Chapter 13

NEONATAL SEPSIS

Neonatal sepsis is the most important cause of neonatal deaths in the community, accounting for over half of them. If diagnosed early and treated with good supportive care and antibiotics, it is possible to save most cases of neonatal sepsis.

Learning objectives:

The participant after completing this module should be able to:
1) Enumerate the aetiological organisms of neonatal sepsis.
2) Identify clinical features of neonatal sepsis.
3) Describe methods to diagnose neonatal sepsis.
4) Interpret the ‘sepsis screen’.
5) Enumerate the steps of supportive care of septicemic neonates.
6) Chart antibiotic therapy for a septic neonate.

Etiology

Most cases of neonatal sepsis in the community are caused by *Escherichia coli* and *Staphylococcus aureus*. In hospitals, *Klebsiella pneumoniae* is also a common organism.

Early-onset (< 72 hrs) infections are caused by organisms prevalent in the maternal genital tract or in the delivery area. The risk factors for early-onset sepsis include
- Low birth weight,
- Prolonged rupture of membranes >24 hrs;
- Foul smelling liquor,
- Multiple per vaginum examinations,
- Intrapatum maternal fever,
- Difficult or prolonged labour

Early onset sepsis manifests frequently as pneumonia and less commonly as septicemia or meningitis.

Late-onset sepsis is caused by the organisms thriving in the external environment of the home or the hospital. The infection is often transmitted through the hands of the care-providers. The onset of symptoms is usually delayed beyond 72 hours after birth and the presentation is that of septicemia, pneumonia or meningitis. The associated factors of late-onset sepsis include:
- Low birth weight,
- Lack of breastfeeding,
- Superficial infections (pyoderma, umbilical sepsis),
- Disruption of skin integrity with needle pricks and use of intravenous fluids.
Clinical features
The most common characteristics and manifestations are depicted in Table 13.1.

**TABLE 13.1: Clinical manifestations of neonatal sepsis**

<table>
<thead>
<tr>
<th>Clinical manifestation</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Lethargy</td>
<td>Cyanosis*</td>
</tr>
<tr>
<td>Refusal to suckle</td>
<td>Tachypnea*</td>
</tr>
<tr>
<td>Poor cry</td>
<td>Chest retractions*</td>
</tr>
<tr>
<td>Not arousalbe, comatose</td>
<td>Grunt*</td>
</tr>
<tr>
<td>Abdominal distension</td>
<td>Apnea/gasping*</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>Fever#</td>
</tr>
<tr>
<td>Vomiting</td>
<td>Seizures#</td>
</tr>
<tr>
<td>Hypothermia</td>
<td>Blank look#</td>
</tr>
<tr>
<td>Poor perfusion</td>
<td>High pitched cry#</td>
</tr>
<tr>
<td>Sclerema</td>
<td>Excessive crying/irritability#</td>
</tr>
<tr>
<td>Poor weight gain</td>
<td>Neck retraction#</td>
</tr>
<tr>
<td>Shock</td>
<td>Bulging fontanel#</td>
</tr>
<tr>
<td>Bleeding</td>
<td></td>
</tr>
<tr>
<td>Renal failure</td>
<td></td>
</tr>
</tbody>
</table>

*Particularly suggestive of pneumonia, #Particularly suggestive of meningitis

Meningitis is often silent, the clinical picture being dominated by manifestations of associated septicemia. However, the appearance of excessive or high-pitched crying, fever, seizures, blank look, neck retraction or bulging anterior fontanel are highly suggestive of meningitis.

In sick neonates, the skin may become tight giving a hide-bound feel (sclerema) and the perfusion becomes poor (capillary refill time of over 3 seconds). Cyanosis may appear. A critical neonate may develop shock, bleeding and renal failure.

**Diagnosis**
In presence of risk factors, assess the baby’s gestation and presence of symptoms. If the baby’s gestation is ≥ 35 weeks and the neonate is asymptomatic, do a sepsis screen. In case of a positive screen or if the baby develops symptoms start first line antibiotics.

