REPERFUSION after cerebral ischemia is a common clinical event. It occurs after the spontaneous break-up of cerebral emboli and follows the removal of clips used for temporary hemostasis during surgery for aneurysm and arteriovenous malformation. Operations such as extracranial-intracranial by-pass are designed to increase circulation to chronically ischemic brain.

The initial period of recirculation after ischemia is of paramount importance and two patterns of post-ischemic circulatory disturbance have been described, the 'no-reflow phenomenon' and 'hyperemia-hypoperfusion'. The no-reflow phenomenon was originally demonstrated as an absence of carbon black staining after 5–7 minutes global cerebral ischemia in rabbits and has also been demonstrated in primates and rats. No-reflow can be reversed or prevented by recirculation at a satisfactory blood pressure, even if ischemia is prolonged. Explanations for the no-reflow phenomenon have included blockage of the vascular lumen by platelets or red cell aggregates; change in blood viscosity; local intravascular coagulation; and direct capillary compression from edematous endothelial and glial cells. The alternative pattern of post-ischemic circulatory disturbance is where an initial increase in cerebral blood flow, 'reactive hyperemia', is followed by a reduction in flow, 'delayed hypoperfusion'. This secondary hypoperfusion has been demonstrated in the isolated canine brain; following global cerebral ischemia in the cat, dog, monkey and rat and following focal cerebral ischemia in the cat.

It has been difficult to reconcile these two post-ischemic circulatory changes. Recent work has suggested that the no-reflow phenomenon will follow complete cessation of cerebral blood flow and does not occur if there is any residual flow, however small. Delayed hypoperfusion, by contrast, may follow both complete and incomplete cerebral ischemia.

It is important to define the factors in ischemia that influence post-ischemic circulatory changes. In these studies, we have chosen to vary the duration of ischemia with a fixed ischemic flow in order to decide whether post-ischemic hyperemia and hypoperfusion are universal phenomena or whether the degree and duration of these events are influenced by the duration of the preceding ischemia.

Methods

Animal Preparation

Experiments were performed in a standard manner by one person (N.V.T.) using a Zeiss operating microscope. Adult, male, Sprague-Dawley rats (200–300 g) were allowed free access to food and water pre-operatively and were premedicated with atropine 60 µg s.c. After induction of anesthesia with approximately 2% halothane, animals were paralysed (2 mg/kg d-tubocurarine i.p.) and ventilated via a tracheostomy with 70% nitrous oxide, 30% oxygen and 1.5% halothane delivered by a small animal ventilator (Harvard 683). The carotid arteries were isolated from the vagus nerve and jugular vein to facilitate subsequent clipping. The left femoral vein and left and right femoral arteries were cannulated with polyethylene catheters (PE50). The animal was then turned prone and the first cervical vertebra (C1) exposed through a muscle splitting incision. The alar foramina on each side was drilled to expose the underlying vertebral vessels lying in the foramen transversarium and they were then divided with bipolar diathermy under direct vision. Burr holes were made in the skull and platinum electrodes placed into three cortical regions, frontal, parietal and occipital on each side using micro-manipulators. The electrodes were cemented into place using cold-setting methylmethacrylate cement which also re-established the closed cranial cavity. A silver/silver-chloride reference electrode was placed subcutaneously in the back. Following surgery, the animal was placed in lateral decubitus and the halothane concentration reduced to 0.5%.

Systemic blood pressure was measured continuous-
ly with a Statham P50 transducer and recorded on a
Lectromed chart recorder. Arterial blood was sampled
anaerobically in microhematocrit tubes (0.1 ml) and
\( \text{PaCO}_2, \text{PaO}_2 \) and pH were measured on a blood gas
analysrer (ABL30 Radiometer, Copenhagen). pH was
corrected where necessary by i.v. infusion of bicar-
bonate. Body temperature was maintained at 36.5 to
37.5°C by external warming. The hematocrit was mea-
sured at the end of the experiment.

With the vertebral arteries divided, cerebral ischemia
was produced by bilateral carotid artery occlusion
using Scoville-Lewis aneurysm clips. Removal of the
carotid clips permitted recirculation.

rCBF

Six Teflon-coated platinum electrode (75 \( \mu \) diam.)
were placed into specific cortical regions stereotacti-
cally as described above and polarised at +400 mV to
the reference electrode. CBF was measured by clear-
ance of hydrogen (approximately 4% hydrogen in the
inspired gas mixture), and the flow calculated by the
initial slope technique between 30 and 90 seconds.

