Int J Biol Med Res. 2011; 2(1): 398-403

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International Journal of Biological & Medical Research

Journal homepage: www.biomedscidirect.com

Original Article

Microscopic study of aorta in relation of different age groups: an observational study

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ARTICLE INFO

Keywords:
Aortas,
Histological feature,
Tunica intima,
Tunica media,
Elastic laminae

ABSTRACT

A detailed microscopic study was carried out to see the changes in histological pattern of abdominal aorta in different age group ranging from new born to 70 years. 62 formalin-fixed specimens of either sex were studied. Thickness of tunica intima was minimal during infancy and it could not be measured, where as in the age group 60 years and above thickness of tunica intima ranged between 385 and 450 µs. While during infancy mean thickness of tunica media was 335 µs [ranged 240-385 µs]. It reaches to the maximum mean thickness of 805 in the age group 40-60 years. But in 60 years and above age group mean thickness of tunica media decreased to 660. All three layers of the arterial wall can be identified in infants. Tunica intima consists of internal elastic lamina and endothelium. Sub-endothelial layer is scarcely perceptible. Elastic fibers on tunica media are long and parallel, uniformly arranged and thicker than adult aorta. In the earlier childhood sub-endothelial connective tissue layer becomes more apparent. In adults thickness of tunica intima increases while tunica media appears thin over regional intimal hypertrophy, but in the old age diffuse intimal hypertrophy is seen. Tunica intima become half, to two third of tunica media. Hyalination of collagen tissue of media occurs with loss of normal staining properties of elastic tissue. Elastic laminae become thinned and show fragmentation with occasional clumping. These changes are more prominent near inner media. Adventitia is thicker than media in infants and becomes thinner with age.z z

1. Introduction

The age changes in systems organs and tissues are those, which occur in the period of decline of life. In man some of the general bodily changes with age are of course, as much matter of common observation as of scientific scrutiny. The longetarians show a high forehead with sparse hair of a gray or mixed gray color, eyes deep set, and mouth sunken with a greatly sunken lower jaw, prominent cheekbones, deep wrinkled traversed entire face, nose and eyes prominent because of the atrophic changes of neighboring parts.

At present there are several theories for age related change in different organs with special reference to the relation of anatomical evidence to their validity; these are (i) Gene mutation theory: The gene mutation theory states that during the life of an animal or man spontaneous somatic mutations occur in the cells of various tissues. From anatomical stand point, it is not yet possible to gather direct evidence relating to gene mutation theory but nuclear changes seen in cells, seem to add some indirect evidence in favor of the theory. (ii) Collagen deposit theory: The gradual accumulation of collagen protein substance which apparently is reabsorbed at a very slow rate or not at all, interferes with the supply of oxygen and nutrients to the cells. Earlier studies noted that changes in collagenous fibers are probably an important factor in senile change [1]. (iii) Wear and tear theory: It is an old and perhaps a natural one. According to Rubner there is a direct proportion, such that each animal and perhaps each cell, has a particular amount of metabolic energy, the rate of expenditure of which will determine its length of life [2]. A study showed that when rats were kept in a cold environment considerable increase in their metabolic rate was accompanied by a decrease in their life span. Studies also found that extending the life span of rats by decreasing the amount of food consumed is an example of reciprocal effect on longevity [3]. Anatomical support for wear and tear concept is difficult to assess. (iv)Autoimmune theory: Every cell in an individual is immunologically similar to every other cell in that individual. Earlier studies indicated that where

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organisms carry cells or tissue other than their own, their lifespan will be shortened [4]. An important feature of this theory is that it may provide the basis for explanation of both "natural biological" processes of aging and of a number of its common pathological manifestation.

Among the cardiovascular diseases, degenerative diseases of blood vessels are responsible for about 20-25% cases. There is a considerable morphological difference between vessels fixed in a collapsed or physiological distended state. In collapsed vessels, the endothelium is thick; the sub-endothelium gap appears distended near nuclei, the internal elastic lamina and in elastic vessels the elastic fibers are undulating and loosely arranged and the gap between them varies in width. The fibers of distended elastic type vessels are straight and the gaps between them are uniformly wide.

