Pediatr Radiol (1989) 19: 71-78

Pediatric Radiology

Selected papers from the ESPR meeting in Montreux, Switzerland, 13-16 April 1988

Pulsed Doppler sonographic measurement of normal values for the flow velocities in the intracranial arteries of healthy newborns*

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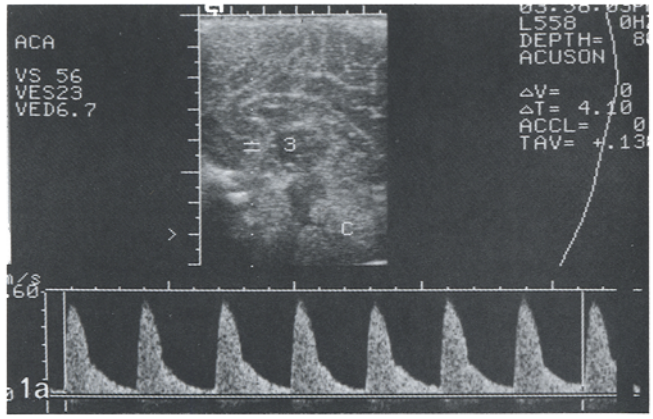
Abstract. 121 healthy premature born infants and full term newborns (corrected gestational age 29 to 45 weeks, weight at investigation 1070 to 3750 g) were investigated by pulsed Doppler sonography with a 5 MHz transducer. In all infants pulsed Doppler recordings were obtained from the internal carotid arteries (ICA), the basilar artery (BA) and both anterior cerebral arteries (ACA). From the flow profile the maximal systolic velocity (V_s), the endsystolic velocity (V_{es}) and the enddiastolic velocity (V_{ed}), the time average velocity (TAV) and the time average maximal velocity (TAMX) as well as the resistance-index (RI) and the pulsatility-index (PI) were measured. For all parameters the relationship to the gestational age was analysed and normal values were established. There was a linear increase of all flow velocities with increasing gestational age. V_s in the ICA was about 20% higher than in the ACA and BA whereas V_{es} and V_{ed} were not significantly different in the three arteries. The TAV in the ICA was 9% higher than in the ACA and 15% higher than in the BA. The TAMX in the ICA was 10% higher than in the ACA and 14% higher than in the BA. In contrast to the increase of the flow velocities neither the RI nor the PI showed a signficant age dependency. For the RI in the ICA 0.77 ± 0.08, in the ACA 0.73 ± 0.08 and in the BA 0.72 ± 0.09 were measured. The PI in the ICA was 3.0 ± 0.08, in the ACA 2.7 ± 0.09 and in the BA 2.7 ± 0.7. Because of the age dependency of the flow velocities in the cerebral arteries the corrected gestational age must be taken into consideration when pathologic flow velocities are analysed.

Although pulsed Doppler sonography of the flow parameters in the intracranial arteries of infants is widely used in neonatology little data relating to normal values for the flow velocities in the cerebral arteries have been published in the literature [3, 12]. Flow velocities in the intracranial arteries are influenced by a great number of physiologic and pathophysiologic factors in the normal child. The age and weight of the patient, the pCO_2 and the vigilance of the child all influence the flow velocities. Under pathologic circumstances cardiovascular diseases as well as diseases of the central nervous system can influence the flow profile and the flow velocities in the cerebral arteries. The most common cardiovascular diseases with pathologic flow profiles in the cerebral arteries of infants are patent ductus arteriosus and other cardiac malformations with a leakage of the aortic "Windkessel" and obstructions of the left ventricular outflow tract [4, 5, 13, 14, 18]. Diseases of the central nervous system with pathologic flow profiles and flow velocities in the cerebral arteries of infants are brain hemorrhage, hydrocephalus, brain edema and the determination of brain death [6, 7, 15]. Physiologic alterations and pathologic influences often occur in the same patients. To establish whether a velocity is normal or abnormal the influence of physiologic circumstances like age have to be exluded. In this study we tried to establish normal values for the flow velocities in the great intracranial arteries of otherwise healthy premature born infants and full term newborns.

Patients and method

121 healthy premature born infants and healthy newborns were investigated by pulsed Doppler sonography. All children with diseases of the central nervous system and children with sus-

