Indian Academy of Pediatrics (IAP)

STANDARD TREATMENT GUIDELINES 2022

Neonatal Sepsis

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Neonatal Sepsis

Definitions and Nomenclature of Neonatal Sepsis

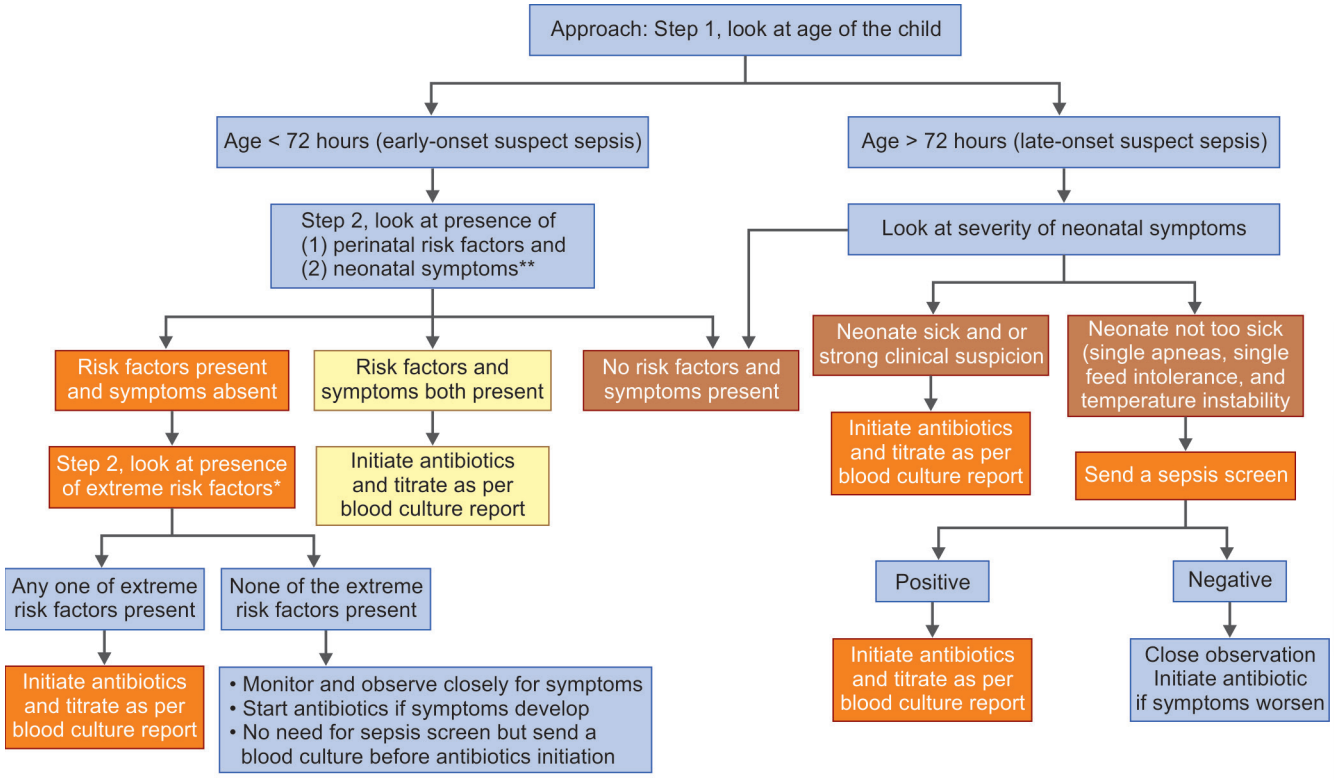
- ☑ *Probable sepsis:* Is clinical and laboratory findings consistent with bacterial infection without a positive culture.
- ☑ *Clinical sepsis:* When the screen and blood/cerebrospinal fluid (CSF) culture is negative, but there is a suggestive history with a high clinical suspicion.
- ☑ *Culture proven or definitive sepsis*: Culture positive sepsis.
- ☑ *Neonatal sepsis:* Best defined as presence of systemic features associated with pure growth of bacteria from one or more sites.
- ☑ *At risk (ruling out sepsis)*: Often we "suspect" sepsis based on risk factors and clinical features, but the clinical course (rapid recovery within few hours) and "screening tests" are not suggestive; we should not label these as "suspected sepsis". They are more like "rule out sepsis".