The final differentiation of various components of vessels wall is not complete until adult life. The three main coats of the arteries are acquired during the 4th month of fetal life but intimas of aorta were not completed for about 30 years. In an aorta of 4th month old human embryo, the intima consists only of endothelium & of rather thick internal elastic membrane while the media consists of several layers of circular smooth muscles cells between which are flat networks of elastic fibers embryonic connective tissue. At the end of embryonic life the internal elastic membrane becomes thicker, and the network of elastic fibers in media becomes thick elastic membrane. The smooth muscles have increased slightly in number but are still inconspicuous. The adventitia by this time becomes smaller. After birth, in muscular arteries, in addition to the thickening of the wall as a whole a connective tissue layer gradually develops between endothelium and internal elastic membrane [5]. Other study also describes that, at birth endothelium lies almost directly upon the internal elastic lamina, but even in childhood these layers become separated by loose mesh of connective tissue [6]. Intimal thickening is the most important aging change for it appears to carry the seeds of arterial disease. The elements added to in time include fibrocytes, smooth muscle cells collagen fibers and ground substance rich in mucopolysacchrides. In this way the intima comes to approach in thickness of media and it is not uncommon to find that in the coronary arteries of men aged 60 years or so intima equals or exceeds the media without any disease process being identifiable. In the middle and later age degenerative changes develop in the elastic fibres of internal and external elastic laminae and in the media [7]. There is often some reparative process shown by the development of thinner fibers irregularly oriented around the original membrane [8].

2. Materials and methods

The present study was carried out in the department of Anatomy at Gandhi Medical College, Bhopal, Madhya Pradesh, India.

2.1.Study subjects

These were 62 human abdominal aortas (41 were male and rest of them female) of different age groups from infant to seventy years collected from embalmed cadavers.

They are classified as follows:-

Group I0	1 year
Group II1	5 years
Group III5	15 years
Group IV15	40 years
Group V 40	60 years
Group VIabove	60 years

2.2. Study tools and technique

These blood vessels were preserved in 10% formal saline immediately after its removal at room temperature before it was taken for histological examination. After preparing the tissue blocks, serial section were cut of 5 µ thickness with the help of rotatory microtome. Sections were mounted on micro slides and the slides were kept at 37° C in an incubator.

2.3.Staining

Various staining techniques were employed for the demonstration of general differentiation of the tissue and for specific tissue component of the organ. These are Haematoxylin and Eosin, Masson's Trichome, Orcein, PATH, Gomeri. Observations were recorded under light microscope. Thickness of intima and media were measured with standardized micrometer; mean values were calculated.

2.4.Ethical clearance

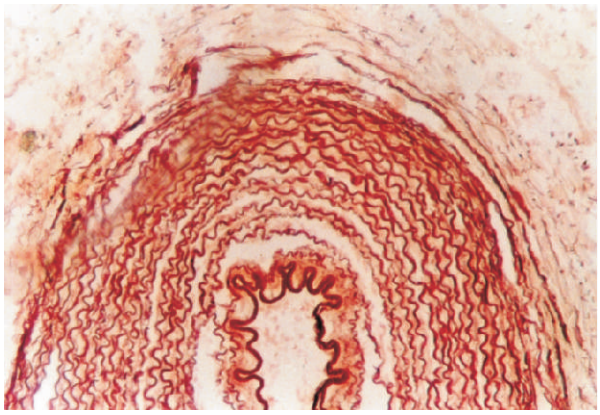
Ethical clearance for conducting the study was taken from the ethical committee of the institution i.e. Gandhi Medical College, and associate Hospital Bhopal, with the assurance that confidentiality will be maintained and the information obtained for this study will not be used for any other purpose except for academic purpose.

