal aspirate, serology, histology	None, euthanized
7	Mongrel	6	M	Red, painful left eye	Uveitis, left eye	Osteomyelitis	Histology	None, euthanized
8	Mongrel	3	M	Red, painful left eye	Panophthalmitis, retinal separation, left eye	Pneumonia	Subretinal aspirate, histology	None, euthanized
9	Bulldog	1.5	M	Red, painful left eye	Panophthalmitis, retinal separation, left eye	Pneumonia, lymphadenopathy, dermatitis	Subretinal, lymph node and subcutaneous mass aspirates, serology, histology	Left eye enucleated, IV amphotericin B, alive
10	Mongrel	2	M	Red, painful right eye	Panophthalmitis, retinal separation, right eye	Pneumonia, osteomyelitis	Histology	None, euthanized
11	Golden Retriever	3	FS	Red, painful left eye	Panophthalmitis, retinal separation, left eye	None	Serology, histology	Left eye enucleated, alive
12	Cocker Spaniel X Poodle	3	M	Red, painful left eye	Panophthalmitis, glaucoma, retinal separation, left eye	Pneumonia	Subretinal aspirate, histology	Left eye enucleated, IV amphotericin B, alive
13	German Shepherd Dog	2	M	Red, painful right eye	Panophthalmitis, glaucoma, retinal separation, right eye	Unknown	Subretinal aspirate, histology	None, euthanized
14	English Setter	2	FS	Red, painful left eye	Keratitis, uveitis, glaucoma, left eye	Pneumonia	Histology	Left eye enucleated, alive
15	Doberman Pinscher	2.5	M	Red, painful eyes	Panophthalmitis, each eye; retinal separation, right eye; glaucoma, left eye	Pneumonia	Subretinal aspirate, serology, histology	None, euthanized
16	Irish Setter	3	M	Red, painful right eye	Keratitis, uveitis, glaucoma, right eye	Pneumonia	Subretinal aspirate, histology	Right eye enucleated, IV amphotericin B, alive
17	Doberman Pinscher	1.5	M	Red, painful right eye	Panophthalmitis, glaucoma, right eye; uveitis, left eye	Pneumonia, lymphadenopathy, dermatitis, meningitis	Smear from skin lesion, lymph node aspirate, histology	None, died
18	Bluetick Hound	3	M	Swollen right eye	Panophthalmitis, glaucoma, right eye; choroiditis, left eye	Pneumonia, lymphadenopathy, orchitis	Lymph node aspirate, serology	IV amphotericin B, alive
19	Coonhound	2	M	Cloudy left eye	Iridocyclitis, retinitis, right eye; panophthalmitis, glaucoma, scleral staphyloma, left eye	Pneumonia, lymphadenopathy, dermatitis, orchitis	Lymph node aspirate	IV amphotericin B, alive
20	Cocker Spaniel	2	M	Blindness	Amaurosis; conjunctivitis of 3rd eyelid, left eye	Pneumonia, lymphadenopathy	Smear from 3rd eyelid lesion	None, died
21	German Shepherd Dog	3	FS	Painful, protruding left eye	Space-occupying lesion of left orbit	Pneumonia	Serology, histology	None, euthanized

*If an eye is not mentioned, the findings were unremarkable.
FS = female spayed.

by palpation. Other early changes included mild swelling and erythema of the iris, hazy vitreous, and areas of choroiditis sometimes causing elevation of overlying sensory retina. In more advanced cases, the lesions had progressed to cause panophthalmitis, often with glaucoma. Affected eyes usually were enlarged, more firm than normal on palpation, and quite sensitive to the animal. Corneal vascularization and edema were marked, often preventing clear visualization of deeper structures. When corneal clarity permitted, the following were found in some of the dogs: hyphema or hypopyon, posterior synechiae, marked swelling and erythema of the iris, cataract, vitreal hemorrhage, and massive retinal separation.