* Presented at the ESPR meeting in Montreux 1988. Selected for publication by an International Group of the ESPR.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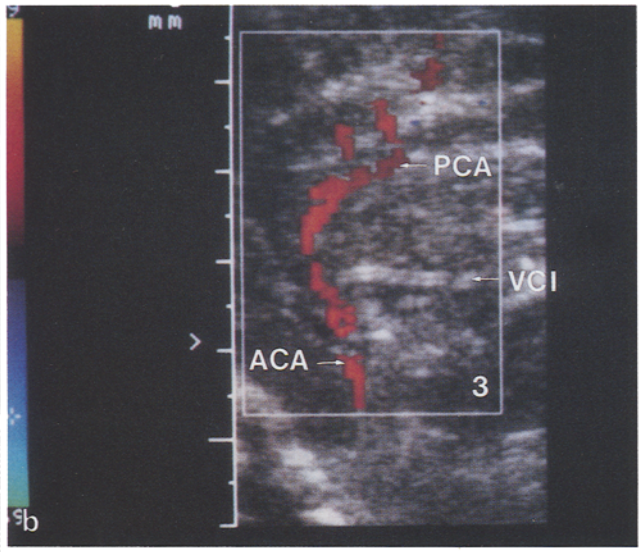
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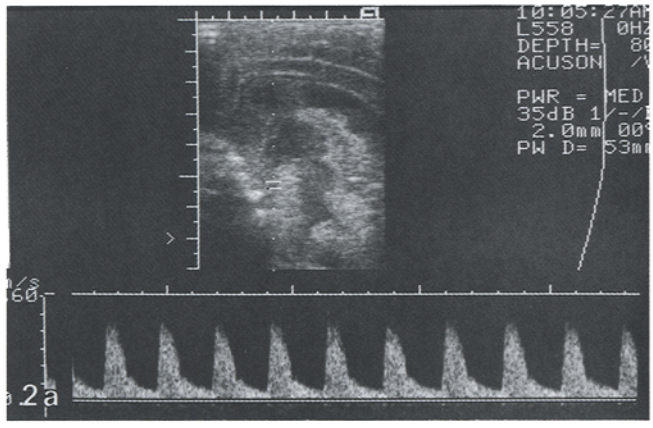
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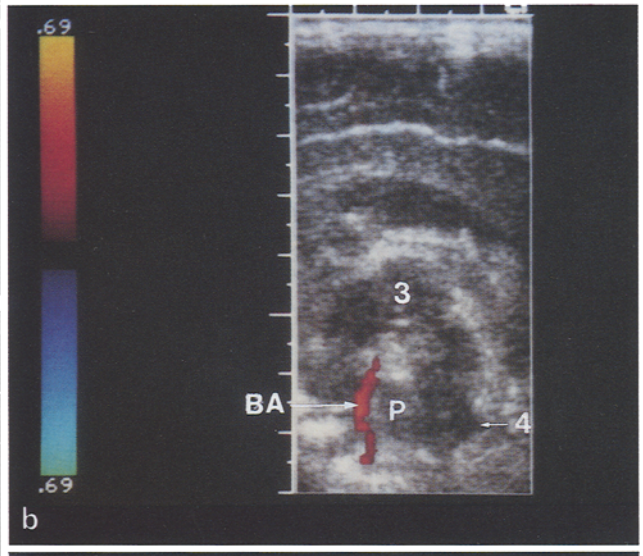
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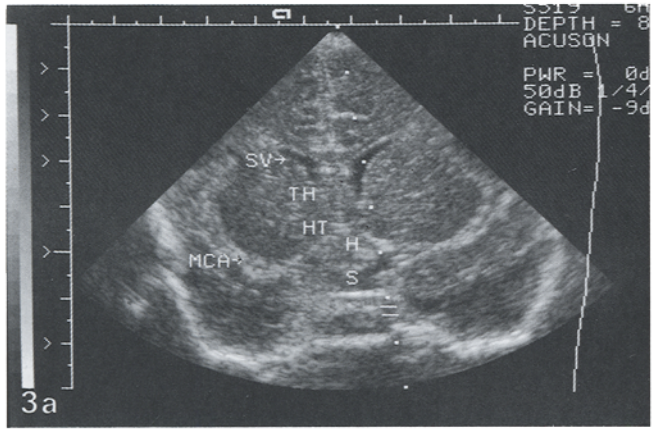
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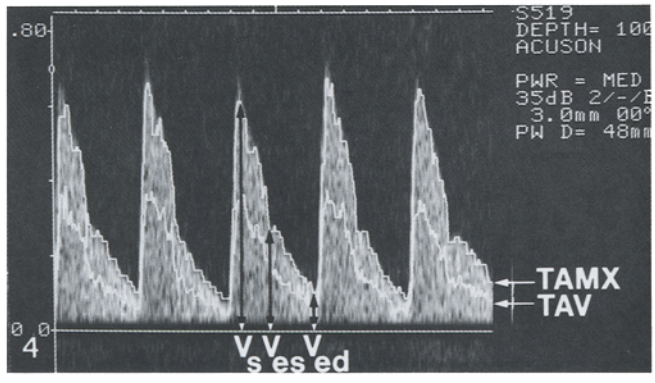
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TAMX
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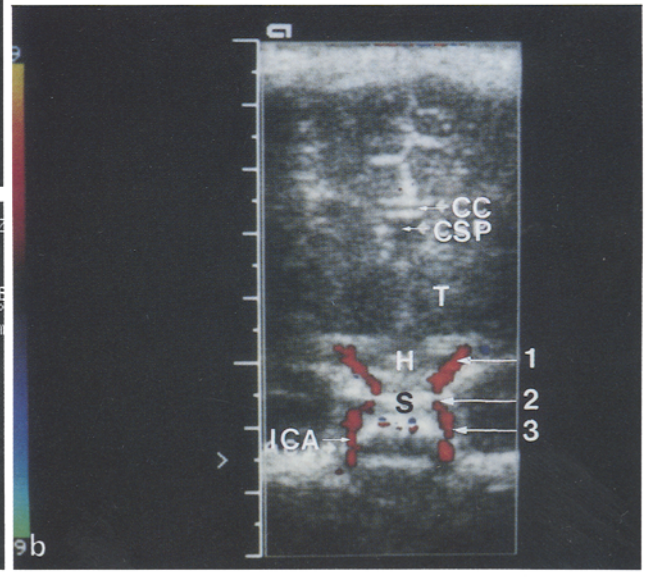
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pected congenital heart disease were excluded. We also rejected results from cases of lung disease or those that were restless or crying.

