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Monitoring the injured brain: ICP and CBF

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Raised intracranial pressure (ICP) and low cerebral blood flow (CBF) are associated with ischaemia and poor outcome after brain injury. Therefore, many management protocols target these parameters. This overview summarizes the technical aspects of ICP and CBF monitoring, and their role in the clinical management of brain-injured patients. Furthermore, some applications of these methods in current research are highlighted. ICP is typically measured using probes that are inserted into one of the lateral ventricles or the brain parenchyma. Therapeutic measures used to control ICP have relevant side-effects and continuous monitoring is essential to guide such therapies. ICP is also required to calculate cerebral perfusion pressure which is one of the most important therapeutic targets in brain-injured patients. Several bedside CBF monitoring devices are available. However, most do not measure CBF but rather a parameter that is thought to be proportional to CBF. Frequently used methods include transcranial Doppler which measures blood flow velocity and may be helpful for the diagnosis and monitoring of cerebral vasospasm after subarachnoid haemorrhage or jugular bulb oximetry which gives information on adequacy of CBF in relation to the metabolic demand of the brain. However, there is no clear evidence that incorporating data from CBF monitors into our management strategies improves outcome in brain-injured patients.

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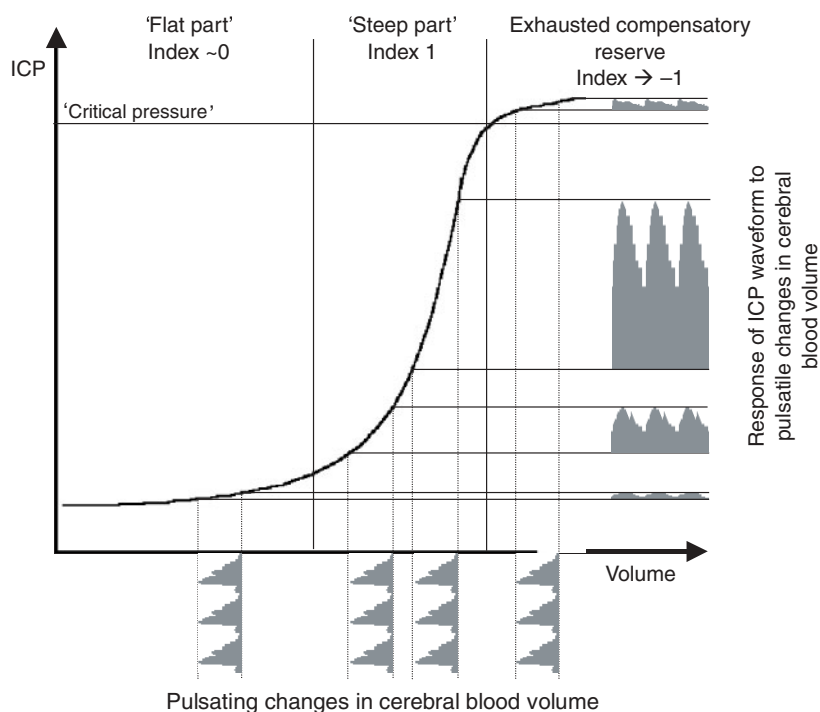
Intracranial pressure

What are we monitoring and how does it work

The fundamental principles of raised intracranial pressure (ICP) are condensed in the doctrine credited to Professors Monro (1783) and Kellie (1824), which states, once the fontanelles and sutures are closed, that (i) the brain is enclosed in a non-expandable case of bone; (ii) the brain parenchyma is nearly incompressible; (iii) the volume of the blood in the cranial cavity is therefore nearly constant; and (iv) a continuous outflow of venous blood from the cranial cavity is required to make room for continuous incoming arterial blood.[5]

The relationship between ICP and intracranial volume is described by the non-linear pressure–volume curve (Fig. 1).[62] Classically, three parts of the intracranial pressure–volume curve are described:[62] a flat part at lower intracerebral volumes, where good compensatory reserve is found, that is ICP remains low and stable despite changes in intracranial volume. This is attributable to compensatory mechanisms, that is the reduction of the volume of cerebrospinal fluid (CSF) or intracranial blood. Once these mechanisms are exhausted, the curve rapidly turns upwards, acquiring an exponentially rising shape. This part of the curve represents low compensatory reserve, that is ICP increases considerably even with relatively small increases in intracerebral volume. Finally, at high levels of ICP, the curve plateaus again, denoting terminal disturbance in cerebrovascular responses, when cerebral perfusion pressure (CPP) is very low and ICP equals mean arterial pressure (MAP). The cerebral arterial bed cannot dilate any more and starts to collapse because of the further increase in brain tissue pressure. Therefore, the system 'gains' some extra buffering capacity previously occupied by arterial blood volume. This third part of the pressure–volume curve has been confirmed experimentally[46 62] and also observed clinically, although only indirectly.[30 84]

Raised ICP is a common problem in neurosurgical and neurological patients. Frequent causes are intracranial mass lesions, disorders of CSF circulation, or more diffuse pathological processes. The gold standard for assessing ICP is an

Fig 1 Intracranial pressure–volume curve. Illustration of the intracranial pressure–volume curve and the relationship between pulsating changes in CBV and the ICP waveform. Index: index of cerebrospinal compensatory reserve calculated as the moving correlation coefficient between the amplitude of the fundamental harmonic of the ICP pulse wave and mean ICP. Steiner and colleagues,[96] reprinted with permission of the publisher.

intraventricular drain inserted into one of the lateral ventricles and connected to an external pressure transducer.[1] The foramen of Monro or for clinical purposes the external auditory meatus is the reference point for zeroing a transducer and repetitive zeroing may be performed after insertion of the catheter. In addition to monitoring pressure, these catheters allow withdrawal of CSF to treat raised ICP. The main limitation of this method is the risk of infection that increases over time and is in the range 6–11%.[9 68] The insertion of ventricular catheters may be difficult in patients with severe brain swelling. The best alternative to the ventricular catheter are intraparenchymal probes.[21] These devices either use a miniature strain gauge pressure sensor mounted at the tip of a thin catheter, or a fibreoptic catheter. With the former system a change of ICP results in a change in resistance and in the latter a change of ICP results in a change in reflection of the light beam. The main limitation of intraparenchymal probes is a small drift of the zero reference.[1] *In vitro* testing of modern probes has found drift as low as 0.6 (0.9) mm Hg (SD) after 5 days of testing.[22] Recalibration can generally not be performed once the sensor has been inserted. The infection rate of intraparenchymal probes is very low. Alternatively, subarachnoid, subdural and epidural devices can be used (Fig. 2). However, the accuracy of these devices is lower than that of intraventricular or intraparenchymal sensors.[16] Pressure measured in the lumbar CSF space is not a reliable estimator of ICP in brain-injured patients,[6] and such measurements may be

dangerous in patients with space occupying lesions. When it is not possible to insert an ICP monitoring device, for example because of severe coagulopathy, it is possible to estimate ICP from a transcranial Doppler examination with an absolute accuracy in the range ±10–15 mm Hg in most cases (Table 1).[2 31] Techniques using tympanic membrane displacement to measure ICP have been unsatisfactory so far[90] but, ultrasound wave transmission has shown some promise.

