

## Perinatal Infectious Diseases Screening

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#### Disclosures

Dr. Relucio is a stockholder for the following publicly traded companies:

- Johnson & Johnson
- Medtronic
- Pfizer
- **3**M
- Walgreens
- •GE Healthcare

#### Objectives

#### Identify

 which infectious diseases screening should be performed during the first and third trimester and at birth

#### **Understand**

- prevalence of disease by gender and race/ethnicity
- clinical manifestations of infectious diseases in neonates where maternal screening was not performed

#### Treat

- maternal syphilis to prevent congenital syphilis
- maternal gonorrhea and chlamydia to prevent opthalmia neonatorum

#### Refer or Treat

 patients with HIV, Hepatitis B and C for maternal treatment and perinatal prevention

#### Identify

 which patients should undergo TB screening using a riskbased strategy

#### Understand

 why TORCH screening is no longer routinely recommended

# Overall Recommendations for Perinatal Infectious Disease Screening

### CDC Recommendations — First Prenatal Visit

All pregnant women

- Syphilis
- Hepatitis B
- Hepatitis C
- HIV

Women <25 years or older women at increased risk

- Gonorrhea
- Chlamydia

### CDC Recommendations – Third Trimester

Syphilis – Certain groups of pregnant women at 28 weeks at risk for infection or reinfection

HIV – Certain groups of pregnant women before 36 weeks

Hepatitis C – Pregnant women with ongoing risk factors

Gonorrhea – Pregnant women with ongoing risk factors

Chlamydia – Pregnant women less than 25 years of age or continued high risk

www.cdc.gov/pregnancy-hiv-std-tb-hepatitis/php/screening/index.html

### CDC Recommendations - At Delivery

Syphilis: Certain groups of pregnant women at risk for infection or reinfection this pregnancy, pregnant women with no previously established syphilis screening this pregnancy, and all pregnant women who deliver a stillborn infant

HIV: Pregnant women not screened during pregnancy

HBV: Pregnant women not screened during pregnancy who are at high risk, or with signs or symptoms of hepatitis

HCV: Pregnant women not previously screened

www.cdc.gov/pregnancy-hiv-std-tb-hepatitis/php/screening/index.html

### CDC Recommendations – Targeted Testing for TB



Testing and treatment for LTBI of asymptomatic women during pregnancy should be pursued only in the context of known risk factors for exposure to TB or for progression to TB disease.



LTBI treatment should be delayed until three or more months after delivery, when possible, to minimize the risk of hepatitis

Treatment may be indicated for contacts and those at highest risk for progression to TB disease.

Providers should closely monitor those receiving LTBI treatment for adverse events and to ensure adherence.



Women with signs or symptoms of TB disease or a positive test for TB infection should be further evaluated for TB disease.

Targeted Testing for TB - Risk factors for exposure to TB disease

Close contact with persons known or suspected to have TB

Having been born or lived in high TB prevalence countries

Living or working in congregate settings, such as correctional institutions, homeless facilities, or healthcare facilities

### Targeted Testing for TB - Risk of progressing to TB disease once infected

**HIV** infection

Potent immunosuppressive therapy (e.g. immunosuppressive drugs such as prednisone or TNFa antagonists)

Diabetes

Cancer

Substance use

### American College of Obstetrics and Gynecology (ACOG) ID Screening Guidelines

- Infections listed in CDC guidance --AND--
- ✓ Rubella titer
- U/A and reflex urine culture for UTI/asymptomatic bacteriuria between 11- and 16- weeks gestation
- Group B strep culture performed between 35- and 37-weeks gestation

Current Screening Rates for Infections Approximately 75%–80% of pregnant women are screened for HIV infection

Approximately 84%–88% of pregnant women are screened for HBV infection

Approximately 85% of commercially insured pregnant women are screened for syphilis

Approximately 41% of pregnant women are screened for HCV infection

www.cdc.gov/pregnancy-hiv-std-tb-hepatitis/php/screening/index.html

Prevalence
Rates of
Reportable
Infections in
Pregnancy in
the US

Prevalence of chronic hepatitis B infection in pregnancy is estimated to be 0.7% to 0.9%

1-2.5% of pregnant women are infected with hepatitis C virus

0.6% of pregnant women are infected with HIV

More than 10,000 US women who gave birth in 2022 had syphilis, about 1 maternal syphilis case for every 357 births.



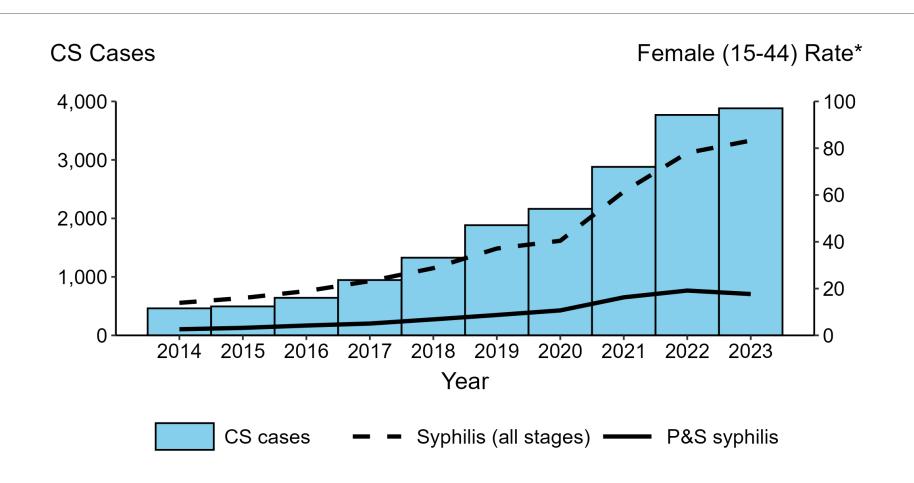
#### Syphilis Overview

Overall, syphilis increased by only 1% after years of double-digit increases.

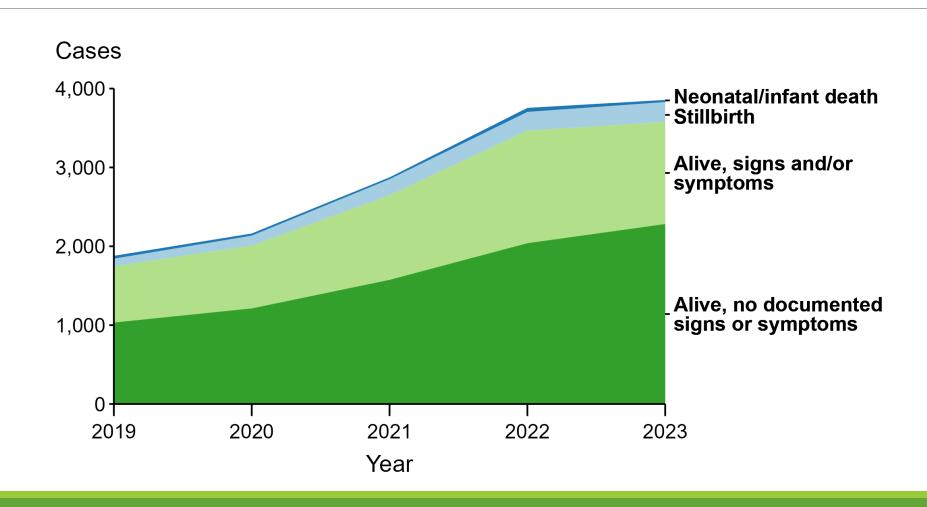
Primary and secondary syphilis declined for the first time in more than two decades, down 10% since 2022.