The ocular changes alone usually suggested blastomycosis. Concurrent lymph node, lung, skin, or bone involvement further raised the likelihood that the clinical signs were attributable to blastomycosis. The degree of clinically evident involvement of nonocular organ systems varied considerably and did not always correlate with the degree of ocular involvement.

The following cases are representative of the range of ocular lesions seen in this series of dogs with blastomycosis. The case numbers refer to those listed in Table 1.

Case 1—A 7-year-old Great Dane was diagnosed

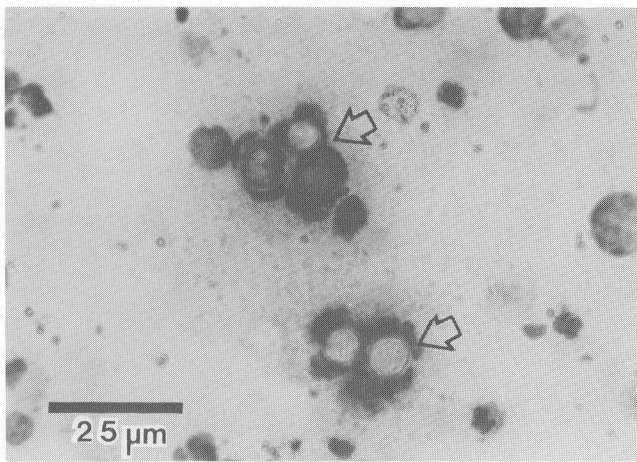


Fig 1—Smear made from subretinal fluid of a dog with ocular blastomycosis. In addition to inflammatory cells, there are 5 *B dermatitidis* organisms (open arrows). Wright's stain.

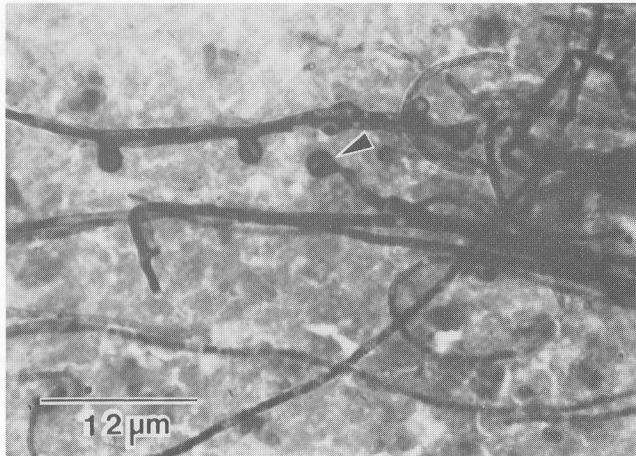


Fig 2—Mycelia and conidia of *B dermatitidis* resulting from culture of subretinal fluid taken from a dog with ocular blastomycosis. Arrowhead denotes one of the conidia. Degenerating inflammatory debris from the subretinal fluid is still distinct in this 6-week culture specimen. Periodic acid-Schiff stain.

as having disseminated blastomycosis on the basis of histologic examination of an inflamed testicle several weeks earlier. The client complained that the eyes had been "runny" for the last few days and requested an ophthalmic examination. Examination of the right eye revealed mild conjunctival hyperemia, slight corneal edema, moderate aqueous flare, and miosis. The left eye was normal. The dog also had pneumonia and dermatitis. Histologic examination of impression smears from a skin lesion on a paw revealed *B dermatitidis*.

The client requested euthanasia of the dog. Examination of histologic sections of the right eye revealed a small focus of inflammatory infiltrate and organisms in a peripheral zone of the posterior ocular segment not visible clinically.

Case 2—A 1-year-old male Doberman Pinscher was referred because of pneumonia, dermatitis, lymphadenopathy, and a reddened, sensitive left eye. The right eye showed slight corneal edema, fine keratic precipitates, and moderate aqueous flare.

