Calcifications of Iliac Arteries in Newborns and Infants

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Meyer, W. W., and Lind, J. (1972). Archives of Disease in Childhood, 47, 364. Calcifications of iliac arteries in newborns and infants. Calcific incrustations of the primary internal elastic membrane in the common and internal iliac arteries could be shown grossly by a modified Von Kossa reaction in one-half of all necropsied newborns and infants in the first 4 weeks of life. The calcium content of the Von Kossa positive lesions was verified by Voigt’s technique. After the age of 1 year calcific deposits were found in nearly every case. It is unlikely that resorption of these early calcific deposits occurs with growth.

The early development of calcific incrustations in the common and internal iliac arteries is obviously related to their position and function in the fetal circulation, i.e. to the higher haemodynamic load which results from the rapid increase in blood flow to the placenta during fetal development, and is associated with an accelerated growth and widening of both vessels.

In both iliac arteries only the well-differentiated, thick primary internal elastic membrane becomes calcified in childhood. This membrane is not present throughout the circumference of these arteries, but is developed in certain sectors only. Hence, the predilection site of the calcific incrustations, as well as their gross and microscopical patterns, is determined by the structural peculiarities of both iliac arteries, i.e. by the heterogeneous differentiation of the elastic elements in the vessel’s tube. The significance of this heterogeneous structure for the development of later atherosclerotic lesions is still to be evaluated.

The common and internal iliac arteries are the site of the earliest pathological changes in the human vascular system. As reported in a previous pilot study (Meyer, 1968), pronounced calcifications in these arteries could be shown grossly, even in newborn infants, when an appropriate method was used (Meyer and Stelzig, 1969).

In this report, based on a larger number of cases, we confirmed the frequent occurrence of calcifications in the iliac arteries. Moreover, the close relation of the calcific deposits to some structural peculiarities of the arterial wall was also established. These peculiarities probably represent a structural accommodation to the increasing haemodynamic load on both the common and internal iliac arteries which, during fetal development, connect the aorta and the umbilical arteries and are therefore subject to the full impact of the large blood volume in the placental circuit.

Materials and Methods

The lower part of the abdominal aorta together with the common, internal, and external iliac arteries and a short proximal segment of the umbilical arteries, was laid free and removed from the body in 63 unselected necropsy cases including 24 newborns and infants in the first 4 weeks of life, 11 infants aged 1 to 11 months, and 28 infants and children aged 1 to 12 years.

In most cases, the common and internal iliac arteries were opened longitudinally along their medial retraction folds (see below) and the external iliac artery along its anterior wall. In 41 cases, arterial circumferences were measured in the abdominal aorta above the bifurcation, in the middle part of the common iliac artery, and in the external and internal iliac arteries approximately 5–10 mm below their origin in the common iliac artery (Table I). The arterial specimens were then rinsed in distilled water, and the calcific deposits demonstrated grossly with the modified Von Kossa reaction (Meyer and Stelzig, 1969). The extent of the calcifications which became visible after this reaction was arbitrarily classified into grades I–III (see Results). Frozen cryostat sections were prepared for microscopical examination and stained with Gomori’s aldehyde fuchsin. In 25 cases, the Von Kossa reaction was grossly performed on
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Circumferences of Abdominal Aorta, Common, Internal, and External Iliac Arteries in Children

