Supplementary webappendix

This webappendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

### Diagnostic criteria for the insult during pregnancy or the neonatal period

<table>
<thead>
<tr>
<th>Neonatal Insult</th>
<th>Diagnostic criteria</th>
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| Neonatal Jaundice               | • Significant jaundice based on bilirubin level for age and weight of newborn based on internationally accepted criteria [39] [40]  
  • Non-obstructive jaundice [41] |
| Neonatal Tetanus                | • Initially well and then onset of spasms that maybe provoked or spontaneous  
  • Trismus and difficulty feeding |
| Neonatal Meningitis             | • Cerebrospinal fluid (CSF) culture positive for a causative organisms  
  Or positive antigen test [42]  
  • White cell count in cerebrospinal fluid of more than 50 cells per microlitre [42]  
    • Positive blood culture and/or gram stain  
    • Glucose blood/CSF ratio < 0.1  
    •  |
| Neonatal Sepsis                 | • Positive blood culture  
  • Clinical definition of neonatal sepsis based on an accepted algorithm |
| Hypoxic Ischemic Encephalopathy | • Onset within 2 days of birth of severe or moderate neonatal encephalopathy in infants born at 34 or more weeks of gestation  
  • Acute perinatal event, and/or a 10 minute APGAR less than 5 or assisted ventilation for more than 10 minutes.  
  • Ideally also the following:  
    • Evidence of metabolic acidosis (pH <7 or less or base deficit < 12 mmol per liter [43]) |
Other identifiable aetiologies such as trauma, coagulation disorders, infectious conditions, or genetic disorders were excluded [43].

**Preterm birth**

Documentation of gestation age below 37 completed weeks by:-

- Where last menstrual period is known and expected date of delivery can calculated
- Acceptable gestation age estimation criteria with
  - Ultrasound, ideally first trimester
  - Dubowitz score [44]
  - Other clinical scores with validation published eg Eregie [45]

**HIV**

- Polymerase Chain Reactions (PCR) test that shows infection with the HIV virus,

**Toxoplasmosis**

- Serological diagnosis of infection in the mother through seroconversion, presence of IgA and IgM, low avidity IgG, or PCR in amniotic fluid [46, 47]
- Immunological diagnosis in the newborn with suggestive clinical history [46, 47]
- Histological diagnosis of the central nervous system tissues where post-mortem is done

**Rubella**

- Clinical diagnosis based on the classical triad of congenital heart disease, deafness and congenital cataracts, and history of maternal infection
- Ideally also supportive laboratory evidence such as
  - increased antibody titres
  - Persistence of rubella-specific IgG in the infant after 6 to 12 months
  - Virus isolation from any site such as fetal blood or chorionic villus biopsy

**Cytomegalovirus**

- Documentation of maternal infections by either IgG avidity testing or documented seroconversion
**Detection of virus in the newborn from urine, saliva or blood**

<table>
<thead>
<tr>
<th>Herpes</th>
<th>Syphilis</th>
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<tr>
<td>• Isolation of Herpes simplex virus (HSV) from skin lesions, CSF, urine, throat, nasopharynx or conjunctivae</td>
<td>• High neonatal antibody titres: ≥ 4 times above the maternal levels</td>
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<td>• Detection of HSV DNA in CSF by PCR</td>
<td>• Positive rapid plasma regain or venereal disease research laboratory (VDRL) will also be considered</td>
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<td>• Laboratory microscopic visualization of spirochetes</td>
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<td>Preterm birth</td>
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<td>Birth asphyxia</td>
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<td>Sequel* OR Outcome* OR Morbidity OR Prognosis</td>
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<td>OR Impairment OR Deficit OR follow-up OR long-term OR Incidence OR Prevalence</td>
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</table>
References of publications reviewed

Preterm births


Hypoxic-ischemic encephalopathy


**Neonatal jaundice**


Neonatal Meningitis


Neonatal sepsis


Cytomegalovirus


**Herpes**


**Rubella**


Toxoplasmosis


Neonatal tetanus


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