During subsequent post-ischemic hypoperfusion, in both C0reaktivity and autoregulation are abolished. 

In reactive hyperemia, cerebral vessels are paralyzed, and increased metabolic demand of the tissue and therefore oxygen availability is in misrelationship to an increased oxygen content of cerebral venous blood increases (luxury perfusion).


The hemodynamic changes are caused by or associated with disturbances of flow regulation. During reactive hyperemia, oxygen availability exceeds the oxygen requirements of the tissue, and oxygen content of cerebral venous blood increases (luxury perfusion). During post-ischemic hypoperfusion, the decreased oxygen requirements of the tissue, and oxygen content of cerebral venous blood increases (luxury perfusion). During both phases, energy-producing metabolism and blood flow are uncoupled: in reactive hyperemia, oxygen availability exceeds the oxygen requirements of the tissue, and oxygen content of cerebral venous blood increases (luxury perfusion).

During post-ischemic hypoperfusion, the decreased oxygen availability is in misrelationship to an increased metabolic demand of the tissue and therefore may result in relative cerebral hypoxia.

The hemodynamic changes are caused by or associated with disturbances of flow regulation. During reactive hyperemia, cerebral vessels are paralyzed, and both CO2-reactivity and autoregulation are abolished. During subsequent post-ischemic hypoperfusion, in contrast, vascular tone is increased although CO2-reactivity is abolished, and a rise of blood pressure now causes an autoregulatory constriction of the resistance vessels. In consequence, blood flow in this period of hypoperfusion cannot be improved by either increasing blood pressure or increasing arterial or tissue pCO2.

The hemodynamic changes observed during post-ischemic hypoperfusion resemble the pharmacological effect of indomethacin, an inhibitor of prostaglandin synthesis, which also reduces blood flow and abolishes CO2-reactivity without interfering with autoregulation. Prostaglandins have been shown to play an important role in the hemodynamic balance of local blood flow, whereby prostacyclin (PGI2) and thromboxane A2 (TXA2) are mainly involved. The respective precursors are the cyclic endoperoxides PGG2 and PGH2, that are synthetized from arachidonic acid by cyclo-oxygenases. These endoperoxides are transformed in the vascular wall by prostacyclin synthetase into PGI2 and in the blood platelets by thromboxane-synthetase into TXA2.

No Effect of Prostacyclin on Blood Flow, Regulation of Blood Flow and Blood Coagulation Following Global Cerebral Ischemia

W. van den Kerckhoff, K.-A. Hossmann and V. Hossmann*

SUMMARY In normothermic cats under light barbiturate anesthesia, cerebral blood flow was arrested for one hour by intrathoracic occlusion of the innominate, the left subclavian, and both mammarian arteries. Recirculation of the brain after ischemia resulted in reactive hyperemia, followed by a decrease of blood flow to about 70% of control (post-ischemic hypoperfusion). During postischemic hypoperfusion, CO2-reactivity was completely abolished. Intravenous infusion of prostacyclin 2 hours after ischemia (1.8 μg/kg/min) decreased systemic arterial blood pressure and reduced platelet aggregability but did not improve cerebral blood flow, did not restore CO2-reactivity, and did not influence postischemic changes of blood coagulation. It is concluded that prostacyclin deficiency is not or not the only reason for the development of post-ischemic hypoperfusion and the associated disturbance of flow regulation.

STROKE Vol 14, No 5, September-October 1983

Received November 29, 1982; revision accepted March 3, 1983.

From the Max-Planck-Institut für neurologische Forschung, Abteilung für experimentelle Neurologie, und Lehrstuhl Innere Medizin II, Universität Köln, Ostmerheimer Str. 200 D-5000 Köln 91 (Merheim), Republic of West Germany.

*This study was supported in part by Landesamt für Wissenschaft und Forschung, NRW.

Address correspondence to: W. van den Kerckhoff, Max-Planck-Institut für neurologische Forschung, Abteilung für experimentelle Neurologie Köln, Ostmerheimer Str. 200 D-5000 Köln 91 (Merheim), Republic of West Germany.