<table>
<thead>
<tr>
<th>Age Groups</th>
<th>No. of Cases</th>
<th>Aorta (above bifurcation)</th>
<th>Common Iliac Artery</th>
<th>Internal Iliac Artery</th>
<th>External Iliac Artery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newborns</td>
<td>10</td>
<td>12.9 ± 0.2</td>
<td>7.7 ± 1.0</td>
<td>7.2 ± 0.7</td>
<td>4.1 ± 0.4</td>
</tr>
<tr>
<td>6 dy-6 wk</td>
<td>7</td>
<td>12.4 ± 1.6</td>
<td>7.5 ± 1.4</td>
<td>6.2 ± 0.4</td>
<td>4.4 ± 0.9</td>
</tr>
<tr>
<td>3-8 mth</td>
<td>5</td>
<td>12.5 ± 0.4</td>
<td>8.0 ± 0.3</td>
<td>6.1 ± 0.2</td>
<td>5.7 ± 0.5</td>
</tr>
<tr>
<td>10-18 mth</td>
<td>6</td>
<td>14.3 ± 0.7</td>
<td>8.8 ± 0.6</td>
<td>6.2 ± 0.6</td>
<td>7.1 ± 0.5</td>
</tr>
<tr>
<td>3-5 yr</td>
<td>7</td>
<td>17.0 ± 2.0</td>
<td>10.9 ± 0.7</td>
<td>7.4 ± 0.3</td>
<td>8.7 ± 0.9</td>
</tr>
<tr>
<td>7-12 yr</td>
<td>6</td>
<td>21.4 ± 2.2</td>
<td>15.6 ± 2.3</td>
<td>9.3 ± 1.0</td>
<td>11.3 ± 1.7</td>
</tr>
</tbody>
</table>

the arteries of one side of the body only. The arteries of the opposite side were not opened longitudinally, but first fixed in a neutral formaldehyde solution and used to determine structural differences in the individual arterial sectors. Frozen cross-sections of the common, internal, and external iliac arteries were prepared for this purpose. In order to identify the respective arterial sectors in the microscopic sections, the adventitia of the lateral and anterior walls of the vessels was labelled with India ink before cutting. Elastic tissue was stained with Gomori’s aldehyde fuchsin, orcein, and Weigert’s resorcin fuchsin. For microscopic demonstration of calcific deposits both the Von Kossa reaction and Voigt’s technique (Voigt, 1957) were used on the step or serial cryostat sections.

**Results**

**Postnatal changes in size and ratio.** The common and internal iliac arteries represent a direct continuation of the abdominal aorta. In fetuses and newborns they form wide vascular channels which merge with the umbilical arteries. On the other hand, the external iliac and femoral arteries, which supply the entire lower extremity, appear as relatively thin vessels (Fig. 1, 2, and 4). Measurements at birth reveal that the common and internal iliac arteries are approximately twice as wide as the external iliac artery (Table I). This difference in size and ratio alters after birth. The calibre of the external iliac and femoral arteries increases with the growth and development of the lower extremity, while the internal iliac artery becomes relatively smaller because, after birth, it only supplies the pelvic viscera and the surrounding tissues. Between 1 and 2 years of age the circumference of the internal and external iliac arteries becomes approximately equal, and by the end of the first decade the ratio is reversed (Table I, see Fig. 7). Thus, the common and internal iliac arteries exhibit an accelerated antenatal growth rate and attain a larger calibre than the other fetal vessels as a consequence of the large blood flow in the placental circuit.

Whereas only a few tiny arteries originate in the common iliac artery, many arterial branches arise from the internal iliac artery. However, in fetuses and newborns the orifices of these branches also appear small in comparison with the wide trunk of the artery. The orifices are predominantly located on the dorsomedial wall of the trunk.

**Postmortem changes.** After death the tube of the collapsed and retracted common and iliac arteries is no longer roundish in cross-section, but oval. In the common iliac artery the sides of the oval are formed by the folded lateral and medial walls. On the luminal surface of each of these folded parts, a narrow, flat longitudinal groove can be discerned. In the internal iliac artery, the dorsomedial and anterolateral walls become folded.

**Fig. 1.** Postmortem angiogram of a newborn. The common (C) and internal (I) iliac arteries appear wide, while the external iliac arteries (E) and femoral arteries (F) are comparatively narrow. (A) abdominal aorta.
and form both sides of the oval cross-sectional area of the vessel. On the luminal surface of the opened artery, a narrow, flat longitudinal groove can be discerned in the middle of these folded parts, as in the common iliac artery, these grooves represent a retraction product and are not seen in arteries which are fixed under an appropriate filling pressure.

**Gross calcifications.** In newborns and infants the early calcifications become grossly visible as fine, scattered dot-like black deposits on the luminal surface of both the common and internal iliac arteries (grade I). In the common iliac artery they appear first on the lateral wall above the origin of the internal iliac artery. With more pronounced involvement, tiny roundish or polygonal deposits spread out proximally along the lateral wall, i.e. along the lateral retraction groove of this vessel. In the internal iliac artery the dorsomedial wall is the predominant site of calcifications. In both these predilection sites, even with the moderate involvement (grade II, Fig. 3), the lesions often appear to be grouped around circularly orientated calcific-free bands. With severe involvement (grade III), these bands become clearly visible (Fig. 4, 7, colour plates A and B).

