

Medical care & clinical practice

european standards of care for newborn health

EFCNI european foundation for the care of newborn infants

Topic Expert Group

Medical care and clinical practice

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Topic Expert Group: **Medical care and clinical practice**

Overview

Preterm and ill infants, treated in the neonatal intensive care unit have multiple medical clinical conditions, resulting in an extremely vulnerable patient group. (1–4) Enormous improvements in neonatal care during the last years have also made care increasingly complex.

The most important neonatal event is the postnatal adaptation to extrauterine life during which air breathing is established and circulatory changes take place. Difficulties may occur with transition in situations such as preterm birth and following perinatal asphyxia, accounting for much of the associated neonatal mortality and morbidity. (5–8) Other conditions that are of great relevance for preterm and other ill infants are bronchopulmonary dysplasia, necrotising enterocolitis (NEC), respiratory distress syndrome, suspected early onset neonatal sepsis, hypoglycaemia, hypoxic ischaemic encephalopathy, persistent pulmonary hypertension of the newborn infant, neonatal jaundice, Retinopathy of Prematurity, and vitamin K deficiency bleeding.

Additionally, infants requiring neonatal intensive care constitute a high-risk population for developing brain injury, particularly full term and preterm infants exposed to hypoxia-ischaemia, CNS infections, or with congenital anomalies. Therefore, early recognition of disturbed brain function or structural brain injury is important in the institution of preventive or treatment strategies, and appropriate follow-up. Early identification of impaired function will improve clinical management and long-term functional outcomes. (9–14)

The Topic Expert Group on Medical care and clinical practice develops standards on the prevention, diagnosis and management of the main medical conditions and challenges affecting preterm or ill babies. Additionally, standards on specific clinical procedures and techniques are developed.

Source

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Hypoglycaemia in at risk term infants

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Target group
Term newborn infants and parents

User group
Healthcare professionals, neonatal units, hospitals, and health services

Statement of standard
Measures are taken to identify, prevent, and manage hypoglycaemia in newborn infants who are at risk for impaired metabolic adaptation within the first 72 hours of life, including those with prolonged fetal distress, growth restriction, maternal diabetes, asphyxia, maternal beta-blocker medication.

Rationale
The goal is to prevent the adverse effect of hypoglycaemia while minimising unnecessary separation of mother and the newborn infant.

At birth, the discontinuation of nutrients from the mother results in a decline in plasma glucose level during the first two hours of postnatal life. Studies that have documented blood glucose concentration during the first 2-4 h of life reported values from as low as 1.1-1.4 mmol/L (20-25 mg/dL). (1) Although levels may be low early postnatally this stabilises within 48-72 hours post-delivery to levels more typical of later childhood.

Healthy newborn infants tolerate these initially low blood glucose levels even though glucose is the major oxidative fuel of the brain, because the neonatal brain also has the capacity to oxidise ketone bodies and lactate. During this period, endogenous production of glucose is promoted by glycogenolysis and gluconeogenesis. Enhancement of fat oxidative metabolism also contributes to the production of ketone bodies. Metabolic neonatal transition is integrated under the influence of a postnatal hormonal surge and timely production of key regulatory enzymes. (1)

However, the increased risk of hypoglycaemic exposure per se and impaired metabolic adaption resulting in inability to liberate alternative fuels such as ketones and lactate place some infants at increased risk from the adverse outcomes related to hypoglycaemia.

In addition to the risk categories listed above, perturbations of adaptive responses can occur in infants with sepsis, haemolytic disease and specific inborn errors of metabolism. They can also occur in term infants with congenital disorders that prevent infants from mounting an adequate counter-regulatory metabolic and endocrine response, such as hyperinsulinism. (2)

There are other well-known risk situations for hypoglycaemia such as preterm or late preterm birth, but these situations are not under the scope of this topic.

Benefits

Short-term benefits
- Reduced exposure to potentially harmful hypoglycaemia in at risk infants (3)
- Reduced unnecessary investigations and interventions (4)
- Minimised separation of mother and infant (consensus)

- Increased rate of diagnoses of infants with hypoglycaemic disorders before discharge (5)

Long-term benefits

- Improved neurologic outcome (consensus)

Components of the standard

Component	Grading of evidence	Indicator of meeting the standard
For parents and family		
1. Parents are informed by healthcare professionals about the importance of early energy provision and blood glucose monitoring. (6)	A (Low quality) B (High quality)	Patient information sheet
For healthcare professionals		
2. A unit guideline on identification, prevention, and management of hypoglycaemia is adhered to by all healthcare professionals.	B (High quality)	Guideline
3. Training on identification, prevention, and management of hypoglycaemia is attended by all responsible healthcare professionals.	B (High quality)	Training documentation
4. Risk factors for hypoglycaemia are identified at birth, and within the first days of life according to the clinical situation. (7)	A (Moderate quality)	Clinical records, guideline
5. An early feed, within one hour, is provided. (8,9)	A (High quality)	Clinical records, guideline
6. Thermal care, ideally given by skin-to-skin positioning, is provided. (10)	A (Moderate quality)	Clinical records, guideline
7. Blood glucose is measured at predetermined times. (3)	A (Moderate quality)	Clinical records, guideline
8. Observation of well-being and feeding documentation is conducted. (11)	B (High quality)	Clinical records, guideline
9. Interventions are administered according to operational thresholds approach. (12)	B (High quality)	Clinical records, guideline

For neonatal unit		
10. A unit guideline based on an operational threshold approach using values advocated by professional bodies is available and regularly updated in all maternity and neonatal units. (13)	A (Low quality) B (High quality)	Guideline
For hospital		
11. Training on identification, prevention, and management of hypoglycaemia is ensured.	A (High quality) B (High quality)	Training documentation
12. Equipment suitable for immediate and reliable blood glucose measurements is provided. (14)	A (High quality) B (High quality)	Audit report
13. Training in awareness of the limitations of the devices used for blood glucose monitoring is ensured. (14)	A (High quality) B (High quality)	Training documentation
For health service		
14. A national guideline based on an operational threshold approach using values advocated by professional bodies is available and regularly updated.	B (High quality)	Guideline

Where to go – further development of care

Further development	**Grading of evidence**
For parents and family	
N/A	
For healthcare professionals	
N/A	
For neonatal unit	
N/A	
For hospital	
N/A	
For health service	
• Prioritise scientific studies investigating impaired metabolic adaptation, and the long-term consequences of hypoglycaemia with or without clinical symptoms.	B (Moderate quality)

Getting started

Initial steps
For parents and family
• Parents are verbally informed by healthcare professionals about the importance of early energy provision and blood glucose monitoring.

For healthcare professionals

- Attend training on identification, prevention, and management of hypoglycaemia.
- Promote early skin-to-skin contact and breastfeeding as standard care.

For neonatal unit

- Develop and implement a unit guideline on identification, prevention, and management of hypoglycaemia, based on an operational threshold approach using values advocated by professional bodies.
- Develop information material about the importance of early energy provision and blood glucose monitoring for parents.

For hospital

- Support healthcare professionals to participate in training on identification, prevention, and management of hypoglycaemia.

For health service

- Develop and implement a national guideline on prevention, diagnosis and management of hypoglycaemia, based on an operational threshold approach using values advocated by professional bodies.

Description

Glucose levels and neurological outcomes

The association of neonatal hypoglycaemia with poor long-term neurodevelopment and neurocognition remains controversial. A systematic review showed that in early childhood (2-5 years), there was no neurodevelopmental impairment but an increased risk of visual impairment and executive dysfunction, and in mild childhood (6-11 years), an increased risk of neurodevelopmental impairment and low literacy and numeracy scores. However, there were important variations across the studies on blood glucose threshold (1.1 to < 2.6 mmol/L), as well as methods of glucose measurement, management strategies and treatments, outcome assessment methods, characteristics of the populations studied (low birth weight, preterm, infants of diabetic mothers), and other aspects of study designs that all raise the possibility of confounding. The authors concluded: "*Carefully designed randomized trials are required to determine the optimal management of neonates at risk of hypoglycaemia with long-term follow-up at least to school age.*" (15)

Also, the relationship between the severity, the frequency and the duration of low blood glucose level remains unclear. (15,16)

Recently, the HypoEXIT trial that randomised newborn at 35 weeks of gestation or later at risk for hypoglycaemia found that a 2.0 mmol/L threshold was not inferior to 2.6 mmol/L for psychomotor development at 18 months. None of the infants with hypoglycaemia had any clinical signs or symptoms of hypoglycaemia. (17) However, caution needs to be exercised in terms of extrapolation to all at risk neonates with hypoglycaemia. Firstly, the trial population of infants ‘at risk’ was formed with a third of infants whose risk was the classification of being large for gestational age (LGA). The level of risk for such infants is low and many centres would not consider this group would warrant screening as infants at risk for hypoglycaemia. (18) The study also excluded all neonates with severe hypoglycaemia before trial entry, and therefore may well have excluded neonates who could have a persistent hypoglycaemia-related disorder, such as congenital hyperinsulinism. Furthermore, the study reported on psychomotor development at 18 months, which is too young to investigate possible differences in neurocognitive function and is not a reliable marker of (potential) subtle influence of lower glucose concentrations on neurodevelopment. Studies that include follow-up to age 5 are required.

To date, there are strong arguments that symptomatic hypoglycaemia in newborn infants is associated with risk for brain damage and neurodevelopmental sequelae. (19) The potential for adverse outcome also exists if neonatal hypoglycaemia is over treated with a rapid rise in glucose concentrations after initial hypoglycaemia and in infants with less stable glucose concentrations, even within the normal range. (16)

Glucose thresholds for intervention

A recent study that determined postnatal changes in plasma glucose concentration in healthy infants receiving current recommended cares (breastfeeding and skin-to-skin as soon as possible after birth) reported that the 10th percentile for the first 48 hours approximated 2.6 mmol/L (47 mg/dL), although 39% showed at least one episode below this threshold of <2.6 mmol/L. There was a small increase in glucose concentration over the first 18 hours and a second increase after 48 hours, reaching values similar to adult's one after 96 hours. (20)

Data from the Sugar Babies Study which reported in a well-phenotyped group of infants (35–42 weeks gestational age) with risk factors for hypoglycaemia showed that blood glucose concentrations were <2.6mmol/L and < 2.0 mmol/L in 51% and 19%, respectively, but very few had abnormal clinical signs. 15% were too sleepy to feed when hypoglycaemic and 7% were noted to be jittery but 79% showed no clinical signs. (7)

- It is currently unknown at which glucose concentrations and after what duration neurologic injuries occur in newborn infants.
- Blood glucose levels below 1.0 mmol/L (18 mg/dL) that are associated with acute neurological dysfunction present the greatest risk of cerebral injury. (21–24)
- The tolerance to low glucose levels probably varies due to the newborn infant's ability to produce alternative substrates. (25)
- The concept of the "operational threshold" aims to provide clinicians with blood glucose values at which clinical interventions should be considered.

→ We need to implement practices that prevent harm which results from unrecognised or untreated hypoglycaemia whilst minimising unnecessary interventions and admission in neonatal unit.

- Measures to prevent and detect hypoglycaemia should be undertaken after birth in infants at risk, including: thermal care with skin-to-skin; support of breastfeeding; early energy provision and monitoring of blood glucose starting within the first hours of life.
- Feeding should be observed and abnormal feeding (not waking for feeds, not latching at the breast, not sucking effectively, appearing unsettled) should be recorded by the healthcare team.
- Glucose monitoring should be initiated before the second feed and no later than four hours after birth in asymptomatic infants, or at any time if there are abnormal clinical signs.
- Blood glucose concentration should be measured with validated devices. Local guidelines should be based on the operational threshold approach, using values advocated by professional bodies in their own country.

The lack of a clear evidence base for defining cerebral energy sufficiency is reflected in the contrast of recommendations between different organisations. (26)

1. Cornblath Operational Thresholds (2000) updated review of the literature subsequently (11), and used by the British Association of Perinatal Medicine (2017). (18) The suggested operational threshold concentrations at which clinicians should consider intervention are (12):

- Blood glucose level <2 mmol/L (36 mg/dL) in an asymptomatic baby, that remains below the same value at next measurement.
- A single measurement <2.5 mmol/L (45 mg/dL) in a newborn with abnormal clinical signs.
- A very low concentration of blood glucose <1.0 mmol/L (<18 mg/dL) indicates the need for intravenous glucose infusion aimed at raising plasma glucose concentration above 2.5 mmol/L (45 mg/dL). The low value of 18 mg/dL is presumed to be near blood glucose concentrations that can cause brain damage.

In symptomatic newborn infants with documented profound recurrent or persistent hyperinsulinic hypoglycaemia, therapeutic levels of 3.5 mmol/L (60 mg/dL) are recommended. (18) Infants with hypoxic ischemic encephalopathy have abnormal clinical signs by definition and the threshold of 2.5 mmol/L (45 mg/dL) should be used. (27)

2. The American Academy of Pediatrics (AAP) (2011)

   The American Academy of Pediatrics (AAP) proposed an algorithm with suggested thresholds for intervention in at risk newborn infants at ≥34 weeks' gestation depending upon postnatal age: 1.4-2.2 mmol/L (25-40 mg/dL) in the first 4 hours, 1.9-2.5 mmol/L (35-45mg/dL) from 4-24 hours and 2.5 mmol/L (45 mg/dL) after 24 hours. (8)

3. The Paediatric Endocrine Society (2015)
   The Paediatric Endocrine Society (PES) recommended higher plasma glucose levels to be considered safe in newborn infants: plasma glucose should be kept above 2.8 mmol/L (50 mg/dL) during the first 48 hours and above 3.3 mmol/L (60 mg/dL) for infants older than 48 hours. (5)

Measurement of glucose levels

- Accurate measurement of blood glucose level is essential for diagnosis and management of neonatal hypoglycaemia.
- The ward-based blood gas biosensor should be considered the reference standard for measuring blood glucose based on accuracy and speed of result availability.
- Blood gas analysers will produce glucose results as a calculated 'plasma glucose equivalent' concentration that should agree with laboratory plasma glucose results in the majority of cases.
- Most handheld glucometers also report results as 'plasma glucose equivalents', some devices are available that measure true whole blood glucose by rupturing the blood cells and measuring combined plasma and cellular glucose.
- This true whole blood glucose may be 10-15% lower than the corresponding plasma glucose. Practitioners should be aware that all current cot side technologies are prone to some inaccuracy, particularly in the range 0-2.0 mmol/l.
- If handheld glucometers are being used to screen for low blood glucose, only those devices conforming to the ISO 15197:2013 standard should be used and their limitations should be understood: possible error of +/- 0.8 mmol/l (14.4 mg/dL) for values <5.5 mmol/l (<99 mg/dL).
- If a handheld glucometer is used, low values should be confirmed using an accurate method. (14)

Most common clinical symptoms in low blood glucose levels

Abnormal cry, pallor, hypothermia, lethargy, irritability, tremor/jitteriness, poor sucking, hypotonia, apnoea, bradycardia, respiratory distress, seizures, coma.

Clinical symptoms are not specific and not related to the severity of low blood glucose levels. All these clinical signs could be important signs of acute neurological dysfunction in the context of low blood glucose so need to be acted upon in the same way i.e. measurement of blood glucose.

Infants who initially had none of the risk factors for hypoglycaemia with abnormal feeding behaviour or with important loss of weight (>10%) become at risk and need clinical evaluation and may need glycaemia monitoring. Any healthy baby at birth who experiences adverse event during the neonatal period should also be monitored for hypoglycaemia.

