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Contribution to the knowledge of senile arterial changes. (On the senile fibrosis of the arterial wall.)

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Translated from: Frankfurter Zeitschrift fuer Pathologie, 41: 120-135 (1931).

Although the literature dealing with arterial changes at various age levels is quite extensive, this question has not been investigated with sufficient versatility and finality heretofore. In the past, researchers (Jores, Alb. Aschoff, Hallenberger, Oppenheim, Wolkoff) directed their attention almost exclusively to the senile changes of the inner arterial membrane and subjected the development and alterations of its layers to a thorough investigation. The senile alterations of the central arterial membrane have been treated relatively little (K. Dietrich). Only a few authors (Gruenstein, Staemmler) dealt in detail with its structure in correlation with age. And yet, the senile changes of the central membrane undoubtedly are of great importance for the understanding of socalled arterial "detrition" in advanced age.

From this point of view, Staemmler's work, in which he points to an increase in the amount of connective tissue present in the media of muscular type arteries with advanced age, deserves particular attention. He observed this process in the art. lienalis and art. renalis and calls it "fibrous degeneration" of the arterial musculature. However, Ssobolew, long before Staemmler, reported a considerable development of connective tissue in the wall of the art. iliaca com. and in the aortal wall, indicating a type of "cirrhosis" of the arterial wall. He did not present an exacter description of this process and failed to point out a correlation to age.

Finally, K. Dietrich recently mentions an increase in the collagenous substance in the media with reference to age. However, he did not investigate this process more closely, since his attention was directed primarily to the changes in the muscular elements in dependence on blood pressure fluctuations.

In view of the great interest inherent in the investigation of senile changes of the media of both muscular as well as eleastic arteries, I have undertaken research into the structural alterations of the central arterial membrane in correlation with age, with principal stress on the development of the collagenous substance occurring therein.

Material and method of the investigations.

In order to gain a more precise idea of the amount of collagenous substance in the media for every single case, consideration had to be given to the fact that the connective tissue fibers are covered by a chromotropic intermediate substance upon ordinary staining (Ssolowjew, Schultz). Hence it is absolutely necessary to differentiate between the collagenous substance and the intermediate substance in any evaluation of the change in the former's quantity in the arterial walls with respect to age. According to Ssolowjew data, sparse, lossely situated connective tissue fibers appear in the arterial wall when exposed to the effects of potassium and soda lye solutions in concentrations of 0.1% to 1%, which are no longer covered by the chromotropic intermediary substance. Based on these data as well as on the investigations of other authors (Hansen, Tretjakow), a number of materials may be used to dissolve the chromotropic, mucoid substance; in addition to caustic soda solutions, these include chromic acid, picric acid, osmic acid, potassium manganate and the lye solution recommended by Hansen, consisting of equal parts baryta water and lime water and 10% NaCl.

Based on the literature quoted here, I treated a number of arterial specimens with the reagents indicated in preliminary tests, in an attempt to effect a complete dissolution of the intermediary substance without noteworthy damage to the structure of the arterial wall. Pieces of aorta, fixed in 95% alcohol, were submerged in various solutions (2-6-12-24 hours), i.e. in a KOH and NaOH solution in a concentration of 3:100, up to 1:1,000, as well as in 1% chromic acid and picric acid, and in Hansen's mixture.

After treatment with the reagents, the specimens were washed for several hours under running water and imbedded in paraffin following preparation with alcohol and chloroform. Staining of the sections with van Gieson, Mallory and Unna's polychromic methylene blue. I was able to determine as a result of these tests that Hansen's mixture is most suitable and completely meets the requirements. Staining with polychromic methylene blue eliminates the chromotropic substance, while the remaining elements of the arterial wall stain normally and do not suffer noteworthy damage. The preparations stained with van Gieson and Mallory merely showed a somewhat looser arrangement of the collagenous substance when compared to non-treated control sections.

