Systemic necrotizing vasculitis in nine young Beagles

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Summary: *A systemic necrotizing vasculitis of unknown etiopathogenesis may be termed juvenile polyarteritis syndrome (JPS). The syndrome has been recognized primarily in young Beagles used for toxicologic studies. We studied 9 young Beagles with JPS. Affected dogs had fever (40 to 41.5 C), anorexia, and signs of pain in the cervical area. They had a characteristic hunched stance, and were unwilling to move. Laboratory abnormalities in all dogs included nonregenerative anemia, hypoalbuminemia, and leukocytosis characterized by a mature neutrophilia. Analysis of CSF revealed a moderate to severe neutrophilic pleocytosis and a mildly high protein concentration in most dogs. Signs of disease resolved rapidly with high doses (2.2 mg/kg of body weight, PO) of prednisone. If untreated, clinical signs and laboratory abnormalities had a remitting and relapsing course in most dogs. Findings at necropsy included necrotizing arteritis with fibrinoid necrosis, periarteritis, thrombosis, and intimal proliferation that most frequently affected small- to medium-sized vessels in the cervical spinal cord, mediastinum, and heart. An immune-mediated pathogenesis for this disease is suspected.*

A systemic necrotizing vasculitis that may be called juvenile polyarteritis syndrome (JPS) has been most commonly reported in young Beagles used for toxicologic studies.[1-3] This syndrome also has been called canine pain syndrome. A similar, if not identical, syndrome has been reported in other breeds of dogs.[4-6]

We evaluated 9 young laboratory-bred Beagles with clinical signs of JPS to clarify the clinical and laboratory abnormalities associated with JPS, to correlate the clinical findings with histologic lesions, to investigate the etiopathogenesis of JPS, and to identify a clinically useful antemortem marker.

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Materials and Methods

Nine dogs were obtained from a commercial Beagle breeding kennel as soon as clinical signs typical of JPS were recognized. At the time of first evaluation, dogs ranged from 4 to 10 months old (median, 8 months). Both sexes were equally represented, and weights ranged from 4.6 to 8.2 kg (median, 6.7 kg). All dogs had been vaccinated for *Bordetella bronchiseptica,* canine parainfluenza, canine parvovirus, *Leptospira* sp (serovars *canicola* and *icterohaemorrhagiae*), papilloma virus, canine distemper virus, canine adenovirus type II, and rabies. Dogs also had been routinely treated with pyrantel pamoate and ivermectin. All dogs received a clinical evaluation (including ophthalmologic and neurologic examinations) at the time of arrival, each time clinical signs of JPS were detected, and monthly thereafter. Dogs were housed in groups of 2 to 4 dogs per pen and fed a dry, kibbled maintenance ration.[a] Water was provided ad libitum by an automatic water system. Vaccination for canine distemper virus, canine parvovirus, canine parainfluenza virus, leptospirosis, canine adenovirus type II, and rabies was performed yearly. Dogs were observed daily for signs of JPS. Rectal temperature was measured daily.

Standard hematologic and serum biochemical determinations, serum electrophoresis, urinalysis, urine protein:creatinine ratios, and fecal examinations for parasites were performed multiple times in all dogs. Other procedures that were performed in all or a majority of dogs included CSF analysis (n = 9), synovial fluid analysis (n = 7), thoracic and abdominal radiography (n = 8), survey cervical radiography (n = 6), cervical myelography (n = 3), electrocardiography (n = 9), echocardiography (n = 9), and thyroid function evaluation (n = 6). Selective angiography was performed in 1 dog.

