Neonatal Infections

Bacterial

viral

Early sepsis

1st 7 days

late sepsis

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Part I

Bacterial Infections in the Neonate

- 2nd M.C serious disease -after jaundice- is Prematurity, it has alot of complications.
- Are RDS occurs only with Premature babies, or may occur with full term babies?
  it mainly occur with Premature infants, but also may occur in full term babies in cases of GBS, it obscure the function of surfactant → so leads to RDS
- RDS is common as Prematurity.
- one of the most common causes of Prematurity occurs because of maternal infection (About 20٪), so prevention & treatment of it will decrease occurance of Prematurity = decrease RDS.
- Prematurity is the most serious disease in neonatal period

Bacterial Infections in the Neonate

- (GBS)
- (GC)
- Lesteria
- ureaplasma
- Chlamydia
- Gram negative sepsis

sever RDS is the first signs on baby then septic shock starts to occur

- Rapid fulminant sepsis
- inheaden function of surfactant
- about 70% of cases. of early sepsis

To Prevent maternal infection and Prematurity

Neonatal sepsis

any change from normal it is sepsis until proven otherwise

- An ill-appearing infants less than ~~1~~ 3 month with a positive blood culture
  - * Gold standard for diagnosis of sepsis
  - * don't depend on CRP to diagnose
- Incidence is 1-8/1000 live births
- One third of septic neonates develop meningitis
  - Early sepsis = 35% → But incidince of meningitis with early sepsis more dangerous and more complication
  - ⊛ in late sepsis 75%

3 not 1, because GBS may affect baby until 3 months.

⊛ most common cause of false -ve blood culture is Tecnigal problem

Routes of Infection

- Bacteria can infect a previously sterile fetus:
  - transplacental (syphilis, listeria, mycobacterium)
  - ascending immediately before delivery, (early onset GBS)
  - during passage through birth canal (gonococcal ophthalmia, E. coli) any Gram -ve organism cause rapid fulminant sepsis
  - *colonization at time of birth*, with subsequent late onset infection (GBS, listeria)

CLASSIFICATION OF SEPSIS

Early onset sepsis *Risk factors*

it is important to know because you will depend on it if there are no blood culture

- Sepsis during the first 7 days of life.
- Incidence is greater among preterm infants.
- ***Risk factors interconnected with vertical transmission of causative organisms include:***
  - Premature
  - prolonged rupture of chorioamniotic membranes (PROM).
  - Maternal colonization with group B beta-hemolytic streptococcus (GBS).
  - Intrapartum maternal fever.
  - Maternal UTI.
  - Preterm delivery.
  - Chorioamnionitis.
  - Meconium aspiration.

most important risk factors

Chorioamnionitis

excretion of meconium intrauterine and aspiration of it.

2 types of Pneumonia
- Chemical Pneumonitis - first 3 days
- Bacterial Pneumonia

Early onset sepsis *Causative organisms:*

EARLY

- GBS 69%
- GN bacilli 15%
- Enterococcus 3%
- Coag Neg staph 2%
- Staph Aureus 2%
- Other 8%
  - Gram-negative organisms: Escherichia coli is the most common. → in Jordan = Klebsella
  - Gram-positive organisms Group B beta hemolytic streptococcus is the most common and is associated with the rapid onset of fatal respiratory disease and shock.

Early onset sepsis

Presentation → most early symptoms is RDS

- ***Presentation signs are nonspecific and may include any of the following:***
  - Poor feedingLethargy
  - Temperature instability
  - Irritability
  - Apnea → Cessation of breathing >20s with CV manifistations
  - Respiratory distress
  - Hypo/hyperglycemia
  - Shock
  - Metabolic acidosis
  - Cyanosis and skin color change
  - Seizures + convulsions
  - Hypotonia
  - Gastro intestinal symptoms such as vomiting and diarrhea.
  - Jaundice.

Bad Prognostic sign

Bad Prognostic sign

Late onset sepsis → gradual deterioration and less severity, except of Pseudomonas

- Acute infections which occur from 8-28 days of life.
- Among healthy term infants this is much less than early onset sepsis.
- ***Risk factors:*** Late onset bacterial infections are closely related to
  - endotracheal intubations → most important risk factor for Pseudomonas late sepsis which causes Fulminant rapid sever sepsis
  - indwelling urinary and vascular catheters
  - Lack of enteric feeding → Feeding activate bacteria in the gut & prevent infection
  - Inborn error of metabolism
  - Exposure to broad spectrum antibiotics, which may alter normal flora and permit overgrowth and dissemination of fungal species and resistant bacteria.

Late onset sepsis *Causative organisms*

LATE

- GBS 11%
- GN Bacilli 15%
- Enterococcus 5%
- Coag Neg staph 43% → M.C
- Staph Aureus 4%
- MRSA 2%
- Fungal 2%
  - In contrast to early onset infections, gram-positive organisms predominate most of the cases.
  - Coagulase-negative Staphylococcus species (common skin flora) are most common isolates, especially among preterm infants.
  - Gram-negative bacteria e.g. E. coli and Klebsiella pneumoniae are also significant.
  - Fungal infections with Candida species occur frequently in small preterm infants.

Presentations

- In most cases of late onset, sepsis is gradual, rather than rapid.
  - Feeding intolerance.
  - Need for increased environmental oxygen
  - persistent tachycardia.
  - In Pseudomonas infections (ventilated infants) the presentation may include any signs mentioned in the early onset sepsis.

* How to dignose?

