

# THE LANCET

## Supplementary webappendix

This webappendix formed part of the original submission and has been peer reviewed.  
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neurodevelopmental outcomes after intrauterine and neonatal insults: a systematic  
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Diagnostic criteria for the insult during [pregnancy or the neonatal period

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<b>Neonatal Insult</b>	<b>Diagnostic criteria</b>
<i>Neonatal Jaundice</i>	<ul style="list-style-type: none"><li>• Significant jaundice based on bilirubin level for age and weight of newborn based on internationally accepted criteria [39] [40]</li><li>• Non-obstructive jaundice [41]</li></ul>
<i>Neonatal Tetanus</i>	<ul style="list-style-type: none"><li>• Initially well and then onset of spasms that maybe provoked or spontaneous</li><li>• Trismus and difficulty feeding</li></ul>
<i>Neonatal Meningitis</i>	<ul style="list-style-type: none"><li>• Cerebrospinal fluid (CSF) culture positive for a causative organisms</li><li>• Or positive antigen test [42]</li><li>• White cell count in cerebrospinal fluid of more than 50 cells per microlitre [42]<ul style="list-style-type: none"><li>◦ Positive blood culture and/or gram stain</li><li>◦ Glucose blood/CSF ratio &lt; 0.1</li><li>◦</li></ul></li></ul>
<i>Neonatal Sepsis</i>	<ul style="list-style-type: none"><li>• Positive blood culture</li><li>• Clinical definition of neonatal sepsis based on an accepted algorithm</li></ul>
<i>Hypoxic Ischemic Encephalopathy</i>	<ul style="list-style-type: none"><li>• Onset within 2 days of birth of severe or moderate neonatal encephalopathy in infants born at 34 or more weeks of gestation</li><li>• Acute perinatal event, and/or a 10 minute APGAR less than 5 or assisted ventilation for more than 10 minutes.</li><li>• Ideally also the following:<ul style="list-style-type: none"><li>◦ Evidence of metabolic acidosis (pH &lt;7 or less or base deficit &lt; 12 mmol per liter [43])</li></ul></li></ul>

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- Other identifiable aetiologies such as trauma, coagulation disorders, infectious conditions, or genetic disorders were excluded [43].
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*Preterm birth* Documentation of gestation age below 37 completed weeks by:-

- Where last menstrual period is known and expected date of delivery can be calculated
  - Acceptable gestation age estimation criteria with
    - Ultrasound, ideally first trimester
    - Dubowitz score [44]
    - Other clinical scores with validation published eg Eregie [45]
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*HIV* • Polymerase Chain Reactions (PCR) test that shows infection with the HIV virus,

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*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

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*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

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*Cytomegalovirus* • Documentation of maternal infections by either IgG avidity testing or documented seroconversion

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	<ul style="list-style-type: none"><li>• Detection of virus in the newborn from urine, saliva or blood</li></ul>
<i>Herpes</i>	<ul style="list-style-type: none"><li>• Isolation of Herpes simplex virus (HSV) from skin lesions, CSF, urine, throat, nasopharynx or conjunctivae</li></ul>
<i>Syphilis</i>	<ul style="list-style-type: none"><li>• Detection of HSV DNA in CSF by PCR</li><li>• High neonatal antibody titres: <math>\geq</math> 4 times above the maternal levels</li><li>• Positive rapid plasma regain or venereal disease research laboratory [VDRL]) will also be considered</li><li>• Laboratory microscopic visualization of spirochetes</li></ul>

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## Search Terms

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Search element	MEDLINE	EMBASE	PSYCHINFO	CINHAL
<b>Exposure</b>	Thesaurus terms exploded	Thesaurus terms exploded	Thesaurus terms exploded	Thesaurus terms exploded
	Jaundice	Jaundice	Jaundice	Jaundice
	Tetanus	Tetanus	Tetanus	MH "Hyperbilirubinemia, Neonatal+"I
	Meningitis	Meningitis	Meningitis	
	Sepsis	Sepsis	Sepsis	Infections
	Preterm birth	Preterm birth	Preterm birth	
	Birth asphyxia	Birth asphyxia	Birth asphyxia	Infant, premature
	HIV	HIV	HIV	MH "Asphyxia Neonatorum"
	Toxoplasmosis	Toxoplasmosis	Toxoplasmosis	
	Rubella	Rubella	Rubella	MH "Birth Injuries+"Syphilis, congenital
	Cytomegalovirus	Cytomegalovirus	Cytomegalovirus	
	Herpes	Herpes	Herpes	
	Syphilis	Syphilis	Syphilis	
+Subheadings:				
Complications				

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Diagnosis

Epidemiology

Aetiology

Mortality

Prevention/control

Psychology

Rehabilitation

Therapy

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<b>Keywords</b>	Sequel* OR Outcome*OR Morbidity OR Prognosis OR Impairment OR Deficit OR follow-up OR long-term OR Incidence OR Prevalence			
<b>Outcome</b>	Thesaurus terms exploded  Neurological impairment  Neurologic manifestation  Dyskinesias  Gait Disorders  Neurobehavioral manifestations  Neuromuscular manifestations  Meningism  Pain	Thesaurus terms exploded  Neurological impairment  Neurological impairment  Neurological impairment  MH "Outcomes of Prematurity"  MH "Outcomes (Health Care)+"  MH "Treatment Outcomes+"	Thesaurus terms exploded  Neurological impairment  Neurological impairment  MH "Outcome Assessment"	Thesaurus terms exploded  MH "Problem Rating Scale for Outcomes (Omaha)"+

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Paralysis

Paresis

Reflex-abnormal

Seizures

Sensation disorder

Voice Disorders

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Population Age=newborn Infant, newborn

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Language All All All All

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## **Neonatal jaundice**

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