Sexually Transmitted Infections in Pregnancy

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Disclosures

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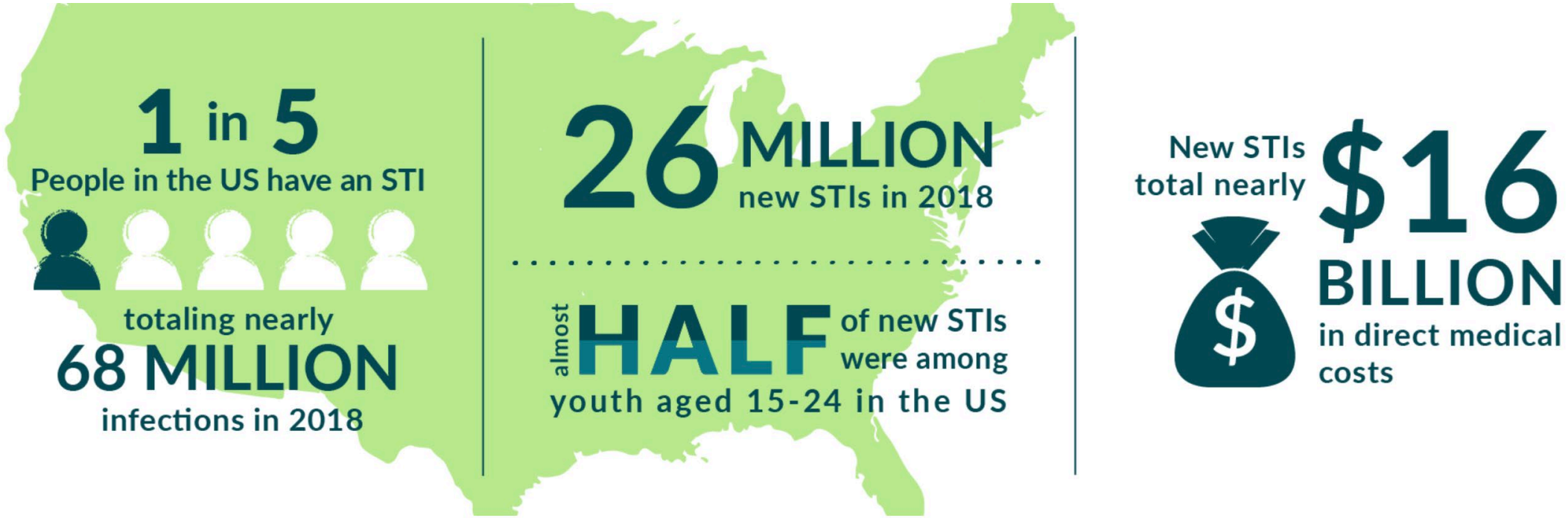
Learning Objectives

- *By the end of this session, each participant will be able to list the:*
  - *Screening recommendations for STIs in pregnant persons*
  - *Recommended treatment regimens for STIs in pregnant persons*
  - *Potential impact of STIs on the pregnancy as well as the neonate*

- STIs Covered:
  - HIV
  - Syphilis
  - Hepatitis B Virus
  - Hepatitis C Virus
  - Chlamydia
  - Gonorrhea
  - Trichomonas
  - Herpes Simplex Virus

STI – Scope of the Problem



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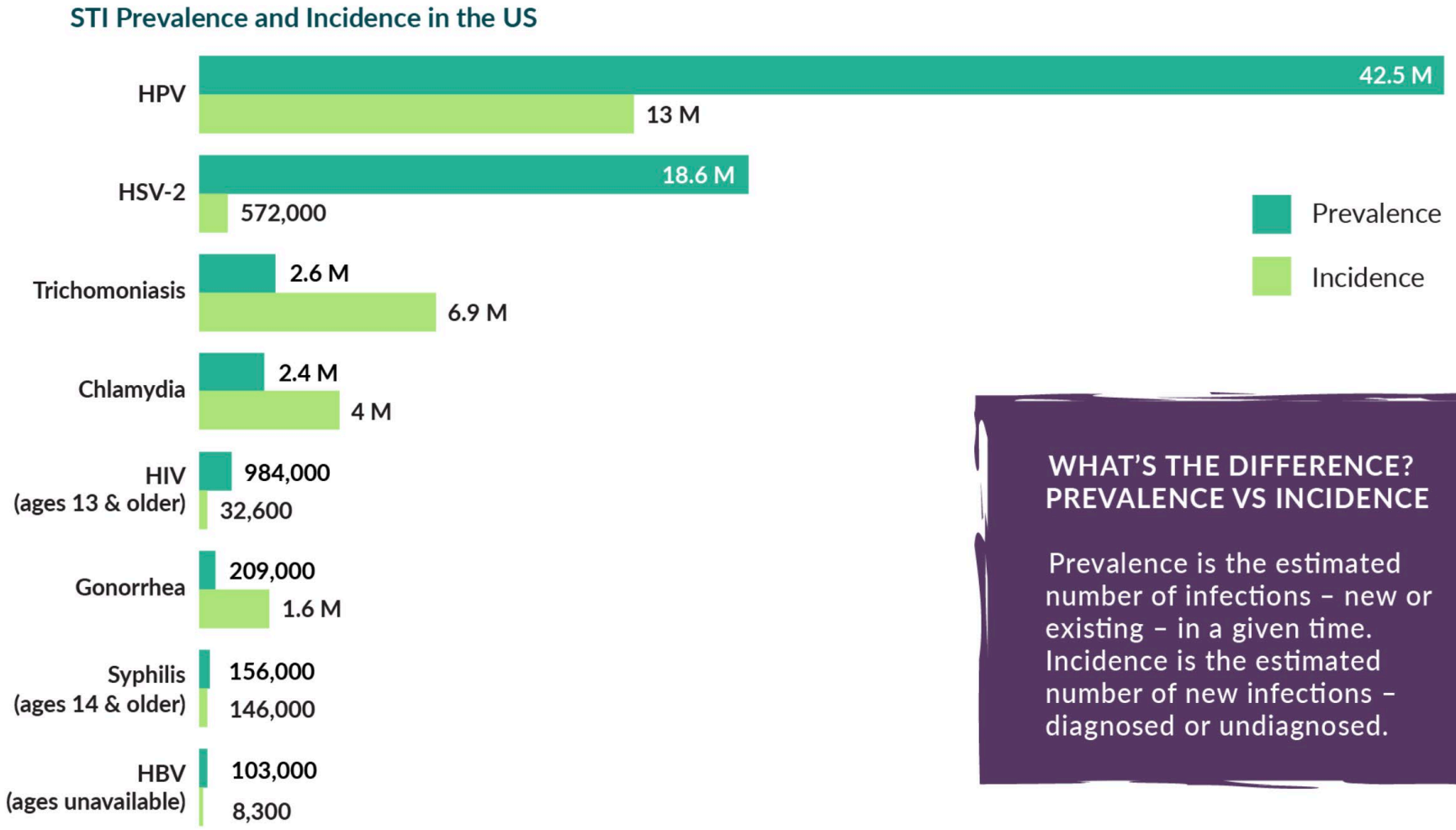
Source: CDC.gov

Scope of the problem by STI



WHAT'S THE DIFFERENCE? PREVALENCE VS INCIDENCE

Prevalence is the estimated number of infections – new or existing – in a given time. Incidence is the estimated number of new infections – diagnosed or undiagnosed.

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Source: CDC.gov

- Pregnant women fall under the “special population” according to the CDC

- Recommended screening tests for ALL pregnant women
  - HIV, Syphilis, Hepatitis B, Hepatitis C

- Recommended screening tests for pregnant women AT RISK
  - Chlamydia, Gonorrhea

- Screen only if symptomatic
  - Bacterial vaginosis, trichomonas, HSV-2

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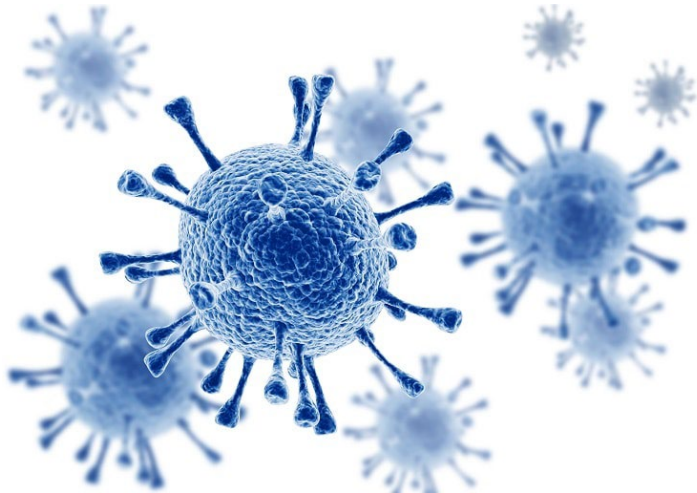
Human immunodeficiency virus (HIV)

A sentinel event

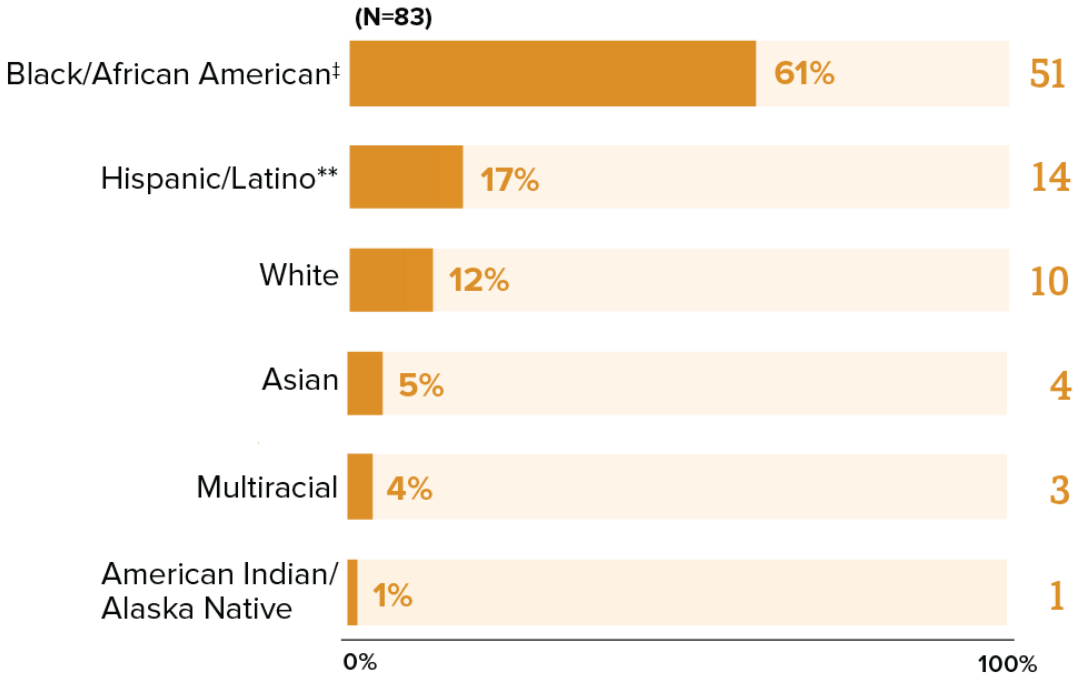
HIV

- A single-stranded, positive-sense, enveloped RNA virus
- Transmitted via sexual contact, needle-sharing, or perinatally
- Women comprise 50% of the people worldwide living with HIV
  - In the US, females made up 19% of the new HIV diagnoses in 2019



