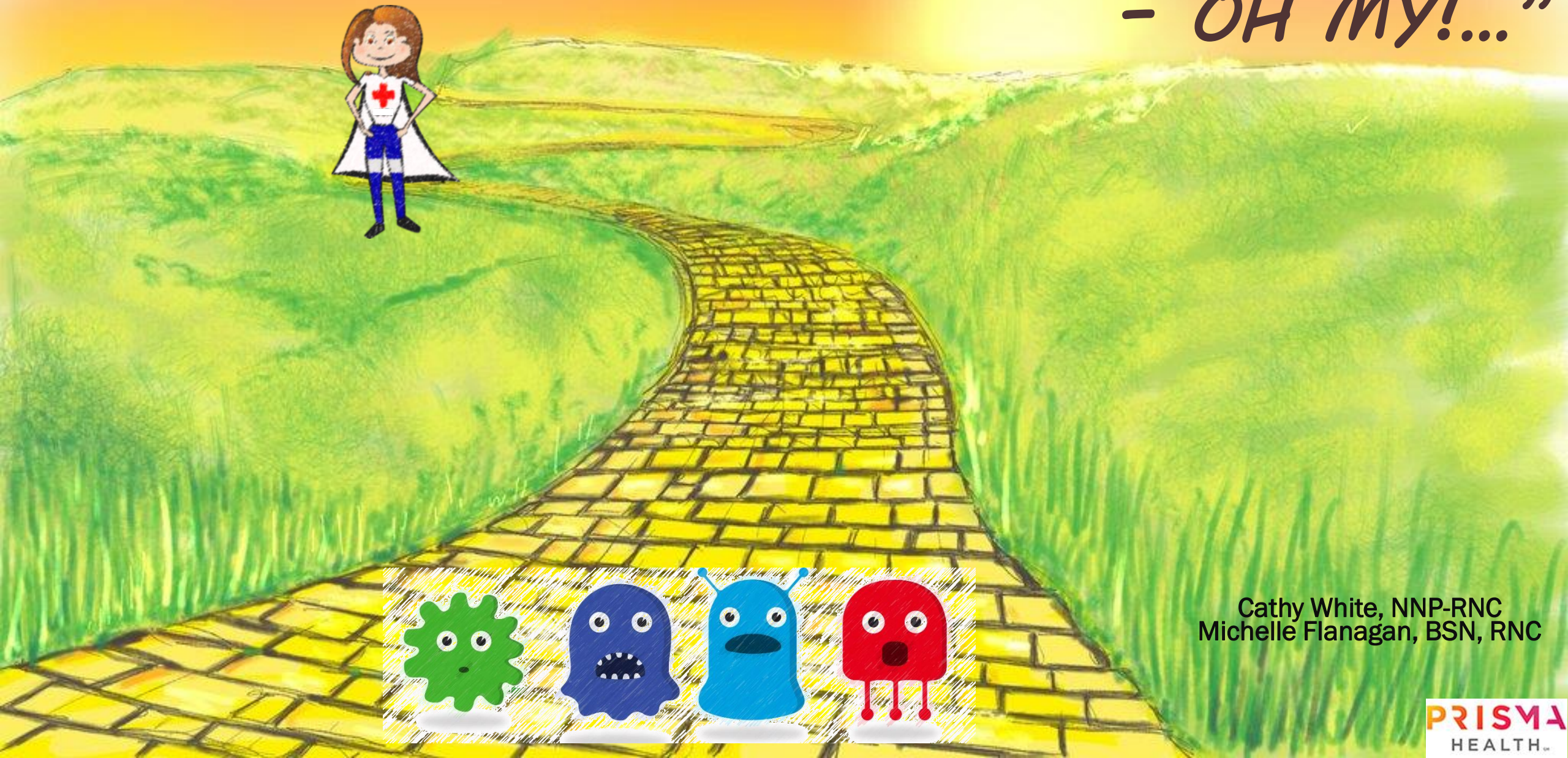
2019 Perinatal Systems Education Series
Self Study Module

"VIRUSES, BACTERIA & YEAST – OH MY!..."



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PRISMA HEALTH

Directions

- Please read the following module and complete the Post-Test and Evaluation.
- ***This module was designed to be completed on your computer, rather than printed if possible.***
- If you have any questions, please contact Perinatal Systems at 803-434-2912 or PerinatalSystems@PrismaHealth.org

Objectives

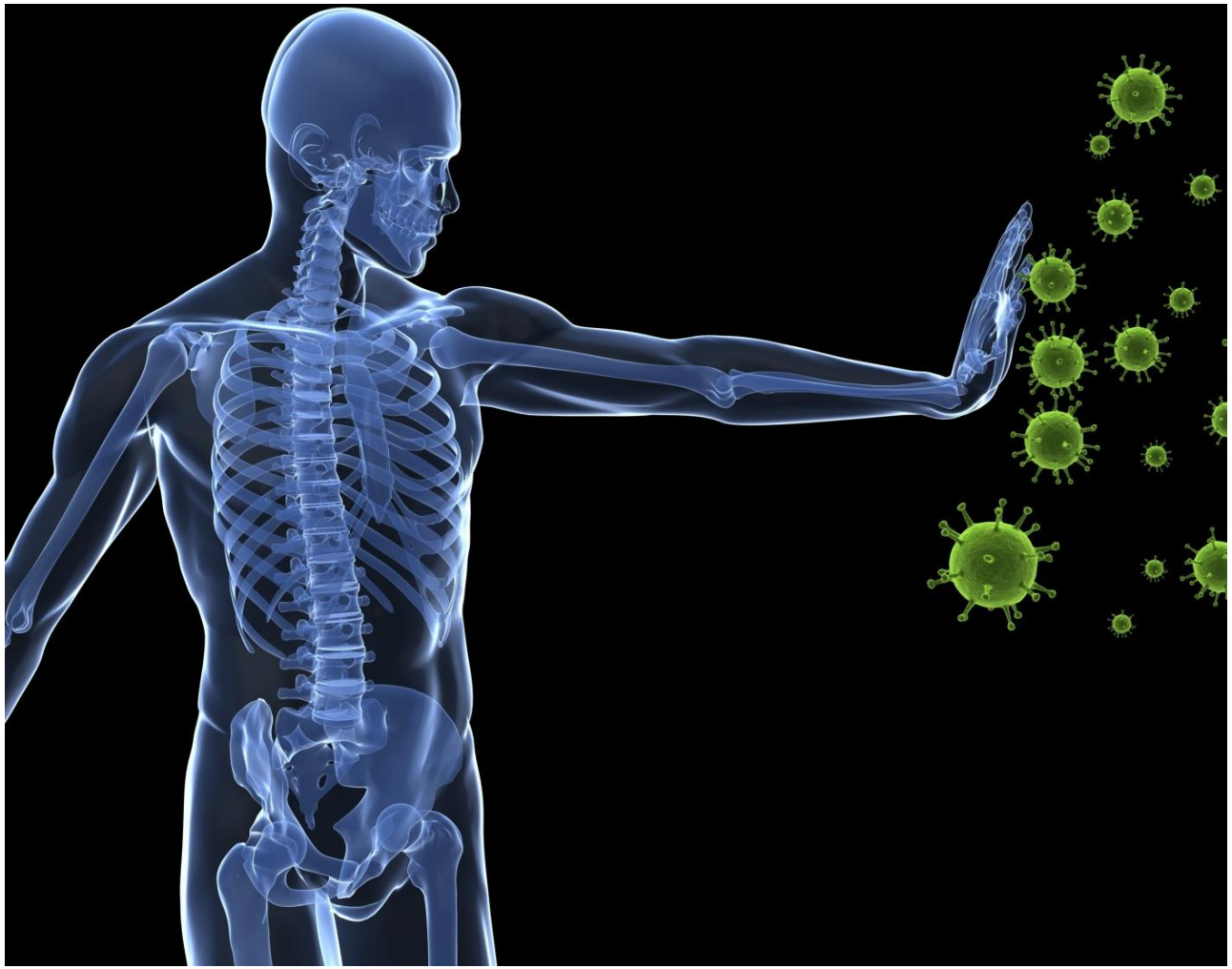
- By the end of the program, participants will:
  - have a better understanding of the maternal and neonatal immune system
  - current statistics and rate of increase with sexually transmitted diseases
  - be able to verbalize the most common TORCH infections and the effects on mother and fetus
  - be able to identify bacterial infections seen in mother and infant
  - be able to verbalize fungal infections seen in mother and infant

