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CALCIFICATION OF THE MEDIA OF THE HUMAN AORTA AND ITS RELATION TO INTIMAL ARTERIOSCLEROSIS, AGEING AND DISEASE *

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In recent years the emphasis in the etiology of atheromatosis and arteriosclerosis has been placed on the intimal changes. This has been based mainly on the fact that numerous experiments in animals, particularly in the rabbit, have demonstrated the production of atheromatous lesions following the administration of large amounts of lipoid substances such as cholesterol. However, there is also evidence that other factors play an important rôle in the genesis of arteriosclerosis and that the lipoids may be secondarily deposited in the intima. It has not been possible to show, except in rare instances, that there exists in human beings an elevated lipoid content of the serum which might account for the presence of atheromatous lesions in the intima of the aorta. The experiments of Anitschkow [1] and also of Harrison [2] have demonstrated that the presence of medial defects in the rabbit's aorta will influence the deposition of intimal lipoids following cholesterol feeding. There are also certain histological differences between the character of the intimal lesions in experimental animals and in man, although these differences may be considered of relatively minor importance.

The association between the elastic properties of arteries and the development of the intimal lesions of arteriosclerosis has been a point of interest for many years. It appears to have been first stressed by Polotebnow,[3] in 1868, who observed that a sclerotic artery could be stretched only one-fourth as much as a normal one. Kaufmann [4] found that the size of the aorta depended on age and body build, the enlargement of the aorta with age being due to a loss of elasticity. More recently the experiments of Wilens [5] showed that with advancing age there is a progressive loss of elasticity which varies in degree in differ-

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ent areas but proceeds at a constant rate for a given area and affects all persons to approximately the same degree. He has further observed that the development of intimal plaques is not directly related to this loss of elasticity, for a greatly thickened intima can restrict the elasticity of the media only to a relatively slight degree. Loss of elasticity of the media proceeds as rapidly in those subjects who develop slight intimal atheromas as in those who exhibit profound changes. The earliest and largest intimal accumulations of lipoids appear in those areas which are subject to the earliest and most marked loss of elasticity.

The theory that loss of elasticity and weakening of the vessel wall are the primary factors that precipitate all subsequent intimal lesions is an old one. It was propounded by Thoma and Kaefer,[6] in 1889, and has been supported by Faber,[7] Klotz [8] and, more recently, by Wells.[9] The latter stated that the changes in the physicochemical properties of arteries support the view that arteriosclerosis depends primarily on the reduction in elasticity of the media, and that the subsequent changes seem to be due to the yielding of the media. To support this theory numerous lesions have been described as occurring in the media; among these can be listed swelling, fragmentation, diminution in volume, fatty infiltration, and calcification of elastic fibers. The problem is apparently complicated by the belief that there is considerable diversity in the vascular manifestations, depending upon the site and type of vessels involved. Thus, Winternitz, Thomas and LeCompte [10] have recently restated a generally accepted concept that "the muscular arteries, for example, are very prone to undergo medial change ending in calcification, without necessarily involving either the intimal or adventitial coats, whereas this type of change in the larger elastic arteries is rare."

However, calcification of the media of the aorta has been observed by Klotz,[8] Ribbert,[11] Ravault,[12] Farkas and Fasal,[13] as well as by Faber.[7] Of these investigators, only Faber believed that there was a relationship between calcification of the media of the aorta and the production of intimal arteriosclerosis; the others could find no direct parallelism between the amount of calcium deposited in the media and arteriosclerosis of the intima. In all these investigations it was recognized that calcification of the media rarely occurred in young persons, but no organized attempt was made to correlate this change with age. It would thus appear that while calcification of the media of the human aorta has been recognized, little is known of its significance. Faber, as well as Farkas and Fasal, attempted to study calcification of the media of the aorta and its relation to ageing and disease, but they were unable to reach any definite conclusion from the limited number of cases studied.

In the course of study of human aortas from routine autopsies, we noted the frequent occurrence of a blue-staining, finely granular material in the media of the aorta which was apparently similar in character to that described by Björling [14] as mucoid degeneration. However, subsequent analysis by micro-incineration showed this material to be composed largely of calcium, and on the basis of this observation it was decided to investigate the relationship of calcification of the media of the aorta to intimal arteriosclerosis, ageing and disease.

Materials and Methods

A preliminary experiment was carried out in an attempt to determine whether the dark blue granular material in the media of aortas stained with alkaline Delafield's hematoxylin was calcium. Sections were made from 10 aortas imbedded in paraffin in the usual manner. These were mounted on slides for study by micro-incineration, and control slides were stained with alkaline Delafield's hematoxylin and eosin. The technic of micro-incineration was the same as that developed by Scott,[15] and also employed by one of us (Lansing).[16] Examination of these incinerated preparations by darkfield microscopy revealed areas containing large amounts of white ash which corresponded in general to the areas of dark blue granular material in the hematoxylin and eosin preparations. This white ash has been identified clearly as calcium by Lansing and Scott.[17] That the blue granular material represents calcium is also indicated by the observation that this staining reaction can be prevented by decalcification in dilute nitric acid (Figs. 7 and 8).

In a second experiment 50 specimens of aortas of various ages taken from the proximal part of the arch, and showing varying degrees of blue-granular material in the media, were examined also by the technic of micro-incineration. It was noted that the areas showing the greatest concentration of calcium in the micro-incinerated preparations corresponded to the sites of deposition of the blue-granular substances in the hematoxylin and eosin preparation. There were, however, other areas in the micro-incinerated preparation in which there was more finely dispersed calcium, and these could not be identified in the hematoxylin and eosin preparations. This indicates the greater sensitivity of the method of micro-incineration for the demonstration of calcium.

