Chapter 9  
Doppler assessment of the fetal and neonatal brain  
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INTRODUCTION

Doppler ultrasound has been used to investigate the human circulation since 1957 (Satomura 1957), but it was in 1977 that Fitzgerald & Drumm developed a Doppler system to obtain velocity waveforms from the umbilical artery and suggested its use in the evaluation of the fetal condition in cases with pre-eclampsia and intrauterine growth restriction. Since that time Doppler ultrasound has become increasingly utilized as a non-invasive tool to evaluate the hemodynamics of the uteroplacental and fetoplacental circulations. Continuing technical developments in Doppler ultrasound equipment, particularly highly sensitive color flow imaging techniques, have made it possible to study the fetal circulation in even greater detail. Neonatal Doppler studies date from 1979 (Bada et al. 1979). Doppler ultrasound has mainly been used as a research tool, but a number of clinical applications have been recognized.

Doppler ultrasound is a non-invasive method of measuring blood flow velocity, which detects hemodynamic changes instantly. Repeated measurements can conveniently be made at the bedside or cotside. However, it is important to understand the limitations of the method before considering its uses in obstetric and neonatal practice.

DOPPLER MEASUREMENTS

When an ultrasound signal is directed towards a moving object (e.g. red blood cells within a vessel) the frequency of the reflected signal is altered. The size of this change or Doppler shift is directly proportional to the velocity of the moving object (Doppler 1842):

\[ D = \frac{2Fv \cos \Theta}{C} \]

where \( D \) is the Doppler shift, \( F \) is the transmitted frequency, \( v \) is the blood flow velocity (m/s), \( \Theta \) is the angle of insonation and \( C \) is the velocity of sound in tissue, which is a constant (1540 m/s). The Doppler-shifted frequencies received by the same ultrasound probe are within the audible range and can be displayed in real-time as a spectral display of repeated flow velocity waveforms. The maximum frequencies of the waveform envelope or outline are proportional to the maximum velocities of erythrocytes within the vessel, usually in the center of the blood vessel. The accuracy of the technique is partly operator dependent, including uniform insonation of vessels and the correct setting of high-pass filters. Doppler waveforms can be assessed either quantitatively or qualitatively.

QUANTITATIVE MEASUREMENT

Accurate quantitative assessment of the blood flow depends upon several variables.

Angle of insonation

The measurement of the blood flow velocity depends upon the angle between the Doppler beam and the longitudinal axis of the vessel studied. The angle of insonation should be kept as small as possible. The greater the angle, the less accurate the velocity measurement becomes, and an angle of greater than 60° should not be used. In neonatal cerebral studies the angle should be kept as close to zero as possible. Duplex or color Doppler equipment can be used to measure the angle of insonation to correct blood flow velocity measurements (Eik-Nes et al. 1980; Griffin et al. 1983).

Vessel cross-sectional area

The volume flow depends upon the radius of the vessel studied. Errors in vessel diameter measurement will be doubled in the calculation of absolute blood flow, which is a particular problem when measuring smaller blood vessels such as fetal cerebral arteries. The blood vessel is also assumed to be circular with a constant diameter but this is known to vary with arterial pressure during each cardiac cycle (Eik-Nes et al. 1984):

\[ \text{volume flow} = \pi r^2 v \]

where \( v \) is the time average mean velocity and \( r \) is the radius of the vessel studied.

There is evidence that the neonatal cerebral arteries do change in diameter (Michelidishvili 1985; Sonesson & Herin 1988). However, if the angle of insonation is fixed, Doppler ultrasound may give a reliable measure of changes in cerebral hemodynamics but this may not be directly comparable between infants.

QUALITATIVE MEASUREMENT

Methods of extracting hemodynamic information from Doppler signals that avoid the problems associated with measurement of absolute velocity and flow have been developed. These methods include the calculation of simple ratios or indices using certain points on the maximum frequency.
outline of the waveforms. They have the advantage that they are angle independent, as the angle of insonation appears in both the numerator and the denominator of the ratio and its effect is cancelled out.

The three main indices used in clinical studies are (Fig. 9.1):

\[
\begin{align*}
A/B &= \text{(S/D ratio)} \quad \text{(Stuart et al. 1980)} \\
\text{peak systolic velocity} &= \frac{A}{B} \\
\text{PI (pulsatility index)} \quad \text{(Gosling et al. 1971)} &= \frac{\text{peak systolic velocity} - \text{end-diastolic velocity}}{\text{mean velocity}} \\
\text{RI (resistance index)} \quad \text{(Pourcelot 1975)} &= \frac{\text{peak systolic velocity} - \text{end-diastolic velocity}}{\text{peak systolic velocity}}
\end{align*}
\]

These Doppler indices are generally used as a measure of downstream resistance in the circulation, values increasing with a reduction in end-diastolic flow or higher downstream resistance. When there is absent end-diastolic velocity (AEDV), PI provides the most useful information since the \(A/B\) ratio will be infinity and the RI unity (\(A/B = \infty, RI = (A-0)/A = 1\)). It should also be noted that completely different alterations in the waveform shape can result in the same change in ratio. Central circulatory changes can contribute to alterations in waveform shape, particularly as all the indices are dependent on heart rate or length of the cardiac cycle (Mires et al. 1987; Maulik et al. 1992). It is important to recognize that with acute hemodynamic changes, the measurement of PI can yield misleading results. In a recent report Gunnarson et al. (1998) used cerebral Doppler blood flow velocimetry to study central hemodynamics in the ovine fetus during conditions of hypoxemia and acidemia. An increase in blood velocities occurred within a cerebral vessel during hypoxemia and hypoxic–acidotic periods, whereas PI remained unchanged due to the effects of a reduced heart rate. This highlights the potential problems with the interpretation of PI.

In vitro studies and in vivo cerebral studies in neonates and animals have shown a good correlation between Doppler velocity measurements and cerebral blood flow measured by other techniques (Blennow et al. 1983; Greisen et al. 1984, Smith 1984; Raja et al. 1987). The RI is the index favored by neonatologists and has been shown to be of clinical value in asphyxiated infants (see below). Although it may be assumed to be a measure of cerebral vascular resistance, this has been disputed and its correlation with resistance in animal models is not good.

**DOPPLER EQUIPMENT**

Continuous-wave Doppler probes transmit ultrasonic waves and receive the Doppler-shifted frequencies continually. Doppler signals are therefore obtained blindly from all moving structures in the line of the Doppler beam. Visualization of the vessels cannot be achieved using this equipment, which excludes its use in the fetal cerebral circulation. In neonatal cerebral studies the two main acoustic windows are transfontanellar for the anterior cerebral arteries and transtemporal for the middle cerebral arteries (Figs 9.2 and 9.3). Continuous-wave Doppler will sample all vessels in the path of the ultrasound beam, which may confuse the origin of the signal. Also, the angle of insonation may be impossible to estimate. These problems reduce the reproducibility of the technique and pulsed-wave Doppler is preferred.