Immune System Overview

Maternal

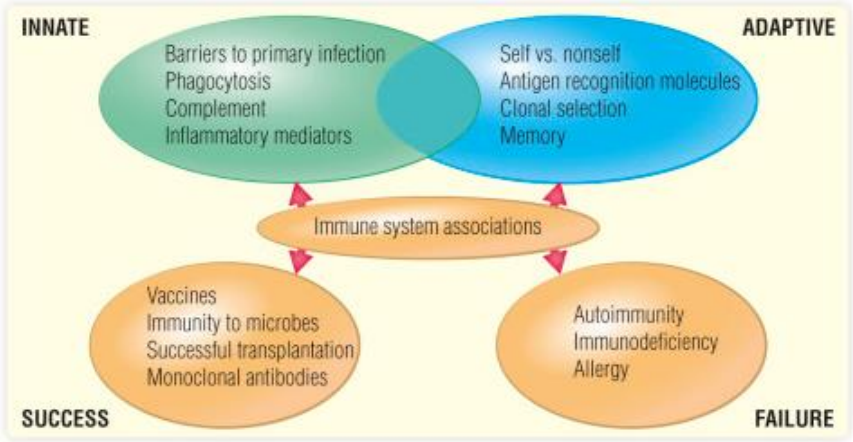
Fetal

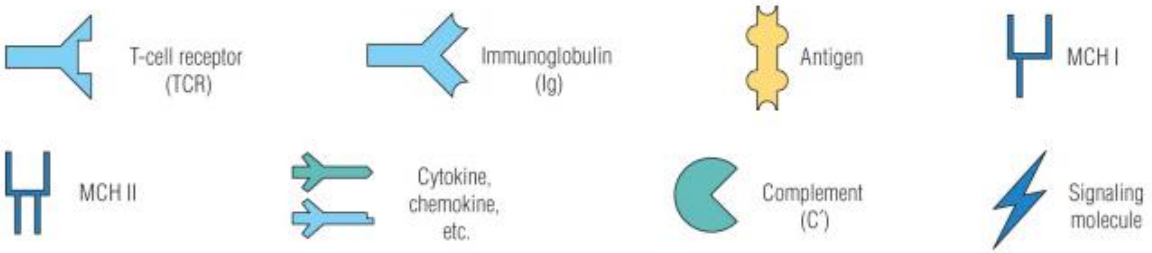
Neonatal



Immune System – General Review

- The overall function of the immune system is to prevent or limit infection





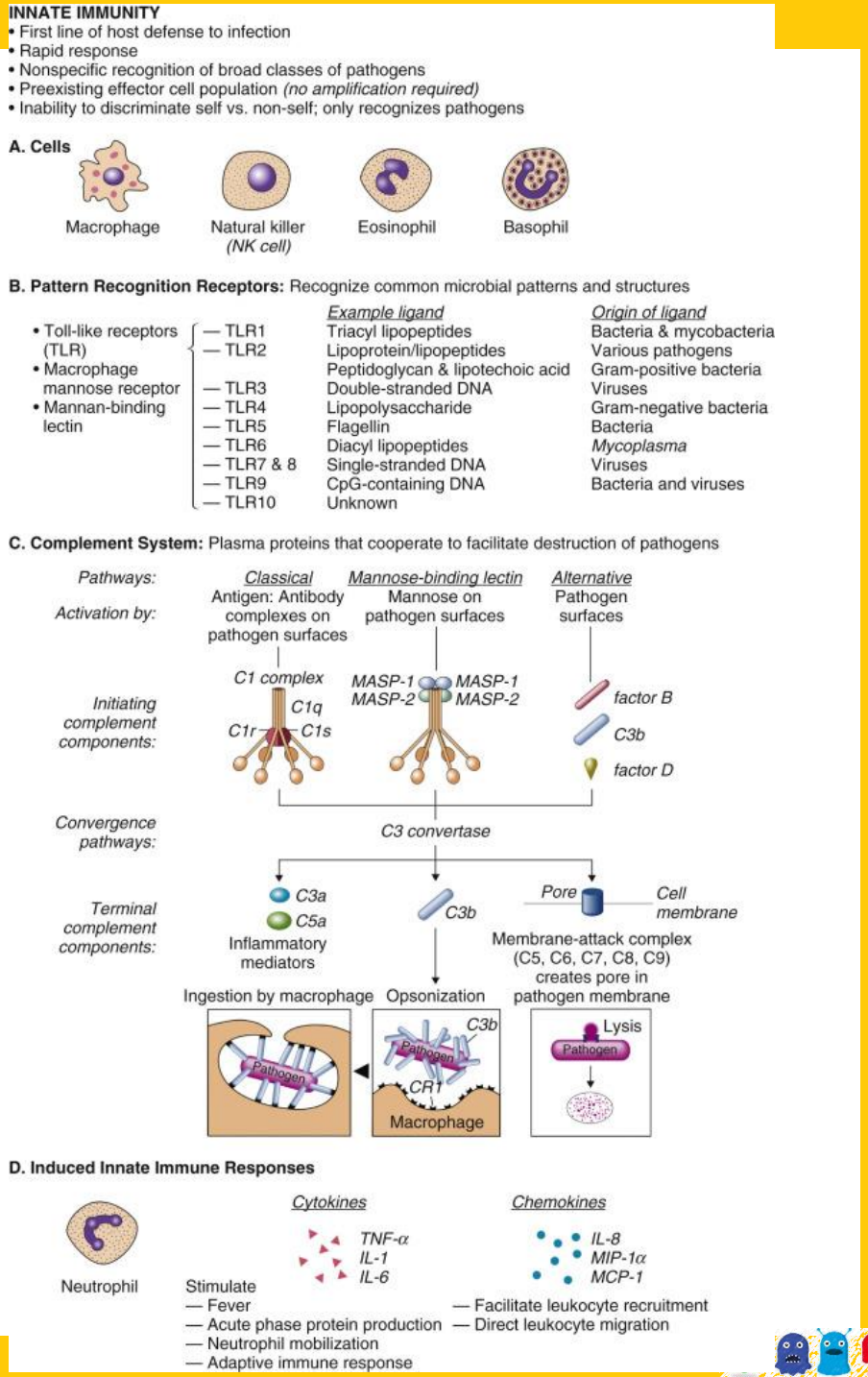
We inhabit a world dominated by microbes, many of which can cause harm (Box 1.1). The immune system is the body's primary defense system against invasion by microbes. This chapter briefly introduces the major components of the human immune system, what they do, and how they accomplish their host defense role.

https://www.niaid.nih.gov/research/immune-system-overview

Introduction to the Immune System - Immunology for Medical Students. Helbert, Matthew, MBChB, FRCP, FRCPath, PhD. Published December 31, 2016. Pages 1-6. © 2017.

Innate Immunity

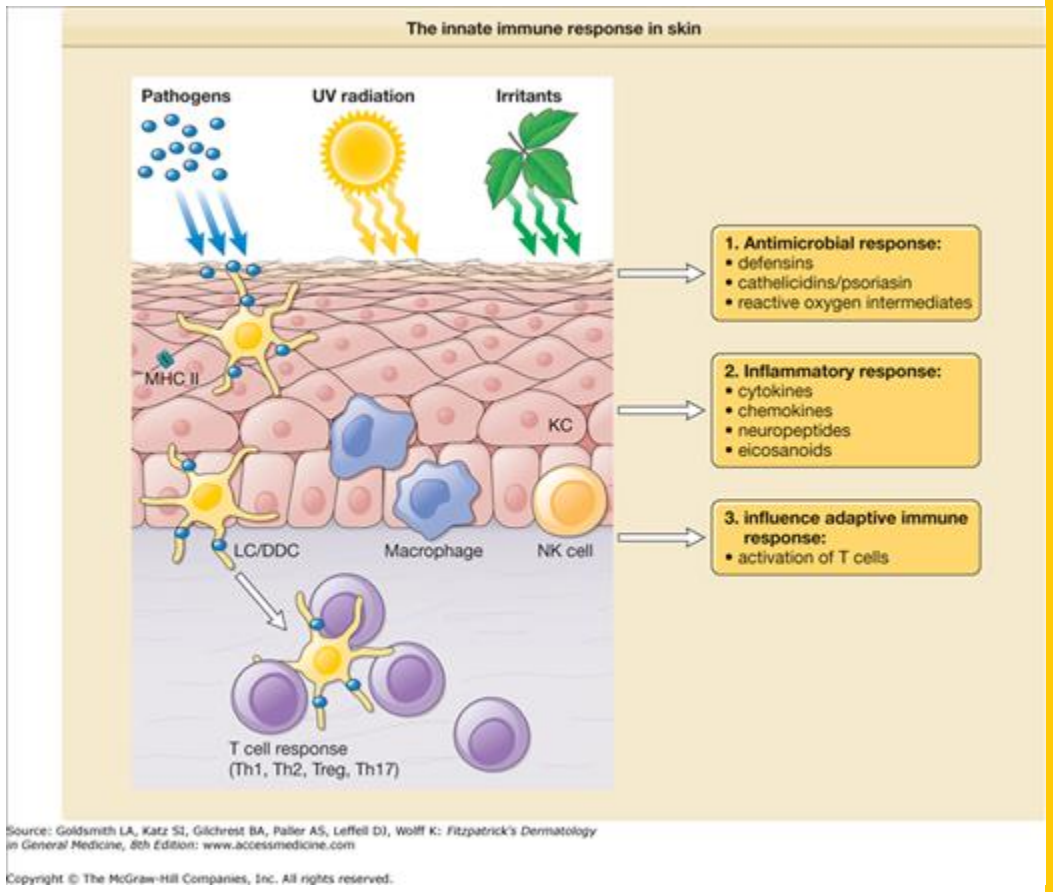
- The innate immune system constitutes the first-line barrier, the rapid-response mechanism, to prevent microbial invasion.
- Its components are inherited from parent to child and directed against molecules expressed only by micro-organisms.
- "Innate" immunity refers to immune responses that are present from birth and not learned, adapted, or permanently heightened as a result of exposure to micro-organisms



- Introduction to the Immune System - Immunology for Medical Students. Helbert, Matthew, MBChB, FRCP, FRCPath, PhD. Published December 31, 2016. Pages 1-6. © 2017.
- Image from: Gabbe, et al. OBSTETRICS: NORMAL AND PROBLEM PREGNANCIES, 7th Ed 2017 by Elsevier, Inc.

Components of the innate immune system:

- Host components
  - Physical barriers
    - Tight junctions in the skin, epithelial and mucous membrane surfaces, mucus itself, and vascular endothelial cells that prevent pathogen penetration of the intestines.
  - Enzymes in epithelial and phagocytic cells
    - Ex: lysozyme
  - Inflammation-related serum proteins
    - Ex: complement components, C-reactive protein, lectins, and ficolins.
  - Antimicrobial peptides on the surfaces of cells and within phagocyte granules.
  - Cell receptors that sense micro-organisms and signal a defensive response
    - Ex: toll-like receptors
  - Cells that release cytokines and other inflammatory mediators
    - Ex: macrophages, mast cells, natural killer cells, innate lymphoid cells
  - Phagocytes
    - neutrophils, monocytes, macrophages



- https://www.uptodate.com/contents/an-overview-of-the-innate-immune-system?search=innate%20immune%20system&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1
- Image from: https://accessmedicine.mhmedical.com/content.aspx?bookid=392&sectionid=41138705

Components of the innate immune system continued

- The Microbiome
  - The human microbiome is the collection of bacteria, fungi, and viruses that live in and on the human body, which may also be considered a component of the innate immune system, as it impacts mechanisms of host defense
  - directly effects the maturation of the immune response and its continued effectiveness, protects against pathogen overgrowth, and modulates the balance between inflammation and immune homeostasis
    - Example: coagulase-negative staphylococci on the skin produce an antimicrobial peptide that can inhibit growth of Staphylococcus aureus.
  - Alteration in the composition, diversity, or metabolites of the microbiome, such as that caused by antibiotic use, is associated with diseases affecting a variety of organ systems

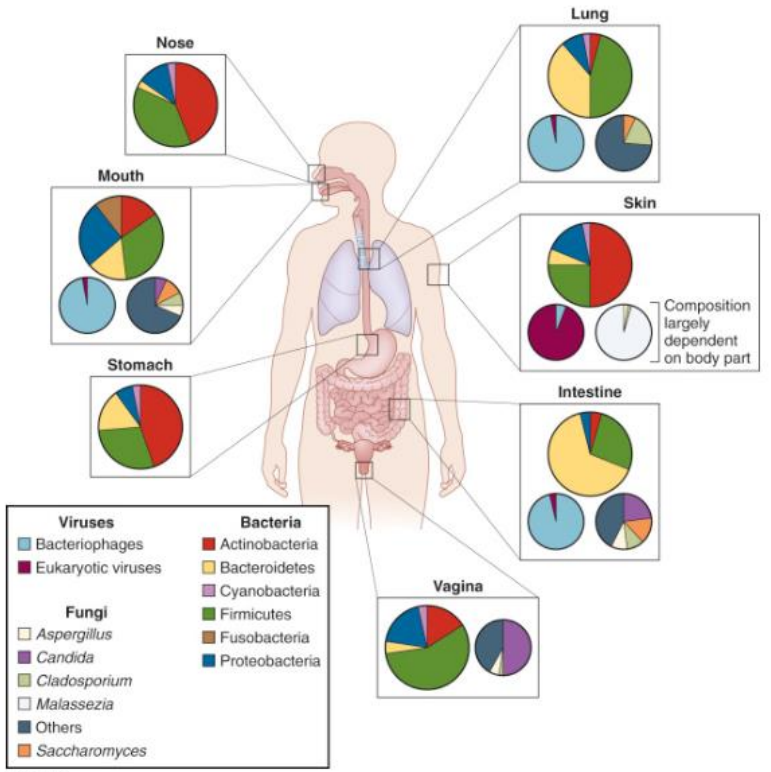


FIG. 5.1

The composition of bacterial, fungal, and viral microbiota at distinct body sites. This figure shows the distribution and relative abundance of bacterial, fungal, and viral communities at different sites on the human body that are exposed to the external environment. Bacterial composition is represented by the six most abundant phyla, fungal composition by the most prominent genera, and viral composition as bacteriophages or eukaryotic viruses.

(Modified from Marsland BJ, Gollwitzer ES. Host-microorganism interactions in lung diseases. *Nat Rev Immunol.* 2014;14:827–35.)

