THE INTERRELATION OF ELASTIC TISSUE AND CALCIUM IN THE GENESIS OF ARTERIOSCLEROSIS *

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According to Wells,[1] "the disorganization of arterial walls with advancing age presents features which seem to indicate that this is, primarily, only the natural behavior of colloidal membranes." A study of the age changes in the "elastic colloid" might therefore be expected to yield important information on the genesis of arteriosclerosis. Yet such an approach has received relatively little attention among investigators. Instead, major effort has been put on the study of lipid metabolism and its relation to the formation of atheromatous plaques.

Extending Wells' line of reasoning, it was thought that there would be similarities between age changes in arterial walls and the processes of ageing of tissues generally; in 1944 we[2] had observed, as in other soft tissues, a progressive increase in the calcium content of the media of the aorta with increasing age. These changes precede the formation of intimal plaques and probably condition their genesis. At that time we reviewed the evidence in favor of the concept that medial changes are, in large part, responsible for the subsequent formation of intimal atheromata. Subsequently Yater, Traum, Brown, Fitzgerald, Geisler, and Wilcox[3] have presented further evidence, based on a study of human autopsy material, indicating that the deposition of lipids in the intima is secondary rather than primary. Experiments with cockerels[4] also have indicated that medial degeneration is the primary lesion in coronary arteriosclerosis.

Our recent study[5] of ageing processes in coronary arteries has demonstrated further that calcification is related to changes in elastic tissue. In these arteries there appears to be a splitting and fragmenting of the internal elastic lamella accompanied by calcification of the fragments. It would thus appear that two processes common to ageing tissues occur in arterial walls: changes in the state of certain colloidal elements as indicated by Wells,[1] and calcification of these elements.

The present report is a continuation of these studies; a comparison has been made of the changes in elastic tissue and calcium in some arteries in which atheromatous plaques are commonly found with those

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in arteries in which atheromata occur relatively infrequently. By such a comparison it may be possible to characterize further the process of elastic tissue calcification and to determine its relation to the formation of intimal plaques.

Material and Method

We have studied the hepatic, renal, and iliac arteries in approximately 140 human autopsy cases. The vessels were fixed in 10 per cent formalin in absolute alcohol and sections prepared as in previous studies.[2,5] In each instance a micro-incinerated section, one stained for elastic tissue with resorcin-fuchsin, and a third stained with hematoxylin and eosin were compared. Grading of the severity of calcification, 1 to 4 plus, was carried out as in previous investigations.[2,5]

Table I

Distribution of Cases by Age Groups *

Age group	Number of cases		
	Hepatic	Renal	Iliac
0–19 yrs.	6	9	8
20–39 yrs.	13	9	12
40–49 yrs.	17	19	20
50–59 yrs.	19	21	17
60–69 yrs.	35	38	34
70–79 yrs.	25	31	29
Over 80 yrs.	13	13	11
Total	128	140	131

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The distribution of cases is shown in Table I. A comparison of the changes in elastic tissue and calcium over the span of years shown in Table I was carried out with each of the arteries listed. In most instances it was possible to compare the three vessels in the same individual, although in occasional cases all three arteries were not available for study. A comparison was made also of the rate of calcification of the arteries presented in this and previous reports. In addition, an attempt was made to correlate the severity of these processes with some of the diseases commonly encountered in an autopsy series; namely, diabetes, hypertension, tuberculosis, and cancer.

Results

Alterations in Elastic Tissue and Calcium with Age

Hepatic Artery

During the first 2 decades of life the internal elastic lamella lay in juxtaposition to the endothelial lining of the hepatic artery. The ex-

ternal lamella consisted of one or several parallel wavy bands. The media was essentially devoid of elastic elements until the latter part of the second decade when scattered fine filaments of elastic tissue were found in the media. These appeared to arise from either lamella, but in most instances these filaments were more numerous near the internal elastic layer. Micro-incinerated preparations showed a thread-like line of calcium along the inner surface of the vessel. The external lamella showed no evidence of calcification and the media presented only a cellular distribution of calcium corresponding to the nuclear elements. The pattern was essentially the same in the succeeding 2 decades except that there was a progressively increasing number of elastic filaments in the media. The latter showed no particular tendency to calcify up to age 40 (Figs. 1 and 2).

No general thickening of the intima was noted prior to the fifth decade of life. In occasional specimens there were focal areas of duplication of the internal elastica toward the intima; the latter were thinner than the parent membrane, which could be easily identified. In such areas deeper, fine, wavy, elastic fibrils also extended into the media and broke off continuity with the internal elastica. The external elastica was composed of numerous parallel wavy fibrils from which fragments of elastic elements also extended into the media as well as into the adventitial fat. It was during the fifth decade that foci of calcification appeared in the media and duplicated the pattern of the elastic elements in this layer; most of this calcification was toward the intimal half of the media and was generally about 1 plus in intensity.

After the fifth decade the hyaline thickening of the intima and duplication of the internal elastic lamella became progressively more marked. The fragmentation and granulation of elastic elements which appeared to arise at the base of this membrane also became progressively more intense and gradually extended deeper into the media. An increasing number of fragments also extended from the external lamella. While there was diffuse hyaline thickening of the intima, plaques were encountered rarely. Calcification of the elastic elements in the media became progressively more severe with advancing age, but seldom exceeded 3 plus in intensity. The external elastica calcified only rarely, and in such exceptional cases it occurred in areas adjacent to fragments of elastic tissue. Intact elastic membranes calcified only slightly. Calcification was much more severe in elastic fibrils and fragments; the wormy and granular pattern in elastic tissue preparations was frequently duplicated in the micro-incinerated specimens (Figs. 3 and 4).

