Brain Sonography

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Abstract

Ultrasonography is the most easily available imaging technique to study the newborn and infant brain. It is non-invasive, non-irradiating and easily repeatable. The aim of this chapter is to review the US findings of normal brain anatomy, congenital malformations, hypoxic-ischemic encephalopathy, hemorrhagic lesions and their complications, and intracranial infections. A review of gray-scale and Doppler techniques is also included.

Technique and Normal Anatomy

The current standard technique for performing neurosonography is through an anterior fontanelle approach with both coronal and sagittal scans. The anterior fontanelle approach provides the most readily accessible view and reveals the best anatomic detail because of the relative large size and acoustic window of the anterior fontanelle (Lowe and Bailey 2011a; Epelman et al. 2010). Actually, the exclusive use of transfontanellar scanning can cause some limitations, which might reduce the diagnostic efficacy of cranial ultrasound (Di Salvo 2001; Luna and Goldstein 2000). The transducer position, being fixed by the location of the anterior fontanelle, may be inadequate in relation to the reflecting interfaces, with practical problems such as “blind” areas, particularly in the upper parieto-occipital region, and an unfavorable angle of incidence with insufficient demonstration of structural details in case of parallel interfaces (i.e., lateral walls of the third ventricle) to the direction of propagation of the ultrasound beam.

The most obvious improvement may be achieved by transcranial examination. Moreover, concerning Doppler investigations, the transcranial approach is one of the most important methods to avoid errors due to angle ambiguity (Winkler and Helmke 1990).

The same transducers are used for both morphological assessment and hemodynamic evaluation of the brain. Probes with a small footprint are necessary because of the small size of the ultrasonic window of the open fontanelles (Van Wezel-Meijler et al. 2010). Five- to 10-MHz real-time sector or vector transducers are adequate for the transfontanellar approach. High-frequency broadband linear array transducers, ranging from 5 MHz up to 15 MHz and more, are generally used to evaluate the extra-axial fluid space, dura, meninges, and convolutional marking. Lower insonating frequencies are used for the transcranial approaches. Options such as multifrequency, multi-focus, image-compounding, or speckle-reduction filters may be helpful.

Transcranial approaches – such as transtemporal or mastoid accesses – can be very useful for the study of the posterior fossa (Riccabona 2014; Correa et al. 2006).

Regarding spectral and color Doppler imaging (Couture and Veyrac 2001), the sensitivity to low-volume and low-velocity flow in small cerebral vessels depends on the frequency of the ultrasound beam, which has to be tailored (as high as possible) by the operator to any specific application. A software able to detect low blood velocity (approximately 1 cm/s) is needed. Wall filter setting should be low (between 30 and 50 Hz), the size of the anatomic and color windows should be adapted to the size of the region of interest, and persistence should be moderate or high.
Fissures, Sulci, and Gyri

Fissures, sulci, and gyri develop in an orderly sequence and constitute a good indicator for gestational age (Govaert and De Vries 2010; Huang and Yeh 1991; Huang 1991; Naidich et al. 1994; Worthen et al. 1986). In premature infants, the brain is rather featureless because the gyri and sulci are underdeveloped (physiologic pachygyria) (see Fig. 24) (Siegel 2011). Compared to the embryological development, there is a 2–4-week delay between the first enfolding of the brain and the visualization of a sulcus by sonography (Bernard et al. 1988). The sulci and fissures have variable echogenicity depending on their size and on the vessels they contain (Naidich et al. 1986a). When they are narrow, they appear as echodense linear structures separating the gyri. An echogenic parenchymal pseudolesion can be seen when a sulcus is imaged through its long axis (Bowerman 1987). Hyperechogenicity is caused by blood vessels and collagen in the pia mater (Slovis and Kuhns 1981). When they are wider, the anechoic CSF is resolved and they appear hypoechoic (Naidich et al. 1986a). A high-frequency linear array transducer is recommended for evaluation of sulci and gyri along the convexity of the cerebrum (subfontanellar structures) (Fig. 1).

Hemispheric Brain Parenchyma

High-frequency sections can display the normal gray-white matter junction in different locations. In fact, the thin cerebral cortex appears as a relatively hypoechoic stripe between the hyperechoic pia mater and white matter. The echoes of the white matter are due to its numerous vessels (Naidich et al. 1986a). A coronal section through the anterior fontanelle with a high-frequency linear array transducer permits the best view of the corticomedullary differentiation (Fig. 1).

Corpus Callosum

It is visible on both coronal and sagittal scans as a thin, hypoechoic, crescentic, midline structure (Figs. 2 and 3). True midline sections are not suitable to display the corpus callosum, since the fibrous falx shadow obscures the desired anatomy. Instead, “midline” sections are obtained by angling toward the midline from a point just lateral to the falx (Naidich et al. 1986a). At term, the genu is about 4–5 mm, the splenium about 3.5–4 mm, and the body about 2–2.5 mm thick. In a preterm newborn, the genu is about 3 mm, the splenium about 2.8 mm, and the body about 1.7 mm thick. At 9 months, the corpus callosum has the adult
shape and the genu is about 8.4 mm, the splenium about 8.2 mm, and the body about 3.7 mm thick (Couture et al. 1994; Barkovich and Kjos 1988).

Gray Nuclei and Deep White Matter

Coronal sonograms (Fig. 2) depict the anterior limb, genu, posterior limb, and sublenticular parts of the internal capsule, the caudate nucleus, the putamen, the lateral and medial nuclei of globus pallidus, the lateral and medial medullary laminae of the lenticular nucleus, the nucleus accumbens septi, and some of the thalamic nuclei (Naidich et al. 1986a, 1985). On coronal view, the internal capsule represents the most useful and reliable semiotic element (Couture et al. 1994). The anterior limb is hyperechoic, the genu is mildly echoic, and the posterior limb is hypoechoic (Naidich et al. 1986a, 1985). This phenomenon depends on both the scan angle and the perpendicular interposition of the fibers of the capsule and the caudoputaminal connections. In the section through the posterior limb, the fibers are nearly parallel to the ultrasound beam.

A sagittal sonogram (Fig. 3) through the caudothalamic groove is the best way of showing the thalamus, the lentiform nucleus, the internal capsule, and their relationships (Govaert and De Vries 2010; Naidich et al. 1986a, b). It routinely displays a gangliothalamic ovoid delimited by the lateral ventricle, the perimesencephalic cistern, and the radiations of the corpus callosum. The gangliothalamic ovoid exhibits four obliquely oriented bands of increased and decreased echogenicity. The anterior-most hyperechoic band 1 corresponds to the head of the caudate nucleus and parts of the lenticular nucleus.
Hypoechoic band 2 corresponds to the globus pallidus, genu, and posterior limb of the internal capsule and cerebral peduncle. Hyperechoic band 3 corresponds to the ventral and lateral thalamic nuclei (except the pulvinar). Hypoechoic band 4 corresponds to the pulvinar. According to Couture et al. (1994), the bands detectable by sonography are five. These authors subdivided band 1 into a superior hypoechoic part, corresponding to the caudate nucleus, and an inferior hyperechoic part, corresponding to the putamen.

**Supratentorial Ventricular Cavities**

The lateral ventricles appear as anechoic paramedian fluid-filled spaces. On coronal sections (Fig. 2) the frontal horns have the typical crescent shape configuration; at the level of the trigones the lateral ventricles diverge laterally. On sagittal sections (Fig. 3), the entire transducer must be angled laterally and the posterior portion of the transducer must be swept further from the midline to either side in order to display the full contour of the lateral ventricle including the frontal horn, body, atrium, occipital horn, and temporal horn (Naidich et al. 1986a). Actually, the temporal horn is hardly visible in normal newborns as its lumen is very often virtual. Different methods have been proposed to define the normal size of the lateral ventricles (Govaert and De Vries 2010; Poland et al. 1985; Perry et al. 1985; Helmke and Winkler 1987; Levene 1981). The ventricle-to-hemisphere ratio (cella media width/hemisphere width) is calculated from measurements on both sides in the axial plane. Normal values are between 0.2 and 0.33. On a
frontal section through the head of the caudate nucleus, the ratio of the laterolateral diameter between the points of the frontal horns to the distance between the left and right internal table on that section averages 0.32 (95 % reliability margin: 0.23–0.42). Slightly higher ratios have been found in preterm (0.32–0.36) than in full-term infants (0.25–0.30). Term values are achieved at about 36 weeks of gestation. The same ratio measured behind the foramen of Monro tends to be 0.35 at term. The term ventriculomegaly is appropriate for values between 0.36 and 0.4 and hydrocephalus for values above 0.4. The third ventricle is usually slit-like on coronal view (Fig. 2) when normal, because its transverse diameter is very small. On midline sagittal scans (Fig. 3), the third ventricle appears as a vaguely triangular hypoechogenic zone that angles anteroinferiorly from the foramen of Monro. The massa intermedia that crosses the third ventricle is highly variable in size. It often appears hyperechoic with a hypoechogenic center (Naidich et al. 1986a). On axial sections, the anterior recesses of the third ventricle come into view as one or two echoic parentheses (the lateral borders) inside the hypothalamus, which appears in the basal cistern as an ovoid hypoechogenic structure (Naidich et al. 1986a). According to Helmke and Winkler, the mean values of the width of the third ventricle, examined in coronal and axial sections, are 2.8 mm in the first 3 months and 3.8 mm between the 9th and 12th month of life (Helmke and Winkler 1987).

**Choroid Plexus**
The choroid plexus of the lateral ventricle is the most striking landmark of the neonatal brain because of its highly echogenic structure (Figs. 2 and 3). It presents micropulsations and a smooth, sharply defined outline. Its echogenic appearance is due to frequent liquid–solid transitions in the villous crypts and to its marked vascularity (Govaert and De Vries 2010). In the sagittal view it runs in a semicircular direction around the thalamus, and at the atrium it widens and thickens to form the glomus. It never extends beyond the caudothalamic groove and, at the level of the foramen of Monro, it passes through the foramen, and, together with its contralateral counterpart, runs posteriorly in the roof of the third ventricle to the suprapineal recess. In the temporal horn the plexus adheres to its roof medially and is thin, while it is well visible, in the sagittal view, in case of hydrocephalus. The two temporal plexuses can also be studied on midline coronal cuts and are seen as two small, hyperechoic, rounded, symmetrical spots. On coronal sections through the trigone, where the lateral ventricles diverge laterally, the glomus almost fills the whole ventricular lumen (Guermazi et al. 2000).

**Posterior Fossa**
The study is mainly based on sagittal and axial sections. The best sagittal images are obtained via the anterior fontanelle although, in comparison with the study of supratentorial structures, this approach offers a worse image quality due to the relatively large distance to be covered (i.e., need of lower insonating frequencies) (Couture et al. 1994). Satisfactory true axial images can be obtained directly through the thin temporal squama and the posterior and posterolateral fontanelles (Epelman et al. 2010; Di Salvo 2001; Steggerda et al. 2012).

Midline and paramedian sagittal transfonntanellar sections (Fig. 3) display the bony posterior fossa, basal cisterns, brainstem, fourth ventricle, and cerebellum. The fluid-filled cisterna magna is anechoic. Normal values of the midsagittal height of the cisterna magna and of the distance of the fastigium of the fourth ventricle from the plane of the foramen magnum are 4.52 +/− 1.29 mm and 16.05 +/− 3.03 mm, respectively (Goodwin and Quisling 1983). Usually, the other cisterns are strongly echogenic as their walls consist of leptomeninges and blood vessels. The cerebral peduncles, pons, and medulla oblongata appear as echo-poor structures. The fourth ventricle is almost anechoic and triangular.

