



## CHORIOAMNIONITIS (I.E. INTRA-AMNIOTIC INFECTION)

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# Goals and Objectives

- I.C.3a Know the significance of a maternal temperature increase during labor
- I.C.3b Know the complications and effects of chorioamnionitis in the mother and the fetus.
- XVII.A.3f Mycoplasma and ureaplasma 1. Know the epidemiology pathogenesis and prevention of perinatal infection with mycoplasma and ureaplasma
- Know the clinical manifestations diagnostic features, management and complications of perinatal infection with mycoplasma and ureaplasma

You have a 31 yo G3P2 mother who is A+, GBS unknown, serology negative mother who is 38 weeks who has been in labor. She had an epidural placed 1 hour ago and has rapidly progressed to fully dilated. The patient's nurse reports that she has developed a fever of 100.6 degrees Fahrenheit, HR is 110, and the fetal baseline HR is 165 with good beat to beat variability.

Based on current guidelines what do you do next?

- A. Allow patient to push and monitor for further signs of infection
- B. Start Ampicillin/Gentamicin and allow patient to start to push
- C. Start Ampicillin/Gentamicin and take back for an urgent C/S
- D. Start Ampicillin/Gentamicin/Clindamycin and allow to push
- E. Start Erythro and co-amoxiclav and take for an urgent C/S

The infant is born and is well appearing. The physical exam is unremarkable.

Based on current guidelines what do you do?

- A. Draw a blood culture, CBC, CRP, and start Ampicillin and Gentamicin
- B. Draw a blood culture, CBC, CRP, and start Ampicillin and Cefotaxime
- C. Draw a blood culture, CBC, CRP and monitor for signs and symptoms
- D. The baby is well appearing, continue to monitor closely for 48 hours

# Chorioamnionitis (Intra-amniotic Infection)

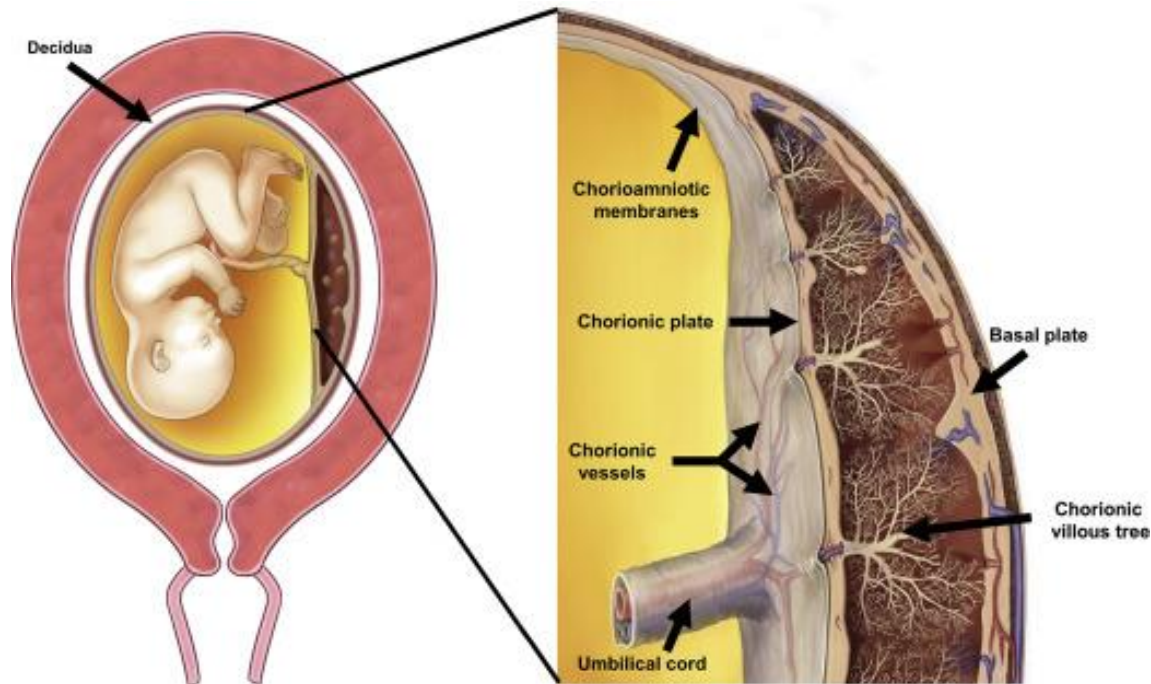
- Acute chorio is the most frequent diagnosis in placental pathology reports.
- Cause of neonatal and maternal morbidity and mortality
- Associations with
  - Preterm birth
  - EOS
  - BPD
  - ROP
  - PVL
- Lack of complete understanding due to lack of precision in the diagnosis