HIV in Pregnancy

- Of the 36,801 new HIV diagnoses in the US and dependent areas in 2019, <1% were due to perinatal transmission



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Source: CDC.gov

HIV – Screening in pregnancy

- "Opt-out screening" at first prenatal visit or as early in pregnancy as possible
- Retest in the 3rd trimester (before 36 weeks) if at high risk:
  - Illicit drug use
  - STI during pregnancy
  - Multiple sex partners during pregnancy
  - Live in areas of high HIV incidence
  - Partner has HIV
  - Signs or symptoms of acute HIV infection
- Rapid HIV testing should be performed on any woman in labor who has not been screening during pregnancy

HIV – vertical transmission

- Transplacentally or by exposure to maternal cervicovaginal secretions and blood at delivery
  - Risk proportional to concentration of virus in the maternal plasma
- Mode of delivery should be driven by obstetrical indications when maternal viral load is low/undetectable
  - If viral load >1000 copies/mL, potential benefit to scheduling a pre-labor cesarean delivery
- Combined antiretroviral therapy can reduce vertical transmission risks to 1-2% if maternal viral loads of ≤ 1000 copies/mL can be sustained
- Intrapartum zidovudine
  - Achieves adequate drug levels in both maternal and fetal circulation if given 3-6 hours prior to delivery
  - May be considered in those with viral loads ≥50 but ≤1000 copies/mL
  - Recommended for all with a viral load >1000 copies/mL within 4 weeks of delivery

HIV – Exposed Neonates

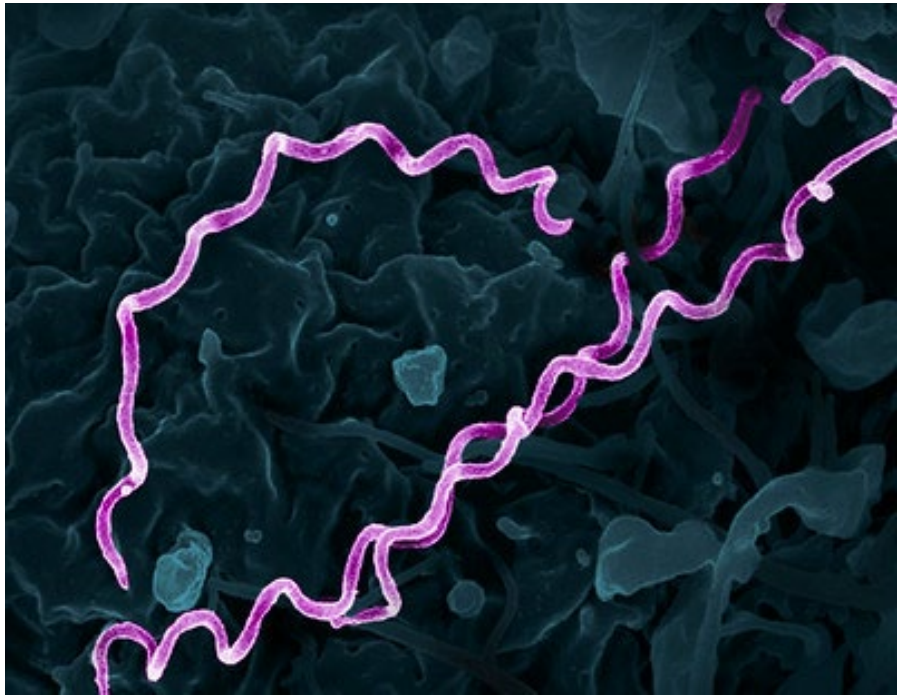
- All infants born to mothers with HIV should have postexposure prophylaxis initiated as soon as possible after birth
- Regimen depends on maternal viral load, and will be given from 2-6 weeks postnatally
- Breast/chest feeding should be discouraged as cumulative additional vertical transmission risk is ~15%

Syphilis

Not a thing of the past

Syphilis

- Cause by the highly motile, spiral-shaped, gram-negative bacterium T. palladium entering via direct contact with a mucosal surface or skin abrasion



Stages of Syphilis

Primary Syphilis

- 3-90 days after exposure
- Single painless ulcer or chancre

Secondary Syphilis

- 4-10 weeks after initial infection
- Skin rash, mucocutaneous lesions, and lymphadenopathy

Tertiary Syphilis

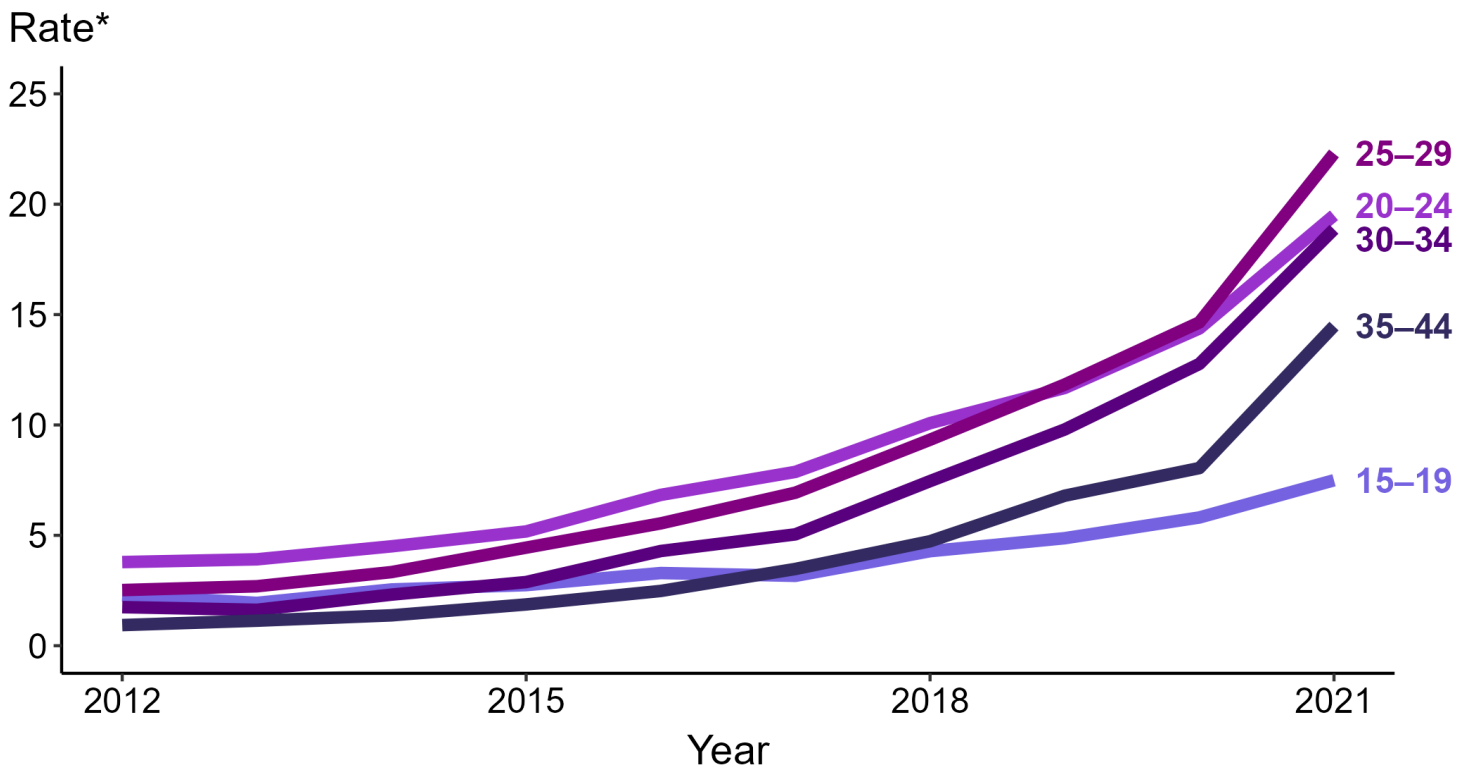
- 3-15 years after initial infection
- Cardiac involvement, gummatous lesions, tabes dorsalis, and general paresis

Latent Syphilis

- Detected by serologic testing and lacking clinical manifestations

**Neurosyphilis, ocular syphilis or otosyphilis can occur at any stage

Primary and Secondary Syphilis Among US Women of Reproductive age



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Source: CDC.gov

Syphilis – Screening in Pregnancy

- Serologic testing at first prenatal visit
- 2 step process: traditional vs reverse sequence
- Reportable to local or state health department
- Serologic retesting in the third trimester and at delivery for those at high risk
- Test woman in case of stillborn or infant death

Risk Factors for Syphilis:

- Sex with multiple partners
- Transactional sex
- Late or limited prenatal care
- IV drug use
- Incarceration of woman or her partner
- Unstable housing

Traditional

Initial non-treponemal test → Confirmatory treponemal test

Reverse Sequence

Automated treponemal test → Quantitative non-treponemal test

Treponemal Tests

- Detect antibodies against specific treponemal antigens
- Qualitative only
- FTA-ABS, MHA-TP, EIA, CIA, TP-PA

Non-Treponemal Tests

- Based on serum reactivity to an antigen
- Quantify the total IgG and IgM antibodies released
- VDRL, RPR

Prenatal syphilis screening laws

2015 → 2019

- Congenital syphilis rate increased **291%** to 48.5 cases per 100,000 live births

Legal requirements for syphilis screening among pregnant women by time of test and state, 2018

