Topic Expert Group: **Follow-up & continuing care**

Immunisation of preterm infants

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Target group
Infants born very preterm and those preterm infants with risk factors (see preamble of Follow-up & continuing care), parents, and families

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

Statement of standard
Preterm infants are immunised according to their chronological age, regardless of gestational age and weight at birth. In very preterm infants, immunisations are started and monitored in hospital, once the target age for the first immunisation (usually 8-12 weeks) is reached.

Rationale
Preterm infants have a high vulnerability for infections due to the immaturity of the immune system including skin and mucosa barriers and reduced amounts of protective antibodies transferred through the placenta. This susceptibility is of particular importance for vaccine-preventable diseases such as pertussis, pneumococcal, H. influenzae type B, influenza and rotavirus infections. Severe disease courses of Rotavirus infections (including sepsis-like cases) have been noted for preterm infants. The vulnerable lung of preterm infants renders them susceptible for infections with respiratory syncytial virus (RSV), which often require hospitalisation and respiratory support. Preterm infants are at higher risk for long-term morbidities associated with complicated courses of infections, e.g. chronic lung disease. (1–3)

There are historical scepticism and uncertainties of healthcare professionals and parents about the immunogenicity and safety of vaccines administered to preterm infants. (4,5) While no apparent justifications for delaying vaccine administration exist, preterm infants are often not vaccinated according to national standards. (6,7) Studies, however, demonstrate that the preterm infant's immune system is competent to generate protective immune responses to vaccines which are similar to that obtained in term infants. (4,8) Schedule-based vaccination of preterm infants is known to prompt accelerated priming of protective immune components and therefore adds a benefit for vulnerable infants by reducing the risk for infectious and respiratory morbidity during childhood. (4–6,8–11) Combination vaccines such as hexavalent vaccines (diphtheria, pertussis, tetanus, polio, haemophilus type B and hepatitis B), pneumococcal vaccines and live vaccines such as rotavirus are suitable for preterm infants, well tolerated, safe and immunogenic. (9)

Infants <28 weeks of gestation or <32 weeks of gestation (as per national guideline) have a higher risk to respond to vaccination with apnoea, desaturations with SaO2 <80% and bradycardia within 24 hours. Adequate monitoring in a hospital setting is justified as apnoea and desaturations with SaO2 <80% for longer than 60 seconds increase the risk for adverse neurodevelopmental outcome. If the first vaccination is well tolerated (without apnoea/bradycardia) and the patient is discharged from hospital, subsequent immunisations can be performed in an outpatient setting. (2,12,13)

Epidemiological variations for vaccine-preventable diseases in Europe (e.g. tuberculosis, meningococcus B and meningococcus C infections) need consideration for country-specific vaccination schedules of preterm infants. A few countries mostly in Eastern Europe recommend immunisation with Bacillus Calmette-Guerin against tuberculosis as soon as possible after birth for late to moderate preterm infants >31 weeks of gestation.

Non-specific hygienic measures are important. Preterm and term infants benefit from non-specific preventive measures against infections including breastfeeding, up-to-date immunisation schedule of family members and avoiding the exposure to tobacco smoke, contact with ill individuals and crowds. (3)

Equal access to timely vaccinations for preterm and term infants across the EU should be promoted.

Benefits

Short-term benefits

- Improved awareness among parents and healthcare professionals for vaccine-preventable diseases and the immunological competence of preterm infants (consensus)
- Increased information of parents about immunisations during hospital stay to avoid missed opportunities (see Transition from hospital to home) (7)
- Increased vaccine coverage in this risk group which leads to reduced general burden of infectious diseases (2)
- Intensified safety monitoring and avoidance of unnecessary sepsis evaluations in the post-vaccination period (7)

