Secondary ischaemic brain damage after head injury

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When the brain is examined within a few days of injury it can be surprisingly difficult to establish what has been the cause of death, or to determine with certainty which lesions are primary and which are secondary, apart from clear-cut complications such as intracranial haematoma or infection. Recent reports of continuous measurements of intracranial pressure after head injury (Lundberg, Troupp, and Lorin, 1965; Troupp, 1965 and 1967) suggest that many patients who die after head injury develop very high intracranial pressure before death without necessarily having a focal expanding lesion. The effect of a generalized increase in intracranial pressure on the brain is ultimately to produce a reduced perfusion of blood and the brain will then suffer hypoxic damage. In the belief that this may be one of the mechanisms contributing to brain damage after head injuries (and other lesions causing raised pressure) we have explored various aspects of the relationships between intracranial pressure and cerebral blood flow.

The oxygen supply to the brain depends, as in any other tissue, on the equation: available oxygen = haemoglobin × oxygen saturation × blood flow. A reduced oxygen content of the blood is not uncommon after head injury, which makes the brain much more critically dependent on blood flow. Blood loss from associated injuries, which occurs in a third of all cases of head injury admitted to hospital, commonly gives a low haemoglobin. Respiratory difficulties are also frequent after head injury, either due to the unconscious state or to associated chest injuries, and as a result of ventilatory insufficiency the oxygen saturation is then reduced.

Blood flow in the brain has a characteristic peculiar to its situation within a rigid closed cavity, namely, its susceptibility to surrounding tissue pressure. Indeed the supply of blood to the brain depends on cerebral perfusion pressure, which is the difference between systemic arterial pressure and intracranial pressure. Cerebral perfusion may be altered not only by systemic hypotension but also by raised intracranial pressure. Whilst hypotension is uncommon in patients suffering from head injury alone, the

GLIA 700-900ml.
NEURONES 500-700ml.
BLOOD 100-150ml.
CSF 100-150ml.
ECF <75ml.

Fig. 1 Volume of various intracranial tissues (ECF = extracelullar fluid).
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**Fig. 2** Rise of cerebrospinal fluid pressure exactly mirrors rise in PaCO₂ (measured by an infrared analyzer, on expired air).


**Fig. 3** Effect of halothane on ventricular pressure in a patient with intracranial tumour. Controlled respiration, on nitrous oxide-oxygen before halothane was introduced; normocapnia.

Figure 3 from Jennett et al (1967).

**Fig. 4** Each line records a change in ventricular pressure in a patient with an intracranial mass lesion under the same conditions as shown in Figure 3 (Halo = halothane; TCE = trichlorethylene; MOF = methoxyflurane).

Figure 1 from Jennett et al (1969).
intracranial pressure may rise due to several factors. A common cause of rising pressure is an increase in the intracranial blood volume. Although blood forms only a small proportion of the total intracranial volume (Fig. 1), it is the only component of the intracranial contents which is subject to rapid changes in volume. An abrupt rise in pressure may result from the vaso-dilatation consequent on increasing the arterial CO\(_2\) or reducing the arterial PO\(_2\) (Fig. 2). Both of these factors will operate when there is respiratory insufficiency; but this will also cause cerebral venous congestion, due to the transmission to the intracranial cavity of the rising intrathoracic pressure, there being no venous valves between the right atrium and the intracranial cavities. Apart from this the brain itself may swell as a result of contusions and the accumulation of extravascular blood or cerebral oedema.

