

Color Doppler study of the venous circulation in the fetal brain and hemodynamic study of the cerebral transverse sinus

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ABSTRACT

Objectives To describe the venous circulation in the fetal brain; to describe the normal blood flow velocity waveform in the transverse sinus and to establish normal reference ranges for the second half of gestation.

Population A total of 126 pregnant women with uncomplicated pregnancies at 20–42 weeks of gestation.

Methods A combination of color-coded Doppler and two-dimensional real-time ultrasound was used to identify the main venous systems in the fetal brain. Blood flow velocity waveforms of the transverse sinus were obtained from a transverse plane of the head at the level of the cerebellum.

Results A waveform could be obtained in the cerebral transverse sinus in 98% of the cases. The waveform obtained was triphasic with a forward systolic component, a forward early diastolic component and a lower forward component in late diastole. Reverse flow during atrial contraction was seen before 28 weeks and the diastolic flow increased with gestation thereafter. Pulsatility and resistance indices decreased and flow velocities increased in the transverse sinus throughout gestation.

Conclusion The venous circulation of the fetal brain can be identified by color Doppler. The gestational age-related decrease in resistance and increase in flow velocities suggest that hemodynamic studies of the cerebral transverse sinus might have clinical implications in studying compromised fetuses.

INTRODUCTION

Doppler ultrasound examination has been used over the past 15 years to investigate fetal hemodynamics. The major

fetal arterial vessels have been identified and ranges for blood flow velocities and impedance to flow as well as their changes with chronic fetal hypoxia have been established^{1–3}. More recently, some predictive value has also been attributed to hemodynamic changes in the inferior vena cava and the ductus venosus in severely growth-restricted fetuses^{4,5}. In contrast, sparse information is available on the developmental pattern of the cerebral venous circulation in normal and compromised human fetuses.

The venous return of the cerebral hemispheres is established by 15 weeks of gestation^{6,7} and is supported by two systems draining into the dural system⁸. The first consists of a deep system converging into the vein of Galen and the inferior sagittal sinus which empties into the straight sinus. The second system is superficial and reaches the superior sagittal sinus after running through the pia mater and the arachnoid space (Figure 1a).

The straight and the sagittal sinuses drain into the two transverse sinuses. Each transverse sinus runs peripherally to the parietal region of the brain in an anterior direction to join the sigmoid sinus, which in turn anastomoses with the internal jugular vein on both sides of the neck (Figure 1b and c). At 20 weeks, the inferior sagittal sinus is less than 0.5 mm in diameter whilst the straight sinus is larger. Interestingly, there is a greater number of capillaries in the posterior half of the falx cerebri at this gestation (Figure 1d).

The aims of this study were:

- (1) To describe the venous circulation in the fetal brain and to establish the ultrasound–anatomical correlates;
- (2) To establish reference ranges for venous blood flow velocities in the cerebral transverse sinus during the second half of pregnancy.