Increases in congenital syphilis cases appear to be slowing in some areas—with a 3% increase over 2022 nationally, compared to 30% annual increases in prior years.

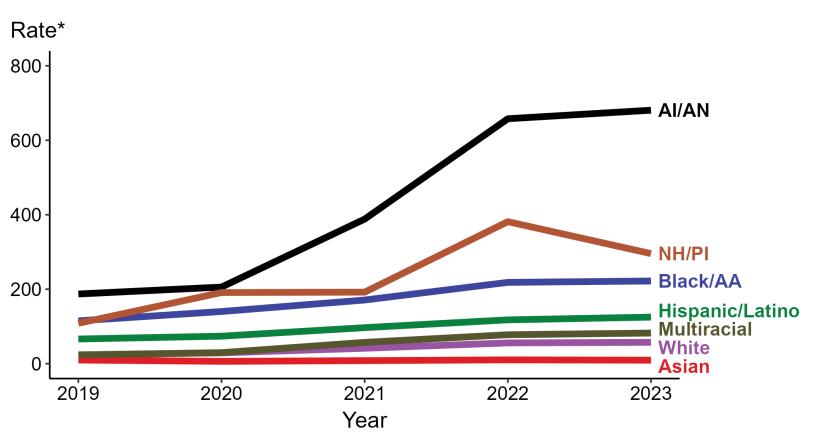
### Congenital Syphilis — Reported Cases by Year of Birth and Rates of Reported Cases of Primary and Secondary Syphilis and Syphilis (All Stages) Among Women Aged 15–44 Years, United States, 2014–2023



#### Congenital Syphilis — Reported Cases by Vital Status and Clinical Signs and Symptoms of Infection, United States, 2018–2023



### Congenital Syphilis — Rates of Reported Cases by Race/Hispanic Ethnicity of Birth Parent and Year of Birth, United States, 2019–2023



\* Per 100,000

ACRONYMS: AI/AN =
American Indian or Alaska
Native; Black/AA = Black or
African American; NH/PI =
Native Hawaiian or other
Pacific Islander

#### Congenital Syphilis (CS)

- **Early** manifestations
  - < 2 years of age</p>
  - Due to hematogenous spread (via blood) of *T. pallidum* and the resultant inflammatory response in various organs and tissues
  - Immune-mediated

- > Late manifestations
  - > 2 years of age
  - Scarring or stigmata from early disease
  - Reaction to persistent inflammation
  - Noninfectious

### CDPH guidelines for syphilis screening of pregnant people – differ from CDC

All pregnant patients, regardless of risk behaviors, should be screened for syphilis three times during pregnancy:

- Once at either confirmation of pregnancy or at the first prenatal encounter (ideally during the first trimester);
- •Second: Early in the third trimester (at approximately 28 weeks gestation or as soon as possible thereafter); and
- •Third: At delivery.
- **AND:** Emergency departments and hospital-affiliated urgent care clinics should screen all pregnant persons for syphilis prior to discharge if syphilis test results are not available for the current pregnancy.

SB 306 Fact Sheet - Prenatal Syphilis Testing

#### Early manifestations (birth to age 2)

#### Gestation

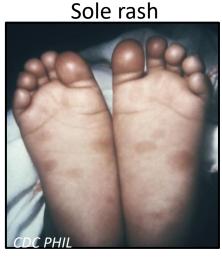
- Placental thickening, hydrops fetalis, IUGR
- Preterm and/or SGA

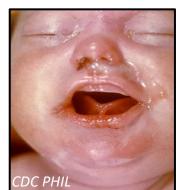
#### Constitutional

Fever and irritability

#### Skin and Mucosa

- Rash and lesions
- Nasal secretions (snuffles)
- Mucous patches
- Adenopathy





**Nasal secretions** 

#### Desquamating rash













Umbilical lesion

#### Early manifestations (birth to age 2)

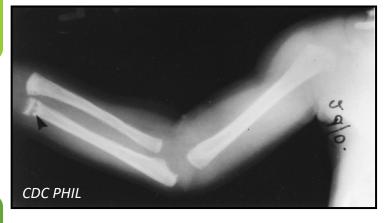
#### Neurologic

- Abnormal reflexes or motor development
- Failed hearing screens

#### Musculoskeletal

- Osteochondritis
- Periostitis
- Pseudoparalysis

**Periostitis** 





Osteochondritis



#### Early manifestations (birth to age 2)

#### Pulmonary

Pneumonia alba

#### Cardiac

Myocardits

#### GI

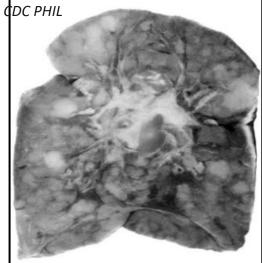
- Pancreatitis
- Malabsorption
- Hepatomegaly (with or without jaundice)
- Splenomegaly



Hepatosplenomegaly



#### Pneumonia alba



#### Late manifestations (> 2 years of age)

#### Neurologic

- Interstitial keratitis
- 8<sup>th</sup> cranial nerve deafness

#### Dental

- Peg-shaped & notched central incisors (Hutchinson teeth)
- Multicuspid first molars (Mulberry molars)

#### Skeletal

- Anterior bowing of the shins (saber shins)
- Frontal bossing
- Symmetric painless swelling of the knees (Clutton joints)

#### **Facial**

- Saddle nose
- Fissures and scaring around body orifices (rhagades)

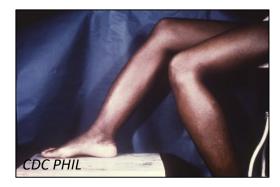
Interstitial keratitis



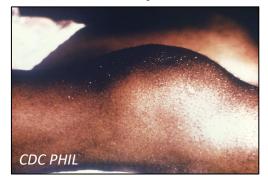
Hutchinson teeth



Saber shins



Clutton joints





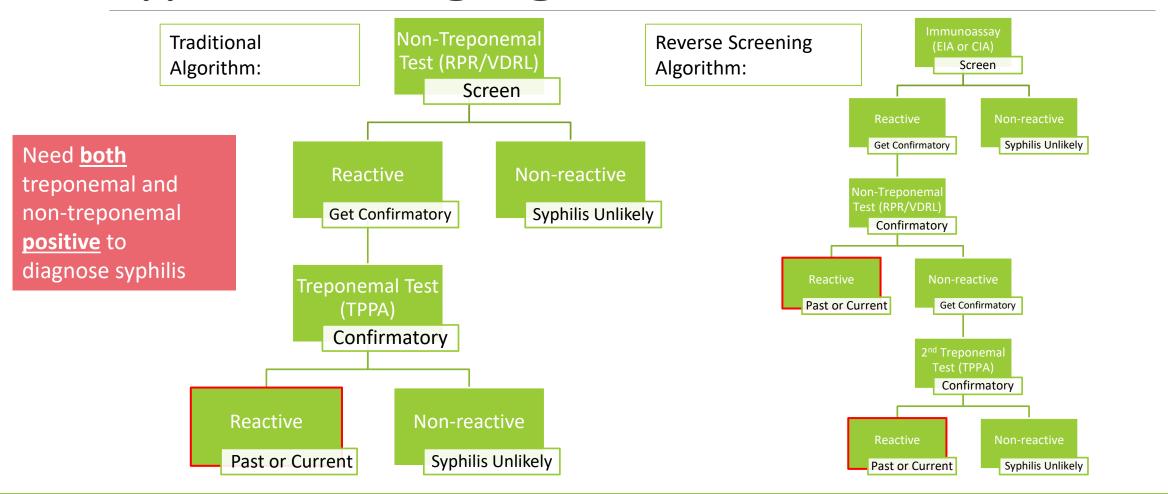
#### Syphilis: Diagnosis

- Organisms on microscopy using dark field
- Positive serology on blood or cerebrospinal fluid (CSF)
   Non-Specific Treponemal Tests:
  - 1. Venereal Disease Research Laboratory (VDRL)
  - 2. Rapid Plasma Reagin (RPR)