1. Clinical Presentation [se notes which written about it]
2. Full sepsis work up [CBC, I:T ratio, Platelets]

1- CBC:

① * normal readings WBCs → Adult = 4000-12000, Neonate = 4000-25000 → so neonate with 16000 WBCs shouldn't go to NIC !!

* WBCs lower than 4000 = sepsis + bad Prognosis [Leukopenia is bad prognosis]
* WBCs 25000-50000 = sepsis
* WBCs > 50000 = Leukomoid reaction + very bad Prognosis [may be ALL, septic shock, Leukomoid reaction, syphilis] congenital

2 I:T ratio [neutrophils]

[Immature : Total] neutrophils

* Normal : < 20 %
* I:T > 20% = septic shock
* I:T > 40% = impeding septic joint ??
* Any serious infection will affect bone marrow to produce immature neutrophils, which known as shifting to the left

3 Platelets:

Thrombocytopenia will occur, because Platelets is negative acute Phase reactants

● Note:

CRP is Positive acute Phase reactant, but when it indicates high index of suspecion ? we don't depend on absolute readings of CRP, we depend on titer of CRP.

* negative CRP: ≤ 5
* if CRP > 5 → Positive

} → but we don't depend on this readings, we depend on CRP titer
↳ if serial titer of CRP tend to increased → high index of suspecion of sepsis

* Half life of CRP = 6 hrs → so to see CRP titer you take it every 6 hrs to see tendincy for increasing, if increased → high suspecion of sepsis
* But first of all you start treatment by empirical antibiocs → if CRP titer decreased = sepsis + Good choice of antibiotics

So, CRP neither sensitive or specific, it is not diagnostic, but we use it for suspecion & follow up

* Pt. is 4hrs age has run fulminant sepsis, is it GBS or E coli? best steps to diagnose?

1 Do gram Staining :- if it Gram +ve → GBs, so give Penicilline & vancomycine
- if it Gram -ve → E. coli, so give cephalosporins

2 Latix agglutination test.

3 culture of all body fluids [Blood, urine, CSF → CSF: 1 analysis, 2 culture]

4 CXR.

1) Chemistry
2) cells → WBC: * normal adult : < 5, * normal Peds < 25 } → this will be normal with norm differentials
3) Protien → RBC: * normal adult : zero, * normal Peds : ≤ 100
4) sugar

because normal vaginal delivary may cause compression on head and sheering of blood
* if it > 500 → it may be sepsis with HSV

* HSV treated by acyclouir
* HSV sepsis very dangerous bec. it cause temporal lobe hemorrhage → temp. lobe epilipsy for ever & mental retardation

neonatal sepsis
Diagnosis

- **Clinical manifestations**:
  - early signs of sepsis in infants are usually ***nonspecific***
  - other early signs may include：
    - tachycardia
    - poor feeding
    - “just not looking well”
  - more obvious findings include：
    - shock
    - respiratory distress
    - apnea
    - Jaundice
    - lethargy
    - vomiting
    - diarrhea

neonatal sepsis
Diagnosis

50% of septic neonates don't have fever
* mainly occurs with full term babies, Preterm babies mainly has no fever

- ***Fever***:
  - more commonly in *term infants than preterm*
  - a temperature of 38.0ºC measured is the lower limit of the definition of fever
  - temperature instability is seen in only 50-60% of septic infants

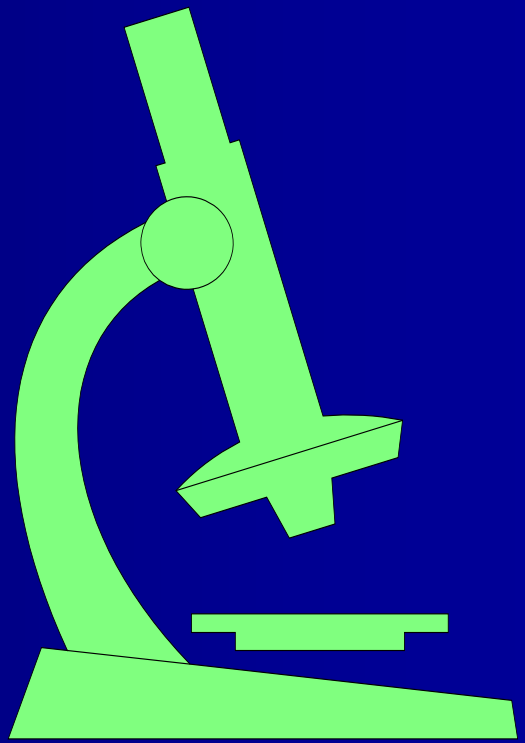
neonatal sepsis
Diagnosis

- ***Respiratory distress***
  - signs of respiratory distress are **common** in infected infants and include :
    - tachypnea, grunting
    - flaring, retractions
    - rales, decreased breath sounds
  - apnea can occur, and is usually a **later sign**
- ***Cardiovascular***
  - signs of CV effects can include :
    - Tachycardia
    - poor peripheral perfusion
    - Hypotension
- The *most reliable signs* of sepsis in infants ages 0 - 8 weeks:
  - change in *behavior, respiratory effort and peripheral perfusion*

neonatal sepsis

Diagnosis → Full septic work up

- ***Blood culture***:
  - the **most specific** method of diagnosis
  - usually positive by 48 hours
- ***Lumbar puncture***
  - approximately 1/4 of infants with sepsis have meningitis



