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Syphilis and HIV in Pregnancy

management of infants

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SCHOOL OF - to apply in all slides at the same time edit in Insert > Header & Footer

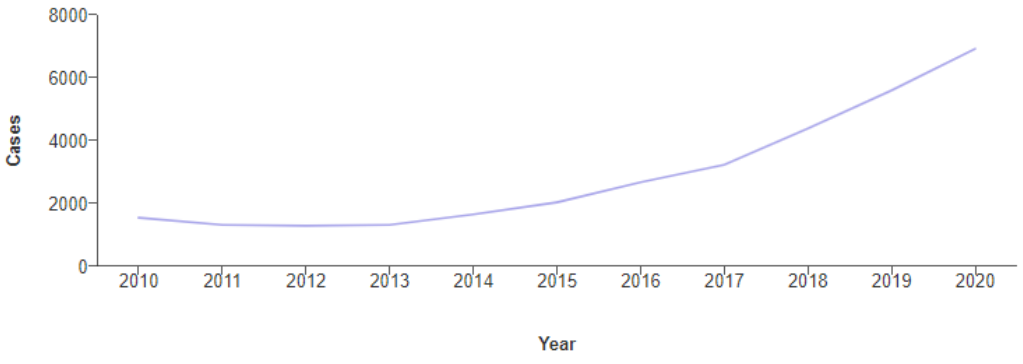
Nothing to disclose

Learning Objectives

1. Understand the trends of syphilis and HIV in Alabama
2. Understand the updated screening for syphilis and HIV during pregnancy
3. Describe limitations of various syphilis diagnostics
4. Describe the management of a baby born to a mother with a h/o syphilis during pregnancy
5. HIV management at delivery
6. Care of HIV exposed infants

Syphilis in pregnancy is on the rise

Number of primary and secondary syphilis cases among women aged 15 to 44 years, United States[4]

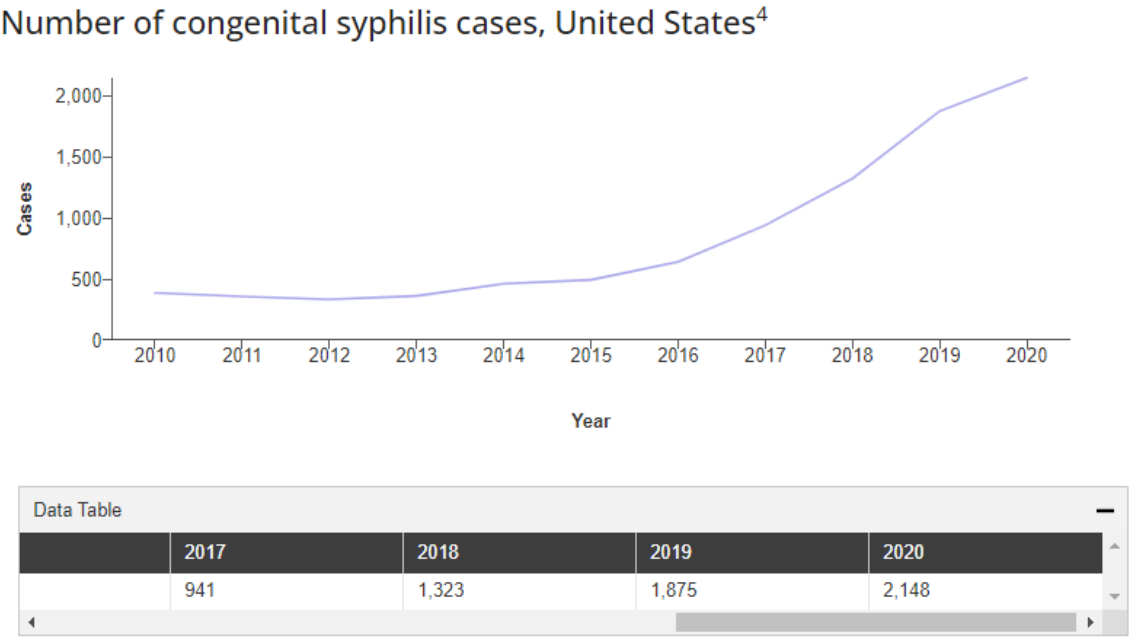


Data Table

	2017	2018	2019	2020
	3232	4390	5600	6924

Source: Centers for Disease Control and Prevention. *Sexually Transmitted Disease Surveillance 2020.* Syphilis.

