A Pathological Study on Arteriosclerosis of Carotid

Tadanaga KAWAUCHI*

Department of Pathology Nagasaki University School of Medicine Nagasaki, Japan

Received for publication, January 5, 1965

The studies made by the elders of our department have revealed that the degree of advancement of sclerotic lesions in the arteries which are distributed in various organs and that of aortic sclerosis in the same individual are not necessarily parallel with each other. The same trend between the aorta and the carotid artery has been confirmed by the author's observation in which the degree of advancement of arteriosclerotic lesions was measured by applying the Gore's mathod to the aorta and the Thickening Index to the carotid artery. Particularly, arteriosclerosis of the siphon portion is further advanced in many cases than that of the aorta. The main lesion of the siphon portion is atheromatous lesion being followed by calcic deposit. Calcification may begin as early as at the age of 12 and it often results in calcic tubes. In the sinus portion where frequency of atheromatous lesion is the highest, complicated lesion or occlusion is common among the Occidentals. Contrarily, however, the author's investigation showed a low frequency of ulcer, calcification, thrombosis and complete occlusion. The pattern of an early lesions of arteriosclerosis in the elastic type portion is different from that in the muscular type portion. Changes of the media precede in the former and those of the internal elastic membrane are found in the latter. It is manifest that sclerotic lesions of the carotid artery are fairly different in frequency and character between the Occidentals and the Japanese.

There have been many technical reports on sclerosis of the aorta and the coronary artery and, furthermore, there is also no little literature on sclerosis of the cerebral artery, cerebral hemorrhage and vascular disease^{31,32,34,55}. There have also been several treatises of radiological study on the carotid artery which connects the aorta and the cerebral artery, so-called organ-artery, and which plays an important role in central nervous circulation^{6,8,1,66}, and some reports from the standpoint of vascular surgery pertaining particularly to the thrombosis

*川内忠脩

of individual incidences^{1),36)}. Recently, function of the carotid artery has been clinically studied with various methods such as measuring carotid arterial pressure though use of Resonance electrosphygmograph³⁾ and Oscillometry⁹⁾. However, the literature is few, either in Japan or abroad, that describes sclerotic disease of the carotid artery as a result of the systematic observations from patho-morphological point of view. The actual state of arteriosclerosis of carotid of the Japanese has been clarified to some extent by the author from morphological point of view, and the outline is herewith reported in comparison with other literature.

MATERIALS AND METHODS:

The main material of the study consisted of 186 pieces of carotid artery collected at random from among the 1288 cases of autopsy performed during the period from May 1961 to the end of December 1963. The common carotid artery was obtained from the origin (thoracic portion) to the sinus portion where the internal and external carotid arteries are bifurcated; the internal carotid artery was obtained from its origin through the petrosus portion and the cavernous portion which run within the arterial canal of the base of the skull, to the "carotid siphon" as named by MONIZ and WICKBOM; and the external carotid artery was obtained from its origin to the resectable peripheral end—all of these as a series of specimen. The aorta of the same individual was also the material of the study. The age-composition ranging from newborn to 87 and sex ratio are as shown in Tables 1 and 2. With 32 additional cases, observation was made only for the proximal half of the common carotid artery, but these cases are excluded from the tables.

Age Group Sex	1	2	3	4	5	6	7	8	Total
Male	3	8	7	10	4	9	10	13	64
Female	3	3	2	4	5	7	7	6	37
Total	6	11	9	14	9	16	17	19	101

Table	1.	Number	of	Cases	Studied	(By	Sex	and	Age	Group))
-------	----	--------	----	-------	---------	-----	-----	-----	-----	--------	---

Table	2.	Number	of	Arteries	Studied	(By	Sex	and	Age	Group))
-------	----	--------	----	----------	---------	-----	-----	-----	-----	--------	---

Age Group Sex	1	2	3	4	5	6	7	8	Total
Male	6	15	12	19	7	18	15	25	117
Female	6	6	6	8	8	14	12	9	69
Total	12	21	18	27	15	32	27	34	186

ARTERIOSCLEROSIS OF CAROTID

METHOD OF OBSERVATION :

The aorta was fixed in 10% formalin and the degree of its sclerosis was indicated by a numerical index according to GORE's method¹⁴ which is most generally adapted at present. The carotid artery was macroscopically observed for its full length, and then, a microscopic section was obtained from each "5 the" ollowing portions : thoracic portion of the left common carotid artery being 1 cm peripheral from the aortic arch, and its distal end or 1 cm cardiac side from the sinus portion where the internal and external carotid arteries are bifurcated; 1 cm peripheral portion from the bifurcation, petrosus portion, cavernous portion and siphon portion of the internal carotid artery; and 1 cm peripheral portion of the external carotid artery from the bifurcation. The right carotid artery was sampled at 1 cm peripheral portion of the common carotid artery from where it is bifurcated from the brachiocephalic artery. The sampling of the other portions followed the same method as for the left side. The samples of the cases below 15 years of age were all excised at 0.5 cm peripheral side. The samples were embedded in paraffin and carbowax and cut into 100 serial sections with thickness of 7μ . The sections were dyed with hematoxylin-eosin, Weigert's elastic fiber stain, van Gieson's stain, and Weigert-Masson-Goldner's multiple stain. The fat was dyed with Sudan III and Oil red 0.

RESULTS

I Macroscopic Findings

Common Carotid Artery:

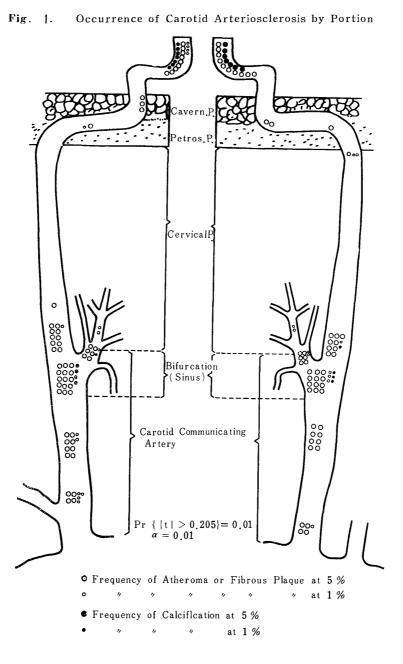
Macroscopic findings of the common carotid artery were similar to the sclerotic lesions which are usually seen in the aorta, and the severity of lesions increased as the age advanced. Fatty streak and yellow dot appeared scatteringly in the low-teenage; the intima showed milk white diffused turbid thickening and localized gross unevenness. As the age advanced a little further, there were seen some small white circumscribed fibrous plaques and atheromatous flecks protruded to the size of milium or in the shape of line. These lesions were most frequently observed in the sinus portion and, next to that, in the thoracic portion. Among the lesions which appeared in younger age, atheromatous fleck and yellow dot were often difficult to be macroscopically distinguished from each other, but, in the 30's such distinction became easier. In the 40's, there appeared a minimal narrowing of the vessel, though it was circumscribed, particularly in the sinus portion due to fibrous plaque and atheroma. In the 60's or more, calcification appeared in the sinus portion (7 cases out of 64, 10.9%) and in the thoracic portion (1.6%), and even ulcerous lesion was seen

particularly in the sinus portion (1 case, 1.6%). The narrowing of vessel as shown in Photo. 1 or more advanced stenosis was observed in 9 cases (14.1%) of over 60-year-old samples, but there was no case of complete obstruction which is due solely to sclerotic mural thickening. There was one case of complete obstruction of the left sinus portion due to thrombus in a 77-year-old male sample. This is equivalent to 0.45% of the total of 118 cases of the study of common carotid artery and 1.6% of the cases over the age of 60. Accordingly, it is suggested that atheroma and fibrous plaque are the main lesions of the common carotid artery and they apt to occur in the sinus portion.

