The Effect of Nicotinic Acid on the Cerebral Circulation, with Observations on Extracerebral Contamination of Cerebral Venous Blood in the Nitrous Oxide Procedure for Cerebral Blood Flow

By Peritz Scheinberg, M.D.

Measurement of cerebral blood flow by the nitrous oxide method before and during intravenous administration of nicotinic acid indicates that cerebral vessels do not respond to this drug. Evidence that contamination of cerebral by extracerebral blood occurs in about 20 per cent of subjects is deduced from the effects of nicotinic acid on the measured cerebral blood flows; studies making use of the intravascular catheter technic to sample internal jugular blood tend to confirm this hypothesis.

The nitrous oxide method for measuring cerebral blood flow, as devised by Kety and Schmidt, is based on the assumption that blood collected from a needle placed in the internal jugular bulb is not significantly contaminated by blood from extracerebral sources. This problem was investigated by Shenkin, Harmel and Kety, who calculated the percentage contamination of internal jugular by extracerebral blood by injecting dye into the external carotid artery and drawing blood samples from the internal jugular bulb and external jugular vein. They concluded that in the 8 subjects studied, an average of only 3 per cent of the blood in the internal jugular bulb is derived from extracerebral sources. These data are useful in studying normal subjects at ordinary room temperatures; they do not help in determining whether contamination has occurred in any given subject. Furthermore, it appeared possible that the frequency and degree of contamination might be different when the vessels of the extracerebral circulation were widely dilated, as following local heating or the administration of various drugs. Since nicotinic acid produces an intense flushing of the face, scalp, and neck and is thought to produce an increase in blood flow in these areas, this drug was employed with the following objectives in mind: (1) To determine the effect of nicotinic acid on the cerebral circulation; (2) to determine the frequency and extent of contamination of internal jugular by extracerebral blood; and (3) to devise a simple test to determine whether contamination had occurred in any given subject.

Method

The subjects were chosen at random from the hospital wards and included patients with various disease states, as well as 2 normal subjects. While several of the patients showed evidence of chronic cerebral vascular disease, none were studied immediately after an acute cerebral vascular accident. All the subjects were studied under fasting conditions. The nitrous oxide procedure for measuring the cerebral blood flow has been described in detail by Kety and Schmidt, and the modification in use in this laboratory of drawing continuous ten minute blood samples simultaneously from the femoral artery and the internal jugular bulb for the determination of the mean arterio-venous nitrous oxide difference has been reported previously, together with data on values for normal young subjects. The gas mixture used in the determination consisted of 15 per cent N₂O, 64 per cent N₂ and 21 per cent O₂. Arterial pressures were measured by the auscultatory method, with the arm held at heart level, every two minutes during the blood flow determination. Mean pressures were calculated from these readings by adding one-third the pulse pressure to the diastolic pressure. Blood oxygen contents were determined by the spectrophotometric method of Hickam and Frayser. Glucose was determined by Nelson's photometric adaptation of the Somogyi method. Cerebral oxygen utilization, cerebral glucose utilization, and cerebrovascular resistance were calculated as previously described.

The nicotinic acid was administered intravenously
in a normal saline infusion; doses of 300 to 800 mg. in 200 to 300 ml. of saline, over a twenty to twenty-
five minute period were used. In all instances, a very
pronounced flush was produced over the blush area,
with lesser degrees of flushing over other parts of
the body. The control blood flow determination was al
ways done prior to the administration of nicotinic
acid.

RESULTS

Effect of Nicotinic Acid on the Cerebral Cir-
culation. The data are presented in table 1. Intra-
venuous nicotinic acid in large, flushing doses
produced no significant change in any of
the cerebral metabolic functions. The relatively
large standard errors are the result of
the heterogeneity of the population studied.
Taken in this way, these nicotinic acid studies
are of no great positive value. Examination of
figure 1, however, reveals a finding of interest.
This chart plots, for comparison, the individual
determinations of cerebral blood flow and
A-V \( O_2 \) difference expressed as percentage
change from the control values resulting from
the administration of nicotinic acid or pro-
caine block of the stellate ganglion. The latter
results are taken from a previous study. The
spread of the changes occurring from these two
procedures (neither of which revealed statis-
tically significant change when considered as a
group) are about the same except for the
determinations enclosed in the blocks. These
subjects showed changes following the admin-
istration of nicotinic acid which were
strikingly different from the whole group; two
of the subjects showed large changes in cerebral
blood flow, whereas four had significant changes
in A-V \( O_2 \) difference. The large decreases in
A-V \( O_2 \) difference in these 4 subjects (out of a
group of 20) suggest that in approximately one
out of 5 persons the cerebral vessels are dilated
by the nicotinic acid, or that the internal
jugular blood is contaminated by extracerebral
blood. The results to be reported strongly
support the thesis of extracerebral contamina-
tion.

