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 > 4 days 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

dalima.astrawanata@gmail.com/HKKI/Juli/2017
**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 continuous 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 (non-specific)
  – Detect shift to the left
  – I/T ratio (immature vs total neutrophil) \( \rightarrow \)
    Normal: -24hrs < 0,16 -60 hrs < 0,12
    Limited positive predictive value

• White blood cell counts:
  – Low positive predictive value \( \rightarrow \) 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 $\rightarrow$ produced in liver, monocytes
  - More sensitive $>$ CRP
  - More specific to bacterial vs viral
  - Useful after age $>$ 24 hrs
  - Elevated in non sepsis $\rightarrow$ RDS (respiratory distress syndrome, infants of DM mother)
  - Rapid TAT (turn around time) $<$ 2 hrs $\rightarrow$ 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 predominantly PMNs
  - GBS infection $\rightarrow$ 29% within normal range
  - Gram negative meningitis > 95% increased
  - Elevated protein level
    - Increased > 80% $\rightarrow$ Gram negative meningitis
    - Normal 50% $\rightarrow$ GBS meningitis
  - Decreased glucose concentration
    - Does not necessarily hypoglycemia
    - More severe $\rightarrow$ 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