FUNGAL AND VIRAL INFECTIONS

DILLON S. JOINER, M.D.

LEARNING OBJECTIVES

- You will be better able to describe the epidemiology, clinical presentation, diagnosis, management, and prevention of infection among neonates with:
  - Herpesvirus infections including herpes simplex virus (HSV), cytomegalovirus (CMV), Epstein-Barr virus (EBV), and varicella-zoster virus (VZV)
  - Hepatitis A, B, C, D, E
  - Rubella
  - Respiratory syncytial virus (RSV)
  - Rotavirus
  - HIV
  - Parvovirus
  - Influenza
  - *Candida*

QUESTION TIME

What is the most common congenital viral infection in the U.S.?

A. Hepatitis C
B. Cytomegalovirus
C. Herpes simplex virus
D. Respiratory syncytial virus
E. Rubella

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CYTOMEGALOVIRUS (CMV)

Betaherpesvirus group, ds-DNA, ubiquitous. Persists after primary infection with shedding.

Chronic infection: necrosis in specific tissues. Reinfection with other strains can occur.

Transmission:

- Horizontally, vertically, via transfusion/transplant, rarely breastmilk
- Maternal 1° infection (< 10% mothers demonstrate flu-like symptoms, 40% lymphocytosis, 50% transaminitis)
  - 50% transmission rate and more severe neonatal disease
- Maternal 2° infection (reactivation)
  - 0.5% - 2% transmission rate and less severe neonatal disease

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True or false:

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CMV: PRESENTATION

0.15% - 2% of live infants have congenital CMV in the U.S.

Majority (85% - 90%) asymptomatic; ~10% symptomatic, which can include: IUGR, hepatitis, hepatosplenomegaly, pneumonitis, enteritis, encephalitis, bone marrow suppression, petechiae, purpura (“blueberry muffin rash”), chorioretinitis, **microcephaly, CSF pleocytosis, periventricular calcifications**

Late: sensorineural hearing loss (develops up to 3 years of age)

Bold above are predictors of poor prognosis.

CYTOMEGALOVIRUS

Diagnosis: shell vial culture (1-2 days), urine viral culture (2-6 weeks) or PCR (rapid). Must be identified by 21 days of age to be certain it is congenital.

Management:
If symptomatic: IV ganciclovir or oral valganciclovir before 1 month of age for 6 months to improve developmental/auditory outcomes.
If asymptomatic: treatment not currently recommended due to adverse effects (neutropenia in up to 20%).

Prevention: hand hygiene for all – standard precautions. Passive immunization of infected pregnant women with hyperimmune globulin (HIG) has been studied, but is not routinely advised due to no significant improvement in fetal transmission rate, and higher rate of obstetric complications.

QUESTION TIME

Which of the following is TRUE about neonatal HSV infections?

A. Approximately 20% of infants with HSV encephalitis have long term neurodevelopmental impairments
B. Mortality rate of those with disseminated disease approaches 50-70%
C. SEM (skin, eye, mucous membrane) disease is usually present at birth

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HERPES SIMPLEX VIRUS

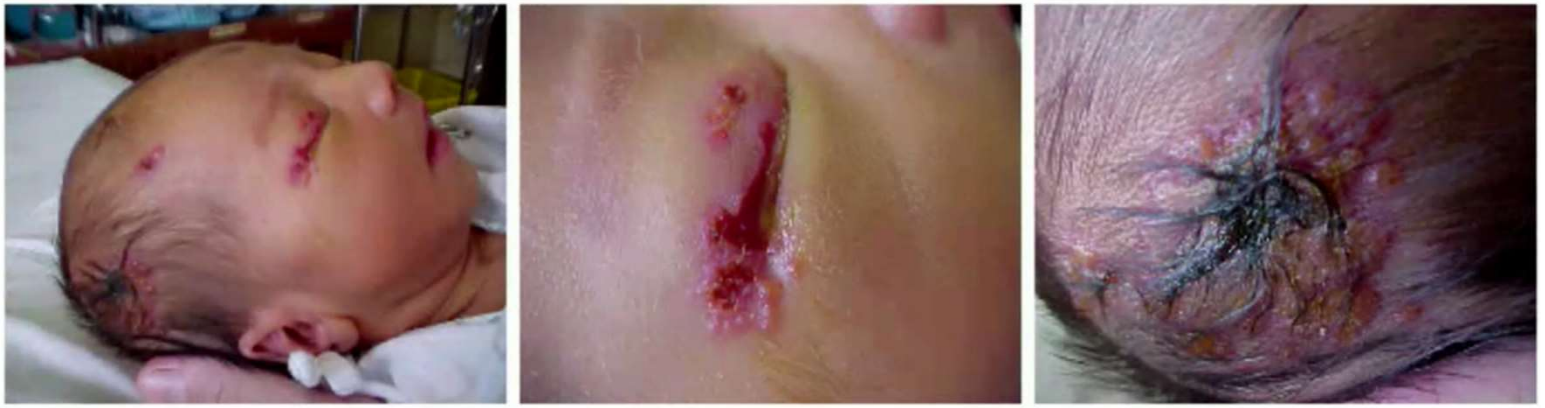
- Incidence 1/3000-1/20,000 live births
- HSV1 (oral), HSV2 (genital)
- HSV infection acquired during 3 time periods
  - Intrauterine (5%)
  - Intrapartum (85%)
  - Postpartum (10%)
- **20-40% are premature**
- ~75% due to HSV2
- 30-50% infants infected through birth canal in 1° infection
- 0-5% infants infected in 2° infection
- > 50% of infected infants due to 2° infections in mother
- 60-80% women asymptomatic when infant infected
- C-section without ROM decreases risk (< 4 hours)

HSV: PRESENTATION

- Majority of neonates asymptomatic at birth
- 3 patterns of illness from birth to 4 weeks
  - Skin, eye, and mouth (SEM) ~45%
  - CNS disease 30-35%
  - Disseminated disease 20%
    - Multiple visceral organs: lung, liver, adrenals, skin, eye, and/or brain

HSV: SEM DISEASE

- Presents at 5-12 days of life
- Single or grouped vesicles/pustules with red base, on “presenting part”
- Crusted papules or erosions
- Poor healing at scalp monitor or electrode sites
- Oral ulcers