Examinations of the arterial wall for the presence of collagenous substance in conjunction with age could be undertaken only after these preliminary steps. I utilized the same technique as described above: The sections, treated with Hansen's mixture for one day, were rinsed for a few minutes in a 1/10 normal solution of hydrochloric acid, since the phenol-phthalein test had shown that the lye remains in the tissue for a long period of time. In addition to the stains listed above, I used Foot's method for the impregnation of gitter cells; here the sections were not pre-treated with lye.

My material consisted of the following arteries: Aorta (the ascending portion of the arch, the thoracic aorta and the abdominal aorta), art. carotis communis, a. femoralis, a. brachialis, a. lienalis, a. mesenterica superior, a. coronaris cordis dex. and sin.

The arteries listed were examined in 21 cases of the following age levels: 9 days - 3 cases; 5, 10, 23 and 40 years - 2 cases each; 16, 20, 24, 27, 42, 53, 56, 62 and 83 years - 1 case each.

In microscopic examination of the arteries of older persons, sections from arterial portions without visible pathologic lesions were used exclusively, the material being selected from individuals with acute causes of death, whenever possible.

Arteries of the elastic type.

Art. carotis communis. 9 days old (Fig. 1). The collagenous substance is already well defined and represented in considerable quantity in the first days of life. The coarser fibers stain dark blue with Mallory, the finer precollagenous ones turn light blue. The intima is thin at this age and shows (with Mallory) a large amount of interlaced light blue fibrils; in addition, dark blue collagenous fibers are present here that border primarily on the inner side of the l. elast. int. Similar, rather coarse fibers are located in the media, progressing along the outside of the l. elast. int.

The central layer contains well pronounced, rather thick collagenous fibers at this age, being for the most part located outwards, before the membranes. These fibers hug the elastic laminae quite intimately by following their undulating course. They are the source of fine fibrils which surround the elastic membranes and form networks between them. Everywhere, precollagenous, fine fibers run through the gaps in the elastic membranes and penetrate the intima from the media through the gaps in the l. elast. int. (see also Benninghoff's data). The total amount of collagen increases toward the outer arterial layer which contains thick collagenous fibers. A large number of muscle fibers with circular courses are located between the membranes of the media in early childhood; their arrangement throughout the entire vascular circumference is very regular, with a swollen, juicy appearance.

The art. carotis communis at this age shows approximately the same conditions upon treatment either with Foot's stain or Mallory's. The gitter cells entwine the elastic membranes in places and form networks between them.

Age 5. In addition to a general thickening of the vascular wall, the comparison with the preceding age group reveals an increase in collagen, expressed by an increase in collagenous and precollagenous fibers as well as by a thickening of the individual fibers. The network of fine fibrils in the intima is considerably denser than at the preceding age level, accompanied by a rise in the amount of coarse fibers staining dark blue

with Mallory. The central layer contains fairly coarse collagenous fibers which border on the elastic lamellae, not only from the outside, as had been the case with newborn, but also from the inside. The spaces between the elastic membranes are considerably wider than at the earlier age, and are filled with a dense network of fine fibrils that stain light blue with Mallory and are impregnable with silver by Foot's method.

Age 10 and 16. The structure of the media fails to reveal essential deviations from the conditions described above, but the quantity of collagenous and precollagenous fibers is slightly greater than at the earlier age.

Starting with the third decade (age 24), especially dense accumulations of collagenous fibers are found in the inner as well as the central layer. The latter harbors thick bundles of collagenous fibers, stained dark blue by Mallory, not only on the inside and outside of the elastic membranes, but also in the space between them, next to the network of fine fibers observed in the earlier age groups. Particularly thick bundles of collagenous fibers are situated predominantly in the outer layers of the media, as already observed in earliest childhood. At this age the gaps in the elastic membranes are much more noticeable than before (Gruenstein, Voigt). Precollagenous fibers penetrate these gaps everywhere. The amount of muscle fibers in the media seems to have increased in comparison with earlier years. Their arrangement is no longer as regular along the entire vascular circumference as noted in childhood. As early as age 5-10, the muscle fibers group themselves into individual bundles separated by collagenous fibers.

Material of the fourth decade failed to reveal additional increases in collagenous fibers, although isolated coarse fibers came into greater prominence. The gaps in the elastic membranes are everywhere filled with networks of collagenous and precollagenous fibers. The quantity of muscle fibers seems to be increased somewhat in comparison to earlier age groups; the bundles are frequently rather short.