It should be pointed out that within wide
limits the oxygen consumption of areas drained
by the internal and external jugular veins is not
changed by increasing the blood flow. As the
calculated blood flow increases, the arterio-
venous oxygen difference falls, and the product
of the two remains the same. It is important to
emphasize that the finding of a constant
cerebral oxygen consumption before and after
the administration of nicotinic acid does not
bear on the question of contamination. It will
be noted that blood flow studies before and
during nicotinic acid were obtained on only
3 of the 4 subjects in whom the arteriovenous
oxygen difference decreased during nicotinic
acid. In 2 of these 3, the calculated cerebral
blood flow during nicotinic acid increased
proportionately and oxygen consumption was
not changed. In the one instance in which the
calculated blood flow did not increase, the fall
in oxygen consumption was 0.8 ml. \( O_2 \) per
minute per 100 Gm. brain, a change which is
probably in the range of variation due to
technical inaccuracies. As mentioned before,
when the patients are considered as a group,
there was no significant change in cerebral oxy-
gen consumption.

The Nitrous Oxide and Oxygen Content of
Blood Draining from the Face and Neck. These
data are summarized in table 2. The blood flow
procedure and calculations were performed in
the same way as the cerebral blood flow, except
that venous blood was drawn from the external
jugular vein or from the internal jugular vein
about 5 cm. inferior to the jugular bulb. This
gives a value for blood flow which does not
represent facial blood flow, as the solubility
coefficient for nitrous oxide in the tissues of
the face and neck is unknown, and it is doubtful
if the facial and neck tissues are homogeneous
enough to make the nitrous oxide method ap-
licable. It does indicate the direction of error
which results if blood from these tissues are
mixed with blood draining from the brain.
The nitrous oxide and oxygen contents of the
external jugular blood were studied in eight
observations on 7 subjects. The calculated
average blood flow was 29 ml. per minute per
100 Gm. tissue, less than half of the expected
average cerebral blood flow; the average A-V
\( O_2 \) difference was 2.96 volumes per cent, less
than half of the expected average cerebral
A-V \( O_2 \) difference. Thus, contamination from
facial and neck blood ordinarily gives a falsely
low value for cerebral blood flow and cerebral
\( O_2 \) consumption.
TABLE 1.—The Effects of Intravenous Nicotinic Acid on Cerebral Metabolic Functions