- https://www.uptodate.com/contents/an-overview-of-the-innate-immune-system?search=innate%20immune%20system&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1
- Image: Feigin and Cherry's Textbook of Pediatric Infectious Diseases 8th Ed. 2019 Elsevier https://www.clinicalkey.com/#!/content/book/3-s2.0-B9780323376921000058?scrollTo=%233-s2.0-B9780323376921000058-f005-001-9780323376921

Essential functions of the innate immune system include the following:

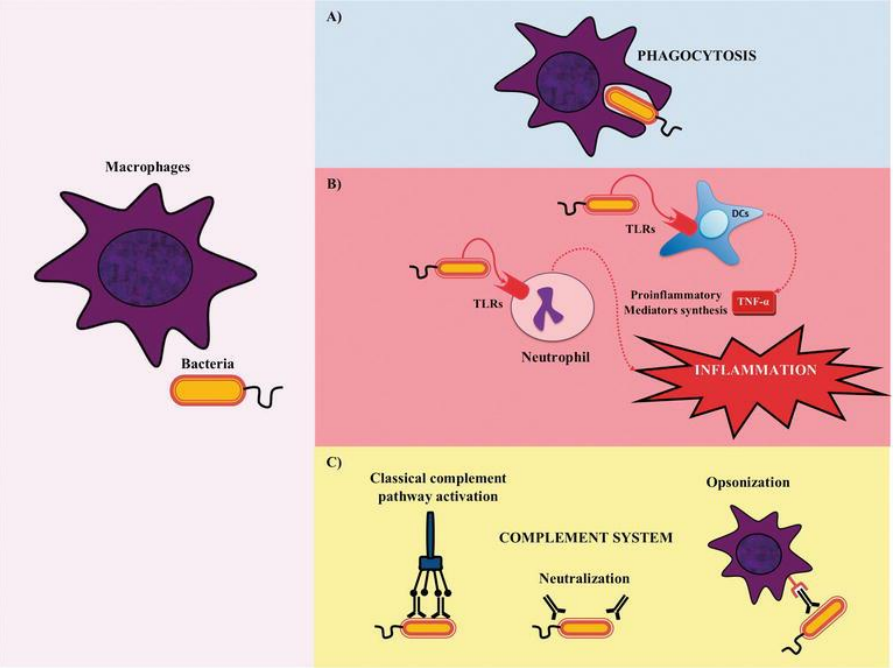


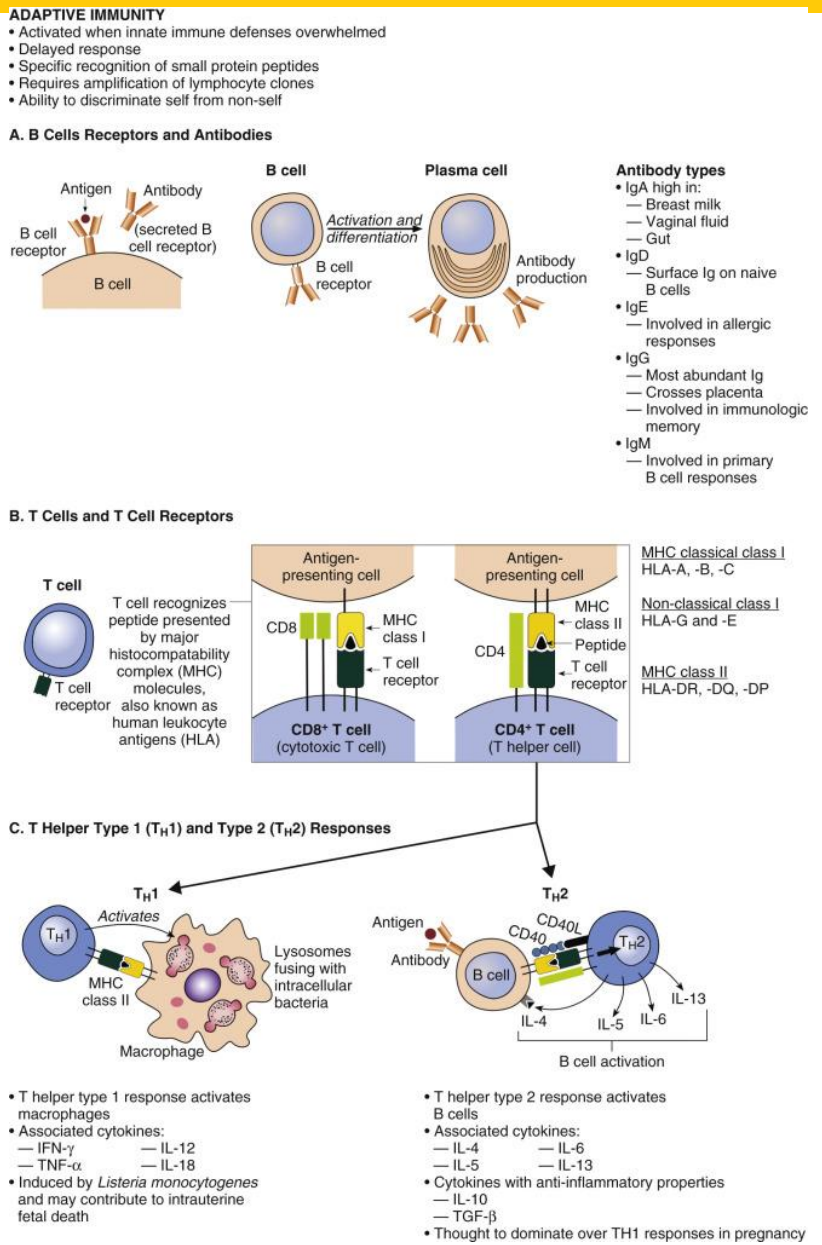
Figure 1.
Immune response against bacteria. Mechanisms of the innate immune response to eradicate bacteria are (A) phagocytosis, (B) inflammatory response, and (C) participation of the complement system.

- Detection of micro-organisms and first-line defense against invasion and infection.
- Regulation of inflammation
- Maintenance of "immunologic homeostasis" within the host.
- Activation and instruction of adaptive immune responses.

- https://www.uptodate.com/contents/an-overview-of-the-innate-immune-system?search=innate%20immune%20system&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1
- Image: https://www.intechopen.com/books/physiology-and-pathology-of-immunology/physiology-and-pathology-of-innate-immune-response-against-pathogens

Adaptive Immunity

- The adaptive immune system is capable of specifically distinguishing self from non-self.
- This is accomplished by creating an anticipatory defense system of recognition molecules that interact with foreign, non-self antigen.



- Introduction to the Immune System - Immunology for Medical Students. Helbert, Matthew, MBChB, FRCP, FRCPath, PhD. Published December 31, 2016. Pages 1-6. © 2017.
- Image from: Gabbe, et al. OBSTETRICS: NORMAL AND PROBLEM PREGNANCIES, 7th Ed 2017 by Elsevier, Inc.

Active and Passive Immunity

- Active immunity
  - Occurs when the individual plays a direct role in responding to the antigen—for example, after an encounter with a virus
- Passive immunity
  - Immunity is transferred from one individual to another by transferring immune cells or serum from an immunized individual to an unimmunized individual
  - Antibodies produced in one host can be passively transferred to another and convey meaningful immunity. This occurs normally during fetal development and can be leveraged for treatment in the form of immune globulin and hyperimmune globulins.
  - During fetal development — Transplacental transfer of maternal immunoglobulin G into fetal circulation is an example of passive immunity.
  - After birth — After birth, neonates begin to passively receive IgA and innate humoral elements via oral intake of colostrum and breast milk.
  - Antibody levels in infants and children — Infants develop the ability to respond to an array of microbial challenges in the first years of life.
    - **IgG** – Since the half-life of passively transferred IgG is 20 to 30 days, maternal IgG is largely cleared from an infant's circulation by six months of age. At the same time, endogenously produced IgG rises gradually during the first year of life. Since these two process occur simultaneously, serum IgG concentrations reach a physiologic nadir between the third to the eighth month of life
    - **IgM and IgA** – IgM production begins in utero, increases rapidly during the first month of life, and then slowly rises thereafter to reach about 70 percent of adult serum concentrations by one year of age.

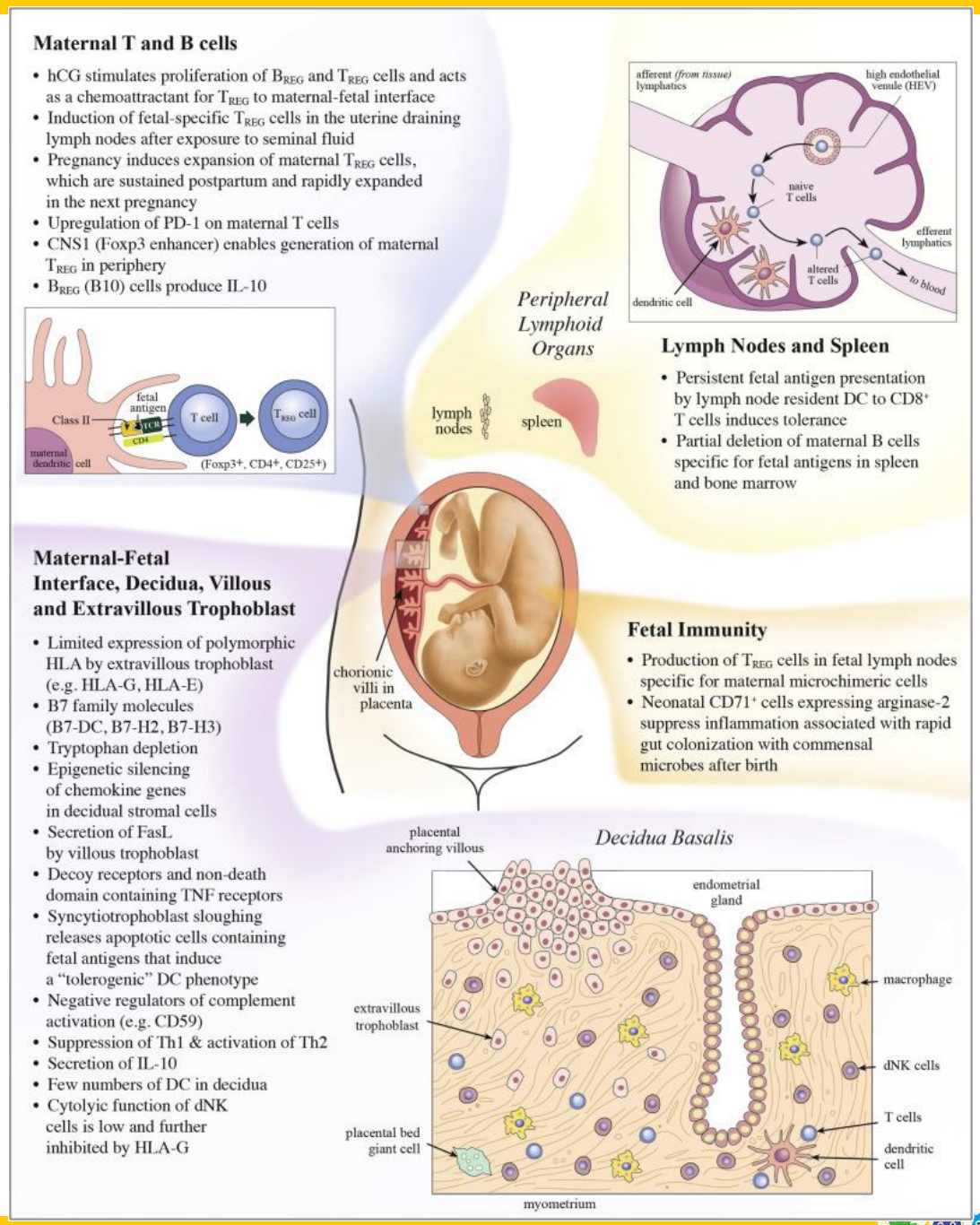
- Introduction to the Immune System - Immunology for Medical Students. Helbert, Matthew, MBChB, FRCP, FRCPath, PhD. Published December 31, 2016. Pages 1-6. © 2017.
- https://www.uptodate.com/contents/the-adaptive-humoral-immune-response?search=adaptive%20immune%20system&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1#H1

Immunity in Pregnancy

- In pregnancy there is an enhancement of the innate immunity and suppression of the adaptive immunity
  - The cell-mediated response is less functional
  - Antibody mediated response is enhanced
- This prevents the mother's immune response from rejecting the fetus – but increased her risk to infections but generally maintains the mother's overall immune function.
- Both protective and potentially harmful maternal antibodies cross the placenta.
  - Maternal IgG crosses in significant amounts
  - This transfer across the placenta give the fetus passive immunity from the maternal antibody complement

Immunity in Pregnancy

- Pregnancy is a unique immunologic phenomenon in which the normal immune rejection of foreign tissues does not occur.
  - The maternal immune system clearly recognizes fetal cells as foreign, and about 30% of primiparous and multiparous women develop antibodies against the inherited paternal HLA of the fetus.
  - The continued presence of these antibodies does not appear to be harmful to the fetus.
  - Persistent fetal cells in the mother may play a role in maintaining the levels of these antibodies because in some women, the antibodies persist, whereas in others they disappear.
  - The normal growth and development of the fetus despite maternal immune recognition requires several maternal and fetal adaptations that in most women allow pregnancy to be carried uneventfully to term.
- Achieving fetal tolerance requires changes to maternal immunity in multiple locations and by many different cell types because maternal and fetal cells are in direct contact with each other.
- In summary, the complex nature of the cells and the many locations of the maternal-fetal interface necessitate a number of different immune mechanisms to prevent fetal rejection.



Gabbe, et al. OBSTETRICS: NORMAL AND PROBLEM PREGNANCIES, 7th Ed 2017 by Elsevier, Inc.