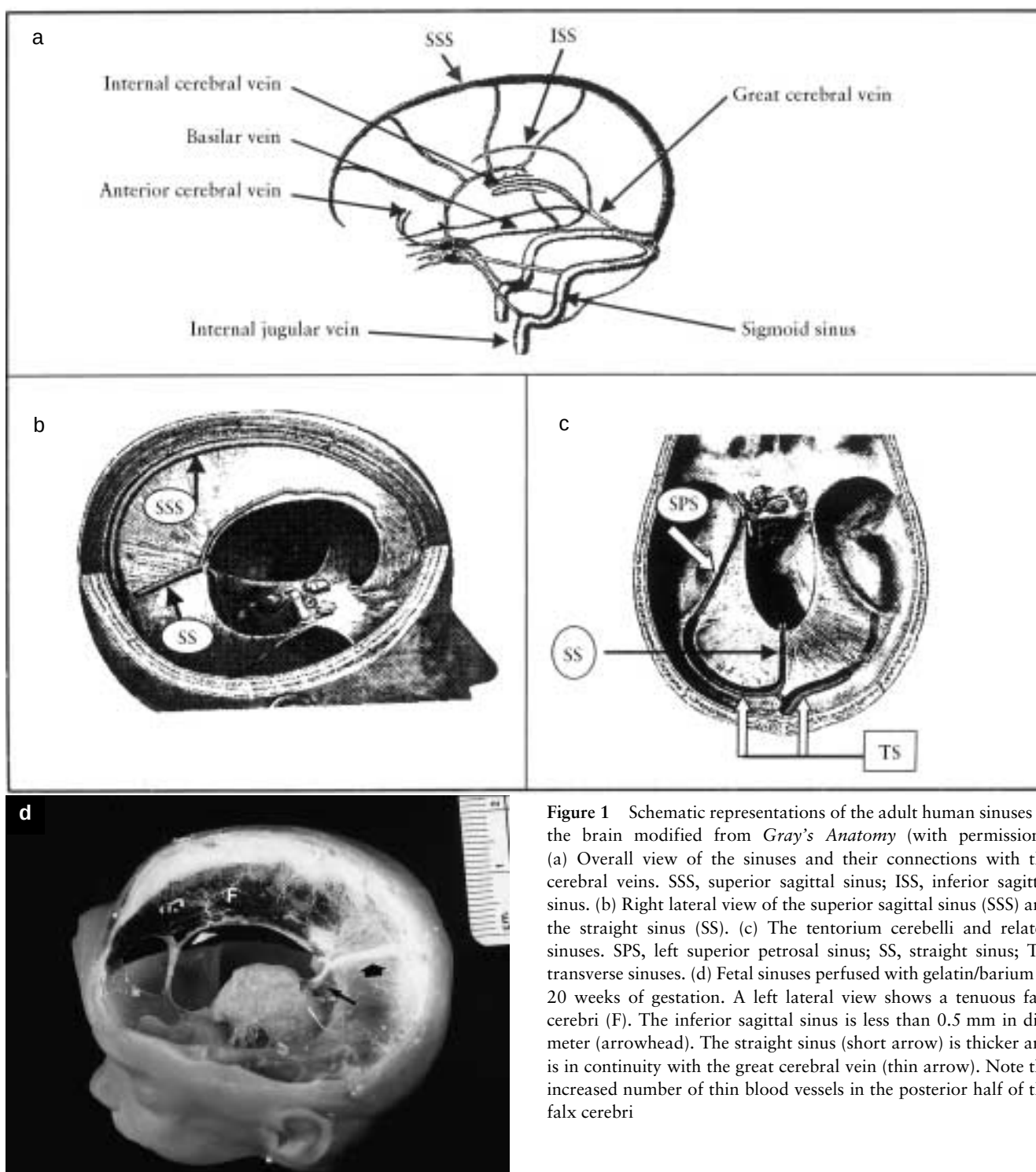


Figure 1 Schematic representations of the adult human sinuses of the brain modified from *Gray's Anatomy* (with permission). (a) Overall view of the sinuses and their connections with the cerebral veins. SSS, superior sagittal sinus; ISS, inferior sagittal sinus. (b) Right lateral view of the superior sagittal sinus (SSS) and the straight sinus (SS). (c) The tentorium cerebelli and related sinuses. SPS, left superior petrosal sinus; SS, straight sinus; TS, transverse sinuses. (d) Fetal sinuses perfused with gelatin/barium at 20 weeks of gestation. A left lateral view shows a tenuous falx cerebri (F). The inferior sagittal sinus is less than 0.5 mm in diameter (arrowhead). The straight sinus (short arrow) is thicker and is in continuity with the great cerebral vein (thin arrow). Note the increased number of thin blood vessels in the posterior half of the falx cerebri

MATERIALS AND METHODS

Study population

Flow velocity waveforms were recorded from the cerebral transverse sinus in a cross-sectional study of 126 fetuses at 20–42 weeks, in order to establish reference ranges for velocities and indices for impedance to flow, with gestation.

A longitudinal study of the evolution of these waveforms and indices throughout pregnancy was also performed in 37 of these cases with a time interval of 4–6

weeks. The mean number of examinations per patient was 3.7 (3–6). In these cases, color Doppler examination of the fetal brain was used to establish ultrasound–anatomical correlates of the main vessels of the venous circulation.

A total of 126 women with normal singleton pregnancies were recruited during a 1-year period. The gestational age was calculated from the last menstrual period and confirmed by crown–rump length measurement at 10–14 weeks. All fetuses were found to be normally grown and anatomically normal at the 20-week scan and this was confirmed at delivery. Doppler ultrasound examination of