Even in cases with a severe involvement the calcifications do not spread diffusely throughout the entire luminal surface of the iliac arteries. In the common iliac artery they remain confined to the lateral wall of the vessel and the adjacent parts of the anterior and/or posterior wall. An unstained longitudinal stripe, free of calcifications, then becomes clearly visible beside the densely incrustated parts of the luminal surface (Fig. 4, 7, and colour plates A and B). In the internal iliac artery the affected and nonaffected parts are even more clearly demarcated. In this artery, the anterolateral wall of the tube of the vessel stays free of calcific deposits and the incrustations appear predominantly on its dorsomedial wall. Numerous black incrustations often form a continuous black longitudinal stripe, which is sharply delineated from the calcific-free anterolateral wall (see Fig. 5, colour plate C).

In some cases in which the Von Kossa reaction has been performed on the arterial segments after fixation in formaldehyde, further structural details appear on their luminal surface. The areas which include a well-developed internal elastic membrane become brown, whereas the membrane-free areas stay whitish. Hence, not only the circular gaps in the internal membrane (see below), partly delineated by the calcific incrustations, but also other areas free of the internal elastic membrane become clearly visible on the luminal surface of both iliac arteries. In some parts a peculiar striated pattern could be discerned grossly, indicating numerous fine interruptions of the internal elastic lamina.

No calcific incrustations could be found, grossly or microscopically, in the external iliac and femoral
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Fig. 3.—Calcifications (black) in the common iliac (CI) and internal iliac (II) arteries of a 16-month-old infant who died of pyaemia. Grade II lesion. Von Kossa reaction. Millimetre scale to the left. (A) bifurcation of the aorta. (EI) external iliac arteries. (OU) obliterated umbilical arteries.

Fig. 4.—Calcific deposits (black) in the left iliac arteries of a 6-day-old newborn (birthweight 2700 g). Von Kossa reaction. Pronounced calcific incrustations in the common iliac artery (CI) and finer point-like lesions in the internal iliac artery (II). External iliac artery (EI) is free of deposits. In the midst of calcific incrustations, calcific free, circularly arranged stripes (arrows) are seen. Circumference of internal iliac artery (II) is nearly twice as wide as external iliac artery (EI) (see Fig. 2).

arteries of the newborns, even when the common and internal iliac arteries were severely involved (Fig. 4). In the external iliac and femoral arteries the calcific deposits usually appear later in childhood and up to the end of the first decade of life, scattered tiny calcific incrustations only could be shown grossly on the luminal surface of these vessels.

Microscopical findings. The lesions of the common and internal iliac arteries represent the incrustated parts of the primary internal elastic membrane, which often becomes irregularly undulated and thicker than in the neighbouring unaffected sectors (see Fig. 6, colour plate D). On the longitudinal sections the calcification-free circular bands which are seen grossly on the luminal surface of the arteries represent wide gaps in the internal elastic membrane. The incrustations often spread out up to the edge of these membrane gaps (colour plate E). On tangential sections the sometimes roundish incrustations appear sharply interrupted at the membrane edge. The preformed small fenestrae in the elastic membrane remain free of calcific deposits, and are clearly seen as tiny round openings in the black or brownish membrane (colour plate F).

As we have shown in the serial frozen cryostat sections, the lesions of the internal elastic membrane, which turn black after the Von Kossa reaction, prove in the following sections to be anisotropic when the Voigt technique for identification of calcium is used. This method is considered to be
specific and sensitive enough for calcium deposits in animal tissues (Voigt, 1957).