Routes of Transmission

- ☑ *Vertical transmission*: This transmission is in utero, either hematogenous or through amniotic fluid or during birth. The symptoms usually manifest within the first 72 hours of life.
- ☑ *Horizontal transmission:* These are hospital-acquired infections, majority being late-onset sepsis (>72 hours of life). However, breach in asepsis during resuscitation, immediately after delivery, is also horizontal transmission, but the symptoms may manifest within the first 72 hours of life.

Perinatal Risk Factors	Extreme Risk Factors
Rupture of membranes > 24 hours	Rupture of membranes > 72 hours
Spontaneous preterm labor	Chorioamnionitis (intra-amniotic infection)
Chorioamnionitis (intra-amniotic infection)	Foul smelling liquor
Prolonged labor	
Unclean per vaginal examinations	
Perinatal asphyxia	

Definition of Intra-amniotic Infection Or Inflammation Or Both (Triple I)
Maternal fever: Maternal oral temperature ≥ 39°C on any one occasion. If oral temperature is 38 (100.4) to 38.9 (102°F), repeat after 30 minutes, if repeat value remains at least 38°C (100.4) it is defined as fever
Suspected triple I: Fever without a clear source plus any of: (1) baseline fetal tachycardia (>160 bpm for >10 minutes)
Maternal total leukocyte count (TLC) > 15,000/cmm in absence of corticosteroids
Definite purulent fluid from cervical os
Confirmed triple I: All the above plus laboratory findings such as:
Positive amniotic fluid Gram stain/culture
Histopathological evidence of infection or inflammation or both in placenta


Approach: Step 1, look at age of the child
Age < 72 hours (early-onset suspect sepsis)
Age > 72 hours (late-onset suspect sepsis)
Step 2, look at presence of (1) perinatal risk factors and (2) neonatal symptoms**
Look at severity of neonatal symptoms
Risk factors present and symptoms absent
Risk factors and symptoms both present
No risk factors and symptoms present
Neonate sick and or strong clinical suspicion
Neonate not too sick (single apneas, single feed intolerance, and temperature instability
Step 2, look at presence of extreme risk factors*
Initiate antibiotics and titrate as per blood culture report
Initiate antibiotics and titrate as per blood culture report
Send a sepsis screen
Any one of extreme risk factors present
None of the extreme risk factors present
Positive
Negative
Initiate antibiotics and titrate as per blood culture report
• Monitor and observe closely for symptoms
• Start antibiotics if symptoms develop
• No need for sepsis screen but send a blood culture before antibiotics initiation
Initiate antibiotics and titrate as per blood culture report
Close observation Initiate antibiotic if symptoms worsen
Symptoms of sepsis**
• Lethargy
• Poor feeding
• Mother/nurse reports that baby is not well
• Fever
• Hypothermia
• Vomiting, diarrhea, and abdominal distension
• Seizures and encephalopathy
• Poor perfusion and shock
• Rarely: Bleeding, sclerema, and renal failure
Components of sepsis screen
• Total leukocyte count (TLC)
• Absolute neutrophil count (ANC)
• Micro-erythrocyte sedimentation rate (ESR)
• C-reactive protein (CRP)
• Immature-to-total count (I/T ratio)
TLC < 5,000/cmm, ANC below cutoff for age (<1,800/cmm), Micro-ESR > 15 mm Hg, CRP > 10 mg per dL and I/T ratio > 0.2—any two of the above constitute a positive sepsis screen

- ☑ It is not possible to recommend a single antibiotic policy for use in all newborn units.
- ☑ It should be based on local culture and sensitivity data and profile of organisms for last 6–12 months. If not available, use data from nearby units or National Neonatal Perinatal Database (NNPD).
- ☑ Individual antibiotics and rational combinations of antibiotics must be evaluated for the percentage of organisms that they cover. The simplest and cheapest rational combination of antibiotics must be selected for each line
  - *First line*: Must cover approximately 75–80% of isolates
  - *Second line*: Must cover approximately 90–95% of isolates
  - *Third line*: Must cover approximately 95–100% of isolates
- ☑ Initial combination should cover both gram-negative and gram-positive organisms. One should use the lowest generation antibiotic combination which would cover about 70% of organisms. This is to ensure you have something to fall back on.
- ☑ Avoid cephalosporins as first-line antibiotics—proven harm [high risk of extended-spectrum beta-lactamases (ESBL) organisms, increased *Candida* infections, necrotizing enterocolitis (NEC), and mortality]—units who do not use have shown multiple benefits.
- ☑ Have a written unit/departmental/institutional antibiotic policy and practice antibiotic stewardship (reasons for starting the antibiotics, review the plan for antibiotics at 48 hours and again at 5 days based on culture reports and clinical course, have an exit plan, do not use reserve drugs without consultation)