There appeared to be no change from the average degree of calcification in such diseases as hypertension, cancer, and tuberculosis. A single

case, a 65-year-old patient with diabetes, showed 4 plus calcification as compared with an average of 1.8 for that age group. Four patients with cirrhosis of the liver, whose ages ranged from 30 to 69 years, showed a higher degree of calcification by about 1 plus than the average for the corresponding age groups, and in 2 cases of primary carcinoma of the liver there was a quantitatively similar deviation. It thus appears that local obstruction to the flow of blood through the hepatic artery may intensify these age changes.

Renal Artery

Until approximately age 30, with few exceptions, the internal elastic lamella of the renal artery lay in contact with the lining endothelium as in the hepatic artery; and in the micro-incinerated preparations this was again represented by a thin, distinct, wavy line of calcium. On the other hand, the external elastic lamella showed an increase in the number of fibers relatively early, beginning in the second decade of life when the identity of the parent membrane was lost, and usually appearing in the third decade as 6 to 8 parallel, wavy, elastic bands extending well into the adventitia. Correspondingly, by the age of 20 years there was already notable calcification of the external elastic lamella, usually somewhat less than 1 plus. During the third decade also, filaments and granules of material showing the staining qualities of elastic tissue appeared along the inner side of the external elastic bands and extended into the media. Along these extensions foci of calcification began to appear; one case showed areas of 3 plus calcification at this time, but on the average calcium deposition was 1 plus (Figs. 5 and 6).

From the fourth decade on, the intima became progressively thicker due to hyalinization, until in very old specimens it occupied about one-third of the thickness of the wall. The internal elastica lay at the base of the intima, and the parent membrane easily could be identified even in very old specimens. Occasionally there were focal duplications of the internal elastic lamella into the intima; this sometimes was associated with the appearance of gaps in the continuity of the internal elastica. Calcification in such areas was proportional to the degree of elastic multiplication, but rarely exceeded 2 plus in intensity. In the fifth and sixth decades filaments and granules of material with the staining properties of elastic tissue appeared beneath the internal elastic lamella and extended into the media. However, these extensions neither penetrated as deeply nor did they appear as concentrated as those arising adjacent to the external lamella. Intimal plaques were encountered only rarely,

but when they were present there was an intensified duplication of elastic fibrils across the base of the plaque. Some increase in the intensity of granular and filamentous extensions of elastic material into the media was noted also. The latter process is similar to that previously observed in the coronary artery.

As would be expected from the pattern of elastic tissue alteration, calcification was most intense along the external lamella and extended into the media in a pattern duplicating the elastic extensions (Figs. 7 and 8). During the sixth decade approximately one-third of the cases showed many such foci of calcification of 3 plus or greater intensity, and the number of cases showing areas of intense calcification increased with succeeding decades until in the ninth and tenth only a rare case presented less than a 3 plus degree of calcification.

Beginning at about age 50, occasional renal arteries showed a different pattern from that described. Instead of fibrillar and granular extensions moving into the media from the elastic membranes, there was a diffuse arrangement of fine, elongated, elastic filaments through the media, oriented parallel to the internal and external elastic lamellae. Between these filaments there were clumps of elastic material in the form of fine filaments and granules, the quantity of the latter depending upon the age of the vessel. The pattern, therefore, resembled that seen in the aorta, and we have termed this process "aortification." However, the parallel elastic fibrils were thinner and more widely spaced than in the aorta. For the most part, the degree of calcification depended upon the concentration of elastic material between these fibrils, but even when the latter process was not marked, the intensity of calcification was rarely less than 2 plus.

Of the four major categories of disease with which a correlation of the degree of elastic tissue change and intensity of calcium deposition was attempted, hypertension, tuberculosis, and carcinoma did not appear to alter the rate or intensity of these processes except in patients over 80 years of age. In that group, cases with hypertension or carcinoma showed less calcium and a more moderate degree of elastic tissue alteration than the average for that age period. In 3 cases of hypertension the average degree of calcification was 1.2 plus less than for the total age group, while in 4 patients with carcinoma it was 0.5 plus less. There was only one patient with diabetes, age 65, who showed 3.5 plus calcification of the renal artery as compared with an average of 2.6 for the decade 60 to 69. No significance is attached to these findings because of the relatively few cases studied.

Iliac Artery

As in the hepatic and renal arteries described, the inner elastic membrane of the iliac artery lay along the inner surface of the vessel during the first decade of life; it appeared in the micro-incinerated specimen as a finely accentuated white line of calcium. Beneath this there were fairly broad elastic fibers arranged in rows parallel to the inner elastic lamella. The external elastica at first consisted of several wavy bands coursing in the same axis as those noted above, perhaps slightly thicker than those seen in the media. The incinerated specimens showed a cellular distribution of calcium until the latter part of the second decade when granules and fragments of elastic material appeared between the fibers in the media coincidentally with clump formation of calcium in the incinerated sections (Figs. 9 and 10). This deposition of elastic material occurred somewhat more intensely along the outer third of the media usually adjacent to the external lamella. Such clumping was observed only in occasional cases during the latter part of the second decade, but gradually increased in intensity and in area during the next 2 decades, so that by age 39 there was, on the average, a well developed 2 plus calcification.