Other considerations

- Neonates with congenital hyperinsulinism have to be identified at an early stage and receive appropriate treatment with a combination of high glucose intakes and sometimes, specific medication (glucagon, diazoxide…). Hyperinsulinism suppresses lipolysis and reduces ketones, which act as alternative fuels to maintain brain neuronal function; therefore, hypoglycaemia caused by congenital hyperinsulinism is detrimental to the brain, with adverse neurodevelopment in a third to half of children. (28,29)
- In term infants with hypoxic-ischaemic encephalopathy (HIE), glucose profiles vary widely during the first 72 hours of life. Early hypoglycaemia can occur, mainly in infants with severe HIE. (30)The optimal target blood glucose level for ensuring adequate energy provision to HIE remains unknown. However, data support guidance to maintain a blood glucose concentration of 2.5 mmol/L (45 mg/dL) or more in neonates with HIE. (27)
- Oral dextrose gel may be considered as an adjunct to a feeding plan in newborn infants at risk of hypoglycaemia. Prophylactic dextrose gel can reduce the incidence of neonatal hypoglycaemia, thus potentially reducing separation of mother and baby and supporting breastfeeding. (31,32)
- Newborn infants presenting with clinical signs of hypoglycaemia or with very low glucose levels should be treated with intravenous dextrose (an intravenous bolus of 2.5 ml/kg 10% glucose) as soon as possible, followed by constant rate infusion of glucose.
- Newborn infants with risk factors should not be discharged until at least two adequate-level consecutive pre-feed blood glucose measurements have been made, and effective feeding has been established over several fast-feed cycles.
- Hypoglycaemia that persists beyond 72 hours after birth might have a different aetiology than “transitional neonatal hypoglycaemia” and requires specific investigations. (5)

Source

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Diagnosis and management of necrotising enterocolitis (NEC)

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Target group
Infants at risk of or being treated for necrotising enterocolitis (NEC) and parents

User group
Healthcare professionals, neonatal units, hospitals, health services

Statement of standard
Neonatal services provide a high standard of care in terms of diagnosis and treatment of necrotising enterocolitis (NEC) and infant/family experience and strive to continuously improve care and outcomes for NEC.

Rationale
Necrotising enterocolitis (NEC) is a leading cause of mortality and morbidity in preterm infants. About 40-50% of preterm infants who require surgery for NEC do not survive. Our improved understanding of the causation of NEC has not yet translated into improved outcomes, especially for surgical NEC. (1)

Outcomes for newborns at risk of NEC are best improved by preventing NEC. In those in whom NEC occurs, a much earlier diagnosis and intervention can improve outcomes. Unfortunately, we do not at present have reliable biomarkers to predict or detect NEC early or delineate it from various confounders. (2,3)

It is estimated that 1 per 1.000 live-born infants develop NEC and among these about 25% progress to surgical NEC. Apart from mortality, NEC can have life-long severe impact on infants and families and a significant socio-economic burden on society. (3,4) Among survivors of NEC, the average length of hospital stay increases by approximately 3 weeks for medical NEC and about 2 months for surgical NEC. (5) NEC can account for nearly 20% of the annual neonatal unit expenditure and a potential cost-saving of $200,000 per patient could be achieved if progression to surgery is prevented. (2,3,6–10)

Optimising long-term neurodevelopment is critical and we need to shift the focus from survival alone to minimising impairment as the primary goal. (3) There is evidence that the overall mortality rate and rate of neurodevelopmental impairments (NDI) is very high for infants with surgical NEC. Surgical NEC significantly increases the odds ratio of cerebral palsy (mean=1.55), visual impairment (mean=2.31), cognitive impairment (mean=1.44) and psychomotor impairment (mean=1.72). (9,11–13) Hence, prevention should be the primary quality improvement goal but if NEC does develop, the early detection and attempt to prevent progression to surgical NEC is of paramount importance.

While the last 6 decades have seen a lot of research into the pathogenesis of NEC to try to generate a ‘cure’ (1,14), we have missed opportunities for quality improvement (QI) and standardisation. In parallel with efforts to improve our understanding of etiology of NEC, we need to focus on our standards of care with regard to diagnosis and treatment of NEC as well as family experience. We need to focus on improvements that units can make tomorrow, over the coming weeks and months.

Reports on variation in incidence and mortality (incidence between 2-7% overall – fourfold difference, between 5-22% in <1kg- almost fivefold difference) also suggest that QI efforts to improve standards of care may help in decreasing unwanted variation and improve outcomes. (15)

Benefits

Short-term benefits

- Earlier identification of NEC (16–18)
- Reduced mortality and morbidity (19)
- Decreased need for surgery (20)
- Improved surgical outcomes (e.g. extent of resection required) (17,19,21)
- Reduced risk of complications of NEC (22)
- Decreased other neonatal morbidities which are worsened by NEC e.g. chronic lung disease (22)
- Reduced length of hospital stay (consensus)
- Improved growth and nutrition (23–25)
- Improved family experience (consensus)
- Timely access to appropriate surgical opinion (26)
- Timely access to appropriate pain relief/comfort care (27)

Long-term benefits

- Reduced mortality (28)
- Decreased need for repeated surgery (21,22)
- Improved surgical outcomes (22)
- Decrease in complications of NEC e.g. short gut syndrome, long-term parenteral nutrition, need for transplantation (17,22,29)
- Improved quality of life (30,31)
- Reduced rate of readmissions (consensus)
- Reduced healthcare costs (32)

Components of the standard

Component	**Grading of evidence**	**Indicator of meeting the standard**
For parents and family		
1. Parents are informed by healthcare professionals about risk factors and symptoms of NEC.	B (High quality)	Audit report, patient information sheet
2. Parents are informed about clinical course of illness, possible complications and treatment options.	B (High quality)	Audit report, patient information sheet
3. Parents are provided up-to-date information about outcomes of NEC.	B (High quality)	Parent feedback
4. Parents are offered support and counselling.	B (High quality)	Audit report, parent feedback
For healthcare professionals		
5. Up-to-date education and training on detection and management of NEC is attended by all responsible healthcare professionals.	B (High quality)	Training documentation

6. A unit guideline on detection and management of NEC is adhered to by all healthcare professionals.	B (High quality)	Guideline
7. Appropriate equipment for diagnosis and management of NEC is available for all healthcare professionals (as appropriate to role).	B (High quality) C (High quality)	Audit report, healthcare professional feedback
8. Surgical opinion regarding diagnosis and management of NEC is available for healthcare professionals 24/7.	B (High quality)	Audit report, healthcare professional feedback
For neonatal unit		
9. A unit guideline on diagnosis and management of NEC is available and regularly updated. (1,33–35)	B (High quality)	Guideline
10. Clear guidance is available to healthcare professionals regarding indications for surgical opinion and transfer of neonates with NEC to surgical centre (if appropriate). (36–41)	B (High quality)	Guideline
11. Relevant equipment and products are available and appropriate guidance for use e.g. X-ray & US machines, central venous lines, peritoneal drain, parenteral nutrition. (36,37,39,40)	B (High quality)	Audit report, healthcare professional feedback
12. All cases of NEC are discussed with the relevant surgical team in a proactive and timely manner. (36–41)	B (High quality) C (High quality)	Minutes of debriefings
13. Data regarding NEC outcomes is collected and reviewed on a regular basis including parental/family feedback.	B (High quality) C (High quality)	Audit report, parent feedback
14. A well-defined process for post discharge care and multi-disciplinary follow-up of infants treated for NEC is available and regularly updated.	B (High quality)	Guideline
15. Quality indicators regarding NEC outcomes are contributed to regional and national databases (see standard Quality indicators).	B (Low quality)	Audit report
For hospital		
16. Appropriate staffing, expertise and equipment required for optimal diagnosis and management of NEC is provided. (36,37,39,40,42)	B (High quality) C (High quality)	Audit report, healthcare professional feedback

17. Appropriate locations for operating facilities for NEC are provided. (36,37,39,40,42)	B (High quality) C (High quality)	Guideline, healthcare professional feedback
18. Robust processes to ensure appropriate management of NEC and regular audit of all relevant outcomes are in place.	B (High quality)	Audit report guideline,
For health service		
19. A national guideline on management of NEC is available and regularly updated.	B (High quality)	Guideline
20. Services are configured in terms of location and access to medical and surgical NEC care such that equity and effectiveness of provision is optimised.	B (High quality)	Regional network agreements, guideline, parent feedback
21. Clear guidelines in terms of retrieval of neonates with NEC to surgical and higher acuity centres including timelines are available to transport services.	B (High quality)	Audit report, guideline

Where to go – further development of care

Further development	**Grading of evidence**
For parents and family	
• Parents and family are provided options to feedback on the care provision and family experience and encouraged to offer suggestions for improvement.	B (High quality)
• Parents of infants diagnosed with NEC and adult survivors of NEC are engaged with, to develop priorities for research and quality improvement (QI) in various aspects of NEC.	B (High quality)
• Parents of infants diagnosed with NEC are encouraged and supported to be involved in research studies related to NEC.	B (High quality)
For healthcare professionals	
• Review practice and outcomes on a regular basis (at least annually) and share learning and latest advances.	B (High quality) C (Moderate quality)
• Engage in quality improvement work related to NEC and explore newer practices e.g. use of abdominal ultrasound in the diagnosis and monitoring of NEC.	B (High quality)
For neonatal unit	
• Encourage and support healthcare professionals to engage in quality improvement work related to NEC and explore newer practices in the diagnosis and monitoring of NEC.	B (High quality) C (Moderate quality)
• Review and act upon parental feedback and outcomes data of patients with NEC including family experience regularly (at least annually). (36,39,40)	B (High quality)

For hospital	
• Facilitate continuing professional development and training of staff and involvement with collaborative research and innovative and improvement practices in terms of NEC diagnosis and management. (36,39,40,43)	B (High quality) C (Moderate quality)
For health service	
• Review outcomes of NEC regularly including family experience and ensure learning from variation, adverse incidents and feedback.	B (High quality)
• Optimise provision of care for NEC in terms of its safety, timeliness, efficiency, effectiveness, equitability and family centredness.	B (High quality)

Getting started

Initial steps
For parents and family
• Parents are verbally informed by healthcare professionals about a suspected or confirmed NEC diagnosis in a timely way by a senior member of the neonatal team and their questions are appropriately answered.
• Parents receive relevant information about NEC and advised on suitable websites or resources.
• Parents of infants diagnosed with NEC are offered support and counselling.
For healthcare professionals
• Attend training on management of NEC to receive relevant up-to-date information about NEC and advise on suitable websites and other resources for education and training.
For neonatal unit
• Develop and implement a comprehensive unit guideline for diagnosis and management of NEC and audit their practice at least annually.
• Develop information material on NEC for parents.
For hospital
• Benchmark NEC rates and outcomes against regional/national or other relevant comparators (e.g. eNewborn, VON data).
• Support healthcare professionals to participate in training on management of NEC.
For health service
• Benchmark NEC rates and outcomes of various providers of care against regional/national or other relevant comparators (e.g. eNewborn, VON data).

Description

This standard focusses on key general standards of care provision that can positively impact on infant and family outcomes. We have chosen not to include specific diagnostics or therapies that may have a role in diagnosis and management of NEC. Many of these have variable degrees of evidence supporting them and are dynamic and evolving.

The standard highlights areas with poor evidence as well as areas that have robust evidence but are not part of day to day practice in all neonatal units. We are

elaborating the former as recommendations for research and the latter as key priorities for quality improvement.

Key priorities for research

While all of the listed standards would benefit from more robust evidence, the following areas are especially recommended as priorities for further research:

- Impact of standards on implementation of good practice and improving outcomes
- Impact of better communication and support for parents on parental experience and improving outcomes
- Impact of earlier diagnosis on NEC outcomes
- Newer diagnostic and treatment modalities for NEC
- Development of large datasets to test relevant hypothesis regarding diagnosis and management of NEC
- Development of machine learning and other forms of AI to improve outcomes of NEC
- Optimising post-discharge care and follow up of infants with NEC
- Long-term outcomes of NEC
- Optimising care for NEC survivors

Key priorities for quality improvement (QI)

- Review of standards, gap analysis and development of appropriate action plan and timelines
- Standardisation in various aspects of NEC diagnosis and treatment
- Every neonatal unit and relevant provider of services should review their NEC service provision and outcome data regularly (including parental and staff feedback), benchmark and develop a plan for improvement with appropriate timelines
- Every neonatal unit and relevant provider of services should develop key priorities for their service in terms of NEC e.g. early diagnosis, optimal communication and support for parents, implementation of 'better' modalities like ultrasound, appropriate multi-disciplinary follow-up and support for NEC survivors and their families, development of appropriate datasets and optimal use of data to understand risks as well as effectiveness of various interventions

Source

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EFCNI, Khashu M, Zimmermann LJI et al., European Standards of Care for Newborn Health: Diagnosis and management of necrotising enterocolitis (NEC). 2022.

Management of persistent pulmonary hypertension of the newborn infant (PPHN)

Reiss I, Zimmermann LJI, Hellström-Westas L, Buonocore G, Greenough A, Rabe H, Villamor E

Target group
Term and near-term infants >34 weeks of gestational age and parents

User group
Healthcare professionals, perinatal and neonatal units, hospitals, and health services

Statement of standard
Management of newborn infants with persistent pulmonary hypertension (PPHN) in a specialised centre improves mortality and morbidity.

Rationale
Persistent pulmonary hypertension of the newborn (PPHN) is characterised by sustained elevation of pulmonary vascular resistance (PVR) after birth resulting in extrapulmonary shunting from right to left via the fetal circulatory pathways (patent ductus arteriosus and patent foramen ovale). (1) PHN leads to severe hypoxaemia that may not respond to conventional respiratory support and to avoid severe cardiorespiratory failure. (2) The management of delivery and neonatal care should be transferred to a specialised centre to ensure optimal outcomes. (3,4)

Benefits

Short-term benefits
- Reduced mortality and morbidity (2,4,5)
- Reduced need for extra-corporeal membrane oxygenation (ECMO) (6)

Long-term benefits
- Reduced long-term morbidity (neurodevelopmental and cardiopulmonary outcome) (7)

Components of the standard

Component	Grading of evidence	Indicator of meeting the standard
For parents and family		
1. Parents are informed by healthcare professionals about persistent pulmonary hypertension (PPHN) in the newborn infant, treatment strategies as well as short- and long-term consequences.	B (High quality)	Patient information sheet
For healthcare professionals		
2. A unit guideline on indications of pre- or postnatal transfer to a specialised centre, which may include facilities for ECMO, is adhered to by all healthcare	A (High quality) B (High quality)	Guideline

professionals (see Birth & transfer). (4,5)		
3. Training on the management of PPHN is attended by all responsible healthcare professionals.	B (High quality)	Training documentation
For perinatal and neonatal unit		
4. A unit guideline on indications of pre- or postnatal transfer to a specialised centre, which may include facilities for ECMO is available and regularly updated, to include: (4,5) • Resuscitation and early management are focused on optimal lung recruitment and ventilation, and based on neonatal resuscitation guidelines. (2) • Diagnosis is confirmed by detection of pre- and post-ductal saturation difference of 5-10%. • 2D echocardiography is performed to rule out the presence of cardiac anomalies and assess right heart function; the degree of pulmonary hypertension is classified relative to systemic blood pressure. (5) • Inotropic drugs are used to support organ perfusion. (5) • In case of poor organ perfusion, treatment with inhaled nitric oxide (iNO) is started. (5,7,8) • If there is insufficient response to iNO despite optimal lung recruitment, i.v. drugs such as phosphodiesterase inhibitors (sildenafil, milrinone) or prostaglandin are considered. (3) • ECMO is considered according the extracorporeal life support organisation (ELSO) guidelines (OI>20). (4) • Local protocols are updated in regular intervals to ensure individualised therapy.	A (High quality) B (High quality)	Guideline
For hospital		
5. Training on the management of PPHN is ensured.	B (High quality)	Training documentation
6. Access to 24/7 echocardiography, radiology, and laboratory support is ensured.	B (High quality)	Guideline

7. ECMO is only provided in designated centres.	B (High quality)	Guideline
For health service		
8. A national guideline on indications of pre- or postnatal transfer to a specialised centre, which may include facilities for ECMO, is available and regularly updated (see Birth & transfer).	B (High quality)	Guideline

Where to go – further development of care

Further development	**Grading of evidence**
For parents and family	
N/A	
For healthcare professionals	
N/A	
For perinatal and neonatal unit	
N/A	
For hospital	
N/A	
For health service	
• Develop research into optimal saturation targets, use of inodilators and additional drugs to treat persistent pulmonary hypertension (PPHN).	A (Low quality)
• Provide long-term multidisciplinary standardised follow-up after discharge. (7)	A (Moderate quality)
• Set up a European-wide database for newborn infants with PPHN.	A (Low quality)

Getting started

Initial steps
For parents and family
• Parents and family are verbally informed by healthcare professionals about persistent pulmonary hypertension (PPHN), treatment strategies as well as short- and long-term consequences.
For healthcare professionals
• Attend training on management of PPHN. • Raise awareness to diagnose PPHN.
For perinatal and neonatal unit
• Develop and implement a unit guideline on indications of pre- or postnatal transfer to a specialised centre, which may include facilities for ECMO. • Develop information material about PPHN, treatment strategies as well as short- and long-term consequences for parents.
For hospital
• Support healthcare professionals to participate in training on management of PPHN and the use of licensed drugs.