In the 6th and 7th decades, the collagenous fibers of the cases examined by me (age 53, 56 and 62) show a dull blue hue after staining with Mallory when compared to younger material; van Gieson's stain produces a homogeneous appearance, the bundle contours are indistinct (see also Voigt's description). The gaps in the elastic membranes are noticeable more frequently and stretch over greater distances than earlier. The total amount of muscle fibers seems greater at this age, their number is smaller, however, in proportion to the collagenous substance which has undergone intense development. At some points the media reveals small amounts of longitudinal muscle fibers.

The 6th and 7th decades produce considerable amounts of gitter cells in the wall of the art. carotis communis. As in earlier age groups, they form dense networks in the intima and between the elastic membranes of the media. However, this age group shows more of the coarse fibers, and the network is less ramified.

The aorta. All of the aortal sections examined by me gave nearly identical results, and for this reason they may be described together. Considerable amounts of well defined collagenous and precollagenous fibers are found in the aortal wall as early as on the 9th day of life. In addition to rather coarse fibers staining blue with Mallory, we can see numerous delicate, fine, light blue precollagenous fibrils. The intima consists of fine interlaced fibers; well defined collagenous longitudinal fibers are also present. In the media, the collagenous fibers border on the elastic membranes (just as in the art. carotis communis), showing a well pronounced, primarily circular orientation in the thoracic and abdominal aorta; however, their direction is no longer as regular in the ascending portion of the aorta and in the aortal arch. The collagenous fibers follow the convolutions of the elastic membranes and border on their outer side. In this age group the elastic membranes undulate very strongly, almost without interruptions; there are only a few points with small gaps that are penetrated by bundles of collagenous or precollagenous fibers (Benninghoff). Similar holes occur also in the lamina elastica int., through which collagenous and precollagenous fibers enter the intima from the media. The fibers become progressively coarser toward the outer layer. The central layer harbors networks of fine precollagenous fibers between the elastic membranes, in addition to the fibers bordering on them. These networks are less strongly defined in the abdominal portion of the aorta, where the elastic laminae are arranged more compactly. The muscle fibers lie between the membranes and at times hug them quite closely (see also Benninghoff).

At age 10 the amount of collagenous fibers in all layers of the aortal wall is considerably greater than in early childhood. The collagenous longitudinal fibers are coarser in the inner layer. The network of thin precollagenous fibers is denser. The muscular-elastic layer is distinctly defined. The bundles of collagenous fibers in the media are thicker than in the preceding age group; they lie on both sides of the elastic membranes. The latter have a greater number of disruptions than before. The spaces between the elastic membranes are wider, and contain a fairly dense network of fine precollagenous fibers that also penetrate the membranes' gaps at every point. In places, smaller sections with considerable aggregations of collagenous fibers are found, especially in the proximity of the adventitia.

At age 20-27 the quantity of collagenous fibers is increased in the intima and media in comparison to the previous group, and their bundles are coarser and thicker. The central layer now shows coarse collagenous fibers also in the spaces between the elastic membranes, where the preceding age group merely had a thin network of precollagenous fibers. The interruptions in the elastic membranes are more pronounced than before: they are penetrated not only by thin collagenous fibers, as previously, but also by coarser ones.

The following age group (4th and 5th decade) reveals another increase in collagenous fibers in the aortal wall. The intima is thickened, contains copious networks of precollagenous fibers; bundles of longitudinal

fibers are located on their internal side. In the media the thicker collagenous fibers neighbor on the elastic membranes, in which connection the coarser bundles proximate the adventitia, as in childhood. The gaps in the elastic membranes are even more pronounced, their interspaces are occupied by coarse collagenous fibers. Muscle fibers are arranged in long and short bundles here; some cases reveal bundles of longitudinal muscle distributed arbitrarily.