Although both PGI2 and TXA2 synthesis are inhibited by indomethacin, the main factor responsible for the hemodynamic changes seems to be the reduced synthesis of PGI2, because substitution of this compound reverses the reduction of cerebral blood flow and restores.
CO₂-reactivity.\textsuperscript{15-18} In view of these findings, the ques-
tion arose whether post-ischemic hypoperfusion and
the associated disturbance of CO₂-reactivity can be
reversed by therapeutic application of prostacyclin.
Post-ischemic hypoperfusion is frequently associated
with regional disturbances of metabolic activity\textsuperscript{2}
and of the blood coagulation system;\textsuperscript{19, 20} these effects,
therefore, were also studied. In this communication
the hemodynamic and hemostatic, and in an accompa-
nying paper the metabolic observations will be
described.\textsuperscript{1}

Material and Methods

Thirteen adult cats of both sexes, weighing 2–3.5
kg, were used. The animals were anesthetized with
pentobarbital (Nembutal\textsuperscript{®}, 30 mg/kg intraperitoneal-
ly). Following tracheotomy, the animals were immo-
bilized by pancuronium bromide (Pancuronium\textsuperscript{®},
Or-
ganon, FRG) and mechanically ventilated with a
Harvard respirator. Arterial pCO₂ was maintained
close to 30 mm Hg and arterial pO₂ above 100 mm Hg
by appropriate adjustment of tidal volume and oxygen
content of the inhaled air. Tidal CO₂ was continuously
monitored using a CO₂-analyzer (URAS, Hartmann
and Braun, Frankfurt, FRG). Body temperature was
maintained at 37°C with a thermocontrolled heating
pad.

Catheters were placed into the following vessels:
into the innominate artery via the left brachial artery
for estimation of cerebral blood flow by bolus injection
of \textsuperscript{133}Xenon; into the left femoral artery for monitoring
the systemic arterial blood pressure and for withdrawal
of arterial blood samples; into both femoral veins
for drug infusion and stabilization of systemic blood
pressure by withdrawal or reinfusion of blood, if
necessary.

Blood flow of the total brain was completely arrest-
ed for one hour by intrathoracal occlusion of the in-
nominate, the left subclavian and both mammarian
arteries. Collateral blood supply via the ascending spi-
nal arteries was prevented by lowering the systolic
blood pressure below 80 mm Hg with trimethaphan-
camphorsulfonate (Arfonad\textsuperscript{®}) and — if necessary —
by withdrawal of blood. The completeness of ischemia
was controlled by recording the clearance of \textsuperscript{133}Xenon,
that was injected immediately before the occlusion of
the arteries. Ischemia was considered to be complete
when radioactivity over the head decreased by less
than 10% during the total length of ischemia.

In order to promote blood recirculation after isch-
emia, the animals were submitted to the following
procedure. Ten minutes before the end of the ischemia,
30 ml Tris buffer (Sterofundin-Tris\textsuperscript{®}, 15 mM/L) were
infused at a rate of 1 ml/min for equilibration of the
acid-base balance during the early recirculation peri-
od. Five minutes before recirculation, infusion of 10
ml/kg 20% mannitol (Osmosteral\textsuperscript{®}), was started at a
rate of 1 ml/min to reduce brain swelling which regu-
larly occurs during reperfusion. Immediately before
recirculation, systolic blood pressure was abruptly ele-
rated to more than 180 mm Hg by intravenous infusion
of norfenefrine (Novadral\textsuperscript{®}), and the vascular clamps
were removed from the innominate and subclavian
arteries at the peak of the pressure pulse. Blood reper-
fusion of the ischemic brain resulted in a steep increase
of arterial pCO₂, as evidenced by the rise of tidal CO₂.
Respiration rate and volume, therefore, were increased
until tidal pCO₂ returned to normal values. Arterial
blood samples were taken in short intervals (5–10 min)
to control buffer infusion and ventilation rate until
acid-base balance and arterial blood gases returned to
normal.

