



Universiteit
Leiden
The Netherlands

State-of-the-art cranial ultrasound in clinical scenarios for infants born at term and near-term

Valverde, E.; Ybarra, M.; Bravo, M.C.; Dudink, J.; Govaert, P.; Horsch, S.; ... ; EurUS Brain Grp

Citation

Valverde, E., Ybarra, M., Bravo, M. C., Dudink, J., Govaert, P., Horsch, S., ... Pellicer, A. (2024). State-of-the-art cranial ultrasound in clinical scenarios for infants born at term and near-term. *Developmental Medicine & Child Neurology*, 67(3), 322-347.
doi:10.1111/dmcn.16133

Version: Publisher's Version

License: [Licensed under Article 25fa Copyright Act/Law \(Amendment Taverne\)](#)

Downloaded from: <https://hdl.handle.net/1887/4302728>

Note: To cite this publication please use the final published version (if applicable).

INVITED REVIEW

State-of-the-art cranial ultrasound in clinical scenarios for infants born at term and near-term

Eva Valverde¹  | Marta Ybarra¹ | Maria Carmen Bravo¹ | Jeroen Dudink² | Paul Govaert^{3,4}  | Sandra Horsch⁵  | Sylke Steggerda⁶ | Adelina Pellicer¹ | on behalf of The EurUS.Brain Group[#]

¹Department of Neonatology, La Paz University Hospital, Madrid, Spain

²Department of Neonatology, UMCU-Wilhelmina Children's Hospital, Utrecht, the Netherlands

³Department of Neonatology, UZBrussels, Brussels, Belgium

⁴Department of Neonatology, ZNA Middelheim, Antwerp, Belgium

⁵Department of Neonatology, Helios Klinikum Berlin Buch, Berlin, Germany

⁶Department of Neonatology, Leiden University Medical Center, Leiden, the Netherlands

Correspondence

Eva Valverde, Department of Neonatology, La Paz University Hospital, Madrid 28046, Spain.
Email: evam.valverde@salud.madrid.org

Abstract

Neonates admitted to the intensive care unit are at risk of brain injury. Importantly, infants with signs of neurological impairment need prompt diagnosis to guide intervention. Cranial ultrasound (CUS) is the first-line imaging tool for infants born preterm. New developments in this technology, which now incorporates high-resolution equipment, have notably improved the performance of CUS in infants born at term and near-term. On the other hand, the potential of CUS as a diagnostic tool in older infants is less established. The lack of studies focusing on this topic, local protocol variability among clinical sites, and divergent opinions on CUS patterns of disease entities are the main constraints. This review provides an overview of state-of-the-art CUS as a decision-making tool under different clinical scenarios, such as neonatal encephalopathy, seizures, and suspected central nervous system infection. The CUS features that characterize several patterns supporting a diagnosis are detailed, focusing on haemorrhage and infection.

Newborn infants who show abnormal neurological signs need a prompt diagnosis to be managed optimally. Neuroimaging is core to their work-up.¹ Cranial ultrasound (CUS) is a non-invasive bedside tool that can be used serially. It is currently the first-line imaging modality in the neonatal intensive care unit.^{2–5} Magnetic resonance imaging (MRI) provides a detailed extent of damage and the effect on myelination, and informs on cortical involvement, thereby increasing prognostic capacity.⁶ The need to transport the neonate, the associated costs, and scarcity in low- and middle-income countries constrain its clinical use. However, the complementarity of both imaging tools is very high, with CUS used at the start of the work-up and followed by information provided by an MRI, thus serially addressing the

evolution of the process. Due to radiation, the use of computed tomography (CT) should be restricted to emergencies.

The evolution of ultrasound devices, and multi-array micro-convex and linear high-frequency probes, has overcome previous limitations, such as poor image resolution. While the role of CUS in the diagnosis of brain injury in infants born preterm is well established,^{4,5} its value in infants born at term and near-term has yet to be confirmed. Advances in understanding the cause and course of traumatic brain injury, infarction, and metabolic and developmental problems, have changed attitudes towards CUS.^{4,5,7–9} A lack of studies focusing on the capacity of CUS in diagnosing brain injury in infants born at term, absence of uniform protocols, and divergent opinions on CUS patterns are some

Abbreviations: AIS, arterial ischaemic stroke; CSVT, cerebral sinovenous thrombosis; CUS, cranial ultrasound; HIE, hypoxic–ischaemic encephalopathy; ICH, intracranial haemorrhage; SDH, subdural haematoma.

Plain language summary: <https://onlinelibrary.wiley.com/doi/10.1111/dmcn.16172>

[#]Members of the EurUS.Brain study group are listed in the Acknowledgements.

© 2024 Mac Keith Press.

of the constraints. There is no consensus about the best use of CUS in emergency situations, such as seizures or acute neonatal encephalopathy. Whether CUS can alter the time frame of a definite diagnosis, reducing the number of MRIs (or not) remains to be evaluated.

This review summarizes the current role of CUS in the diagnosis and management of neonatal encephalopathy, birth trauma, seizures, and suspected central nervous system (CNS) infection. Congenital brain anomalies and preterm brain injury are not included in this review. We particularly focused on the evolving features and timing of brain injury patterns.

METHOD

A standard literature search was conducted in October 2021 using PubMed and medical subject headings (MeSH terms). A second search was done in August 2023. The search was carried out combining the concepts of neonate, CUS and hypoxic–ischaemic injury, hypoxic–ischaemic encephalopathy (HIE), intracranial haemorrhage (ICH), brain trauma, CNS infection, meningitis, stroke, and sinovenous thrombosis. Case reports, including detailed CUS findings, were also used. Four hundred and one abstracts were selected for review; among them, 110 (27%) were relevant for the issues

What this paper adds

- Using cranial ultrasound (CUS) systematically to diagnose several disease processes in infants born near-term and at term strengthens its potential.
- Large and clinically significant intracranial haemorrhages can be detected using CUS, thereby speeding up diagnosis and neurosurgical intervention.

to be addressed. This was supplemented by cross-references. No randomized clinical trials were found.

NEONATAL ENCEPHALOPATHY

Neonatal encephalopathy is a clinical entity characterized by abnormal consciousness, seizures, and deranged tone and reflexes.¹⁰ It is not cause-specific, and the aetiology may vary from hypoxia–ischaemia or infection to metabolic or genetic conditions.¹¹ In trying to establish the cause of neonatal encephalopathy, a detailed prenatal and perinatal history, a

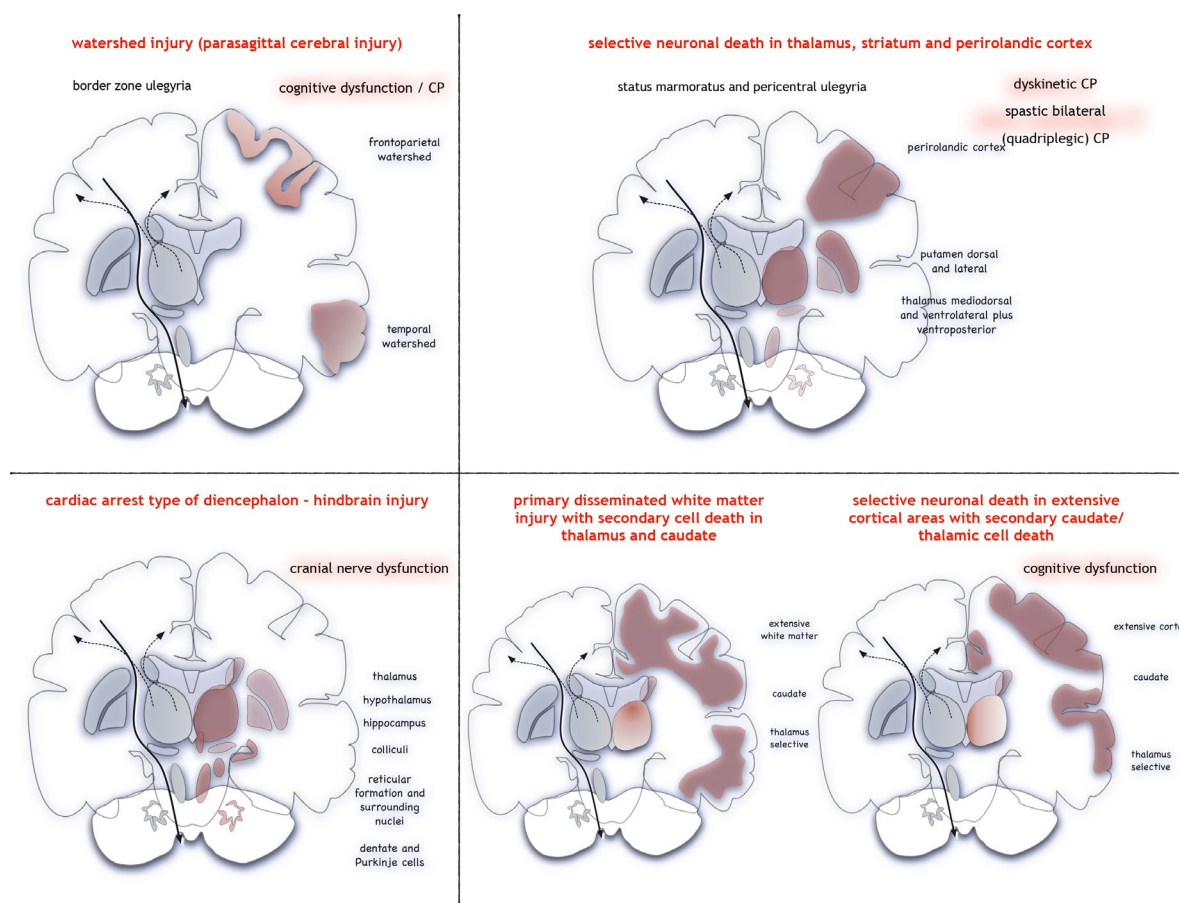


FIGURE 1 The most common brain injury patterns seen in infants born at term with intrapartum asphyxia and the most likely associated neurodevelopmental outcome. Abbreviation: CP, cerebral palsy.

clinical exam, laboratory and imaging studies, are part of the work-up. MRI and CUS are the two imaging modalities that should be used complementarily in these infants. Despite the high value of serial CUS imaging in an infant with neonatal encephalopathy we describe below, MRI should be considered in all infants that present with neonatal encephalopathy.

HYPOXIC-ISCHAEMIC ENCEPHALOPATHY

HIE refers to a specific diagnostic category in which functional alteration of the CNS is attributed to a hypoxic-ischaemic insult. Features of intrapartum asphyxia, such as acidosis, low Apgar score, need for advanced resuscitation at birth, and early organ failure linked to an acute peripartum hypoxic-ischaemic event point to a diagnosis of HIE. The presence of abnormal neurological signs immediately after birth and their evolving course, together with markers of tissue ischaemia in other organs, help in differentiating

hypoxia-ischaemia from other causes of neonatal encephalopathy, where there is a symptom-free interval (i.e. metabolic neonatal encephalopathy) or a more static course (i.e. genetic or malformative neonatal encephalopathy). The timing of the insult in relation to birth (antenatal or perinatal), and the type of insult (partial or total asphyxia), determine the pattern of damage and the extent of the injury.^{12, 13}

Two main pathophysiological patterns stand out in experimental work and human observations.^{14–16} The first concerns abrupt cessation of cerebral blood flow and involves the basal ganglia and thalamus region, often in relation to sentinel events like umbilical cord prolapse, uterine rupture, placental abruption, or fetal-maternal transfusion. Such dramatic events prevent redistribution of cerebral blood flow, inducing damage to the deep nuclei with high metabolic activity, and are associated with brainstem and peri-rolandic cortical injury in severe cases. The second pattern concerns a subacute type of asphyxia, usually related to placental or cord complications, which often results in a watershed injury to the cerebral (sub)cortex, with typical

TABLE 1 Spectrum and timing of sonographic findings in neonatal HIE.

Pattern	Description
Brain swelling	Slit-like ventricles, loss of cortical grey to white matter differentiation, and loss of the normal sulcal landmarks. These signs emerge 12–24 hours after the insult. If the insult is severe or antenatal, the changes may be present earlier.
Basal ganglia-thalamic injury	Increased echogenicity at the basal ganglia and thalami develops gradually between 2 and 4 days after an acute hypoxic-ischaemic insult. The thalami are symmetrically hyperechoic and the PLIC is visible as a hypoechoic line between the hyperechoic putamen and thalamus (four-column sign). The echogenic central grey matter and the hypoechoic PLIC can also be seen on the parasagittal view. Focal (asymmetrical) hyperechoic areas may be found.
Cortical necrosis	The cortex is thickened and hyperechoic, with an inversion of the normal grey to white matter pattern. This may only become obvious near the end of the first week.
Periventricular or subcortical white matter injury	As an early finding, the cortex may appear hypoechogenic because of hyperechogenicity of the subcortical white matter, giving the characteristic image of 'tramline sign' (accentuation of the normal grey to white matter pattern). This is often an early sign, influenced by congestion, which rarely may evolve into white matter destruction.
Altered Doppler flow patterns	Luxury perfusion is characterized by high diastolic flow velocity, with the resistance index gradually dropping below 0.55. High velocity may also be observed in deep veins like the internal cerebral vein. Absent or reversed diastolic flow associated with brain swelling and high intracranial pressure is an ominous sign.

Abbreviations: HIE, hypoxic-ischaemic encephalopathy; PLIC, posterior limb of the internal capsule.

TABLE 2 Proposed imaging schedule in perinatal HIE.

Day and diagnostic imaging	Description
Day 1 CUS with Doppler	It can help to rule out antenatal injury and conditions that mimic HIE (intracranial haemorrhage, stroke, infection, metabolic or genetic/structural aetiology). Carried out to establish the timing of the hypoxic-ischaemic insult (legal implications).
Days 2–3 CUS with Doppler	Recognition of an emerging injury pattern. Spectral analysis of the blood flow velocity curve. Comparison with the aEEG findings.
Day 5 CUS with Doppler and MRI	Definition of the location and extent of the injury. Spectral analysis of the blood flow velocity curve. It is advisable to perform an MRI days 4 to 10 after birth. Carried out 4–6 days after birth (with diffusion sequences) for redirection of care.
Days 7–10 CUS	Confirmation of injury pattern and prediction of the outcome.

Abbreviations: aEEG, amplitude-integrated electroencephalography; CUS, cranial ultrasound; HIE, hypoxic-ischaemic encephalopathy; MRI, magnetic resonance imaging.

parasagittal distribution on the convexity, as cerebral blood flow autoregulation does not prevent a reduction of flow to the interarterial border zones. Variable mixtures of these two patterns are found in HIE (Figure 1); white matter injury also may occur in this context.

The timing of imaging is crucial because changes usually take between 2 and 7 days to appear after the original insult.¹⁷ CUS has traditionally been used to rule out antenatal injury, detect contraindications to hypothermia, or recognize entities that mimic HIE, such as stroke or haemorrhage. However, studies reporting a high sensitivity and accuracy of CUS to detect brain injury^{8, 18, 19} have extended its use in HIE.

The spectrum and timing of CUS findings in HIE are detailed in Tables 1 and 2,^{3,7–9,17,19–21} together with several examples (Figure 2). Although not fully characterized, the evolution of CUS patterns in HIE are usually addressed using early (on day 1 from admission) and serial exams (Table 2). After an intrapartum insult, hyperechoic changes in the thalami and basal ganglia can appear early after birth (from 12 hours onwards); they become obvious

by day 3 to 4 in cooled infants. The posterior limb of the internal capsule is visible as a hypoechoic line between the hyperechoic putamen and the thalamus, giving the appearance of a four-column sign. When asphyxia occurs a few to several days before delivery, the thalami can have a normal appearance at birth. In these cases, the chronic injury is fully expressed as hyperechoic thalami due to neuronal ferrugination (a process where iron and calcium are deposited in dead neurons), not earlier than 2 weeks after the hypoxic–ischaemic injury occurred. In contrast, in long-lasting (chronic) antepartum global forebrain ischaemia, the thalami and related structures will appear hyperechoic at birth (Figure 3). Defining thalamic injury during therapeutic hypothermia can be challenging, even with MRI, where the prognostic value early in the clinical course (by day 4) is influenced by cooling; discrepancy between the techniques is common. White matter changes on CUS are often present around day 4. Cortical necrosis with selective hyperechoic change of cortex (increased cortical echogenicity) may only become obvious between day 5 and day 7.

