Oxidative Capacity of Atherosclerotic Tissue of Rabbit and Dog, With Special Reference to Succinic Dehydrogenase and Cytochrome Oxidase

By Nelicia Maier, M.D., Ph.D., and Henry Haimovici, M.D.

The difference in susceptibility of various species to spontaneous or experimental atherosclerosis and the predilection of this pathologic process for certain sites in the same artery, such as the aorta, have not received as yet a satisfactory explanation. While there is ample evidence that an abnormal lipid metabolism, as indicated by chemical changes in the circulating blood, plays a role in the development of atherosclerosis, the factors responsible for the formation and location of the atherosclerotic lesions are not fully understood.

In previous work it was demonstrated that canine thoracic aorta, usually refractory to experimental atherosclerosis, remains so even when implanted into the abdominal aorta, site of maximum involvement in the dog, whereas abdominal implants remain susceptible. Similar results were obtained with aortic homografts implanted into the thoracic aorta. These findings suggest a biologic dissimilarity between thoracic and abdominal aorta in the dog. Similarly, a species difference was noted in the oxidative capacity of the succinic oxidase and cytochrome oxidase systems studied in normal aortic tissue slices of man, rabbit and dog. The homogenate technic used in conjunction with the slice technic was helpful in indicating to which of the components of the cytochrome system the species difference may be ascribed. These two enzymatic systems appeared of particular interest since it was shown in various tissues that they are affected by the level of thyroid function which in turn plays a major role in rendering certain species susceptible to atherosclerosis.

Accumulated evidence indicates that the arterial wall contains a large number of enzymes and is capable of metabolic activity. The question that arises is whether the arterial wall plays a metabolic role during the development of atherosclerosis and, if so, at what stage. Investigation of the metabolism of arterial tissue in various species, and in various segments of the aorta, both in the normal and in the pathologic state, may be helpful in understanding, at least partly, the factors involved in the development of atherosclerosis. The present study deals with the oxidative capacity of atherosclerotic tissue with special reference to the succinic oxidase and cytochrome oxidase systems.

Methods

The oxidative capacity, with reference to the two enzymatic systems mentioned above, was studied in the aorta of rabbit and dog, as well as in the liver as control tissue.

RABBITS

Male chinchilla rabbits, four to five months old, were used. Only those animals showing a gain in weight during an observation period of several weeks were retained. Biweekly blood cholesterol determinations were made, using blood from the central artery of the ear. The average control blood cholesterol in normal animals was 45.3 mg/100 ml of serum, with a range of variation from 19.0 to 90.2 mg. Cholesterol was administered in the food by dissolving it in ether and mixing it with Purina pellets and then allowing the ether to evaporate. The pellets contained 0.6 g cholesterol per cent. The daily cholesterol
intake per animal was 0.6 to 0.8 g. Within four
weeks the average serum cholesterol rose to about
1000.0 mg/100 ml, with a range of variation from
590.0 to 1400.0 mg. The animals on this
atherogenic regimen appeared in good health and
showed increase of weight, rapid in the begin-
ning and tending to level off after several
months. Animals showing a loss of weight were
discarded. The rabbits were sacrificed by ex-
sanguination after two to eight months.

The above atherogenic regimen seemed the
most suitable for the development of a relative-
ly slow atherosclerosis, compatible with good
health of the animals for a prolonged period of
time. Indeed, larger cholesterol content of the
pellets, resulting in a larger daily cholesterol in-
take, appeared to be unsuitable because the
animals showed rapid deterioration, loss of appe-
tite, and loss of weight associated invariably with
marked fatty degeneration of the liver.

DOGS

Mongrel dogs, ranging in age from two to
three years and weighing between 14 and 20
kg, were used. The atherogenic regimen consisted of
thiouracil and Purina kibbled meal containing
2.5% cholesterol. The cholesterol was dissolved in
ether, the solution was mixed with kibbled
Purina and the ether allowed to evaporate. The
average daily cholesterol intake was 0.6 to 0.8
g/kg body wt. Thiouracil was administered in
powdered form, mixed with meat. The average
amounts of thiouracil used daily ranged from 70
to 100 mg/kg body wt, the dosage being ad-
justed according to blood cholesterol level and
the dog's appetite. Blood cholesterol levels were
determined biweekly by the method of Abell and
associates. During administration of the above
diet, the dogs appeared in good condition. They
were sacrificed by light pentobarbital anesthesia
and exsanguination from 9 to 15 months after the
beginning of the atherogenic regimen. Rabbits
and dogs kept on Purina pellets only were used as
controls.