	First Visit	Third Trimester	Delivery
Alabama	X	O	X
Alaska	X		
Arizona	X	X	X
Arkansas	X	X	
California	X		
Colorado	X		
Connecticut	X	X	
Delaware	X	X	
DC	X	X	
Florida	X	X	O
Georgia	X	X	O
Hawaii			
Idaho	X		
Illinois	X	X	
Indiana	X	O	
Iowa			
Kansas	X		
Kentucky	X		
Louisiana	X	X	O
Maine			
Maryland	X	X	O
Massachusetts	X		
Michigan	X	X	O
Minnesota			
Mississippi			
Missouri	X	O	O
Montana	X		
Nebraska	X		
Nevada	X	X	
New Hampshire			
New Jersey	X		X
New Mexico	X		
New York	X		
North Carolina	X	X	X
North Dakota			
Ohio	X		
Oklahoma	X		
Oregon	X		
Pennsylvania	X	O	
Rhode Island	X		
South Carolina	X		
South Dakota	X		
Tennessee	X	O	
Texas	X	X	
Utah	X		
Vermont	X		
Virginia	X		
Washington	X		
West Virginia	X		
Wisconsin			
Wyoming	X		

X	Screening required
O	Screening Required only if at increased risk

Source: CDC.gov

Syphilis – Vertical transmission

- Fetus most commonly acquires syphilis via transplacental passage of spirochetes
- Risk is highest in early states of infection
- After 20 weeks, maternal syphilis without treatment is associated with abortion, fetal death, or congenital syphilis
- Treatment dramatically reduces the risk of vertical transmission to **1-2%**

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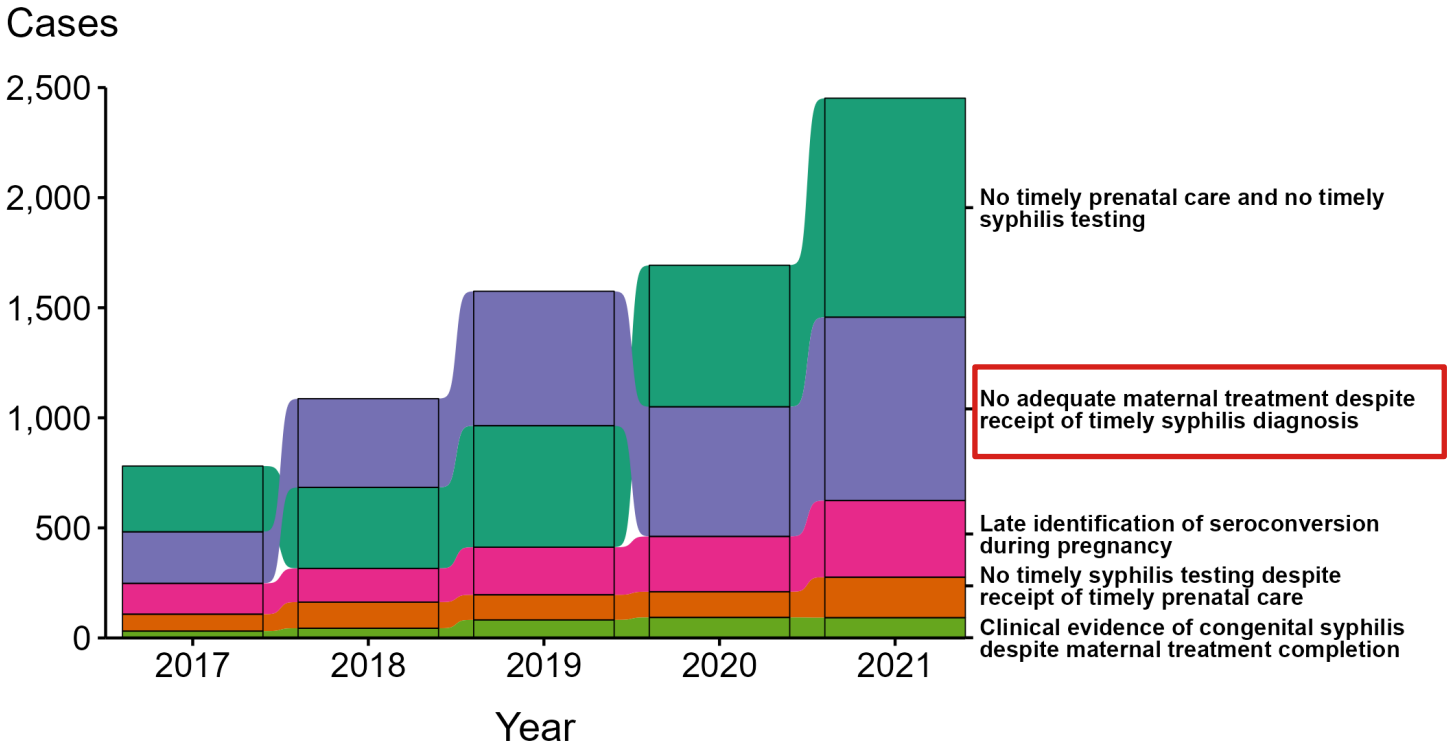
Congenital Syphilis

- Missed prevention opportunities among mothers delivering infants with congenital syphilis in the United States from 2017-2021



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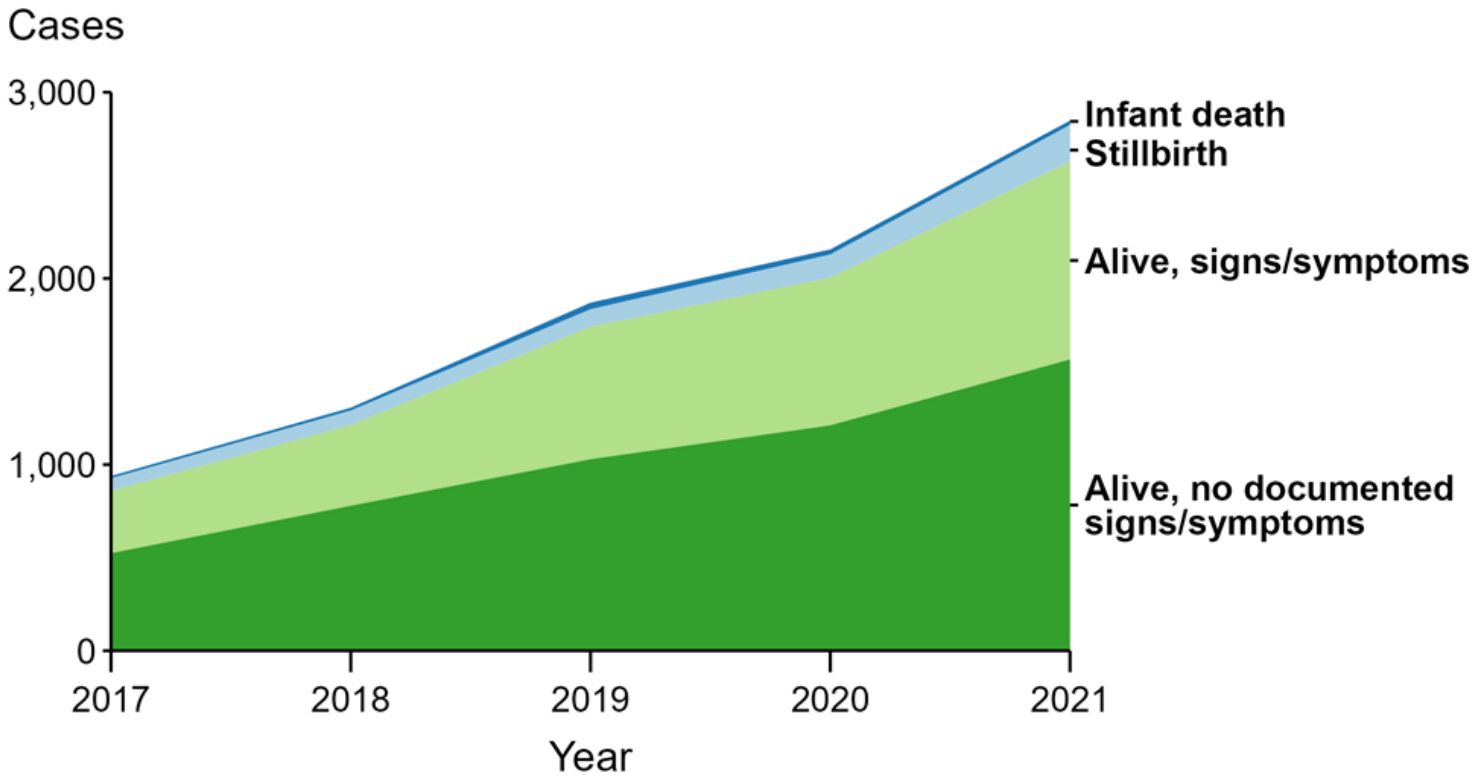
Source: CDC.gov

Congenital Syphilis

- Routine screening in pregnancy typically identifies latent syphilis
- Complications of congenital syphilis:
  - Hepatic injury, anemia, thrombocytopenia, fetal growth restriction, and rarely hydrops and stillbirth
- Up to 12% of neonates with a normal prenatal ultrasound will require treatment for syphilis at birth