Internal Carotid Artery:

The wall of the internal carotid artery which is bifurcated from the distal terminal of the common carotid artery, is somewhat thin and is slightly dilated in the shape of a bag ranging from 0.5 cm (infant) to 1.5 cm towards the peripheral side. This portion is somewhat elastic muscular type artery; the intima is semitransparent milk white and somewhat glossy. The sclerotic lesions of the common carotid artery which appear in the low-teenage also extended to this portion and increased along with the advancement of age, but the frequency of atheroma and fibrous plaque was generally lower than that of the former (Fig. 1). The ulcer, calcification or complete obstruction which is circumscribed only in this portion was hardly seen even after the age of 60. In the further peripheral portion from there, the arterial wall was thick and fine transverse wrinkles ran circle on the surface of the intima. Again in the further peripheral portion, numberless fine longitudinal wrinkles were also added. From the petrosus portion, the artery is a pure-muscular type and fatty streak and yellow dot were vary rare. Small atheromas and fibrous plaques were the main lesions in this portion but their frequency was the lowest of all portions in the internal carotid artery. A coarse irregular unevenness was seen in the intima in the portion of vessel which runs through arterial canal of the skull and in the siphon portion, and the intima could be easily detached from the media. In the latter part of the 30's, there appeared circumscribed milk white or yellow fibrous plaque mostly in the intima of the interior wall of the tortuous portion. However, stenosis of the vessel due to atheroma as shown in Photo. 2 was very rare (1.36%) of the total cases). At the age of over 50, calcification of the intraosseous vessel was frequent-it occurred in 11 cases (16.1%) out of 68 cases of the samples over 50. Naturally, the frequency become higher in proportion to the advancement of age.

The frequency of atheroma and fibrous plaque in the siphon portion among the total cases of this study was as shown in Fig. 1, and was the second highest next to that in the sinus portion of the common carotid artery. It is especially noteworthy that the frequency of calcified focus, either by itself or complicated with atheroma, was very high,



being 34.7% of the total cases. When the cases are limited to those of over 50 years of age, the frequency increased as high as 46 cases out of 78 (59.0%) and it is interesting in consideration of the microscopic finding which is stated later (i.e., calcification of the internal elastic membrane is already noted at the age of 15). The sclerotic lesion in such a high degree naturally produced narrowing of the vessel (Photo. 1), and stenosis covering 1/2 or more of the lumen was seen in 19.8%

of the total cases.

There was no significant difference between the two lateral sides in frequency of fibrous plaque and atheroma throughout the entire length of the carotid artery as shown in Fig. 1.

External Carotid Artery:

The portion from the bifurcation to 0.5-1.0 cm peripheral side of the external carotid artery is similar in characteristics to the equivalent portion of the internal carotid artery except for lower frequency of atheroma and fibrous plaque. In some cases, however, there are noted stenosis of the vessel caused by a lesion continued from the sinus portion, and obstruction of the vessels with Y-shaped thrombus (Photo. omitted). The further peripheral portion is a pure muscular type artery with fine trasverse wrinkles. Lesions rarely occur in this portion with the lowest frequency in the entire carotid artery.

II Relation between Aorta and Carotid in the Degree of Arteriosclerosis

KAMURA²⁶⁾ applied GORE's athero index (hereinafter called G. I.) which is used for quantitative and qualitative measurements of arteriosclerosis of the aorta and circle of WILLS which are organ type arteries. He has reported the average value of G. I. for that region to be at most 2.5 despide the fact that the most servere sclesotic lesion is found in the terminal of the internal carotid artery. DEGUCHI^{T)} has reported that the G. I. average for the gastric artery of the samples in their 80's was 0.16 and that for the aorta was 38.3. Similar relations have been noted in the gastric or renal artery (FUKUDA¹²⁾, FUJITA¹¹⁾, NogucHI⁴²⁾ et al.). It is thus indicated to be improper that G. I. is equally applied to the aorta and organ arteries which are different from each other both in structure and in diameter.

Hence, with the purpose of finding a quantitative expression of sclerosis of minor arteries, $H_{IERONYMI^{17}}$, $K_{LINGELHOEFER^{27}}$ and others, having measured the interior diameter of the vessel and the thickness of the intima and media, obtained the degree of thickening, and compared the degrees of sclerosis among main organ arteries of the body. $K_{AMEYAMA^{24}}$, $O_{TSU^{43}}$ and $S_{HOZAWA^{47}}$ tried to express the degree of thickening by M/I, the ratio between the thickness of intima and that of media; and the degree of stenosis by L/W, the ratio between the thickness of the wall (W) and the interior diameter (L) of the artery.

As it has already been reported by FUKUDA¹²⁾ and FUJITA¹¹⁾, the method to indicate the degree of sclerosis or thickening of minor arteries by the ratio of intima against media in weight has been practiced in our department since 1961: The microscopic figure is drawn by projection on a sheet of specific paper (MITSUBISHI KENT Paper 5); the intima and media are cut out of the paper for measurement of respective weight through use of the SHIMAZU's balance L-II, (the values are

indicated by I and M, respectively), and the ratio $I/M \times 100$ is regarded as the Thickening Index (hereinafter called T. I.) of the arteries. This method is deemed adequate since sclerosis of an artery of this size mostly consists, as a rule, in the thickening of the intima whereas there is hardly any change in the thickness of the media.

Tables 3, 4 and 5 show the relation between T. I. of the carotid artery and G. I. of the aorta. The coefficients of correlation of these three tables are calculated as r = 0.72, r = 0.35, r = 0.74, respectively. A fairly close correlation is noted. However, the correlation between carotid and aortic sclerosis (Table 4) is quite weak and it has a significant difference from the other two (Table 3 and 5). It is manifest in Table 5 that, although the coefficient of general correlation of arteriosclerosis in the siphon portion to the aorta is rather high, sclerotic incidence in the siphon portion of individual case is relatively numerous in comparison with sclerosis of the aorta. In this sense, it is deemed that the degree of arteriosclerosis of the carotid and that of the aorta are

Table	3.	T. I. in Sinus Portion of Common Carotid
		and Gore's Index in Aorta

GORE's Index T. I	~5.0	~ 10.0	\sim 15.0	~ 20.0	~ 25.0	~ 30.0	30 ~	Total
~ 10.0	25	3						28
\sim 20.0	44	7	1	ĺ	4	1		57
\sim 30.0	16	8	2		1			27
\sim 40.0	1	3	· 1	2			1	8
\sim 50.0				3		1		4
50 \sim	1	2	2	1	3	1	8	18
Total	87	23	6	6	8	3	9	142

r = 0.72

Table	4.	T. I. in Intraosseous Portion of Carotid
		Artery and GORE'S Index of Aorta

GROE'S Inder T.I	~ 2.5	~ 5.0	\sim 7.5	~10.0	~15.0	15 ~	Total
~ 5.0	24					1	25
\sim 10.0	6	1					7
\sim 15.0	21			2	1	1	25
\sim 20.0	16	3					19
~ 30.0	24	3		2	3	6	38
$_{30}\sim$	22	12	. 7	7	10	12	70
Total	113	19	7	11	14	20	184

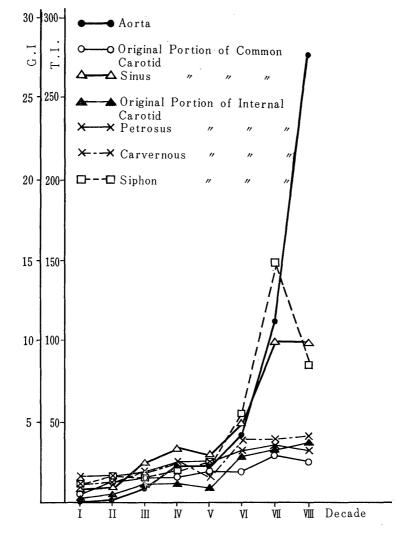
·. 1

GORE, S Index	~ 2.5	~ 5.0	~ 7.5	~ 10.0	\sim 15.0	~ 20.0	$_{20}\sim$	Total
~ 5.0	6							6
\sim 10.0	7							7
\sim 15.0	7			1				8
\sim 20.0	8	1		1				10
\sim 30.0	10	6		1	2	2		21
$_{30}\sim$	13	13	4	4	4	2	11	51
Total	51	20	4	7	6	4	11	103