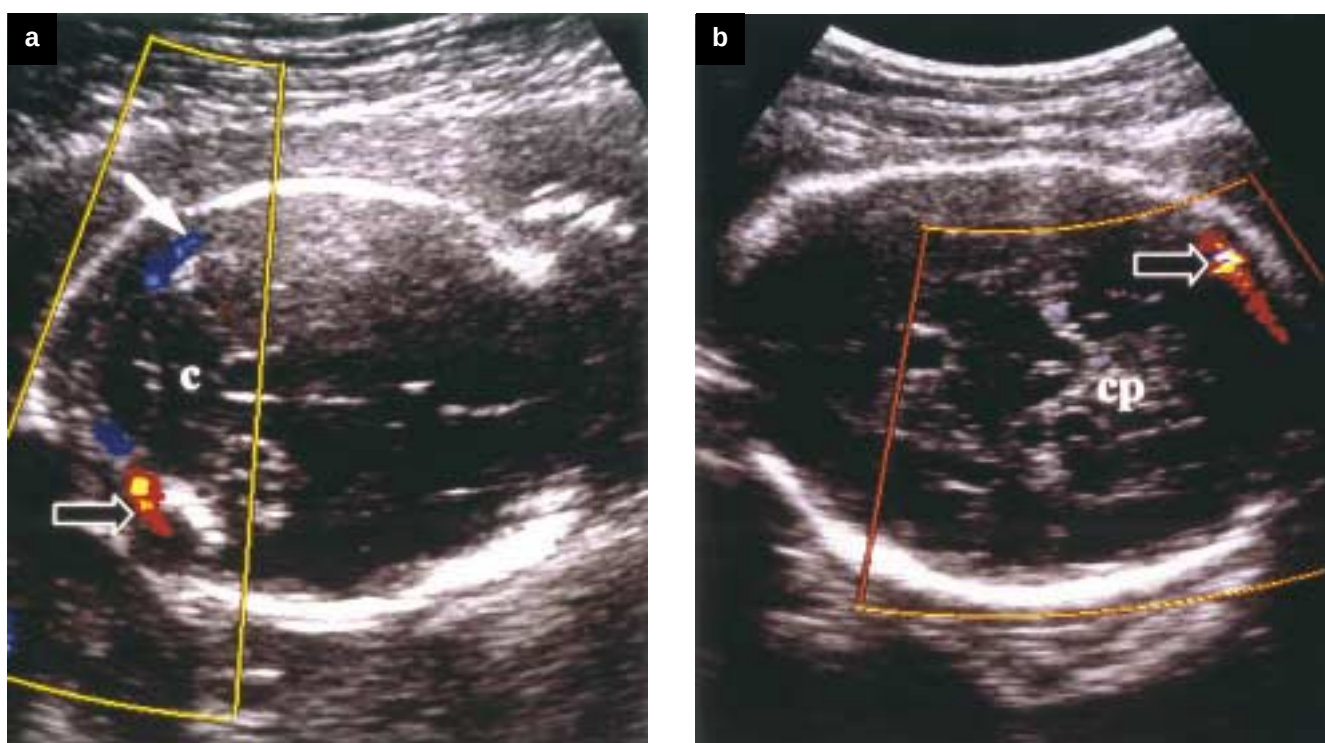


Figure 2 Visualization of the transverse sinus (arrows) in transverse planes: (a) at the level of the cerebellum (c) or (b) just below, at the level of the cerebral peduncles (cp)

the uterine arteries was systematically performed and patients presenting with bilateral notches or high resistance indices after 24 weeks were excluded. Fetal head and abdominal circumference, fetal heart rate and pulsatility index (PI) in the umbilical and middle cerebral arteries were found to be normal. The study was approved by the local hospital Ethics Committee.

Examination protocol

Doppler measurements were recorded in the absence of fetal breathing movements. Color Doppler was used to visualize the dural sinuses. Low values for scale, gain, filter setting and sample volume were selected to allow visual and acoustic recognition of low-flow venous signals. The transverse sinus was visualized in a transverse plane of the brain at the level of the cerebellum or just below it (Figure 2). Increased sweep speed was used for clear individualization of the waveforms. The angle between the Doppler signal and the long axis of the transverse sinus was always less than 60°. Depending on the fetal position, the sample volume was placed over the best visualized vessel, either right or left, and independently of the position of the vessel on the plane obtained. Five parameters, namely, peak systolic velocity, minimum diastolic velocity, time-averaged maximum velocity, PI for veins and resistance index (RI) were measured within a time limit of 15 min, following angle correction with the software included in the ultrasound system.

Doppler recordings

The transverse sinus, middle cerebral artery and umbilical artery flow velocity waveforms were recorded by using a two-dimensional real-time color Doppler system, with a 5-MHz curvilinear transducer (General Electric 500, Gif/Yvette, France). By the manufacturer's specifications, the spatial peak temporal average power output was less than 100 mW/cm². The high-pass filter was set low.

Reproducibility

As the left and right transverse sinuses are two vessels with identical flow, the right/left variations were studied. In order to assess the reproducibility of measurements, maximum and minimum velocity, time-averaged maximum velocity, PI for veins⁹ and RI were recorded from right and left transverse sinuses in 14 fetuses. The intraobserver coefficient of variation for the same parameters was determined by examining 21 fetuses, 15 min apart.

All measurements in the study population were performed by the same operator (H.L.D.). However, the interobserver coefficient of variation was evaluated between two different operators (H.L.D. and Y.V.) on 11 fetuses.

Statistical analysis

The reproducibility of measurements (intraobserver, interobserver and right vs. left measurements) was assessed by analysis of variance.

Age-related reference ranges were obtained following the method outlined by Bland and Altman¹⁰. Logarithmic or exponential transformations of the data were used in cases of positive or negative skewness, respectively. The transformed distributions were found to be normal. The 50th centile was derived first by fitting a straight line re-



Figure 3 Visualization of cerebral and dural venous system at 30 weeks' gestation in a sagittal and median plane: superior sagittal sinus (thin white arrow), inferior sagittal sinus (yellow arrow), straight sinus (turquoise arrow), the torcular or confluence of sinuses (thick white arrow), the internal cerebral vein (thick unfilled arrow). Note the aliasing effect in the straight sinus due to the turbulent flow coming from the vein of Galen which cannot be visualized in this plane

gression. It was then tested whether additional quadratic terms were statistically significant, and whether they improved the visual fit of the model. The 5th and 95th centiles were derived from the standard deviation of the residuals. When the latter were found to depend on gestational age (i.e. presence of heteroscedasticity), the method described by Altman¹¹ was used. This involved regressing the absolute residuals on gestational age and applying a regression equation to derive the standard deviation.

RESULTS

Anatomical study

During the second half of pregnancy, part of the venous cerebral circulation could be visualized by color Doppler, as shown in Figures 3 and 4. The torcular or confluence of sinuses was imaged on a sagittal and median plane at the level of the cerebellum and near the internal occipital protuberance. This dilated posterior extremity of the superior sagittal sinus receives the straight sinus running backwards and downwards at the junction of the falx and the tentorium. On the same plane, the internal cerebral vein was imaged (in blue), running backwards just below the splenium of the corpus callosum and leading into the great cerebral vein or vein of Galen, the anterior part of which could be imaged (in red) only where it curved sharply upwards around the splenium; in this part the blood flow was towards the probe (Figure 3). The inferior sagittal sinus, a small vessel with very low flow, is usually partially imaged on this median plane.