# Epidemiology

- 1-5% of all pregnancies
- Histologic chorioamnionitis ranges from 50-70% in VLBW to 10-15% in term infants
- 30% in PTL have histologic chorio
- 80% with PPROM

# Placental Anatomy

- 3 major structures
  - Placental disc
  - Chorioamnionic membranes
  - Umbilical cord



# Types of Chorioamnionitis

## Clinical Chorio

- Divided into:
  - Acute Chorio (symptomatic mother)
    - Strongly associated with EOS (RDS, CV instability)
    - Assoc w/ GBS, E. Coli, Strep viridans
  - Subclinical Chorio (PTL or asymptomatic)
    - May contribute to CLD and PVL
    - Assoc w/ Ureaplasma, Mycoplasma, Gardnerella

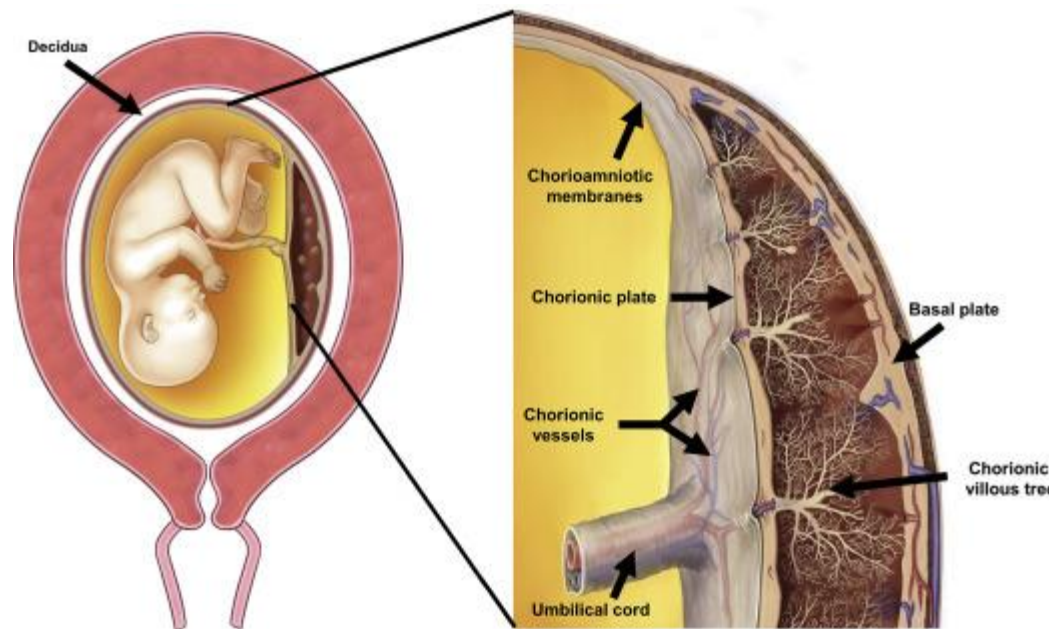
## Histologic Chorio

- 3x as common as clinical chorio (confirmed by amniotic fluid culture)
- Typically ascending infection
- Difficult to identify
  - Chronic and can be silent
  - Organisms are difficult to culture