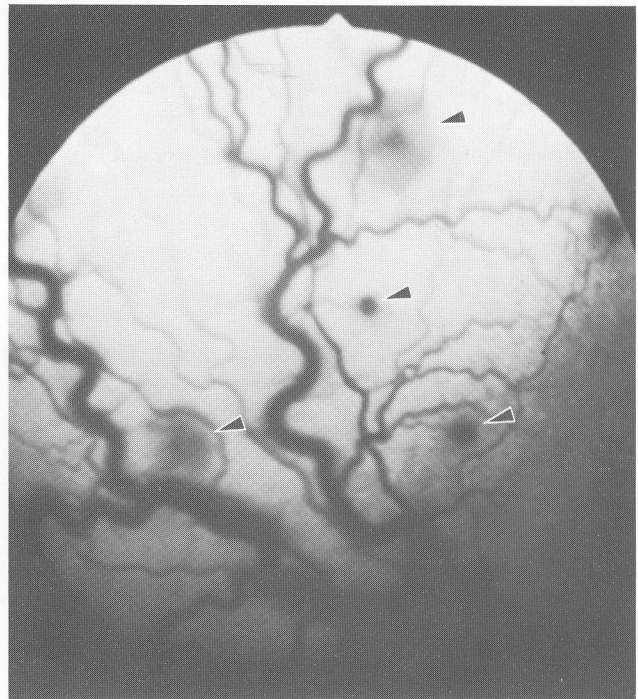


Fig 3—Tapetal area of right ocular fundus from a dog with ocular blastomycosis. The arrowheads point to areas of choroidal and retinal inflammation. The retinal vasculature is dilated and somewhat tortuous.

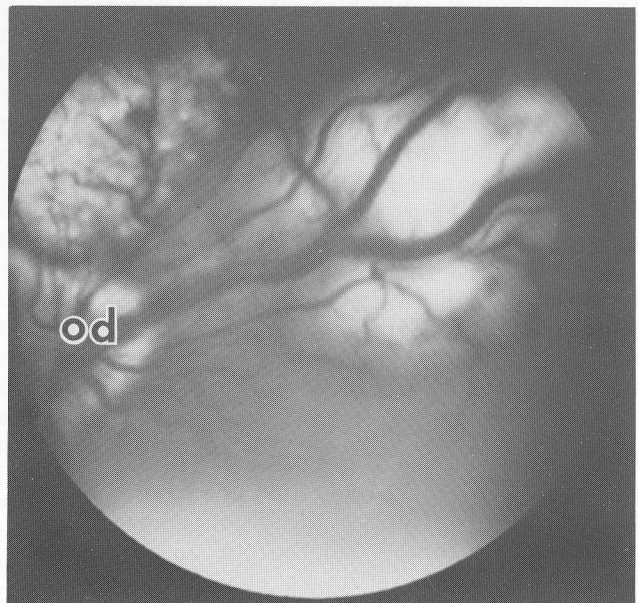


Fig 4—Optic disk (od) and nontapetal area of right ocular fundus from a dog with ocular blastomycosis. The large white mass to the right of the optic disk is a granuloma arising from the choroid and causing elevation of the overlying sensory retina.

Within the tapetal area of the right ocular fundus were many brown-to-purple, blurred spots, which were interpreted as focal areas of choroiditis with separation and edema of the overlying sensory retina (Fig 3); in the nontapetal fundus, there were several large areas of fluffy white exudate, with elevation of the sensory retina (Fig 4). The right optic disk was swollen, and the retinal vasculature was engorged.

