Effects of High Static Pressures on Human Cerebral Arteries in Vitro

D. A. COPE, M.SC. AND MARGOT R. ROACH, M.D., PH.D.

SUMMARY Static elastic properties were obtained from pressure, volume, and length measurements of 34 isolated human cerebral arteries from 23 circles of Willis of patients aged 23-76 years. No significant difference in initial or final elastance was observed with age or branch in the circle of Willis. Twenty-four of the arteries from 18 circles of Willis were then subjected to transmural pressures of 200-300 mm Hg for periods of ≤ 5 minutes and the elastic properties restudied. In general, this had little effect on the arteries except for a significant increase in initial elastance than the males. Histological studies to look for elastin fragmentation in the intima were inconclusive.

THERE IS INCREASING EVIDENCE that human intracranial saccular aneurysms are acquired rather than congenital.1 Hassler2 and Nystrom3 have both stressed the importance of elastin fragmentation in aneurysms, and it seems likely that a break in the internal elastic membrane at the apex of an intracranial bifurcation may be the factor which initiates the development of an aneurysm. While Ferguson and Roach4 postulated that some hemodynamic force caused the fragmentation, this has not been proven.

Scott et al.5 showed clearly that the elastic properties of human cerebral arteries and aneurysms were different, and that the elastin part of the curve (i.e. the low pressure part) was absent in aneurysms. They also found, in a few arteries, that repeating the pressure-volume curves more than three times appeared to change the elastic properties of the artery to elastic properties more like those of an aneurysm. Since all of their arteries were subjected to pressures of at least 200 mm Hg, they postulated that high pressures might fragment the elastin, but could not say what pressure, or what duration of high pressure cause this alteration. Fragmentation of the elastin was postulated to be associated both with an increase in initial radius, and also with a change in the initial slope of the tension-strain diagram.6

Our experiments were designed to determine, if possible, whether pressure would fragment the elastin in isolated human cerebral arteries, and to determine if the age of the artery altered the response.

Methods

Thirty-four arteries were gently dissected from 23 circles of Willis of age 23-76 years at autopsy, and stored in saline at 4°C until use. Previous studies had demonstrated that the static elastic properties did not change for at least ten days under these conditions.4 All arteries were studied in less than one week after death.

One end of the artery was cannulated and connected to a
The initial slope has increased from the previous run, while the final slope is virtually unchanged.

Table 2 shows that the site of origin of the arteries from different age groups. There were no significant differences (at the 95% level) with age in either the initial or final slopes, although the two are quite different from each other. Table 2 shows that the site of origin of the arteries from the circle of Willis had no significant effect on the initial and final elastance. However, the initial radius was significantly different between groups when tested by analysis of variance.
Table 3  Effect of Short Pressure Subjections With Age

<table>
<thead>
<tr>
<th></th>
<th>≤ 40 yrs.</th>
<th>40-60 yrs.</th>
<th>≥ 60 yrs.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in average initial elastance (AE) (dynes/cm × 10⁻⁴)</td>
<td>N</td>
<td>10</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>s</td>
<td>0.214</td>
<td>0.024</td>
</tr>
<tr>
<td>after 1st pressure subjection</td>
<td>p</td>
<td>0.10 &lt; p &lt; 0.20</td>
<td>0.198</td>
</tr>
<tr>
<td>Change in average initial elastance (AE) (dynes/cm × 10⁻⁴)</td>
<td>N</td>
<td>10</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>s</td>
<td>0.205</td>
<td>-0.069</td>
</tr>
<tr>
<td>after all pressure subjections</td>
<td>p</td>
<td>0.10 &lt; p &lt; 0.20</td>
<td>0.187</td>
</tr>
<tr>
<td>Change in average final elastance (AE) (dynes/cm × 10⁻⁴)</td>
<td>N</td>
<td>9</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>s</td>
<td>0.557</td>
<td>8.304</td>
</tr>
<tr>
<td>after 1st pressure subjection</td>
<td>p</td>
<td>1.167</td>
<td>7.496</td>
</tr>
<tr>
<td>Change in average initial radius (AR) cm</td>
<td>N</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>s</td>
<td>0.0058</td>
<td>0.0041</td>
</tr>
<tr>
<td>after 1st pressure subjection</td>
<td>p</td>
<td>0.001 &lt; p &lt; 0.01</td>
<td>0.0087</td>
</tr>
<tr>
<td>Change in average initial radius (AR) cm</td>
<td>N</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>s</td>
<td>0.0063</td>
<td>0.0027</td>
</tr>
<tr>
<td>after all pressure subjections</td>
<td>p</td>
<td>0.0019</td>
<td>0.0029</td>
</tr>
</tbody>
</table>

*Tests of paired comparisons before and after high pressure subjections; N = number of arterial segments; s = mean of the differences; s = standard error of the mean (SEM); p = probability. Only significant change is in initial radius.

(except for the middle and anterior cerebral arteries). The biggest difference was between the vertebrae and the posterior cerebral arteries.