Table 5. T. I. in Siphon Portion and GORE's Index in Aorta

r = 0.74

Fig. 2. Sclerotic Index of Aorta (G. I) and Thickening Index (T.I) by Age Group



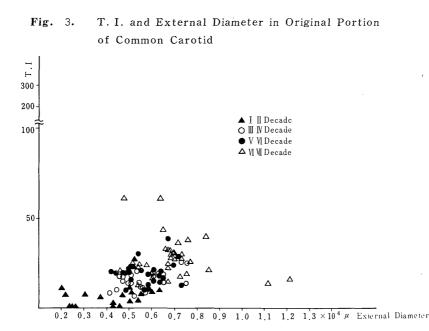
not so steadilyparallel in an individual body.

Figure 2 shows the relation by age group between the aorta and various portions of the carotid artery. The G. I. and T. I. are approximately parallel up to the 40's, and both G. I. of the aorta and T. I. of the siphon portion and the sinus portion of the carotid rapidly increase after the 40's. There is no remarkable difference in T. I. among various portions of the carotid up to the 40's but after the 40's, the T. I. increases in the siphon portion and then in the sinus portion, and these two portions predominate the other portions in the aspect of T. I. However, the values of T. I. are not necessarily proportional to the frequency of atheroma and fibrous plaque.

III Comparison of the Thickening Index among Various Portions of the Carotid Artery

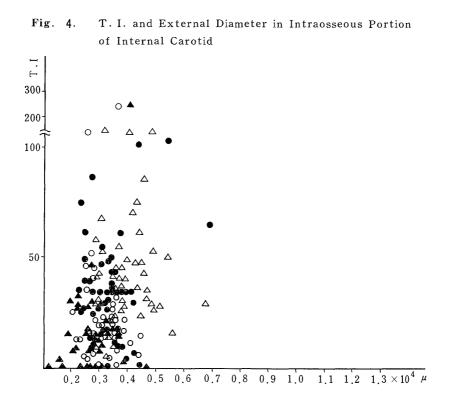
A comparison of T. I. measurements in various portions indicates, as shown in Fig. 2, that the thickening index in the siphon portion of the internal carotid and in the sinus portion of the common carotid shows a sudden increase in the 40's, and it is rather high compared to that in the other portions in the 60's.

According to the study by $M_{IYAKE^{383}}$, the intima of the intraosseous artery is thickened much more remarkably than that of the aorta, and it is similar to that of the cardiac coronary, cerebral and renal arteries. However, according to the author's study with the T. I. method, it is not necessarily true with the aged although this portion shows a higher T. I. than the other portions in the younger group. The T. I. in the



Vol. 9

thoracic portion of the common carotid and in the bifurcated portion of the external carotid gradually increases along with the advancement of age, but the rate of the increase is small. Since the function of a vessel is effected by its diameter and by the thickening of the media and intima, the relation between the diameter and the T. I. of the vessel was first investigated. For example, in the thoracic portion of the common carotid which is elastic type, a trend is noted from Fig. 3 that the external diameter and the T. I. increase proportionally. On the other hand, in the intraosseous portion of the internal carotid which is pure muscular type and of the small diameter, the T. I. attains about four times as high as that in the thoracic portion of the common carotid while the external diameter is about 1/2 in size (Fig. 4). This



means that, if it is neglected to take into consideration the difference in structure of the arterial wall, bifurcation angle and other conditions, the intraosseous portion of the internal carotid should receive about four times as much mural pressure as the original portion of the common carotid receives. It may be important to analyze the T. I. of the carotid artery which varies by portion, by dividing it into two factors, namely, the dimensions of the media (M) and the dimensions of the intima (I) as well as to microscopically study the structure of the arterial wall.

Fig. 5. Increasing Rate of Intima, Media and Thickening Index (Orignal Portion of Comm. Carotid)

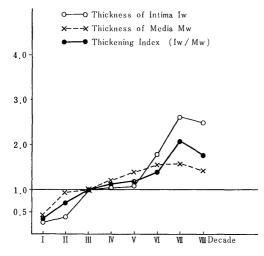


Fig. 6. Increasing Rate of Intima, Media and Thickening Index (Original Portion of Intern Carotid)

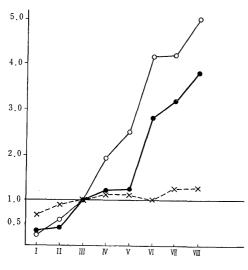
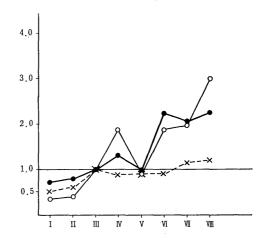


Fig. 7. Increasing Rate of Intima, Media and Thickening Index (Cavernous Portion of Internal Carotid)



The rate of increase in thickness of the intima and media of the carotid artery in its various portions was reviewed for various age groups against the thickness in the early 20's which was considered as the basic value of 1, since it is generally believed that the growth of an artery is completed at about that age (Figs. 5, 6, 7). As for elastic type arteries, the growth of the media is rapid in the childhood; it is rather slow in the teenage but it still continues even after the 20's. With the aged, the thickness becomes 1.5 times as much as in the 20's and 3.0 times as much as in the childhood. The intima, on the other hand, smoothly grows up to the age of

20 but it is not so thickend up to the 40's. After the 40's, howevever, the thickness of the intima rapidly increases so that it becomes 2.5 and 4.5 times as much as in the 20's and in the childhood, respectively. In the internal carotid artery, as shown in Fig. 6, the media smoothly grows up to the 20's and then it continues to increase in thickness although it is very slow, so that the thickness in the advanced age becomes 1.25 and 1.7 times as much as in the 20's and in the childhood,

respectively. In contrast to this, the thickness of the intima which increases along with aging, becomes 5 and 10 times as much as that in the 20's and in the childhood, respectively. A similar relation is also seen in the sinus portion of the common carotid artery and in the siphon portion (Fig. omitted).

As it is noted in Fig. 7, the rate of increase in thickness of the media as well as of the intima in the intraosseous portion of the internal carotid, is placed between that in the original portion of the common carotid and that in the sinus portion of the common carotid or in the siphon portion. The bifurcated portion of the external carotid is also similar to this pattern.

IV Microscopic Findings

The literature which systematically describes microscopic findings of human carotid artery covering its full length, is few in number, having been provided by HIERONTMI¹⁷⁾ (1956), KAMEYAMA²³⁾ (1960), OTSU⁴³⁾ (1962), and SHOZAWA⁴⁷⁾ (1963).

As the carotid artery various in the degree of thickening by portion, each portion has a different characteristics also from the histological point of view.

1) Original Portion of the Common Carotid Artery

In the original (thoracic) portion of the common carotid which is elastic type, some fibrous connective tissue is noted directly under the endothelial cells since the age of 2. The internal elastic membrane is mostly a series of single layers but it is partially composed of some layers like some loose threads. In the media, there are about 15 layers of lamella in a series. Soon after the birth, the elastic lamellae of the media which are directly under the internal elastic membrane are delicate; the interval spaces are wide; and collagenous substance is noted in those spaces. The external elastic membrane can not yet be clearly distinguished from the lamella of the media and collagenous substance is also noted in the external 1/3 of the media and in the adventitia. Since the age of 10, there are added intima thickening and collagenous change, and the internal elastic membrane sees disruption and multiplication of layers. Inside the media, some homogenized collagenous substances are increased and fine waste-silk-like elastic fibers are noted. The number of lamella of the media at this age is about 20. In an 11-year-old case of intracerebral teratoma, an atheromatous lesion was noted at mural side of the fibrously thickened intima and a vertical arrangement of spindle or oval cells of the intima was observed in the innermost laver.

