Sudden Death in Doberman Pinschers

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SUMMARY **In a postmortem study of 11 Doberman Pinschers that had died suddenly, an identical cardiac lesion was found in 10. This was a nearly complete focal degeneration of the His bundle, which was associated with cartilage and bone formation in the adjacent central fibrous body. The cause of these lesions is considered to be luminal narrowing of the local small coronary arteries, which may be a heritable fault. It is postulated that sudden unexpected death in these dogs may be due to a form of Adams-Stokes attack. Pertinence of these observations to human cardiac disease is discussed.**

UNEXPECTED SUDDEN DEATH, which is one of the greatest problems in cardiology today, too often remains unexplained. Any knowledge contributing to an elucidation of this problem deserves attention. This report describes the findings resulting from a study of sudden unexpected death as it occurs in the Doberman Pinscher dog. It has long been known among admirers of this breed that these dogs occasionally die suddenly and unexpectedly, but efforts to determine the cause have previously left it a mystery. The deaths have characteristically been in presumably healthy dogs, often with an unanticipated sudden collapse but usually preceded by one or more convulsions. Because of the convulsion, a cerebral lesion has been considered, but examinations of the brain have failed to demonstrate significant pathology there (1). Since a cardiac lesion could cause both convulsions and sudden death, the present study was undertaken to determine whether there was pathology in the heart, with particular attention to the conduction system.

SUBJECTS

Hearts from two Doberman Pinschers that died suddenly and unexpectedly were originally examined, and an identical lesion was found in the bundle of His and central fibrous body (2). The likely significance of this pathology was then communicated to owners and breeders of these dogs, and over the course of the past 3 years we have now had the opportunity to study the hearts from a total of 11 Dobermans that died suddenly at a time when they were considered in excellent health. All were purebred dogs. General data for all the dogs are presented in Table 1, but a brief summary of details for each is as follows.

DOG 1

This 5-year-old black, male Doberman from Michigan developed recurring convulsions one evening, with no apparent cause, and died during one of these the next morning. This dog and Dog 2 were owned by different persons and did not share kennel or other facilities, but they did have a common ancestor, a magnificent red Doberman that was an international show champion. This common ancestor (Red "B") died suddenly and unexpectedly at the age of 10 years while in apparent good health. Red

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TABLE 1. Clinical and Necropsy Data on 11 Doberman Pinscher Dogs*

Number in Series	Age, Sex	Cause of Death	Condition of AV Bundle	Cartilage in CFB	Bone in CFB	Abnormal Coronary Arteries
1	5 yr, M	Sudden and unexpected	Degenerate	Yes	Yes	Yes
2	6 yr, M	Sudden and unexpected	Degenerate	Yes	Yes	Yes
3	3 yr, F	Sudden and unexpected	Degenerate	Yes	No	Yes
4	4 yr, M	Sudden and unexpected	Degenerate	Yes	Yes	Yes
5	3½ yr, F	Sudden and unexpected	Degenerate	Yes	Yes	Yes
6	3 days, M	Sudden and unexpected	Intact	No	No	No
7	9 yr, M	Sudden and unexpected	Degenerate	Yes	Yes	Yes
8	6½ yr, F	Sudden and unexpected	Degenerate	Yes	Yes	Yes
9	8½ wk, F	Sudden and unexpected	Degenerate	Yes	Yes	Yes
10	10½ yr, F	Sudden but expected	Degenerate	Yes	Yes	Yes
11	9 wk, F	Sudden and unexpected	Degenerate	Yes	No	Yes

* CFB = central fibrous body; AV = atrioventricular.

"B" had been mated with a dam that produced three pups: a female that died in an accident, a male that is living and well, and Dog 1 in this study; this dam died at the age of 10 of "tetanus" that had not responded to appropriate treatment with tetanus antitoxin. Red "B" was later mated with another dam, the health of which is unknown, producing a litter that included the mother of Dog 2 in the present study. The mother of Dog 2 is living and well, but the father died unexpectedly at the age of 5 years of unknown cause. Necropsy findings in all dogs in this study were so similar they will be described together, with any pertinent exceptions noted.