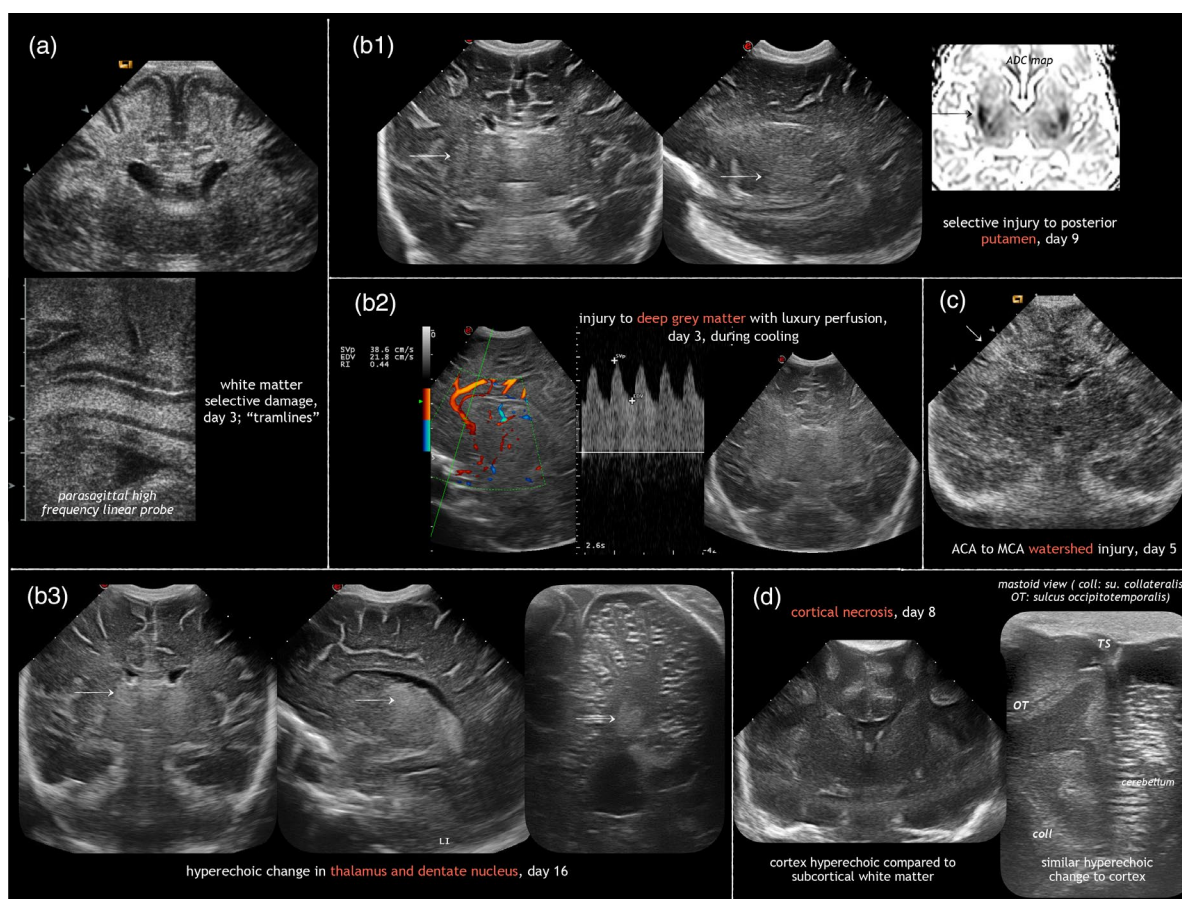


FIGURE 2 Typical cranial ultrasound (CUS) patterns in term birth asphyxia. (a) Tramline effect around the cortex from very echogenic white matter. (b) Basal ganglia-thalamic injury. (b1) Hyperechoic putamen (selective injury to the posterior putamen). (b2) Increased echogenicity in the basal ganglia and thalami with loss of differentiation of central structures (day 3 CUS). Luxury perfusion: high diastolic flow velocity and low resistance index (below 0.55). (b3) Hyperechoic thalamus and dentate nucleus (day 16 CUS). (c) Subcortical white matter hyperechogenicity in the territory bordering the anterior cerebral artery (ACA) and middle cerebral artery (MCA) (watershed injury). (d) Hyperechoic and thickened cortex (cortical necrosis). Abbreviation: ADC, apparent diffusion coefficient; Coll, sulcus collateralis; OT, sulcus occipitotemporalis.

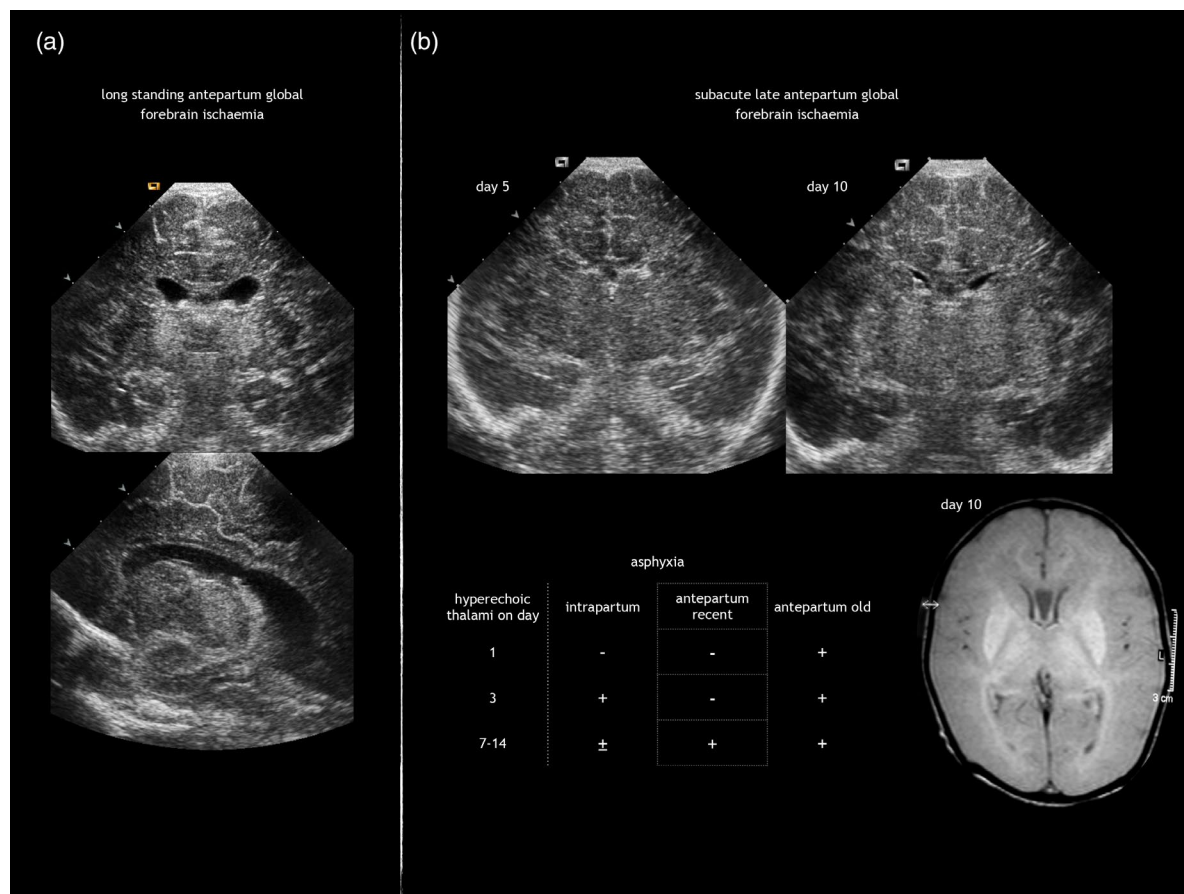


FIGURE 3 Timing of thalamic ischaemic insult and images after birth. (a) Chronic antepartum brain injury. Seizures occurred immediately after an emergency caesarean section due to absent fetal heart rate variability and reduced movements. The day 1 cranial ultrasound (CUS) shows hyperechoic thalami at the ventrolateral nuclei and dilated ventricles (ex vacuo). (b) Subacute antepartum ischaemia in an infant born at term with low Apgar scores and reduced fetal movements during the 8 days before delivery. The basal ganglia and thalami were normal on the earlier CUS but have become hyperechoic, showing the four-column sign by day 10. Equivalent findings are seen on the magnetic resonance imaging scan.

A CUS grading system has been validated to predict outcome in cooled infants with HIE.¹⁹ In the study, abnormalities found on days 3 to 7 after birth were predictive of an adverse outcome. The negative predictive value was high (96% for a cut-off value <3), indicating that a normal scan was reassuring.

Non-invasive haemodynamic assessment using CUS with Doppler is a complementary tool while parenchymal changes take place and evolve. Analysis of the peak systolic flow velocity and end-diastolic flow velocity curves, as well as the derived resistance index (resistance index = peak systolic flow velocity – end-diastolic flow velocity / peak systolic flow velocity), lead to the recognition of several abnormal arterial patterns. Luxury perfusion (resistance index ≤ 0.55) beyond 24 hours from birth, indicating a poor outcome, is found in infants with HIE who do not undergo therapeutic hypothermia.^{22–25} Early assessment of the resistance index loses predictive value in cooled infants (sensitivity 63%, specificity 76%).²⁶ This low predictive value does not preclude its use. A low resistance index after rewarming is correlated with severe brain injury on diffusion-weighted MRI²⁷ and poor outcomes.^{25, 28}

NEONATAL ENCEPHALOPATHY OTHER THAN HIE

Neonatal encephalopathy in the absence of a history of perinatal asphyxia suggests a focal ischaemic, infectious, metabolic, genetic, or structural aetiology. Non-specific but suggestive neuroimaging features can be found in infants who suffer from inborn errors of metabolism (Figure 4).²⁹ Consistent CUS and MRI findings include ventriculomegaly, germinolysis, abnormal basal ganglia and thalami, white matter changes, or structural anomalies (abnormal cortical folding, absent or thin corpus callosum, abnormal cerebellum).¹⁸ Changes like structural anomalies, ventriculomegaly, or germinolytic cysts are not found during the acute phase of HIE.¹⁸

ISCHAEMIC ENCEPHALOPATHY CAUSED BY CRANIAL COMPRESSION

Complicated labour can result in neonatal encephalopathy and multifocal brain injury without the features of traumatic

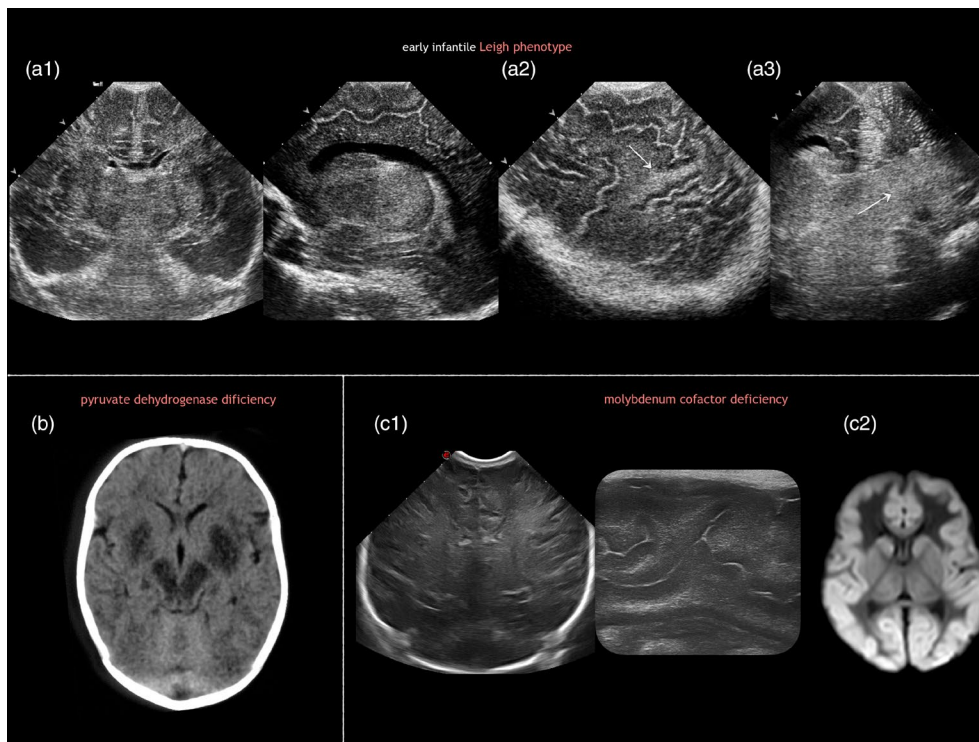


FIGURE 4 Metabolic stroke-like lesions: mitochondrial disorders and molybdenum cofactor deficiency. (a) Cranial ultrasound (CUS) findings in early infantile Leigh phenotype: progressive hyperechogenicity (within 3 weeks) mirroring that of hypoxic–ischaemic deep gray matter injury. (a1) Coronal and parasagittal planes, hyperechoic thalamus and putamen (four-column sign). (a2) Subcortical white matter hyperechogenicity (tramline sign). (a3) Hyperechoic brainstem tegmentum (mastoid view). (b) Pyruvate dehydrogenase deficiency causing apnoea and lactic acidosis at birth. Computed tomography scan showing extensive damage in the mesencephalon, pons, thalamus, and striatum. (c) Molybdenum cofactor deficiency. (c1) CUS displaying hyperechoic white and deep gray matter. (c2) The corresponding diffusion-weighted magnetic resonance imaging changes.

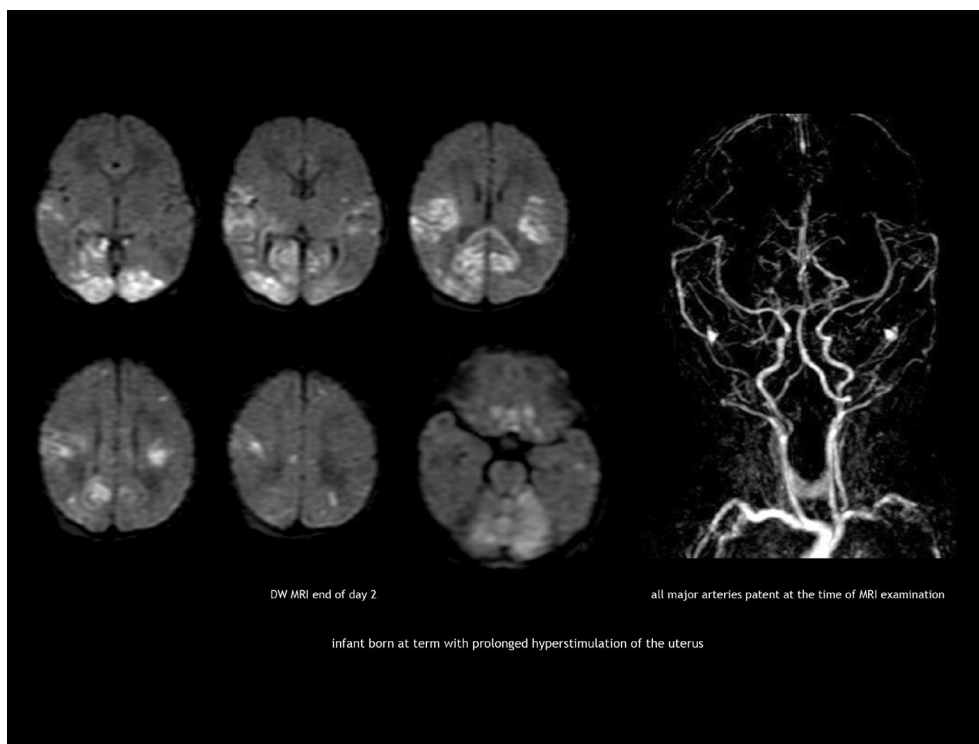


FIGURE 5 Cranial compression ischaemic encephalopathy associated with uterine hyperstimulation. Multifocal areas of diffusion-weighted (DW) magnetic resonance imaging (MRI) restriction but normal arterial pattern (no occlusion) at the time of the exam (day 2 after birth).

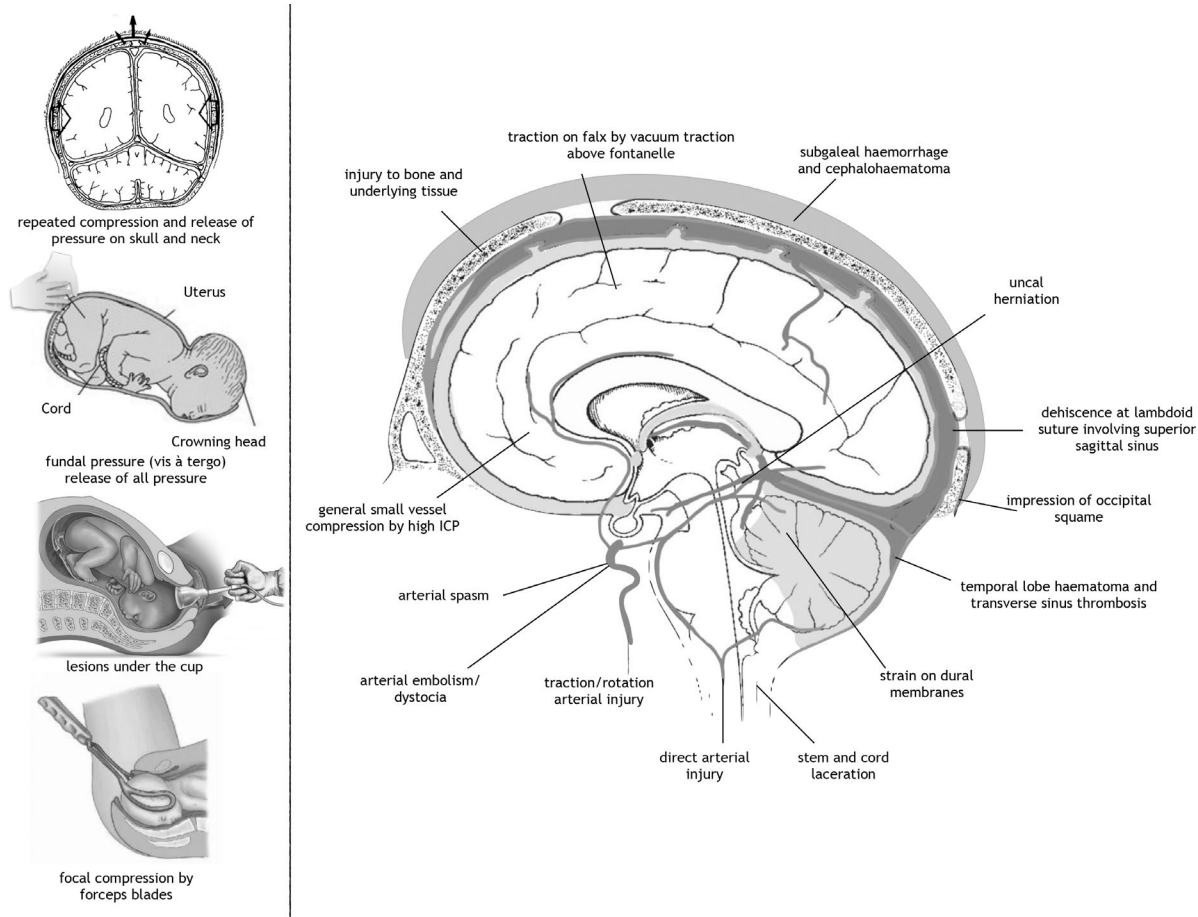


FIGURE 6 Mechanisms and sites of possible mechanical injury to the cranium during cephalic or breech vaginal delivery. Abbreviation: ICP, intracranial pressure.

haemorrhage (i.e. ischaemic encephalopathy caused by cranial compression). The underlying mechanism is probably related to relentless compression of the vascular bed during high intrapartum intracranial pressure (Figure 5).³⁰ Multiple, mainly non-haemorrhagic infarcts defy explanation according to arterial thrombosis or embolism. Significant impairment of cerebral circulation from head compression can produce injury during labour without systemic asphyxia or multiorgan failure. Uterine contractions raise fetal intracranial pressure potentially to a level two to four times that of the associated intrauterine pressure; if maintained, it may significantly reduce cerebral blood flow.³⁰

Pressure distribution depends on the presentation of the head, mostly exerting itself on the brain regions facing the pubic bone. Microvascular compression is probably the first injurious mechanism before pressure leads to arterial occlusion.