Such changes increase along with aging. Increase and vertical arragement of elastic substance are generally noted in the "basal layer" of the intima as called by $J_{ORE5^{21.2}}$, and hyalinization or atheromatous lesion of collagenous fiber is more frequently noted in the innermost

101

basal layer of the intima than in the superficial layer. Fat-positive granules appear in the endothelial cells and in the layer directly underneath or in the vertically arranged cells about the internal elastic membrane (Photo. 14). After the age of 70, the internal elastic membrane is swelled, disrupted or made into fine fibers, and finally disappears.

In the media, the number of lamella is about 35 from the second half of the 20's to the first half of the 30's but it decreases along with aging. In the 80's, it becomes about the same as that in the childhood and, since the space between one another is markedly expanded and placed in a straight line, the distribution of lamellae looks like a pile of boards. In the spaces among the linearly distributed lamellae, hypertrophied muscular cells and collagenous substance are noted; in the interior 1/3 of the layer, sclerotic lesions are especially remarkable due to the coarseness and disruption of the lamellae themselves and due to the swelling and abnormal distribution of muscular cells. The fat which is often noted from the 20's appears in such a layer. Vascularization is noted in the interior and exterior layers of the media which corresponds to the atheromatous intima.

The external elastic membrane is either thick and linear or it is made into fine fibers, but in either case it is deeply dyed with Weigert's stain and then several lines are distributed close together in a bundle.

2) Sinus Portion of the Common Carotid Artery

Lesions which appear in the original portion age also noted in the sinus portion being advanced by 1 decade. In a 7-day-old infant, fibrous thickening of the intima was noted on 1 8 of the circumference of the vessel and the internal elastic membrane was disrupted into small pieces though it was minimal. The diffused fibrous thickening of the intima is always found in the teenage. An atheromatous lesion was noted on the 1/3 of circumference of the thickened intima in a leukemia case of 19-year-old sample. Generally, atheroma is more expanded here than in the original portion and it often expands to the internal layer of the media. In the internal layer of the media, fine elastic fibers and connective fibers are increased and the space between lamellae is expanded and the lamellae have been partially disrupted. Such changes of the media are observed even among younger samples (Photo, 5, 6). However, the number of lamella of the media, rapidly increases through the teenage and it is at most 30 in the 30's, being somewhat less numerous than in the original portion. The timing of linear distribution is also earlier than that in the original portion. Atheroma is frequently noted in the medium or innermost layer of the intima. In this portion and in the internal layer of the media, vertical arrangement of cells occurs since about 6 years of age and fatty granules appear covering a fairly large area since about 20 years of age (Photo. 15).

In the common carotid artery, sclerotic lesions which are common

among elastic type arteries are scatteringly seen but there are some local variations during the progress to the diffused thickening of the intima. There are certain localities where edematous hyaline swelling of collagenous fibers is seen only in the intima whereas any such change is hardly seen in the media (Photo. 4), and there are some portions where thickening is hardly noted in the intima while swelling or colliquation of the muscular cells is seen in the media, particularly in the layer near the intima (Photo. 5). In another portion, chages of the intima and media are sometimes seen simultaneously such as thickening of the intima, disruption of the internal elastic membrane, increase of dust-shaped or linear-dust-shaped elastic fibers in the internal layer of the media, and hyaline change of stroma (Photo. 6). Thus, presclerotic changes are not necessarily definite.

3) Cervical Portion of the Internal Carotid Artery

The region of the internal carotid about 1 cm distal to the bifurcation from the common carotid is an elastic-type-predominating muscular type vessel although the nature varies by each individual. In the intima, collagenous fibers and elastic fibers increase from the age of 2 and vertical arrangement of spindle muscular cells occurs in the innermost laver. Disruption, duplication or multiplication of the internal elastic membrane also appears from this age. In the internal layer of the media, lesions such as increase of fine tortuous elastic fibers and vertical arrangement and hypertrophy of muscular cells, and the degree of expansion of a lesion around the vessel are similar to those in the sinus portion of the common carotid artery (Photo. 11, 12). In some regions where the internal elastic membrane is weak or disappeared, the internal layer of the media is collagenized and the muscular cells are swelled and distributed irregularly; they seem to transfer from the media towards the intima (Photo. 13). It is thought somewhat different from pure elastic type arteries in that the internal elastic membrane is generally big and atheroma appears both in the internal and superficial layers of the intima. It is very rarely observed that a relatively big fibric bundle of muscular cells running in the longitudinal direction of the vessel appears in the medium or external layer of the media in the bifurcated portion of the internal carotid and the sinus portion of the common carotid. Such a fibric bundle of muscle shows a similar reaction to the adjacent tissue of the media in case of sclerosis, and this may be said a deformity of the vascular wall structure (Photo. 11).

The so-called cervical portion, further peripheral portion of the internal and external carotid artery, is a muscular type artery and the intima is least changeable but it appears in the form of "elastic-hyperplastic intima thickening" in which Fuchselin positive granules or fine fibers increase diffusely. A bifurcation or duplication of the thick distinctive internal elastic membrane, if any, is minimal. The media is relatively thick and it has fine elastic fibers in a small quantity. These changes resemble those in the main portion of the hepatic and gastic arteries.

4) Intraosseous Artery

In the portion of carotid artery running through the petrosus portion, the internal elastic membrane is very thick and dark, and its surface is either linear or coarsely uneven consisting of some small tortuosity. The direct canal side of such elastic membrane is covered with a layer of endothelial cells, but where the intima is thickened, there are seen inside the internal elastic membrane Fuchelin positive substance which looks like a fine network or accumulated dust and is dyed homogeneous red by van Gieson's stain. As the thickening is advanced, the internal elastic membrane is duplicated in layer and becomes fine. Atheroma is sometimes formed in the surface layer of the "elastic-hyperplastic intima thickening" due to fibrous thickening and its degeneration.

There are some cases in which organized mural thrombi are adhered to the surface of the thickened intima (Photo. 9, 10).

Atheroma mostly appears in the surface layer of the intima. Vertical arrangement of muscular cells is also seen in the innermost layer of the thickened intima and in its adjacent media (Photo. 16, 18).

The cells which are arranged vertically to the inner surface of the vessel are spindle and they can be well dyed in yellowish red with van Gieson's stain and in bricque color with Masson-Trichrom's stain. In the basal region of the young muscular cells which are vertically distributed, there are fine elastic fibers running at right angles to these muscular cells and they seem to make a boundary against the natural muscular fibers of the media (Photo. 15, 16,18).

In serial sections, the both ends of the elastic fibers seem to be connected to the thick internal elastic membrane which originally existed (Photo. 17, 18). That a complicated duplication or multiplication of the internal elastic membrane is the prerequisite of the thickening of intima as stated by IwAO^{18),19)} in his observation of the radial artery, can be referred only to the radial, basilar artery and intraosseous portion of the vertebral arteries even among muscular type arteries. Not every thickening of intima follows this procedure. It is a matter of course that most of the thickening of intima is due to the thickening of elastic layer and to the proliferation of cells of the intima itself; and that the thickening of media is also due to the proliferation of cells which constitute the media. However, it is interesting to note the relation between "vertical arrangement" which is observed on the boundary between two lamellae, and the duplication of internal elastic membrane.

The growth of the adventitia of the intraosseous artery is consider-

ably weak. The connective fiber is small in number. Besides the external elastic membrane which is bright running with a somewhat minimal tortuosity, there are seen only a few elastic fibers which are disrupted running circle outside the external elastic membrane.

