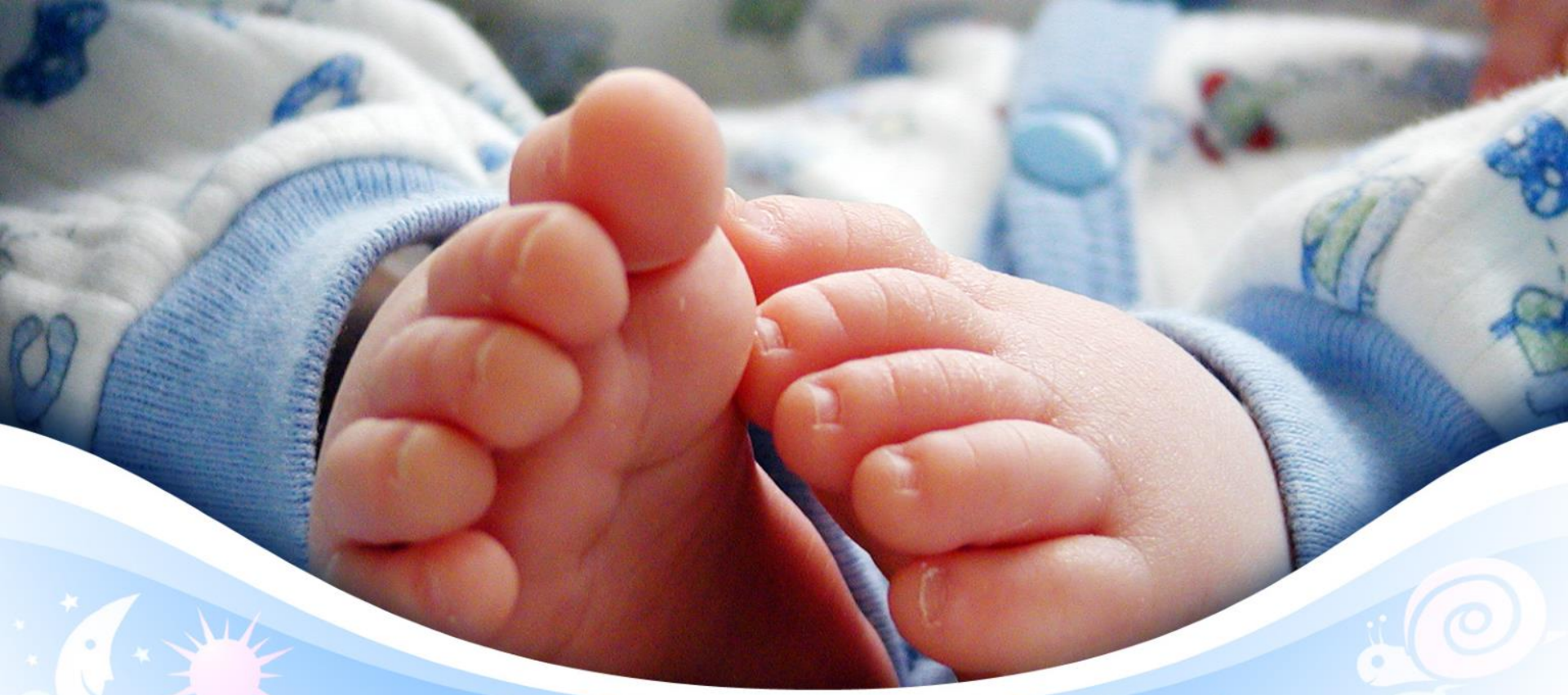

NEONATAL SEPSIS

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Background

- Neonatal sepsis :
  - Early-onset
  - Late-onset
- Early-onset : mostly premature neonates
  - Within 24 hours → 85%
  - 24-48 hours → 5%
  - 48-72 hours → < 5%
- Microorganisms from mother → acquires as passes thru birth canal

Microbes common in early-onset

- Group B *Streptococcus*
- *Escherichia coli*
- Coagulase-negative *Staphylococcus*
- *Haemophilus influenzae*
- *Listeria monocytogenes*
- Most common → pneumonia

Late-onset Sepsis

- Occurs > 4days after birth up to 90 days
- Microbes mostly causing :
  - Coagulase-negative *Staphylococcus* (CNS)
  - *Staphylococcus aureus*
  - *Escherichia coli*
  - *Klebsiella sp*
  - *Pseudomonas sp*
  - *Enterobacter sp*
  - *Candida sp*
  - Group B *Streptococcus* (GBS)
  - *Serratia sp*
  - *Acinetobacter sp*

Late-onset Sepsis

- Increase CNS (cogulase-negative *Staph*) sepsis
- Colonization of infant skin, respiratory tract, conjunctivae, GI tract, umbilicus → from environment
- Port of entry → catheters (vascular, urine), indwelling lines
- Contact with caregivers, healthcare workers
- Most common → bacteremia, meningitis

Staphylococcus epidermidis

- CN *Staphylococcus* → normal skin flora
- CNS → increasingly cause late-onset and nosocomial sepsis
- Adhere to plastic iv catheters, shunts → by bacterial polysaccharide capsules
- Capsules formed between microbes and catheter → prevent phagocytosis and C3 deposition
- Biofilm formed on catheters → slime produced by organisms extracellular material → acts as barrier to host defence and antimicrobial action

Cellular Immunity

- Neonatal polymorphonuclear (PMN) :
  - Deficient in chemotaxis, killing capacity
  - Decreased adherence to endothelial blood vessels → decreased ability to migrate into tissues
  - Failure to degranulate
  - Limited capacity of phagocytosis
  - Diminished bone marrow response → neutrophil reserves depleted
  - Impaired macrophage chemotaxis
  - Decreased cytokine production → decreased T-cell production → decreased B-cell stimulation and granulocyte proliferation