From the fifth decade on, the internal elastic membrane appeared to split off fine filaments which contributed to the intima which had thickened somewhat by a process of hyalinization; filaments also penetrated into the media. During the sixth decade, in most instances the identity of the inner elastic membrane was lost in a dense mass of elastic material. The external elastic lamella also appeared to split off elastic elements which contributed to the elastic mass in the media. Consequently, calcification occurred first as two bands along the outer and inner thirds of the media, with later extension into the middle third, as the elastic material progressively accumulated in this area. This process began at about age 40, and by the sixth decade there was a well developed 3 plus calcification in most vessels, with elastic material and calcium distributed diffusely through the whole thickness of the wall (Figs. 11 and 12). There usually was less calcification along the inner 20 per cent of the wall which constituted the intima than through the remainder of the vessel, but elastic elements infiltrated the intima and some degree of calcification of this layer was present in almost every vessel after age 60. Succeeding age periods showed only a progressive intensification of this process.

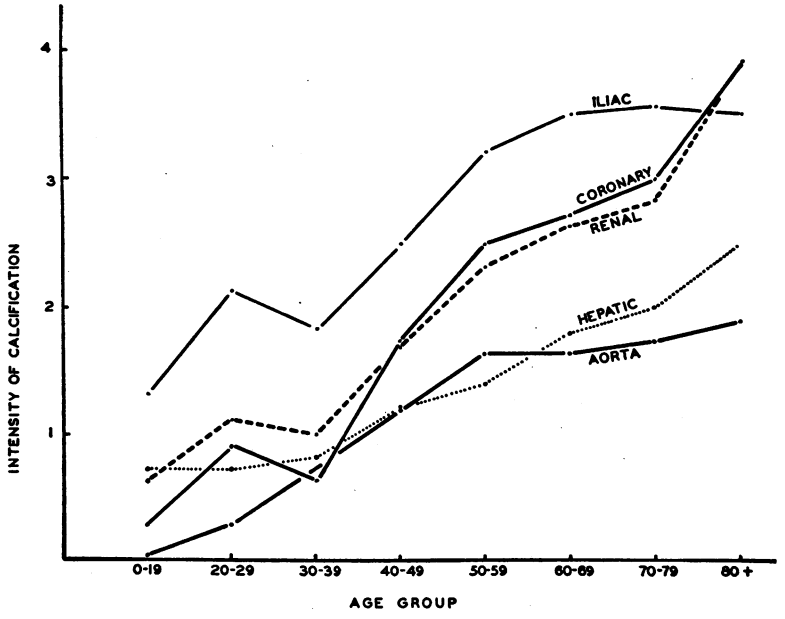
Occasional vessels gave an indication of the mechanism of Mönckeberg's sclerosis. Dense concentrations of granules and filaments of elastic material developed deep in the media of some vessels and these

areas showed intense calcification, some of which was apparent even with routine hematoxylin and eosin stains.

The iliac vessels of hypertensive patients showed no intensification of this process. In patients below age 50 with malignant disease (8 cases), the degree of calcification was less than the general average by approximately 0.5 plus, but in those over 60 (15 cases) the intensity of calcification was higher than the average for the decade 60 to 69 years by about the same average difference. There was no significant deviation from the average in a single case of diabetes and in 12 patients with tuberculosis.

COMPARISON OF THE RATE OF CALCIFICATION IN SEVERAL MAJOR ARTERIES

In Text-Figure 1 we have charted the rate of calcification in the several major arteries studied to date. It should be pointed out, however, that calcification varies from site to site in a given vessel, and the data represent an impression of the average intensity and frequency



Text-Figure 1. A comparison of the rate of calcification of several major human arteries.

of distribution of such foci. The intensity in each instance is based upon arbitrary standards established in the initial studies on the aorta. Quantitative chemical studies will be made at a later date. It is apparent from these curves that the aorta and hepatic arteries calcify relatively slowly compared with the other vessels in the chart. We have

no data on the intensity of elastic tissue fragmentation and granulation in the aorta; a comparison of these changes in the aorta and pulmonary artery are now in progress. However, in the hepatic artery, as noted earlier in this paper, these changes are not as intense as in the coronary, renal, and iliac arteries. Thus, even in relatively old persons, the degree of calcification is rarely more than 2 plus in the hepatic artery and the aorta.

The curves representing the coronary, renal, and iliac arteries have certain similarities. In each instance there is a lower degree of calcification in the fourth than in the third decade, although this difference may not be significant. Furthermore, all three vessels show a relatively rapid rise in calcium content between the fourth and seventh decades; calcification in the iliac artery then tends to level off, whereas in the coronary and renal arteries it continues to increase through succeeding age periods. The curves representing the rates of calcification of the coronary and renal arteries are almost superimposed upon each other; the differences at corresponding age periods are probably not significant.

These data do not show that in all age periods in which there is a notable average degree of calcification there are cases showing a low degree of elastic change and a low degree of calcification. Even in patients over 80 years, occasional vessels are encountered showing only a 1 plus degree of calcium deposition. Such data suggest that the maximum degree of calcification is approximated in the third or fourth decades, following which the curve tends to level off.