**Direct method**
Isolation of microorganisms from blood, CSF, urine, pleural fluid or pus is diagnostic. In clinically suspected cases of sepsis, send blood culture prior to starting antibiotics.
**Indirect method**

There are a variety of tests which are helpful for screening of neonates with sepsis

- **TLC**: A total leucocyte count below 5000/mm$^3$
- An **absolute neutrophil count** of < 1800 per cu mm is an indicator of infection. Neutropenia is more predictive of neonatal sepsis than neutrophilia.
- **Immature neutrophils** (Band cells + myelocytes + metamyelocytes) to total neutrophils ratio (I/T) > 0.20 means that immature neutrophils are over 20 percent of the total neutrophils because bone marrow pushes even the premature cells into circulation, to fight infection.
- The **micro-ESR** may be elevated with sepsis and a fall of > 15 mm during first hour indicates infection.
- **C-reactive protein** (CRP): A CRP value of > 10mg/L is taken as positive. A negative CRP is reassuring. The CRP can be affected by asphyxia, shock, meconium aspiration and prolonged rupture of membranes.

There are a variety of other tests which can be used to predict sepsis but it may be difficult to perform them at all places and hence the clinical acumen remains crucial. A practical positive "sepsis screen" takes into account two or more positive tests out of the five given below:

1. Leukopenia (TLC <5000/cmm)
2. Neutropenia (ANC <1800/cmm)
3. Immature neutrophil to total neutrophil (I/T) ratio (> 0.2)
4. Micro ESR (> 15mm 1st hour)
5. CRP +ve

All neonates with late onset sepsis should be evaluated by doing a lumbar puncture to rule out meningitis. The CSF cytology and the biochemistry values need to be interpreted in the light of the normal range of the values for CSF in the term and preterm neonates (Table 13.2).

### TABLE 13.2: Normal CSF Values

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Term neonates</th>
<th>Preterm neonates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein</td>
<td>20-150 mg%</td>
<td>65 –180 mg%</td>
</tr>
<tr>
<td>Glucose</td>
<td>44-128 mg%</td>
<td>24-63 mg%</td>
</tr>
<tr>
<td>White cell count</td>
<td>0-22/mm3 (61% polys)</td>
<td>0-26 / mm3 (57% polys)</td>
</tr>
</tbody>
</table>

**Treatment**

Early treatment is crucial. Supportive care and antibiotics are two equally important components of the treatment. The supportive care makes the difference between life and death early in septicemia.
Supportive care
The purpose of supportive care is to normalize the temperature, stabilize the cardio-pulmonary status, correct hypoglycemia and prevent bleeding tendency (Table- 13.3).

**TABLE – 13.3 : Supportive care of a septic neonate**

1. Provide warmth, ensure consistently normal temperature.
2. Start intravenous line.
3. Infuse normal saline 10 ml/kg over 20-30 minutes, if perfusion is poor as evidenced by capillary refill time (CRT) of more than 3 seconds. Repeat the same dose 1-2 times over the next 30-45 minutes, if perfusion continues to be poor.
4. Infuse glucose (10 percent) 2 ml/kg stat.
5. Inject Vitamin K 1 mg intramuscularly.
6. Start oxygen by hood or mask, if cyanosed or grunting.
7. Provide gentle physical stimulation, if apneic.
8. Provide bag and mask ventilation with oxygen if breathing is inadequate.
9. Avoid enteral feed if hemodynamically compromised, give maintenance IV fluids.
10. Consider use of dopamine if perfusion is persistently poor.
11. Consider exchange transfusion if there is sclerema.

Antibiotic therapy
Antibiotic therapy should cover the common causative bacteria, namely, *Escherichia coli*, *Staphylococcus aureus* and *Klebsiella pneumoniae*. A combination of ampicillin and gentamicin is recommended for treatment of sepsis and pneumonia. In cases of suspected meningitis, cefotaxime should be used along with an aminoglycoside. Table 13.4 shows detailed guidelines about antibiotic therapy.

**TABLE 13.4 : Antibiotic therapy of neonatal sepsis**

**I. Septicemia or pneumonia**

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Each dose</th>
<th>Frequency</th>
<th>Route</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;7 days age</td>
<td>&gt; 7 days age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inj Ampicillin or</td>
<td>50 mg/kg/dose</td>
<td>12 hrly</td>
<td>8 hrly</td>
<td>IV</td>
</tr>
<tr>
<td>Inj cloxacillin</td>
<td>50 mg/kg/ dose</td>
<td>12 hrly</td>
<td>8 hrly</td>
<td>IV</td>
</tr>
<tr>
<td>AND</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inj Gentamicin or</td>
<td>5 mg/kg/dose</td>
<td>24 hrly</td>
<td>24 hrly</td>
<td>IV</td>
</tr>
<tr>
<td>Inj Amikacin</td>
<td>15 mg/kg/dose</td>
<td>24 hrly</td>
<td>24 hrly</td>
<td>IV</td>
</tr>
</tbody>
</table>
II. Meningitis