Congenital syphilis is on the rise

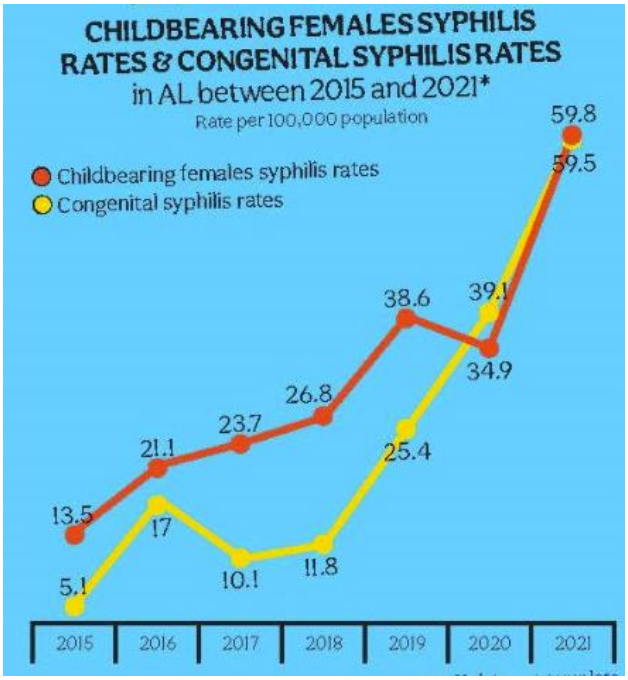


Data Table

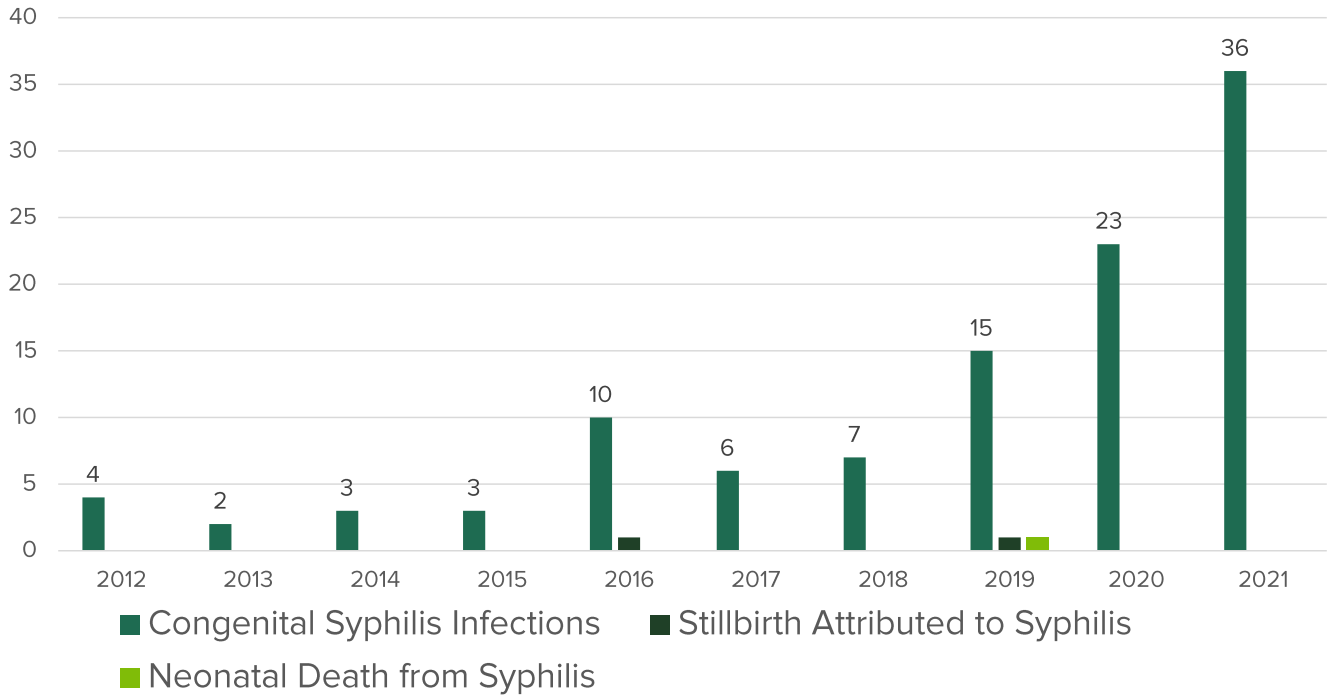
	2017	2018	2019	2020
	941	1,323	1,875	2,148

Source: Centers for Disease Control and Prevention. *Sexually Transmitted Disease Surveillance 2020*. Syphilis.

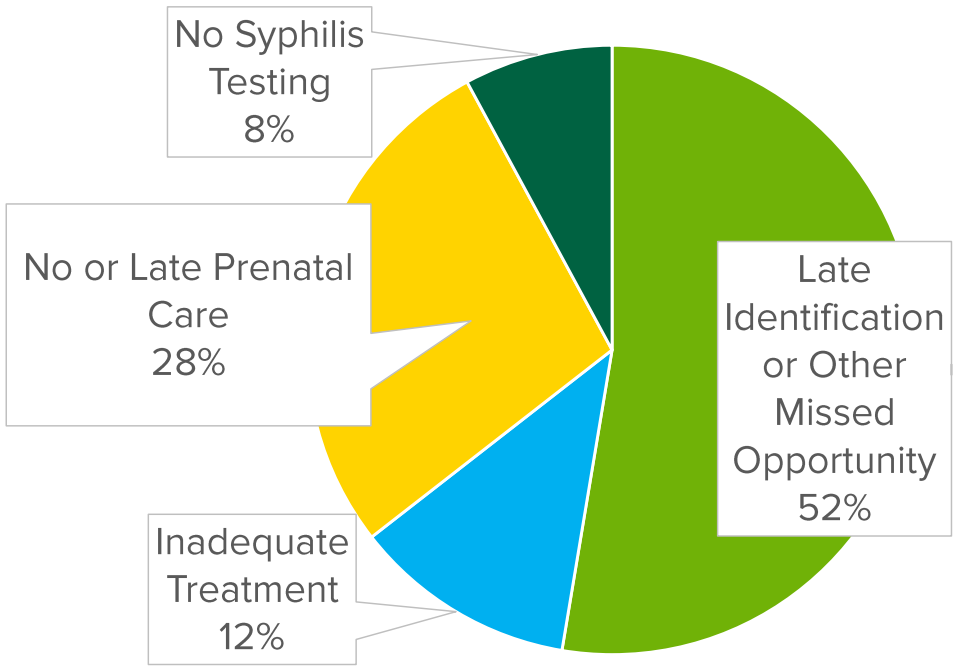
Rates of Syphilis in Alabama



Congenital Syphilis Infections and Outcomes in Alabama 2012-2021

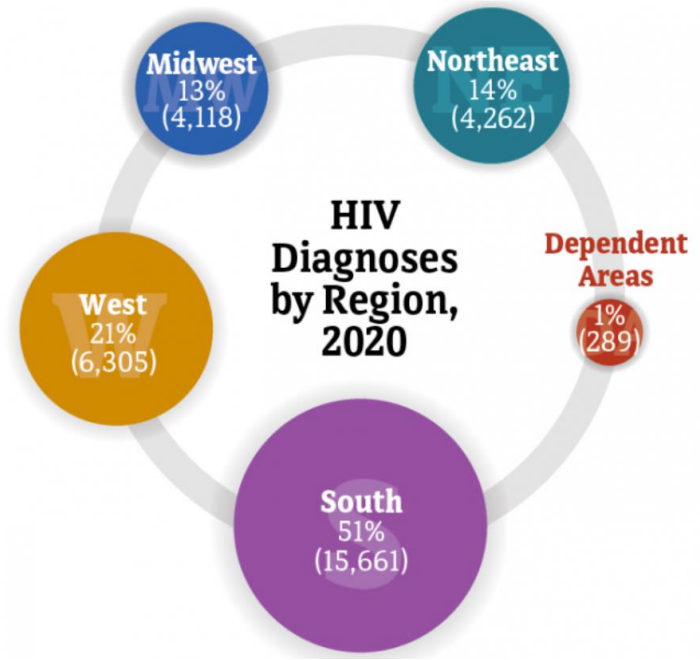


Missed Opportunities to Prevent Congenital Syphilis in Alabama, 2018-2021



New HIV Diagnoses by Region, 2020

† Among adults, adolescents, and children under the age of 13.

