

# Regional cerebral blood flow and intraventricular pressure in acute head injuries<sup>1</sup>

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**SYNOPSIS** Twelve patients who were comatose after head injuries were studied with serial determinations of regional cerebral blood flow, jugular PO<sub>2</sub> tension, and intraventricular pressure. These determinations began a few hours after the injury, and were followed throughout the clinical course. Diffuse derangement of cerebral vasomotor regulation is confirmed after severe head trauma, which may contribute to deterioration and poor prognosis, and which indicates a need for therapeutic maintenance of rich oxygenation, hyperventilation with moderate hypocapnia, and steady blood pressure. Continuous recording of IVP (eventually sensitized by fluid infusion or CO<sub>2</sub> inhalation tests) may give an early indication of the subsequent clinical state and may suggest the need to submit the patients to further investigative and therapeutic procedures.

Treatment of craniocerebral injuries is based on careful clinical and neuroradiological observations with a few essential laboratory findings related to acid-base parameters and blood gas analysis.

An important addition in severe cases is the continuous recording of intracranial pressure by means of epidural transducers or intraventricular catheters (intraventricular pressure, IVP). IVP recording, besides being a possible prognostic indicator (Johnston *et al.*, 1970; Vapalahti, 1970; Bruce *et al.*, 1973), provides early information on the need for effective relief of mounting intracranial hypertension, and, to a certain extent, also provides the means of correcting it through removal of ventricular fluid. The early predictive value of IVP measurements is enhanced by a 'fluid infusion' test as suggested by Miller *et al.* (1973).

Further pathophysiological information can be derived from measurements of cerebral blood flow and metabolism: the value of this information is still in question, in part due to the limited number of patients examined.

The aims of the present study are: (1) to contribute to the description of the changes in regional cerebral blood flow, intraventricular pressure, cerebrovascular reactivity, and oxygen tension of the jugular venous blood (P<sub>jug</sub>O<sub>2</sub>) in man in the early phase after severe head injuries; (2) to analyse the inter-relationships of these variables as they may affect prognosis; (3) to discuss the possible clinical relevance of these measurements.

Our clinical material is composed of 12 patients with a severe closed head injury with a state of coma, studied in the very early phase (four cases <10 hours, two cases <24 hours, four cases <36 hours), and repeatedly thereafter.

Since this is clinical, not experimental, work, results are heterogeneous. However, some conclusions about the prognostic value of such pathophysiological observations, and about general therapeutic indications in similar conditions, can be derived from our study, together with the need for more research on clinico-physiological relationships in acute head injuries.

<sup>1</sup> Supported by the C.N.R.

## METHODS

Ten patients ranging in age from nine to 46 years (average 24.6 years), were studied during the acute phase (seven to 35 hours after the injury). Two more patients aged 18 and 24 years were examined for the first time on the third and 10th day after the accident.

All patients had been subjected to the same treatment, consisting of immediate ventilation with oxygen through nasal intubation and sedation with diazepam. Echoencephalography (EchoEG), was performed followed by carotid angiography, and (in seven cases of this series) by surgery. When necessary, shock was treated by blood and fluid transfusion and  $\beta$ -adrenergic drugs. Ventilation was then continued with 50% air-oxygen, using Engström respirators to maintain the PaCO<sub>2</sub> between 25 and 30 mmHg and high arterial PO<sub>2</sub>.

During the clinical course, in addition to hyper-ventilation, the usual intensive care was given, paying particular attention to fluid balance and high caloric intake. EchoEG and angiography were repeated when necessary.

Of the 12 patients, six died and were subjected to necropsy. Three who died without recovering consciousness and with increasing neurological deterioration were considered 'neurological fatalities' (cerebral death: group A); while three died of extracerebral complications, after recovering consciousness (extracerebral death: group B); of those who survived, although some have permanent neurological sequelae, none is in a permanent vegetative or apallic state (recovery: group C). These three groups were considered as different prognostic entities for the purpose of correlation with pathophysiological findings.

In all cases the regional cerebral blood flow (rCBF) was studied in the hemisphere that seemed most involved clinically. In one case, the contralateral hemisphere was studied simultaneously on the first day; in two more cases bilateral examination was performed at a later stage. Blood flow studies were then repeated on two to six different occasions in each patient, at various time intervals. Our data are thus based on 45 separate runs, each including rCBF, ICP, and P<sub>Jug</sub>O<sub>2</sub> determinations in the resting state, and during test situations, for a total of 172 rCBF determinations.

For the present study, the following techniques were used:

1. Regional cerebral blood flow (rCBF) by <sup>133</sup>Xe, intra-arterial injection method; external recording with eight probes; automatic analysis of the two minute flow index. It was therefore our practice not to submit the patients to prolonged changes in

respiration or in perfusion pressure, as required for tests of CBF responses.