Duplex Doppler ultrasound is a combination of pulsed-wave Doppler and real-time ultrasound in which the same transducer is used both to transmit repetitive ultrasound pulses and receive the echoes. The depth of the signals can be...
be adjusted to allow visualization and targeting of the vessel studied, enabling Doppler assessment in a number of fetal and neonatal vessels including the descending aorta, renal artery, common carotid artery, internal carotid artery, and anterior, middle, and posterior cerebral arteries.

Duplex systems can be rather large and cumbersome for neonatal studies and pulsed-wave probes without real time may offer a good alternative. The facility for altering the depth of the signal acquisition ‘gate’ allows a defined tissue sample to be taken. As the vessels are very small it is possible to sample across the whole artery, providing more complete velocity profiles. Ideally, a fixed probe should be used to maintain a constant angle of insonation during a study, in which case a change in the frequency shift will reflect a change in velocity (assuming vessel diameter remains the same). This is not possible in the fetus. Absolute velocity values can only be measured if the angle of insonation is known (see above). Velocity signals are subject to very marked physiological variations and therefore the recordings should be gathered over as many cardiac cycles as possible.

Using color flow imaging, blood flow information is color-coded, in terms of direction, velocity and turbulence, and superimposed on the gray-scale real-time image. This equipment offers major advantages, especially in the study of small vessels such as in the fetal cerebral circulation. It allows rapid visualization and accurate identification of the desired vessel, which minimizes examination time with reduced exposure to ultrasound energy. It also allows a more accurate estimation of the angle of insonation.

More recently, a new technique of detecting blood flow has been introduced called power Doppler imaging or angiography. Power Doppler displays the intensity or energy of the returning Doppler signal. Although power Doppler provides no information on flow direction, velocity, or flow character, it has improved sensitivity compared to color Doppler imaging in demonstrating slower flow, perfusion in smaller vessels, and continuous imaging of tortuous vessels as it is angle independent. Its potential value in the investigation of fetal cerebral blood flow including intracranial hemorrhage (Guerriero et al. 1997), microcephaly (Pihu et al. 1998), vascular malformations (Paladini et al. 1996), and tumors has been suggested, although the increased sensitivity to tissue motion can be problematic in the fetus (Poon & Aono 1996).

SAFETY OF ULTRASOUND USED IN DOPPLER INVESTIGATIONS

The three main potential mechanisms for damage using ultrasound are heating and cavitation effects and possible sister chromatid exchange:

1. The heating effect arises from the absorption of the ultrasound energy by the tissues through which it passes (Nyborg 1985). Different tissues have varying acoustic absorption coefficients, bone having the highest. All of the studies have been carried out in vitro and they do not take into account the cooling effect that occurs in perfused tissues. Nevertheless, the high intensity of pulsed-wave Doppler used in certain circumstances, such as by vaginal probes in early pregnancy, have the potential to cause significant heating in tissues, a fact underlining the need for care (Ter Haar et al. 1989).

2. Cavitation is the formation of small, gas-filled cavities caused by the negative pressures in the acoustic field. Both stable and unstable cavitation are theoretically possible although evidence of their effects is not available in vivo. However, cavitation is potentially harmful, and in vitro models may cause tissue disruption (O’Brien et al. 1979). No studies suggest that the phenomenon occurs at diagnostic intensities in vivo.

3. Sister chromatid exchange remains a theoretical risk; no adverse clinical results have yet been reported.

Follow-up studies of infants scanned in utero have not shown any detrimental neurodevelopmental outcome (Salvesen et al. 1992; Carstensen & Gales 1983), although one report suggests an increased incidence of non-right-handedness in those infants exposed to ultrasound in utero (Salvesen et al. 1993).

PRACTICAL GUIDANCE FOR SAFE USE OF DOPPLER ULTRASOUND

1. The acoustic power and pulse amplitude should be kept to a minimum commensurate with the production of waveforms which can be accurately measured. The output intensity, $I_{out}$, should be kept below 100 mW/cm², as advised by the American Institute of Ultrasound in Medicine (1984).

2. The lowest pulse repetition frequency (PRF) which still allows measurement of the highest velocities should be used.
3. If the output of the machine used is not known, the local medical physics service should be asked to obtain such information.

4. The maximum temperature that may be reached by the transducer should be ascertained.

5. Particular caution should be taken if the patient has an elevated body temperature.

6. When using duplex Doppler equipment the Doppler beam should be turned-off until the vessel required is identified.

7. The Doppler beam should not be directed towards a particular point for longer than 1 min.

8. Exposure of tissue–bone interfaces should be minimized as much as possible.

9. The total duration of exposure to the ultrasound beam should be minimized.

**TECHNIQUE OF MEASURING FETAL CEREBRAL BLOOD FLOW**

All the cerebral blood flow velocity (CBFV) waveforms should be obtained using a 3.5 MHz transducer, during fetal apnea and in the absence of fetal movements (see below). The pressure exerted on the maternal abdomen by the ultrasound transducer should be kept to a minimum. The fetal head is readily compressed and a significant positive correlation between pressure and PI in the middle carotid artery (MCA) and internal carotid artery (ICA) has been noted (Vyas et al. 1990a), potentially giving rise to spurious results. The vessels studied should be the closest to the Doppler transducer, the angle of insonation always being less than 60°, and the Doppler sample gate length always being 4 mm or less, both to minimize the interference from other small cerebral vessels and to ensure the production of waveforms that can be accurately measured. It is important to identify correctly each cerebral vessel using color flow imaging, as significant fetal regional cerebral blood flow differences are present in utero (Mari 1994). Downstream resistance is highest in the MCA and lowest in an intracerebellar artery. In the majority of published fetal cerebral circulation studies, data have been obtained from the most easily accessible MCA.

Using transabdominal ultrasound, the fetal basal cerebral arteries are visualized in an axial view of the fetal head at the level of the brain stem. An angled horizontal section of the brain including the thalami and cavum septum pellucidum is obtained initially (plane where biparietal diameter is usually measured). If the transducer is moved caudally in a parallel plane, the anterior, middle, and posterior fossae are seen and the circle of Willis can be clearly identified using color flow imaging. This consists of an anastomosis (anterior and posterior communicating arteries) between the paired internal carotid arteries and the basilar artery.

The ICA divides into the anterior and middle cerebral arteries (Fig. 9.4A). The use of duplex Doppler equipment allows detection of the ICA pulsations, but color flow Doppler facilitates visualization and confirmation of the vessel identity as it branches immediately after its exit from the bony canal (Fig. 9.4B).