Age 53 and 62. All layers of the vascular wall contain coarse collagenous fibers in large quantity; many collagenous fibers stain a dirty blue with Mallory, the contours of the individual fibers are indistinct, vague. The thin fibers are well defined in the form of a rather dense network. The elastic membranes show a slight undulation and very frequent disconnections. The muscle fibers of the media have a circular orientation in the form of bundles of various size; longitudinal bundles are also present. The general arrangement of muscle fibers is irregular.

The gitter fibers of the aortal intima have a predominantly longitudinal or oblique direction in early childhood; they give cross sections an appearance of fairly dense points and transverse strips. In the central layer the coarser fibers border on the elastic membranes, entwining the latter in places. Networks of wavy, fine fibers are found between the membranes. The sixth year of life already shows an increase in the amount of gitter fibers in the intima in comparison to early childhood; the longitudinal fibers have a denser arrangement, distinctly defined circular fibers are also found next to the lam. elast. int. The lam. elast. int. as well as the elastic membranes are often entwined by gitter fibers in the central layer. In the media they proceed through the gaps in the elastic membranes; fairly dense networks of fine, ramified gitter fibers are found between the membranes. At age 22, 24 and 27 the gitter fibers of the aortal wall are present in copious amounts (Fig. 2). Their networks in the intima are especially dense near the lam. elast. int. In the media they surround the elastic membranes and muscle bundles, and also form dense networks between the membranes. Gitter fibers are also very copious at higher age levels (50-80 years). In addition to a considerable amount of fairly coarse gitter fibers, we also find dense networks of fine fibrils. At an advanced age the gitter fibers are generally coarser and less ramified than at younger age levels (Fig. 2 and 3).

Thus we find the wall of elastic arteries examined by me to contain quite a large amount of collagenous substance from early childhood, both in the form of thick, collagenous fibers and fine, precollagenous fibrils. At this age the intima harbors predominantly fine fibrils. In the central layer, deposits of fairly thick collagenous fibers are found on the outside of the elastic membranes; networks of fine fibrils are situated between the membranes. With advancing age the total amount of collagenous fibers increases on one hand, and a thickening of the individual fibers is noted, on the other. In this connection a gradual transformation of precollagenous fibers into collagenous ones takes place everywhere.

The intima reveals rather thick collagenous fibers already in childhood, and the network of precollagenous fibers becomes progressively denser. In the media, coarse collagenous fibers appear not only on the external side of the elastic membranes, but also on the internal side. The networks of precollagenous fibers between the elastic membranes become considerably denser, and at age 20 the collagenous, circularly oriented fibers are already well defined. In addition, the media shows many precollagenous fibers that penetrate through the gaps in the elastic membranes. The gaps in the elastic membranes are more numerous at later age levels (Gruenstein, Voigt), and fibers penetrating them become thicker and coarser. Similar fibers proceed through the gaps in the lam. elast. int. and ext. from the central layer into the intima and adventitia. At still later age levels the increase in collagenous fibers is accompanied by their gradual transformation (swelling, homogenization, dullness), which may be called "hyalinosis." The smooth muscle fibers of the central layer are distributed evenly in early childhood. Later, an arrangement of the muscle fibers into bundles is evident. Longitudinal bundles of muscle fibers are seen in subsequent years, their amount being subject to considerable individual fluctuation, according to M. Aresu. In senile years the muscle bundles are of various length, they are unevenly distributed and separated by large amounts of collagenous fibers.

Arteries of the muscular type.

Art. femoralis. 9 days old. The vascular intima is not developed. The endothelium borders directly on the lam. elast. int. The muscle fibers of the media are arranged very regularly in several rows. Fine, precollagenous fibers proceed between the rows of muscle. They are generally distributed evenly, the coarser ones are proximal to the lam. elast. int. The coarser gitter fibers run a serpentine course through the rows of muscle fibers and branch out into finer fibrils that form networks between the muscle fibers. The intima of the art. femoralis is already well defined in the 10-year-old; it contains considerable amounts of collagenous and precollagenous fibers which form fairly thick collagenous longitudinal fibers, as well as circular fibers running along the lam. elast. int., and also thin fibrils forming a dense network. The lam. elast. int. contains disruptions in places, admitting individual collagenous or precollagenous fibers, whole bundles of fibers and, at times, muscle cells, into the inner layer of the intima. The muscle fibers of the media are not arranged as evenly as in the preceding material. The collagenous fibers are coarser than before and less regularly distributed. The gitter fibers are more strongly defined here and take a serpentine course between the rows of muscle fibers. Fairly coarse gitter fibers are proximal to the lam. elast. int. and penetrate through its gaps into the intima.