Humoral Immunity

- Some preformed Ig → nonspesific placental transfer from mother, mostly occur in older gestation
- Prematurity → increased low level immunoglobulin
- IgM synthesized in utero → 10 weeks gestation, generally low at birth
- IgG, IgE → synthesized in utero
- Most IgG → acquired from mother during late gestation
- IgA not secrete until 2-5 weeks post birth
- Response to bacterial polysaccharide Ag diminished during 2 years of age

Complement

- Complement production → as early 6 weeks gestation → varies widely
- Deficiencies in alternative pathway > classic pathway
- Mature complement activity → aged 6-10 months
- Decreased levels fibronectin → assist neutrophil adherence and opsonic function
- Reduced opsonic efficiency → Group B *Strep*, *E.coli*, *Streptococcus pneumoniae*

Early-onset Neonatal Sepsis

- Risk factors :
  - Maternal GBS colonization (untreated)
  - Premature rupture of membrane (PROM)
  - Prolonged rupture of membrane
  - Prematurity
  - Low birth weight
  - Maternal UTI (urinary tract infection)
  - Chorioamnionitis
  - Meconium staining
  - Birth asphyxia

Early-onset Neonatal Sepsis

- Microorganisme commonly associated :
  - Group B *Streptococcus* (GBS)
  - *E. coli*
  - Coagulase-negative *Staphylococcus* (CNS)
  - *H. influenzae*
  - *L.monocytogenes*

Late-onset Neonatal Sepsis

- Risk factors :
  - Prematurity
  - Central Venous Catheterization (CVC) > 10 days
  - Nasal cannula or continous positive airway pressure (CPAP)
  - H2-receptor blocker or proton pump inhibitor
  - Meningitis
  - GI tract pathology

Late-onset Neonatal Sepsis

- Microorganisms commonly associated :
  - GBS (36%)
  - *E.coli* (31%)
  - *Listeria sp* (5-10%)
  - *Streptococcus pneumoniae*
  - *Staphylococcus aureus*
  - *Staphylococcus epidermidis*
  - *H. influenzae*
  - *Pseudomonas sp*
  - *Klebsiella sp*
  - *Serratia sp*
  - *Enterobacter sp*
  - *Proteus sp*

Laboratory Studies

- Complete blood count :
  - Differentiate sepsis vs delivery stress (nonspesific)
  - Detect shift to the left
  - I/T ratio (immature vs total neutrophil) → Normal : -24hrs < 0,16 -60 hrs < 0,12

    Limited positive predictive value
- White blood cell counts :
  - Low positive predictive value → not infected with abnormal WBC
  - Normal WBC in 50% culture positive

Laboratory Studies

- Platelet count :
  - Thrombocytopenia < 100,000/uL → sign of sepsis, can last up to 3 weeks
  - Infant w/ sepsis → 10 – 60% thrombocytopenia
  - Mean Plt Volume (MPV), Plt Distribution Width (PDW) higher > after 2-3 days (newly formed)
- CRP (C-reactive protein) :
  - Rise secondary to → increased macrophage, IL-6, T-cell
  - Rise within 4-6 hrs of infection onset → abnormal rise 24 hrs → peak 2-3 days
  - Serial study → assess antibiotic response, relapse

Laboratory Studies

- PCT (Procalcitonin) :
  - Propeptide of calcitonin → produced in liver, monocytes
  - More sensitive > CRP
  - More spesific to bacterial vs viral
  - Useful after age > 24 hrs
  - Elevated in non sepsis → RDS (respiratory distress syndrome, infants of DM mother)
  - Rapid TAT (turn around time) < 2 hrs → clinical useful

Laboratory Studies

- Coagulation studies :
  - Signs of bleeding → gastric bleeding, intravenous puncture sites
  - To detect possibilities of DIC (disseminated intravascular coagulation)
  - Abnormalities in prothrombin time (PT), partial thromboplastin time (APTT), fibrinogen, D-dimer
- Immunoglobulin M :
  - Elevated IgM → suggest intra uterine infection
- Cytokine :
  - IL-6, IL-8 → useful in combination and serial measurements

Laboratory Studies

- CSF (Cerebrospinal fluid) analysis :
  - Elevated WBC predominan PMNs
    - GBS infection → 29% within normal range
    - Gram negative meningitis > 95% increased
  - Elevated protein level
    - Increased > 80% → Gram negative meningitis
    - Normal 50% → GBS meningitis
  - Decreased glucose concentration
    - Does not necessarily hypoglycemia
    - More severe → Gram negative infection, late-onset sepsis

Laboratory Studies

- Culture :
  - Aerobic culture → within 48 hours positive
  - Anaerobic culture → abscesses, bowel involvement, massive hemolysis, refractory pneumonia
  - Single site blood sampling → effective for neonates sepsis
  - Urine culture → useful in late-onset sepsis
- HSV (Herpes simplex virus) PCR testing :
  - Useful for negative culture, not responding to antibiotics

Should not be based on single test

- Based on :
  - Culture and microscopic results
  - Maternal risk factors
  - Intrapartum risk factors
  - Cerebrospinal fluid results
  - Complete blood count, differential count
  - CRP, PCT serial → to see trends
  - Clinical progress → w/ treatment for 7-10 days

Conclusion

- Management and diagnostic of Neonatal sepsis should consider many aspect such as :
  - Maternal risk factors
  - Intrapartum neonatus risk factors
  - Clinical signs of neonatus and mother
  - Etiology and patogenesis of neonatal sepsis

→ besides Laboratory examinations results

- Trends of Lab results is important to evaluate treatment or progress of clinical conditions

THANK YOU