HSV: CNS DISEASE

- ~16-19 days of life
- Often a component of disseminated disease
- CSF may be normal (virus isolated in less than half of cases), but may have pleocytosis, elevated protein, and (if late), evidence of hemorrhage
- Lethargy, poor feeding, irritability, focal or generalized seizures are presenting manifestations
- EEG nearly always nonspecific (but abnormal)
- ~50% of untreated die from neurologic deterioration 6 months after onset, and virtually all survivors have some severe sequelae

HSV: DISSEMINATED DISEASE

- Usually declared by 10-12 days of life
- Worst prognosis
- Presents with signs similar to bacterial sepsis/shock
- ~20% will not have any SEM findings to aid diagnosis
- Petechiae, purpura, DIC, GI bleeding
- Hepatomegaly, hepatitis, +/- jaundice
- Respiratory distress (pneumonitis, effusion) – marks even poorer prognosis
- 60-80% will have CNS involvement, but many die before these symptoms present
- Death usually occurs at ~2 weeks of age, ~1 week after symptoms

HERPES SIMPLEX VIRUS

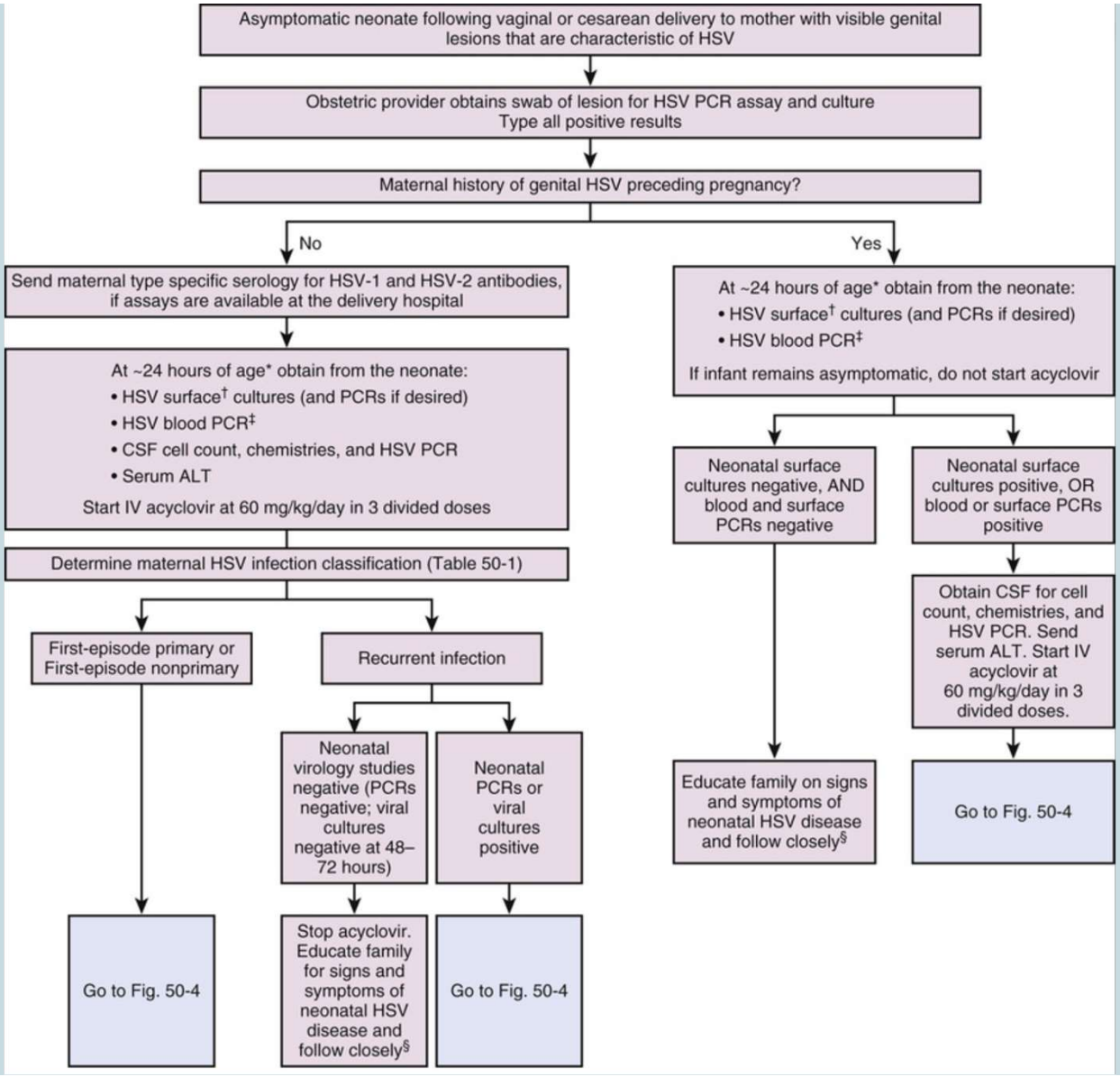
Diagnosis: cell culture, PCR assay of mucosal swab specimens obtained 12-24 hours after birth, PCR of CSF or whole blood