Normal WBCs:
1) neonates → 4000 - 25000
2) adult → 4000 - 12000

neonatal sepsis

Diagnosis

Thrombocytopenia = negative Phase reactant

- CBC & DIFFERNTIAL → *if WBCs < 4000 with sepsis this is bad Prognostic feature.
  * more than 50000 WBCs, it may be leukemoid reaction
- I:T RATIO → determine neutrophils
- CXR
- URINE A&C
- CRP → Not diagnostic, only for index of suspecioun of sepsis

Risk Factors for Perinatal Infection

- Maternal chorioamnionitis
- Premature delivery
- Prolonged premature rupture of membranes
- Maternal colonization or infection of the anogenital tract with specific neonatal pathogens

Chorioamnionitis

- Obstetrical diagnosis:
  - Maternal temperature > (38C)
  - fetal tachycardia
  - uterine irritability or tenderness
  - foul smelling or cloudy amniotic fluid
- Treatment for mother includes antibiotics and delivery of infant

* It may lead to PVL (Periventricular Leuko malacia), healed by cysts and multiple cystic area which cause sever type of cerebral Palsy

Infants of Mothers With Chorioamnionitis

- Treatment ranges from close observation to empiric antibiotics
  - A minimum of screening labs (CBC and blood culture)
  - observation for at least 48 hours is reasonable
- All symptomatic infants require :
  - full sepsis work up
  - empiric ampicillin plus aminoglycoside or 3rd generation cephalosporin pending culture results

Preterm Labor

- Infection may be responsible for up to 20-40% of preterm deliveries:
  - Chorioamnionitis consistently increased
  - Increased clinical infections in preemies
  - Positive amniotic fluid cultures in 10-15% of preterm deliveries

Specific Recommendations

- **Preterm labor with intact membranes**:
  - Group B Streptococcus prophylaxis only
- **Preterm labor with ruptured membranes:**
  - Group B Streptococcus prophylaxis
  - If between 24-32 weeks:
    - Ampicillin plus erythromycin IV for 48 hours, then amoxycillin and erythromycin orally for up to 7 days
    - If vaginosis is present:
      - Substitute clindamycin for erythromycin

Potential Neonatal Pathogens

- Group B streptococcus (GBS)
- *Chlamydia trachomatis*
- *Ureaplasma urealyticum*
- *Neisseria gonorrhoeae*
- *Escherichia coli* and other gram negative enteric organisms
- *Listeria monocytogenes*
- *Trichomonas vaginalis*
- Bacterial vaginosis

"Early" vs "Late" neonatal sepsis

EARLY

- GBS 69%
- GN bacilli 15%
- Enterococcus 3%
- Coag Neg staph 2%
- Staph Aureus 2%
- Other 8%

LATE

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- Enterococcus 5%
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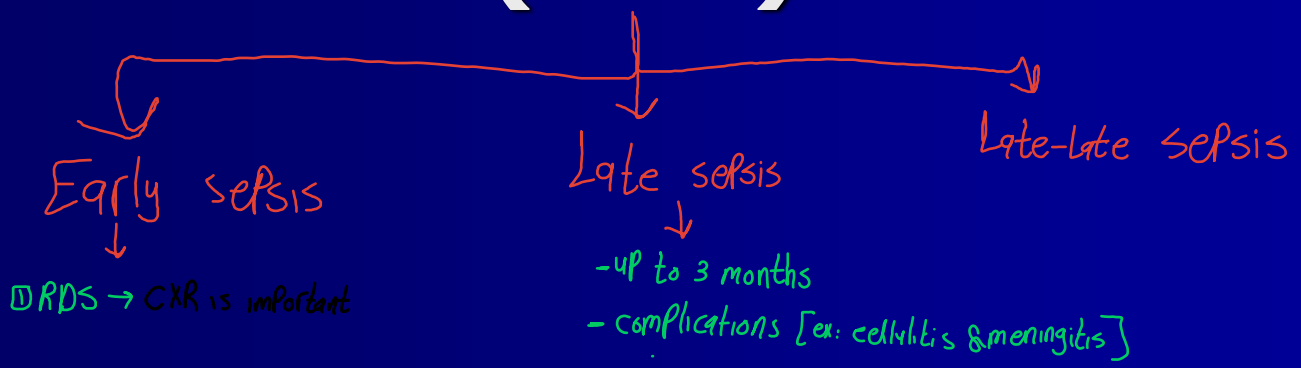
Group B Streptococcus (GBS)



* treatment & Dx + work up is same in all cases.

Group B Streptococcus (GBS)

- *Steptococcus agalactiae*
  - Normal flora of genitourinary tract, gastrointestinal tract, and occasionally the pharynx
  - Colonization of pregnant women ranges from 5-35%

Neonatal GBS Infection

- 1- 4 cases/1000 live births
- Transmission occurs *in utero or shortly after delivery*
- Nosocomial spread can occur via hand contamination

→ as same as risk factors of early sepsis, with adding of ① <20 yrs maternal age. ② Previous GBS child.