Axial sonograms display the contour of the midbrain, the cerebral aqueduct, and the internal structure of the midbrain. The suprasellar cistern anterior to the midbrain appears as a hyperechoic, six-point star.
Axial scans also display the hypoechoic folia and the hyperechogenic fissures of the vermis and cerebellar hemispheres. Coronal sections through the temporal squama and posterolateral fontanellae show the length of the hypoechoic brainstem. A hyperechoic midline stripe probably corresponds to perforating vessels, midline nuclei, and decussating fiber tracts.

**Normal Variants and Pitfalls**

**Asymmetric Lateral Ventricle Size**
It is defined by a difference in ventricular width greater than 2 mm (Shen and Huang 1989). Ventricular asymmetry is usually more pronounced in the most posterior portion of the occipital horn, a fact that should be taken into account particularly when using the posterior fontanelle as an acoustic window. The preservation of the lateral ventricle triangular configuration in coronal views, the presence of thin ventricular walls showing only faint echogenicity, and no increase in size on follow-up scans suggest normality (Lowe and Bailey 2011b).

**Coarctation of the Lateral Ventricles**
This unusual uni- or bilateral variant consists of a focal approximation of the ventricle walls at any point medial to their external angle (Fig. 4). When the approximation is complete or nearly complete, the external part of the ventricle acquires a rounded configuration, simulating a cyst (Rosenfeld et al. 1997). Parasagittal images reveal contiguous cysts extending anteriorly from the level of the thalamocaudate groove (Fig. 4). They are detected in the first week of life. Coarctation should not be confused with germinal matrix cyst, cystic periventricular leukomalacia, and multiple subependymal cystic conglomerates secondary to a viral or chromosomal etiology. The authors who maintain these pathophysiologic mechanisms call this sonographic appearance subependymal pseudocysts, germinolytic cysts, or subependymal germinolysis (Lu et al. 1992; Rademaker et al. 1993; Keller et al. 1987; Zorzi and Angonese 1989; Mito et al. 1989; Shen and Huang 1985; Sudakoff et al. 1991; DiPietro 2002). Actually, the symmetry found in many reported cases would be extraordinarily unusual for a prenatal ischemic or hemorrhagic event (Rosenfeld et al. 1997; Zorzi and Angonese 1989; Sudakoff et al. 1991; DiPietro 2002). To differentiate these entities from coarctation, it is essential to carefully observe the position of the cystic image in relation to the external ventricle angle. A diagnosis of evolving prenatal germinal matrix hemorrhage should be considered when the lesion is located below the external ventricle angle, in utero.

**Fig. 4** Coarctation of the left lateral ventricle. (a) Coronal view through the anterior fontanelle shows bilateral weakly echogenic lines (open white arrows), representing the points of coarctation of the lateral ventricles. The cavum septi pellucidi is evident in the midline, just underneath the corpus callosum. (b) Parasagittal images reveal contiguous cysts (calipers), extending anteriorly from the level of the thalamocaudate groove.
periventricular leukomalacia should be considered when it is above, and viral or chromosomal etiology should be considered when it is located in the thalamus or in the head of the caudate nucleus. In lateral ventricle coarctation, the false cystic image is seen at the external angle. As the etiology can often be difficult to establish, Di Pietro recommends TORCH titers to evaluate a possible in utero infection (DiPietro 2002).

**Choroid Plexus**

Although the choroid plexus has a clear, characteristic form, it can present configuration patterns that may be misinterpreted as choroid pathology. The most common of these are choroid cyst, “split” choroid, and “truncated” choroid (Lowe and Bailey 2011b).

Choroid plexus cysts are well-demarcated, rounded, anechoic structures. They can be bilateral, often asymmetric. They are more often found in the glomus part of the choroid plexus and can also be seen in utero. Choroid cysts are neuroepithelial cysts and could be the result of an enfolding of the neuroepithelium in the choroid plexus mass (Guermazi et al. 2000). They are a common finding in obstetric and postnatal ultrasound studies and usually disappear on serial examinations (DeRoo et al. 1988; Riebel et al. 1992). The likelihood of a congenital infection or a chromosomal anomaly with a unilateral single cyst is negligible (Fernandez Alvarez et al. 2009). Large (greater than 1 cm in diameter) or multiple bilateral plexus cysts in infants are known to present with trisomy 9, 18, and 21 (Siegel 2011; Fernandez Alvarez et al. 2009; Herman and Siegel 1991).

The location of the plexus is relatively constant, while its morphology can vary. It can be bilobed (see Fig. 6) with an appearance that can mimic choroid hemorrhage (“split” choroid). Color Doppler can be helpful in differentiating the normal choroid plexus from intraventricular clot (Di Salvo 2001; Seibert et al. 1998). The “truncated” choroid is a flattening of the lower portion of the plexus giving the appearance of a solid–fluid level (Lowe and Bailey 2011b).

**Cavum Septi Pellucidi and Cavum Vergae**

Both cavities are lined by glia and not by ependyma. They are situated between the fornix and corpus callosum. A frontal view shows the cavum septi pellucidi as a triangular or trapezoid echo-free space with its base under the corpus callosum and its apex against the fornix (Fig. 4). A sagittal section shows an echo-free zone with concave rims toward the base of the brain. The cavum Vergae is visualized as the posterior extension (between the bodies of the lateral ventricles) of the cavum septi pellucidi. Sometimes it can appear separated like a cyst between the choroid glomera.

The cavum septi pellucidi and cavum Vergae are frequently found in premature and term neonates on autopsy. Using cranial ultrasonography through the anterior fontanelle, Nakajima et al. (1986) detected a cavum septi pellucidi in 97 % of premature infants, 56 % of full-term neonates, and 29 % of 1-month-old infants. The incidence of cavum Vergae was 60 % in premature infants and 7 % in full-term neonates. None of the 1-month-old infants were found to have a cavum Vergae. The largest cavum septi pellucidi observed ultrasonographically was 10 mm wide. Bohlayer et al. (1983), using sonography, found a cavum septi pellucidi in 100 out of 642 infants. The highest incidence (52 %) was found among very low gestational age infants (<33 weeks) within the first 7 days of life. After the second month, the incidence decreased rapidly. A cavum Vergae was seen only in combination with a cavum septi pellucidi, less frequently, however, than a cavum septi pellucidi alone (26 out of 642 infants); the incidence was 33 % in very low gestational age infants (<33 weeks) within the first 7 days of life, only 4 % in term neonates, and 0 % after the second month of life. According to the series of 108 normal newborns studied by Mott et al. (1992), a cavum septi pellucidi was seen in all normal infants below 36 weeks of gestational age. At 36, 38, and 40 weeks, only 69 %, 54 %, and 36 %, respectively, had cavum septi pellucidi. There was no significant change in the width, depth, or area of the cavum septum pellucidi with age, birth weight, or
biparietal diameter. According to this study, a cavum septi pellucidi greater than 0.95 cm in width or greater than 0.81 cm in depth is outside the normal range and may represent anomalous development of the midline structures of the brain.

**Peritrigonal Echogenic “Blush”**
Cranial sonography in preterm and some full-term neonates reveals a hyperechoic “blush” (“halo”) posteriorly and superiorly to the ventricular trigones on parasagittal views (Fig. 3) (Grant et al. 1983). This normally increased echogenicity resembles fine brush strokes. It is probably caused by the interfacing of numerous parallel fibers that are nearly perpendicular to the longitudinal axis of a sonographic beam passing through the anterior fontanelle. The same echogenicity is not seen on sonograms obtained through the posterior and posterolateral fontanelles because, with that angle, the long axis of the sonographic beam and the fiber tracts are nearly parallel (DiPietro et al. 1986). This normal sonographic finding must be differentiated from the abnormal peritrigonal hyperechogenicity caused by periventricular leukomalacia. Abnormally increased periventricular echodensity is usually more echogenic than the choroid plexus and more confluent, lumpy, or coarse than the normal blush. True pathologic hyperechogenicity remains when scanned from various angles.

**Doppler Imaging**
There are numerous, obvious limitations to the depiction of the neonatal cerebral circulation. The great arteries and veins are always demonstrated on color imaging, but other vessels are inconstantly seen, and some are never visualized. This is mainly due to anatomic characteristics (small-size and/or low-flow vessels and arteries located deeply in the posterior fossa) (Couture et al. 2006). The anterior fontanelle approach is most appropriate for evaluating the cerebral vessels in the neonate, but it must be combined with transcranial Doppler for a complete assessment of the vasculature (Wong et al. 1989). Some cerebral vessels are particularly unsuited to examination through the anterior fontanelle. The course of some arteries and veins is nearly perpendicular to the Doppler beam, and it is known that an incidence angle of 60° or greater makes the interpretation of the resulting spectra uncertain and may render misleading color-coded images of blood vessels (Winkler and Helmke 1990; Couture and Veyrac 2001; Grant et al. 1987; Horgan et al. 1989).

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**Fig. 5** Normal anatomy. Color Doppler. (a) Coronal view through the anterior fontanelle: the (1) internal carotid artery, (2) middle cerebral artery, (3) anterior cerebral artery, and (4) pericallosal artery; lenticulostriate arteries (white arrows). (b) Midsagittal view through the anterior fontanelle: the (1) anterior cerebral artery, (2) callosal marginal artery, (3) pericallosal artery, (4) internal cerebral vein, (5) posterior medial choroidal artery, (6) superior choroidal artery, and (7) medial frontal arteries.
According to Couture and Veyrac (2001), the arteries always seen by color Doppler are the following (Fig. 5): internal carotid, ophthalmic, anterior choroidal, posterior communicating, basilar, anterior cerebral, pericallosal, callosomarginal, medial frontal, middle cerebral, lenticulostrate, operculo-insular, posterior cerebral, thalamic, and choroidal. The veins always seen by color Doppler are the superior sagittal sinus, medial superficial veins, lateral sinuses, vein of Galen, internal cerebral vein, terminal veins, and basilar veins.

The middle cerebral artery, posterior cerebral artery, and basal vein require a temporal bone approach (Winkler and Helmke 1990). Concerning the circle of Willis, all its arteries may be visualized by a transfontanellar approach, although the transosseous temporal access allows the best depiction of the entire circle (Couture and Veyrac 2001).

The arterial spectral analysis shows a rapid ascending wave up to the peak systolic frequency, followed by a gentle slope down to the end-diastolic frequency. The brain is a low-resistance vascular bed, and a continuous forward flow should be seen throughout the arteries in systole and diastole. A semiquantitative measurement of vascular resistance is obtained by calculating the resistance index (RI: peak systolic frequency minus end-diastolic frequency divided by peak systolic frequency). In preterm infants, the mean RI is 0.7 (range, 0.54–0.86), whereas in term infants it is 0.66 (range, 0.52–0.8) (Zamora et al. 2014). After fontanellar closure, the mean RI decreases to 0.50–0.60 (Seibert et al. 1990). Allison et al. reported 0.726 with a standard deviation of 0.057 (overall mean of all interrogated vessels) as the normal intracranial RI value for a term infant during the first 24 h after birth (Allison et al. 2000).

According to Couture et al., the assessment of blood velocities at birth and during the first month of life should be constantly preferred to RI. RI alone is of poor value and may be the source of severe errors. For example, only the measurement of velocities identifies a low blood flow, which is most often associated with normal RI (Couture and Veyrac 2001). Taylor emphasized that the range of normal values of velocities in cerebral arteries is relatively wide, but the variability for an individual infant is limited: the changes in flow velocity should not exceed 50% above the baseline (Taylor 1998). According to Couture et al., the mean value of peak systolic velocity at 32 weeks of gestation is 43.1 cm/s in the anterior cerebral artery, 37.6 cm/s in the basilar artery, and 43.3 cm/s in the internal carotid artery. At 40 weeks of gestation, the same value rises to 52.9 cm/s in the anterior cerebral artery, 54.2 cm/s in the basilar artery, and 60.2 cm/s in the internal carotid artery (Couture and Veyrac 2001). According to Bode and Wais, a rapid linear increase of flow velocities is found within the first 20 days, with higher velocities in neonates of higher birth weight and gestational age. The mean increase in peak systolic velocity per day is about 1.5 cm/s (Bode and Wais 1988).