With the previous two experiments as a basis, a statistical analysis was carried out for the purpose of determining the relationship of age and disease to calcification of the media. For this purpose we used specimens from 582 aortas, removed from the proximal portion of the arch and stained with alkaline Delafield's hematoxylin and eosin. This

number included the 60 specimens used in the two preliminary experiments. It should be stated that in those cases in which the hematoxylin and eosin stain failed to reveal evidence of calcification of the media, either micro-incinerated preparations were made or the slides were restained. This was done because it was noted that when the hematoxylin became old, or had lost some of its alkalinity, it failed to reveal the presence of the blue-granular material in the media. Also, in some cases in which autopsy had been performed 18 or more hours after death, even fresh hematoxylin preparations failed to show evidence of calcium. In all of these cases, however, the presence of calcium in the media could be demonstrated in micro-incinerated preparations.

The sections were arbitrarily graded as negative, 1 plus, 2 plus, or 3 plus (0, +, ++, or +++) in accordance with the degree of calcification of the media; photomicrographs illustrating these grades, both by micro-incineration and by hematoxylin and eosin staining, are shown in Figures 1 to 9.

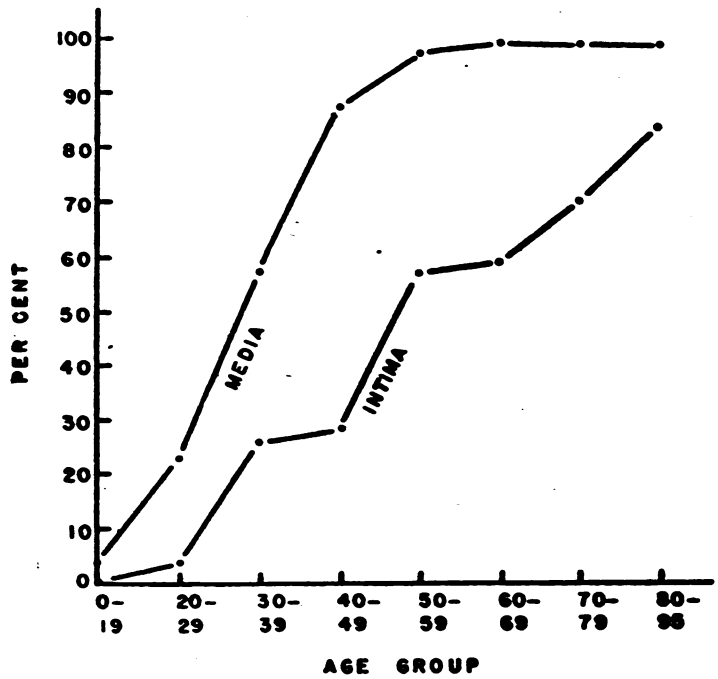
In a final experiment various levels through the whole length of 6 aortas were studied in order to determine whether or not the intensity of calcification of the media is uniform throughout the length of the aorta, as well as to determine if there is any correlation between the intensity of calcification of the media and the site of formation of intimal plaques.

Results

In 60 aortas we carefully compared the site of deposition of the blue-granular material in hematoxylin and eosin sections with the areas of calcification in corresponding micro-incinerated preparations. In those showing a slight degree of calcification of the media, it could be seen that the calcium was deposited between the muscle fibers; this distribution would correspond to the areas usually occupied by elastic fibers. With progressive increase in the amount of calcium, the areas involved became more extensive, and in pronounced cases the cellular structure of the media became entirely obliterated. In the latter instances it was possible to conclude that both muscle and elastic fibers were heavily infiltrated with calcium. This can be seen in Figures 7 and 9. Occasionally in senile specimens discrete concretions of calcium were observed in addition to the general 3 plus calcification of the media. However, such condensations occurred relatively infrequently.

Specimens taken through various areas of 6 whole aortas, from subjects ranging in age between 35 and 83 years, were studied by micro-

incineration. The areas studied included the proximal part of the arch free of intimal plaques, the abdominal aorta free of intimal plaques, and the abdominal aorta including intimal plaques. In general, the intensity of calcification of the media was greater in the abdominal than in the thoracic portion of aortas taken from subjects 35, 55 and 63 years old. In the remaining 3 subjects, 70, 76 and 83 years old, the concentration of calcium in the media was so great throughout the aorta that it was not possible to estimate quantitative differences between the thoracic and abdominal portions. In the three younger cases it could be determined also that the concentration of calcium in the abdominal portion of the aorta was greater in the area immediately under an intimal plaque than where there was no evidence of intimal



Text-Fig. 1. The age-incidence of medial calcification and of intimal sclerosis, based on 540 aortas.

proliferation, while in the three older specimens the concentration of calcium throughout the media was so great that such a difference was no longer discernible.