Risk Factors for Neonatal GBS Infection

- Rupture of membranes > 18 hours
- Maternal chorioamnionitis
- Maternal GBS bacteruria
- Maternal age < 20 years → static finding, not related to immunity
- Gestational age < 37 weeks
- Previous child with GBS
- Twin with GBS

Early Onset Infection

- Usually occurs within the 1st 24 hours
  - Range is 0-6 days
- 3/4 of all neonatal GBS infections
- Occurs in ~ 1 infant/ 100-200 colonized mothers
- Presenting symptoms:
  - Respiratory distress
  - apnea
  - shock
  - pneumonia
  - and *occasionally meningitis*

Late Onset Infection

- 3- 4 weeks of age
  - Range is *7 days - 3 months*
- Presenting symptoms:
  - Occult bacteraemia
  - meningitis
  - Rarely :
    - Cellulitis
    - osteomyelitis
    - septic arthritis

Diagnosis

- Cultures of :
  - blood
  - spinal fluid
  - Urine
  - pleural fluid
  - joint fluid as indicated
    - Organisms will appear as Gram positive cocci on Gram stain preparations
- Latex particle agglutination → about 1hr it may determine the microorganism.
  - Rapid antigen test

* Although not all microorganisms determined by latex agglutination test, but it give you a good clue

⑤ Prevention of GBS

Prepartum Chemoprophylaxis

- Current recommendations offer two different strategies :
  - Option I recommends : ALL women to have surveillance anogenital cultures at 35-37 weeks gestation
  - Option II recommends : a prevention strategy based on risk factors alone and routine cultures are not obtained

Option I: Recommendations for Intrapartum Antibiotics

- Positive GBS colonization documented by surveillance anogenital cultures at 35-37 weeks gestation with or without risk factors
- Unknown GBS status and presence of one of the following risk factors:
  - Gestational age < 37 weeks
  - Rupture of membranes > 18 hours
  - Maternal temperature > 38 → signs of chorioamnionitis

Option II

- Recommendations for intrapartum antibiotics based on presence of risk factors only
  - Gestational age < 37 weeks
  - Rupture of membranes > 18 hours
  - Maternal temperature >38
- No screening cultures are obtained

General Considerations

- Oral antibiotics are not effective for prophylaxis
- Regardless of the prevention strategy adopted, the following women should be treated:
  - *Any women with symptomatic or asymptomatic GBS bacteruria*
  - *Prior infant with GBS infection*

Drugs of Choice

Remember: no role of oral antibiotics, so all are IV.

- Penicillin G:
  - 5 million units IV, then 2.5 million units every 4 hours until delivery
- Ampicillin:
  - 2 grams IV, then 1 gram every 4 hours until delivery

give it for all patients and in all regimins because of Listeria

- Clindamycin or erythromycin acceptable in penicillin allergic patients

added if there are vaginal discharge

General Management of Asymptomatic Infants

- Routine prophylactic antibiotics in newborns of mothers who received intrapartum antibiotics is not recommended
- Routine cultures of infants to document colonization is not recommended
- As always, strict hand washing by hospital personnel is imperative

* Summary to next slide:

1 risk → work up + observe

2 risk → work up + treatment

No risk → No work up OR observe

Asymptomatic Infants with Intrapartum Antibiotic Prophylaxis (IAP)

→ depending on risk factors

- **< 35 weeks gestation and maternal IAP** (1 risk)
  - CBC, blood culture
  - and observe at least 48 hours → without treatment → not Protect
- **< 35 weeks and only 1 dose of antibiotics** (2 risk)
  - CBC, blood culture
  - and treat for 48h while under observation
  - D/C treatment at 48h if cultures negative
- **> 35 weeks and 2 or more doses of antibiotics given to mother:** (no risk)
  - No labs, observe for at least 48 hours
- **> 35 weeks and only 1 dose of antibiotics**: (1 risk)
  - CBC, blood culture,
  - observe for 48 hours

Symptomatic Infants

- Full sepsis work up regardless of risk factors
- Ampicillin plus an aminoglycoside pending cultures
- May use Penicillin G alone when GBS is isolated
- GBS bacteraemia: treat for 10 days
- GBS meningitis: treat for 14-21 days
- GBS osteomyelitis: treat for 4-6 weeks

→ Duration of treatment differs, but same treatment

Chlamydia

- The presence of *Chlamydia trachomatis* in the cervix is associated with *preterm deliveries*
- Neonatal *chlamydial conjunctivitis*
  - 1st few days to several weeks after birth
  - Not prevented by routine eye prophylaxis
- Pneumonitis occurs between 2-19 weeks after birth

Maternal Treatment Recommendations

- Treatment with erythromycin may prevent disease in infant
- routine screening in 1st and 3rd trimesters
- Treat partner
- screen for other sexually transmitted disease

Infant Treatment Recommendations

- Infants born to **untreated** mothers should be treated with oral erythromycin for 14 days
- Neonatal **chlamydial conjunctivitis**
  - Topical therapy is ineffective
  - Oral erythromycin 50mg/kg/day in 4 divided doses for 14 days
  - ~80% effective (may need 2nd course)

Ureaplasma

- Associated with lower respiratory tract infections and chronic lung disease in preemies
- Rarely causes CNS infection in newborns
- *No proven benefit* from prepartum or intrapartum antimicrobial therapy in colonized women

Gonorrhea (GC)

- Preterm deliveries
- Ophthalmia neonatorum:
  - Historically the leading cause of ***acquired blindness*** in the United States
- Less commonly:
  - Scalp abscess
  - vaginitis
  - bacteremia
  - arthritis
  - Endocarditis
  - meningitis

Control Measures

- All pregnant women should have routine cervical cultures for GC as part of their prenatal care
- Repeat culture in 3rd trimester for high risk women
- Positive cultures require work up for other sexually transmitted disease and work up and treatment of partner(s)

Treatment of Infant

- ALL infants should receive routine eye prophylaxis regardless of maternal history:
  - 1% tetracycline, 0.5% erythromycin (1% silver nitrate, of historical interest only)
- **Infants born to mothers with gonorrhea**:
  - Routine eye prophylaxis as before
  - Single dose of ceftriaxone 25-50 mg/kg (125mg maximum) or cefotaxime 100mg/kg