3.Results

Group I (0 1 year): A prominent histological feature in this group was absence of sub-endothelial connective tissue between internal elastic lamina and endothelium in tunica intima of aorta. Internal elastic lamina was continuous and uniformly thick. None of the slides from this group showed intimal thickening or localized intimal hypertrophy. In tunica media elastic laminae were long and parallel to each other and of uniform thickness. They were arranged in a compact manner. Between elastic laminae were circularly arranged smooth muscle cells surrounded by collagen tissue. In this age group proportion of collagen tissue was much less than smooth muscle cells, which forms prominent, layer between laminae. Tunica adventitia in this age group is even thicker than the media. It shows longitudinally arranged collagen and elastic tissue (Figure 1).

Figure.1

Aorta of 6 days old baby showing well defined thick wavy, compactly arranged, parallel to each other internal elastic lamina & sub endothelial layer are absent (orcein staning, ×100)



Group II (1 to 5 years): It was observed that thickness of tunica intima starts appearing in aorta at this age i.e. sub-endothelial connective tissue appears between internal elastic lamina and endothelium. Average thickness of tunica intimae of aorta was 35 µ. Histological features of tunica media in this group were quite similar to the previous group. Elastic laminae were long, uniform and parallel to each other and compactly arranged like previous group. Occasional anastomoses of elastic lamina were also seen. Numbers of elastic laminae were seen increasing. Average thickness of tunica media of aorta in this group was 485 µ (Figures 2 and 3).

Figure.2

Aorta of 2 year old child showing well defined, compactly arranged, long parallel internal elastic lamina & slight thickening of tunica intima (gomeri staning, ×100)

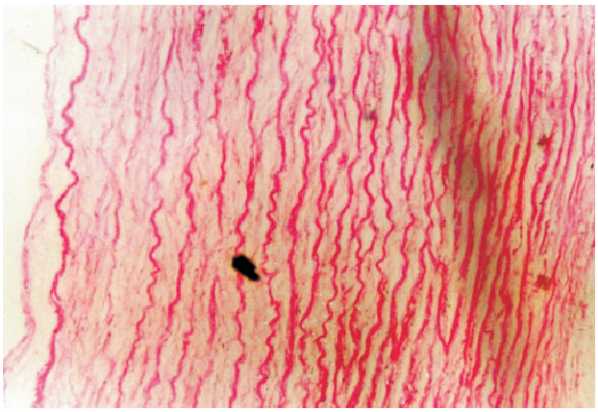
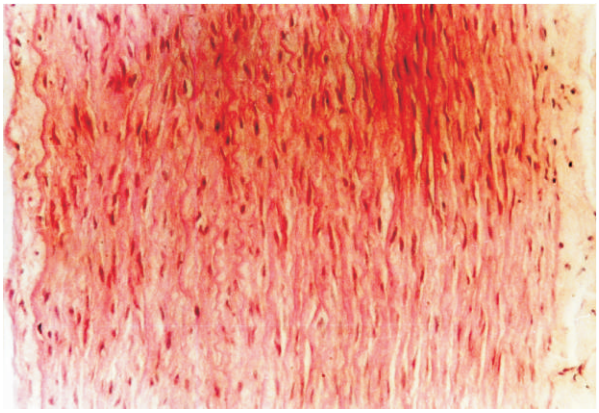


Figure.3

Aorta of 2 year old child showing well defined internal elastic lamina, slight thickening of tunica intima & tunica media consist of laminae by layer of smooth muscle cells (H&E staining, ×100)



Group- III (5 15 years): In this group, microscopic appearance of blood vessels was very much similar to the earlier group except thickness of tunica intima was more than the previous group i.e. average thickness was 95 µ, splitting and stretching of internal elastic lamina can be seen at few places, localized thickening of tunica intima was more prominent with a mean value of 165 µ. Mean thickness of tunica media was 580 µ.

Group IV (15 to 40 years): Tunica media showed consistent increase in thickness. Regional intimal hypertrophy was also seen increasing. It was thicker than previous group. Average thickness of this layer was 135 µ and average regional intimal hypertrophy was 88 µ. Tunica media of aorta showed some irregularity and branching and crenation of elastic laminae. Tunica media appeared thin over areas of regional intimal hypertrophy. There was consistent increase in amount of collagen tissue. Average thickness of media was 712 µ. Tunica adventitia remained similar in appearance.