- Ensure facilities and devices for optimal care and follow-up care.

For health service

- Develop and implement a national guideline on indications of pre- or postnatal transfer to a specialised centre, which may include facilities for ECMO.

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Management of Respiratory Distress Syndrome

Sweet DG, Zimmermann LJI, Hellström-Westas L, Buonocore G, Bohlin K, Herting E

Target group
Newborn infants at risk of Respiratory Distress Syndrome (RDS) and parents

User group
Healthcare professionals, neonatal units, hospitals, and health services

Statement of standard
Newborn infants at risk of Respiratory Distress Syndrome (RDS) receive appropriate perinatal care including place of delivery, antenatal corticosteroids, guidance around optimal strategies for delivery room stabilisation, and ongoing respiratory support.

Rationale
The goal is to promote optimum survival without complications for newborn infants at risk of Respiratory Distress Syndrome (RDS), whilst minimising potential risks of adverse effects such as pulmonary air leak and bronchopulmonary dysplasia. Many available therapies for the management of RDS involve balancing benefits of treatment with potential risks. With modern practice it is essential that anyone involved in the care of newborn infants is able to comply within their setting to standards of care expected to achieve best outcomes. (1,2) Treatment of newborn infants with RDS requires access to specialist skills and equipment that are not readily available outside of the neonatal environment. The overall aim is to treat with early surfactant if it is needed, whilst at the same time trying to avoid unnecessary intubation and mechanical ventilation by maximising the use of non-invasive respiratory support and less invasive surfactant administration. (1,3,4) There are regularly updated European consensus guidelines both for supporting transition and managing RDS which form the basis of this standard, and provide more detail where required.(1,2) With implementation of regional training for standards such as less invasive surfactant administration it is possible at country-wide level to improve quality of care. (5)

Benefits

Short-term benefits
- Reduced mortality (5)
- Reduced pulmonary air leaks (pulmonary interstitial emphysema and pneumothorax) (4,6)
- Reduced need for invasive ventilation (4)

Long-term benefits
- Improved long-term neurodevelopment (7)
- Reduced healthcare costs (8)
- Reduced bronchopulmonary dysplasia (BPD) diagnoses (1,3,4)

Components of the standard

Component	Grading of evidence	Indicator of meeting the standard
For parents and family		
1. Parents are informed by healthcare professionals about Respiratory Distress Syndrome (RDS), survival rates/morbidity, treatment, and short- and long-term care. (9)	A (Low quality) B (High quality)	Patient information sheet
For healthcare professionals		
2. A unit guideline on management of RDS is adhered to by all healthcare professionals.	B (High quality)	Guideline
3. Training on detection and treatment of RDS in the neonatal intensive care unit (NICU) is attended by all healthcare professionals. (10)	A (Low quality) B (High quality)	Training documentation
4. A unit guideline to determine which pregnant women have to be transferred for care to a perinatal centre is adhered to by all healthcare professionals (see Birth & transfer). (11)	A (Moderate quality)	Guideline, audit report
5. Ensure all healthcare professionals involved in neonatal care are trained in the use of **all** modes of respiratory support including volume-targeted modes of synchronised ventilation, high frequency oscillation, nasal ventilation, CPAP, heated humidified high flow oxygen and blended oxygen. (12)	A (High Quality)	Training documentation
For neonatal unit		
6. A unit guideline to ensure a standardised approach to initial stabilisation after birth for newborn infants at risk of RDS is available and regularly updated, including • access to blended oxygen (13) • access to CPAP from birth (3) • access to manual ventilation with devices that control pressures (14) • access to pulse oximetry from birth (15)	B (High quality) A (High quality) A (High quality) A (Moderate quality) A (Low quality)	Guideline

7. A unit guideline is available and regularly updated including surfactant administration, criteria for intubation, and ventilation strategies with optimal lung protection. (1,12–19)	A (High quality) B (High quality)	Guideline
For hospital		
8. Training on management of RDS is ensured.	B (High quality)	Training documentation
9. Access to radiology, biochemistry, and blood gas analysis is provided throughout the 24 hours.	B (High quality)	Audit report
10. A unit guideline and evidence of quality improvement initiatives are available within the obstetric service to optimise the use of prenatal corticosteroid therapy (see Birth & transfer). (7)	A (High quality) B (High quality)	Guideline, audit report
For health service		
11. Women at risk for very preterm birth are referred in a timely fashion for expert care during pregnancy and delivery (see Birth & transfer). (20)	A (High quality)	Audit report

Where to go – further development of care

Further development	**Grading of evidence**
For parents and family	
N/A	
For healthcare professionals	
N/A	
For neonatal unit	
• Update guidelines using the current European consensus guideline and ERC NLS Guidelines.	B (High quality)
For hospital	
N/A	
For health service	
N/A	

Getting started

Initial steps
For parents and family
• Parents are verbally informed by healthcare professionals about Respiratory Distress Syndrome (RDS), survival rates/morbidity treatment, and short- and long-term care.

For healthcare professionals

- Attend training on management of RDS.
- Appraise healthcare professional knowledge in the detection and treatment of RDS and identify gaps in knowledge and training.

For neonatal unit

- Develop and implement a unit guideline on management of RDS based on the European consensus guidelines.
- Develop information material on RDS for parents.
- Develop quality improvement plan for the management of RDS.

For hospital

- Support healthcare professionals to participate in training on management of RDS.

For health service

N/A

Source

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Management of suspected early-onset neonatal sepsis (EONS)

Stocker M, Buonocore G, Zimmermann LJI, Hellström-Westas L, Klingenberg C, Kornelisse R, Maier RF, Metsvaht T

Target group
Term and late-preterm infants with suspected infection within the first 72 hours after birth and parents

User group
Healthcare professionals, neonatal units, hospitals, and health services

Statement of standard
Newborn infants with suspected early-onset infection receive prompt diagnosis and effective treatment of sepsis while avoiding overuse of antibiotics.

Rationale
The goal is to reduce morbidity and mortality from early-onset sepsis and adverse effects of overuse of antibiotics. Early diagnosis and treatment of early-onset neonatal sepsis (EONS) are critical in preventing severe and life-threatening complications and mortality. Diagnosis of EONS is difficult due to the often subtle, nonspecific clinical presentation and low predictive values of biomarkers. (1–4) Uncertainty about the presence of neonatal infection may result in unnecessary and prolonged antibiotic treatment. (5,6) Population-based studies in Norway and Switzerland reported a rate of around 2.5% of all term infants started on antibiotic therapy due to suspected EONS, whereas the incidence of culture-proven EONS was between 0.02 and 0.07% (7,8) In other European countries and the United States of America even higher proportions of all term infants are started on antibiotic therapy. (9) Physician's attitudes, such as complacency and fear, have been described as influential factors on antibiotic prescribing. (10)

Antibiotics may have several effects: life-saving for the individual with a severe infection; beneficial for the community hindering spreads of bacteria; problematic for the community regarding development of resistance and for the individual via collateral damage of the microbiome. In early life, antibiotic mediated alteration of the microbiome may have potential consequences for future health. (11–14) Therefore, reduction of unnecessary or prolonged antibiotic therapy is one of the key steps of antimicrobial stewardship to improve future health of the individual and to impede the emergence of multidrug resistant bacteria. (11–16)

Benefits

Short-term benefits
- Reduced mortality and morbidity (17–20)
- Reduced unnecessary and prolonged antibiotic therapy for suspected infection (7–9)
- Reduced separation of mother and infant with less interfering of breastfeeding (consensus)

Long-term benefits
- Reduced development of multidrug resistance (MDR) (12,15)
- Reduced alteration of the infant microbiome, with implication for later health (11–14)

Components of the standard

Component	Grading of evidence	Indicator of meeting the standard
For parents and family		
1. Parents (at the hospital and at home) are informed by healthcare professionals about signs, treatment and consequences of early-onset neonatal infection (see Infant- & family-centred developmental care). (21–25)	A (Low quality) B (High quality)	Patient information sheet
For healthcare professionals		
2. A unit guideline on management for suspected early-onset neonatal sepsis (EONS) is adhered to by all healthcare professionals.	B (High quality)	Guideline
3. Training on management for suspected EONS is attended by all healthcare professionals.	B (High quality)	Training documentation
4. In healthy infants with risk factors for EONS, vital signs are observed and monitored for 24 hours, and infants do not receive antibiotics unless symptomatic. (8,21–26)	A (Moderate quality)	Guideline
5. Always consider to start parenteral antibiotic therapy if newborn infants have clinical signs possibly related to sepsis. (21–25)	A (Moderate quality)	Guideline
6. An aerobic blood culture (minimum 1ml) is drawn before start of antibiotic therapy. (21–25)	A (Moderate quality)	Guideline
7. The need for antibiotic therapy is re-evaluated after 24-36 hours. (21–25,27,28)	A (Moderate quality)	Guideline
8. Antibiotic therapy is streamlined as soon as blood culture results are available. (21–25)	A (Moderate quality)	Guideline
9. ≥3rd generation cephalosporins or carbapenems are not routinely used for empiric therapy. (12,21–25)	A (Moderate quality)	Guideline
For neonatal unit		
10. A unit guideline for suspected EONS is available and regularly updated in conjunction with obstetric guidance on intrapartum prophylaxis. (21,29)	B (High quality)	Guideline

11. Depending on the current rate of neonates started on antibiotics, implementing the sepsis calculator to decrease exposure of antibiotics is considered. (21,30)	A (moderate quality)	Guideline
12. A unit-based antibiotic stewardship programme is established: minimum for use of ≥3rd generation cephalosporins or carbapenems. (31–33)	A (Moderate quality)	Audit report
For hospital		
13. Training on management for suspected EONS is ensured.	B (High quality)	Training documentation
14. Analysis of blood cultures including determination of antibiotic resistance patterns with daily report of results is conducted. (15,16,34,35)	A (High quality)	Audit report
15. Hospital-based antibiotic stewardship programme is established: minimum recording of multidrug resistance (MDR). (31–33)	A (Moderate quality)	Audit report
For health service		
16. A national guideline on management for suspected EONS is available and regularly updated in conjunction with obstetric guidance on intrapartum prophylaxis. (29,34–36)	A (Moderate quality)	Guideline
17. Regional/national surveillance and reports of antibiotic resistance patterns of positive blood cultures are available. (15,16,34,35)	A (Moderate quality)	Audit report

Where to go – further development of care

Further development	**Grading of evidence**
For parents and family	
N/A	
For healthcare professionals	
N/A	
For neonatal unit	
• Develop an algorithm with biomarker guidance for duration of antibiotic therapy. (37–39)	A (Moderate quality)
For hospital	
• Consolidate an antibiotic stewardship programme. (28–30)	A (Moderate quality)
For health service	
N/A	

Getting started

Initial steps

For parents and family

- Parents are verbally informed by healthcare professionals about signs, treatment and consequences of early-onset neonatal infection.

For healthcare professionals

- Attend training on management for suspected early-onset neonatal sepsis (EONS).
- Reduce the use of unnecessary antibiotic therapy.

For neonatal unit

- Use published guidelines regarding management for suspected EONS.
- Develop and implement a unit guideline on management for suspected EONS in conjunction with obstetric guidance on intrapartum prophylaxis.
- Develop information material on signs, treatment and consequences of early-onset neonatal infection for parents.

For hospital

- Support healthcare professionals to participate in training on management for suspected EONS.
- Ensure facilities for rapid detection of bloodstream infection.
- Start or continue with an antibiotic stewardship programme.

For health service

- Use published guidelines regarding management for suspected EONS.
- Develop and implement a national guideline on management for suspected EONS in conjunction with obstetric guidance on intrapartum prophylaxis.

Description

Different national guidelines for the management of suspected EONS are published and may serve as examples. These guidelines are not uniform and differ in some points. (21,24,25,29,40,41) The diversity of the guidelines reflects the diversity of their national healthcare system. It is also a consequence of a different translation of available data to clinical practice such as the approach of maternal risk factors for EONS. Guidelines for the management of EONS have to be adapted to the specific healthcare practices such as screening for maternal colonisation with Group B streptococci, and possibilities for observation of newborn infants at increased risk for EONS. The introduction of the sepsis calculator as algorithm regarding start of antibiotics is mainly dependent on the current rate of newborn infants started on antibiotics. Whereas start of antibiotics due to risk factors alone is not reasonable (compare component 4), risk factors in combination with clinical signs are part of the algorithm of the sepsis calculator.

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Neonatal jaundice

Borszewska-Kornacka M, Buonocore G, Zimmermann LJI, Hellström-Westas L, Marlow N, Özek E, Perrone S, Tołłoczko J

Target group
Newborn infants and parents

User group
Healthcare professionals, neonatal units, hospital, and health service

Statement of standard
All newborn infants are assessed for neonatal jaundice with the aim of implementing effective prevention of severe hyperbilirubinaemia.