Normal ICP depends on age and body posture. Normal ICP in a supine healthy adult ranges between 7 and 15 mm Hg. In the vertical position it is negative with an approximate mean of −10 mm Hg but not exceeding −15 mm Hg.[32] In term infants 1.5–6 mm Hg are considered normal, whereas in children values between 3 and 7 mm Hg are quoted.[39]

ICP cannot be assumed to be evenly distributed in many pathological states and it is important to realize that even with a ventricular catheter, uniformly distributed ICP will only be observed when CSF circulates freely between all its natural pools. An intraparenchymal probe measures local pressure that can be compartmentalized and is not necessarily identical with intraventricular pressure. Significant pressure gradients may exist in patients with intracranial hypertension. For example supratentorial measurements do not necessarily reflect infratentorial pressure[86] and bilateral ICP monitoring has demonstrated large ICP gradients in patients with expanding mass lesions,[17] subdural haematomas,[18] or even in absence of space occupying lesions.[73]
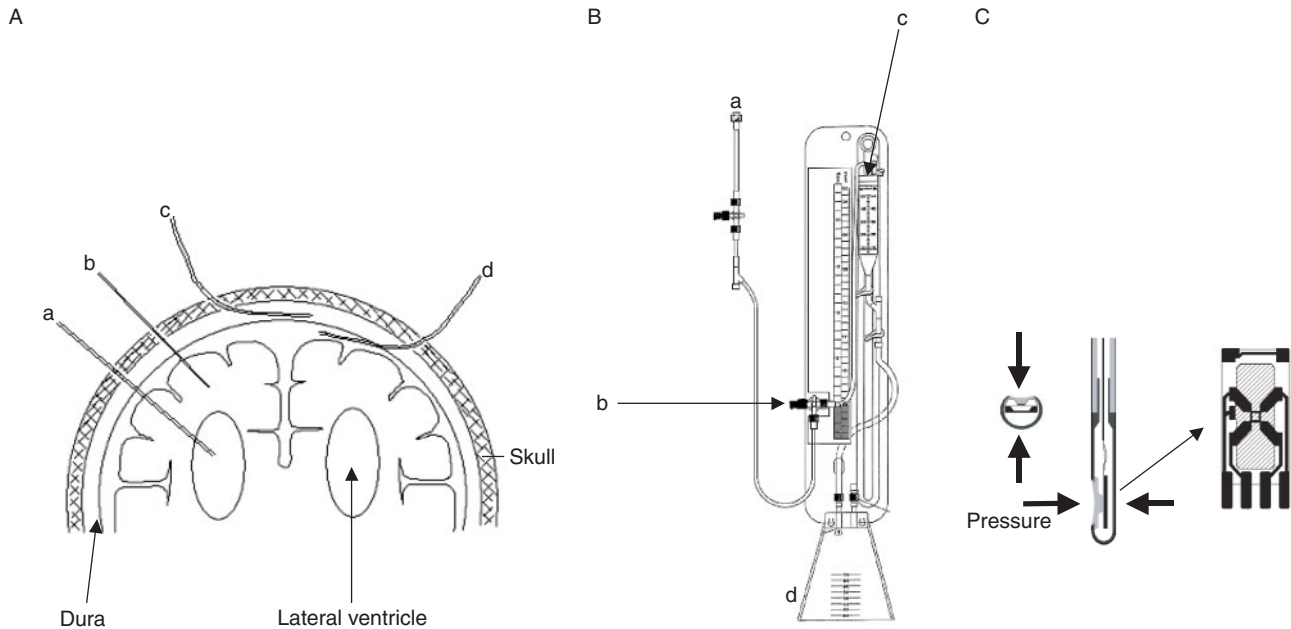
Fig 2 ICP monitoring. (A) Possible sites of ICP monitoring: a: intraventricular drain; b: intraparenchymal probe; c: epidural probe; d: subarachnoid probe. (B) Typical system for ICP measurement via an intraventricular drain: a: connection with drain; b: zero (should be positioned at height of patient's ear) and three-way stopcock for connection with pressure transducer; c: drip chamber, adjustable in height over zero for CSF drainage. Depending on stopcock position (b) either pressure measurements or CSF drainage are possible; and d: CSF reservoir. (C) Possible configuration for intraparenchymal probe. Pressure is sensed at the tip of the probe by a miniature sensor consisting of piezo-elements or other pressure sensitive elements arranged as a Wheatstone bridge.

Table 1 Characteristics of different methods for ICP monitoring. ICP, intracranial pressure; CSF, cerebrospinal fluid

Method	Advantages	Disadvantages
Intraventricular catheter	'Gold standard'	Most invasive method
	Allows drainage of CSF to lower ICP	High infection rate
	Re-zeroing possible	May be difficult to insert
		Simultaneous CSF drainage and
		ICP monitoring not possible
Intraparenchymal probe	Low infection rate	Measures local pressure
		Drift of zero over time
Subarachnoid probe	Low infection rate	Limited accuracy
	No brain penetration	High failure rate
		Periodic flushing necessary
Epidural probe	Low infection rate	Limited accuracy
	Easy to insert	Relatively delicate
	No penetration of dura	
Lumbar CSF pressure	Extracranial procedure	Inaccurate reflection of ICP
		May be dangerous when brain
		oedema is present
Tympanic membrane displacement	Non-invasive	Insufficient precision
Transcranial Doppler	Non-invasive	Limited precision