Grading of the atherosclerotic lesions was done
separately for the three aortic segments and was
based on the percentage of surface involved.
Four grades were thus arbitrarily established as a
guide for the classification of the extent of lesions:
grade 1+: 5 to 25%; grade 2+: 25 to 50%;
grade 3+: 50 to 75%; grade 4+: 75 to 100%.
The aorta and a segment of liver were removed
immediately after sacrifice of the animals and
placed in ice-cooled containers with tight-fitting
covers. The aorta was flushed with ice-cold saline
solution, then freed of adherent fat and con-
nective tissue, rinsed again with ice-cold saline
and blotted with filter paper. The tissues were
used within 60 minutes after sacrifice. Tissue
slices were prepared freehand, with a razor blade,
while the tissue was placed between two frosted
glass plates, the bottom one lying on crushed
ice. The thickness of the liver slices was about
0.5 mm. Studies of aortic tissue were done on
very thin slices of intima and the innermost
media layer (hereafter referred to as intima-
media) and on slices of the entire wall. While it
would have been desirable to study the intimal
layer only, since it is the one primarily involved
in the atherosclerotic process, this was, however,
not practically feasible due to its extreme thin-
ness in the normal aorta. Thus, although the
normal aortic innermost layer was sliced very thin
(0.1 to 0.15 mm), such slices, in addition to in-
tima, still included a certain amount of media.
In the atherosclerotic aorta, the intima-media lay-
er was separated at the cleavage plane, and cut
into slices with thinness similar to that of the
normal tissue. They also included a certain
amount of media. The portions of atherosclerotic
tissue used in our experiments were carefully
freed of surrounding normal appearing tissue.

Studies of aortic tissue were done on its three
segments, i.e., arch and ascending segment (here-
after referred to as "arch"), descending thoracic
and abdominal segments in the rabbit, and on
the descending thoracic and abdominal segments
in the dog.

The tissue slices were collected in ice-cooled
chambers, blotted, weighed, and transferred to
ice-cooled manometer flasks containing Krebs-
Ringer solution pH 7.4, of final phosphate con-
centration 0.023 M, and with the substrate in the
side arm. Oxygen consumption was determined
by the direct method of Warburg at 37.4°C
with oxygen as gas phase. Amounts of fresh tissue
per flask were 100 to 125 mg for the aorta, 30 to
40 mg for rabbit's liver and 20 to 30 mg for
dog's liver. The dog aorta and atherosclerotic
rabbit aorta provided enough material for duplica-
tive determinations, whereas that of the normal
rabbit did not provide enough material, thus
making it necessary to pool tissues from two or
three rabbits. Substrates used were sodium suc-
cinate (pH 7.4) of final concentration 0.05 M and
p-phenylenediamine of final concentration 0.03
M for the determination of the oxidative capaci-
ty of the succinic oxidase and cytochrome oxidase
systems respectively.

The surviving slice technic originated by O.
Warburg offers a means of studying the activity
of an enzymatic system with the cofactors
available at the concentration existing in the
tissues. Among the three substrates considered
specific for the cytochrome oxidase system, ascorbic
acid does not penetrate the cells. Of the other
two substrates, hydroquinone and p-phenylenedi-
amine, the latter because of its low oxidizabili-