Ophthalmia Neonatorum

- Crystalline penicillin G 50,000-75,000 units/kg/day in 2 divided doses for 7-10 days
- Alternatives include ceftriaxone or cefotaxime in a single dose
- Local saline eye washes every 1-2 hours initially, then increased to every 6-12 hours as infant improves
  - Saline washes should be followed by topical administration of chloramphenicol or tetracycline

Disseminated Neonatal GC

- Arthritis or septicemia:
  - Ceftriaxone 25-50 mg/kg once per day for 7 days
  - Cefotaxime 50-100 mg/kg/day in two divided doses for 7 days
- Meningitis:
  - Ceftriaxone or cefotaxime for 10-14 days

Trichomonas

- May cause newborn vaginal discharge
- Inconsistently associated with preterm delivery
- Reasonable to screen and treat high risk or symptomatic mothers
  - Treatment is with metrinidazole

Bacterial Vaginosis

- *Gardnerella vaginalis*
- Clinical or laboratory confirmed bacterial vaginosis consistently associated with preterm delivery
- Pregnancy outcomes improved when treated with metronidazole (with or without erythromycin)

Gram Negative Bacilli

- Gram negative neonatal septicemia or meningitis cannot be differentiated clinically from other pathogens
  - Fever
  - temperature instability
  - apnea
  - cyanosis
  - jaundice
  - Hepatosplenomegaly
  - lethargy, irritability, anorexia
  - vomiting, abdominal distention
- Diagnosis by culture

Treatment
Gram Negative Bacilli

- **Empiric therapy**:
  - Ampicillin plus an aminoglycoside or cephalosporin active against gram negative bacilli (cefotaxime, ceftriaxone, ceftazidine)
- Septicemia: treat for 10-14 days
- Meningitis: treat for 21 days
  - Close follow up for hearing loss or residual neurologic abnormalities

Listeria

- Gram positive bacilli
- Food borne transmission via contaminated dairy products, meats and unwashed vegetables
- Asymptomatic fecal and vaginal carriage can result in :
  - neonatal infection
  - preterm delivery
  - spontaneous abortion
- Nosocomial outbreaks occur

Listeria Antibiotic Therapy

- The organism is sensitive to penicillin and ampicillin
- Combined therapy with an aminoglycoside is more effective
- Cephalosporins are not active against listeria
- Treat sepsis for 10-14 days and meningitis for 21 days

Listeria
Maternal Recommendations

- Antimicrobial therapy for known infection in pregnancy may prevent onset of neonatal disease
- Pregnant women should avoid unpasteurized dairy products and undercooked meats
- All vegetables should be thoroughly washed if eaten raw

Part II

Viral Infections in the Neonate

Vertically Transmitted Viral Infections in the Neonate

- Herpes Simplex Virus (HSV)
- Varicella Zoster Virus (VZV)
- Hepatitis B
- Cytomegalovirus (CMV)

Herpes Simplex Virus (HSV)

- Large, enveloped DNA virus
  - HSV type II (usually genital)
  - HSV type I (usually facial and oral)
  - Either type can exist at either location
- Transmission to the neonate occurs via the birth canal or by ascending infection
- Postnatal transmission can occur

(HSV)
Risk of Neonatal Infection

- Primary maternal infection
  - Risk of transmission to infant 33-50%
- Recurrent maternal infection
  - Risk of transmission to infant 3-5%
- Relative risk varies:
  - Vaginal delivery vs. Cesarean section
  - Length of time membranes ruptured

(HSV) Horizontal Transmission

- Mother or father with non-genital infection
  - hands, mouth, nipple
- Nosocomial spread from infected infant to non infected infant
  - usually via the hands of nursery personnel

(HSV) Clinical Manifestations of Neonatal Disease

- Symptoms usually occur from birth to two weeks but can occur as late as 4-6 weeks
- **Three clinical syndromes**:
  - Multiple organ, systemic infection
  - Localized central nervous system disease
  - Localized infection to skin, eyes (conjunctivitis, keratitis, chorioretinitis), and mouth

(HSV) Skin Lesions

- Vesicles may have already ruptured and may look more like impetigo or mild cellulitis
- Usually at presenting part of baby or site of instrumentation
- 1/3 of infants with systemic disease will lack skin lesions
- Another 1/3 will manifest skin lesions **AFTER** onset of systemic disease

(HSV)
Symptoms of Systemic Disease

- Appearance of sepsis:
  - Fever, lethargy, poor feeding
  - Must rule out bacterial infection as well
- Respiratory distress
- Seizures:
  - Tend to be recurrent and difficult to control
  - Spinal fluid shows elevated white blood cells (mostly lymphocytes), erythrocytes, and protein

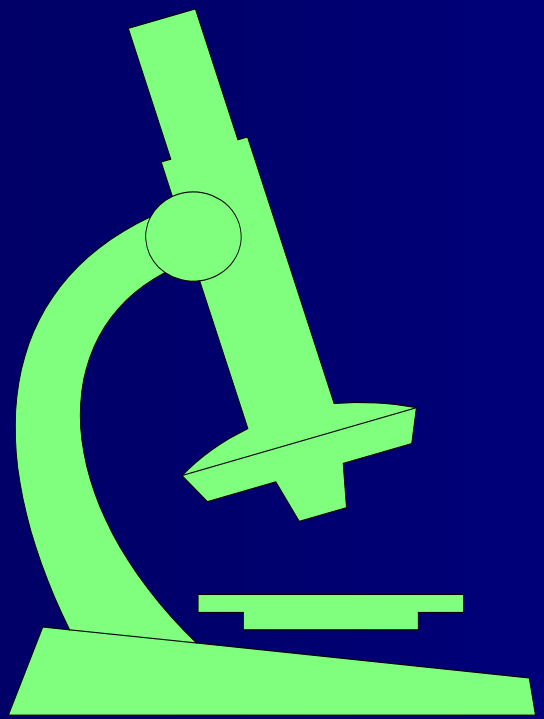
(HSV) Mortality and Morbidity

- Isolated skin, eye, or oral disease (20%)
  - 25% of infants will develop neurologic abnormalities despite lack of symptoms at presentation
- Central nervous system CNS disease (33%)
  - 17-50% mortality
  - 40% of survivors will have neurologic sequelae
    - microcephaly, spasticity, paralysis, seizures, deafness, blindness