INTRACRANIAL HAEMORRHAGE

The incidence of symptomatic ICH ranges from 0.3 to 2.5 per 1000 live births,^{31–34} although data on asymptomatic ICH are

TABLE 3 Mechanisms of haemorrhage and haemostatic work-up.	
Mechanism	
• Within an arterial infarct • Within a venous infarct (thrombosis) • Direct trauma to a vessel • Haemostatic problem • Arterial hypertension • Venous congestion without thrombosis • Vascular anomaly • Tumour	
Haemostatic work-up	
• Thrombocytopenia: iso-immune, autoimmune • Thrombocytopathy: von Willebrand disease, congenital amegakaryocytic thrombocytopenia, thrombocytopenia-absent radius syndrome, Wiskott–Aldrich syndrome; drugs: salicylates or non-steroidal anti-inflammatory medication • Shortage of coagulation factors: congenital (factors V, VII, VIII, X), use of coumarins, diffuse intravascular coagulation • Shortage of anticoagulants: protein C deficiency, factor V Leiden, factor II mutation • Dysfibrinogenaemia • Liver failure • Glutathione synthetase deficiency	

lacking. The diagnosis is based on the recognition of predisposing factors, abnormal clinical features, and neuroimaging. Bleeding-related mechanisms (Figure 6) and haemostatic work-up in the case of suspected/confirmed ICH are listed in Table 3.

Subdural haematoma

A subdural haematoma (SDH) is the most common ICH in infants born at term because of rupture of abnormal, lacerated, congested, or thrombosed veins (Figure 7). MRI and CT studies in asymptomatic newborn infants reported 26% to 46% prevalence of limited SDH.^{35–37}

Epidural haemorrhage

Epidural haemorrhage is rare in the neonate and originates from rupture of the branches of the meningeal arteries, or major veins or venous sinuses; it is always located underneath a linear fracture, with an overlaying cephalohaematoma.

Primary subarachnoid haemorrhage

Primary subarachnoid haemorrhage is common but it is usually clinically benign.

Subarachnoid haematoma

A subarachnoid haematoma occurs in the context of abnormal haemostasis. In the recent literature, the terms subpial and subarachnoid haematoma have been used interchangeably because there is no way to differentiate them using imaging.

BIRTH MECHANICAL TRAUMA AND ASSOCIATED ICH

Birth trauma causes specific haemorrhagic conditions that are briefly described in the following sections.

Ischaemic encephalopathy caused by cranial compression

Bruising of gyral core

Bruising (Figure 8) refers to focal bleeding near a bony edge or fracture, or under a depressed bone, after delivery with excessive head moulding. A peculiar pattern in the frontal gyral core has been reported.³⁸ High-resolution CUS is the diagnostic method of choice shortly after admission, and after a difficult delivery, because the superior frontal gyrus is very accessible. Diffusion-weighted MRI may demonstrate

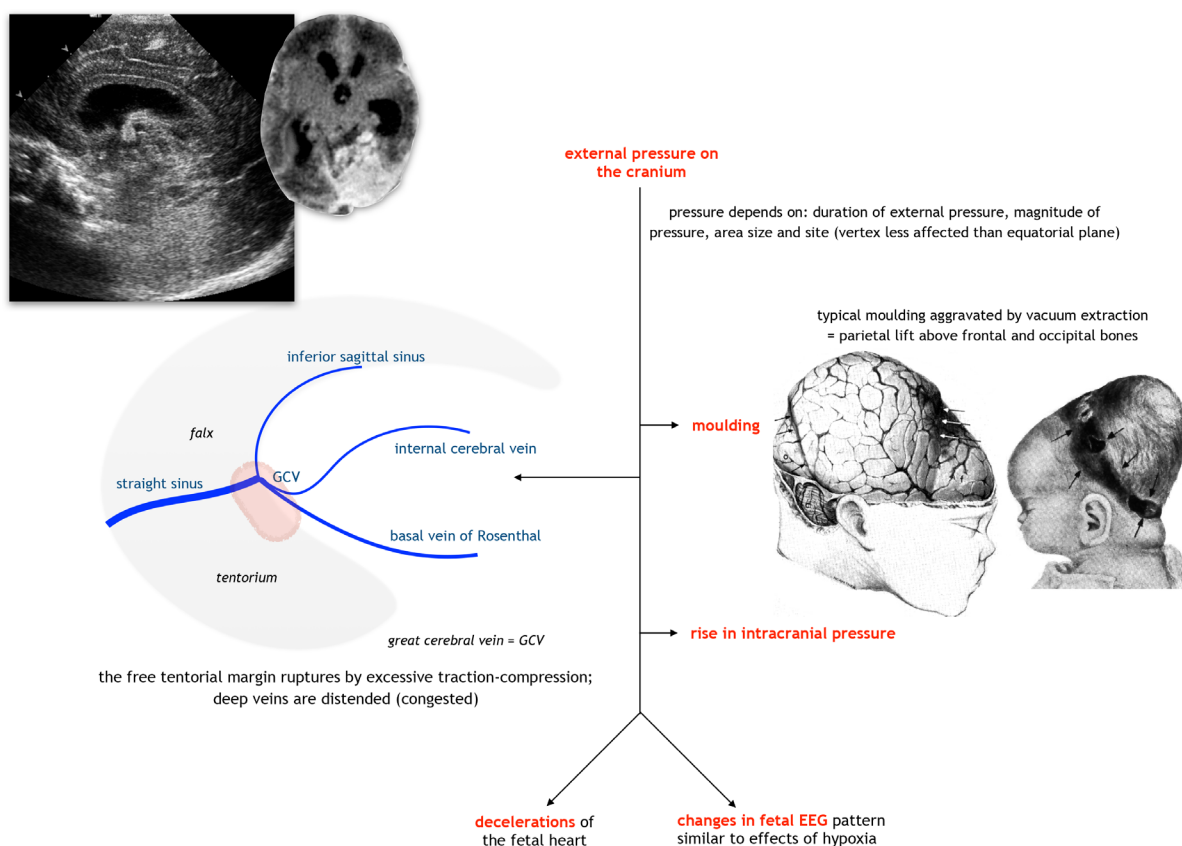


FIGURE 7 Intracranial effects of cranial compression. Abbreviation: EEG, electroencephalogram.

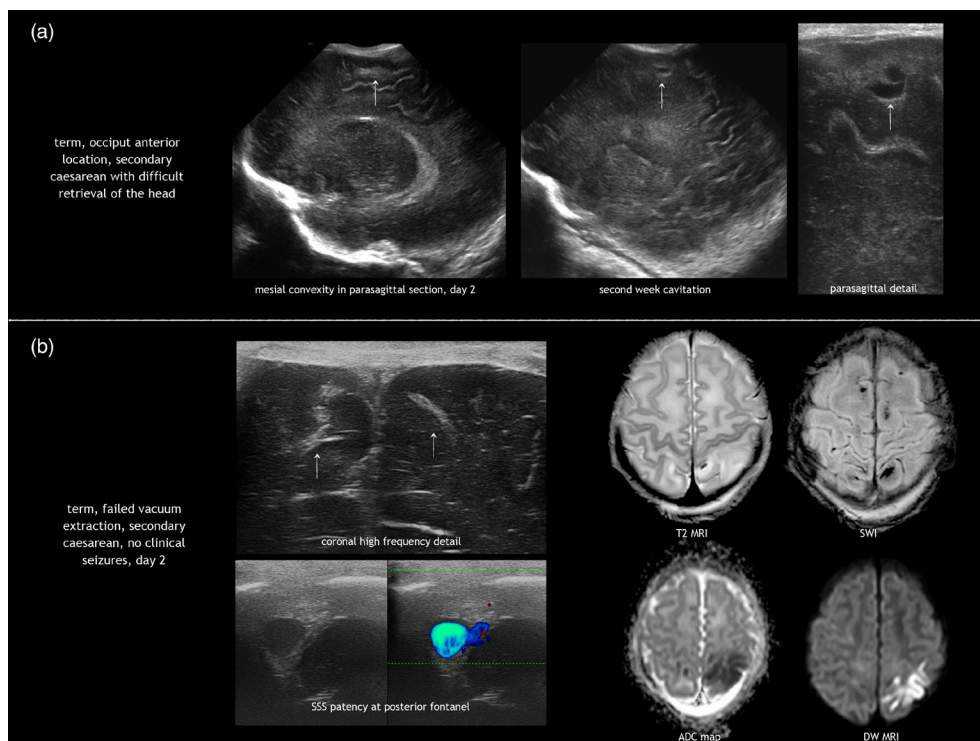


FIGURE 8 Subcortical bruising at the core of the superior frontal gyrus. (a) Cranial ultrasound (CUS) showing focal hyperechogenicity in the frontal white matter evolving into cavitation within 2 weeks (mesial convexity, parasagittal view). (b) Top, CUS showing a hyperechoic and thickened cortex. Bottom, Patency of the superior sagittal sinus. Magnetic resonance imaging (MRI) shows a subcortical haemorrhage. The diffusion-weighted changes extend into the cortex. Abbreviations: ADC, apparent diffusion coefficient; DW, diffusion-weighted; SSS, superior sagittal sinus; SWI, susceptibility-weighted imaging.

a lesion that is surprisingly more extensive than expected on ultrasound.

Occipital osteodiastasis

Traumatic occipital diastasis (Figure 9) may cause a very large SDH in the posterior fossa and cerebellar laceration.³⁹ The squamous part of the occipital bone is pushed into the posterior fossa. CUS of the anterior fontanelle can suggest the diagnosis if hyperechoic changes are seen into or below the inferior cerebellar hemisphere(s), although mastoid insonation should be conducted to gain a better view. The cisterna magna may be filled with blood. MRI illustrates contusion of the inferior hemispheres.

Temporal lobe haematoma with or without transverse sinus thrombosis

Transverse sinus thrombosis (Figure 10) rarely causes temporal lobe haemorrhage.⁴⁰ Arterial infarction may result in bleeding. A lobar haematoma is evidence of trauma, haemostatic failure, a tumour, or vascular malformation.

Intradural haematoma with subdural component

The venules of a dural venous network near the superior sagittal sinus are 'leaky' and could be the source of subdural bleeding at the hemisphere convexity.⁴¹

The context and pathogenesis of the different types of ICHs are listed in Table 4.

CUS WORK-UP AND CLINICAL MANAGEMENT OF ICH

During CUS, the diagnosis is often incidental in the context of a difficult delivery, unexplained hyperbilirubinaemia from a large ICH, or presence of a skull fracture. Symptomatic infants typically present within the first 48 hours after birth with seizures, respiratory depression, irritability, or altered tone or consciousness. Different clinical entities can be identified according to the severity of the haemorrhage (Table 5).⁴² Prognosis depends on whether or not parenchymal involvement or abnormal neurological signs are present.³⁴ Small SDHs resolve without sequelae by a month.^{36, 43}

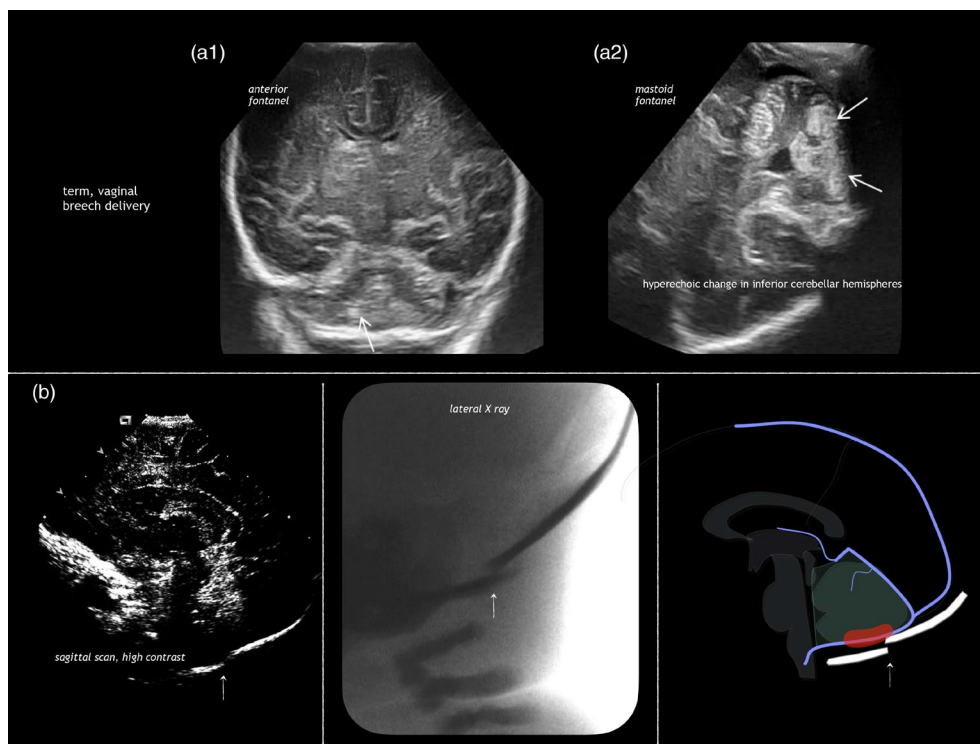


FIGURE 9 Occipital osteodiastasis. (a) Cranial ultrasound (CUS) coronal plane through the anterior fontanelle (a1) and mastoid view (a2): hyperechoic change in the inferior cerebellar hemispheres (arrows) in an infant born at term by vaginal breech delivery. (b) Depressed base of the occipital squame causing cerebellar contusion. Lateral X-ray showing squame overlapping the basal part of the occipital bone.

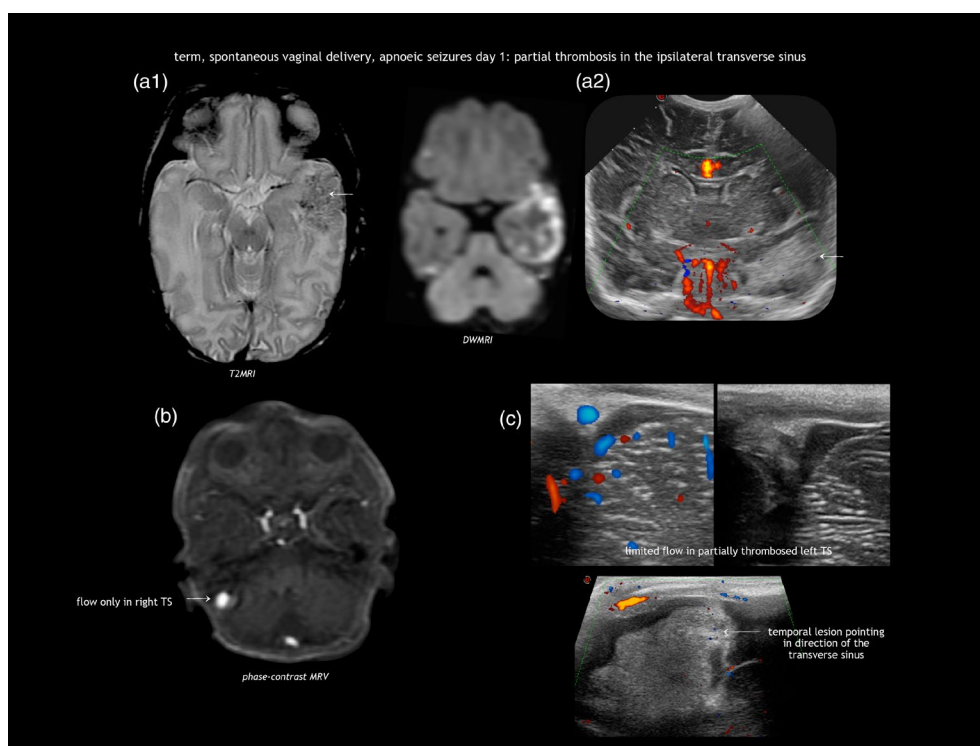


FIGURE 10 Apneic spells within the first day in an infant born at term with transverse sinus thrombosis near a temporal lobe haematoma. (a1) T2-weighted magnetic resonance imaging (MRI)/diffusion-weighted (DW) MRI illustrating a left temporal lobe haematoma (arrow); (a2) Cranial ultrasound (CUS): hyperechoic lesion in the left temporal lobe (arrow). (b) Phase-contrast magnetic resonance venography (MRV) depicts only flow in the right transverse sinus (TS). No flow is seen on the left. (c) Mastoid view CUS showing limited flow through the left transverse sinus (thrombosed) and the associated hyperechoic temporal lobe (arrow).

TABLE 4 Types of intracranial haemorrhage in the infant born at term and near-term.

Type of haemorrhage	Context, pathogenesis, and imaging
Subdural	- More frequent than expected in asymptomatic newborn infants (26%–46%); it resolves within 3–4 weeks.^{35–37} - Associated with birth trauma, prolonged labour, or instrumental birth.^{36, 37, 43} Skull compression leads to cranial moulding, raised intracranial pressure, and venous distension (Figure 7).⁴² - According to the source of the bleeding: tentorial laceration and rupture of the straight sinus, transverse sinus, or the great cerebral vein can result in massive infratentorial haemorrhage and brainstem compression; falx laceration and rupture of the inferior sagittal sinus cause haemorrhage in the longitudinal cerebral fissure; rupture of the bridging superficial cerebral veins causes haemorrhage over the cerebral convexity.
Epidural	- Very infrequent but it is an irrefutable sign of mechanical trauma if haemostasis is normal. - Typical early liquefaction of the clot (within 24–48 hours). - Major haemorrhage can lead to uncal herniation, intracranial hypertension, ipsilateral ventricle compression, and shift of the interhemispheric fissure and third ventricle.
Subarachnoid haemorrhage	- Common in infants after normal vaginal delivery and usually asymptomatic. - It shows as a thin layer of blood covering the pia without associated brain damage. - Although usually asymptomatic, occasionally it can result in seizures or neurological syndromes.
Subarachnoid haematoma	- Generally associated with altered hemostasis, often with platelet dysfunction or thrombocytopenia. - It starts at the molecular layer of the cortex. - Expansive haemorrhage invades the subarachnoid tissue and distends the sulci, leading to haemorrhagic/ischaemic destruction of the subjacent parenchyma.
Bruising of the frontal gyral core	Characteristically, it is focal, unilateral, or asymmetrical (bilateral) hyperechoic change in the core of the superior frontal gyrus, which may cavitate within days (Figure 8). Attributed to shearing forces, the mechanism of this pattern remains elusive. The lesions do not fit within a global hypoxic–ischaemic or macrovascular template. Selective subcortical venous ischaemia secondary to bone displacement is a candidate mechanism.