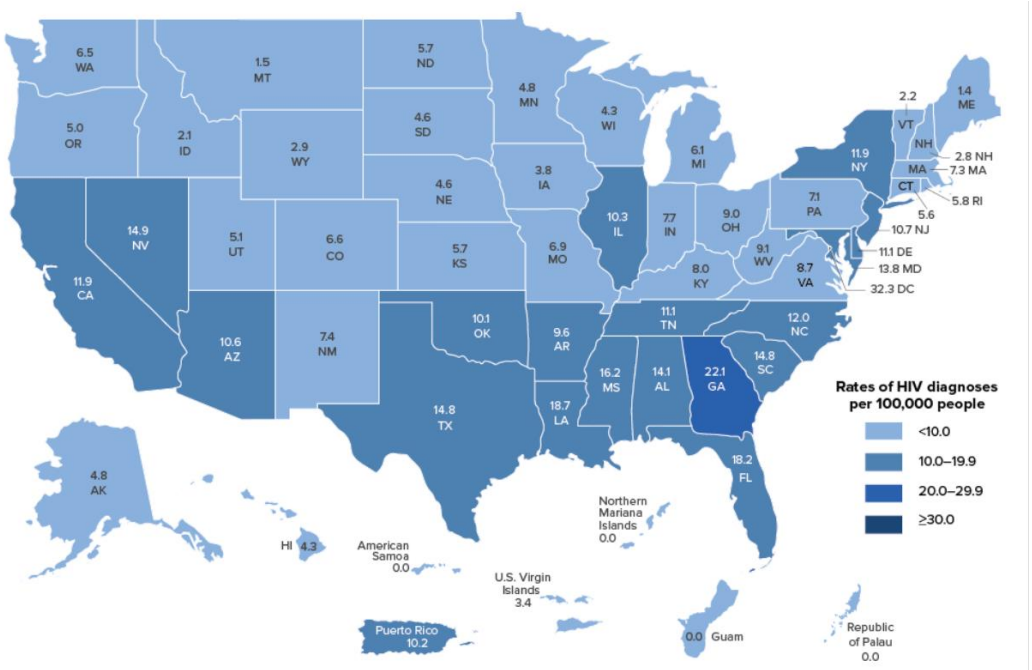


Source: CDC. Diagnoses of HIV infection in the United States and dependent areas, 2020. *HIV Surveillance Report* 2022;33.

Rate of New HIV Diagnoses by Region, 2020

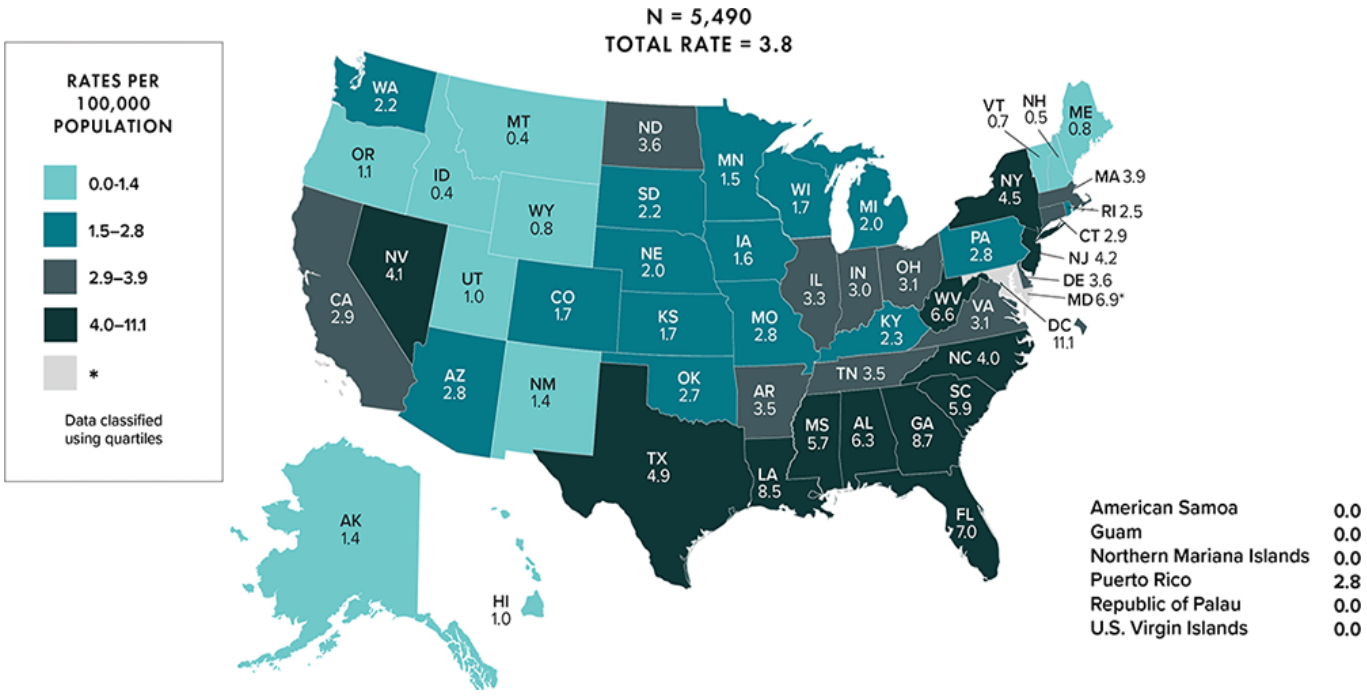
*Rates are per 100,000 people.

† Among adults, adolescents, and children under the age of 13.