The age-incidence of calcification of the media obtained from the examination of 540 aortas of various ages is shown graphically in Text-Figure 1. Prior to 20 years of age medial calcification occurred in only 4 per cent of the cases; between 20 and 30 years this increased

to 58 per cent; between 40 and 50 years 98 per cent showed this change, and after 50 years of age calcification of the media was present in all cases exclusive of certain instances in which there were other diseases of the media. It should be noted that these figures do not take into account the intensity of calcification of the media; they present only the incidence. The data in Table I show that the intensity of calcification of the media as well as the frequency of its occurrence increases with age. Thus, calculations from the data in this table show that prior to 50 years of age 56 per cent of the cases showed no medial calcification, 32 per cent showed slight (+) calcification, and only 12 per cent showed marked calcification (++ and +++). After 50

TABLE I

Age Distribution and Correlation of Calcification of the Media and Intimal Proliferation in the Human Aorta*

Age groups	No intimal lesions				With intimal plaques				Calcified plaques			
	0*	1	2	3	0*	1	2	3	0*	1	2	3
0–19	47	2										
20–29	20	4	1			1						
30–39	16	12				2	4			3		1
40–49	5	20	7			2	3	1		5	2	
50–59		23	11	3	1†	14	11	3	1	10	6	5
60–69		32	15	7		14	13	6		21	20	7
70–79		20	9	3		8	10	4		22	22	14
80–95		4	2	1		1	3	1		13	11	11

* Medial changes are graded 0, 1, 2, and 3 in accordance with the degree of calcium deposition.

† Connective tissue penetration of the media.

years of age there were no cases free of this change, while 48 per cent had slight calcification (+) and 52 per cent showed a marked deposition of calcium in the media (++ and +++). The influence of age on the intensity of medial calcification is shown also in the first two columns of Table II, where it can be seen that there is in both sexes a progressive increase in the mean intensity of calcification with increasing age, at least up to 59 years. Apparently the increase with age is less definite after 60 years.

In Table II we have analyzed statistically the intensity of medial calcification of the aorta on the basis of sex and of various diseases of which there were sufficient cases to allow for the determination of significant differences. There is no significant difference between the intensity of calcification of the media in corresponding decades in the two sexes. The cases in which death was due to a rapidly fatal accident or to an acute infectious disease were used as controls since these would not be expected to have an influence on calcification of the

TABLE II

The Influence of Sex and Disease on the Graded Incidence of Deposition of Calcium in the Media of the Aorta as Correlated with Age

Classification	Age groups							
	0–19	20–29	30–39	40–49	50–59	60–69	70–79	Over 80
Females (all cases)	0.0 ± 0.0	0.4 ± 0.2	0.8 ± 0.2	1.2 ± 0.1	1.7 ± 0.3	1.6 ± 0.1	1.7 ± 0.1	1.8 ± 0.2
Males (all cases)	0.1 ± 0.1	0.1 ± 0.1	0.6 ± 0.2	1.2 ± 0.1	1.5 ± 0.1	1.7 ± 0.1	1.8 ± 0.1	2.1 ± 0.2
Accident or acute disease	0.0 ± 0.0	.....	.....	1.0 ± 0.2	1.2 ± 0.1	1.6 ± 0.1	2.0 ± 0.2	1.9 ± 0.3
Tuberculosis	0.1 ± 0.1	0.3 ± 0.2	0.6 ± 0.1	1.2 ± 0.3	1.4 ± 0.2	1.6 ± 0.2	1.9 ± 0.2	.....
Cancer	.....	.....	1.0 ± 0.6	1.1 ± 0.2	1.8 ± 0.1	1.8 ± 0.1	1.3 ± 0.1	2.3 ± 0.3
Nephrosclerosis and/or hypertension	.....	.....	2.8 (4)	1.6 ± 0.2	1.8 ± 0.3	1.5 ± 0.1	1.5 ± 0.2	1.8 ± 0.3
Coronary thrombosis, cerebral thrombosis and hemorrhage	.....	.....	.....	1.3 (4)	1.6 ± 0.2	1.7 ± 0.2	1.9 ± 0.2	2.1 ± 0.4
Syphilitic aortitis	.....	.....	0.0 (3)	0.0 ± 0.0	0.2 ± 0.1	0.4 ± 0.2	0.1 ± 0.1	.....

Figures in parentheses represent the number of cases when they were relatively few.

media. When this group is compared with the two groups according to sex, it may be noted that the mean values for the three groups are essentially the same for corresponding age groups except for the decade between 50 and 60 years. Here the mean value for the group with accidental death is somewhat lower than those generally obtained in males and females of corresponding age; this difference, however, is of doubtful statistical significance and may be due to the effects of other diseases included in the two groups according to sex, as will be noted later. A comparison of the data from patients dying of tuberculosis with those obtained from groups with deaths from accident and acute diseases does not reveal any significant differences. There were no patients below 30 years of age dying of cancer. The mean values of the various age groups of cancer patients, when compared with the group with accidental death, were essentially similar except during the decades of 50 to 60 and 70 to 80 years; in the former decade the mean intensity of calcification in cancer patients was greater, while in the latter it was lower, than in the group with accidental death. Another group was composed of patients dying of coronary arterial thrombosis and cerebral arterial hemorrhage or thrombosis. As would be expected, there were none younger than 40 years of age in this category, and only 4 in the decade from 40 to 50 years. There were no significant differences betwen this group, the group with accidental death, or the groups according to sex.

The most striking results were obtained from a comparison of the intensity of medial calcification in subjects with syphilitic aortitis and all other groups. Of 42 specimens of syphilitic aortitis studied, 33 showed no calcification of the media and only 9 showed it to a very slight degree (+). Characteristic of these cases was partial replacement of the media by fibrous tissue; an example of this is shown in Figure 10. It may be noted here that there were two other cases with connective tissue penetration into the media which did not show the inflammatory change characteristic of syphilitic aortitis and in which no definite etiology could be established; here also no evidence of calcification of the media could be obtained. In Figure 11 an incinerated preparation of typical syphilitic aortitis is shown; despite the advanced age of this subject (72 years), the calcium content of the media is essentially comparable to that of a child (*cf.* Fig. 2).