The characteristic gross pattern of calcific incrustations, which has been found in the common and internal iliac arteries (see above), depends on the heterogeneous structure of both vessels as well as on a different affinity of some of their structural elements to calcium. Unlike muscular arteries,
the primary internal elastic membrane in the common and internal iliac arteries is not well differentiated throughout the entire circumference. On the cross-sections of the common iliac artery a well-developed, thick and homogeneous internal elastic membrane has been found predominantly in the lateral wall and the neighbouring parts of the circumference (Fig. 9). In the internal iliac artery this kind of membrane is present in the dorsomedial sector (Fig. 8, 9). In other sectors of these arteries the subendothelial or subintimal elastic layer is formed not by a homogeneous elastic membrane, but by one or more layers of fine longitudinally oriented, tightly-packed elastic fibres. On arterial cross-sections rows of dot-like stumps of these fibres are clearly seen. Similarly fine elastic networks often develop over the well-differentiated primary elastic membrane, and with growth form the secondary elastic membrane. The fine intimal elastic networks, as well as the secondary membra-
where the internal elastic membrane is well developed the elastic lamellae of the underlying media are usually more numerous and thicker than in the sectors in which the intimal or subintimal elastic layers are only formed by thin elastic networks (Fig. 9).

**Incidence** (Table II). In the newborns and in infants during the first 4 weeks of life calcifications were found grossly in 13 out of 24 cases, i.e. in approximately half of all necropsied infants. In 11 cases in which calcifications are not observed, 4 were premature with birthweights of 1300–1800 g. In 7 cases, birthweights ranged from 2400–2800 g. Grade III lesions were found in a mature stillborn (birthweight 3050 g), in a term newborn who died 24 hours after birth of an intracranial haemorrhage, in a 7-day-old and a 4-week-old infant who died of an acute tracheobronchitis and kidney malformation, respectively.

In the next age group (1–11 months of age, 11 cases) three cases only were negative.

In all but one of the children who died at ages ranging between 1 to 12 years (28 cases) calcific deposits could be shown grossly. 14 of these children died as a result of traffic or other accidents.

In the group of 15 cases with pronounced calcific incrustations (grade III lesions) 8 children were aged 1 to 4 years, 6 children 5 to 9 years, and 1 was 10 years of age. 8 of these 15 children died as a result of traffic or other accidents. In the remaining cases subdural haematoma (1), congenital heart disease (2), sepsicaemia (1), and internal hydrocephalus (2) were the causes of death. In 1 case no definite cause of death could be found at necropsy.

Thus the frequency of calcific incrustations increases during infancy and childhood. Since the same calcification patterns are also regularly present in young adults, it is unlikely that resorption of calcific deposits occurs with growth.

![Schematic presentation of the cross-sections of the external (EI), common (CI), and internal (II) iliac arteries showing differences in development of the primary internal elastic membrane in newborns and infants.](image)

**FIG. 9.** — Schematic presentation of the cross-sections of the external (EI), common (CI), and internal (II) iliac arteries showing differences in development of the primary internal elastic membrane in newborns and infants. In the external iliac artery (above), a continuous wavy internal elastic membrane is seen in the luminal layer of the vessel. In the common iliac artery (CI) this membrane is predominantly developed in the lateral wall (L, arrow), and in the internal iliac artery (II) it is present in the dorsomedial sector (dm, arrow).

The structural differences in the individual sectors of both iliac arteries are not confined to the internal elastic layer of their walls. In the sectors

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**TABLE II**

**Incidence of Gross Calcifications in Iliac Arteries**

<table>
<thead>
<tr>
<th>Age Groups</th>
<th>Total No. of Cases</th>
<th>No. of Positive Cases</th>
<th>Grade I Lesions</th>
<th>Grade II Lesions</th>
<th>Grade III Lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4</td>
<td>24</td>
<td>13</td>
<td>8</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>1-11 mth</td>
<td>11</td>
<td>8</td>
<td>4</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>1-12 yr</td>
<td>28</td>
<td>27</td>
<td>5</td>
<td>7</td>
<td>15</td>
</tr>
<tr>
<td>Total</td>
<td>63</td>
<td>48</td>
<td>17</td>
<td>11</td>
<td>20</td>
</tr>
</tbody>
</table>

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PLATE A.—Pronounced calcific incrustations of the left common iliac artery (black). Von Kossa reaction. Circularly arranged calcific-free stripes, seen in the midst of the incrustations, correspond to gaps in the internal elastic membrane (see colour plate E). 1-month-old infant. Kidney malformation. Bodyweight 3.065 g. Millimetre scale to the left (see also colour plate B).