Fetal Immunity

- Descriptions of the development of the fetal immune system are relatively limited, but sufficient information exists to determine that the fetus, even very early in gestation, has innate immune capacity.
- Acquired immunity, particularly the capacity to produce a humoral response, develops more slowly and is not completely functional until well after birth.
- Many of the immune protective mechanisms that are present to protect the fetus from both pathogens and maternal immune recognition occur at the maternal-fetal interface.

Fetus age (weeks)	Innate Immunity	Humoral Immunity	Celular Immunity	Passive Immunity
5-6	Macrophages in the liver and blood		T-cell precursor in the liver	
9-10	Start of the complement synthesis	B precursor in the liver	T-cell precursors in the thymus	
12-14	Macrophages in lymphonodes and APC MHC class II	Pre-B cells with IgD, IgG and IgA	T-cells CD4+ and CD8+ in the liver and spleen	Start of mother's IgG transfer
16-17	Mature macrophages in the liver and circulating neutrophils	Large number of B-cells in the spleen, blood and bone marrow	T-cells in the blood and lymphoid tissues/ rearrangement of receptors	
20-30		B-cells secrete antibodies	Gradual increase of T-lymphocytes secreting lymphokines	Gradual increase of IgG transportation

APC : antigen presenting cells; MHC: major histocompatibility antigens

- Gabbe, et al. OBSTETRICS: NORMAL AND PROBLEM PREGNANCIES, 7th Ed 2017 by Elsevier, Inc.
- De La Cochetière, Marie & Rouge, Carole & Darmaun, Dominique & Rozé, Jean Christophe & Potel, Gilles & Leguen, Christele. (2007). Intestinal Microbiota in Neonates and Preterm Infants: A Review. Current Pediatric Reviews. 3. 21-34. 10.2174/157339607779941697.

Fetal Immune System

- The active immunologic capacity of the fetus & neonate is less as compared to older children & adults
- Fetal cell-mediated immunity and humoral immunity begin to develop by 9-15 weeks gestation
- The primary fetal response to infection is IgM (immunoglobin M).
- Passive immunity is through IgG (Immunoglobin G) transferred across the placenta.
  - IgG transfer begins to increase rapidly around 16 weeks gestation
  - By 26 weeks, fetal concentration of IgG is equivalent to Maternal levels.

Cell Mediated Immunity: Adaptive immune mechanism provided by the immune cells. T-helper cells, T-cytotoxic cells and T-regulatory cells provide protection against certain organisms, regulate B-cell function, defend against cancer and mediate graft rejection.

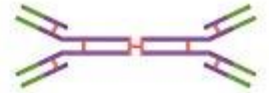
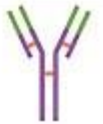
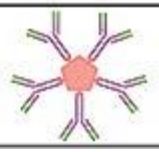
Humoral Immunity (Antibody mediated Immunity): Adaptive immune mechanism mediated by B-cells, which produces antibodies and protects the body from extracellular antigens.

IgM and IgG: 2 out of 5 classes of Antibodies (Proteins – Immunoglobulins) that react to specific antigens

Cunningham, F. G. (2010). Williams Obstetrics 23rd Edition. McGraw-Hill Publishing.
Blackburn, S. (2007) Maternal, Fetal & Neonatal Physiology: A Clinical Perspective. Third edition. Saunders Elsevier – St. Louis, Missouri.

Immune System

- Immunoglobulin
  - Humoral Immunity is a specific antibody-mediated response that functions as if there has been a previous exposure
- Types of Immunoglobulin
  - IgG: provides immunity against bacterial and viral pathogens
    - Crosses placenta
    - Decreased in preterm and postterm infants
  - IgM: does not cross placenta
  - IgA: common in GI and respiratory tract
    - does not cross placenta
    - secreted in colostrum and human milk
  - IgE: plays a major role in allergic reactions

Name	Properties	Structure
IgA	Found in mucous, saliva, tears, and breast milk. Protects against pathogens.	
IgD	Part of the B cell receptor. Activates basophils and mast cells.	
IgE	Protects against parasitic worms. Responsible for allergic reactions.	
IgG	Secreted by plasma cells in the blood. Able to cross the placenta into the fetus.	
IgM	May be attached to the surface of a B cell or secreted into the blood. Responsible for early stages of immunity.	

https://www.bioexplorer.net/types-of-antibodies.html/

Neonatal Immunity - Overview

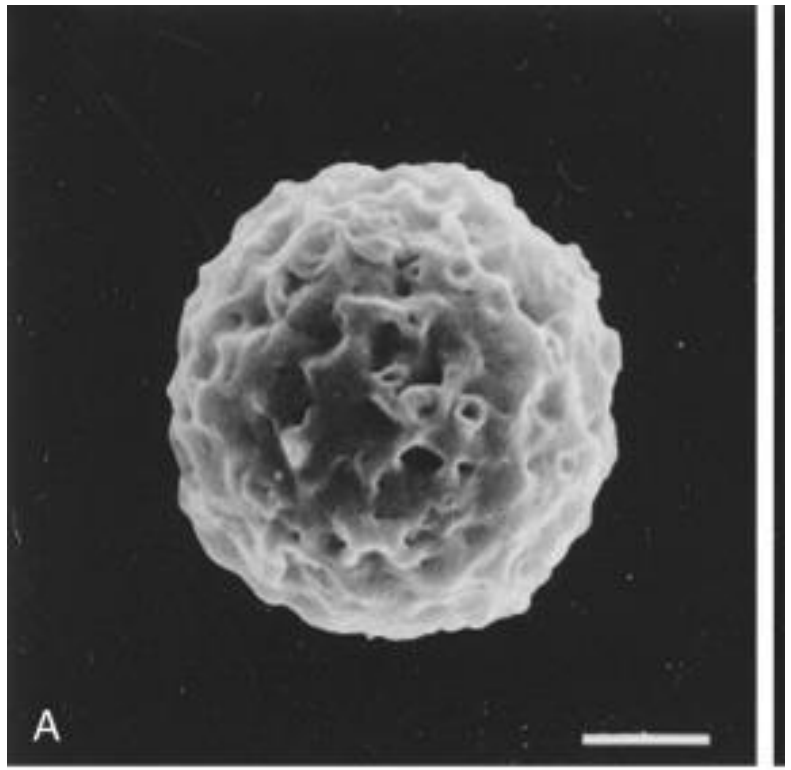
- The neonate inherits a great degree of immunity from the mother because many protein antibodies diffuse from the mother's blood through the placenta into the fetus.
  - The neonate does not form antibodies of its own to a significant extent.
  - By the end of the first month, the baby's gamma globulins, which contain the antibodies, have decreased to less than half the original level, with a corresponding decrease in immunity.
  - Thereafter, the baby's own immune system begins to form antibodies and the gamma globulin concentration returns essentially to normal by the age of 12 to 20 months.

- Despite the decrease in gamma globulins soon after birth, the antibodies inherited from the mother protect the infant for about 6 months against most major childhood infectious diseases, including diphtheria, measles, and polio.
  - Therefore, immunization against these diseases before 6 months is usually not necessary.
  - However, the inherited antibodies against whooping cough are normally insufficient to protect the neonate; therefore, for full safety, the infant requires immunization against this disease within the first month or so of life.

Guton and Hall Textbook of Medical Physiology. 13th Ed. 2016 Elsevier, Inc

Neonatal Immune System

- Neutrophils are a type of white blood cell that are responsible for much of the body's protection against infection. They are produced in the bone marrow and released into the bloodstream to travel to wherever they are needed.
  - We have a storage pool, but in a septic neonate this depletes quickly because of decrease reproduction and proliferation

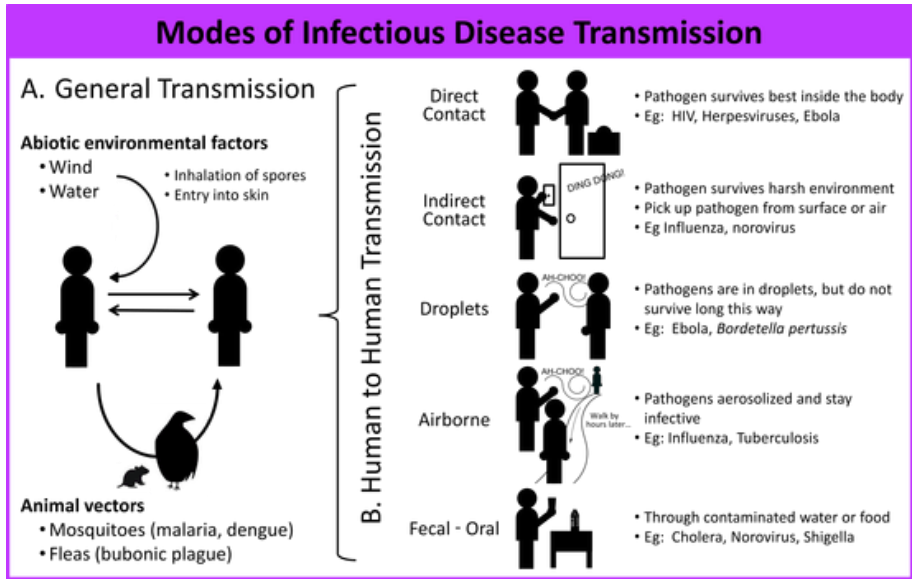


https://www.clinicalkey.com/#!/search/neutrophil/%7B%22facetquery%22:%5B%22+contenttype:IM%22%5D%7D?page=4

Transmission

Transmission refers to the way germs are moved to the susceptible person.

Germs don't move themselves. Germs depend on people, the environment, and/or medical equipment to move in healthcare settings.



- https://www.cdc.gov/infectioncontrol/spread/index.html
- Image: http://sitn.hms.harvard.edu/flash/special-edition-on-infectious-disease/2014/an-introduction-to-infectious-disease/

- There are a few general ways that germs travel in healthcare settings:
  1. Contact moves germs by touch (example: MRSA or VRE).
     - For example, healthcare provider hands become contaminated by touching germs present on medical equipment or high touch surfaces and then carry the germs on their hands and spread to a susceptible person when proper hand hygiene is not performed before touching the susceptible person.
  2. Sprays and splashes occur when an infected person coughs or sneezes, creating droplets which carry germs short distances. These germs can land on a susceptible person's eyes, nose, or mouth and can cause infection
     - Example: pertussis or meningitis
     - Close range inhalation occurs when a droplet containing germs is small enough to breathe in but not durable over distance.
  3. Inhalation occurs when germs are aerosolized in tiny particles that survive on air currents over great distances and time and reach a susceptible person.
     - Airborne transmission can occur when infected patients cough, talk, or sneeze germs into the air (example: TB or measles)
     - When germs are aerosolized by medical equipment or by dust from a construction zone (example: Nontuberculous mycobacteria)
  4. Sharps injuries can lead to infections when bloodborne pathogens enter a person through a skin puncture by a used needle or sharp instrument.
     - Example: HIV, HBV, HCV

Other Types of Transmission

- Droplet contact, also known as the *respiratory route*, and the resultant infection can be termed airborne disease.
  - If an infected person coughs or sneezes on another person the microorganisms, suspended in warm, moist droplets, may enter the body through the nose, mouth or eye surfaces.
- Fecal-oral transmission, wherein foodstuffs or water become contaminated (by people not washing their hands before preparing food, or untreated sewage being released into a drinking water supply) and the people who eat and drink them become infected.
  - Common fecal-oral transmitted pathogens include *Vibrio cholerae*, *Giardia* species, rotaviruses, *Entameba histolytica*, *Escherichia coli*, and tape worms.
- Sexual transmission, with the resulting disease being called sexually transmitted disease
- Oral transmission, diseases that are transmitted primarily by oral means may be caught through direct oral contact
  - Such as kissing, or by indirect contact such as by sharing a drinking glass or a cigarette.
- Transmission by direct contact, Some diseases that are transmissible by direct contact include athlete's foot, impetigo and warts
- Vehicle transmission, transmission by an inanimate reservoir
  - food, water, soil
- Vertical transmission, directly from the mother to an embryo, fetus or baby during pregnancy or childbirth.
  - It can occur when the mother gets an infection as an intercurrent disease in pregnancy.
- Iatrogenic transmission, due to medical procedures such as injection or transplantation of infected material.
- Vector-borne transmission, transmitted by a vector,
  - Vector: an organism that does not cause disease itself but that transmits infection by conveying pathogens from one host to another

https://en.wikipedia.org/wiki/Infection

Vertical Transmission

- We will highlight vertical Transmission as it directly impacts maternal-fetal-neonatal infections
- Vertical transmission of infectious agents from mother to fetus or newborn child is a common mode of transmission of certain pathogens, and may occur through several different routes.
  - *Placental-fetal transmission* . This is most likely to occur when the mother is infected with a pathogen during pregnancy. Some of the resulting infections interfere with fetal development, and understandably the degree and type of damage depend on the age of the fetus at the time of infection. For example, rubella infection during the first trimester can lead to heart malformations, mental retardation, cataracts, or deafness, while rubella infection during the third trimester has little effect.
  - *Transmission during birth* . This mode of transmission is caused by contact with infectious agents during passage through the birth canal. Examples include gonococcal and chlamydial conjunctivitis.
  - *Postnatal transmission in maternal milk* . Agents transmitted in this fashion include cytomegalovirus (CMV), human immunodeficiency virus (HIV), and hepatitis B virus (HBV).