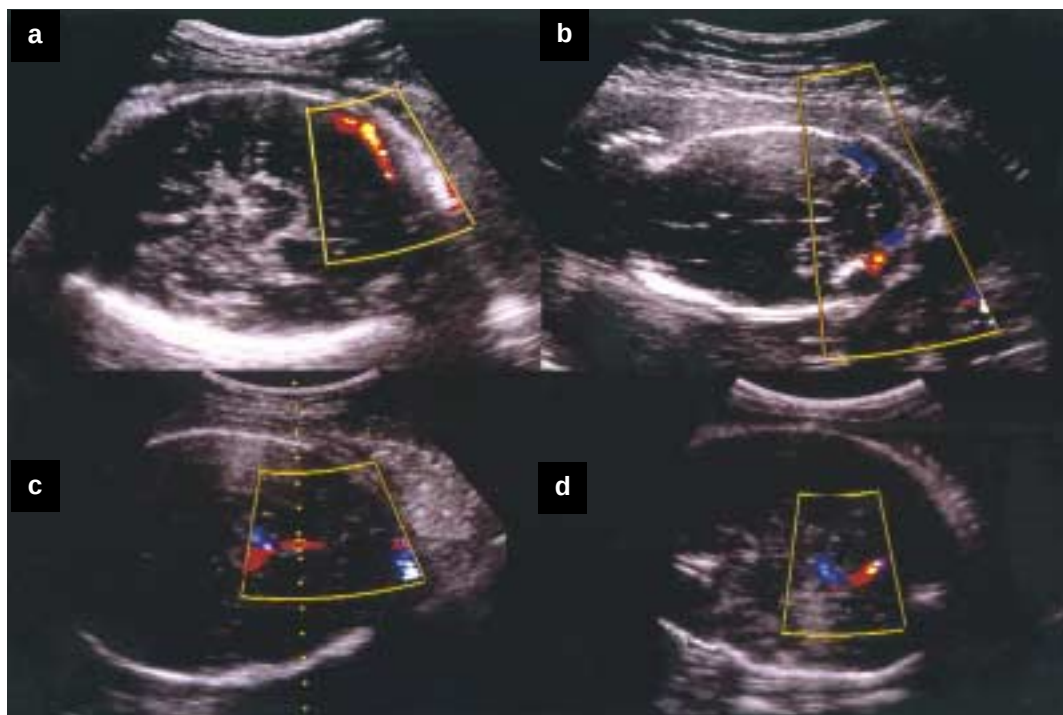


Figure 4 Visualization of cerebral and dural venous system in transverse planes: the right transverse sinus running laterally on the tentorium (a); the external and end parts of the left and right transverse sinuses before they curve down internally to join the sigmoid sinus (b); the straight sinus and the basal veins passing round the cerebral peduncles (c); and the vein of Galen or great cerebral vein curving sharply upwards which explains the two colors observed (d)

At the level of the cerebellum or just below, at the level of the cerebral peduncles, a transverse view demonstrates the transverse sinuses running laterally in an anterior direction on the tentorium and the straight sinus running backwards (Figure 4a and b); this sinus collects the intracerebral blood from the great cerebral vein and joins the transverse sinuses through the torcular. The basal veins were imaged around the cerebral peduncles (Figure 4c) ending in the great cerebral vein, which curves sharply upwards, showing two different colors, explained by the opposite direction of the blood flow (Figure 4d). Flow velocity waveforms were obtained from these vessels and different patterns (flat or pulsatile) were observed (Figures 5 and 6).

Hemodynamic study of the transverse sinus

The mean gestational age at delivery was 39 weeks (± 1.5). The median birth weight was 3280 g (± 676.9). The percentage of neonates below the fifth centile was 2.4% (3/126). The fetal head and abdominal circumferences were within the 90% confidence interval of our normal ranges at the time of the Doppler examination. The fetal heart rate was normal, ranging between 120 and 160 beats/min.

Technically acceptable flow velocity waveforms from the transverse sinus were obtained in 98% (124/126) of the cases in which the velocity waveform could be recorded in less than 2 min. Failure to record waveforms was determined by fetal movements, fetal breathing movements and an unfavorable fetal position.

In 75% (93/124) of the cases, the angle of insonation was less than 40°, in 12% (15/124) between 40 and 50° and in 13% (16/124) between 50 and 60°.

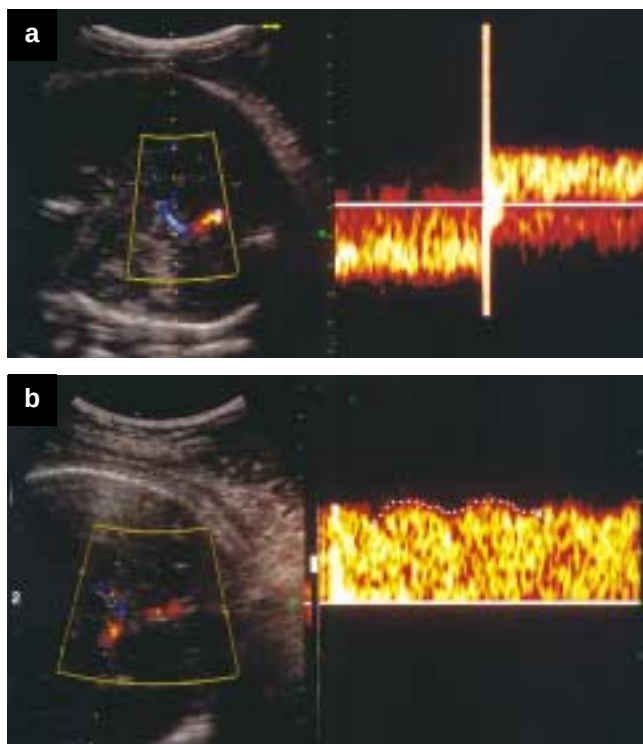


Figure 5 Flat waveforms observed in the vein of Galen (a), the straight sinus and the basal vein (b)

Results of the regression analysis of each parameter are given in Table 1. The PI and RI on both sinuses increased from 20 to 28 weeks and decreased thereafter to term. The velocities increased with gestation. Reference ranges derived from normal pregnancies are shown in Figures 7–11.