DOG 2

This 6-year-old male Doberman from Michigan had been in a veterinarian's kennel for several days because of anorexia. Its appetite had been normal at least 2 days before it was found dead in the cage one morning, with physical evidence suggesting the dog had been violent during the preceding night. Because of a question of poisoning, stomach contents were examined toxicologically and gastrointestinal mucosa histologically, with negative results.

DOG 3

A 4-year-old female Doberman from California was thought to be in good health before sudden unexpected death. At necropsy there were some cecal worms and enteritis, but the cardiac lesions were identical with those in the other dogs. The maternal grandfather of Dog 3, which was located 2,000 miles from Dogs 1 and 2, was also the grandfather of Red "B," the common ancestor of the first two dogs in this series.

DOG 4

This 5-year-old male Doberman was owned by a farmer in Alabama. During dipping of sheep for ticks, the dog entered some of the dip solution. The next day it died during a series of convulsions, which the veterinarian did not consider related to the exposure to sheep dip.

DOG 5

This 3½-year old black and tan female Doberman was owned in Arizona. For several weeks before its sudden death, it had exhibited varying degrees of weakness in both front legs and one rear one. It is not known whether the weakness was the consequence of a preceding convulsion.

DOG 6

This 3-day-old male black Doberman puppy from Michigan was 1 of 11 in a litter presented for routine tail docking and dew claw removal under local anesthesia. When the owners arrived back at their home, they found that this puppy had died.

DOG 7

This 9-year-old male Doberman from Michigan died suddenly and unexpectedly at a time when considered in excellent health. From its pedigree data it was discovered that there were common ancestors with Dogs 1, 2, and 3 of this series.

DOG 8

This 6½-year-old female Doberman from California died suddenly and unexpectedly while in apparent good health. Its relationship to Dogs 1, 2, 7, and 9 is discussed later.

DOG 9

This 8½-week-old female Doberman puppy from Michigan received light general anesthesia with methoxyfluorine (Fluothane®) for the purpose of trimming the ears and was placed in a kennel cage in apparent good condition. Five hours later it was found dead. In addition to the cardiac pathology, necropsy demonstrated pulmonary edema.

DOG 10

This 10½-year-old female Doberman from Michigan suddenly collapsed and became dyspneic. The owner, who had heart disease herself, thought the symptoms resembled a heart attack and gave the dog one of her own nitroglycerin pills, which seemed to relieve it. She continued to treat it in this fashion for 1 day and then sought the consultation of a veterinarian. On examination the dog was found extremely dyspneic with pulmonary congestion and no discernible pulse or heart beat. The mucous membranes were cold but not cyanotic. Within a few minutes after beginning the examination, the veterinarian found the dog was dead. In addition to the cardiac pathology there was pulmonary edema at necropsy.

DOG 11

This 9-week-old puppy, a littermate of Dog 9, died unexpectedly after an ear trimming procedure. It had previously been considered healthy.

GENEALOGICAL SUMMARY DATA

Dogs 1, 2, 3, 7, and 8 all had one common male ancestor; but each of these descendants had different immediate antecedents, none was a littermate of the other, and their relationship to the common ancestor was from two to four generations removed. The two puppies that were littermates (Dogs 9 and 11) are even more distant