Usually, the venous spectrum is uniform and continuous. A sinusoidal pattern, synchronous to arterial pulsation, is less frequent. Mean values of venous flow velocities in normal neonates are 3.0 ± 0.3 for terminal veins, 4.3 ± 0.7 for the vein of Galen, and 9.2 ± 1.1 for the superior sagittal sinus (Taylor 1998).

Pitfalls
Spectral and color Doppler imaging requires operator experience, sensitive Doppler equipment, and operator knowledge of the limitations of Doppler.

1. Physics of sound waves and Doppler instruments: errors due to high-pass filter cutoff (low velocities disappear), aliasing (a flow that appears in opposite direction can give false indication of turbulence), and rapid image update (may cause aliasing; it reduces the sensitivity of the system).
2. Quality and adjustment of the Doppler instrument: errors due to low sensitivity, inappropriate adjustment of Doppler controls, and inadequate wall filter.
3. Examination technique: errors due to an unfavorable incidence angle (no signal in the presence of flow, errors in determination of absolute flow velocities that requires angles greater than 30°) or to a transducer-induced pressure (a decrease in arterial flow velocity, predominantly in diastole, may be detected).

4. Cerebral vascular anatomy: errors due to unfavorable probe position as related to the three-dimensional arrangement of vessels and inadequate separation of closely adjacent vessels or vessel-like structures (erroneous projection of a flow signal in a small cystic lesion).

5. Interpretation: flow velocity or RI is taken to equal cerebral blood flow, RI is taken to equal peripheral vascular resistance (pandiastolic backflow may, e.g., be due both to a patent ductus arteriosus and a reversible edema in a premature infant), and one artery is taken to represent the cerebral circulation.

A simplified interpretation of spectral appearances should be avoided; the absence of Doppler signal does not mean absence of flow, and RI does not depend only on cerebral vascular resistances.

**Congenital Malformations**

**Chiari II Malformation**

Cranial sonography is an inexpensive and convenient method of evaluating the presence of a Chiari II malformation in children with myelomeningocele and of following up its evolution after shunt procedures.

![Fig. 6](https://example.com/fig6.png)

**Fig. 6** Chiari II malformation. (a) Coronal scan: inferior pointing of the frontal horns of the lateral ventricles (“batwing” configuration). (b) Midsagittal scan: extension of the cerebellar vermis into the upper cervical canal (black arrowhead), beaked mesencephalic tectum (white arrow), and prominent massa intermedia (white arrowhead). (c) Parasagittal scan: colpocephaly; “split” choroid (open white arrows)
The detected abnormalities (Fig. 6) can be categorized into ventricular and extraventricular alterations (Deeg 1984; Babcock and Han 1981).

The most frequent alteration of the ventricular system is hydrocephalus with inferior pointing of the frontal horns of the lateral ventricles ("batwing" configuration). Usually, the lateral walls have a squared-off appearance and the occipital horns are dilated more than the frontal horns (colpocephaly). On axial transcranial view the lateral ventricles look enlarged and are referred to as an “American eagle” appearance. A "split" choroid is frequent (Netanyahu and Grant 1986). Heterotopia of abnormally migrated neuronal tissue in the lateral ventricle has been described (Govaert and De Vries 2010). The third ventricle is enlarged and contains a prominent massa intermedia. Herniation of the third ventricle into the suprasellar cistern and a prominent suprapineal recess are occasionally seen in these patients. The fourth ventricle is elongated and flattened and may appear obliterated. When seen, it is usually noted to be in a low position with respect to the occipital bone (Babcock 1986).

Among extraventricular alterations, infants have a downward displaced cerebellum, obliterated cisterna magna, and low positioning of the tentorium cerebelli. Direct scanning at the craniocervical junction allows good evaluation of this area in patients with Chiari II malformation (Cramer et al. 1986; Brennan and Taylor 2010). The interhemispheric fissure is prominent in some patients before shunting and tends to enlarge when the ventricles diminish in size after ventricular shunting (Babcock 1986). Agenesis/dysgenesis of the corpus callosum and agenesis or fenestration of the septum pellucidum are common associated anomalies. On axial and sagittal sections, a beaked mesencephalic tectum can be detected (Govaert and De Vries 2010).

**Cephalocele**
Sonography can contribute to the evaluation of a cephalocele by detecting associated intracranial anomalies and directly examining the contents of the lesion (parenchyma, vessels, ventricular extension, etc.) (Fig. 7) (Barr 1999).

**Holoprosencephaly**
Usually, sonography allows detection of a partial or the complete absence of the interhemispheric fissure (with fusion of the cerebral hemispheres), pathognomonic for holoprosencephaly.

The sonographic pattern of the alobar form of holoprosencephaly is characterized by a huge (horseshoe-shaped on coronal view) ventricle located in the midline. Midline and paramedian sagittal transfontanellar sections show the communication of the monoventricle with a large occipital cyst, the
“dorsal sac.” Both are directly in contact with the calvarium. The brain only consists of a flat mass (pancake-like) of anteriorly fused cerebral hemispheres located in the frontal region. The convolutional markings are sparse and there is a smooth appearance of the brain surface. Both the thalami and choroid plexuses are fused in the midline. The interhemispheric fissure and falx cerebri are absent as well as the corpus callosum and the septum pellucidum (Couture et al. 1994; Barr 1999; Deeg et al. 1989). By color Doppler it is possible to identify some of the vascular anomalies of holoprosencephaly, such as the absence of the anterior cerebral arteries or the presence only of a single vessel and the absence of the midline venous structures (Couture and Veyrac 2001; Barr 1999).

Semilobar holoprosencephaly, the intermediate form, has a smaller monoventricular cavity with partially fused and anteriorly rotated thalami, resulting in a small third ventricle (Fig. 8). The cerebral tissue is moderately developed anteriorly with partial posterior development of an interhemispheric fissure and separate, rudimentary occipital and temporal horns (Couture et al. 1994; Deeg and Gassner 2010a).

Lobar holoprosencephaly, the least severe type, presents more complete formation of lobes, occipital horns, and a third ventricle. The anteroinferior portion of the interhemispheric fissure is incomplete and the cerebral cortex is fused at the frontal pole (usually the frontal lobes are hypoplastic). On coronal sonograms, the frontal horns of the lateral ventricles are squared and fused with flat roofs and angular corners. The septum pellucidum is absent. The corpus callosum is malformed. The use of high-frequency linear array transducers can allow the detection of associated migrational anomalies (Siegel 2011; Couture et al. 1994; Barr 1999). A similar pattern of the frontal horns on coronal view may be found in septo-optic dysplasia, but the interhemispheric fissure is normal (Deeg and Gassner 2010a; Kuban et al. 1989; Nowell 1986). According to Couture et al., as the abnormal vascular distribution is observed not only in alobar holoprosencephaly but also in the semilobar and lobar forms, color Doppler may become of great value in differentiating lobar holoprosencephaly from septal agenesis. These authors reported a case of lobar holoprosencephaly, studied by color Doppler, with a single cerebral artery and an abnormal course of the pericallosal artery running far from the midline because of incomplete hemispheric division (Couture and Veyrac 2001).

Fig. 8 Semilobar holoprosencephaly. Coronal view through the anterior fontanelle: partial absence of the interhemispheric fissure with fusion of the cerebral hemispheres (*). Partially fused thalami (white arrowheads)
Anomalies of the Corpus Callosum

Agenesis

The classical sonographic signs of agenesis of the corpus callosum are (Fig. 9) the absence of the corpus callosum; absence of the pericallosal and cingulate sulci; “sunburst” pattern of sulci along the medial surface of the hemisphere; wide interhemispheric fissure; ventriculomegaly; elevation of the dilated third ventricle with elongation of the foramen of Monro; small, laterally positioned frontal horns with concave medial borders (“bull’s head” appearance on coronal scan) due to protrusion of the large, laterally positioned and inverted cingulate gyri and of the Probst lateral callosal bundles; marked separation of the bodies of the lateral ventricles; and colpocephaly (Babcock 1986; Deeg 2011; Cadier et al. 1982). Interhemispheric cysts occur in about 30% of patients with callosal agenesis. These cysts may or may not communicate with the lateral ventricles (Siegel 2011). A lipoma of the corpus callosum appears as a
highly echogenic mass in the middle of the interhemispheric fissure (Fig. 10). Usually, the normal corpus callosum is replaced by this lipoma (Auriemma et al. 1993; Fisher and Cremin 1988; Lin et al. 1995).

Partial Agenesis
The sonographic diagnosis may be difficult. Significant colpocephaly and elevation of the third ventricle are rare. The main sonographic signs are separation of the lateral ventricles and radial arrangement of the medial sulci (Couture et al. 1994). On color Doppler, in complete agenesis the pericallosal artery remains far from the third ventricle and takes an upward oblique direction (Fig. 9). The value of this sign is yet greater in case of partial callosal agenesis: the pericallosal artery closely follows the normal corpus callosum but loses its normal course where the corpus callosum disappears; at this level it takes an upward posterior oblique direction (Couture and Veyrac 2001).

Disorders of Neuronal Migration

Lissencephaly (Agyria–Pachygyria Complex)
Lissencephaly or “smooth brain” is a malformation due to deficient neuronal migration. In agyria (Fig. 11), coronal sonograms show an hourglass or a figure-eight-shaped brain with a smooth surface (in pachygyria the few gyri are coarse, broad, and shallow). The smooth cortical surface can be best demonstrated both by a transfontanellar approach with high-frequency linear array transducers and on far lateral “sagittal” sonograms displaying the smooth surface of the insula (Deeg 2011; Motte et al. 1987). On coronal scans, the interhemispheric fissure is not flanked by branching sulci and the sylvian grooves appear as wide linear grooves without opercularization of the insula. The ventricles are enlarged with a
fetal configuration (colpocephaly). The subarachnoid spaces are enlarged. The normal interdigitation of gray and white matter is not seen, and hyperechogenicity of the periventricular white matter is detected (Ramirez 1984; Babcock 1983). On parasagittal scans along the lateral ventricles, subcortical heterotopic neurons cause a pseudo-liver pattern of echo reflections in the telencephalic parenchyma (Govaert and De Vries 2010; Cioffi et al. 1991). Anomalies of the corpus callosum can be discovered.

A premature brain (brains that have not completed sulcation) can appear smooth and can mimic lissencephaly.

**Hemimegalencephaly**

Sonography shows enlargement of one hemisphere with ipsilateral ventricular dilatation, pachygyric cortex, thickening of the gray matter, lack of gray-white matter interdigitation, widening of the sylvian fissure, and increased echogenicity of the ipsilateral white matter. The early alteration in echogenicity of the white matter is thought to be caused by gliosis of the centrum semiovale (Fariello et al. 1993).

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**Fig. 11** Lissencephaly. (a) Coronal section through the anterior fontanelle with high-frequency linear array transducer: smooth surface; the interhemispheric fissure is not flanked by branching sulci (black arrows); the ventricles are enlarged. (b) Far lateral sagittal sonogram displaying the smooth surface of the insula

**Fig. 12** Type II (open lips) schizencephaly. Coronal section through the anterior fontanelle: open cleft walls of a bridge containing CSF between the leptomeninges and the dilated lateral ventricle (white arrows)
Schizencephaly
Sonography is limited in its capacity to depict the periphery of the brain, particularly near the vertex. Angulation of the probe toward the imaged side of the brain improves coronal imaging of the parenchyma between the lateral ventricle and its nearby cortical surface. This is especially true at the level of the sylvian fissure, a site of particular concern for schizencephaly. Type II (open lips) schizencephaly is easier to diagnose as sonography demonstrates an open cleft containing CSF between the leptomeninges and the dilated lateral ventricle (Fig. 12). Sonography also allows identification of the gray and white matter and the gray matter infolding within the clefts: cortical echoes are always present along the sides of the cleft. In type I (fused lips) schizencephaly, the walls of the clefts are apposed, and no CSF space is seen. This makes the sonographic diagnosis difficult, but the presence of dimpling of the lateral ventricular wall may aid in the diagnosis. Neuronal heterotopia bordering the fissure can be detected by sonography as crude nodules causing the slit to become undulated (Babcock 1986; Patel et al. 1997; Gedikbasi et al. 2009; Pellicer et al. 1995). Color Doppler may demonstrate a colored vessel within the hyperechoic linear image of the cleft, a pathognomonic finding of schizencephaly (Couture and Veyrac 2001).