The corrected gestational age at investigation ranged from 29 to 45 weeks (mean 37.1 ± 3.1 weeks). The corrected gestational age was the sum of the weeks of pregnancy and the actual weeks of life. The weight of the infants at investigation ranged from 1070 to 3750 g (mean 2190 ± 590 g).

All children were investigated by computer sonography (Acuson 128) with a 5 MHz transducer. The system allows simultaneous display of the two dimensional image and the Doppler spectrum as well as colour flow imaging.

Only infants who were asleep or who were in a quiet condition were investigated. Sometimes feeding during the investigation was helpful in restless children.

Anterior cerebral arteries (ACA)

The flow in the ACA was measured in sagittal sections as it is shown in Figure 1. The artery can be displayed by colour coded Doppler sonography in front of the 3rd. ventricle (Fig. 1b). In this region there is no significant angle between the axis of the vessel and the Doppler line of the pulsed Doppler device which is the optimal condition for accurate flow measurement so flow velocities can be measured without angle correction. Following dimensional imaging of the vessel on the gray scale image the Doppler line was placed in front of the 3rd. ventricle and the sample volume localized within the vessel under two dimensional control. Colour coded Doppler sonography is very helpful but not essential for the correct placement of the sample volume. As the flow in the vessel is directed towards the transducer it is displayed in red colour. When no colour Doppler is available the best location of the sample volume can be found by moving the Doppler line and the sample volume in the region in front of 3rd. ventricle till the highest frequency spectrum can be obtained which is characterized by a clear and loud audiosignal.

Another possible site for measurement of the flow in the ACA are coronal sections through the brain with the transducer slightly angled anteriorly. The ACA can be found in a plane just in front of the 3rd. ventricle. Colour coding is also very helpful at this point. After two dimensional imaging of the ACA the Doppler line is placed in the midline and the sample volume is localised just beneath the genu of the corpus callosum.

Basilar artery (BA)

To measure the flow in the BA sagittal sections through the midline are most helpful although coronal sections tangentially to the base of the skull can also be used. In sagittal sections the BA runs at the base of the skull just in front of the pons cerebri as it is shown in Figure 2. Colour coded Doppler sonography is very helpful to show the exact course of this vessel (Fig. 2b). As the flow is directed towards the transducer the artery is displayed in red. There is no significant angle between the axis of the vessel and the Doppler line of the pulsed Doppler device so optimal Doppler recordings can be obtained without angle correction. After placement of the Doppler line just in front of the pons cerebri the sample volume is localized in the region of the base of the skull and the Doppler recordings are obtained.

Internal carotid arteries (ICA)

The flow in both ICA can be measured in coronal sections through the sella turcica (Fig. 3). Colour flow imaging is able to display the exact course of both ICA within the gray scale image. As the flow is directed towards the transducer the arteries are displayed in red. Colour coded imaging clearly shows the three parts of the vessel: the pars petrosa below the region of the sella, the pars cavernosa with the carotid syphon alongside the sella and the pars cerebralis above the level of the sella (Fig. 3b). Doppler sonographic flow measurements should not be done in the pars cavernosa (carotid syphon) where the vessel describes a lying S and runs out of the plane before it enters it again. In this region the angle of incidence is not exactly known and the flow velocities are underestimated. The best point to measure the flow in the ICA is the pars petrosa below the level of the sella. In this region no significant angle exists between the axis of the vessel and the Doppler line of the duplex device so optimal Doppler curves can be obtained without anglecorrection. When no colour is available, the Doppler line is placed close to the side of the sella. The optimal position of the sample volume can be found by

Fig. 1a and b. Flow measurement in the anterior cerebral artery (ACA) in sagittal sections. **a** Duplex-scan image of the flow measurement in the ACA. The Doppler line and the sample volume are placed in the ACA in its course infront of the 3rd ventricle [3]. C = cerebellum. In the lower part of the image the Doppler frequency spectrum is displayed simultaneously with the cross sectional image. **b** Colour flow imaging of the ACA. As the flow is directed towards the transducer the artery is displayed in red. In the region infront of the 3rd ventricle [3] the angle of incidence approximates zero. PCA = pericallosal artery; VCI = Vena cerebri int. The angle of incidence in the region of the VCI is 90° therefore no colour flow is displayed

Fig. 2a and b. Flow measurement in the basilar artery (BA) in sagittal sections through the midline. **a** Duplex-scan image of the flow measurement in the BA. The Doppler line and the sample volume are placed in the BA infront of the pons cerebri. In the lower part of the image the simultaneously displayed Doppler spectrum is shown. **b** Colour flow mapping of the BA infront of the pons cerebri (P). 3 = 3rd ventricle, 4 = 4th ventricle. As the flow is directed towards the transducer the artery is displayed in red

Fig. 3a and b. Flow measurement in the internal carotid arteries (ICA) in coronal sections. **a** Gray scale image with the Doppler line placed just aside from the sella (S). The sample volume (horizontal lines) is placed just beneath the sella in the pars petrosa of the ICA. H = hypophysis; HT = hypothalamus; TH = thalamus; SV = lateral ventricle; MCA = middle cerebral artery. **b** Colour flow mapping of the ICA. As the flow is directed towards the transducer the artery is displayed in red. 1 = pars cerebralis of the ICA; 2 = pars cavernosa of the ICA (carotid syphon); 3 = pars petrosa of the ICA; S = Sella turcica; H = hypophysis; T = thalamus; CSP = cavum septi pellucidi; CC = Corpus callosum

Fig. 4. Normal flow profile in the intracranial arteries of healthy infants. V_s = Peak systolic flow velocity; V_{es} = endsystolic flow velocity; V_{ed} = enddiastolic flow velocity; TAMX = time average maximal velocity; TAV = time average velocity

moving the Doppler line and the sample volume just around the edges of the sella.