Fig 3 Examples of ICP monitoring. (A) Low and stable ICP. Mean arterial blood pressure (ABP) is plotted along the lower panel. (B) Stable and elevated ICP—this can be seen most of the time in head-injury patients. (C) 'B' waves of ICP. They are seen both in mean ICP and spectrally resolved pulse amplitude of ICP (AMP, upper panel). They are also usually seen in plots of time averaged ABP, but not always. (D) Plateau waves of ICP. Cerebrospinal compensatory reserve is usually low when these waves are recorded [RAP: correlation coefficient (R) between AMP amplitude (A) and mean pressure (P)] close to +1; index of compensatory reserve. At the height of the waves, during maximal vasodilatation, integration between pulse amplitude and mean ICP fails as is indicated by a decrease in RAP. After the plateau wave, ICP usually decreases below baseline level and cerebrospinal compensatory reserve improves. (E) High, spiky waves of ICP caused by sudden increases in ABP. (F) Increase in ICP caused by temporary decrease in ABP. (G) Increase in ICP of 'hyperaemic nature'. Both blood flow velocity and jugular venous oxygen saturation (Sj_{O_2}) increased in parallel with ICP. (H) Refractory intracranial hypertension. ICP increased within a few hours to above 100 mm Hg. The vertical line denotes the moment when the ischaemic wave probably reached the vasomotor centres in the brain stem: heart rate increased and ABP (CPP) decreased abruptly. Note that the pulse amplitude of ICP (AMP) disappeared around 10 min before this terminal event. Czosnyka and Pickard,[32] reprinted with permission from the BMJ Publishing Group.

Why is it important

In contrast to most other organs the brain is protected by a stiff skull. An increase in ICP may therefore impede cerebral blood flow (CBF) and cause ischaemia. Raised ICP is an important secondary insult in brain-injured patients and a predictor of poor outcome after traumatic brain injury. It is used as a target in many treatment algorithms. ICP is also used to calculate CPP, which is the difference between MAP
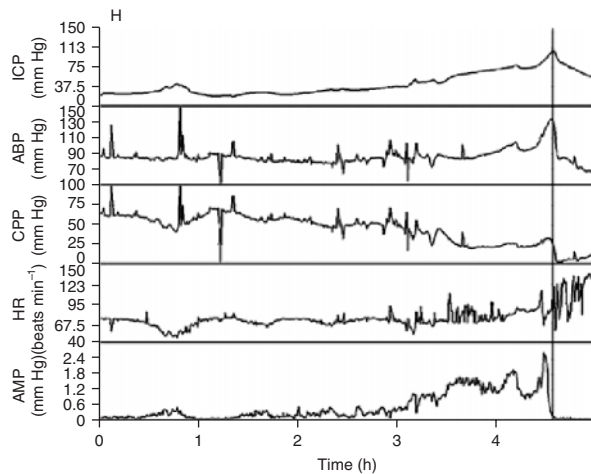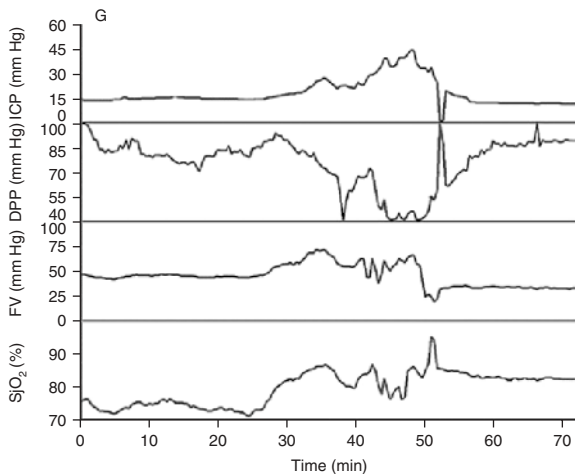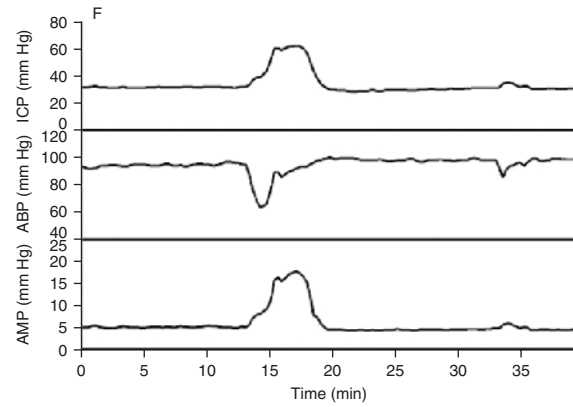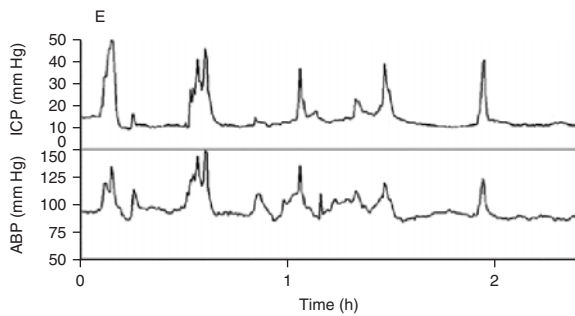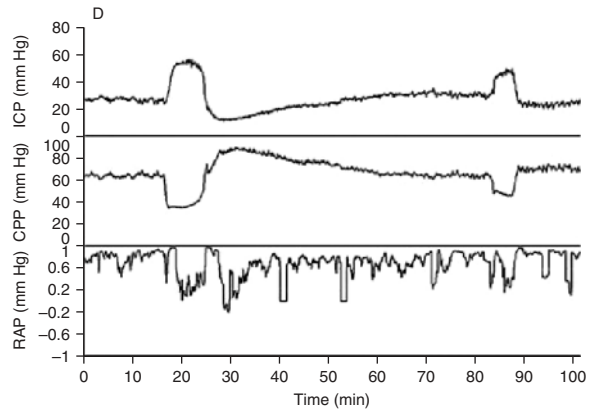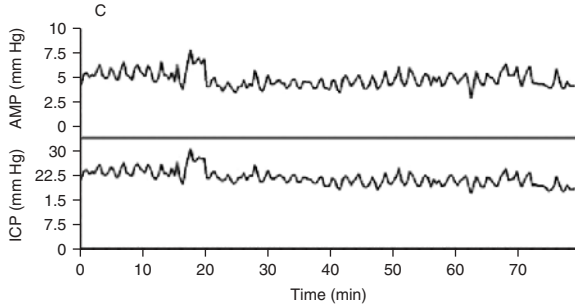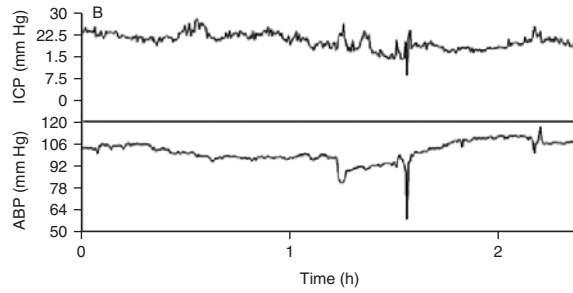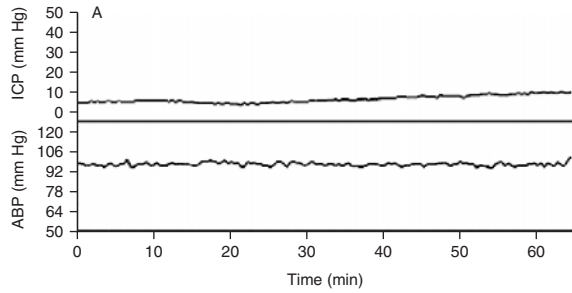
and ICP (CPP=MAP−ICP). CPP represents the pressure gradient across the cerebral vascular bed and is used as a therapeutic target for brain-injured patients in many intensive care units and is recommended by the Brain Trauma Foundation's, evidence based guideline.[1]