Rationale
Hyperbilirubinaemia is common in newborn infants. Physiological jaundice appears after the first 24 hours of life and usually resolves spontaneously within the first week. However, neonatal hyperbilirubinaemia may also become more severe and require treatment to prevent or treat bilirubin encephalopathy and risk of later cerebral palsy and hearing deficiencies. Monitoring of bilirubin levels in all newborn infants, and awareness of risk factors, are vital for adequate management. Risk factors for severe neonatal hyperbilirubinaemia include: prematurity, haemolytic disorders, early jaundice (<24 hours), bruising and haematoma after delivery, infections, excessive weight loss, family history of jaundice – including conditions such as spherocytosis, conjugation disorders, and haemoglobinopathies, for example sickle cell anaemia and glucose-6-phosphate dehydrogenase deficiency (G6PD),which are more prevalent in Mediterranean, African and Asian populations. (1–3)

Phototherapy is effective in reducing bilirubin concentrations. Initiation of phototherapy should take into account the gestational age, postnatal age and risk factors. Phototherapy usually may be implemented without separating mother and infant. Severe hyperbilirubinaemia may be treated effectively by blood exchange transfusion and the use of gammaglobulin may reduce the need for exchange transfusion in the presence of ongoing haemolysis. (4,5)

In most European countries, national professional societies and health services have developed comprehensive guidelines and charts for the management of hyperbilirubinaemia in their populations, which should be followed. (6–12) It is also critical to monitor for prolonged jaundice (greater than 14 days) in newborn infants and investigation should detect the presence of conjugated hyperbilirubinaemia in such infants. (4,13,14)

Benefits

Short-term benefits
- Reduced occurrence of severe neonatal jaundice (4,15,16)
- Reduced length of hospital/NICU stay (5)
- Early detection of cholestasis (17)

Long-term benefits
- Reduced neurological complications (16)
- Reduced occurrence of hearing loss (16)
- Reduced hospital readmission (17)

Components of the standard

Component	Grading of evidence	Indicator of meeting the standard
For parents and family		
1. Parents are informed by healthcare professionals about identification, prevention, and management of hyperbilirubinaemia. (2,14,15)	A (Moderate quality) B (High quality)	Patient information sheet
2. Parents are informed by healthcare professionals about the role of breastfeeding and adequate nutrition in the prevention of hyperbilirubinaemia (see Nutrition and Care procedures). (4)	A (High quality) B (High quality)	Patient information sheet
For healthcare professionals		
3. A unit guideline on hyperbilirubinaemia including management after discharge is adhered to by all healthcare professionals.	B (High quality)	Guideline
4. Transcutaneous bilirubinometers is used to screen newborn infants for hyperbilirubinaemia. (3,18–23)	A (High quality)	Guideline
5. Training in the management of hyperbilirubinaemia is attended by all healthcare professionals. (4,16)	A (High quality) B (High quality)	Training documentation
For neonatal unit		
6. A unit guideline on hyperbilirubinaemia including management after discharge is available and regularly updated.	B (High quality)	Guideline
For hospital		
7. Training in the management of hyperbilirubinaemia is ensured.	B (High quality)	Training documentation
8. Equipment for the diagnosis and management of hyperbilirubinaemia, including transcutaneous bilirubinometers, is provided.	B (High quality)	Audit report
For health service		
9. A national guideline on management of hyperbilirubinaemia including management after discharge is available and regularly updated.	B (High quality)	Guideline
10. Systems for the identification of prolonged jaundice are available and audited. (4)	A (High quality)	Audit report, guideline

Where to go – further development of care

Further development	Grading of evidence
For parents and family	
N/A	
For healthcare professionals	
N/A	
For neonatal unit	
N/A	
For hospital	
N/A	
For health service	
• Support research in new therapeutic modalities, cost effectiveness, and improvement in technology. (24)	A (Moderate quality)

Getting started

Initial steps
For parents and family
• Parents are verbally informed by healthcare professionals about identification, prevention, and management of hyperbilirubinaemia.
For healthcare professionals
• Attend training in the management of hyperbilirubinaemia.
For neonatal unit
• Use published guidelines regarding management of hyperbilirubinaemia including management after discharge. (17) • Develop and implement a unit guideline on hyperbilirubinaemia including management after discharge. • Develop information material about identification, prevention, and management of hyperbilirubinaemia for parents.
For hospital
• Support healthcare professionals to participate in training in the management of hyperbilirubinaemia. • Provide equipment for non-invasive measurement of bilirubin.
For health service
• Develop and implement a national guideline on hyperbilirubinaemia including management after discharge.

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Neurological monitoring of the high-risk infant: EEG and aEEG

Hellström-Westas L, Zimmermann LJI, Buonocore G, Dudink J, Gressens P, Pellicer A

Target group

- Term and preterm infants at risk for brain injury:
  - Infants with hypoxic-ischaemic encephalopathy (HIE)
  - Infants with encephalopathy for other causes (e.g. metabolic)
  - Infants with suspected or verified seizures
  - Infants requiring intensive care and/or surgery
  - Infants with suspected/confirmed congenital central nervous system (CNS) anomalies
- Parents

User group

Healthcare professionals, neonatal units, hospitals, and health services

Statement of standard

In order to improve evaluation and outcomes of newborn infants at risk of brain injury, management includes neurological monitoring using a structured, age-appropriate neurological assessment and a range of devices to evaluate brain haemodynamics, oxygen transport, brain function, and imaging, as required.

Rationale

Newborn infants comprise a high-risk population for developing brain injury, during the first days after birth due to respiratory, haemodynamic, infectious, or metabolic instability. Full term and preterm infants with hypoxia-ischaemia, CNS infections, or congenital anomalies are at particular risk of brain injury. Early recognition of on-going disturbances of brain function or structural damage is important in implementing preventive or treatment strategies, and appropriate follow-up. Early detection of cerebral compromise, such as encephalopathy and seizures, is associated with better management of these conditions. High-risk infants should be identified as early as possible, the patient history together with a structured clinical examination and repeated clinical observations form the basis of the evaluation. The electroencephalogram (EEG) provides sensitive detection of abnormal brain function. (1,2) Continuous monitoring with a full montage EEG or the limited-channel amplitude-integrated EEG (aEEG) has been increasingly used in neonatal units and is excellent in the detection and grading of the severity of cerebral compromise in both term and preterm infants, and can be used for early evaluation before interventions such as therapeutic hypothermia. (3–11) Modern aEEG monitors also display the raw EEG (aEEG/EEG), which improves seizure detection. (12,13) The use of continuous EEG or aEEG/EEG monitoring is associated with earlier seizure diagnosis and better seizure management. (14,15) Studies in asphyxiated newborn infants have shown that aEEG combined with near-infrared spectroscopy is useful. (16,17)

Benefits

Short-term benefits

- Improved evaluation of clinical symptoms, including seizures, and early detection of cerebral compromise (2,6,14,18,19)
- Refined clinical management of neonatal seizures, including more efficient treatment and less use of antiepileptic drugs (14,15,18–20)

- Early prediction of outcome may assist medical decisions such as interventions and redirection of care (5,9,10,21)

Long-term benefits

- Improved long-term outcomes (22–25)
- Improved cost-effectiveness (26,27)
- Reduced exposure to antiepileptic drugs (15,20)

Components of the standard

Component	**Grading of evidence**	**Indicator of meeting the standard**
For parents and family		
1. Parents are informed by healthcare professionals about the role of EEG and aEEG/EEG monitoring.	B (High quality)	Patient information sheet
For healthcare professionals		
2. A unit guideline on neurological monitoring including EEG and aEEG/EEG monitoring is adhered to by all healthcare professionals, to include • asphyxiated newborn infants, including undergoing therapeutic hypothermina (3–5,5,6,16,23,26) • infants at risk of and undergoing treatment for seizures. (6,12–15,18–20,22,23,28)	A (High quality) B (High quality)	Audit report, guideline
3. Specific training on the use of EEG and aEEG/EEG monitoring is attended by all responsible healthcare professionals. (5,11,14,27,29)	A (Moderate quality) B (High quality)	Training documentation
4. Teams with a focus of interest on EEG and aEEG/EEG monitoring (e.g. neonatologists, neurologists, neuro-physiologists, nurses, radiologists, radiographers, and physicists) are established. (29,30)	A (High quality) B (High quality)	Guideline
For neonatal unit		
5. A unit guideline on the implications of EEG and aEEG/EEG monitoring is available and regularly updated.	B (High quality)	Guideline
For hospital		
6. Training on the use of EEG and aEEG/EEG monitoring is ensured. (5,11,14,27,29)	A (Moderate quality) B (High quality)	Guideline
7. An interdisciplinary team for neurological evaluation (including EEG	A (Moderate quality)	Audit report

and aEEG/EEG) of high-risk infants in the NICU is supported. (14,15)		
8. Facilities for EEG and aEEG/EEG monitoring and interpretation are provided.	B (High quality)	Audit report
For health service		
9. High-risk infants are transferred to NICUs with appropriate neuro-monitoring systems and expertise. (31)	A (High quality)	Audit report, guideline

Where to go – further development of care

Further development	**Grading of evidence**
For parents and family	
N/A	
For healthcare professionals	
N/A	
For neonatal unit	
• Develop a full neonatal neuro-critical care concept, including guidelines and close collaboration with neurologists. (13,19,24)	A (Moderate quality)
For hospital	
• Use monitoring systems that allow for expert evaluation of aEEG/EEG or EEG 24/7 also from outside the hospital.	A (Low quality)
For health service	
• Monitor incidence, treatment and long-term outcomes after neonatal seizures. (15,24,25)	A (High quality)
• Develop multi-centre expertise by sharing EEG databases.	B (Moderate quality)

Getting started

Initial steps
For parents and family
• Parents are verbally informed by healthcare professionals about the implications of EEG monitoring.
For healthcare professionals
• Attend training on the use of EEG and aEEG/EEG monitoring. • Identify leading staff with a focus of interest on neonatal neurological evaluation and monitoring.
For neonatal unit
• Develop and implement a unit guideline on the use of EEG and aEEG/EEG monitoring. • Develop parental information material about EEG and aEEG/EEG monitoring, also including parental perspectives. • Provide resources for specific training on EEG and aEEG/EEG monitoring tools.
For hospital
• Support healthcare professionals to participate in training on the use of aEEG/EEG and EEG monitoring.

- Provide technology for EEG or aEEG/EEG monitoring.

For health service

- Create systems to effectively transfer high-risk infants to NICUs with appropriate neuromonitoring systems and expertise.

Description

Electroencephalography (EEG) and amplitude-integrated EEG (aEEG) for evaluation of brain function in high risk infants

A majority of adverse events affecting brain function in term and preterm infants occur during deliver or the first week after birth. Such events include perinatal asphyxia, cerebral haemorrhages, ischaemia, metabolic and infectious conditions. Cerebral symptoms may be vague or entirely absent but may also include encephalopathy and seizures. Evaluation of brain function with conventional EEG or continuous monitoring with the aEEG/EEG gives diagnostic and prognostic information in high-risk term and preterm infants. Continuous video-EEG monitoring can be considered to be the gold standard, but this method is not available in all neonatal intensive care units (NICU) and not feasible for routine monitoring of large numbers of high-risk infants. During the last two decades EEG and aEEG/EEG monitoring have been increasingly used worldwide in compromised newborn infants.

Newborn infants with compromised brain function or at risk for developing severe cerebral complications should be monitored closely by clinical observation and continuously with aEEG/EEG. Conventional EEG should be performed in newborn infants monitored by aEEG/EEG.

Regular knowledge updates and training of healthcare professionals in basic management and evaluation of aEEG/EEG and EEG is of utmost importance. Several studies have reported that insufficient training in aEEG/EEG is associated with poorer and unreliable performance of the monitoring. For this reason, aEEG/EEG monitoring should be conducted in collaboration with clinical neurophysiologists or neurologists, and for most monitored newborn infants at least one standard EEG should be recorded. (13,28–30,32–35)

Several studies have demonstrated that the electrocortical activity is one of the most sensitive measures for early evaluation of brain function and early prediction of outcome in asphyxiated newborn infants. Consequently, it is recommended to record the aEEG/EEG for evaluation of asphyxiated newborn infants before hypothermia treatment. (5,21) In asphyxiated term infants, simultaneous monitoring with aEEG/EEG and NIRS is associated with more precise outcome prediction. (16,17)

Clinical identification of suspected seizures is not reliable since a majority of neonatal seizures have only subtle clinical symptoms or are entirely subclinical. Brain monitoring with aEEG/EEG and EEG in asphyxiated newborn infants allows earlier recognition of seizures in newborn infants with HIE, and with more precise treatment of seizures and the use of fewer antiepileptic drugs. (14,15,18,19,22–25,36)

The compressed aEEG trend alone is not sensitive enough for detection of seizures since especially brief seizures may be missed in the compressed trend. However, if both aEEG and raw-EEG is inspected around 80-90% of all seizures that can be identified in a standard EEG may be detected. (13,37) Development of efficient automated seizure detection alarms is urgently needed in the busy NICU setting.

Many studies have also shown that aEEG and EEG may be sensitive early predictors of outcome in preterm infants (1,7,9,10), but clinical experience of aEEG in very

preterm infants is still limited. The early predictive accuracy of aEEG and EEG can be expected to be lower in preterm infants than in term infants since the long-term outcome of especially very preterm infants may be affected by later complications during the clinical course.

The neonatal neurocritical care concept is an emerging strategy which includes a care concept based on specially trained NICU healthcare professionals and interdisciplinary teams that include neurologists, guidelines and protocols for consistent management of newborn infants at risk of neurological injury, aEEG/EEG and EEG monitoring of high-risk infants, and long-term follow up. (31) The first reports from NICUs practicing neurocritical care show very promising results. (15,24,25,27)

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Neurological monitoring in the high-risk infant: Near-infrared spectroscopy (NIRS)

Pellicer A, Hellström-Westas L, Zimmermann LJI, Buonocore G, Dudink J, Gressens P

Target group

- Term and preterm infants at risk for brain injury:
  - Infants with hypoxic-ischaemic encephalopathy (HIE)
  - Infants with peri-intraventricular haemorrhage (PIVH)
  - Infants with encephalopathy for other causes (e.g. metabolic)
  - Infants with suspected or verified seizures
  - Infants requiring intensive care and/or surgery
  - Infants with suspected/confirmed congenital central nervous system (CNS) anomalies
- Parents

User group

Healthcare professionals, neonatal units, hospitals, and health services

Statement of standard

In order to improve evaluation and outcomes of newborn infants at risk of brain injury, management includes neurological monitoring using a structured, age-appropriate neurological assessment and a range of devices to evaluate brain haemodynamics, oxygen transport, brain function, and imaging, as required.

Rationale

Infants requiring neonatal intensive care constitute a high-risk population for developing brain injury, particularly full term and preterm infants exposed to hypoxia-ischaemia, CNS infections, or with congenital anomalies.

In the first hours after birth, there is imbalance between blood flow and oxygen supply to the brain due to haemodynamic adaptation during transitional circulation, particularly in the very preterm infant. (1) Low and fluctuating cerebral blood flow are associated with adverse outcomes. (2,3) Experimental models and observational studies confirm that both hyper- and hypoxaemia may cause irreversible brain injury. (4–6) The vulnerability of this population, the severity of underlying clinical conditions, and the complexity of care make continuous, cot-side, and non-invasive monitoring tools valuable. Near-infrared spectroscopy (NIRS) derived regional tissue oxygen saturation of haemoglobin ($rStO_2$) is an absolute value, which corresponds to mixed blood saturation, used in the clinical setting as a surrogate measure for venous oxygen saturation (SvO_2). (7) Indirect assessment of cerebral blood flow has been shown to correlate with $rStO_2$. (8) This non-invasive, continuous monitoring system may help to adjust interventions that have effects on blood and oxygen supply to the brain. (9) Bilateral brain monitoring may detect differential perfusion between hemispheres. Yet, sound evidence supporting routine use of NIRS monitoring is still lacking.

Benefits

Short-term benefits

- Reduced burden of cerebral hypo- and hyperoxia in preterm infants in the first 72 h after birth (10,11)
- Early detection of infants at risk of peri-intraventricular haemorrhage (PIVH) (12–14)

- Support in decision-making in post-haemorrhagic ventricular dilatation (PHVD) (15,16)
- Improved neuroprotection after asphyxia using combined NIRS and MRI measurements of brain perfusion (15)
- Improved maintenance of theoretically safe cerebral oxygenation levels in infants with congenital heart defects (16)

Long-term benefits

- Reduced all-cause mortality in extremely preterm infants (10)
- Improved long-term outcomes in extremely preterm infants (17)

Components of the standard

Component	Grading of evidence	Indicator of meeting the standard
For parents and family		
1. Parents are informed by healthcare professionals about the role of near-infrared spectroscopy (NIRS) monitoring.	B (High quality)	Patient information sheet
For healthcare professionals		
2. A unit guideline on neurological monitoring including NIRS is adhered to by all healthcare professionals, to include • Newborn infants during resuscitation at birth (≤15 min) (11,18,19) • Extremely preterm infants in the first 72 h after birth (9,10,20) • Infants at risk of or with peri-intraventricular haemorrhage (PIVH) (12-14); infants who develop post-hemorrhagic ventricular dilatation (PHVD) (21,22) • Asphyxiated newborn infants undergoing therapeutic hypothermia (23–26) • Infants undergoing surgery with cardio-pulmonary bypass (16,27–29)	A (High quality) B (High quality)	Guideline
3. Training on NIRS monitoring is attended by all responsible healthcare professionals. (9,20,27,28,30)	A (High quality) B (High quality)	Training documentation
4. Teams with a focus of interest on neuro-critical care, including neonatologists, neurologists, neuro-physiologists, nurses, radiologists, radiographers, and physicists are established.	B (High quality)	Guideline

For neonatal unit		
5. A unit guideline on neurological monitoring including NIRS is available and regularly updated including standardised operational procedures. (7,9,20,30)	A (High quality) B (High quality)	Guideline
For hospital		
6. Training on NIRS monitoring is ensured. (7,20,27,28,30)	A (High quality) B (High quality)	Training documentation
7. Facilities for NIRS monitoring are provided.	B (High quality)	Audit report
8. An interdisciplinary team for neuro-critical care of high-risk infants in the NICU is supported.	B (Moderate quality)	Audit report
For health service		
9. High-risk infants are transferred to NICUs with appropriate neuro-monitoring systems and expertise. (31–33)	A (High quality)	Audit report, guideline

Where to go – further development of care

Further development	**Grading of evidence**
For parents and family	
N/A	
For healthcare professionals	
• Monitor perioperative near-infrared spectroscopy (NIRS) in infants with non-cardiac complex neonatal surgery. (34,35)	A (Low quality)
For neonatal unit	
N/A	
For hospital	
N/A	
For health service	
N/A	

Getting started

Initial steps
For parents and family
• Parents are verbally informed by healthcare professionals about the role of near-infrared spectroscopy (NIRS).
For healthcare professionals
• Attend training on NIRS monitoring.