Another possibility to measure the flow in the ICA are parasagittal sections close and parallel to the midline. With colour flow mapping the artery can be visualized and the sample volume positioned in a region of the vessel were the angle of incidence is very low. Without colour coded Doppler sonography flow measurements in sagittal sections are much more difficult than flow measurements in coronal sections.

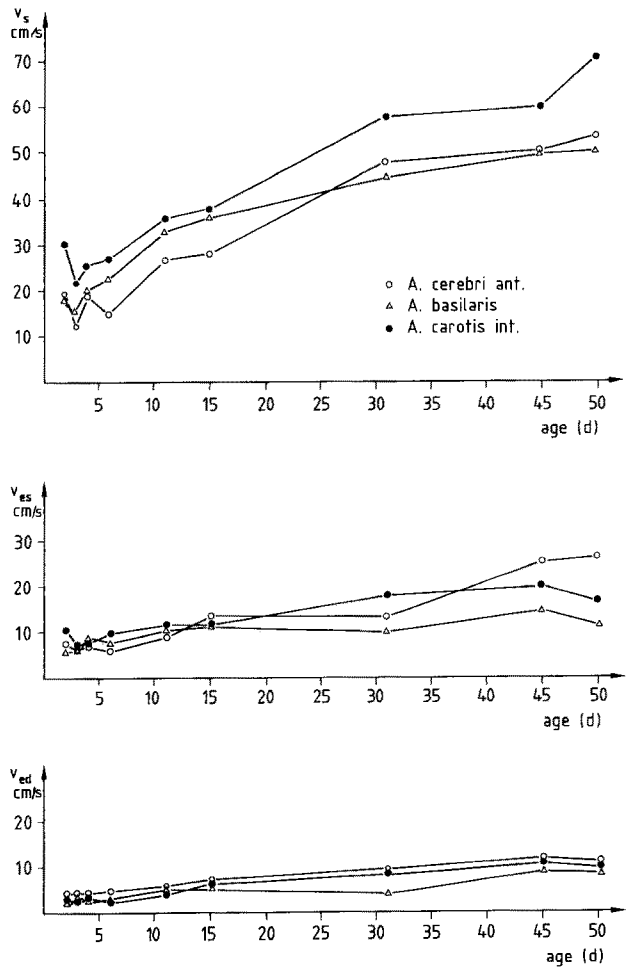


Fig. 5. Increase of the flow velocities in the intracranial arteries of a premature infant born in the 31rd week of gestation with a birth weight of 1350 g. Linear increase of all flow velocities with increasing age. V_s = peak systolic velocity; V_{es} = endsystolic velocity; V_{ed} = enddiastolic velocity; d = days

Quantification of flow velocities and pulsatility-indices

From the flow profile the maximal systolic velocity V_s, the endsystolic velocity V_{es} and the enddiastolic velocity V_{ed} were measured as it is shown in Fig. 4. V_s corresponds to the peak of flow profile, V_{es} to the shoulder in the declining part of the flow profile, whereas V_{ed} marks the end of the pulse cycle (Fig. 4). Two mean flow velocities were measured: The time average maximal velocity (TAMX) and the time average velocity (TAV). TAMX corresponds to the area under the flow velocity curve and is measured by integration of the Doppler curve (Fig. 4). When the flow profile in the measured vessel is flat TAV approximates TAMX. In the small intracranial arteries of preterm infants and full term newborns a parabolic flow profile predominantes. Beside the high velocities in the center of the vessel the flow velocities near the walls are much lower. Therefore TAV in these vessels is lower than TAMX. TAV was calculated by the integrated computer of the system over several pulse cycles (Fig. 4).

Beside these absolute flow velocites the pulsatility-index (PI) defined by Gosling in 1974 [8] and the resistance-index defined by Pourcelot in 1975 [17] were calculated.

The pulsatility-Index (PI) is defined as:

$$PI = \frac{V_s - V_{ed}}{TAV}$$

The resistance-index (RI) is defined as:

$$RI = \frac{V_s - V_{ed}}{V_s}$$

Statistical analysis

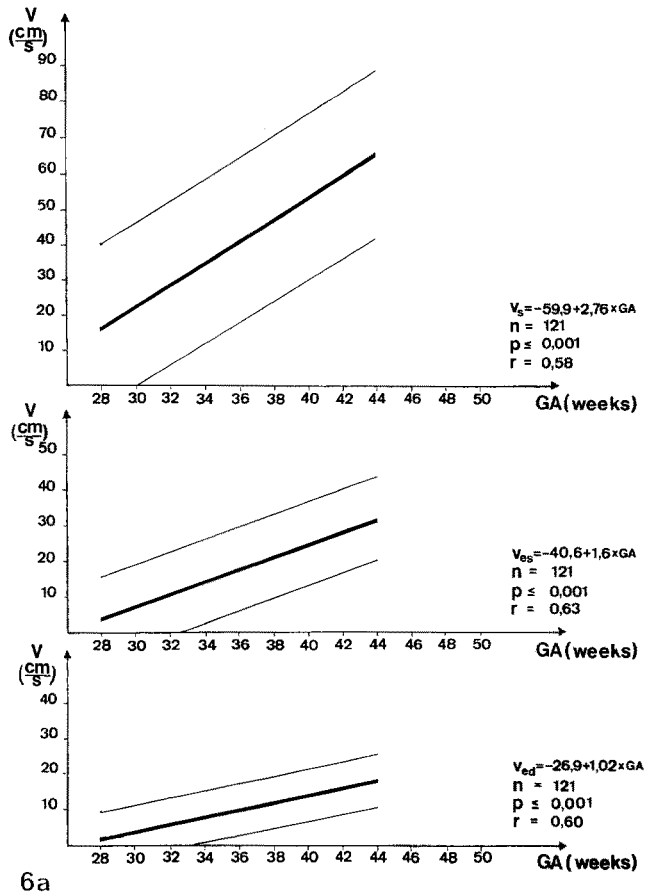
All data were analysed by computer using linear regression and linear regression after linear logarithmic transformation. The reproducibility of our measurements was analysed after the method described by Bland and coworkers [2] in The Lancet.

Results

In healthy premature born infants, newborns and older infants a systolic-diastolic forward flow could be found in all cerebral arteries as it is shown in Figure 4. While the flow profile in the intracranial

Fig. 6. a Dependency of the flow velocities in the anterior cerebral arteries with increasing gestational age (GA) in 121 premature and full-term born infants. Linear increase of all flow velocities. Beside the mean values the two standard deviation is shown. V_s = peak systolic flow velocity (top); V_{es} = endsystolic flow velocity (middle); V_{ed} = enddiastolic flow velocity (bottom). **b** Dependency of the mean flow velocities in the anterior cerebral arteries with increasing gestational age (GA) in 86 premature and full-term born infants. Linear increase of the mean flow velocities with increasing gestational age. Beside the mean values the two standard deviation is shown. TAMX = time average maximal velocity (top); TAV = Time average velocity (bottom)

Fig. 7. a Dependency of the flow velocities in the basilar artery with increasing gestational age (GA) in 110 premature and full-term born infants. Linear increase of all flow velocites. Beside the mean values the two standard deviation is shown. V_s = peak systolic flow velocity (top); V_{es} = endsystolic flow velocity (middle); V_{ed} = enddiastolic flow velocity (bottom). **b** Dependency of the mean flow velocities in the basilar artery with increasing gestational age (GA) in 82 premature and full-term born infants. Linear increase of the mean flow velocities. Beside the mean values the two standard deviation is shown. TAMX = time average maximal velocity (top); TAV = time average velocity (bottom)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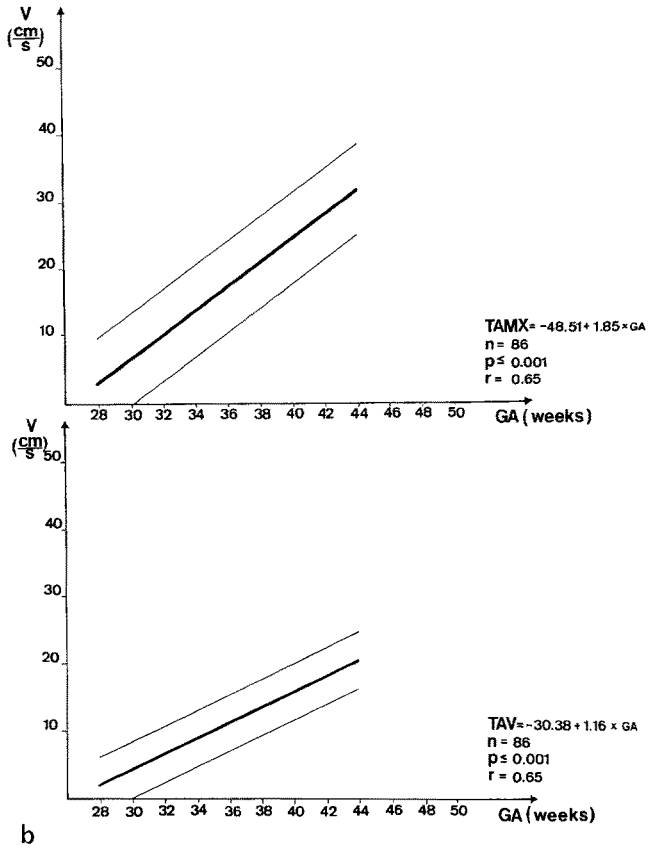
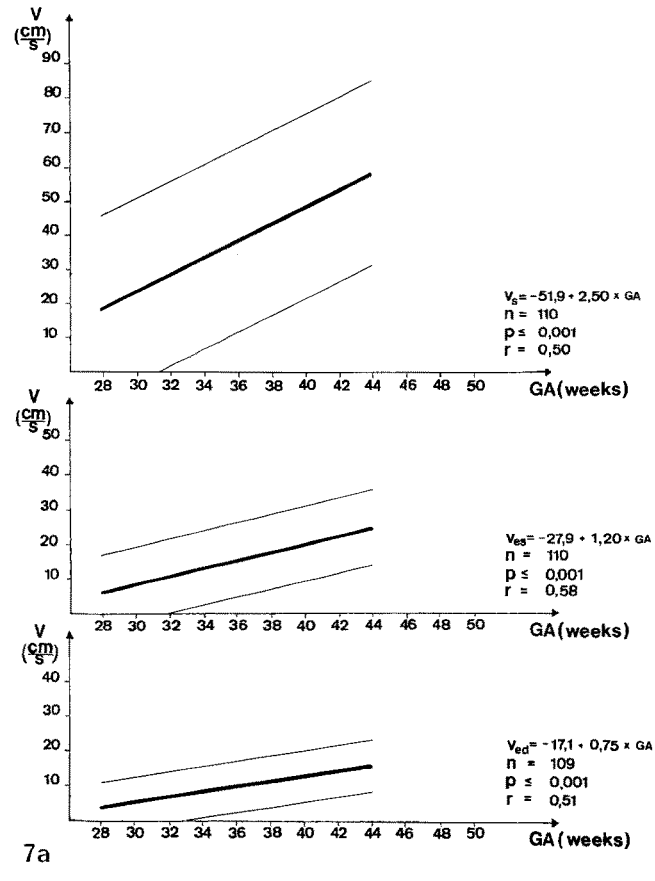
p ≤ 0,001
r = 0,58
GA(weeks)
V_{es}=-40,6+1,6×GA
n = 121
p ≤ 0,001
r = 0,63
V_{ed}=-26,9+1,02×GA
n = 121
p ≤ 0,001
r = 0,60