Clinical role

Indications for ICP monitoring vary from unit to unit and may include severe head injury, intracerebral and subarachnoid haemorrhage, hydrocephalus, or brain oedema after large strokes, hypoxic brain injury, central nervous system infections, or fulminant hepatic failure. ICP thresholds, above which therapy is started, depend on age and disease. In hydrocephalus values greater than 15 mm Hg are regarded as elevated,[32] whereas in head-injured adults the ICP threshold, above which outcome will be affected negatively, is between 20 and 25 mm Hg.[1] Above 25 mm Hg, aggressive treatment is started in most intensive care units. There is controversy concerning critical thresholds for ICP in children. Recently, it has been suggested that ICP should be treated above a threshold of 15 mm Hg in infants, 18 mm Hg in children younger than 8 yr and 20 mm Hg in older children and teenagers.[69] However, it is important to realize that there has never been a randomized controlled trial showing an outcome benefit for patients with ICP monitoring when compared with patients without ICP monitoring. Indeed a recent observational study has suggested that a CPP/ICP oriented therapy will increase treatment intensity and respirator days without an improvement in outcome.[28] It should be noted, that the non-monitored group had intensive cross-sectional imaging and motor score assessment (GCS) in lieu of ICP monitoring.

When CPP is used as a target for therapy there is further controversy as to which thresholds should be used. The Lund protocol suggests a lower limit of 50 mm Hg;[7] the revised guidelines of the Brain Trauma Foundation suggest 60 mm Hg[1] and earlier work suggested that in individual patients a CPP of 80 mm Hg or more may be required.[88] There have been some attempts to identify individual thresholds for CPP management. Methods such as transcranial Doppler and jugular bulb oxymetry,[19] microdialysis,[75] brain tissue oxymetry,[70] and an index of pressure reactivity[99] have been used for this purpose. So far there is no evidence that such an approach improves outcome. More recently it has also been shown that inappropriately high CPP is associated with poor outcome.[10 41] Again there is controversy whether the upper limit should be set at 60,[41] 70,[1] or 90 mm Hg.[10]

The rationale of any CPP augmentation is to increase CBF in brain regions which have critically low blood flow. However, an increase in CPP will only lead to an increase in CBF when autoregulation has failed or CPP is below the lower limit of autoregulation.[66] In a normal brain CBF is constant in the CPP range of about 50–150 mm Hg because of autoregulation[80] and a shift to the right of the autoregulation curve has been suggested after brain injury. Autoregulation is frequently disturbed in brain inured patients;[36 37 47 94] nevertheless, the effects of CPP augmentation are difficult to predict and may be small despite large increases in CPP.[25 98]

When ICP is monitored and recorded continuously typical patterns emerge (Fig. 3). Many patients have relatively stable ICP below or above 20 mm Hg. The term refractory intracranial hypertension is used when ICP increases over a few hours to very high values and leads to the death of the patient unless aggressive measures such as craniectomy are instituted. In some patients, spontaneous ICP waves are observed. Waves can be analysed in the time domain according to the classification proposed by Lundberg in 1960:[63] 'A' waves or plateau waves comprise a steep increase in ICP from near normal values to 40 or more mm Hg persisting for 5–20 min. Plateau waves are always pathological and occur in patients with intact autoregulation and reduced intracranial compliance.[87] 'B' waves are ICP oscillations that occur at 0.5–2 waves min⁻¹. ICP can increase to 20 mm Hg above baseline. These waves are probably related to changes in vascular tone, as transcranial Doppler typically shows increases of blood flow velocity in the middle cerebral artery at the same frequency as the 'B' waves. Lundberg also described 'C' waves as oscillations that occur with a frequency of 4–8 min⁻¹. These waves are probably of little pathological significance. ICP changes can also be the result of changes in CBF or arterial pressure, especially when intracranial compliance is reduced. Any change in cerebral blood volume (CBV) will lead to an increase in ICP. Such changes may be caused by intracranial events, for example seizures, or in response to a change in systemic variables such as, MAP, temperature, blood gases, serum sodium and inflation pressures. It is also worth noting that compliance decreases with age and may account for some of the poor outcome in elderly brain-injury patients.[55]

In chronic disease such as hydrocephalus or benign intracranial hypertension, ICP needs to be interpreted somewhat differently. In hydrocephalus CSF circulation and assessment of pressure volume compensation are important. Overnight ICP monitoring and tests where volume is added to the CSF space are important, especially in patients who present with persisting or recurring symptoms after insertion of a shunt.[51]

Use in research settings

The response of ICP to changes in MAP depends on the pressure reactivity of the cerebral blood vessels. Pressure reactivity is defined as the vascular response to a change in transmural pressure and is a key component of pressure autoregulation. Disturbed pressure reactivity implies disturbed pressure autoregulation. If pressure reactivity is intact, an increase in MAP will lead to a cerebral vasoconstriction within 5–15 s with reductions of both CBV and ICP. If pressure reactivity is impaired, CBV will increase

passively with increasing MAP, and ICP will increase. Opposite effects will occur when MAP is reduced. Disturbed pressure reactivity is associated with poor outcome after head injury. Using the relationship between MAP and ICP pressure reactivity can be monitored continuously.[33] Recent results suggest that pressure reactivity may influence the choice of a treatment strategy in head-injured patients[48] or may be used to define individual CPP targets.[99]