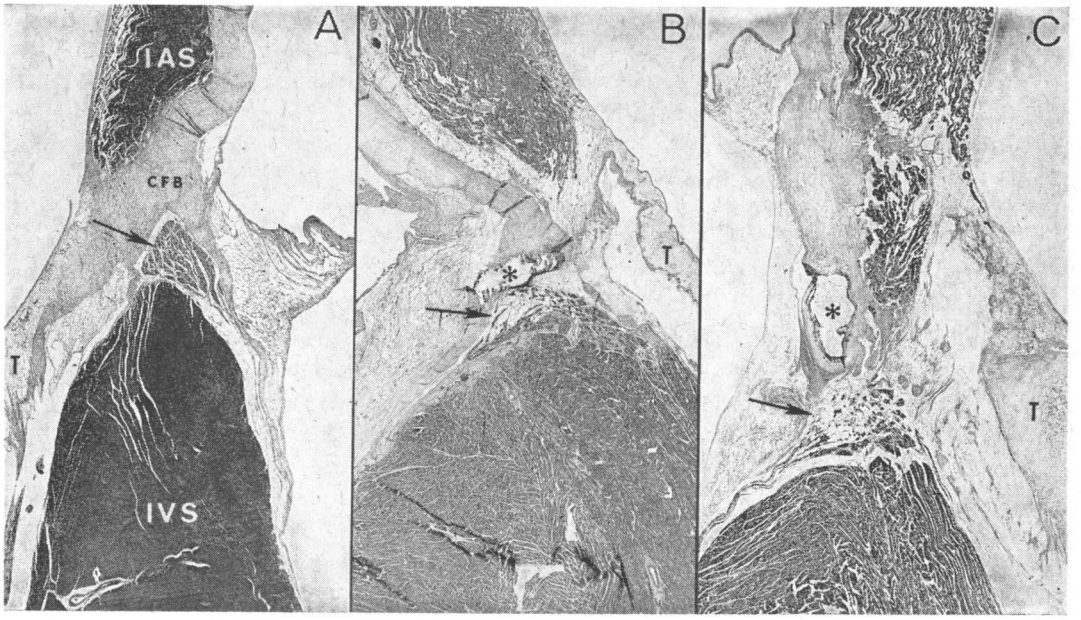

FIGURE 1. The characteristic pathologic lesion of the His bundle described in this study is illustrated here at low magnification. A. An example of normal canine His bundle (*arrow*) for comparison. (× 20). B. Bone cyst (*asterisk*) in the central fibrous body with the degenerated His bundle (*arrow*) adjacent to it in Dog 1. (× 17.) C. Similar pathologic changes in Dog 2. (× 17.) Orientation of the three sections is the same except that the tricuspid valve (*T*) is on the left in *A* but on the right in *B* and *C*. IAS is interatrial septum; IVS, interventricular septum; and CFB, central fibrous body. (Goldner trichrome stain.)

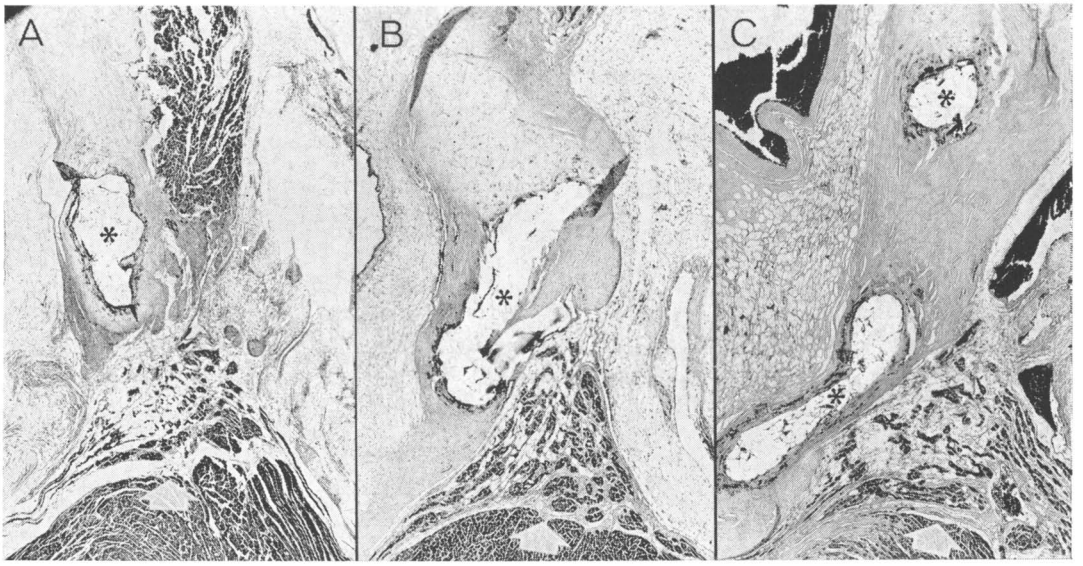

FIGURE 2. The lesions of the His bundle and the central fibrous body are shown here in more detail from Dogs 2 (*A*) (× 28), 5 (*B*) (× 45), and 7 (*C*) (× 45). The bone cyst in each is indicated with an asterisk; two cysts are present in *C*. The degenerating His bundle is indicated with a white arrow. Particles of marrow fat can be seen within the bone, and cartilage is visible nearby. (Goldner trichrome stain.)