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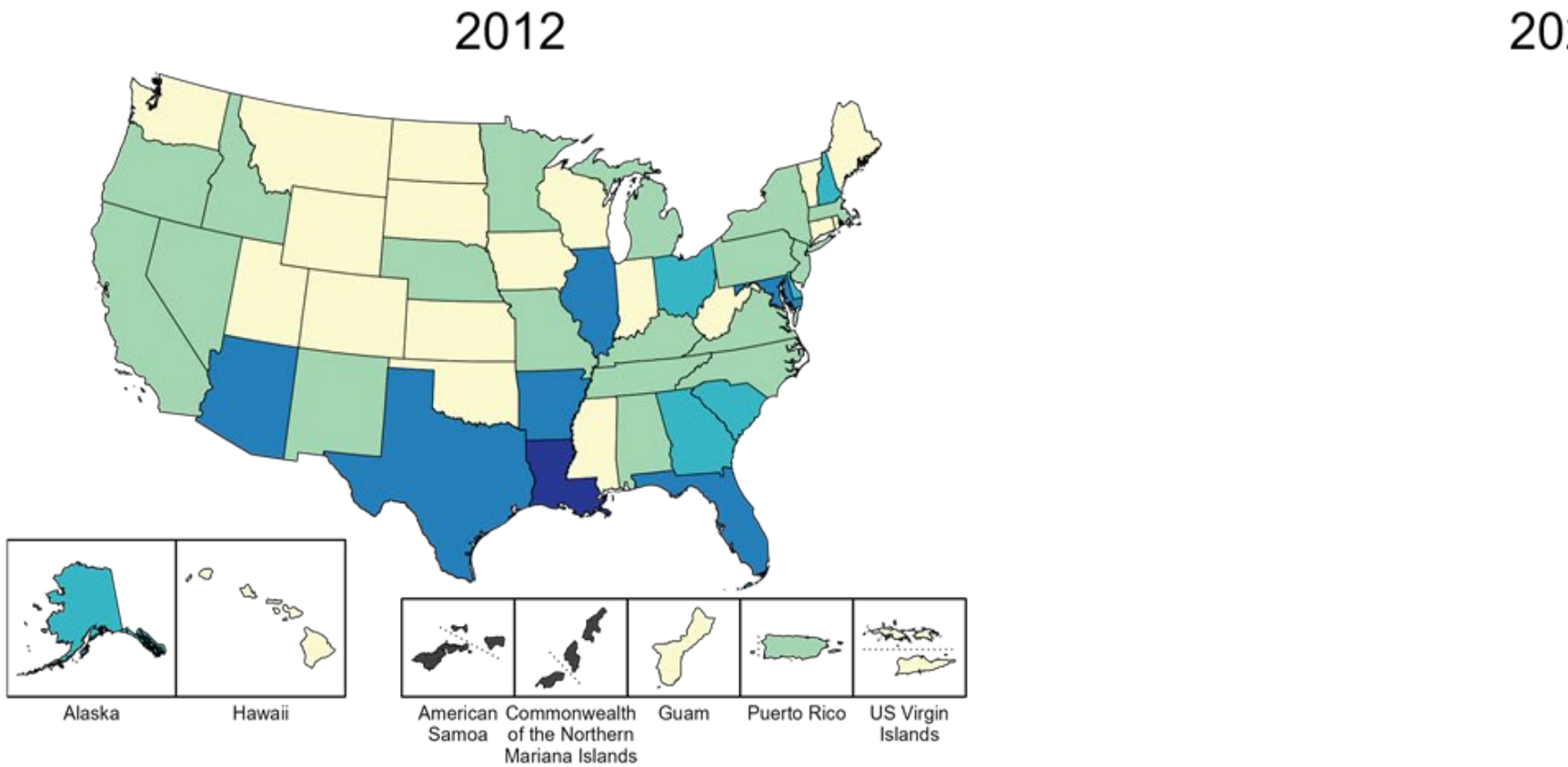
Source: CDC.gov

Congenital Syphilis



Source: CDC.gov

Rank*	State†	Cases	Rate per 100,000 Live Births
1	Arizona	181	232.3
2	New Mexico	44	205.7
3	Louisiana	110	191.5
4	**Mississippi**	64	182.0
5	Texas	680	182.0
6	Oklahoma	85	175.6
7	South Dakota	16	140.7
8	Arkansas	50	139.0
9	Nevada	45	133.6
10	Hawaii	20	128.0
14	**Florida**	180	83.2
	US TOTAL‡	**2,855**	**77.9**
16	**Georgia**	93	75.0
18	**Alabama**	37	63.7
21	**Kentucky**	25	47.9
22	**Tennessee**	39	47.7
28	**North Carolina**	42	34.9
29	**South Carolina**	19	33.2

Source: CDC.gov

Congenital Syphilis – Reported Cases and Rates of Reported Cases by State, Ranked by Rates, United States, 2021

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Syphilis – Treatment

- The **only** safe and adequate treatment option for syphilis for both mother and fetus in pregnancy is penicillin G
  - Those allergic to PCN should undergo desensitization
- Pregnant women with syphilis should be treated immediately
- Treatment ≥ 30 days prior to delivery is likely to prevent most cases of congenital syphilis
- Treatment success with a 4-fold decrease in RPR by 1 year
- Re-treat for latent syphilis if new signs/symptoms, a 4-fold titer increase, or an initially high titer (≥1:32) that fails to decline 4-fold within 1 year after therapy

Syphilis – Treatment

Stage	Treatment
Early Syphilis Primary Secondary Early latent (<1yr)	Benzathine PCN G 2.4 million units IM weekly x 2 doses
Late Syphilis Late latent (>1yr) Tertiary	Benzathine PCN G 2.4 million units IM weekly x 3 doses
Neurosyphilis	Aqueous crystalline PCN G 3-4 million units IV q4h (or a continuous infusion) x 10-14 days

Jarisch-Herxheimer (JH) Reaction

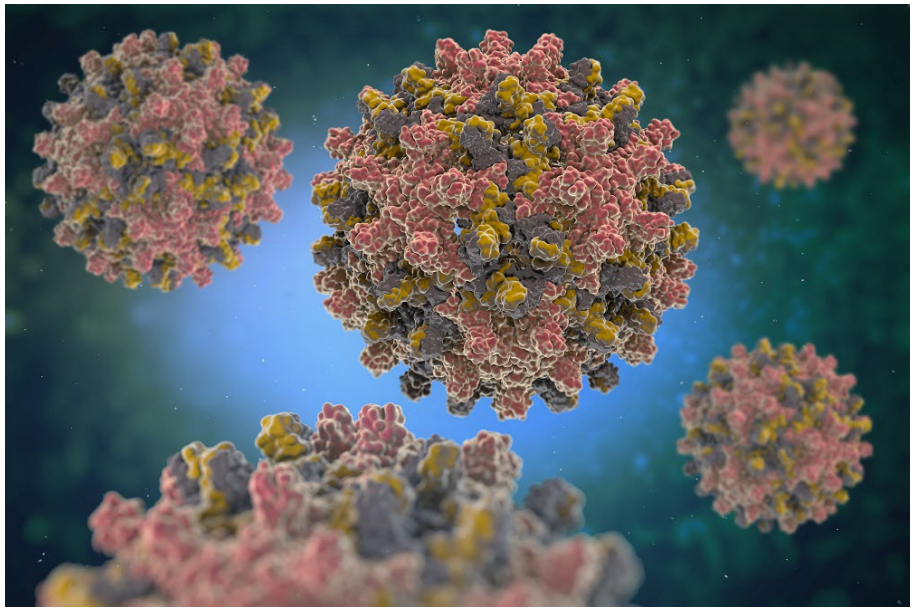
- Acute febrile reaction that can occur within the first 24h after the initiation of therapy
  - Most common among those with early syphilis
- Increased risk of preterm labor and non-reassuring fetal status in the second half of pregnancy
  - Recommend continuous fetal monitoring for up to 24 hours after administration of the first PCN G dose
- Monitoring not required for subsequent doses in those with no evidence of JH reaction with the first

Hepatitis B Virus (HBV)

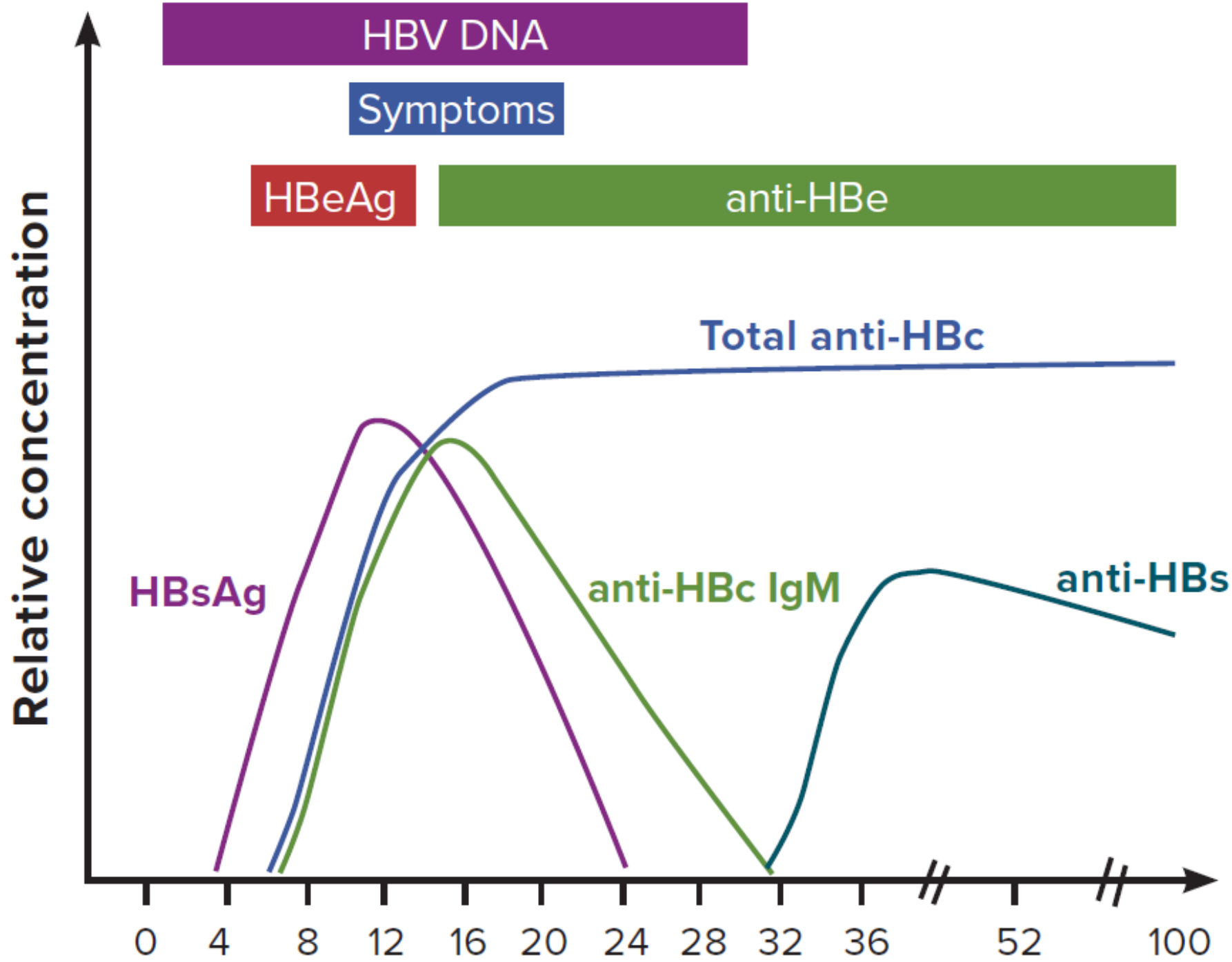
The one with a vaccine

Hepatitis B Virus

- Small DNA virus with an average incubation period of 60 days
- Efficiently transmitted by percutaneous or mucous membrane exposure to HBV-infected blood or body fluids that contain HBV
- Primary risk factors:
  - Unprotected sex with an infected partner
  - Multiple partners
  - MSM
  - History of other STIs
  - Injecting drug use