The ICP waveform consists typically of three components which overlap in the time domain but may be separated by analysis in the frequency domain. The pulse waveform has several harmonics, the fundamental of which corresponds to the frequency of the heart rate. The second component is attributable to the frequency of the respiratory cycle and the third component consists of 'slow waves' which are within the frequency limits of 0.05–0.0055 Hz. This definition of slow waves is less precise as the one used by Lundberg. Recently, the power of these slow waves has been shown to predict the outcome of patients with raised ICP after traumatic brain injury. A low content of slow waves in the overall ICP dynamics was associated with death.[11]

It is possible to obtain information of an individual patient's position on his or her pressure–volume curve from ICP monitoring data. The three parts of the pressure–volume curve can be identified by determining cerebrospinal compensatory reserve using an index, calculated as the moving correlation coefficient between the amplitude of the fundamental harmonic of the ICP pulse wave and mean ICP.[30] The principle on which this index is based is illustrated in Figure 1. Possible values of this index range from −1 to +1 and it makes use of the fact that the amplitude of the ICP waveform increases with mean ICP, at first slowly and, as compensatory reserve decreases, more rapidly. In the flat part of the pressure–volume curve the index equals approximately zero. In the exponentially rising part of the curve the value increases and eventually reaches a value of 1. With very high ICP values (greater than ~ 40 mm Hg), in the third part of the curve, the index will become negative and approach −1.[30] Earlier work showed that this index indicates loss of further vasodilatatory capacity on top of plateau waves[35] and it was demonstrated that the combination of a high ICP (>20 mm Hg) and a value for the index (<0.5) was associated with poor outcome.[30] A patient's position on the pressure–volume curve could be used to predict the risk of deterioration or herniation. In a preliminary study, this index was used to predict the response of ICP to hyperventilation.[96] Alternatively, methods such as the Spiegelberg Brain Compliance monitor have been developed to measure brain compliance. The role of this new device is still under investigation[110] but offers the possibility of an early warning system before decompensation.

Wider applicability

Raised ICP is an important feature of fulminant hepatic failure and associated with a high mortality. Most likely it is a consequence of cytotoxic oedema.[81] Placement of intraparenchymal ICP monitors in these patients has been shown to lead to complications in 20% and fatal haemorrhage in up to 4% of patients.[12] Epidural transducers may be the safest choice for ICP monitoring in such patients, even though they are known to be less precise than the other devices. Treatment strategies of raised ICP in the context of fulminant hepatic failure are still controversial.[58]

In summary, ICP is a complex parameter which contains information about cerebral compensatory mechanisms and mechanisms contributing to CBF regulation. ICP control requires continuous ICP monitoring and integration of the additional information in the ICP waveform and their relationship to MAP to help us understand the underlying pathophysiology.

Cerebral blood flow

What are we monitoring and how does it work

Bedside monitors for CBF can be characterized as quantitative or qualitative monitors. Kety and Schmidt[54] published the first method for quantitative determination of global CBF in patients in 1945. They used N_2O as an inert tracer gas and calculated CBF from the arterio–venous difference of the N_2O concentration based on a non-steady state application of Fick's principle. The method is still used today with some modifications,[108] and new methods of measurement are often compared against it. Recently two groups have proposed new techniques for quantitative determination of global CBF at the bedside. One is continuous jugular thermodilution,[71] the other a double-indicator method based on injections of dye and iced water providing non-continuous measurements.[109] Both methods have not yet gained widespread recognition and their usefulness is currently being evaluated.[52] The above methods are prone to be problematic because of anatomical factors: methods that rely on blood sampling from one of the jugular bulbs can be influenced by the asymmetry of venous drainage. This may introduce the unpredictable risk of acquiring misleading data.[59 72 101] A modification of the Kety–Schmidt technique is the [133]xenon method. [133]Xenon is a γ emitting freely diffusible inert gas that interferes only moderately with cerebral metabolism and is eliminated rapidly and almost completely via the lungs. Application is possible by injection into the carotid artery or i.v.,[4] or by inhalation.[77] Quantitative CBF data are calculated based on washout curves. Several detectors can be placed over each hemisphere and a certain amount of information on regional perfusion can be acquired although without precise anatomical correlation. Accordingly, comparisons of the same region from one study to another are difficult. Moreover, this method measures mainly cortical and subcortical blood flow within the territory of the middle cerebral artery. Low flow can be missed because of under or overlying adequate flow ('look-through phenomenon').[107] The equipment is bulky

and patients are exposed to ionizing radiation. Interpretation of both CBF and oxygen extraction fraction (OEF) require knowledge of arterial blood pressure and more importantly arterial Pa_{CO_2}. Correction of CBF and OEF should be made to normocapnia as modest reductions in Pa_{CO_2} will increase cerebral vascular resistance, OEF and reduce CBF. Large regions of increased OEF may be iatrogenic, and while important and of interest, they do not indicate a primary ischaemia problem.

Thermal diffusion[92] monitors focal cortical blood flow. A probe is inserted through a burr hole and placed on a cortical region of interest. The probe typically consists of two small gold plates, one of which is heated. Local cortical blood flow is calculated from the temperature difference between the two plates, which decreases with rising blood flow. The main advantage of this method is that the measurements are continuous but only local information is obtained. Recently, a modification of this technique using an intra-parenchymal probe incorporating thermistors has been evaluated in brain-injured patients.[106] It provides continuous quantitative real-time data that are in good agreement with values obtained by Xenon-CT for a volume of approximately 5 cm^3 around the tip of the probe. This new technology seems to be promising because of its excellent temporal resolution and potential to monitor a large part of a vascular territory with one probe or several vascular territories with multiple probes.

