Changes in the Character and Location of Arterial Lesions in Mammals and Birds in the Philadelphia Zoological Garden


The frequency of arteriosclerosis (intimal thickening with or without lipid deposits) in mammals and birds of the Philadelphia Zoological Garden has increased 10-fold since 1935. This increase has involved increases in the varieties of animals that develop the disease and has been accompanied by changes in the location and character of the lesions, as well as in the apparent rate of their development. Thus, in recent years lesions of the coronary arteries have become relatively common and, since 1950, have led to deaths of a number of younger animals. In the earlier material, coronary lesions usually were limited to an occasional aged animal that had died of other causes.

The recent paper on frequency listed the varieties of mammals in which arteriosclerosis has developed most often since 1935. This paper also described the conditions that have been related to the rise in frequency. The changes in the character and location of arteriosclerotic lesions in the animals of this zoo will be described and discussed at this time.

Material

The material for this report has been taken largely from autopsies of mammals and birds that have died in the Philadelphia Zoo since 1935. Earlier material from this series of autopsies has been described and illustrated. It is reviewed briefly for comparison with the more recent examples of the disease.

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During 1935 the traditional and often inadequate diets then common to zoological gardens were replaced in the Philadelphia Zoo by controlled diets. Since then nutritional disease has ceased to be a factor in morbidity or mortality. These diets and the conditions under which the material from this zoo has been collected and prepared for study have been described fully.

Observations

Prior to 1935 and the introduction of adequate diets the most striking form of arteriosclerosis developed in birds as atheromata of the thoracic aorta and brachiocephalic arteries. These lesions probably attained their largest size in the parrots and their relatives (Psittacidae), especially in parrots of the genus Amazona. In these birds the thickness of the atheromata often exceeded the diameters of the arteries themselves and, at times, convulsive seizures experienced by parrots could be attributed to partial obstruction of the brachiocephalic arteries by these lesions.

However, this was not exclusively a disease of the psittacine birds. Relatively large atheromata also developed in the thoracic aorta and brachiocephalic arteries of ducks and geese (Anatidae), of pheasants (Phasianidae), of carnivorous birds (Accipitridae), and of the birds-of-Paradise (Paradisidae). Occasional birds of these groups also experienced convulsive seizures that could be related to the lesions.

The microscopic appearances of these atheromata were relatively uniform: loosely arranged fibrous structures with a considerable lipid content. The bases of these lesions usually extended into the media of the arteries, to involve the inner third of this coat and, occasionally, as much as its inner half.
During the same period, atherosclerosis of mammals apparently was limited to the infrahuman primates, chiefly Old World monkeys and baboons (Cercopithecidae). Occasional animals of this group developed relatively small atheromata in the abdominal aorta; these lesions were limited to the intima. In other mammals of the series the chief evidence of arterial disease was segmental necrosis and calcification of the media of the lower thoracic and abdominal aorta. These lesions corresponded more or less closely to Mönckeberg's sclerosis in man. Usually they were accompanied by thickening of the overlying intima.2

Within a year after improved diets had been introduced in the Philadelphia Zoo the appearance and location of the arteriosclerotic lesions, as seen during routine autopsies, seemed to be undergoing changes in both mammals and birds. Thus, in time, the large atheromata of the thoracic aorta and brachiocephalic arteries became rare in birds of all groups. Instead of these larger, softer lesions, birds now developed smaller, more compact atheromata, which have been located most often in the abdominal aorta and its branches. These more recent lesions usually have been limited entirely to the intima. That is, they differ from the atheromata that were seen before 1935 both in their structure and in the degree to which they penetrate the wall of the arteries. Their more common microscopic appearances are illustrated in figure 1 a, b, and c.

Since 1935 occasional examples of the Mönckeberg type of aortic disease still have been found in mammals. The increased frequency of arteriosclerosis in mammals of the Philadelphia Zoo, however, reflects the development of intimal thickening in larger or smaller foci, with or without lipid deposits, in the aorta and its larger branches, as well as in the arteries of the myocardium, the kidneys, the spleen, and other organs.