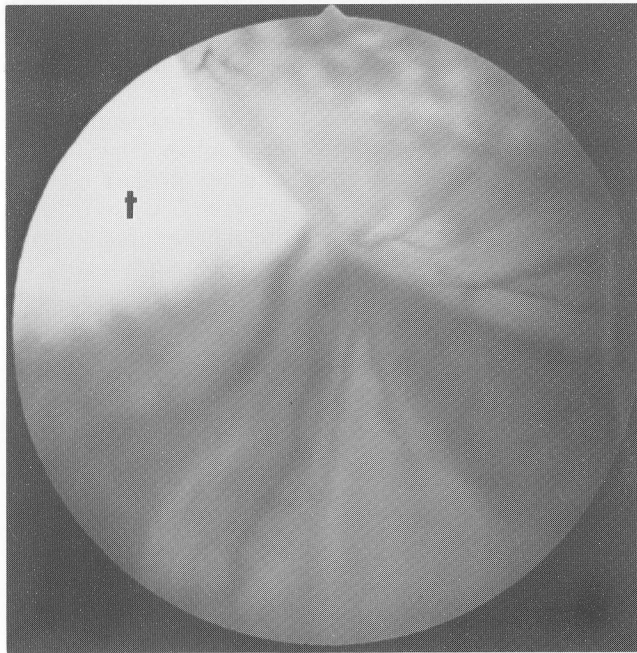


Fig 5—Right ocular fundus of a dog with ocular blastomycosis. Most of the sensory retina is separated in funnel fashion from the retinal epithelium. Ill-defined blood vessels seem to have converged and disappeared from view as they approached the optic disk, which is hidden by retina. A small sector of tapetal area (t) is not involved.

The left eye had dense corneal edema and vascularization, large keratic precipitates, and marked aqueous flare. Although the anterior ocular segment changes prevented clear visualization of the deeper ocular structures, the lack of a consensual pupillary response to light provided indirect evidence that the left eye had massive retinal or optic nerve damage. Examination of impression smears from skin lesions and a tracheal wash revealed *B dermatitidis*.

In spite of iv therapy with amphotericin B, the lesions in the right eye became larger. The dog's general condition deteriorated, and euthanasia was performed. Histologic examination of both eyes revealed *B dermatitidis* in the posterior segments.

Case 3—A 1-year-old male Labrador Retriever was referred because of reddened, sensitive eyes and lameness. The left eye had mild keratitis and a large granulomatous-appearing fluffy white lesion in the ventral ocular fundus adjacent to the ora ciliaris retinae; the sensory retina was elevated in this area. The right eye was enlarged and soft on palpation; it had keratitis, uveitis, incomplete cataract, vitreal hemorrhage, and diffuse retinal separation. Osteomyelitis, pneumonia, and lymphadenopathy also were evident. Examination of an aspirate from 1 of the lymph nodes revealed *B dermatitidis*.

The dog was placed on a regimen of iv amphotericin B therapy. There was remission of the general clinical signs within a week. The granulomatous-appearing lesion in the left eye eventually resolved into a focal scar. The right eye became noninflamed and was no longer sensitive. There was no recurrence of clinical signs in the 6 months this dog's health status was monitored.



Fig 6—Right ocular fundus of same dog as in Figure 5, 1 month after initiating iv therapy with amphotericin B. The sensory retina is now mostly in situ.

Case 4—A 1-year-old male German Shepherd Dog was referred because the left eye had enlarged over a 6-week period. Ulcerative skin lesions also had become evident. Examination revealed a funnel-shaped retinal separation involving most of the retina in the right eye (Fig 5); areas of inflammatory infiltrate were seen, especially along retinal blood vessels. The left eye was enlarged and firmer than normal when palpated; keratitis, uveitis, posterior synechiae with iris bombé, and complete cataract prevented examination of the ocular fundus. The dog's vision was markedly compromised. Dermatitis, orchitis, prostatitis, pneumonia, and lymphadenopathy were evident. Histologic examination of impression smears made from a skin lesion, prostatic secretions, and a lymph node disclosed *B dermatitidis*.

The dog was placed on a regimen of iv amphotericin B therapy. Within 1 month, the retinal separation in the right eye was mostly resolved (Fig 6), the left eye was noninflamed and softer than initially, and vision had improved. Fundus fluorescein angiography of the right eye revealed leakage of dye in a large scarred area, suggesting local breakdown of the blood-retinal barrier, although this appeared to be without consequence to the dog. There were no exacerbations of blastomycosis in the 3 months the dog's health status was monitored.