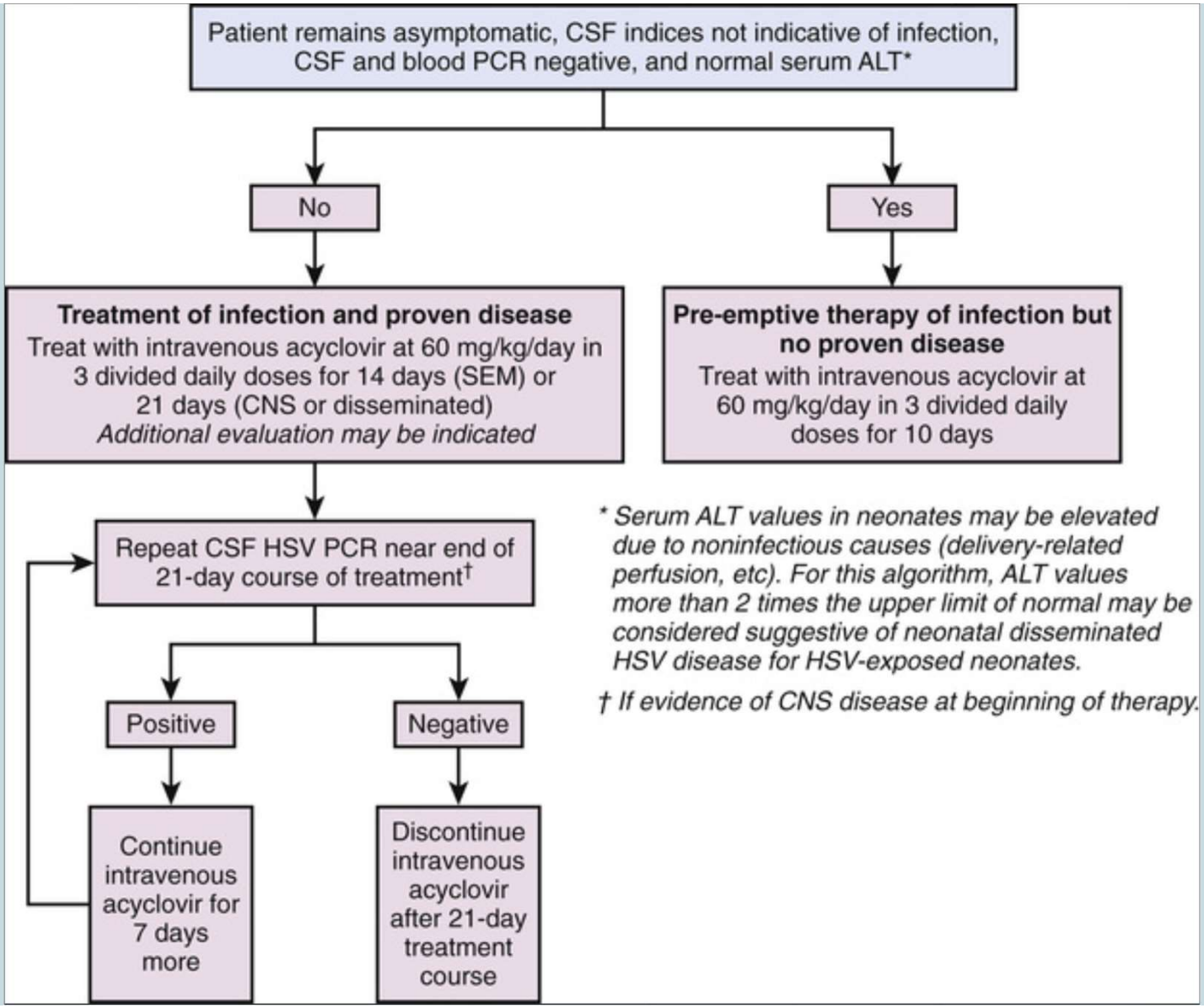
Management: Parenteral acyclovir, 60 mg/kg/day divided Q8H for 14 days (SEM) and minimum 21 days for CNS or disseminated infections. Topical ophthalmic medication (trifluridine, vidarabine) if ocular involvement. Monitor UOP and Cr for renal toxicity.

Prevention: Oral acyclovir suppressive therapy 300 mg/m^2 Q8H for 6 months following treatment of acute disease improves neurodevelopmental outcomes and decreases SEM outbreaks.
3^{rd} trimester prophylactic acyclovir decreases recurrence of lesions or detection of HSV, but no proof of decreased neonatal infection

HSV COMPLICATIONS

- Death
- Severe CNS disease, seizures
- Blindness
  - Cataracts secondary to eye involvement of SEM disease
  - Blindness as sequelae of CNS disease
- Fulminant hepatitis
- Recurrences through 1st year of life (especially of SEM disease)


Asymptomatic neonate following vaginal or cesarean delivery to mother with visible genital lesions that are characteristic of HSV
Obstetric provider obtains swab of lesion for HSV PCR assay and culture
Type all positive results
Maternal history of genital HSV preceding pregnancy?
No
Yes
Send maternal type specific serology for HSV-1 and HSV-2 antibodies, if assays are available at the delivery hospital
At ~24 hours of age* obtain from the neonate:
• HSV surface† cultures (and PCRs if desired)
• HSV blood PCR‡
• CSF cell count, chemistries, and HSV PCR
• Serum ALT
Start IV acyclovir at 60 mg/kg/day in 3 divided doses
Determine maternal HSV infection classification (Table 50-1)
First-episode primary or First-episode nonprimary
Recurrent infection
Go to Fig. 50-4
Neonatal virology studies negative (PCRs negative; viral cultures negative at 48–72 hours)
Neonatal PCRs or viral cultures positive
Stop acyclovir. Educate family for signs and symptoms of neonatal HSV disease and follow closely§
Go to Fig. 50-4
At ~24 hours of age* obtain from the neonate:
• HSV surface† cultures (and PCRs if desired)
• HSV blood PCR‡
If infant remains asymptomatic, do not start acyclovir
Neonatal surface cultures negative, AND blood and surface PCRs negative
Neonatal surface cultures positive, OR blood or surface PCRs positive
Educate family on signs and symptoms of neonatal HSV disease and follow closely§
Obtain CSF for cell count, chemistries, and HSV PCR. Send serum ALT. Start IV acyclovir at 60 mg/kg/day in 3 divided doses.
Go to Fig. 50-4


Patient remains asymptomatic, CSF indices not indicative of infection, CSF and blood PCR negative, and normal serum ALT*
No
Yes
Treatment of infection and proven disease
Treat with intravenous acyclovir at 60 mg/kg/day in 3 divided daily doses for 14 days (SEM) or 21 days (CNS or disseminated)
Additional evaluation may be indicated
Pre-emptive therapy of infection but no proven disease
Treat with intravenous acyclovir at 60 mg/kg/day in 3 divided daily doses for 10 days
Repeat CSF HSV PCR near end of 21-day course of treatment†
Positive
Negative
Continue intravenous acyclovir for 7 days more
Discontinue intravenous acyclovir after 21-day treatment course
* Serum ALT values in neonates may be elevated due to noninfectious causes (delivery-related perfusion, etc). For this algorithm, ALT values more than 2 times the upper limit of normal may be considered suggestive of neonatal disseminated HSV disease for HSV-exposed neonates.
† If evidence of CNS disease at beginning of therapy.

QUESTION TIME

Which of the following is TRUE about varicella infection?