Atherosclerosis of the aorta and its larger branches rarely has contributed to the deaths of mammals or birds in this zoo. In recent years and chiefly since 1950, however, intimal thickening of smaller arteries, particularly of the intramural arteries of the heart, has become a relatively frequent cause of morbidity and mortality. Thus, a description of these lesions of the coronary arteries, and of the conditions under which they have developed in both mammals and birds, may be of considerably more interest than continued concern with atheromata of the aorta and its branches.

Arteriosclerosis of the coronary arteries and associated myocardial damage have developed in a wide variety of animals in the Philadelphia Zoo. The range in body types and food habits of these animals may be illustrated adequately by citing examples from the records of 9 families of mammals and 5 families of birds, which also are among those that have had considerable increases in the frequency of arteriosclerosis.1 These 14 families and their records are listed separately in table 1.

This list of mammals is headed by the Bovidae, which are ruminants—buffalo, sheep, goats, and antelopes. The second family, the Macropodidae, are herbivorous marsupials—kangaroos, wallabys, and wallaroos. The Capromyidae, third, are large fur-bearing rodents, and omnivorous, according to the feeding system of this zoo.

Three families of primates follow in the list. The Cebidae are New World monkeys and include squirrel, cebus, spider, and woolly monkeys. The Cercopithecidae are Old World animals—monkeys and baboons. The Pongidae are anthropoid apes, represented here by gibbons, chimpanzees and orangutans.

Three families of carnivores complete the list of mammals. The Mustelidae include mink, skunks, otters, and badgers; the Canidae, wolves, foxes, and coyotes; and the Felidae, tigers, lions, leopards, and other cats.

Birds are represented in this series by ducks, geese, and swans—Anatidae; by pheasants and quail—Phasianidae; by parrots and macaws—Psittacidae; by cranes—Gruidae; and by hawks and related species—Accipitridae.
Figure 1

a and b, atheromata of the thoracic aorta of geese (Anatidae) × 200 and × 100 respectively; c, atheromata of the abdominal aorta of an Impeyan pheasant (Phasianidae) × 100; d, cross section through the proximal segment of the left coronary artery of a European badger (Mustelidae) × 50; e, cross section through a proximal branch of the left coronary at a focus of thrombosis and recanalization: dourocouli (Cebidae) × 100. (a through e, Verhoeff's elastic tissue stain.)
Birds of the last-named group are carnivores. All the others have received a diet designed for omnivorous animals.

Table 1 presents a summary of observations of 96 mammals and 84 birds of the 14 groups. These examples of coronary disease were collected between January 1, 1945, and December 31, 1958. Each animal of this series was found to have developed intimal thickenings of the coronary arteries that at least equaled the thickness of the medial coat of the vessels. Lesions of this dimension were the requirement for inclusion in the table.

The first 2 columns of the table show the relative frequency with which the deep and the superficial arteries of the myocardium were involved. Disease of the surface arteries always was accompanied by disease of the intramural vessels. The reverse obviously has not been so.

The columns under "myocardium" show the frequency of fibrosis and of infarction in this series. A majority of examples of infarction were combined with fibrosis of the myocardium.

It also seemed of interest to show in this table the relative frequency of atherosclerosis of the aorta, and of intimal thickening of the arteries of the spleen in this series of mammals and birds. The last 2 columns list the animals by sex.