- Identify leading healthcare professionals with a focus of interest on neonatal neurological monitoring.

For neonatal unit

- Develop and implement a unit guideline on neurological monitoring including NIRS.
- Develop parental information material about NIRS monitoring also including parent perspectives.
- Provide resources for specific training on NIRS monitoring.

For hospital

- Support healthcare professionals to participate in training on NIRS monitoring.

For health service

- Create systems to effectively transfer high-risk infants to NICUs with appropriate neuro-monitoring systems and expertise.

Description

The near-infrared spectroscopy (NIRS) sensor is placed at the forehead avoiding cavities, superior sagittal sinus, intra or extra-cranial huge blood collections, or vascular malformations, if known. Scalp oedema will also influence the quality of the NIRS signal. In the smallest newborn infants and those with poor perfusion states sensor position is rotated to avoid tissue injury related to compression or heat. (7,20)

Commercial NIRS devices incorporate similar technology but different wavelengths and computational algorithms translating changes in light absorption into $rStO_2$ absolute values. (7) Systematic approach has evidenced huge differences in $rStO_2$ according to device or probe (30,36), so that device-specific reference ranges or limits have to be used.

Neonatal resuscitation after birth: Clinical assessment of the newborn infant carries high inter-observer variability particularly when scoring preterm or term infants in need of resuscitation. (37) Oxygen saturation targeting and the use of supplemental oxygen during transition remain controversial topics. (38) The use of pulse oximetry or heart rate monitoring during resuscitation has not led to improvements on the short or long-term outcomes. (39) $rStO_2$ and fractional oxygen extraction reference ranges and percentile charts for the interpretation of cerebral oxygenation during immediate transition to avoid hypo- and hyperoxia of the brain during resuscitation appears promising. (11,18,19) Yet, routine interventions based on $rStO_2$ during resuscitation need development and evaluation.

Extremely low gestational age newborn infants: Recent studies have shown an association of cerebral $rStO_2$ levels and clinical outcomes. (40) Low $rStO_2$ on the first day of life associates surrogated measures of compromised systemic blood flow and risk of intraventricular haemorrhage. (12) Impaired cerebral blood flow autoregulation assessed by NIRS and arterial blood pressure monitoring associates abnormal systemic (and cerebral) blood flow distribution, death and severe brain injury. (41,42) Cerebral oxygenation can be stabilised in the preterm infant during the first 72 hours from birth by the combined use of $rStO_2$-NIRS monitoring and a pathophysiological, brain oriented treatment guideline with no record of severe adverse events. (9,10) The quality of evidence supporting some of the listed statements in the intervention algorithm is generally low, however, are all routinely used in clinical care of these patients. (9) Although important early surrogate outcomes, such as aEEG at day 3 of postnatal life or neuroimaging, did not significantly differ between the study groups (43,44), post hoc analyses showed that early burden of cerebral hypoxia was significantly associated with low brain electrical activity and severity of intracranial haemorrhage. (19) So far, definitive evidence of benefit for improvement of long-term

clinical outcomes is needed as the technology is not cheap, requires manipulation and additional staff time, and may have unwanted effects. (10)

*PIVH: C*orrelations between NIRS-derived data immediately after birth and during the transitional circulation and the development of PIVH have been reported. (12–14) Timing of neurosurgical intervention in PHVD could be critical for neurodevelopment (45), and may be guided by standardised ventricular measurements by cranial ultrasound combined with cerebral NIRS and cranial Doppler. (21,22) This approach provides a better understanding of the pathophysiology and the effect of interventions on the long-term outcomes.

HIE: Cerebral hypoperfusion during the first hours after birth is followed by hyperperfusion, even during treatment with moderate hypothermia. Potential differences according to the severity of brain injury (moderate vs severe) have been identified. (15,46) NIRS measurements of oxygenation and MRI measurements of brain perfusion show good correlation. (15) Among neonates with HIE, NIRS demonstrates evolving patterns of brain oxygenation that predict favourable and adverse outcomes both in non-cooled (46) and in those who undergo therapeutic hypothermia. (23,24) As yet, widespread recommendation of NIRS monitoring alone to guide important clinical decisions in asphyxiated newborn infants cannot be made. Used in combination with amplitude-integrated EEG increases the outcomes predictive capacity compared to either modality alone. (24–26)

Congenital heart disease (CHD): NIRS may be a useful adjunct particularly during cardiopulmonary bypass to optimise perfusion. NIRS-derived measures of systemic oxygen balance correlate with global circulatory measures and biochemical indicators of shock. (27) Algorithms have been developed to guide interventions based on $rStO_2$ values during the perioperative period. (28) However, the current literature on the use of NIRS alone does not demonstrate improvement in neurologic outcome. (29) Prospective data evaluating NIRS findings and relevant outcomes in this population is difficult to compare, because of the variable disease physiology, variable baseline values, and small sample sizes. These issues prevent extrapolation to wider CHD population.

Other complex surgical procedures conducted during the neonatal period, such as congenital diaphragmatic hernia or esophageal atresia (34,35), might be additional scenarios where NIRS may guide surgeons and anaesthesiologists during the intervention procedures. A NIRS value out of normal range, or a huge change even within the normal range, may trigger the assessment of the patient's condition when used in combination with other monitoring tools.

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Neurological monitoring in the high-risk infant: ultrasound and MRI scanning

Dudink J, Hellström-Westas L, Zimmermann LJI, Buonocore G, Gressens P, Pellicer A

Target group

- Term and preterm infants at risk for brain injury:
  - Infants with hypoxic-ischaemic encephalopathy (HIE)
  - Infants with encephalopathy for other causes (e.g. metabolic)
  - Infants with suspected or verified seizures
  - Infants requiring intensive care and/or surgery
  - Infants with suspected/confirmed congenital central nervous system (CNS) anomalies
- Parents

User group

Healthcare professionals, neonatal units, hospitals, and health services

Statement of standard

In order to improve evaluation and outcomes of newborn infants at risk of brain injury, management includes neurological monitoring using a structured, age-appropriate neurological assessment and a range of devices to evaluate brain haemodynamics, oxygen transport, brain function, and imaging, as required.

Rationale

Infants requiring neonatal intensive care constitute a high-risk population for developing brain injury, especially during the first days after birth due to respiratory, haemodynamic, infectious, or metabolic instability. Full term and preterm infants exposed to hypoxia-ischaemia or infections, or carrying conditions such as congenital malformations, antenatal (maternal) risk factors, neonatal diseases potentially involving CNS, or late prematurity, among others, are exposed to increased risk of brain injury. Early recognition of on-going disturbances of brain function or structural damage is important in implementing preventive or treatment strategies, and appropriate follow-up. Early detection of cerebral compromise, such as encephalopathy or seizures, is associated with better management of these conditions. High-risk infants should be identified as early as possible, the patient history together with a structured clinical examination and repeated clinical observations form the basis of the evaluation. The vulnerability of this population, the severity of underlying clinical conditions, and the complexity of care deserve preferably continuous, cot-side, and non-invasive monitoring tools. This can be accomplished from four perspectives: haemodynamics and oxygen transport, connectivity and function, structure, and clinical expression. The ultimate goal is to prevent or reduce risk for brain injury by early identification of high-risk infants and improved clinical management.

Benefits

Short-term benefits

- Reduced mortality and morbidity (i.e., detect sinovenous thrombosis, severe haemorraghes or post-haemorrhagic ventricular dilatation) (1–11)
- Direct feedback on neuroprotective interventions (i.e., low molecular weight heparin treatment for cerebral vein thrombosis, ventricular reservoir taps, ventriculo-peritoneal shunt treatment) (1–8)

- Improved assessment of severity of brain damage which might redirect care (i.e., in patients with hypoxic ischaemic encephalopathy (HIE), arterial stroke, venous infarction) (1–12)
- Provides proxy biomarker for outcome for evaluation in neuroprotective intervention trials (11–16)
- Informs prognosis for physicians and parents (11–16)

Long-term benefits

- More focused follow-up programmes (5,16–20)
- Improved understanding of brain injury pathophysiology (5,12,14,17–19)
- Improved assessment of neonatal brain development to guide future prevention and intervention strategies (5,16–19)

Components of the standard

Component	**Grading of evidence**	**Indicator of meeting the standard**
For parents and family		
1. Parents are informed by healthcare professionals about the role of brain imaging. (21)	A (Moderate quality) B (High quality)	Patient information sheet
For healthcare professionals		
2. A unit guideline on neurological monitoring including brain imaging is adhered to by all healthcare professionals, to include • term infants with suspected brain injury (1–5,9–13,15,16) • very preterm infants (1–5,12)	A (High quality) B (High quality)	Audit report, guideline
3. Training on ultrasound and MRI procedures is attended by all responsible healthcare professionals.	B (High quality)	Training documentation
4. Teams with a focus of interest on neuroimaging (e.g. nurses, neonatologists, neurologists, neuro-physiologists, radiologists, radiographers, and physicists) are established. (18)	B (High quality)	Guideline
For neonatal unit		
5. A unit guideline on neurological monitoring including brain imaging is available and regularly updated, to include standardised operational procedures for cranial ultrasound (CUS) (22–24) and magnetic resonance imaging (MRI). (20,21,25–27)	A (High quality) B (High quality)	Guideline

For hospital		
6. Training on ultrasound and MRI procedures is ensured. (20,21,25–27)	A (High quality) B (High quality)	Training documentation
7. An interdisciplinary team for neurological evaluation of high-risk infants in the NICU is supported.	B (Moderate quality)	Audit report
8. Facilities for brain imaging (CUS and MRI) are provided.	B (High quality)	Audit report
For health service		
9. High-risk infants are transferred to NICUs with appropriate neuro-monitoring systems and expertise. (17,28)	A (High quality)	Audit report, guideline

Where to go – further development of care

Further development	**Grading of evidence**
For parents and family	
N/A	
For healthcare professionals	
N/A	
For neonatal unit	
• Develop a full neonatal neuro-critical care concept, including guidelines and close collaboration with neurologists.	B (Moderate quality)
For hospital	
N/A	
For health service	
• Monitor incidence, treatment and long-term outcomes after neonatal brain injury such as intra-ventricular haemorrhage. (18)	A (High quality)
• Develop multi-centre expertise by sharing imaging databases.	B (Moderate quality)

Getting started

Initial steps
For parents and family
• Parents are verbally informed by healthcare professionals about the role of brain imaging.
For healthcare professionals
• Attend training on ultrasound and magnetic resonance imaging (MRI) procedures. • Identify leading healthcare professionals with a focus of interest on neonatal neurological monitoring.
For neonatal unit
• Develop and implement a unit guideline on neurological monitoring including brain imaging.

- Develop parental information material about brain imaging, also including parental perspectives.
- Provide resources for specific training on brain imaging tools.

For hospital

- Support healthcare professionals to participate in training on ultrasound and MRI procedures.

For health service

- Create systems to effectively transfer high-risk infants to NICUs with appropriate neuro-monitoring systems and expertise.

Description

Despite several major advances in fetal and neonatal care, the frequency of neurodevelopmental disability among the survivors of neonatal intensive care remains high. Although mortality for both, preterm infants and severely compromised term infants has decreased, the population of newborn infants at risk for neurological disability is still increasing. (29,30) Neuroimaging is a critical investigation in the provision of adequate diagnostic or prognostic information for parents. (1–5) Neuroimaging in newborn infants at risk of brain damage is oriented to:
a. Diagnosing brain injury to provide the most appropriate medical management.
b. Early detection of lesions associated with long-term neurodevelopmental disabilities.

Early diagnosis of structural brain damage can steer neuroprotective and/or neurorehabilitation treatment strategies, and guide appropriate follow up. It can also give us an understanding of the pathophysiology. (1–5)

Neonatal neuroimaging techniques such as CUS, MRI and CT scanning have been used for many decades and have proven to be extremely helpful assessing brain maturation and injury. However, there are still several challenges associated with neonatal neuroimaging, which will be highlighted below. (5,11,13,25)

Proper assessment of neonatal brain images requires extensive knowledge about neonatal brain injury (aetiology, pathophysiology, prognosis), developmental neuro-anatomy (neuro-embryology), the advantages and disadvantages of the different imaging techniques, pitfalls and optimal timing. (5,11,13,25) Furthermore, the transport and sedation of critically ill neonates for both MRI and CT scanning often represents a major challenge. (25–27) Proper scanning requires a dedicated team. The most common used neonatal neuroimaging modalities are: CUS and MRI. The use of CT is very limited and because of radiation should tried to be avoided. All these factors have to be taken into account when choosing timing and modality to image the neonatal brain.

There are advantages and disadvantages for each of the modalities: (5,11,13,25–27)

Cerebral Ultrasound	
Advantages	Disadvantages
• Bedside, patient friendly, save • Reliable for detection of severe haemorrhagic lesions (e.g. peri-intraventricular haemorrhage-P/IVH- in preterms) and severe white matter damage	• Difficult to detect cortical abnormalities • Difficult to detect posterior fossa abnormalities (the use of posterior fontanel and mastoid fontanel can be of help)

• Doppler technique (detection of thrombosis) • Specific lesions: germinolytic cysts, calcifications, lenticulo-strtriate vasculopathy -LSV • Repeated assessments (i.e., measurements such as the Levene index in posthaemorrhagic ventricle dilatation –PHVD patients)	• Less reliable in detecting small lesions and subtle white matter damage • Difficult to assess myelinisation
MRI	
Advantages	Disadvantages
• Relatively safe (no radiation) • Good assessment of whole brain (including cortex and posterior fossa) • Detailed information about brain development (including myelination) • Reliable information about localisation and extent of brain damage • Reliable for detection of small lesions and subtle white matter damage • Special sequences for different purposes: e.g. diffusion-weighted imaging (DWI) (cytotoxic oedema), diffusion tensor imaging (DTI) (quantitative white matter tract analysis), magnetic resonance venography (MRV) (venous system), susceptibility weighted imaging (SWI) (haemorrhages), contrast (tumour, abscess), magnetic resonance angiography (MRA) (arterial vessels)	• More burden/distress for (often unstable) infants and medical team: transport issues, sedation, time consuming • High costs (depending on hospital) • Some lesions more difficult to assess (LSV, calcifications, germinolytic cysts)
CT	
Advantages	Disadvantages
• Good visualisation of bone structures • Often wider availability than MRI	• Relatively unsafe (radiation) • Poor tissue contrast (low resolution) • To detect haemorrhages beyond one week can be difficult

Disease states and recommended neuroimaging technique:*
*Based on several factors, including local availability, expertise, and protocols.