Discussion

The term "arteriosclerosis" has generally been used to describe various changes in the arteries which lead to their loss of elasticity. In the aorta it denotes a thickening of the intima produced by a new forma-

tion of connective tissue in which there may be found small and large wandering cells laden with fat. In later stages the thickened intima becomes hyaline or necrotic about the more abundant accumulations of fat, and secondary areas of calcification may occur. Medial changes are usually held to be the result of encroachment of the intimal plaques upon the media. Although several investigators have described the frequent occurrence of calcium deposits in the media of the human aorta, this phenomenon has not received general recognition, probably due to a tendency to look for gross or relatively homogeneous concretions such as the calcium plaques which occur in the intima of the aorta and in the media of muscular arteries (Mönckeberg's sclerosis). Calcification of the media of elastic arteries has been described (see Introduction) as being essentially microscopical and has been observed only by the use of special stains or micro-incineration. However, we have observed in a few cases extreme calcification of the media leading to the formation of concretions. From a physiological point of view, the degree of calcification observed in these experiments can be expected to produce functional changes in the contractility of the aortic wall.

Our studies tend to confirm the observations of Ravault [12] that calcification of the media of the aorta is primarily associated with the elastic elements, since in the early stages calcium is deposited between muscle fibers rather than inside the muscle cell. It is of interest in this respect that in syphilitic aortitis, in which the elastic elements of the media are destroyed, the amount of calcium is markedly less, or it may be absent. In more severe changes, the calcium becomes generally deposited and involves all of the elements composing the media. However, Hass [18] has observed the formation of collagenous splints in the media, and the deposition of calcium in these structures as well as in the elastic lamellae must be considered as a possibility.

It is interesting to note that Shelling, Asher and Jackson,[19] as well as Johnson,[20] have observed calcified and degenerative arterial lesions in human beings with adenomas of the parathyroid glands, and similar changes have been described in dogs following the administration of large amounts of parathyroid hormone (Hueper,[21] Learner,[22] McJunkin, Tweedy and Breuhaus [23]). While the experimental lesions mainly involve the media, in man the intima is affected as well as the media. A more extensive lesion involving both the intima and media of elastic as well as muscular arteries has been produced in rabbits, cats, dogs and rats by the administration of large amounts of vitamin D (Kreitmair and Hintzelmann,[24] Schmidtmann,[25] Hueper,[26] Ham and Lewis,[27] Ham and Portuondo,[28] Shohl, Goldblatt and Brown,[29] and

others). Hueper[26] has observed similar results following a lengthy exposure of rats to ultraviolet irradiation. It should be noted that in these lesions there are areas of intimal proliferation in close proximity to the areas of calcification of the media.

We have seen in the present observations a step by step increase in the amount of calcium deposited in the media of the aorta with increasing age. Wilens[5] has demonstrated that in the human aorta the elasticity progressively decreases with age and is primarily dependent upon changes in the elastic elements in the media. Similarly, Saxton[30] has studied the extensibility of the rabbit aorta with respect to age and has been able to show that this vessel becomes more extensible with increasing age; it also becomes less able to return to its original circumference after stretching. However, the results of this investigator suggested that the rabbit aorta does not age as rapidly as the human aorta and is still a relatively young structure at the end of the life span of this species. Hass[18] has used purified elastic tissue preparations, and has observed that the extensibility of purified networks of elastic tissue is greatest in young specimens and usually decreases with age, although occasional aged elastic systems have the characteristic high extensibility of youthful tissue. Unfortunately, it cannot be ascertained from Hass' experiments what rôle calcium plays in this change in extensibility because the method used in the purification of elastic tissue removes the calcium from this tissue. However, it is very likely that with the infiltration into the media of large amounts of calcium with age there would be a profound diminution in both elasticity and contractility of the aorta. Significantly, the curve of reduction of elasticity with age, as demonstrated by Wilens,[5] closely parallels the curve of intensity of calcification of the media with age in the present experiments.

As stated previously, the theory that loss of elasticity and weakening of the vessel wall are the primary factors which precipitate the formation of subsequent intimal lesions has been considered for a long time. The chief supporters of this concept have been Thoma and Kaefer,[6] Faber,[7] Klotz,[8] Wells,[9] and, more recently, Wilens[5] and Hass.[18] The latter investigator believes that "the intimal changes represent a fortuitous accumulation of lipids in a collagenous splint that is deposited in response to a primary failure of medial systems to maintain integrity of function in the presence of imposed tensions." Most of the theories concerning the focal nature of early atheromatous plaques are based on the assumption that there are certain sites subject to particular stresses and strains. Some investigators such as Duguid[31] and Moschcowitz[32] believe that this leads to a localized impairment of elasticity