Jugular oximetry and transcranial Doppler provide non-quantitative or 'adequacy of CBF' data and are the methods which are used most often in intensive care. Jugular oximetry cannot directly measure CBF. Jugular bulb saturation (Sj_{O_2}) or the arterio-jugular oxygen content difference (AJDO$_2$), which is calculated as the difference between the arterial and jugular oxygen content in paired blood samples, provide information about the adequacy of global CBF in relation to metabolic demands (Figs 4 and 5). However, this is only correct if the cerebral metabolic rate for oxygen (CMRO$_2$) does not change independently of CBF, that is coupling between flow and metabolism is intact. The placement of catheters in the jugular bulb allows sampling of blood that almost exclusively drains from the intracranial circulation. Despite the fact that blood is usually sampled from one jugular bulb only, it is assumed that the values relate to global CBF rather than hemispherical CBF. However, typically only two-thirds of the sampled blood are drained from the ipsilateral hemisphere[40] and there is a large inter-individual variability of venous drainage of the brain which explains why methods relying on blood sampling from one of the jugular bulbs are prone to the influence of asymmetry of cerebral venous drainage.[72 101] It is impossible to predict which side in a specific patient will give more important data,[101] and there is no consensus on which side should be cannulated. Generally, the right internal jugular vein is preferred because it often is the dominant vessel. Alternatively, the side with the larger jugular foramen can be
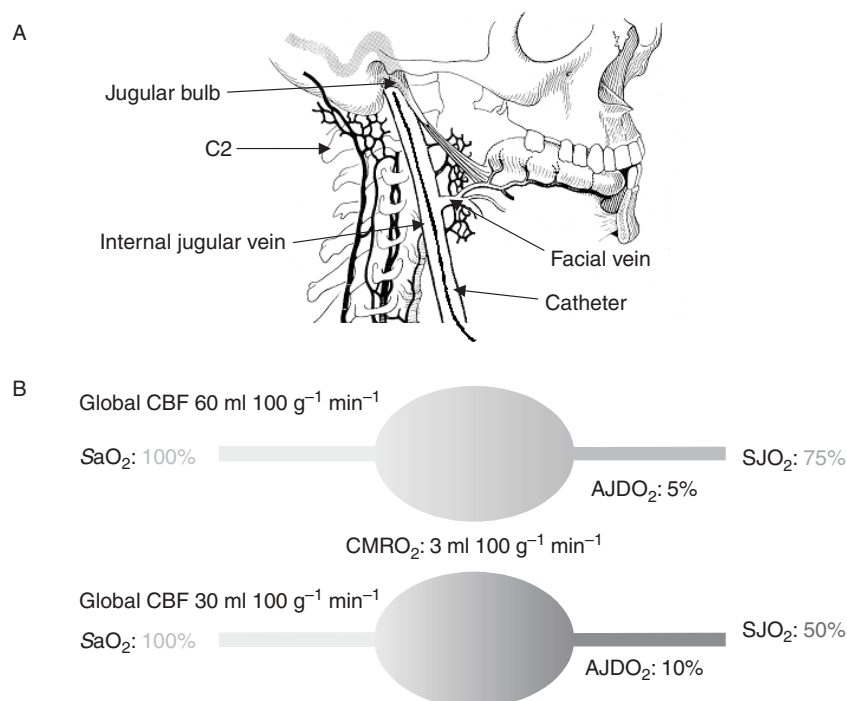
used or the side on which a compression of the jugular vein causes a greater increase in ICP. The catheter tip should lie at the level of the first or second cervical vertebral body, that is above the point at which the jugular vein receives its first extracranial tributary, the facial vein. The extracranial contamination at this level is considered to be about 3%.[40] The correct position of the catheter should be confirmed with a lateral cervical spine X-ray. Blood can be sampled intermittently or a fibreoptic catheter can be used to continuously determine Sj_{O_2}. If samples are withdrawn too quickly falsely elevated values may be found because of retrograde aspiration of extracranial blood. A rate of blood withdrawal of less than 2 ml min^{-1} should be used.[67] Fibreoptic catheters need to be recalibrated at regular intervals and are susceptible to artifacts as a result of the catheter position inside the vessel. It has been shown that when a fibreoptic catheter is used for continuous Sj_{O_2} monitoring 'time of good quality data' can be as low as 43% of the monitoring time.[56]

Normal values for AJDO$_2$ range from 4 to 9 ml 100 ml^{-1}.[42] Low CBF and ischaemia raise oxygen extraction and increase AJDO$_2$, whereas hyperaemia will lead to a decrease in AJDO$_2$. If CMRO$_2$ remains constant between measurements, changes in CBF can be estimated using the following relationship:

$$\text{CBF} = \frac{\text{CMRO}_2}{\text{AJDO}_2} \quad \text{and} \quad \text{CBF} \approx \frac{1}{\text{AJDO}_2}.$$

In view of the anatomical limitations it is not surprising that the estimates of changes in global CBF are not very accurate in head-injured patients with this method.[97] Jugular bulb oximetry is a global monitor and its sensitivity to detect regional ischaemia is small. A recent study in head-injured patients using positron emission tomography (PET) to quantify the ischaemic brain volume found that 170 (63) ml of brain volume were ischaemic at an Sj_{O_2} of 50%,[24] although the PET definition requires refining and lacks correction for Pa_{CO_2}.

Transcranial Doppler was introduced to clinical practice in 1981.[3] It is based on the Doppler principle,[38] easy to use and non-invasive, and can be used repeatedly. Transcranial Doppler measures blood flow velocity in the basal cerebral arteries not CBF, and the linear relationship between CBF and mean flow velocity (CBF=mean flow velocity×area of the insonated vessel×cosine of the angle of insonation) is only present if neither the diameter of the insonated vessel, nor the angle of insonation change during the examination. This assumption is probably fulfilled for most situations where examinations of the basal cerebral arteries are performed[44 49 89] with the possible exception of cases of subarachnoid haemorrhage leading to vasospasm. Examination of the ratio of extracranial internal carotid blood flow velocity to middle cerebral artery blood flow velocity helps differentiate vasospasm from increased CBF (Lindegaard Index).[61] Reasonable correlations have been reported between transcranial Doppler and xenon computed

A

B

Global CBF 60 ml 100 g^{-1} min^{-1}

Sa_{O_2}: 100%

Sj_{O_2}: 75%

AJDO$_2$: 5%

CMRO$_2$: 3 ml 100 g^{-1} min^{-1}

Global CBF 30 ml 100 g^{-1} min^{-1}

Sa_{O_2}: 100%

Sj_{O_2}: 50%

AJDO$_2$: 10%

Fig 4 Jugular bulb oximetry. (A) Catheter inserted into the internal jugular vein. The tip of the catheter must lie in the jugular bulb or at or above the level of the body of the 2nd cervical vertebra (C2). Blood can be sampled intermittently or oxygen saturation can be measured continuously using a fibreoptic catheter. The facial vein is the first large extracranial vein draining into the internal jugular vein. Rapid aspiration of blood samples (>2 ml min^{-1}) will result in extracranial contamination of samples. Jugular bulb catheters should be flushed continuously with normal saline (~2 ml h^{-1}). Thrombosis of the internal jugular vein is a possible complication which may result in raised ICP. (B) Principle of Sj_{O_2} monitoring. Sa_{O_2}, arterial oxygen saturation; CMRO$_2$, cerebral metabolic rate for oxygen; CBF, cerebral blood flow; AJDO$_2$, arterio-jugular difference in oxygen content; Sj_{O_2}, jugular venous oxygen saturation. CMRO$_2$ is identical in the upper and lower half of figure. Upper panel: adequate CBF, normal AJDO$_2$ and Sj_{O_2}. Lower panel: inadequate CBF, increased AJDO$_2$ and low Sj_{O_2}.

tomography and PET CBF measurements.[15 97] As a tool for the rapid estimation of CBF over a wide range of flows with the potential to detect vasospasm, transcranial Doppler is the simplest way to non-invasively obtain repeated real-time estimates of CBF (Fig. 6).