As a specific therapy, prostacyclin (1.8 µg/kg/min)
was applied in 6 cats by continuous intravenous injec-
tion over 60 min after the second hour of recirculation
(PGI\textsubscript{2}-treated group). The drug was freshly prepared
from a stock solution (1 mg prostacyclin in 1 ml gly-
cine buffer, pH 10.5, 4°C) by dilution 1:5 with cold 15
mM Tris buffer immediately before the beginning of
infusion. Infusion rate of PGI\textsubscript{2} was temporarily re-
duced when the systemic blood pressure fell below 130
mm Hg. Seven other cats received an infusion of the
solvent alone (placebo group).

Before ischemia and after 3 hours of reperfusion,
i.e. at the end of the 1 hour’s infusion of PGI\textsubscript{2} or the
solvent, respectively, a battery of blood coagulation
and platelet function tests were carried out. Global
coagulation tests such as PTT, TT, and Quick, the
factors V, X, XII and the concentration of fibrinogen
were measured by use of commercially available test
reagents (Boehringer, Mannheim; Behring-Werke,
Marburg, FRG), whereby the clotting time was mea-
sured with a coagulometer of Schnitger and Gross
(Amelung, Lemgo Brake, FRG).

Plasminogen and AT III-activity were measured
with a chromatographic substrate assay (Kabi, Stockholm,
Sweden), blood platelets with a cell counter (Type
123, Analys Instruments, Stockholm, Sweden), and
platelet aggregation ratio (PAR) was evaluated accord-
ing to the method of Wu and Hoak.\textsuperscript{21} ADP-induced
platelet aggregation was measured in heparinized
whole blood samples immediately after withdrawal
with an electronic aggregometer.\textsuperscript{22}

Cerebral blood flow was measured before and at
various intervals after ischemia using the intraarterial
\textsuperscript{133}Xenon injection technique. For each flow estima-
tion, one mCi \textsuperscript{133}Xenon (dissolved in about 0.2 ml
Ringer solution) was injected as a bolus into the in-
nominate artery, and the \textsuperscript{133}Xenon clearance from the
brain was monitored by an extracranial collimated
scintillation detector placed over the exposed skull.
Muscles and tongue were shielded with lead to avoid
extracerebral contamination of the clearance curves.
Clearance curves were evaluated by the 2 minutes’
slope index.\textsuperscript{23}

CO₂-reactivity of cerebral blood flow was estimated
before ischemia and 3 hours after the beginning of
recirculation by ventilating the animal with a gas mix-
ture containing 6% CO₂, 21% oxygen, and the rest
nitrogen.

The electrocorticogram was recorded from the sen-
sory motor area of the right hemisphere with bipolar
silverball electrodes. The same region was also stimulated with single rectangular pulses (0.3 ms, 10 V), and the evoked pyramidal response was recorded at the bulbar level using a stereotactically implanted concentric needle electrode.

Restitution of electrophysiological function after ischemia was classified 3 hours after the beginning of recirculation as follows:

Recovery was defined as normalization of the pyramidal response, accompanied by the beginning recovery of EEG. Partial recovery was defined as a partial return of the pyramidal response without recovery of EEG. No recovery indicated absence of any neurophysiological functions.

At the end of the experiments the brains were frozen in situ with liquid nitrogen. The brains were sawed in slices of 0.5 cm thickness, and processed for regional biochemical evaluation of NADH, glucose and ATP, as described elsewhere.¹

Results

Two groups of animals were compared. In one group (7 cats, placebo group) global complete cerebral ischemia of one hour was followed by three hours’ blood recirculation using a standardized therapy for prevention of no-reflow (see Methods). In another group of animals (6 cats, PGI₂-treated group) the same therapy was supplemented by continuous intravenous infusion of prostacyclin (1.8 µg/kg/min), starting two hours after beginning of recirculation and continuing until the end of the experiments after 3 hours.

General Physiological Parameters

The data obtained are summarized in table 1: In both groups, the acid-base status of the blood, blood gases and hematocrit remained stable throughout the experiments. During recirculation, the mean arterial blood pressure, after a period of induced hypertension, decreased to about 85 mm Hg after one hour, and subsequently stabilized between 100 and 150 mm Hg after 2 hours of recirculation. In the prostacyclin-treated group, mean arterial blood pressure fell to about 80 mm Hg during drug administration, indicating a general peripheral vasodilating effect.