Culturing for aerobic and anaerobic bacteria, mycoplasma, and fungi was performed on urine (n = 9), blood (n = 8), CSF (n = 9), and synovial fluid (n = 1). Culturing of feces for *Salmonella* spp, *Clostridium* spp, and *Campylobacter* spp also was

[a]Laboratory canine diet No. 5006, Hill's Pet Products, Topeka, Kan.

performed (n = 3). Samples of CSF were evaluated for antibody titers to canine distemper virus. Serum samples were evaluated in all dogs for antibody titers to *Ehrlichia canis, Rickettsia rickettsiae, Toxoplasma gondii, Brucella canis, Borrelia burgdorferi,* and *Chlamydia psittaci*. Standard immunologic tests performed included measurement of antinuclear antibody and rheumatoid factor titers (n = 9), lupus erythematosus cell preparations (n = 5), direct Coombs' tests (n = 5), and lymphocyte stimulation tests (n = 9). Direct immunofluorescence to detect immune complexes in tissue sections also was performed.

Transmission studies were performed by transfusion of blood from 2 dogs clinically affected with JPS and 1 age-matched control dog to 6 clinically normal 4-month-old Beagles. Twenty milliliters of blood was withdrawn from each donor dog and divided between 2 recipient dogs. Each recipient received 5 ml of donor blood, IV, and 5 ml, IP. Recipients were observed daily for 6 months after transfusion. Rectal temperatures of recipients were monitored daily and a CBC was performed weekly for the first 3 months after transfusion.

Medical treatment was attempted in all 9 dogs during an acute episode of JPS. Treatment modalities that were evaluated included broad-spectrum antibiotics (ampicillin, trimethoprim/sulfadiazine, chloramphenicol, tetracycline) and immunosuppressive doses of prednisone and cyclosporine. Detailed necropsies were performed in all 8 dogs that were euthanized and in all transfusion recipient dogs.

Results

Clinical signs—Initial physical examination revealed 3 dogs with clinical signs of acute JPS, 2 dogs with resolving clinical signs, and 4 dogs that were clinically normal. All dogs that were clinically normal on arrival had clinical signs of JPS within the next 14 days. Clinical signs in all affected dogs included pyrexia (40 to 41.5 C), lethargy, little voluntary locomotion, and an unwillingness to move the head and neck. Affected dogs tended to assume a hunched stance, with their necks extended ventrally (Fig 1). All dogs had cervical hyperesthesia and many had signs of pain when touched elsewhere. Some dogs had signs of pain when their mouth was opened; however, this was believed to be attributable to concurrent extension of the neck. Neurologic examination revealed intermittent deficits of conscious proprioception that affected 1 or both forelimbs in all dogs. Ophthalmologic examinations revealed no abnormalities. Clinical evaluation of the heart was normal in all but 1 dog, in which a grade II/V diastolic murmur was heard best on the right side. All dogs lost weight (10 to 15% body weight) during clinical episodes, but dramatic muscle atrophy was not observed. Diarrhea, with melena, developed in 3 dogs, and transient facial edema was observed in 1 dog. All dogs were partially to completely anorectic.

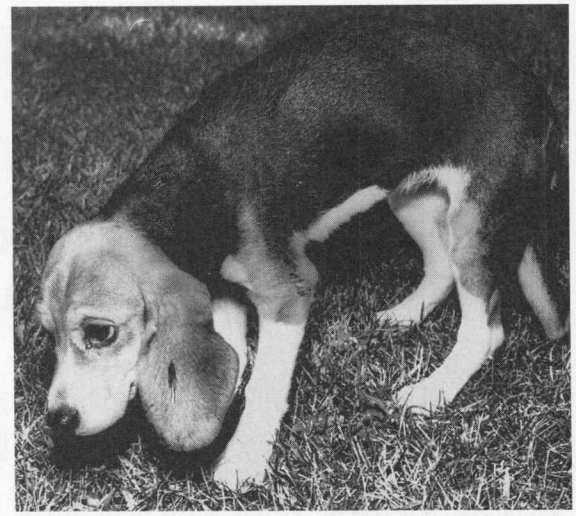
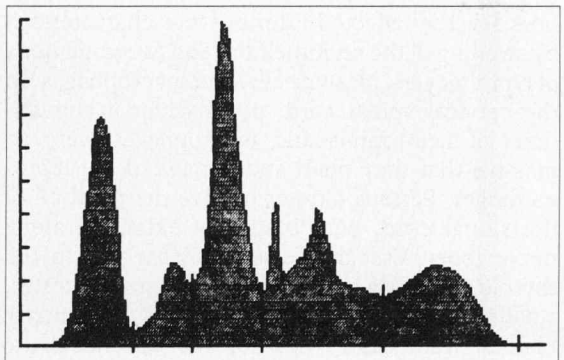


