Executive summary

- Premature and low birth weight infants are at greater risk of increased mortality and morbidity from vaccine preventable diseases.
- With the exception of BCG, immunisations should be given according to the National Immunisation Schedule at the appropriate chronological age.
- Do not adjust age for preterm birth, i.e. National Immunisation Schedule vaccines start at 6 weeks of age from the date of birth.
- The usual vaccine dosage should be used.

### Vaccine immunogenicity

- Inferior immune response to some vaccines although evidence suggests the response is still protective.

### Vaccine safety

- Immunisation in these infants is safe and effective. However, post-vaccination apnoea with or without associated bradycardia up to 48 hours post-immunisation may be increased in some groups.

### Aapnoea

- Factors possibly associated with an increased incidence of post-immunisation apnoea:
  - Apnoea within the 24 hour period before immunisation.
  - More severe illness at birth.
  - Chronological age less than 67 days and/or earlier gestational age in infants with a birth weight of less than 1500g.
  - An apnoeic episode following the first immunisation event.

### Apnoea monitoring

- Consider after the first immunisation event.
- Consider after subsequent immunisation events when an infant has experienced apnoea after their first immunisation event.
- No long term sequelae have been associated with post immunisation apnoic events.
- Immunisation should not be withheld or delayed.

### Vaccine administration

- Preferred site for intramuscular immunisation is the vastus lateralis.
- A 23–25 gauge x 16mm needle inserted at a 90° angle to the skin is usually adequate.

### Targeted immunisation or cocooning

- Consider pertussis and influenza immunisation for all close contacts.
- These vaccines are not usually funded for these groups by the Ministry of Health.

### Recommendations for individual vaccines

#### Infants born to hepatitis B carrier mothers

- Give hepatitis B immunoglobulin (HBIG) and a hepatitis B immunisation (HBvaxPRO®) within 12 hours of birth regardless of birth weight, followed by
- Three doses of hepatitis B containing vaccine (DTaP-IPV-HepB/Hib [Infanrix®-hexa]) beginning at 6 weeks of age, regardless of birth weight. Serology testing for hepatitis B infection (HBsAg) and immunity (antiHBs) is recommended at 9 months of age.

#### Infants of non-hepatitis B carrier mothers

- Three doses of hepatitis B containing vaccine (DTaP-IPV-HepB/Hib [Infanrix-hexa]) beginning at 6 weeks of age, regardless of birth weight.

#### Tuberculosis (BCG)

- Eligible infants born at 34 weeks gestation or later can receive the BCG vaccine soon after birth.
- Eligible infants born before 34 weeks gestation should have their BCG delayed until 34 weeks gestational age.

#### Diphtheria, tetanus, pertussis, polio and *Haemophilus influenzae* type b (Hib)

- Three doses beginning at 6 weeks of age.
- Administer as DTaP-IPV-HepB/Hib (Infanrix-hexa).

#### Pneumococcal disease

- Infants who are not eligible for the high-risk pneumococcal immunisation programme
  - Give the routine National Immunisation Schedule pneumococcal conjugate vaccine (PCV10/Synflorix®) at 6 weeks, 3 months, 5 months and 15 months of age.
- Infants who are eligible for the high-risk pneumococcal immunisation programme
  - PCV13/Prevenar 13® replaces PCV10/Synflorix at 6 weeks, 3 months, 5 months and 15 months of age.
  - Two 23-valent pneumococcal polysaccharide vaccine doses (23PPV/Pneumovax®23) are recommended and funded if the infant continues to be at high-risk of pneumococcal disease, the first at 2 years of age and the second five years after the first.

#### Rotavirus (RV1)

- Two doses of rotavirus vaccine (Rotarix®) beginning at 6 weeks of age.
- Infants in hospital at 6 weeks of age should receive the first Rotarix dose on time.
- There is a theoretical risk of disease resulting from horizontal transfer of the vaccine virus.
- If standard precautions are maintained, the risk of transmission of vaccine strain rotavirus will be minimal.

#### Influenza

- Influenza vaccine annually from 6 months of age.
- Preterm birth alone does not meet the eligibility criteria for receipt of funded vaccine.
- Two doses of vaccine administered one month apart in the first year, then one dose annually in each subsequent year.
Young infants are especially vulnerable to a number of vaccine preventable diseases, particularly pertussis (whooping cough), *Haemophilus influenzae* type b (Hib) disease, pneumococcal disease and influenza. Preterm and low birth weight infants have an even higher risk than full term infants of developing serious complications from vaccine preventable diseases.

Preterm birth is defined as birth before 37 weeks gestation and low birth weight refers to infants born weighing less than 2500 grams. With the exception of the BCG vaccine, gestational age and birth weight are not limiting factors when deciding whether a clinically stable preterm infant is to be immunised at the appropriate chronological age, following the same immunisation schedule as infants born full-term. The recommended dose of each vaccine should be used, doses should not be divided.