(HSV) Disseminated Disease

- Without antiviral therapy:
  - 80% mortality
  - Most, if not all, survivors will have permanent neurologic sequelae
- With antiviral therapy:
  - 15-20% mortality
  - 40-55% of survivors will have permanent neurologic sequelae

Laboratory Diagnosis



- Tzanck smear
- Serology
- Viral cultures
- Polymerase chain reaction

Tzanck Smear

- Scraping from base of vesicle
- Positive slides will show multinucleated giant cells
- Quick screen but only 75% sensitive

Serology

- will demonstrate rising HSV antibody titers
- These rises occur late in the course of disease and are not particularly useful in making treatment decisions
- Recurrent infections in mother often do not produce a rise in titers

Viral Culture

- Still the gold standard
- Viral detection usually positive within 1-3 days of inoculation

Polymerase Chain Reaction

- Not widely available
- Relies on amplification of native HSV DNA…..
- Primary limitations include cost and possibility of false positives

Acyclovir

- Minimum effective dose in neonates is 30 mg/kg/day in three divided doses
  - Most experts recommend higher doses: 45 to 60 mg/kg/day
- Neonatal HSV should be treated with parenteral acyclovir rather than oral therapy
- Minimum length of therapy is 14 days
  - 21 day course may prove more effective

Special Considerations

- Intravenous acyclovir:
  - Ensure adequate hydration to prevent precipitation of drug in kidneys
  - Infuse drug over one hour
- Ocular disease:
  - Topical therapy with 1-2% trifluridine, 1% iododeoxyuridine, or 3% vidarabine
  - Requires acyclovir as well

Recurrent Skin Lesions

- Common in surviving infants
- Greater than three recurrences in the first 6 months of life correlates with adverse neurologic and/or ocular sequelae
- Role of prophylactic oral acyclovir not yet clear
- Prolonged oral acyclovir associated with neutropenia

(HSV) Recommended Obstetric Management

- All women in labor should be questioned regarding a history of HSV in themselves or sexual partners
- During the physical exam care should be taken to look for genital and non-genital lesions
- If Cesarean section is to be performed, it is best done within 4-6 hours of membrane rupture
- Scalp monitors should be avoided

(HSV)
Preterm Infants

- When a woman presents in
  - preterm labor
  - active HSV lesions,
  - AND ruptured membranes
    - ***the course is not clear:***
- Options include:
  - Allow labor to progress (*consider acyclovir for mother*)
  - Delay delivery and give *steroids for lung maturation*
  - *Immediate Cesarean section*

HSV
Management of Infants Born to Mothers With ***Active HSV***

- Viral cultures from the conjunctiva, naso-pharynx, mouth, stool, and urine at 24-48 hours of life
- Cultures sooner if ***symptomatic***
  - All of the above plus cultures of any *skin lesions* and the spinal fluid
- Always obtain cultures prior to starting empiric acyclovir

(HSV)
Vaginal Delivery Over a Primary Genital Infection

- 33-50% risk of infection in the newborn
- Risk is higher if :
  - premature
  - instrumentation during delivery, or if lacerations occur
- Most experts recommend empiric acyclovir treatment at birth
- Obtain viral cultures prior to starting therapy

HSV Vaginal Delivery Over a *Recurrent* Genital Lesion

- Risk of neonatal infection 5% or less
- No emperic therapy required
- Surveillance cultures at 24- 48 hours
- Careful examination for vesicles and systemic signs of infection

HSV
Delivery by Cesarean Section with Active Maternal HSV

- Obtain surveillance cultures at 24-48 hours of life
- Empiric therapy not recommended
  - Consider if primary lesion and membranes ruptured *greater than 6 hours prior to delivery*

HSV
Maternal History of HSV
No Active Lesions

- Not an indication for Cesarean section
- No special isolation required for infant
- Routine viral cultures not necessary

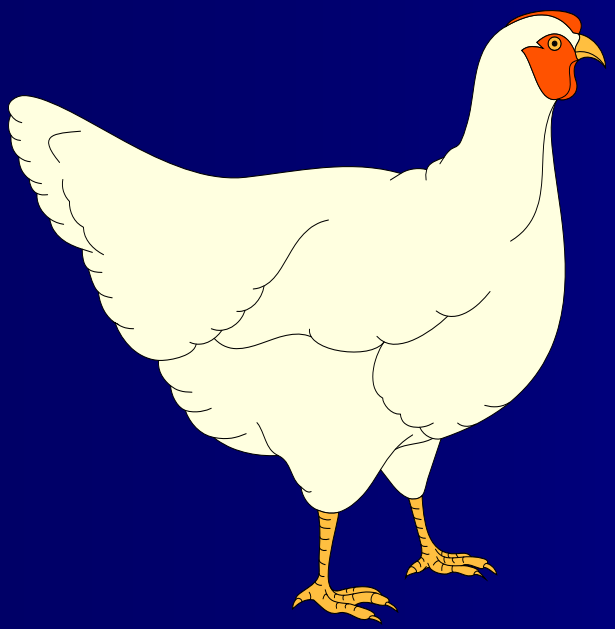
HSV
General Recommendations

- Infants exposed to active lesions should be isolated from other infants in nursery
- Parents should be instructed in *strict hand washing techniques*
- Parents with cold sores should not kiss infants until lesions healed
- Other non-genital herpetic lesions should be covered

HSV
General Considerations

- Breast feeding is NOT contraindicated unless there are lesions on the breast
- Elective circumcisions should be delayed at least one month in high risk infants
- Infection can manifest as late as 6 WEEKS!