descendants of the same male ancestor and were not closely related to the five grown dogs cited. Since this large kindred covered a number of generations and was owned in widely scattered geographic areas, only the broadest genetic implications can be made relative to the present study. These include the fact of some blood relationship of several members of the study, and 1 ancestor in common for 6 of the 11 dogs dying suddenly. If the lethal factor is heritable, its presence or absence in other members of these generations is unknown, and therefore its mode of transmittance remains obscure.

NECROPSY FINDINGS

Every dog in this study was necropsied, although in Dogs 1 and 11 the examination was limited to the heart and lungs. Pertinent extracardiac findings are presented with each case above, but in none were such findings considered the likely cause of death. Because a cardiac lesion responsible for sudden death might logically be suspected to be in the atrioventricular (AV) node or the His bundle, in every dog this region was sectioned subserially at 1-mm intervals in a manner described previously (3, 4). From these blocks, selected areas of AV node and His bundle were then sectioned serially at 6-μ intervals. A similar study was routinely conducted for the sinus node (5) and for selected sites in the free walls of the four cardiac chambers. In 10 of the 11 dogs studied because of sudden death the important abnormalities were in the heart. Furthermore, the observed changes were similar in every instance and consisted of the following. In the undivided His bundle of these 10 dogs there was a point of almost complete replacement by fat (Figures 1 and 2) with no associated inflammation. Adjacent to this lesion in the His bundle there was regularly a striking transformation in the central fibrous body that included a bone cyst (Figure 3) in 8 of the 11 dogs and contiguous islands of cartilage in 10 of the 11. The one dog that did not show any of these changes was a