Heterotopia
Usually, the heterotopic gray matter is isoechoic to the normal brain so that it may be suspected only when the walls of the lateral ventricles are corrugated and rounded bulges in the ventricular cavity are present (Govaert and De Vries 2010; Patel et al. 1997, Pellicer et al. 1995).

Posterior Fossa Anomalies

Dandy–Walker Malformation
The typical sonographic features of the Dandy–Walker malformation are (Fig. 13) (1) a large triangular anechoic structure in the posterior fossa, whose base is inferior, in close contact with the occipital bone; (2) an elevation of the tentorium cerebelli, as shown by the separation of the occipital horns on coronal scan; (3) an absence of a normal fourth ventricle; (4) a dilated cerebral aqueduct in communication with the cyst; (5) vermian remnants, often rotated dorsally and cranially, which appear as a small hyperechoic structure wedged between the cyst inferiorly and the posterior part of the third ventricle.

Fig. 13 Dandy–Walker malformation. Midsagittal scan through the anterior fontanelle: large anechoic structure in the posterior fossa (black arrows), vermian remnants (open white arrows), and dilated third ventricle (3). Compare with Fig. 18 (large posterior fossa arachnoid cyst)
superiorly (vermian agenesis/hypoplasia is better demonstrated on coronal scans where the cystic structure separates the small cerebral hemispheres); and (6) a variable dilatation of the third and lateral ventricles (Deeg and Gassner 2010b; Veyrac et al. 1986; Groenhout et al. 1984; Barkovich et al. 1989).

The Dandy–Walker malformation must be differentiated from a large posterior fossa arachnoid cyst (Fig. 18) and a mega cisterna magna. In both these malformations, the fourth ventricle, cerebellar hemispheres, and vermis appear normally developed, although they are compressed and displaced in case of an arachnoid cyst. The differential diagnosis between a mega cisterna magna and vermian hypoplasia or dysgenesis without ventricular dilatation requires MRI (Siegel 2011; Bowerman 1987). A detailed study of the spine should be performed, as dysraphic malformations of the spine may coexist (Coley and Siegel 2011).

**Vascular Malformations**

Arteriovenous malformations of the brain may occur in any location, most commonly in the parietal lobes, followed by the occipital lobes. Large malformations, such as vein of Galen aneurysmal malformations, can be easily demonstrated by sonography, while smaller, more peripheral ones may not (Babcock 1986). However, color Doppler could be attempted in cases of congestive heart failure or neonatal seizure, before more invasive investigations are performed (Couture and Veyrac 2001).

**Vein of Galen Aneurysmal Malformation**

On coronal view (Fig. 14), a two-dimensional ultrasound shows a midline cystic structure placed between the lateral ventricles. On sagittal view it is located behind the third ventricle and the quadrigeminal plate. The cyst may compress the posterior part of the third ventricle and the aqueduct, causing obstructive hydrocephalus. Posteriorly, it extends into the dilated straight sinus and torcular Herophili. When thrombosed, it becomes echoic. Pulsations of the mass or surrounding dilated feeding arteries can be identified. Brain atrophy with parenchymal calcifications may result from the ischemia due to vascular steal. Areas of decreased echogenicity represent regions of necrosis (Mansour and Veyrac 1987; Mullaart et al. 1982; Newlin et al. 1981; Cubberley et al. 1982; Abbitt et al. 1990). The differential diagnosis includes other supratentorial cystic lesions, particularly quadrigeminal cysts.

Doppler evaluation (Fig. 14) immediately excludes a cyst or cisternal dilatation, showing turbulent flow within the aneurysm as well as feeding arteries and markedly dilated straight sinus and torcular Herophili (Govaert and De Vries 2010). Both systolic and end-diastolic velocities in the internal carotid arteries, anterior cerebral arteries, and basilar arteries are pathologically high (up to >1 and >0.5 m/s, respectively) with pathologic low RI (Meila et al. 2015). According to Couture et al., color and pulsed Doppler may be useful to diagnose and estimate the prognosis of vein of Galen aneurysmal malformations. Ideally, they should be used antenatally. All criteria of postnatal sonography may be applied to the fetus, including color Doppler diagnosis and color/pulsed Doppler determination of the prognosis (feeding arteries, draining veins, degree of heart failure). The concept of stealing and deprived arteries appears extremely valuable. It is essential to analyze the entire intracerebral vasculature by pulsed Doppler to define the risk of ischemic brain damage. This requires a prolonged and difficult study protocol of the fetal brain (arterial and venous network) in order to distinguish cases with good and poor prognosis and to predict a poor outcome (wide shunt, heart failure, ischemic brain damage) (Couture and Veyrac 2001; Deeg and Scharf 1990; Eltohami and Robida 1992; Westra et al. 1993; White et al. 1992; Tessler et al. 1989; Stockberger et al. 1993).

Hemodynamic changes after embolization include improvement in blood supply to uninvolved portions of the brain and increase in caliber and flow of feeding vessels that have not been occluded during embolization. Serial volume flow measurements must be performed with Doppler sonography in major extracranial arteries. The success of embolization is indicated by substantial decrease of total
Fig. 14 Vein of Galen aneurysmal malformation. (a) Posterior coronal view through the anterior fontanelle: grayscale ultrasound shows a midline cystic structure (open white arrowhead) placed between the lateral ventricles. (b) On midsagittal view the cyst is located behind the third ventricle and the quadrigeminal plate. The color Doppler ((c): coronal scan, (d): midsagittal scan) shows a counterclockwise swirling appearance of the flow within the lesion; the feeding arteries have an increased velocity. (e) The spectral analysis of the aneurysmal pouch shows an arterial spectrum with a turbulent high-velocity flow.

carotid artery flow and increase of RI (Meila et al. 2015). Color Doppler may be a noninvasive modality that adds important imaging and hemodynamic data to those provided by angiography (Westra et al. 1993).
Sinus Pericranii

Color Doppler can be diagnostic in displaying a venous vessel crossing the hyperechoic cranial vault (Kim et al. 2011; Antoun et al. 1997). Because of the mirror-image artifact caused by a bone (an acoustic mirror), a superficial vessel may artifactually appear to cross the cranial vault and to extend intracranially.

Sonography is important to perform the differential diagnosis with other extracranial lesions and malformations, such as cavernous hemangioma, meningocele (Fig. 15), leptomeningeal cyst, dermoid (Fig. 16), and epidermoid cyst (Fig. 17).

Fig. 15 Meningocele. (a) High-resolution coronal section through the anterior fontanelle and (b) high-resolution midsagittal section with color Doppler. An extracranial mass above the anterior fontanelle with a cystic and avascular appearance (arrowheads); SS superior sagittal sinus

Fig. 16 Dermoid cyst at the nasal bridge. High-resolution longitudinal scan (color Doppler): avascular mass filled with low-level echoes

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Intracranial Fluid Collections

Arachnoid Cysts
Two-thirds of these lesions are located supratentorially, especially in the middle cranial fossa and along the sylvian fissure (Gosalakkal 2002). They appear as anechoic fluid spaces that do not communicate with the subarachnoid space or ventricles (Fig. 18). Since vascular structures appear anechoic, Doppler should be used to differentiate them from arachnoid cysts (Govaert and De Vries 2010; Couture et al. 1994; Barr 1999; Chuang and Harwood-Nash 1986).

Hydrocephalus
Hydrocephalus refers to the dilatation of the ventricular system associated with increased intraventricular pressure. Usually, the cause is an obstruction to the circulation of the CSF (congenital aqueductal stenosis, posthemorrhagic in premature infants, postinfectious, myelomeningocele, and tumor). It must be distinguished from ventriculomegaly due to parenchymal loss (ex vacuo). Sonography identifies the level of obstruction as the point of transition from a dilated to a small ventricle. According to Govaert and deVries (2010), sonography may suggest the differential diagnosis between true hydrocephalus and ventriculomegaly ex vacuo. In the latter situation one deals with microcephalic children, with normal fontanelle.
tension. Occipital as well as frontal ventricular segments are affected in ventriculomegaly ex vacuo, whereas prominent occipital dilatation is typical of obstructive hydrocephalus. In case of brain atrophy, dilated subarachnoid spaces and interhemispheric fissure are found. Changes in the velocity of the cerebral arterial flow may be seen only with obstructive hydrocephalus.

Doppler ultrasound has been increasingly used to assess changes of cerebral hemodynamics in infants and children with hydrocephalus. There is general agreement that a direct correlation exists between the intracranial pressure (from experimental, fontanometric, and direct measurement evidence) and the RI. In addition, this increasing index is predominantly due to a reduction in the end-diastolic velocity. Stable ventriculomegaly is associated with normal pulsatility. Cerebral blood flow velocity parameters change significantly following CSF drainage by tapping or shunting. The measurements of intracranial pressure and cerebral blood flow velocity are currently the best ways of assessing the need for CSF diversion and monitoring subsequent shunt function (Couture and Veyrac 2001; Goh and Minns 1995). Actually, in cases of slowly progressive or stabilized dilatation, the hemodynamic assessment (velocities and indices) is usually normal, probably because of compensatory mechanisms. On this subject, Taylor and Madsen (1996) described a statistically significant correlation between the change in RI during fontanelle compression and elevated intracranial pressure (Fig. 19). These authors demonstrated that the hemodynamic response to fontanelle compression during Doppler sonography could be used to indirectly assess the intracranial pressure and help to determine the need for shunt placement in hydrocephalic infants. They proposed a sensitization test by a single, brief (3–5 s), and firm fontanellar compression, with measurement of pre- and postcompression RI and of ΔRI (percentage of change in RI defined as fontanellar compression RI – baseline RI/baseline RI, normal value, 1–19 %). If cerebral compliance is disturbed, shunting is required. The neurosurgical placement of extraventricular shunts aims to avoid increasing intracranial pressure with possible subsequent herniation. Infants with shunts can be followed reliably with sonography, avoiding repeated CT or MRI scans (Kipphuth et al. 2011; Mandiwanza et al. 2013).

The most frequently used parameter for monitoring ventricular size in infants with intraventricular hemorrhage is the ventricular index (VI): $VI = \text{total width of the lateral ventricle on coronal view}/\text{total biparietal width in the same image}$ (Brouwer et al. 2010). 3D sonography can be a useful tool to reduce examination time and facilitate follow-up (McLean et al. 2012).
Pericerebral Fluid Collections

Extracerebral fluid collections are a frequent finding on ultrasonography. The differential diagnosis includes communicating hydrocephalus due to extraventricular obstruction (hemorrhage, infection), subdural collections, and benign subarachnoid effusions, which represent the great majority and the most common reason for large heads in children.

In infants with macrocrania, increased CSF in the extra-axial spaces with normal to slightly enlarged ventricles is a common abnormality, but it is usually associated with a normal neurologic outcome and represents the so-called benign macrocrania. Affected infants usually present between 2 and 7 months of age with an enlarged or enlarging head. Usually, they are studied after neurologic examination and head circumference measurement. Sonography is the recommended initial procedure since it accurately evaluates ventricular size, extra-axial fluid, and congenital malformations. If sonography is normal or shows mildly increased fluid spaces, a follow-up with head circumference measurement and clinical evaluation will probably suffice. CT is indicated if there is a significant abnormality on sonography that requires further clarification (Babcock et al. 1988). The wide spaces are thought to be the result of immature arachnoid villi and impaired CSF absorption. The dilatation usually resolves by the second year of life (Siegel 2011). Often there is a family history of large heads.