2. Arterial (MABP) and intracranial (ICP) pressures through catheters inserted into a systemic artery and a lateral cerebral ventricle, connected with Statham transducers.

3. Blood gases (arterial and cerebral mixed venous) with an IL apparatus, blood samples drawn from a systemic artery and the superior bulb of the jugular vein; readings corrected for temperature.

In 10 instances, ventricular cerebrospinal fluid (VCSF) was sampled. Lactate and pyruvate in VCSF were measured enzymatically after immediate cold PCA addition and freezing of the sample.

Measurements were done in the resting hyper-ventilated state, and during tests of acute hypercapnia (+10/20 mmHg PaCO<sub>2</sub>); hypocapnia (-5/10 mmHg), trimetaphan and/or angiotensin infusion ( $\pm$ 15/30 mmHg MABP), and occasionally during mannitol infusion or withdrawal of VCSF.

CO<sub>2</sub> reactivity was expressed as preserved or impaired, according to the cerebral blood flow changes per mmHg PaCO<sub>2</sub>, in absence of significant MABP changes.

Autoregulation was expressed as preserved or impaired, according to the CBF changes per mmHg, in absence of significant PaCO<sub>2</sub> changes. These 'all or none' definitions are arbitrary, although operationally valid, and they are standard in our laboratory (Fieschi *et al.*, 1966, 1969; Agnoli *et al.*, 1968).

## RESULTS

rCBF Since regional variations are negligible in

TABLE 1  
AVERAGE CBF (ml/100 g/min), ICP (mmHg), AND PaCO<sub>2</sub> (mmHg) VALUES IN PATIENTS WITH ACUTE HEAD INJURIES DURING RESPIRATOR TREATMENT

Final outcome	Hours			
	< 12	12-36	36-96	> 96
<b>Cerebral death</b>				
CBF	—	27.1	53.1	38.1
ICP	—	9.0	18.7	11.0
PaCO <sub>2</sub>	—	28.0	27.1	28.5
<b>Extracerebral death</b>				
CBF	17.0	22.5	35.8	32.0
ICP	7.0	1.5	5.1	4.5
PaCO <sub>2</sub>	24.0	22.9	32.1	30.5
<b>Recovery</b>				
CBF	28.0	36.3	35.3	32.2
ICP	3.5	2.5	11.1	3.4
PaCO <sub>2</sub>	27.3	33.0	31.4	27.4

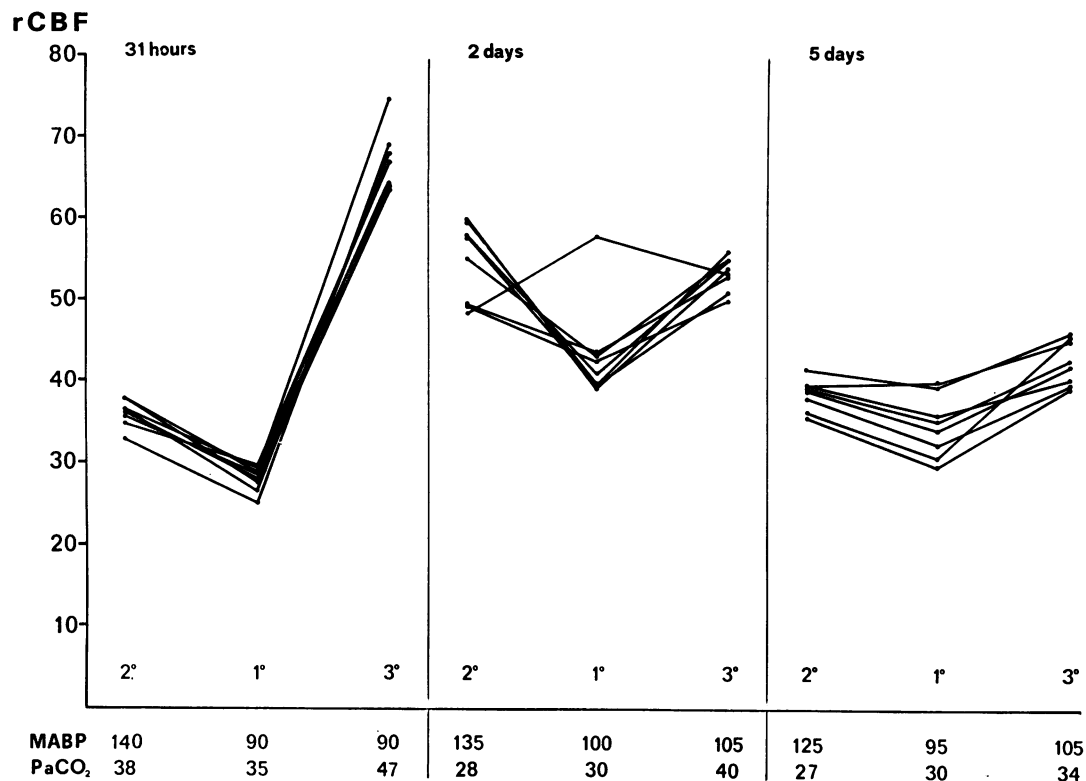


FIG. 1. Three studies of rCBF during CO<sub>2</sub> and angiotensin tests in the same subject, at different time intervals after injury. Each line represents one cerebral region. 1°: resting value, 2°: values during angiotensin, 3°: values during CO<sub>2</sub> inhalation. CBF is higher after two days, when the region with highest flow shows paradoxical responses.