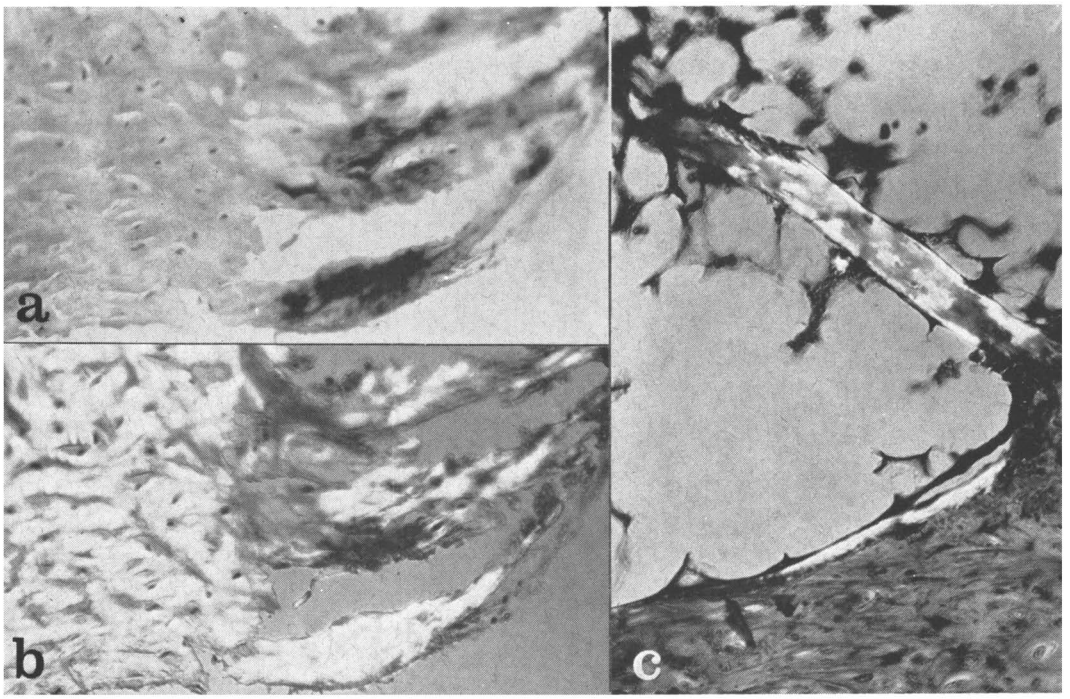

FIGURE 3. Margins of the bone cysts are shown here from Dogs 1 (*a* and *b*) and 2 (*c*). The spicules of bone stain darkly when viewed with ordinary light (*a*) but exhibit characteristic birefringence when viewed with polarized light (*b* and *c*). *a* and *b* are the same section. (Goldner trichrome stain, × 192.)

3-day-old puppy (Dog 6). In the 10 dogs with the changes in the central fibrous body there were additional islands of cartilage in the tricuspid valve in 4, with bone formation in 2 of these, and islands of cartilage (without bone) in the root of the aorta of 4 dogs and in the mitral valve in 2. Except for scattered small foci of fibrosis, the ventricular myocardium appeared normal. In every heart the tricuspid valve was variably thickened, but except for the cartilage as noted above, the other 3 cardiac valves were normal. There was no unusual hypertrophy or dilation of the cardiac chambers. The coronary arteries were grossly normal throughout their course.

To explain the degeneration of the His bundle, which appeared to have been a gradual process with fatty replacement, two possibilities were considered. One was trauma to the His bundle by the adjacent bone, but this possibility was rejected when it was found that the His bundle of the beef heart was not degenerated despite the normal consistent presence of a large bone (the os cordis) directly adjacent to it (Figure 4) (6). The second possibility was chronic ischemic degeneration of the His bundle as a consequence of unsuccessful competition for available blood supply with the adjacent cartilage and newly forming bone, which have a high metabolic requirement. To explore this latter point, studies were conducted in the beef heart to determine if there was a single blood supply to both the os cordis and the His bundle or whether they had separate nutrient arteries, since in the latter case the survival of bovine His bundle adjacent to bone might be attributable to separate blood supply. The os cordis and the His bundle in the beef heart are supplied by a single artery (6).

On closer examination of the small coronary arteries in the region of the His bundle