The widening of the subarachnoid spaces can be echographically quantified. To differentiate normal from pathologically dilated subarachnoid spaces, the following upper limits have been proposed on the basis of the 95th percentile: 3 mm for sinocortical width, 4 mm for craniocortical width, and 6 mm for interhemispheric width (Libicher and Troger 1992).

High-frequency grayscale imaging can also differentiate subarachnoid effusions from subdural collections (Figs. 20 and 21). Subdural effusions are often of traumatic origin and frequently require neurosurgical intervention (subdural shunting). When the subdural fluid is not compressive, the subarachnoid space remains quite large, the sulci are widened, and the subarachnoid vessels are still visible, detached from the brain surface. The two compartments are separated by an echogenic membrane. When the subdural collection produces a mass effect, the subarachnoid space is embedded in the brain surface, the

Fig. 20 Benign macrocrania. High-resolution coronal section through the anterior fontanelle (color Doppler): arachnoid vessels (*) cross the enlarged subarachnoid space; SS superior sagittal sinus
subarachnoid vessels are not visible, and the sulci are narrowed or even closed (Couture et al. 1994). Color Doppler also supports the diagnosis based on the presence or absence of vessels bridging the fluid collection and on their appearance, situation, and direction (Figs. 20 and 21). In patients with benign subarachnoid space enlargement, color Doppler sonography detects arachnoid vessels (arteries and veins) within the fluid collection (cortical vein sign). On the contrary, the veins are displaced and embedded within the echogenic pia-arachnoid that surrounds the brain or are trapped in the subarachnoid spaces between the neo-membrane and the cortical surface in patients with subdural collections (Chen et al. 1996; Rupprecht et al. 1996). Actually, also subdural collections are bridged by some vessels: not the multiple small arteries and veins as in the subarachnoid space but some large veins that drain venous flow from the superficial venous network toward the superior sagittal sinus (Couture and Veyrac 2001). The fluid content of the subdural space may be characterized by sonography: hygroma is anechoic, whereas an acute subdural hematoma is echogenic with multiple thin echoes spread homogeneously. Empyema must be differentiated from reactive subdural effusion in infants with meningitis. The pattern is characterized by heterogeneous to hyperechoic convexity collections, hyperechoic strands, thick echogenic inner membrane, increased echogenicity of pia-arachnoid, exudates in the subarachnoid space, mass effect, and loculated extra-axial collections (Chen et al. 1998). Color Doppler detects intense hyperemia in the wall of the collection, in the septations, and in the underlying brain surface (Couture and Veyrac 2001).
Intracranial Hemorrhage

Premature Infants

Pathophysiology
Premature infants are at high risk for intracranial hemorrhage, which usually originates in the subependymal germinal matrix. It occurs in approximately 15% of premature infants with birth weight below 1,500 g (Volpe 2008; Sheth 1998). The germinal matrix is the site of origin for migrating cerebral neuroblasts between approximately 10–20 weeks of gestation. In the third trimester it provides glial precursors (Volpe 2008; Szymonowicz et al. 1984). It is located along the wall of the lateral ventricle and at 28–30 weeks is prevalent in the region of the caudothalamic groove at the head of the caudate nucleus, where it is not longer well visualized by 35 weeks (Yikilmaz and Taylor 2008). The germinal matrix is highly cellular, gelatinous in texture, and richly vascularized. The vessels within its capillary bed are immature and thin walled and, thus, prone to bleeding. The vascular origin of hemorrhage in premature infants is controversial and has been variously attributed to arteries, veins, arterioles, capillaries, or sinusoids (Brown et al. 1994). Recent studies (Govaert and De Vries 2010; Ghazi-Birry et al. 1997; Taylor 1997) show that the germinal matrix hemorrhage (GMH) in preterm neonates is primarily venous in origin. Hemorrhage can tunnel along the venous perivascular space, collapsing the vein and rupturing the tethered connecting tributaries (Fig. 22). The extravasation of blood from the arterial circulation appears to be much less common. In approximately 80% of cases, blood spills over from the germinal matrix to the lateral ventricles (Volpe 2008) because of loss of cerebral autoregulation with subsequent hypoxic damage to the sensitive capillaries in the germinal matrix (Heck et al. 2012). As the infant approaches term, the germinal matrix slowly involutes and the choroid plexus becomes the exclusive site of origin of the intraventricular hemorrhage (IVH) (Lacey and Terplan 1982). Actually, 46% of infants weighing less than 1,500 g with GMH and IVH also have choroid plexus hemorrhage (Armstrong et al. 1987).

Several factors may lead to intracranial hemorrhage, including intravascular, vascular, and extravascular ones. Intravascular causes include fluctuating cerebral blood flow (detectable by Doppler), increase in cerebral blood flow, increase in cerebral venous pressure, decrease in cerebral blood flow, and platelet and coagulation disturbances. Vascular factors are represented by tenuous capillary integrity and vulnerability of matrix capillaries to hypoxic–ischemic injury. Extravascular factors are classified in three categories: deficient vascular support, fibrinolytic activity, and postnatal decrease in extravascular tissue pressure (Volpe 2008).
The neuropathological consequences of IVH are germinal matrix destruction, periventricular hemorrhagic infarction, and posthemorrhagic hydrocephalus.

GMH regresses with cyst formation and/or gliosis, with possible noxious effects on later brain development.

Hemorrhage into the cerebral parenchymal tissue superolaterally to the angles of the lateral ventricles is a major cause of death and disability in preterm infants. It is associated with GMH/IVH, and its pathogenesis was previously referred to an extension of IVH. More recent studies have suggested that it is due to bleeding into tissue previously damaged by ischemia following cerebral hypoperfusion. The anatomic distribution and histological features of these hemorrhages suggest that they result from venous infarction and that the venous drainage of the periventricular tissues is obstructed by a large GMH/IVH at the level of the terminal veins, which run within the germinal matrix (Takashima et al. 1986; Gould et al. 1987). According to Volpe (2008; Guzzetta et al. 1986), parenchymal lesions are associated with large areas of the GMH/IVH in about 80% of cases, occur on the same side as the larger amount of the GMH/IVH, and develop and progress after the occurrence of the GMH/IVH. Also the high incidence of visceral intravascular thrombi and the fan-shaped appearance of the hemorrhage suggest venous hemorrhagic infarction (Perlman et al. 1993). Using color Doppler (coronal scans) to test this hypothesis in vivo, Taylor confirmed that obstruction of terminal veins by the GMH may play an important role in the pathogenesis of periventricular white matter hemorrhage (Fig. 25). The abnormality of the terminal veins occurs more frequently with GMH/parenchymal lesions (90%) than with the GMH alone (52%), and complete occlusion of the terminal veins is more common in GMH/parenchymal lesions (82%) than in the GMH alone (16%). GMH size correlates with increasing terminal vein abnormality (Taylor 1995; Dean and Taylor 1995). Counsell et al. (1999) reported an MRI study of a preterm neonate with bilateral GMH/IVH and hemorrhagic infarction in the periventricular white matter on the side of the larger amount of germinal matrix and intraventricular blood. In this case, they found a fan-shaped pattern along the course of the medullary veins consistent with a combination of intravascular thrombi and perivascular hemorrhage.

Posthemorrhagic hydrocephalus is due to the obstruction caused by blood clots (arachnoid villi, aqueductal obstruction), obliterative arachnoiditis (posterior fossa), disrupted ependyma, and reactive gliosis (aqueductal obstruction) (Volpe 2008).

**Sonography**

The GMH is seen as an echogenic focus due to the formation of a fibrin mesh within the organized clot. On coronal sections, the hyperechoic area is found underneath the floor of the frontal horn, whereas on parasagittal scans the bleeding appears as a prominence anterior to the caudothalamic groove (Shackelford and Volpe 1985). It appears as a rounded thickening of the choroid plexus near the foramen of Monro. Normal plexus is not present in the frontal and occipital horns, produces a symmetric picture, and contains micropulsations. Rarely, the GMH occurs in other areas along the body of the lateral ventricle where the germinal matrix has not involuted (at the level of the anterior part of the caudate nucleus at 24–26 gestational weeks). Over a period of weeks, the GMH liquefies and finally vanishes or evolves into a subependymal cyst. Hyperechoic subependymal nodules encountered in tuberous sclerosis, consisting of immature neuroglial cells, may mimic the GMH (Toma et al. 1997).

If a hemorrhage ruptures through the ependymal lining, the echogenic material can be identified within the ventricle (Shackelford and Volpe 1985; Bellah 1996; Bulas and Vezina 1999). Power Doppler sonography through the posterior fontanelle enhances the ability to distinguish normal choroid plexus (a vascular structure) from IVH in normal-sized ventricles (Di Salvo 2001; Seibert et al. 1998). The diagnosis of hemorrhage into the choroid plexus may be difficult. Appearances indicative of plexus bleeding are fuzziness of plexus outlines, hyperechogenicity of the cranial plexus on coronal section,
asymmetric hyperechogenicity within glomus tissue, and subsequent local cyst formation. Indirectly, the absence of an evident GMH may support this diagnosis (Govaert and De Vries 2010; Guermazi et al. 2000). Besides, at color/power Doppler choroid hemorrhage remains avascular, but this sign may be misleading since, frequently, the normal choroid plexus is not uniformly vascular (Seibert et al. 1998). According to Tatsuno et al. (1992), on color Doppler, colored CSF is a very early sign of IVH and may precede direct visualization of abnormal ventricular echoes. This sign is related to the presence of small particles in the CSF, and it appears as an alternatively red and blue signal in the sylvian aqueduct and fourth ventricle. This finding may be more easily evoked by movements of the child, such as sucking and crying.

When hemorrhage is extensive, an echogenic material can be seen to dilate the ventricles (Fig. 23). With severe IVH, the ventricle is completely filled with echogenic blood and has a cast-like appearance. IVH may be bilateral and symmetrical or it may be confined to one ventricle. In severe cases, even the third and fourth ventricles are filled with blood. After 2 or 3 weeks and persisting for several weeks, the ependymal lining of a ventricle that contains blood becomes irregular and hyperechogenic due to glial reaction to clot (Figs. 23, 24, and 25) (Gaisie et al. 1990). Over a period of weeks, the clot within the ventricle retracts and becomes progressively isoechoic from the center outward (Fig. 26), occasionally producing a “ventricle-within-a-ventricle” appearance and leaving behind a jumble of clot fragments in the cavity. Diffuse low-level echoes or blood/CSF levels can also be detected. Posthemorrhagic

Fig. 23 Intraventricular hemorrhage and parenchymal hemorrhagic infarction. (a) Coronal section through the anterior fontanelle: the frontal horn of the left ventricle is filled with echogenic blood; a hyperechoic parenchymal hemorrhagic infarction is adjacent to the same ventricle (white arrowheads); the frontal horn of the right ventricle (open white arrows) and the temporal horns (white arrows) are dilated; the ependymal lining of the ventricles is irregular and hyperechogenic. (b) Left parasagittal section: the lateral ventricle is flooded with hyperechoic blood (white arrowheads). (c) Coronal section through the anterior fontanelle after two months: the parenchymal hemorrhagic infarction is liquefied and integrated in a dilated lateral ventricle (white arrowhead); also the left temporal horn (white arrow) is dilated
hydrocephalus can be shown very well by cranial sonography (Govaert and De Vries 2010; Siegel 2011; Couture et al. 1994; Grant et al. 1987; Bellah 1996).