Experimental Protocol (table 1)

A total of 48 animals were used. The study mea-
sured rCBF, brain edema and blood-brain barrier
(BBB) permeability in each animal. Brain edema and
BBB permeability measurements required sacrifice of
the animal and the results are reported in the accompa-
nying paper.

Animals were divided into three experi-
mental groups:

Group A — ischemia = 15 mins, followed by recircu-
lation.

Group B — ischemia = 30 mins, followed by recircu-
lation.

Group C — ischemia = 60 mins, followed by recircu-
lation.

All animals were allowed to stabilise for 60 minutes
after surgery. Anesthesia was maintained at a constant
level (70% nitrous oxide, 30% oxygen, 0.5% halo-
thane). rCBF was measured before ischemia, through-
out ischemia and in recirculation at 5, 15, 30, 60, 120
and 180 minutes (or until sacrifice, if sooner). \( \text{PaCO}_2, \text{PaO}_2 \)
and pH were measured before each flow.

Statistical Analysis

The flow data were compared by analysis of vari-
ance, using the BMDP program package. Data reduc-
tion and analysis were performed on the University of
London CDC6600 computer.

Seven variables were used (Group + 6 electrodes,
for each animal). The electrode data were transformed
to give mean regional data.

At specified times in recirculation the design depen-
dants were 3 x 3 (frontal, parietal, occipital x
Groups A, B, C). The differences between the depen-
dants means were compared to an error term. The
degrees of freedom were calculated for independent
cases (i.e., for animals, rather than electrodes).

Results

Three groups of animals were compared. The three
groups were each of 16 animals made ischemic for
either 15, 30 or 60 minutes. In all groups ischemia was
followed by three hours reperfusion.

General Physiological Parameters (table 2)

Systemic arterial pressure \( \text{PaCO}_2, \text{PaO}_2 \), and systemic
pH remained stable throughout the experiment. Four-
vessel occlusion did not lead to systemic metab-
olic upset. On recirculation there was a slight reduc-
tion in systemic pH greater following 60 minutes
ischemia. This was corrected by i.v. infusion of bicar-
bonate and never required more than 1–2 mmol of
bicarbonate to return the systemic pH to normal limits.
Whole blood hematocrit lay between 0.45–0.40.

Cerebral Blood Flow (table 3)

Halothane concentration was maintained at 0.5% at
all times. There were differences in the pre-ischemic
CBF regionally (table 3). Mean cortical CBF before
ischemia was not significantly different between the
three experimental groups.

Forty-eight rats underwent four-vessel occlusion
and they all became ischemic. The hydrogen clearance
curve showed an equilibration phase in the first 45
seconds after carotid clipping and then settled to a
steady ischemic clearance which was maintained until
the clips were removed. The mean ischemic flow was
5.8 ± 0.4 mls/100 g/min (mean all cortical regions ±
S.E.M.). There were no significant differences be-
 tween the levels of flow regionally or between the
three experimental groups.

Removal of the carotid clips permitted reperfusion
and there was a similar pattern of reflow in all cortical
regions and in the three experimental groups (fig. 1).

There was an immediate increase in rCBF. After a
variable period of time this hyperemia was succeeded
by 'delayed hypoperfusion' with flows reduced below
control values. There were differences between the

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|c|c|}
\hline
 \textbf{Group} & \textbf{Pre} & \textbf{Ischemia} & \textbf{Recirculation} & \textbf{Recirculation} & \textbf{Recirculation} \\
 & \textbf{mins} & \textbf{mins} & \textbf{mins} & \textbf{mins} & \textbf{mins} \\
\hline
\textbf{Group A} & & & & & \\
15 mins & n = 16 & 16 & n = 12 & 8 & 4 \\
30 mins & n = 16 & 16 & n = 12 & 8 & 4 \\
60 mins & n = 16 & 16 & n = 12 & 8 & 4 \\
\hline
\end{tabular}
\caption{Experimental Design}
\end{table}
TABLE 2  General Physiological Parameters