The MCA is the largest branch of the ICA supplying approximately 80% of the blood flow to the cerebral hemisphere. It passes anterolaterally from the circle of Willis in the Sylvian fissure, to supply the corpus striatum, basal ganglia, cortex of the insula, and the inferior frontal gyrus. The greater wings of the sphenoid bone, between the anterior and middle fossae are good reference points for locating the MCA. As the fetal head is often in a lateral position, an acute angle of insonation (which may reach zero) can be achieved to produce a clear waveform, an advantage for velocity measurements. Locci et al. (1992) demonstrated that PI values obtained from the proximal MCA are significantly lower

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Figure 9.4 (A) Diagramatic representation of the cerebral arteries through a cross-section of the fetal head showing the cerebral peduncles (CP), internal carotid (I), and the anterior (A), middle (M) and posterior (P) cerebral arteries. (B) Fetal cerebral circulation shown by color flow Doppler.
than from the distal segment. The MCA is recognized to consist of four segments: M1, M2, M3, and M4 (Aaslid 1986). The M1 segment maintains a more constant diameter and is the preferable site for Doppler studies.

The anterior cerebral artery (ACA) leaves the ICA at the anterior perforating substance and passes forwards, above the optic nerve towards the orbital surface of the frontal lobe. With color flow imaging the vessel can be easily identified as it leaves the anterior boundary of the circle of Willis and tracks towards the frontal lobe (Fig. 9.4B). Accurate measurements of the ACA can sometimes be difficult as the angle of insonation would be greater than 60° when the fetal head is in the lateral position.

The posterior cerebral artery (PCA) is the terminal branch of the basilar artery and curls back around the cerebral peduncles before passing backwards above the tentorium towards the occipital lobe. The superior cerebellar arteries (SCA) originate from the basilar artery, just before it terminates into the PCAs. The SCA can be localized running parallel and caudal to the PCA (Erkpairejikit et al. 1996).

Transvaginal Doppler assessment has been shown to have some advantages over transabdominal scanning in that a coronal section of the fetal brain is produced, allowing better distinction between the ICA and MCA and producing signals of equal quality from both cerebral hemispheres (Lewinsky et al. 1991). In addition, it may be superior at early gestations (Kurjak et al. 1992), in obese patients, and when the fetal head is deeply engaged in the pelvis (Lewinsky et al. 1991).

PHYSIOLOGICAL VARIABLES AFFECTING FETAL CEREBRAL BLOOD FLOW

A number of physiological variables will influence Doppler measurements in the fetal cerebral arteries. GESTATIONAL AGE

Transvaginal color Doppler imaging has made it possible to visualize the fetal intracranial circulation earlier in gestation than with transabdominal ultrasound (Kurjak et al. 1992). Fetal intracranial blood flow has been detected as early as 8 weeks’ gestation. End-diastolic frequencies in the Doppler waveform become more common with advancing gestational age, being constantly present after 13 weeks’ gestation (Kurjak et al. 1992). Earlier cross-sectional studies noted a weak parabolic correlation of PI with gestational age from intracerebral arteries in normal pregnancy. There was a slight rise in PI between 15 and 20 weeks’ and a fall towards term (van den Wijngaard et al. 1989; Arduini et al. 1990b; Mari & Deter 1992). This is in contrast to changes in the umbilical artery (UA), which indicate a steady fall in the vascular resistance with increasing gestation (Trudinger et al. 1985). However, in a longitudinal study Veille et al. (1993) found that although the diameter of the MCA, the time velocity integral and the peak flow velocity all increased progressively with gestational age, the standard Doppler indices did not demonstrate a significant decrease. Only PI showed a weak correlation with gestational age. Blood flow within the MCA ranged between 23 ml/min at 19 weeks’ gestation to 133 ml/min at term, paralleling the increase in fetal weight and total cardiac output. Therefore, the proportion of the cardiac output received by each MCA remained constant throughout gestation, between approximately 3 and 7%.

Other studies have noted a downward trend, but not always reaching levels of statistical significance, in Doppler resistance indices within the ICA (Wladimiroff et al. 1986, 1987) and the MCA (Meerman et al. 1990; Rizzo & Arduini 1991; Harrington et al. 1995; Kurmanavicius et al. 1997) in the third trimester. However, an increase in cerebral blood flow velocity with advancing gestational age is a consistent finding (Meerman et al. 1990; Vyas et al. 1990b; Mari et al. 1995). In a cross-sectional study Joernt et al. (1996) calculated maximum systolic, mean and maximum end-diastolic velocities in the MCA after correcting for the angle of insonation. The maximum end-diastolic velocity increased to a relatively greater extent than the maximum systolic velocity throughout the third trimester and this was interpreted as a constant decrease in cerebral vascular resistance up to 42 weeks’ gestation. This illustrates the problems associated with Doppler waveform analysis in the interpretation of changing downstream resistance or impedance in terms of absolute blood velocity or actual blood flow and vice versa. However, it is apparent that under normal circumstances the MCA is a low-resistance, high-capacitance bed, even early in gestation (Wladimiroff et al. 1992).

FETAL BREATHING MOVEMENTS

Wladimiroff (1989) recorded a wide range of PI values in the ICA in the presence of fetal breathing movements, demonstrating measurements taken during that time are unreliable. Therefore, all studies of cerebral and other fetal vessels should be made during fetal apnea.

FETAL HEART RATE

Measurements of the Doppler velocity waveforms have been shown to be inversely correlated with fetal heart rate due to the alteration in end-diastolic frequencies with length of cardiac cycle. Calculation of the indices can be standardized for a particular heart rate of 140 bpm (Mires et al. 1987). A decrease in the PI was found with increased fetal heart rates in the ICA, descending aorta and UA in appropriately grown and growth-restricted fetuses (van Eyck et al. 1985, 1986). When the heart rate is within the normal range (110–150 bpm), its influence on the waveform indices is of little clinical importance. However, fetal heart rate decelerations (Mari et al. 1991) or a fetal tachycardia secondary to rital drine (Rasanen 1990) will have a significant effect.
FETAL BEHAVIORAL STATES (see p. 94)

Nijhuis et al. (1982) provided clear evidence for the existence of fetal behavioral states in the human fetus, during the last few weeks of pregnancy. Four states were defined based on fetal heart rate patterns, eye movements, and body movements. Van Eyck et al. (1987) studied the ICA and the UA in relation to fetal behavioral states in normal pregnancy at 37–38 weeks' gestation. The PI in the ICA was found to be significantly lower during the ZF state (active sleep) compared with the IF state (quiet sleep) whereas the PI in the UA did not significantly change. The reduction in PI was not related to differences in fetal heart rate and was interpreted as representing an increase in cerebral blood flow. In pregnancies complicated by intrauterine growth restriction (van Eyck et al., 1988), this behavior dependency during the IF and ZF states disappeared in the ICA, the PI being constantly lower.