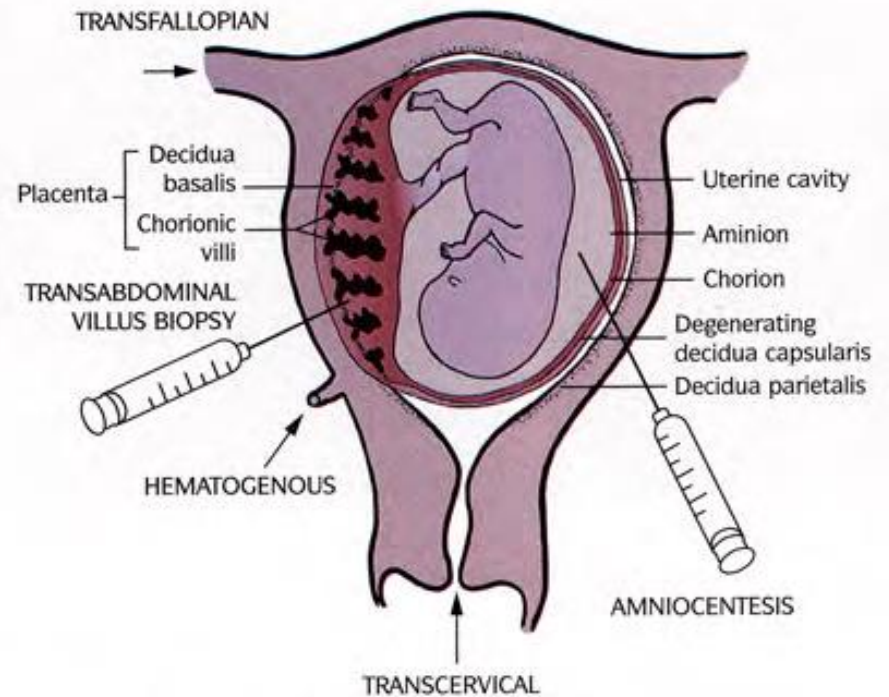
# Histologic Definition

- Neutrophil invasion into the
  - Chorio decidual space (between maternal and fetal membranes) OR
  - Fetal membrane OR
  - Placenta OR
  - Amniotic fluid OR
  - Umbilical cord OR
  - Fetus



# Pathogenesis

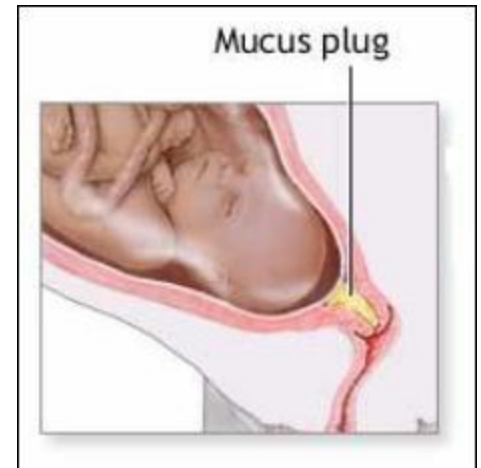
- Ascending – typical
- Retrograde through abdominal cavity
- Hematogenous from placenta
- Iatrogenic via amniocentesis



5.31. Routes of fetal infection.

# Protective barriers

- Cervical mucus plug
  - Anatomic barrier
  - Contains numerous antibacterial peptides with bactericidal activity
- Fetal membranes
- Placenta