Parenchymal hemorrhagic infarction may be seen as a usually unilateral asymmetric echodensity, globular, crescentic, or fan-shaped in configuration, in the frontal and parietal regions adjacent to the lateral ventricle. Over 1–2 months, this area liquefies and is integrated into a curved, dilated lateral ventricle (Fig. 23) (Govaert and De Vries 2010; Volpe 1989, 2008; Perlman et al. 1993).
A standard grading system is important for reporting, record keeping, epidemiological studies, and prognostication (DiPietro 2002). The single score system of Papile et al. (1978), originally described for CT and the most commonly used, has been modified by Volpe (Volpe 2008):

- Grade 1 (35 %): GMH with no or minimal IVH (10 % of ventricular area on parasagittal view)
- Grade 2 (40 %): IVH (10 –50 % of ventricular area on parasagittal view)
- Grade 3 (25 %): IVH (>50 % of ventricular area on parasagittal view; usually distends the lateral ventricle)
- Separate notation: periventricular echodensity (15 %)

In the majority of cases, intracranial hemorrhage is a clinically silent syndrome (Dubowitz et al. 1981); therefore, a cranial sonographic examination has an appropriate and important role in screening the preterm infant (Volpe 2008; Bellah 1996). Serial ultrasound scans in infants with IVH have shown that the approximate time of occurrence of a GMH/IVH is on the first postnatal day in 50 % of cases, by day 2 in 25 %, by day 3 in 15 %, and beyond the fourth day in 10 %. Thus, one can expect that a scan on the fourth postnatal day would detect at least 90 % of the cases. Besides, since the hemorrhage progresses in about 20–40 % of all cases and typically reaches its maximal extent in 3–5 days, a second scan after about 5 days is generally recommended. According to Boal et al. (1995), routine screening could be delayed until the 2nd week without any risk to the patient’s health. The widespread use of a similar screening protocol would result in significantly fewer studies being performed, with an estimated saving, in the USA, of more than $3 million annually. Once an IVH is detected, infants should be followed at weekly intervals to screen the possible development of hydrocephalus, as the traditional clinical signs do not appear for days to weeks after onset of ventricular dilatation. Typically, the posterior horns of the lateral ventricles dilate before, and more severely than, the anterior horns. However, ventriculomegaly identified by sonography does not necessarily equate with hydrocephalus (progressive ventricular dilatation secondary to a disturbance in CSF dynamics), because ventricular dilatation may occur after IVH as a result of periventricular leukomalacia (PVL) or periventricular hemorrhagic infarction.

According to Volpe (2008), a progressive ventricular dilatation begins within 1–3 weeks after IVH. Sixty-five percent of infants with IVH exhibit no progressive ventricular dilatation, while the remaining 35 % develop a slowly progressive ventricular dilatation. Volpe emphasized the role of sonography for the management of this 35 %, based on the estimation of rate and severity of progression of ventricular dilatation and the Doppler measurements of RI (see above).
According to Couture and Veyrac (2001), with a knowledge and understanding of the multiple physiopathogenic mechanisms underlying the development of IVH in preterm infants, Doppler sonography may provide criteria indicating a risk of hemorrhage (predictive role) and severity of brain damage (prognostic role). Pulsed and color Doppler examination of the neonatal brain should be aimed at identifying the following:

1. Temporal fluctuations of the Doppler waveform, requiring a correction of unsynchronized ventilation by muscle paralysis or any other means (Perlman et al. 1983a)
2. Diagnosis of IVH based on alternate red and blue color Doppler signal in the sylvian aqueduct and fourth ventricle (Tatsuno et al. 1992)
3. Low blood flow velocities, suggesting possible risk of hypoxic–ischemic injury or germinal matrix hemorrhage during the reperfusion phase
4. High blood flow velocities, often associated with increased mean arterial blood pressure and suggesting direct rupture of germinal matrix vessels
5. Lack of cerebral autoregulation, appearing as intense changes in blood velocities during changes in mean arterial blood pressure
6. Increased RI, which can be associated with an increase in intracranial pressure, and with a patent ductus arteriosus, thus requiring heart sonography

Unfortunately, Doppler investigation, as performed in clinical practice, represents the hemodynamic situation of a short period, where only abnormal results have a predictive or prognostic value.

**Term Infants**

Intracranial hemorrhage of the term neonate includes extra-axial, intracerebellar, intraventricular, lobar, and basal ganglia hemorrhages. Actually, primary subarachnoid, intracerebellar, and intraventricular hemorrhage are more frequent in premature infants (Volpe 2008).

**Extradural Hemorrhage**

Neonatal extradural hematomas are a sign of mechanical trauma and usually follow a complicated delivery (Orman et al. 2015). Constant ultrasonographic features include a biconvex, echogenic, intracranial mass adjacent to the inner table of the skull. It is often located beneath a cranial fracture usually associated with a cephalohematoma. On the other hand, cephalohematoma may cause a mirror-image artifact mimicking epidural hematoma: color Doppler may help to avoid this pitfall (Cakmakci et al. 2003). Early liquefaction of the clot (within 24–48 h) is typical for this lesion. The diagnosis is best verified by CT (Govaert and De Vries 2010; Lam et al. 1991).

**Subdural Hemorrhage**

Usually, subdural hemorrhages are caused by trauma, such as grossly traumatic delivery or nonaccidental trauma. Bleeding is due to tentorial laceration with rupture of the straight sinus (infra-/supratentorial hemorrhage), occipital osteodiastasis with rupture of the occipital sinus (infratentorial hemorrhage), falx laceration with rupture of the inferior sagittal sinus (longitudinal cerebral fissure hemorrhage), and rupture of bridging, superficial cerebral veins (surface of cerebral convexity hemorrhage) (Volpe 2008). CT and MRI are the best techniques to examine these lesions (Govaert and De Vries 2010). The centrotentorial tear cannot be directly identified by sonography. However, a perilesional hemorrhage of sufficient size will show up in coronal sections as an echogenicity between the hyperechoic strips of choroid plexus. On sagittal sections, a hyperechogenicity is found behind the usual retrotectal white echo line of the quadrigeminal cistern (Govaert and De Vries 2010; Huang and Shen 1991). Hemorrhages with a
laterotentorial epicenter (basal subdural hematoma) look like a lobar temporal hemorrhage. Convexity subdural hemorrhage appears as a crescentic mass overlying the cerebral hemisphere and producing medial displacement of the sylvian fissure, midline shift, ventricular compression, sutural diastasis, changes in the sulcal pattern, and echogenicity of the ipsilateral side of the brain. Hydrocephalus is the most common complication (Lam and Cruz 1991). The echogenicity of the lesions depends on the presence of fibrin.

Subarachnoid Hemorrhage
Primary subarachnoid hemorrhage is caused by trauma or circulatory events related to prematurity. Sonography is relatively insensitive for detection of small amounts of blood. Hyperechogenicity or a fluid collection over the cerebral convexity or in the sylvian fissure can suggest a large hemorrhage (Govaert and De Vries 2010; Siegel 2011; Volpe 2008). A highly specific, although somewhat insensitive, sonographic diagnosis of subarachnoid hemorrhage can be made from the appearance of the subarachnoid cisterns: increased echogenicity and/or increased echo-free content (Kazam et al. 1994).

Cerebellar Hemorrhage
In premature infants cerebellar hemorrhage is due to increased venous pressure, pressure-passive cerebellar circulation, and intrinsic vulnerability of certain capillaries (subependymal and subpial germinal matrices) (McCarthy et al. 2011). In term neonates, trauma and disturbed coagulation are the most common causes. The possible lesions are primary intracerebellar hemorrhage, venous infarction, extension into the cerebellum of IVH or subarachnoid hemorrhage, and laceration of the cerebellum or rupture of major veins of the occipital sinus (in term infants with a traumatic delivery) (Volpe 2008). Due to the

![Cerebellar Hemorrhage](image)

*Fig. 27* Cerebellar hemorrhage. Coronal section through the anterior fontanelle: echogenic focus within the cerebellum (*white arrows*)
echogenicity of the cerebellum, areas of infarction and hemorrhage can easily be missed sonographically. Through anterior fontanelle scanning, the lesions are best identified on the coronal scan, but imaging via the posterolateral fontanelle may demonstrate cerebellar hemorrhage missed by the anterior fontanellar approach (Soudack et al. 2013). Sonography demonstrates an ill-defined echogenic focus within the cerebellar region (Fig. 27) (Perlman et al. 1983b; Foy et al. 1982; Benders et al. 2014). Hemorrhages occurring while the patients are on anticoagulant therapy (e.g., during extracorporeal membrane oxygenation – ECMO) are less echogenic than those in babies with normal clotting factors (Govaert and De Vries 2010; Barr 1999). Cerebellar hemorrhage is an underrecognized and poorly visualized complication in preterm infants. In low birth weight infants, it may be clinically silent and not associated with significant supratentorial hemorrhage. Studies performed by MRI show that cerebellar hemorrhage is not unusual following perinatal hemorrhagic/ischemic anoxic injury. Cerebellar atrophy may also occur as a result of a vascular disease (Mercuri et al. 1997).

**Intraventricular Hemorrhage**

The site of origin of IVH in term infants is not only the choroid plexus but also the thalamus and the subependymal germinal matrix. The causes are trauma and the same pathologic factors of the preterm babies. The sonographic patterns are also the same (Volpe 2008; Montoya et al. 1987).

**Lobar and Basal Ganglia Hemorrhages**

Parenchymal hemorrhages may have different causes: trauma, infarction (the unilateral thalamic/gray nuclei lesions are typical), coagulation disturbances, vascular defects, cerebral tumors, unknown causes, and ECMO (Volpe 2008; Hanigan et al. 1995; Pierre-Kahn et al. 1985; Govaert et al. 1992; Trounce et al. 1985). By sonography, lobar hematomas appear as round or elliptic echogenic masses (Fig. 28). After a few weeks, a cystic regression of a part of the affected lobe occurs. The overlying cortex is often necrotic. IVH and extra-axial hemorrhages can coexist. In basal ganglia hemorrhages, sonography depicts asymmetric or unilateral particularly echogenic lesions in the thalamus and/or caudate nucleus (Fig. 29) (Govaert and De Vries 2010).

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Fig. 28  Bilateral anterior cerebral artery hemorrhagic infarction in an infant after surgery for necrotizing enterocolitis. (a, b) Coronal views through the anterior fontanelle: bilateral lobar echogenic masses.
Brain injury in the premature infant is an extremely important problem, partly because of the large absolute number of infants affected accounting about 2–9 of every 1,000 live births (Swarte et al. 2009). The two principal brain lesions that underlie the neurological manifestations subsequently observed in premature infants are periventricular hemorrhagic infarction (see above) and PVL (Volpe 1998).

**Hypoxic–Ischemic Encephalopathy**

**Premature Infants**

Brain injury in the premature infant is an extremely important problem, partly because of the large absolute number of infants affected accounting about 2–9 of every 1,000 live births (Swarte et al. 2009). The two principal brain lesions that underlie the neurological manifestations subsequently observed in premature infants are periventricular hemorrhagic infarction (see above) and PVL (Volpe 1998).

**Periventricular Leukomalacia**

Pathophysiology  PVL is an important cause of perinatal morbidity: visual impairment, spastic diplegia, and quadriplegia are common long-term sequelae. The incidence of sonographic PVL (5–25 % in
premature infants) is much lower than that observed at autopsy (Govaert and De Vries 2010; Volpe 2008). It can occur also in utero or perinatally. The neuropathological pattern is characterized by both focal periventricular necrosis and more diffuse cerebral white matter injury. Focal necrotic lesions occur at the level of the deep cerebral white matter, more frequently near the trigone of the lateral ventricles and around the foramen of Monro. They are characterized by coagulation (6–12 h) and later (1–3 weeks) by cystic necrosis (Banker and Larroche 1962). Subsequently, the fluid is absorbed, and gliosis, deficient myelin, and focal ventricular dilatation are the sequelae. Necrotic white matter may bleed secondarily (25 % of cases) (Paneth et al. 1990). Unlike the hemorrhagic venous infarction associated to IVH, the hemorrhage in PVL occurs on a background of coagulation necrosis. The diffuse component of PVL (telencephalic leukoencephalopathy) is nonnecrotic, gliotic, and noncystic. The sequelae are hypomyelination and ventriculomegaly (Gilles and Murphy 1969).