Table 3 summarizes the effects of short (<5 min) pressure exposure on the elastic properties of the three age groups. Note that, with the number of vessels studied, pressure has no effect on either the initial or the final elastance. By contrast, pressure of >200 mm Hg increased the initial radius in the young arteries (those <40 years), but had no effect on the others. Table 4 shows that there were no significant differences in any one group of arteries after short time exposure to high pressures. In the <40 year group, there were arteries from four males and six females (table 5). Pressure altered the initial elastance of the female arteries more. (An increase of 0.315 ± 0.127 S.E.M. for the female compared to 0.057 ± 0.298 for the males.) Neither difference was significant but the p value for the female was 0.05 < p < 0.10. Before the application of pressure ≥200

Table 4  Effect of Short Pressure Subjections with Origin

<table>
<thead>
<tr>
<th></th>
<th>Vertebral</th>
<th>Mid. Cerebral</th>
<th>Ant. Cerebral</th>
<th>Post. Cerebral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in average initial elastance (AE) (dynes/cm × 10⁻⁴)</td>
<td>N</td>
<td>3</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>s</td>
<td>0.593</td>
<td>0.0314</td>
<td>+ 0.366</td>
</tr>
<tr>
<td>after 1st pressure subjection</td>
<td>p</td>
<td>&lt;.50</td>
<td>0.2624</td>
<td>0.265</td>
</tr>
<tr>
<td>Change in average final elastance (AE) (dynes/cm × 10⁻⁴)</td>
<td>N</td>
<td>3</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>s</td>
<td>0.517</td>
<td>17.72</td>
<td>+ 0.29</td>
</tr>
<tr>
<td>after 1st pressure subjection</td>
<td>p</td>
<td>2.475</td>
<td>14.350</td>
<td>2.106</td>
</tr>
<tr>
<td>Change in average initial radius (AR) cm</td>
<td>N</td>
<td>2</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>s</td>
<td>0.0055</td>
<td>+ 0.0051</td>
<td>+ 0.0018</td>
</tr>
<tr>
<td>after 1st pressure subjection</td>
<td>p</td>
<td>0.0065</td>
<td>0.0034</td>
<td>0.0012</td>
</tr>
</tbody>
</table>

*Tests of paired comparisons before and after high pressure subjections; N = number of arterial segments; s = mean of the differences; s = standard error of the mean (SEM); p = probability; No significant changes.
differences; sample only small parts of each artery. In retrospect, we
microscope, but this was not done.

mm Hg, there was no significant difference between male
and female initial elastances (table 6).

For technical reasons, our histological slides were too poor
in quality to determine if the elastin had been fragmented
before or after the sections were cut. They also allowed us to
sample only small parts of each artery. In retrospect, we
should have assessed this with the scanning electron
microscope, but this was not done.

Discussion

We still have no quantitative information to determine if
static pressures can fragment the elastin in human cerebral
arteries. Our results show that young arteries become larger
(i.e. increase their initial radius) in response to pressures of
≥200 mm Hg. This response appears to be slightly more
pronounced in arteries from young females. While arteries
from different parts of the circle of Willis had different ini-
tial radii, they did not appear to respond differently to
pressure. Busby and Burton found that young cerebral
arteries (30-59 years) were more distensible than old ones
(60-89 years), and that both initial and final elastance in-
creased with age in the same manner described for human il-
iac arteries by Roach and Burton. Our results did not show
any significant difference between young and old arteries,
perhaps because of group sizes. On the other hand, Scott et
al. found an extremely wide variation between arteries from
the same circle of Willis. The pattern for any one artery was
not consistent in our results.

Stehbens has pointed out that the anterior circulation ac-
counts for 85-95% of aneurysms found at autopsy. Since we
found no significant differences between arteries in the
anterior and posterior circulations (table 4), we cannot ex-
plain this predisposition toward aneurysm formation in the
anterior cerebral arteries. However, we have no evidence
that the elastic properties of the bifurcation are comparable
to those of the arteries from which they arise. In fact, recent
work by Macfarlane shows clearly that measurement of the
elastic properties of arterial bifurcations is very complex.

Locksley, Sahs and Stehbens have found a higher incidence of
aneurysms in females ≥45 years of age. It is interesting to
speculate if the elastin in arterial bifurcations in females is
different, as our results for arteries suggest (but do not prove)
or if the increased incidence of hypertension in young females
may be the major factor.

Other diseases, such as hypertension and atherosclerosis,
are known to be associated with elastin fragmentation. There
is no good evidence whether the disease or the elastin
fragmentation appears first.

We still have no clear idea why we have failed to duplicate
the results of Scott et al. The difference could be due to
differences in age, differences in degree of atherosclerosis,
differences in arteries chosen, or a variety of other factors.

The results here suggest that the original assumption of Scott et
al. that static pressure of ≥200 mm Hg might fragment
elastin in human cerebral arteries may be an oversimplifica-

In order to reach some definite conclusions about the
effects of high pressure with age a sample size of 15-20
would be needed. For the male-female difference in the ≤40
year group a sample size of 20-25 would be needed for
significance. To determine the effects of high pressure on the
various branches, a sample size of 15-20 would be needed
with the branches grouped according to age. All estimates of
sample sizes needed assume that the t-values remain the
same.

Acknowledgment

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<table>
<thead>
<tr>
<th>Table 5</th>
<th>Effect of Sex on Initial Elastance Before Pressure Subjection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>N</td>
<td>4</td>
</tr>
<tr>
<td>x</td>
<td>+0.0575</td>
</tr>
<tr>
<td>s_x</td>
<td>0.298</td>
</tr>
<tr>
<td>p</td>
<td>(NS) 0.05 &lt; p &lt; 0.10</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 6</th>
<th>Effect of Sex on Initial Elastance Before Pressure Subjection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>N</td>
<td>6</td>
</tr>
<tr>
<td>x</td>
<td>1.370</td>
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<tr>
<td>s_x</td>
<td>0.773</td>
</tr>
<tr>
<td>p</td>
<td>(NS)</td>
</tr>
</tbody>
</table>
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