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ty proved more satisfactory to us for the study of arterial tissue, whose oxygen consumption is low. The experimental conditions for using the slice technic in the determination of the oxidative capacity of the above two systems, in presence of succinate and p-phenylenediamine, were described and analyzed by Rosenthal et al. 18 Optimal concentration of substrate, and proportionality between enzyme action and amount of tissue, were determined in our experiments. The oxygen consumption per hour was computed from the period of linearity. While for normal tissues comparison of enzymatic activities on a dry weight basis may be valid, in tissues infiltrated by inert deposits, such as lipids, the dry weight basis may introduce serious errors. To avoid this source of error, the oxygen consumption of all tissues studied was related to their nitrogen content. It was expressed as QO2 = oxygen consumption/mg nitrogen/hour. The nitrogen content was obtained at the end of the experiment on the entire content of the flask by micro-Kjeldahl determination. 17

Results

RABBIT
(a) Entire Atherosclerotic Aortic Wall
Table 1 summarizes the results obtained with the rabbit's entire aortic wall. From this table it appears that during the first two to four months the development of atherosclerosis is associated with an increase (P<0.05) in oxidative capacity of the succinic oxidase system, in the arch and descending thoracic, as well as an increase in oxidative capacity of the cytochrome oxidase system in the arch. The latter system was not studied in the descending thoracic and abdominal segments. At a later stage (six to eight months) a reverse trend seems to occur, and a significant decrease (P<0.001) is noted in the arch for the succinic oxidase system.

(b) Atherosclerotic Intima-media
Because atherosclerosis involves mainly the intima and the immediately adjacent media, it is possible that changes occurring in this superficial layer may be masked by the underlying normal tissue. Table 2 summarizes the results obtained with the atherosclerotic layer, separated at the cleavage plane, and indicates that the development of atherosclerosis is associated in the first two to four months with an increase (P<0.05) of the oxidative capacity of both systems. At a later stage (six to eight months) a significant decrease (P<0.05) of the oxidative capacity takes place, for the succinic oxidase system in both the arch and descending thoracic aorta and for the cytochrome oxidase system in the three aortic segments.

<table>
<thead>
<tr>
<th>Substrate: succinate</th>
<th>Substrate: p-phenylenediamine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Arc</td>
</tr>
<tr>
<td>QO2 ± SEM (mm3 O2/mg tissue nitrogen/hour)</td>
<td>21.2 ± 1.31</td>
</tr>
<tr>
<td>No. of cases</td>
<td>8</td>
</tr>
<tr>
<td>Change, % of control</td>
<td>+34.0</td>
</tr>
<tr>
<td>P</td>
<td>&lt;0.02</td>
</tr>
</tbody>
</table>

Atherosclerotic: duration of atherogenic regimen, two to four months

| QO2 ± SEM | 28.4 ± 2.06 | 23.7 ± 2.62 | 20.4 ± 4.62 | 31.6 ± 4.30 |
| No. of cases | 7 | 7 | 7 | 6 |
| Change, % of control | +34.0 | +39.4 | +17.2 | -54.9 |
| P | <0.02 | <0.05 | >0.5 | <0.05 |

Atherosclerotic: duration of atherogenic regimen, six to eight months

| QO2 ± SEM | 16.6 ± 0.82 | 14.9 ± 1.14 | 17.7 ± 1.76 | 16.4 ± 2.08 | 15.3 ± 0.95 | 19.2 ± 2.44 |
| No. of cases | 13 | 8 | 7 | 11 | 8 | 8 |
| Change, % of control | -21.7 | -13.4 | +1.7 | -19.6 | -10.9 | +7.9 |
| P | <0.001 | >0.1 | >0.5 | >0.05 | >0.1 | >0.5 |

*Portions of aorta used in experiments were 100% atherosclerotic.
1QO2 = mm3 O2/mg tissue nitrogen/hour.
<table>
<thead>
<tr>
<th>Substrate: succinate</th>
<th>Substrate: p-phenylenediamine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Arch</td>
</tr>
<tr>
<td>QO$_2$  ± SEM</td>
<td></td>
</tr>
<tr>
<td>No. of cases</td>
<td>10</td>
</tr>
<tr>
<td>Change, % of control</td>
<td>+44.3</td>
</tr>
<tr>
<td></td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Atherosclerotic: duration of atherogenic regimen, two to four months</td>
<td></td>
</tr>
<tr>
<td>QO$_2$ ± SEM</td>
<td>14.3</td>
</tr>
<tr>
<td>No. of cases</td>
<td>13</td>
</tr>
<tr>
<td>Change, % of control</td>
<td>-37.8</td>
</tr>
<tr>
<td></td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Portions of aorta used in experiments were 100% atherosclerotic.
†QO$_2$ = mm$^3$ O$_2$/mg tissue nitrogen/hour.
In contrast to aortic tissue, the liver, although always undergoing a certain degree of fatty degeneration, showed no change in oxidative capacity at any time during the administration of the atherogenic regimen.