Cerebral Blood Flow

In both groups, mean cerebral blood flow was about 40 ml/100 g/min before ischemia (table 1). After vascular occlusion blood flow completely stopped, as confirmed by the absence of ¹³³Xenon-clearance. Immediately after ischemia, reactive hyperemia developed, the degree of which depended on the individual blood pressure. One hour after the onset of recirculation, blood flow stabilized between 30 and 35 ml/100 g/min, i.e. about 25% below the control level. During prostacyclin infusion, blood flow further decreased to 27 ± 3 ml/100 g/min, but this value was not significantly different from that of the untreated animals in which blood flow after 3 hours' recirculation was 29 ± 6 ml/100 g/min. This finding does not exclude that prostacyclin slightly reduced cerebrovascular resistance because blood pressure was lower than in the untreated animals.

CO₂-reactivity of blood flow was tested before and three hours after cerebral ischemia (fig. 1). Both before and after ischemia, the ventilation of the animals with 6% CO₂ caused an increase of arterial pCO₂ from 30 to about 60 mm Hg. Before ischemia, hypercapnia led to an increase of blood flow up to 350%. Three hours after recirculation, CO₂-reactivity was completely abolished in both the placebo and prostacyclin-treated group. Prostacyclin, in consequence, was not

<table>
<thead>
<tr>
<th>Table 1 General Physiological Parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>Placebo group</td>
</tr>
<tr>
<td>pH</td>
</tr>
<tr>
<td>pCO₂ (mm Hg)</td>
</tr>
<tr>
<td>pO₂ (mm Hg)</td>
</tr>
<tr>
<td>HCO₃⁻ (mmol/l)</td>
</tr>
<tr>
<td>Hct (vol%)</td>
</tr>
<tr>
<td>SAP (mm Hg)</td>
</tr>
<tr>
<td>CBF (ml/100 g/min)</td>
</tr>
<tr>
<td>PGI₂-treated group</td>
</tr>
<tr>
<td>pH</td>
</tr>
<tr>
<td>pCO₂ (mm Hg)</td>
</tr>
<tr>
<td>pO₂ (mm Hg)</td>
</tr>
<tr>
<td>HCO₂⁻ (mmol/l)</td>
</tr>
<tr>
<td>Hct (vol%)</td>
</tr>
<tr>
<td>SAP (mm Hg)</td>
</tr>
<tr>
<td>CBF (ml/100 g/min)</td>
</tr>
</tbody>
</table>

General physiological parameters before and at various recirculation times following 1 hour complete ischemia of the cat brain. PGI₂ was infused between 2 and 3 hours after ischemia. Values are means ± SEM.
able to reverse the post-ischemic suppression of CO₂-reactivity.

Electrophysiological Function

Electrophysiological suppression and recovery after ischemia was evaluated by recording spontaneous ECoG activity, and the pyramidal response following electrical stimulation of the motor cortex (fig. 2). During ischemia, ECoG activity ceased within 15 sec and the pyramidal response after 3–5 min. After restoration of blood flow, in 5 out of 13 animals pyramidal response began to reappear within 10 min, and initial signs of electro-cortical activity were recorded after 1–2 hours (functional recovery). In 5 animals, only the pyramidal response but not the ECoG reappeared after 30–60 min (partial recovery), and in the remaining 3 animals, electrophysiological recovery was absent or a secondary suppression of electrophysiological functions occurred (no recovery). There was no difference in the incidence of no recovery between treated and untreated animals. This is not surprising because prostacyclin infusion was started 2 hours after the beginning of recirculation, i.e. at a time when a clear distinction between animals with and without recovery could already be made. However, there was also no influence of prostacyclin infusion on the progression of recovery in those animals in which electrophysiological signs of function had returned.