Figure 1—Female Beagle (5 months old) with clinical signs of juvenile polyarteritis syndrome (JPS). Notice the hunched stance and position of the neck.

In 3 dogs, clinical signs were severe and persistent, lasting from 9 to 17 days. Two of these dogs initially were treated with prednisone, but were euthanized because they could not be maintained in good condition without continuous prednisone treatment. The third dog did not receive prednisone treatment and was euthanized after 8 days of severe clinical signs. In the remaining 6 dogs, the clinical signs persisted from 2 to 7 days and then resolved. These dogs appeared clinically normal for several weeks to months, but then each dog had 2 to 8 episodes of clinical signs during the next 18 months of observation. Although there was considerable variation between dogs in the duration of clinical episodes and the severity of clinical signs, these variables tended to be consistent within individual dogs. The interval between episodes varied from 12 to 133 days. In 3 of the 6 dogs with cyclic disease, clinical episodes ceased after they were 12 to 18 months old. Two of these dogs were subsequently euthanized, and 1 is still alive and has been clinically normal for 2 years. Three dogs were euthanized during or between cyclic episodes.

Laboratory and radiologic abnormalities—Consistent clinicopathologic abnormalities were detected in all dogs during clinical episodes of JPS. All dogs had leukocytosis characterized by neutrophilia and monocytosis. The neutrophilia usually was composed of mature neutrophils; however, low numbers of band cells were observed in some dogs. The peak total WBC count ranged from 25.3 to 80.2 $\times 10^3$ cells/μl (median, 36.2 $\times 10^3$ cells/μl). The peak neutrophil count ranged from 21.5 to 76.4 $\times 10^3$ cells/μl (median, 30.7 $\times 10^3$ cells/μl), and the peak monocyte count ranged from 1.3 to 11.3 $\times 10^3$ cells/μl (median, 3.3 $\times 10^3$ cells/μl). All dogs developed a normocytic, normochromic, nonregenerative anemia during clinical episodes, which was manifested by low PCV, RBC count, and



FRACTION	%	G/DL	NORMAL
Albumin	20.9	1.0	2.3-3.2
Alpha 1	7.7	0.4	0.2-0.5
Alpha 2	29.5	1.5	0.3-1.1
Beta	24.8	1.2	0.6-1.2
Gamma	17.2	0.9	0.5-1.8
TOTAL		5.0	5.3-7.8

Figure 2—Serum protein electrophoretogram from an acutely ill dog with JPS. Notice the high α_2-globulin fraction.

hemoglobin concentration. The minimal PCV ranged from 21 to 32% (median, 30%). The reticulocyte count during episodes of anemia was always < 60,000 cells/μl and the reticulocyte production index was always < 0.6. Platelet counts were usually normal. A transient thrombocytopenia was detected once each in 3 of 9 dogs. Fibrinogen concentration was measured whenever CBC were performed. Fibrinogen concentrations ranged from 0 to 600 mg/dl, with no consistent trend.