TABLE 5 Neurological syndromes with extra-axial ICH.

Rapidly lethal syndrome	Less severe, progressive neurological syndrome	Neurological syndrome associated with subdural or epidural haemorrhage of the cerebral convexity	No neurological signs
Tentorial laceration, occipital osteodiasis, extensive posterior fossa subdural hematoma.	Smaller tentorium tears or rupture of bridging veins around the superior part of the cerebellum (limited to the posterior fossa clot).	Tissue pressure at the cerebral convexity or from below the temporal lobe.	The most common presentation of subdural haemorrhage.
Neurological impairment present from birth; it rapidly progresses in minutes to hours. Clinical signs of mid-brain and upper pons compression: stupor or coma, skew deviation of the eyes, unequal and poorly light-reactive pupils, retrocollis/opisthotonos, depressed respiratory drive.	Neurological impairment in three phases: 1. Symptom-free period (< 24 hours). 2. Signs of increased intracranial pressure (full fontanelle, irritability, lethargy) due to cerebrospinal fluid flow blockage at the posterior fossa. 3. Clinical signs of brainstem compression (abnormal respiratory pattern, apnoea, bradycardia, oculomotor abnormalities).	Minor or no clinical signs. Focal signs: hemiparesis, eye deviation, focal seizures, ipsilateral pupillary changes (uncal herniation), tongue paralysis.	Unexplained hyperbilirubinaemia or low-grade fever. Skull fracture. Antecedent of difficult labour or delivery.

Abbreviation: ICH, intracranial haemorrhage.

MRI is the diagnostic method of choice in the diagnosis of extra-axial haemorrhage because it can detect the location and extent of the bleeding. CUS has a more limited value. In a prospective study of asymptomatic neonates, only 55% of the posterior fossa SDH diagnosed using MRI were identified using CUS, and no supratentorial haemorrhages were detected.³⁶ In this study, most SDHs were 3 mm or less in size. In a retrospective study on CUS in the diagnosis of ICH, using CT or MRI as standard, the sensitivity of CUS to detect significant ICH was 78% (33% in the case of insignificant bleeding).⁴⁴

In our experience, CUS can be used as the first-line tool, speeding up the diagnosis in symptomatic infants

with suspected ICH. If bleeding is suggested by CUS, it is best followed by MRI to define the extent of bleeding and the associated parenchymal injury. Supratentorial SDH can be suspected on CUS as an extra-axial hypoechoic or hyperechoic lentiform or flat image along the convexity of the hemisphere (Figure 11). A central tentorial haematoma can be suspected when the midline structures under the splenium (vermis cerebellum, pons, and cisterns) are poorly delineated, or by the presence of a hyperechoic area above the vermis that prevents identification of the quadrigeminal cistern. An epidural haematoma is seen as extracerebral echogenicity with biconvex contours.^{45–47} Small and eccentric haemorrhages are difficult to visualize using CUS.

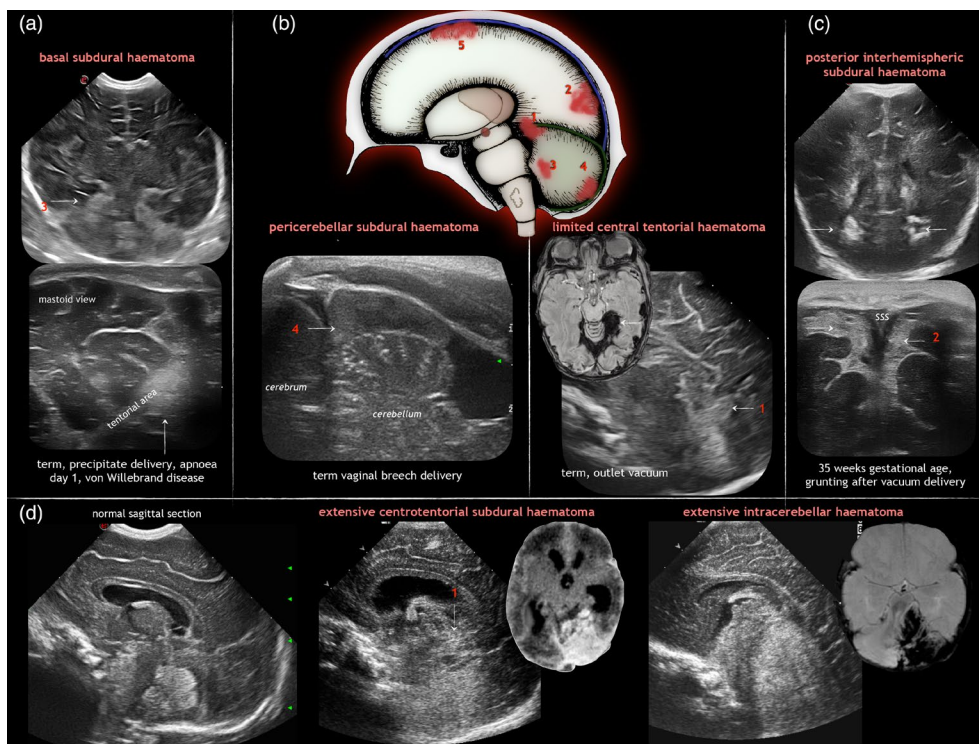


FIGURE 11 Examples of subdural bleeding on cranial ultrasound. (a) Basal temporal (lateral tentorial) haematoma visible via both the anterior fontanelle and mastoid fontanelles. (b) Central tentorial haematoma. (c) Posterior interhemispheric haematoma. (d) Normal midline section, centrotentorial haematoma, and intracerebellar haematoma. Abbreviation: SSS, superior sagittal sinus.

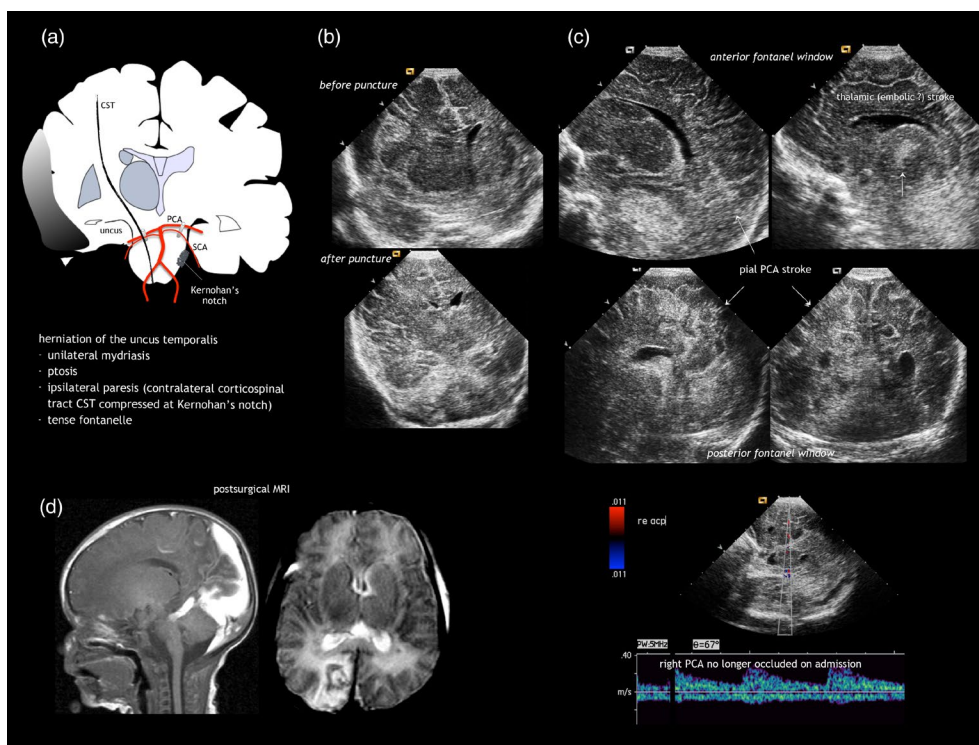


FIGURE 12 Posterior cerebral artery (PCA) stroke associated with right-sided subdural haematoma causing uncus herniation. (a) Schematic representation of uncus herniation-related clinical signs. (b) Uncus herniation aetiopathogenesis: basal subdural haematoma causing midline shift of the ipsilateral structures. Cranial ultrasound, coronal view: extra-axial hypoechoic lenticular area (subdural haematoma on the convexity) before and after puncture. (c) PCA stroke secondary to uncus herniation: hyperechoic area in the occipital lobe (arrow) visible through the anterior and posterior fontanelles. (d) T1 sagittal and T2-weighted coronal magnetic resonance imaging. Abbreviations: CST, corticospinal tract; SCA, superior cerebellar artery.

A supratentorial haematoma may cause a mass effect, driving the uncus through the tentorial notch (uncal herniation).⁴⁸ This compresses the basal vein and the fork of the posterior cerebral artery and superior cerebellar artery, which hold the oculomotor nerve, resulting in unilateral mydriasis and ptosis (Figure 12). This requires emergency subdural puncture via the superior or lateral fontanelle.

Although rare in the newborn infant, an extensive posterior fossa haematoma is best treated by relief of pressure in the posterior fossa. Ventricular drainage, in case of dilatation of the supratentorial ventricles by posterior fossa crowding, can lead to upward herniation of the cerebellum and brainstem, with compression of major arteries of the circle of Willis and subsequent brain destruction (Figure 13).

ACUTE PERINATAL CNS INFECTION

CNS infection is an important cause of mortality and morbidity.⁴⁹ Early diagnosis is challenging because of frequent lumbar puncture contraindication; even if conducted,

the micro-organism responsible for the infection may not be isolated. Therefore, the diagnosis is often established based on cerebrospinal fluid findings and blood culture.^{50, 51} Imaging defines the infection's impact on the CNS and points to a potential aetiology, as specific patterns to several micro-organisms have been reported.⁵¹ CUS is usually the first imaging tool in suspected meningitis. Acute bacterial meningitis leads to characteristic CUS changes in up to 65% of patients, figures that rise to 100% in the newborn infant with atypical neurological signs.^{52, 53} We recommend a baseline CUS on admission in neonates with suspected CNS infection. If meningitis is confirmed, or the condition of the infant deteriorates, serial studies are then performed to rule out complications that need further attention. Optimized settings include a high-frequency linear probe for assessment of the meninges and extra-axial space, as well as Doppler assessment to exclude sinovous thrombosis. CUS provides us with the optimal timing to determine the extent of the injury using MRI.

A spectrum of CUS findings in neonatal CNS infection has been reported in clinical series and reviews.^{49, 52–68}

Initial and evolving changes observed using CUS during neonatal CNS infection include meningeal

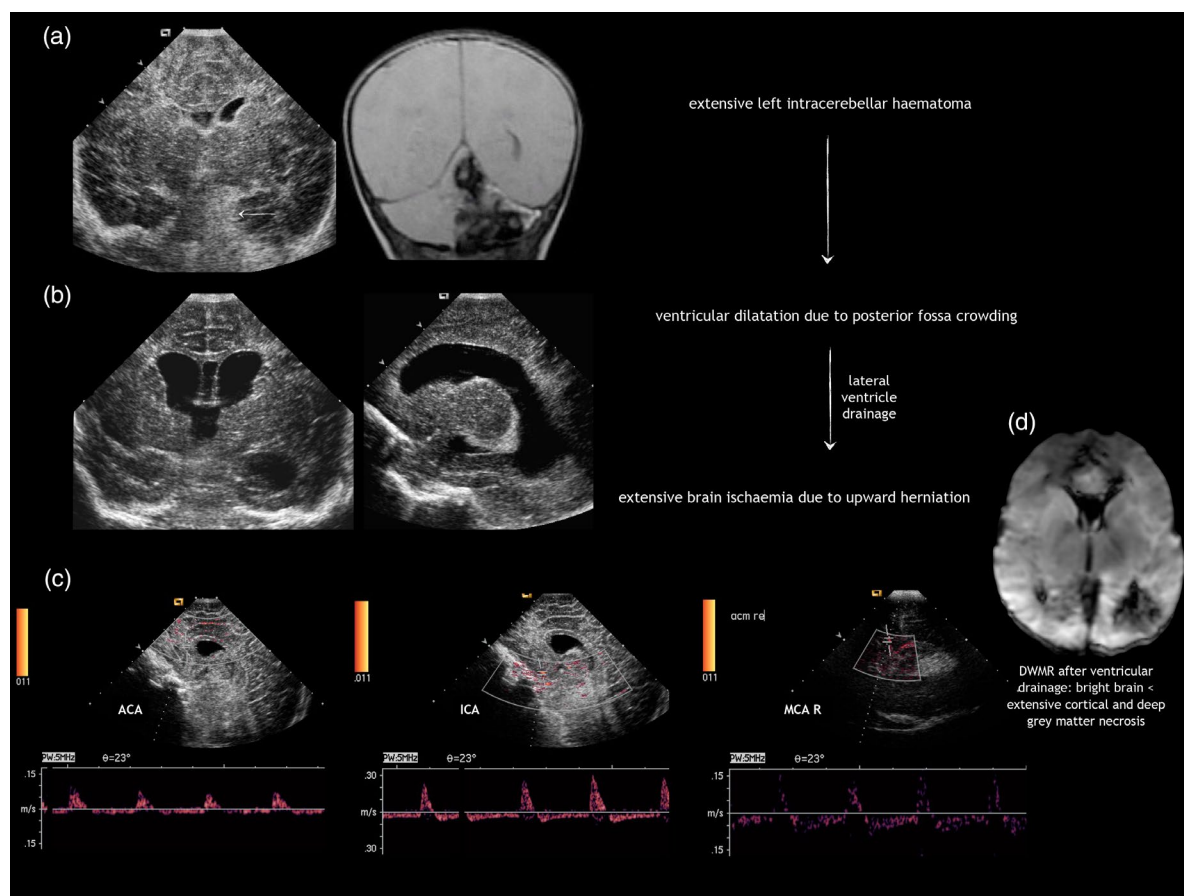


FIGURE 13 Upward herniation due to ventricular drainage. (a) Cranial ultrasound (CUS)/magnetic resonance imaging (MRI): left intracerebellar haematoma causing obstruction of the cerebrospinal fluid. (b) Secondary ventricular dilatation. (c) Ventricular drainage causes upward herniation of cerebellum and brainstem with compression of the major arteries in the circle of Willis: abnormal CUS Doppler findings in the anterior cerebral artery (ACA), internal carotid artery (ICA), and middle cerebral artery (MCA) showing reverse diastolic flow. (d) Diffusion-weighted (DW) MRI after ventricular drainage: note the cortical and deep grey matter necrosis.

TABLE 6 Lesion patterns caused by neonatal brain infection.

Cranial ultrasound findings in bacterial infections	
Meningeal thickening	• Hyperechoic widening of the sulcus is the earliest and most common finding (23% to 83% of cases);⁵³ transient and without outcome correlation.^{50, 56} • Measurements can be taken in the coronal plane, at the level of the foramen of Monro, and outside the gyrus frontalis superior (Figure 15): meningeal thickening is defined when ≥1.3 mm, if measured from the gyral surface, or ≥2 mm when measured within a groove.^{52, 65}
Enlarged subarachnoid spaces	• Hyperechoic area with strands and cavities is suggestive of empyema (Figure 15); Doppler helps to differentiate empyema from benign enlargement of the subarachnoid spaces, where cortical vessels are surrounded by cerebrospinal fluid.^{50, 53, 65}
Parenchymal destruction	• Described in Gram-negative encephalitis as a liquefaction necrosis;^{53, 60, 64, 65} the periventricular or subcortical white matter is especially vulnerable to infection,⁶⁰ appearing as areas of increased echogenicity (Figure 16).
Ventriculitis/plexitis	• Carries an increased risk of hydrocephalus and neurological morbidity^{64, 69} and determines treatment duration. • Sonographic findings: increased ependymal echogenicity, intraventricular debris or septae, intraventricular hyperechoic content, and increased echogenicity or irregularity of the plexus (Figure 17);⁶⁴ Doppler detection of cerebrospinal fluid flow at the aqueduct may add to the diagnosis.^{54, 57} Purulent inflammation near the ventricle lining may lead to thrombophlebitis with periventricular infarction.
Hydrocephalus	• Variable reported prevalence after bacterial meningitis (16%–60% of cases).⁵³ Ventriculomegaly occurs during the acute phase due to increased cerebrospinal fluid production, hindered circulation, and decreased absorption (Figure 28); hydrocephalus can develop later due to adhesions, aqueduct stenosis, progressive fourth ventricle trapping, or multiloculated cyst formation.⁴⁹ • Static ventricular dilatation may also be due to atrophy.^{49, 65}
Abscess formation	• Associated with bacterial and yeast infection;⁵¹ some abscesses follow focal infarction of either venous or arterial origin. • Round echogenicity followed by central dissolution and a hyperechoic rim, sometimes with a level between fluid and necrotic debris (Figure 19).^{49, 60} Micro-abscesses in the subcortical and periventricular white matter and basal ganglia have been described in fungal meningitis as scattered, small, round hyperechoic lesions.⁵⁹
Cerebrovascular complications	• Up to 5%–10% of bacterial meningitis (particularly group B <i>Streptococcus</i>) are associated with arterial ischaemic stroke,^{70, 71} with wide brain involvement (cortical multifocal ischaemia, basal ganglia involvement, or a large territorial arterial infarction) due to inflammation of pial arteries and superficial veins, or subarachnoid inflammation at the base of the brain and secondary vasospasm at the level of the circle of Willis or perforator arteries (Figure 20).⁶³ • Sinovenous thrombosis is diagnosed in up to 7%–16% of cases with meningitis⁷² when changes are near a fontanelle.
Cranial ultrasound findings in viral infections	• For perinatal infection, human parechovirus and enterovirus are frequently identified. • Clinical signs and disease severity are variable and a high index of suspicion is needed. In symptomatic infants, the clinical picture simulates a sepsis-like disease with fever, hepatitis, or abnormal neurological signs.⁶⁸ • Neuroimaging is recommended when facing abnormal neurological signs or severe illness to rule out white matter abnormalities;⁶⁷ increased echogenicity in the periventricular and deep white matter is the most frequent sonographic finding (Figure 22). • Some characteristic patterns can be recognized according to the type of virus: abnormal echogenicity at the level of the frontal and temporal lobes in herpes simplex virus infection; extensive frontal cystic evolution in rotavirus infection; there are limited neuroimaging findings in prenatal parvovirus infection. Parenchymal calcifications, cerebellar haemorrhage, and arterial infarction have been reported.^{61, 67}

thickening, enlargement of extra-axial spaces, direct parenchymal destruction, ventriculitis and plexitis, hydrocephalus, abscess formation, or cerebrovascular complications^{69–72} (Table 6 and Figures 14–22).