In the cases aged 20 and 24 the inner layer of the art. femoralis contains a considerable amount of thick collagenous fibers; the particularly thick ones are deposited between the lam. elast. int. and the newly formed inner border lamella. In the central layer the irregularities of

arrangement of muscular and collagenous fibers is even more distinct than in the preceding age group. There are isolated instances of small sections of the media with a considerable amount of muscle fibers consisting of coarse, collagenous fibers or of a dense network of finer fibers. The quantity of gitter fibers seems to have increased over the preceding age group. They usually have a longitudinal course in the intima, and show a circular orientation in the media. They entwine the muscle fibers and form networks at this point. In places the precollagenous fibers become coarser and turn into collagenous ones.

At age 53, all layers of the vascular wall reveal a large quantity of collagenous fibers. They are coarser than at the preceding age level, are dull in places and have vague contours. The number of collagenous fibers in the central layer is larger than before; the number of muscle bundles, on the other hand, is relatively small, and their arrangement is less regular.

The gitter fibers of the media are quite well defined and present in considerable numbers. As in the earlier material, they again prefer the proximity of muscle bundles which they surround. The coarse fibers bordering on the lam. elast. int. from the outside, are particularly characteristic.

Art. brachialis. The process of increase in collagenous substance in the walls of the art. brachialis with advancing age is as distinct as in the art. femoralis. In early childhood the central layer of the art. brachialis contains smooth muscle fibers which are arranged in dense, almost regular processions, forming regular rows separated by fine, collagenous and precollagenous fibers. At age 5-10 these fibers appear to be coarser and thicker. At age 25-30 a certain irregularity may already be noted in the arrangement of muscle fibers. The media, particularly in the outer layers, shows isolated, small spots consisting of bundles of fairly coarse, collagenous fibers. At later age levels (40-50 years) these areas become progressively larger and are found more often. At the highest age level the collagenous substance in the media exceeds the muscle fibers quantitatively. Thus the muscle bundles in the art. brachialis of a 62-year-old are very thin and scattered between the coarse collagenous fibers in relatively small amounts. In addition, particularly thick collagenous fibers are found primarily on the outside of the lam. el. interna. Precollagenous fibers are found everywhere in large amounts next to the collagenous ones. The former have a circular course in the media, entwine the muscle fibers and form networks between them. Compared to younger material, they seem coarser in advanced age; the networks are less dense and a transformation to collagenous fibers is evident everywhere. The structure of the inner layer in relation to the proportion of collagenous to precollagenous fibers does not differ from that of the art. femoralis.

[illegible] The senile changes of the art. lienalis have been [illegible] by Stuhlmacher, who points to a fibrous degeneration of the [illegible] in the media. The art. lienalis has a thin central layer in [illegible] childhood (9 days), consisting of a few relatively proximal [illegible] of muscle fiber. There are collagenous and precollagenous fibers between them. The strongly pronounced adventitia consists of coarse collagenous and elastic fibers.

[illegible] to a newly formed intima may be observed; it contains fine collagenous and precollagenous fibers that enter from the media through the gaps in the lam. elast. int. The amount of collagenous fibers in the media at this age has increased when compared to the preceding material. At age 23 the number of collagenous and precollagenous fibers in the central and inner layers has increased considerably over childhood. The fibers are quite coarse and form considerable aggregates in places. A particularly characteristic sign is the arrangement of coarse fibers along the lam. elast. int., both inside and out.

The 4th and 5th decades reveal an irregular arrangement of the muscular and collagenous fibers. The media is permeated with fairly large areas consisting of copious collagenous fibers. The amount of muscle fiber has decreased relatively, they are scattered in irregular bundles. A large quantity of collagenous fibers is found also in the intima, where they occur everywhere between the muscular and elastic fibers. In later age the collagenous fibers are especially coarse; they have a certain dull appearance and the contours of the individual bundles are vague in places.