the vast majority of cases, we shall deal with an average of the eight regions (average rCBF).

**RESTING CBF** The initial CBF (less than 12 hours after injury) was quite low (26 ml/100 g/min). This low value is hardly explained by the low PaCO<sub>2</sub>, or by reduced cerebral perfusion pressure (CPP), since CO<sub>2</sub> reactivity is absent in this acute stage, while the CPP is normal. The initial reduction must be related either to the state of coma and the consequent decreased metabolism (Ingvar, 1973), or to primary-impact *diffuse* brain damage—that is, not restricted to the brain-stem—as suggested by Mitchell and Adams (1973).

The spontaneous course of rCBF in the following days differs in the three prognostic groups (Table 1).

In cases of group A (cerebral death), CBF increased to reach high values (reactive hyperaemia) between 36 and 96 hours. Late hyperaemia despite a persistently low PaCO<sub>2</sub> is thus an indication of poor prognosis.

In case of group B (extracerebral death) rCBF slowly increased towards normal after the second day, without instances of reactive hyperaemia.

A similar course of rCBF was observed in group C (recovery) with the main difference consisting in a milder CBF impairment in the early stages. The late reduction below 30 ml/min in this group is clearly related to lower values of PaCO<sub>2</sub>.

Therefore, in patients with neurological recovery, the course of CBF is roughly parallel with their clinical status.

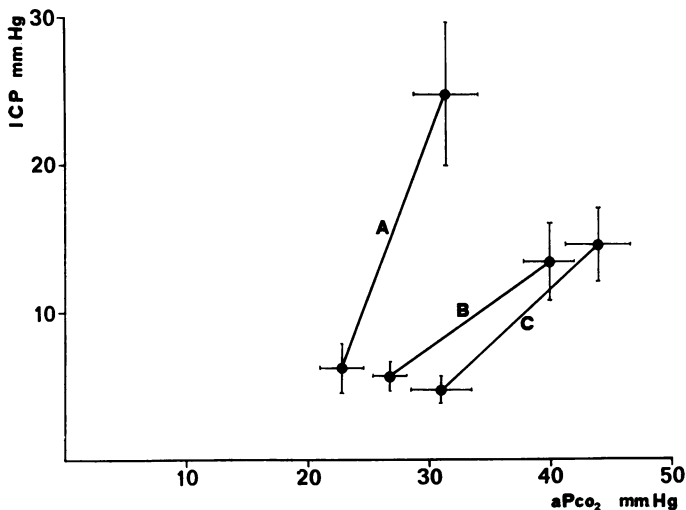


FIG. 2. Response of ICP during CO<sub>2</sub> inhalation at constant MABP. The slope is steeper in group A. A: cerebral death; B: recovery; C: extracerebral death.

**REGIONAL DIFFERENCES** As already stated, in our material rCBF is quite uniform over the entire hemisphere<sup>2</sup> being evenly low or evenly high without much inter-regional variability. In only seven out of 45 'resting' measurements did the rCBF show regional differences, flow in one or more regions being 25% higher or lower than the hemispheric mean.

**RESPONSE TO CO<sub>2</sub>** Our 12 subjects were tested 33 times with either hyper- or hypocapnia or both; the vascular reactivity to CO<sub>2</sub> was simply considered as *present* whenever the rCBF changed more than 0.8 ml/100 g/min per mmHg of pCO<sub>2</sub> change: *impaired* whenever the response was equal or lower than 0.8.

An additional 12 CO<sub>2</sub> tests were performed but discarded because the MABP changed, concurrently with the PaCO<sub>2</sub>, by more than 10 mmHg; in such cases one could not tell whether one was testing the CO<sub>2</sub> responses or the autoregulation. The minimal and average PaCO<sub>2</sub> changes during effective tests were 6 mmHg and 12.6 mmHg respectively.

CO<sub>2</sub> reactivity was abolished in 44% of the head injury cases tested within four days of the

trauma, while it gradually recovered from the fourth day.

Usually rCBF responses to CO<sub>2</sub> are quite uniform without much inter-regional difference. Paradoxical responses of 'steal' or 'counter-steal' were rarely observed (four times: 10.8%), and then only in the acute phase (Fig. 1).