Group - V (40 - 60 years): Tunica intima showed consistent increase in thickness and diffuse intimal hypertrophy. Internal elastic lamina was thick, and there was a replication of internal elastic lamina. Sub endothelial layer showed fibrocytes, collagen fibers, elastic fibers and smooth muscle cells. Average thickness of tunica media in this group was 310 µ. Localized intimal hypertrophy was 375 µ. Tunica media of aorta showed that laminae were thin and fragmented. Thinning of elastic laminae as well as increase in collagen tissue was more evident near inner part of media. Elastic laminae of outer media were seen like previous group. Average thickness of tunica media of aorta was 805µ (Figures 4 and 5).

Figure.4

Aorta of 45 year old men showing internal elastic lamina thin and broken at many places, thickened of tunica intima & elastic lamina in media is thin and fragmented smooth muscle cells decreased (H&E staining, ×100)

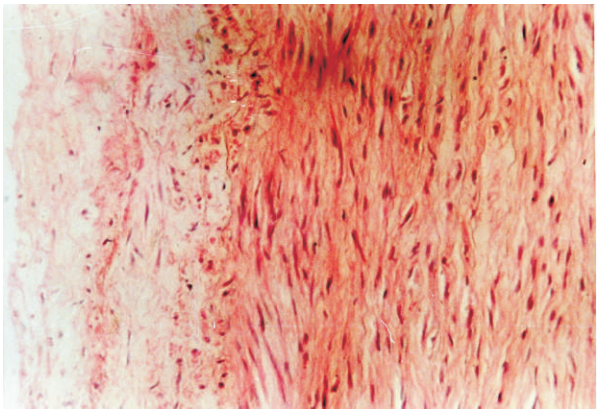
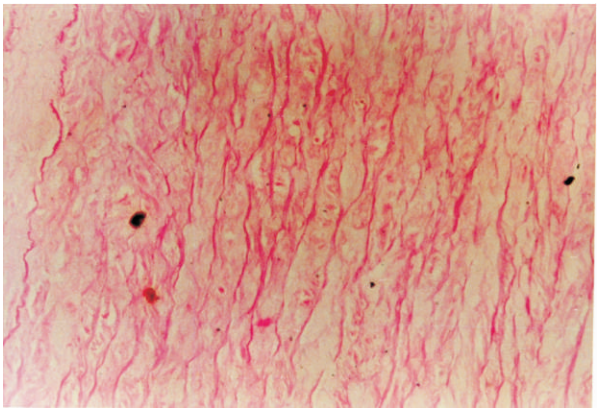


Figure.5

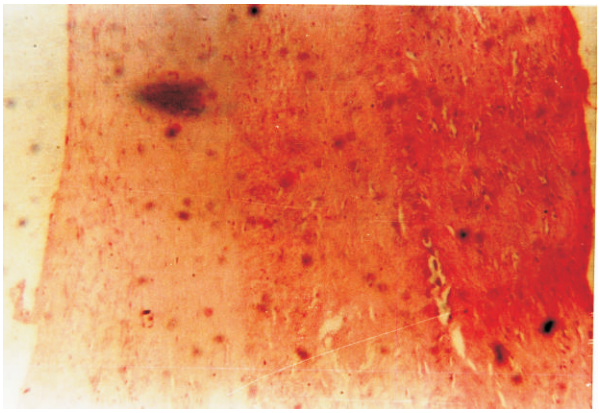
Aorta of 50 year old men showing replication of internal elastic lamina with highly thickened tunica intima elastic lamina are thin; short fragmented and anastomoses (gomeri staning, ×100)



Group VI - (Above 60 years): Tunica intima of aorta showed increased thickening as well as reduplication of internal elastic lamina. Average thickness of tunica intima was 417µ. At this stage regional intimal hypetrophy becomes diffuse in nature. Average thickness of regional intimal hypertrophy was 650µ. Tunica media of aorta in this group was more or less similar to the previous group except elastic laminae showed a little more branching and became more thinner and fragmented; average thickness was 660µ (figure 6).