The doctor himself may aggravate this situation by giving analgesic or sedative drugs which are respiratory depressants, or by anaesthesia. Neurosurgeons have long been familiar with the deterioration of patients suffering from multiple injuries, including a head injury, following an anaesthetic given for some orthopaedic procedure. This deterioration was previously ascribed to faulty anaesthetic technique, causing either respiratory insufficiency or hypotension or both. However, a series of investigations carried out in Glasgow (McDowall, Barker, and Jennett, 1966; Jennett, McDowall, and Barker, 1967; Jennett, Barker, Fitch, and McDowall, 1969) suggests that volatile anaesthetic agents themselves may be an important factor. Observation of the vasodilatory effect of volatile agents on the cerebral blood vessels in animal experiments led us to predict that intracranial pressure would rise in patients, even if the anaesthetic technique was impeccable in avoiding ventilatory insufficiency. This proved to be the case, even in patients with no intracranial abnormality; when there was already an intracranial space-occupying lesion the rise in pressure could be alarming (Fig. 3). In a series of such patients, exposed to one of three different volatile agents (trichlorethylene, halothane, and methoxyflurane) the intracranial pressure rose in every single case, sometimes quite dramatically (Fig. 4). But that is not all, because these agents may cause hypotension and the net effect on the perfusion pressure could therefore be very considerable (Fig. 5); indeed it could approach the level at which the perfusion of even fully oxygenated blood becomes inadequate to meet tissue requirements in the brain as indicated in experiments on dogs (Zwetnow, Kjällquist, and Siesjö, 1968) and in primates (Brierley, Brown, Excell, and Meldrum, 1969).

In the situations described the blood flow was primarily altered and the effects of this on intracranial pressure and perfusion pressure were observed. But after head injury the intracranial and perfusion pressures may be altered and the question is what effect this may have on blood flow. To explore this we carried out a series of experiments on baboons in which the perfusion pressure was altered, either by raising intracranial pressure by the cisternal infusion of mock cerebrospinal fluid, or by lowering systemic arterial pressure by limited exsanguination followed by sympathetic blockade and tilting of the table (Rowan, Harper, Miller, Tedeschi, and Jennett, 1970). The volume blood flow was measured by the radioactive inert gas clearance method and the velocity of the circulation by the radioactive transit time technique. We discovered that volume flow was maintained until perfusion pressure fell below about 40 mm Hg, ie, there was autoregulation; this was achieved by vasodilatation rather than by an increase in the velocity of the circulation.

Eventually increased intracranial pressure produces maximal vasodilatation, and the vessels then no longer react normally, ie, by vasodilatation to hypercapnia or by vasoconstriction to hypocapnia. This is the state described by Langfitt, Weinstein, and Kassell (1965) as ‘vasomotor paralysis’, on the basis of animal experiments. In this situation measures which depend on reducing intracranial pressure by inducing cerebral vasoconstriction are ineffective, for

![](image)

Fig. 5 Reduction in perfusion pressure during administration of methoxyflurane in a patient with an intracranial mass lesion.
example, hyperventilation or hyperbaric oxygen (Miller, Fitch, Ledingham, and Jennett, 1970). Another consequence of this condition of the cerebral vasculature is that a passive relationship is established between the systemic arterial pressure and intracranial pressure; as arterial pressure increases autoregulation no longer operates and the intracranial blood volume increases with a resultant rise in intracranial pressure. Measures designed to raise the systemic arterial pressure may then have a catastrophic effect on the intracranial pressure. We have demonstrated this phenomenon in patients after head injury in whom continuous monitoring of intraventricular pressure has been carried out. When a falling blood pressure was restored to normal limits by plasma expanders in some patients, and by noradrenalin in others, we observed sudden rises in intracranial pressure, sometimes leading to apnoea. We have also recorded this phenomenon when hypertonic solutions (mannitol) were given with the intention of reducing intracranial pressure; increased blood volume caused such a sharp rise of systemic arterial pressure that the net effect on the intracranial pressure was to increase it.

These various observations led us to postulate that episodes of inadequate cerebral perfusion may occur more frequently after head injury than we had previously suspected. The question is whether neuropathologists can find, in the brains of patients dying after head injury, any evidence of reduced cerebral perfusion and hypoxia, which would support the hypothesis that this is an important factor in causing secondary brain damage.

References


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W B Jennett

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