Source: CDC.gov



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Hepatitis B Virus In Pregnancy

- Perinatal transmission represents the single largest cause of chronic infection worldwide
- Hepatitis B virus vaccine is recommended for all pregnant adults who were not previously vaccinated
- Vertically acquired HBV:
  - Results in a chronic carrier state in up to 90% of infected infants
  - ~ 25% of infants who develop chronic HBV infection will eventually die from chronic liver disease

HBV – Vertical transmission

- Vertical transmission is more frequent in women acutely infected in the third trimester
  - 80-90% vs 10% in the first trimester
- Vertical transmission rates:
  - 10-20% in mothers seropositive for HBsAg alone
  - 90% in mothers seropositive or both HBsAg and HBeAg
- Risk drops to <5% with prophylaxis and antiviral treatments
- Breastfeeding is not contraindicated as long as immunoprophylaxis is given to the neonate at birth

HBV – Screening in Pregnancy

- Screen during each pregnancy during first trimester
- All pregnant patients who are HBsAg positive need HBV DNA quantitative testing
- Retest upon admission for delivery if:
  - High risk
  - Was not screened prenatally
  - Has clinical hepatitis
- HBsAg positive must be reported to local or state health department

Risk Factors for HBV:
- More than one sex partner in the previous 6 months
- Evaluation or treatment for STI
- IV drug use
- HBsAg positive sex partner

HBV – Management in Pregnancy

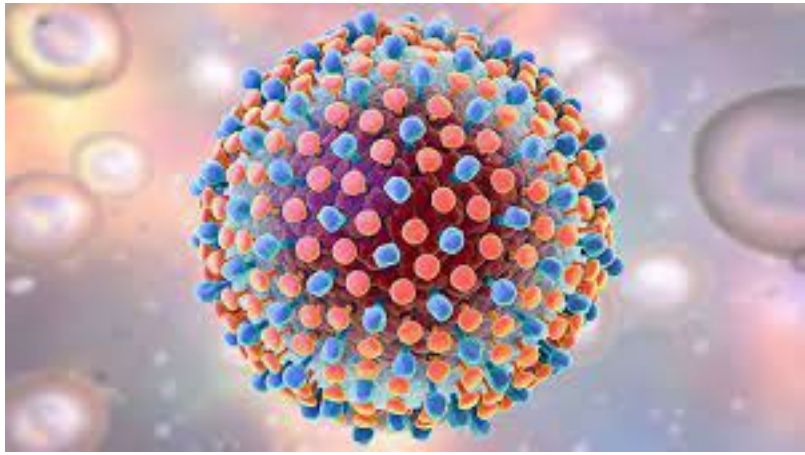
- Uninfected pregnant women exposed to HBV should receive HBIG and start the immunization series
  - Within 24 hours and not later than 14 days after exposure
  - 85-95% effective in prevention of neonatal infection
- Use antivirals during pregnancy if viral load is >200,000 iu/mL at the beginning of the third trimester
- Neonates born to HBsAg positive moms, should receive HBV vaccination and HB immunoglobulin within 12 hours of birth
  - Reduces risk of neonatal HBV infection to 1%

Hepatitis C Virus (HCV)

Not just for boomers

Hepatitis C Virus

- Small, enveloped virus with a positive-sense single-stranded RNA genome
- Most commonly reported bloodborne infection in the US
- Primarily transmitted via IV drugs or sexually
  - Hemodialysis patients, healthcare workers
- 75% are asymptomatic and at least 50% of infected individuals progress to chronic infection



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HCV – Screening in Pregnancy

- Screen all patients during each pregnancy for Hepatitis C
  - Except in areas where the prevalence of HCV infection is <0.1%
- If HCV antibody screen is positive, HCV RNA PCR testing is needed to confirm

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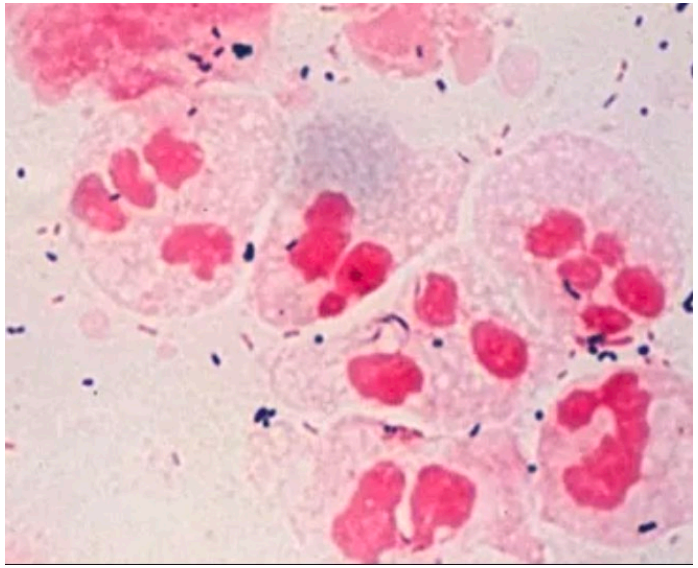
HCV – Vertical Transmission

- Perinatal transmission is approximately 3-8%
  - Up to 44% if the mother has HIV
- More frequent in women acutely infected in the third trimester
  - 80-90% vs 10% in the first trimester
- No effective treatment or practice reduces this risk
- Rates of HCV transmission to breast-fed infants are similar to rates observed in those not breast-fed
  - Avoid breast feeding if nipples are cracked or bleeding

Chlamydia

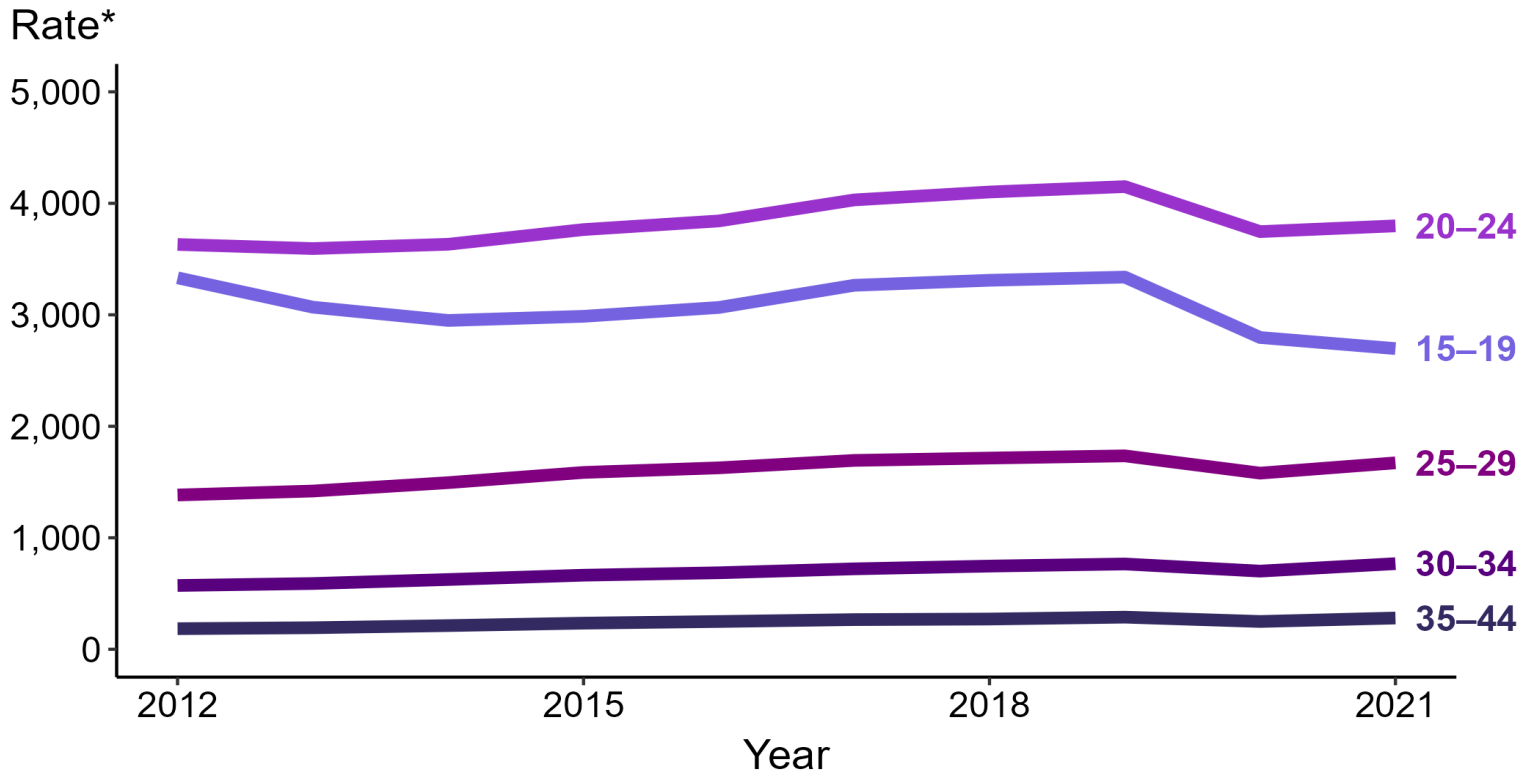
The one that always seems to be around

Chlamydia Trachomatis



- Obligate, intracellular gram negative rod
- Most frequently reported bacterial STI in the US
- 2/3 of new infections occur among youth aged 15-24 years
- Infection is typically insidious and symptoms are minimal or absent in most
- Slow replication cycle, so symptoms may not appear until several weeks after exposure

Chlamydia – Rates of reported cases among US women of reproductive age



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Source: CDC.gov

Chlamydia In Pregnancy

- Untreated chlamydial infection has been linked to preterm labor, premature rupture of membranes, and low birth weight

- The newborn may also become infected during delivery as the baby passes through the birth canal