Case 15—A 2.5-year-old male Doberman Pinscher had had a 3-week history of bilateral ocular sensitivity and redness that failed to respond to various topical medications. When blindness became evident, he was referred. Examination disclosed keratitis, uveitis, and complete, funnel-shaped retinal separation in the right eye; the sensory retina, clearly visible behind the lens, contained fluffy white

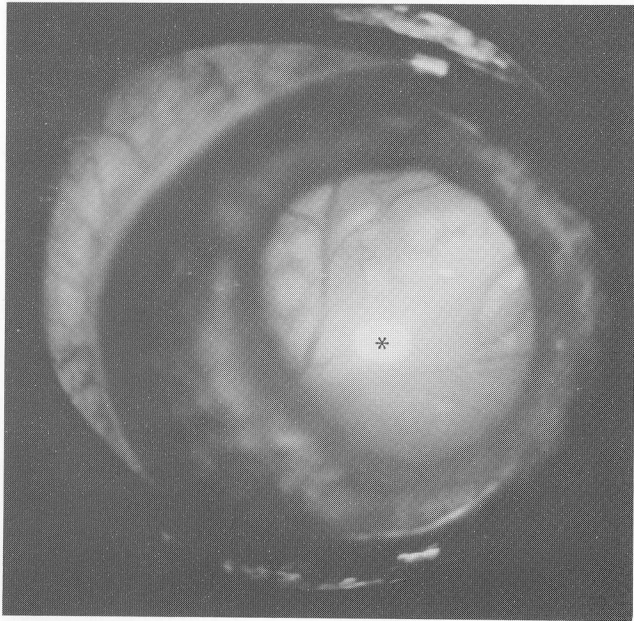


Fig 7—Right eye of a dog with ocular blastomycosis. The sensory retina has been displaced anteriorly to a position just behind the lens. The retinal blood vessels are easily seen through the pupil; white subretinal granulomas also are visible. The asterisk denotes the camera flash reflection.

exudates deep within it (Fig 7). The left eye was enlarged and firmer than normal on palpation; panophthalmitis with vitreal hemorrhage prevented visualization of the fundus. Histologic examination of a subretinal aspirate from the right eye showed *B dermatitidis*.

The client elected to have the dog euthanized. *Blastomyces dermatitidis* was demonstrated histologically in the left ocular tissues and within miliary granulomas of the lungs.

Case 20—A 2-year-old male Cocker Spaniel was referred because of blindness. Examination failed to reveal ocular lesions of sufficient magnitude to account for the dog's total vision loss. The left nictitating membrane had a soft, proliferative lesion on the palpebral surface. Examination of smears made of scrapings from this lesion revealed *B dermatitidis*. Pneumonia and lymphadenopathy also were evident.

Within 24 hours after admission, the dog died. Permission for necropsy was not granted.

Case 21—A 3-year-old spayed female German Shepherd Dog was referred because the left eye had been swollen and reddened for 2 months. Topical medication and orbital drainage through the mouth had had no effect. Examination revealed that the left eye was displaced forward and dorsolaterally; it could not be pushed into the orbit. There was conjunctival hyperemia and epiphora, but the left globe itself was normal. The right eye was normal.

Because the clinical signs suggested neoplasia of the left orbit, a cavernous sinus venogram was obtained and thoracic radiographs were made. The venogram demonstrated a large filling defect in the left orbit. The thoracic radiographs revealed diffuse

interstitial and nodular pulmonary disease compatible with mycotic pneumonia. A blood sample was drawn for serologic testing and was positive for blastomycosis.

The client requested euthanasia of the dog. At necropsy, a large, firm mass was found in the ventromedial aspect of the left orbit. Histologic examination of this tissue revealed numerous granulomas containing *B dermatitidis*.