The waveform in the transverse sinus was triphasic, and consisted of a systolic (S) forward flow component during ventricular systole, another forward flow component (D) in early diastole, corresponding to passive ventricular filling, and a late diastolic component (a) during atrial

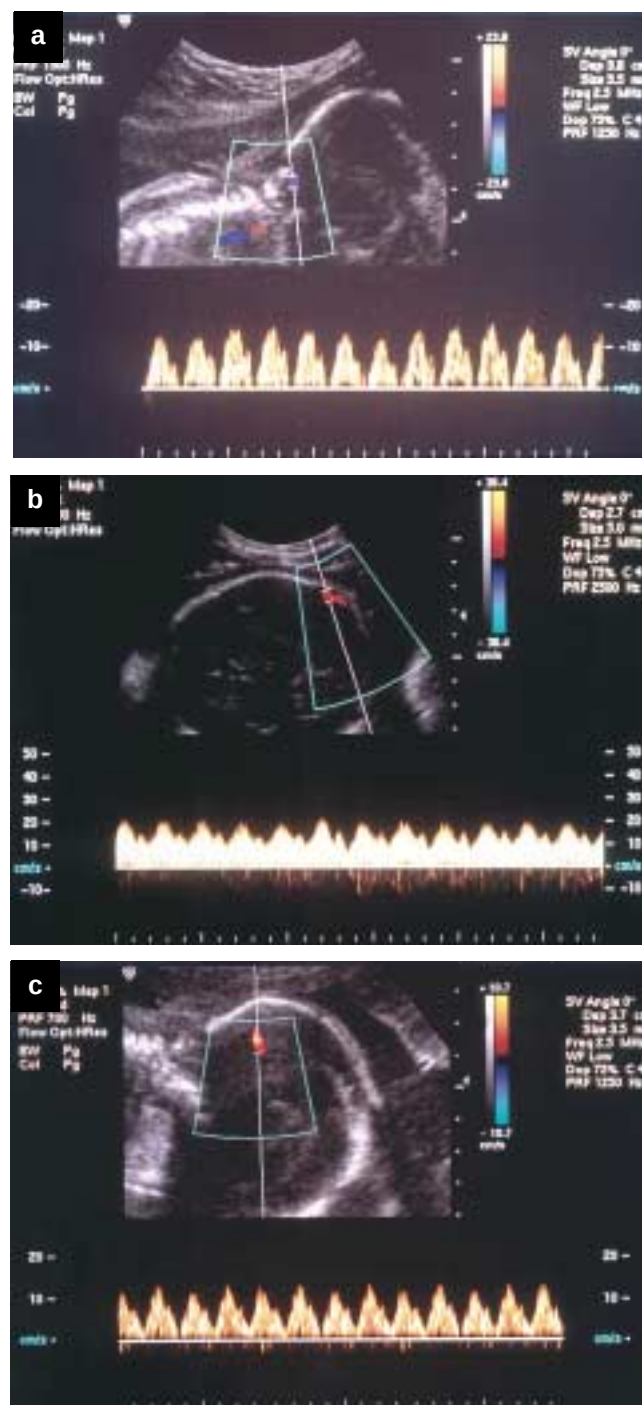


Figure 6 Pulsatile waveforms observed in the inferior sagittal sinus (a), the transverse sinus (b) and the superior sagittal sinus (c)