Long-term benefits

- Alleviated parent and provider vaccine safety concerns and improved confidence in vaccinating high-risk infants after hospital discharge (consensus)
- Increased rate of complete, schedule-based immunisation in preterm infants (7)
- Reduced healthcare costs and costs for the family (i.e. hospital readmissions) (consensus)
- Reduced risk of transmitting vaccine-preventable infectious diseases in childcare and school settings (consensus)
- Increased sensitivity for preterm birth related complications including problems of parent-infant interaction due to schedule-based immunisation appointments (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 immunisations given during hospitalisation. (14)	A (High quality) B (High quality)	Parent feedback, patient information sheet
2. Parents are informed by healthcare professionals about immunisations given at discharge from neonatal care.	A (High quality) B (High quality)	Parent feedback, patient information sheet

	Also including information on the importance of completion of immunisation according to the immunisation schedule and avoiding delays so infants are reliably protected when attending early day care. (14)		
3.	Family members, household and other close contacts of the preterm infant are immunised according to national recommendations, considering the risk of transmission of vaccine-preventable diseases, e.g. pertussis or influenza (preventive concept of "cocooning"). (15)	A (High quality)	Parent feedback, patient information sheet
4.	Discharge planning includes information about non-specific hygienic measures and avoidance of unnecessary exposures, and an individualised immunisation schedule adapted to the infants' medical conditions and risk factors. (14–17)	A (High quality) B (High quality)	Parent feedback, patient information sheet
For healthcare professionals			
5.	A unit guideline on immunisation during and after hospitalisation (neonatal care/follow-up care) is adhered to by all healthcare professionals, e.g. verification of immunisation status at every follow-up visit.	B (High quality)	Guideline, training documentation, clinical record
6.	Training on current national immunisation guidelines, including safety and efficacy data of vaccines related to preterm infants, is attended by all responsible healthcare professionals. Training of communication skills as of provider vaccine communication in paediatric populations is critical to alleviate scepticism.	B (High quality)	Guideline, training documentation
7.	Immunisation is initiated according to the chronological age of preterm babies, regardless of gestational age and weight at birth. In very preterm infants, immunisations are started in hospital, once the target age of 8-12 weeks for the first immunisation is reached. (3,4,6,18)	A (High quality) B (High quality)	Guideline
8.	Primary immunisation includes vaccination against Diphtheria, Pertussis, Tetanus, Polio, Haemophilus	A (High quality) B (High quality)	Guideline

	type B and Hepatitis B according to national immunisation schedule. This is initiated in early infancy (e.g. at 2, 3, 4 months of age) followed by a booster immunisation e.g. at 11-24 months of age. (3,4,11)		
9.	Immunisation against Streptococcus pneumoniae (pneumococci) and Neisseria meningitides (meningococci) is initiated as per national or unit guideline. Rotavirus vaccination can be given at age 6 weeks if ward infrastructure allows prevention of nosocomial transmission (immunised individuals may shed the virus, single room). Otherwise, rotavirus vaccination can be administered at discharge from neonatal care. Infants with signs or family history of immunodeficiency should not be vaccinated with live vaccines (BCG, rotavirus). (2,3,8–10)	A (High quality) B (High quality)	Guideline
10.	Passive immune-prophylaxis against RSV are considered before hospital discharge of extremely preterm infants with additional risk factors during season. At six months of chronological age, preterm infants should be evaluated if they qualify for influenza immunisation, e.g. infants with chronic lung or heart disease.	B (High quality)	Guideline
11.	Training on application of vaccines in preterm infants, including injection and pain management procedures is attended by all responsible healthcare professionals.	B (High quality)	Guideline, training documentation
12.	Training on necessary safety monitoring precautions during and after immunisation during hospitalisation is attended by all responsible healthcare professionals. (2,12,13,19)	A (High quality) B (High quality)	Guideline, training documentation
13.	Healthcare professionals document all provided immunisations in a standardised WHO standard compatible immunisation card.	B (High quality)	Guideline, training documentation
14.	A written proposal for an individualised immunisation schedule (included in the discharge summary) is communicated with the primary care physician and	B (Moderate quality)	Clinical records