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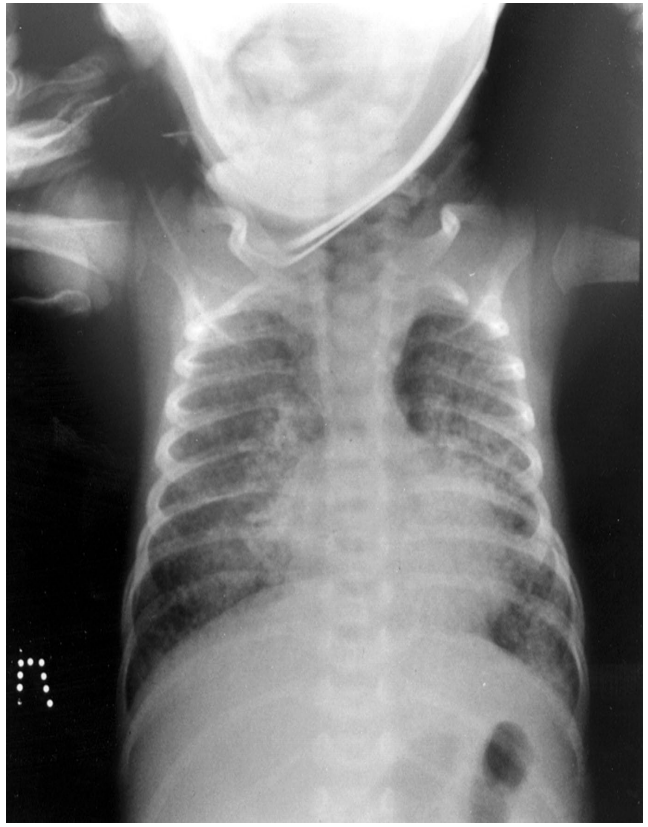
Chlamydia – Screening in Pregnancy

- Test all pregnant women <25yo at first prenatal visit
- Test all "older" women if at high risk
  - More than one sex partner
  - A sex partner with concurrent partners or has an STI
- Retest in 3rd trimester
- After treatment, test of cure 3-4 weeks later
- NAATs are the most sensitive tests and can be performed on vaginal swabs or urine

Chlamydia – Vertical Transmission



- Nearly 2/3 of infants born to women with C. trachomatis become infected
- Perinatal morbidity includes neonatal conjunctivitis and pneumonitis
  - Despite the effectiveness of ophthalmic prophylaxis with erythromycin, 15% may still develop conjunctivitis
  - C. trachomatis pneumonitis during the first few months of life affects up to 16% of exposed infants
- Perinatally transmitted *C. trachomatis* infection of the nasopharynx, urogenital tract, and rectum might persist for 2-3 years

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Chlamydia – Treatment in Pregnancy

Recommended regimen:

- Azithromycin 1gm orally in a single dose

Alternative regimen:

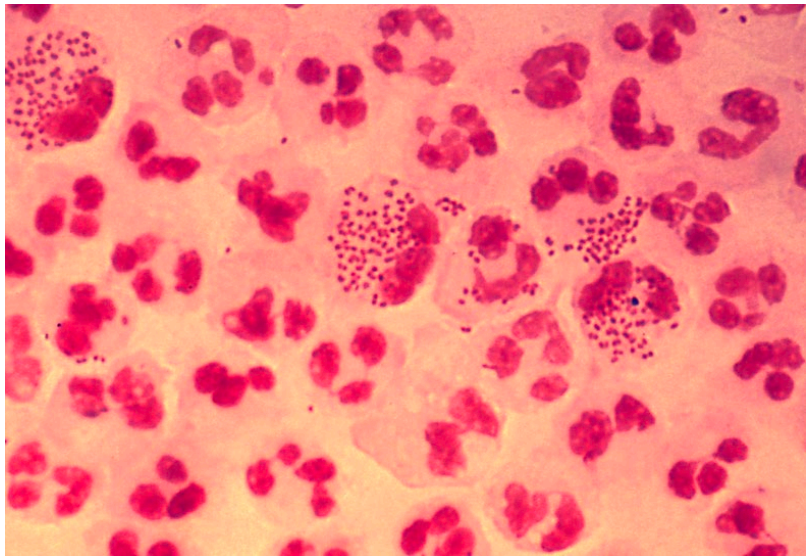
- Amoxicillin 500mg orally TID x 7 days

- Abstain from sexual activity for 7 days after single dose antibiotics or until completion of a 7-day course of antibiotics to prevent spread

Gonorrhea

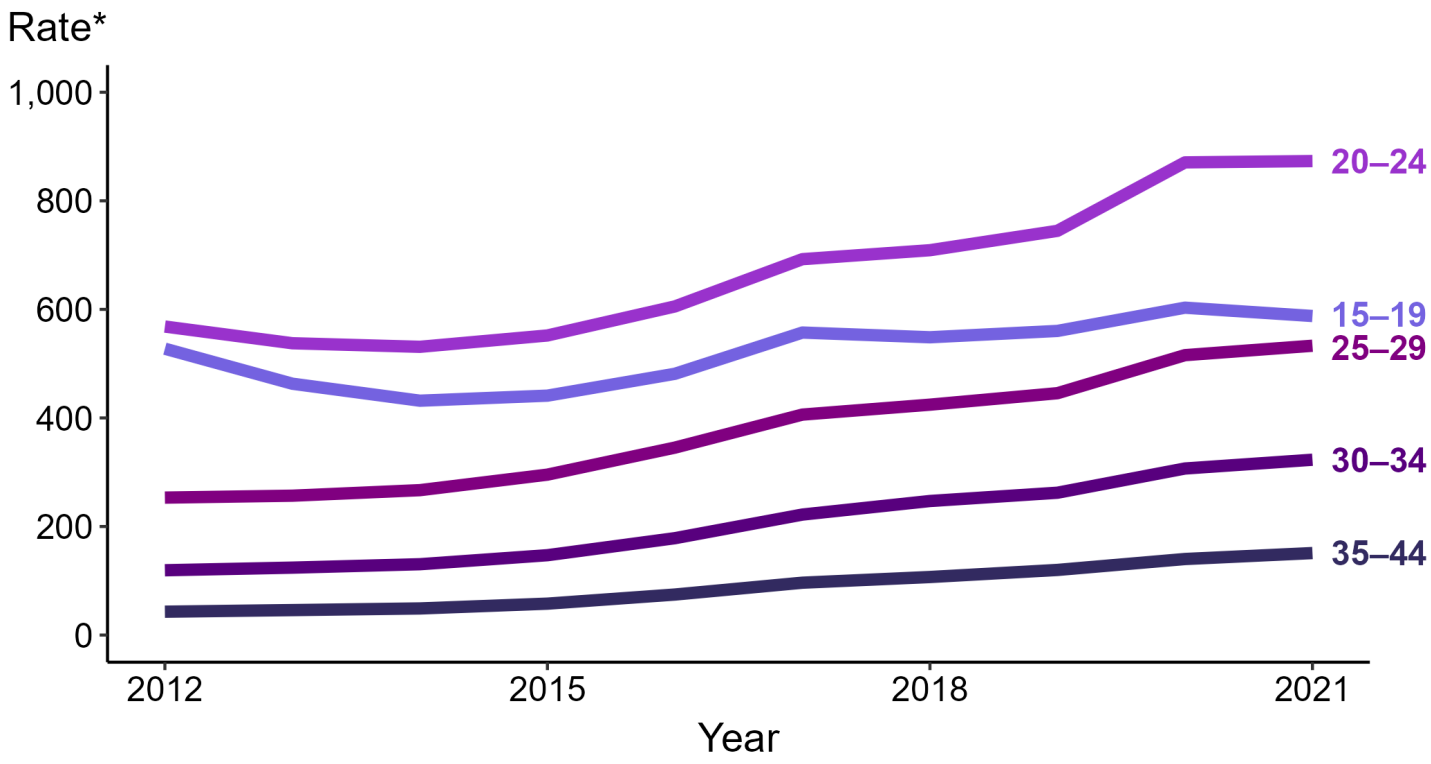
The partner in crime

Neisseria Gonorrhea



- Obligate, fastidious, gram negative diplococcus
- Second most commonly reported bacterial STI in the US
- 1.6 million new gonococcal infections occurred in the US in 2018
  - More than half occur among young people age 15-24
- Most women are asymptomatic
- Antimicrobial resistance is of increasing concern

Gonorrhea — Reported cases among women of reproductive age in the US



* Cases per 100,000

Source: CDC.gov

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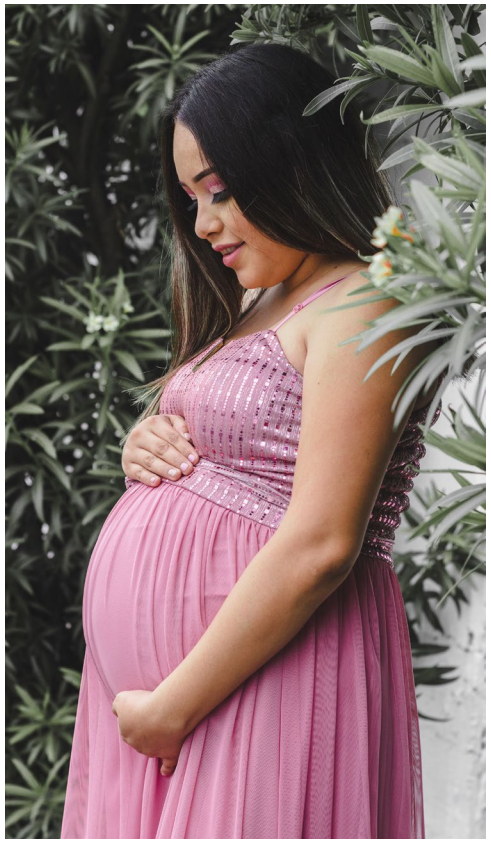
Gonorrhea in Pregnancy

- Untreated gonococcal infection in pregnancy has been linked to miscarriages, premature birth, low birth weight, premature rupture of membranes, and chorioamnionitis

- Gonorrhea can also infect an infant during delivery as the infant passes through the birth canal

Gonorrhea – Screening In Pregnancy

- Test all pregnant women <25yo at first prenatal visit
- Test all "older" women if at high risk
  - More than one sex partner
  - A sex partner with concurrent partners or has an STI
  - Inconsistent condom use in non-monogamous relationships
  - Previous or co-existing STIs
  - Transactional sex
  - Elevated risk based on geographic location
- Treat all positive patients immediately and retest in 3 months
- Retest in 3rd trimester