The blood coagulation data are shown in table 2. In both groups global coagulation times, and coagulation times for the factors V, X, XII increased after ischemia and fibrinogen concentration decreased significantly and similarly. An increased activation of the fibrinolytic system was also evident in both groups with a significant and similar fall of plasminogen from 0.94 ± 0.7 to 0.57 ± 0.2I IU/ml in the placebo group (p < 0.01) and from 0.98 ± 0.14 to 0.43 ± 0.09 IU/ml in the PGI₂-treated group (p < 0.01).

A significant reduction of active AT III, indicating an increased thrombin turnover with formation of inactive AT III-thrombin-complexes, was also measured in both groups (p < 0.01). The only difference between treated and untreated animals concerned platelet aggregability (fig. 3). During PGI₂-infusion platelet aggregation ratio (PAR) significantly increased in both

FIGURE 2. Electrocorticogram and pyramidal response following electrical stimulation of the motor cortex before (control) and 3 hours after total cerebro-circulatory arrest of 60 min. Recordings are from animals with different degrees of functional disturbances after ischemia.

FIGURE 1. CO₂ reactivity of cerebral blood flow before and 3 hours after complete cerebro-circulatory arrest of 60 min. Above: untreated animals, below: animals treated with prostacyclin (1.8 µg/kg/min intravenously). Arterial pCO₂ was increased by ventilating the animals with 6% CO₂.
TABLE 2  Coagulation Parameters

<table>
<thead>
<tr>
<th></th>
<th>Placebo group</th>
<th>PGI&lt;sub&gt;2&lt;/sub&gt;-treated group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control 3 hours</td>
<td>3 hours</td>
</tr>
<tr>
<td></td>
<td>Control 3 hours</td>
<td></td>
</tr>
<tr>
<td>Prothrombin time (sec)</td>
<td>11.5±0.6</td>
<td>19.5±3.3</td>
</tr>
<tr>
<td>PTT (sec)</td>
<td>18.3±2.1</td>
<td>177.8±54.0</td>
</tr>
<tr>
<td>TT (sec)</td>
<td>15.0±1.1</td>
<td>145.4±64.1</td>
</tr>
<tr>
<td>Fibrinogen (mg/dl)</td>
<td>151±32</td>
<td>109±30</td>
</tr>
<tr>
<td>Factor V (sec)</td>
<td>17.5±1.2</td>
<td>20.0±1.5</td>
</tr>
<tr>
<td>Factor X (sec)</td>
<td>39.6±0.8</td>
<td>50.1±3.6</td>
</tr>
<tr>
<td>Factor XII (sec)</td>
<td>28.9±2.9</td>
<td>40.7±2.8</td>
</tr>
<tr>
<td>Plasminogen (CTA-U/ml)</td>
<td>0.94±0.70</td>
<td>0.57±0.21</td>
</tr>
<tr>
<td>AT III (IU/ml)</td>
<td>17.0±2.2</td>
<td>11.5±1.9</td>
</tr>
<tr>
<td>PAR % venous</td>
<td>0.87±0.06</td>
<td>0.75±0.17</td>
</tr>
<tr>
<td>PAR % arterial</td>
<td>0.97±0.03</td>
<td>0.85±0.15</td>
</tr>
</tbody>
</table>

Changes of blood coagulation parameters, fibrinolysis and platelet aggregation ratio (PAR according to Wu and Hoak<sup>21</sup>) before and 3 hours following 1 hour complete ischemia. PGI<sub>2</sub> was infused between 2 and 3 hours after ischemia. Values are means ± SEM.

the arterial and venous blood, when compared with the preinfusion value (p < 0.05). In the placebo group, on the other hand, platelet aggregation ratio fell. This indicates an increase in in-vivo platelet aggregation during solvent (glycine/Tris buffer 1:5) infusion in contrast to the platelet disaggregating effect of PGI<sub>2</sub>.