The precollagenous fibers of the art. lienalis are well defined from earliest childhood. In the intima they prefer a longitudinal orientation. In the media they follow a serpentine course along the muscle fibers and form networks between them. Some of them are coarser, others finer, a few coarser fibers border on the outside of the lam. elast. int. Later age bring a thickening of the gitter fibers, their coarse is less serpentine and they change into collagenous fibers throughout.

Art. mesenterica superior. In early childhood the media contains only fine collagenous and precollagenous fibrils which have a circular orientation between the muscle fibers. Their amount in the media is increased from the 5th year on and they appear to be coarser. At age 10 the central and inner layers contain a good number of collagenous fibers which follow the course of the lam. elast. int. in the intima, whereas they are situated in bundles between the muscle fibers of the media. At age 24 this picture is more pronounced; this age reveals a particularly strong development of collagenous fibers at several points of the media. The arrangement of muscular and collagenous fibers usually is irregular. At age 40 and 50 the amount of muscle fiber has experienced a relative decrease; bundles of various size are scattered between the collagenous network.

The alterations just described agree completely with those observed by Schmiedl. He points to a "fibrosis" of the central layer of the art. mesenterica sup. which starts around the third decade and increases with age.

The coronary arteries of the heart. Well defined collagenous fibers are present in the inner and central layer at the earliest age, both in the left and right coronary arteries.

According to Wolkoff, the intima of these arteries is distinctly pronounced in childhood. There are a good number of coarse collagenous fibers inward from the lam. elast. int.; they are longitudinal in the inner layer of the intima and circular in the proximity of the lam. elast. int. In addition, the intima shows a network of fine fibers that proceed in various directions. The muscle fibers of the central layer are arranged in regular rows separated by undulating, fine collagenous and precollagenous fibers.

At age 10 the inner and central layers of the right and left coronary arteries betray an increase in the number and thickness of collagenous fibers. The network of fine collagenous or precollagenous fibers of diverse orientation is considerably denser in the intima compared to the earlier age levels. Isolated fibers lead from the media to the intima through gaps in the lam. elast. int. The central layer contains collagenous fibers embedded between the muscles. They are coarser and occupy more space than previously.

Age 16 and 20 brings an increase in collagenous fibers in the walls of the coronary arteries. The outer portions of the intima contain whole bundles of rather coarse collagenous fibers which penetrate into the media via gaps in the lam. elast. int. The network of fine, interlacing precollagenous fibrils is also more distinct in the intima. The collagenous fibers of the central layer are coarser and cover greater areas than in the preceding material. The foci of collagenous fibers have an oblong shape and are found more often in the section of the media proximal to the adventitia; apparently they relate to the vasa vasorum. The muscle fibers are separated due to a proliferation of collagenous fibers and lose their regular arrangement known from childhood. At higher age levels the amount of collagenous fibers increases considerably in the central and inner layers.

At age 53 the central layer contains ubiquitous and considerable aggregates of collagenous fibers in the form of large individual strata that are wedged between the muscle fibers. The amount of muscle fibers is decreased, their bundles are thinner than at earlier age levels. Unusually great changes involving the development of large masses of collagenous fibers and the decrease in muscle fibers were noted in the coronary arteries of a 62-year-old man. In this case, aggregates of coarse collagenous fibers were present in the form of extensive interspaced strata. At this age the collagenous fibers assume a dull blue color after staining with Mallory, and the individual fibers lose the distinctiveness of their contours.

The gitter fibers in the wall of the coronary arteries (Fig. 4,5,6) are distinctly visible in early childhood, both in the intima and media. In the intima they are usually oriented longitudinally and border on the lam. elast. int., while the media shows them proximal to the elastic membranes. In the central layer the coarser gitter fibers proceed in spiral undulations parallel to the muscle bundles, while the thinner ones form networks between the muscle bundles. At age 26-27 the number of gitter fibers is even larger. In the intima, a dense network of them is found close to the elastic plates of the hyperplastic layer. In addition, fibers are seen here that are scattered without any form of arrangement. In the media they entwine the muscle fibers quite densely and form copious networks between them, consisting of strongly serpentine fibers. The 5th and 6th decades reveal well developed gitter fiber networks in the intima and media, although the fibers are generally coarser and not as undulating as in the preceding age group; transitions to collagenous fibers take place everywhere.