Figure.6

Aorta of 45 year old men showing, internal elastic lamina and elastic lamina are not clear, highly thickened tunica intima and thinning of tunica media with atrophy smooth muscle cells (H&E staining, ×100)



A direct relationship was observed between numbers of elastic laminae of tunica media of aorta with increasing age being 23, 28, 43, in group I, II and III respectively. Because of branching anastomoses fragmentation and fraying in the adult hood and in old age it is difficult to count the no. of elastic laminae.

In this present study 40% of study subjects belonged to 40 - 60 years age (Table 1). There was increase in thickness of tunica intima of aorta with age. During infancy thickness of tunica intima was minimal and it could not be measured, where as in the age group 60 years and above, mean thickness of tunica intima was 417 (385-450) (Table 2).

Table 1. Distribution of aorta according to age

Age Group	Aorta No.	%
0 - 1 year	03	50
1 - 5 year	05	8
5 - 15 year	04	6
15 - 40 year	14	22
40 - 60 year	25	40
60 + year	11	19
Total	**62**	**100**

Table 2. Thickness range and mean thickness of tunica intima of aorta

Age Group	Thickness range (µ)	Mean Thickness (µ)
0 - 1 year		
1 - 5 year	15 - 20	35
5 - 15 year	50 - 115	95
15 - 40 year	65 - 215	135
40 - 60 year	265 - 400	310
Above 60 year	385 - 450	417

Increase in thickness of tunica media was also observed with age. During infancy mean thickness of tunica media was 335 (240-385) and reached to the maximum mean thickness of 805 in the age group 40-60 years. But in 60 years and above age group, mean thickness of tunica media decreased to 660 (Table 3).

Table 3. Thickness range and mean thickness of tunica media of aorta

Age Group	Thickness range (µ)	Mean Thickness (µ)
0 - 1 year	240 - 385	335
1 - 5 year	350 - 570	485
5 - 15 year	485 - 750	580
15 - 40 year	485 - 1050	712
40 - 60 year	550 - 965	805
Above 60 year	615 - 700	660

During infancy no localized thickening of tunica intima was seen, where as in the age group 60 years and above localized thickening of tunica intima was frequently noted and ranged from 450-810 (Table 4).

Table 4. Localized thickness range and mean localised thickness of tunica intima of aorta

Age Group	Thickness range (µ)	Mean Thickness (µ)
0 - 1 year		Not Seen
1 - 5 year	45 - 80	60
5 - 15 year	115 - 195	165
15 - 40 year	85 - 300	188
40 - 60 year	285 - 515	375
Above 60 year	450 - 810	650

4. Discussion

In our study it was found that in arteries of infants all three layers were present. Tunica intima consists of only internal elastic laminae and one endothelium with scarcely perceptible sub-endothelial connective tissue layer. We have not found intact endothelium as it was lost during preparation but only few endothelial cells nuclei could be seen projecting in to lumen. So the internal elastic lamina appeared as inner most layer and was continuous, thick wavy in appearance.

The tunica media of infant aorta shows circularly arranged elastic laminae. These elastic laminae are long and run parallel to each other and are uniform in thickness. They appear thicker than those of adult aorta and are fairly compactly arranged. Similar findings also suggested by Robert J et al (1964), [9] when they compared the pulmonary trunk and aorta at different ages. Between elastic fibers smooth muscle cell layers surrounded by collagen tissue are present.

Lakatta EG [10] showed that elastic fibers in the media of infants aorta was thick elastic membranes while tunica adventitia was smaller than media. He also found that sub-endothelium connective tissue was absent at birth. Crawford T [6] also described similar changes at birth.