followed by fibrous overgrowth of the intima at that site, or to a wrinkling with formation of connective tissue interstices. Other investigators stress primarily the intimal changes. Thus Aschoff [33] described swelling of the ground substance, while Krafka [34] observed separation or actual intimal herniation. Moon [35] placed emphasis on a local anemia, while Winternitz, Thomas and LeCompte [10] described in great detail the increased intimal vascularity and hemorrhage. It is particularly the latter group of investigators who have demonstrated the rich network of small vessels which supply the arterial wall; some of these are derived from the vasa vasorum in the adventitia, while others have their origin as tiny openings in the endothelial lining of the aorta. These vessels are generally composed of a single layer of endothelial cells and depend upon the contraction of the aorta to propel their contained blood. It then becomes apparent how a change in the elasticity and contractility of the aortic wall would influence the rate of flow of blood through these small vessels. A diminution in contractility could account for a hemostasis which would result in small thrombi and hemorrhages which Winternitz, Thomas and LeCompte described as the earliest changes in the formation of atheromatous plaques; it would also account for a diminution in the amount of oxygen supplied to the intima to which Hueper [26] attributes importance in the formation of intimal plaques. Recently Wilens [36] has immobilized segments of vessels by placing silver cuffs about the femoral and carotid arteries of rabbits. This produces an adventitial thickening and fibrosis, and a thinning of the media due to atrophy of smooth muscle and condensation and fragmentation of elastic fibers. He then observed that cholesterol feeding usually leads to a selective localization of lipids in the intima of arteries at the region of the cuffs. Two observations in the present series may be in essential agreement with the interpretation that local immobility may influence the site of formation of intimal plaques. Although we have studied only 6 complete aortas, it appears that the abdominal portion undergoes a more pronounced degree of calcification of the media than does the thoracic segment; it is generally agreed that the intimal involvement in arteriosclerosis is more extensive in the abdominal than in the thoracic part of the aorta. In addition, in 3 cases we have observed that within a single aorta calcification of the media is more intense in the immediate vicinity of intimal plaques than elsewhere. The first of these two observations is contrary to a previous observation by Ravault [12] who noted a higher degree of calcification in the thoracic than in the abdominal portion of the aorta.

The assumption that in the aorta medial involvement is secondary to intimal changes is without support if the present results are valid. It

would appear more likely that intimal plaques are a result of medial injury plus, probably, other localized conditions. This contention is supported by the observations that calcification of the media precedes the formation of intimal plaques and that intimal plaques do not occur without medial calcification or some other injury to the media.

The present experiments also show that calcification of the media of the aorta is apparently not influenced by sex and by most of the diseases analyzed in our statistical data. Chronic disease *per se* apparently has no influence on this change. However, the mechanism of calcification of the media may be influenced by certain diseases. Thus, in the analysis of the 42 cases of syphilitic aortitis, 33 cases show no evidence of calcification, while in 9 cases there was only a mild degree of this change. Characteristic of syphilitic aortitis is the breakdown of the muscular and elastic elements of the media and the infiltration of scar tissue. The end-product of syphilitic aortitis, namely, the scarring of the media, results in a disruption of the normal vasa vasorum as well as a loss of contractility and elasticity. This can be expected to produce an effect upon the intima comparable to that of calcification of the media; and, indeed, thickening of the intima is a common finding in syphilitic aortitis, although the plaques may not become calcified as readily as those seen in arteriosclerosis. Also characteristic of syphilitic aortitis is the fact that plaques are more concentrated in the thoracic portion of the aorta, and therefore it would be of interest to determine if there is any difference in the degree of scarring and decalcification between the thoracic and abdominal portions of the aorta. This we hope to do in future experiments.

The data on hypertension lead to the interesting observation that calcification of the media of the aorta in the third, fourth and possibly the fifth decades is more pronounced than in the other diseases studied. It cannot be stated at present whether this is the effect of an existing hypertension or whether it is a factor in the etiology of the latter disease. However, it is conceivable that calcification of the media of the renal artery resulting in relative hemostasis could have an effect similar to that of the Goldblatt kidney. This also must await further investigation.

We have seen, therefore, how calcification of the media of the aorta may play a specific rôle in the genesis of arteriosclerosis. But the present observations also have a broader biological significance, namely, their relationship to processes of ageing in general. The present work demonstrates that the variations in frequency of calcification of the media as well as in the intensity of this phenomenon are correlated with ageing. The increase in calcium deposition in the soft tissues in human

beings is entirely in line with the fact that the calcium concentration increases with age in a variety of tissues and organs of various species. (See Lansing [16] for a review of the literature on this subject.) Calcification of the media of the aorta, in particular, has been seen in a wide variety of lower mammals and birds by Fox.[37] Barnes [38] has observed that in rats the incidence of calcification of the heart is an increasing function of the age at death. It has been suggested by Lansing [16] that this increase in calcium is a general characteristic of the ageing process. He has demonstrated that calcium increases with age not only in the vertebrates but also in invertebrates and even in plants. It is interesting to note that the age-intensity curve of medial calcification of the aorta (Table II) closely parallels the age-calcium concentration curve which he obtained on the water plant, Elodea. It appears, therefore, that we are dealing with a fundamental process in the biology of ageing, which in the specific instance of the aorta may result in secondary intimal changes producing the phenomenon of arteriosclerosis.

Summary

The frequency of occurrence and the influence of age, sex and disease on calcification of the media of the human aorta were studied by means of sections prepared by hematoxylin and eosin staining and by micro-incineration. The results showed that calcification of the media precedes the formation of intimal plaques; that medial calcification occurs more frequently than do intimal plaques; that intimal plaques do not occur without calcification of the media or other medial change such as syphilitic aortitis, or marked connective tissue infiltration of the media; and that within a single aorta medial calcification is probably more intense in the immediate vicinity of an intimal plaque than elsewhere. In a few observations it was noted also that calcification of the human aorta was more pronounced in the abdominal than in the thoracic portion of the aorta.

Calcification of the media of the aorta was shown to be primarily a function of age and was not influenced by sex and various chronic infectious diseases. However, specimens from hypertensive persons between the ages of 30 and 60 years showed considerably more medial calcification than did the "controls." Of 42 cases of syphilitic aortitis, 33 showed no medial calcification and 9 showed only slight calcification of the media.

The relationship between calcification of the media of the human aorta and the loss of elasticity and contractility with age, as well as the possible relationship of these changes to the formation of intimal plaques, is discussed.

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[*Illustrations follow*]

DESCRIPTION OF PLATES

PLATE 131

FIG. 1. Section of the aorta of a 14-year-old male stained with hematoxylin and eosin. There are no abnormal deposits in the media. × 90, thickness 4 μ.