The above description reveals that the general arrangement of collagenous fibers in the wall of muscular type arteries examined by me is nearly uniform within a given age group. Earliest childhood shows relatively few thin, collagenous fibers in the central layer of these arteries. The intima contains them only in the coronary arteries of the heart, where many precollagenous fibers are found as well. In the media, the collagenous fibers are located between the muscle fibers which are arranged in regular rows in close proximity. The gitter fibers entwine the muscle fibers and form networks between them. The coarser gitter fibers border on the outside of the lam. elast. int.; they surround the latter frequently and proceed through its gaps into the intima. Fairly coarse gitter fibers lead a spiral course parallel to the muscle fibers.

With advancing age there occurs a uniform thickening of the existing collagenous fibers and a formation of new fibers. Bundles of longitudinal fibers are found in the intima at age 5-10, and the circular fibers located on the inside of the lam. elast. int. are also well defined. Moreover, the intima already shows a network of fine precollagenous fibers. Particularly thick collagenous longitudinal fibers are found in the intima of the heart's coronary arteries. The deposits of collagenous fibers in the media become progressively thicker with advancing age and consist of coarser fibers than in early childhood. The increase in collagenous fibers continues in later age groups (toward age 20-25). The muscle bundles in the media are separated more and more by the developing collagenous fibers; in addition, areas appear in which the coarse collagenous fibers are more strongly developed, especially in the outer portions of the media. In the 3rd and 4th decades these areas appear in the entire central layer, whereby the muscle fiber bundles are separated over considerable distances due to the collagenous substance. At about age 40 the preponderance of collagenous substance over the muscular elements becomes quite clear in all arteries examined. Material of advanced age (5th, 6th and 7th decades) reveals continued increase in collagenous fibers, and the muscle fibers are arranged in relatively thin, short bundles scattered throughout the collagenous substance in the media; the collagenous fibers lose their sharp contours and stain diffusely.

The amount of fine fibers as well as coarser precollagenous fibers grows with advancing age; they are everywhere transformed into collagenous fibers. The third decade brings particularly dense networks of gitter fibers. In later life the number of gitter fibers is quite considerable; the coarser fibers are present in greater quantity and the fine ones show a slightly serpentine orientation.

Summary.

A study of the senile changes in arteries of the elastic and muscular type leads to the conclusion that all arteries examined by me reveal a steady increas in collagenous substance or collagenous fibers with advancing age. However, each type of artery discussed shows certain peculiarities within the context of the existing senile changes. The arteries of the elastic type give evidence of a good number of coarse collagenous fibers from earliest childhood, occupying a considerable portion of the vascular wall. The collagenous and precollagenous fibers of the media are arranged in a circular pattern and anastomose mutually through the gaps in the elastic membranes as well as with the collagenous fiber system of the intima and adventitia. Advancing age brings a thickening of the collagenous fibers and formation of new collagenous and precollagenous fibers.

The arteries of the muscular type contain only a few collagenous and precollagenous fibers at an early age. Here we meet the agenous substane in theform of fine fibrils situated between the uscle fibers. With advancing age the arteries of the muscular type experience a thickening and proliferation of the collagenous and precollagenous fibers; the latter change to collagenous fibers. The muscle fibers are distributed on isolated, irregular groups. This process is analogous to that described by Staemmler for the art. renalis and lienalis and by Schmiedl for the art. mesenterica sup.

The attrition of muscle fibers with age is not as distinct in the arteries of the elastic type; it might even be said that the total amount of muscular elements is frequently greater at an advanced age than in early childhood. Owing to the proliferation of collagenous fibers, the regular arrangement of muscle fibers in the media is disturbed and the muscle fibers are distributed on irregular groups, just as in the muscular type arteries.