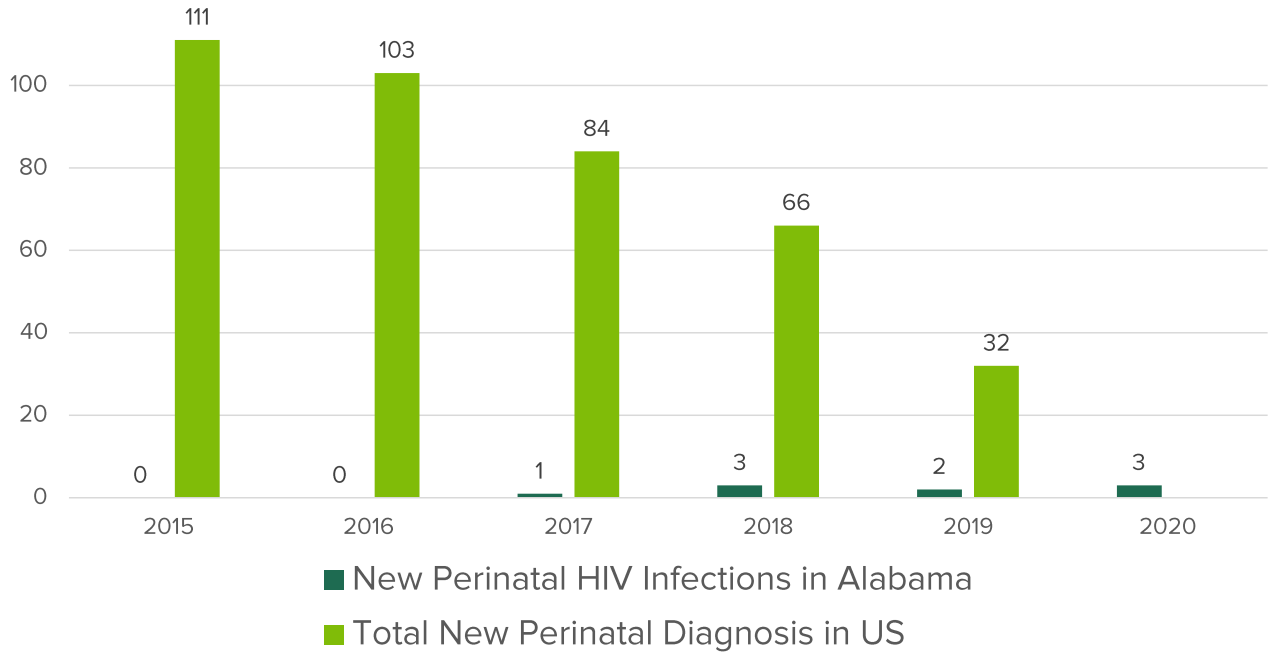
Source: CDC. Diagnoses of HIV infection in the United States and dependent areas, 2020. *HIV Surveillance Report* 2022;33.

Rate of HIV Diagnoses in Women by Region, 2020



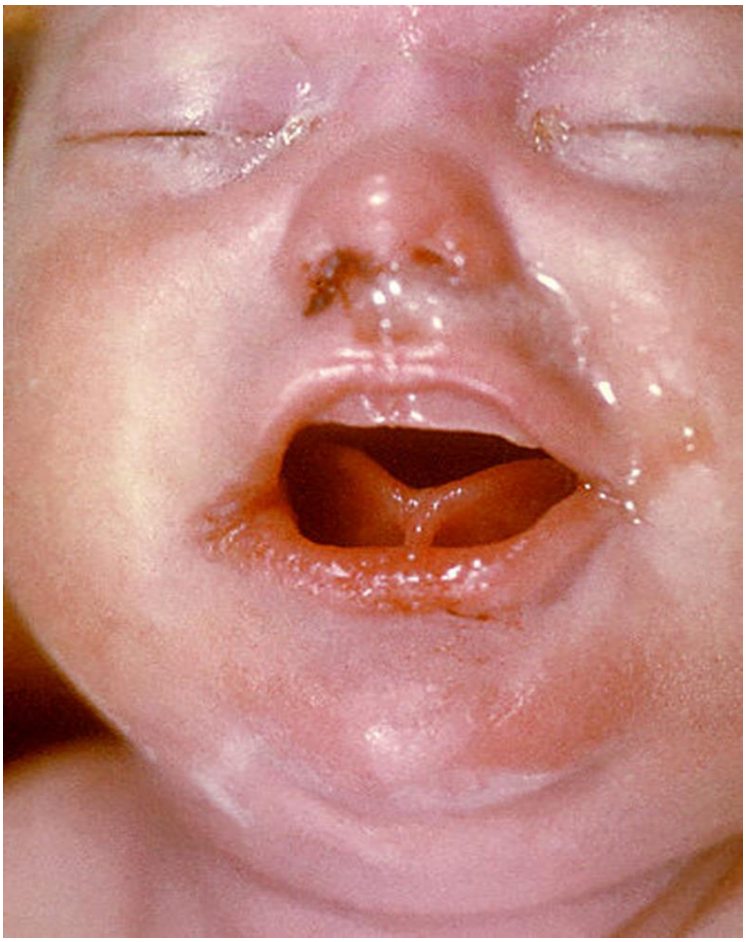
CDC, Diagnoses of HIV Infection in the United States and Dependent Areas 2020: Special Focus Profiles
https://www.cdc.gov/hiv/library/reports/hiv-surveillance/vol-33/content/special-focus-profiles.html

Perinatally Acquired HIV Trends in Alabama and the United States



Congenital Syphilis

- Spirochetes can cross placenta during all stages of pregnancy
- Infant can be infected during delivery
- Untreated early syphilis – 40% of pregnancies miscarriage, still birth, perinatal death
- Maternal – fetal transmission = 60 – 100% for primary or secondary infection (40% for early latent)
- Syphilis + HIV infection – increase risk of HIV transmission to infant
- Most infected infants – ASYMPTOMATIC at birth