6a


V (cm/s)
TAMX= -48.51+1.85×GA
n= 86
p≤ 0.001
r= 0.65
GA (weeks)
TAV=-30.38+1.16 x GA
n = 86
p≤ 0.001
r = 0.65

b


V (cm/s)
V_s= -51,9 + 2,50 x GA
n = 110
p ≤ 0,001
r = 0,50
GA(weeks)
V_{es}= -27,9 + 1,20 x GA
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r = 0,58
V_{ed}= -17,1 + 0,75 x GA
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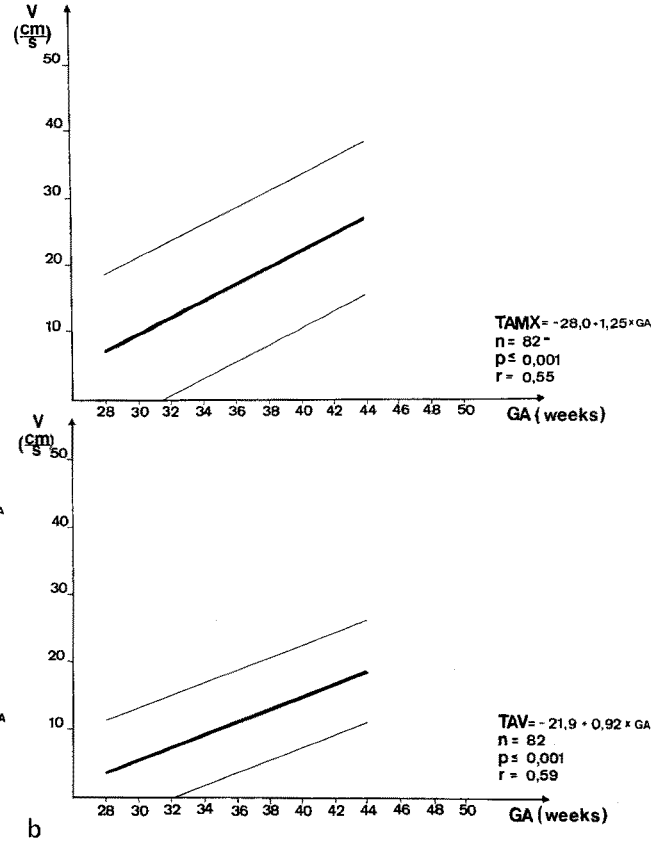
p ≤ 0,001
r = 0,51

7a


V (cm/s)
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GA (weeks)
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p≤ 0,001
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b