provided by healthcare professionals at the hospital.		
For neonatal unit, hospital, and follow-up team		
15. A unit guideline on immunisation during and after hospitalisation (neonatal care) is available and regularly updated.	B (High quality)	Guideline
16. Training on current national immunisation guidelines, including safety and efficacy data of vaccines related to preterm infants is ensured.	B (High quality)	Guideline, training documentation
17. For immunisations during neonatal care preterm infants are clinically stable and not expecting surgery within the next 3 days for inactivated vaccines and 14 days for live virus vaccines.	B (High quality)	Guideline, clinical records
18. First immunisation of preterm infants <28 weeks of age in hospital is ensured, i.e. during primary stay or readmission, and monitored for 24-72 hours post immunisation as per local guideline in order to detect apnoea and/or bradycardia events. In addition, critical indication of sepsis evaluations post-vaccination is ensured.	B (High quality)	Guideline, clinical records
For health service		
19. A national guideline on recommended preterm immunisations 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	
• Conduct more research on yet neglected aspects of immunisation practice in preterm infants (e.g. role of breast-milk feeding, probiotics, microbiome on vaccine responses)	B (Moderate quality)
For health service	
• Provide financial resources for research on yet neglected aspects of immunisation practice in preterm infants	B (Moderate quality)

Getting started

Initial steps

For parents and family

- Parents and family receive flyer and information sheets about specific preterm oriented prevention of infectious diseases by active and passive immunisation strategies.

For healthcare professionals

- Attend training on the assessment of discharge readiness using current national immunisation guidelines, including safety and efficacy data of vaccines related to preterm infants.
- Establish a structure of communication with primary care physician, community/healthcare services and follow-up services regarding the timing of immunisations.

For neonatal unit, hospital, and follow-up team

- Develop and implement a unit guideline for the assessment of the preterm child's immunisation status at the time of discharge from hospital and at every follow-up visit (e.g. 3, 6 and 12 months).
- Develop and implement a unit guideline on the immunisations to be recommended after discharge from hospital to home.
- Develop information material on different vaccine-preventable infectious diseases and the related vaccines for parents.
- Support healthcare professionals to participate in training on the assessment of discharge readiness using current national immunisation guidelines, including safety and efficacy data of vaccines related to preterm infants.

For health service

- Develop and implement a national guideline on immunisation in preterm infants.
- Enable easy access for parents to vaccination through paediatricians in outpatient care.
- Define quality markers for discharge care.

Description

Core elements of immunisations in preterm infants are:

- **Infant**: completion of immunisations according to infants age and underlying chronic conditions
- **Family**: check immunisation status of family members and household contacts including influenza, pneumococcal and pertussis boosters of family members (cocooning strategy). Inform parents/mothers of vaccines recommended during pregnancy (Influenza, pertussis) for protection of infants via active antibody transfer to newborn infants, especially during the third trimester. Consider pertussis booster immunisations in adolescence and adulthood to increase immunity against pertussis and prevent transmission to newborn infants. Seasonal influenza immunisation of pregnant women is associated with reduced risk for preterm birth and respiratory morbidity in the offspring.
- **Community/healthcare system**: development of a comprehensive individualised immunisation schedule for further completing immunisation series started in the hospital during preterm care. Make appointments for further booster immunisations, which require post immunisation cardio-respiratory monitoring.

Example of a checklist used to address immunisation during discharge management

1. Discharge readiness

a. INFANT

- Immunisation status adequate according to chronological age and underlying conditions?
- Infant qualifies for specific vaccines at discharge, as influenza, or Rotavirus vaccine or passive immunisation against RSV

b. PARENTS

- Counsel about necessary immunisations according to infants chronological age and underlying conditions.
- Inform parents about update of the immunisation status in all family and household or other close contacts (e.g. grandparents).

c. COMMUNITY/HEALTHCARE SYSTEM

- Primary care and medical special care physicians informed about infant's immunisation status and further necessary booster and primary vaccine doses (individualised immunisation plan).
- If necessary, provide information to primary care and medical special care physicians about previous vaccine responses/side effects and if necessary safety monitoring in further vaccine doses.
- Appointments for follow-up immunisations documented in discharge letter, are arranged and confirmed with parents and primary care physician.

2. Pre-discharge screening and care procedures

- Start full immunisation following chronologic age, consider RSV prophylaxis and influenza immunisation, if applicable.

3. Parental competencies

- Strengthen knowledge about immunisation importance, appointments and documentation.

Source

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