<table>
<thead>
<tr>
<th>Duration of ischemia</th>
<th>SAP (mm Hg)</th>
<th>PaCO₂ (mm Hg)</th>
<th>PaO₂ (mm Hg)</th>
<th>pH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-ischemia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15 mins</td>
<td>124 ± 3</td>
<td>38.9 ± 0.7</td>
<td>171 ± 18</td>
<td>7.374 ± 0.005</td>
</tr>
<tr>
<td>30 mins</td>
<td>121 ± 2</td>
<td>37.7 ± 0.7</td>
<td>158 ± 14</td>
<td>7.356 ± 0.010</td>
</tr>
<tr>
<td>60 mins</td>
<td>127 ± 3</td>
<td>40.8 ± 0.7</td>
<td>192 ± 20</td>
<td>7.380 ± 0.012</td>
</tr>
<tr>
<td>Ischemia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15 mins</td>
<td>120 ± 4</td>
<td>39.7 ± 0.6</td>
<td>161 ± 11</td>
<td>7.377 ± 0.016</td>
</tr>
<tr>
<td>30 mins</td>
<td>117 ± 3</td>
<td>38.5 ± 0.5</td>
<td>150 ± 7</td>
<td>7.367 ± 0.014</td>
</tr>
<tr>
<td>60 mins</td>
<td>126 ± 5</td>
<td>39.3 ± 0.4</td>
<td>175 ± 19</td>
<td>7.353 ± 0.017</td>
</tr>
<tr>
<td>5 mins reperfusion</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15 mins</td>
<td>124 ± 3</td>
<td>42.2 ± 1.2</td>
<td>150 ± 7</td>
<td>7.343 ± 0.012</td>
</tr>
<tr>
<td>30 mins</td>
<td>123 ± 2</td>
<td>38.8 ± 1.0</td>
<td>142 ± 10</td>
<td>7.389 ± 0.021</td>
</tr>
<tr>
<td>60 mins</td>
<td>126 ± 4</td>
<td>41.0 ± 0.8</td>
<td>176 ± 22</td>
<td>7.390 ± 0.021</td>
</tr>
<tr>
<td>60 mins reperfusion</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15 mins</td>
<td>126 ± 4</td>
<td>38.4 ± 1.1</td>
<td>149 ± 13</td>
<td>7.386 ± 0.010</td>
</tr>
<tr>
<td>30 mins</td>
<td>121 ± 2</td>
<td>39.2 ± 1.0</td>
<td>137 ± 8</td>
<td>7.388 ± 0.021</td>
</tr>
<tr>
<td>60 mins</td>
<td>132 ± 4</td>
<td>39.7 ± 1.0</td>
<td>161 ± 23</td>
<td>7.351 ± 0.029</td>
</tr>
<tr>
<td>180 mins reperfusion</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15 mins</td>
<td>116 ± 3</td>
<td>38.0 ± 0.8</td>
<td>156 ± 15</td>
<td>7.392 ± 0.007</td>
</tr>
<tr>
<td>30 mins</td>
<td>120 ± 2</td>
<td>40.6 ± 1.5</td>
<td>136 ± 12</td>
<td>7.354 ± 0.017</td>
</tr>
<tr>
<td>60 mins</td>
<td>130 ± 3</td>
<td>38.7 ± 1.1</td>
<td>179 ± 18</td>
<td>7.344 ± 0.017</td>
</tr>
</tbody>
</table>

SAP = systemic arterial blood pressure.
Values = mean ± SEM.

three experimental groups in each of these phases of recirculation, and we have considered the data under the headings 1) no-reflow, 2) hyperemia, 3) duration of hyperemia and 4) hypoperfusion.

No-Reflow

On removal of the carotid clips there was an immediate clearance of any hydrogen still present in the brain. The first flow was measured at 5 minutes of recirculation and from a total of 210 electrodes in 36 rats, not one electrode failed to show reflow. Some brain regions failed to mount a typical hyperemia and this was related to the duration of the preceding ischemia. After 15 minutes ischemia, only 2.5% of electrodes showed flows lower than their pre-ischemic value. This increased to 11.7% after 30 minutes ischemia and to 15.7% after 60 minutes ischemia. Those regions that did not show post-ischemic hyperemia nevertheless followed a similar pattern of later reflow with a reduction in CBF until during hypoperfusion they were not separate from the group as a whole.