Discussion

It has been demonstrated in these and previous studies that the basic ageing process in the major arteries of man is primarily a calcification of the media with extension of this process into the intima and adventitia. The calcification appears to be intimately associated with certain alterations in the physical character and in the pattern of distribution of the elastic tissue, these changes in the elastic elements being an integral part of the ageing process. Thus, in the coronary artery the greater part of the elastic fragments and granules seem to be deposited in the area about the internal elastic lamella, and this is the site in which calcium deposition is most extensive[5]; in the renal artery these changes are predominant about the external lamella, and the most extensive calcification occurs in this location. The hepatic artery develops an intermediate pattern with both lamellae apparently contributing to the ageing process, although it is more prominent in

the region of the internal elastic band; furthermore, the rate and intensity are considerably diminished. In the iliac artery the ageing process produces a distribution of elastic elements in the media resembling that found in the aorta, but the process is most intense in the areas adjacent to the elastic lamellae, and in these locations calcification also is most intense. A similar process which we have termed "aortification" is observed occasionally in the renal and coronary arteries, but it is a relatively rare occurrence in these vessels, and appears to have no relation to any of the several diseases for which a statistical correlation was attempted.

It has been shown also that the intensity and rate of calcium deposition are directly proportional to the intensity and rate of these elastic tissue changes. Thus in the iliac artery there is a more intense deposition of filaments, fragments, and granules of elastic staining material than in the other arteries in corresponding age groups. The intensity and rate of deposition of elastic material and calcium are about the same in the coronary and renal arteries at corresponding ages, and less in the hepatic artery. No histologic studies of elastic tissue changes in the aorta have been reported because of the difficulty in estimating the quantity of these altered forms of elastic material in a vessel containing an abundance of elastic tissue even in very young patients. Instead, the aorta is being studied by analytical chemical technics.

No significant intensification or retardation of these processes has been noted in relation to such diseases as hypertension, diabetes, malignant tumors, or tuberculosis in the relatively few cases included in this report. It has been noted, however, that in diseases such as cirrhosis or carcinoma of the liver, which may produce obstruction of the hepatic artery, there is an intensification of the ageing processes in this vessel.

We have made the point in our introduction that these are ageing processes common to many tissues, and not distinctive of blood vessels; as such they represent manifestations of fundamental age changes in tissues. The problems connected with the ageing of blood vessels, therefore, are not basically different from those of other tissues. Lansing[6] has demonstrated that an increase in tissue calcium is a fundamental part of the ageing process in lower forms of animal life, as well as in mammals. Furthermore, the elastic tissue changes do not represent a phenomenon specifically encountered in the vascular system. Unna[7] described similar changes in the skin in aged persons, and Weidman[8] has studied the phenomenon of "elastosis senilis," which he considered

a physiologic accompaniment of cutaneous senescence. Weidman was of the opinion that it should cause no surprise if calcification is found in the cutaneous deposits of elastic tissue, but this process apparently has not been studied in the skin. Calcification is, however, an accompaniment of pseudoxanthoma elastica, a skin condition in which an increase in elastic elements occurs. Bittrolff[9] also has observed calcification in association with changes in elastic elements in the lungs similar to those which we have described in arteries. Wells[1] stated that similar processes occur in the elastic cartilage of certain joints and in this structure the changes in elastic elements and the increase in calcium are accompanied by the appearance of cholesterol.

The association of calcium deposition with changes in the elastic elements in human vessels likewise has been observed previously. Ravault[10] suggested 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. Similarly, Ku[11] has noted a parallelism between the increase in elastic tissue and the ash in several coronary arteries, and Zinkant[12] has observed a similar association in micro-incineration studies of human uterine arteries. We have pointed out previously that the loss of elasticity of the aorta parallels the rate of increase of calcium in the media.[2]

This association of elastic tissue changes and calcium deposition is not limited to human arteries. It has been described by Fox[13] in several species of animals, and is perhaps most pronounced in the rabbit, cow, and bird. In the rabbit the intimal changes seem to be due to a fibrillar thickening in which fine elastic fibrils participate and to which a small deposit of sudan-staining material and narrow strips of calcium may be added. In the muscle of the media there are clear calcium plates both near and removed from the lumen. These appear to be nearest the elastic fibers, and, when in the intima, they occupy a position just below the internal elastic lamella. Lucien and Parisot[14] maintained that rabbit arteriosclerosis is comparable to the human disease and that severe spontaneous cases are the same as experimental cases. Ophüls[15] likewise was of the opinion that severe spontaneous rabbit arteriosclerosis is quite similar to the natural human disease. Jaffé[16] emphasized the occurrence of calcification of the media in the rabbit aorta and scarcely credited the appearance of atheroma.