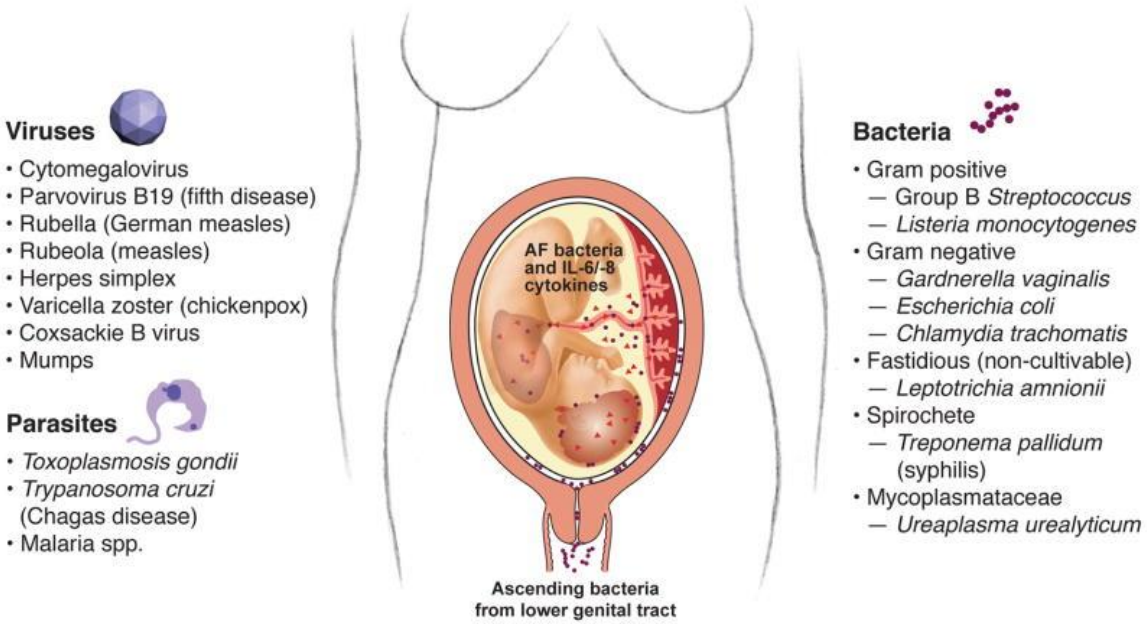
Robbins and Cotran Pathologic Basis of Disease, 9th Ed. 2015 Elsevier, Inc.

Other Perinatal Infections - Transmission

- Transcervical, or ascending, infections are caused by spread of microbes from the cervicovaginal canal and may be acquired in utero or during birth.
  - Most bacterial infections and a few viral infections are acquired in this manner.
  - In general, the fetus acquires the infection by "inhaling" infected amniotic fluid into the lungs or by passing through an infected birth canal during delivery.
  - Fetal infection usually is associated with inflammation of the placental membranes and inflammation of the umbilical cord.
- Transplacental infections gain access to the fetal bloodstream by crossing the placenta via the chorionic villi, and may occur at any time during gestation or occasionally, as may be the case with hepatitis B and human immunodeficiency virus, at the time of delivery via maternal-to-fetal transfusion.
  - Most parasitic and viral infections, and a few bacterial infections, follow this mode of hematogenous transmission.
  - The clinical manifestations of these infections are highly variable, depending largely on the gestational timing and the microorganism involved.

Robbins Basic Pathology, 10th Edition. 2018, Elsevier Inc. https://www.clinicalkey.com/#!/content/book/3-s2.0-B9780323353175000077?scrollTo=%23hl0002516

Does infection affect the fetus?



- Infection by bacteria, viruses and parasites may lead to fetal death, organ injury or limited sequelae depending on the pathogen.
- The majority of early preterm births are associated with intrauterine infection, which triggers an inflammatory response believed to result in preterm labor (PTL) and injury to the developing fetal lung and brain
- Multiple factors may influence the extent of fetal injury associated with an inflammatory response including the triggering pathogen or cytokine profile, timing of the exposure, duration of the insult, concurrent insults (e.g., hypoxia, ischemia), infant demographic variables (e.g., ethnicity, sex), maternal factors (e.g., antenatal steroids, tobacco use), and genetic or epigenetic determinants.

Reproduction. 2013; 146(5): R151–R162. Published online 2013 Oct 1. Influence of Infection During Pregnancy on Fetal Development Kristina M. Adams Waldorf[1] and Ryan M. McAdams[2]
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4060827/

Specific Causes of Some Fetal/Neonatal Infections

Intrauterine

Transplacental

- Viruses: Varicella-zoster, coxsackie; human parvovirus B19, rubella, CMV, HIV
- Bacteria: listeria, syphillis, Borrelia
- Protozoa: Toxoplasmosis, malaria

Ascending infections

- Bacteria: GBS, Coliforms
- Viruses: HSV

Intrapartum

Maternal Exposure

- Bacteria: gonorrhea, chlamydia, GBS, Tuberculosis, mycoplasmas
- Viral: HSV, Papillomavirus, HIV, HBV, HCV

External Contamination

- Bacteria: Staphylococcus, Coliforms
- Viruses: HSV, Varicella Xoster

Neonatal:

Human transmission:

- Staphylococcus, HSV

Respirators & Catheters:

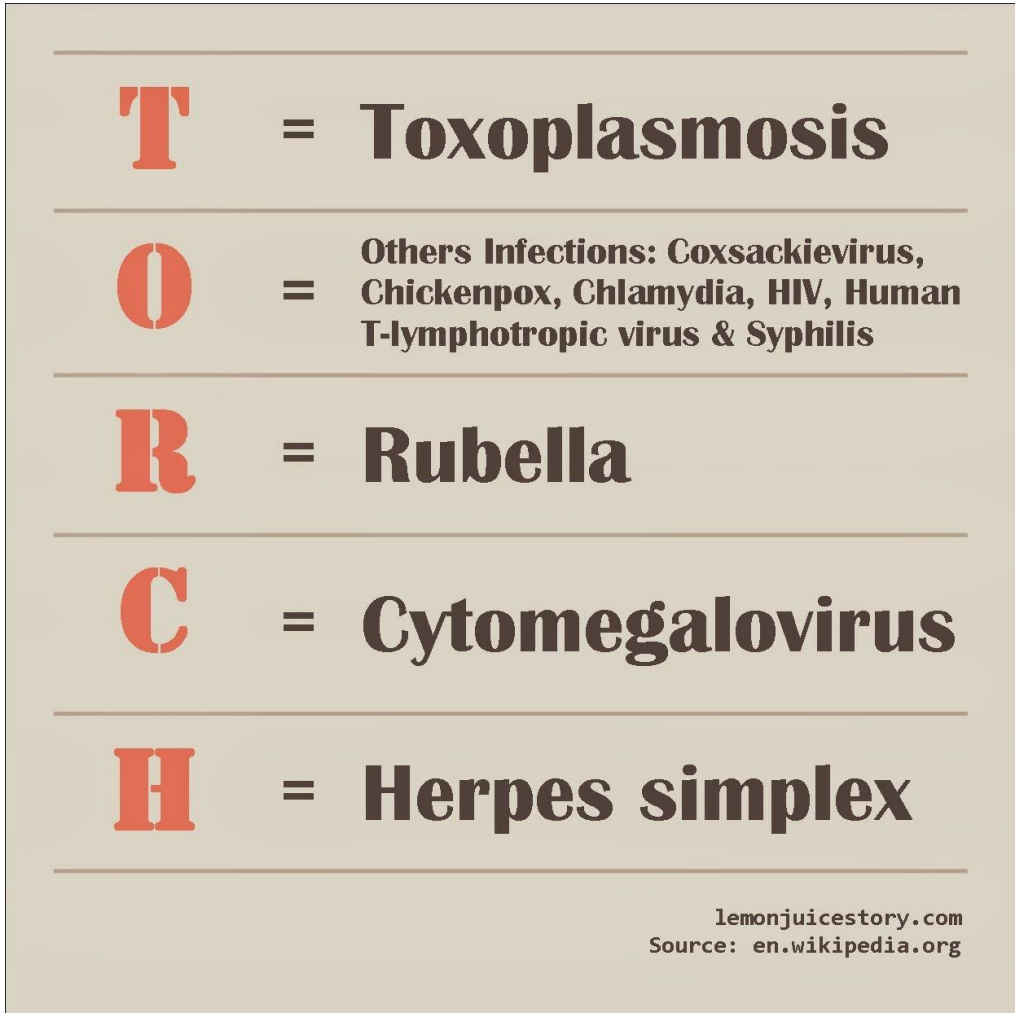
- Staphylococcus, coliforms

Cunningham, F.G. (2010). Williams Obstetrics 23rd Ed. McGraw Hill Publishing

TORCH Infections

What is TORCH?

- Perinatal infections account for 2% to 3% of all congenital anomalies.
- TORCH, which includes Toxoplasmosis, Other (syphilis, varicella-zoster, parvovirus B19), Rubella, Cytomegalovirus, and Herpes infections, are some of the most common infections associated with congenital anomalies.
- Most of the TORCH infections cause mild maternal morbidity, but have serious fetal consequences, and treatment of maternal infection frequently has no impact on fetal outcome.
- Recognition of maternal disease and fetal monitoring once disease is recognized are important for all clinicians.
- Knowledge of these diseases will help the clinician appropriately counsel mothers on preventive measures to avoid these infections, and will aid in counseling parents on the potential for adverse fetal outcomes when these infections are present.



https://www.ncbi.nlm.nih.gov/pubmed/12150751

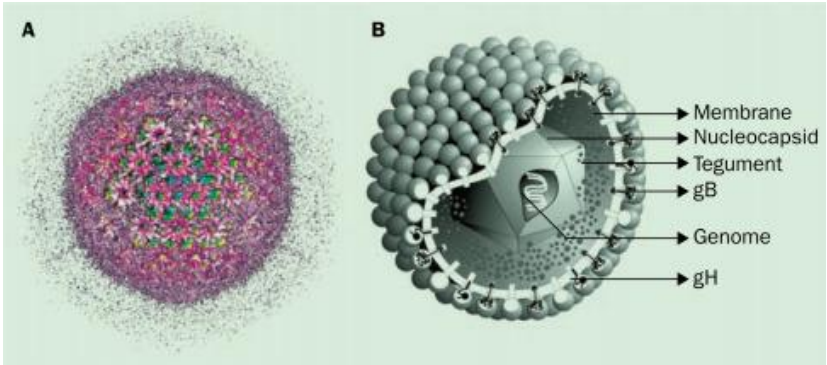
TORCH Infections

- The practice of screening pregnant women for TORCH infection varies geographically. In the United States, the American College of Obstetricians and Gynecologists (ACOG) recommends that pregnant women be screened for rubella and syphilis at the first prenatal visit.
  - Asymptomatic infants generally are not screened for congenital infections.
  - Screening with TORCH titers is expensive and has a poor diagnostic yield.
  - Infant with suspected congenital infections will be screened for specific pathogens based upon their clinical presentation.
  - Signs and symptoms of TORCH are consistent in the neonate. They will include hepatosplenomegaly, fever, lethargy, anemia, petechiae, purpurae, jaundice and chorioretinitis.
- Due to the need to keep the module within a certain time frame, we will only focus on the most common Maternal/Neonatal TORCH infection.