#### **Specific Treponemal Tests:**

- 1. Fluorescent Treponemal Antibody Absorption (FTA-ABS)
- 2. Microhemagglutination-Treponema pallidum (MHA-TP)
- 3. Syphilis enzyme immunoassays (EIA)
- 4. Syphilis chemiluminescence immunoassays (CIA)
- 5. T. pallidum passive particle agglutination (TPPA)

#### Syphilis testing algorithms



#### Treatment of syphilis in pregnancy

The only treatment of syphilis in pregnancy is penicillin

If type-1 penicillin allergy, patient should be desensitized in collaboration with an allergist in the hospital and treated with penicillin

#### Recommended Regimen for Syphilis During Pregnancy

Pregnant women should be treated with the recommended penicillin regimen for their stage of infection.

#### Recommended Regimen for Primary and Secondary Syphilis\* Among Adults

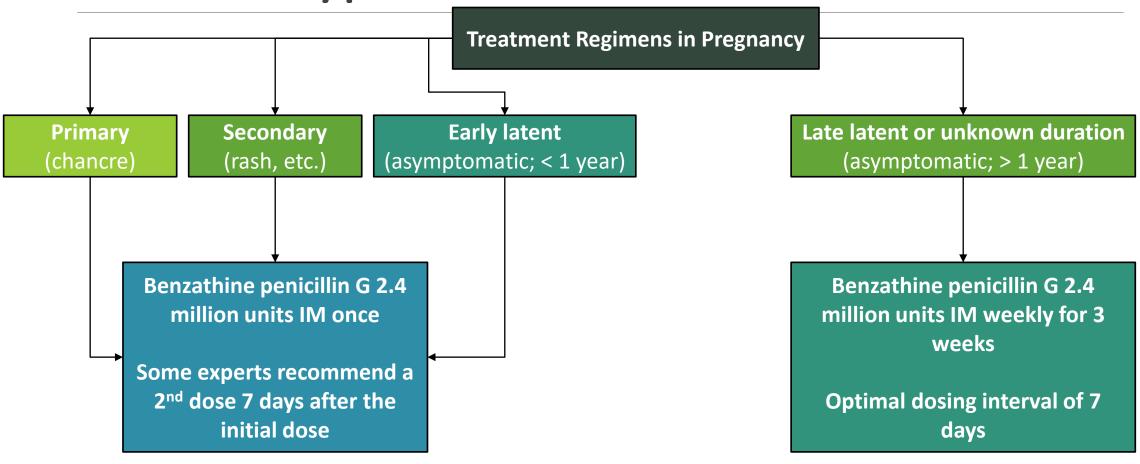
Benzathine penicillin G 2.4 million units IM in a single dose

#### Recommended Regimens for Latent Syphilis\* Among Adults

Early Latent Syphilis: Benzathine penicillin G 2.4 million units IM in a single dose

**Late Latent Syphilis: Benzathine penicillin G** 7.2 million units total, administered as 3 doses of 2.4 million units IM each at 1-week intervals

#### Prenatal syphilis treatment

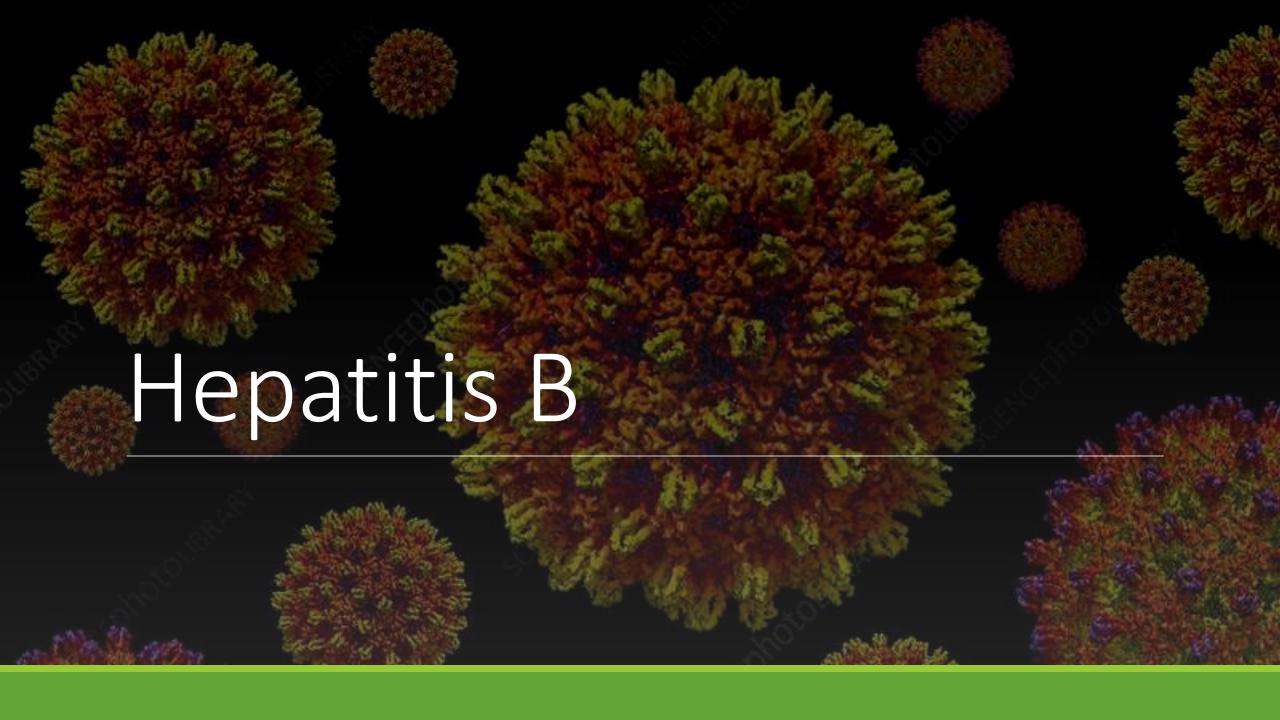


#### Syphilis serologies at delivery

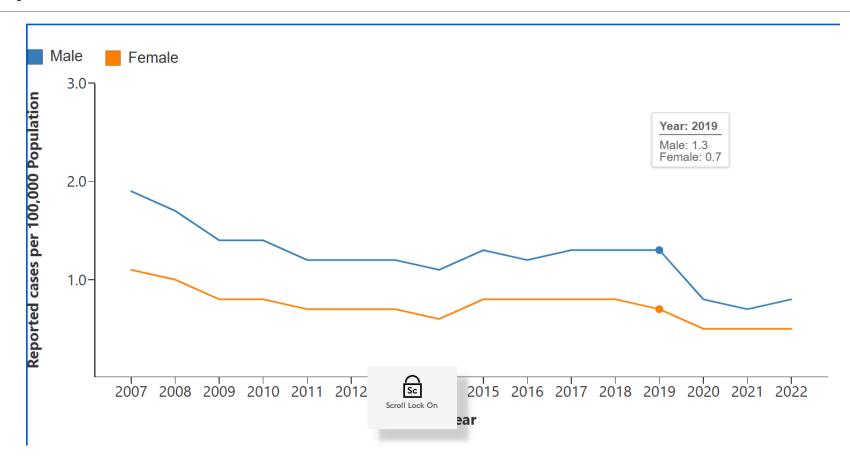
#### Non-treponemal (RPR/VDRL)