Serum biochemical analyses revealed a rapid and progressive hypoalbuminemia during episodes of clinical disease in 8 dogs. The minimal total albumin concentration ranged from 1.7 to 2.9 g/dl (median, 2.2 g/dl). The total serum protein concentration usually was normal despite the hypoalbuminemia. Other biochemical abnormalities that were intermittently detected in all dogs included mild to moderate hypoglycemia that ranged from 38 to 72 mg/dl (median, 65 mg/dl), moderate depletion of sodium, potassium, and chloride ions, and increased alkaline phosphatase, cholesterol, and amylase concentrations. Changes in serum lipase concentration were not observed in any dog. Bilirubinemia was intermittently detected in 1 dog during clinical episodes. Thyroid function was normal in all dogs. In all dogs, serum electrophoresis revealed hypoalbuminemia with a high α_2-globulin fraction (Fig 2). The peak α_2-globulin fraction ranged from 1.1 to 1.8 g/dl (reference range, 0.3 to 1.1 g/dl), with a median of 1.7 g/dl. Urinalysis in all dogs was normal. Urine protein: creatinine ratios were transiently increased (1:1.5 to 1:6.6) in 3 of 9 dogs on 1 occasion each. Multiple urine protein:creatinine ratios on follow-up evaluations, however, were normal.

Cerebrospinal fluid analysis revealed neutrophilic pleocytosis, with a mild to moderate increase in microprotein in 6 dogs. Analysis of CSF was normal in 3 dogs. Peak WBC count in the CSF ranged from 1 to 1,850 WBC/mm^3 (median, 65 cells/mm^3), and peak microprotein concentrations ranged from 15 to 67 mg/dl (median, 29 mg/dl). The Pándy's test for globulins in the CSF was positive on 1 occasion in 2 dogs. Synovial fluid analysis revealed severe neutrophilic inflammation in 1 dog, mild to moderate inflammation in 4 dogs, and no abnormalities in 2 dogs. Clinicopathologic abnormalities generally resolved completely within 7 to 21 days of resolution of clinical signs, except for a persistent mildly high α_2-globulin fraction in 6 dogs.

Thoracic radiography and echocardiography were normal in all but 1 dog in which left ventricular hypertrophy and dilatation of the aortic outflow tract were detected. Myocardial contractility, however, was normal. Selective angiography revealed congenital anomalies of the aortic sinus, aortic root, and coronary vessels, with no evidence of an acquired abnormality. Findings on electrocardiography were normal in all but 2 dogs, in which intermittent sinus arrest and a wandering pacemaker were detected on 1 occasion in each dog. Abdominal radiography revealed mild hepatomegaly in 5 dogs. Results of survey cervical radiography and cervical myelography were normal in all dogs.

During the acute phase of the disease, all dogs had suppression of the blastogenic response to mitogenic stimulation. Antinuclear-antibody and rheumatoid-factor titers were absent and lupus erythematosus cells were not detected. Attempts to identify immune complexes in tissue sections have been inconclusive.

Bacteria were not isolated from the CSF in any dog. Bacteriologic culturing revealed no organisms in the blood from 6 of 8 dogs, in the urine from 8 of 9 dogs, or in the synovial fluid from 2 of 2 dogs. Bacteriologic culturing revealed no abnormal bacterial flora in the feces from 2 of 3 dogs. Bacterial organisms were recovered from the blood in 2 dogs (*C perfringens, Enterobacter agglomerans*), urine in 1 dog (*Enterococcus* sp, group D), and feces in 1 dog (*C perfringens*). Significant antibody titers to *Ehrlichia canis, Rickettsia rickettsiae, Toxoplasma gondii, Brucella canis, Borrelia burgdorferi,* or *Chlamydia psittaci* were not detected in serum samples from any dog. Cerebrospinal fluid samples from all dogs had no antibodies to canine distemper virus.

All recipient dogs were clinically normal for 6 months after transfusion. Necropsy of recipient transmission dogs did not reveal any evidence of transmission of JPS.

