Cooling in Mild Encephalopathy (COMET) trial

Expanded Modified Sarnat Staging in Term Infants

IMPERIAL

Encephalopathy can be diagnosed only by clinical examination. Although neurological examination is subjective, standardisation of the assessment and certification minimises examiner variability and promotes the enrolment of appropriate infants in clinical trials.

This examination involves nine signs under six categories (Table 1); each category contributes one point. Primitive reflexes (suck and Moro) and the autonomic nervous system (pupils, heart rate, and respiration) have multiple signs, but these contribute only one point; when multiple signs within a category differ, assign the highest category. For example, if suck is normal and Moro is absent, assign 'severe' under the primitive reflexes category.

The neurological examination should be conducted in two phases:

A) Observation phase (spontaneous activity, posture, heart rate, and respiration)
B) Active manipulation phase (level of consciousness, tone, suck, Moro, and pupils).

The infant should always be assessed in an awake state (Shankaran et al., NEJM 2005).

A. Observation part of the assessment

1. Spontaneous activity

Assess spontaneous activity when the infant is awake. The first examination should be performed before sedation. If the infant is markedly sedated a clinical judgment must be used to decide whether the examination is reliable. Administration of a muscle relaxant will preclude a meaningful exam.

1. Circle normal if infant is active.
2. Circle mild if spontaneous activity is slightly reduced.
3. Circle moderate if spontaneous activity is markedly reduced.
4. Circle severe if spontaneous activity is absent.

2. Posture

Observe infant in awake state.

1. Circle normal if infant is moving around and does not maintain one posture and has flexion of lower extremity at hip and/or knees.
2. Circle mild if there is mild flexion of distal joints (fingers and wrist usually)
3. Circle moderate if there is complete extension or frog-legged" position (complete abduction); moderate flexion of distal joints.
4. Circle severe if decerebrate or decorticate with or without stimulation.

If posture is abnormal, but does not fit moderate or severe, code as moderate.

3. Respiratory pattern (Autonomic Nervous System)

1. Circle normal if breathing spontaneously.
2. Circle mild if tachypnoeic or on supplemental oxygen.
3. Circle moderate if requiring CPAP or high flow.
4. Circle severe if apnoeic or requiring ventilator support

An intubated infant with spontaneous breaths is coded as severe as it cannot be ascertained if the spontaneous breaths can sustain respiration without ventilator support.

4. Heart rate (Autonomic Nervous System)

Heart rate should be evaluated based on documented rate over the previous min/hrs. If cooling has been already initiated heart rate cannot be assessed as the infant may have bradycardia in response to cooling.

1. Circle normal if the heart rate is between 100 to 160.
2. Circle mild if there is tachycardia (>160 per minute)
3. Circle moderate if there is bradycardia (< 100/min) with only occasional increases to >120/min.
4. Circle severe if the heart rate is not constant and varies widely between <100 and >120.

B. Active manipulation part of the assessment

1. Level of consciousness

Level of conscious can be assessed only by stimulating the infant and assessing the response to stimuli, and not by merely observing the infant. Level of consciousness is the deciding factor if categories of moderate and severe categories are equal.

1. Circle normal if the infant is alert and responsive to external stimuli when awake.
2. Circle mild if infant is hyper-alert, has an exaggerated response to minimal stimuli, has a stare, is inconsolable.
3. Circle moderate if the infant is lethargic. Lethargy is delayed but complete response to external stimuli (start with mild stimuli first then proceed to more noxious stimuli). It is important not to confuse reduced spontaneous activity with lethargy.
4. Circle severe if infant is in stupor or coma and is not arousable and is non-responsive to external stimuli. The infant may have a delayed but incomplete response to stimuli.

2. Tone

Tone is the resistance to passive movement. Evaluate extremities, trunk and neck tone and make clinical judgment of tone based on tone in these areas. If possible, evaluate infant prone over your hands to assess neck and trunk. If varying tone, code the predominant state

1. Circle normal if there is strong flexor tone in all extremities, including at the hip.
2. Circle mild if there is slightly increased peripheral tone in the limbs only.
3. Circle moderate if hypotonic or floppy either focal or generalized, or if both peripheral and truncal tone are increased.
4. Circle severe if flaccid (like a rag doll) or if rigid (stiffness or inflexibility)

3. Suck (Primitive reflex)

Put a gloved finger inside the infant's mouth to assess suck.

1. Circle normal if the infant vigorously sucks the examiners finger.
2. Circle mild if suck is weak.
3. Circle moderate if suck has a bite.
4. Circle severe if suck is absent.