- Need both birthing parent and infant titers at delivery
- Perform the same test on both (e.g. compare RPR with RPR) drawn at the same time

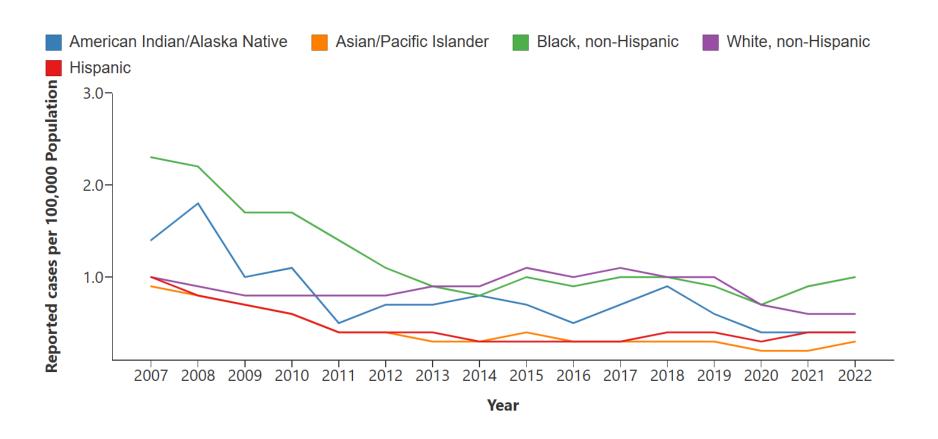
- Treponemal (FTA-ABS/TP-PA EIA)
  - TP-PA from a birthing parent can stay positive in Infant serum for up to 15 months.
  - NOT NEEDED IN INFANT SCREENING



### Rates of reported cases of acute hepatitis B, by sex — United States, 2007–2022



### Rates of reported cases of acute hepatitis B, by race/ethnicity — United States, 2007–2022



Total <sup>§</sup>	16,729	5.8
0–19	252	0.4
20–29	1,564	4.1
30–39	3,881	9.9
40–49	3,912	11.1
50–59	3,206	8.8
≥60	3,892	5.6
Male	9,348	
Female	7,334	5.1
American Indian/Alaska Native, non-Hispanic	73	3.2
Asian/Pacific Islander, non-Hispanic	3,651	20.1
Black, non-Hispanic	2,759	7.7
White, non-Hispanic	3,112	1.8
Hispanic	817	1.6
Other	1,098	n/a

Number and rate\* of newly reported cases† of chronic hepatitis B, by demographic characteristics — United States, 2022

State or Jurisdiction	▲ No
Alabama	_
Alaska	_
Arizona	_
Arkansas	_
California	2
Colorado	_
Connecticut	_
Delaware	_

Number of newly reported cases\* of perinatal hepatitis B, by state or jurisdiction — United States, 2022

During 2022, a total of 13 cases of perinatal hepatitis B to CDC, compared with 17 perinatal hepatitis B cases reported during 2021.

#### Clinical manifestations



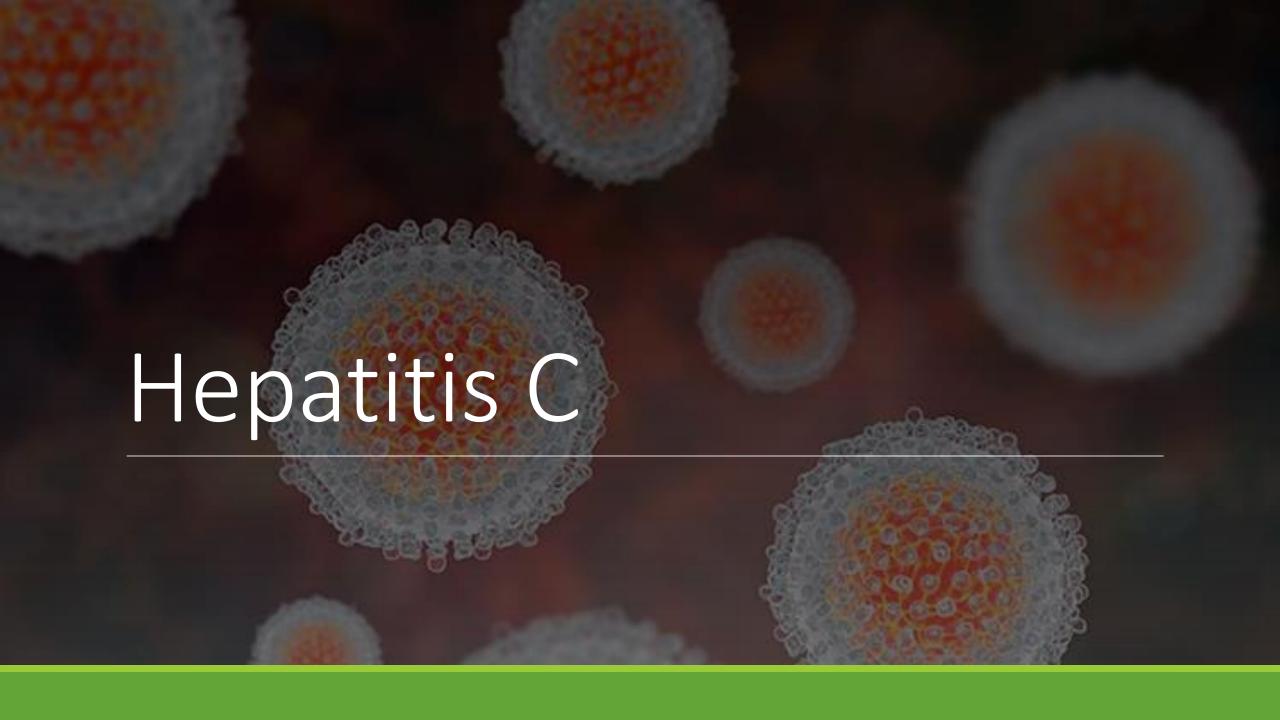
#### Hepatitis B: Diagnosis

TABLE 5. Interpretation of serologic test results\* for hepatitis B virus infection