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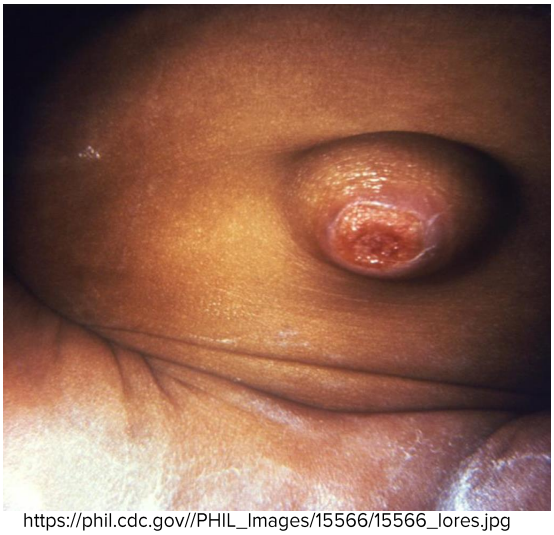

https://phil.cdc.gov//PHIL_Images/15566/15566_lores.jpg

CONGENITAL SYPHILIS
< 2 YEARS

- Most asymptomatic
- Rhinitis “snuffles”
- Rash
- Skeletal abnormalities
- CNS disease

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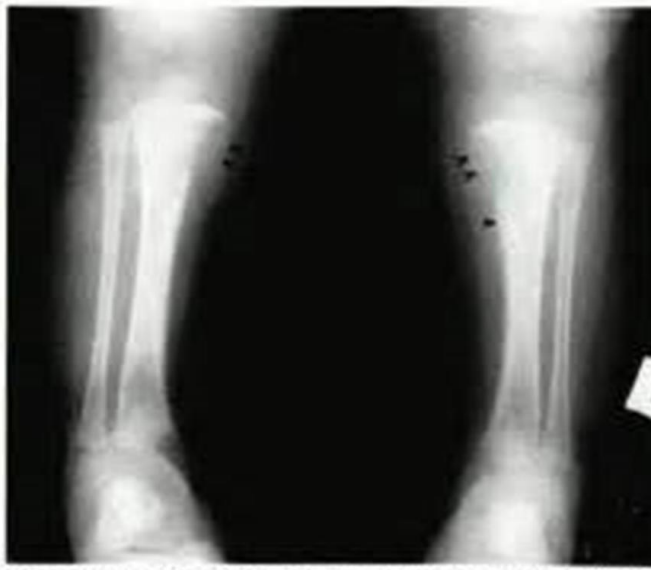
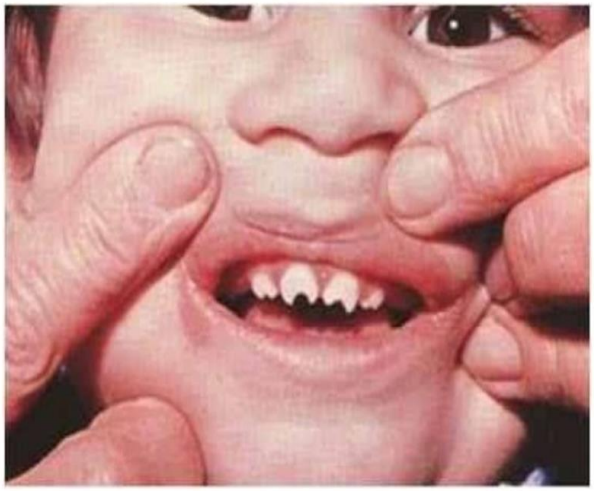


https://www.healio.com/orthopedics/journals/ortho/1983-4-6-4/%7Ba1913b33-0067-4489-8694-7584dbf0e4b6%7D/radiologic-case-study



http://image.slidesharecdn.com/congenitalsyphilis-140810152305-phpapp02/95/congenital-syphilis-35-638.jpg?cb=1407684228

CONGENITAL SYPHILIS > 2 YEARS:
All systems affected (developmental delay, seizures, deafness, visual disturbance, bone and teeth deformities, aortitis)

Perinatally acquired HIV

- Maternal – infant transmission in untreated women about 30%
- If delay in diagnosis of infant – often presents with AIDS
- Result in life-long infection requiring ART (complicated medication regimens in childhood, frequent follow-up, medication side-effects)
- With appropriate screening and treatment of pregnant women maternal – infant transmission < 1%

A 28 year old G2P1 woman is seen for her first antenatal care visit at 20 weeks GA. Her screening labs included a negative Syphilis EIA, a negative HIV, HebB surface Ag positive, negative gonorrhea but positive chlamydia. She received treatment. Should she be retested for syphilis and if so when?

1. No the syphilis EIA is highly sensitive with a very low false negative rate.
2. Yes, a repeat test should be done at the next visit with a non-treponemal test such as the RPR due to limited sensitivity of the treponemal EIA
3. Yes, a repeat treponemal EIA should be done again at 28 weeks GA and again at delivery as this woman has some risk factors for syphilis infection during her pregnancy
4. Yes a repeat treponemal EIA or RPR should be done again at 28 weeks and again at delivery as this is recommended for all pregnant women

A 32 year old G3P2 woman enters antenatal care at 10 weeks GA. Her treponemal EIA is positive. You order a RPR which is negative. What should you do next?

1. No further testing is needed as the negative RPR is more specific and less likely to have false negatives while the treponemal EIA is known to have a high false positive rate.
2. Inquire about her prior syphilis history. If she was previously adequately treated no further testing is needed.
3. Obtain a treponemal specific test such as the TP-PA, if negative then can assume the initial EIA was a false positive, if positive, inquire about prior syphilis history.
4. Obtain a VDRL as this is more sensitive and specific than the RPR

You are covering newborn nursery. A full term infant with a normal physical exam born to a mom who was treated at 22 weeks GA for syphilis with IM penicillin. Her RPR went down from 1:64 to 1:4 and then went up to 1:16 at time of delivery. The infant RPR is 1:4. What should you do for the baby?

1. No further evaluation is needed as the mom was adequately treated for syphilis, it is not unusual to have fluctuations of the RPR during pregnancy post treatment and the infant RPR is < 4 times the maternal RPR.
2. Treat the baby with 10 days of IV penicillin for presumed congenital syphilis due to the fourfold increase in the maternal RPR at delivery.
3. Evaluate the infant with CBC, platelet count, CSF, and long-bone x-rays – if abnormal then treat with 10 days of IV penicillin, if normal then no treatment.
4. Evaluate the infant with CBC, platelet count, CSF, and long-bone x-rays – if abnormal then treat with 10 days of IV penicillin, if normal then single dose of IM penicillin.