About 10 per cent of the mammals and birds of this series had developed atheromata of the larger coronary arteries. These lesions, whether they developed in mammals or in birds, corresponded closely in both macroscopic and microscopic appearances to lesions of the same sites in man (fig. 1d and 1e). The occurrence of this type of coronary lesion does not appear to have been related to the size of the animal or to the type of diet. Atheromata have been found in the larger coronary arteries of animals that ranged from large bovines to small monkeys and carnivores, and in representatives of 4 of the 5 families of birds. The ages of animals in which these lesions developed also ranged widely, but in a majority of the cases they appeared in the older animals. Sex apparently was not directly related to their development.
**Figure 2**

Intimal thickening of the intramural branches of the coronary arteries in the walls of the left ventricle: a, from a crowned crane (Gruidae); b, from a kalege pheasant (Phasianidae); c, from a timber wolf (Canidae); and d, from a snow leopard (Felidae). The lesions seen in c and d were associated with infarction; necrotic muscle lies adjacent to the occluded artery in d. All × 200. (a and b, Verhoeff's stain, c and d, hematoxylin and eosin.)
In this series of animals the atheromata of the coronaries have been accompanied by more or less intimal thickening of the smaller intramural branches of the arteries, and also in some instances by scars in the myocardium. The values in table 1, however, show that neither fibrosis nor infarction was dependent upon the occurrence of atheromata in the larger arteries. In fact, none of the examples of infarction in this series was associated with atheromata in the larger arteries. Instead, intimal disease of the deeper intramural arteries apparently has been the only cause of myocardial infarction or fibrosis.

Figures 2 and 3a and 3b illustrate some of the variations in the microscopic appearances of the lesions of the smaller vessels, which incidentally were essentially the same whether in mammals or in birds. Usually they seemed to have developed as relatively localized changes, often involving short segments of the arteries, and ranging from densely cellular to almost completely acellular homogeneous lesions.

Differential stains suggested that the more cellular of these lesions were composed of fibrous tissue. Less cellular ones contained finely divided elastic fibers or fibers that corresponded, in their staining qualities, to elastic fibers. The more homogeneous lesions lacked fibers and nuclei and perhaps are best described as "hyalinized," although occasional ones apparently contained lipid droplets.

The development of these lesions of the deeper coronary arteries accounts for both fibrosis and infarction of the myocardium. Sections of the hearts of approximately half of the mammals and birds that have been included in the table contain one or more foci of fibrosis.

Infarcts have been found in about 25 per cent of the series. Invariably, infarcts in the hearts of these animals have been multiple small lesions from 1 to 10 mm. in their greatest diameters and, with few exceptions, visible macroscopically only in the walls of the left ventricle.

Coronary disease in this series was accompanied by atherosclerosis of the aorta in about 25 per cent of the mammals and in about 50 per cent of the birds. Intimal disease of the splenic arteries was found in about half of both mammals and birds. These records are given simply to illustrate again that arteriosclerosis of the coronary arteries develops in a wide variety of animals independently of the disease in other sites.

Discussion

Improved diets for mammals and birds in the Philadelphia Zoological Garden have been associated with changes in the character and location of arteriosclerotic lesions. The first changes were noted within 5 years after new diets were introduced. Thus, they may have been related to improvement in nutrition.

More recently, beginning at least 10 years after the improved diets started, lesions of the coronary arteries have become increasingly frequent and severe. This later change has been associated with increasing population densities in the zoo, and increased breeding activity. Present evidence suggests that the increase has been a response to psychologic disturbances in the exhibition groups.

The validity of this hypothesis must depend upon the results of experimental studies that are now under way. Meanwhile, it may be noted that intimal thickening and occlusions of the distal segments of the coronary arteries have been known for many years as a common disease of man. Moreover, narrowing and occlusion at this level of the coronary system are well recognized causes of myocardial damage in man. Recently the lesion also has been described in dogs, cats, baboons, and in at least 1 "ape"—apparently a chimpanzee. The present material demonstrates that the lesion may develop in a great variety of mammals and birds, and in all of them may lead to infarction and fibrosis of the myocardium.