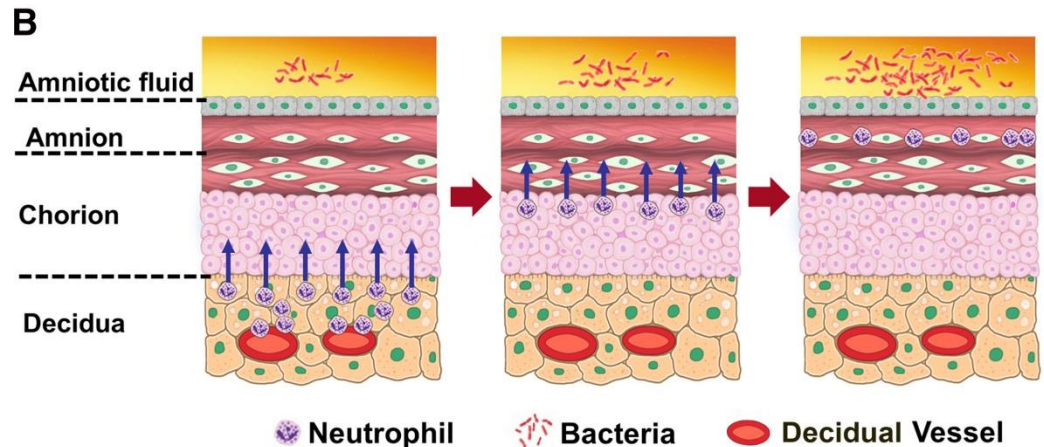
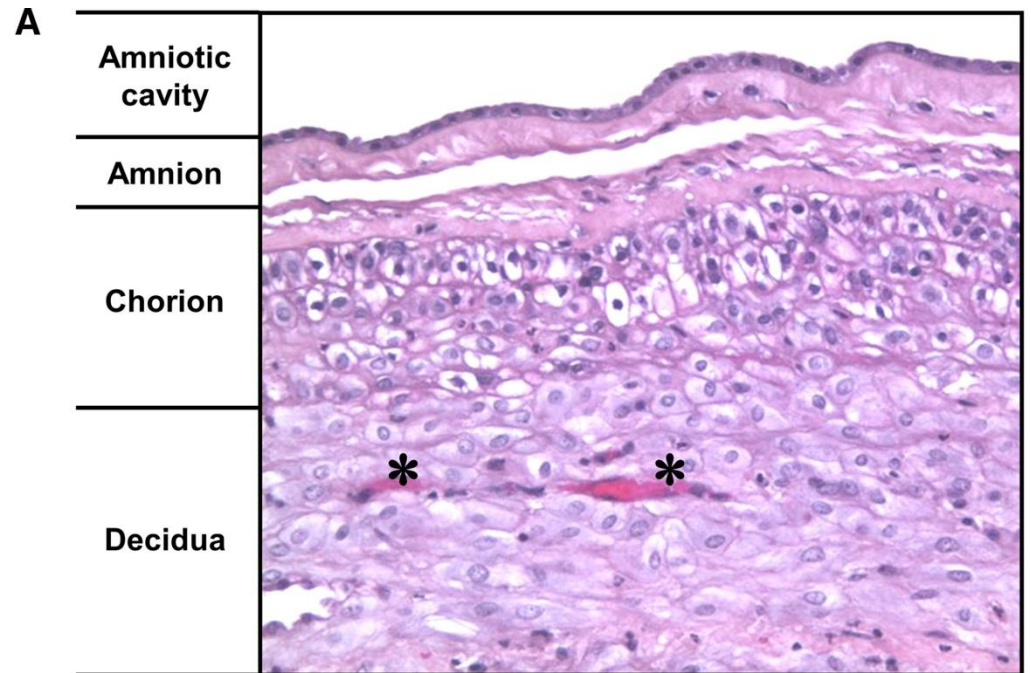
# Chorioamnionitis: Visual





# Pathology

- Maternal neutrophils migrate from the Decidua to the Amniotic Cavity
- Maternal inflammatory response
- 90% of neutrophils derived from the membranes are maternal