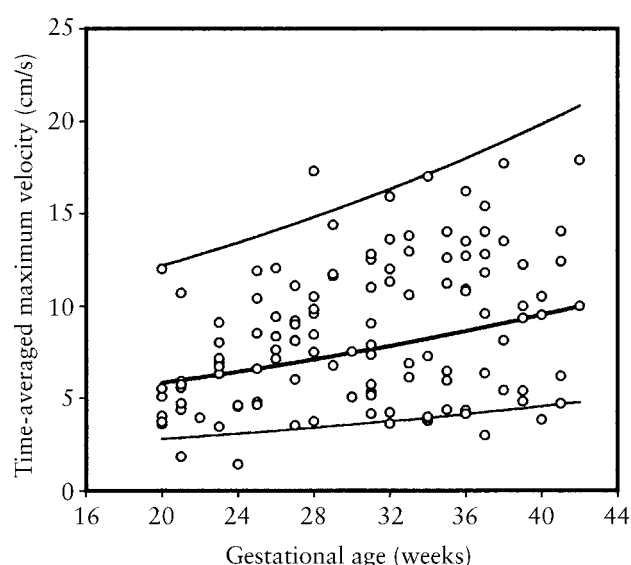
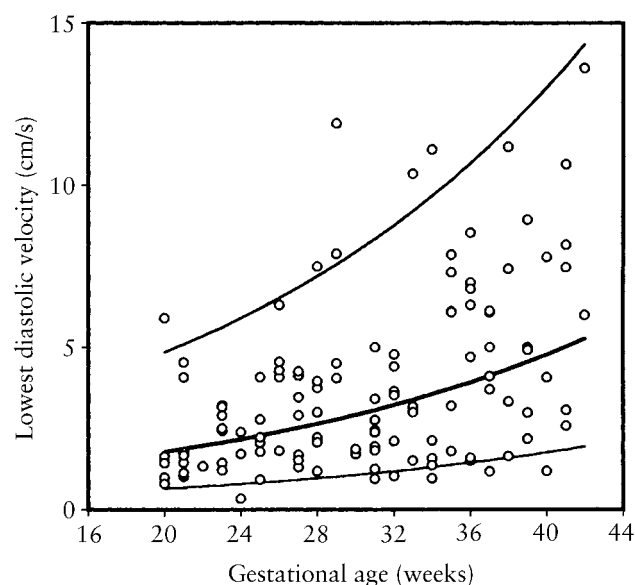
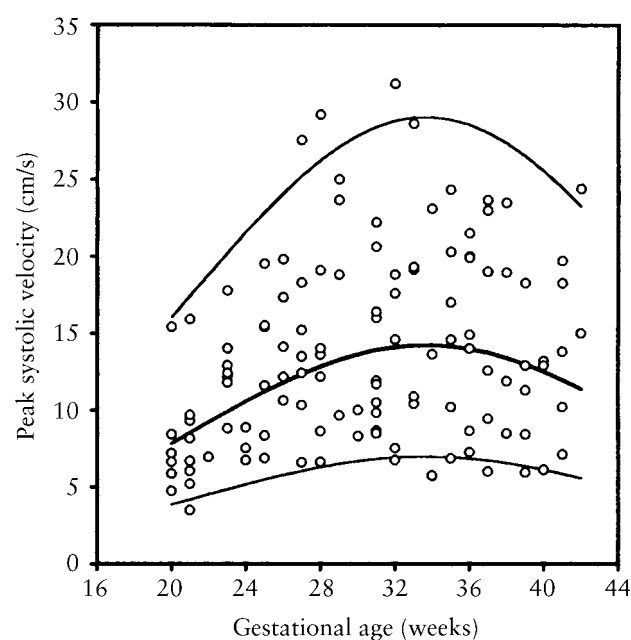
Table 1 Regression formulae for various Doppler measurements. TAMV, time-averaged maximum velocity; RI, resistance index; PIV, pulsatility index for veins; *a*, minimum diastolic velocity; *S*, peak systolic velocity

Index	Transformation	Constant	Linear coefficient	Quadratic coefficient	Standard deviation	Outliers
TAMV	log	1.275683	0.024453		0.446473	2
<i>a</i>	log	-0.404096	0.049257		0.607431	1
<i>S</i>	log	-0.952512	0.214447	-0.003186	0.433541	0
RI	exp	1.116368	0.089565	-0.001805	*	0
PIV	none	-0.553070	0.143659	-0.002718	†	0

*SD of RI = $\log [1.253314 \times (0.025471 + (0.004784 \times \text{GA}))]$

†SD of PIV = $1.2533314 \times [-0.519598 + (0.044708 \times \text{GA}) + (-0.000654 \times \text{GA}^2)]$

GA, gestational age

**Figure 7** Individual values for time-averaged maximum velocity in the transverse sinus of 126 normal fetuses plotted on the appropriate reference range (mean, 5th centile, 95th centile) with gestation**Figure 9** Individual values for the lowest diastolic velocity in the transverse sinus of 126 normal fetuses plotted on the appropriate reference range (mean, 5th centile, 95th centile) with gestation**Figure 8** Individual values for the peak systolic velocity in the transverse sinus of 126 normal fetuses plotted on the appropriate reference range (mean, 5th centile, 95th centile) with gestation

contraction. The latter was typically a lower forward flow component and rarely a reverse flow (Figure 12).

The blood flow pattern can change throughout pregnancy, as demonstrated by reversed flow during atrial contraction (*a*), which was observed in a decreasing number of cases up to 28 weeks (40.5% (15/37), 20.6% (7/34) and 16.7% (6/36) at 20–22, 23–25 and 26–28 weeks, respectively) and could not be observed after 30 weeks. Thereafter, diastolic flow was present throughout the heart cycle and increased to term. In all cases, the *D* wave in early diastole tended to decrease and the waveform tended to become biphasic during the last month of gestation. The relationship between the different components and gestational age is shown in Figure 12.

Reproducibility of measurements

The intraobserver reproducibility of measurements is presented in Table 2. This shows that interpatient variance was greater than inpatient variance for PI of veins and RI, but only marginally for time-averaged maximum velocity. Means and standard deviations according to observers and right or left side of measurements are shown in

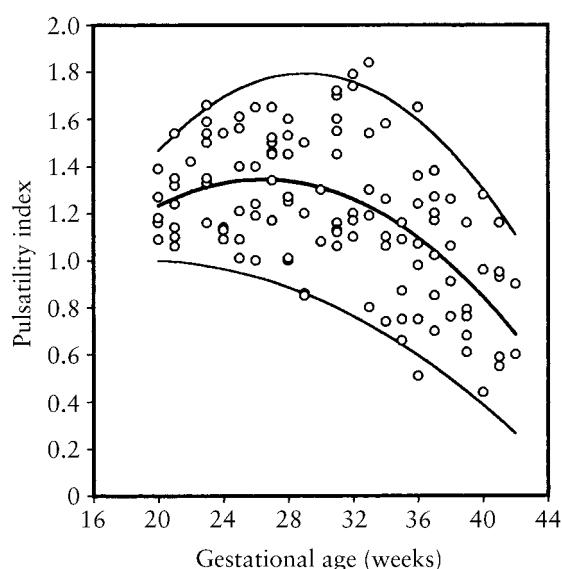


Figure 10 Individual values for the pulsatility index for veins [(peak systolic velocity minus lowest velocity during atrial contraction)/time averaged maximum velocity], in the transverse sinus of 126 normal fetuses plotted on the appropriate reference range (mean, 5th centile, 95th centile) with gestation