<table>
<thead>
<tr>
<th>Pt.</th>
<th>Age</th>
<th>Diagnosis</th>
<th>Cerebral Blood Flow (ml/min./100 Gm. brain)</th>
<th>Arterial-Cerebral Venous O2 Difference (vol. %)</th>
<th>Arterial-Cerebral Venous Glucose Difference (mg. %)</th>
<th>Cerebral O2 Consumption (ml. O2/min./100 Gm. brain)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Before N.A.</td>
<td>During N.A.</td>
<td>Before N.A.</td>
<td>During N.A.</td>
</tr>
<tr>
<td>S. C.</td>
<td>50</td>
<td>Pernicious anemia</td>
<td>36</td>
<td>6.10</td>
<td>4.37</td>
<td>12</td>
</tr>
<tr>
<td>H. S.</td>
<td>55</td>
<td>HVD; Diabetes</td>
<td>48</td>
<td>4.92</td>
<td>4.16</td>
<td>11</td>
</tr>
<tr>
<td>T. M. S.</td>
<td>48</td>
<td>Cerebral vasc. dis.</td>
<td>48</td>
<td>3.75</td>
<td>2.80</td>
<td>14</td>
</tr>
<tr>
<td>C. P.</td>
<td>49</td>
<td>Cerebral vasc. dis.</td>
<td>39</td>
<td>5.86</td>
<td>5.60</td>
<td>18</td>
</tr>
<tr>
<td>M. S.</td>
<td>23</td>
<td>RHD and Congestive heart failure</td>
<td>49</td>
<td>5.15</td>
<td>6.05</td>
<td>15</td>
</tr>
<tr>
<td>E. G.</td>
<td>58</td>
<td>Myxedema</td>
<td>40</td>
<td>5.47</td>
<td>6.35</td>
<td>15</td>
</tr>
<tr>
<td>W. P.</td>
<td>60</td>
<td>Pernicious anemia</td>
<td>25</td>
<td>4.26</td>
<td>6.25</td>
<td>7</td>
</tr>
<tr>
<td>W. W.</td>
<td>28</td>
<td>RHD; Congestive heart failure</td>
<td>41</td>
<td>5.28</td>
<td>4.06</td>
<td>11</td>
</tr>
<tr>
<td>T. R.</td>
<td>42</td>
<td>HVD</td>
<td>58</td>
<td>6.28</td>
<td>5.84</td>
<td>12</td>
</tr>
<tr>
<td>C. L.</td>
<td>23</td>
<td>Hysteria</td>
<td>76</td>
<td>4.52</td>
<td>4.05</td>
<td>12</td>
</tr>
<tr>
<td>H. F.</td>
<td>45</td>
<td>HVD</td>
<td>48</td>
<td>5.65</td>
<td>5.75</td>
<td>12</td>
</tr>
<tr>
<td>J. W.</td>
<td>36</td>
<td>HVD</td>
<td>65</td>
<td>5.41</td>
<td>4.15</td>
<td>12</td>
</tr>
<tr>
<td>N. B.</td>
<td>26</td>
<td>HVD</td>
<td>84</td>
<td>5.84</td>
<td>5.84</td>
<td>8</td>
</tr>
<tr>
<td>A. S.</td>
<td>29</td>
<td>Normal</td>
<td>61</td>
<td>6.78</td>
<td>7.04</td>
<td>11</td>
</tr>
<tr>
<td>M. S.</td>
<td>19</td>
<td>Hysteria</td>
<td>64</td>
<td>5.03</td>
<td>5.95</td>
<td>6</td>
</tr>
<tr>
<td>J. B.</td>
<td>33</td>
<td>Normal</td>
<td>78</td>
<td>5.11</td>
<td>5.42</td>
<td>8</td>
</tr>
<tr>
<td>M. M.</td>
<td>54</td>
<td>Myxedema</td>
<td>54</td>
<td>7.15</td>
<td>7.06</td>
<td>12</td>
</tr>
<tr>
<td>G. H.</td>
<td>39</td>
<td>HVD</td>
<td>54</td>
<td>6.21</td>
<td>6.43</td>
<td>15</td>
</tr>
<tr>
<td>M. L.</td>
<td>32</td>
<td>HVD</td>
<td>50</td>
<td>8.11</td>
<td>8.40</td>
<td>11</td>
</tr>
<tr>
<td>H. S.</td>
<td>50</td>
<td>HVD</td>
<td>48</td>
<td>5.60</td>
<td>6.00</td>
<td>8</td>
</tr>
</tbody>
</table>

Mean.................................        54                  6.40              0.94                   11.3                                        10.5                                            | 3.39                                          |
St. Dev.†..............................    14.6                17.5               1.6                     2.7                                                  3.53                                            | 3.33                                          |
St. Error‡.............................    3.3                 4.1                 0.35                    0.59                                                  0.79                                            | 0.74                                          |

<table>
<thead>
<tr>
<th>Pt.</th>
<th>Cerebral Glucose Consumption (mg. glucose/min./100 Gm. brain)</th>
<th>Mean Arterial Pressure (mm. Hg)</th>
<th>Cerebral Vascular Resistance (units)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before N.A.</td>
<td>During N.A.</td>
<td>Before N.A.</td>
</tr>
<tr>
<td></td>
<td>4.32</td>
<td>3.92</td>
<td>91</td>
</tr>
<tr>
<td>S. C.</td>
<td>5.28</td>
<td>4.30</td>
<td>107</td>
</tr>
<tr>
<td>H. S.</td>
<td>6.72</td>
<td>6.84</td>
<td>125</td>
</tr>
<tr>
<td>T. M. S.</td>
<td>5.14</td>
<td>6.14</td>
<td>87</td>
</tr>
<tr>
<td>C. P.</td>
<td>6.22</td>
<td>7.20</td>
<td>137</td>
</tr>
<tr>
<td>M. S.</td>
<td>7.20</td>
<td>6.15</td>
<td>91</td>
</tr>
<tr>
<td>E. G.</td>
<td>2.25</td>
<td>5.25</td>
<td>100</td>
</tr>
<tr>
<td>W. P.</td>
<td></td>
<td></td>
<td>97</td>
</tr>
<tr>
<td>W. W.</td>
<td></td>
<td></td>
<td>2.44</td>
</tr>
</tbody>
</table>

* For age and diagnosis, see top half of table.
† Standard deviation = $s = \sqrt{\frac{S^2 - (Sx)^2}{n}}$
‡ Standard error = $s/\sqrt{n}$
HVD = Hypertensive vascular disease
RHD = Rheumatic heart disease
N. A. = Nicotinic Acid
The p values, calculated from the changes resulting in individual cases following nicotinic acid administration, range from 0.06 to 0.35, indicating that the changes are not statistically significant.