NEWBORN INFANTS WITH SEIZURES

Seizures are the most frequent neurological sign in neonatal intensive care units, with an incidence of 1 to 5 per 1000 live births.⁷³ A prompt diagnosis to determine the aetiology is crucial where intervention is needed. Neuroimaging is essential not only to establish the diagnosis, but also to advance a prognosis. HIE and perinatal arterial stroke are responsible for up to 75% of seizures in the infant born at term, while ICH is the leading cause of seizures in infants born preterm.⁷⁴

Description of all entities causing neonatal seizures is beyond the scope of this article. Perinatal stroke encompasses three entities: arterial ischaemic stroke (AIS), cerebral sinovenous thrombosis (CSVT), and haemorrhagic infarction.

ARTERIAL ISCHAEMIC STROKE

AIS accounts for most perinatal strokes (up to 80%); more than half of children present with focal seizures in the first 72 hours after birth; neonates are typically asymptomatic between ictal episodes; however, clinical signs of neonatal encephalopathy can be present if the infarct is extensive. Maternal and fetal factors and intrapartum complications have been associated with AIS, but in many cases no single cause is identified.⁷⁵ AIS usually affects the left middle

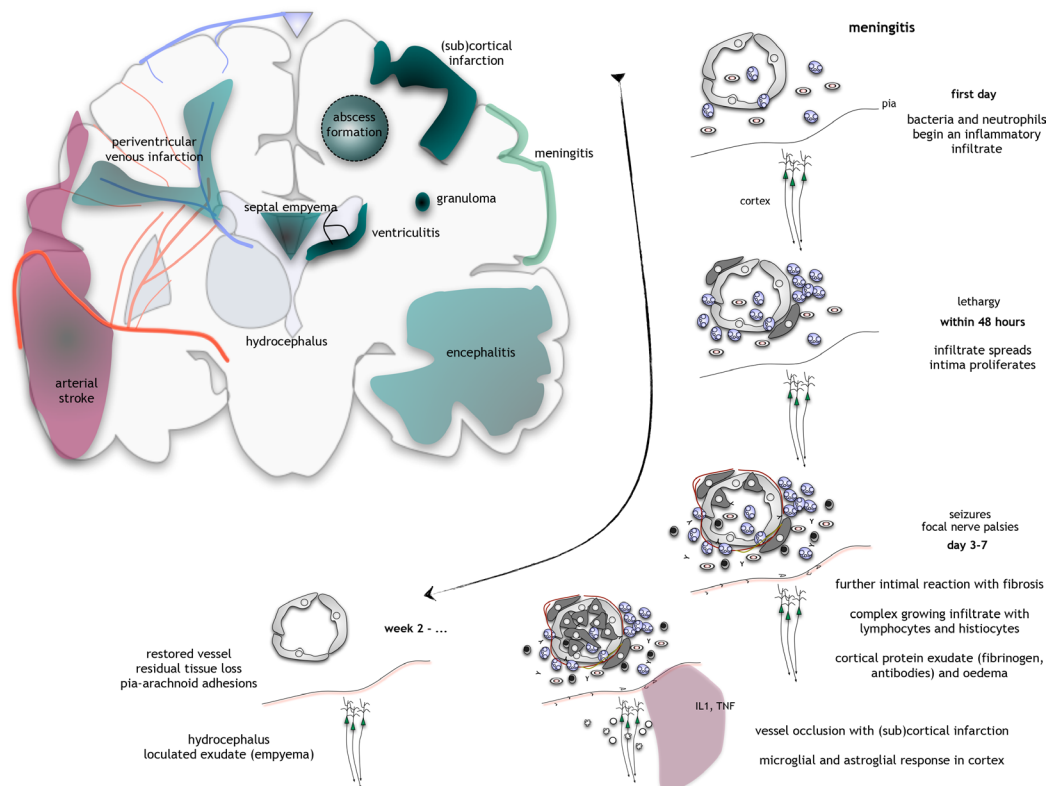


FIGURE 14 Schematic representation of brain injury patterns in the newborn infant caused by bacterial infection. Abbreviations: IL-1, interleukin-1; TNF, tumour necrosis factor.

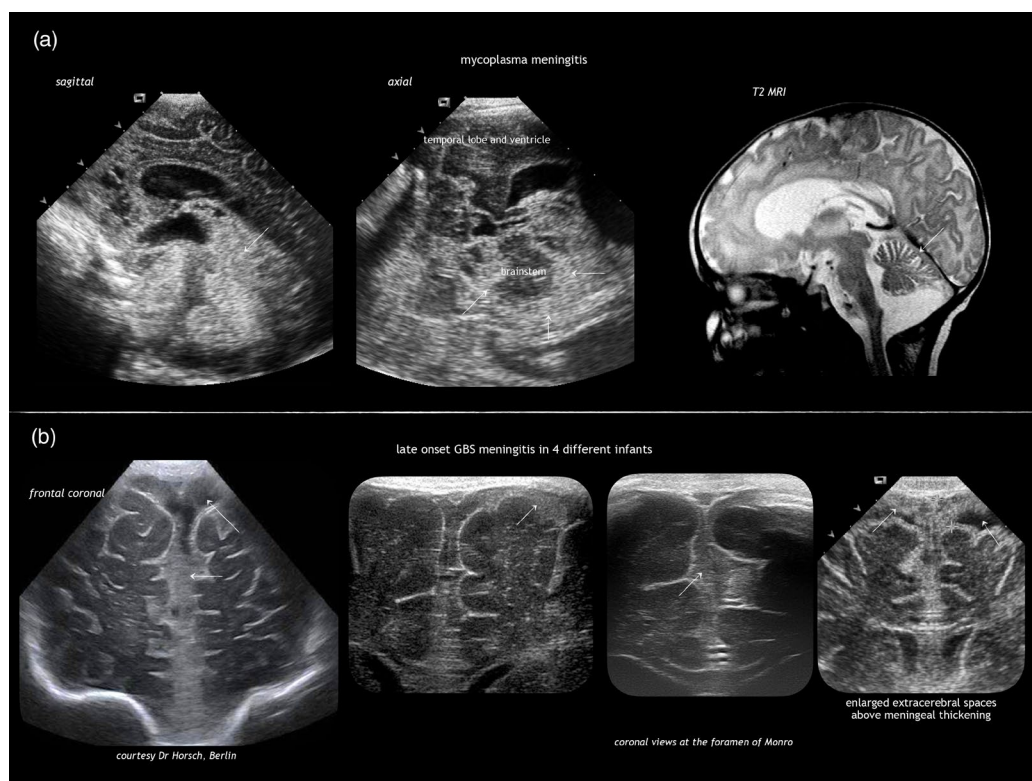


FIGURE 15 Cranial ultrasound (CUS) findings in bacterial infection. (a) Meningeal thickening: sagittal plane showing hyperechoic thickening between the vermis and tentorium (arrow). CUS axial view (temporal fontanelle). T2-weighted magnetic resonance imaging (MRI) (arrow). (b) CUS examples of four infants with enlarged subarachnoid spaces with hyperechoic content and meningeal thickening (far right image). Abbreviation: GBS, group B *Streptococcus*.

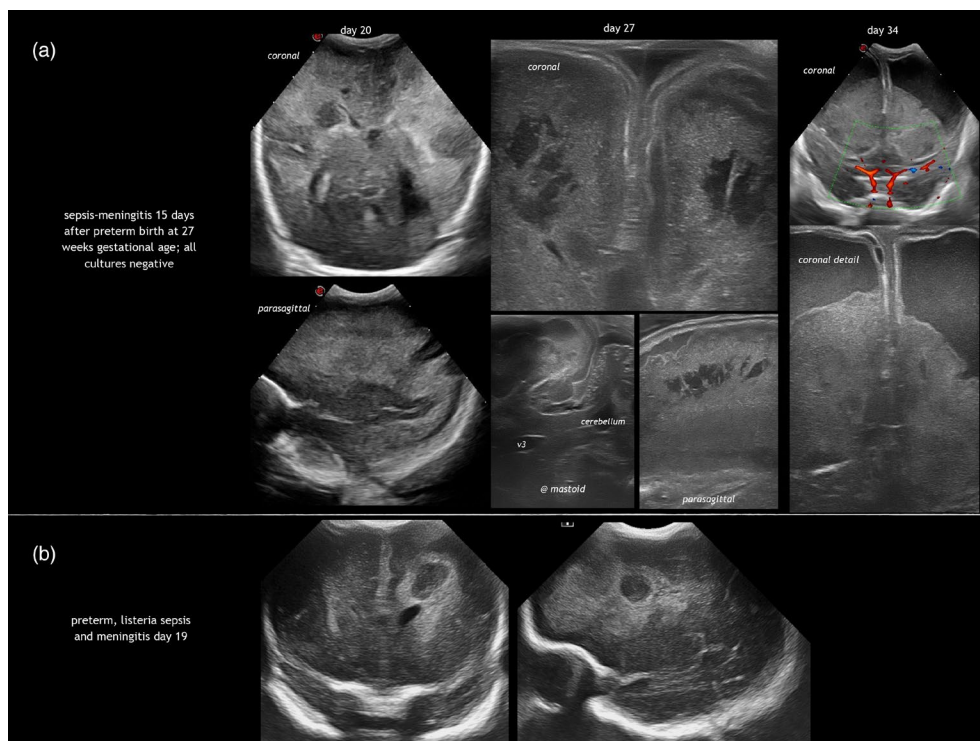


FIGURE 16 Direct non-vascular parenchymal destruction: liquefaction necrosis. (a) Increased echogenicity in the periventricular and subcortical white matter evolving into cavitation, sparing the cerebellum and parts of the deep grey matter in a 15-day-old (27 weeks gestational age) with meningitis-like syndrome and no microbiological findings. (b) Coronal and parasagittal views of a 19-day-old infant born preterm with sepsis-meningitis caused by *Listeria monocytogenes*.

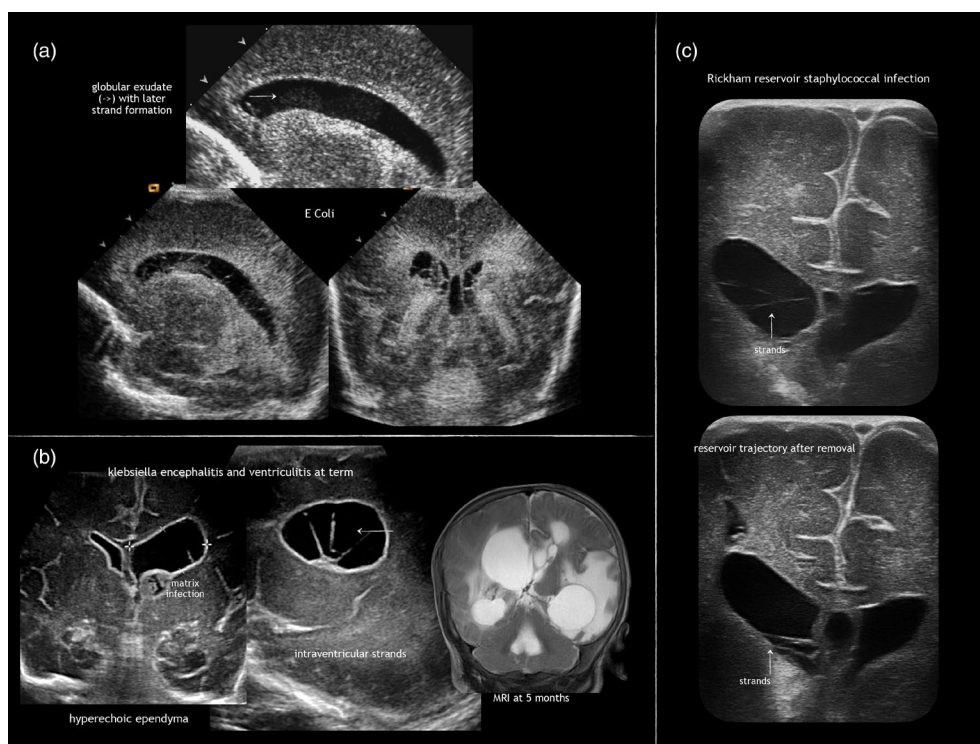


FIGURE 17 Bacterial ventriculitis/plexitis. (a) Ventriculitis; caused by *Escherichia coli*. (b) Encephalitis and ventriculitis caused by *Klebsiella*. (c) Rickham reservoir staphylococcal infection. Ventricular dilatation, increased ependymal echogenicity, intraventricular strands, and debris. Abbreviation: MRI, magnetic resonance imaging.

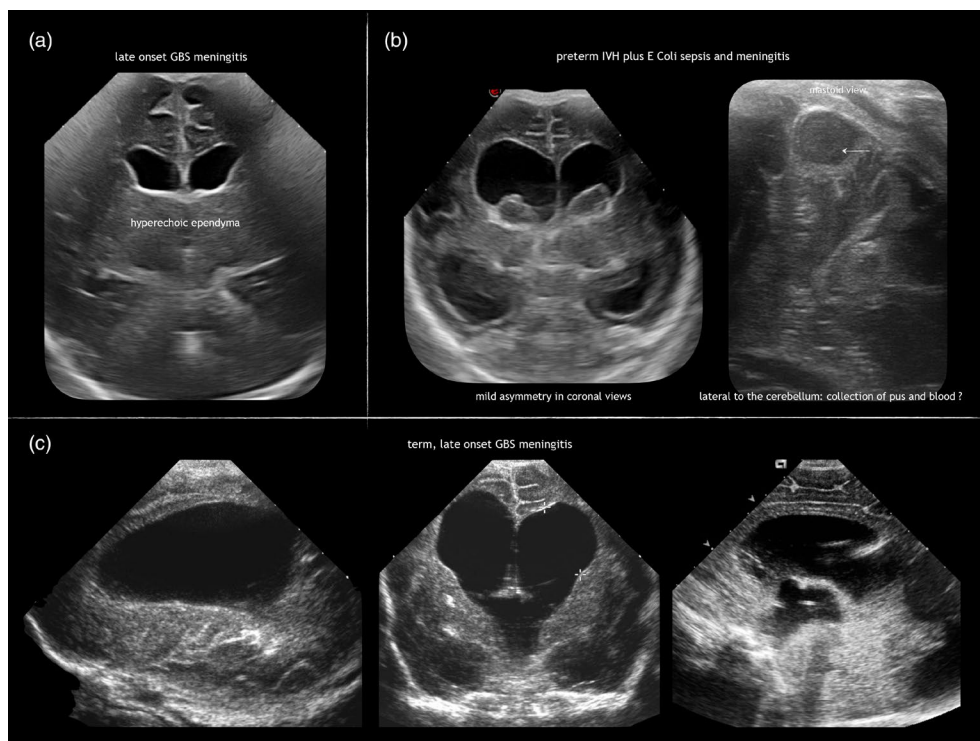


FIGURE 18 Post-meningitis hydrocephalus. (a) Late-onset group B *Streptococcus* (GBS) meningitis complicated by hydrocephalus: note the dilated lateral ventricles and hyperechoic ependyma. (b) Infant born preterm with intraventricular hemorrhage (IVH) and meningitis caused by *Escherichia coli*: note the mild asymmetry of the lateral ventricles on the coronal view; there is a collection of blood or pus lateral to the cerebellum (arrow). (c) Infant born at term with late-onset GBS meningitis who developed delayed hydrocephalus with dilatation of the lateral and third ventricles.