Discussion

The present experiment was designed in order to test the hypothesis that a reduction of PGI<sub>2</sub> may be responsible for the disturbance of the CO<sub>2</sub>-reactivity and the decrease of CBF observed during the phase of post-ischemic hyperperfusion following a period of prolonged cerebro-circulatory arrest. This hypothesis was derived from the hemodynamic similarities between post-ischemic hyperperfusion and the reduction of blood flow by indomethacin which causes an inhibition of prostaglandin synthesis and which is reversed by systemic application of prostacyclin<sup>15</sup>. During ischemia, arachidonic acid accumulates in the brain tissue and during the early recirculation phase triggers a shortlasting burst of production of prostaglandins via prostaglandin endoperoxides<sup>25-27</sup>. These endoperoxides have a free radical character and may be able to inactive their respective enzymes<sup>28-30</sup>. The preferential inactivation of prostacyclin synthetase can be explained by its location in the wall of cerebral vessels. Thromboxane A<sub>2</sub> synthetase, on the other hand, is less affected because only a small fraction of total platelet content resides in the brain during ischemia. This could lead to an imbalance of vasoactive prostaglandins: the reduced synthesis of the vasodilating and platelet disaggregating PGI<sub>2</sub> in the vessel wall may cause a relative increase of the vasoconstricting and platelet aggregating TXA<sub>2</sub> and, in consequence, produce the observed hemodynamic alterations.

Our findings, however, do not support this hypothesis. In the present experimental situation infusion of prostacyclin did not influence blood flow or flow regulation during delayed postsischemic hyperperfusion following one hour of cerebrocirculatory arrest. A methodological error due to inactivation of PGI<sub>2</sub> before or during infusion can be excluded because its vasodilatory effect was confirmed by the fall of systemic arterial pressure<sup>6</sup>, and its effect on platelet function by the reduction of platelet aggregability<sup>9,31</sup>. It is not likely, either, that the drug did not reach the brain vessels because previous studies have shown that in animals with functional recovery blood reperfusion is not disturbed<sup>3</sup>. However, it should be considered that the absence of cerebral vascular effects may be due to a reduced activity of PGI<sub>2</sub> at the effector site in the vascular smooth muscle cells, e.g. by a disturbed passage across the cerebrovascular wall.

As has been shown in previous experiments, disseminated intravascular coagulation develops during the ischemic impact being initiated by an activation of factor XII and increased platelet aggregation in the brain and systemic vascular bed. This is in contrast to the findings in the present work where, although the ischemic impact was identical, no significant changes of coagulation parameters were observed. This may be due to the reduced platelet aggregability during PGI<sub>2</sub> infusion.

![Figure 3](http://stroke.ahajournals.org/)

**Figure 3.** ADP-induced platelet aggregation 2–3 hours after total cerebro-circulatory arrest of 60 min. Measurements were carried out with an electronic aggregometer before, during and after intravenous infusion of prostacyclin (1.8 µg/kg/min). Note the reduction of platelet aggregability during PGI<sub>2</sub> infusion.
microvasculature. The activation of blood platelets as well as of the procoagulant and fibrinolytic system with liberation of 5-hydroxytryptamine and other proaggregatory compounds from the platelets and formation of fibrin degradation products has been shown to increase the toxicity of cerebral and other vessels. The failing response of PGI₂ on the vascular smooth muscles could, therefore, also be influenced by this disturbance of the haemostatic system which was not affected by the PGI₂ infusion started 2 hours postischemia.

Our findings, on the first sight, seem to contradict the earlier observations of Hallenbeck and Furlow who reported an amelioration of post-ischemic recirculation by prostacyclin. However, these authors studied the early recirculation phase and not the delayed post-ischemic hypoperfusion phenomenon. Immediately after ischemia, recirculation may be impaired by the so-called no-reflow phenomenon which is the combined result of intravascular aggregation of blood particles, increased vascular tone, microvascular compression by swollen glial cells and post-ischemic hypotension.

Prostacyclin seems to improve this disturbance by reducing platelet aggregation because the flow-promoting effect can be enhanced by additional application of indomethacin. Indomethacin, besides its effect on prostacyclin synthesis, also causes an inhibition of thromboxane A₂ which is a platelet aggregant. Inhibition of these two compounds and substitution of prostacyclin, therefore, considerably decreases platelet aggregability.