Interestingly, when Kofinas et al. (1996) investigated the effect of vibroacoustic stimulation on fetal MCA waveforms in 160 normal pregnant women at various gestations, they noted a reduction in PI values in fetuses over 28 weeks. The influence of fetal heart rate changes was thought to be negligible and an explanation for the response is not clear.

TECHNIQUE OF MEASURING NEONATAL CBV

As described above, the ACA and MCA are the most commonly studied vessels. A pulsed-wave transducer which may be securely fixed over the anterior fontanelle or temporal area to give a constant angle of insonation is preferred. Collection of data continuously for up to a minute will allow assessment to give a constant angle of insonation is preferred. Collection of data continuously for up to a minute will allow assessment of beat-to-beat and cycling variability (see below).

Other vessels which have been studied are the PCA, basilar artery and the circle of Willis. Color flow mapping has also made it possible to study the internal cerebral veins, the vein of Galen and the sagittal sinus.

PHYSIOLOGICAL VARIABLES AFFECTING NEONATAL CBV

GESTATIONAL AGE AND POSTNATAL AGE

Several studies of the MCA and ACA have shown that cerebral blood velocity increases with increasing gestational age and with each postnatal day, but for each day after birth a wide range of velocity values has been reported. The major change occurs within the first 12 h of life and is associated with a fall in the RI (Archer et al., 1985; Deeg & Rupprecht 1988; Horgan et al., 1989, Fenton et al. 1990). These physiological changes must be taken into account in recordings between babies or in repeated measurements made in the same baby (see Table 9.1).

CYCLING VARIATION AND BEAT-TO-BEAT VARIABILITY

Marked beat-to-beat variability of the velocity signal has been recognized for many years (Perlman et al. 1983a).

When recordings were made over periods of one or more minutes, it became apparent that the cycling variations occur at several frequencies (Anthony et al., 1991). Both preterm and healthy full-term infants show similar patterns of variation (Anthony et al., 1991). One of the major components of this variability appears to be respiration (Bignall et al., 1988). The influence of respiration is greatest in preterm infants who are artificially ventilated, presumably representing entrainment to that of the ventilator frequency (Coughtry et al., 1993). The influence of respiration is accentuated in hypovolemic states (Rennie 1989).

Ferrar et al. (1994) observed slow frequency CBV variations of significantly greater amplitude during quiet sleep compared with active sleep, in full-term infants. The frequency was similar to that described in preterm babies and adults, at a similar frequency to Lundberg B waves in intracranial pressure. These may represent vasmotor waves in the small autoregulatory arteries of the brain. Greater variability in CBV has also been described during rapid eye movement sleep than non-rapid eye movement sleep in both full-term and preterm infants (Cowen 1985; Rehan et al., 1996). Rehan et al. (1996) also describe greater CBV variability with periodic and apneic breathing than with regular breathing.

Therefore, it is important to be aware of such influences upon CBV so that observed changes are not necessarily ascribed to pathological states.

OXYGEN, CARBON DIOXIDE AND ARTERIAL PRESSURE

Transient hyperoxia has been shown to induce a small but consistent reduction in CBV (Nijima et al. 1988; approximately 3% per 1 kPa rise in PO2). The effect of carbon dioxide upon CBV, however, is much greater than that of oxygen. There is an approximate rise of 30% per 1 kPa rise in CO2 (Menke et al. 1993). Hypercapnia in full-term healthy neonates provokes a rise in diastolic velocity, due to cerebral vasodilatation (Archer et al. 1986a). On the first day of life, sick preterm infants show a blunted

<table>
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<tr>
<th>Age (hours)</th>
<th>ACA Term</th>
<th>ACA Preterm</th>
<th>MCA Term</th>
<th>MCA Preterm</th>
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Table 9.1 Mean velocities for postnatal age in the ACA and MCA in term and preterm infants (Fenton et al. 1990)

Source: Reproduced, with permission, from Anthony & Levene (1993).
CBFV response to increasing carbon dioxide tension, which becomes exaggerated after 24 h of age (Levene et al. 1988). The CBFV response to carbon dioxide changes on the first day of life appears largely dependent on the concomitant change in arterial pressure (Fenton et al. 1992).

Conversely, in the cerebral circulation, early reduction in downstream resistance (Wladimiroff et al. 1993) suggest there is an 8% rise in CBFV per 1 kPa rise in arterial pressure. The change is greater in infants below 30 weeks gestation, implying that these infants have immature autoregulatory control of cerebral blood flow (Joreh & Joreh 1987).

PLASMA VISCOSITY
In both adults and neonates, it is known that a low hematocrit is associated with an increased velocity, and the hematocrit should therefore be noted in each study (Rosenkrantz & Oh 1982; Brass et al. 1988). Hemodilution in nine neonates resulted in a significant decrease in hematocrit, an increase in cardiac output and 20% increases in blood flow velocities of the internal carotid artery and the celiac artery (Mandellbaum et al. 1994).

CEREBRAL BLOOD FLOW IN COMPLICATED PREGNANCIES
FETAL INTRAUTERINE GROWTH RESTRICTION
In intrauterine growth restriction (IUGR) secondary to placental insufficiency there is an increase in downstream resistance in the fetoplacental circulation, with reduced, absent or even reversed end-diastolic flow in the UA Doppler waveforms (Trudinger et al. 1985; Morrow et al. 1989; Battaglia et al. 1993). Conversely, in the cerebral circulation, early studies noted an increase in end-diastolic flow suggesting a reduction in downstream resistance (Wladimiroff et al. 1986, 1987; van den Wijngaard et al. 1989). These findings are consistent with the phenomenon of 'brain-sparing' or redistribution of blood flow in response to fetal hypoxia demonstrated in animal models. Flow is preferentially increased in favor of the vital organs such as the brain, heart, and adrenal glands to maintain adequate oxygen supply, with a decrease in the blood flow to the gut, kidneys, and carcass (Cohn et al. 1974; Peeters et al. 1979). During acute fetal lamb asphyxia, induced by obstruction of the maternal aortic blood flow, Malcus et al. (1991) observed significant changes in vessel diameter using ultrasound. A decrease in the aortic diameter and aortic blood flow occurred with fetal acidemia whereas in the common carotid artery, vessel diameter and blood flow significantly increased, i.e. there was apparent vasodilatation. In the chronic hypoxic state of the growth-restricted fetus, a preservation of head growth at the expense of the abdominal circumference or liver size is well recognized. In a recent longitudinal study of fetuses that developed IUGR, Harrington et al. (1999) demonstrated that a reduction in abdominal circumference mirrored the rise in UA PI and preceded waveform changes in the MCA and thoracic aorta. Interestingly, when growth restriction was associated with either a structural or chromosomal abnormality, Wladimiroff et al. (1988) noted that PI in the ICA was always within the normal range (suggesting the absence of circulatory redistribution) whereas the PI was raised in 33% of cases in the UA.