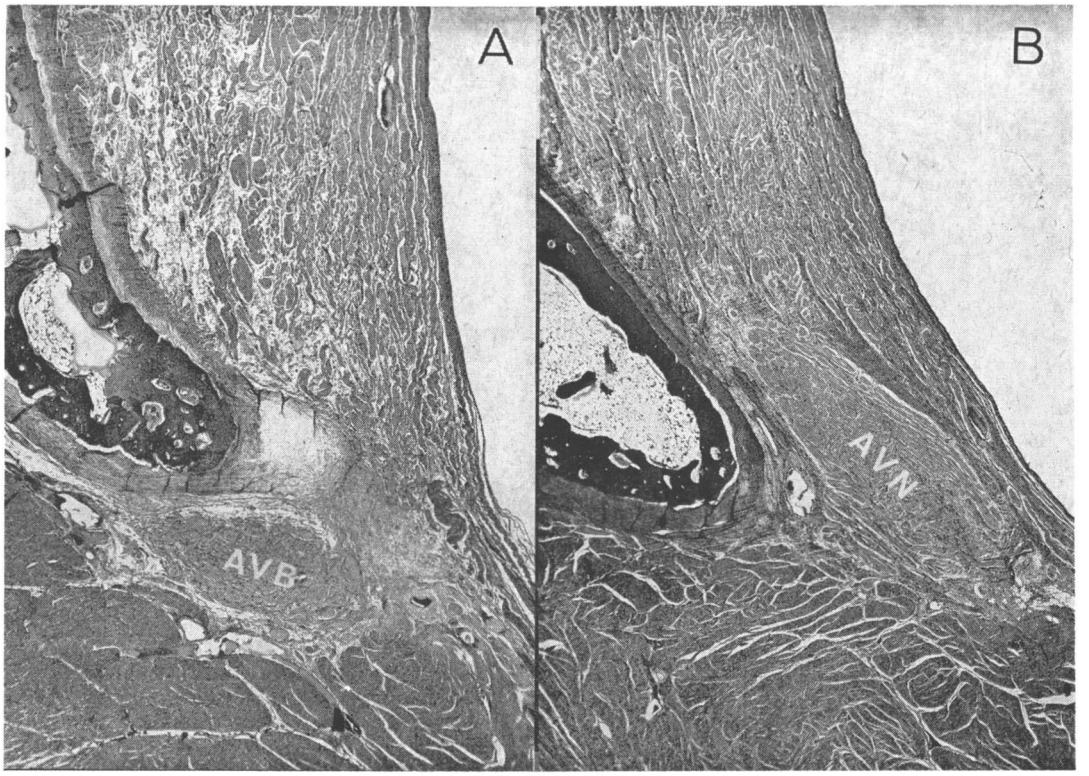

FIGURE 4. Examples of the bovine os cordis directly adjacent to the His bundle (AVB in *A*) and atrioventricular node (AVN in *B*) are shown here from a normal steer heart. Note the absence of any degeneration despite a large, well-developed adjacent bone. (Goldner trichrome stain, × 16.)

of the Doberman dogs, it was found that the lumens were markedly narrowed (Figure 5). The arterial lesions were focal and on serial examinations of a single artery were often found to be located between long adjacent normal segments. Histologically, the arteriopathy consisted of both medial degeneration and endothelial proliferation. There were no amyloid and no inflammation of the arteries or their adventitia. Similar lesions could be found in ventricular myocardium, but very infrequently compared with the distribution in the region of the AV node and the His bundle. Since focal ischemia was one of the etiologic considerations relative to the focal degeneration of the His bundle, these arterial lesions were interpreted to be of functional significance. Whether they may have also been responsible for earlier metaplasia of collagen in the central fibrous body into cartilage and eventually bone is a logical question for which there is presently no answer.

No electrocardiograms or examinations of the pulse or heartbeat are available in any of the dogs except Dog 10, in which the pulse was found to be absent shortly before death. To see whether apparently normal Doberman Pinschers had any evidence of heart block or other cardiac electrical disturbance, we made electrocardiograms on 15 purebred Dobermans, and all were normal. There were specifically no arrhythmias, no prolongation of the PR interval, and no change in configuration of QRS. We have not sacrificed any healthy Dobermans to study their hearts.

Bone in the central fibrous body and degeneration of the His bundle have been observed in 2 mongrels, 1 of uncertain origin and the other mainly terrier, but they have not been observed in over 65 other mongrel dogs. Disturbances in AV conduction as a spontaneous occurrence in apparently healthy dogs are rare (7) and have not been observed in over 600 dogs studied here with electrocardiograms in the course of physiologic experiments. A different type of pathology, also associated with an arteriopathy, has been found in the sinus node of certain Dalmation coach hounds (8), but their His bundles were normal, and there was no cartilage or bone in the central fibrous body.

Discussion

Focal degeneration of the His bundle with cartilage and bone in the adjacent central fibrous body was consistently present in the hearts of 10 of 11 Doberman Pinschers consecutively studied because of sudden death. Whatever the cause of this lesion, it is logical to suspect that it was related to the sudden death and that death was due to a form of Adams-Stokes attack. On comparative studies with the beef heart, which normally contains an os cordis directly adjacent to the His bundle, the significant difference was that the local small coronary arteries were normal in the steer but were focally narrowed in the Dobermans. On this basis it is concluded that the degeneration of the His bundle is due to chronic ischemia, compounded by metabolic competition with cartilage and newly formed bone for a much diminished blood supply.

Bone in the heart is not a new observation (9, 10), but except for the os cordis of the steer and some related vertebrates, there has been no consistency in its location within the heart, being most often present in a site of chronic inflammation. It should be stressed that there is an important difference between simple calcification and formation of bone, since the former is not uncommon in many locations in the heart while the latter is rare. Calcification in association with chronic aortic valvulitis, for example, is a frequent necropsy finding in patients with rheumatic heart disease and complete heart block. However, in 8 such human hearts personally examined specifically for either cartilage or bone in the central fibrous body, there was none; nor has bone in the central fibrous body been seen in over 250 other human hearts.