5) Siphon Portion

The thickening of the arterial wall rapidly becomes remarkable from the age of 40 (Fig. 1). This portion shows the strongest sclerosis among various portions of the carotid artery. Thickening of the intima is mostly a lesion composed of a mixture of atheroma and calcification as shown in Photo. 1. It begins to appear at the age of 2, and "elastichyperplastic intima thickening" is noted circumscribedly together with duplication or multiplication of the internal elastic membrane. The internal elastic membrane in the region without intima thickening looks thick and firm, but it is mixed in various degrees with degenerations such as swelling, "caterpillar type" as named by HIERONYMI, disruption (Photo. 19, 20, 21) and calcification (Photo. 26). In contrast to such various degenerations of the internal elastic fiber, multiplication of the internal elastic membrane accompanied by intima thickening is a "hyperplastic" change and it is an interesting finding being contrasted to the previous finding up to the first half of the 30's (Photo. 7, 8).

However, the relation between a hyperplastic change of the elastic membrane with inntima thickening and various degenerations of the internal elastic membrane without intima thickening becomes vague from the latter half of the 30's; fibrous-diffused intima thickening covers the circumference; swelling and calcification occur even in the duplicated layer and fibrous portion of the internal elastic membrane; such intima can form atheroma by fusion or homogenization of the cells and fatty degeneration of the fibrous tissue in the superficial layer.

The media, together with the intraosseous portion, is originally thin and hardly causes microscopic changes, but fine spiral elastic fibers are noted in the internal layer of the media at the portion of intima thickening and compensatory hypertrophy (?) of muscular cells is also seen. However, such change of the media is much less than that in elastic type arteries.

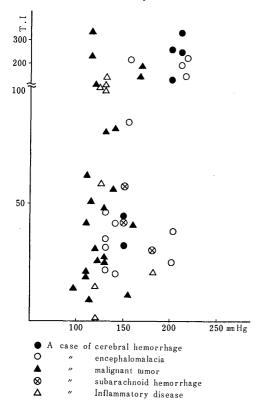
Fine elastic fibers which lie on the base of the muscular cells vertically arranged in the internal layer of the media are also found in the siphon portion. As previously stated, calcification appears in the internal elastic membrane, gradually grows into a mass or knob, and, passing though the internal elastic membrane, extends to the adjacent tissue (Photo. 22, 23). Calcification rarely begins in the external elastic membrane as shown in Photo. 24 and extends toward the external layer of the media and the adventitia.

Generally, the growth of the adventitia is very weak and in case of the aged with marked arteriosclerosis, the adventitia has sometimes almost disappeared.

V Blood Pressure and the Degree of Thickening

KAMEYAMA has preported that 96% of the cases of severe arteriosclerosis in the siphon portion showed hypertension which was moderate

Fig. 8. Blood Pressure and Thickening Index in Siphon Portion of Carotid Artery



or more in severity. However, according to the observation of the author on the relation between the systolic blood pressure and the degree of the thickening in the siphon portion with autopsied cases of over the age of 40, hypertensive cases did not necessarily show higher degree of thickening, as indicated in Fig. 8. From the point of view of pathological cause of death, cases of cerebral hemorrhage indicated hypertension of higher than 200 mmHg and T.I. of above 100; cases of traumatic subdural or cortical hemorrhage indicated the blood pressure of 150 mmHg and T.I. of 44.13.

With the cases of encephalomalacia, the blood pressure ranged from 130 mmHg to 215 mmHg and T. I. was scattered widely from 20 to 200 or more. It is deemed that, whereas cases of cerebral hemorrhage suggest some relation between T. I. in the siphon portion and blood pressure, encephalomalacia cases indicate

no relation whatsoever between the two.

With some cases of irradiated cervical lymphosarcoma, compression and stenosis of the vessel due to tumor were noted in the sinus portion of the common carotid and its periphery; with the cases of intracranial tumor and tuberculous meningitis which might cause elevation of cerebral pressure, T. I. in the siphon portion was high although they were not hypertensive. With 2 leukemia cases out of 3, infiltration of leukemic cells was seen in the adventitia of the siphon portion and of the intraosseus portion, and T. I. was higher than the standard value of same age.

DISCUSSION

According to the macroscopic and microscopic observations of the carotid artery in its full length, there is noted a certain characteristics in early and last stage of sclerotic lesions in each portion.

a. Characteristics of sclerotic lesion by portion

1) The common carotid is an elastic type artery, and its lesion is mostly common with the aortic change which has been reported by MOVAT³⁹⁾, TAYLOR⁴⁸⁾, GRESHAM¹⁵⁾ and WILLENS⁵¹⁾, and it is based on diffused thickening of the intima.

At the time of birth there is a defined and relatively thick internal elastic membrane adjacent to the endothelial cells, and fine granular elastic substance exists inside the membrane. Soon, connective tissue and a few elastic fibers appear under the endothelial cells. The internal elastic membrane shows some localized disruption or fragmentation. Elastic fiber, collagenous fiber and smooth muscle fiber appear in the deep layer of the intima. WILLENS classifed the intima into subendothelialfibrous zone and musculo-elastic layer but HIERONYMI classified it into elastic-hyperplastic layer and elastic-muscular layer. He further explained that the layer directly under the endothelium where previously insudated plasma and argentaffine fiber existed will become later a connective tissue layer and that the thickening of the intima consists mostly in proliferation of the elastic-hyperplastic layer.

In the media, many lamellae which are thiner than the internal elastic membrane are lined up, and among the lamellae, collagenous fibers and smooth muscle fibers are arranged mostly annularly but in part longitudinally. The arrangement of the lammellae and muscle cells at internal 1/3 of the media is coarse and irregular.

The phenomenon such as increase and accumulation of mucopolysaccharide or degeneration and disappearance of elastic fibers mostly in the innermost layer of the intima and at the internal layer of the media is the most primary histological finding of sclerotic lesion of the aorta, which phenomenon is called "edematous swelling" by MOVAT, ARAI², et al. According to the observation of the common carotid artery by the author, the primary lesion varies by location even in the same specimen: where no change is noted either in the intima or in the media; where slightly edematous and fibrous thickening is noted only in the intima; just opposite to this, where edematous change is noted only in the media; or where hyperplastic or edematous change is noted both in the intima and the media. In order to explain the fact that there are various kinds of sclerotic lesion from its start, a mere description that arteriosclerosis is started by the "insudation" of plasma into the intima is not adequate, but it is deemed that metabolism of the arterial wall and the effect caused by the hemodynamics at that location are important factors. In any case, these localized changes gradually extend to the entire arterial wall and become fibrous diffused intima thickening.

Macroscopic findings of the primary lesion are fatty streaks or yellow dots, in which fat deposits in the thickened intima. This fatty substance scatteringly exists in the endothelial cells and in the cytoplasm of the superficial layer of the intima which is directly under the former.

On the contrary, atheroma is often observed microscopically as a fatty deposit mostly in the middle or innermost layer of the intima. In the layers of the intima and media adjacent to the internal elastic membrane, there appear spindle muscle cells which are vertically arranged in the direction to the canal side. These cells are deemed to transfer in the primary sclerotic lesion³⁵⁾. The portion where such a phenomenon occurs is called by ARAI as the "area of vital reaction of the artery" and this layer as the "functional layer". In the cells which are vertically arranged in the so-called functional layer, there appears fine granular fat, and they then seem to transit to form cells which are numerously seen in the middle layer of the intima. Such fatty cells become swelled and fused and, together with hyalinization of stroma, they finally form atheroma. This process coincides with the view that edematous swelling plays an important role in the formation of atheroma.