**AUTOREGULATION** Autoregulation was tested 33 times by *increasing* MABP with controlled angiotensin infusion and 15 times by decreasing with controlled infusion of trimetaphan. The MABP was respectively increased or decreased by 25 mmHg on the average. In five more cases, since arterial CO<sub>2</sub> changed—concurrently with MABP—by more than 5 mmHg, the autoregulation tests were discarded.

Autoregulation was considered as *present* whenever the rCBF change was lower than 0.2 ml/100 g/min per mmHg of MABP change, *impaired* whenever this response was equal to or more than 0.2.

Autoregulation to induced hypertension was preserved in the early hours (we shall discuss later why this does not seem to be a case of 'false autoregulation'); it was abolished in more than 50% of the cases between 36 and 96 hours and recovered in the majority of cases thereafter.

Impairment of autoregulation between 36 and 96 hours seemed to bear some relationship to

<sup>2</sup> This study cannot exclude the existence of significant differences between hemispheres, in fact in one out of two simultaneous bilateral recordings average hemispheric flow was 42.6 and 28.8 ml/100 g/min respectively.

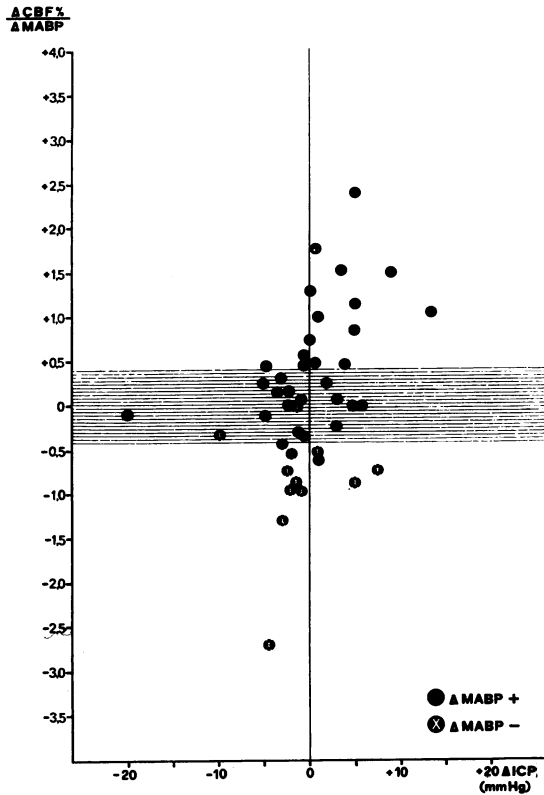


FIG. 3. Response of ICP and CBF during autoregulation tests. Shaded area: preserved autoregulation.

poor prognosis. The trimetaphan test also indicated that the impairment of autoregulation during hypotension lasted longer than impairment of autoregulation during hypertension. This might mean simply that the threshold for autoregulation was higher than normal, since during the trimetaphan test the MABP was usually reduced to about 80–85 mmHg, which is close to the threshold for autoregulation in control subjects.

**INTRACRANIAL PRESSURE 1. Resting intraventricular pressure (IVP)** Intraventricular pressures recorded in our cases at rest (during moderate hyperventilation) were in most instances low (Table 1). In only four cases was a (slightly) elevated IVP recorded (over 15 mmHg) and three of them were the 'neurological fatalities': the fourth case (no. 6) had a resting IVP of 12 mmHg at seven hours from the injury increasing to 25–30 mmHg on the third day. After this intracranial hypertension, angiography was repeated and a right temporal haematoma removed, which had not been noted at the first angiographic study. The IVP returned to normal (9 mmHg) on the second day after the operation, and this patient eventually recovered. In the remaining three cases of intracranial hypertension (18, 19, and 26 mmHg respectively), the patients died without recover-

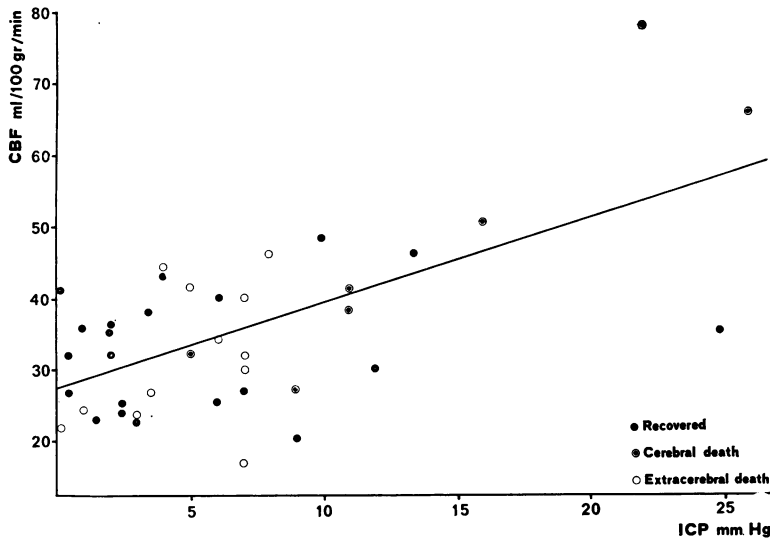


FIG. 4. Resting CBF and ICP in the case record; sample regression equation:  $y = 27.5 + 1.15x$ .