https://www.uptodate.com/contents/overview-of-torch-infections

Maternal/Fetal - CMV

- Cytomegalovirus (CMV) is a large, enveloped, double-stranded DNA virus that is a β-herpesvirus.
- CMV is not highly contagious; transmission primarily occurs by contact with infected saliva or urine, and it can also be transmitted via blood or by sexual contact.
- The incubation period is about 40 days following exposure.
- In the United States, primary CMV infection in pregnant women ranges from 0.7% to 4%, and recurrent infection can be as high as 13.5%.



https://www.sciencedirect.com/science/article/abs/pii/S1473309904012022

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CMV in the Pregnant Woman

- Clinical Manifestations
  - Infected patients may be asymptomatic or they may have a mononucleosis-like syndrome with fever, malaise, myalgias, chills, and cervical lymphadenopathy.
  - Infrequent complications include pneumonia, hepatitis, Guillain-Barre syndrome, and aseptic meningitis. Laboratory abnormalities include atypical lymphocytosis, elevated hepatic transaminases, and a negative heterophile antibody response
- Diagnosis
  - Active, maternal CMV infection is best diagnosed by culture, detection of CMV antigens, or DNA PCR of blood, urine, saliva, amniotic fluid, or cervical secretions.
  - Serologic tests are available, but antibody levels may not be detectable for up to 4 weeks after primary infection, and titers can remain elevated; this makes a serologic diagnosis of reinfection difficult.
    - Fetal serology and blood culture are much less sensitive. Fetal CMV infection can occur weeks to months following maternal infection; thus repeat testing may be considered at 7-week intervals.
    - Antepartum CMV detection does not predict the severity of congenital CMV infection, and 80% to 90% of children with congenital CMV infection have no neurologic sequelae.
- Management of Cytomegalovirus During Pregnancy
  - Pregnant women should be counseled regarding preventive measures:
    - careful handling of potentially infected articles such as diapers, clothing, and toys;
    - avoidance of sharing food and utensils; and
    - frequent hand washing.
  - Antiviral therapy is not indicated in immunocompetent infected individuals, and ganciclovir is not effective for intrauterine treatment of congenital CMV infection.
  - Avoiding maternal CMV infection is the only effective prevention for congenital CMV infection.

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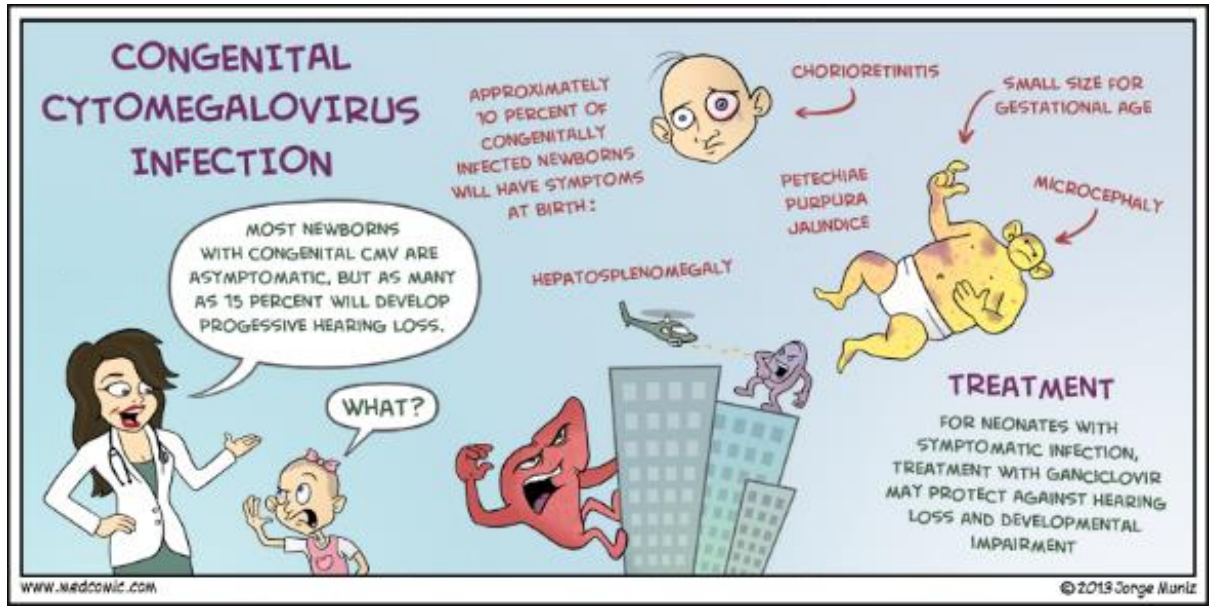
Congenital Cytomegalovirus

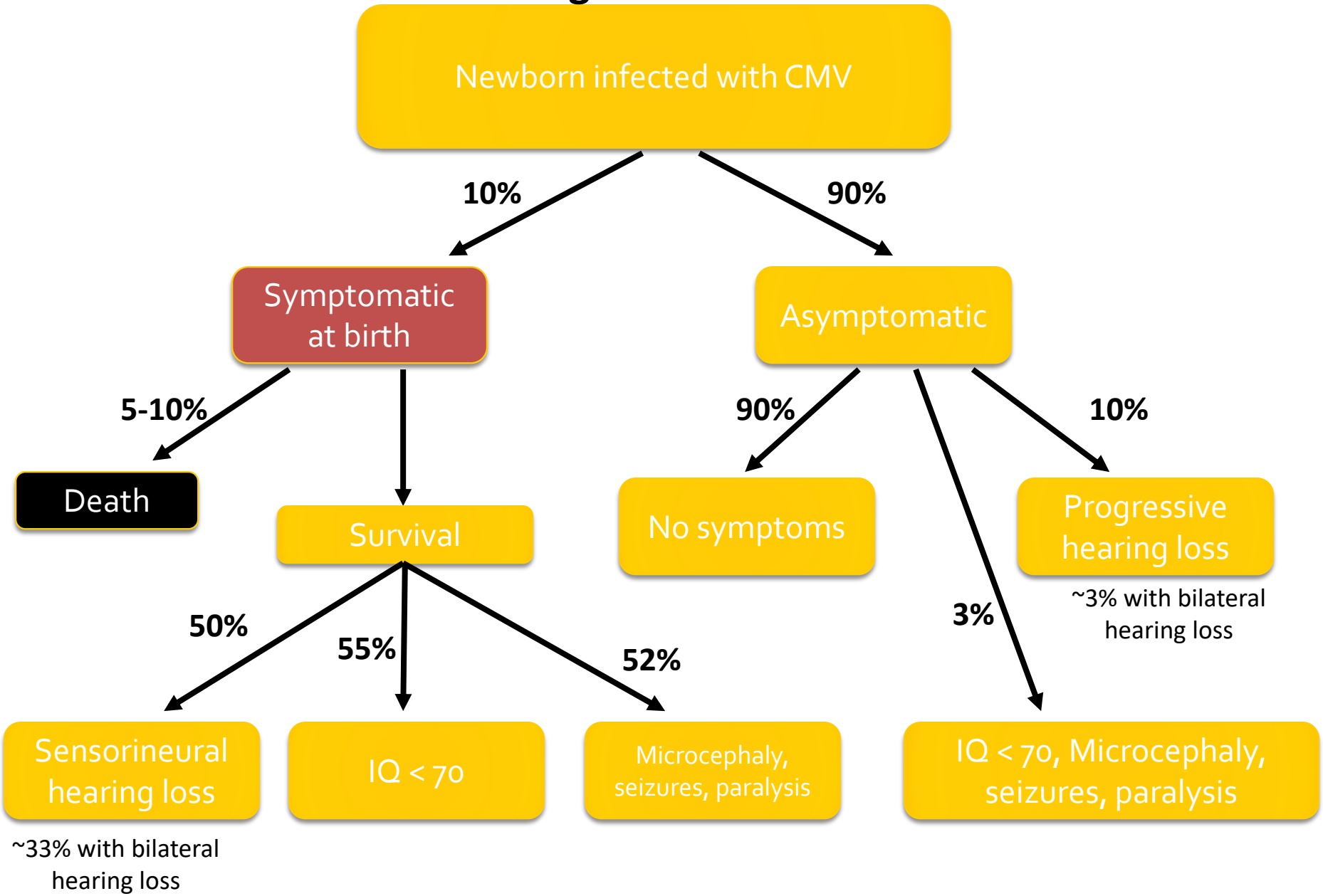
- Congenital Cytomegalovirus is the most common congenital viral infection. The causative organism is the Human Herpesvirus 5. Transmission of CMV from mother to infant can occur via transplacental, intrapartum and breastmilk.
- Transplacental transmission: Maternal viremia leads to placental infection followed by transplacental transmission to the fetus is the major source of fetal infection
- Intrapartum transmission: Postnatal infection can occur via intrapartum exposure to cervical/vaginal viral shedding
- Breast milk transmission: Consumption of infected breast milk.

Congenital Cytomegalovirus

- About one out of every 200 infants is born with congenital cytomegalovirus infection.
- Around one in five babies born with congenital CMV infection will have long-term sequel.
- Risk of transmission for primary infection is 30-40% in the first and second trimesters, and 40 to 70% in third trimester.
- The risk for transmission with non-primary infection is much lower, 3%.
- The risk of complications to the fetus is greatest if a primary infection occurs during the first trimester

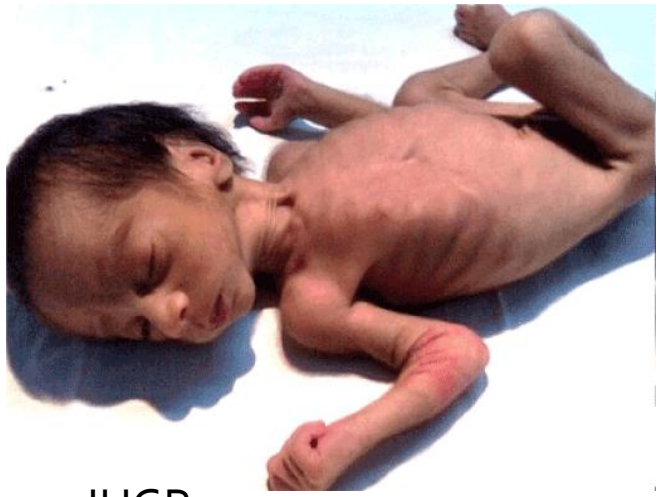


Congenital CMV



Congenital Cytomegalovirus

- About 10% of infants with congenital CMV infection will have signs and symptoms that are apparent at birth:
- Petechiae
- Jaundice
- IUGR
- Hepatosplenomegaly
- The most significant manifestations of Congenital Cytomegalovirus are the CNS.
- Microcephaly
- Ventriculomegaly
- Chorioretinitis
- Sensorineural hearing loss



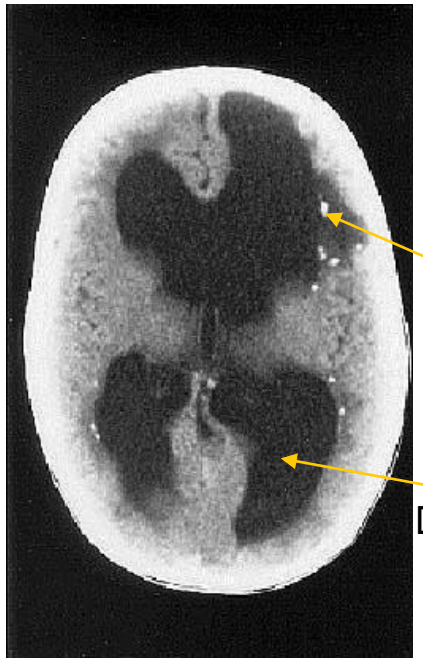
IUGR

Microcephaly

358 Blueberry muffin' rash compatible with congenital infection with CMV or rubella.

Congenital Cytomegalovirus

- Intracranial calcifications is predictive of cognitive and audiologic deficits in later life and predicts a poor neurodevelopmental prognosis
  - Cranial CT of infant born with symptomatic congenital cytomegalovirus infection. The CT scan shows ventriculomegaly and periventricular calcifications
- Sensorineural hearing loss
  - 15% of infants have unilateral or bilateral deafness
  - CMV associated hearing loss may develop months or even years after birth