It is well known that atherosclerotic lesions, especially in their early phase, display a patchy or segmental distribution in man as well as in the dog and rabbit. As a result of this morphologic pattern, atheromatous and nonatheromatous arterial tissue may exist side by side. The characteristics of the nonatheromatous tissue were those of normal tissue as disclosed by smooth, glistening intima and a normal histologic picture of the arterial wall. The question arose whether any enzymatic changes occurred in this nonatherosclerotic tissue.

Table 3 shows the results obtained with the intima-media of atheromatous and nonatheromatous segments of the thoracic aorta of rabbits fed the cholesterol diet for three to four months. These results reveal that in contrast to the atherosclerotic tissue the nonatherosclerotic segment shows no change in the oxidative capacity of the succinic oxidase system and a decrease of about 19% ($P > 0.05$) in that of the cytochrome oxidase.

### Table 3

<table>
<thead>
<tr>
<th>Substrate: succinate</th>
<th>Atherosclerotic tissue</th>
<th>Nonatherosclerotic tissue</th>
<th>Change, % of control</th>
<th>$P$</th>
<th>Control</th>
<th>Atherosclerotic tissue</th>
<th>Nonatherosclerotic tissue</th>
<th>Change of nonatherosclerotic, %</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td>Atheromatous tissue</td>
<td></td>
<td></td>
<td>Nonatheromatous tissue</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>19.0 ± 1.20</td>
<td>16.4 ± 0.91</td>
<td>28.5 ± 3.24</td>
<td></td>
<td>21.4 ± 1.10</td>
<td>17.4 ± 0.67</td>
<td>31.7 ± 1.55</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of cases</td>
<td>10</td>
<td>6</td>
<td>6</td>
<td></td>
<td>7</td>
<td>6</td>
<td>6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change, %</td>
<td>-13.7</td>
<td>+50.0</td>
<td></td>
<td></td>
<td>-18.7</td>
<td>+48.1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>$&gt;0.05$</td>
<td>$&lt;0.02$</td>
<td></td>
<td></td>
<td>$&lt;0.01$</td>
<td>$&lt;0.001$</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Portions of aorta used in experiments were 100% atherosclerotic (by area involved).

Table 5 summarizes the results obtained with the entire wall of the descending thoracic and abdominal aorta from dogs with marked atherosclerosis in the peripheral vessels, but none yet in the aorta. This table indicates that no significant changes are seen in the entire aortic wall at that stage. It is, however, possible that a change may have taken place in the intima and that the normal underlying tissue, by its important mass, may mask it.

### TABLE 3

Oxidative Capacity of Atherosclerotic* and Nonatherosclerotic Adjacent Intima-media of Descending Thoracic Aorta from Rabbits on an Atherogenic Regimen for Three to Four Months

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*Portions of aorta used in experiments were 100% atherosclerotic (by area involved).

$1O_2 = mm^3 O_2/mg tissue nitrogen/hour.$
in the peripheral vessels only, displays a decrease of about 33% (P < 0.01) in oxidative capacity of the cytochrome oxidase system in the abdominal segment and no change in the thoracic, whereas the succinic oxidase system appears unaffected in both segments (P > 0.05).

Table 7 shows that the intima-media of the thoracic aorta from dogs with more advanced atherosclerosis, involving only the peripheral vessels and the abdominal aorta, exhibits a decrease of about 24% (P < 0.01) in the oxidative capacity of the former system and no change in that of the latter.