ing consciousness. We may suppose that at normal  $p\text{CO}_2$  values the IVP would be higher in these patients. Indeed, higher values of IVP were recorded during  $\text{CO}_2$  inhalation tests (Fig. 2). Instead, at hypocapnia (such as during our standard treatment) an intracranial pressure of 20 mmHg already present usually indicates a very poor risk. Spontaneous increase of a previously normal IVP to this level or higher indicates the need for prompt correction whenever possible. Surgery, correction of an iatrogenic or neurogenic hypo-osmolality, induction of deliberate hyperosmolality, or withdrawal of cerebrospinal fluid are among the measures to be quickly decided upon and undertaken.

The predictive value of IVP may be enhanced by the saline infusion test of Miller, or by the hypercapnic test discussed in the following paragraph.

2. *ICP and  $\text{CO}_2$*  Miller *et al.* (1973) state that an increase of ICP of more than 25% obtained by infusing 1 ml of mock CSF in one minute, yields useful information, indicating that the intracranial volume-pressure relationship has reached a critical stage of brain 'tightness'. Their test was performed by directly altering the CSF volume. Inhaling  $\text{CO}_2$  is another means of increasing the intracranial volume provided that some  $\text{CO}_2$  reactivity is preserved. Therefore it is not surprising that patients showing a big increase of ICP during  $\text{CO}_2$  inhalation usually presented the worst neurological prognosis.

This test may not always be reliable in cases with diffuse vascular lack of reactivity to  $\text{CO}_2$ . Except in these extreme circumstances, however, this test further supports the use of moderate prolonged hyperventilation as a means of controlling the intracranial volume that might be close to the critical threshold.

3. *ICP and autoregulation* During MABP changes, in cases of preserved autoregulation, the IVP remains steady, whereas if autoregulation is impaired the IVP also changes in the same direction as the arterial pressure. Therefore IVP recording provides information on the state of vasomotor regulation (Fig. 3).

The rise in ICP produced by arterial hypertension also stresses the need to control such pressure changes by means of well monitored intensive care.

ICP AND CBF 1. *In resting state* In our experience (which does not include severe intracranial hypertension) CBF and ICP run parallel. This points to two facts: (a) ICP is not in itself, within these ranges of IVP, such a limiting factor to blood flow as to lead to brain ischaemia. (b) Elevated ICP is a poor risk sign because it signals subjacent vasodilatation, which expresses a diffuse metabolic and vasoregulatory derangement. Only at higher levels of IVP (25–30 mmHg) can pressure become a limiting factor to CBF and require treatment by means of dehydration. Otherwise there is no need to use osmotic agents systematically (Fig. 4).

TABLE 2

LACTATE AND PYRUVATE CONCENTRATION IN VENTRICULAR FLUID OF UNCONSCIOUS PATIENTS WITH SEVERE BRAIN INJURIES

<i>Final outcome</i>	<i>Day of treatment</i>	<i>CSF lactate (mmol/l)</i>	<i>CSF pyruvate (mmol/l)</i>	<i>L/P</i>	<i>PaO<sub>2</sub> (mmHg)</i>	<i>PjugO<sub>2</sub> (mmHg)</i>	<i>PaCO<sub>2</sub> (mmHg)</i>
Recovery	3	3.06	0.29	10.5	230	43	37
	3	2.21	0.18	12.3	102	36	28–40
	5	2.82	0.19	14.8	180	38	30
	10	2.88	0.23	12.5	290	—	30
	22	1.09	0.15	7.2	220	26	24
Extracerebral death	15	2.07	0.17	12.2	280	34	30
	28	5.89	0.47	12.5	94	29	27
Cerebral death	1	2.38	0.22	10.8	320	45	29
	2	4.68	0.29	16.8	280	45	32
	4	1.61	0.15	10.7	250	32	28

2.  $CO_2$  tests Blood flow and ICP increase in parallel during  $CO_2$  changes: in cases with severe neurological prognosis the slope of ICP rise is steeper, indicating an ICP near the critical threshold.