# Grading and Staging of Histologic Chorioamnionitis

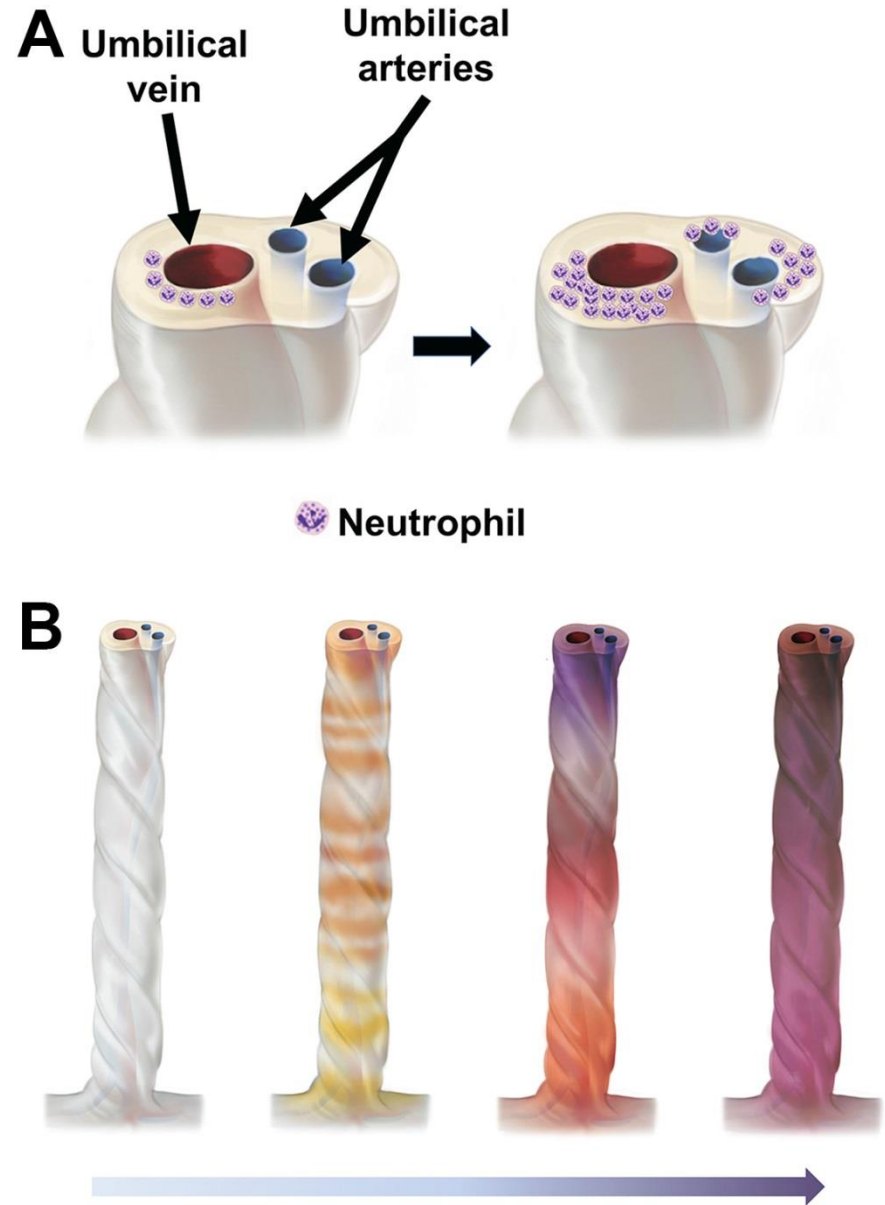
- Amniotic Fluid Infection Nosology Committee
  - Stage – progression based on anatomical regions infiltrated by neutrophils
  - Grade intensity of the acute inflammatory process at a particular site.
- Maternal inflammatory response vs fetal

# Maternal inflammatory response

- Stage I – neutrophils in chorion or subchorionic space
- St. 2 0 chorionic connective tissue and/or amnion or the chorionic plate
- St. 3 – necrotizing chorioamnionitis with amnion epithelial necrosis
- Grade 1 (mild to mod) – individual or small clusters of maternal neutrophils that infiltrate the chorion laeve, chorionic plate, subchorionic fibrin, or amnion
- Grade 2 (severe) – presence of 3 or more chorionic microabscesses (confluence of neutrophils)

# Funisitis

- St. 1 in umbilical vein (phlebitis)
- St. 2 when they are seen in the artery (arteritis)
- St. 3 when they progress to the Wharton jelly (funisitis)





# Fetal Inflammatory response

- Staging – refers to the location of neutrophil infiltration
  - More important than grading in the assessment of the severity.