Cerebral Ultrasound (examples)

- High-risk neonatal conditions: e.g. preterms (gestational age (GA) less than 32 weeks), intrauterine growth restriction, congenital abnormalities (syndromes), post-resuscitation, HIE, meningitis/encephalitis, metabolic diseases, symptomatic

hypoglycaemia, hyperbilirubinemia (above exchange transfusion threshold), sudden severe anaemia, congenital heart defects, post-surgery, pre-extracorporeal membrane oxygenation (ECMO), post-ECMO, sudden clinical deterioration.

- Newborn infants with neurological symptoms/signs: e.g. seizures, hyper- or hypotonia, abnormal movements, abnormal consciousness, unexplained central apneas, unexplained irritability and restlessness, micro- or macrocephaly.

MRI (examples)

- Neurological symptoms not explained by other diagnoses
- Convulsions
- Symptomatic hypoglycaemia
- Severe hyperbilirubinemia and neurological symptoms or abnormal ultrasound
- HIE grade II or III
- P/IVH with PHVD or periventricular haemorrhagic infarction (PVHI)
- (Suspected) congenital CNS abnormalities
- (Suspected) sinovenous thrombosis
- Abnormalities in posterior fossa
- Parenchymal injury (periventricular leukomalacia -PVL>II, intraparenchymal haemorrhage, stroke, inhomogeneous periventricular echogenicity -PVE)
- Symptomatic extra-cerebral haemorrhage

Suggested timing of neuroimaging:

Cerebral Ultrasound

Term infants:

- Neurological symptoms suggesting brain injury: as soon as possible (to exclude acute conditions that need intervention)
- Suspected congenital CNS abnormalities: 1st day after birth

Preterm infants:

- GA >28 weeks: scan on day 1-3-7-14,21,28, at 6 weeks and at term equivalent age (TEA)
- GA< 28 weeks: scan on day 1-3-7-14-21-28- than every two weeks until 34 weeks GA and at term equivalent age (TEA)
- Intensify CUS in case of abnormalities or after episode of clinical deterioration (e.g. unexplained anaemia, neurological symptoms, P/IVH, PHVD, inhomogeneous PVE, cerebellar haemorrhage, surgery, HIE, CNS infection, metabolic disease, etc.)

MRI

Term infants (examples):

- Neurological symptoms of unknown origin: as soon as possible
- Hypoxic Ischemic Encephalopathy: between day 4-7
- Suspected parenchymal damage (e.g. stroke): between 3-7 days after insult

Preterm infants (examples):

- Neurological symptoms of unknown origin: as soon as possible
- Routine neuroimaging in extreme preterm infants: preferred timing around TEA

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Neurological monitoring in the high-risk infant: clinical neurological evaluation

Gressens P, Hellström-Westas L, Zimmermann LJI, Buonocore G, Dudink J, Pellicer A

Target group

- Term and preterm infants at risk for brain injury:
  - Infants with hypoxic-ischaemic encephalopathy (HIE)
  - Infants with encephalopathy for other causes (e.g. metabolic)
  - Infants with suspected or verified seizures
  - Infants requiring intensive care and/or surgery
  - Infants with suspected/confirmed congenital central nervous system (CNS) anomalies
- Parents

User group

Healthcare professionals, neonatal units, hospitals, follow-up teams, and health services

Statement of standard

In order to improve evaluation and outcomes of newborn infants at risk of brain injury, management includes neurological monitoring using a structured, age-appropriate neurological assessment and a range of devices to evaluate brain haemodynamics, oxygen transport, brain function, and imaging, as well as long-term follow-up of neuro-motor function as required.

Rationale

Infants requiring neonatal intensive care constitute a high-risk population for developing brain injury, particularly full term and preterm infants exposed to hypoxia-ischaemia, CNS infections, or with congenital anomalies.

Early recognition of disturbed brain function or structural brain injury is important in the institution of preventive or treatment strategies, and appropriate follow-up. Early detection of neurological compromise, such as encephalopathy or seizures, is associated with better management of these conditions. (1–4)

The patient history, a structured neurological examination and repeated clinical observations form the basis of evaluation. After discharge, standardised follow-up and assessment of neurological, motor, cognitive and behavioural function are the mainstay of monitoring, to identify sequelae of perinatal brain injury (see Follow-up & continuing care). Early identification of impaired function will improve clinical management and long-term functional outcomes. (5–10) Parental questionnaires can be combined with formal motor assessment in high-risk populations. (11) Motor assessment tests should be validated in their specific cultural settings. (12)

Benefits

Short-term benefits

- Early identification of neuromotor impairments (5–8)

Long-term benefits

- Improved long-term neuromotor outcomes (8)

Components of the standard

Component	Grading of evidence	Indicator of meeting the standard
For parents and family		
1. Parents are informed by healthcare professionals about the role of clinical neurological evaluation and the importance of neurological follow-up.	B (High quality)	Patient information sheet
For healthcare professionals		
2. A unit guideline on comprehensive clinical neurological evaluation and the use of technological investigation is adhered to by all healthcare professionals (see Medical care & clinical practice). (5–9)	A (High quality) B (High quality)	Guideline
3. Specific training on clinical neurological evaluation of high-risk infants is attended by all responsible healthcare professionals. (5–7,9)	A (High quality) B (High quality)	Training documentation
4. Teams with a focus of interest on neuro-critical care, including neonatologists, neurologists, neuro-physiologists, nurses, radiologists, radiographers, and physicists are established.	B (High quality)	Guideline
For neonatal unit		
5. A unit guideline on comprehensive clinical neurological evaluation and the use of technological investigation is available and regularly updated. (5–9)	A (High quality) B (High quality)	Guideline
For hospital and follow-up team		
6. Specific training on clinical neurological evaluation of high-risk infants is attended is ensured. (5–7,9)	A (High quality) B (High quality)	Training documentation
7. Facilities for clinical neurological evaluation of high-risk infants are provided.	B (High quality)	Audit report
8. An interdisciplinary team for neuro-critical care of high-risk infants in the NICU is supported.	B (Moderate quality)	Audit report
9. An organised follow-up programme for high-risk infants including neurological, motor and behavioural assessments is established.	B (High quality)	Guideline

For health service		
10. Pregnant women with fetuses with identified neurological problems and high-risk newborn infants are transferred to centres with appropriate clinical neurological evaluation systems and expertise (see Birth & transfer). (13)	A (High quality)	Audit report, guideline
11. Follow-up programme for high-risk newborn infants, including neurological, motor and behavioural assessments, as well as parental questionnaires is ensured.	B (High quality)	Guideline
12. Benchmarking of long-term neurological outcomes of high-risk infants is established. (11,14)	A (High quality) B (High quality)	Audit report

Where to go – further development of care

Further development	**Grading of evidence**
For parents and family	
N/A	
For healthcare professionals	
N/A	
For neonatal unit	
N/A	
For hospital	
N/A	
For health service	
N/A	

Getting started

Initial steps
For parents and family
• Parents are verbally informed about the role of clinical neurological evaluation and the importance of neurological follow-up.
For healthcare professionals
• Attend training on clinical neurological evaluation of high-risk infants. • Identify leading healthcare professionals with a focus of interest on neonatal neurological evaluation.
For neonatal unit
• Develop and implement a unit guideline comprehensive clinical neurological evaluation and the use of technological investigation. • Develop parental information material on clinical neurological evaluation and the importance of follow-up also including parent perspectives.

- Provide resources for specific training on the various neonatal neurological examination tools.

For hospital

- Support healthcare professionals to participate in training on clinical neurological evaluation of high-risk infants.

For health service

- Create systems to effectively transfer high-risk infants to NICUs with appropriate neuro-monitoring systems and expertise.
- Establish a follow-up programme for high-risk newborn infants including neurological, motor and behavioural assessments as well as parental questionnaires.

Description

The standardised clinical neurological examination constitutes the basis of the evaluation of high-risk infants and should be performed repeatedly in the acute phase and later on in infants at risk for neurodevelopmental sequels.

In the neonatal intensive care unit (NICU)

- Neurological assessment should be performed repeatedly in term and preterm infants with overt or suspected clinical signs from the central and/or peripheral nervous system, including seizures. Several validated methods are available for term (1,5,6) and preterm infants (7–9), including for example the Dubowitz Neurological Assessment of the Preterm and Full-term Infant (5,7), the neurological assessment by Amiel-Tison (6), the Assessment of Preterm Infants' Behaviour (APIB) (15), Neonatal Intensive Care Unit Network Neurobehavioural Scale (NNNS) (16), Prechtl's Assessment of General Movements (GMs) (17), and other. (8,9,18)
- Moderately preterm and term infants with hypoxic-ischaemic encephalopathy (HIE), including infants subjected to therapeutic hypothermia, should be repeatedly assessed during the first days of life to produce gradings of encephalopathy using Sarnat criteria or Thompson scores. (1–3)
- Neonatal pain/comfort assessments are used for repeated assessments of infant behaviour during, intensive care and pain should always be excluded as a potential cause of abnormal behaviour in infants. (19)

Long-term outcomes

First two years after birth

Several neurodevelopmental and neuropsychological tests have been developed for postnatal evaluation of high-risk infants in different countries and hence in different languages. Some of them have been translated and validated in different (but not all) languages, making in some way, general recommendations very difficult. Accordingly, the following description is based on relatively largely adopted tests but might require some adaptations, depending on the considered part of the world. It is important to remember that a translated test must be validated prior to its generalised use.

- The follow-up should aim at early diagnosis and categorisation of neurodevelopmental problems, including cerebral palsy, motor function, hearing and vision impairments, alongside medical problems such as feeding problems, growth and respiratory function.
- Systematic neuro-motor evaluation can be valuable using well validated tests, such as the Alberta Infant Motor Scale (AIMS) (20), and the Peabody

Developmental Motor Scales. (21)

- The clinical neurodevelopmental evaluation should be combined with other assessment methods as required and which may include cerebral ultrasound and MRI, NIRS, aEEG/EEG, EEG, hearing tests, ophthalmological and genetic testing, as appropriate.

Evaluation around 2 and 5-5½ years of age

Long-term follow-up should be offered to infants with a significant risk of developing long-term neurodevelopmental sequels, and who could benefit in their function and quality of life from early detection and special intervention/training for these sequels. High-risk groups include: extremely preterm infants (gestational age <28 weeks), severely growth restricted infants, infants with morphological brain injury (intraventricular haemorrhage grade 3-4, periventricular leukomalacia, stroke, posthaemorrhagic ventricular dilatation, malformations), infants with moderate-severe HIE including infants who needed hypothermia treatment, infants with severe encephalopathies of other causes (e.g. kernicterus, seizures due to hypoglycaemia, metabolic diseases), central nervous system infection and severe neonatal morbidities (e.g. major surgery, sepsis, necrotising enterocolitis, need for nitric oxide or extracorporeal membrane oxygenation). (11,14)

There seems to be some international agreement that 2 and 5-5½ years of (corrected for prematurity, when relevant) age are suitable for evaluation of high-risk infants. These age levels have been chosen since children with adverse development, including cerebral palsy, benefit from early diagnosis and training by physiotherapists. The standardised age-groups also allow for better international comparisons of outcomes.

The present standard has a focus on neurological and motor assessment which should be combined with evaluation of cognitive, behavioural and psychiatric outcomes (see Follow-up & continuing care). Several methods are available, e.g. the Bayley Scales of Infant and Toddler Development (BSID) (22) and the Brunet-Lezine assessment in the younger children. (23) Neurological examination should be performed in a standardised way (24), and e.g. the Movement Assessment Battery for Children (Movement ABC) (25) and other motor assessment tests can be used for evaluation of motor function, including developmental coordination disorders (DCD). Cognitive testing is often done with the Wechsler Preschool and Primary Scale of Intelligence (WPPSI) or the Wechsler Intelligence Scale for Children (WISC).

Categorisation of motor outcome should preferably be done according to the Gross Motor Function Classification System (GMFCS) (26), which also facilitates international comparisons of outcomes. Hand function in children with cerebral palsy can easily be classified with the Manual Ability Classification System (MACS) (27), also in children younger than 4 years.

Follow-up at 2 years should include:

Neurological and neurodevelopmental testing, including cognition and language (e.g. BSID, Brunet-Lezine or equivalent). Assessment of motor function (e.g. Peabody, Movement ABC). Behavioural and autism screening as required (see Follow-up & continuing care).

Follow up at 5-5½ years should include:

Neurological testing (standardised) and motor function (e.g. Movement-ABC) cognitive function (WPPSI IV or WISC), behavioural tests. Reading and writing

evaluation at school age (see Follow-up & continuing care).

For infants at risk of developing motor deficits it is recommended to have a dedicated paediatric physiotherapist present during follow up visits for motor assessments (preferably using standardised test). Hand function should preferably be assessed in conjunction with motor assessment in children with suspected or deviant motor function. (28)

A high proportion of children with morphological brain injury develop cerebral visual impairments, including preterm infants with white matter injury, term infants with stroke or other perinatal brain injury. In order to optimise long-term outcomes by early support of visual functioning in compromised children, it is recommended to screen children with known perinatal brain injury for cerebral visual impairments. (29)

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Postnatal management of newborn infants with hypoxic ischaemic encephalopathy (HIE)

Van Bel F, Hellström-Westas L, Zimmermann LJI, Buonocore G, Murray D, Saliba E, Thoresen M

Target group
Term and near term infants with hypoxic ischaemic encephalopathy (HIE) and parents

User group
Healthcare professionals, neonatal units, hospitals, and health services

Statement of standard
Newborn infants who have suffered from severe hypoxic-ischaemia receive early evaluation and appropriate postnatal management including therapeutic hypothermia and monitoring.

Rationale
The goal is to reduce long-term effects of hypoxic ischaemic brain injury. Moderate to severe perinatal asphyxia in term and near term infants is one of the most important causes of neonatal death and adverse motor and cognitive outcome, with an incidence of 2-20 per 1000 live born infants, depending in which part of the world they are born. (1) Until recently, therapy was limited to stabilisation of the newborn infant and treatment of hypoxic ischaemic encephalopathy (HIE) induced seizures. Reduction of the body temperature to 33.5°C is the only established therapy which has shown a decrease in adverse outcomes after perinatal asphyxia (death or substantial disability at 18 months of age) from about 66% for non-cooled infants to 50% in cooled infants. (2,3) Intensive research is ongoing to explore (pharmacological) neuroprotective interventions which could be used in addition to hypothermia to improve outcome. (4–7)

Benefits

Short-term benefits
- Reduced brain injury due to excitatory neurotransmitters and reactive oxygen species (8,9)
- Improved prognosis using stratified hypoxic ischaemic encephalopathy (HIE) severity, e.g. using neurophysiological monitoring (a-EEG (10–12) or EEG) (see Medical care & clinical practice) (13)
- Reduced brain injury by early treatment of seizures (13,14)
- Reduced mortality (3)

Long-term benefits
- Improved neurocognitive outcome, increasing the rate of disability free outcome at 5 years (3,15) reduced health and societal costs (16), reduced occurrence of epilepsy at 2 years (7), less severe cerebral palsy in survivors (15)

Components of the standard

Component	Grading of evidence	Indicator of meeting the standard
For parents and family		
1. Parents are informed by healthcare professionals about the management and outcome of hypoxic ischaemic encephalopathy (HIE). (17–20)	A (Low quality) B (High quality) C (Moderate quality)	Patient information sheet
2. Parents receive counselling regarding the expected short- and long-term outcome and prognosis related to HIE prior to discharge by healthcare professionals. (20)	B (High quality) C (Moderate quality)	Clinical records
For healthcare professionals		
3. A unit guideline on management of HIE including criteria for hypothermia treatment is adhered to by all healthcare professionals.	B (High quality)	Guideline
4. Training in assessment and management of encephalopathic infants is attended by all responsible healthcare professionals. (21,22)	A (Moderate quality) B (High quality)	Training documentation
5. Moderate hypothermia treatment is started within 6 hours and continued for 72 hours after birth of eligible infants. (2,23)	A (High quality)	Audit report
For neonatal unit		
6. A unit guideline on management of HIE (22) including monitoring blood glucose, a-EEG, seizures (14), heart rate (24), oxygen saturation (25), PCO_2 (14,25), and blood pressure is available and regularly updated.	A (Moderate quality) B (High quality)	Guideline
7. Infants who require hypothermia treatment are managed in centres with documented expertise and experience including necessary transfer (see Birth & transfer).	B (Moderate quality)	Guideline
For hospital		
8. Training in assessment and management of encephalopathic infants is ensured.	B (High quality)	Training documentation
9. At designated units, cooling devices and monitoring equipment are available.	B (High quality)	Audit report

For health service		
10. A national guideline on management of HIE including criteria for hypothermia treatment is available and regularly updated.	B (High quality)	Guideline
11. Hypothermia treatment including documented follow-up at 2 years (e.g. Bayley III or similar) and necessary education is coordinated and organised.	B (High quality)	Audit report
12. Support services for families with infants with HIE are available.	B (High quality)	Audit report

Where to go – further development of care

Further development	**Grading of evidence**
For parents and family	
• Use routine health service and education data for long-term follow-up programmes.	B (Moderate quality)
For healthcare professionals	
N/A	
For neonatal unit	
• Develop regional training programmes on early assessment and management of hypoxic ischaemic encephalopathy (HIE).	B (High quality)
• Research on improved interventions, monitoring care and outcome predictors.	B (Moderate quality)
For hospital	
N/A	
For health service	
• Develop asphyxia registry service including outcome at 2 years. (14,18)	B (Moderate quality)

Getting started

Initial steps
For parents and family
• Parents are verbally informed by healthcare professionals about the management and outcome of hypoxic ischaemic encephalopathy (HIE) by healthcare professionals.
For healthcare professionals
• Attend training in assessment and management of encephalopathic infants.
• Join post-graduate education with respect to hypothermia and a-EEG or EEG monitoring and interpretation technique/knowledge.
• Develop appropriate neurodevelopmental follow-up expertise.
For neonatal unit
• Develop and implement a unit guideline on management of HIE including criteria for hypothermia treatment.
• Develop information material on management and outcome of HIE for parents.