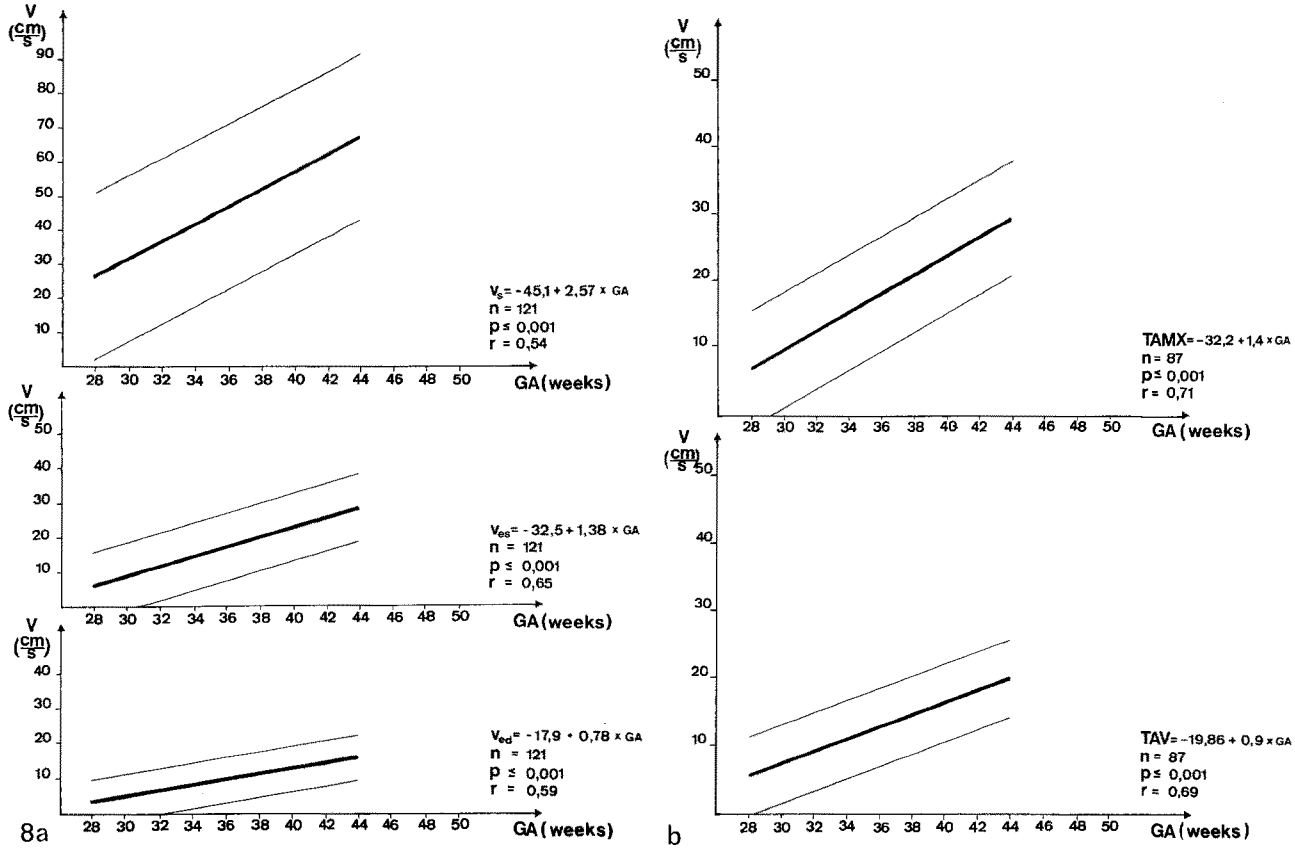

Fig. 8. a Dependency of the flow velocities in the internal carotid arteries with increasing gestational age (GA) in 121 premature and full-term born infants. Linear increase of all flow velocities. Beside the mean values the two standard deviation is shown. V_s = peak systolic flow velocity (top); V_{es} = endsystolic flow velocity (middle); V_{ed} = enddiastolic flow velocity (bottom). **b** Dependency of the mean flow velocities in the internal carotid arteries with increasing gestational age (GA) in 87 premature and full-term born infants. Linear increase of the mean flow velocities. Beside the mean values the two standard deviation is shown. TAMX = time average maximal velocity (top); TAV = time average velocity (bottom)

arteries is age independent a significant increase of all flow velocities with increasing gestational age could be found as it is shown in Figure 5. In this figure the flow velocities in the ICA, ACA and BA are shown with increasing gestational age in a premature infant born in the 31st week of gestation with a birth weight of 1350 g. With increasing age an increase of all flow velocities could be found. At the age of 1 month the initial measured flow velocities had already doubled.

Flow velocities

In all children we found a linear increase of all flow velocities with increasing gestational age in all measured intracranial arteries as it is shown in Figures 6, 7 and 8. In these figures beside the mean values of the flow velocities the two standard deviation is shown.

V_s in the ICA was about 20% higher than in the ACA and BA whereas V_{es} and V_{ed} were not significantly different in the three arteries. The TAV in the ICA was 9% higher than in the ACA and 15% higher than in the BA. The TAMX in the ICA was 10% higher than in the ACA and 14% higher than in the BA.

Pulsatility-index and resistance-index

In contrast to the increase of all flow velocities with increasing gestational age neither the pulsatility-index nor the resistance index showed such variation. For the RI in the ICA 0.77 ± 0.08, in the ACA 0.73 ± 0.08 and in the BA 0.72 ± 0.09 were measured. The PI in the ICA was 3.0 ± 0.08, in the ACA 2.7 ± 0.09 and in the BA 2.7 ± 0.7.

Discussion

The use of pulsed Doppler sonography combined with gray scale imaging, called duplex scanning enables the investigator to measure absolute flow velocities. This technique has two major advantages:

1. The possibility of precise location of the sample volume of the Doppler system within the region of interest. This allows measurement of flow velocities in definite vessels.

2. As the angle between the Doppler line and the axis of the vessel is accurately known, angle corrections can be performed. This allows a more precise quantification of flow velocities.

The early investigations of the flow within the intracranial arteries of newborns performed by Henrietta Bada [1] were done with a continuous Doppler (CW-Doppler) device. These systems lack range resolution and two dimensional imaging. Therefore flow measurements cannot be done in definite vessels. As the angle of incidence is not exactly known, flow velocities cannot be calculated by CW Doppler systems.