In the present investigation, the no-reflow phenomenon was prevented in a different way. Since the degree of no-reflow is mainly determined by the degree of microvascular compression and the post-ischemic perfusion pressure, blood pressure was increased immediately before recirculation to hypertensive levels, and perivascular glial swelling was reduced by osmotherapy. With this approach it was possible to prevent the no-reflow phenomenon without application of specific drugs, and the effect of prostacyclin could be studied at a later stage without previous interference with prostaglandin metabolism. The absence of a hemodynamic effect of prostacyclin after 2 hours' recirculation, therefore, is a strong argument against its role for the development of post-ischemic hypoperfusion. However, if prostacyclin synthetase is inactivated by free radicals, as suggested by Siesjö, its role for the development of post-ischemic recirculation, therefore, is a strong argument against the presence of a hemodynamic effect of prostacyclin after 2 hours' recirculation. However, if prostacyclin synthetase is inactivated by free radicals, as suggested by Siesjö, it is conceivable that not only the enzyme but also the prostacyclin effector site at the vascular smooth muscle is destroyed. Substitution of prostacyclin, in this case, would be without hemodynamic effects. Further studies, therefore, should focus on this particular problem.

Acknowledgment
The excellent technical and secretarial help of Mrs. Sörensen and Mrs. Langer is gratefully acknowledged.

References

Occlusive Thromboaortopathy (Takayasu’s Disease): Cervical Arterial Stenoses, Retinal Arterial Pressure, Retinal Microaneurysms and Prognosis

KAICHIRO ISHIKAWA, M.D.,* MASANOBU UYAMA, M.D.,† AND KUNIO ASAYAMA, M.D.†

SUMMARY Eighty-one young Japanese patients with occlusive thromboaortopathy (Takayasu’s disease) were classed into three groups according to the degree and extent of diameter stenosis in the 4 cervical arterial systems, as determined by serial aortography. Class I was made up of 63 patients with 70% or greater stenosis in less than 3 systems, including 33 patients without systemic hypertension (Class Ia). Class II was made up of 6 patients with 70% or greater stenosis in 3 systems and less than 50% stenosis in the remaining 1, including 5 patients without systemic hypertension (Class Iia). Class III was made up of 12 patients with 70% or greater stenosis in 3 systems and 50% or greater stenosis in 1 system. Ophthalmodynamometric systolic pressure in patients in Class III was significantly lower than that in patients in Class Iia (p < 0.001), but there was no significant difference between patients in Classes Ia and Iia. Microaneurysms and/or arteriovenous anastomoses in the retinal vessels were found in all but one patient in Class III and in only one patient in combined Classes I and II. These results indicate that each of the ophthalmodynamometric values and fundoscopic findings are very helpful in identifying the markedly severe occlusive lesions (Class III) of the 4 cervical arterial systems. In this chronic disease, however, angiography is most useful for evaluation of these severe lesions, to monitor progression from Classes I and II to Class III, in which the prognosis is rather poor.

RELATIONSHIP among cervical arterial stenoses, retinal arterial pressure and retinal vascular changes in occlusive thromboaortopathy (Takayasu’s disease) is not clear. The disease is a chronic inflammatory arteriopathy of unknown origin and the site of occurrence is the aorta and/or its main branches.1 2 Intracranial arteries and the distal segments of the bifurcation of the common carotid arteries and those of the vertebral arteries are usually spared in this disease.3 4 Therefore, these patients appropriately serve as unique subjects for assessment of the influence of gradually developing stenoses in the proximal segments of the aortic arch vessels, as related to retinal arterial pressure and ischemic retinopathy. A severe retinopathy of arteriovenous anastomoses5 and microaneurysms, a characteristic manifestation of Takayasu’s retinopathy6 is one of the ominous signs in prediction of a poor prognosis in patients with this disease.7 8 Consequently, it is very important to investigate stepwise, the cervical arterial stenoses which cause severe ischemic retinopathy.
No effect of prostacyclin on blood flow, regulation of blood flow and blood coagulation following global cerebral ischemia.
W van den Kerckhoff, K A Hossmann and V Hossmann

Stroke. 1983;14:724-730
doi: 10.1161/01.STR.14.5.724

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/14/5/724