FIG. 2. Section of the aorta of a 14-year-old male prepared by the microincineration technic. The white ash represents deposits of calcium which correspond to the location of the nuclei in hematoxylin and eosin specimen. × 90, thickness 4 μ.

FIG. 3. Section of aorta of a 40-year-old male stained with hematoxylin and eosin. A few plaque-like deposits in the media can be seen. This illustrates a 1 plus (+) deposition of calcium. × 90, thickness 4 μ.

FIG. 4. Section of aorta of a 38-year-old male prepared by the microincineration technic. The deposits of calcium in the media are larger than those seen in Figure 2. This illustrates a 1 plus (+) deposition of calcium. × 90, thickness 4 μ.

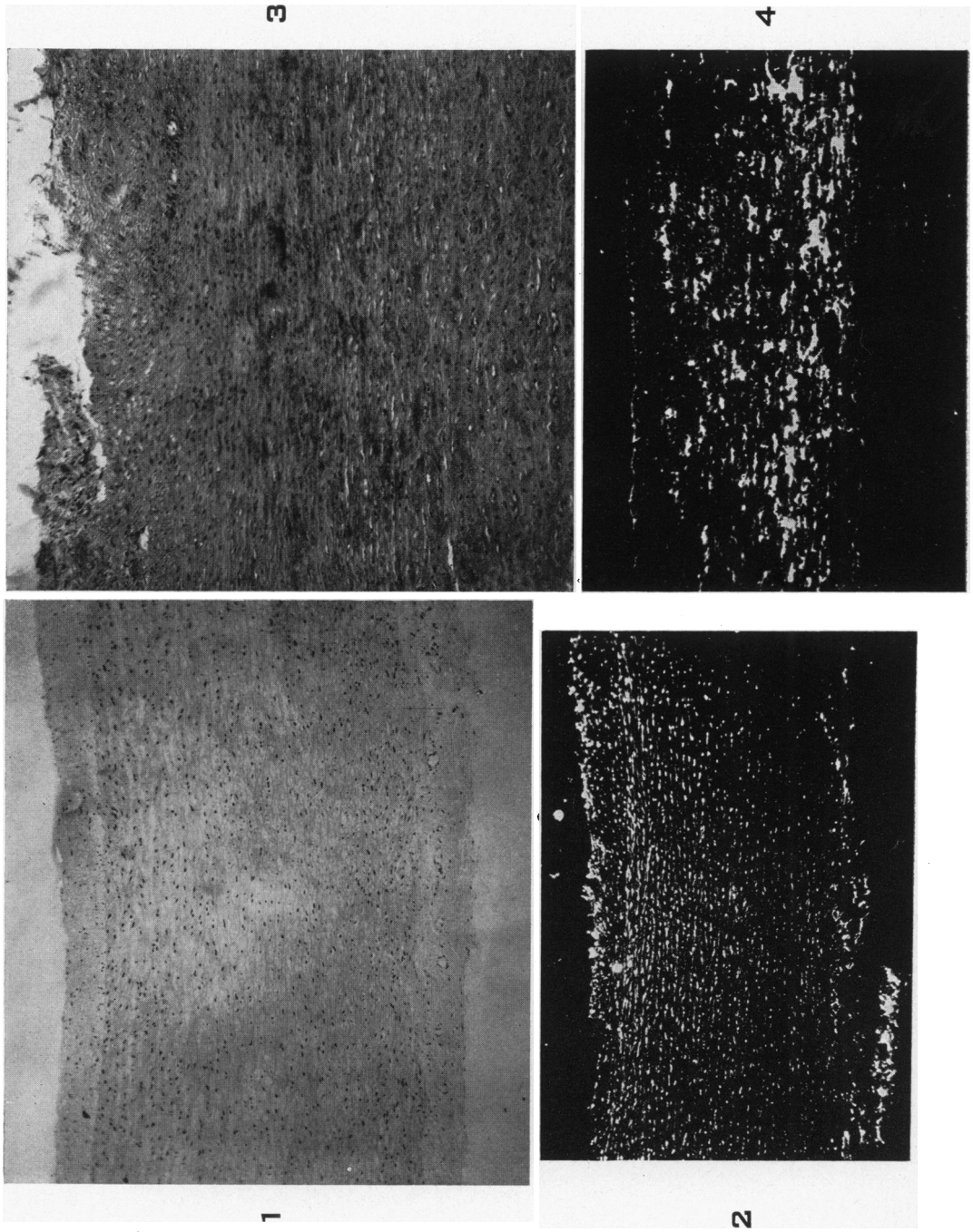

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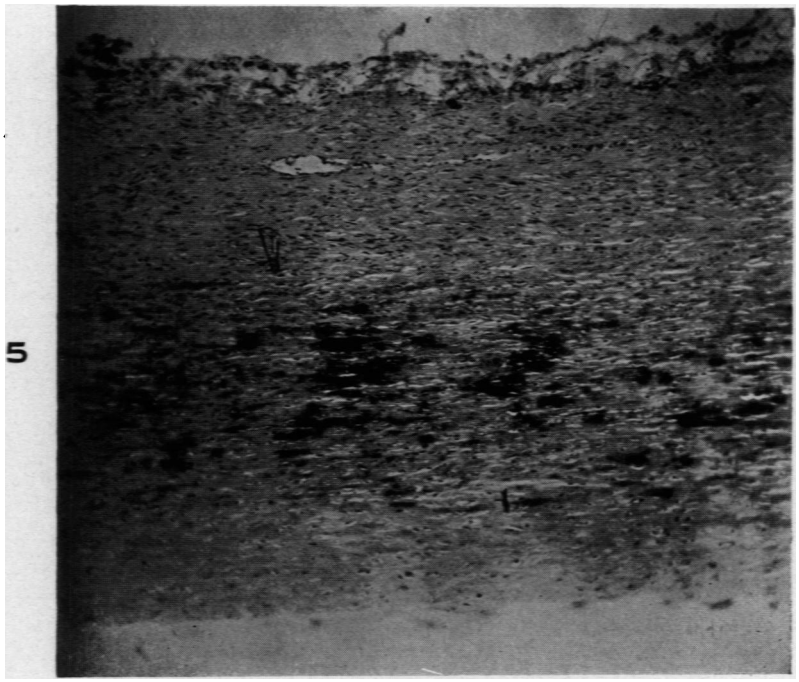
PLATE 132