2) In the thoracic portion of the carotid artery which is a submuscular type, the media has many fine elastic fibers and is thick in width. The internal elastic membrane is thick and defined being similar respectively to that of organ arteries, f. i. gastric, hepatic, coronary, radial and renal arteries which are muscular type. During the course of sclerosis, a change of this internal elastic membrane antecedes; and "elastic-hyperplastic intima thickening" as called by JORES²¹⁾ is generally observed in the intima, and when the thickening is remarkable, it is covered with a layer of connective tissue. The intima thickened like this is hardly deposited by fatty substance, and accordingly, formation of atheroma is also very rare.

3) In the intraosseous and siphon portions of the internal carotid artery which belongs to the muscular type, the intima thickening is generally nodular. After having studied the basilar artery, KAMURA has reported that the internal elastic membrane of the basilar artery is so thick that, during the course of diffused thickening, very conspicuous is the period without intima thickening but only with the change of internal elastic membrane. The nodular intima thickening begins with the change that dust-like elastic fibers increase concurrently with the bifurcation, duplication or splitting of the internal elastic membrane and then the fibrous connective tissue grows in the superficial layer, Degeneration of this fibrous tissue later forms atheroma. This is frequent in the middle or superficial layer of the intima. The internal elastic membrane which originally seemed firm is now decreased in its stainability, swelled and joined by calcification and deposit of fatty substance; and it looks like an acid-corroded wire and is seemingly fragile. Sometimes a series of lump-like unevenness also appears in the elastic membrane.

This is a change from HIERONYMI's caterpillar type elastica, and it is equivalent to OTSURU'S A-type or B type⁴⁴⁾ and KAMURA'S nodular type elastic membrane. Anyway, there is noted no thickening of the intima in the portion where there is such a change of the internal elastic membrane.

As for the reason why, on the one hand, there is localized nodular thickening of the intima and, on the other hand, there appears a portion with degenerative change of the internal elastic membrane at the opposite side but without thickening of the the intima, no adequate clarification has been given. For example, NARITA⁴¹⁾ reported that when the common carotid artery of the rabbit is bent into the shape of "S" and covered with resin, remarkable fibrous intima thickening was caused on the wall of the interior curvature; and SHOZAWA⁴⁷⁾ reported that an observation of the intraosseous curvature of the internal carotid artery revealed strong collagenation and more atheromatous change on the exterior curvature. Thus, the finding or the prospect in this connection is not necessarily definitive. However, according to the author's observation, the interior curvature seems to be more with intima thickening and atheroma, and the exterior curvature more with degenerative change of the internal elastic membrane. Anyway, the regional difference in such changes seems to be affected by a hemodynamic factor-particularly, change of the internal elastic membrane seems to be frequent on the side of hemodynamic impact against the arterial wall, and atheroma formation on the other side.

According to DROPMANN¹⁰⁾ who analyzed, from the point of view of hemodynamics, the portions in the curvature of the artery and in the bifurcated portion of the common carotid where atherosclerosis is frequent, atheroma appears at the inside wall of the curvature, and at the outside wall of the bifurcated portion if the bifurcated angle is large or at the inside wall of the bifurcated portion if the bifurcated angle is small; and change of elastic lamella appears at the opposite side of the wall in each case. For the cause of these phenomena, he has attached great importance to the hemodynamic impact which affects the arterial wall, and has theoretically explained that atheroma apts to occur at "hydrostatic minimum" where the impact is minimum, or where wall pressure is decreased. On the other hand, DUGUID, CRAWFORD⁵⁾, LEVENE, et al., explained that thickening of the intima is caused by organization of mural thrombi. However, according to the author's observation, such was rare but secondary mural thrombi were seen rather often. The vertical arrangement of muscle fiber which occurs in the innermost layer of the intima adjacent to the internal elastic membrane and in the internal layer of the media is seen both in elastic type arteries and in muscular type ones. Particularly in muscular type arteries, fine elastic fiber is sometimes shining in the basal portion of the vertically arranged muscular cell line. This fine fiber separates the vertically arranged muscular cells in the inner layer from the ring muscular fiber in the outer layer, and it is connected to the original elastic membrane at the both ends. Such a finding suggests that the elastic fiber or elastic substance grows in the intercellar spaces which have some differences in metabolism or potential energy.

It is previously mentioned that arteriosclerosis appears differently both in quantity and in function according to the size and locality of the artery. This seems to be based on the difference in the "area of vital reaction" of the arterial wall. In elastic type arteries, the deepest elastic muscular layer of the thickened intima plays a functional role in the deposit of fatty substance and the atheroma formation. In muscular type arteries, such as the carotid artery which runs though the base of the skull, there is little elastic-muscular layer; calcification can occur in this layer, but it dose not participate in the thickening of the intima. OTSU⁴³ has also pointed out that the thickening of the intima is due to the change of the internal elastic membrane. It is particularly interesting to note the vertical arrangement of muscular cells of the media directly under the internal elastic membrane in relation with the function of the media against the thickend intima.

b. Calcification

Calcification was macroscopically seen in the siphon portion in as high as 59% of the samples over the age of 50, and microscopically in a part of the internal elastic membrane already at the age of 12. KAMEYAMA⁴²⁾ reported that deposit of calcic element in the intima was almost always noted in the aged samples even in the form of calcified ring. Since the siphon portion indicates not only the highest value for fibrous or atheromatous thickening of the intima among various portions of the internal carotid but also calcification, it is deemed naturally that elasticity of the wall is remarkably decreased and functional disturbance is caused. PENDERGRASS (1948)⁴⁵⁾ reported a case of calcification in the siphon portion in a 4-year-old patient with hypertension and vitamin intoxication. It is stated in the literature of COLE⁴⁾ that calcification in cases of defect of visual field, exophthalmus, and FOSTER KENNEDY syndrome was reported by SCHIFF-WERTHEIMER, HARTMAN, and GUILLAUMAT, respectively.

Having radiologically reviewed calcification in the siphon portion, $COLE^{4}$ reported that calcification was noted in 50 cases (1.2%) among 4,100 skull X-ray films; that the average age for the cases of

calcification was 63.3; that cerebral circulation disturbance was seen in 27 cases; and that MENIERE'S syndrome and paralysis of oculomotorius nerve were also noted. The frequency of calcification observed radiologically is much less than that in the author's study of autopsied specimens.

According to the results of radiological study of calcification in the cervical portion of the carotid by $R_{ING^{40}}$ et al., calcification was noted in 216 cases (21.6%) among 1,000 cases over the age of 40 and in more than 70% of the cases over the age of 80. The author's study with 64 cases over the age of 60 revealed only 7 cases (10.9%) of calcification in the sinus portion, 1 case (1.6%) in the cervical portion of the external carotid and 1 case (1.6%) in the cervical portion of the internal carotid.

According to the report of KAMEYAMA, embolism of the carotid artery was seen in 2 cases (1.2%) out of 166 cases over the age of 60; according to the author, 1 case (1.6%) out of 64. GURDJIAN's¹⁶ observation by vascular X-ray revealed stenosis of the sinus portion of the common carotid in 20% and complete embolism of that portion in 18%; and WHISNANT'S⁵⁰ autopsy study revealed stenosis of more than $\frac{1}{20}$ of the canal in 40% of the cases over the age of 50. These figures are much different from the author's 14% over the age of 60.

It may be inevitable to see a difference in the results between radiological study and autopsy study, but, among the Japanese, calcification is remarkably frequent in the siphon portion whereas it is rare in the sinus and cervical portions of the carotid artery. In the comparison of the trend among the Japanese with that in western nations such as high frequency of calcification in the carotid artery, particularly in the sinus portion, in addition to the high occurrence of ulcer, thrombogenesis, narrowing and obstruction, it is imagined that such difference is affected by the difference in the mode of life, food and metabolism, and furthermore in the customs and internal spiritual life.

CONCLUSION

For the observation of arteriosclerosis of the carotid, macroscopic and microscopic studies were performed on a total of 186 pieces of carotid artery and aorta for the full length obtained from 101 autopsied cases ranging in age from the 0's to the 70's. The following conclusions were obtained.