In advanced years, and sometimes sooner, the proliferating collagenous fibers of arteries of both types stain more diffusely and turbidly, their contours are indistinct. These changes of the collagenous fibers in the arterial wall may be designated as "hyalinosis" after Voigt.

The senile increase in collagenous fibers in the arteries examined by me takes place diffusely; no focal accumulations of these fibers were noted. However, the media consistently shows small areas, especially toward the adventitia, that probably correspond to the course of the vasa vasorum and in which the collagenous fibers reveal particularly strong development.

In view of the consistency of such collagenous areas, they cannot be considered a pathological manifestation, especially since signs of an inflammatory nature are absent. A correlation between the atherosclerotic changes in the intima and the collagenous-fibrous proliferations in the media could not be established from my material. It is true that my material did not contain severe atherosclerotic changes, although such alterations of low degree occurred sporadically. I was unable to discover any special changes in the media at such places in comparison with neighboring areas, where the intima did not contain atherosclerotic changes. This observation agrees with Staemmler's opinion that the development of fibrous tissue in the central layer takes place independently of the atherosclerotic changes in the intima.

The progressive increase in collagenous fibers with advancing age occurs in the arteries at the expense of a vigorous development of gitter fibers, thanks to the transformation of precollagenous fibers into collagenous ones. The amount of gitter fibers is quite considerable even in childhood, and their number grows with advancing age. In later years they become coarser and less wavy, especially in senile years when the major part of these fibers is converted to collagenous ones.

It may be concluded from the facts listed here that the senile increase in collagen in the central arterial layer pointed out by Staemmler and Schmiedl relative to certain arteries, are valid for the walls of the large muscular and elastic type arteries as such. According to Staemmler's data the development of fibrous tissue is more pronounced in the media of the art. lienalis than in the art. brachialis, an opinion that is not shared by Hesse, however. According to my observations, the senile development of collagenous fibers generally takes place at about the same rate in all arteries examined.

I cannot say anything definite about the significance of changes in blood pressure for the structure of the arterial media (K. Dietrich), since my material was chosen from cases that failed to indicate deviations from normal blood pressure.

Since the main manifestation of the changes described above consists in progressive accumulation of collagenous substance in the media, it ought to be appropriate to designate it as "senile fibrosis (or collagenosis") of the arteries.

The basis of arterial fibrosis is apparently found in mechanical influences (Staemmler), but a primary change in the physico-chemical structure of the intermediate substance ("hysteresis") with advancing age is also possible. At any rate, fibrosis of the media, coupled with senile changes of the intima (Jores, Alb. Aschoff, Wolkoff and others) and the elastic framework of the arteries (Voigt, Gruenstein), as well as the increase in chromotropic substance (Schultz, Ssolowjew) represents a typical alteration characterizing the morphologic picture of the arteries in advanced years.

Illustrations.

Fig. 1. From the cross section of the art. carotis of a 9-day-old child. Treatment according to Foot. The gitter fibers entwine the lamellae of the media. (Magnification about 800 X).

Fig. 2. From the cross section of the thoracic aorta of a 27-year-old woman. Foot's preparation. The gitter fibers of the media entwine the elastic lamellae and form dense networks between them. The gitter fibers have a longitudinal or oblique course in the intima (800 X).

Fig. 3. From the cross section of the thoracic aorta of an 83-year-old woman. Foot's preparation. Generous development of coarse, extended gitter and collagenous fibers in the media (800 X).

Fig. 4. From the cross section of the right coronary artery of the heart of a 5-year-old child. Treatment after Foot. The media reveals numerous fine, serpentine gitter fibers that proceed between the muscle fibers or entwine the latter (800 X).

Fig. 5. From the cross section of the right coronary artery of the heart of a 23-year-old man. Foot's preparation. The gitter fibers of the media are thicker, more generously developed, than in childhood and form dense networks (800 X).

Fig. 6. From the cross section of the same artery of a 56-year-old man. Foot's treatment. The gitter fibers of the media are very coarse, extended, decreased in number and form isolated, compact networks between the muscle fibers (800 X).