Hyperemia (fig. 2)

All brain regions and all three experimental groups showed post-ischemic hyperemia, defined as mean flows in recirculation significantly greater than pre-ischemic values. This hyperemia was always maximal immediately on recirculation (measured at 5 minutes) and it developed in the presence of a normal systemic blood pressure (mean = 124 mmHg). The data are shown in table 3. There were 35° of freedom. There was a significant group effect (F = 4.16; p = 0.0249) with peak hyperemia being greatest in Group A, least in Group C. There was also a site effect (F = 13.49; p < 0.001) with occipital flows being significantly reduced, compared to the frontal and parietal flow. The

TABLE 3  Post-Ischemic Cerebral Blood Flow — Rat Cortex

<table>
<thead>
<tr>
<th>Ischemic Time</th>
<th>Frontal</th>
<th>Parietal</th>
<th>Occipital</th>
</tr>
</thead>
<tbody>
<tr>
<td>15 min</td>
<td>80 ± 5</td>
<td>93 ± 9</td>
<td>86 ± 9</td>
</tr>
<tr>
<td>30 min</td>
<td>5.5 ± 0.4</td>
<td>6.3 ± 0.9</td>
<td>5.8 ± 0.5</td>
</tr>
<tr>
<td>60 min</td>
<td>108 ± 7</td>
<td>104 ± 8</td>
<td>125 ± 13</td>
</tr>
<tr>
<td>15 min</td>
<td>85 ± 5</td>
<td>87 ± 9</td>
<td>80 ± 6</td>
</tr>
<tr>
<td>30 min</td>
<td>5.9 ± 0.6</td>
<td>5.7 ± 0.8</td>
<td>5.6 ± 0.5</td>
</tr>
<tr>
<td>60 min</td>
<td>6.6 ± 0.5</td>
<td>6.2 ± 0.7</td>
<td>5.7 ± 0.4</td>
</tr>
<tr>
<td>15 min</td>
<td>193 ± 14</td>
<td>142 ± 14</td>
<td>110 ± 9</td>
</tr>
<tr>
<td>30 min</td>
<td>91 ± 10</td>
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<td>60 min</td>
<td>193 ± 14</td>
<td>142 ± 14</td>
<td>110 ± 9</td>
</tr>
</tbody>
</table>

CBF ml/100 g/min in 3 cortical regions.
Flows were measured at rest, during ischemia and during reperfusion (5, 15, 30, 60 min and 2, 3 hrs). Three experimental groups with ischemic times of 15, 30, 60 min followed by reperfusion.
Results are mean ± SEM.
For statistical analysis refer to text.
Reperfusion after Cerebral Ischemia

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Figure 1. CBF following cerebral ischemia. Pre-ischemic flow was 94 ± 8 ml/100 g/min (there was no significant difference between the three experimental groups). During ischemia, flow was reduced to 5.8 ± 0.4 ml/100 g/min. On reperfusion, there was an immediate hyperemia followed by delayed hypoperfusion in all groups. ◊ 15 minutes ischemia, ◊ 30 minutes ischemia, ◊ 60 minutes ischemia. a — all flows significantly greater than pre-ischemic flows, 'hyperemia', p < 0.01, b — all flows significantly lower than pre-ischemic flow, 'hypoperfusion', p < 0.01.

Group and site effects were independent (site/group interaction, F = 1.35; p = 0.261).

Duration of Hyperemia (fig. 3)

There was not an abrupt change from hyperemia to hypoperfusion and we calculated the time for the hyperemic flow to reach control values for each electrode. There was no regional difference, so the regional data were summed to give a mean cortical value for each animal. The duration of hyperemia in the three groups was A = 16.9 ± 0.5 mins; B = 21.9 ± 1.3 mins; C = 62.1 ± 7.4 mins (results = mean ± S.E.M.). Differences between the means were compared using one-way ANOVA (p < 0.001) and we concluded that longer ischemia prolonged post-ischemic hyperemia.

Delayed Hypoperfusion (fig. 4)

All three experimental groups and all brain regions showed hypoperfusion, i.e., a reduction in CBF to levels significantly lower than pre-ischemic values (table 3). There was a difference in the rate of onset of hypoperfusion as described above. During established hypoperfusion (at two and three hours recirculation) differences between design dependants, brain region
('site') and the experimental groups were compared using analysis of variance. There were 11 degrees of freedom for each term. At 120 minutes recirculation, there was no significant difference (F = 0.13; p = 0.878) and no site difference (F = 1.41; p = 0.130). Similar results were found at 180 minutes recirculation. Indeed in this study, during hypoperfusion, there was a remarkable similarity of flow, despite the differences in the duration of the preceding ischemia. These flows were approximately 65% of the pre-ischemic levels.