Current discussions of coronary disease of man, however, generally have been concerned with atherosclerosis of the proximal segments of the arteries. Intimal thickening and occlusion of the smaller, intramural branches of these arteries often seem to be considered
Figure 3

Intimal thickening in the intramural branches of the coronary arteries in the walls of the left ventricle: a and b, male orang-utan (Pongidae) young adult, 18 years of age, captive-born in the Philadelphia Zoo. Note in a the perivascular fibrosis and occlusion of a lateral branch of the artery. In b atrophy and fibrosis of the myocardium are associated with occlusion of 2 smaller arteries; c, d, and e from man, postoperative deaths; c and e men, 70 and 68. d women 67 years of age. All × 100. (a through e. Verhoeff’s stain.)
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a separate entity, or else are ignored as being of little or no significance.

At this time, one opinion attributes this lesion of the smaller vessels to inflammatory processes, either of the myocardium, as in rheumatic fever, or of more generalized disturbances, as in sensitivity reactions and infections.9 21, 22 Others have suggested, however, that this lesion is an integral part of the whole process of coronary arteriosclerosis or atherosclerosis.23, 24

According to this second view, intimal thickening may be initiated in foci at any and all levels of the coronary arteries. The mechanism by which this is accomplished is unknown, but it may involve fibrosis, elastosis, endotheliosis, thrombosis, etc.20, 23–25 The proximal segments of these vessels, by virtue of both size and anastomoses,11 provide space and time needed for the development of the more spectacular lesion—atheroma with hemorrhage and thrombosis. More distal branches of these arteries undergo occlusion and disappear into the scar tissue that replaces the myocardium, before more conspicuous changes may take place.

Observations on lesions of the coronary arteries of both mammals and birds in the Philadelphia Zoological Garden support this latter opinion. Moreover, concurrent observations on coronary arteries of man and a series of domesticated animals are in keeping with this view (fig. 3c, d, and e). Certainly we have found nothing to suggest that coronary disease in these zoo animals can be related to infectious disease or to sensitization. If these conditions (infections and sensitivity) had contributed to arterial disease in these populations some of the earlier stages should have been seen, for the animals listed here are a small fraction of the number autopsied since 1945. Still, neither thrombosis nor inflammatory reactions in or about arteries have been found. Furthermore, coronary disease was unknown in these animals for about a decade after improved nutrition had virtually eliminated infectious disease as a cause of morbidity and mortality. This interval suggests, as well, that lesions of the coronary arteries have not been related to diets. Nevertheless, improved diets apparently have contributed to the development of these lesions through increased vigor and a more intense response of the animals to population densities.1 4

Summary

Improved nutrition for mammals and birds at the Philadelphia Zoological Garden has been followed by continued increases in the frequency of arteriosclerosis and by changes in the character and location of the lesions. During the first decade after diets were improved the large atheromata of the proximal aorta and brachiocephalic arteries of birds were replaced by smaller, more compact lesions, usually of the abdominal aorta. At the same time many species of mammals developed atheromata of the aorta, whereas earlier these lesions had been found chiefly in baboons and monkeys (Cercopithecidae).

During the second decade of adequate nutrition, and especially since 1950, arteriosclerosis of the coronary arteries has become relatively common in both mammals and birds. Usually this lesion has developed in the distal, intramural segments of the coronary arteries, as intimal thickening and occlusion. Most frequently it has been associated with myocardial fibrosis, but it also has led to myocardial infarction and sudden death in both mammals and birds. Present evidence suggests that this lesion reflects a response of adequately nourished animals to population densities.

Summario in Interlingua

Le meliorate alimentation del mammales e aves al jardin zoologique de Philadelphia ha essite sequite per un continue augmento del frequenti de arteriosclerosis e per alterationes in le character e in le sito del lesiones. Durante le prime decennio post le melioration del dietas, le grande atheromas del aorta proximal e del arterias brachiocephalic in le aves esseva remplaciate per plus miere e plus compacte lesiones, usualmente in le aorta abdominal. Simultaneemente multe species de mammales disveloppava atheromas del aorta, durante que previamente iste lesiones haveva occurrirte principalmente in babuinos e simias longiegudate (Cercopithecidas).
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References

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