Response to treatment—Response to treatment with any broad-spectrum antibiotics, regardless of whether an organism was recovered from blood, urine, or feces was not evident. A dramatic clinical response was observed 12 hours after prednisone administration (1.1 mg/kg of body weight, PO, q 12 h). Rapid resolution of fever, clinical signs, and

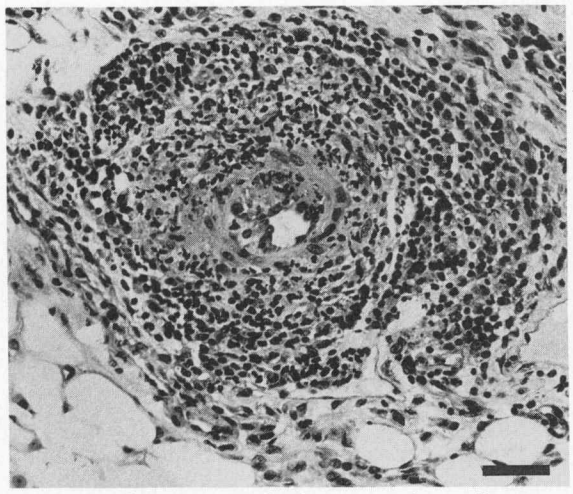


Figure 3—Photomicrograph of a section of a small muscular artery in the cranial mediastinum of a dog with JPS. Notice the necrosis of the tunica media and expansion of the tunica adventitia by inflammatory cells that extend perivascularly. H&E stain; bar = 50 μm.

laboratory abnormalities was detected in all 6 dogs in which corticosteroid treatment was initiated. Dogs could be maintained free of clinical signs on a low-dose, alternate-day maintenance regimen of prednisone (0.25 to 0.5 mg/kg, every other day) for several months. Clinical signs returned within 2 weeks of withdrawal of corticosteroid treatment. Cyclosporine (20 mg/kg, PO, q 24 h) given to 1 dog resulted in no improvement in clinical signs. Cyclosporine concentrations in blood were not measured.

Histologic abnormalities—Three dogs were euthanatized while having persistent clinical signs of JPS. Two dogs were euthanatized during subsequent clinical episodes, and 3 dogs were euthanatized while clinically normal. Gross abnormalities in the 5 dogs with clinical signs of JPS at time of euthanasia included multiple foci of hemorrhage within the coronary grooves of the heart, cranial mediastinum, and the leptomeninges of the cervical spinal cord. Regional lymph nodes were often enlarged and hemorrhagic. Gross lesions were not observed in the dogs that were clinically normal at the time of euthanasia.

Histologically, all dogs with clinical signs of JPS had severe necrotizing vasculitis of small- to medium-sized arteries in the cranial mediastinum, the extramural coronary arteries of the heart, and the leptomeninges of the cervical spinal cord. The most severe changes were characterized by acute necrotizing vasculitis and perivasculitis (Fig 3). Fibrin thrombi, partially filling or occluding vessel lumens, were common, and perivascular inflammatory infiltrates produced massive eccentrically placed nodules that completely encircled smaller arteries. The perivascular nodules usually were composed of neutrophils, but lymphocytes, plasma cells, and macrophages predominated in some. Less severely affected arteries were characterized by swelling of the endothelium, and accumulations of lymphocytes, plasma cells, and macrophages. In the cervical spinal cord, perivascular accumulations of neutrophils and macrophages were so massive that they filled and expanded the leptomeninges. Lesions did not involve the neuropil of the spinal cord, but commonly extended along nerve roots. Vasculitis also was observed in the thyroid gland, thymus gland, lymph nodes, testes, small intestine, diaphragm, esophagus, and urinary bladder in some dogs. In 1 dog, the vasculitis of the small intestinal arteries was severe enough to have caused thrombosis and ulceration of the duodenal mucosa, which had caused severe melena. This same dog had amyloidosis of the liver, which probably had caused the intermittent hyperbilirubinemia. Dogs that were clinically normal at the time of euthanasia had minimal vascular lesions. The principal histopathologic alterations were subintimal and perivascular fibrosis, and mild lymphoplasmacytic perivasculitis.