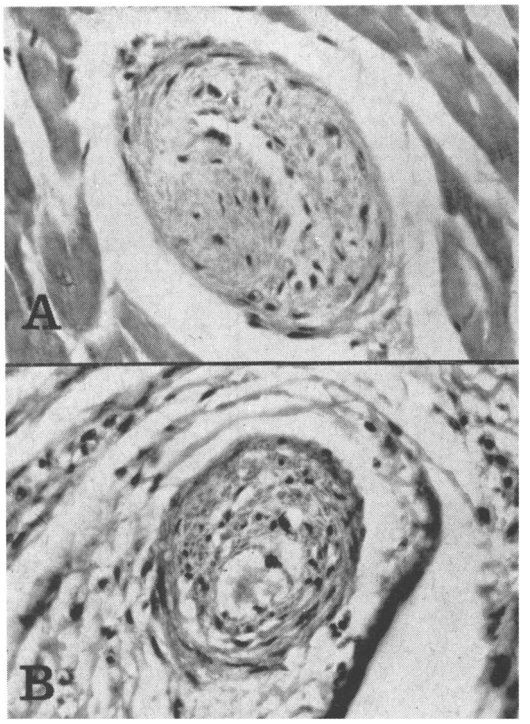

Figure 5. Two examples of characteristic lesions producing luminal narrowing of small arteries in and near the His bundle of these Doberman dogs are shown here. A. From Dog 1. B. From Dog 2. (Goldner trichrome stain, × 480.)

The possibility that the central fibrous body is either under unusual physical stress, as suggested by Keith and Flack (11), or some other influence (perhaps metabolic), is supported by the normal presence of bone in this location in the beef heart. It has recently been demonstrated that the combination of focal ischemia and an appro-

priate antigenic stimulus can consistently produce focal new growth of cartilage in the myocardium of the chicken (12). It seems likely, therefore, that both the cartilage (and new bone) formation and the His bundle degeneration are the consequence of local ischemia caused by narrowing of the small coronary arteries of the region and that once the mutation of collagen to cartilage occurs, the His bundle is at a compounded disadvantage in the competition for the diminished arterial circulation.

Focal narrowing of small coronary arteries is not uncommon within the canine myocardium (13–15), but the resulting scattered focal degeneration and replacement by fat or collagen in ventricular myocardium is of little functional significance unless the process is exceptionally widespread.

Since the same pathologic changes were observed in the His bundle of 10 of the 11 dogs dying suddenly, and their ages ranged from 8 weeks to 10 years, the lesions must develop at different rates of speed in different dogs but may not be present in the immediate postnatal period (for example, Dog 6). A difference in speed of development of the lesions is further indicated by the fact that the ones in Dog 9 were far more extensive than those in Dog 11, even though these two dogs were littermates of the same sex and died at approximately the same age (8 to 9 weeks).

Whether the apparent rarity of such changes in the His bundle of mongrel dogs is due to less inbreeding than in purebred dogs is conjectural. It would be desirable to know, for example, whether similar pathology occurs in the hearts of other purebred dogs dying suddenly and unexpectedly. Similarly, a systematic study of mongrels selected in the same manner as the Dobermans (for example, sudden unexpected death) might yield different results, since the present groups are not directly comparable. We are aware of no reason why this lesion should be unique in the Doberman Pinscher and anticipate that it will eventually be found in other breeds of dog and possibly other animals.

From this study of Doberman dogs there are two points that have value in understanding human cardiac disease. It seems likely that the abnormalities in the small coronary arteries of these dogs were inherited, resembling both in this way and in the histologic appearance a disease observed in human patients dying with certain forms of obscure myocardiopathies (16–18). The second point concerns the focal degeneration of the His bundle secondary to narrowing of its nutrient arteries, a condition also observed in certain human examples (16–18). In fact, the appearance of the His bundle of the dog in this report illustrated in Figures 2 and 3 is virtually identical with a lesion found in a patient with thrombotic thrombocytopenic purpura dying with a documented Adams-Stokes seizure (Figure 4A in reference 19). Destruction of the His bundle in both instances was due to occlusion of nutrient arteries of the bundle. Further study of this interesting problem in the dog may increase our knowledge of both canine and human cardiac disease.