Farkas and Fasal[17] have noted that calcification of arterial walls becomes visible before the formation of intimal plaques. As in some of

our specimens, they encountered plaques beginning with the 20th year, but believed that this change has no causal relationship to arteriosclerosis. We also have presented evidence[2] to show that in man medial calcification precedes the formation of intimal plaques. This may be the case likewise in spontaneous arteriosclerosis in the animals commonly used in the experimental production of arteriosclerotic lesions, namely, rabbits and birds. It is likely, in many instances, that if sufficiently old animals are used, the ease with which atheromatous plaques are produced by cholesterol administration is dependent upon the state of development of the spontaneous process of elastic calcification. There is evidence to substantiate such an opinion. Anitschkow[18] and also Harrison[19] have shown that the production of medial defects in the rabbit aorta influences the deposition of intimal lipids, and Wilens[20] has immobilized segments of vessels by placing silver cuffs about the femoral and carotid arteries of rabbits, a procedure which results in adventitial thickening and fibrosis as well as a thinning of the media and condensation and fragmentation of elastic fibers. This latter process leads to a selective localization of lipids in the intima of arteries at the region of the cuffs when cholesterol is subsequently administered. It has been observed by Schmidtmann and Hüttich[21] that adrenalin injected into rabbits produces medial necrosis and facilitates the deposition of administered cholesterol. It is of pertinent interest that in unpublished studies we have not been able to demonstrate the elastic tissue changes and calcium deposition in several major arteries in the mouse, and that this species is notoriously resistant to experimental cholesterol atheromatosis.

Wells[1] recognized that the alterations that constitute arteriosclerosis depend chiefly on the colloidal properties of elastin, and that the changes in the elastic elements of arteries are in striking agreement with the well known behavior of ageing colloids in general. Among these alterations with age he noted (1) a reduced capacity to bind water, (2) a decrease in elasticity and flexibility, (3) a decrease in permeability, and finally (4) a tendency for the gel to be transformed into a granular state with a marked decrease in the colloidal properties. Bürger and Schlomka[22] looked upon the loss of water as the primary process, with a resulting decrease in the capacity of the colloids to hold soluble constituents such as cholesterol and calcium in solution.

As to the granular changes in the elastic elements which have been described here, Wells[1] attributed this also to a loss of water, but recognized the likelihood that some chemical change also had occurred

as indicated by the increased tendency to bind basic stains, often associated with a decreased affinity for the usual elastic stains. Little is known of the properties of elastin, or even of its origin. Cytologists believe that there are no specific cells that produce elastin; elastin appears to be laid down by fibroblasts of the same type as those which produce collagen. Despite this lack of knowledge, it is generally assumed that the granular material is a degeneration product of elastin. If this were so, the result in old persons would be a decrease in elastic material. Such a conclusion cannot be reached from the present studies; the amount of granular and filamentous elements far exceeds that which one would expect to be derived from the intact elastic lamellae. It must be assumed that either new elastic material is laid down to reconstitute the inner and outer lamellae, and that these then undergo degeneration, or that the granular and filamentous elements are laid down as such in progressively increasing amounts with increasing age. In favor of the former view are the recent observations of Gross[23] that normal elastic tissue contains two distinct chemical and morphologic components, namely, threads and an amorphous binding substance, which are associated to form the elastic fiber. In this connection it is interesting that there is a tendency of the threads to aggregate on the acid side and to fray into finer threads at higher pH. It would thus appear that a higher pH in the vessel wall would facilitate not only fraying and breakdown of elastic elements, but also the precipitation of calcium salts. Against this hypothesis is the fact that the identity of the parent elastic membranes is frequently lost with the marked increase in filaments and granules. It is possible, however, that in old arteries intact elastic fibers break down into their component elements as rapidly as they are formed.

Likewise our knowledge of the chemical constitution of elastic tissue is scant. It is apparently a protein which Wells[1] considered of an unusual sort in that it appears to be about half glycine and leucine. Most of the studies to date have been rather crude. Its affinity for orcein may be taken as indirect evidence that it probably contains a carbohydrate moiety, and this may be of importance in that Hass[24] has observed that in ageing of costal cartilage the polysaccharide moiety decreases as calcium is deposited. This may explain the loss of affinity for orcein of the filamentous and granular material as it progressively calcifies. Despite this meager state of our knowledge of elastic tissue, the material constituting this component of arterial walls is referred to as a chemical unit called elastin. Weidman[8] has postulated that in ageing processes in the skin, collagenic fibers be-

come impregnated with a substance which he calls pre-elacin, and in this way he accounts for the increase in elastic elements. Unna[7] showed that the elastic material in skin changes from an acidophilic to a basophilic state in the course of ageing, and he referred to this altered form as elacin, thereby indicating a chemical transformation to a new form of elastic material. Until more is known of the chemical nature of the intact elastic membrane as well as of the granular and filamentous forms, we would prefer to term the latter elements elastoid, thus indicating that they retain, in large part, the specific staining properties of elastic tissue, but have an altered physical form which has resulted in a loss of elastic efficiency.

Finally, it should be pointed out that the process of elastoid deposition and calcification in arteries is not uniform but, like the formation of atheromata, it is focal in character; neither is it uniform in any group. As we have pointed out, there are occasional young vessels showing active elastic change and calcification, and conversely, there are relatively old vessels in which these alterations are minimal. The pattern of these ageing processes appears to be determined in the third or fourth decade of life. Like Thoma and Kaefer,[25] Klotz,[26] Beitzke,[27] and Wells,[1] we believe that arteriosclerosis consists primarily of the progression of chemical and physical changes in elastic tissue which reduce the resiliency of the arterial wall and result in dilatation of the vessel. The subsequent changes, such as the formation of atheromata, seem to be secondary to these processes in the media.