PVL is seen more often in premature infants, low birth weight infants, and infants requiring prolonged ventilator support. Many factors contribute to the development of PVL: periventricular vascular anatomic and physiological factors, cerebral ischemia–impaired cerebrovascular autoregulation–pressure-passive cerebral circulation, intrinsic vulnerability of cerebral white matter of premature newborns, intrauterine infection–inflammation–cytokine release, and glutamate toxicity (Volpe 2008). The lesions of primary leukomalacia are localized in watershed areas called arterial end zones. The cerebral vascular supply of the immediate periventricular region explains the occurrence of PVL, which is focal where long and basal penetrating vessels terminate or diffuse resulting from lack of interconnection between long and short
penetrating vessels. The infants with leukomalacia have either poorly developed vessels (a function of gestational age) or severe clinical complications producing ischemia, or both (Volpe 1997; Rorke 1992; Takashima and Tanaka 1978). In addition, a very low physiological blood flow to cerebral white matter in premature infants has been demonstrated, and the periventricular vessels have immature autoregulation (limited ability to dilate in response to demand), insufficient to compensate for transient hypoxia, hypercapnia, and hypotension (Volpe 2008).

**Sonography** In preterm infants, PVL can occur up to term age (Govaert and De Vries 2010). Initially, it appears as bilateral echogenic intraparenchymal lesions at the external angle of the lateral ventricles, radiating anteriorly from the trigone to the foramen of Monro (Fig. 30). The echodensities can be coarse, punctate, patchy, and occasionally asymmetric (Bellah 1996; Bowerman et al. 1984). The increased echogenicity usually occurs within a few days after the insult and is transient. Scans must not be limited to the central germinal matrix regions of the brain. To adequately see the white matter, the scanning fields must extend as far forward as possible into the frontal lobes, posteriorly into the occipital lobes, and as laterally to the left and to the right as possible (DiPietro 2002). With time (1–3 weeks), cystic components develop within the echogenic zone (Fig. 31). The cysts grow and then gradually disappear (1–3 months), leaving an irregularly dilated, angular lateral ventricle. The entity of the cystic leukomalacia and of the ventricular dilatation strongly correlates with the residual neuromotor dysfunction (Volpe 2008; Holling and Leviton 1999). This is the pattern of the deep focal necrotic lesions of PVL. The diffuse, nonnecrotic component of PVL is not visualized well by sonography (Volpe 2008). Actually, the correlation between cranial sonograms and postmortem examination neurodiagnoses demonstrates the sensitivity of sonography is low: as much as 70 % of injuries are not detected, and not only the diffuse components but also small focal necrotic components (<1 cm) can be missed (Volpe 2008; Adcock et al. 1998). About specificity, the crucial problem is the differential diagnosis with the normal periventricular echogenic blush, which is more pronounced the shorter the gestation (see above). Abnormal hyperechogenicities usually match or exceed plexus density (DiPietro et al. 1986). The changes of the pattern, such as increased echogenicity, presence of small cysts, and ventricular dilatation, are signs of PVL. In vivo distinction between PVL and hemorrhagic venous infarction may be difficult because the pathogeneses overlap and they can coexist. Anyway, hemorrhagic venous infarction versus PVL is always grossly hemorrhagic, markedly asymmetric, on the same side as IVH, usually more anterior, and with a roughly triangular appearance. The single large porencephalic cyst detectable during the evolution differs from the multiple small cysts observed as a consequence of PVL, which never communicate with the lateral ventricle. Infants with unilateral localized damage to the frontal white matter associated with hemorrhagic venous infarction have a better neurodevelopmental outcome than those with PVL (Volpe 2008; Bellah 1996).

According to Couture and Veyrac, hemodynamic assessment remains extremely disappointing in PVL, and one is still unable to help in preventing this damage and its severe motor consequences (Couture and Veyrac 2001). On the contrary, Blankenberg et al., evaluating the lenticulostriate arteries with power and pulsed wave Doppler, demonstrated fluctuations in cerebral blood flow, increased velocities, and significantly lower RI in neonates with a PVL, a GMH, or both than in neonates without (Blankenberg et al. 1997).

**Term Infants**

Sonography is less sensitive in the identification of selective cortical (difficult to evaluate) or brainstem neuronal injuries (too far from the transducer). Lesions of the basal ganglia and thalamus can be better detected (Volpe 2008; Babcock 1995). Pathologically, ischemic injury in the term infant produces edema, neuronal necrosis, and white matter gliosis (Barkovich and Truwit 1990). With moderate or severe edema,
the brain parenchyma becomes hyperechoic, the sulci disappear, and the ventricles collapse (Siegel et al. 1984). Unlike the majority of the authors, Couture et al. (1994) emphasized the role of sonography in the identification of the main neuropathological entities.

**Selective Neuronal Necrosis**

High-frequency linear array transducers are necessary. Selective neuronal necrosis appears as a thick hyperechoic ribbon surrounding the normal subcortical white matter (Fig. 32). When the injury is

**Fig. 32** Selective neuronal necrosis. (a, b) Coronal and parasagittal sections through the anterior fontanelle with high-frequency linear array transducer: hyperechogenicity of the gray matter close to the interhemispheric fissure *(white arrows)*

**Fig. 33** Severe hypoxic–ischemic encephalopathy. (a, b) Coronal and parasagittal sections through the anterior fontanelle: gray matter involvement with extension to the subcortical white matter; ischemic lesion involving the right lenticulate nucleus *(white arrowhead)*. (c) Negative diastolic flow at pulsed Doppler suggests poor prognosis
massive, the gyri of the convexity and basal ganglia look like a hyperechoic patchwork (Fig. 33). The subcortical white matter may be involved, with disappearance of the cortico-subcortical differentiation (when the ischemia is only subcortical, it is increased). Sonography is inadequate to detect infratentorial extension of the injury (Couture et al. 1994).

Parasagittal Cerebral Injury

The areas of cortico-subcortical necrosis are in the border zones between the end fields of the major cerebral arteries, i.e., in the parasagittal superomedial aspects of cerebral convexities (Volpe 2008). High-resolution sonography may detect cortico-subcortical triangular echodensities, with their base toward the surface, under both the anterior and posterior fontanelles. Focal cystic lesions or atrophic scars follow in a short time (Govaert and De Vries 2010; Huang et al. 1987).

Ischemia and Necrosis in the Diencephalon and Basal Ganglia

The sonographic pattern (Fig. 34) is characterized by a symmetric hyperechogenicity, with regular contours, soft at first, visible from day 2–3, and by sparing of internal capsule, without ventricular bleeding. These signs allow differential diagnosis with hemorrhage. Cysts are never seen. Persistence (a bright thalamus may persist for months) and increase of density suggest genuine necrosis. Cerebral atrophy localized in the gangliothalamic region contributes to the development of ventriculomegaly (Naidich et al. 1986b; Connolly et al. 1994; Shen 1984; Cabanas et al. 1991).

According to Couture et al. (2006), hemodynamic assessment (color and pulsed Doppler imaging) provides extremely valuable information. It requires an investigator to be available within the intensive care unit. It also requires caution, because it reflects a brief instant in the course of the disease, with changing hemodynamic alterations. Perinatal asphyxia causes a prolonged drop in RI by increased diastolic amplitude and increased velocities (vasodilatation mainly due to hypoxemia, hypercapnia, and fetal acidosis). Persistence of low RI in the first days of life after restoration of biological parameters is a sign of tissue necrosis (Stark and Seibert 1994). Different hypotheses have been proposed: vasodilatation due to acidosis, paralysis of arteriolar vasomotricity (Levene et al. 1989), brain edema with compression of brain vessels, and increased diastolic flow (Deeg et al. 1990). Rarely, newborns demonstrate decreased diastolic flow velocities (excessive vascular compression from edema?); these patients have the worst outcome (Fig. 33).

Many authors emphasized the study of velocimetric measures versus RI in evaluating the prognosis. In the series of Levene et al. (1989), the positive predictive value of cerebral blood flow velocity measurements less than 2 SD or greater than 3 SD for death or severe impairment is 94 %, compared with 83 % for

Fig. 34 Ischemia and necrosis in the basal ganglia. Coronal and parasagittal sections through the anterior fontanelle: symmetric hyperechogenicity of the basal ganglia (open white arrowheads)
low RI alone. Ilves et al. (1998) studied by pulsed Doppler 39 asphyxiated and 35 healthy term newborn infants during the first days of life. Asphyxiated infants, investigated at the age of 12 +/− 2 h, with moderate-stage and severe-stage hypoxic–ischemic encephalopathy had respectively decreased (15.6 +/− 3.9 cm/s) and increased (26.5 +/− 9.6 cm/s) mean cerebral blood flow velocity in the middle cerebral artery compared to the control group (20.9 +/− 3.7 cm/s). Four out of six infants with severe-stage and mean cerebral blood flow velocity of 3 SD above the mean for normal infants at the age of 12 h died, and two developed multicystic encephalopathy during the neonatal period. Four out of six infants had a normal RI, which became low only at 24 h of life. Thus, measuring RI alone in the first 12 h is insufficient. Also, Eken et al. (1995) demonstrated that ultrasonography and Doppler RI were of little value in the early stage. In 34 full-term infants with hypoxic–ischemic encephalopathy studied within 6 h of life, cerebral blood flow velocity measurements provided the most useful information about the expected course of encephalopathy and subsequent neurodevelopmental outcome. According to Couture and Veyrac, velocimetric alterations appear to be the most reliable guarantee of an accurate early prognostic assessment (Couture and Veyrac 2001).

**Focal or Multifocal Ischemic Brain Necrosis**

According to Volpe, this group comprises the localized areas of necrosis that occur within the distribution of single or multiple major cerebral vessels (left, right, or bilateral middle cerebral artery, other arteries, venous thrombosis, etc.) (Volpe 2008).

The most characteristic sonographic findings of infarction (Figs. 28 and 29) are absence of gyral definition, absence of vascular pulsations, altered parenchymal echogenicity, and territorial distribution. The affected areas are brighter due to edema and, later, necrosis with glial reaction and new capillary formation. Mass effect, reflected in ventricular size and shift of midline structures, may also be seen and largely parallels the extent of the infarction. Evolution of infarcts is characterized by a gradual resumption of arterial pulsations and concurrent development of cystic spaces (Govaert and De Vries 2010; Balcom and Redmond 1997; de Vries et al. 1997, 1988; Hernanz-Schulman et al. 1988).

Doppler study in infants with hypoxic–ischemic infarcts shows increased size and number of visible vessels in the periphery of the infarct and increased mean blood flow velocity in vessels supplying or draining the infarcted areas. The hyperemia may be due to breakdown of the blood–brain barrier and neuronal disruption with release of vasoactive substances. Actually, luxury perfusion may extend also in the contralateral hemisphere. The visualization of the vessels in the infarct is decreased, and the signal in the arteries that supply the region is absent. Color Doppler imaging may be used to follow the slow vascular recovery after neonatal infarction (Couture and Veyrac 2001; Taylor 1994).

Occasionally, focal small nodular hyperechogenicities at the level of thalami, basal ganglia, capsules, and periventricular region may be seen. The pathogenesis is as yet insufficiently understood (Govaert and De Vries 2010).