# Clinical Chorioamnionitis (Diagnosis)

- Fever
- AND 2
  - Maternal Leukocytosis (>15,000 cells)
  - Uterine fundal tenderness
  - Maternal tachycardia (>100 bpm)
  - Fetal tachycardia (>160 bmp)
  - Purulent amniotic fluid
  - Foul smelling amniotic fluid

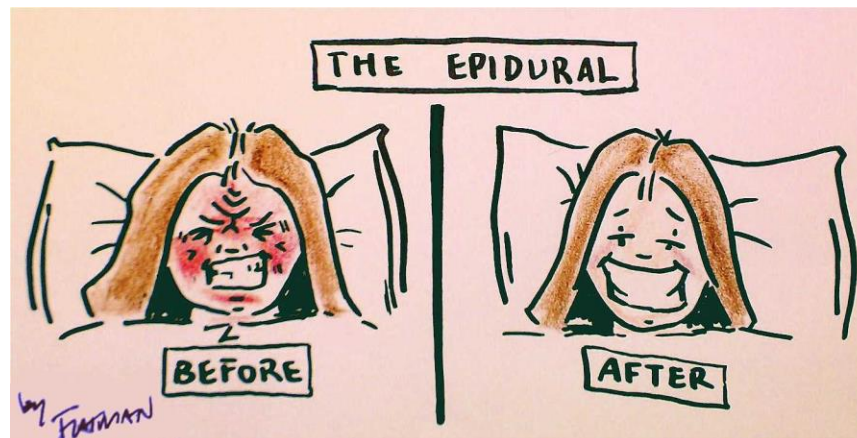


# Risk Factors

- Clinical Chorio
  - GBS colonization or bacteriuria
  - Nulliparity
  - Internal monitoring devices
  - Meconium stained amniotic fluid
  - Serial vaginal digital exams
  - Duration of active labor
  - Duration of ROM
  - Chorio in prior pregnancy
  - Single nucleotide PMNS in immunoregulatory genes (IL-10, IL-16)

# Sensitivity and Specificity of Diagnostic Criteria

- Much variation
- Fever – 42-95% sensitivity, 85% specificity and 61% accuracy
- Fever, maternal tachycardia and fetal tachycardia – 18% sensitivity, 98% specificity, and 52% accuracy.
- Leukocytosis in 70-90% of patients with clinical chorio.



# Microbiology

- Usually polymicrobial.
- Culture proven Chorio –
  - Ureaplasma (47%)
  - Mycoplasma (30%)
- Other organisms found include:
  - Gardnerella (25%)
  - Bacteroides (30%)
  - GBS (15%)
  - E. coli (8%)
- Anaerobes more in Pre term delivery

# Microbiology

- PCR techniques identify 30-50% more organisms than culture-based methods
- 5 phyla commonly present
  - Firmicutes, Actinobacteria, Bacteroidetes, Proteobacteria, Fusobacteria
- Differing patterns in PTL vs. PPRM

# Microbiology

- Ureaplasma commonly found in asymptomatic women (16-20 wk gestation undergoing amniocentesis).
- Many of these women developed a robust inflammatory response and went on to develop adverse pregnancy outcomes.
- May cause a much more robust inflammatory response than other pathogens