FIG. 5. Section of aorta of a 53-year-old male stained with hematoxylin and eosin. There is an increase in the number and size of calcium deposits over those seen in Figure 3. This illustrates a 2 plus (+,+) deposition of calcium. × 100, thickness 4 μ.

FIG. 6. Section of aorta of a 49-year-old male prepared by the microincineration technic. The deposits of calcium are large and confluent. This illustrates a 2 plus (++) deposition of calcium. × 100, thickness 4 μ.



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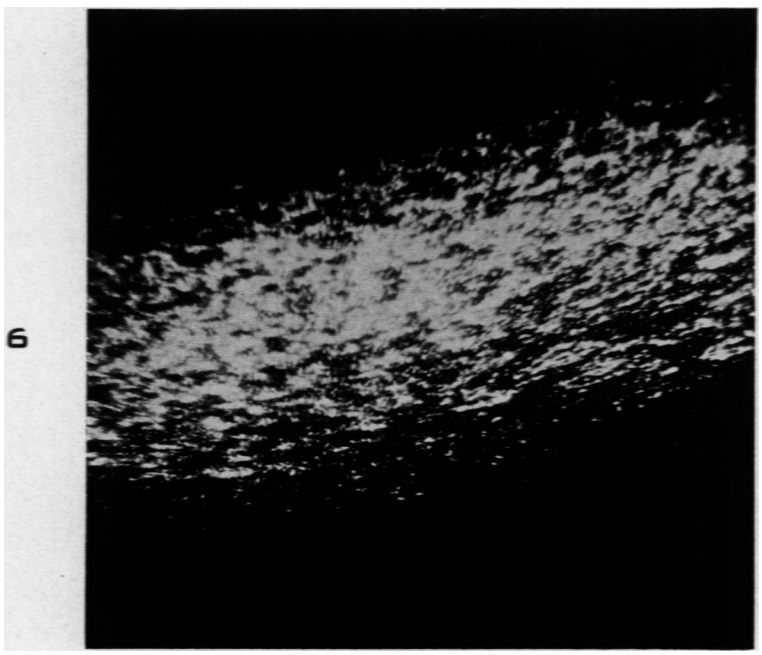

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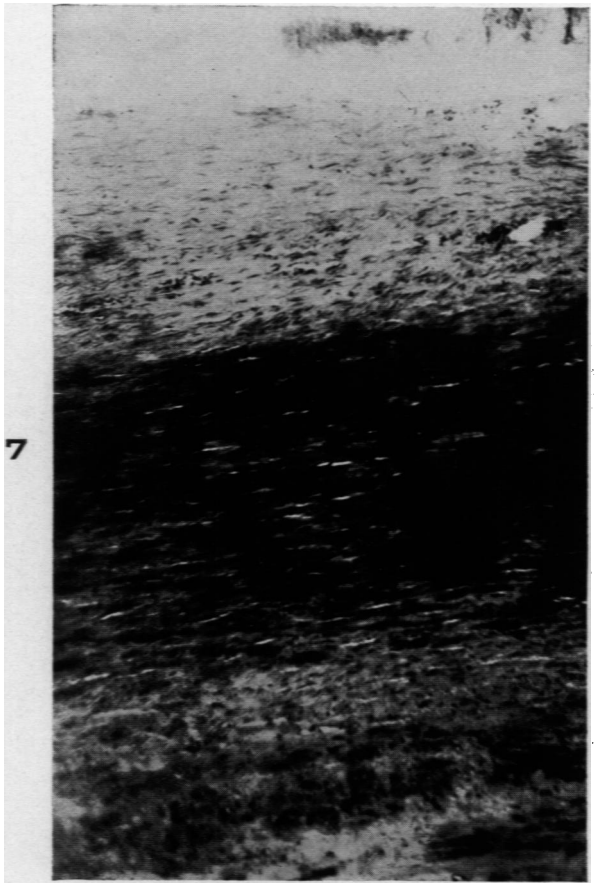
PLATE 133

FIG. 7. Section of aorta of an 80-year-old male stained with hematoxylin and eosin. A large confluent area of calcium in the media can be seen. This illustrates a 3 plus (+++) deposition of calcium. × 100, thickness 4 μ.

FIG. 8. Same specimen as that shown in Figure 7, after decalcification with dilute nitric acid. This illustrates the removal of the blue-granular material from the media by decalcification.

FIG. 9. Section of aorta of a 75-year-old male prepared by the microincineration technic. This demonstrates a marked deposition of calcium in the media, and represents a 3 plus (+++) deposition of this substance. × 100, thickness 4 μ.