**Passive immunity in preterm infants**

Transplacental transfer of maternal immunoglobulin G (IgG) that can protect an infant against some vaccine preventable diseases is affected by a range of factors including the mother’s past exposure to the disease and vaccination history, antibody half-life, and the infant’s gestational age. Infants born at less than 32 weeks gestation have significantly less IgG compared with those born at 32–36 weeks. Furthermore, IgG wanes more rapidly rendering preterm infants at increased and earlier risk for vaccine preventable diseases.

**Vaccine immunogenicity**

Preterm infants have an inferior immune response to some vaccines although evidence suggests that the response is still adequate for protection.

**Vaccine safety**

Vaccines in preterm and/or low birth weight infants have excellent safety profiles, comparable to those in full term infants, with the exception of a possible increase in apnoea with or without associated bradycardia up to 48 hours post-immunisation.

**Apnoea**

Factors that have been identified as possibly being associated with an increased incidence of post-immunisation apnoea include apnoea within the 24 hour period before immunisation, more severe illness at birth, chronological age less than 67 days, and/or earlier gestational age in infants with a birth weight of less than 1500g. Although apnoic episodes are not necessarily causally associated with immunisation, an apnoeic episode following the first immunisation event is a significant risk factor for an apnoeic episode following the second immunisation event. No long term sequelae have been associated with post immunisation apnoeic events.

**Apnoea monitoring**

Apnoea monitoring of preterm and/or low birth weight infants, particularly those with a history of respiratory immaturity, should be considered after the first immunisation event. When an infant has experienced apnoea after their first immunisation event, apnoea monitoring (for both medical reasons and to maintain parental confidence in immunisation) should be considered after subsequent immunisation events. Immunisation should not be withheld or delayed.

**Vaccine administration**

The preferred site for intramuscular immunisation in preterm or low birth weight infants is the same as for full term infants, the vastus lateralis. A 23–25 gauge x 16mm needle inserted at a 90° angle to the skin is usually adequate.

**Targeted immunisation or cocooning**

Research suggests that most infants acquire diseases such as whooping cough and influenza from family members. “Cocooning” or “targeted immunisation” involves ensuring siblings are up to date with their immunisations, and immunising the infant’s close contacts (parents, grandparents and carers) to reduce the risk of disease exposure for the infant. Important vaccines to consider include pertussis-containing vaccines and influenza vaccines.

Estimates of pertussis vaccine efficacy in adolescents and adults vary from 51–92%. In those who develop immunity, protection against disease is highest over the first year after immunisation and wanes rapidly over 4–6 years. Reducing the risk of close contacts having active disease is beneficial for infants. However, pertussis carriage and transmission of bacteria from asymptomatic contacts may be possible. Studies measuring the “cocoon” effect from targeted pertussis immunisation report ‘no benefit’ to around a 50% reduction in the pertussis disease risk in infants aged under 4 months.

Any adult with a cough needs to have pertussis excluded before spending time with infants even if they have received a pertussis booster immunisation. Despite a relatively rapid loss of protection in vaccine responders, booster doses of pertussis-containing vaccine are recommended no more frequently than 10-yearly for non-pregnant adolescents and adults.

Influenza and pertussis-containing vaccines are not funded by the Ministry of Health on the basis of a person being a close contact but can be purchased through the person’s general practice.

**Recommendations for individual vaccines**

**Hepatitis B**

Infants born to hepatitis B carrier mothers

Infants born to HBsAg-positive (hepatitis B surface antigen-positive) mothers require hepatitis B immunoglobulin (HBIG) and a hepatitis B immunisation within 12 hours of birth. Without hepatitis B immunoprophylaxis these infants have up to a 50% risk of acquiring the disease perinatally and more than 90% likelihood of progressing to chronic hepatitis if they do acquire the disease with the associated lifelong risk of developing liver cirrhosis and cancer.

When the mother is also HBeAg-positive (a marker for high viral replication) at the time of delivery, the risk of perinatal hepatitis B infection increases to 90%. However, routine testing for HBeAg is not done because infection can still be transmitted when the HBeAg is non-detectable.
Immunisation for the low birth weight and/or preterm infant (updated September 2017)

Hepatitis B
Infants born to hepatitis B carrier mothers continued
HBIG is expected to be effective in very low birth weight infants. In a small study 10 infants, all weighing less than 1750g when born to hepatitis B carrier mothers, received HBIG at birth but no hepatitis B immunisation until 11–59 days old. No infants became hepatitis B surface antigen positive.

Some studies suggest that infants weighing less than 2000g at birth have decreased seroconversion to hepatitis B vaccine. Corticosteroid use and hyperbilirubinaemia may also reduce the immune response to hepatitis B vaccine. However, these are not reasons to delay the birth hepatitis B immunisation. By 4 weeks of age all infants, independent of gestational age and birth weight, are expected to respond to the hepatitis B vaccine and develop protection against the disease.

In New Zealand, a complete course of three hepatitis B vaccine doses are administered from 6 weeks of age irrespective of whether the infant had a birth dose of vaccine. Serology testing for hepatitis B infection (HBsAg) and immunity (antiHBs) is recommended at 9 months of age for all infants born to hepatitis B carrier mothers.

Infants born to mothers whose hepatitis B carrier status is not known
Infants born to mothers whose HBsAg status is unable to be demonstrated as negative within 12 hours of delivery should also receive hepatitis B immunoprophylaxis regardless of their birth weight.