Congenital Cytomegalovirus Diagnoses and Treatment

- Congenital CMV infection is diagnosed by detection of CMV DNA in the urine, saliva, or blood within three weeks after birth. Congenital CMV cannot be diagnosed using samples collected more than three weeks after birth because testing after this time cannot distinguish between congenital infection and an infection acquired during or after delivery
- Treatment of congenital CMV infection with antivirals should be started in infants with evidence of central nervous system involvement. Two antiviral used are ganciclovir or valganciclovir. They may improve hearing and developmental outcomes.
- Most infants with congenital CMV grow up healthy. They will need regular hearing and vision screening

Sexually Transmitted Infections (STI's)

CDC STD Fact Sheet – from October 2019 CDC Press Release – 2018 *Sexually Transmitted Disease Surveillance Report* https://www.cdc.gov/nchhstp/newsroom/docs/factsheets/STD-Trends-508.pdf

CDC FACT SHEET

Reported STDs in the United States, 2018

Sexually transmitted diseases (STDs) are a substantial health challenge facing the United States, and the epidemic disproportionately affects certain populations. Many cases of chlamydia, gonorrhea, and syphilis continue to go undiagnosed and unreported, and data on several other STDs, such as human papillomavirus and herpes simplex virus, are not routinely reported to CDC. As a result, national surveillance data only captures a fraction of America's STD epidemic. CDC's STD Surveillance Report provides important insight into the scope, distribution, and trends in STD diagnoses in the country. Strong public health infrastructure is critical to prevent and control STDs, especially among the most vulnerable groups.

RECORD HIGH STDS THREATEN MILLIONS OF AMERICANS

2,457,118
COMBINED CASES REPORTED IN 2018

Chlamydia
1,758,668 cases
540 per 100,000 people

Gonorrhea
583,405 cases
179 per 100,000 people

Syphilis (all stages)
115,045 cases
35 per 100,000 people

Syphilis (primary and secondary)	Syphilis (congenital)
35,063 cases	1,306 cases
11 per 100,000 people	33 per 100,000 live births

STD PREVENTION CHALLENGES

Maintaining and strengthening core prevention infrastructure is essential to mounting an effective national response. LIMITED RESOURCES make it challenging to quickly identify and treat STDs. Many state and local STD program budgets have been cut in recent years—resulting in staff layoffs, reduced clinic hours, and increased patient co-pays that can limit access to essential diagnosis and treatment services.

Antibiotics can cure chlamydia, gonorrhea, and syphilis. However, LEFT UNTREATED, these STDs put men, women, and infants at risk for severe, lifelong health outcomes like chronic pain, severe reproductive health complications, and HIV.

People who CANNOT GET STD CARE remain vulnerable to short- and long-term health consequences and are more likely to transmit infections to others—further compounding America's STD burden.

SOME GROUPS ARE MORE LIKELY TO BE AFFECTED BY STDS

Syphilis

NEWBORNS

MORE THAN 1,300 CASES of congenital syphilis were reported in 2018, which resulted in severe health complications and deaths among newborns. From 2017 to 2018 syphilis among newborns INCREASED 40%, from 24 TO 33 CASES PER 100,000 LIVE BIRTHS.

WOMEN

- Diagnoses of primary and secondary syphilis, the most infectious stages of the disease, INCREASED 34% from 2017 to 2018 (3,722 CASES TO 4,995 CASES) among women overall.
- The rise in congenital syphilis parallels increases in primary and secondary syphilis among women of reproductive age (a 36% INCREASE from 2017 to 2018).

GAY AND BISEXUAL MEN

- Primary and secondary syphilis rates increased among men by 11%—from 17 CASES PER 100,000 men in 2017 to 19 PER 100,000 MEN in 2018.
- Men accounted for nearly 86% (30,034) of all primary and secondary syphilis cases in 2018, and gay, bisexual, and other men who have sex with men accounted for 54% (18,760) of all syphilis cases.
- CDC estimates ABOUT HALF of MSM who have syphilis also have HIV.

Gonorrhea

WOMEN

Gonorrhea diagnoses among women have increased for several consecutive years—from 232,587 CASES in 2017 to 241,074 CASES in 2018.

GAY AND BISEXUAL MEN

Gonorrhea diagnoses nearly doubled among men over the past five years (from 186,943 TO 341,401 CASES). Data suggest that men who have sex with men are disproportionately affected by this disease.

Chlamydia

WOMEN

- Chlamydia is the most commonly reported STD, with nearly 1.8 MILLION CASES reported in 2018.
- Young women (ages 15-24) account for 44% of reported cases and face the most severe consequences of an undiagnosed infection.
- It is estimated that UNDIAGNOSED STDS CAUSE INFERTILITY IN MORE THAN 20,000 WOMEN each year.

WHAT CAN BE DONE?

TURNING BACK THE RISE IN STDS WILL REQUIRE RENEWED COMMITMENT FROM ALL PLAYERS:

CDC detects and rapidly responds to evolving STD threats, trains frontline health workers, and provides prevention resources to state and local health departments.

Providers should make STD screening and timely treatment a standard part of medical care, especially for adolescents, pregnant women and MSM.

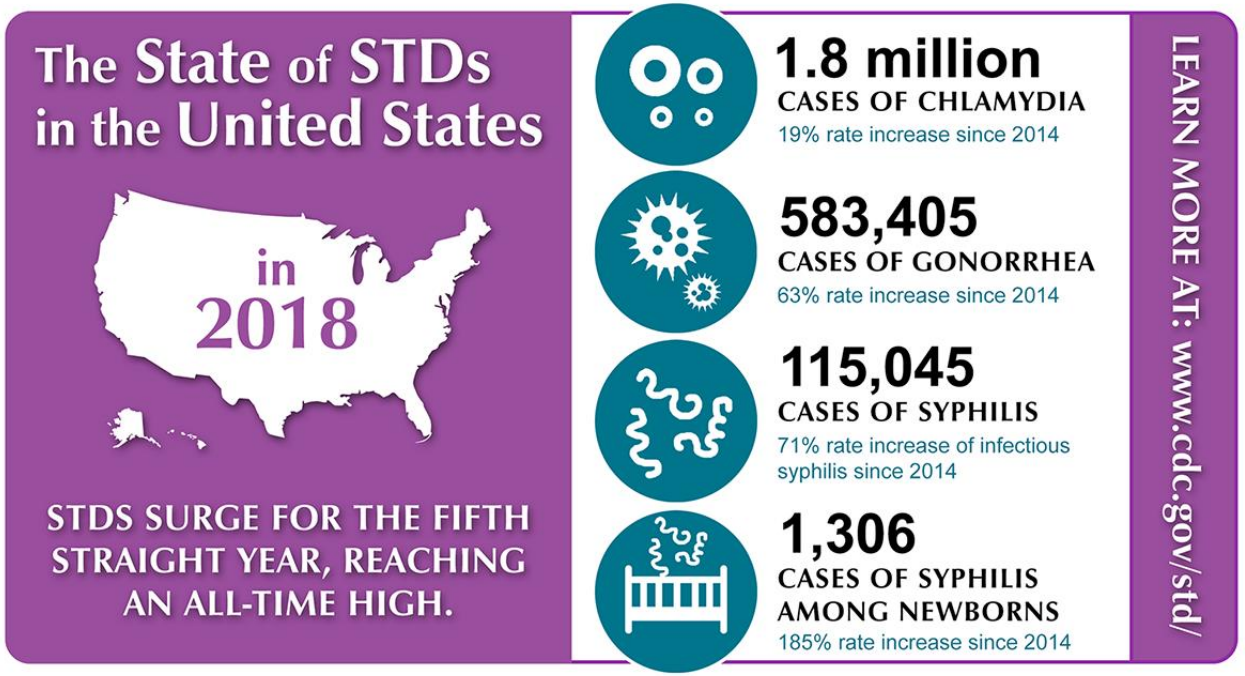
State and local health departments should direct resources to STD investigation and clinical service infrastructure for rapid detection and treatment for people living in areas hardest hit by the STD epidemic.

Everyone should talk openly about STDs, get tested regularly, and reduce risk by using condoms or practicing mutual monogamy.

For more information visit ***www.cdc.gov/nchhstp/newsroom***

CDC Press Release Report: "October 8, 2019 – Growing threat of newborn deaths from syphilis"

- Combined cases of syphilis, gonorrhea, and chlamydia reached an all-time high in the United States in 2018, according to the annual Sexually Transmitted Disease Surveillance Report released today by the Centers for Disease Control and Prevention.
- Sexually transmitted diseases can have severe health consequences.
  - Among the most tragic are newborn deaths related to congenital syphilis, which increased 22 percent from 2017 to 2018 (from 77 to 94 deaths).
- The new report shows that from 2017 to 2018, there were increases in the three most commonly reported STDs:
  - There were more than 115,000 syphilis cases. ◦The number of primary and secondary syphilis cases – the most infectious stages of syphilis – increased 14 percent to more than 35,000 cases, the highest number reported since 1991.
    - Among newborns, syphilis cases increased 40 percent to more than 1,300 cases.
  - Gonorrhea increased 5 percent to more than 580,000 cases – also the highest number reported since 1991.
  - Chlamydia increased 3 percent to more than 1.7 million cases – the most ever reported to CDC.



"2018 STD SURVEILLANCE REPORT HIGHLIGHTS ALARMING THREAT: NEWBORN DEATHS FROM SYPHILIS - 22 PERCENT INCREASE FROM 2017 TO 2018 (FROM 77 TO 94 DEATHS)"

https://www.cdc.gov/nchhstp/newsroom/2019/2018-STD-surveillance-report-press-release.html

Why Such in Increase?

- Multiple factors drive the continued increase in STDs
- Data suggest that multiple factors are contributing to the overall increase in STDs, including:
  - Drug use, poverty, stigma, and unstable housing, which can reduce access to STD prevention and care
  - Decreased condom use among vulnerable groups, including young people and gay and bisexual men
  - Cuts to STD programs at the state and local level – in recent years, more than half of local programs have experienced budget cuts, resulting in clinic closures, reduced screening, staff loss, and reduced patient follow-up and linkage to care services

https://www.cdc.gov/nchhstp/newsroom/2019/2018-STD-surveillance-report-press-release.html

Overview: Sexually Transmitted Infections in Women

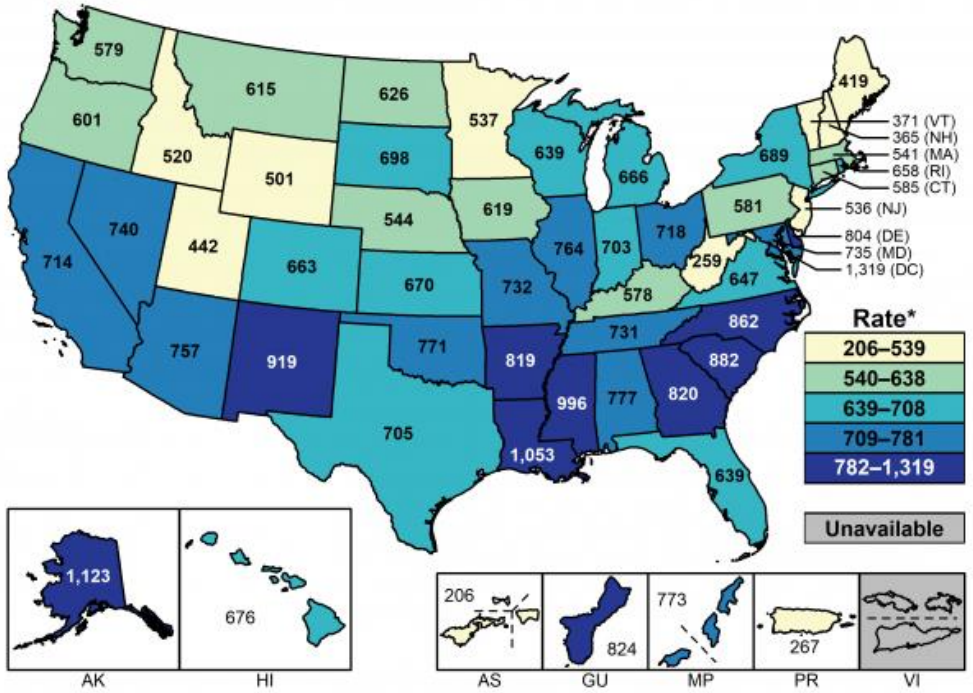
- Complications of sexually transmitted infections disproportionately affect women of all ages, with important implications for women of reproductive age.
- Undiagnosed and untreated STDs can lead to pelvic inflammatory disease, ectopic pregnancy, as well as adverse fetal and neonatal outcomes.
- STD-related morbidity disproportionately occurs in women for a number of reasons.
  - Women are biologically more susceptible than men to the acquisition of some STDs and more likely to suffer from complications.
  - It is also important to note that STDs are often asymptomatic in women, delaying diagnosis and treatment until there is a symptomatic complication.
  - A female's sexual and reproductive health can also be interrelated to her particular social, cultural, and economic environment, creating conditions for risky sexual behaviors.