Why is it important?

Autopsy data have repeatedly shown that brain ischaemia is common in non-survivors of traumatic head injury and it is likely that inadequate CBF significantly contributes to the occurrence of post-traumatic secondary brain insults and therefore increases the probability of a poor outcome after brain injury.[13 50 79 83] CBF thresholds for ischaemia have initially been established in baboons by the group of Symon and colleagues[103] at ~15 ml 100 g^{-1} min^{-1}. The same group has also introduced the concept of the penumbra, defined as a zone of brain where because of inadequate perfusion neuronal function is lost but can be recovered when adequate perfusion is restored.[8 14] Using PET in humans suffering from ischaemic stroke the threshold for infarction was established at a CBF of 8 ml 100 g^{-1} min^{-1} and that for the penumbra at 20 ml 100 g^{-1} min^{-1}, that is the tissue with a CBF between these two thresholds is

potentially salvageable but will proceed to infarction if CBF is not restored within a limited time window.[43 64] Therefore, CBF or adequacy of CBF monitoring offers a rational approach to detect and prevent secondary insults and improve the outcome of these patients. The situation is less clear with high CBF (absolute or relative) as both beneficial and detrimental effects are possible and the relationship between elevated CBF and ICP is still unclear.[53]

Clinical role

Techniques to alter CBF are double-edged 'scalpels' and reliable and reproducible effects vary between and within patients when effects are assessed regionally and globally.[98] Even if we were able to adjust CBF to a certain target value, it would still be unclear what the appropriate value should be. The metabolic demands of the brain influence the thresholds for ischaemia and hyperaemia and our therapeutic interventions such as sedation or hypothermia will change these thresholds in an unpredictable manner. It is therefore not possible to use the absolute CBF thresholds for ischaemia cited above. Because of the shortcomings of technology, qualitative CBF trend monitoring rather than quantitative measurements of CBF is the clinical reality.
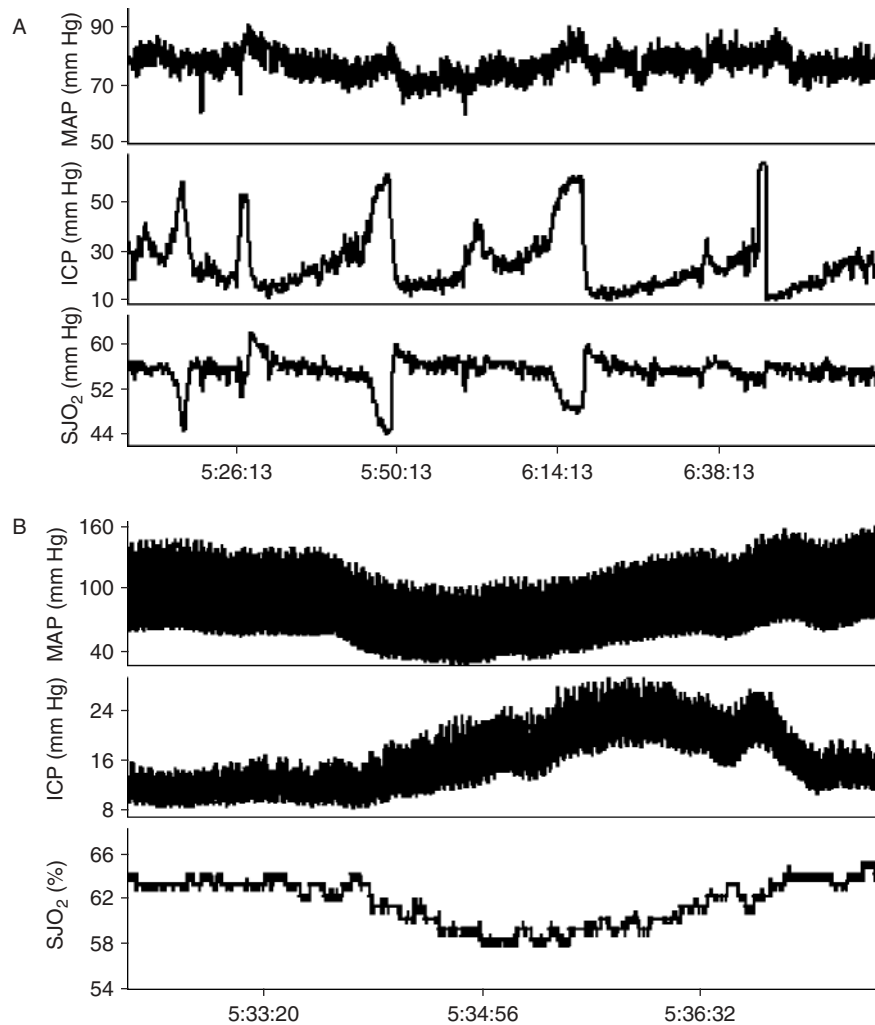
Fig 5 Adequacy of CBF monitoring: clinical examples of jugular bulb oximetry. MAP, mean arterial pressure; ICP, intracranial pressure; Sj_{O_2}, jugular bulb oxygen saturation. (A) Change in Sj_{O_2} with increases in ICP. (B) Change in Sj_{O_2} with low CPP (=MAP−ICP).

Despite the many limitations of the method, interest has focused on Sj_{O_2} monitoring. In head-injured patients it has been shown that repetitive reductions of Sj_{O_2},[45] and high values[27] are associated with poor outcome. There are only two studies[29][85] that compare a CBF-targeted treatment strategy with another approach and both used Sj_{O_2}, as a qualitative monitor with good temporal resolution, to estimate adequacy of CBF. The first study,[85] a randomized trial, was designed to answer the question, whether a CBF-targeted protocol, using a higher arterial blood pressure and optimized volume management to augment CBF, without targeting a specific range of CBF and or Sj_{O_2}, was superior to a conventional ICP-based strategy. It failed to demonstrate a difference in outcome for these two strategies. The main limitation of this study is that in the ICP-based strategy group episodes of low Sj_{O_2} were treated in the same way as in the CBF group. However, despite not finding a difference in outcome, the authors concluded that a CBF-targeted management protocol could prevent secondary injury because the CBF-targeted protocol reduced the frequency of jugular desaturations, and therefore the risk of cerebral ischaemia significantly. This study reported one unexpected observation: 15% of patients in the treatment group developed an adult respiratory distress syndrome (ARDS). While this percentage is well within the reported incidence in trauma patients, it was nevertheless surprising that the rate was almost five times that of the control group. The data were later reanalysed to assess whether ARDS is a complication of induced hypertension. Using a logistic regression model, administration of ephedrine, administration of larger doses of dopamine (median dose in patients without ARDS: 35 mg kg^{-1} 24 h^{-1}, in patients with ARDS: 215 mg kg^{-1} 24 h^{-1}), and a history of drug abuse were found to be associated with an increased risk to develop ARDS.[26] It is therefore likely that the beneficial effects of the CBF-targeted management were partially offset by the morbidity and mortality associated with ARDS. The second study,[29] providing class II