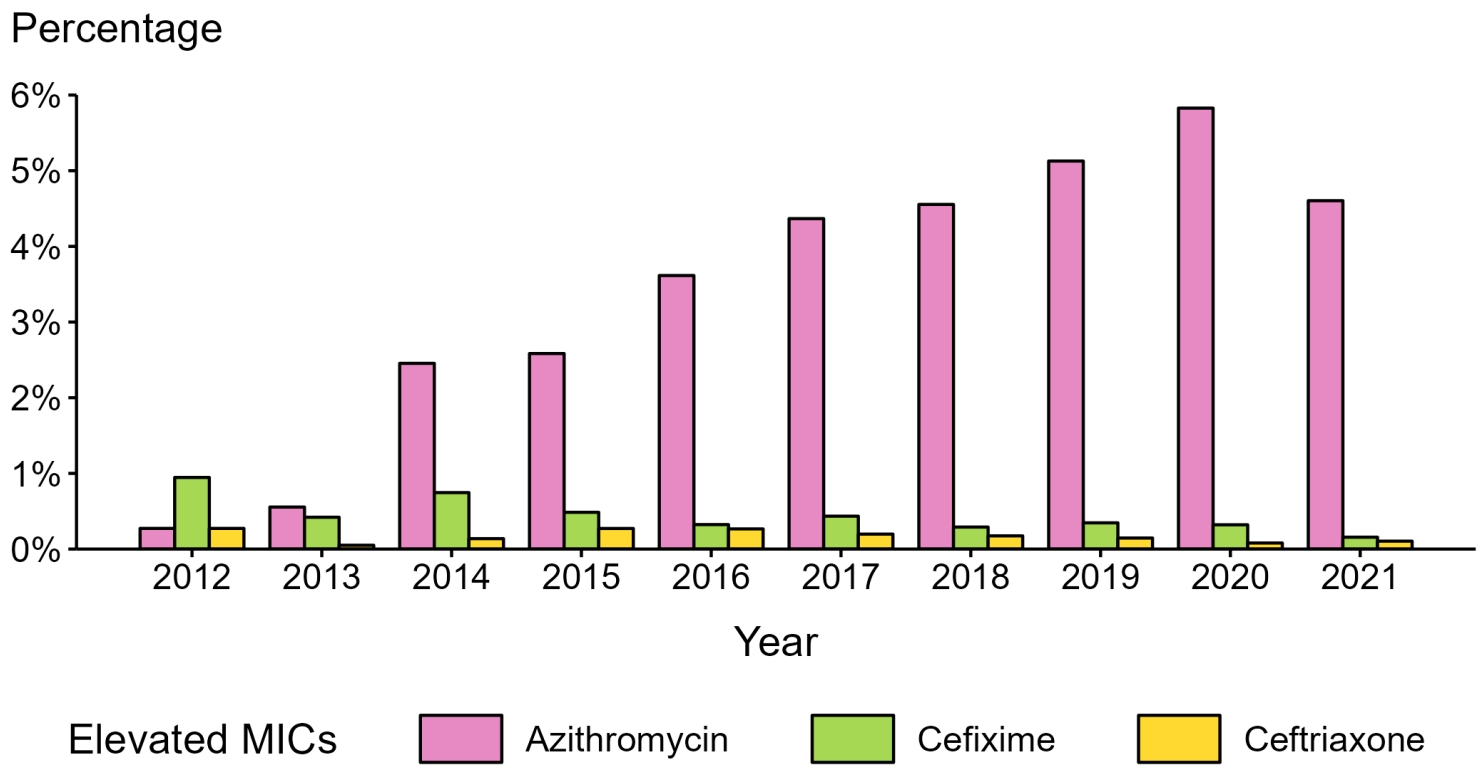
Gonorrhea – Neonatal Infection

- An acute illness manifesting 2-5 days post birth
- Most severe manifestations are ophthalmia neonatorum and sepsis
- Less severe manifestations: rhinitis, vaginitis, urethritis, and scalp infection
- Disseminated gonococcal infection is rare
  - Sepsis, arthritis or meningitis

Gonorrhea – Treatment in Pregnancy

- Ceftriaxone 500mg IM x 1
- If chlamydia has not been excluded, treat with azithromycin 1gm orally in a single dose

Neisseria gonorrhoeae — Percentage of Isolates with Elevated Minimum Inhibitory Concentrations (MICs) to Azithromycin, Cefixime, and Ceftriaxone, (GISP), 2012-2021



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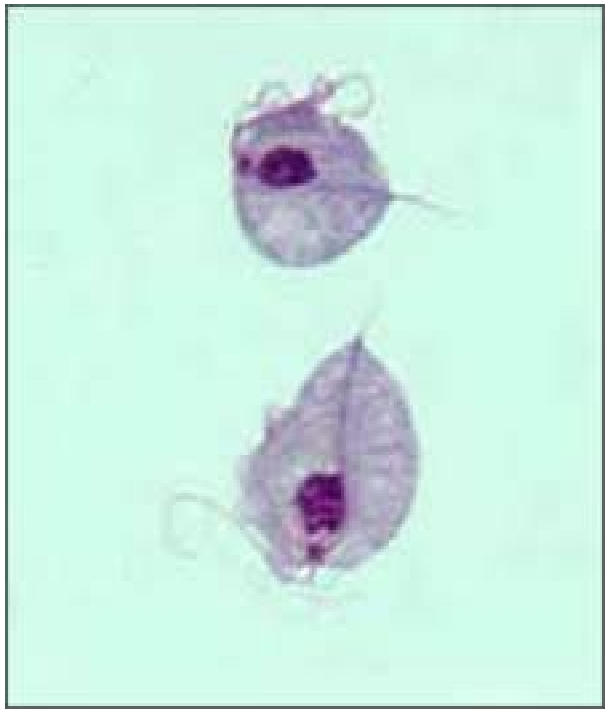
Source: CDC.gov

Trichomonas

A dime a dozen

Trichomonas Vaginalis

- Most prevalent nonviral STI worldwide
- ~70% of those infected do not have signs or symptoms
- Women with a history of incarceration are 2-5x more likely to have T. vaginalis
- Other risk factors:
  - Two or more sex partners during the previous year
  - Having less than a high school education
  - Living below the national poverty level



Trichomonas in Pregnancy

- Linked to premature rupture of membranes, preterm birth, and low birth weight infants
- Very rarely, the female newborn can acquire the infection when passing through the birth canal during delivery and have vaginal discharge after birth
- Evidence does not support routine screening
- Evaluate and screen symptomatic women
  - Wet mount has a low sensitivity (44-68%) which decreases quickly to 20% within 1 hour of collection
  - NAATs are highly sensitive

Trichomoniasis – Treatment

- Regimen is the same for non-pregnant women

Preferred Treatment :

- Metronidazole 500mg orally BID x 7 days

Alternative Treatment:

- Tinidazole 2gm orally in a single dose

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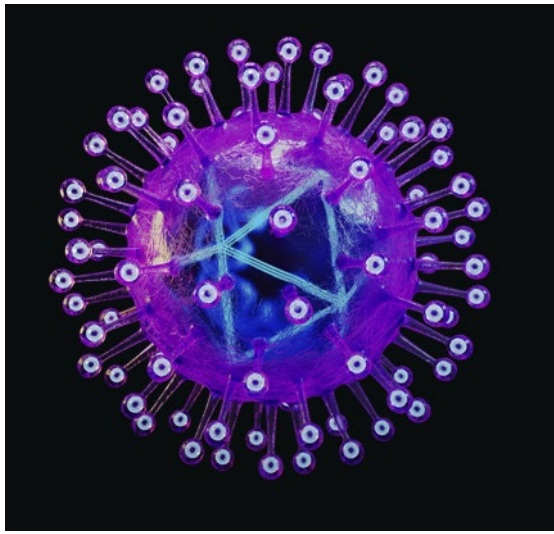
Herpes Simplex Virus (HSV)

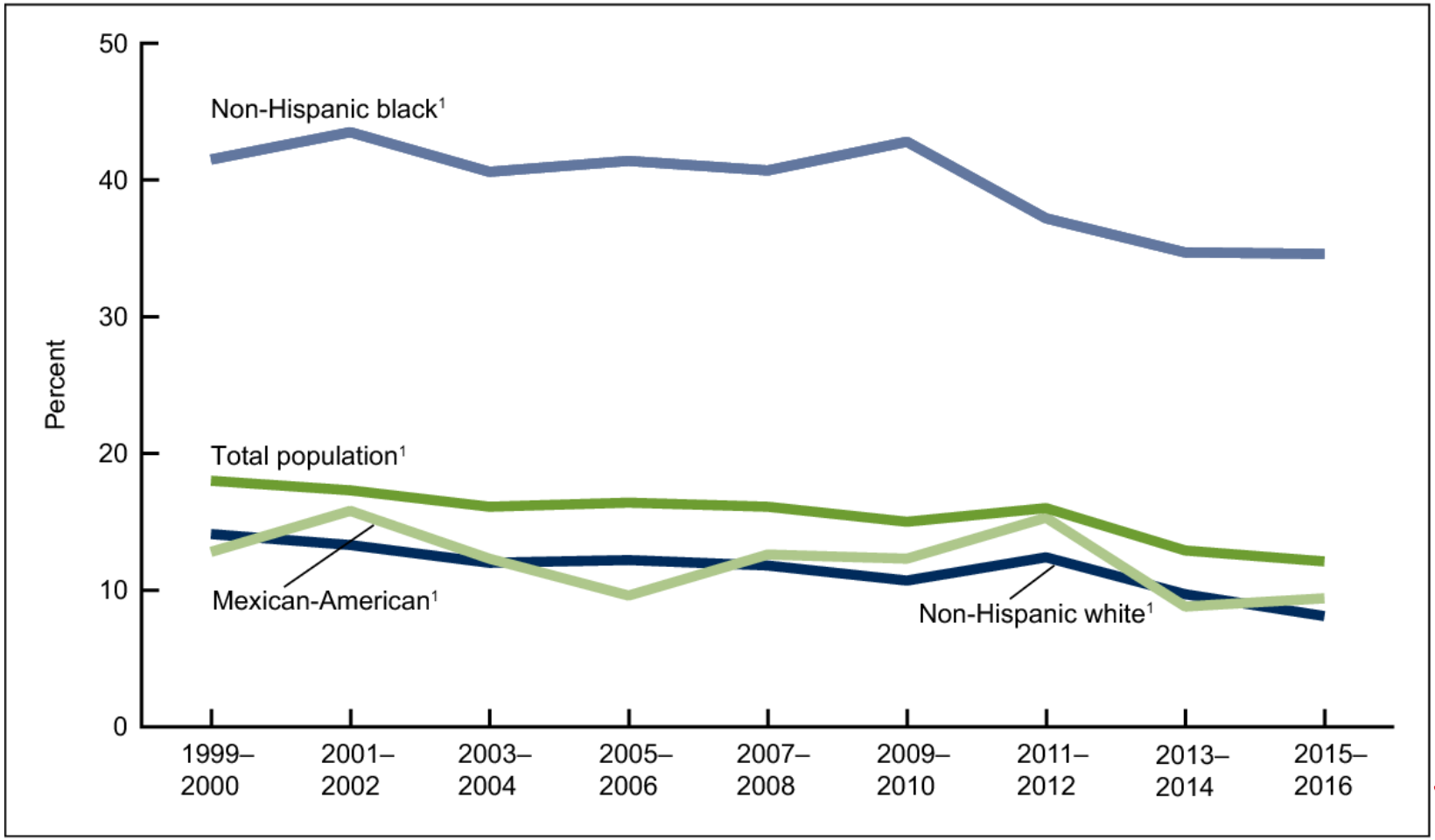
The gift that keeps giving

Herpes Simplex Virus



- An estimated 50 million people infected in the US
  - Only 5-15% of infected individuals report recognition of their disease
- HSV Type 1 or Type 2 - both double-stranded DNA viruses
- Establishes latency as persistent infection of the sacral and paraspinal ganglia
  - Genital HSV recurrences can occur throughout the distribution innervated by the sacral ganglia, including the buttocks and thighs