A. All infants with congenital varicella syndrome should be placed in airborne and contact isolation
B. An infant born to a mother who develops varicella between 5 days before delivery to 2 days after delivery should receive VZIG
C. If a mother develops varicella during pregnancy, she should receive varicella vaccine and VZIG
D. All of the above

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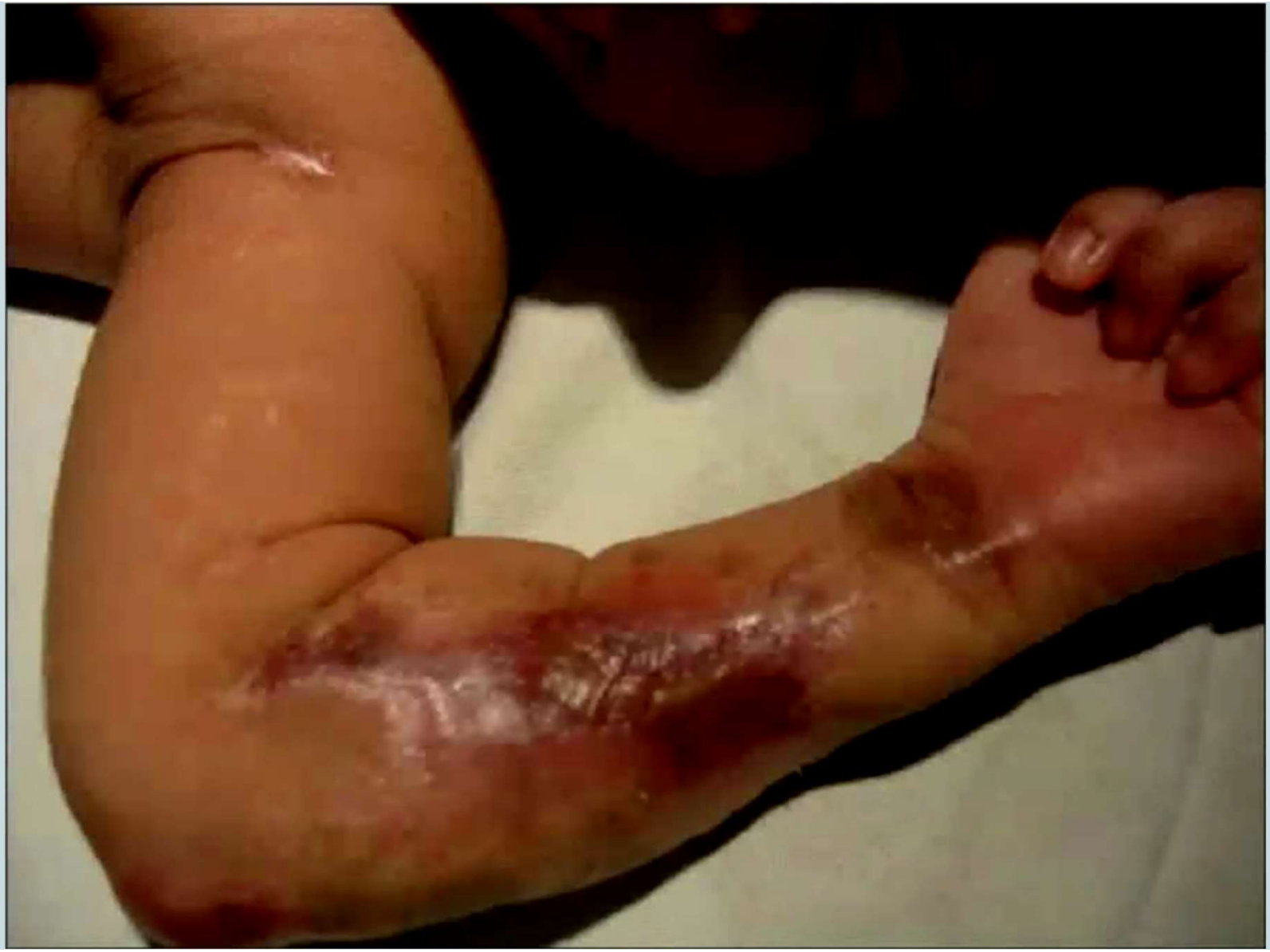
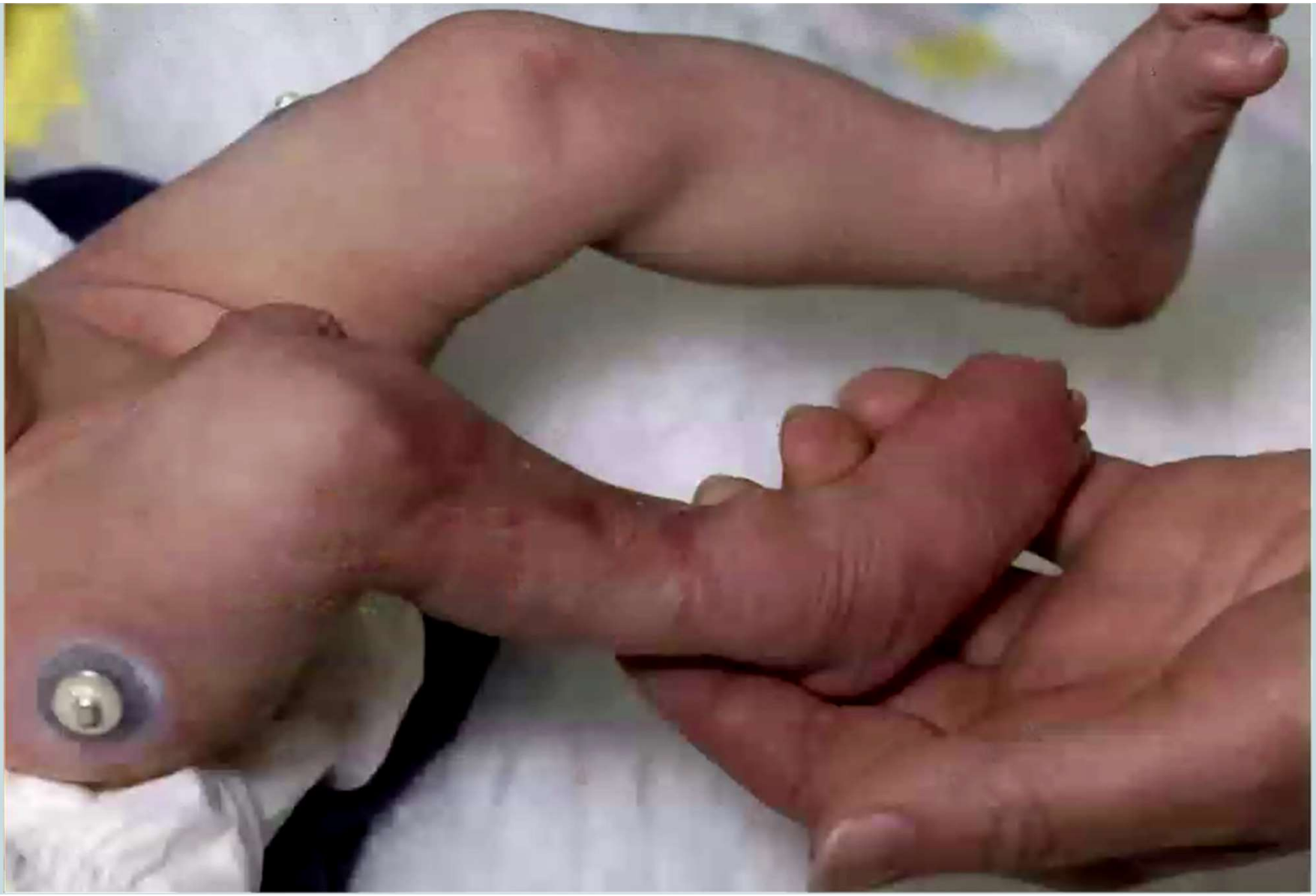
VARICELLA-ZOSTER VIRUS