The development of colour coded Doppler sonography allows simultaneous display of the intracranial vessels within the gray scale image. Flow directed towards the transducer is displayed in red, flow away from the transducer is displayed in blue. This new technique allows a more precise localisation of the sample volume of the duplex system within the vessel than gray scale imaging alone. Some parts of the vessel can be found, with minimal or no angle between the Doppler line and the axis of the vessel greatly increasing the accuracy of measurement. Colour coded Doppler sonography is therefore very helpful for the definition of the best localisation of the sample volume. This is for the anterior cerebral artery the course in front of the 3rd. ventricle, for the basilar artery the course in front of the pons cerebri and for the internal carotid arteries the pars petrosa beneath the sella. In these regions the angle between the Doppler line and the axis of the vessel approximates zero and can be neglected. Colour coded Doppler sonography is very helpful but no essentially necessary for the Doppler sonographic flow measurements in intracranial arteries of infants.

As pulsed Doppler sonography is increasingly used in neonatology one has to ask what flow velocities are normal. To our knowledge only two papers have been published in the literature where reference values for the flow velocities in the intracranial arteries of newborns were reported [3, 12]. Jorch and coworkers found a linear increase of the flow velocities in all intracranial arteries with increasing weight. Normal values for the flow velocities in the intracranial arteries of healthy preterm infants and full term newborns according to increasing gestational age and actual age have not been previously published. In our patients we found a better correlation of the flow velocities in the intracranial arteries with increasing gestational age than with the weight at investigation [3]. As the flow velocities show a strong age (and weight) dependency these parameters must be taken into consideration when pathologic flow velocities are analysed. In contrast to the increase of the flow velocities neither the pulsatility-index nor the resistance-index showed a age and weight dependency. Both parameters are ratios which describe the flow profile: As the peak systolic flow velocity and the enddiastolic flow velocity as well as the time average flow velocity increase in a similar way the pulsatility-index and the resistance-index did not change significantly. Both parameters are age independent values which can be used for the description of the flow profile. They will alter when either the maximal systolic or the enddiastolic flow velocities change but will keep constant when both velocities increase or decrease simultaneously. Therefore the quantification of the absolute flow velocities in intracranial arteries are better parameters for the description of flow, although brain perfusion cannot be calculated by Doppler sonography unless the cross sectional area of the vessels of investigation can be measured. Volume flow could theoretically be determined by Doppler sonography according to the following formula: $Q = A \times \bar{V}$ (Q is the volume flow in ml/s, A the cross sectional area of the vessel measured in mm^2 and $\bar{V}$ the mean flow velocity in the vessel measured in mm/s. $\bar{V}$ can be measured by Doppler sonography). The cross sectional area of the small intracranial arteries of infants however cannot be measured accurately. Therefore volume flow cannot be calculated. The investigations of Greisen [9], Hansen [10] and Perlman [16] however found a good correlation of Doppler sonographic determined flow velocities within the intracranial arteries and the brain perfusion determined by Xenon-133-clearance [9], the microsphere method [10] and positron emission tomography [16]. Therefore an increase or decrease of the mean flow velocities in the same patient may reflect an increase or decrease of brain perfusion especially as the great intracranial arteries are relatively calibre constant as the angiographic studies of Hilal showed [11].

Beside the physiologic factors of gestational age and weight influencing the flow velocities in brain arteries especially the pCO_2 and the vigilance of the patient must be taken into consideration. A high pCO_2 results in a dramatic increase, whereas a fall in pCO_2 leads to a decrease of the flow velocities. A rise of blood pressure in crying children is followed by an increase of all flow velocities especially in diastole.

Under pathologic circumstances cardiovascular abnormalities especially like patent ductus arteriosus [5, 13, 14] result in a decrease of diastolic forward

flow. Hemodynamic relevant ductus arteriosus are characterized by an absent or retrograd diastolic flow. The patent ductus can be defined as a leakage of the "Windkessel" of the aorta. Other cardiovascular abnormalities which can be defined as a leakage of the aortic "Windkessel" are truncus arteriosus communis, aorto-pulmonary window, aortic insufficiency and great arterio-venous fistulas. In these cases flow profiles in intracranial arteries show similar changes to patent ductus arteriosus. In left ventricular outlet obstructions like severe aortic stenosis or hypoplastic left heart syndrome a non-pulsatile flow with low peak-systolic flow velocities and low acceleration slope and deceleration slope can be found [18]. In contrast to this in coarctation of the aorta higher peak-systolic flow velocities in the intracranial arteries can be found than in healthy infants, whereas the flow velocities in the lower parts of the body are decreased [4]. All diseases of the central nervous system with a raised intracranial pressure result in a decrease of diastolic forward flow, especially severe rapidly progressive hydrocephalus, severe brain edema and rapidly evolving subdural and subarachnoid hemorrhage [6, 7]. In infectious diseases of the brain however and postasphyxially an increase of diastolic flow velocities can be found. In preterm born infants who developed intracranial hemorrhage we could find significant lower flow velocities within the anterior cerebral arteries than in comparable infants without hemorhage [6]. Low flow velocities in preterm born infants with lung disease may be a major risk factor for the development of intracranial hemorrhage. Early flow measurements in these infants may be valuable in the prevention of intracranial hemorrhage by optimal fluid uptake, treatment with catecholamines and last not least optimal ventilation. This means a pCO_2 not too low, as low pCO_2 levels lead to a further decrease of the flow velocities within the intracranial arteries and probably cause a further reduction of brain perfusion.

With the help of pulsed Doppler sonography better management of severely ill preterm born infants and newborns seem probable. Severe life threatening complications can perhaps earlier be detected and as we hope in many cases be prevented.

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