- Provide appropriate devices and knowledge how to use device(s). (22)

For hospital

- Support healthcare professionals to participate in training assessment and management of encephalopathic infants.
- Provide appropriate budget and technical support for training and equipment.

For health service

- Develop and implement a national guideline on management of HIE including criteria for hypothermia treatment and follow-up.
- Recognise that therapies discussed in this statement are mandatory.

Description

Apart from the supportive therapies such as stabilisation of haemodynamics, support of respiration, monitoring of physiological parameters and metabolism (e.g. glucose metabolism, electrolytes, etc.) and treatment of seizures, moderate hypothermia (target; 33-34˚C) should be initiated as soon as possible and not later than six hours after birth (within the so-called therapeutic window) and continued for 72 hours, with appropriate sedation and pain management. (2,23) It is important to anticipate the possible side effects of induced hypothermia; including thrombocytopenia; hypotension; arrhythmia/bradycardia and hearing loss. (3,26) If sepsis or infection is suspected, antibiotic treatment should be considered. Although beyond the scope of this topic, appropriate (brain) monitoring is mandatory. Depression of background amplitude on early amplitude-integrated EEG (a-EEG) or abnormal multi-channel EEG activity is an excellent indicator of severity, and can be used to stratify babies for therapeutic hypothermia. Continuous a-EEG/EEG monitoring is essential to detect electrographic seizures and the effect of anticonvulsant treatment. In addition, the use of near infrared spectroscopy-monitored cerebral oxygenation ($rScO_2$) can be useful to estimate severity. Proper documentation of brain injury, including serial neurological examination (cranial ultrasound; MRI, preferably with diffusion sequences) as well as biochemical markers in blood/serum or plasma is important to determine the prognosis in the first week of life. Be aware of the effect of hypothermia per se on biochemical markers (27–29) and physiological variables. (21) Systematic neurobehavioural testing and documentation at two years follow-up in survivors (e.g. Bayley III (30) or Griffiths (31) as well as at early school age for long term, e.g. 5-8 years (see Follow-up & continuing care). (18)

1. General measures (hemodynamic/respiratory stabilisation; treatment of convulsions; metabolic/electrolyte surveillance)
2. Moderate whole body hypothermia (33.5±0.5˚C)
3. Add-on therapies when such are proven effective in trials (e.g. pharmacology/noble gasses/repair with umbilical cord stem cells)

1 and 2 are established therapies and are standard clinical practice, 3 are experimental and are currently under clinical investigation.

Several phase II and III studies are underway for assessment as add-on therapies to be used with hypothermia, mostly pharmacological therapy (rhEPO; melatonin; allopurinol) and ventilation with noble gases (Xenon); Repair with stem cells (e.g. mesenchymal stem cells, autologous (UMBC cells) and allogeneic transplantation are being investigated). (4,13,32–34)

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EFCNI, van Bel F, Hellström-Westas L et al., European Standards of Care for Newborn Health: Postnatal management of newborn infants with hypoxic ischaemic encephalopathy (HIE). 2018.

Postnatal support of transition and resuscitation

Schouten ES, Buonocore G, Zimmermann LJI, Hellström-Westas L, Flemmer AW, Rüdiger M, Saugstad OD, Trevisanuto D, Vento M

Target group
Newborn infants, pregnant women with risk factors, their partners, and parents

User group
Healthcare professionals (including community midwives), neonatal units, hospitals, and health services

Statement of standard
Support of postnatal transition to extrauterine life is based on internationally consented guidelines, which are based on scientific evidence, and is performed in an appropriate structured and equipped environment by trained personnel.

Rationale
Postnatal adaptation to extrauterine life is a complex process during which air breathing is established and circulatory changes take place. Difficulties may occur with transition in situations such as preterm birth or perinatal asphyxia. These situations account for much of the associated neonatal mortality and morbidity. (1–4) Certain problems that arise during birth may be anticipated. (5) Transition should be supported appropriately and resuscitation instituted when necessary. High-risk deliveries should be attended by individuals trained in advanced neonatal resuscitation, but all healthcare professionals attending deliveries should be trained in basic neonatal resuscitation techniques.

The International Liaison Committee on Resuscitation (ILCOR) provides comprehensive recommendations for the management at transition and resuscitation of the newborn infant, which are adapted by international bodies such as the American Heart Association (AHA) and the European Resuscitation Councils (ERC). (6–8) These recommendations are updated regularly, translated and adapted by the respective regional or national organisations. A recent survey showed that available equipment and clinical practices recommended by the international guidelines are already implemented by centers in Europe, but a large variance still persists. (9) Training in the practical skills of resuscitation should be undertaken in all maternity settings, including all responsible disciplines, using a neonatal resuscitation courses (see Education & training).

Benefits

Short-term benefits
- Reduced mortality and morbidity (6–8)

Long-term benefits
- Improved neurodevelopmental outcome (6–8)

Components of the standard

Component	Grading of evidence	Indicator of meeting the standard
For parents and family		
1. Pregnant women with risk factors and their partners are informed by healthcare professionals and counseled before birth (see Birth & transfer).	B (High quality)	Patient information sheet
2. Parents of infants at high-risk for resuscitation are informed by healthcare professionals about the possible need for support at transition and its risks. They are informed about the outcome of equivalent infants cared for in the current facility and if applicable are given alternatives.	B (Moderate quality)	Patient information sheet
3. Parents are invited to be present during resuscitation. (8,10,11)	A (High quality)	Guideline
4. Parents are provided with opportunities to debrief following a resuscitation of their infant.	B (High quality)	Clinical record, parent feedback
For healthcare professionals		
5. A guideline on resuscitation, including post-resuscitation care, is adhered to by all healthcare professionals. (6–8)	B (High quality)	Guideline
6. Training on current resuscitation recommendations, guidelines and local equipment is attended by all responsible healthcare professionals using accredited courses (see Education & training). (6–8)	A (Moderate quality) B (High quality)	Training documentation
7. Equipment needed for resuscitation is regularly checked.	B (High quality)	Audit report
For neonatal unit		
8. A guideline on neonatal resuscitation (aligned to relevant (inter)national resuscitation guidelines), including post-resuscitation care, and local arrangements for transfer to expert services where necessary, is available and regularly updated. (6–8)	B (High quality)	Guideline

9. Information to support emergency calls is clearly displayed within the delivery suite and neonatal unit to cover: • further help (manpower) • consultation (knowledge) • neonatal transport	B (High quality)	Guideline
10. Team debriefing after resuscitation is provided.	B (High quality)	Healthcare professional feedback
11. Healthcare professionals trained in resuscitation are available throughout the 24 hours.	B (High quality)	Audit report
For hospital		
12. Training on resuscitation including simulation scenarios is ensured.	B (High quality)	Training documentation
13. Facilities for appropriate resuscitation and for resuscitation training (e.g. mannequins for simulation) are provided. (12,13)	A (High quality) B (High quality)	Audit report
For health service		
14. A national guideline on neonatal resuscitation is available and regularly updated.	B (High quality)	Guideline

Where to go – further development of care

Further development	**Grading of evidence**
For parents and family	
N/A	
For healthcare professionals	
• Video recording of transition management is conducted and structured feedback is given, using video recording of resuscitation situations for learning purposes demands good debriefing skills, clear local policy concerning archiving and medico-legal implications of the video material. (14)	B (Moderate quality)
• Elicit options for providing emergency telemedicine consultation for neonatal resuscitation. (15)	A (Low quality)
For neonatal unit	
• Establish debriefing rounds for resuscitation situations, including interdisciplinary work with psychologist for complex cases.	B (Moderate quality)
• Establish regular quality meetings within one week after delivery to check defined quality parameters of pre- and postnatal management (antenatal lung maturation, admission temperature etc.) together with nurses, midwifes, obstetricians, neonatologists, psychologists, alternatively cases of complex deliveries can be debriefed collectively to address general or	B (Moderate quality)

structural aspects that need quality improvement.

For hospital	
• Establish the chance of bonding with the mother immediately after successful support of postnatal transition.	B (High quality)
For health service	
• Support research into new techniques and approaches for neonatal resuscitation.	B (High quality)

Getting started

Initial steps
For parents and family
• Parents are verbally informed by healthcare professionals about resuscitation.
For healthcare professionals
• Offer prenatal counseling by neonatologists. • Attend regular training on basic neonatal resuscitation, for example a local Newborn Life Support course provided by the ERC. • Establish centralisation for high-risk deliveries in advance.
For neonatal unit
• Develop and implement a guideline on resuscitation. • Develop information material on neonatal transition phase and potential resuscitation for parents. • Provide adequate training for healthcare professionals.
For hospital
• Support healthcare professionals to participate in resuscitation training. • Support healthcare professionals in implementing measures for quality improvement.
For health service
• Develop and implement a national guideline on neonatal resuscitation.

Source

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Prevention, detection, documentation, and treatment of retinopathy of prematurity (ROP)

Hellström A, Hellström-Westas L, Zimmermann LJI, Buonocore, G, Hård AL, Stahl A

Target group
Preterm infants at risk of severe retinopathy of prematurity (ROP) defined by national guidelines and their parents

User group
Healthcare professionals, eye units, neonatal units, hospitals, and health services

Statement of standard
Programmes for preventive measures such as control of oxygen supplementation and promotion of optimal nutrition are established as well as screening programmes for detection, documentation, and treatment of sight threatening retinopathy of prematurity (ROP) in all units caring for very preterm infants.

Rationale
The goal is to prevent visual impairment and blindness due to retinopathy of prematurity (ROP), which is a major cause of childhood blindness and mainly affects extremely preterm infants. (1,2) Uncontrolled oxygen supplementation and poor neonatal monitoring are important factors contributing to increased ROP risk, even in more mature infants. (3)

Hospitals caring for very preterm infants need programmes promoting adherence to oxygen saturation targets and avoidance of hyperoxia, through implementation of appropriate alarm levels, education of healthcare professionals, oxygen titration guidelines, and sufficient number of skilled attendants. Automated oxygen control can improve SpO_2 targeting and may be an alternative. (4) Prevention and management of ROP require close inter-disciplinary collaboration.

Hospitals caring for very preterm infants should adhere to screening and treatment programmes for ROP, based on existing evidence.

These programmes define:

- screening inclusion criteria,
- timing of eye examination
- choice of dilating drops and information on how to avoid systemic absorption
- pain and stress control at screening examinations (5)
- indication for treatment
- anaesthesia/analgesia during laser treatment (5)
- follow-up of treated infants following appropriate protocols based on the treatment

Currently, most hospitals adhere to the US recommendations for screening (6) and for treatment, the recommendations of the Early Treatment for Retinopathy of Prematurity Group (7) are followed in many countries.

Benefits

Short-term benefits

- Reduced occurrence of severe retinopathy of prematurity (ROP) needing treatment (8–10)
- Improved identification of infants needing treatment for ROP (6)

- Increased percentage of infants treated timely (6,11)
- Reduced stress for parents (12)

Long-term benefits

- Reduced occurrence of visual impairment and blindness caused by ROP (8–10)

Components of the standard

Component	Grading of evidence	Indicator of meeting the standard
For parents and family		
1. Parents are informed by healthcare professionals about retinopathy of prematurity (ROP), screening, treatment, and outcomes including the importance of provision of mother's own milk for the prevention of ROP (see Care procedures). (12,13)	A (Low quality) B (High quality)	Patient information sheet
For healthcare professionals		
2. Available guidelines on prevention and management of ROP are adhered to by all involved healthcare professionals.	B (High quality)	Guideline
3. Training on oxygen saturation targets is attended by all responsible healthcare professionals. (13)	A (High quality) B (High quality)	Training documentation
For neonatal unit		
4. Unit guidelines on prevention of ROP are available and regularly updated. (6,7,13)	A (High quality) B (High quality)	Guideline
5. Unit guidelines for control of oxygen supplementation and promotion of maternal milk feeding are available and regularly updated. (14,15)	A (Moderate quality) B (High quality)	Audit report, guideline
For eye unit		
6. Guidelines on screening, documentation and management of ROP are available and regularly updated. (2)	A (High quality) B (High quality)	Guideline
For hospital		
7. Training on prevention and management of ROP is ensured.	B (High quality)	Training documentation
8. Availability of expert personnel for fail-safe system of ophthalmological screening and treatment is ensured. (6)	A (Moderate quality) B (High quality)	Audit report

For health service		
9. National guidelines on prevention and management of ROP are available and regularly updated.	B (High quality)	Guideline
10. Rate of blindness and impaired vision due to ROP is monitored nationally.	B (High quality)	Audit report

Where to go – further development of care

Further development	**Grading of evidence**
For parents and family	
N/A	
For healthcare professionals	
N/A	
For neonatal and eye unit	
• Initiate seamless information transfer systems between clinics and hospitals and measures to improve patient adherence to ophthalmological follow-up during screening and after treatment (see Follow-up & continuing care). (16–18)	B (Moderate quality)
For hospital	
N/A	
For health service	
• Consider telemedicine support for screening for retinopathy of prematurity (ROP). (11,19)	A (Moderate quality)
• Support research into causes and treatment of ROP. (20)	B (Moderate quality)

Getting started

Initial steps
For parents and family
• Parents are verbally informed by healthcare professionals about retinopathy of prematurity (ROP), screening, treatment and outcomes including the importance of provision of maternal milk for the prevention of ROP.
For healthcare professionals
• Attend training on prevention and management of ROP.
For neonatal unit
• Develop and implement a unit guideline on prevention of ROP. • Develop formalised programmes for education in oxygen saturation targets. • Develop formalised programmes for promotion of mother's own milk feeding.
For eye unit
• Develop and implement a unit guideline for management of ROP. • Develop information material on ROP for parents. • Develop fail-safe systems for the identification of infants at risk of ROP. • Ensure fail safe systems for referral and continuous cover by ophthalmologist.
For hospital
• Support healthcare professionals to participate in training on prevention and management of ROP.

- Identify pathways for infants with progressive ROP to receive expert assessment and treatment.