3. Autoregulation tests Simultaneous measurements of CBF and IVP during a pressure test allow us to discuss the role of 'false autoregulation'. In such a case, during arterial hypertension IVP would increase while the CBF remained constant: the IVP would in fact counteract MABP changes, and the effective cerebral perfusion pressure (CPP) would remain unchanged. The fact that this was not the case in our patients shows that false autoregulation is an unlikely or rare phenomenon in head injuries,

although a final statement on this point requires that we know the state of the local tissue pressure.

JUGULAR OXYGEN TENSION ( $P_{jugO_2}$ ) 1. *In the resting state* Most values of  $P_{jugO_2}$  ranged from 30 to 40 mmHg in the resting state. Almost all measurements were performed during hyper-ventilation and in the presence of arterial hyperoxia ( $aPO_2$  ranging from 190 to 260 mmHg), which may have contributed to the relatively high values of  $P_{jugO_2}$  recorded (Table 2). Differences between prognostic groups or at different stages after injury are not significant.

2.  $P_{jugO_2}$  and  $PaCO_2$  A relationship between  $P_{jugO_2}$  and  $PaCO_2$  was found in all periods after head trauma. A vasodilator response is thus elicited by  $CO_2$  in the brain as a whole, although 'regionally' or even in an entire hemisphere the vascular reactivity to  $CO_2$  may be absent (*vide infra*).

3.  $P_{jugO_2}$  and CBF In Fig. 5 the values of  $P_{jugO_2}$  have been plotted against the mean hemispheric rCBF values recorded at the same time, both in the resting state and during  $CO_2$  tests (at constant blood pressure).

There is a great dispersion of values during the first period of study, between 0 and 96 hours, while a highly significant correlation between CBF and  $P_{jugO_2}$  is found subsequently.

The acute changes of blood pH due to the change in  $pCO_2$  may interfere with the result of  $PO_2$  measurements. To exclude this interference, the relation between  $P_{jugO_2}$  and mean hemispheric rCBF was examined during the tests of autoregulation when  $PaCO_2$  and blood pH are unaffected, but results are similar to those observed during the  $CO_2$  test (Fig. 6).

The higher dispersion of relationships between cerebral venous  $pO_2$  and mean hemispheric rCBF during the first four days of a brain injury may be due either to a reversible increase in extracerebral contamination of the blood in the jugular bulb or to maldistribution of the blood flow in the brain, with changing amounts of non-nutritional flow.

An artefact due to extracerebral contamination cannot be ruled out entirely. However, no rationale exists for variability of extracerebral

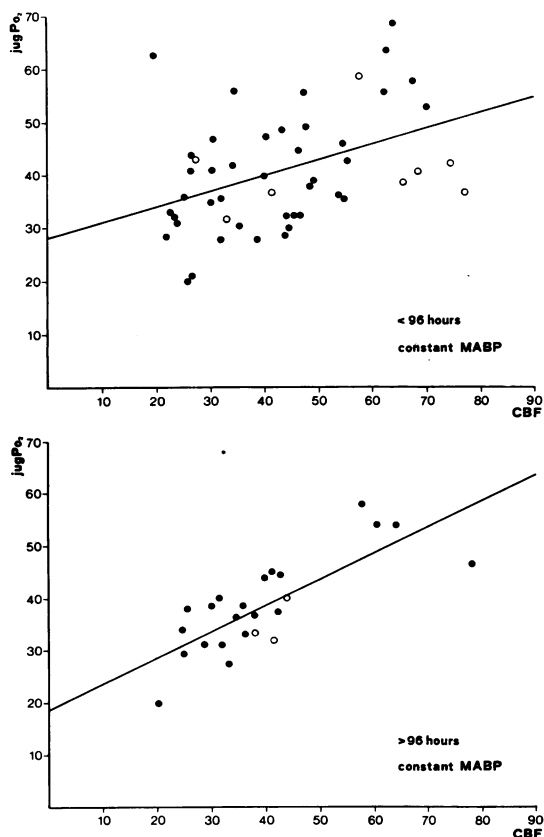


FIG. 5. rCBF and  $P_{jugO_2}$  during  $CO_2$  test. Upper:  $r=0.41$ ,  $P<0.01$ . Lower:  $r=0.78$ ,  $P<0.001$ . ●: Recovered and extracerebral death. ●: Cerebral death.