- Tropism: skin, nerve, eye, and CNS
- Highly contagious, airborne
- Congenital infection very rare, more often perinatal/postnatal
- Transmitted person to person via direct contact, droplets, airborne
- More severe disease in infants < 1 month, pregnant women, adolescents, immunocompromised
- Incubation period of 10-21 days

VZV PRESENTATION

- **Congenital** – "Zoster in newborn"
  - Highest risk if maternal infection between 13-20 weeks of pregnancy
  - Overall risk of transmission from maternal infection during pregnancy < 1%
  - Chorioretinitis, microcephaly, IC calcifications, hepatosplenomegaly, thrombocytopenia; scarred skin and limbs with damaged nerves, muscle, and bone
  - Children infected with VZV in utero may develop zoster without extrauterine varicella
- **Perinatal**
  - Maternal rash 5 days before to 2 days after delivery
  - High case fatality rate due to disseminated varicella
  - Insufficient time for protective antibodies to cross to fetus
  - Rash, sepsis, encephalitis, pneumonitis, hepatitis





VARICELLA-ZOSTER VIRUS

- **Diagnosis:** VZV PCR of lesion/CSF, DFA – scraping, cells Tzanck prep. Serology (IgM/IgG).
- **Management:** Acyclovir – "high dose": 20 mg/kg Q8H. VZIG or IVIG – targeted for exposure
  - Exposure from mother 5 days prior-2 days post delivery
  - Premature < 28 weeks regardless of maternal immune status
  - > 28 weeks with no maternal immunity
- **Prevention:** VZV vaccine prior to pregnancy (95% protection), VZIG if 3-5 days of maternal exposure. Acyclovir for pregnant women with varicella in 2nd – 3rd trimesters. Isolate mother from infant if active lesions at delivery (airborne and contact). No isolation for embryopathy (no active lesions).

EPSTEIN-BARR VIRUS

- **Epidemiology:** Humans only known reservoir, 90% adults infected; close personal contact (saliva), blood transfusion, transplantation; incubation period 30-50 days. Intrauterine infection not documented.
- **Presentation:** Fever, exudative pharyngitis with petechiae, lymphadenopathy, hepatosplenomegaly, EBV-associated lymphoproliferative disorders.
- **Diagnosis:** Serological testing and PCR of immunocompromised
- **Management:** Symptomatic
- **Prevention:** Hand hygiene for all – standard precautions

HEPATITIS A VIRUS

- **Epidemiology:** ssRNA. Person to person; fecal-oral; vertical transmission rare. Incubation period of 4 weeks.
- **Presentation:** Acute, self-limited fever, malaise, anorexia, and jaundice. No increased risk of congenital malformations
- **Diagnosis:** anti-HAV IgM (up to 3 months)
- **Management:** Supportive care
- **Prevention:** Contact precautions for 1 week following symptom onset. Some experts would administer IGIM (0.02 mL/kg) to infant if maternal symptoms began between 2 weeks before and 1 week after delivery. Efficacy has not been established.

HEPATITIS B VIRUS

- **Epidemiology:** dsDNA. Transmitted via blood and body fluids. Up to 90% infected in the first year of life will develop chronic HBV. Immune tolerant "silent" phase for years, some with growth impairment.
  - Risk of neonatal HBV from HBsAg+ and HBeAg+ mother: 70-90%
  - Risk of neonatal HBV from HBsAg+ and HBeAg- mother: 5-20%
- **Presentation:** Subacute (nonspecific) to clinical and fulminant hepatitis. Extrahepatic manifestations.

HBV SEROLOGIES

Antigens

- HBsAg (vaccine)
- HBcAg (C is “covert” – not in circulation)
- HBeAg (E for “enfectivity”, rapidly replicating)

Antibodies

- C – true exposure, anti-HBc IgM and IgG
- S – only in acute and chronic infection

	S antigen	E antigen	C antibody	S antibody
Acute infection	+	+	+	
Window phase			+	
Chronic infection	+	+	+	
Recovery			+	+
Immunization				+

HBV MANAGEMENT

- **HBsAg negative:** universal immunization of all term infants at birth and preterm infants when 2 kg, at 30 DOL, or discharge
- **HBsAg unknown:**
  - Hep B vaccine within 12 HOL
  - Test mother as soon as possible
- **HBsAg positive:**
  - Infant > 2 kg: HBIG before 7 days of life
  - Infant < 2 kg: HBIG before 12 hours of life
  - 3 additional doses of monovalent Hep B vaccine when neonate 1 month chronological age
- Early active and passive HBIG and Hep B vaccine (within 12 HOL) prevents 95% of perinatal HBV infections
- No therapy for acute HBV; screened periodically and referred; goal to prevent progression to hepatocellular carcinoma

HBV MANAGEMENT

Maternal HepB status	Baby with BW ≥ 2 kg	Baby with BW < 2 kg
HepBsAg NEGATIVE	HepB vaccine soon after birth 2 more doses to complete series	Delay HepB vaccine until 2 kg or 30 days or discharge (whichever is 1st) If < 2 kg at 1st dose, 3 additional doses needed to complete series
HepBsAg UNKNOWN	TEST MOM HepB vaccine ≤ 12 hours HBIG by 7 days of age if + *Complete vaccine series*	TEST MOM HepB vaccine ≤ 12 hours HBIG within 12 hours *Complete vaccine series*
HepBsAg POSITIVE	HepB vaccine ≤ 12 hours HBIG by 12 hours (different site than vaccine) Test after vaccine series (9-18 months)	HepB vaccine ≤ 12 hours HBIG within 12 hours (different site than vaccine) Test after vaccine series (9-18 months)