4. Moro (Primitive reflex)

If infant has fracture of clavicle or brachial plexus injury, evaluate other extremities.

1. Circle normal if, with stimulus, there is extension of limbs, opening of hands, extension with abduction of upper arm followed by flexion (embrace)
2. Circle mild if low threshold to elicit.
3. Circle moderate if incomplete or delayed response
4. Circle severe if absent.

5. Pupil (Autonomic Nervous System)

Pupils are difficult to assess in the newborn infant with edema of eyelids. You will need to gently separate the eyelids while a second person shines light. Always use a pupil torch to assess the size of the pupil.

1. Circle normal if, in the dark size is 2.5-4.5 mm & in light, reactive & 1.5-2.5mm
2. Circle mild if mydriasis.
3. Circle moderate if constricted and reacting to light.
4. Circle severe if skew deviation of eyes, pupils are dilated or non-reactive to light. If pupils asymmetric, assign severe.

Please laminate this document and keep in your NICU and refer to it when performing a neurological assessment.

Assignment of mild encephalopathy in the COMET trial
The COMET trial requires the infant to have 2 or more abnormalities in the 6 categories, but not more than 3 categories in moderate and severe. It is mandatory that there should be a normal transcranial (single channel) aEEG background for at least 30 minutes or no seizures.

The above definitions are adapted from a) the NICHD Neonatal Research (NRN) Neurological Examination for HIE available on the NICHD NRN website and b) The PRIME study (Prospective Research on Infants with Mild Encephalopathy) and c) The COMET Pilot study (Whole-Body Hypothermia vs Targeted Normothermia for Neonates with Mild Encephalopathy)

https://neonatal.rti.org/pdf/Neurocertification_HIE_Trials_SS_05212019.pdf

Dr Reema Garegrat, Professor Sudhin Thayyil, Professor Seetha Shankaran.

Table 1. Expanded Modified Sarnat Staging for Hypoxic Ischaemic Encephalopathy.

CATEGORIES (TOTAL 6)	CIRCLE THE COMPONENTS OF NEUROLOGICAL EXAMINATION (TOTAL 9 circles)			
	NORMAL	MILD	MODERATE	SEVERE
1. Level of consciousness				
	Alert, Responsive to external stimuli when awake.	Hyper-alert, has an exaggerated response to minimal stimuli, has a stare, is inconsolable.	Lethargic – i.e. delayed but complete response to a stimulus.	Stupor/coma
2. Spontaneous activity				
	Active (Changes position when awake)	Slightly reduced activity	Markedly reduced activity	Absent
3. Posture				
	Predominantly flexed when quiet	Mild flexion of distal joints (fingers and wrist usually)	Complete extension, frog legged (complete abduction) moderate flexion of distal joints	Decerebrate or decorticate
4. Tone				
	Strong flexor tone in all extremities, including at the hip	Slightly increased peripheral tone in limbs	Hypotonia/floppy (focal or general) or Hypertonia (peripheral + truncal)	Flaccid or Rigid
5. Primitive reflexes (Assign based on the highest of the two sub-categories)				
Suck	Strong, easy to elicit	Weak suck	Suck has a bite	Absent
Moro	Complete	Low threshold to elicit	Incomplete or delayed response	Absent
6. Autonomic system (Assign based on the highest of the three sub-categories)				
Pupils	In dark: 2.5-4.5 mm. In light, reactive: 1.5-2.5 mm	Dilated (Mydriasis) and reacting to light	Constricted (Miosis) and reacting to light	Deviation/ Fixed dilated/ asymmetric/non-reactive to light
Heart rate	100-160 bpm	Tachycardia (HR > 160 bpm)	Bradycardia (HR <100 bpm)	Variable HR
Respiration	Breathing spontaneously	Tachypnoeic (RR >60/min) or requiring supplemental oxygen	CPAP or High flow	Apnoea or requires ventilator
TOTAL SCORE (CIRCLES)				

The final level of encephalopathy is assigned based on which level (mild, moderate or severe) predominates among the 6 categories. If moderate and severe categories are equally distributed, the neonate's level of consciousness then determines the final level of encephalopathy. Any neonate with seizure should be classified as moderate or severe encephalopathy depending on their neurological examination.
Mild encephalopathy varies between the mildest end of a spectrum which has 4 categories under normal and 2 categories under mild while the severe most end has 4 categories under mild and a total of 2 categories under moderate and severe.