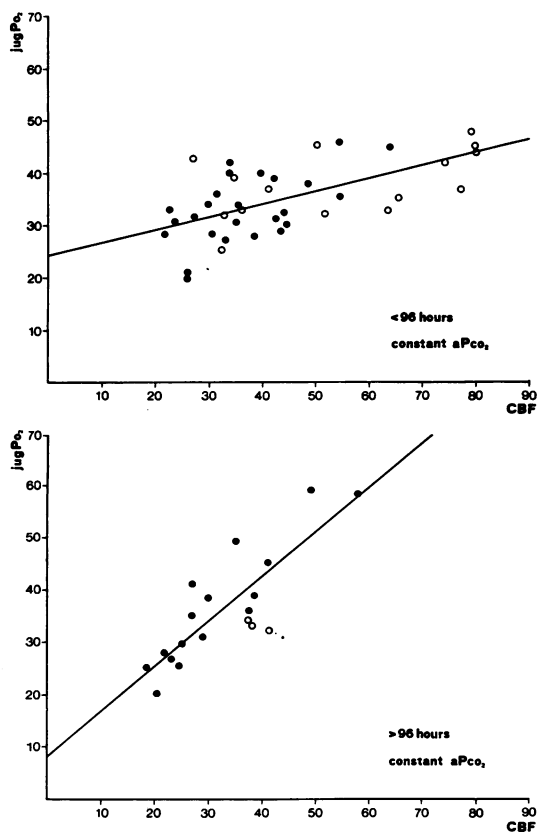


FIG. 6.  $rCBF$  and  $P_{jugO_2}$  during autoregulation test. Upper:  $r=0.60$ ,  $P<0.001$ . Lower:  $r=0.83$ ,  $P<0.001$ . ●: Recovered and extracerebral death. ●: Cerebral death.

contamination so we favour the hypothesis of CBF maldistribution in the acute phase. A macroscopic example of uneven distribution and reactivity of CBF can be found in the different behaviour of the two hemispheres. In one case, a patient showed a definite increase in jugular venous  $PO_2$  under  $CO_2$  testing, while the CBF was greatly reduced over the whole hemisphere studied. This case leads one to infer a steal effect on the other hemisphere.

Whatever the explanation, one point must be stressed, namely, the lack of real clinical significance of  $P_{jugO_2}$  during the first days of a trauma in our setting—that is, in presence of an elevated arterial hyperoxia induced by the respirator treatment. This is at variance with the

statements of Zupping *et al.* (1972) on the prognostic value of  $P_{jugO_2}$  in brain injury.

In fact, since the jugular blood  $O_2$  tension is not in equilibrium with the mean tissue oxygen tension, the most direct approach to the measurement of cerebral hypoxia in this pathological situation is the oxygen tension in the CSF.

**CSF LACTATE AND PYRUVATE (Table 2)** In 10 patients the CSF was sampled from the lateral ventricle for measurements of lactate (L), pyruvate (P), and L/P ratio. In only two patients was this measurement possible in the very early phase. In all cases the patients had already been subjected to hyperoxic and usually hypocapnic ventilation for at least some hours before sampling.

CSF lactate values were fairly high (above 3 mmol/l) in three samples, two of which were taken within the first days: in the third case the patient had developed septic complications and was in a poor general state at the time of sampling on the 28th day.

The L/P ratio was high in only one sample, taken at 40 hours in a patient who later underwent 'neurological death'.

The near-normal values found in this series are at variance with those reported by Metzel and Zimmermann (1971), Crockard and Taylor (1972) and King *et al.* (1974). This may be the consequence of a treatment specifically intended to minimize secondary brain hypoxia: in fact, our only patient with high L/P ratio came from another hospital where he was not hyperventilated for the first 36 hours.

## DISCUSSION

**PATHOPHYSIOLOGY OF HEAD INJURIES** Severe trauma to the head is constantly followed by impairment of cerebral vasomotor regulation. Similar findings have been demonstrated in experimental models in animals (Reivich *et al.* 1969). This impairment consists of disturbed autoregulation, diminished or lost response to  $CO_2$  (to the extent of possible paradoxical 'steal' responses), and reactive hyperaemia. In this context, it is important to note that the vaso-paralysis does not take place in the hours immediately after the injury, but only on the second to third day.



This derangement may be of importance in determining one of the most serious complications of head trauma (apart from tissue laceration and haemorrhage)—namely, brain oedema. Therefore, interrupting this chain of events by means designed to restore autoregulation, such as hyperventilation, seems feasible (Paulson *et al.* 1972).

The importance of the vascular factor is further indicated by the 'maldistribution' of CBF. This concept is derived from experimental models (Hossman and Lechtape-Grüter, 1972), and by pathological studies such as that of Graham and Adams (1971), and it is further suggested in this study by the dissociation between the  $P_{jugO_2}$ -rCBF.

If the brain is not homogeneously perfused, however, we must make explicit that what we measure as rCBF in these pathological circumstances is the mean flow of the *perfused* areas in the region under study, not the true average rCBF to the whole region. This may be the reason why the rCBF appears to be rather uniform throughout the hemisphere, without important differences between the eight regions explored by our system.

The state of the circulation and the vasoparalysis is reflected in the ICP measurements. Actually, ICP and CBF are correlated in both acute and late phases, intracranial pressure being higher in cases of reactive hyperaemia, or during  $CO_2$  tests, and in cases with impaired autoregulation it is also influenced by the MABP head.