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Each dose</th>
<th>Frequency &lt;7 days age</th>
<th>Route</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inj Ampicillin and</td>
<td>100 mg/kg/dose</td>
<td>12 hrly</td>
<td>IV</td>
<td>3 weeks</td>
</tr>
<tr>
<td>Inj Gentamicin</td>
<td>2.5 mg/kg/dose</td>
<td>12 hrly</td>
<td>IV</td>
<td>3 weeks</td>
</tr>
<tr>
<td>OR</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inj Cefotaxime and</td>
<td>50 mg/kg/dose</td>
<td>12 hrly</td>
<td>IV</td>
<td>3 weeks</td>
</tr>
<tr>
<td>Inj Gentamicin</td>
<td>2.5 mg/kg/dose</td>
<td>12 hrly</td>
<td>IV</td>
<td>3 weeks</td>
</tr>
</tbody>
</table>

In late-onset sepsis to cover nosocomial staphylococcal infection, first line of antibiotics may comprise of cloxacillin 100 mg per kg per day and an aminoglycoside (gentamicin or amikacin). In nosocomial sepsis, antibiotic sensitivity pattern of organisms responsible for nursery infection should be known and the antibiotic therapy should be started accordingly. Usually *staphylococci* and gram negative bacilli (*Pseudomonas, Klebsiella*) should be covered using aminoglycoside (gentamicin or amikacin) and a third generation cephalosporin (cefoxaxime). For resistant *staphylococcal* infection, vancomycin (30 mg per kg per day) should be used.

On confirmation of sensitivity pattern, appropriate antibiotics are used singly or in combination. In a baby in whom the antibiotics were started on low suspicion, these may be stopped after 3 days, if baby is clinically well and the culture is negative. However, if a baby appears ill even though the cultures are negative, antibiotic therapy should be continued for 7 to 10 days as bacterial infection can occur with negative cultures.

The duration of antibiotic therapy in sepsis depends upon the pathogen, site of infection and the clinical response of the baby. 7-10 days therapy is required for soft tissue infections or pneumonia. Septicemia should be treated for 10-14 days. Meningitis should be treated for a period of 3 weeks. Deep-seated infections (Septic arthritis, osteomyelitis or ventriculitis) may require therapy for 3-6 weeks and are best managed at a higher centre. Change antibiotics if there is no improvement.

**Prevention of infections**

A good antenatal care goes a long way in decreasing the incidence, morbidity and mortality from neonatal sepsis. All mothers should be immunized against tetanus. All types of infections should be diagnosed early and treated vigorously in pregnant mothers. Babies should be fed early and exclusively with expressed breast milk (or breastfed) without any pre-lacteal feeds. Cord should be kept clean and dry. Unnecessary interventions should be avoided.
**Hand washing**
This is the simplest and the most effective method for control of infection in the hospital. All persons taking care of the baby should strictly follow hand washing policies before touching any baby. The technique of handwashing is given in skill section & shall be practiced at the skill station.

**Prevention of infection in hospital**
The nursery environment should be clean and dry with 24 hour water supply and electricity. There should be adequate ventilation and lighting. The nursery temperature should be maintained between 30 $\pm$ 2$^\circ$C. Overcrowding should be avoided. All procedures should be performed after wearing mask and gloves. Unnecessary invasive interventions such as needle pricks and setting of intravenous lines should be kept to the barest minimum. *The use of prophylactic antibiotics for prevention of nosocomial infections is strongly condemned.* They are not only useless but dangerous due to the potential risk of emergence of resistant strains of bacteria.
VIDEO ON PREVENTION OF INFECTIONS

This video will demonstrate the skill of proper hand washing for prevention of infection. It also includes the methods of disinfecting instruments and equipments in the nursery.
Disinfection of Equipment