A

B
Doppler probe (2MHz)

C

Middle cerebral artery
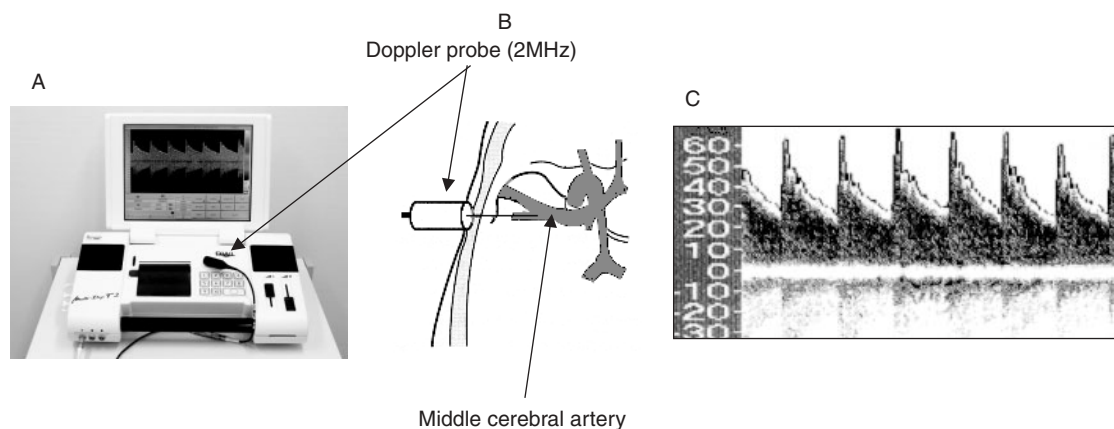
Fig 6 Transcranial Doppler. (A) Typical transcranial Doppler machine. (B) Illustration of insonation of middle cerebral artery through temporal bone. (C) Typical printout of signal from the middle cerebral artery. y-axis, blood flow velocity in cm s^{-1}.

evidence, compared a CBF-targeted approach using manipulation of Pa_{CO_2}, that is 'optimized hyperventilation', to maintain cerebral oxygen extraction at 24–42%, based on the AJDO$_2$, to a management based on maintaining CPP above 60 mm Hg. This study found that the outcome was better with the optimized hyperventilation protocol. However, there are several issues, such as the choice of the CPP threshold in the control group and the use of vasodilators, that prevent this publication from serving as a strong argument that control of CBF by optimized hyperventilation is clearly superior to a CPP-targeted management.[20]

Transcranial Doppler is used frequently for the detection and monitoring of vasospasm in patients after aneurysmal subarachnoid haemorrhage. Reasonable sensitivity and specificity are reported especially for the middle cerebral artery and the basilar artery, however, it is currently unknown whether monitoring of vasospasm with transcranial Doppler has an impact on outcome.[93]

Use in research settings

Monitoring of CBF also gives us the possibility to assess the reactivity of the cerebrovascular bed to changes in CPP, arterial partial pressure of CO_2 (Pa_{CO_2}) or brain metabolism. For the assessment of vascular reactivity, mostly transcranial Doppler is used to measure changes in CBF velocity. While assessment of CO_2-reactivity has its place in the assessment of patients with stenotic carotid artery disease, the response of CBF velocity to stimuli such as changes in MAP, arterial partial pressure of CO_2, or metabolic suppression are used primarily in research. Intact autoregulation has been shown to be a powerful protective mechanism for the injured brain as it is associated with good outcome[33 34 36 57 78] and several methods for determination of the autoregulatory status are available. Most methods measure the CBF response to a single reduction in MAP or CPP. A distinction is made between dynamic measurements evaluating changes within the first seconds after the stimulus and steady-state measurements. However, there is a

good correlation between these two types of measurement.[104 105] More sophisticated methods evaluate the phase shift, correlation or spectral coherence between changes in CBF and CPP[34 100] or fit various dynamic models to transcranial Doppler blood flow velocity and arterial blood pressure data.[91] These methods generally give non-continuous information. Continuous monitoring of autoregulation is also possible using methods that calculate an index of autoregulation[34] based on the response of flow velocity to slow spontaneous changes in CPP. After trauma, reactivity to changes in Pa_{CO_2} seems to be less vulnerable than autoregulation as intact CO_2 reactivity is frequently found in the presence of disturbed autoregulation, a phenomenon called 'dissociated vasoparalysis'.[23] Loss of reactivity to changes in Pa_{CO_2} is associated with poor outcome.[65 76] Also, the response of flow velocity to metabolic suppression for instance by using propofol titrated to achieve burst suppression can be measured.[60] Finally, non-invasive estimation of ICP and CPP is an area of interest and transcranial Doppler has been used to achieve this.[2 31]

Wider applicability

Postoperative neurological complications are frequently found in patients undergoing cardiac surgery. Cerebral infarction and encephalopathy have been reported in 15% of patients who undergo coronary-artery bypass grafting[82] and more than 50% of such patients may have postoperative cognitive deficits.[74] The aetiology of these complications is still not completely understood and jugular oximetry,[95] and transcranial Doppler[102] have been used in this context.

Conclusion

Current management strategies for acute brain injury patients encompass the principle of physiological stability. Although there is debate about which precise thresholds should be striven for, without monitoring ICP, considerable information is missing and objective management of the

patient not possible. Interventions to reduce ICP are double-edged swords and direct measurement will reduce their indiscriminate usage. ICP monitors are inexpensive and have an acceptably low complication rate. They offer a high yield in information and should be the cornerstone of all critical care management of acute brain injury. The role of CBF monitoring is less clear. Currently, Sj_{O_2} and transcranial Doppler are the methods that are used most frequently. However, there is no clear evidence that incorporating data from these methods into our management strategies improves the outcome in brain-injured patients.

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