“ALL pregnant women should get tested for syphilis and HIV at their
1. first prenatal visit,
2. between 28 and 32 weeks GA
3. and at time of delivery.”

So no more “risk assessment”!

ADPH Prenatal STD testing (updated Aug 5, 2022)

Alabama Prenatal STD Testing

Test (All tests must be FDA approved)	Initial Prenatal Visit	Third Trimester	Labor and Delivery (L&D)
Syphilis	All pregnant persons.	All pregnant persons at 28-32 weeks gestation, regardless of risk factors.	All pregnant persons.
HIV	All pregnant persons not previously confirmed as HIV infected.	All pregnant persons at 28-32 weeks gestation, regardless of risk factors unless previously confirmed as HIV infected.	All pregnant persons unless already confirmed as HIV infected.
Chlamydia	All pregnant persons.	All pregnant persons at 36 weeks gestation if the initial test was positive, have signs and symptoms, or at high risk of infections.	
Gonorrhea	All pregnant persons.	All pregnant persons at 36 weeks gestation if the initial test was positive, have signs and symptoms, or at high risk of infections.	
HBV	All pregnant persons.		All pregnant persons if no prior testing or have signs and symptoms of hepatitis.
HCV	All pregnant persons.		

No Prenatal Care –Patient Presents at Delivery

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Gonorrhea	All pregnant persons.
HBV	All pregnant persons.
HCV	All pregnant persons.

Revised 12/21/22

Understanding Syphilis tests: Essentially 3 types

Non-specific, non-treponemal

RPR / VDRL

directed against lipoidal antigens

Manual treponemal specific serology:

FTA-ABS

Fluorescent Treponemal Antibody Absorbed test manual indirect fluorescence measures IgG and IgM

TP-PA

Treponema pallidum Particle Agglutination assay manual agglutination assay that measures IgG and IgM

Automated treponemal tests:

EIA

enzyme immunoassay

CIA

chemiluminescence immunoassay

MBIA

microbead immunoassay

RPR and VDRL

Strength	Weakness
• Distinguish new infection from past treated infection • Monitor response to treatment • Titers go up with infection and down with treatment	• Non-specific – other conditions can give a positive RPR • Not sensitive • Delay in response with acute infection

FTA-Abs and TP-PA

Strength	Weakness
• specific for syphilis – so can confirm that the positive RPR is due to syphilis. • TP-PA has the highest sensitivity (94 – 96% for primary syphilis, 100% for secondary and 95% for latent syphilis), • FTA-ABS- less sensitive for primary syphilis (65 – 88%) • 100% specific	• once positive – positive for life - can't distinguish between past treated infection and new re-infection • Labor intensive – not practical for screening

Automated EIA, CIA, MBIA

Strength	Weakness
• automated high throughput so cost effective for mass screening (as in pregnancy) • Very sensitive: 94 – 96% for primary syphilis and 100% for secondary syphilis, 95 – 100% for early latent and 86 – 98% for late latent	• Not as specific (i.e. can have false positives, especially in low pre-test probability like in pregnancy screening) e.g. Trep-Sure EIA specificity of 78 – 86%) • Can't distinguish between past treated and new infection

Bottom line – especially in screening can't rely on a single test if positive – Will ALWAYS need at least 2 sometimes 3 to make a diagnosis

- So most pregnancy screening will use an automated treponemal test – EIA, CIA or MBIA
- If negative – No syphilis at that time but need to retest during pregnancy!
- If positive need to get a RPR
- If RPR positive – then have made a diagnosis of syphilis in pregnancy – need to decide on stage and treat accordingly and can use RPR for monitoring
- If RPR negative – need to get the TP-PA – if negative – no syphilis at that time.
- If TP-PA positive (maybe detecting prior h/o treated syphilis OR new infection in pregnancy) NEED history. If determine new infection - need to stage and treat accordingly (worth repeating RPR during treatment – will often have a delayed response)

Treatment of syphilis in pregnancy

- Primary, secondary, or early latent syphilis – Benzathine penicillin G 2.4 million units IM at 1 week interval **x 2**
- Late latent or tertiary (no CNS disease) syphilis – Benzathine penicillin G 2.4 million units IM at 1 week intervals x 3 (**must be given at 7 day intervals** if more than 9 days have passed then need to repeat)
- If diagnosed in second half of pregnancy – need to monitor fetus with US for signs of congenital syphilis – may require more treatment
- If diagnosed and treated for syphilis before this pregnancy – but continues to have positive RPR – recommend retreating the woman
- CAN ONLY USE PENICILLIN in pregnancy – so if patient allergic need to desensitize and treat.
- If **baby born within 30 days of treatment** = inadequate fetal treatment

So mom had syphilis during pregnancy and was treated – what to do with baby?

- Was mom treated with penicillin 2 - 3 weeks apart (depending on stage of disease) at least 30 days before delivery? **Need to call and ask the Health Department!**
- What was mom's RPR at diagnosis, after treatment and at time of delivery? **Need to call and ask the Health Department!**
- Need to obtain RPR on infant and do a physical exam

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Management of baby after you have called health department and obtained RPR.