Mean difference

Formula: $t = \frac{\text{Std. error of mean diff.}}{\text{Mean difference}}$. 

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Table 1.—Continued

<table>
<thead>
<tr>
<th></th>
<th>Cerebral Glucose Consumption (mg. glucose/min./100 Gm. brain)</th>
<th>Mean Arterial Pressure (mm. Hg)</th>
<th>Cerebral Vascular Resistance (units)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before N.A.</td>
<td>During N.A.</td>
<td>Before N.A.</td>
</tr>
<tr>
<td>T. R.</td>
<td>6.96</td>
<td>7.40</td>
<td>181</td>
</tr>
<tr>
<td>C. L.</td>
<td>8.36</td>
<td>8.65</td>
<td>91</td>
</tr>
<tr>
<td>H. F.</td>
<td>5.28</td>
<td>5.52</td>
<td>158</td>
</tr>
<tr>
<td>J. W.</td>
<td>3.96</td>
<td>2.90</td>
<td>133</td>
</tr>
<tr>
<td>N. B.</td>
<td>6.72</td>
<td>8.10</td>
<td>133</td>
</tr>
<tr>
<td>A. S.</td>
<td>6.40</td>
<td>7.75</td>
<td>93</td>
</tr>
<tr>
<td>M. S.</td>
<td>7.58</td>
<td>7.00</td>
<td>94</td>
</tr>
<tr>
<td>J. B.</td>
<td>4.20</td>
<td>6.80</td>
<td>68</td>
</tr>
<tr>
<td>M. M.</td>
<td>6.30</td>
<td>7.20</td>
<td>119</td>
</tr>
<tr>
<td>G. H.</td>
<td>8.10</td>
<td>6.20</td>
<td>113</td>
</tr>
<tr>
<td>M. L.</td>
<td>5.40</td>
<td>4.40</td>
<td>126</td>
</tr>
<tr>
<td>H. S.</td>
<td>3.80</td>
<td>2.90</td>
<td>115</td>
</tr>
</tbody>
</table>

Mean: 5.83 5.66 114 100 2.32 2.12
St. Dev.: 1.58 1.69 29 26 0.88 0.82
St. Error: 0.37 0.40 6.5 5.8 0.2 0.19

Fig. 1.—Individual determinations of cerebral blood flow and A-V O₂ difference, expressed as percentage change from the control values resulting from the administration of nicotinic acid or procaine block of the stellate ganglion.

In 5 subjects given nicotinic acid, the flow calculated from blood in the external jugular vein increased from an average of 29 to 91 ml. per minute per 100 Gm. tissue. (It must be remembered that this does not represent true blood flow, but rather an increase in the nitrous oxide content of the venous blood.) Of these, only two subjects (J. W. and L. J., table 2) showed an increase to levels that would have caused a significant increase in the cerebral blood flow above normal had this blood been contaminating cerebral venous...
blood. The others would have caused only a small increase in the original cerebral blood flow, and might not be recognized because of the errors inherent in the method. The average A-V \(O_2\) difference in these 5 subjects fell from 3.0 to 0.9 volumes per cent, and in every instance the change was striking and would cause a falsely low A-V \(O_2\) difference if this blood had been contaminating cerebral venous blood. The mean oxygen consumption of the tissues drained by the external jugular vein was not altered significantly by the nicotinic acid. In Subject L. J., blood was obtained from the internal jugular bulb simultaneously with that taken from the external jugular vein; there was no change in either cerebral blood flow or A-V \(O_2\) difference with nicotinic acid, indicating that no contamination was present.