These observations indicate the importance of studies of the metabolism of the arterial wall and its component parts along the lines recently reported by Briggs, Chernick, and Chaikoff[28] and by Chernick, Srere, and Chaikoff.[29] Such experiments may serve to determine whether there is an intramural origin of lipids responsible for the atheromata rather than the time-honored concept of diffusion of these substances from the plasma through the endothelial lining. Studies of this type may also yield information concerning the release of substances having an injurious effect upon the muscular component of the arterial wall as recently suggested by Szent-Györgyi.[30]

Summary

The hepatic, renal, and iliac arteries of approximately 140 human cases have been studied by means of routine hematoxylin and eosin and elastic tissue preparations, and by micro-incineration; a comparison has been made of the age changes in these vessels and those in the aorta and coronary artery as previously reported.

The present investigations reaffirm our previous conclusion that the basic age change in the major arteries of man is primarily calcification of the media. These studies show that the calcification is intimately associated with alterations in the physical character and pattern of distribution of the elastic tissue, which are described; the intensity and rate of calcium deposition is directly proportional to the intensity and rate of the elastic tissue changes.

It has been demonstrated further that the location of these processes within the wall is different in different vessels, as is also the rate of calcification. The iliac artery calcifies most rapidly, followed by the renal and coronary arteries which show an almost identical rate of calcium deposition. The aorta and hepatic artery calcify relatively slowly.

An attempt has been made to correlate certain disease processes with the intensity of the age changes. In general, the number of cases of a specific disease in a given age group is too small to warrant any conclusion, but there appears to be an intensification of the ageing processes in the hepatic artery of individuals with diseases such as cirrhosis and carcinoma of the liver which may obstruct the hepatic blood flow.

These observations yield additional information on the life history of elastic tissue. The term elastoid is suggested for the fragments and granules of elastic material which increase in the ageing process of arteries, pending further knowledge of their physical and chemical characteristics.

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DESCRIPTION OF PLATES

PLATE 141

FIG. 1. Section of the hepatic artery of a male, 19 years old, showing beginning extension into the media of elastic fragments and granules from both elastic lamellae. Resorcin-fuchsin stain. × 90.

FIG. 2. From the same case as Figure 1. Micro-incinerated section. The calcium line along the inner surface of the vessel corresponds to the inner elastic lamella. × 90.

FIG. 3. Section of the hepatic artery of a male, 65 years old. Of note are the elastic extensions into the intima from the inner elastica and the extensions into the media from both elastic layers. The external elastica has thickened also. Resorcin-fuchsin stain. × 90.

FIG. 4. From the same case as Figure 3. Micro-incinerated section, showing calcification of the inner elastica and extensions of elastic tissue into the intima. In this case there is also calcification of the external lamella. Moderate calcification of elastic extensions into the media may be seen. × 90.