HEPATITIS C VIRUS

- **Epidemiology:** ssRNA. Bloodborne in adults and maternal-fetal transmission in children. Chronic infection. 6 HCV genotypes with multiple subtypes. Seroprevalance in U.S. pregnant women 1-2%, risk of perinatal transmission 5-6%; 10-20% if HIV coinfection, occurring only from women who are HCV RNA+ at delivery.
- **Presentation:** Mild and insidious; jaundice < 20%, less hepatitis than HBV
- **Diagnosis:** HCV IgG serology and NAA to detect HCV RNA – may be performed at 1-2 months of age; passively acquired maternal antibody may persist in infants up to 18 months
- **Management:** Antivirals aimed at inhibiting HCV replication and eradicating infection
- **Prevention:** Standard precautions

HEPATITIS D VIRUS

- **Epidemiology:** defective RNA, needs HBsAg for surface coat, converting HBV into more rapidly progressing or fulminant disease. Present worldwide. Acquisition by parenteral, mucous membrane, or percutaneous.
- **Presentation:** Mild and insidious; jaundice < 20%, less hepatitis than HBV
- **Diagnosis:** Anti-HDV IgG antibodies in a person with HBV; HDV RNA if IgG positive
- **Management:** Pegylated IFN-α for 1+ years or combination therapy
- **Prevention:** Standard precautions. HBV immunization protects against HDV infection.

HEPATITIS E VIRUS

- Rare in the U.S.
- High maternal mortality
- Increased risk of stillbirth and premature delivery

RUBELLA

- **Epidemiology:** RNA, humans only source; transmitted through direct or droplet contact with nasopharyngeal secretions. Communicability few days before to 7 days after rash onset. Infants may shed and transmit for 1 year following infection.
- **Presentation:** Many subclinical; generalized erythematous maculopapular rash, lymphadenopathy, mild fever (infant). Transient polyarthralgia and polyarthritis (mother). Encephalitis and thrombocytopenia are complications.
- **Diagnosis:** Rubella IgM from birth to 3 months of age (false positives occur) and stable or increasing rubella IgG first 7-11 months of life. Isolation of virus from throat, NP, or urine in cell culture
- **Management:** Supportive
- **Prevention:** Droplet precautions until 7 days after rash onset. Contact precautions for known/suspected CRS until 1 year of age or cultures obtained 1 month apart after 3 months of age are negative. MMR immunization.

CONGENITAL RUBELLA SYNDROME

- Maternal rubella during pregnancy: miscarriage, fetal death, or congenital manifestations (hydrops)
- Congenital defects occur in up to 85% if maternal infection during 1st trimester; 50% if infection 13-16 weeks; 25% if infection near end of 2nd trimester
- Ophthalmologic (cataracts, salt and pepper chorioretinitis, microphthalmos, and congenital glaucoma), cardiac (PDA, peripheral pulmonary artery stenosis), auditory (sensorineural hearing loss), or neurologic (microcephaly, learning impairment), growth restriction, interstitial pneumonitis, radiolucent bone disease, hepatosplenomegaly, thrombocytopenia, and dermal erythropoiesis (blueberry muffin rash).
- Mild forms of CRS exist without manifestations at birth
- Report known or suspected CRS to local and state health departments.

RESPIRATORY SYNCYTIAL VIRUS

- **Epidemiology:** RNA paramyxovirus, acute respiratory tract infection. Most RSV hospitalizations within the first 3 months of life. Predisposed are premature, cyanotic or complex cardiac disease, pulmonary hypertension, CLD of prematurity, immunodeficiency. Occurs in annual epidemics during winter and early spring. Viral shedding from 3-8 days up to 3-4 weeks. Incubation period of 2-8 days.
- **Presentation:** Rhinitis, cough, wheezing, tachypnea. Preterm infants may not manifest respiratory symptoms – lethargy, anorexia, apnea.
- **Diagnosis:** Antigen detection assays, RVP-PCR (30% coinfected)
- **Management:** Supportive – hydration and ventilation if indicated. Ribavirin not recommended for routine use; consider for severe infections. Corticosteroids, antimicrobials, and bronchodilators are not recommended.
- **Prevention:** Palivizumab (humanized mouse IgG monoclonal antibody) may reduce the risk of hospitalization with RSV (55%). Administered IM Q30Days for 5 months during RSV season. Not effective as treatment of RSV or in controlling outbreaks. Infants in NICU may receive first dose 48-72 hours prior to discharge.

ROTAVIRUS

- **Epidemiology:** dsRNA, most common etiology of acute gastroenteritis in community and healthcare settings prior to universal immunization. Transmission by fecal-oral route and possibly via fomites. Incubation period 1-3 days. Intestinal lactase may be a receptor (lower incidence in preterm)
- **Presentation:** Acute onset of fever and vomiting followed by watery diarrhea for 3-8 days. Dehydration, electrolyte abnormalities, and persistent diarrhea
- **Diagnosis:** Enzyme immunoassays, RT-PCR to detect viral DNA
- **Management:** Supportive: Hydration.
- **Prevention:** Contact precautions for the duration of illness for incontinent children. Consumption of human milk is associated with milder rotavirus disease. Bleach (1:2 with water) and 70% ethanol inactivates rotavirus on environmental surfaces. Preterm infants may be immunized when > 6 weeks postnatal age and clinically stable. Standard precautions after receipt of rotavirus vaccine. Debatable administration in NICU.

PERINATAL HIV: EPIDEMIOLOGY

- RNA
- HIV-1 and HIV-2
- 100-200 perinatal cases per year
- Blood, semen, cervicovaginal secretions, and human milk
- Mother to child transmission in utero, in labor/delivery, and via breastfeeding
- Untreated MTC 25-30%. Decreased MTC due to antenatal testing, antiretroviral prophylaxis, C-section before labor and ROM, and avoidance of breastfeeding.

PERINATAL HIV: DIAGNOSIS

- Detection of virus or nucleic acid. Antibody assays valuable if negative up to 24 months of infant age (positive could represent maternal serology)
- In U.S. preferred diagnostic in infants is HIV DNA PCR. Positive result by 48 hours in utero transmission; 93% HIV DNA PCR+ by 2 weeks of age and 95% DNA PCR+ by 4 weeks of age.
- HIV RNA may be falsely negative in ARV recipients (detects plasma viral load)
- Infants infected via MTC have high viral set-points with progressive immune dysfunction and immunosuppression.