In 3 subjects, a catheter was inserted into the internal jugular vein under fluoroscopic observation to a point 5 cm. inferior to a needle which had been placed in the internal jugular

### Table 2.—Comparative Blood Flows and Arteriovenous Oxygen Differences when Venous Blood is Obtained from the Internal Jugular Bulb, Internal Jugular Vein, and External Jugular Vein

<table>
<thead>
<tr>
<th>Pt.</th>
<th>Age</th>
<th>Type of Procedure</th>
<th>Blood Flow (ml./min./100 Gm. tissue)</th>
<th>Arteriovenous (O_2) Difference (volumes %)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Before N.A.</td>
<td>During N.A.</td>
</tr>
<tr>
<td>L. B.</td>
<td>38</td>
<td>External jugular blood flow</td>
<td>20</td>
<td>2.60</td>
</tr>
<tr>
<td>J. S.</td>
<td>30</td>
<td>External jugular blood flow</td>
<td>27</td>
<td>2.78</td>
</tr>
<tr>
<td>J. M.</td>
<td>44</td>
<td>External jugular blood flows, before and during N.A.</td>
<td>18</td>
<td>2.43</td>
</tr>
<tr>
<td>J. W.</td>
<td>34</td>
<td>Same as above</td>
<td>46</td>
<td>0.97</td>
</tr>
<tr>
<td>N. S.</td>
<td>44</td>
<td>Same as above</td>
<td>37</td>
<td>5.24</td>
</tr>
<tr>
<td>Z. B.</td>
<td>40</td>
<td>Same as above</td>
<td>23</td>
<td>4.82</td>
</tr>
<tr>
<td>L. J.</td>
<td>20</td>
<td>Simultaneous int. and ext. jug. blood flows, before and during N.A.</td>
<td>67</td>
<td>5.74</td>
</tr>
<tr>
<td>R. C.</td>
<td>25</td>
<td>Catheter in int. jug. vein. Needle in int. jug. bulb. Simultaneous blood flows before and during N.A.</td>
<td>42</td>
<td>7.65</td>
</tr>
<tr>
<td>R. D.</td>
<td>33</td>
<td>Same as above (oxygens only)</td>
<td>7.49</td>
<td>5.96</td>
</tr>
<tr>
<td>H. S.</td>
<td>50</td>
<td>Same as above</td>
<td>48</td>
<td>6.40</td>
</tr>
<tr>
<td>Mean</td>
<td></td>
<td></td>
<td>52</td>
<td>6.82</td>
</tr>
</tbody>
</table>

I. J. B. = Internal Jugular Bulb.  
Cath. = Catheter.  
E.J.V. = External Jugular Vein.  
N.A. = Nicotinic Acid.
Nicotinic acid increased the blood flow and decreased the A-V O\textsubscript{2} difference when calculated from samples collected by the catheter. In 2 patients, the oxygen content of the blood from the needle was unchanged; in one it rose. In this instance, the assumed contamination from extracerebral blood did not change the calculated flow.

The observations indicate that contamination from extracerebral sources consistently decreases the A-V O\textsubscript{2} difference, but has a more variable effect on the nitrous oxide calculation for cerebral blood flow.

Discussion

The finding that intravenous nicotinic acid in flushing doses does not produce cerebral vasodilatation indicates that this drug probably has no place in the treatment of cerebral vascular disease unless it possesses some therapeutic action aside from its effect on cerebral vessels. No inferences can be drawn from these studies, however, concerning the effectiveness of nicotinic acid in the treatment of acute cerebral embolism in young persons, for no such subject was included in these observations. Our findings are in agreement with those of Loman, Rinkel, and Myerson,\textsuperscript{7} who showed that intravenous nicotinic acid in doses of 100 to 150 mg. produced no significant changes in the cerebral arteriovenous oxygen difference in 4 cases and no changes in the cerebrospinal fluid pressure in 8 cases. They also showed that intracarotid nicotinic acid did not alter the cerebral arteriovenous oxygen difference. Our findings do not support the observations of Aring and his colleagues,\textsuperscript{8} who found an increased intracranial blood flow following the administration of nicotinic acid. These workers used the method devised by Ferris\textsuperscript{4} to measure relative intracranial blood flow; we feel that they did not measure the effect of nicotinic acid on the cerebral vessels, but rather on the vessels of the face. In this method, the skull is used as a type of plethysmograph, and changes in intracranial blood flow are measured by changes in the displacement of spinal fluid through a large needle in the lumbar region. A cuff is applied to the neck with sufficient pressure to prevent venous return from the head; the increased facial flow caused by nicotinic acid could have increased the pressure in the internal jugular system since the common facial vein enters into the internal jugular vein, and the venous return from the face is trapped by the cuff as effectively as the cerebral venous return. The only valves in the internal jugular vein are too far inferior to prevent this transmission of increased pressure into the internal jugular system and thence to the cerebrospinal fluid, thus producing an increased rate of spinal fluid displacement, due to increased facial blood flow, and not related to increased cerebral blood flow.