In growth-restricted fetuses the MCA PI demonstrates a significant inverse correlation with the degree of fetal hypoxemia, measured by cordocentesis (Vyast al. 1990b; Akalin-Sel et al. 1994). Simultaneous intrapartum pulse oximetry has also shown significantly higher blood flow velocity in the MCA in the presence of reduced oxygen saturation (Sutterlin et al. 1999). However, with severe degrees of hypoxemia (>4 SD below the mean for gestation), Vyast et al. (1990b) noted a tendency for PI to rise (Fig. 9.5). This has been attributed to increased intracranial pressure due to cerebral edema. There appears to be a limit to the adaptive mechanism present in that the severely compromised fetus may lose its ability to vasodilate the cerebral circulation.

Arduini et al. (1992a) performed Doppler velocimetry on 36 growth-restricted fetuses at weekly intervals after the diagnosis of a 'brain-sparing' effect, until the onset of antepartum late fetal heart rate decelerations were observed. In the cerebral circulation a nadir of vasodilatation was reached 2 weeks before the onset of decelerations, whereas a further dramatic increase in PI occurred within the UA and descending aorta close to the development of the abnormal heart rate tracing. These results are consistent with data

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\Delta \text{MCA cerebral artery pulsatility index (SD from mean)}
\]

Figure 9.5. Fetal hypoxia and the PI in the MCA. Open circles represent acidic freatures and closed circles represent non-acidemic fetuses. (Reproduced with permission from Vyast et al. 1990b.)
from fetal lamb experiments, showing that changes in the cerebral circulation take place at an early stage of fetal hypoxemia when only slight alterations in peripheral blood flow are detected (Peeters et al. 1979). However, in more severe hypoxemia, there are marked increases in peripheral vascular resistance and minimal increases, or even decreases, in cerebral blood flow. Individual values of PI may be difficult to interpret due to this variable effect. Indeed, as discussed above, studies on the cerebral circulation have shown that velocity is better correlated with brain blood flow than is PI (Rosenberg et al. 1985; Martin et al. 1990; Gunnarsson et al. 1998).

The possibility that a reduction in MCA PI can predict adverse perinatal outcome, such as preterm delivery, growth restriction, Cesarean section for fetal distress and neonatal complications, has been investigated. Several studies have used a ratio of Doppler indices, comparing the MCA or ICA to the umbilical artery or descending thoracic aorta, as a better indicator of centralization of the fetal circulation and subsequent perinatal problems (Arduini & Rizzo 1992b; Gramellini et al. 1992; Scherjon et al. 1992; Hecher et al. 1995a; Chan et al. 1996; Luzzi et al. 1996; Ozcan et al. 1998; Harrington et al. 1999; Ott 1999; Ozeren et al. 1999). In an ovine model of acute fetal hypoxia secondary to reduced umbilical or maternal aortic flow, Arbeille et al. (1995) found the cerebroplacental ratio (cerebral RI : umbilical RI) to be the hemodynamic parameter that most closely followed the changes in PI. Bahado-Singh et al. (1999) evaluated the screening efficiency of the cerebroplacental ratio for the prediction of IUGR and associated perinatal complications in 201 at-risk fetuses. A highly significant increase in perinatal morbidity and mortality was observed in cases with an abnormal ratio (Fig. 9.6). The cerebroplacental ratio appeared superior to umbilical artery Doppler in predicting perinatal complications. There was a progressive increase in screening efficiency as the interval between Doppler study and delivery fell. An unexplained finding of the study was that the ratio did not appear to correlate significantly with outcome in fetuses over 34 weeks' gestation. An immaturity of the mechanisms that autoregulate cerebral blood flow in preterm fetuses was postulated to explain the difference in results.

The hemodynamic effect appears to be a protective mechanism to prevent fetal brain hypoxia, as follow-up studies to date have not shown an increase in neurologic problems in the neonate or up to 3 years of age (Scherjon et al. 1993; Chan et al. 1996; Scherjon et al. 1998). Interestingly, Scherjon et al. (1996) recorded shorter visual-evoked potential latencies at 6 months of age in infants with abnormal ratios. They postulated that this accelerated neurophysiologic maturation could be the result of a beneficial adaptation to severe fetal growth restriction. In a cohort of 77 growth-restricted fetuses, Yoshimura et al. (1998) found no relationship between abnormal MCA : UA PI ratios and follow-up growth at 6 and 12 months of age, despite initially lower birth weight, increased admission, and length of stay in the neonatal unit. The available evidence suggests that an abnormal cerebroplacental ratio is not an indication to intervene too early and deliver a preterm fetus, but that increased surveillance is required. However, the value of cerebral Doppler velocimetry in improving clinical outcome has not yet been assessed by a randomized controlled trial. Neither has the issue of cost-effectiveness in clinical practice been addressed. With increasingly adverse conditions there is a preferential shift in cardiac output in favor of the left ventricle (Al Ghazali et al. 1988) with increasing right ventricular afterload (Rizzo & Arduini 1991). This has prompted investigators to assess the venous side of the fetal circulation as well as the arterial vessels. As pressure in the right atrium increases, ‘a’ wave decelerations are seen in the ductus venous and there is an increase in reversed flow within the inferior vena cava (Hecher et al. 1995b). Such abnormalities in venous flow are associated with metabolic acidemia whereas arterial redistribution affecting only the MCA does not appear to be associated with acidemia in IUGR (Rizzo et al. 1995). Longitudinal observations in preterm growth-restricted fetuses have demonstrated that abnormal venous waveforms precede abnormally reduced short-term variation of fetal heart rate (Hecher & Hackeloer 1997). Short-term heart rate variation, assessed by computer analysis, is itself considered a better predictor of acidemia compared to decelerations (Guzman et al. 1995).

Using arterial and venous Doppler velocimetry in a prospective study of 19 severely growth-restricted fetuses, Ozcan et al. (1998) found that absent or reversed flow in the ductus venous was the only significant parameter associated with perinatal death and 5 min Apgar scores. Randomized controlled trials are needed to determine...
whether additional venous Doppler assessment will enable obstetricians to assess more accurately the optimal time for delivery before the development of abnormal cardiotocography (Hecher et al. 1995a; Black & Campbell 1997; Hecher & Hackeloer 1997). This is particularly important in the management of the very preterm or growth-restricted fetus, aiming to minimize perinatal morbidity and any subsequent complications. It must always be appreciated that there is a variation in fetal responses to adverse intrauterine conditions (Hecher & Hackeloer 1997). Long-term follow-up studies are indicated to assess minor differences in neurologic development. It is also possible that the combined use of arterial and venous Doppler assessment may allow more women to be monitored as outpatients. However, because of the requirement for expensive color flow Doppler equipment and technical expertise, they are likely to be of limited value as a screening tool in normal pregnancy.