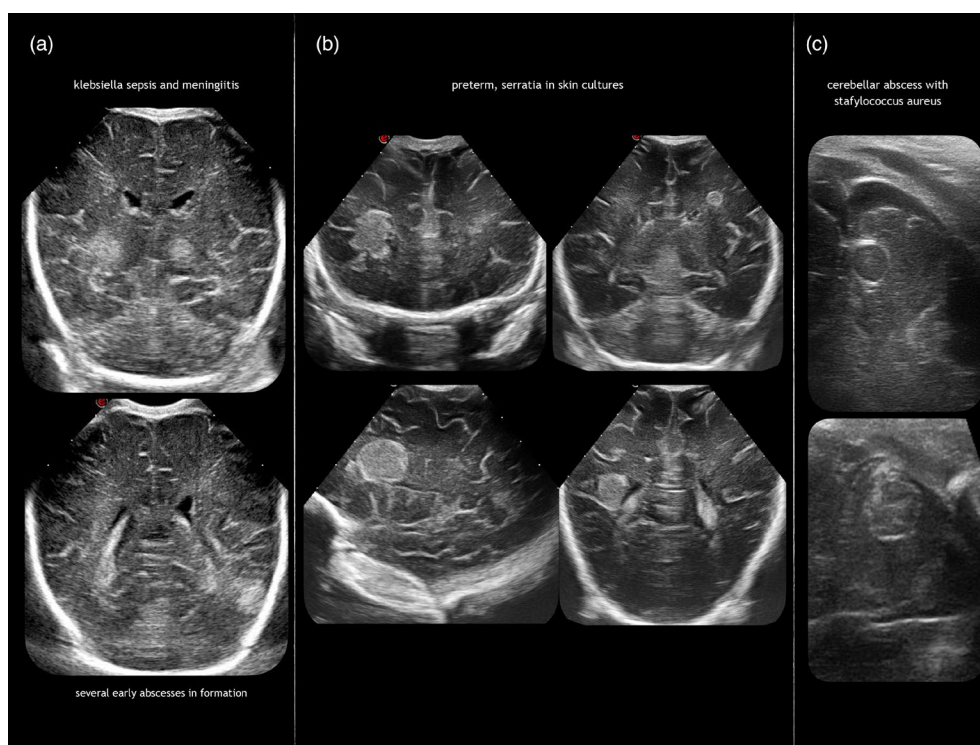


FIGURE 19 Brain abscess. Hyperechoic rounded lesions. (a) Cranial ultrasound (CUS), coronal view: infant born preterm with meningitis caused by *Klebsiella*. (b) Coronal and parasagittal CUS: unexpected findings in an infant born preterm without signs of ongoing infection but *Serratia* on skin cultures. (c) CUS, mastoid view: cerebellar abscess in two infants born preterm with *Staphylococcus aureus* infection.

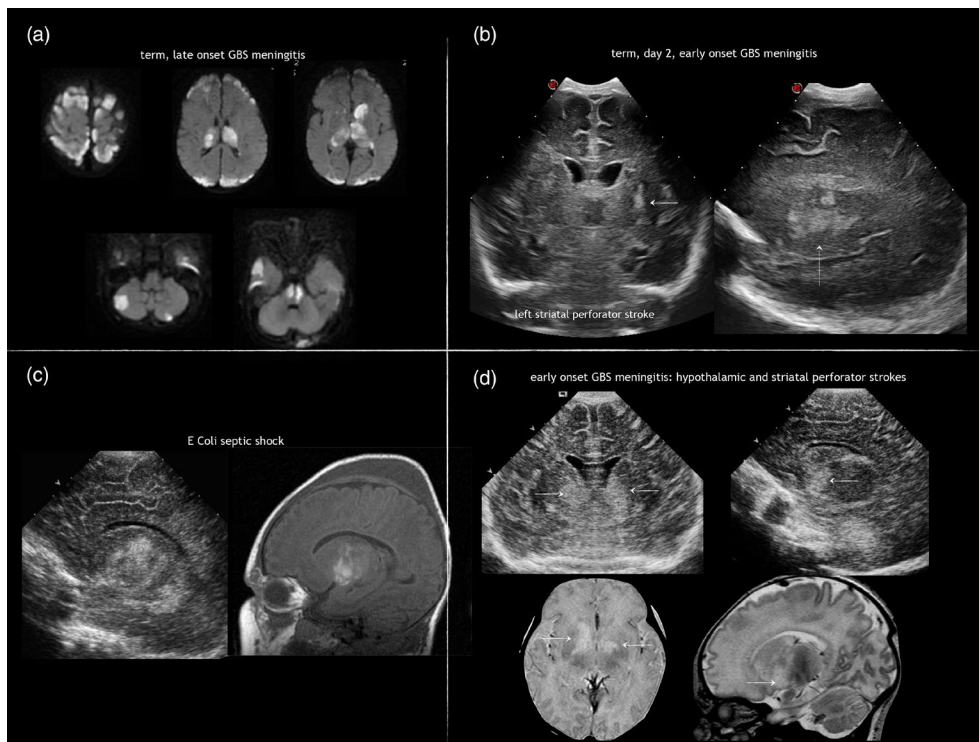


FIGURE 20 Several magnetic resonance imaging (MRI) and cranial ultrasound (CUS) examples of bacterial infection-related arterial infarction. (a) Diffusion-weighted (DW) MRI in an infant born at term with late-onset group B *Streptococcus* (GBS) meningitis: note the multiple cerebral, cerebellar, and brainstem arterial infarcts. (b) Left striatal perforator stroke in an infant born at term with early-onset GBS meningitis. (c) Anterior choroidal artery stroke in *Escherichia coli* meningitis. (d) Hypothalamic and striatal perforator strokes after early-onset GBS sepsis-meningitis in an infant born at term: CUS and MRI findings (arrows).

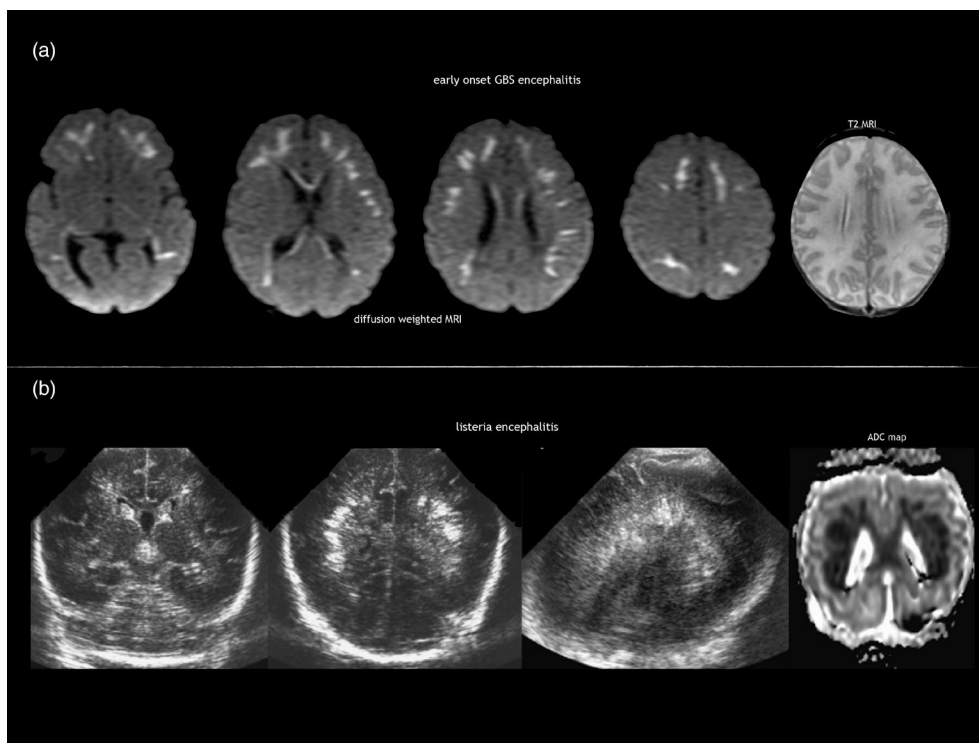


FIGURE 21 Striped appearance in the white matter seen in bacterial infection. (a) Early-onset group B *Streptococcus* (GBS) encephalitis: diffusion-weighted (DW) and T2-weighted magnetic resonance imaging (MRI). (b) Neonatal encephalitis caused by *Listeria monocytogenes*: cranial ultrasound and apparent diffusion coefficient (ADC) map.

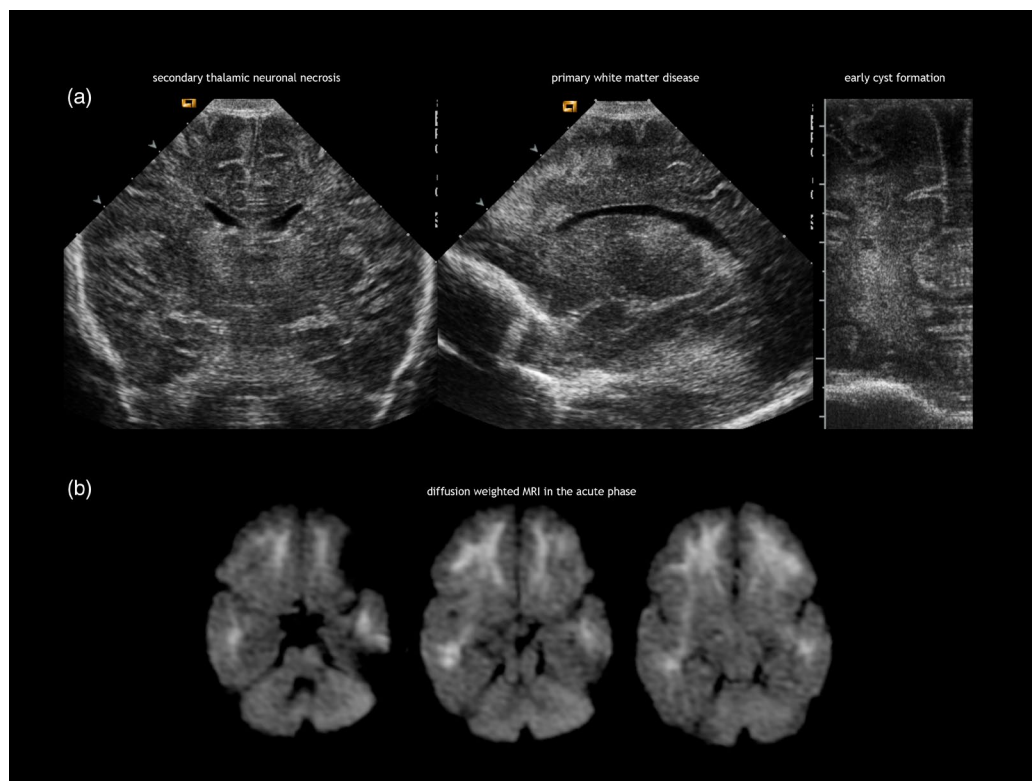


FIGURE 22 Parechovirus encephalitis. (a) Cranial ultrasound showing secondary thalamic necrosis, primary white matter disease, and early cyst formation. (b) Diffusion-weighted (DW) magnetic resonance imaging (MRI) during the acute phase.

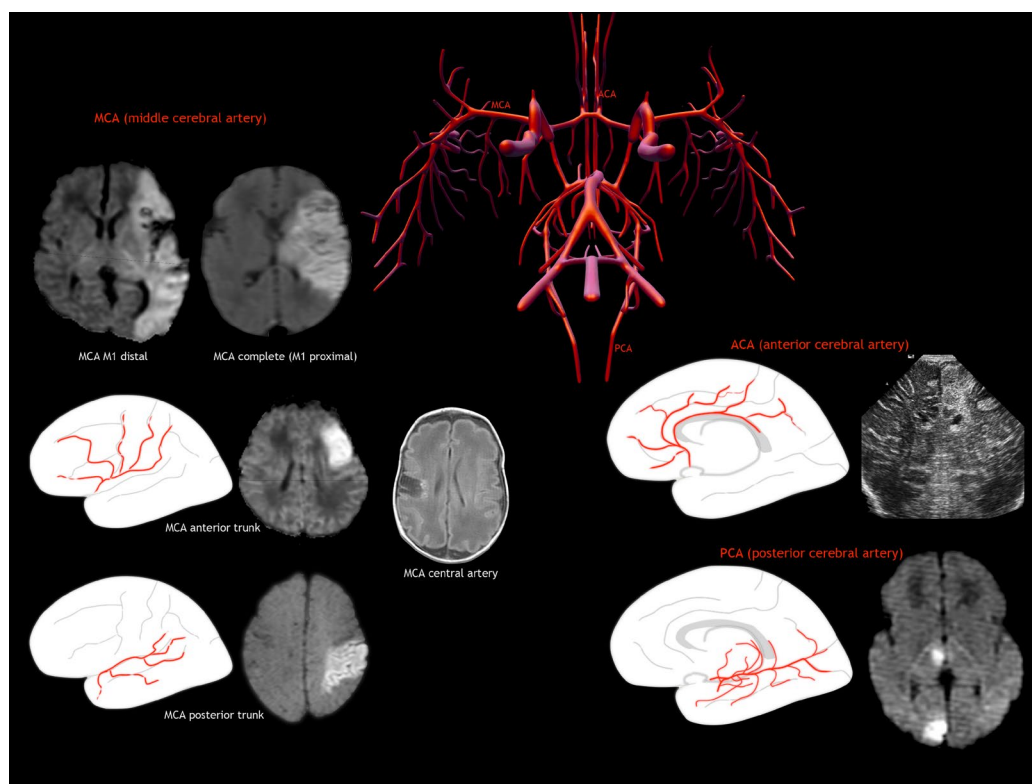


FIGURE 23 Templates illustrating brain parenchyma-affected territories in large arterial ischaemic stroke.

cerebral artery; its posterior trunk is most frequently involved.⁷⁶ In the past, CUS was considered inadequate to detect AIS. Two reasons must be considered. First, AIS can be missed if CUS is performed only on admission. In fact, the reported sensitivity to detect AIS increases if the CUS scan is repeated beyond 48 hours from admission of a neonate with seizures.^{77–79} A sensitivity up to 93% has been reported for middle cerebral artery territory strokes. The high sensitivity of CUS in this context is due to the location of the middle cerebral artery at the centre of the field of view.⁷⁹ Second, the experience of the examiner is crucial, especially in the first 48 hours during which AIS recognition using CUS is challenging.⁷⁹ Technique upgrading, and routine use of accessory acoustic windows, such as the posterior fontanelle, have increased the strength of CUS in detecting AIS. Templates help to delineate the affected arterial territory (Figure 23).⁸⁰ Crucial to early detection is a perfectly symmetrical scanning routine to detect subtle hyperechoic changes in one hemisphere. On day one, AIS appears as a subtle hyperechogenic area within the affected arterial territory. Between 24 and 72 hours, increased echogenicity defines a wedge-shaped area near the surface of the brain (Figures 24 and 25). Large infarcts evolve into cavitation within 2 to 4 weeks.⁷⁸ Focal areas of echogenicity—not typically triangular—can also be visualized, especially with distal pial artery occlusion (e.g. stroke in the area of the central groove) (Figure 26), or deep grey matter

infarction secondary to occlusion of a perforator artery. Early in the clinical course, asymmetrical blood flow velocity (lower in the affected side), or loss of pulsatile flow, can be present. In large infarcts, high-flow diastolic velocity (luxury perfusion) in the affected artery can be detected between 24 and 72 hours of the initial insult. MRI can depict small cortical infarcts, allows better delineation of the location and extent, and provides more precise prognostic information.

CEREBRAL SINOVENOUS THROMBOSIS

CSVST is underestimated because many infants remain asymptomatic or have non-specific clinical signs. Therefore, the diagnosis of CSVST requires a high index of suspicion. Seizures are the heralding sign in 55% to 70%; other associated clinical features are lethargy, apnoea, or a sepsis-like syndrome.⁸¹ Risk factors related to CSVST include instrumental (vacuum, forceps) delivery, asphyxia, sepsis or meningitis, dehydration, or a congenital heart defect.⁸¹ In experienced hands, CUS with Doppler has demonstrated strengths when evaluating the venous system; it is particularly useful in infants at high risk of developing this complication.^{82, 83} Any neonate with seizures should undergo a complete CUS evaluation of venous flow using both the anterior fontanelle,

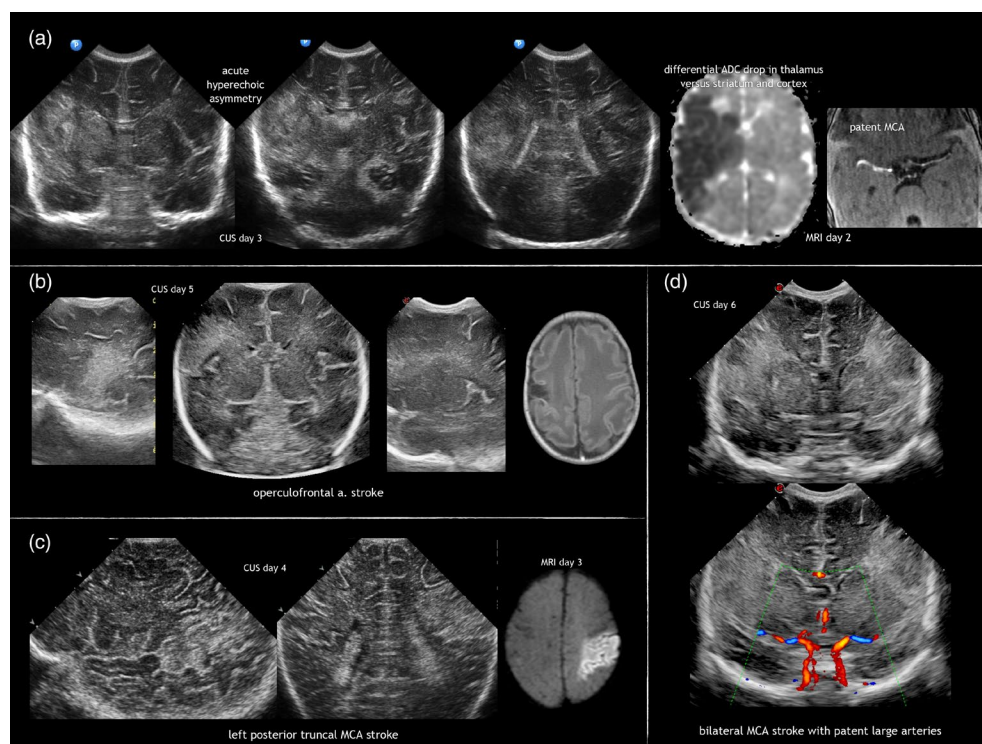


FIGURE 24 Middle cerebral artery (MCA) stroke. (a) Acute stroke in the right main branch (M1 proximal): cranial ultrasound (CUS) on day 3 displaying hyperechoic asymmetry (coronal view) and day 2 magnetic resonance imaging (MRI) with differential apparent diffusion coefficient (ADC) drop in the thalamus versus the striatum and cortex, and patent MCA. (b) Right ascending frontal stroke causing supraventricular and insular hyperechogenicity. (c) Posterior and retroinsular hyperechogenicity in left posterior truncal MCA stroke (CUS day 4 and MRI day 3). (d) Acute bilateral MCA stroke with patent large arteries on day 6 CUS with Doppler.