The observations presented here indicate that a significant amount of contamination of cerebral venous blood by blood from the face or neck, when vasodilatation in the face or neck has not been produced by heat or drugs, would result in a falsely low cerebral blood flow, A-V O\textsubscript{2} difference, and rate of O\textsubscript{2} consumption, and a falsely high cerebrovascular resistance. When vasodilatation in the face or neck has been produced, as by the administration of nicotinic acid, extracerebral contamination of cerebral venous blood may then result in a falsely high cerebral blood flow and a falsely low A-V O\textsubscript{2} difference. It is also demonstrated that nicotinic acid greatly increases the nitrous oxide content of the blood draining from the face and neck without altering the nitrous oxide content of cerebral venous blood, and therefore not altering cerebral blood flow.

The finding that the nitrous oxide content of blood draining from the external jugular vein (and hence the calculated flow through that vein) is not increased by a similar magnitude in different persons, whereas A-V O\textsubscript{2} difference is consistently and greatly decreased, is not explained by this study. It is possible that this variation of response by different individuals to nicotinic acid depends upon whether the increased blood flow to the tissues of the face and neck goes through capillaries or arteriovenous shunts. Increased capillary flow would allow the nitrous oxide to be absorbed by the tissues and yield a slower rise in the venous nitrous oxide curve than if arterial blood passed directly into the veins. It is also possible that
the individual characteristics of the tissues of the face and neck in different persons may influence the response of the venous nitrous oxide content to nicotinic acid. Finally, it is technically easier to measure changes in A-V O₂ difference than in blood flow, and this may well account for some of the disparity.

The consistently decreased A-V O₂ difference which results from the administration of nicotinic acid when extracerebral contamination is present offers a useful and simple test for determining the presence of extracerebral contamination in any subject. The patient can be given 50 to 100 mg. of nicotinic acid intravenously to produce flushing of the face, and then another sample can be drawn from the internal jugular bulb for oxygen analysis. If the oxygen content of the blood increases significantly, contamination has occurred. Certainly any observations on the effect of drugs on cerebral metabolism, as measured by the nitrous oxide method, should take into consideration the effects of the drug in question on the circulation in the face and neck.

These data also seem to indicate that extracerebral contamination of some degree is to be expected in about 20 per cent of the subjects studied by the nitrous oxide technic. Unless facial circulation is greatly increased, as by heat or drugs, the degree of contamination is probably quite small and should rarely affect a series of results.

SUMMARY AND CONCLUSIONS

1. Intravenous nicotinic acid in flushing doses produces no change in cerebral blood flow, arteriovenous oxygen and glucose difference, oxygen and glucose consumption, or vascular resistance.

2. The incidence of extracerebral contamination of cerebral venous blood in performing the nitrous oxide procedure for cerebral blood flow is thought to be around 20 per cent. This contamination is usually not of significant magnitude unless the facial circulation is increased by heat or drugs.

3. Significant contamination of cerebral venous blood by facial or neck blood in the resting subject at ordinary room temperature produces falsely low values for cerebral blood flow, A-V O₂ difference, and oxygen consumption by the nitrous oxide procedure. If contamination occurs when vasodilatation has been produced in the face and neck by nicotinic acid, a decreased A-V O₂ difference will consistently result, and also, in some cases, a falsely high value for cerebral blood flow.

4. For workers who use the nitrous oxide technic for measuring the effects of drugs on the cerebral circulation, a test for contamination of cerebral venous blood by extracerebral blood is suggested, using nicotinic acid as the testing substance.

ACKNOWLEDGEMENTS

The author is indebted to Dr. Eugene A. Stead, Jr., for much valuable advice and assistance in this work. The procedures were greatly assisted by the capable technical work of Miss Frances Morgan, Miss Dorothy Frederick, and Mrs. Louise Allen.

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The Effect of Nicotinic Acid on the Cerebral Circulation, with Observations on Extracerebral Contamination of Cerebral Venous Blood in the Nitrous Oxide Procedure for Cerebral Blood Flow
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Circulation. 1950;1:1148-1154
doi: 10.1161/01.CIR.1.5.1148

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/1/5/1148

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