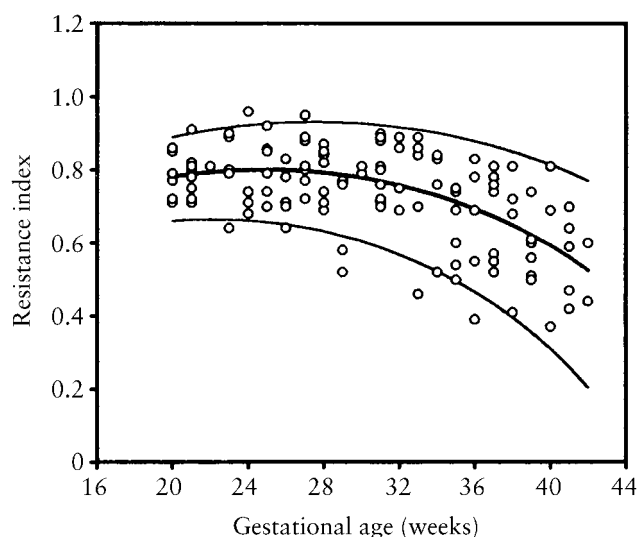


Figure 11 Individual values for resistance index [(peak systolic velocity minus lowest velocity during atrial contraction)/peak systolic velocity] in the transverse sinus of 126 normal fetuses plotted on the appropriate reference range (mean, 5th centile, 95th centile) with gestation

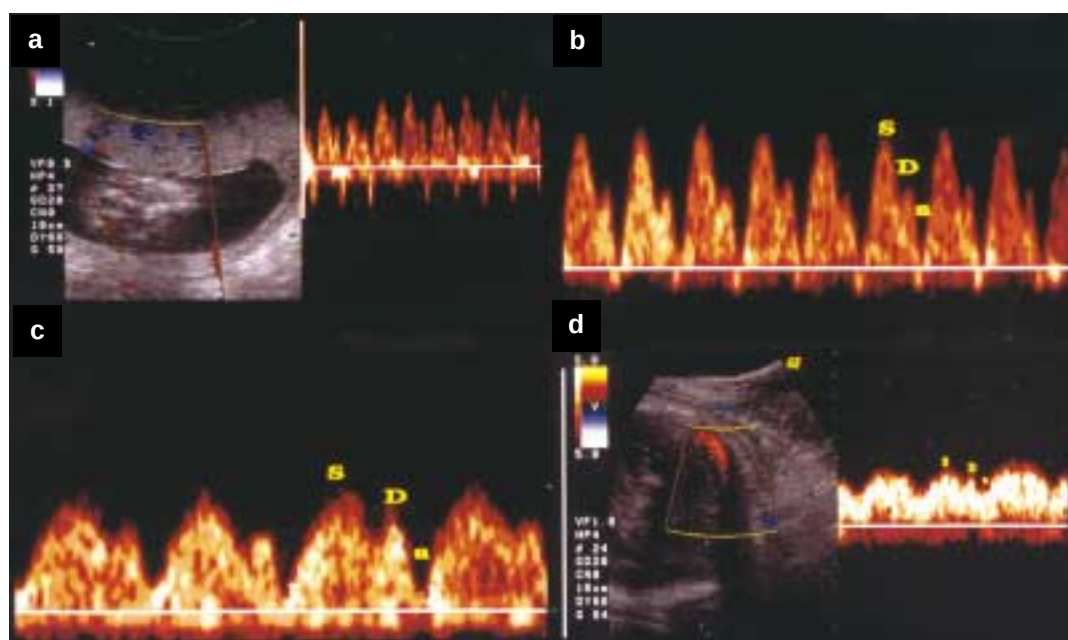


Figure 12 Transverse sinus flow velocity waveform consisting of triphasic forward flow component. Relationship between the different components and gestational age: (a) 14 weeks; (b) 23 weeks; (c) 30 weeks; (d) 41 weeks. S, peak systole; D, peak diastole. Note the common reverse flow before 22 weeks in relation to the atrial contraction, a, during late diastole

Table 3. Two-way analysis of variance suggested that variations between observers and between sides of measurements were not statistically significant.

DISCUSSION

Although the fetal cerebral arterial circulation has been well described both anatomically and hemodynamically, sparse data are available on the venous cerebral system. In normal neonates, color Doppler examination has enabled

visualization of the intracranial venous system¹², and establishment of normal ranges for flow velocities in many vessels, such as the vein of Galen, internal cerebral vein, inferior and superior sagittal sinuses and straight and transverse sinuses¹²⁻¹⁴. Very low-amplitude pulsatile flow within the venous system in newborns and infants is a common finding in more central venous channels such as the transverse sinus (36% of cases) or the straight sinus (32%), but is uncommon in smaller or deeper veins such as the vein of Galen (15%), whose pattern is typically flat^{15,16}.