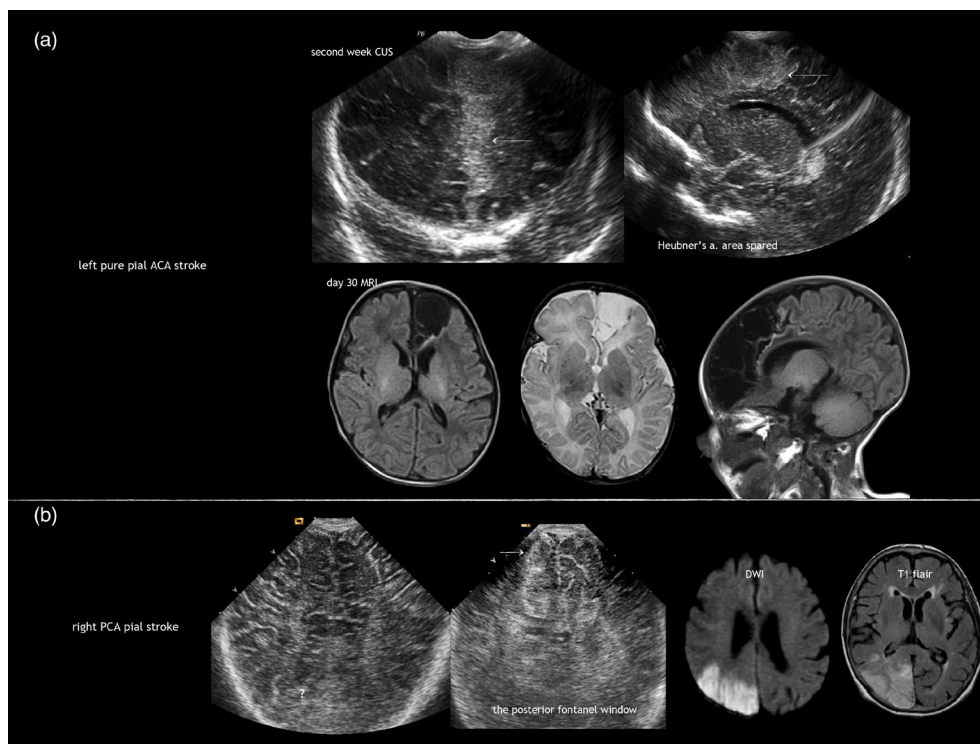


FIGURE 25 Anterior cerebral artery (ACA) and posterior cerebral artery (PCA) stroke. (a) Left pial ACA stroke after extracorporeal membrane oxygenation decannulation: second-week cranial ultrasound showing frontal hyperechogenicity and spared Heubner's artery (arrows), as well as 30-day magnetic resonance imaging (MRI). (b) Infant born at term with right-sided PCA stroke: anterior fontanelle, posterior fontanelle, and MRI (diffusion-weighted and T1 flair).

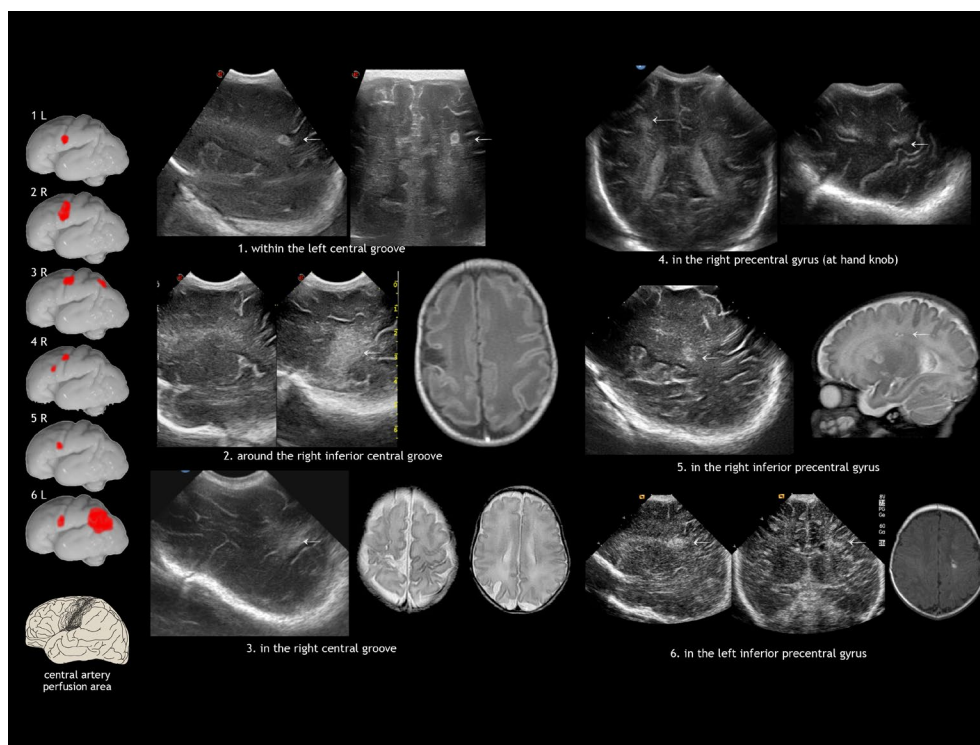


FIGURE 26 Middle cerebral artery distal (peri)central artery stroke.

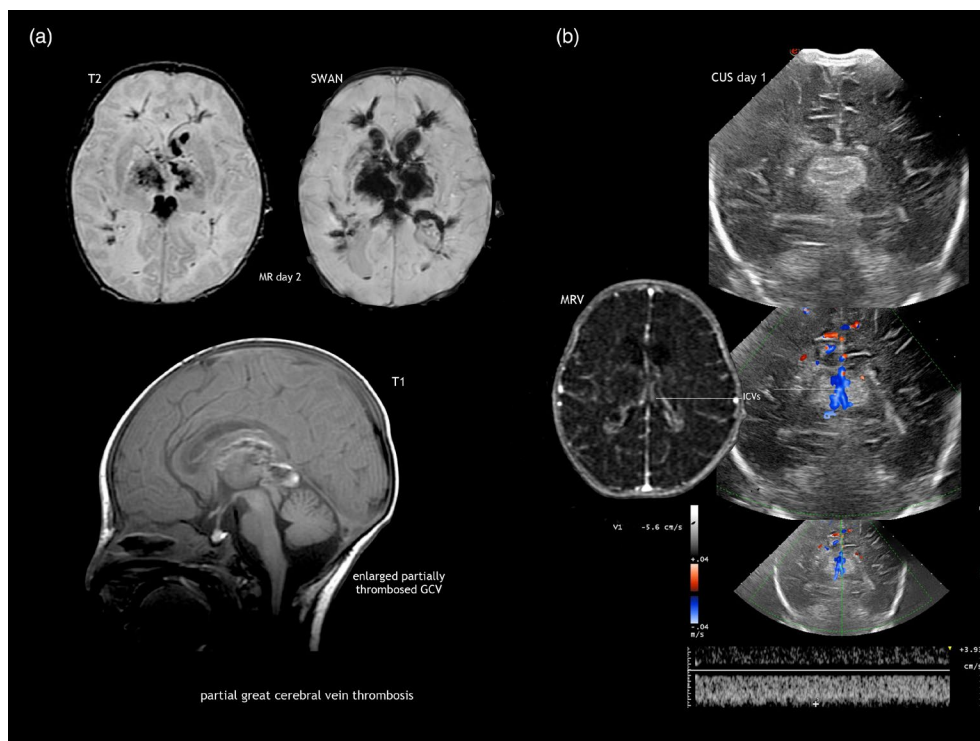


FIGURE 27 Bilateral thalamic haemorrhage. (a) Enlarged, partially thrombosed great cerebral vein (T1). (b) Patent internal cerebral veins (ICV) at the time of presentation. Abbreviations: CUS, cranial ultrasound; GCV, great sphenous vein; MRI, magnetic resonance imaging; MRV, magnetic resonance venography; SWAN, susceptibility-weighted angiography.

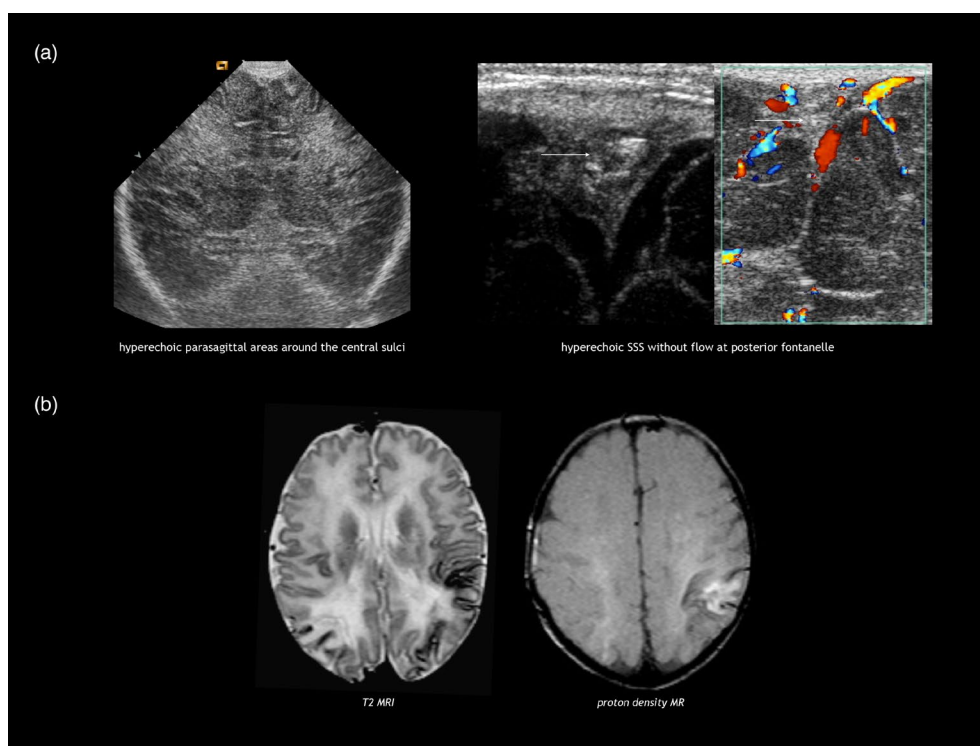


FIGURE 28 Sinus thrombosis in an infant (and mother) with factor II mutation (also prothrombin G202110A genotype). (a) Cranial ultrasound (CUS) via the anterior fontanelle showing bilateral hyperechoic parasagittal white matter around the central sulci and hyperechoic superior sagittal sinus (SSS) without flow as viewed through the posterior fontanelle. (b) T2-weighted magnetic resonance imaging (MRI) displaying bilateral asymmetric hyposignal in affected cortical areas, indicating bleeding and very high signal in the white matter, which is consistent with the changes noted on the CUS; proton density MRI sequence with the haemorrhagic hypersignal.

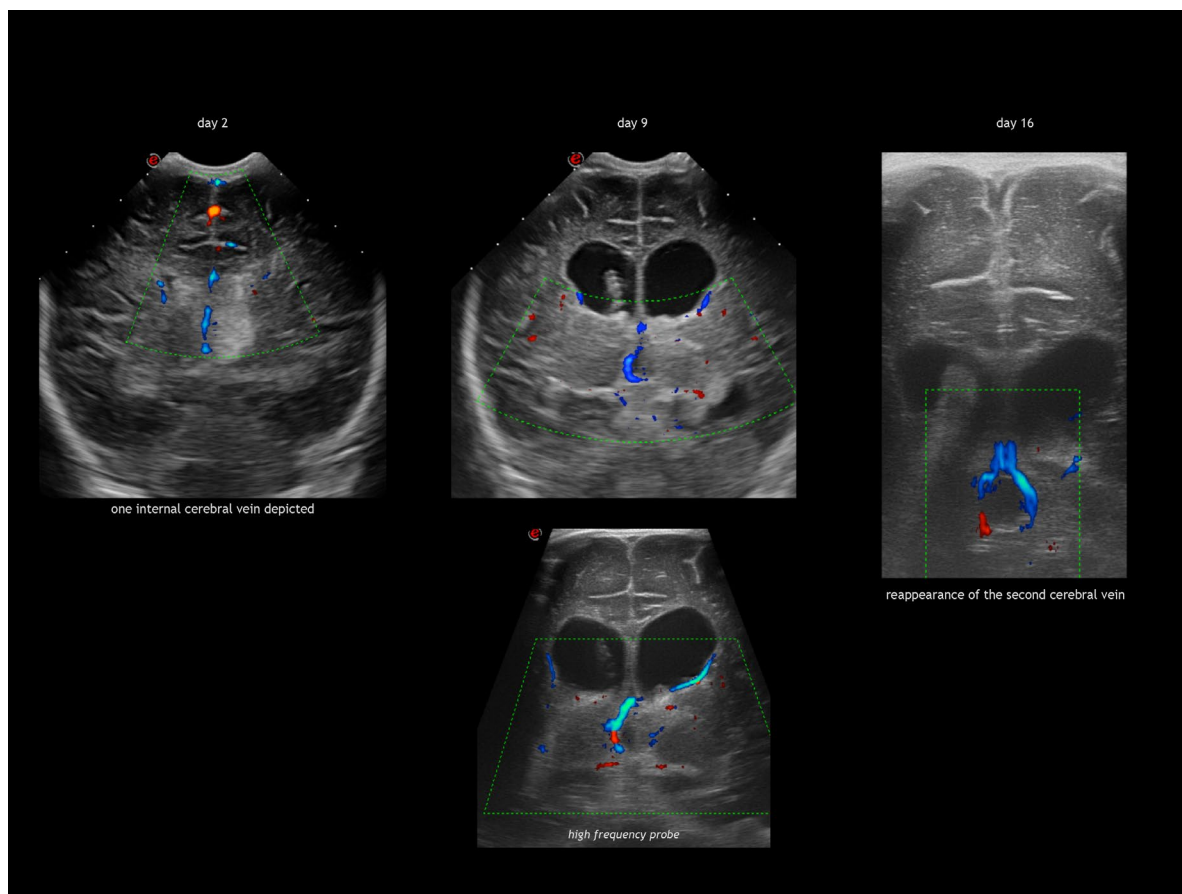


FIGURE 29 Internal cerebral vein thrombosis in an infant born at term after uncomplicated delivery. On days 2 and 9, only one internal vein is clearly visualized using a Doppler ultrasound. The right thalamus appears hyperechoic; on day 16, both internal veins are clearly visible.

to explore the internal cerebral veins, great cerebral vein, straight sinus, superior sagittal, and transverse sinus, and the mastoid fontanelle to examine the transverse and sigmoid sinus. The presence of an intraventricular haemorrhage in an infant born at term, especially if associated with thalamic or white matter haemorrhage, should raise a high index of suspicion for CSVT (Figure 27).⁸¹ On CUS with Doppler, CSVT is characterized by increased echogenicity in the thrombosed sinus together with absent or reduced flow during the acute stage (Figure 28).⁸² If CSVT is suspected, MRI is another optional diagnostic tool. In our experience, when clinical suspicion arises, CUS facilitates the expedited diagnosis of CSVT. Serial CUS scanning permits the assessment of recanalization of large vessels within a time span of a couple of weeks (Figure 29).

CONCLUSIONS

CUS is a valuable tool in the decision-making process for neonates born at term and near-term admitted to the neonatal intensive care unit, who display abnormal neurological signs or when there is a strong suspicion of CNS infection, neonatal encephalopathy, or birth trauma after

a complicated delivery. Therefore, CUS should be part of the routine work-up in these infants. Although evidence on the strengths of this technology has increased, systematic approaches to define timing and evolving patterns of sonographic features in the different pathological entities are still needed.

ACKNOWLEDGEMENTS

The members of the EurUS.Brain study group are as follows: Thais Agut, Roberta Arena, Ana Alarcon, Juan Arnaez, Marco Bartocci, Isabel Benavente-Fernández, Fernando Cabañas, Nuria Carreras Blesa, Olivier Claris, Monica Fumagalli, Alfredo Garcia-Alix, Pedro Lubián-López Simón, Tobias Mühlbacher, Alessandro Parodi, Luca Ramenghi, Charles C. Roehr, Simone Schwarz.

DATA AVAILABILITY STATEMENT

Data sharing not applicable - no new data generated.