Infants of non-hepatitis B carrier mothers
Infants born to hepatitis B negative (HBsAg negative) mothers prematurely and/or weighing less than 2000g are expected to be adequately protected against hepatitis B after three doses of vaccine beginning at 6 weeks of age.

BCG
The BCG Immunisation Programme is currently suspended due to a vaccine supply issue. When the Programme is operational, in New Zealand it is recommended that the BCG immunisation is administered soon after birth to infants who are at increased risk of tuberculosis and meet the eligibility criteria (refer to Section 20.5.2 in the Immunisation Handbook 2017). Studies measuring the preterm and/or low birth weight infant’s response to the BCG immunisation have used BCG scar, Mantoux response and/or the lymphocyte migration inhibition test to assess the infant’s response. Some data indicates that administering the BCG immunisation at a gestational age of 34 weeks or later provides a good immune response. Other data suggests that the BCG immunisation can be given as early as a gestational age or 31 weeks. As these methods are now known to provide false negative indicators of immune response, and in the absence of recent data using modern and more accurate tests, a conservative approach to administering the BCG to preterm and/or low birth weight infants is advised. Infants born at 34 weeks gestation or later can receive the vaccine soon after birth. Infants born before 34 weeks gestation should have their BCG delayed until they reach a gestational age of 34 weeks.

Diphtheria, tetanus, pertussis, polio and Haemophilus influenzae type b (Hib)
Diphtheria and tetanus toxoid vaccines are highly immunogenic in preterm infants. The immune response to the acellular pertussis vaccine components in preterm infants has been shown to be lower than in those born at full term, but still expected to be higher than that required for protection. The acellular pertussis vaccine has been shown to be efficacious when administered to preterm infants.

Pneumococcal
Both the 10-valent (PCV10/Synflorix) and 13-valent pneumococcal conjugate (PCV13/Prevenar 13) vaccines have been shown to be immunogenic in infants born before 37 weeks gestation and infants born at less than 2500g but earlier gestational age and/or extremely low birth weight may influence the magnitude of antibody response and duration of protection following the primary vaccine course. Timely administration of the booster/fourth dose in the second year of life is recommended. PCV10 and PCV13 have also been shown to be safe and generally well tolerated in preterm and/or low birth weight infants.

Infants who are not eligible for the high-risk pneumococcal immunisation programme are recommended to receive the routine National Immunisation Schedule pneumococcal conjugate vaccine (PCV10/Synflorix) at ages 6 weeks, 3 months, 5 months and 15 months.

Infants who are eligible for the high-risk of pneumococcal immunisation programme are recommended to receive PCV13/Prevenar 13 instead of PCV10/Synflorix at ages 6 weeks, 3 months, 5 months and 15 months. Two 23-valent pneumococcal polysaccharide vaccine doses (23PPV/Pneumovax23) are recommended and funded if the infant continues to be at high-risk of pneumococcal disease, the first at 2 years of age and the second 5 years after the first.

In infants and children aged under 5 years, the following conditions are eligible for the high-risk pneumococcal immunisation programme:

- Cardiac disease with cyanosis or failure
- Cerebrospinal fluid leak
- Chronic pulmonary disease, including asthma treated with high-dose corticosteroid therapy
- Cochlear implant
- Corticosteroid therapy for more than two weeks and who are on an equivalent daily dosage of prednisone of 2 mg/kg per day or greater, or children who weigh more than 10 kg on a total daily dosage of 20 mg or greater
- Diabetes
- Down syndrome
- Functional asplenia
- HIV-positive
- Immunosuppressive therapy
- Intracranial shunt
- Nephrotic syndrome
- Pre-or post-splenectomy
- Pre-term infant born before 28 weeks gestation
- Primary immune deficiency
- Post-haematopoietic stem cell transplantation
- Post-solid organ transplantation
- Radiation therapy
- Renal failure

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Rotavirus
Rotarix has been shown to be safe and efficacious when given to preterm infants born between 27–36 weeks gestation following the same schedule as full term infants. Adverse events and vaccine immunogenicity were comparable with the preterm cohort receiving the placebo and term infants in an earlier Rotarix safety and immunogenicity study. The weakened (attenuated) rotavirus from Rotarix may be found in stool for up to 28 days after the first immunisation and up to 15 days after the second. A theoretical risk of disease resulting from horizontal transfer of the vaccine virus exists. If standard precautions are maintained, the risk of transmission of vaccine strain rotavirus will be minimal.

Preterm infants are at increased risk for hospitalisation from rotavirus during their early years of life. Rotarix can be administered to medically stable, hospitalised infants at 6 weeks of age. The vaccine has been shown to be well-tolerated in these infants, and no increase in nosocomial rotavirus transmission was observed within the neonatal intensive care unit (NICU).

Influenza
Annual influenza vaccine is recommended for all preterm infants from 6 months of age. However, preterm birth alone does not meet the eligibility criteria for receipt of funded vaccine. All infants and children aged under 9 years receiving influenza vaccine for the first time require two doses of vaccine administered one month apart, then one dose annually in each subsequent year.

References

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References continued