Autoregulation and  $CO_2$  reactivity are sometimes dissociated. Both may be impaired, but with a different time course and to a different degree. As previously shown in other pathological circumstances, this dissociation supports

the view of dual control of cerebral circulation (Yoshida *et al.*, 1966). The question arises whether the preserved autoregulation in the first measurements, when  $CO_2$  response is already impaired, is an example of a 'false' autoregulation.

Simultaneous measurements of CBF, IVP, and MABP indicate that in our cases (hyperventilation, early surgery when necessary), intracranial hypertension was not an important limiting factor to brain tissue perfusion, and suggest that false autoregulation is seldom, if ever, present after head injuries.

Bruce *et al.* (1972) have reached similar conclusions that 'pseudoautoregulation appears to be an uncommon phenomenon' and that 'in many patients . . . CBF was independent of the level of ICP before or after mannitol infusion'.

Since the level of IVP does not necessarily reflect local tissue pressures in areas of a developing mass lesion or cerebral oedema, we can hypothesize focal vascular compressions, due to localized oedema and pressure gradients, at a time when the ICP recorded from a lateral ventricle is not significantly elevated.

**PROGNOSTIC ASPECTS** Table 2 shows positive relationships existing between some pathophysiological data obtained in the first four days after a severe injury and the neurological outcome. Severe brain damage (once surgical lesions are removed) is indicated by (1) the rCBF increasing to levels of reactive hyperaemia; (2) a higher than normal ICP in the range of 15–30 mmHg during moderate hyperventilation; (3) severe impairment of autoregulation. All these data are significant not in the immediate hours after the injury, but in the second to fourth day.

TABLE 3  
AVERAGE RESTING VALUES DURING FIRST 96 HOURS AFTER ACUTE HEAD INJURIES RELATED TO PROGNOSIS

Final outcome	ICP (mmHg)	MABP (mmHg)	PaCO <sub>2</sub> (mmHg)	$\Delta$ CBF $\Delta$ MABP	$\Delta$ CBF $\Delta$ PaCO <sub>2</sub>	CBF (ml/100 g/min)	$P_{jugO_2}$ (mmHg)
Cerebral death	16.8 ± 3.2	92.3 ± 7.2	27.4 ± 1.7	0.34 ± 0.22	1.08 ± 0.50	46.6 ± 9.6	38.3 ± 2.3
Extracerebral death	4.2 ± 1.2	99.5 ± 3.9	30.2 ± 3.7	0.22 ± 0.10	0.46 ± 0.16	26.7 ± 4.8	36.2 ± 3.4
Recovery	5.5 ± 2.0	107.1 ± 3.7	31.0 ± 1.2	0.14 ± 0.07	0.97 ± 0.27	34.0 ± 2.0	34.8 ± 1.7

All values: mean ± SE.

Student's *t* test: between values linked by braces, \*  $P < 0.05$ , †  $P < 0.01$ .

PjugO<sub>2</sub>, at the same time, has minimal prognostic value. For practical purposes then, continuous ICP recording is an effective prognostic indicator, although not an absolute one, and for this purpose it can be sensitized by tests of 'tightness' such as saline infusion or CO<sub>2</sub> inhalation. Further information given by rCBF measurements is of little practical use in individual patients.

**THERAPEUTIC IMPLICATIONS** Prevention of a severe rise in ICP in our group of patients can be attributed to the early treatment instituted—that is, (1) very early detection and removal of mass lesions; (2) immediate and continuous hyperventilation at PaCO<sub>2</sub> 25–30 mmHg and high PaO<sub>2</sub>; (3) sedation preventing ICP waves and lactacidosis; (4) control of arterial pressure and prevention of secondary ischaemic episodes. Search for, and emergency relief of, intracranial hypertension must be continued for several days, since new therapeutic indications may develop subsequently.

In addition to surgically removable lesions, an incorrect osmotic equilibrium causing brain oedema may also be responsible for a delayed but still reversible ICP rise.

As far as prevention is concerned, we submit the evidence of diffuse cerebral vasomotor disturbances and of their prognostic importance (mediated through the maldistribution, uneven oxygenation of the brain and brain oedema). Twenty-four hours' support of blood pressure and of the blood oxygen carrying capacity, hyperventilation with oxygen-rich mixtures, and perhaps steroid treatment to counter oedema are helpful to limit the effects of impaired autoregulation and vasoparalysis. In particular, the hyperventilation may act through its 'counter-steal' effects, through reduction of ICP, and through counteraction of cerebral metabolic acidosis and its consequences.

These procedures, the effectiveness of which has already been reported (Rossanda *et al.*, 1966), may be partly responsible for the reduction in the number of cases with vegetative survival or apallic states after severe head injuries.

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