# Treatment





# Treatment

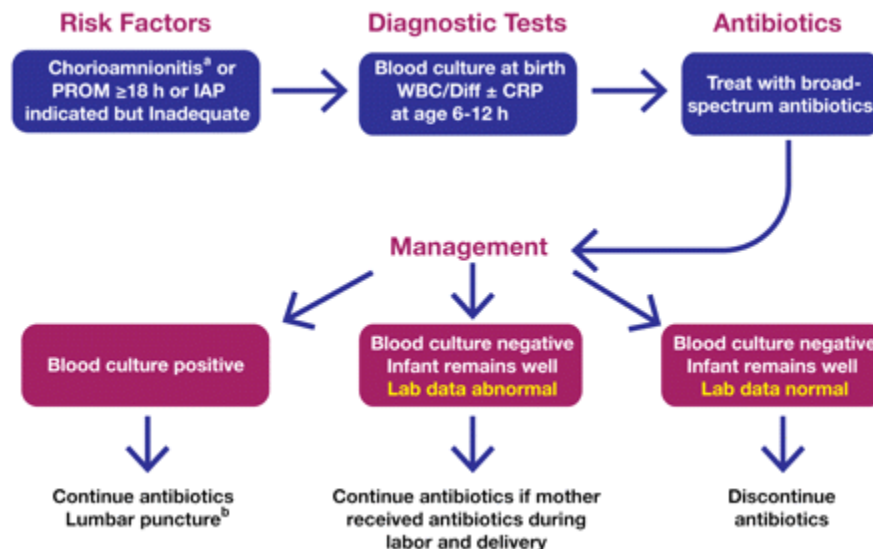
- Obstetric Management
  - Broad spectrum antibiotics (A/G).
  - Prompt delivery reduces both maternal and fetal morbidity
- Controversies
  - Length of treatment
  - Mycoplasma and Ureaplasma are not covered.
  - Antibiotic administration in PTL w/ intact membranes
  - Antibiotics in some circumstances may be harmful.

# Outcomes

- 2 fold increase in abnormal progression of labor, increased risk of C/S, postpartum hemorrhage, poor cervical dilation, and placental abruption.
- Surgical complications after c/s and chorio include endometritis, pelvic abscess, wound infection, thromboembolism, and bacteremia

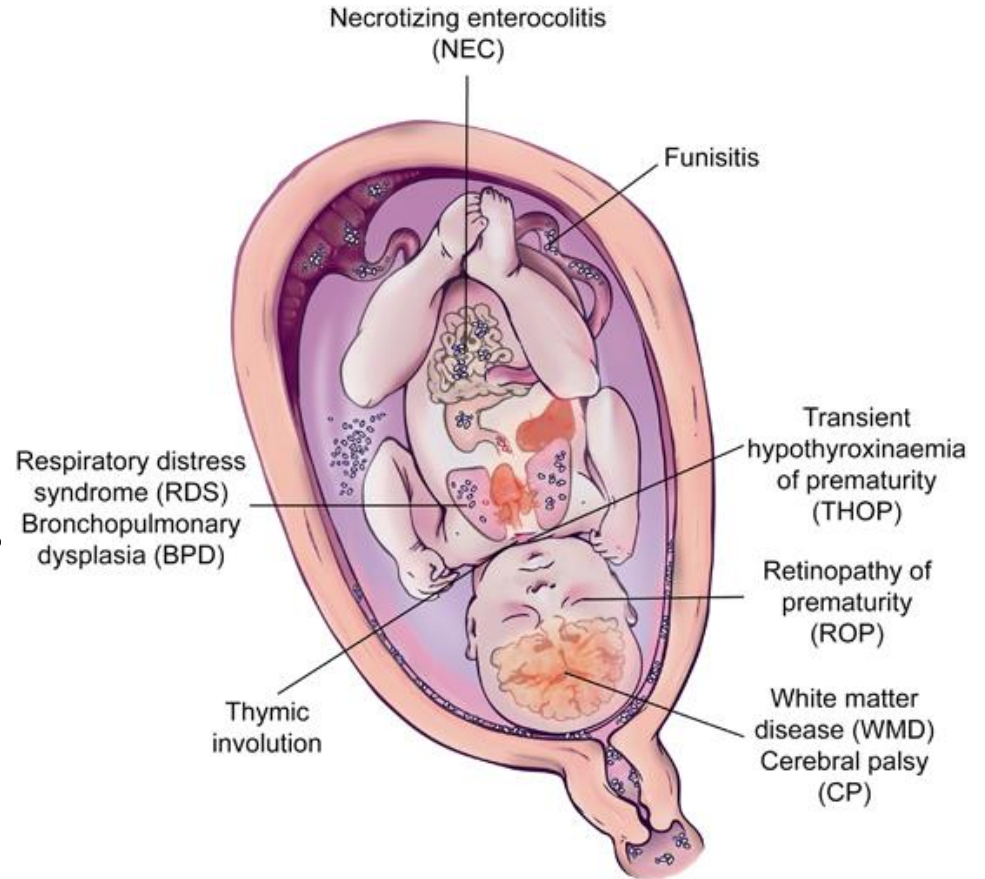
# Neonatal Treatment

- CDC and Committee on Fetus and Newborn (2012):
- Full sepsis evaluation and initiation of antimicrobial therapy (even in well appearing infants)