1) In the macroscopic finding of the carotid artery, sclerotic change mostly consists of fibrous plaque and atheroma and localities of these changes were, in descending order, sinus portion of the common carotid, siphon portion, bifurcated portion of the internal carotid, thoracic portion of the common carotid, intraosseous portion of the internal carotid (arterial canal) and cervical portion of the internal carotid. In the cervical portions of the internal and external carotid arteries, milk white turbid thickening is the main change and atheroma and fibrous plaques are hardly seen.

2) In comparison of the thickening index (T.I.) for the carotid artery, the value of intima/media $\times 100$, with GORE's index (G.I.) for the aorta, arteriosclerosis is increased with the advance of age in both cases and the degree of sclerosis in the aorta and in the sinus portion and the siphon portion of the carotid rapidly increases after the 40's.

3) It is revealed in the observation of the same individual regardless of his age that the aorta and the carotid are not necessarily parallel in the degree of arteriosclerosis. Particularly sclerosis of the siphon portion is far advanced in many cases than that of the aorta.

4) In the original portion (thoracic portion) and the bifurcated portion (sinus portion) of the common carotid, external diameter of the vessel is enlarged as the thickening index is increased. This is due to the fact that thickening and extension of the media itself appears along with the aging and the progress of arteriosclerosis. In contrast to this, in the intraosseous portion of the internal carotid, the media is hardly affected by the increase in the thickening index and accordingly the external diameter is not enlarged.

5) Primary sclerotic lesions which can be pointed out macroscopically are fatty streaks and yellow dots and their microscopic lesion consists in fatty deposit in the endothelial cells and directly thereunder. These lesions appear in elastic type arteries or at elastic-type-dominant arterial walls such as the common carotid and the aorta, but they do not occur in muscular type arteries. Atheroma and fibrous plaque are seen in both.

6) For these lesions, however, the main locality of deposit of fatty substance and cholesterol varies more or less by the nature of the arterial wall. Deposit is frequent in the middle or innermost layer of the intima in case of the common carotid artery which is an elastic type, and in the middle or superficial layer in case of the intraosseous portion and the siphon portion of the internal carotid artery.

7) From the common carotid artery to the siphon portion, the ultimate phase of arteriosclerosis assumes a form of diffused intima thickening but nodular or localized intima thickening appears during the process. However, its initial change varies by locality: Thickening is often preceded by a change of the media in elastic type arteries and of the internal elastic membrane in muscular type arteries especially in the siphon and intraosseous portions.

8) The "vertical arrangement" of muscular cells, which generally appears as one of the hyperplastic changes at the primary stage of arteriosclerosis in the innermost layer of the intima and in the superficial layer of the media both being adjacent to the internal elastic membrane, can be seen anywhere throughout the entire carotid artery.

9) Calcification is dense in the siphon portion. Calcification in the internal elastic membrane is already noted at the age of 12. Calcification in other portions is very rare among the Japanese.

10) Sclerotic lesions in the carotid artery which would cause narrowing of more than $\frac{1}{2}$ of the canal are fairly frequent when one is aged, but it is very rare among the Japanese to see complete obstruction due to thrombus, etc.

11) Among cerebral hemorrhage cases, many indicate high thickening index in the siphon portion, but among encephalomalacia cases the locality of high thickening index is not definite.

This study was made with the support of scientific research fund of the Education Ministry.

The author sincerely wishes to thank Professor MATSUOKA for his cordial direction and review during the course of this study.

REFERENCES

- 1) Adams, J. E. and Smith, M.C. and Wylle, E. J. : Surg. 53 : 449 (1963).
- 2) ARAI, T. : Tr. Soc. Path. Jap. 51 (2) : 290 (1962) (Japanese).
- 3) CHLEBUS, H. : Amer. Heart J. 64 : 22 (1962).
- 4) COLE, M. and DAVIES, H. : Brit. J. Radiol. 36 : 289 (1963).
- 5) CRAWFORD, T. : J. Atheroscler. Res. 1 : 3 (1961).
- 6) DECKER, K. : Ann. Radiol. 6: 37 (1963).
- 7) DEGUCHI, N. : J. Nagasaki Med. Ass. 38 (3.4) : 223 (1963) (Japanese).
- 8) DILENGE, D. : Ann. Radiol. 6 : 27 (1963).
- 9) DOGULU, S. : Neurol. 11 : 22 (1961).
- 10) DROPMANN, K. : Z. Kreislaufforsch. 52 : 171 (1963).
- 11) FUJITA, T. : J. Nagasaki Med. Ass. 39 (7) : 613 (1964) (Japanese).
- 12) FUKUDA, N. : J. Nagasaki Med. Ass. 39 (3) : 222 (1964) (Japanese).
- 13) FRIEDMAN, M. and BYERS, S. O. : Arch. Path. 76 : 99 (1963).
- 14) GORE, I. and TEJADA, C. : Am. J. Path. 33 (5) : 875 (1957).
- 15) GRESHAM, G. A. and HOWARD, A. M. : J. Atheroscler. Res. 3 : 161 (1963).
- 16) GURDJIAN, E. S., et al. : J. A. M. A. 176 (3) : 194 (1961).
- 17) HIERONYMI, G.: Über die altensbedingten Formwändel elastischer und muskulärer Arterien. Sitzungsberichte der Heiderberger Akademie der Wissenschaften. 3 (1956).
- 18) Імао, Ј., Матѕиока, S., et al : Tr. Soc. Path. Jap. 49 (3) : 719 (1960) (Japanese).
- 19) INAO, J.: J. Nagasaki Med. Ass. 36 (5.6): 379 (1961) (Japanese).
- 20) JETT, J. and SCOTT, G. : J. Am. Geriat. Soc. 8: 245 (1960).
- 21) JORES, L. : Wesen und Entwickelung der Arteriosklerose. Siesenbaden,

J. F. Bergman. (1903).

- 22) JULIAN, O. C., Dye, W. S., et al. : Arch. Surg. 86 : 803 (1963).
- 23) KAMEYAMA, M. and OKINAKA, Sh. : Neurol. 13 : 279 (1963).
- 24) MAMEYAMA, M., et al. : J. Jap. Soc. Intern. Med. 49 (5): 529 (1960) (Japanese).
- 25) KAMURA, S., et. al. : Tr. Soc. Path. Jap. 49 (3) : 720 (1960) (Japanese).
- 26) KAMURA, S.: J. Nagasaki Med. Ass. 37 (11): 368 (1962) (Japanese).
- 27) KLINGELHÖFER, D. and MEYER, W. W. : Virch. Arch. Path. Anat. 335 : 529 (1962).
- 28) LLENAS, S. J. : Ann. Radiol. 6 : 75 (1963).
- 29) LUSZTIG, G. : Z. Ges. Inn. Med. 18 : 320 (1963).
- 30) Матѕиока, S. et al. : Tr. Soc. Path. Jap. 50(2) : 220 (1961) (Japanese).
- 31) MATSUOKA, S. : Psychiat. Neurol. Jap. 43 : 146 (1934) (Japanese).
- 32) MATSUOKA, S. : Tr. Soc. Path. Jap. 33 : 380 (1938) (Japanese).
- 33) MATSUOKA, S. : Jap. J. Clin. Exp. Med. 39 (9) : 20 (1955) (Japanese).
- 34) MATSUOKA, S. : SAISHIN IGAKU 11 (4) : 780 (1956) (Japanese).
- 35) MATSUOKA, S. : Tr. Soc. Path. Jap. 52 : 115 (1963) (Japanese).
- 36) MCMULLEN, J. B. : J. Lancet 83 : 236 (1963).
- 37) MIYAKE, M. : Acta anat. Nippon. 2 : 953 (1929) (Japanese).
- 38) MIYAKE, M. : Acta anat. Nippon. 2 : 449 (1929) (Japanese).
- 39) MOVAT, H.Z., HAUST, M. D. and MORE, R. H. : Am. J. Path. 35 (1): 93 (1959).
- 40) NAKAGAWA, S. and MATSUOKA, S. : Acta. med. Nagasa'i. 7 (1.2): 38 (1962).
- 41) NARITA, F. et al. : J. Geriat. 6 : 268 (1962) (Japanese).
- 42) NOGUCHI, T. et al. : Tr. Soc. Path. Jap. 52 : 112 (1963) (Japanese).
- 43) OTSU, S. : J. Geriat. 6 : 38 (1962) (Japanese).
- 44) Orsuru, S.: J. Nagasaki. Med. Ass. 36 (9.10): 468 (1961) (Japanese).
- 45) PENDERGRASS, E. P. : J. A. M. A. 137 (12): 1030 (1948).
- 46) RING, B. A. and EDDY, W. M. : J. A. M. A. 184 : 866 (1963).
- 47) SHOZAWA, T. : J. Geriat. 81 (1963) (Japanese).
- 48) TAYLOR, C. B. et al. : Arch. Path. 76 : 449 (1963).
- 49) WEXLER, B. C. and TRUE, C.W. : Circ. Res. 12 : 659 (1963).
- 50) WHISNANT, J. P. et al : Arch. Neurol. 4 : 119 (1961).
- 51) WILLENS, S.L.: Am. J. Med. 17 (4): 825 (1951).
- 52) YANO, T. : Acta med. 29 (9) : 115 (1958) (Japanese)
- 53) YOSHIDA, Y., et al. : Tr. Soc. Path. Jap. 49 (3) : 820 (1960) (Japanese).