A broad guide to initial antibiotics is mentioned below:

I. Septicemia or Pneumonia

Birth weight < 2 kg

Antibiotic	*Each dose*	*Frequency*		*Route*	*Duration (Days)*
	0–14 days age	*>14 days age*			
Injection ampicillin* or	50 mg/kg/dose	12 hourly	8 hourly	IV	7–10
Injection cloxacillin#	50 mg/kg/ dose	12 hourly	8 hourly	IV	7–10
AND					
Injection gentamicin	5 mg/kg/dose	24 hourly	24 hourly	IV	7–10

Birth weight ≥ 2 kg

Antibiotic	*Each dose*	*Frequency*		*Route*	*Duration (Days)*
	0–7days age	*>7 days age*			
Injection ampicillin* or	50 mg/kg/dose	12 hourly	8 hourly	IV	7–10
Injection cloxacillin#	50 mg/kg/ dose	12 hourly	8 hourly	IV	7–10
AND					
Injection gentamicin	5 mg/kg/dose	24 hourly	24 hourly	IV	7–10

II. Septicemia Second-Line Drugs

Birth weight < 2 kg

Antibiotic	*Each dose*	*Frequency*		*Route*	*Duration (Days)*
	0–14 days age	*>14 days age*			
Injection piperacillin#					
Tazobactam***	50 mg/kg/dose	12 hourly	8 hourly	IV	7–10
Injection amikacin**	15 mg/kg/ dose	24 hourly	24 hourly	IV	7–10

Birth weight ≥ 2 kg

Antibiotic	*Each dose*	*Frequency*		*Route*	*Duration (Days)*
	0–7 days age	*>7 days age*			
Injection piperacillin#					
Tazobactam***	50 mg/kg/dose	12 hourly	8 hourly	IV	7–10
Injection amikacin**	15 mg/kg/ dose	24 hourly	24 hourly	IV	7–10

III. Meningitis (for Confirmed Meningitis)

Birth weight < 2 kg

Antibiotic	*Each dose*	*Frequency*		*Route*	*Duration (Weeks)*
	0–7 days age	*>7 days age*			
Injection cefotaxime*	50 mg/kg/dose	12 hourly	8 hourly	IV	3
Injection amikacin**	15 mg/kg/ dose	24 hourly	24 hourly	IV	3

Birth weight ≥ 2 kg

Antibiotic	*Each dose*	*Frequency*		*Route*	*Duration (Weeks)*
	0–7 days age	*>7 days age*			
Injection cefotaxime*	50 mg/kg/dose	8 hourly	6 hourly	IV	3
Injection amikacin**	15 mg/kg/ dose	24 hourly	24 hourly	IV	3

IV. Meningitis—Second-line Drugs

Antibiotic	*Each dose*	*Frequency*		*Route*	*Duration (Weeks)*
	0–7 days age	*>7 days age*			
Injection meropenem****	40 mg/kg/dose	8 hourly	8 hourly	IV	3
Injection amikacin**	15 mg/kg/ dose	24 hourly	24 hourly	IV	3

\# Start if pustules/umbilical sepsis.
* Infuse as an IV infusion using syringe infusion pump over 30 minutes or longer. Use a concentration not >100 mg/mL for infusion.
** Infuse as an IV infusion using syringe infusion pump over 30 minutes or longer. Use a concentration not >5 mg/mL for infusion.
*** Infuse as an IV infusion using syringe infusion pump over 30 minutes or longer. Use a concentration not >50 mg/mL for infusion.
**** Infuse as an IV infusion using syringe infusion pump over 30 minutes or longer.

Points to Remember

- ☑ As neonatal sepsis is a dynamic, complex, and heterogeneous condition, intense monitoring (subjective and objective) of the baby is warranted. A repeat sepsis screen within 12 hours may be adopted if initial screen is negative and suspicion of sepsis is strong.
- ☑ *Process of taking blood culture*: Take all aseptic barrier precaution [local disinfection of site with 70% alcohol, povidone iodine (avoid in extremely low birth weight), then alcohol), 1 mL of blood to be put containing at least 5 mL of broth for culture, take blood from fresh puncture site (preferably from freshly inserted intravenous cannula.

Further Reading

- ☑ Investigators of the Delhi Neonatal Infection Study (DeNIS) collaboration. Characterisation and antimicrobial resistance of sepsis pathogens in neonates born in tertiary care centres in Delhi, India: a cohort study. Lancet Glob Health. 2016;4(10):e752-60.
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