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

<table>
<thead>
<tr>
<th>Preterm birth</th>
<th>Documentation of gestation age below 37 completed weeks by:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Where last menstrual period is known and expected date of delivery can be calculated</td>
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<tr>
<td></td>
<td>• Acceptable gestation age estimation criteria with</td>
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<td></td>
<td>- Ultrasound, ideally first trimester</td>
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<td></td>
<td>- Dubowitz score [44]</td>
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<td></td>
<td>- Other clinical scores with validation published eg Eregie [45]</td>
</tr>
</tbody>
</table>

| 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><strong>Herpes</strong></th>
<th>Isolation of Herpes simplex virus (HSV) from skin lesions, CSF, urine, throat, nasopharynx or conjunctivae</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Detection of HSV DNA in CSF by PCR</td>
</tr>
</tbody>
</table>

<p>| <strong>Syphilis</strong>          | High neonatal antibody titres: ( \geq 4 ) times above the maternal levels                                         |
|                       | Positive rapid plasma regain or venereal disease research laboratory (VDRL) will also be considered               |
|                       | Laboratory microscopic visualization of spirochetes                                                                |</p>
<table>
<thead>
<tr>
<th>Search element</th>
<th>MEDLINE</th>
<th>EMBASE</th>
<th>PSYCHINFO</th>
<th>CINHAL</th>
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<tbody>
<tr>
<td><strong>Exposure</strong></td>
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<tr>
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<td>Jaundice</td>
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<td></td>
<td>Tetanus</td>
<td>Tetanus</td>
<td>Tetanus</td>
<td>MH &quot;Hyperbilirubinemia, Neonatal&quot;</td>
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<td></td>
<td>Meningitis</td>
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<td>Meningitis</td>
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<td>Sepsis</td>
<td>Sepsis</td>
<td>Sepsis</td>
<td>Infections</td>
</tr>
<tr>
<td></td>
<td>Preterm birth</td>
<td>Preterm birth</td>
<td>Preterm birth</td>
<td>Infant, premature</td>
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<td></td>
<td>Birth asphyxia</td>
<td>Birth asphyxia</td>
<td>Birth asphyxia</td>
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<tr>
<td>HIV</td>
<td>HIV</td>
<td>HIV</td>
<td>HIV</td>
<td>MH &quot;Asphyxia Neonatorum&quot;</td>
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<tr>
<td>Toxoplasmosis</td>
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<tr>
<td>Rubella</td>
<td>Rubella</td>
<td>Rubella</td>
<td>Rubella</td>
<td>MH &quot;Birth Injuries&quot;</td>
</tr>
<tr>
<td>Cytomegalovirus</td>
<td>Cytomegalovirus</td>
<td>Cytomegalovirus</td>
<td>Cytomegalovirus</td>
<td>&quot;Syphilis, congenital&quot;</td>
</tr>
<tr>
<td>Herpes</td>
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<td>Herpes</td>
<td>Herpes</td>
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<tr>
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<tr>
<td>+Subheadings:</td>
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<tr>
<td>Complications</td>
<td></td>
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</tbody>
</table>
Diagnosis
Epidemiology
Aetiology
Mortality
Prevention/control
Psychology
Rehabilitation
Therapy
### Keywords

Sequel* OR Outcome* OR Morbidity OR Prognosis OR Impairment OR Deficit OR follow-up OR long-term OR Incidence OR Prevalence

### Outcome

<table>
<thead>
<tr>
<th>Thesaurus terms exploded</th>
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</thead>
<tbody>
<tr>
<td>Neurological impairment</td>
<td>Neurological impairment</td>
<td>Neurological impairment</td>
<td>MH &quot;Outcomes of Prematurity&quot;</td>
</tr>
<tr>
<td>Neurologic manifestation</td>
<td>Neurologic manifestation</td>
<td>Neurologic manifestation</td>
<td>MH &quot;Outcomes (Health Care)+&quot;</td>
</tr>
<tr>
<td>Dyskinesias</td>
<td>Dyskinesias</td>
<td>Dyskinesias</td>
<td>MH &quot;Treatment Outcomes+&quot;</td>
</tr>
<tr>
<td>Gait Disorders</td>
<td>Gait Disorders</td>
<td>Gait Disorders</td>
<td>MH &quot;Outcome Assessment&quot;</td>
</tr>
<tr>
<td>Neurobehavioral manifestations</td>
<td>Neurobehavioral manifestations</td>
<td>Neurobehavioral manifestations</td>
<td>MH &quot;Problem Rating Scale for Outcomes (Omaha)+&quot;</td>
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<tr>
<td>Neuromuscular manifestations</td>
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<td>Meningism</td>
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</tr>
<tr>
<td>Disorder</td>
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<td>Age</td>
<td>Language</td>
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<td>--------------------------------</td>
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<td>----------</td>
</tr>
<tr>
<td>Paralysis</td>
<td>Infant, newborn</td>
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<td>All</td>
</tr>
<tr>
<td>Paresis</td>
<td>Infant, newborn</td>
<td></td>
<td>All</td>
</tr>
<tr>
<td>Reflex-abnormal</td>
<td>Infant, newborn</td>
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<td>All</td>
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<tr>
<td>Seizures</td>
<td>Infant, newborn</td>
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</tr>
<tr>
<td>Sensation disorder</td>
<td>Infant, newborn</td>
<td></td>
<td>All</td>
</tr>
<tr>
<td>Voice Disorders</td>
<td>Infant, newborn</td>
<td></td>
<td>All</td>
</tr>
</tbody>
</table>

The table represents a summary of the disorders and their associated populations. The entries indicate that all disorders are present in the infant and newborn populations.
References of publications reviewed

Preterm births


Hypoxic-ischemic encephalopathy


Neonatal jaundice


Neonatal Meningitis


Neonatal sepsis


Cytomegalovirus


**Herpes**


**Rubella**


**Toxoplasmosis**


**Neonatal tetanus**


HIV