For health service

- Develop and implement a national guideline on prevention and management of ROP.

Description

Despite the success of retinopathy of prematurity (ROP) screening and treatment much is unknown about the progression and response to treatment.

There is controversy over the precise oxygen saturation targets but current evidence suggests that, whereas ROP is less frequent when saturations are targeted at 85-89%, mortality is increased. Thus, most units maintain targets of 91-95%. (21) However, recent European consensus guidelines recommend a target range of 90-94% with alarm limits set at 89% and 95%. (22) It is important to avoid higher saturations and research is ongoing into whether these targets can be refined further. Most importantly better adherence to saturation targets is associated with lower rates of ROP. (14)

Furthermore, early provision of mother's own milk is associated with a reduced risk of ROP. (13,23)

If treated at the appropriate stage, vision of infants with severe ROP can be preserved by laser therapy or anti-VEGF therapy where indicated. (20) The long-term safety of anti-VEGF treatment needs further research. (24) If left untreated, severe ROP may lead to irreversible blindness – often in both eyes. (25) Importantly, even less severe ROP affects vision (26) and infants treated for ROP have an increased risk of retinal detachment, myopia, and other complications throughout life. (27,28)

Source

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Prevention of Bronchopulmonary Dysplasia (BPD)

Poets C, Zimmermann LJI, Hellström-Westas L, Buonocore G, Hallman M, Lista G, van Kaam A, Kramer B

Target group
Very preterm and particularly extremely preterm infants, intrauterine growth restricted (IUGR) and small-for-gestational-age (SGA) infants, and parents

User group
Healthcare professionals, neonatal units, hospitals, and health services

Statement of standard
Bronchopulmonary Dysplasia (BPD) is best prevented using evidence-based strategies, including continuous distending pressure or non-invasive ventilation to maintain patency of airways and avoiding invasive mechanical ventilation and intermittent hypoxemia when possible, minimally invasive early administration of exogenous surfactant, aiming at volume targeted ventilation and early caffeine, administration of systemic steroids in infants still requiring mechanical ventilation during their 2nd postnatal week, and supporting parental involvement in preterm infant care starting shortly after birth.

Rationale
Bronchopulmonary Dysplasia BPD results from the effects of non-physiologic stimuli (e.g. inflammation, ventilator induced lung injury, high supplemental oxygen levels) in an infant with underdeveloped lungs and defence mechanisms (e.g. anti-oxidant capacity). (1) Interventions that reduce inflammation (e.g. steroids) or any of these non-physiologic stimuli (e.g. mechanical ventilation) are likely to reduce BPD rates. Improving patient comfort through the early involvement of parents and/or family-centred care is also associated with a reduction in BPD rates. (2–4) Some of these interventions may additionally promote the survival of the target group; none decreases the chances of survival. (5)

BPD is defined as supplemental oxygen or ventilator requirement at 36 weeks post-menstrual age (PMA). According to one proposal these requirements last for ≥3 consecutive days to maintain arterial oxygen saturation in the 90-95% range plus the presence of persistent parenchymal lung disease. (6) There are proposals for defining the grade of BPD at 36 weeks PMA which differ in their predictive power. (7) BPD is a risk factor for later respiratory hospitalisation in infancy, compromised lung function in childhood, neurodevelopmental impairment, and a potential risk factor for chronic obstructive pulmonary disease in later life. (1,8) However, the risk of BPD has not decreased in population-based studies of extremely preterm infants (9), suggesting that more innovative research is needed to enhance the benefits.

Benefits

Short-term benefits
- Reduced risk of BPD by avoiding invasive mechanical ventilation (risk ratio (RR), 0.91; 95% Confidence Interval 0.84-0.99) (5)
- Reduced risk of BPD by use of minimally invasive surfactant administration (RR 0.75; 0.59-0.94) (10,11)
- Reduced risk of BPD by use of volume targeted ventilation (as opposed to pressure targeting) (RR 0.61; 0.46-0.82) (12)

- Reduced risk of BPD by starting caffeine on postnatal day one or two instead of later (RR 0.51; 0.40-0.64) (13,14)
- Reduced risk of BPD by administration of vitamin A intramuscularly for the first four postnatal weeks (RR 0.87; 0.77-0.98) (15)
- Reduced risk of BPD by involving parents early in their infants' care and/or by applying NIDCAP (OR 0.42; 0.18-0.95). (3,4)
- Reduced rate of death or BPD by administration of systemic steroids to respirator-dependent infants after the first postnatal week (RR 0.75; 0.67-0.84) without increasing the risks of cerebral palsy (16)
- Reduced risk of BPD by avoiding intermittent hypoxemia (IH) in extremely low gestational age infants, e.g. through closed-loop oxygen control (9,17)
- Reduced risk of BPD by feeding breast milk (particularly if given as raw milk) (18)

Long-term benefits

- Reduced adverse neurodevelopmental outcome if BPD can be prevented (8)
- Reduced risk of pulmonary arterial hypertension through reduced numbers BPD (consensus)
- Reduced risk of chronic obstructive lung disease in adulthood (consensus)

Components of the standard

Component	**Grading of evidence**	**Indicator of meeting the standard**
For parents and family		
1. Parents are informed by healthcare professionals about Bronchopulmonary Dysplasia (BPD) and strategies to minimise its risk. (1)	A (High quality)	Patient information sheet
2. Parents are closely involved in their baby's care, e.g. through family-integration or NIDCAP. (2–4)	A (Moderate quality)	Parent feedback
For healthcare professionals		
3. A unit guideline on the management and prevention of BPD is adhered to by all healthcare professionals, and includes the following advice:	A (Moderate quality)	Guideline
• Surfactant is administered via a thin intra-tracheal catheter if FiO2 is >0.30 or using INSURE (intubation surfactant and extubation). (19) Some extremely immature infants still require early intubation, ventilation and surfactant.	A (High quality)	Guideline
• Volume targeted ventilation (at 5-7 ml/kg) is used plus adequate PEEP level, if intubation cannot be avoided. (12)	A (High quality)	Guideline
• Infants on n-CPAP are switched to synchronised nasal ventilation if	A (High quality)	Guideline

respiratory distress visible while on CPAP. (20)		
• Caffeine is administered from day 1-2 after birth (10 mg/kg loading, 5 mg/kg/d maintenance for caffeine base). (13,14)	A (High quality)	Guideline
• Vitamin A is considered (5000 IE i.m. three times/week for week 1-4 after birth). (15)	A (High quality)	Guideline
• If mechanical ventilation is still necessary during postnatal week 2, postnatal steroid use is considered (dexamethasone at the lowest effective dose possible). (21,22)	A (High quality)	Guideline
• In infants receiving additional inspired oxygen, avoiding IH is considered, e.g. through closed-loop oxygen control. (9,17)	A (Moderate quality)	Guideline
• Breast milk is the preferred nutrient. (18)	A (Moderate quality)	Guideline
• Efforts to reduce rates of infection, as a risk factor for BPD, are made. (23)	A (Moderate quality)	Guideline
4. Training on the management and prevention of BPD is attended by all responsible healthcare professionals.	B (High quality)	Training documentation
For neonatal unit		
5. A unit guideline on prevention and management of BPD is available and regularly updated.	B (High quality)	Guideline
6. A protocol is in place for how to involve parents early on in their baby's care.	A (Moderate quality)	Clinical records
For hospital		
7. Training on management and prevention of BPD is ensured.	B (High quality)	Training documentation
8. Institutional BPD rates are monitored together with length of hospital stay and use of supplemental oxygen.	B (High quality)	Audit report
For health service		
9. A national guideline on management and prevention of BPD is available and regularly updated.	B (High quality)	Guideline

Where to go – further development of care

Further development	**Grading of evidence**
For parents and family	
N/A	
For healthcare professionals	
• Investigate in larger numbers whether using synchronised nasal ventilation rather than n-CPAP is the preferred mode of nasal respiratory support. (12)	A (Moderate quality)
• Evaluate alternative anti-inflammatory strategies, e.g. hydrocortisone, inhaled budesonide, or tracheal instillation of budesonide together with exogenous surfactant to generate more data on their long-term effectiveness and safety. (16,24,25)	A (High quality)
• Investigate the benefits of high frequency oscillatory ventilation for preventing BPD, particularly in infants with significant oxygen requirement and low lung compliance despite surfactant treatment and mechanical ventilation. (12)	A (Moderate quality)
• Investigate whether high-flow nasal cannula, compared to n-CPAP, can reduce the risk of developing BPD. (26,27)	A (Moderate quality)
• Investigate the role of eradicating Ureaplasma urealyticum shortly after birth. (28)	A (Moderate quality)
• Investigate oral Vitamin A administration as well as the role of other nutrients. (15,29)	A (High quality)
• Find the optimal drug and dose for postnatal steroid treatment. (15)	A (High quality)
• Investigate the potential of mesenchymal stem cells in repairing the injured immature lung. (30,31)	A (Moderate quality)
• Investigate the effect of various delivery-room practices and of early enteral feeding on the prevention of BPD. (22)	A (High quality)
• Investigate the role of inhaled nitric oxide (NO) in preventing BPD, and of vasodilators, particularly inhaled NO, in the early persistence of pulmonary hypertension, for possible prevention of BPD. (32)	A (Moderate quality)
• Investigate the role of serum markers (e.g. Clara cell secretory protein 16 (CC16), KL-6 and end-tidal carbon monoxide) and develop advanced prediction models for the early identification of infants at increased risk of BPD. (33)	A (Moderate quality)
• Investigate new management practices during very high-risk perinatal transition; among them antenatal N-acetylcysteine, prophylactic acetaminophen to extremely preterm infants for prevention of BPD. (34,35)	A (Moderate quality)
• Investigate towards improving the anti-inflammatory properties of surfactant drugs (36) and the use of surfactant as carrier of other drugs.	A (Moderate quality)
• Investigate methods for advancing the perinatal transition of high-risk extremely preterm infants.	A (Moderate quality)
For neonatal unit	
• Identify further synergies between family-oriented care and advanced neonatal management practices	A (Moderate quality)
For hospital	
• Encourage multidisciplinary collaboration between perinatal and neonatal teams, as well as neonatal and paediatric teams.	A (Moderate quality)

For health service

- Promote research on medicines for very high-risk neonates through legislation similar to medicines for children. B (Moderate quality)

Getting started

Initial steps

For parents and family

- Parents are verbally informed by healthcare professionals about BPD and strategies to minimise its risk. (1)
- Parents are educated by healthcare professionals about the particular need of a smoke-free environment.

For healthcare professionals

- Attend training on management and prevention of BPD.
- Apply exogenous surfactant via less/minimally invasive administration via a thin catheter, i.e. without using an endotracheal tube (LISA or MIST), or via the INSURE method (intubation, surfactant, extubation); under investigation: nebulisation, pharyngeal instillation and laryngeal mask airway (LMA) surfactant administration.
- Use nasal continuous positive airway pressure (n-CPAP) instead of intubation and mechanical ventilation. (37)
- Start caffeine on postnatal day 1 or 2 instead of later.

For neonatal unit

- Develop and implement a unit guideline on management and prevention of BPD.
- Develop information material about BPD for parents.

For hospital

- Support healthcare professionals to participate in training on management and prevention of BPD.

For health service

- Develop and implement a national guideline on management and prevention of BPD.

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Prevention of vitamin K deficiency bleeding (VKDB) at birth

Koletzko B, Buonocore G, Zimmermann LJI, Hellström-Westas L, Fewtrell M, Perrone S, Verkade H

Target group
Newborn infants and parents

User group
Healthcare professionals, neonatal units, hospitals, and health services

Statement of standard
Prophylactic supplementation with vitamin K for all infants is given to prevent vitamin K deficiency bleeding (VKDB).

Rationale
Vitamin K deficiency bleeding (VKDB) in infants is prevented by vitamin K supplementation. Healthy newborn infants have low hepatic stores of vitamin K (1) and are at risk of developing serious bleeding, including intracranial hemorrhage, due to low hepatic synthesis of vitamin K–dependent clotting factors. (2,3) Preterm infants appear to be at even higher risk. (4) Postnatal supplementation of vitamin K can markedly reduce the incidence of VKDB, associated morbidity, including devastating brain injury, neurodevelopmental impairment and mortality. (5–7)

Healthy infants should either receive 1 mg of vitamin K intramuscular at birth, or three doses of 2 mg vitamin K orally at birth, at four to six days and at four to six weeks; or 2 mg vitamin K orally at birth followed by weekly doses of 1 mg orally for three months for breastfed infants. (3) Intramuscular application has the best preventive efficiency. (3) The administration of low daily oral doses (e.g. 25-150 µg/d) is less effective than either of the earlier mentioned alternatives and is thus not recommended. (8) Vitamin K should be administered parenterally to newborn infants who are unwell, those who have cholestasis or impaired intestinal absorption, or who are unable to take oral vitamin K, those whose mothers have taken medications that interfere with vitamin K metabolism, and to preterm infants. (9)

Preterm infants may require reduced doses of vitamin K prophylaxis such as 0.5 mg intramuscular for infants >1000 g or 0.2 mg intramuscular/intravenous for infants <1000 g. (8) Vitamin K supplementation protocols should be developed and implemented in all obstetric and neonatal units. (3,10)

Benefits

Short-term benefits

- Reduced risk of Vitamin K deficiency bleeding and related infant mortality and morbidity (11–13)

Long-term benefits

- Reduced long-term damage and neurodevelopmental handicap (12)
- Reduced healthcare costs arising from chronic morbidity (consensus)

Components of the standard

Component	Grading of evidence	Indicator of meeting the standard
For parents and family		
1. Parents are informed before and after birth by healthcare professionals about the importance of vitamin K supplementation and its benefits. (10)	A (High quality) B (High quality)	Patient information sheet
For healthcare professionals		
2. A unit guideline on Vitamin K supplementation in all infants is adhered to by all healthcare professionals. (3)	A (High quality) B (High quality)	Guideline
3. Training on prevention of vitamin K deficiency bleeding (VKDB) is attended by all healthcare professionals.	A (Low quality) B (High quality)	Training documentation
4. Parental refusal of vitamin K prophylaxis is clearly documented.	B (High quality)	Clinical records
For neonatal unit		
5. A unit guideline on vitamin K supplementation in all infants is available and regularly updated. (3)	A (High quality) B (High quality)	Guideline
6. Administration of vitamin K supplementation is monitored.	A (Low quality) B (High quality)	Audit report
For hospital		
7. Training on prevention of VKDB is ensured.	A (Low quality) B (High quality)	Training documentation
For health service		
8. A national guideline on vitamin K supplementation in all infants is available and regularly updated. (3)	A (High quality) B (High quality)	Guideline
9. Rate of vitamin K deficiency related haemorrhage in infants is monitored.	A (Low quality)	Audit report

Where to go – further development of care

Further development	Grading of evidence
For parents and family	
N/A	
For healthcare professionals	
N/A	
For neonatal unit	
N/A	
For hospital	
• Participate in and implement communication strategies to promote acceptance of universal vitamin K supplementation.	A (Low quality)
For health service	
• Develop and implement communication strategies to promote acceptance of universal vitamin K supplementation.	A (Low quality)
• Monitor the proportion of infants who receive vitamin K supplementation according to established standards across the population.	B (High quality)

Getting started

Initial steps
For parents and family
• Parents are verbally informed by healthcare professionals before and after birth about the importance of vitamin K supplementation and its benefits.
For healthcare professionals
• Attend training on prevention of vitamin K deficiency bleeding (VKDB).
For neonatal unit
• Develop a unit guideline on vitamin K supplementation in all infants.
• Develop information material on the importance of vitamin K supplementation and its benefits for parents.
For hospital
• Support healthcare professionals to participate in training on prevention of VKDB.
For health service
• Develop and implement a national guideline for vitamin K supplementation in all infants.
• Raise awareness of the importance of vitamin k supplementation to effectively address common concerns and disinformation.

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