TWIN PREGNANCY

Twin–twin transfusion syndrome (TTTS) is a specific complication of monochorionic diamniotic twin pregnancies associated with extremely high perinatal morbidity and mortality. A hemodynamic mismatch is thought to occur between the twins because of placental vascular communications between their circulations (Bajoria et al. 1995). Cardiac and venous Doppler studies of the fetal circulation in TTTS are more complex with hypovolemia and increased placental resistance in the smaller donor twin and hypervolemic congestive heart failure in the larger recipient twin (Hecher et al. 1995c). Significantly decreased PI was found in the MCA of the larger recipient twin but not in the smaller donor twin (Hecher et al. 1995c). Mean blood flow velocity in the MCA of both twins was normal for gestational age whereas it was decreased in the thoracic aorta.

In contrast, small-for-gestational-age fetuses of monochorionic diamniotic twin pregnancies unaffected by TTTS are more likely to demonstrate the 'brain-sparing effect' (with decreased resistance in the MCA) compared to diamniotic dichorionic twins of similar low birth weights (Gazzano et al. 1998). Cardiac and Doppler ultrasound biometry and Doppler ultrasound from the fetal descending aorta, UA and MCA in the prediction of placental insufficiency in 130 multiple pregnancies. Doppler results from all three vessels rather than a single vessel was the best predictor of IUGR (sensitivity 75.9%) and of an adverse fetal outcome in terms of Apgar score, UA pH < 7.10 and neonatal unit admission.

ABNORMAL AMNIOTIC FLUID VOLUME

Doppler velocity waveforms of the ICA were studied in pregnancies complicated with prolonged severe oligohydramnios due to bilateral renal agenesis (van den Wijngaard et al. 1988). The end-diastolic velocity was reduced, absent or even reversed with a raised PI (>2 SD), suggesting very high peripheral vascular resistance, which Van den Wijngaard and colleagues postulated was due to head compression. The same mechanism was applicable in the newborn when Newton & Gooding (1975) demonstrated that molding of the skull compressed the superior sagittal sinus, resulting in decreased cerebral blood flow.

In post-term fetuses with oligohydramnios, Weiner et al. found the MCA PI was lower compared to post-term fetuses with normal amniotic fluid volume or compared to term fetuses, but this was associated with a reduced left cardiac output and normal PI in the UA and abdominal aorta (Weiner et al. 1996).

Mari et al. (1992) noted a significant decrease in fetal MCA PI after decompression amniocentesis for symptomatic polyhydramnios in twin pregnancies, suggesting a possible improvement in cerebral perfusion.

FETAL ANEMIA

Vyas et al. (1990c) studied 24 red cell isoimmunized pregnancies and found mean blood flow velocity in the fetal MCA to be increased with anemia. Although PI was decreased in anemic fetuses, there was no significant association with the difference in hemoglobin concentration. These hemodynamic changes were not significantly associated with the difference in blood PI. Therefore, the hyperdynamic circulation was considered to be a consequence of the reduced blood viscosity. Mari et al. (1997) noted a decrease in MCA peak systolic velocity with an increase in fetal hematocrit after intrauterine transfusion.

The value of blood flow velocity measurements in the MCA for the non-invasive diagnosis of fetal anemia due to maternal red cell alloimmunization has been recently addressed in a prospective multicenter study involving 111 at-risk fetuses (Mari 2000). All of the fetuses with moderate or severe anemia had peak systolic velocity values above 1.5 times the median (Fig. 9.7). The multiple of the median of peak systolic velocity was a strong predictor of anemia regardless of the presence or absence of hydrops. Measurements of the peak systolic velocity were found to predict the presence of moderate or severe anemia with a sensitivity of 100% and a false positive rate of 12%. Potentially, this could decrease the number of fetuses subjected to invasive amniocentesis or cordocentesis for this condition.

FETAL BLOOD SAMPLING

A significant decrease in PI occurs within the MCA as well as the UA and descending aorta following cordocentesis but not amniocentesis, even when performed transcervically (Capponi et al. 1996; Chitrit et al. 1997). This may reflect the release of vasoactive substances (Bizzo et al. 1996a).

LABOR

Conflicting results have been published using MCA Doppler in normal labor with some investigators reporting
no significant change in PI (Maesek et al. 1990, 1994; Kurjak et al. 1996) and others noting decreased values (Yagel et al. 1992; Chen et al. 1999). Decreased impedance to cerebral blood flow may be a protective mechanism to prevent fetal hypoxia during labor, although no significant difference was detected between downstream resistance in the MCA during uncomplicated labor and in labor with variable decelerations (Yagel et al. 1992). Contrary to their findings during spontaneous labor, Chen et al. (1999) found no significant change in MCA Doppler indices when labor was induced with prostaglandin E₂. It may therefore be significant that these induced labors were more frequently associated with abnormal UA pH values.

In pregnancies complicated by preterm labor, significantly lower MCA PI values were also noted in fetuses delivered within 24-48 h compared to fetuses delivered later or at term (Ghezzi et al. 1995; Rizzo et al. 1996b). Recent randomized trials involving tocolysis with sulindac or terbutaline (Kramer et al. 1999) and indomethacin or magnesium sulfate (Parilla et al. 1997) have reported no significant effects of the drug therapy on downstream resistance in the MCA.

**CLINICAL ASSOCIATION OF CEREBRAL BLOOD FLOW IN THE NEONATE**

There have been many studies describing the association of certain disease states and drugs with changes in CBPFV measurements. Few studies have addressed the clinical consequences and relevance of the associations described.

**CBPFV AND DRUGS**

**SURFACTANT ADMINISTRATION**

The literature describing the effects of surfactant administration on neonatal CBPFV gives conflicting results, with increased, unchanged, and decreased states being described. These differences may arise from the different types of surfactant studied (natural versus synthetic), the different methods of delivery (bolus versus slower administration), and the timescale of CBPFV measurements.

Jorch et al. (1989a) found no change in CBPFV when measured every 10 minutes following bovine surfactant administration to preterm infants in a controlled study. Van de Bor et al. (1994) studied 25 preterm infants given synthetic Exosurf for respiratory distress syndrome and found that mean CBPFV increased by 33% at 5 minutes, returning to baseline by 30 minutes. Cowan et al. (1991) used continuous CBPFV measurement of 10 preterm infants and found a 36% reduction in CBPFV and a 16% reduction in mean arterial pressure, within 2 minutes of administering natural Curosurf. There was also loss of the end-diastolic velocity, thought to be due to ductal shunting following the fall in the pulmonary vascular resistance. Van Bel et al. (1992) noted a fall in CBPFV during the instillation of prophylactic natural Curosurf but the velocities rose to above baseline values 10 minutes after administration.