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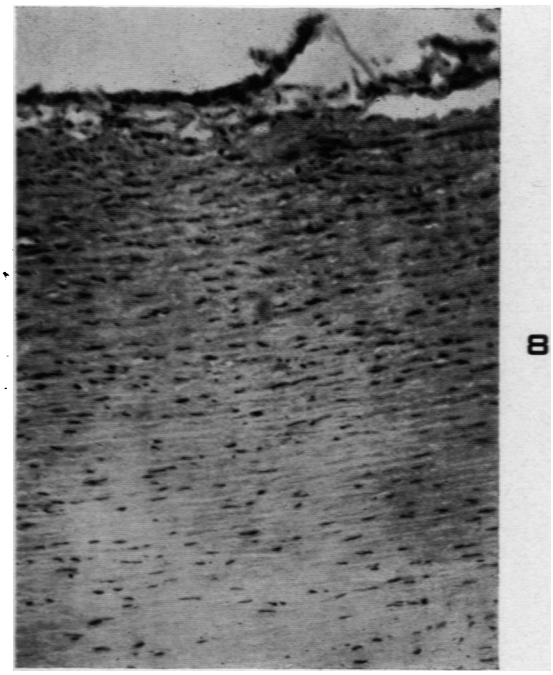

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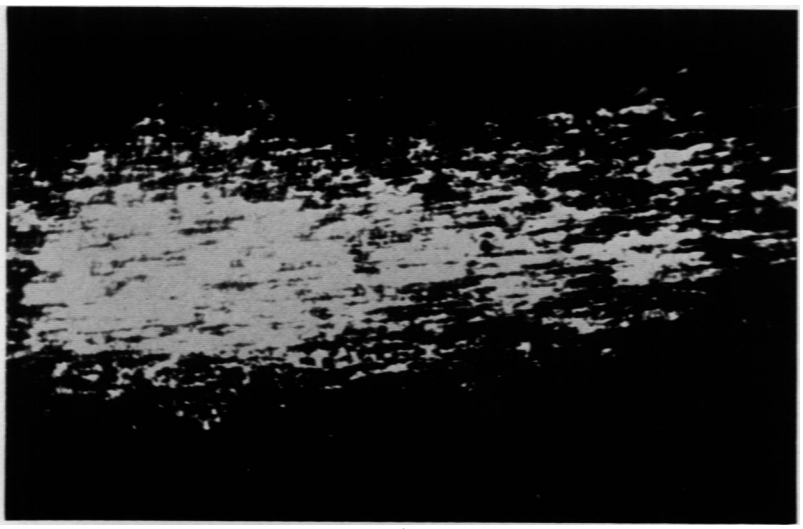

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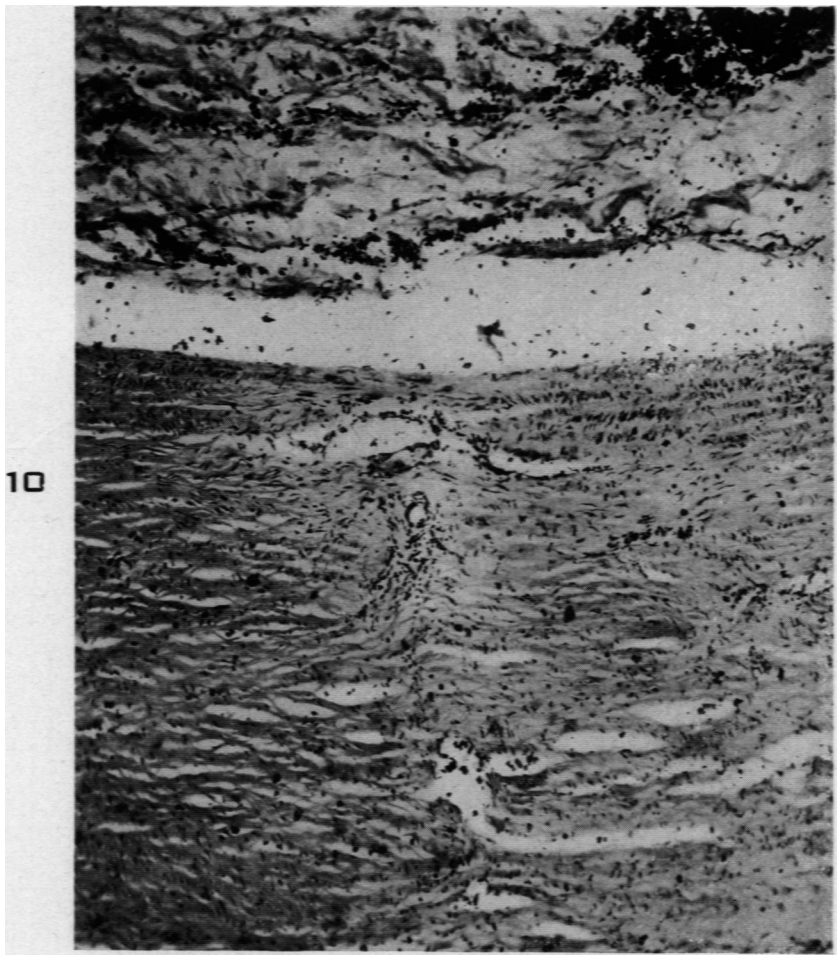
PLATE 134

FIG. 10. Section of aorta of a 72-year-old male stained with hematoxylin and eosin. There is a complete absence of calcareous patches in the media. A transverse medial scar is present. The adventitia, infiltrated with lymphocytes, is at the top of the figure. × 100, thickness 4 μ.

FIG. 11. Same specimen as that shown in Figure 10 prepared by the microincineration technic. A marked diminution in calcium content of the media is apparent. × 100, thickness 4 μ.



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