Table 2 Reproducibility of measurements: results of one-way analysis of variance for repeated measurements of three indices in 21 patients (intraobserver variation)

Source of variation	Degrees of freedom	Sum of squares	Mean square	F ratio	Probability
<i>Time-averaged maximum velocity</i>					
Between patients	20	212.82	10.641	2.25	0.03
Within patients	23	108.98	4.738		
Total	43	321.8			
<i>Resistance index</i>					
Between patients	20	1.02077	0.05104	3.88	0.001
Within patients	23	0.30275	0.01316		
Total	43	1.32352			
<i>Pulsatility index for veins</i>					
Between patients	20	3.376181	1.68809	9.99	$< 10^{-6}$
Within patients	23	0.389445	0.016932		
Total	43	3.765626			

Table 3 Reproducibility of measurements: interobserver and right/left variations. Results are means (SD). TAMV, time-averaged maximum velocity; RI, resistance index; PIV, pulsatility index for veins; *a*, minimum diastolic velocity; *S*, peak systolic velocity

	TAMV	RI	PIV	<i>a</i> (cm/s)	<i>S</i> (cm/s)
<i>Interobserver</i>					
<i>n</i>	10	11	11		
Observer 1	8.02 (4.30)	0.72 (0.17)	1.144 (0.41)		
Observer 2	6.96 (4.55)	0.74 (0.15)	1.145 (0.33)		
<i>Right/left</i>					
<i>n</i>	13	14	14	13	13
Right	6.57 (4.00)	0.73 (0.15)	1.15 (0.35)	2.57 (1.45)	11.02 (3.31)
Left	7.19 (2.42)	0.71 (0.16)	1.085 (0.34)	2.27 (1.30)	9.76 (5.72)

Velocities and waveform patterns have been investigated in different pathological conditions after birth such as persistent ductus arteriosus, malformation of the vein of Galen and respiratory distress. Triphasic venous pulsations of wide amplitude or reversed flow are observed with abnormally increased intrathoracic pressure^{15,16}. One study¹⁷ reported a successful attempt at imaging the dural sinuses in human fetuses after 27 weeks, but no hemodynamic data were generated.

Our study demonstrates that the posterior venous dural system can be imaged *in utero* by conventional trans-abdominal color Doppler ultrasound. The superior and inferior sagittal sinuses, the transverse sinuses, the straight sinus and part of the intracerebral venous system with basal and internal veins and the great cerebral vein could be individualized (Figures 3 and 4). The transverse sinus collects the entire intracerebral venous flow. Changes in the waveform pattern observed in the transverse sinus could be visualized from 13 weeks onwards and studied during the second and third trimesters in up to 98% of the cases. This vessel was therefore chosen as that on which to conduct the hemodynamic study and to generate reference ranges throughout gestation. The transverse sinus shows a triphasic pulsatile forward flow velocity pattern (Figure 12) similar to that described in other fetal venous vessels^{5,18}. This suggests that the fetal cerebral venous flow, at this level, is dependent upon dynamic changes resulting from atrial and ventricular contraction and relaxation.

Our longitudinal studies suggest that the pattern can evolve throughout pregnancy with reversed flow during atrial contraction commonly observed before 23 weeks and

occasionally afterwards, but not after 30 weeks. The diastolic flow progressively increased until term and remained present throughout the heart cycle. During the last month of gestation, the waveform tended to be less pulsatile, with a decrease of the *D* wave together with an increase of the *a* component ending in near fusion of these two waves. The waveform became more similar to the waveform obtained in the neonatal period and could be described as a sinusoidal or even continuous waveform¹⁴.

The marked pulsatility observed in the transverse sinus until the second half of the third trimester and the changes towards a sinusoidal waveform late in pregnancy are supported by two hypotheses:

- (1) The short distance between the heart and the cerebral vessels reflects the difference of pressure between the heart and the vessel during the cardiac cycle. This distance increases with gestation, and the transmission of cardiac pulsatility to the cerebral vessels could therefore decrease late in pregnancy. However, a pulsatile waveform is present in the deep inferior sagittal sinus (Figure 6) until term, while a flat or sinusoidal waveform exists in the basal veins and the straight sinus (Figure 5).
- (2) Histological changes in the vessel wall near term occur as an expression of the maturation of their muscular component and would support an increase in the compliance of the vessel that may resemble that seen in the newborn. Histological studies are being conducted to document such possible structural modifications.

Pulsatility and resistance indices in the cerebral sinuses showed the same evolution as that observed in the cerebral arteries. There was an increase up to 28–30 weeks and a subsequent drop towards term which is consistent with the physiological decrease in placental resistance¹⁹ and in cardiac afterload together with an increasing fraction of cardiac output directed towards the fetal brain²⁰. A similar evolution characterizes the velocities in both cerebral arteries and veins increasing with gestation. This has been reported in previous studies of other fetal veins such as the ductus venosus, pulmonary veins, inferior vena cava and hepatic veins^{5,21,22}, and appears to be a consequence of the increased velocities in the arterial side, considering that arterial output and venous return have to be balanced during pregnancy. A fall in pO_2 levels and a concomitant rise in pCO_2 in the last month of gestation is seen together with an increase of blood supply to the fetal head, suggesting a vasodilatory response in order to guarantee adequate oxygenation to the fetal brain²³. The changes of resistance and pulsatility values in the transverse sinus also reflect the increased brain perfusion and the homeostatic readjustment related to the changes in blood pO_2 and pCO_2 levels with advancing gestation.

It may be concluded that flow velocity waveforms can be reliably obtained from the human fetal cerebral transverse sinus. A gestational age-related increase in flow velocities and a reduction in resistance and pulsatility indices support the hypothesis that hemodynamic study of the fetal cerebral transverse sinus could have clinical implications. Further investigations should be conducted in relation to pathological conditions such as intrauterine growth restriction in chronic hypoxemia.

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