Discussion

In our experience and that of others,18 the extent of aortic lesions in the rabbit, despite some individual variations, may be predictable since it appears to depend upon the blood cholesterol level and the duration of the atherogenic regimen. With our diet, during the first two months, the atherosclerotic changes were minimal and almost exclusively situated in the proximal thoracic aorta. With the passage of time the entire aorta was involved in the following sequence: 1) ascending and arch, 2) descending thoracic, and 3) abdominal. It was thus possible to separate the development of atherosclerosis into two phases, according to the duration of the atherogenic regimen, namely: early phase, two to four months and late, six to eight months.

In contrast to the rabbit, the dog presents greater individual variation and the extent of the lesions does not seem always to parallel the level and duration of cholesterolemia. This individual variation seems to be related to the breed. The development of the atherosclerotic lesions in the dog follows, however, a definite pattern involving first the peripheral vessels and subsequently the abdominal aorta. The descending thoracic aorta, usually refractory to atherosclerosis, may in some instances develop such lesions at a later stage, of a minimal degree only as compared to the abdominal segment.

For the reasons outlined above, early and late atherosclerosis in the dog could not be grouped according to the duration of the atherogenic regimen. The severity of involvement of the abdominal segment was therefore chosen as a criterion for the grouping in two
### Table 5

**Oxidative Capacity of Dog Aorta (entire wall). Marked Atherosclerosis in Peripheral Vessels. No Atherosclerosis in Aorta**

<table>
<thead>
<tr>
<th>Substrate: succinate</th>
<th>Control</th>
<th>Atherogenic regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thoracic</td>
<td>Abdominal</td>
<td>Thoracic</td>
</tr>
<tr>
<td>15.5 ± 1.71</td>
<td>12.5 ± 0.95</td>
<td>15.3 ± 1.06</td>
</tr>
<tr>
<td>No. of cases</td>
<td>7</td>
<td>12</td>
</tr>
<tr>
<td>Change, % of control</td>
<td>-1.3</td>
<td>-10.4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Substrate: 2-phenylenediamine</th>
<th>Control</th>
<th>Atherogenic regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thoracic</td>
<td>Abdominal</td>
<td>Thoracic</td>
</tr>
<tr>
<td>17.7 ± 1.19</td>
<td>19.8 ± 1.21</td>
<td>17.8 ± 0.84</td>
</tr>
<tr>
<td>No. of cases</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Change, % of control</td>
<td>+0.6</td>
<td>-13.2</td>
</tr>
</tbody>
</table>

*\( \Delta QO_2 = \text{nm}^3 \text{O}_2/\text{mg tissue nitrogen/hour.}*

### Table 6

**Oxidative Capacity of Dog Aorta (intima-media). Marked Atherosclerosis in Peripheral Vessels. No Atherosclerosis in Aorta**

<table>
<thead>
<tr>
<th>Substrate: succinate</th>
<th>Control</th>
<th>Atherogenic regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thoracic</td>
<td>Abdominal</td>
<td>Thoracic</td>
</tr>
<tr>
<td>16.1 ± 0.87</td>
<td>12.4 ± 0.66</td>
<td>13.4 ± 1.10</td>
</tr>
<tr>
<td>No. of cases</td>
<td>8</td>
<td>10</td>
</tr>
<tr>
<td>Change, % of control</td>
<td>-1.3</td>
<td>-10.4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Substrate: 2-phenylenediamine</th>
<th>Control</th>
<th>Atherogenic regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thoracic</td>
<td>Abdominal</td>
<td>Thoracic</td>
</tr>
<tr>
<td>16.0 ± 1.01</td>
<td>18.6 ± 0.96</td>
<td>13.2 ± 1.09</td>
</tr>
<tr>
<td>No. of cases</td>
<td>8</td>
<td>10</td>
</tr>
<tr>
<td>Change, % of control</td>
<td>-17.5</td>
<td>-33.1</td>
</tr>
</tbody>
</table>

*\( \Delta QO_2 = \text{nm}^3 \text{O}_2/\text{mg tissue nitrogen/hour.}*

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*Oxidative Capacity of Atherosclerotic Tissue*
Oxidative Capacity of Dog Thoracic Aorta (intima-media). Marked Atherosclerosis in Peripheral Vessels and Abdominal Aorta. No Atherosclerosis in Thoracic Aorta