EXPLANATION OF PLATES

- Photo. 1. 5550, 66 year old male (Lymphosarcoma. G. I.: 4.55, T. I.: 348.70).
 Siphon portion. Canal stenosis is remarkable; extensive calcified focus (black) and fatty focus (grayish white) are coexisting in the intima and the media. Sudan III stain.6×. (G.I.: Sclerotic index of the aorta; T. I.: Thickening index)
- Photo. 2. 5750, 87 year old male (Intracerebral hemorrhage, G. I. : 46, T.1. : 226. 39). Sinus Portion of the common carotid artery. Calcificaion (white portion at the right lower area) in the thickened intima and media. Weigert stain. 4.3×.
- Photo. 3. 6076, 62 year old male (Rectal cancer. G. I. : 41.5, T. I. : 390.34 Petrosus portion. Atheromatous intima thickening is covered with "fibrous Cap". Weigert-Masson-Goldner stain. 7.3×.
- Photo. 4. 5856, 12 year old male (Pineal tumor. G. I. : 0.03, T. I. : 22.25). Bifurcated portion of the internal carotid artery. Edematous intima thickening is noted in part but the media is hardly remarkable. Weigert stain. $100 \times$
- Phoro. 5. 5548, 19 year old female (Acute myeloid leukmia). G. I. : 0.03, T. I. : 16.02) Sinus portion of the common carotid artery. Intima thickening is minimal but remarkable edematous thickening is noted in the interior -1/2 of the media. Mallory stain. 100×.
- Photo. 6. 5856, 12 year old male. (Same as photo. 4). This portion indicates atheromatous thickening of the intima and edematous thickening of the media. Weigert stain. 100×.
- Photo. 7. 5712, 21 year old famale (Acute myeloid leukdmia. G. I.: 0.73, T. I.: 43.66). Siphon portion. "Elastic-hyperplastic intima thickening" is noted on one side of the vascular wall (lower part of the picture) and calcification of the internal elastic membrane on the other side. H. E. stain. 40×
- Phhto. 8. 6160, 10 year old male (Pineal tumor. G. I. : 0.6875, T. I. : 21.78). Siphon portion. One side of the internal elastic membrane indicates localized swelling and disruption without intima thickening; the opposite side indicates "elastic-hyperplastic intima thickening". Weigert-Masson-Goldner stain. 200×.
- Photo. 9. 6495, 60 year old male (Intracerebral hemorrhage. G. I. : 16.2, T. I. : 45.41). Petrosus portion. The intima shows "elastic-hyperplastic thickening" in its lower layer and deposit of organized mural thrombus in its upper layer. H.E. stain. 100×.
- Photo. 10. 6495, 60 year old male. (Same as above). Weigert stain $100 \times$.
- Photo. 11. 6018, 17 year old male (Mitral stenosis. G. I. : 0.148, T. I. : 12.55). Bifur cated portion of the internal carotid artery. The intima shows "vertical arrangement" of cells and the media shows running anormaly of a group of muscular cells. H. E. stain. 100×.
- Photo. 12. 6018, 17 year old male. (Same sample as above). In this portion, "vertical arrangement" is seen in the intima and in the media directly under the internal elastic membrane. Cells of the intima and of the media are alike. H. E. stain. 200×.
- Photo. 13. 6018, 17 year old male. (Same sample as above). The internal elastic membrane has become fine or disappeared. Muscular cells of the media seem to have trespassed on the intima. H. E. stain. 200×.
- Photo. 14. 5704, 29 year old male (Rheumatic aortic insufficiency. G. I.: 0.51, T. I.: 23.98). Original portion of the common carotid artery. In the vertically arranged cells of the intima adjacent to the internal elastic membrane, fat is stained. Sudan III stain. 200×.

ARTÉRIOSCLÉROSIS OF CAROTID

- Photo. 15. 5583, 50 year old male (Rectal cancer. G. I. : 6.4, T.I. : 63.09). Siphon portion. Vertical arrangement of cells is seen in the lower layer of the internal elastic membrane or inside of the media. H. E. stain. 100×.
- Photo. 16. 5518, 10 year old male (Cerebral tumor; glioblastoma. G. I. : 0.03, T. I. : 8.50). Petrosus portion. Vertical arrangement of cells is seen in the media adjacent to the internal elastic membrane. Weigert-Masson-Goldner stain. 200×.
- Photo. 17. 6110, 15 year old female (Subacute necrotic encephalopathy. G. I.: 0.03, T. I.: 11.90). Siphon portion. A delicate new elastic membrane is bifurcated from the thick firm internal elastic membrane and a double layer is formed. Weigert-van Gieson stain. 100×.
- Photo. 18. 5583 (Same as Photo. 15. T. I. : 48.12) Petrosus portion. There are fine elastic fibers in the base of vertical arrangement inside of the media. Weigert-Masson-Goldner stain. 200×.
- Photo. 19. 5865, 25 year old female (Rheumatic mitral stenosis. G. I. : 0.03, T. I.
 : 22.50). Siphon portion. Mural thrombus (mt) is noted in a part of the internal elastic membrane which is swelled or disrupted. The media is thin and the external elastic membrane is very fine. Weigert stain. 100×.
- Photo. 20. 5865, 25 year old female. Continued from the left end of the above picture. The internal elastic membrane is doubled; the one on the canalside is swelled and fragile, and it has become a caterpillar type. Weigert stain. 200×.
- Photo. 21. 6085, 54 year old female (Encephalomalacia. G. I. : 14.5, T. I. : 25.61).
 Siphon portion. The internal elastic membrane has calcification and disruption and it has partially disappeared. Weigert stain. 100×.
- Photo. 22. 6085, 54 year old female. (Same sample as above). Vertical arrangement of muscular cells has appeared where the internal elastic membrane disappeared. H. E. stain. $100 \times .$
- Photo. 23. 5515, 52 year old female (Pancreatic cancer. G. I. : 0.32, T. I. : 39.90). Siphon portion. Calcic deposit extends from the internal elastic membrane towards the intima. H. E. stain. 100×.
- Photo. 24. 5515 (Same as above. T. I. : 26.99). Cavernous portion. Calcic deposit is remarkable in the external elastic membrane. 200×.