Bloom & Fawcet (1967) [5] have stated that in intima between endothelium and internal elastic lamina sub-endothelial elastic muscular layer appears in early childhood. It arises partly by a splitting of internal elastic membrane and partly by the new formation of collagenous and elastic fibers. It gradually increases in thickness and produces progressive thickening. They have also shown that number and thickness of elastic membranes in media of aorta gradually increase in early childhood.

Crawford T [6] has also shown that in early childhood internal elastic lamina and endothelium layers become separated by loose mesh of connective tissue and it tend to increase in among and density with passage of years.

We have also found that in 1 - 5 years age group sub-endothelial connective tissue becomes clearer between internal elastic lamina and endothelium. Elastic laminae in the aorta are long and parallel to each other, and similar to the elastic laminae of infant aorta with exception of occasional anastomoses of elastic laminae. There is a localized splitting of internal elastic lamina with some intimal thickening over elastic splitting. An increase in thickness of tunica media was observed in aorta in comparison to the previous group.

Ross R [11] has shown that in older children more definite intimal thickening appears and almost invariably there is some stretching, splitting or fraying of underlying internal elastic lamina. With increasing age these features become more pronounced.

According to Homan R et al [12] intimal thickening beings to appears in 1st decade of life and covers increasing proportion of intimal surface. Prior & Hutter [13] has shown that continued deposition of sub-endothelial connective tissue throughout life produces progressive thickening of this layer. The elastic fibers deteriorate and are replaced by fibrous tissue; with this loss of elasticity these vessels expand less readily. Tyagi SP et al [14] have shown that the collagen fibers are less numerous and adventitia is rich in cells in young animal than older one. Lakatta EG [10] also found that in childhood intima of aorta has highly developed layer of circular elastic fibres. According to Crawford T [6] arteries of the arm in early adult life show scarcely perceptible amount of sub-endothelial connective tissue and abdominal aorta and large arteries of lower limb shows intimal thickening even in early childhood.

In the present study we also found that gradual increase in thickening of intima in 5-15 years age group. Along with this internal elastic lamina showed localized splitting.

The elastic laminae of tunica media of the aorta are similar to earlier age group. The laminae are still long uniform and parallel and only occasional laminae anastomose. Movat HZ et al [15] have also found similar structure in early adult life. We have also found that elastic laminae of media of aorta increase in number. Apart from increased thickness of intima as a whole, localized or regional intimal thickening is also seen with increasing age. Rebert Deucek and Ruth Takeshita (1963) [16] have also shown that this regional intimal hypertrophy is present by 12 years of age and it increases in amount and diffuseness with age. This regional or localized intimal hypertrophy is present only up to 40 years of age. Robert J (1963) [17] have shown that after 40 years there is diffuse hypertrophy of tunica intima and it is associated with atrophy of media and adventitia. They have also shown that this regional intimal hypertrophy appears at sites where unusually physical stresses can be predicted to occur within the arterial wall.

According to Velican & Velican [18] elastic laminae of aorta in adult life have shown some branching and irregularity of elastic fibers and the laminae are crenated. We also found similar changes in elastic laminae between 15 to 40 years of age. In present study we have measured the thickness of normal intima and media and found that thickness of intima increases with age where as the thickness of the media increases until the 6th decade and thereafter it decreases, possibly due to atrophy of smooth muscle cells and deposition of collagen tissue. The relative measurements of the intima and media of the arteries show that localized thickening of intima is usually associated with thinning of the media. Similar result was also shown by T. Crawford (1961) [19]. The possible explanation of thinning of media over regional intimal hypertrophy is that at parts where intima is thickened, the diastolic rebound of the vessel wall will be reduced and it will tend to remain in a more or less distended position after death. But there is also the possibility that the thinning may represent a basic weakness of the muscular coat.

According to Schlatmann TJ et al [7] in middle and old age degenerative changes develop in the elastic fibers of internal and external elastic laminae and the media. These changes are most noticeable in the internal elastic lamina and there was often some reparative process shown by the development of thinner fibers irregularly oriented around the original membrane. Studies have also shown that concentrations of both collagen and elastin increased significantly with age, substantially after the age of 45 [20].