1. Thermometer
   - Ideal to have separate for each baby
   - Wipe with alcohol after use
   - Store in bottle containing dry cotton
2. Resuscitation bag & mask
   Face mask (Disinfect daily and sterilize weekly)
   - Clean with detergent daily and after each use
   - Immerse in 2% glutaraldehyde
   - Rinse with clean water and dry with sterile linen (washed and sun dried)
   Resuscitation bag (Disinfect daily and sterilize weekly)
   - Dismantle parts
   - Clean with detergent
   - Immerse in 2% gluteraldehyde
   - Rinse with clean water and dry with sterile linen
   - Reassemble the parts
3. Laryngoscope
   - Wipe blade with 70% isopropyl alcohol after use
4. Suction apparatus
   - Suction bottle should contain 3% phenol or 5% Lysol
   - Suction bottle should be cleaned with detergent and changed daily
   - Change tube connected to bottle daily. Flush with water and dry. Soak for disinfection in 2% gluteraldehyde
   - Ideally suction catheter should be for single use.
5. Cots and mattresses
   - Clean everyday with 3% phenol or 5% lysol
   - Replace mattress whenever surface covering is broken
6. Incubator
   - Canopy and mattress should be cleaned with detergent solution and dried.
   - Through cleaning after dismantling every 7 days or after discharge of a baby.
7. Oxygen hood
   - Cleaned everyday of after each use with detergent
8. Rubber tubes and catheters
   - Disinfect in 2% gluteraldehyde
9. IV equipment
   - Disposable needles and infusion sets should be changed every 2-3 days
10. Feeding utensils
    - Clean with soap and water and boil in water for ten minutes

DRILL ON DISINFECTION OF COMMON NEWBORN CARE ARTICLES
Housekeeping Routines

1. **Floor & walls**
   Walls and sinks must be cleaned with 3% phenol or 5% Lysol at least once a day.
   Wet mopping of the room should be done at least 3 times a day.
   Sweeping and dry dusting be avoided.

2. **Disposal of waste and soiled lines**
   Closed bins should be available.
   The bin must be kept closed and emptied at regular intervals.
   Plastic bag can be used in dustbin and these bags should be sealed before they are removed.
   The dustbin should be cleaned and washed properly in running water every day.

3. **Cleaning of spills and splashed with suitable disinfectants**
   Use 10 gm of bleach in 1 ltr of water. Cover the area with solution for at least 20 minutes and mop with newspaper or cloth.

4. **Needles and sharp objects**
   Discard in polar bleach in a needle proof container.
   Cup, spoon and paladai should be boiled far at least 15 min before use.
   Feeding tubes should be preferably disposable.

   All individual item like stethoscope, measuring tape and probe tips should be cleaned with 70% isopropyl alcohol daily or whenever being used for another baby.

Disinfection is killing of the live micro-organism and this can be achieved by 20 minutes contact period with 2% gluteraldehyed.  
Sterilization is killing of live micro-organism along with spore. This can be done by 4 hour contact period with 2% gluteraldehyde.
Ensure that fumes of gluteraldehyde are aired out or rinsed completely with water from objects before using on infants because these can be damaging to the baby.  
2% gluteraldehyde once prepared is active for 14 days.

**DRILL ON WASTE DISPOSAL IN A NEONATAL UNIT**
EVALUATION

1. What are the common pathogens causing sepsis in neonates?
_________________________________________________________________
_________________________________________________________________
_________________________________________________________________
_________________________________________________________________
_________________________________________________________________

2. Enumerate the common clinical features of neonatal sepsis.
_________________________________________________________________
_________________________________________________________________
_________________________________________________________________
_________________________________________________________________
_________________________________________________________________

3. Interpret the following Sepsis screen(s) as positive or negative –
a. TLC -3800/cu mm, CRP Positive, ANC 2020, IT ratio NA, uESR 12 mm
b. TLC -9900/cu mm, CRP Positive, ANC 2020, IT ratio NA, uESR 12 mm
c. TLC -9200/cu mm, CRP Negative, ANC 1270, IT ratio NA, uESR 18 mm
d. TLC -8800/cu mm, CRP Positive, ANC 1920, IT ratio 0.02, uESR 14 mm

4. Write treatment orders for a 2000 gm 9 days old baby diagnosed to have sepsis today.
_________________________________________________________________
_________________________________________________________________
_________________________________________________________________
_________________________________________________________________
_________________________________________________________________

5. Describe measures to prevent infection.
_________________________________________________________________
_________________________________________________________________
_________________________________________________________________
_________________________________________________________________
_________________________________________________________________