_	Serologic marker				
	HBSAG	Total anti-HBc	IgM anti-HBc	Anti-HBs	Interpretation
_	_	_	_	_	Never infected
	+†	_	_	_	Early acute infection; transient (≤18 days) after vaccination
	+	+	+	_	Acute infection
	-	+	+	_	Acute resolving infection
	-	+	_	+	Recovered from past infection and immune
	+	+	_	_	Chronic infection
	-	+	-	-	Past infection; low-level chronic infection <sup>§</sup> ; passive transfer to infant born to HBsAg- positive mother; false positive (no infection)
_	-	-	_	+	Immune if concentration is >10 mIU/mL after vaccination, passive transfer after HBIG administration

#### Treatment and Referral

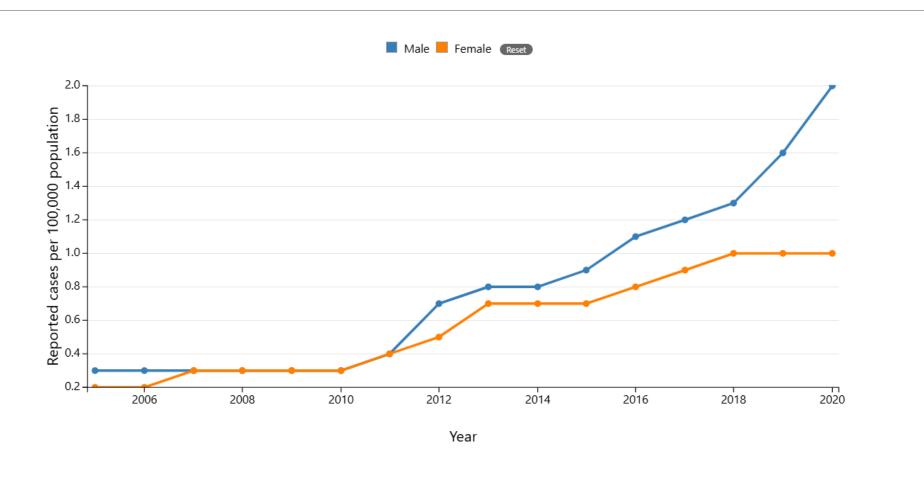
- Check HBV DNA, Hep Be antigen
- The American Association for the Study of Liver Diseases (AASLD) suggests maternal antiviral therapy when the maternal HBV DNA is greater than 200,000 IU/mL
- Refer for treatment Tenofovir first line therapy
- Refer to local health department perinatal Hep B prevention program
- Infant should receive Hep B vaccination and Hep B Immune Globulin



#### Hepatitis C Surveillance Overview

- •There were 4,848 new cases of acute hepatitis C reported during 2022.
- •There were 67,400 estimated acute HCV infections during 2022.
- •There were 93,805 cases of newly reported chronic hepatitis C during 2022.
- •There were 12,717 hepatitis C-related deaths reported during 2022

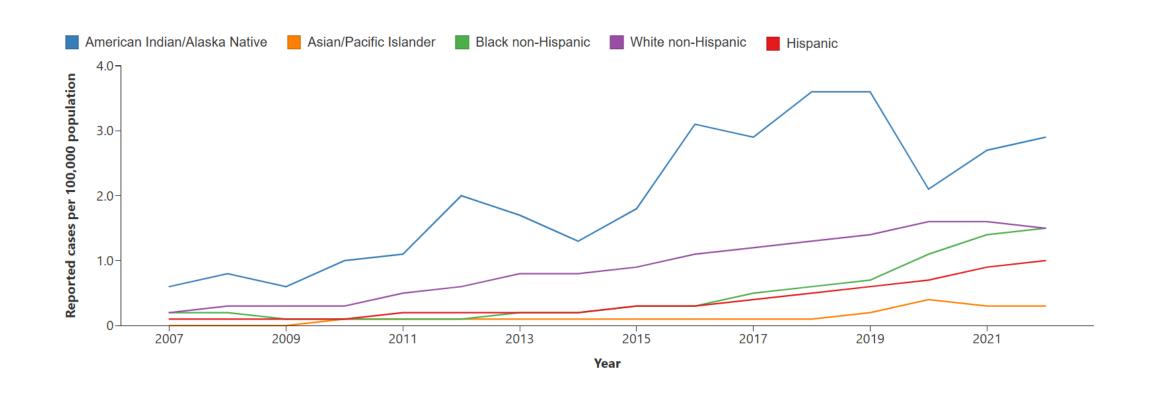
Rates\* of reported cases† of acute hepatitis C virus infection, by sex — United States, 2005-2020



Number of newly reported\* chronic hepatitis C cases† by sex and age — United States, 2022



# Rates\* of reported cases† of acute hepatitis C, by race/ethnicity — United States, 2007–2022



Number and rate\* of newly reported cases† of chronic hepatitis C, by demographic characteristics — United States, 2022

Total <sup>§</sup>	93,805	40.2	
0–19	885	1.6	
20–29	10,833	35.0	
30–39	25,192	80.2	
40–49	18,414	64.9	
50–59	15,805	53.5	
≥60	22,338	38.9	
Male	60,646	52.5	
Female	32,553	27.6	
Race/ethnicity			
American Indian/Alaska Native, non-Hispanic	1,834	104.8	
Asian/Pacific Islander, non-Hispanic	740	6.5	
Black, non-Hispanic	9,938	30.6	
White, non-Hispanic	47,269	31.3	
Hispanic	4,112	13.1	
Other	4,704	n/a	
Urban	71,904	37.1	
Rural	21,016	58.5	