PERINATAL HIV: PRESENTATION

- Asymptomatic at birth
- Symptoms in 1-2 years of life (1-2 months in rapid progressors)
- *Pneumocystis jirovecii* PNA in 1st months of life
- Poorly controlled perinatal infections: recurrent bacterial infections, persistent mucocutaneous candidiasis, abdominal organomegaly, diffuse lymphadenopathy, chronic diarrhea, failure to thrive, and developmental delay
- Virologic testing should be performed at birth, 14 to 21 days of life, at 1 to 2 months, and again at 4 to 6 months
- Prognosis: median survival without therapy 8-13 years, now much improved

PERINATAL HIV: MANAGEMENT

- **Maternal:** Combination ARV regimens during pregnancy = lower rates MTC transmission than zidovudine monotherapy taken antenatally. In U.S., 3-drug combination ARV regimens for own treatment or to prevent MTC.
  - U.S. guidelines recommend Cesarean delivery at 38 weeks, before labor and ROM, for HIV-infected women with a viral load > 1000 copies/mL (irrespective of use of ARVs during pregnancy) and for unknown viral load near the time of delivery.
- **Neonatal:** Infant bathed immediately after birth, start ARV prophylaxis with AZT ASAP within 6-12 hours. Treatment based on risk of exposure – **all get AZT at a minimum**
  - Low = mom received ARV from 1st or 2nd trimester **AND** < 50 copies/mL within 4-6 weeks of delivery **AND** no primary/acute HIV infection during pregnancy **AND** adherent to Tx
  - ≥ 34 weeks: 3-drug combo ARV regimens (AZT, 3TC [lamivudine], and either nevirapine or raltegravir)as soon as possible after Dx
  - 32-33 weeks and ≥ 1.5 kg: no 3TC or raltegravir; < 32 or < 1.5 kg: AZT and ID recs

PARVOVIRUS B19

- **Epidemiology:** ssDNA; contact with respiratory secretions, percutaneous exposure to blood, and vertical transmission. Infectious before rash onset and noninfectious after rash appears.
- **Presentation:** Fever and “slapped-cheek” rash with circumoral pallor; polyarthropathy, chronic anemia, pure red cell aplasia, transient aplastic crisis, petechial-papular-purpuric “gloves-and-socks” rash. During pregnancy, can cause fetal hydrops, IUGR, isolated pleural and pericardial effusions, and death (but majority are normal)
- **Diagnosis:** Parvovirus IgM+: infection past 2-3 months. Parvovirus IgG appears on day 2 of rash and persists for life. Parvovirus B19 DNA at high titer may indicate infection.
- **Management:** Supportive: aplastic crisis may require transfusion. IVIG considered for chronic infection. Hydrops fetalis has been treated successfully with intrauterine blood transfusions of the fetus
- **Prevention:** Neonates with hydrops – standard precautions if hydrops resolved at birth. Parvovirus nonimmune pregnant HCW excluded from care of immunocompromised with parvovirus

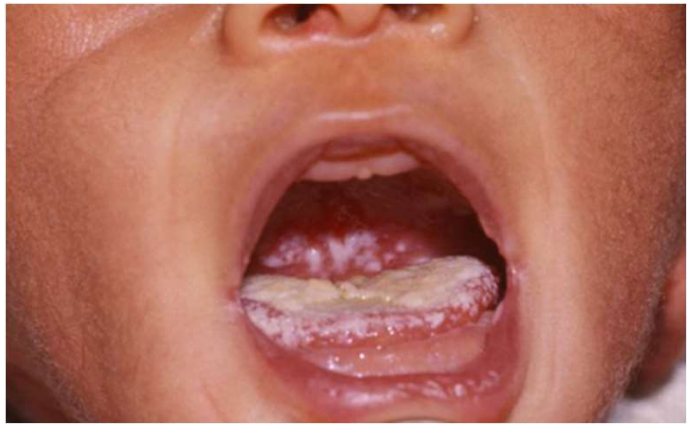
INFLUENZA

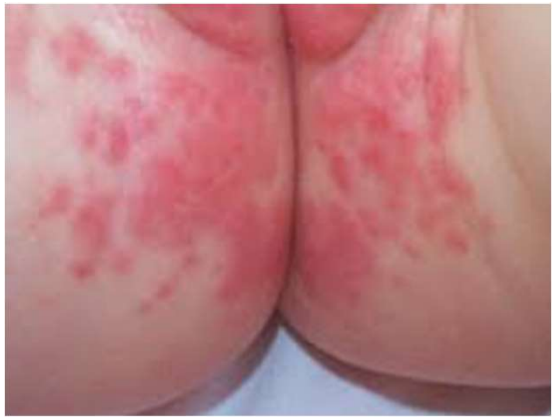
- ssRNA; A, B, and C – A is classified by hemagglutinin (H) and neuraminidase (N)
- Up to 15% of general population affected each year
  - Greater severity of illness if infected during pregnancy
  - Broad range of severity in neonates (new onset apnea common)
  - Infants with signs of URI/LRI
- Diagnosis by PCR, rapid antigen tests, culture
- Management is supportive
  - If maternal infection, isolation from infant if possible
  - Oseltamivir (Tamiflu) can be used ≥ 2 weeks old, even preterm
  - Droplet/standard precautions for the longer of: 1) 7 days after illness onset or 2) 24 hours after fever/respiratory signs resolve
- Prevention: vaccination ≥ 6 months of age (inactivated)

FINALLY… A FUNGUS

THRUSH + DIAPER RASH

- *Candida albicans*
- Rarely progressive
- Diaper dermatitis can progress to ICI in extreme prematurity
- More common when antibiotics given
- Topical treatment with nystatin/miconazole/clotrimazole or systemic therapy with fluconazole/capsofungin