In present study it was observed that between 41-60 years thickness of tunica intima continues to increase an average thickness of tunica intima may reach upto 30-40 percent of the thickness of the tunica media.

There was a reduplication of the internal elastic lamina. The intimal thickening is irregular and causes asymmetrical lumen, collagen tissue in media also increases in quantity. This increase in collagen tissue is more noticeable near junction of media and

adventitia. These possibly correspond to the course of vasavasorum. Increase in collagen tissue causes atrophic changes in smooth muscles of media and bring tortusity of vessel. The increase in collagen tissue and its lack of association with any inflammatory process seem to favor the phenomenon of physical aging. Robert J et al (1963) [17] have also shown that after 40 years of age muscle bundles become atrophied in certain region and adventitia become thinned. All these changes suggest that with age arteries lose their active function and assume a more passive role as conduit for transport of blood. Tunica adventitia also becomes thinned. Donalt Tames and Edward (1954) have shown that elastic laminae become thinned and show much fragmentation by the age of 45 with occasional clumping. The thinning is much more prevalent to the inner media, where there is much fibrosis. The elastic laminas of the outer media were thicker and appear like the lamina of younger age. We also found the similar structure of elastic lamina after 40 years.

According to T Craford et al (1961) [19] intima by the age of 68 years may equal or even exceed the media in thickness and internal elastic lamina become thickened and there may be second incomplete ring inside the original lamina. The thickened intima shows the presence of smooth muscle cells, collagen and elastic fibres and round cells.

Crawfort T [21] has shown that with more advanced age collagen fibers tend to undergo hyaline degeneration and appear swollen, glassy and increasingly eosinophilic.

In the present study in 60 years and above age group, decrease in thickness of tunica media of aorta was recorded, while thickness of tunica intima continues to increase. It becomes half or two third of tunica media. As explained earlier it could be due to atrophy of smooth muscle cells and deposition of connective tissue in media. Elastic laminae of tunica media become thinner and fragmented.

5. Conclusion

Light microscopy of aortas revealed different characteristics in various age groups. A detailed microscopic study was carried out to seen the changes in histological pattern of abdominal aorta. All three layers of the arterial wall can be identified in infants. Tunica intima consists of internal elastic lamina and endothelium. Sub-endothelial layer is scarcely perceptible. Elastic fibers on tunica media of aorta are long and parallel, uniformly arranged and thicker than adult aorta. In the earlier childhood sub-endothelial connective tissue layer becomes more apparent. There is occasional localized splitting of internal elastic laminate. Adventitia is thinner than media. In adults thickness of tunica intima increases while tunica media appears thin over regional intimal hypertrophy, but in the old age diffuse intimal hypertrophy is seen. Tunica intima become half to two third of tunica media. Lumen becomes asymmetrical. There is complete reduplication of internal elastic lamina. Hyalination of collagen tissue of media occurs with loss of normal staining properties of elastic tissue. Elastic laminae become thinned and show fragmentation with occasional clumping. These changes are more prominent near inner media. Elastic laminae of inner media appear liked adult.
From the finding in the present study one might conclude that there is definite intimal hypertrophy and media fibrosis with increasing age. These degenerative changes that develop gradually with the age lead to arteriosclerosis or hardening of the arteries. The gross morphological effect of all these changes is that the arteries tend to dilate and elongate. These inevitably lead to tortuosity of the artery. The arteries become harder and easily palpable in such sites as the wrist and neck. They loss some of their active function and assume a more passive role as a conduit for transport of blood.

Contribution of authors in the present study

Dr. Shankar Dayal Gupta: Conception and design of the study; Prime investigator for the conduction of study.

Dr. Sanjeev K. Gupta: Prime investigator and Analysis & manuscript preparation.

Dr. Dinesh Kumar Pal: Critical analysis and justification of results & interpretation of data.

Dr. Radha Sarawagi : Critical revision of the manuscript.
All authors commented on drafts of the manuscript and approved the final version.

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