Discussion

During the past 15 years, there have been several reports of a systemic necrotizing vasculitis in Beagle colonies.[1-3,7] The vasculitis in some cases was initially attributed to administration of certain drugs. It soon became apparent, however, that this syndrome resulted after exposure to a wide variety of unrelated test compounds and in untreated control dogs.[3] A vasculitis with similar characteristics to this syndrome in Beagles also has been reported for other breeds.[4-6]

The vasculitis generally is characterized by fever, anorexia, and signs of cervical pain; however, a number of investigators have reported a subclinical vasculitis in Beagle colonies that affected either the coronary vessels alone[8,9] or the coronary vessels and numerous other sites.[10] These subclinical lesions were histologically similar to those reported by Hayes et al[3] and others.[1,2] It is still unclear whether these clinical and subclinical vasculitides are 2 distinct syndromes or reflect a continuum of canine systemic necrotizing vasculitis. The clinical syndrome of necrotizing vasculitis in young Beagles (JPS) appears to be clinically distinct from vasculitides that cause primarily dermatologic manifestations in dogs.[11-14] The distinction between JPS and some cases of idiopathic, corticosteroid-responsive, spinal meningitis or vasculitis is less clear.[15-17] One of 2 reported cases of necrotizing vasculitis of the CNS also had vascular lesions in the epicardium, myocardium, and pharyngeal mucosa similar to those described for dogs with JPS.[6] It is possible that some clinical cases of JPS are misdiagnosed as corticosteroid-responsive, sterile meningitis, because of the prominence of the clinical signs related to meningitis and the lack of clinical signs relating to vasculitis elsewhere.

The clinical and laboratory abnormalities that

result with JPS, although differing in severity, are consistent between dogs. This was true for dogs in our study and for those in other reports of JPS.[1-3,7] The changes generally correlated well with the histologic lesions. All 5 dogs that were euthanatized while having clinical signs of JPS had severe spinal meningitis and vasculitis of the arteries of the cervical spinal cord and meninges. In 1 of 3 dogs with melena, duodenal ulceration was evident grossly and histologically. A similar lesion may have accounted for melena observed in 2 other dogs. Conversely, despite severe coronary artery vasculitis, there were no cardiac arrhythmias or other acquired cardiac abnormalities. These results probably reflect the varying amounts of inflammation that can be tolerated by tissues before function is affected. The hypoalbuminemia that was detected during clinical episodes of JPS was probably caused by increased vascular permeability attributable to vasculitis. There was evidence of transient proteinuria in 3 dogs, but this was not a consistent finding. Protein-losing enteropathy could not be entirely ruled out; however, diarrhea was not a consistent finding in these dogs, and hypoglobulinemia was not detected in any dog.

Amyloidosis was found in the liver of 1 severely affected dog of our study. Amyloidosis affecting the spleen, liver, pancreas, and testes has been reported for dogs of another study.[3] Deposition of amyloid appeared to result in dogs undergoing severe repeated clinical episodes.

We were unable to document a viral or bacterial etiopathogenesis. In most dogs, culturing of CSF, blood, urine, synovial fluid, and feces multiple times was unproductive. Bacterial organisms were isolated from blood in 2 dogs, urine in 1 dog, and feces in 1 dog. Despite isolation of these organisms, clinical response to appropriate antibiotic treatment, on the basis of susceptibility testing, was not observed. Histologic evidence of bacterial infection was not observed in any dog at necropsy, including necropsy of 2 dogs in which organisms had been recovered from the blood. Further evidence against a primary bacterial cause of JPS was the clinical response to immunosuppressive doses of corticosteroids. An initial improvement of a bacterial infection might be expected with prednisone treatment because of its anti-inflammatory effects; however, long-term immunosuppressive corticosteroid treatment would likely result in exacerbation of a bacterial disease. The bacteria isolated in our group of dogs were probably nosocomial infections attributable to gastrointestinal tract mucosal breakdown, prolonged hospitalization, or repeated blood, CSF, and synovial fluid sampling. In all cases in which bacteria were isolated, there was no growth on prior or subsequent cultures.