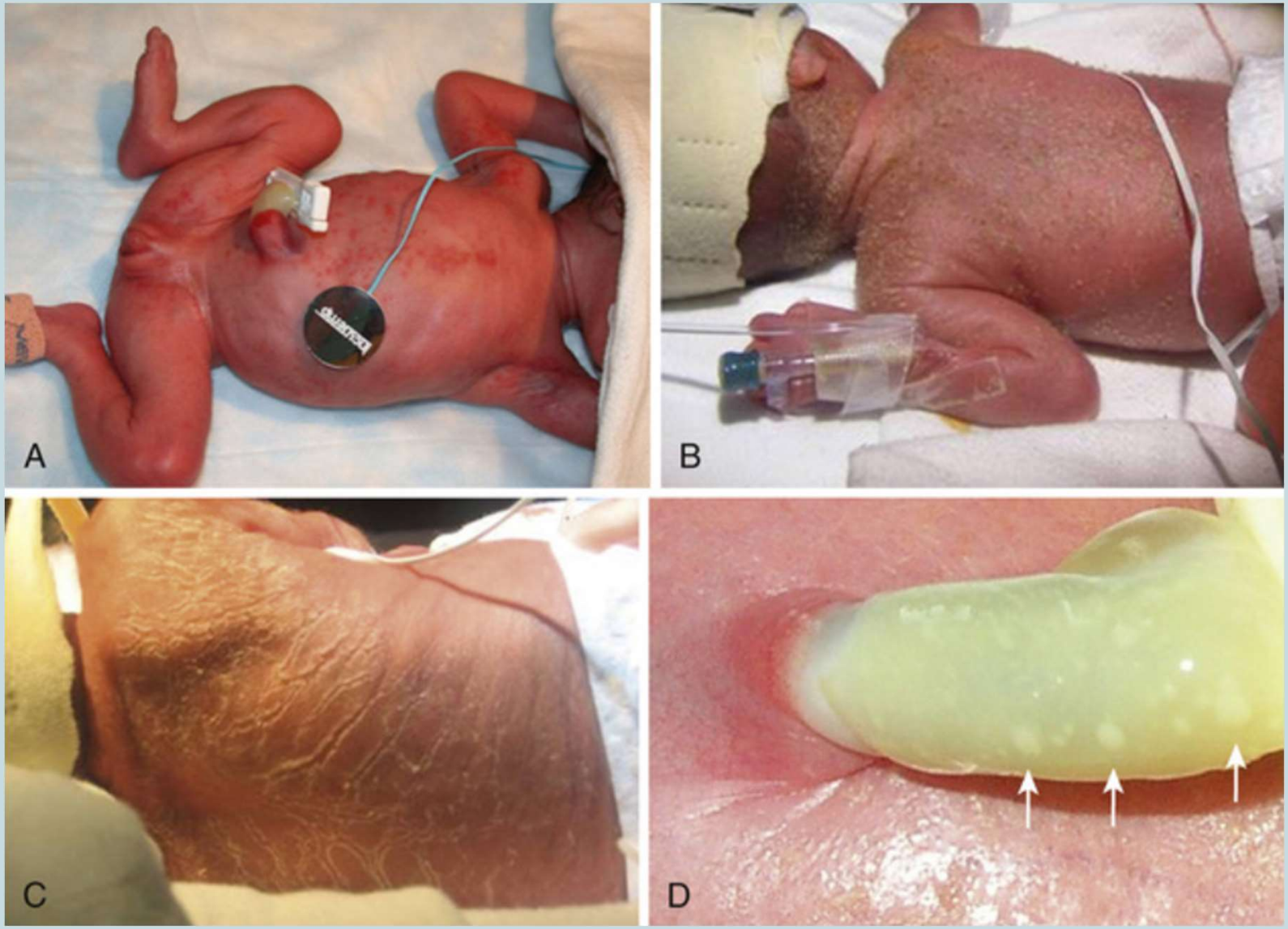


INVASIVE FUNGI IN THE NICU

- Invasive fungal infections are largely caused by *Candida* species
- Small portion from *Aspergillus, Zygomycetes, Malassezia,* and *Trichosporin*.
- Large impact, affects 4-6% of ELBW; Neurodevelopmental impairment in 50%.
- Patient groups in the NICU at higher risk:
  - The extremely premature infant
  - Patients with complex gastrointestinal disease (NEC, gastroschisis, SIPs)
  - Congenital heart disease
  - ECMO
  - Prolonged antibiotics
  - Empiric 3rd gen cephalosporin (doubles risk)
  - Central lines
  - H2 blockers, steroids, ET intubation

CONGENITAL CUTANEOUS CANDIDIASIS

- Presents most commonly at birth, but still “congenital” if presents in first week
- Desquamating maculopapular, papulopustular, erythematous rash. May be desquamation alone.
- Widespread over chest, abdomen, back, extremities, groin, neck, face
- May also include white plaques on umbilical cord
- May disseminate into pneumonia, CSF, or bloodstream infection (11% in term infants, 33% in infants 1000-2500 g, 66% in infants < 1000 g) if untreated.
- Diagnosis: Culture of skin surface for fungi and bacteria; Placental or cord identification (silver stain)
- Treatment: 14-day course of systemic antifungal therapy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D

BLOODSTREAM INFECTION

- Spectrum of symptoms (similar to bacteremia):
  - Common (> 50%): Thrombocytopenia, elevated I:T ratio, elevated CRP, increased or new ABD events, increased FiO2 requirement, increased ventilator support requirement
  - Frequent (~33%): Lethargy, hypotonia, gastrointestinal symptoms (gastric aspirates, distention, bloody stools)
  - Less common (10-15%): Hypotension, hyperglycemia, elevated WBC count, metabolic acidosis
  - Can occur (< 3%): Diminished ANC
- Diagnose with culture – *Candida* grows well in standard aerobic bottle
- Evaluate for cardiac, liver, renal, ophthalmologic, and CNS involvement
- Prompt central line removal is **needed** for clearance and to improve outcomes

CANDIDEMIA TREATMENT

- **REMOVE CENTRAL LINES**
- 21 days of IV therapy recommended, although no clear-cut guidelines
- CNS infection should be presumed (> 15% with invasive candidiasis have meningoencephalitis)
- Kidney involvement guides therapy
  - Liposomal amphotericin B should no be used if renal involvement (doesn't penetrate kidney well)
- Sensitivity varies by species:
  - *C. albicans* sensitive to ampho B and fluconazole; *C. parapsilosis* less sensitive to ampho B; *C. tropicalis* and *glabrata* less sensitive to fluconazole; *C. kruzeii* resistant to fluconazole; *C. lusitaniae* resistant to ampho B

FLUCONAZOLE PROPHYLAXIS

- For patients with long-term IV access, in facilities where risk of invasive candidiasis > 5% in VLBW
- Decreases CVC, skin, GI, and respiratory colonization
- Efficacy 80% in all studies, >90% in < 1000 g
- *Candida*-related mortality decreased by 96%
- Can be given in setting of NEC, ileus, or other GI disease
- Twice weekly IV dosing
- Continue until no longer needing IV access

THE
END