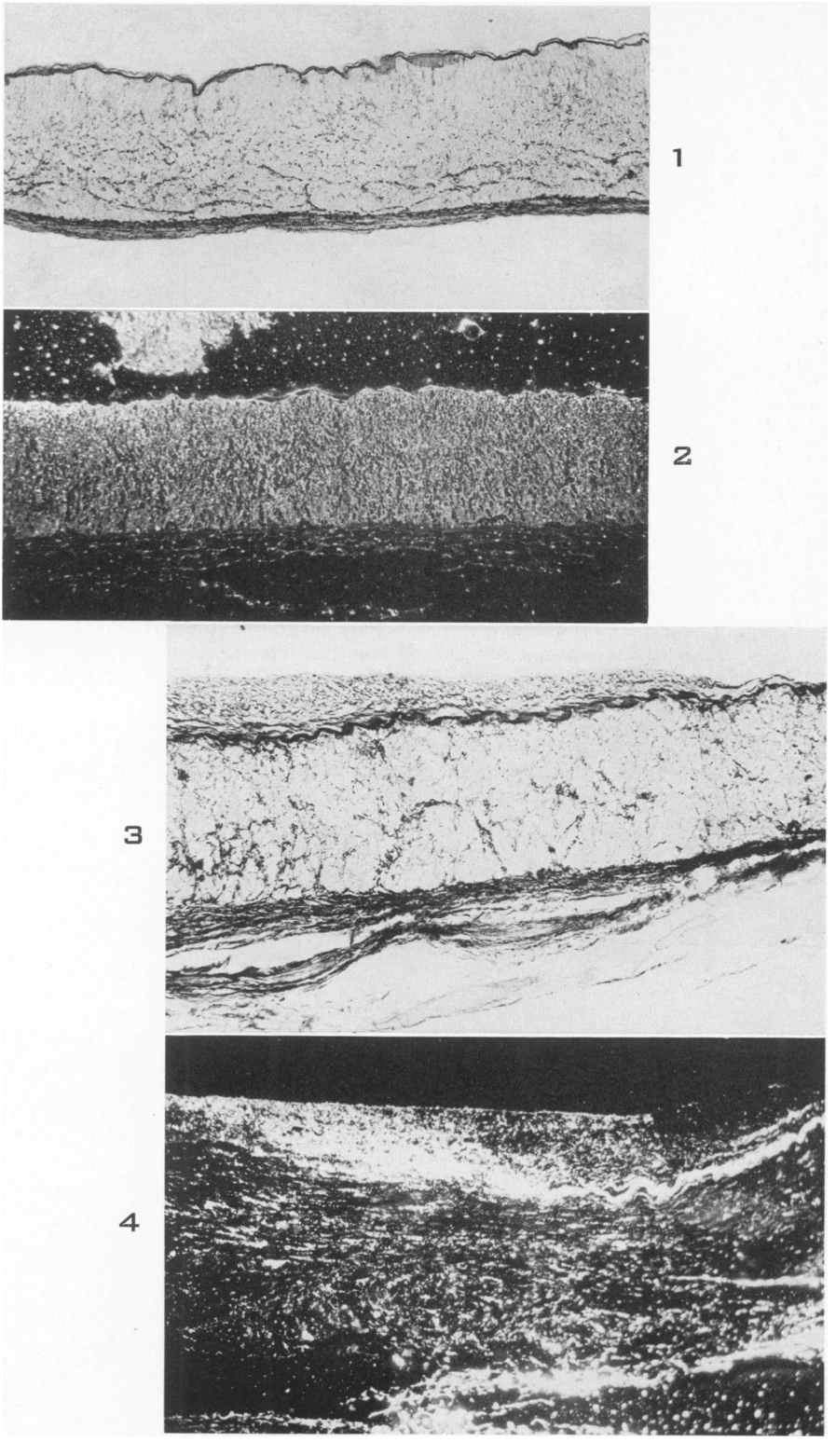

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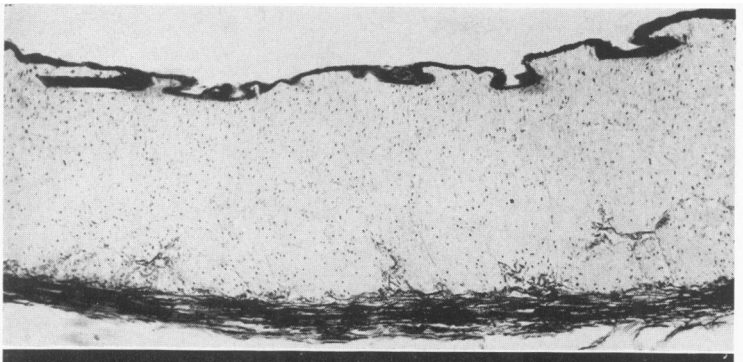
PLATE 142

FIG. 5. Section of the renal artery of a male, 19 years of age, showing a relatively thick external elastic lamella and beginning extension of elastic elements into the outer media. Resorcin-fuchsin stain. × 90.

FIG. 6. From the same case as Figure 5. Micro-incinerated section. The fine calcium line corresponds to the inner elastic lamella. × 90.

FIG. 7. Section of the renal artery of a male, 62 years old. Marked elastic proliferation of the external lamella and numerous elastic extensions into the media may be seen. The inner elastic bundle remains as a single band in most areas. Resorcin-fuchsin stain. × 90.

FIG. 8. From the same case as Figure 7. Micro-incinerated section. Of note is the intense calcification of elastic elements in the media and of the external elastic lamella. The inner elastic lamella can still be identified as a fine line of calcium. × 90.



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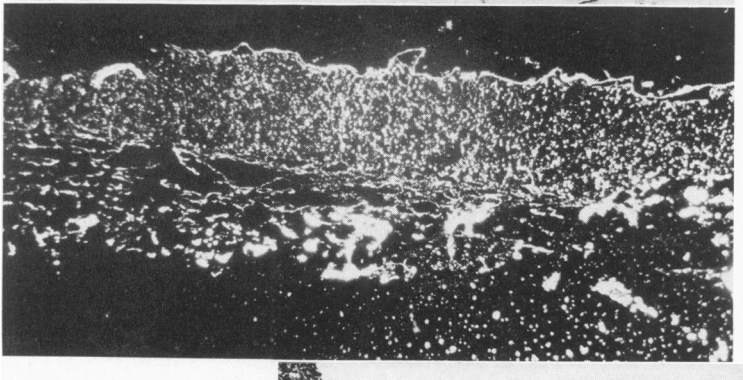

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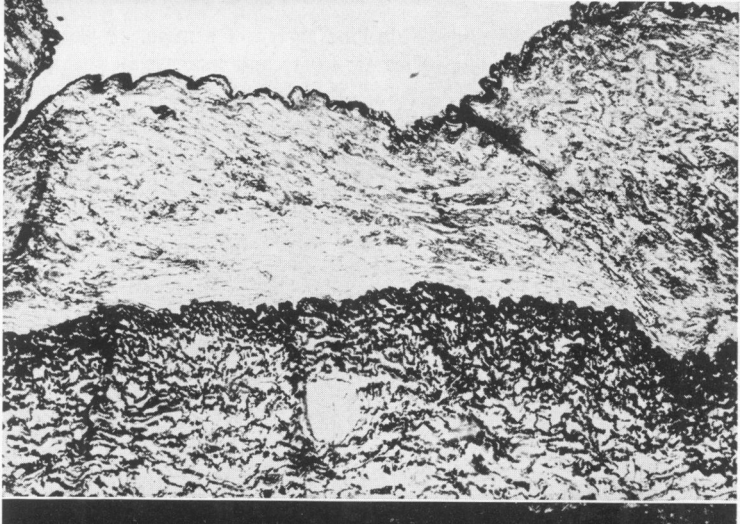