(VZV)
Varicella Zoster Virus



- Causes chicken pox and shingles
- Humans are the *only known reservoir*
- *Highly contagious*
- Transmission is by contact or airborne droplets

(VZV) Epidemiology

- Exposure to a household results in infection in virtually all susceptible members
- Incubation period usually 14-16 days
  - Can range 10-21 days
- Patients are contagious from *2 days prior to and 5 days* after the onset of the rash
  - Immunocompromised patients contagious for duration of rash

(VZV) Congenital Varicella

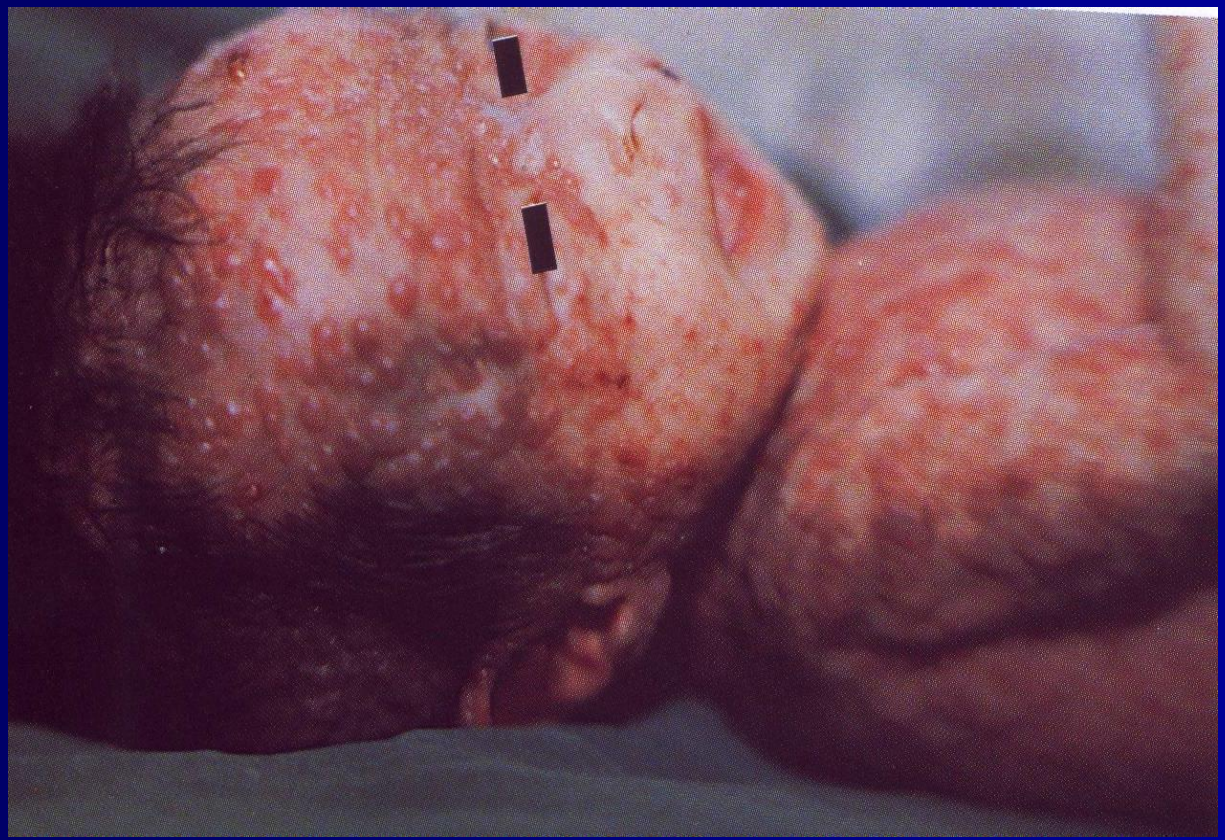
- Caused by maternal infection in the *1st trimester to early 2nd trimester*
  - Greatest risk between 13-20 weeks gestation

- Limb atrophy and scarring
- Chronic encephalopathy and cortical atrophy
- Chorioretinitis, micropthalmia, cataracts

(VZV)
Neonatal Varicella

- Transplacental exposure
- At risk when mother develops varicella *from 5 days prior to 2 days after delivery*
- Can manifest from 1-16 days after delivery
- High risk for disseminated varicella
  - Mortality rates as high as 30%
  - Prognosis much better if lesions develop greater than 5 days after delivery

(VZV)
Neonatal varicella



(VZV) Nosocomial Transmission

- Well documented in pediatric wards

- Rare in newborn nurseries
- High risk infants:
  - Premature infants (> 28 weeks gestation and > 1000 grams) whose mother has no history of varicella
  - Premature infants (≤ 28 weeks gestation or ≤ 1000 grams) *regardless of maternal history*

