The brain does not have significant stores of energy. A constant and plentiful supply of oxygenated blood and glucose is required. If cerebral perfusion pressure (CPP) decreases, caused by either hypotension or increased intracranial pressure (ICP), the cerebral arteries dilate, cerebrovascular resistance decreases and cerebral blood flow (CBF) is maintained despite the reduction in CPP [1]. This process of pressure autoregulation operates within finite limits. If arterial pressure is raised high enough, a "breakthrough" increase in CBF occurs [2]. Conversely, if CPP is lowered sufficiently, CBF must eventually decrease. The threshold values of CPP at which these flow changes occur are not fixed. In patients with long-standing arterial hypertension the thresholds are shifted upwards, hence patients with arterial hypertension tolerate hypotensive anaesthesia poorly. The lower threshold for a declining CBF is at a higher level when CPP is reduced by arterial hypotension than when it is reduced by raised ICP. It is also higher with haemorrhagic than with drug-induced hypotension, and if sympathetic block is used with haemorrhagic hypotension, the CPP threshold is lowered [3]. Within the autoregulatory limits, CBF does not, in any case, remain absolutely constant; there is a small reduction in CBF resulting from decreasing CPP. Dilatation of the resistance vessels is phased. Larger vessels of 200 μm dilate first as CPP decreases, followed by smaller vessels, down to 50 μm as the pressure reduces further [4].

Autoregulation is said to be impaired by several pathophysiological circumstances, including subarachnoid haemorrhage, traumatic brain injury or an episode of global brain ischaemia. Regional loss of autoregulation is observed around brain contusions, infarcts and brain tumours. The conclusion that autoregulation is impaired is drawn from an observation that a pressure-passive change in global or regional CBF occurs in response to a spontaneous or induced change in CPP. How sound is this conclusion? If autoregulation is an important mechanism for protecting the blood supply of the brain, why should it be impaired so easily? In testing for autoregulation, for ethical reasons the patient cannot be submitted to a sufficient change in CPP to test the full autoregulatory curve, from lower to upper limits. When we observe a pressure-passive change in CBF, how do we know that the lower limit of regulation does not lie above the current level of our patient’s CPP? What are we observing may simply be the effect of increasing CPP towards a "new" and elevated threshold value for that patient at that time.

In experimental fluid percussion brain injury, the lower autoregulatory threshold increases to a higher level of CPP with increasing severity of injury [5]. We already know that this threshold is affected by sympathetic tone, by arterial carbon dioxide tension and, presumably, by any other factor that has a powerful effect on cerebral resistance vessels. In an experimental study in which autoregulation was thought to have been impaired by previous cerebral ischaemia, CBF was measured while arterial pressure and ICP were raised in parallel, in order to keep CPP constant. CBF increased with increasing arterial pressure. Cerebral resistance vessels must have increased in calibre to account for an increase in flow, despite constant CPP [6]. It has been hypothesized that the increase in intravascular (arterial) pressure may have stimulated release of the endothelium-derived relaxing factor, nitric oxide. Administration of a nitric oxide inhibitor (L-NAME) can raise the upper threshold for breakthrough of CBF as blood pressure increases [7]. In subarachnoid haemorrhage, endothelin release has been proposed as the cause of the cerebral vasoconstriction that is known to occur in these cases. This powerful cerebral vasoconstritor would be expected to cause an increase in the lower autoregulatory threshold [8]. If this is so, induction of arterial hypertension, to increase CPP, should result in an increase in cerebral perfusion.

In two studies of a group of patients with severe head injury, Chan and colleagues identified a threshold level of CPP of 70 mm Hg, below which there was a progressive increase in the transcranial Doppler pulsatility index, caused largely by a reduction in diastolic flow velocity, and a progressive reduction in jugular venous oxygen saturation (SjV02) [9, 10]. Defining the actual CPP threshold in individual patients is much more difficult, however, because it would be necessary in each patient to measure CBF or SjV02 over a wider range of CPP values than would be acceptable as part of clinical management [11].

The work reported by Moss, Dearden and Berridge in this issue is a nice illustration of this concept [12]. They studied patients under general anaesthesia during neurosurgical operations to clip intracranial aneurysms. Some but not all patients had suffered a subarachnoid haemorrhage. Changes in CBF were inferred from measurements of jugular venous oxygen saturation. This is valid only if inter-regional variations in CBF are small and if cerebral oxygen metabolism remains uniform, so that changes in oxygen saturation essentially reflect flow changes. Such conditions apply under general anaesthesia. With only one exception, an increase in an initially low jugular oxygen saturation that followed an increase in arterial pressure was observed in patients who had suffered a subarachnoid haemorrhage. It is tempting to conclude that these patients had increased their lower autoregulatory threshold because of the vasoconstrictor influence of endothelin released at the time of haemorrhage, but although one might infer that some patients were below threshold at the start of the study, it is not possible from the data presented to define what that threshold value would have been.

With the imminent availability of specific endo-
the lin antagonist drugs for use in humans, it is important that this type of research is pursued, so that the anaesthetist can obtain optimum conditions for brain perfusion in the operating theatre during neurosurgical operations, and in the intensive care unit afterwards.

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References