#### Clinical manifestations



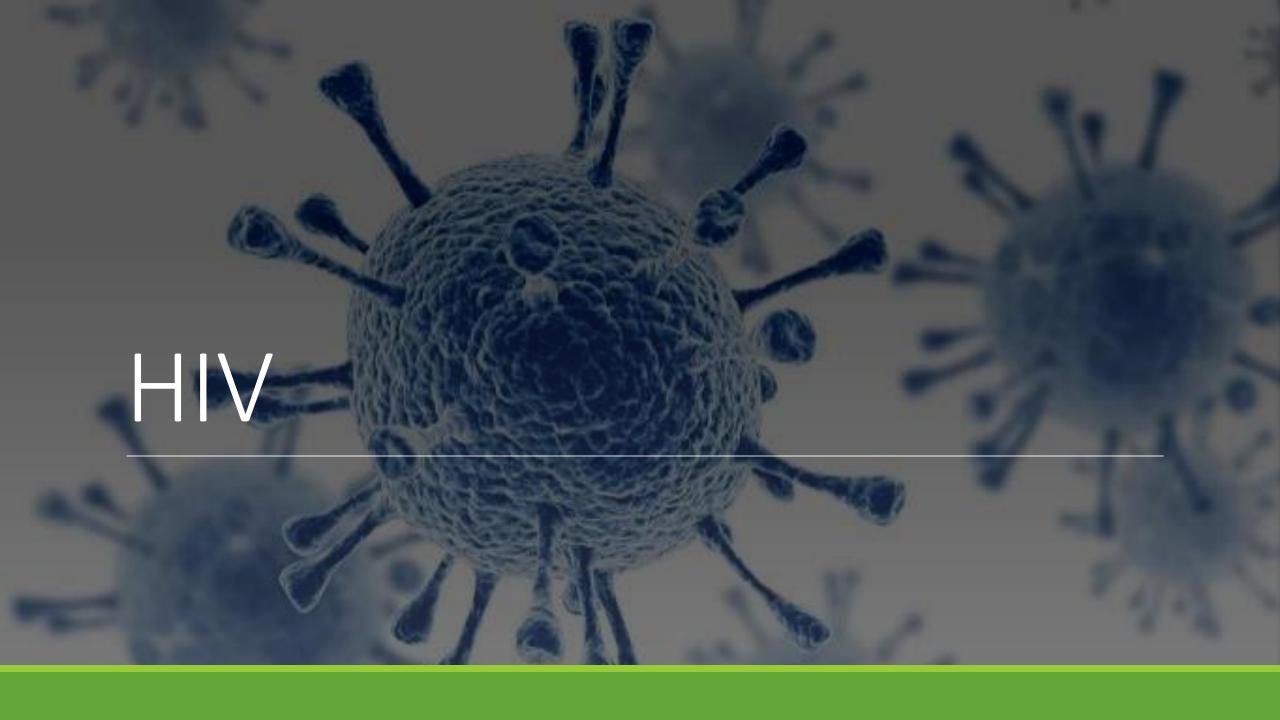


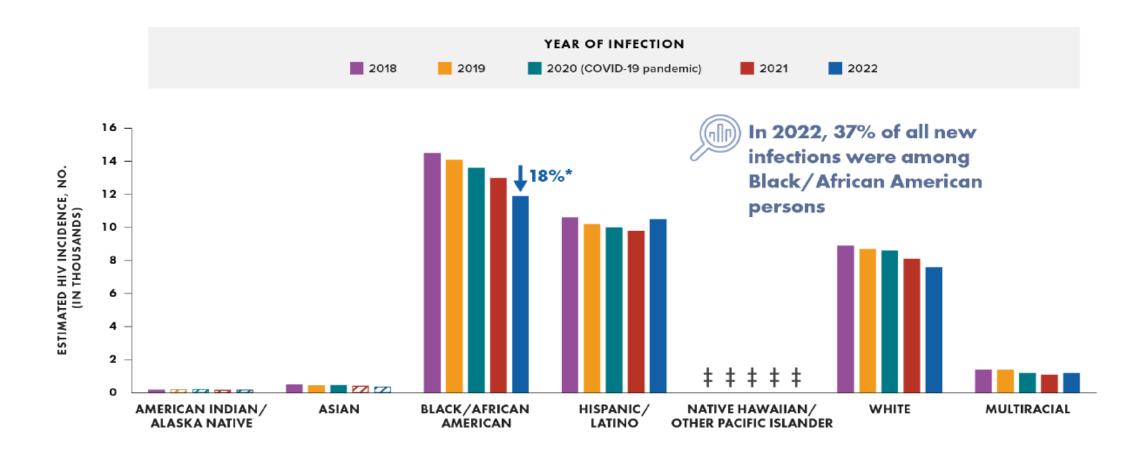
#### Hepatitis C: Diagnosis

- Antibody to HCV (i.e., immunoassay, EIA, or enhanced CIA and, if recommended, a supplemental antibody test)
- Follow up NAAT to detect HCV RNA for those with a positive antibody result
- Antibody to HCV remains positive after spontaneously resolving or successful treatment; therefore, subsequent testing for HCV reinfection among persons with ongoing risk factors should be limited to HCV RNA

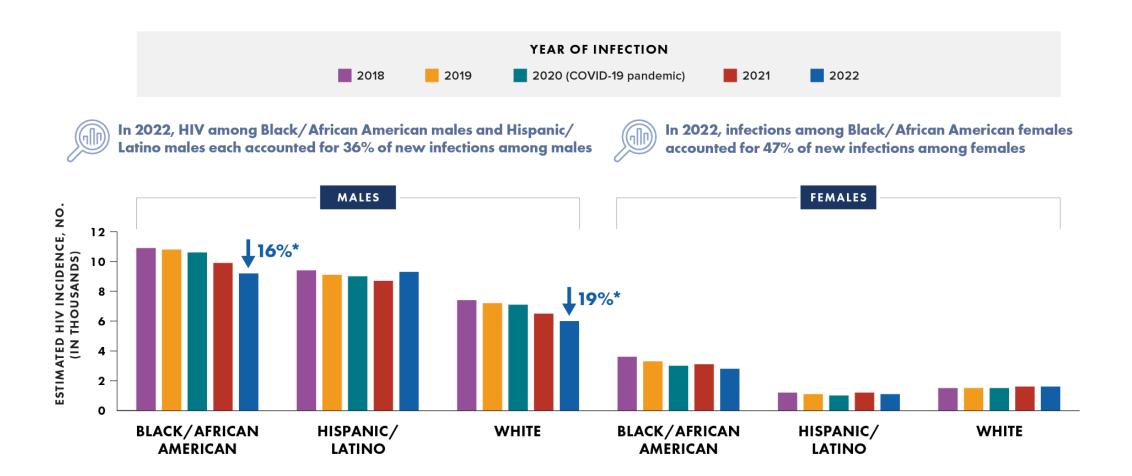
#### Treatment-- Limitations

- There are no large-scale clinical trials evaluating the safety of direct-acting antivirals (DAAs) in pregnancy.
- Currently, there are no available data on the use of pangenotypic regimens during pregnancy.
- DAAs have not been formally studied as a way to interrupt MTCT.
- Despite the lack of a recommendation, treatment can be considered during pregnancy on an individual basis after a patient-physician discussion about the potential risks and benefits. Refer to ID or hepatology
- Treatment would need to be offered postpartum and infant monitored for infection with HCV RNA at 2 months, HCV Ab at 18 months and if positive, check HCV RNA 3 years of age or older – treatment is offered > 3 y of age





Estimated HIV incidence among persons aged ≥ 13 years, by race/ethnicity, 2018–2022—United States



Estimated HIV incidence among Black/African American, Hispanic/Latino, and White persons aged ≥ 13 years, by sex assigned at birth, 2018–2022—United States

## Testing and Referral



HIV-1/HIV-2 Ag/Ab combination assay



If positive, reflex to supplemental HIV-1/HIV-2 antibody differentiation



If positive – check HIV RNA and CD4 count



Refer to ID or HIV specialist for HAART

#### Treatment

- Preferred regimens
  - Dolutegravir/Abacavir/Lamivudine (Triumeq)
  - Dolutegravir + Tenofovir disproxil fumarate + Emtricitabine
  - Dolutegravir + Tenofovir alafenamide + Emtricitabine
  - Dolutegravir + TDF+ Lamivudine
  - Dolutegravir+ TAF + Lamivudine
  - Darunavir/ritonavir + NRTI backbones listed above

#### How about IV Zidovudine



IV ZDV is **not** required for people who meet **ALL** of the following criteria: (1) are receiving ART, (2) have HIV RNA <50 copies/mL within 4 weeks of delivery, and (3) are adherent to their ARV regimen



IV ZDV may be considered for people with HIV RNA ≥50 copies/mL and ≤1,000 copies/mL within 4 weeks of delivery. Data insufficient whether administration of IV ZDV to people with HIV RNA levels between 50 copies/mL and 1,000 copies/mL provides any additional protection against perinatal HIV transmission