Discussion

The four-vessel occlusion model of Pulvinelli and Brierley is an important model of ischemia and it produces severe cerebral ischemia in the rat, without added systemic insults such as anoxia or hypotension. Our modification of the surgical technique allows us to see the vertebral vessels and to be sure that they are divided and all 48 rats in this study became ischemic when the carotid arteries were clipped. There was no post-operative selection of animals and the preparation was completed in one stage. The model is a most stable preparation with no significant change in systemic blood-pressure, PaCO₂, PaO₂ or pH during the course of the experiment (table 2).

Pre-ischemic flow values were not significantly different between the three experimental groups but there were significant differences in flow between the three brain regions and this probably reflects differences in local metabolic rate. The flow values are comparable with results obtained with hydrogen clearance and autoradiography in anesthetised and awake rats.

During four-vessel occlusion, severe hemispheric ischemia was produced in all animals with an overall mean flow of 5.8 ± 0.4 mls/100 g/min (all groups and all regions). We selected three periods of ischemia, 15, 30 and 60 minutes (Groups A, B, C) giving a progressive increase in the duration of ischemia. The pattern of cerebral blood flow in recirculation was similar in the three experimental groups and our results confirm the view that the sequence 'hyperemia-hypoperfusion' is the rule following incomplete ischemia. We have extended this by demonstrating that the peak and duration of hyperemia were dependent upon the duration of incomplete cerebral ischemia, whereas flow during hypoperfusion appeared to be independent of the duration of the preceding ischemia.

Hyperemia occurred in all experiments and in all brain regions. During ischemia, powerful vasodilator substances such as adenosine, K⁺, H⁺ and CO₂ accumulate and dilation of pial vessels has been confirmed by direct observation. Hyperemia represents flow in this dilated vascular bed, and it might be expected that there would be a maximal vasodilatation with even short periods of cerebral ischemia. The similarity of flow in the frontal and parietal cortices within each group was striking and this may represent a state of maximal vasodilatation. Flow was lower in the occipital cortex despite the same degree of ischemia, and this probably reflects a difference in effective arterial blood-pressure. In the four-vessel occlusion model, all cortical regions reperfuse from the carotid arteries and the occipital cortex is furthest from the 'head' of pressure. If this explanation is correct, it suggests that manipulation of the blood pressure in early recirculation may be a method of increasing or decreasing hyperemia. There were differences in the degree of hyperemia between the three experimental groups with Group A showing the fastest flow and Group C the slowest. If we assume maximal vasodilatation in all groups, then this difference in flow must be due to a difference in perfusion pressure (= systemic arterial pressure - intracranial pressure). Since arterial blood-pressure was the same, variations in perfusion pressure are probably accounted for by changes in intracranial pressure (ICP) which is associated with brain edema. We found the amount of edema to be greater with increasing duration of ischemia and this probably accounts for the reduction in post-ischemic hyperemia in Groups B & C.

We would therefore suggest that following incomplete ischemia, immediate hyperemia is the rule and that this is a consequence of maximal vasodilatation. Differences in hyperemic flow represent changes in perfusion pressure, either a change in systemic blood-pressure or ICP. After longer ischemia, the duration of hyperemia was prolonged. Metabolic vasodilator products produced during ischemia lead to post-ischemic vasodilatation. With prolonged ischemia, the volume of these products is greater and also the cellular mechanism necessary for their metabolism and/or excretion are probably damaged to a greater extent. It is therefore likely that the prolongation of hyperemia following longer ischemia is secondary to reduced clearance of vaso-active products.

We have shown that hypoperfusion started significantly sooner after short periods of ischemia. Although it is difficult to compare results from different species and different experimental methods, previous work tends to confirm this. Hypoperfusion starts about 15 to 20 minutes after five minutes global ischemia in the dog; 40 minutes after 30 minutes global ischemia in the cat and about 80 minutes after 60 minutes global ischemia in the cat. Hypoperfusion occurred in our experiments despite maintenance of a normal systemic blood-pressure and PaCO₂ and must be due to an increase in vascular resistance. This may be caused by (I) intravascular, (II) extravascular, or (III) vascular factors.

