
Downloaded from: http://researchonline.lshtm.ac.uk/799081/

DOI: 10.1016/S0140-6736(11)61577-8

Usage Guidelines

Please refer to usage guidelines at http://researchonline.lshtm.ac.uk/policies.html or alternatively contact researchonline@lshtm.ac.uk.

Available under license: http://creativecommons.org/licenses/by-nc-nd/2.5/
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><strong>Neonatal Insult</strong></th>
<th><strong>Diagnostic criteria</strong></th>
</tr>
</thead>
</table>
| **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></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Isolation of Herpes simplex virus (HSV) from skin lesions, CSF, urine, throat, nasopharynx or conjunctivae</td>
</tr>
<tr>
<td></td>
<td>Detection of HSV DNA in CSF by PCR</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Syphilis</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>High neonatal antibody titres: ≥ 4 times above the maternal levels</td>
</tr>
<tr>
<td></td>
<td>Positive rapid plasma regain or venereal disease research laboratory [VDRL]) will also be considered</td>
</tr>
<tr>
<td></td>
<td>Laboratory microscopic visualization of spirochetes</td>
</tr>
</tbody>
</table>
## Search Terms

<table>
<thead>
<tr>
<th>Search element</th>
<th>MEDLINE</th>
<th>EMBASE</th>
<th>PSYCHINFO</th>
<th>CINHAL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Exposure</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thesaurus terms exploded</td>
<td>Thesaurus terms exploded</td>
<td>Thesaurus terms exploded</td>
<td>Thesaurus terms exploded</td>
<td>Thesaurus terms exploded</td>
</tr>
<tr>
<td>Jaundice</td>
<td>Jaundice</td>
<td>Jaundice</td>
<td></td>
<td>Jaundice</td>
</tr>
<tr>
<td>Tetanus</td>
<td>Tetanus</td>
<td>Tetanus</td>
<td></td>
<td>Tetanus</td>
</tr>
<tr>
<td>Meningitis</td>
<td>Meningitis</td>
<td>Meningitis</td>
<td>Meningitis</td>
<td>Meningitis</td>
</tr>
<tr>
<td>Sepsis</td>
<td>Sepsis</td>
<td>Sepsis</td>
<td></td>
<td>Sepsis</td>
</tr>
<tr>
<td>Preterm birth</td>
<td>Preterm birth</td>
<td>Preterm birth</td>
<td>Preterm birth</td>
<td>Preterm birth</td>
</tr>
<tr>
<td>Birth asphyxia</td>
<td>Birth asphyxia</td>
<td>Birth asphyxia</td>
<td>Birth asphyxia</td>
<td>Birth asphyxia</td>
</tr>
<tr>
<td>HIV</td>
<td>HIV</td>
<td>HIV</td>
<td></td>
<td>HIV</td>
</tr>
<tr>
<td>Toxoplasmosis</td>
<td>Toxoplasmosis</td>
<td>Toxoplasmosis</td>
<td>Toxoplasmosis</td>
<td>Toxoplasmosis</td>
</tr>
<tr>
<td>Rubella</td>
<td>Rubella</td>
<td>Rubella</td>
<td></td>
<td>Rubella</td>
</tr>
<tr>
<td>Cytomegalovirus</td>
<td>Cytomegalovirus</td>
<td>Cytomegalovirus</td>
<td>Cytomegalovirus</td>
<td>Cytomegalovirus</td>
</tr>
<tr>
<td>Herpes</td>
<td>Herpes</td>
<td>Herpes</td>
<td></td>
<td>Herpes</td>
</tr>
<tr>
<td>Syphilis</td>
<td>Syphilis</td>
<td>Syphilis</td>
<td></td>
<td>Syphilis</td>
</tr>
<tr>
<td><strong>+Subheadings:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complications</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diagnosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-------------</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epidemiology</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aetiology</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mortality</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prevention/control</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychology</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rehabilitation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Therapy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Keywords</td>
<td>Outcome</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-------------------------------</td>
<td>-------------------------------------------------------------------------</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>sequel* OR outcome* OR</td>
<td>thesaurus terms exploded</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>morbidity OR prognosis</td>
<td>neurological impairment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OR impairment OR deficit</td>
<td>neurological impairment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OR follow-up OR long-term</td>
<td>neurological impairment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OR incidence OR</td>
<td>neurological impairment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>prevalence</td>
<td>neurological impairment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>neurologic manifestation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>dyskinesias</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>gait disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>neurobehavioral manifestations</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>neuromuscular manifestations</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>meningism</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>pain</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>mh &quot;outcomes of prematurity&quot;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>mh &quot;outcomes (health care)+&quot;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>mh &quot;treatment outcomes+&quot;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>mh &quot;outcome assessment&quot;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>mh &quot;problem rating scale for outcomes (omaha)+&quot;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paralysis</td>
<td>Paresis</td>
<td>Reflex-abnormal</td>
<td>Seizures</td>
<td></td>
</tr>
<tr>
<td>-------------------</td>
<td>----------------</td>
<td>----------------</td>
<td>------------</td>
<td></td>
</tr>
<tr>
<td>Sensation disorder</td>
<td>Voice Disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Population</th>
<th>Age=newborn</th>
<th>Infant, newborn</th>
</tr>
</thead>
<tbody>
<tr>
<td>Language</td>
<td>All</td>
<td>All</td>
</tr>
</tbody>
</table>
References of publications reviewed

Preterm births


Hypoxic-ischemic encephalopathy


### Neonatal jaundice


Neonatal Meningitis


Neonatal sepsis


Cytomegalovirus


**Herpes**


**Rubella**


**Toxoplasmosis**


**Neonatal tetanus**


**HIV**