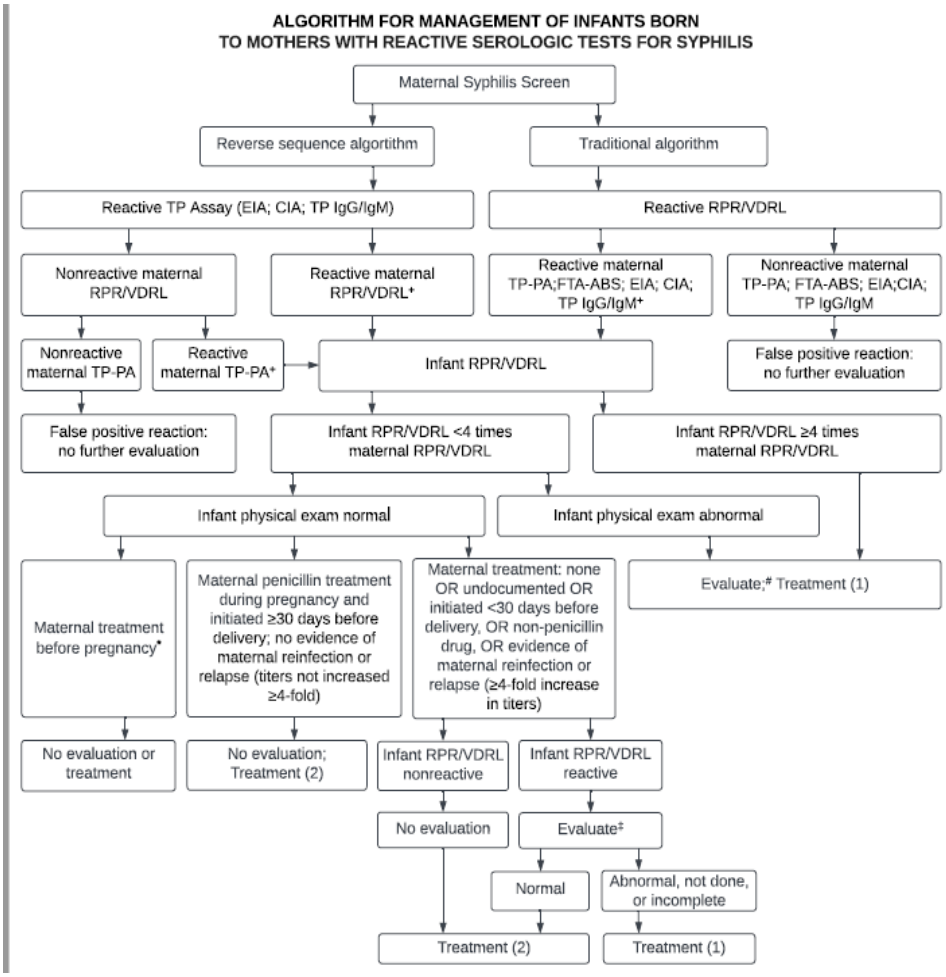
- Baby concerning PE / RPR > 4 x mom's = congenital syphilis - do full eval and treat for 10 days
- Baby normal PE and RPR < 4 x mom's and no concern for inadequate maternal treatment / reinfection – **baby does not have CS** -if mom treated before this pregnancy then no treatment for baby, if treated during the pregnancy then 1 x IM dose penicillin to baby to complete treatment to prevent CS
- Baby normal PE and RPR < 4 times mom's – but concern for inadequate maternal treatment or reinfection – then full eval of baby if normal – baby does not have CS but give 1 IM dose penicillin to prevent CS; if eval abnormal – baby has CS - treat 10 days (IF RPR non-reactive, no eval, 1xIM PCN)

Evaluation of Baby if concern for CS once RPR obtained

- CBC with diff, CSF for white blood cell count, protein and VDRL and long-bone x-rays
- If baby has abnormal PE – tests as indicated (LFT's, abdominal US, neuroimaging, eye exam, ECHO etc.)
- To prevent CS in a baby in whom you've excluded CS – give single dose of IM Benzathine penicillin G 50,000 U/kg
- To treat CS – Aqueous penicillin G 50,000 U/kg IV q 12 hours if < 7 days old, then q 8 hours to complete a total of 10 days. If an interruption in treatment of 1 day, then need to restart whole 10 day course.

Follow-up of babies born to mother with h/o syphilis during pregnancy

- Baby with negative RPR at birth – needs a RPR checked at 3 months – if now positive needs eval and treatment for CS
- Baby with RPR < 4 x mom's and not treated for CS – needs RPR checked at 2 month, 4 month and 6 month check-up – if still positive needs eval and treatment for CS
- Baby treated for CS – needs RPR checked at 4 months, 6 months and 1 year – if persistent needs re-evaluation and referral to ID specialist
- BABIES NEED FOLLOW-UP WITH REPEAT RPRs!!! – this will only happen if the pediatrician knows that there was a maternal history of syphilis



+ Test for HIV-antibody. Infants of HIV-infected mothers do not require different evaluation or treatment.
* Women who maintain a VDRL titer ≤1:2 (RPR ≤1:4) beyond 1 year following successful treatment are considered serofast.
# Evaluation consists of hemoglobin/hematocrit, platelet count; CSF examination for cell count, protein, and quantitative VDRL. Other tests as clinically indicated: long-bone x-rays, neuroimaging, auditory brainstem response, eye exam, chest x-ray, liver function tests.
‡ Hemoglobin/hematocrit, platelet count; CSF examination for cell count, protein, and quantitative VDRL; long-bone x-rays

TREATMENT:

(1) Aqueous penicillin G 50,000 U/kg IV q 12 hr (≤1 wk of age), q 8 hr (>1 wk), or procaine penicillin G 50,000 U/kg IM single daily dose, x 10 days
(2) Benzathine penicillin G 50,000 U/kg IM x 1 dose

07/17/2022

Williams JE.P, Graf RJ, Miller CA, et al. Maternal and Congenital Syphilis: A Call for Improved Diagnostics and Education. Pediatrics. 2022;150(3):e2022057927
PEDIATRICS

HIV in Alabama

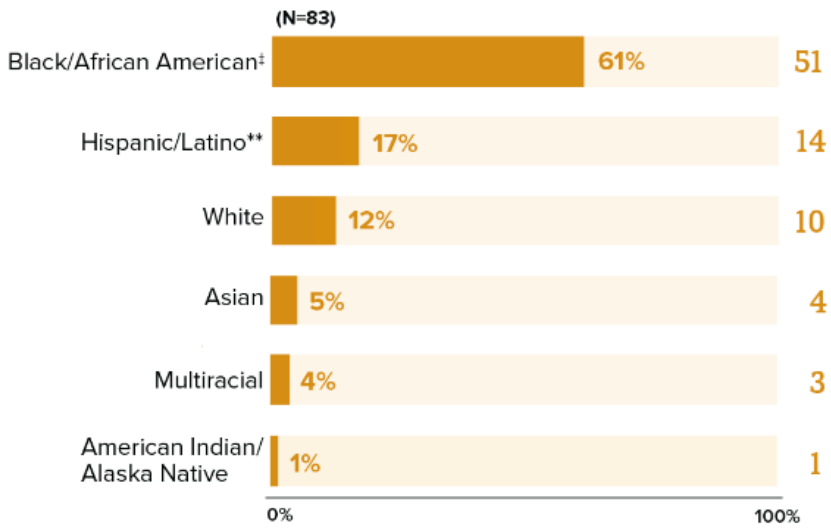
Risk of perinatal HIV remains high in Alabama

- High incidence of new HIV infections
- High number of women with HIV

Alabama Perinatal HIV Infections in Context

- Perinatal HIV Infection is a NEVER event
- The number of perinatal HIV cases has decreased 71% nationally since 2015 but has increased 300% in Alabama
- Alabama makes a disproportionate number of perinatal HIV infections

New Perinatal HIV Diagnoses in the US and Dependent Areas by Race and Ethnicity, 2019



Source: CDC. Diagnoses of HIV infection in the United States and dependent areas, 2019. *HIV Surveillance Report* 2021;32.