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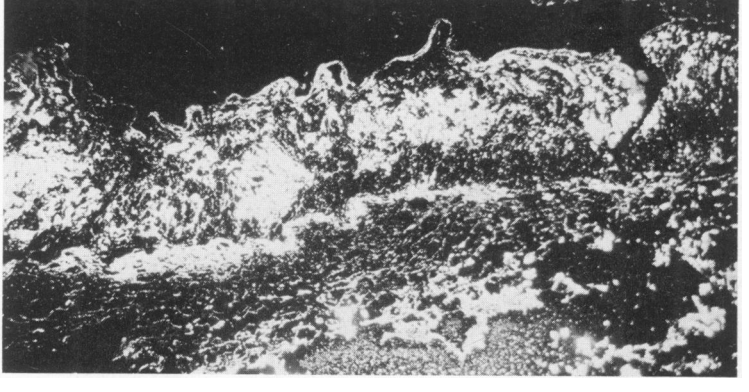

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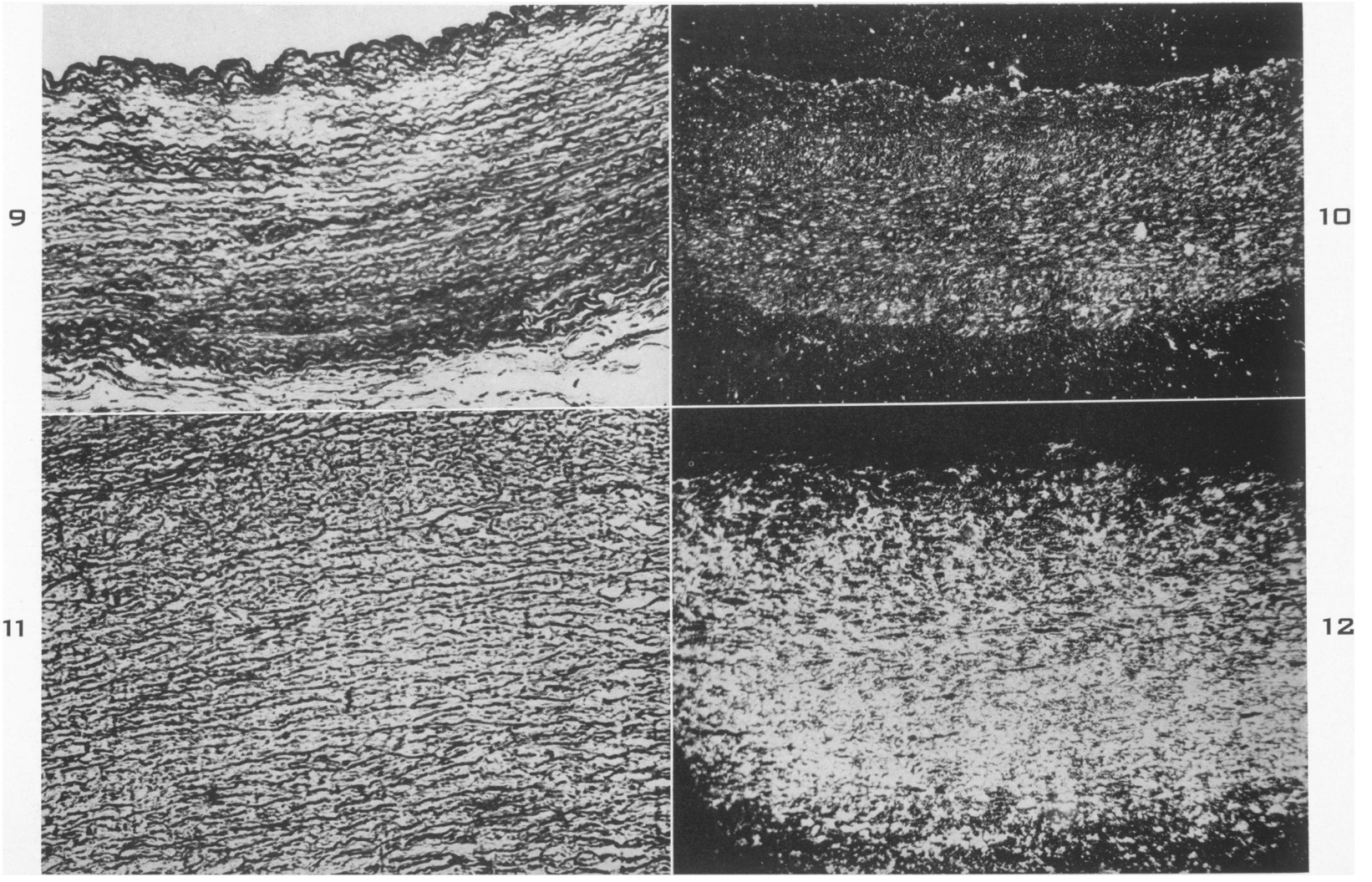
PLATE 143

FIG. 9. Section of the iliac artery of a male, 18 years old, showing a distinct inner elastic lamella, but a relatively indistinct external elastic band. Many plump elastic fibers are present in the media, but discontinuities are beginning to develop. Resorcin-fuchsin stain. × 90.

FIG. 10. From the same case as Figure 9. Micro-incinerated section, showing slight intensification of calcium along the inner surface of the vessel and slight clumping in some areas of the media. × 90.

FIG. 11. Section of the iliac artery of a male, 58 years of age, showing a decrease in thickness of elastic fibers and increase in granular elements between fibers. Loss of identity of the elastic lamellae may be noted. Resorcin-fuchsin stain. × 90.

FIG. 12. From the same case as Figure 11. Micro-incinerated section. There is a diffuse distribution of calcium with loss of calcium lines by which elastic lamellae can be identified. × 90.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