Dehydration, congenital heart diseases, infectious diseases, and perinatal asphyxia mainly cause sinus/venous thrombosis. Ultrasonography provides important information for diagnosing cerebral venous thrombosis (Fig. 29). Sonographic diagnosis of superior sagittal sinus thrombosis is easy; detection of extensive or deep vein thrombosis (internal cerebral vein, vein of Galen, straight sinus) is possible. The thrombosed superior sagittal sinus appears as a large hyperechoic triangle with convex walls. The absence of flow at color Doppler confirms the diagnosis. Usually, thromboses in other sinuses and cerebral veins represent the extension of a superior sagittal sinus thrombosis; morphological sonography provides no information, and color Doppler is required. After 1 month of age, since a normal straight sinus may not be displayed, MRI is required for a complete evaluation. In the case of venous infarction, a subcortical zone in the adjacent brain parenchyma will be hyperechoic. During follow-up, detection of complications, such as edema, intracranial hypertension (increased RI), or pericerebral collection, and evaluation of resolution
may be based on ultrasonography. Usually, the progressive decrease in size of the clot precedes recanalization. Several authors described the presence of collateral circulation around the sinus (Couture and Veyrac 2001; Govaert and De Vries 2010; Couture et al. 1994; Dean and Taylor 1995; Lam 1995; Pedespan et al. 1996; Raets et al. 2013).

**Intracranial Infections**

**Congenital Infections**

Common causes of meningoencephalitis in the fetus are TORCH group infections. Cranial ultrasonography defines subependymal cysts, mild ventriculomegaly, periventricular calcifications, intraventricular strands with dense ependymal borders (ventriculitis), and hyperechogenicity followed by cysts in the white matter due to leukomalacia. Calcifications appear as brightly echogenic foci, varying in number, with or without distal acoustic shadowing. As a rule, cytomegalovirus infection is suggested when calcifications are located near the ventricular wall. However, periventricular calcifications also occur in congenital rubella and herpesvirus infection. Toxoplasmosis is characterized by parenchymal calcifications (difficult to detect by sonography if small and peripheral) and periaqueductal calcifications. About the subependymal cysts, see the previous discussion. The sonographic findings are not specific (Govaert

**Fig. 35** Lenticulostriate vasculopathy. (a–c) Coronal and parasagittal sections through the anterior fontanelle: echogenic streaks in the basal ganglia (white arrowheads); color Doppler shows the stripes are arteries.

Neonatal branching echogenic streaks in the basal ganglia and thalami or “lenticulostriate vasculopathy” (LSV) had originally been associated with prenatal TORCH infection, especially cytomegalovirus. They resemble a “branched candlestick.” Different patterns have been described, including punctuate, linear, and mixed. The lenticulostriate arteries are not normally visible by grayscale sonography, but their Doppler signal may be elicited in normal children and they are rendered vividly visible by color Doppler, which shows these stripes in vivo to be arteries (Fig. 35). Usually, CT and MRI fail to indicate this abnormality. Necropsy reveals basophilic deposits in the walls of involved arteries. Likely, sonographic LSV is a nonspecific marker of a previous insult to the developing brain. Other diagnoses encountered include HIV infection, trisomy 13, Down syndrome, neonatal asphyxia, nonimmune hydrops, fetal alcohol syndrome, neonatal lupus, neonatal hypoglycemia, neonatal sialidosis, Zellweger syndrome, galactosemia, etc. Albeit nonspecific, this finding should alert the physician to the possibility of congenital infection or chromosomal abnormality, and patients need complete screening for possible in utero infection and perhaps also chromosomal analysis (Govaert and De Vries 2010; DiPietro 2002; Hughes et al. 1991; Teele et al. 1988; Ben-Ami et al. 1990; Cabanas et al. 1994; Toma et al. 1989; Bode and Rudin 1995; Kriss and Kriss 1996; Wang et al. 1995; Coley et al. 2000; El Ayoubi et al. 2003). The prognostic significance of this finding is yet to be determined. In the series of Wang and Kuo, the rates of neuropsychiatric disorders were 10 % in the symptomatic group and 54 % in the cryptogenic group; they concluded that idiopathic sonographic LSV in infancy may predict development of neuropsychiatric disorders later in childhood (Wang and Kuo 2003). According to El Ayoubi et al., minor or moderate isolated LSV generally have a good long-term prognosis, and associated forms of any severity depend mainly upon the severity of PVL; major forms of LSV must be a warning sign of a possible underlying congenital anomaly which will rule the vital and functional prognosis (El Ayoubi et al. 2004). On the contrary, Makhoul et al. concluded that, except for more multiple births, neonates with LSV do not display more adverse findings than their matched controls (Makhoul et al. 2003).

Neonatal Bacterial Infections

Transfontanellar real-time sonographic examination of the brain is a reliable, informative, and relatively inexpensive method of documenting and monitoring complicated bacterial meningitis. The spectrum of sonographic features of meningitis includes normal scans, echogenic sulci, evidence of ventriculitis, ventriculomegaly, extra-axial fluid collections, abnormal parenchymal echogenicity, brain abscess, and dural sinus thrombosis (Reeder and Sanders 1983; Rosenberg et al. 1983; Han et al. 1985).

The initial sonographic sign is brain swelling with small ventricular cavities and bright convolutional markings (Govaert and De Vries 2010). In this phase, increased cerebrovascular resistance may contribute to a relative impairment of cerebral perfusion. Couture described also a decrease in peak systolic and mean flow velocities and fluctuation of the Doppler waveform (sign of loss of cerebral autoregulation). Noninvasive monitoring by Doppler ultrasound may be helpful for early detection of deterioration in cerebral hemodynamic trends (Couture and Veyrac 2001; Goh and Minns 1993). According to Okten et al., cranial Doppler ultrasonography is useful for prediction of neurologic sequelae in infants with bacterial meningitis (Okten et al. 2002).

In the neonate, ventriculitis and inflammatory infiltration of the choroid plexus often accompany meningitis. Sonography detects ventricular dilatation with dense ventricular lining and increased periventricular echogenicity. The choroid plexus margins also appear poorly defined with loss of the normally smooth contour. Echogenic material is seen within the lateral ventricles, and intraventricular septa formation results in ventricular compartmentalization (Reeder and Sanders 1983). The detection of CSF flow in the aqueduct on color Doppler may indicate ventriculitis. The CSF flow demonstrates a
to-and-fro motion synchronized with cardiac pulsation and respiration. A prerequisite is the presence of scattering particles within the CSF (minimum concentration in the order of 1,000 cells/μl) (Winkler 1992; Tatsuno et al. 1993).

Venous infarcts (thrombi), frequently hemorrhagic, appear as hyperechoic nodules. They tend to be cortical, subcortical, periventricular, or subependymal in location. Eventually they give rise to cysts, sometimes of porencephalic nature. Arterial occlusions (arteritis) result in an arterial infarction (see above) (Rosenberg et al. 1983; Han et al. 1985).

Brain abscess at the early stage appears hyperechoic (Couture et al. 1994). All following stages of abscess evolution are characterized by an appearance of an echogenic rim with a hypoechoic center (Fig. 36). In the early stages, the echogenicity of the abscess is related primarily to marked cellular infiltration, while in the late stages extensive collagen deposition correlates closely with the echo pattern. The size of the abscess in the cerebritis stage appears smaller on sonography than on CT scan, because the latter detects the extensive cerebritis around the developing necrotic center, whereas sonography does not. This discrepancy disappears in the capsule stages. Sonography provides a more accurate depiction of the neuropathologic characteristics of necrosis compared to CT scan. Healing of the abscess, indicated by a decrease in size of the hypoechoic center, is accurately detected by sonography (Enzmann et al. 1982). Early perilesional hyperemia may be found by color Doppler. As the abscess wall gradually thickens, small peripheral vessels penetrate and colonize it (Couture and Veyrac 2001). Regarding extra-axial fluid collections and dural sinus thrombosis, see the previous discussion.

**Fig. 36** Brain abscess. (a, b) Coronal and parasagittal sections through the anterior fontanelle; (c) transcranial approach: well-circumscribed, thick-walled, fluid-filled lesions
Brain Tumors

Due to its simplicity, sonography is a good exploratory tool. It may be used as a screening procedure in infants with a large head or an abnormal neurologic examination and may be the first examination to demonstrate the tumor mass. Sonography must be performed very carefully in infants with hemorrhage without any identifiable case, because tumors can be associated with hemorrhage or might be misinterpreted as hemorrhage (Orman et al. 2015). MRI is essential (Han et al. 1984).

The hallmark of all tumors is mass effect and obliteration of normal anatomic landmarks. Hydrocephalus is usually present. Most solid neoplasms are hyperechoic when compared with the normal brain (Fig. 37). The internal structure is heterogeneous with cysts and calcifications in teratomas and extremely dense in choroid plexus papillomas. Astrocytomas of the posterior fossa are often cystic. Lipomas present as hyperechoic masses usually located at the level of the corpus callosum. They can also occur in the hypothalamus, in the subarachnoid spaces and in the glomus of the choroid plexus (Fig. 10) (Govaert and De Vries 2010; Couture et al. 1994; Barr 1999; Simanovsky and Taylor 2001; Suflanov et al. 1999; Puvabanditsin et al. 2002).

Doppler sonography can determine tumor vascularity. Choroid plexus papillomas (Fig. 38), which usually arise in the glomera of the lateral or third ventricle, are hypervascular with low-velocity shifts and bidirectional flow during diastole (Chow et al. 1986; Schellhas et al. 1988).

Fig. 37 Chiasmatic–hypothalamic glioma. (a–c) Coronal and midsagittal sections through the anterior fontanelle: poorly defined echogenic mass (open white arrowheads); internal structure is heterogeneous with cysts; (d) Color Doppler: the internal carotid artery and basilar artery, surrounding the mass, are displaced; 1 quadrigeminal plate; 2 fourth ventricle
The intraoperative use of ultrasound imaging is a reliable method for determining the size, shape, and localization of lesions. It can be used as a practicable, cost-effective, and time-saving real-time navigation system (Fig. 39) (Reinacher and van Velthoven 2003; Unsgaard et al. 2002).

**Brain Death**

McMenamin and Volpe (1983) described the characteristic changes in the flow velocity pattern in the anterior cerebral and common carotid arteries studied from the anterior fontanelle of the newborn. They defined a characteristic sequence of deterioration of the flow velocity waveform in both vessels. This sequence consists of loss of diastolic flow, appearance of retrograde flow during diastole, diminution in systolic flow in the anterior cerebral artery, and, ultimately, no detectable flow in the anterior cerebral artery, despite considerable flow in the common carotid artery. This constellation of findings suggests a progressive increase in cerebrovascular resistance and a progressive decrease in cerebral perfusion,
compatible with the diffuse cerebral necrosis and edema documented postmortem. Bode et al. (1988) recorded the blood flow velocities in the basal cerebral arteries by transcranial Doppler sonography and found a typical reverberating flow pattern, characterized by a counterbalancing short forward flow in systole and a short retrograde flow in early diastole. This indicates arrest of cerebral blood flow. In their series, no patient had the typical reverberating flow pattern without being clinically brain dead. However, the same authors observed one neonatal case in which the major basal vessels showed normal flow despite the presence of clinical and EEG criteria of brain death. Glasier et al. 1989 reported a similar experience. Shunting of blood through the circle of Willis without effective cerebral perfusion may explain this phenomenon. Sanker et al. (1992) described a case in which transcranial Doppler sonography demonstrated nearly normal cerebral perfusion, which even increased day by day despite persistence of other signs of brain death. This phenomenon of “cerebral reperfusion” was concluded to be compatible with the diagnosis of brain death. Besides, the cessation of flow velocity in the cerebral arteries may occur in the death of cerebrum but with preservation of the brainstem and, therefore, capacity of survival (Volpe 2008). Couture and Veyrac (2001) concluded that the literature review tends to demonstrate the inconsistency of Doppler changes in brain death. They emphasized that the clinical context remains an essential element to evaluate the hemodynamic patterns.

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