Endotracheal suction and disconnection from the ventilator are common procedures during the administration of surfactant. Transient airway obstruction will lead to a rapid fall in carbon dioxide and cerebral blood flow. Surfactant acts to improve lung compliance and ventilation, leading to a subsequent fall in carbon dioxide and cerebral blood flow. Could the effects of surfactant on CBPFV be due to fluctuations in carbon dioxide? Bell et al. (1994) used the Xenon clearance technique to measure cerebral blood flow and concluded that the observed reduction following natural Curosurf was due to the fall in carbon dioxide levels. Saliba et al. (1994) studied different rates of instillation of synthetic Exosurf (5 versus 15 minutes) and, although increases in CBPFV and PCO₂ were observed following more rapid instillation, the increase in CBPFV could not wholly be explained by the fluctuation in PCO₂. In this study, there was no evidence that CBPFV changes were mediated by alterations in cardiac output, blood pressure, and ductal patency. Rey et al. (1994) demonstrated that the fall in CBPFV following natural Curosurf was more marked at higher doses (200 mg/kg...
The literature therefore suggests that synthetic surfactant is associated with increases in CBFV (van de Bor et al 1991; Saliba et al 1994), whereas natural surfactants appear to reduce CBFV (Cowan et al 1991; Rey et al 1994; van Bel et al 1992). This was tested by Murdoch & Kempley (1998) in a randomized controlled trial of 20 ventilated preterm infants undergoing surfactant treatment (synthetic Exosurf versus natural Curosurf). There was a slow and sustained rise in CBFV with synthetic surfactant. In contrast, with natural surfactant, there was an abrupt fall in CBFV. This was maximal at 1 minute and had largely resolved by 15 minutes. The rapid recovery in CBFV may explain why other groups using NIRS have not observed such changes (Edwards et al 1992), as the technique requires that stability in oxygenation is achieved before measurements are carried out.

Most investigators who claim surfactant has an effect on cerebral blood flow independent of changes in PCO2, and arterial blood pressure have endeavored to measure these parameters. However, fluctuations in PCO2 and arterial pressure may be rapid and go undetected (Halley et al 1995). The observed changes in CBFV following surfactant instillation have led to fears that surfactant therapy may be associated with an increased risk of intraventricular hemorrhage (IVH). The evidence suggests that these fears are unfounded. A meta-analysis of the randomized controlled trials evaluating the efficacy of surfactant therapy in the treatment of respiratory distress syndrome shows a reduction in the risk of all IVH (relative risk 0.88; 95% CI 0.77 to 0.99) (Soll 1999).

**ANALGESIA, SEDATION, AND PARALYSIS**

A bolus of 0.1 mg/kg midazolam produces a minor reduction in CBFV, associated with a transient fall in blood pressure (Harte et al 1997; van Straaten et al 1992). Diazepam also appears only to produce minor changes in CBFV (Jorch et al 1988b). Neuromuscular blockade and, to a lesser extent, morphine sedation decrease fluctuations in CBFV in preterm infants (Perlman et al 1985; Solditz et al 1988). Perlman et al (1985) suggest that using paralysis to reduce CBFV fluctuations results in a decreased risk of intraventricular hemorrhage in ventilated preterm infants.

**SEIZURES AND ANTICONVULSANTS**

Seizures in adults and children produce a substantial increase in cerebral blood flow. Perlman & Volpe (1983b) studied clinical seizures in 12 preterm infants and found that CBFV, blood pressure, and intracranial pressure all rose during seizure activity. The increase in CBFV appears independent of motor activity, as it has also been observed in EEG seizures during paralysis (Boyle 1992). Boylan et al. (1999) found an increase in CBFV during both electroclinical and electrographic (clinically silent) seizures; regression analysis suggested that the increase in CBFV was not wholly explained by changes in blood pressure or PCO2 during the seizure. A regional increase in cerebral perfusion has been demonstrated by SPECT, but it was not possible to correlate the area of hyperperfusion with the epileptiform focus (Borch et al 1998).

Phenobarbital does not produce any significant change in CBFV when given as a 20 mg/kg loading dose (Saliba et al 1991a) and appears not to reduce CBFV fluctuations (Kuban et al 1988).

**INDOMETHACIN**

When used as treatment for patent ductus arteriosus (PDA) at doses of 0.1 and 0.2 mg/kg, indomethacin is associated with a 20–50% reduction in mean CBFV. The effect appears maximal around 30–40 minutes after giving indomethacin and persists for 120 minutes (Laudignon et al 1988; van Bel et al 1989b; Saliba et al 1991b; Austin et al 1992; van Bel et al 1993). A slow infusion over 30 minutes produces a more gradual fall but the overall magnitude is similar to bolus administration (Austin et al 1992). Other methods, such as NIRS and Xe clearance, show a similar magnitude and timescale of reduced cerebral blood flow (Pyrdy et al 1988, Edwards et al 1990).

A PDA can have profound effects upon CBFV. It is associated with a raised RI and a decrease in CBFV (Lipman et al 1982, Martin et al 1982). In some infants, a single bolus injection of aminophylline, Rosenkrantz et al 0h (1984) demonstrated a 21% reduction in anterior cerebral artery CBFV, 60 minutes following aminophylline administration to nine infants. A substantial reduction in PCO2, was also seen, suggesting that CBFV changes may be mediated via CO2 changes. Two studies also demonstrated a fall in CBFV following aminophylline but the magnitude of the fall was too great to be explained solely by CO2 changes (Chang et al 1994, Goven et al 1993). These findings have been confirmed by NIRS (McDonnell et al 1992; Bucher et al 1994) and Xe clearance (Pyrdy et al Schneider 1991).
Aminophylline at steady state, therapeutic concentrations does not appear to alter CBFV (Ghai et al. 1989).

Caffeine therapy has not been shown to reduce CBFV, despite causing a reduction in CO₂ (Saliba et al. 1989a, b; van Bel et al. 1989c), although it has not been compared directly with aminophylline.

**DEXAMETHASONE**

Cabanas et al. (1997) measured CBFV around the first, third, and fifth doses of dexamethasone given to ten ventilated infants with chronic lung disease. There was a short-term increase in CBFV around two hours required by a rise in mean arterial pressure. Progressive doses of dexamethasone produced larger increases in CBFV. Using NIRS, the same group confirmed the increase in CBFV and found that the effect was independent of changes in mean arterial pressure and CO₂ (Pellicer et al. 1998).