#### How about IV Zidovudine

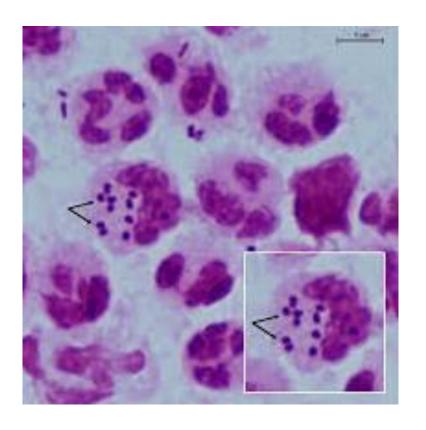


Intrapartum IV ZDV should be administered in the following situations based on laboratory and clinical information near the time of delivery: (a) HIV RNA >1,000 copies/mL, (b) unknown HIV RNA, (c) known or suspected lack of adherence since the last HIV RNA result, or (d) a positive expedited antigen/antibody HIV test result during labor



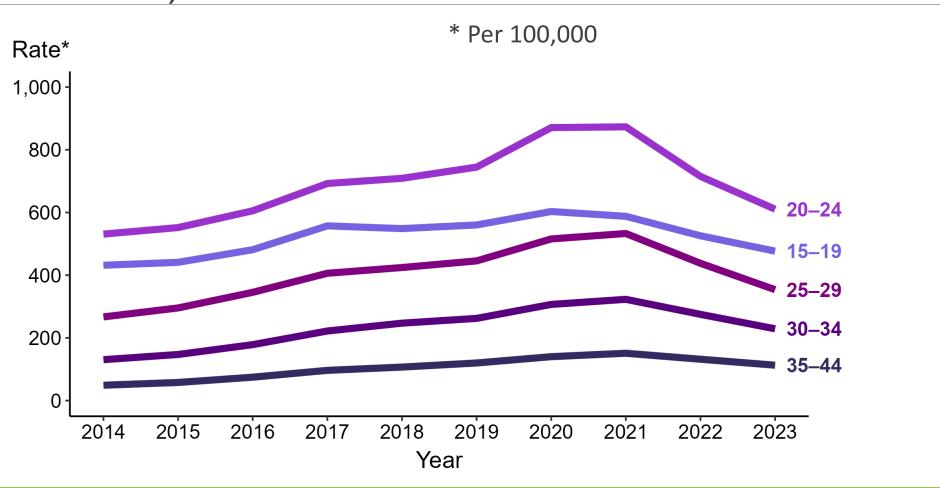
When HIV RNA is >1,000 copies/mL or is unknown near the time of delivery, scheduled cesarean delivery at 38 weeks gestation is recommended to minimize perinatal HIV transmission, irrespective of administration of antepartum ART



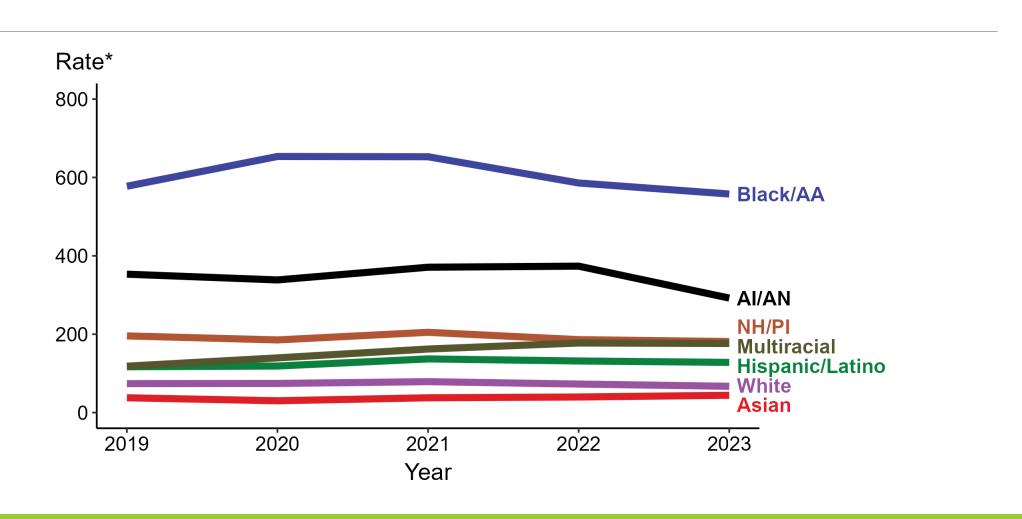


#### Chlamydia and Gonorrhea

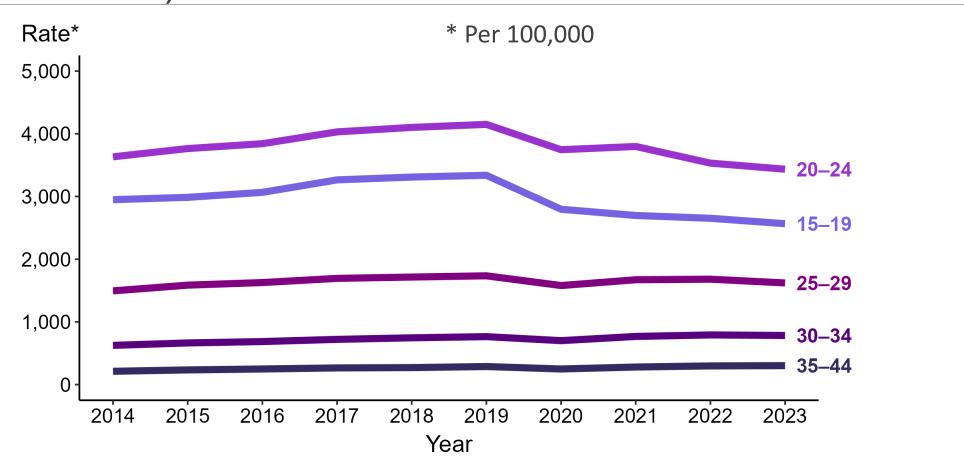
# Gonorrhea — Rates of Reported Cases Among Women Aged 15–44 Years by Age Group and Year, United States, 2014–2023



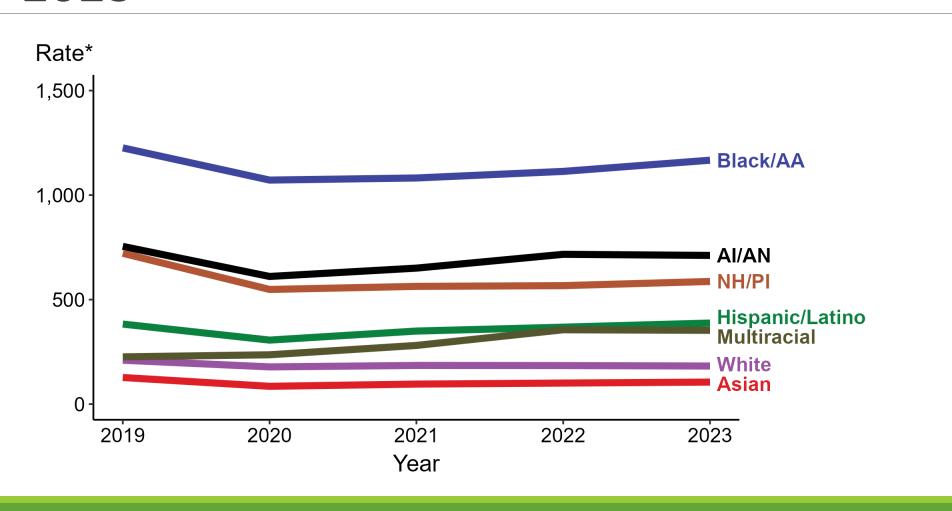
## Gonorrhea — Rates of Reported Cases by Race/Hispanic Ethnicity, United States, 2019–2023