Discussion

The mode of entry by *B dermatitidis* into the body is uncertain but is most likely inhalation.¹² The large number of dogs with pulmonary involvement in this series supports this theory. The variety of ocular lesions in this series of dogs suggests the following hypothesis for progression of the disease in the eye. The organisms became established in the choroid, presumably by hematogenous spread. With or without a variable period of growth, a pyogranulomatous inflammatory response ensues. It is during this period that the first signs of anterior uveitis develop (aqueous flare, miosis, conjunctival hyperemia, photophobia, blepharospasm). Choroidal involvement, although responsible for the anterior uveal changes, may or may not be visible in the ocular fundus. The choroidal inflammation soon becomes exudative and extends from the choroid through the retinal epithelium, causing elevation of the overlying sensory retina. At this time, the lesions may become visible as circular, inflamed, and out-of-focus zones in the tapetal area or as fluffy white granulomatous-appearing masses in the nontapetal area. If the inflammatory process continues, the sensory retina becomes totally separated from the retinal epithelium and may become visible behind the lens. Visualization of this phenomenon may be obscured because of vitreal hemorrhage attributable to intraocular necrosis or because of anterior ocular changes such as inflammatory cataract, occlusion of the pupil, and corneal edema; the anterior changes are secondary to the posterior segment processes and are not caused by the organism itself, which is infrequently found in the anterior ocular tissues. In some cases, the choroidal inflammatory process may break through the sclera, causing its destruction as well as an intense fibrovascular proliferation amongst the orbital tissues, which is seen histologically. Many of the eyes at this stage have angle-closure glaucoma and, with or without the orbital changes, protrude from the orbit. This hypothetical progression of changes in these natural cases is consistent with the results found in experimental studies.^{13,a}

In dogs 20 and 21, there were no changes typical of what one might expect when the eye becomes involved in blastomycosis. The solitary nictitating membrane lesion in dog 20 can best be explained by local invasion of the organism. Alternatively, assuming the lymphadenopathy and pneumonia repre-

^aGross MA: *Experimental Canine Blastomycosis*, MS thesis. Ohio State University, Columbus, Ohio, 1956.

sented disseminated infection, organisms could have arrived at the nictitating membrane hematogenously and begun growing there. In light of the pulmonary involvement, the orbital lesion in dog 21 was almost certainly attributable to hematogenous spread, with atypical localization of the organism.

The reason for the male bias in this series of animals is unknown but is similar to that seen in human beings with blastomycosis.¹⁴

In previous reports, blastomycosis was often not suspected until late in the clinical course or until the dog had died or had been euthanatized and necropsied. This was unfortunate because most of the dogs had similar initial signs and had come from central United States, east of the Mississippi River, an area known to be endemic for blastomycosis.¹² It was clear from the present study that uveal inflammation of any degree in dogs from this area was often associated with and was commonly the hallmark of blastomycosis when not explained by other causes. The finding of uveitis in dogs from this locale should raise the clinician's index of suspicion to blastomycosis and prompt a thorough ocular and general physical examination. When the uveitis is associated with lung, lymph node, skin, bone, or testicular lesions, the suspicion of blastomycosis is greatly strengthened.

Ocular fundus examination would have been important in further increasing the clinician's index of suspicion to blastomycosis. Of all the dogs that were referred with advanced disease, none had had a fundus examination during the initial period of ocular signs. This was important in that early diagnosis and iv treatment with amphotericin B sometimes prevented progression of the early ocular lesions to secondary blinding changes and saved the animal's life.⁴

Confirmation of the diagnosis of blastomycosis was simple once the disease was suspected. Serologic evaluation and examination of aspirates from various

nonocular tissues frequently were rewarding. Intraocular aspiration and examination of smears made from the material also were important in making the diagnosis of blastomycosis in dogs with advanced disease in which the eye was the major organ involved. These procedures were easily performed and quickly established the presence of organisms, particularly in those dogs without skin lesions or lymphadenopathy. The intraocular aspiration was innocuous to the eyes inasmuch as they were already permanently blind from retinal and choroidal degeneration.

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