**CBFV AND PREDICTION**

**HYDROCEPHALUS**

Many investigators have documented the association between higher CBFV resistivity index (RI) values and hydrocephalus in neonates and children (Hill et al. 1982; Alvisi et al. 1985). Following CSF drainage in neonates with hydrocephalus, the RI falls and the mean CBFV rises (Hill & Volpe 1982; van Bel et al. 1989c). The RI predicted a blocked shunt with a sensitivity of 56% and a specificity of 97%. The RI correlated with intracranial pressure and CO₂ (Pellicer et al. 1998). Westra et al. (1998) applied this technique to infants and children for possible tapping or shunt placement. Using an RI > 0.90 during transducer pressure, they predicted raised ICP with a specificity of 100% and sensitivity of 76%.

**PRETERM BRAIN INJURY**

Calvert et al. (1988) undertook serial CBFV measurement in 29 preterm infants. Three infants, who had evidence of intraventricular hemorrhage on cranial ultrasound, had similar CBFV compared with the infants with no evidence of hemorrhage. Two infants, accompanied by evidence of periventricular leukomalacia at autopsy, both of whom had had a prolonged period of low CBFV. Shorland et al. (1990) studied 120 preterm infants and found no association between CBFV and intracranial lesions. Van Bel et al. (1989a) found that preterm infants who were later found to have major impairment at two years of age had a consistently higher RI in the first week of life, although the predictive ability of RI was not formally tested. Rennie et al. (1995) performed CBFV measurements in 74 very low birth weight infants and found no association with subsequent outcome when formally assessed at 18 months of age.

Thus, the absolute values of RI or CBFV do not appear useful in the prediction of preterm brain injury or neurodevelopmental outcome. Eurenius et al. (1979) found no correlation with outcome when cerebral blood flow was measured during the neonatal period using Xe clearance. The lack of predictive ability when considering the absolute values of CBFV has prompted investigators to examine the relationship between fluctuations in CBFV and outcome. Perlman et al. (1983a) studied 50 preterm infants and concluded that a fluctuating pattern of CBFV was associated with a risk of developing intraventricular hemorrhage (likelihood ratio 8; 95% CI 2 to 31). No such association was seen by Coughtry et al. (1997) or Kuban et al. (1988). The reactivity of CBFV to a CO₂ challenge was also found not to be associated with ultrasound evidence of neurologic injury (Fenton et al. 1992).

Therefore, CBFV measurement is not a proven and reliable method of predicting brain injury or long-term outcome in preterm infants.

**HYPOXIC–ISCHAEMIC INJURY IN TERM INFANTS**

The original Doppler study in neonates after intrapartum hypoxic–ischaemic injury demonstrated a low RI, due to an increase in end-diastolic velocity, which was thought to represent impairment in cerebrovascular autoregulation (Bada et al. 1979). Archer et al. (1986b) performed repeated Doppler measurements on infants after intrapartum hypoxia–ischemia and related the findings to the neurodevelopmental outcome at follow-up. Of the 18 infants with an abnormal RI (≤0.55), 12 died or were severely handicapped. All the abnormal results were apparent between 24 and 62 hours of
age. All the infants with normal RI values were normal at follow-up. A RI > 0.55 gives a likelihood ratio of 5.1 (95% CI 2.5 to 10.6) for the prediction of death or neurodevelopmental handicap. The association of reduced RI and poor outcome after hypoxia-ischemia has been confirmed by other workers (Deeg et al. 1990; Stark & Seibert 1994).

The abnormalities in Doppler waveform take 24 hours to emerge and are usually normal in the first 6 hours, despite significant injury (Eken et al. 1995). Levene et al. (1989) have shown that an increase in CBFV (absolute value as opposed to RI) in the second 24 hours and a lack of reactivity to Pco2 predicted a poor outcome. An increase in global cerebral blood flow has also been demonstrated with Xe clearance (Przyd et al. 1990) and NIRS techniques (Meek et al. 1999).

Therefore, measurement of CBFV and estimation of RI can be of some prognostic value, provided it is performed 24 hours after the hypoxic-ischemic insult.

CONCLUSION

It is possible that Doppler assessment of the fetal cerebral circulation could identify the extent of fetal compromise and aid in judging the time of delivery of such pregnancies. However, the problem of implementing such a policy is substantial. Not only is the equipment expensive, but the measurements are sometimes difficult, even in skilled hands. Nevertheless, tertiary referral centers may eventually establish that abnormal venous Doppler in the presence of redistribution of cerebral blood flow is a clear indication for delivery. Further long-term follow-up studies must be performed to ensure that by this time cerebral damage has not already occurred.

The limitations in using Doppler indices to assess cerebral hemodynamics, particularly acute changes in blood flow, should be recognized. However, the potential of peak systolic velocity measurements in the MCA to predict fetal anemia will hopefully improve our management of alloimmunized pregnancies.

In the neonate, Doppler measurements have been shown to have a clinical role in the prediction of outcome following hypoxic-ischemic injury in term infants. There is no convincing proof that CBFV measurements are likely to be of clinical use in the prediction of outcome in preterm infants. Although initially promising, the use of CBFV assessment to detect infants with raised intracranial pressure likely to require surgical CSF drainage procedures has been difficult to apply in the clinical arena. There are many studies reporting CBFV changes with different physiological states and pharmacological interventions. As yet, these remain research interests with little clinical application. Techniques for continuous measurement of the CBFV and analysis of variability may be a useful non-invasive research tool for studying neonatal cerebral hemodynamics.

Key Points

- The interpretation of changes in Doppler indices and cerebral blood flow velocity in terms of actual cerebral blood flow has certain limitations.
- The observation of trends rather than individual Doppler measurements from the MCA may be of more clinical value.
- An increase in end diastolic flow occurs in the MCA Doppler waveform during fetal and neonatal hypoxia.
- An abnormal cerebroplacental ratio is associated with a significant increase in perinatal morbidity and mortality but the value of cerebral Doppler velocimetry in improving clinical outcome has not yet been assessed by a randomized controlled trial.
- The non-invasive measurement of peak systolic velocity in the MCA has been shown to predict moderate or severe fetal anemia in maternal red cell alloimmunization. The potential to decrease the number of invasive procedures performed for this condition requires further study.
- Following intrapartum hypoxia-ischemia, an abnormal Resistance Index (RI > 0.55) in the term neonate is predictive of adverse outcome (death or neurodevelopmental handicap), when the examination is performed 24–60 hours of age (Likelihood ratio 5.1; 95% CI 2.5 to 10.6).
- Doppler CBFV measurement is not a proven and reliable method for the prediction of neurodevelopmental outcome following preterm brain injury.


Functional assessment of CNS development


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(1980) Fetal middle cerebral blood flow velocity waveform 
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