HSV-2 seroprevalence, US persons of reproductive age (14-49yo)

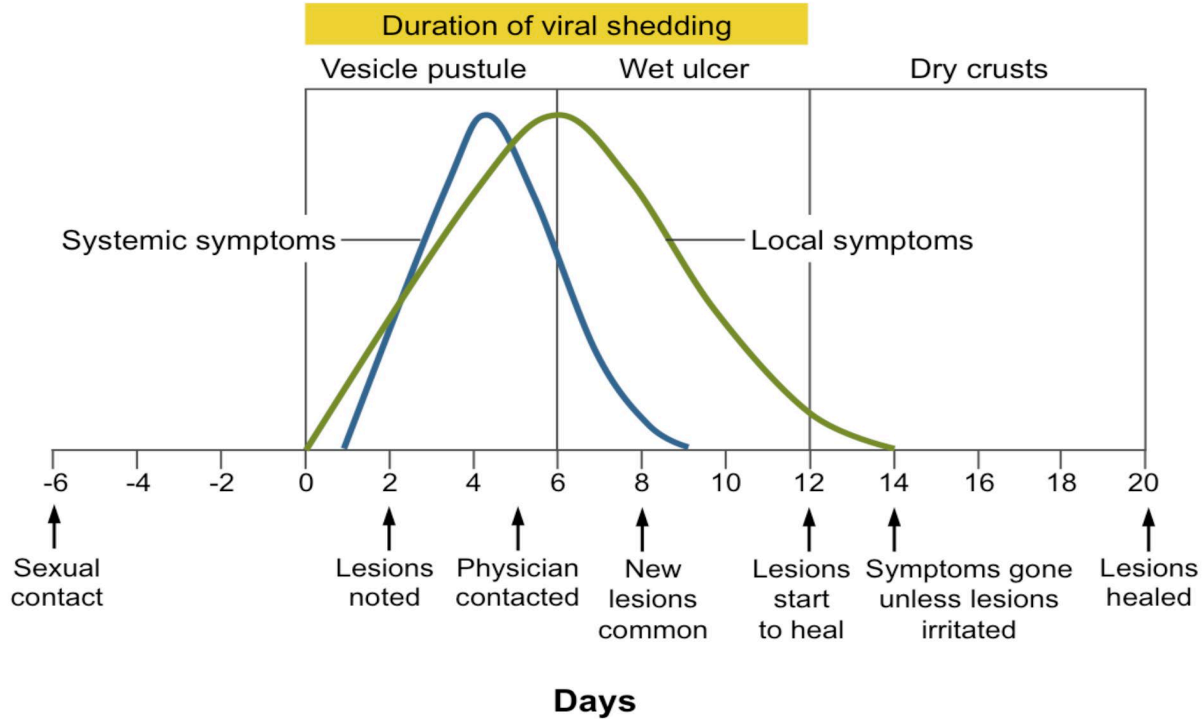


Source: CDC.gov

AETC AIDS Education & Training Center Program Southeast

HSV Transmission

- Genital-to-genital, oral-to-genital, or genital-to-oral contact
- Transmission of HSV-2 most often involves asymptomatic shedding
- Approximately 80% of persons seropositive for HSV-2 have never received a diagnosis of genital HSV



Kimberlin DW, Rouse DJ. Clinical practice. Genital herpes. N Engl J Med. 2004;350:1970-7

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HSV – Screening in Pregnancy

- Evidence does not support routine screening
- In the absence of lesions during the 3rd trimester, routine cultures are not indicated for women who have a history of recurrent genital herpes
- Type-specific serologies may help identify pregnant women at risk for HSV and to help guide counseling regarding the risk of acquiring herpes during pregnancy
- Testing = type-specific virologic testing of a lesion by NAAT or culture
  - Serology can be used to determine if this is primary or a recurrence

HSV – Vertical Transmission

- During a primary outbreak at the time of delivery, risk of transmission is 30-60%
  - Recurrent genital lesions at the time of delivery = 3% risk of transmission
  - Risk of transmission with no visible lesions = 2/10,000
- Systemic antivirals can be used to diminish signs and symptoms but will not remove latent virus
- Antiviral suppressive therapy from 36 weeks to delivery has been shown to decrease HSV recurrences and asymptomatic shedding at delivery
- Cesarean delivery is indicated in women with active genital lesions or prodromal symptoms at delivery

Neonatal HSV

- Usually acquired during the intrapartum period through exposure with the virus in the genital tract
  - 25% disseminated disease, 30% CNS disease, 45% limited to skin or mouth
- Mortality: 30% for disseminated disease, 4% for CNS disease
  - ~20% of survivors of neonatal HSV have long-term neurologic sequalae
- Approximately 80% of infected infants are born to mothers with no reported history of HSV infection
- Estimated 1200-1500 neonatal HSV infections in the US per year
  - 2/3 due to HSV-2, 1/3 due to HSV-1

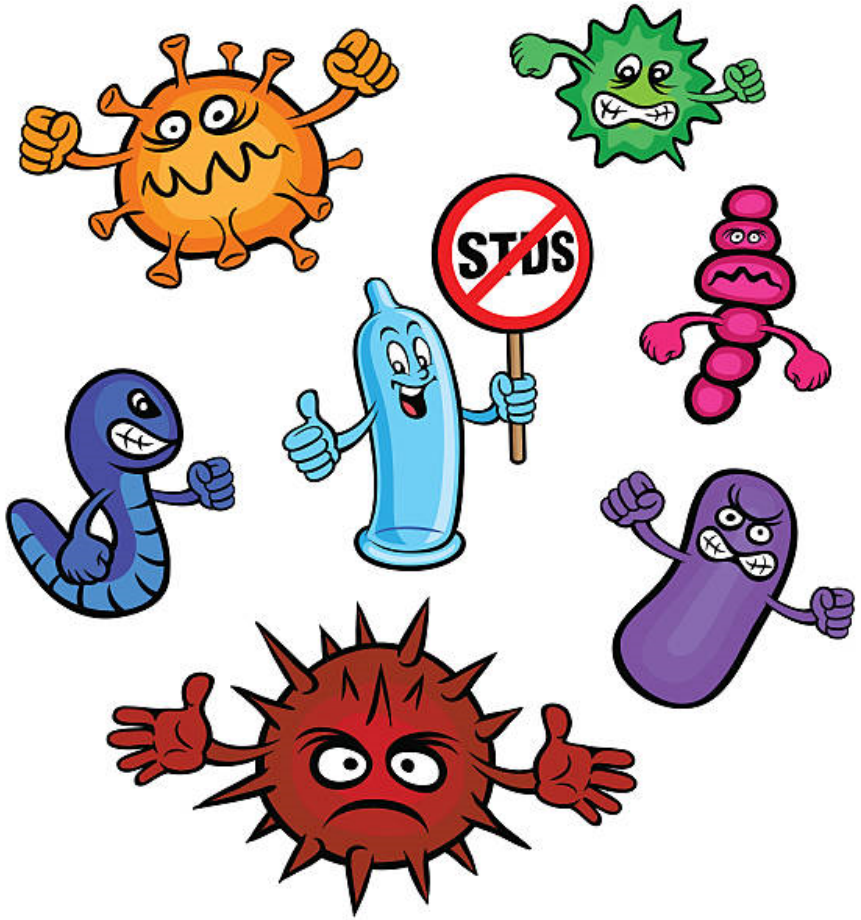
HSV – Treatment in Pregnancy

- Episodic treatment the same as if non-pregnant
  - Acyclovir, Valacylovir, Famciclovir
  - Dose and regimen vary on clinical scenario

- Daily suppressive therapy in pregnant women:
  - Acyclovir 400mg TID *OR*
  - Valacylovir 500mg BID

Disease	CDC Recommendation
Chlamydia	**First prenatal visit**: Screen all pregnant women <25yo and older pregnant women at increased risk **Third trimester**: Re-screen if <25yo or at continued high risk Risk factors: New or multiple sex partners, sex partner with concurrent partners, sex partner who has a STD
Gonorrhea	**First prenatal visit**: Screen all pregnant women <25yo and older pregnant women at increased risk **Third trimester**: Re-screen if at continued high risk Risk factors: Living in a high-morbidity area, previous or co-existing STI, new or multiple sex partners, inconsistent condom use among persons not in mutually monogamous relationships, exchanging sex for money or drugs
Syphilis	**First prenatal visit**: Screen all pregnant women **Third trimester**: Re-screen if at risk for syphilis during pregnancy, live in areas with high numbers of syphilis cases, were not previously tested, or had a positive test in the first trimester
Trichomoniasis	Evidence does not support routine screening in asymptomatic pregnant women
Herpes (HSV)	Evidence does not support routine HSV-2 serologic testing among asymptomatic pregnant women
HIV	**First prenatal visit**: Screen all pregnant women **Third trimester**: Re-screen if at high risk for acquiring HIV infection
Hepatitis B (HBV)	**First prenatal visit**: Screen all pregnant women **Third trimester**: Test those not previously screening, those who engage in behaviors that put them at high risk for infection, and those with signs/symptoms at the time of admission for delivery Risk factors: Having more than one sex partner in the previous 6 months, evaluation or treatment for an STD, recent or current IVDU, an HBsAg-positive sex partner
Hepatitis C (HCV)	**First prenatal visit**: Screen all pregnant women during each pregnancy, except in setting where the prevalence of HCV infection is <0.1%.

STI prevention



References

- **Centers for Disease Control and Prevention (CDC)**
  - www.cdc.gov/std

- **American College of Obstetricians and Gynecologists (ACOG)**
  - Clinical Practice Guidelines: No. 6 – Viral Hepatitis in Pregnancy
  - Committee Opinions:
    - No. 751 – Labor and Delivery Management of Women with HIV Infection
    - No. 752 – Prenatal and Perinatal HIV Testing
  - Practice Bulletin No. 220 – Management of Genital Herpes in Pregnancy