An immune-mediated pathogenesis for JPS is consistent with the cyclic nature of the clinical signs, the immunologic abnormalities observed in affected dogs, the inability to detect an infectious cause, the response to corticosteroid treatment, and the lack of response to antibiotics. Seropositive antinuclear-antibody and rheumatoid-factor titers were reported in a few dogs in 1 report of JPS.[3] The lack of antinuclear-antibody and rheumatoid-factor titers in the dogs in this study does not rule out the possibility of immune-mediated disease. The immunologic changes detected in dogs with JPS have been described.[18]

Immune-mediated vasculitis may result from primary immunopathogenic mechanisms or secondary to infectious organisms, drug administration, or neoplasia.[19-21] None of the dogs of our study had evidence of neoplasia or prior drug exposure, other than routine vaccines and anthelmintics. Immune-mediated disease triggered by a bacterial antigen, virus, or toxin is a possible cause of JPS. Epidemiologic studies of the kennel of origin of these dogs failed to detect any correlation between prior bacterial or viral infections and development of JPS.[b]

A genetic predisposition has been established for many immune-mediated diseases in human beings and laboratory animals.[21] A familial link between dogs with JPS has been suggested by Stejkal et al.[22] Pedigree analysis from the breeding kennel of our dogs with JPS has suggested that the progeny of certain breeding males are more likely to be affected with JPS. A test breeding of 2 of our affected dogs resulted in a litter of 7 pups, of which 1 was affected with JPS.

The characteristic combination of clinical and laboratory abnormalities observed in dogs with JPS allow diagnosis of the syndrome in most cases. We have not been able to identify an antemortem marker that will allow identification of dogs predisposed to JPS, because most abnormalities resolve completely between episodes. High concentrations of α_2-globulins persist in some, but not all dogs, and the decreased response to lymphocyte stimulation persists between episodes. Unfortunately, neither of these abnormalities are specific for JPS.

[b]Glickman LT, Department of Veterinary Pathobiology, Purdue University, West Lafayette, Ind: Personal communication, 1990.

References

1. Brooks PN. Necrotizing vasculitis in a group of Beagles. *Lab Anim* 1984;18:285–290.
2. Harcourt RA. Polyarteritis in a colony of Beagles. *Vet Rec* 1978;102:519–522.
3. Hayes TJ, Roberts GKS, Halliwell WH. An idiopathic febrile necrotizing arteritis syndrome in the dog: Beagle pain syndrome. *Toxicol Pathol* 1989;17:129–137.
4. Joshua JO, Ishmael J. Pain syndrome associated with spinal haemorrhage in the dog. *Vet Rec* 1968;83:165–169.
5. Kelly DF, Grunsell CSG, Kenyon CJ. Polyarteritis in the dog: a case report. *Vet Rec* 1973;92:363–366.
6. Hoff EJ, Vandevelde M. Case report: necrotizing vasculitis in the central nervous systems of two dogs. *Vet Pathol* 1981;18:219–223.
7. Albassam MA, Houston BJ, Greaves P, et al. Polyarteritis in a Beagle. *J Am Vet Med Assoc* 1989;194:1595–1597.

8. Spencer A, Greaves P. Periarteritis in a Beagle colony. *J Comp Pathol* 1987;97:121–128.

9. Hartman HA. Idiopathic extramural coronary arteritis in Beagle and mongrel dogs. *Vet Pathol* 1987;24:537–544.

10. Ruben Z, Deslex P, Nash G, et al. Spontaneous disseminated panarteritis in laboratory Beagle dogs in a toxicity study: a possible genetic predilection. *Toxicol Pathol* 1989; 17:145–152.