References

1. Colmore, J. P.: Personal communication. University of Oklahoma Medical Center, Oklahoma City, Okla.
2. James, T. N., Drake, E. H.: Sudden death in Doberman Pinschers. *Henry Ford Hosp. Med. Bull.* 13: 183, 1965.
3. James, T. N.: Anatomy of the A-V node of the dog. *Anat. Rec.* 148: 15, 1964.
4. James, T. N.: Morphology of the human atrioventricular node, with remarks pertinent to its electrophysiology. *Amer. Heart J.* 62: 756, 1961.
5. James, T. N.: Anatomy of the sinus node of the dog. *Anat. Rec.* 143: 251, 1962.
6. James, T. N.: Anatomy of the sinus node, AV node and os cordis of the beef heart. *Anat. Rec.* 153: 361, 1965.
7. Patterson, D. F., Detweiler, D. K., Hubben, K., Botts, R. P.: Spontaneous abnormal cardiac arrhythmias and conduction disturbances in the dog. A clinical and pathologic study of 3,000 dogs. *Amer. J. Vet. Res.* 22: 355, 1961.
8. James, T. N.: Congenital deafness and cardiac arrhythmias. *Amer. J. Cardiol.* 19: 627, 1967.

9. TOPHAM, J. A.: Bone formations in the heart. *Brit. Med. J.* 2: 953, 1906.
10. FINESTONE, A. J., GESCHICKTER, C. F.: Bone formation in the heart. *Amer. J. Clin. Path.* 19: 974, 1949.
11. KEITH, A., FLACK, M. W.: The auriculo-ventricular bundle of the human heart. *Lancet* 2: 359, 1906.
12. LEHOCZKY-MONA, J., MCCANDLESS, E. L.: Ischemic induction of chondrogenesis in myocardium. *Arch. Path. (Chicago)* 78: 37, 1964.
13. RATCLIFFE, H. L., YERASIMIDES, T. G., ELLIOTT, G. A.: Changes in the character and location of arterial lesions in mammals and birds in the Philadelphia Zoological Garden. *Circulation* 21: 730, 1960.
14. DETWEILER, D. K.: Cardiovascular diseases in animals: clinical consideration, in *Cardiology*, edited by LUISADA, A. A., McGraw-Hill Book Co., Inc., New York, 1961, chap. 2.
15. DETWEILER, D. K.: Genetic aspects of cardiovascular diseases in animals. *Circulation* 30: 114, 1964.
16. JAMES, T. N.: An etiologic concept concerning the obscure myocardiopathies. *Progr. Cardiov. Dis.* 7: 43, 1964.
17. JAMES, T. N.: Anatomy of the coronary arteries in health and disease. *Circulation* 32: 1020, 1965.
18. JAMES, T. N.: Pathology of the small coronary arteries. *Amer. J. Cardiol.* 20: 679, 1967.

QUESTION OF THE MONTH

(Rheumatology)

87. For the past three months, an obese 60-year-old carpenter has had recurrent pain in the region of the right hip. The pain occurs when he climbs stairs, stands up after prolonged sitting, or when he lies on his right side.

On examination, there is tenderness over the right lateral thigh about six inches below the iliac crest. On internal rotation and adduction of the right hip, there is slight limitation of motion with pain on extremes of these motions. Roentgenograms, sedimentation rate, hemoglobin, leukocyte count and urinalysis are within normal limits.

Which of the following is the most likely diagnosis?

(A) Osteoarthritis of the hip
(B) Avascular necrosis of the femoral head
(C) Degenerative lumbar disc disease with referred pain
(D) Monarticullar rheumatoid arthritis
(E) Trochanteric bursitis

[*This* Question of the Month *is from the* Medical Knowledge Self-Assessment Program *of the ACP. The answer and a reference are given on p. 866 of this issue.*—Ed.]