# Fetal Outcomes

- Depend on timing of the inflammatory process.
- Chorio is a risk factor for early-onset sepsis and hemodynamic instability.
- Subclinical infections have been associated with PVL, BPD, ROP, NEC, and thymus involution



# Chorio and Preterm Birth

- Important cause of Preterm birth.
  - Up to 25% of preterm births are caused by an intrauterine infection.
- The evidence includes:
  - Intrauterine infection in animals results in preterm delivery
  - Extrauterine infections (pyelo) are associated with preterm labor
  - In animal models , antibiotic treatment of intrauterine infections can prevent prematurity
  - Treatment of asymptomatic bacteriuria prevents prematurity
  - Administration of antibiotics to women with preterm premature rupture of membranes prolongs gestation
  - Microorganisms can be cultured from the placenta in a high percentage of women with preterm labor

# Chorio and Preterm Birth

- ? Adverse effects due to chorio versus prematurity
- Alabama Preterm Birth Study
  - PMN infiltrations in the free membranes, chorionic plate, and umbilical cord associated with positive intrauterine cultures and a fetal inflammatory response, but not with mortality or intraventricular hemorrhage.
  - Decreased incidence of RDS.
  - At 6 years there was strong association of neurodevelopmental outcomes with gestational age at delivery and caregiver IQ but not with in utero exposure to acute inflammation.

# Chorio and CLD

- Inflammation and CLD
- Association is indirect and based on experimental observations.
- Incidence of RDS is increased with clinical chorio but decreased with histologic chorio.
- Animal studies show bacterial cell wall products (LPS) and inflammatory mediators (IL-6) accelerate surfactant production.

# Clinical chorio and white matter disease

- Controversial
- Increased Cytokine levels in cord blood – Increased PVL
- ? Chorio and CP
- ELGAN study
  - 900 placentas were cultured and biopsied.
  - The Odds Ratios for ventriculomegaly and echolucent lesions were significantly increased with recovery of any aerobic or anaerobic organism.
  - Dose-response relationship between the number of species found and the risk of ventriculomegaly, echolucent lesions, quadriparesis, and diaparesis.
  - Those associations did not persist if there was only histologic chorioamnionitis without recovery of an organism.



# Acute chorio and neonatal sepsis

- Guidelines of antibiotics were based data that stated in newborns greater than or equal to 37 weeks with EOS, histologic chorioamnionitis was present in 90%.
- Adoption of intrapartum antibiotic prophylaxis in 1990s
  - 85% reduction in the rate of culture proven EO GBS sepsis
  - 0.2-0.25% of EOS in 1980s-90s to 0.08-0.1% in 2005 and 0.05-0.06% in infants greater than or equal to 35 weeks.

# Acute chorio and neonatal sepsis

- Risk is dependent on gestational age.
  - In 3 studies with 1892 pts. Infants greater than or equal to 35 weeks born to mothers with chorio the rates of EOS (culture proven) was only 0.47-1.24% (NNT 80-210)
  - In preterm infants 4.8-16.9% (NNT 6-21)

# Acute chorio and neonatal sepsis

- In 1 study of 1413 clinically well infants – no cases of EOS GBS sepsis.
- 1662 at-risk infants 1 instance of a positive blood culture (in a preterm infant).
- “These data make it apparent that it is time to abandon the policy of treating well-appearing infants greater than or equal to 34 weeks’ gestation because of chorioamnionitis alone”

# What is coming?

- Changes to definition and treatment
- Continued research
  - Healthy maternal-fetal microbiome
  - Abnormal colonization of the lower genital tract
  - Immune responses to specific pathogens
  - Risk factors that put women at increased risk for infectious complications of pregnancy
  - Preventive strategies