<table>
<thead>
<tr>
<th>Substrate: succinate</th>
<th>Substrate: p-phenylenediamine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
</tr>
<tr>
<td><strong>QO₂</strong> ± SEM</td>
<td>17.7 ± 1.19</td>
</tr>
<tr>
<td>No. of cases</td>
<td>10</td>
</tr>
<tr>
<td>Change, % of control</td>
<td>-13.0</td>
</tr>
</tbody>
</table>

*QO₂ = mm³ O₂/mg tissue nitrogen/hour.

Our results seem to indicate that, in both rabbit and dog, the development of atherosclerosis is associated with metabolic alterations of the arterial tissue. Thus, at a relatively early stage, the oxidative capacity of the succinic oxidase and cytochrome oxidase systems is increased in the atherosclerotic intima-media of the aortic tissue of both animals, whereas at a late stage it is decreased. Our results agree with previous findings which indicated an increased oxidative capacity of the succinic oxidase system in the atherosclerotic aortic intima-media of rabbits on an atherogenic regimen for three to four months.

While greater oxidative capacity in the early phase may be the result of "adaptation" due to an increased energy requirement, lesser oxidative capacity in the later phase may be attributed to the known development of fibrosis and of degenerative changes accompanying the "death" of the tissue.

It is noteworthy that in contrast to the aorta, the liver which is the site of massive deposition of lipids, in the rabbit particularly, does not exhibit any significant changes in oxidative capacity, at any time during the administration of the atherogenic regimen.

The question arose whether any enzymatic changes preceded the development of atheroma. It appeared that the answer to this question could be provided by studying uninvolved portions of the aorta. The patchy or segmental distribution of the lesions at an early stage in the development of atherosclerosis offered ideal conditions for such an investigation. Tables 3, 6, 7 indicate that the oxidative capacity of the cytochrome oxidase system was decreased in the uninvolved segments in both the rabbit and the dog, whereas that of the succinic oxidase system remained unchanged.

In addition, in the dog, the decrease of enzymatic activity in the uninvolved aorta paralleled the sequence in the development of the atherosclerotic lesions. When only the peripheral vessels were affected, the enzymatic decrease was noted in the abdominal but not in the thoracic aorta (table 6), whereas when the abdominal aorta was also involved, the enzymatic decrease was found in the thoracic segment (table 7).

Since it is well known that experimental canine atherosclerosis involves first the abdominal aorta and occasionally at a later stage the thoracic, the above enzymatic change assumes greater significance. It seems to be preatherosclerotic because it precedes and parallels the sequence of atheromatous lesions in the aorta.

It may be argued that the uninvolved segments which appeared normal by histologic criteria, may already have an elevated concentration of lipids, derived from the lipid-rich plasma. The mere presence of lipids, however, could not account for the above change since the liver, site of massive lipid deposition, did not display any alteration in oxidative capacity.

Elucidation of the mechanism whereby the decrease of the oxidative capacity of the cytochrome oxidase system occurs and the signifi-
Oxidative Capacity of Atherosclerotic Tissue

cance of this decrease in the development of atherosclerosis must await further investigation.

Summary

The oxidative capacity of the succinic oxidase and cytochrome oxidase systems, as measured by the oxidative response to succinate and p-phenylenediamine was studied in slices of aortas from rabbits and dogs subjected to an atherogenic regimen, and in the liver as reference tissue.

In both animals, at an early stage in the atherosclerotic process, the oxidative capacity of both systems was increased in the atherosclerotic intima-media layer, separated at the cleavage plane, while at a later stage it was decreased.

The intima-media of the uninvolved portions of the aorta showed a decrease in the oxidative capacity of the cytochrome oxidase system, whereas that of the succinic oxidase system remained unchanged.

The liver, although the site of massive deposition of lipids, in the rabbit particularly, showed no enzymatic changes at any time during the administration of the atherogenic regimen.

These findings indicate that metabolic alterations of the arterial wall are associated with the development of atherosclerosis.

References


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