ORCID

Eva Valverde <https://orcid.org/0000-0002-2598-9172>

Paul Govaert <https://orcid.org/0000-0002-2011-4529>

Sandra Horsch <https://orcid.org/0000-0002-2412-7319>

REFERENCES

- Wisnowski JL, Wintermark P, Bonifacio SL, Smyser CD, Barkovich AJ, Edwards AD, et al. Neuroimaging in the term newborn with neonatal encephalopathy. *Seminars in Fetal and Neonatal Medicine* 2021; 26(5):101304.
- Dudink J, Steggerda S, Horsch S, Agut T, Alarcon A, Arena R, et al. State-of-the-art neonatal cerebral ultrasound: technique and reporting. *Pediatric Research* 2020; 87:3–12.
- van Wezel-Meijler G, Steggerda SJ, Leijser LM. Cranial Ultrasonography in Neonates: Role and Limitations. *Seminars in Perinatology* 2010; 34(1):28–38.
- Agut T, Alarcon A, Cabañas F, Bartocci M, Martinez-Biarge M, Horsch S, et al. Preterm white matter injury: ultrasound diagnosis and classification. *Pediatric Research* 2020; 87:37–49. Springer Nature.
- Parodi A, Govaert P, Horsch S, Bravo MC, Ramenghi LA, Agut T, et al. Cranial ultrasound findings in preterm germinal matrix haemorrhage, sequelae and outcome. *Pediatric Research* 2020; 87:13–24. Springer Nature.
- Sanchez Fernandez I, Morales-Quezada JL, Kim P. Prognostic value of brain magnetic resonance imaging in neonatal hypoxic-ischemic encephalopathy: A meta-analysis. *J Child Neurol* 2017; 32(13):1065–73.
- Daneman A, Epelman M, Blaser S, Jarrin JR. Imaging of the brain in full-term neonates: does sonography still play a role? *Pediatr Radiol* 2006; 36:636–46.
- Epelman M, Daneman A, Kellenberger CJ, Aziz A, Konen O, Moineddin R, et al. Neonatal encephalopathy: A prospective comparison of head US and MRI. *Pediatric Radiology* 2010; 40(10):1640–50.
- Dinan D, Daneman A, Guimaraes CV, Chauvin NA, Victoria T, Epelman M. Easily overlooked sonographic findings in the evaluation of neonatal encephalopathy: Lessons learned from magnetic resonance imaging. *Seminars in Ultrasound, CT and MRI* 2014; 35(6):627–51.
- D'Alton. Executive summary: Neonatal Encephalopathy and Neurologic Outcome, Second Edition. *Obstetrics and Gynecology* 2014; 123(4):896–901.
- Cowan F, Rutherford M, Groenendaal F, Eken P, Mercuri E, Bydder GM, et al. Origin and timing of brain lesions in term infants with neonatal encephalopathy. *Lancet* 2003; 361(9359):736–42.
- Pasternak JF, Gorey MT. The syndrome of acute near-total intrauterine asphyxia in the term infant. *Pediatr Neurol* 1998; 18:391–8.
- Ikeda T, Murata Y, Quilligan EJ, Choi BH, Parer JT, Doi S, et al. Physiologic and histologic changes in near-term fetal lambs exposed to asphyxia by partial umbilical cord occlusion. *Am J Obstet Gynecol* 1988; 178(1 Pt 1):24–32.
- Brann AW, Myers RE. Central nervous system findings in the newborn monkey following severe in utero partial asphyxia. *Neurology* 1975; 25:327–38.
- Miller SP, Ramaswamy V, Michelson D, Barkovich AJ, Holshouser B, Wycliffe N, et al. Patterns of brain injury in term neonatal encephalopathy. *J Pediatr* 2005; 146:453–60.
- de Vries LS, Groenendaal F. Patterns of neonatal hypoxic-ischemic brain injury. *Neuroradiology* 2010; 52:555–66.
- Swarte R, Lequin M, Cherian P, Zecic A, Van Goudoever J, Govaert P. Imaging patterns of brain injury in term-birth asphyxia. *Acta Paediatrica, International Journal of Paediatrics* 2009; 98(3):586–92.
- Leijser LM, De Vries LS, Rutherford MA, Manzur AY, Groenendaal F, De Koning TJ, et al. Cranial ultrasound in metabolic disorders presenting in the neonatal period: Characteristic features and comparison with MR imaging. *American Journal of Neuroradiology* 2007; 28(7):1223–31.
- Annink KV, de Vries LS, Groenendaal F, Vijlbrief DC, Weeke LC, Roehr CC, et al. The development and validation of a cerebral ultrasound scoring system for infants with hypoxic-ischaemic encephalopathy. *Pediatric Research* 2020; 87:59–66.
- Pinto PS, Tekes A, Singhi S, Northington FJ, Parkinson C, Huisman TAGM. White-gray matter echogenicity ratio and resistive index: sonographic bedside markers of cerebral hypoxic-ischemic injury/edema? *J Perinatol* 2012; 32(6):448–53.
- Salas J, Tekes A, Hwang M, Northington FJ, Huisman TAGM. Head ultrasound in neonatal hypoxic-ischemic injury and its mimickers for clinicians: A review of the patterns of injury and the evolution of findings over time. *Neonatology* 2018; 114(3):185–97.
- Archer LN, Levene MI, Evans DH. Cerebral artery Doppler ultrasonography for prediction of outcome after perinatal asphyxia. *Lancet* 1986; 2(8516):116–8.
- Pryds O, Greisen G, Lou H, Friis-Hansen B. Vasoparalysis associated with brain damage in asphyxiated term infants. *J Pediatr* 1990; 117:119–25.
- Meek JH, Elwell CE, McCormick DC, Edwards AD, Townsend JP, Stewart AL, et al. Abnormal cerebral haemodynamics in perinatally asphyxiated neonates related to outcome. *Arch Dis Child Fetal Neonatal Ed* 1999; 81(2).
- Skranes JH, Elstad M, Thoresen M, Cowan FM, Stiris T, Fugelseth D. Hypothermia makes cerebral resistance index a poor prognostic tool in encephalopathic newborns. *Neonatology* 2014; 106(1):17–23.
- Elstad M, Whitelaw A, Thoresen M. Cerebral resistance index is less predictive in hypothermic encephalopathic newborns. *Acta Paediatrica, International Journal of Paediatrics* 2011; 100(10):1344–1349.
- Snyder EJ, Perin J, Chavez-Valdez R, Northington FJ, Lee JK, Tekes A. Head ultrasound resistive indices are associated with brain injury on diffusion tensor imaging magnetic resonance imaging in neonates with hypoxic-ischemic encephalopathy. *Journal of Computer Assisted Tomography* 2020; 44(5):687–91.
- Gerner G, Burton JV, Poretti A, Bosemani T, Cristofalo E, Tekes A, et al. Transfontanelar Duplex brain ultrasonography resistive indices as a prognostic tool in neonatal hypoxic-ischemic encephalopathy before and after treatment with therapeutic hypothermia. *J Perinatol* 2016; 36(3):202–6.
- Mankad K, Talenti G, Tan AP, Gonçalves FG, Robles C, Kan EYL, et al. Neurometabolic disorders of the newborn. *Topics in Magnetic Resonance Imaging* 2018; 27(4):179–96.
- Schiffrin BS, Ater S. Fetal hypoxic and ischemic injuries. *Curr Opin Obstet Gynecol* 2006; 18:112–22.
- Hobbs C, Childs AM, Wynne J, Livingston J, Seal A. Subdural haematoma and effusion in infancy: An epidemiological study. *Arch Dis Child* 2005; 90(9):952–5.
- Gupta SN, Kechli AM, Kanamalla US. Intracranial Hemorrhage in Term Newborns: Management and Outcomes. *Pediatr Neurol* 2009; 40(1):1–12.
- Åberg K, Norman M, Pettersson K, Järnbert-Pettersson H, Ekéus C. Protracted vacuum extraction and neonatal intracranial hemorrhage among infants born at term: A nationwide case-control study. *Acta Obstet Gynecol Scand* 2019; 98(4):523–32.
- Brouwer AJ, Groenendaal F, Koopman C, Nievelstein RJA, Han SK, de Vries LS. Intracranial hemorrhage in full-term newborns: A hospital-based cohort study. *Neuroradiology* 2010; 52(6):567–76.
- Looney CB, Smith JK, Merck LH, Wolfe HM, Chescheir NC, Hamer RM, et al. Intracranial hemorrhage in asymptomatic neonates: Prevalence on MR images and relationship to obstetric and neonatal risk factors. *Radiology* 2007; 242(2):535–41.
- Rooks VJ, Eaton JP, Ruess L, Petermann GW, Keck-Wherley J, Pedersen RC. Prevalence and evolution of intracranial hemorrhage in asymptomatic term infants. *AJNR Am J Neuroradiol* 2008; 29(6):1082–9.
- Nikam RM, Kandula VV, Yue X, Krishnan V, Kumbhar SS, Averill LW, et al. Birth-related subdural hemorrhage: prevalence and imaging morphology. *Pediatr Radiol* 2021; 51(6):939–46.

38. Delanghe G, Squier W, Sonnaert M, Dudink J, Lequin M, Govaert P. Neonatal subcortical bruising. *Clin Case Rep* 2018; 6(2):407–15.
39. Currarino G. Occipital osteodiaschisis: Presentation of four cases and review of the literature. *Pediatr Radiol* 2000; 30(12):823–9.
40. Baram TZ, Butler JJ, Nelson MD Jr., McArdle CB. Transverse sinus thrombosis in newborns: clinical and magnetic resonance imaging findings. *Ann Neurol* 1988; 24(6):792–4.
41. MacK J, Squier W, Eastman JT. Anatomy and development of the meninges: Implications for subdural collections and CSF circulation. *Pediatr Radiol* 2009; 39(3):200–10.
42. Inder TE, Perlman JM, Volpe JJ. Intracranial hemorrhage: Subdural, subarachnoid, intraventricular (term infant), miscellaneous. Chapter 22, 593–622. In: Volpe's Neurology of the Newborn. 2018; 6th Ed. Elsevier.
43. Jhavar BS, Ranger A, Steven D, Del Maestro RF, Cohen AR, McComb JG, et al. Risk factors for intracranial hemorrhage among full-term infants: A case-control study. *Neurosurgery* 2003; 52(3):581–90.
44. Elkhunovich M, Sirody J, McCormick T, Goodarzi F, Claudius I. The utility of cranial ultrasound for detection of intracranial hemorrhage in infants. *Pediatr Emerg Care* 2018; 34(2):96–101.
45. Aoki N. Epidural haematoma in the newborn infants: therapeutic consequences from the correlation between haematoma content and computed tomography features. *Acta Neurochir* 1990; 106:65–7.
46. Vachharajani A, Mathur A. Ultrasound-guided needle aspiration of cranial epidural hematoma in a neonate: treating a rare complication of vacuum extraction. *Am J Perinatol* 2002; 19(8):401–4.
47. Lam A, Cruz GB, Johnson I. Extradural hematoma in neonates. *J Ultrasound Med* 1991; 10:205–9.
48. Govaert P. Cranial haemorrhage in the term newborn infant. *Clinics Dev Med* nr. 129, London: Mac Keith Press, 1993; ISBN 0 901260 98 3.
49. de Vries LS, Verboon-Macielek MA, Cowan FM, Groenendaal F. The role of cranial ultrasound and magnetic resonance imaging in the diagnosis of infections of the central nervous system. *Early Hum Dev* 2006; 82(12):819–25.
50. Kim KS. Acute bacterial meningitis in infants and children. *Lancet Infect Dis* 2010; 10(1):32–42.
51. Jaremko JL, Moon AS, Kumbha S. Patterns of complications of neonatal and infant meningitis on MRI by organism: A 10-year review. *Eur J Radiol* 2011; 80(3):821–7.
52. Mahajan R, Lodha A, Anand R, Patwari AK, Anand VK, Garg DP. Cranial sonography in bacterial meningitis. *Indian Pediatr* 1995; 32(9):989–93.
53. Yikilmaz A, Taylor GA. Sonographic findings in bacterial meningitis in neonates and young infants. *Pediatr Radiol* 2008; 38(2):129–37.
54. Tatsuno M, Uchida K, Okuyama K, Kawauchi A. Color Doppler flow imaging of CSF flow in an infant with intraventricular hemorrhage. *Brain Dev* 1992; 14:110–3.
55. Rudas G, Almássy Z, Papp B, Varga E, Méder Ü, Taylor GA. Echodense spinal subarachnoid space in neonates with progressive ventricular dilatation: A marker of noncommunicating hydrocephalus. *AJR Am J Roentgenol* 1998; 171(4):1119–21.
56. Jéquier S, Jéquier J-C. Sonographic Nomogram of the Leptomeninges (Pia-Glial Plate) and Its Usefulness for Evaluating Bacterial Meningitis in Infants. *AJNR Am J Neuroradiol* 1999; 20(7):1359–64.
57. Couture A, Veyrac C, Baud C, Saguin M, Ferran JL. Advanced cranial ultrasound: Transfontanellar Doppler imaging in neonates. *Eur Radiol* 2001; 11(12):2399–410.
58. Miyairi I, Causey KT, DeVincenzo JP, Buckingham SC. Group B Streptococcal Ventriculitis: A Report of Three Cases and Literature Review. *Pediatr Neurol* 2006; 34(5):395–9.
59. Rennie JM, Hagmann CF, Robertson N. The baby with a suspected infection. Chapter 13; 270. In: Neonatal Cerebral Investigation. Ed: Cambridge. 2008; ISBN-13 978–0–511–41368-1.
60. Govaert P, de Vries LS. Chapter 63; Bacterial meningitis, ventriculitis, 384. In: An Atlas of Neonatal Brain Sonography. Clinics in Developmental Medicine 2010, No.182-183. Mc Keith Press 2nd Ed.
61. Verboon-Macielek MA, Truttmann AC, Groenendaal F, Skranes J, Döllner H, Hunt RW, et al. Development of cystic periventricular leukomalacia in newborn infants after rotavirus infection. *J Pediatr* 2012; 160(1):165–8.
62. Kumar R, Singhi P, Dekate P, Singh M, Singhi S. Meningitis related ventriculitis - Experience from a tertiary care centre in Northern India. *Indian J Pediatr* 2015; 82(4):315–20.
63. Tibussek D, Sinclair A, Yau I, Teatero S, Fittipaldi N, Richardson SE, et al. Late-onset group B streptococcal meningitis has cerebrovascular complications. *J Pediatr* 2015; 166(5):1187–1192.e1.
64. Gupta N, Grover H, Bansal I, Hooda K, Sapire JM, Anand R, et al. Neonatal cranial sonography: Ultrasound findings in neonatal meningitis - A pictorial review. *Quant Imaging Med Surg* 2017; 7(1):123–31.
65. Littwin B, Pomiećko A, Stępień-Roman M, Spárcz Z, Kosiak W. Bacterial meningitis in neonates and infants – The sonographic picture. *J Ultrason* 2018; 18(72):63–70.
66. Peros T, van Schuppen J, Bohte A, Hodiament C, Aronica E, de Haan T. Neonatal bacterial meningitis versus ventriculitis: A cohort-based overview of clinical characteristics, microbiology, and imaging. *Eur J Pediatr* 2020; 179(12):1969–77.
67. de Vries LS. Viral infections and the neonatal brain. *Semin Pediatr Neurol* 2019; 32:100769.
68. Bucci S, Coltella L, Martini L, Santisi A, De Rose DU, Piccioni L, et al. Clinical and Neurodevelopmental Characteristics of Enterovirus and Parechovirus Meningitis in Neonates. *Front Pediatr* 2022; 10(May):1–7.
69. Mactier H, Galea P, McWilliam R. Acute obstructive hydrocephalus complicating bacterial meningitis in childhood. *BMJ* 1998; 316:1887–9.
70. Chang CJ, Chang WN, Huang LT, Chang YC, Huang SC, Hung PL, et al. Cerebral infarction in perinatal and childhood bacterial meningitis. *QJM* 2003; 96(10):755–62.
71. Hernández MI, Sandoval CC, Tapia JL, Mesa T, Escobar R, Huete I, et al. Stroke patterns in neonatal group B streptococcal meningitis. *Pediatr Neurol* 2011; 44(4):282–8.
72. Fitzgerald KC, Golomb MR. Neonatal arterial ischemic stroke and sinovenous thrombosis associated with meningitis. *J Child Neurol* 2007; 22(7):818–22.
73. Pisani F, Spagnoli C, Falsaperla R, Nagarajan L, Ramantani G. Seizures in the neonate: A review of etiologies and outcomes. *Seizure* 2021; 85:48–56.
74. Hallberg B, Blennow M. Investigations for neonatal seizures. *Semin Fetal Neonatal Med* 2013; 18(4):196–201.
75. Ferriero DM, Fullerton HJ, Bernard TJ, Billingham L, Daniels SR, DeBaun MR, et al. Management of Stroke in Neonates and Children: A Scientific Statement From the American Heart Association/American Stroke Association. *Stroke* 2019; 50(3):e51–e96.
76. Gunny RS, Lin D. Imaging of Perinatal Stroke. *Magn Reson Imaging Clin N Am* 2012; 20(1):1–33.
77. Golomb MR, Dick PT, MacGregor DL, Armstrong DC, deVeber GA. Cranial ultrasonography has a low sensitivity for detecting arterial ischemic stroke in term neonates. *J Child Neurol* 2003; 18(2):98–103.
78. Cowan F, Mercuri E, Groenendaal F, Bassi L, Ricci D, Rutherford M, et al. Does cranial ultrasound imaging identify arterial cerebral infarction in term neonates? *Arch Dis Child Fetal Neonatal Ed* 2005; 90(3):252–6.
79. Olivé G, Agut T, Echeverría-Palacio CM, Arca G, García-Alix A. Usefulness of Cranial Ultrasound for Detecting Neonatal Middle Cerebral Artery Stroke. *Ultrasound Med Biol* 2019; 45(3):885–90.

80. Govaert P, Ramenghi L, Taal R, Dudink J, Lequin M. Diagnosis of perinatal stroke II: mechanisms and clinical phenotypes. *Acta Paediatr* 2009; 98(11):1720–6.
81. Berfelo FJ, Kersbergen KJ, Van Ommen CH, Govaert P, Van Straaten HLM, Poll-The BT, et al. Neonatal cerebral sinovenous thrombosis from symptom to outcome. *Stroke* 2010; 41(7):1382–8.
82. Miller E, Daneman A, Doria AS, Blaser S, Traubici J, Jarrin J, et al. Color Doppler US of normal cerebral venous sinuses in neonates: A comparison with MR venography. *Pediatr Radiol* 2012; 42(9):1070–9.
83. Raets MA, Sol JJ, Govaert P, Lequin MH, Reiss IKM, Kroon AA, et al. Serial cranial US for detection of cerebral sinovenous thrombosis in preterm infants. *Radiology* 2013; 269(3):879–86.

How to cite this article: Valverde E, Ybarra M, Bravo MC, Dudink J, Govaert P, Horsch S, et al. State-of-the-art cranial ultrasound in clinical scenarios for infants born at term and near-term. *Dev Med Child Neurol*. 2025;67:322–347. <https://doi.org/10.1111/dmcn.16133>



Mac Keith Press



Spastic Hemiplegia–Unilateral Cerebral Palsy

Understanding and managing the condition across the lifespan: A practical guide for families

Marcie Ward, Lily Collison, and Eimear Gabbett

Spastic hemiplegia is a very common subtype of cerebral palsy (CP), and CP itself is the most common cause of childhood-onset physical disability. An estimated 17 million people worldwide have CP. Spastic hemiplegia is also known as unilateral spastic CP or, simply, unilateral CP. Spastic hemiplegia affects the upper and lower limbs of one side of the body. The upper limb is usually more affected than the lower limb. This practical guide addresses spastic hemiplegia across the lifespan and the evidence-based, best-practice treatments. It also includes the lived experience of families.

Dec 2024 / 400 pages / ISBN 9781952181139 / Paperback £45.00 / eBook £10.00

www.macketh.co.uk/book/spastic-hemiplegia-unilateral-cerebral-palsy