Perinatal HIV should be a NEVER EVENT

It is almost entirely preventable

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Revised 12/21/22

National HIV Screening Guidelines Continued

- All pregnant women - tested for HIV early - **opt out** after counseling
- If decline - offer testing again during the third trimester.
- If maternal HIV status is unknown at time of labor, a rapid HIV test should be performed immediately.
- Women who were not tested for HIV before or during labor should undergo expedited HIV antibody testing in the immediate postpartum period.

National HIV Screening Guidelines Continued

- Test of choice = immunoassay that is capable of detecting HIV-1 antibodies, HIV-2 antibodies, and HIV-1 p24 antigen (i.e., antigen/antibody combination immunoassay).
  - "4th Generation Screening"
- Decreased "Window Period" then older testing
  - Average of 18 days
  - **95-99.8%** sensitivity at 28 days
  - Decreased false positives
- **Testing should be available 24 hours a day and results available within one hour.**

Types of HIV tests

- Antibody
- Will detect Ab that develop 23 – 90 days post infection
- Most rapid tests

- Antigen / antibody
- Will detect Ab and p24 antigen
- Can detect HIV 18 – 45 days post infection

- NAT / PCR
- Use PCR to amplify virus in the blood
- DNA or RNA
- Qualitative or quantitative
- Can detect HIV 10 – 33 days post infection

Perinatal HIV Transmission is Preventable

The risk of perinatal HIV infection can be less than **1%**

1. Mother takes antiretroviral (ARV) treatment as prescribed throughout pregnancy and delivery.
2. Baby is treated for 2 to 6 weeks of ARV after birth.
3. Formula feeding

(breastfeeding can be considered: shared decision, need to counsel pre-delivery, requires close support and follow-up, and only recommended in ***specific*** *cases*) – contact us at UAB Family Clinic to discuss

Pre-exposure Prophylaxis (PreP) in Pregnancy

- Pill taken everyday to decrease risk of HIV acquisition through sex
- Tenofovir disoproxil fumarate/Emtricitabine (TDF/FTC)
  - Truvada
- Uninfected individuals who are trying to conceive, are pregnant, postpartum, or breastfeeding
- Risk factors for acquiring HIV
  - Such as condomless sex with a partner with HIV whose HIV-RNA level is detectable or unknown,
  - Recent sexually transmitted infection (STI)
  - Injection drug use.

Management of HIV Infection During Delivery

- At the start of labor, initiate IV zidovudine and administer throughout delivery
- If HIV viral load (VL) is >1000 or HIV VL is unknown within 4 weeks of delivery, consider scheduled cesarean section at 38 weeks
- If unknown, maternal HIV status should be confirmed prior to discharge of the women and/or neonate from the hospital.

Classification of Exposed Infants

LOW RISK

- Received ARV during pregnancy with viral suppression
  - HIV RNA level **<50** copies/mL within **4 weeks** prior to delivery
- No concerns related to adherence
- Did not acquire HIV during pregnancy

HIGH RISK

- No prenatal care
- No antepartum ARVs or only intrapartum ARV drugs
- Initiated ARV late in pregnancy
  - late second or third trimester
- Diagnosed **acute HIV** infection during pregnancy
- HIV viral loads **≥50** copies/mL within **4 weeks** of delivery
  - Includes those who received ARV and did not have sustained viral suppression.

Management of Low-Risk HIV Exposed Infants

- Never send a Antibody test!!! (will detect maternal Ab up to 18 – 24 months of age)
- Start infant on **Zidovudine (AZT)** within 6 hours of birth.
  - continue for 4 weeks
- Send CBC to discharge
- Obtain HIV RNA / DNA PCR at
  - 2 weeks (with CBC)
  - 2 months
  - ≥4 months

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Management of High-Risk HIV Exposed Infants

- Send HIV DNA or RNA PCR prior to starting ARV. (At Birth)
- Start infant 3 drug therapy within 6 hours of birth
  - Zidovudine (will continue for 6 weeks)
  - Lamivudine
  - Nevirapine or Raltegravir
- Send CBC prior to Discharge
- Obtain HIV RNA / DNA PCR at
  - 2 weeks (with CBC)
  - 1 - 2 months
  - ≥4 months

Reason for testing recommendations

- ARV influences sensitivity of HIV NAT tests (no need to send birth test for low risk infants
- Zidovudine (AZT) can cause profound anemia (need for CBC at baseline and while on treatment)
- Want to diagnose infected infant ASAP to start appropriate treatment
- Bactrim for PJP px – start at 4 – 6 weeks unless 2 neg HIV NAT tests where one is done ≥ 4 weeks
- Definitively exclude HIV infection with 2 neg HIV NAT tests at ≥ 1 month and ≥ 4 months

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Please contact us about HIV exposed infants:
Call: (205)638 9400
email: FamilyClinic@uabmc.edu
fax: (205) 934 8658

Better to plan ahead.

HIV meds for infants NOT available at retail pharmacies, and NOT stocked in all hospitals

Resources

- Clinicalinfo.hiv.gov for clear guidance on HIV treatment and screening
- National Clinician Consultation Center provides consultations on issues related to the management of perinatal HIV infection 1-888-448-8765; 24 hours a day, 7 days a week.
- Pediatric Antiretroviral Guidelines for antiviral dosing based on gestational age and weight