PLATE B.—Calcific deposits stained red with alizarin in the opposite right common iliac artery of the same case (see colour plate A). Specimen was photographed after clearing in glycerine. (x 5.)

PLATE C.—Marked calcific incrustations (black) of the internal iliac artery of a 13-month-old infant. The incrustations are predominantly located on the dorsomedial wall of the vessel, along which it was opened. Von Kossa reaction (see Fig. 5).

PLATE D.—Cross section of the internal iliac artery. Part of the internal elastic membrane (violet) is calcified (black) to the right. Von Kossa reaction and Gomori’s stain for elastic tissue. (x 330.) 6-month-old infant.

PLATE E.—Calcified edge of the interrupted internal elastic membrane (black). Longitudinal section of the common iliac artery shown in colour plate A. Part of the membrane gap which corresponds to a stainless, calcific-free stripe in colour plate A, is seen above. Von Kossa reaction and Gomori’s stain for elastic tissue. (x 330.)

PLATE F.—Calcific incrustation of the internal elastic membrane shown in a tangential section of the common iliac artery of a 5-year-old child. Von Kossa reaction and Orange G stain. The small preformed round fenestrae of the membrane stay free of calcifications. The incrustations are sharply interrupted at the membrane gap (below) (see colour plate E). (x 130.)
Discussion

The early development of calcific incrustations in the common and internal iliac arteries is probably related to their position and function in the fetal circulation. In the fetus both arteries represent a link between the systemic fetal circulation and the placental circuit. Hence, during gestation they are subjected to the rapidly increasing blood flow directed to the placenta and therefore grow faster than other vessels of the fetal systemic circulation. As seen from angiograms and direct measurements in fetuses and newborns, the calibre of the common and internal iliac arteries greatly exceeds that of the external and femoral arteries (Fig. 1, 2, Table I). The rapid increase in calibre is associated with the higher haemodynamic load on the arterial wall because the total wall tension is directly proportional not only to the blood pressure, but also to the radius of the vessel's tube (Law of Laplace). Thus in the arteries with larger radii the wall tension is greater even when the pressure stays at the same level. The greatest increase in tension probably occurs in the inner layer of the arterial wall (Müller, 1959). The structural peculiarities which were found in the subendothelial elastic layer of both iliac arteries, i.e. the numerous circular gaps in the internal elastic membrane and the lack of this membrane in large parts of the circumference, may therefore be related to the rapid widening of the vessel during fetal development, and represent a structural adaptation to the accelerated arterial growth. The greater increase in tension in the elastic elements could simultaneously result in an early 'wear and tear' and cause structural changes which favour the formation of calcific incrustations. The findings in the iliac arteries of an infant with a single umbilical artery are in accord with this view. Distinct calcifications were shown with the Von Kossa reaction in the wide internal iliac artery on the same side as the single umbilical artery. On the other hand, only a few dot-like incrustations were present in the common iliac artery and in the narrow internal iliac artery on the opposite side. In another case the hypoplastic internal iliac artery of the side where the umbilical artery was absent likewise showed only a few dot-like lesions.

As the extent of the calcifications varies greatly, other factors must also be considered. The occurrence of pronounced calcific deposits in the iliac arteries, as well as in the other arteries in congenital heart disease, indicates that hypoxaemia could favour arterial calcifications. In the fetus intrauterine asphyxia may probably play a similar role. However, on the basis of a small number of such cases no assessment of this factor could be made. Since no calcification has been found in the prematures, maturity as a factor should also be considered. The possible general factors promoting the arterial calcifications have been discussed in the previous paper (Meyer and Lind, 1972).

As stated above, it is unlikely that resorption of the calcific incrustations occurs in the iliac arteries during childhood. Thus, pronounced early calcifications of the internal elastic membrane may impair the normal remodelling of the affected arterial tube during growth, and in this way influence the development of intimal lipid deposits which also often appear in both iliac arteries in childhood. The predilection site of these deposits and their progression to the atherosclerotic plaques could be related to the heterogeneous structure of the vessel's wall which was found during this study in both common and internal iliac arteries.

References


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