Although intravascular stasis, (I), is important in the no-reflow phenomenon, it is difficult to postulate spontaneous sludging occurring after hyperemia, and thrombi cannot be demonstrated in the cerebral vessels after 30 minutes incomplete ischemia in the rat. 'Intracerebral squeeze' (II) or vascular compression from brain swelling is a potential mechanism of post-ischemic hypoperfusion. However, the changes in flow do not follow the known changes in brain water, and CBF is most consistently reduced at 1–4 hours of reperfusion, at a time when brain water is resolving. We could not correlate reduced post-ischemic CBF.
with brain edema. Hypoperfusion occurred soonest (Group A) where brain edema was least and was delayed (Group C) where brain edema was maximal. Equally at two hours recirculation, all groups showed the same hypoperfusion despite marked differences in brain edema. A more likely explanation is that these hypoperfusion are not clear. The mechanism and consequences of post-ischemic hyperperfusion are not clear. The reduction in CBF may simply reflect a reduced CMR and this would imply CBF/CMR coupling during hyperperfusion. Some workers have shown a steady rise in post-ischemic CMR and it may be that CBF and CMR remain uncoupled in later recirculation and very fast flows are inappropriate to the metabolic needs. It would therefore appear that CBF and CMR are uncoupled in early recirculation.

The mechanism and consequences of post-ischemic hyperperfusion are not clear. The reduction in CBF may simply reflect a reduced CMR and this would imply CBF/CMR coupling during hyperperfusion. Some workers have shown a steady rise in post-ischemic CMR and it may be that CBF and CMR remain uncoupled in later recirculation. If so, this would permit a CBF/CMR mismatch during delayed hyperperfusion with relative hypoxia producing secondary neuronal damage. Although we did not measure CMR, we feel that CMR is unlikely to have been the same in our experimental groups. We found no difference in CBF between the three groups and we would suggest that CBF and CMR remain uncoupled during the phase of hyperperfusion. Further work is required to clarify this point and also to determine the mechanisms of post-ischemic hyperperfusion.

In conclusion, after incomplete cerebral ischemia there is an immediate hyperemia followed by hyperperfusion and these flow changes may reflect changes in vascular smooth muscle tone. Hyperemia is a consequence of reperfusion into a maximally vasodilated bed and is reduced following longer periods of ischemia where the ICP is raised. Hyperperfusion starts most quickly after the shortest period of ischemia and this may be due to a return of vascular tone. In established hyperperfusion, flow is 60 to 70% of control values, regardless of the duration of the preceding ischemia.
BRAIN SWELLING due to water accumulation is an important complication of cerebral ischemia and will frequently lead to trans-tentorial herniation and death.1-3 The amount of water accumulating during ischemia depends on the level of flow during ischemia4-5 and its duration,6-7 and on whether the ischemia is complete or incomplete.8 Restoration of blood flow to ischemic brain may improve outcome and operations to revascularize the ischemic brain have been devised. Unfortunately reperfusion may lead to an increase in brain water, occurring either immediately9,10 or later, when it is associated with breakdown of the blood-brain barrier and leakage of protein-rich fluid into the brain interstitial space.5

We have used the model of cerebral ischemia described earlier11 to measure cerebral blood flow (CBF), brain edema and blood-brain barrier (BBB) permeability quantitatively and on a regional basis in the same animal. This study examined the effect of increasing duration of ischemia on the development and resolution of brain edema and blood-brain barrier permeability in recirculation after temporary, severe cerebral ischemia.

Duration of Ischemia Influences the Development and Resolution of Ischemic Brain Edema

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SUMMARY The influence of the duration of ischemia on the development and resolution of post-ischemic brain edema (SG method) was studied in anesthetized rats. Edema developed during ischemia and the amount of edema was related to the duration of ischemia (r = 0.843, p < 0.001). With recirculation to three hours, the major determinant of the amount of edema was still the duration of the preceding ischemia (p < 0.001). Resolution of brain edema only occurred following fifteen minutes ischemia. Post-ischemic blood-brain barrier breakdown [(4)nC-AIB, EB albumin] was greatest following longer ischemia. Where present, the BBB leakage was simultaneously to large and small molecules.
Reperfusion after cerebral ischemia: influence of duration of ischemia.
N V Todd, P Picozzi, H A Crockard and R R Russell

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