#### Chlamydia — Rates of Reported Cases Among Women Aged 15–44 Years by Age Group and Year, United States, 2014–2023



# Chlamydia — Rates of Reported Cases by Race/Hispanic Ethnicity and Year, United States, 2019–2023



#### Clinical manifestations in neonates

#### Chlamydia

- Ophthalmia neonatorum
- Pneumonia



#### Gonorrhea

- Ophthalmia neonatorum
- Scalp abscesses
- Meningitis
- Arthritis
- Pharyngitis
- Rhinitis
- Vaginitis
- Urethritis
- Pneumonia

#### Testing

Urine or vaginal swab GC/CT nucleic acid amplification test

#### Treatment

#### Gonorrhea

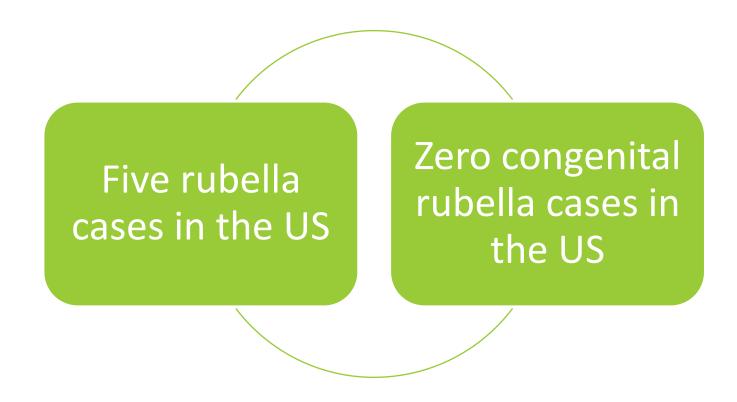
- Ceftriaxone 500 mg IM x 1
- Alternative: Cefpodoxime 800 mg po x 1
- Allergy: Get an ID consult

#### Chlamydia

- Azithromycin 1 g orally in a single dose
- Alternative Regimen:Amoxicillin 500 mg orally 3 times/day for 7 days

### Rubella

#### CDC Rubella Surveillance



Weekly cases\* of notifiable diseases, United States, U.S. Territories, and Non-U.S. Residents week ending November 4, 2023 (Week 44) Table 1110 Rubella, congenital syndrome

# Impact of maternal rubella infection on fetus

Rubella virus infection is a leading cause of vaccine-preventable birth defects, known as congenital rubella syndrome (CRS).

Rubella infection during pregnancy can also lead to miscarriage (loss of the fetus within 20 weeks of conception) and stillbirth (death of the fetus after 20 weeks of pregnancy).

When a pregnant woman is infected with rubella in early pregnancy, she has up to a 90% chance of giving birth to a baby with CRS

33% of infants born with CRS die before their first birthday

#### Clinical manifestations of CRS

- Sensorineural hearing loss
- Cataracts
- Cardiac malformations
- •Microcephaly
- Low birth weight

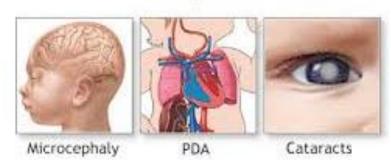
- Radiolucent bone lesions
- Jaundice
- Thrombocytopenia
- Purpuric skin lesions (blueberry muffin lesions)

#### Clinical manifestations of CRS





Rubella syndrome





#### Testing

Serologic testing of rubella immunity: Rubella IgG. Positive test denotes immunity.

Testing for Rubella IgM is not indicated in asymptomatic patients as false positives may cause confusion

The only indication for testing rubella IgM is for suspected rubella infection

#### Vaccination

- Pregnant women who do not have evidence of immunity should be vaccinated immediately after giving birth.
- There is no postexposure prophylaxis if exposed to rubella



#### Epidemiology

The prevalence of GBS colonization in pregnant women in the United States is estimated to be between 10% and 30%

Advancements in screening for GBS colonization and antibiotic prophylaxis have significantly decreased the incidence of GBS-early onset disease from approximately 1.8 cases of GBS-EOD per 1000 live births to approximately 0.23 per 1000 live births

#### Clinical manifestations in neonate

- Group B strep early onset disease occurs from birth through 6 days of age
- Late-onset disease occurs when infant is 7–89 days old and antibiotic prophylaxis does not impact this
- Group B disease manifests as
  - Bacteremia
  - Sepsis
  - Pneumonia
  - Meningitis

#### Testing

- •Universal antenatal testing of pregnant women for GBS colonization at 36 0/7 to 37 6/7 weeks' gestation or for pregnant women who present in preterm labor and/or with PROM before 37 0/7 weeks' gestation.
- Vaginal or rectal swab for culture or NAAT-based methods
- Urine culture

#### Risk Assessment if unknown GBS status

- History of a previous infant with GBS disease
- •Unknown GBS status and preterm labor or preterm premature rupture of membranes (<37 0/7 weeks)
- •Unknown GBS status with any of the following risk factors at ≥37 0/7 weeks of gestation
- Maternal fever ≥100.4 °F (38 °C)
- Prolonged rupture of membranes (≥18 hours)
- Positive point-of-care NAAT for GBS
- History of GBS colonization in a previous pregnancy
- •Negative intrapartum NAAT, but risk factors develop during labor, such as maternal fever and prolonged rupture of membranes
- •Suspected intra-amniotic infection (broad-spectrum antibiotics, including GBS coverage, should be given)

#### Prophylaxis

- If not PCN allergic
  - Penicillin G, 5 million units IV initial dose, then 2.5-3.0 million units every 4 hours until birth.
  - Ampicillin 2 g IV initial dose, then 1 g IV every 4 hours until birth
- If PCN allergic:
  - Clindamycin 900 mg IV every 8 hours until delivery OR
  - Vancomycin 20 mg/kg IV q 12 hours until delivery



# What about TORCH testing?

#### TORCH Testing

#### Toxoplasma

#### Other

- Parvovirus B19
- Syphilis
- Zika
- Varicella Zoster Virus
- Enteroviruses
- Lymphocytic choriomeningitis virus

#### Rubella

#### Cytomegalovirus

#### Herpes

#### Issues with TORCH testing

Indiscriminate screening for TORCH infections with a battery of tests is costly and has poor diagnostic yield.

Current approach is to test infants with suspected congenital infections based upon their clinical presentation and maternal history.

Testing for fetal growth retardation also has low yield

USPSTF Position on Herpes Simplex Screening in Pregnancy

Recommends against routine serologic screening for genital herpes simplex virus infection in asymptomatic adolescents and adults, including pregnant persons.

Routine serologic screening for genital herpes is limited by the low predictive value of the widely available serologic screening tests and the expected high rate of false-positive results likely to occur with routine screening of asymptomatic persons in the US.

The harms outweigh the benefits tor population-based screening tor genital HSV infection in asymptomatic adolescents and adults, including pregnant persons.

#### Questions?