(VZV)
Varicella Zoster Immune Globulin
(***VZIG***)

- Provides passive immunity
- Not effective once active disease occurs
- Dosage: 125 units/10 kg
  - Minimum dose: 125 units
  - Maximum dose: 625 units
- Never administer intravenously
- Best given within 96 hours of exposure

Indications for VZIG (assuming significant exposure)

- Susceptible pregnant women
- Newborn with onset of maternal varicella within 5 days prior through 2 days following delivery
- Hospitalized premature ≥ 28 weeks gestation and no maternal history of varicella
- Hospitalized premature ≤ 28 weeks gestation or ≤ 1000 grams regardless of maternal history

VZIG

- Term infants exposed after 2 days of life are not at increased risk
  - VZIG not indicated
- All infants who receive VZIG should be in strict isolation
  - 50% of infants still develop varicella though disease tends to be milder
  - VZIG may prolong incubation as long as 28 days

Hepatitis B Virus (HBV)

- HBV is a DNA hepadenavirus
- The virus can be isolated from
  - blood
  - wound exudate
  - semen
  - cervical secretions
  - saliva
- It is not transmitted via the fecal oral route

HBV Serology

- ***HBsAg*** : (surface antigen)
  - Detection of acutely or chronically infected patients
- ***Anti-HBs*** : (antibody to HbsAg)
  - Patients with immunity following :
    - infection
    - or vaccination
- ***HBeAg*** : ('e' antigen)
  - Patients at increased risk for transmitting HBV

HBV Serology

- ***Anti-HBe*** : (antibody to HBe)
  - Low risk for transmitting HBV
- ***Anti-HBc*** : (Antibody to core antigen, HBcAg)
  - Evidence of acute or past infection
  - *Not present after immunization*
- ***IgM Anti-HBc***: (IgM antibody to HBcAg)
  - Acute or recent HBV infection

HBV
Risk to Newborn

- *Chronic HBV infection* occurs in 70-90% of infants delivered to mothers who are HBeAg positive
- Those who escape perinatal infection remain at high risk for horizontal transmission during the first 5 years

HBV
Chronic HBV Infection

- High risk of acquiring :
  - chronic active hepatitis
  - cirrhosis
  - primary hepatocellular carcinoma
- The risk of chronic infection is inversely proportional to the age at time of infection
- Asymptomatic HBV carriers coinfected with the Hepatitis D virus can develop fulminant liver disease

HBV
Hepatitis B Immune Globulin

- Reserved for *post exposure prophylaxis*
- Prepared from human donors with high anti-HBs titers
- Standard Immune Globulin (IVIG) ineffective

HBV
Hepatitis B ***Vaccine***

- Two commercial preparations available in the United States
  - Both products of recombinant DNA technology
- The current vaccines produce an antibody response (after 3 doses) in > 90% of adults and > 95% of infants and children

HBV
Routine HBV Vaccination

- First dose at 0-2 months of age
- Minimal interval between 1st and 2nd dose is one month
- Minimal interval between 2nd and 3rd dose is two months
- Minimal interval between 1st and 3rd dose is four months
- When 1st dose is given between 0-2 months, give 3rd dose after 6 months

HBV
Infants of ***HBsAg + Mothers***

- HBIG 0.5 ml IM
- Hepatitis B Vaccine 0.5 ml IM
  - Both should be given within 12 hours of birth
  - inject at different sites
- No contraindication to breast feeding

HBV
Unknown Maternal Status

- Obtain maternal blood for HBV serology
- Administer HBV vaccine while awaiting results
- If mother determined to be HBsAg +, then give HBIG as previously recommended
  - Dose should be given as soon as possible after results known and within 7 days of birth

HBV
Follow Up

- Vaccinate at 0, 1, and 6 months
- Infants given their first vaccine at < 2 kg, *should be given a 4th dose*

Cytomegalovirus (CMV)

- DNA herpes virus
- 1% of all newborns have CMV infection at birth and are excreting virus
- Virus is transmitted both vertically and horizontally

CMV
Modes of Transmission

- Transplacental
- Via birth canal
- Contact with infected urine or saliva
- Blood transfusions and organ transplants

- Breast milk
  - Most infants infected this way *do not manifest clinical illness*

CMV
High Risk Infants

- Severe disease in *~5% of in utero infections*
- Primary maternal infection at *highest risk* :
  - 10-20% will have mental retardation or hearing loss
  - Fetal risks greatest in first half of pregnancy
- Premature infants
- Immunosuppressed patients

CMV
Clinical Disease

- Most infants are asymptomatic
- Mild to moderate disease:
  - Petechiae
  - Hepatosplenomegaly
  - jaundice
  - intrauterine growth retardation
- Severe (Cytomegalic Inclusion Disease)
  - The above findings plus:
    - Microcephaly
    - brain damage,
    - cerebral calcifications
    - chorioretinitis

CMV Diagnosis

- Virus can be cultured from urine, pharyngeal cultures, leukocytes, human milk, semen, and cervical secretions, tissue and other body fluids
- Fourfold antibody titer rise
- Polymerase chain reaction
  - Proof of congenital infection requires cultures or serology within three weeks of birth

CMV Treatment

- Gancyclovir
  - Beneficial in treating retinitis
  - Limited data on congenital infections though potentially helpful
- CMV Immune Globulin
- Vaccine is currently experimental

CMV Prevention

- STRICT HAND WASHING by hospital personnel
- Use only CMV negative blood in premies and immune suppressed patients
- Human Milk
  - Donor milk should be frozen or pasteurized

Any Questions?