11. Manning TO, Scott DW. Cutaneous vasculitis in a dog. *J Am Anim Hosp Assoc* 1980;16:61–67.

12. Randell MG, Hurvitz AI. Immune-mediated vasculitis in five dogs. *J Am Vet Med Assoc* 1983;183:207–211.

13. Fadok VA, Barrie J. Sulfasalazine responsive vasculitis in the dog: a case report. *J Am Anim Hosp Assoc* 1984;20: 161–167.

14. Rachofsky MA, Chester DK, Read WK, et al. Probable hypersensitivity vasculitis in a dog. *J Am Vet Med Assoc* 1989;194:1592–1594.

15. Meric SM, Child G, Higgins RJ. Necrotizing vasculitis of the spinal pachyleptomeningeal arteries in three Bernese mountain dog littermates. *J Am Anim Hosp Assoc* 1986;22:459–465.

16. Irving G, Chrisman C. Long-term outcome of five cases of corticosteroid-responsive meningomyelitis. *J Am Anim Hosp Assoc* 1990;26:324–328.

17. Russo EA, Lees GE, Hall CL. Corticosteroid-responsive aseptic suppurative meningitis in three dogs. *Southwest Vet* 1983;35:197–201.

18. Felsburg PJ, HogenEsch H, Somberg RL, et al. Immunologic abnormalities in canine juvenile polyarteritis syndrome: a naturally occurring animal model of kawasaki disease. *Clin Immunol Immunopathol,* in press.

19. Faucci AS. The spectrum of vasculitis. Clinical, pathologic, immunologic and therapeutic considerations. *Ann Intern Med* 1978;89:660–676.

20. Crawford MA, Foil CS. Vasculitis: clinical syndromes in small animals. *Compend Cont Educ Pract Vet* 1989;11:400–415.

21. Bishop SP. Animal models of vasculitis. *Toxicol Pathol* 1989;17:109–117.

22. Stejkal V, Havn N, Malmfors T. Necrotizing vasculitis as an immunological complication in toxicity study. *Arch Toxicol Suppl* 1982;5:283–286.

Book Review: Parasites of Laboratory Animals

This unique handbook brings together descriptions and illustrations of the common, and some not so common, parasites of laboratory animals, principally rodents. Parasites considered include those of rats, mice, hamsters, gerbils, guinea pigs, rabbits, rhesus and cynomolgus monkeys, baboons, squirrel monkeys, marmosets, and tamarins.

Other sections cover isolation and preservation techniques, and there are brief sections on serodiagnosis and treatment. The appendices include a rather comprehensive host-parasite list of less common parasites of laboratory rodents, lagomorphs, and new and old world monkeys. The appendices also contain formulas for making histologic fixatives and stains, along with descriptions of concentration methods for fecal material and microfilariae. The book also contains a table of contents, a list of nearly 400 references, a glossary, and an index.

This handbook is the product of the author's career-long interest in parasites of laboratory animals, which spans over 20 years—appointments at the Liverpool School of Tropical Medicine, the Medical Research Council Laboratory Animals Center, Carshalton, the field station of the London School of Hygiene and Tropical Medicine at St. Albans, and the Department of Pathology at Cambridge University. The handbook is liberally illustrated with photographs, drawings, and photomicrographs of good to excellent quality. As such, it will provide researchers and diagnosticians a rapid and practical means of identifying common ecto- and endoparasites of laboratory animals.

Although little new information is presented and the information is readily available in the ACLAM/Academic Press monographs, this handbook is especially useful as a concise handy reference to aid in identifying parasites of laboratory animals. *[Parasites of Laboratory Animals. (Laboratory Animal Handbooks, No. 12) By Dawn Owen. 180 pages; illustrated. Royal Society of Medicine Services Limited, 1 Wimpole St, London W1M 8AE United Kingdom. 1992. Price $60.00.]*—JOSEPH E. WAGNER