https://www.cdc.gov/nchhstp/newsroom/2019/2018-STD-surveillance-report-press-release.html

https://www.cdc.gov/std/stats18/womenandinf.htm

Statistics of STD's Related to Women/Pregnancy

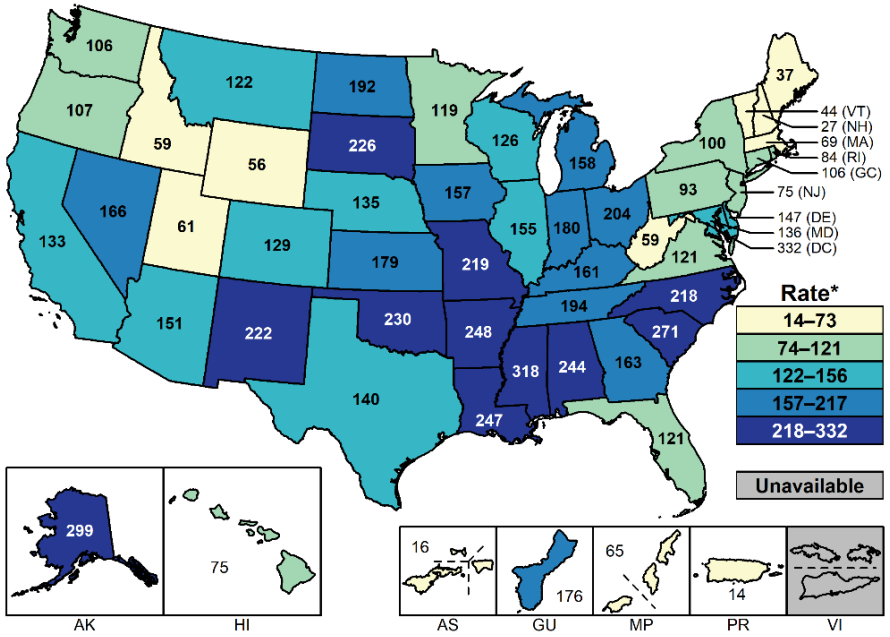
Figure A. Chlamydia — Rates of Reported Cases Among Females by State and Territory, United States, 2018



* Per 100,000.
NOTE: See Sections A1.11 in the Appendix for more information on interpreting reported rates in US territories.

During 2011–2013, chlamydia case rates decreased from 643.4 to 619.0 cases per 100,000 females and then increased 11.9% over the next five years, resulting in a rate of 692.7 cases per 100,000 females in 2018

Figure C. Gonorrhea — Rates of Reported Cases Among Females by State and Territory, United States, 2018



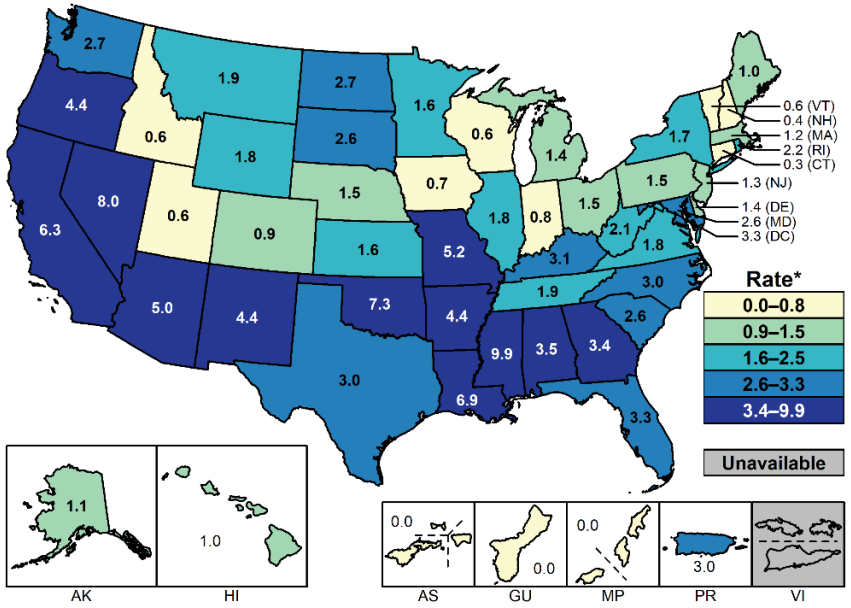
* Per 100,000.
NOTE: See Sections A1.11 in the Appendix for more information on interpreting reported rates in US territories.

During 2015–2018, the gonorrhea rate among women increased 37.2% to 145.8 cases per 100,000 females

https://www.cdc.gov/std/stats18/womenandinf.htm

Statistics of STD's Related to Women/Pregnancy

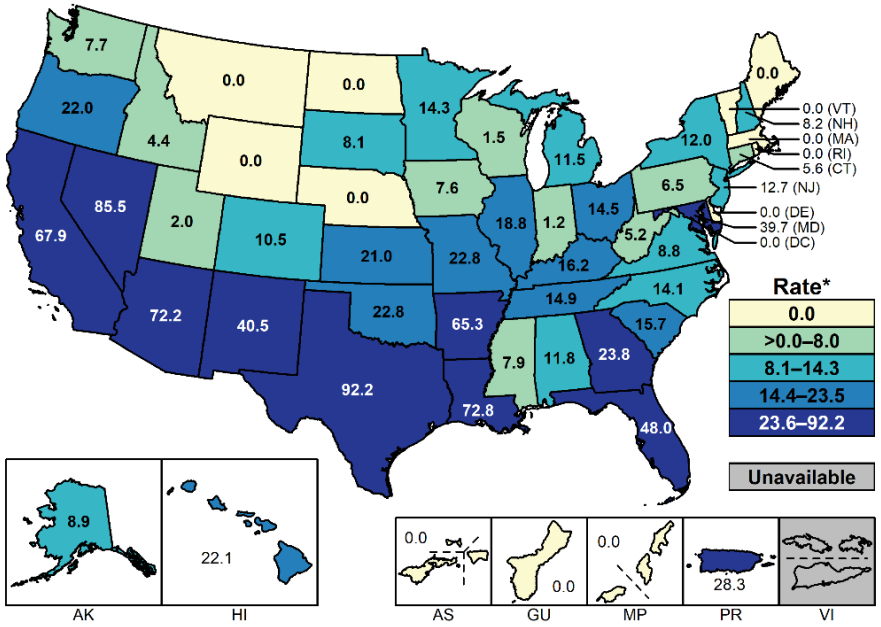
Figure J. Primary and Secondary Syphilis — Rates of Reported Cases Among Females by State and Territory, United States, 2018



* Per 100,000.
NOTE: See Sections A1.11 in the Appendix for more information on interpreting reported rates in US territories.

During 2014–2018, the rate among women increased 172.7%, from 1.1 to 3.0 cases per 100,000 females. During this same period, the rate among reproductive-aged women (women aged 15–44 years) increased 165.4%, from 2.6 to 6.9 cases per 100,000 females aged 15–44 years.

Figure I. Congenital Syphilis — Rates of Reported Cases by State and Territory, United States, 2018



* Per 100,000 live births.
NOTE: See Section A1.11 in the Appendix for more information on interpreting rates for US territories.

In 2018, there were 1,306 reported cases of congenital syphilis, with a rate of 33.1 cases per 100,000 live births, the highest rate reported since 1995. This increase in 2018 represents a 39.7% increase relative to 2017 and a 291.0% increase relative to 2012

We will give some specific information related to syphilis due to the increased rates.

Image from: https://www.npr.org/sections/health-shots/2016/06/10/480643381/despite-rise-of-superbugs-syphilis-still-has-a-kryptonite

General Information: Syphilis

https://www.cdc.gov/std/syphilis/stdfact-syphilis-detailed.htm

Primary Stage

- The appearance of a single chancre marks the primary (first) stage of syphilis symptoms, but there may be multiple sores.
- The chancre is usually (but not always) firm, round, and painless.
- It appears at the location where syphilis entered the body.
- These painless chancres can occur in locations that make them difficult to notice (e.g., the vagina or anus).
- The chancre lasts 3 to 6 weeks and heals regardless of whether a person is treated or not.
- However, if the infected person does not receive adequate treatment, the infection progresses to the secondary stage.

Secondary Stage

- Skin rashes and/or mucous membrane lesions (sores in the mouth, vagina, or anus) mark the second stage of symptoms.
- This stage typically starts with the development of a rash on one or more areas of the body.
- The characteristic rash of secondary syphilis may appear as rough, red, or reddish brown spots both on the palms of the hands and the bottoms of the feet.
- In addition to rashes, symptoms of secondary syphilis may include fever, swollen lymph glands, sore throat, patchy hair loss, headaches, weight loss, muscle aches, and fatigue.
- The symptoms of secondary syphilis will go away with or without treatment.
- However, without treatment, the infection will progress to the latent and possibly tertiary stage of disease.

Latent Stage

- The latent (hidden) stage of syphilis is a period of time when there are no visible signs or symptoms of syphilis.
- Without treatment, the infected person will continue to have syphilis in their body even though there are no signs or symptoms.
- *Early latent syphilis* is latent syphilis where infection occurred within the past 12 months.
- *Late latent syphilis* is latent syphilis where infection occurred more than 12 months ago.
- Latent syphilis can last for years.

Tertiary Syphilis

- Tertiary syphilis is rare and develops in a subset of untreated syphilis infections; it can appear 10–30 years after infection was first acquired, and it can be fatal.
- Tertiary syphilis can affect multiple organ systems, including the brain, nerves, eyes, heart, blood vessels, liver, bones, and joints.
- Symptoms of tertiary syphilis vary depending on the organ system affected.

Neurosyphilis and Ocular Syphilis

- Neurosyphilis:
  - Syphilis can invade the nervous system at any stage of infection, and causes a wide range of symptoms, including headache, altered behavior, difficulty coordinating muscle movements, paralysis, sensory deficits, and dementia.
- Ocular syphilis
  - Can occur at any stage of infection.
  - Ocular syphilis can involve almost any eye structure, but posterior uveitis and panuveitis are the most common.
  - Symptoms include vision changes, decreased visual acuity, and permanent blindness.

Syphilis in Pregnancy

- When a pregnant woman has syphilis, the infection can be transmitted to her unborn baby.
  - All pregnant women should be tested for syphilis at the first prenatal visit.
  - For women who are at high risk, live in areas of high syphilis morbidity, are previously untested, or had a positive screening test in the first trimester, the syphilis screening test should be repeated during the third trimester and again at delivery.
  - Any woman who delivers a stillborn infant after 20 week's gestation should also be tested for syphilis.
- Untreated syphilis in pregnant women results in infant death in up to 40 percent of cases.
- An infected baby born alive may not have any signs or symptoms of disease.
- For pregnant women only penicillin therapy can be used to treat syphilis and prevent passing the disease to her baby
  - Treatment with penicillin is extremely effective (success rate of 98%) in preventing mother-to-child transmission.
  - Pregnant women who are allergic to penicillin should be referred to a specialist for desensitization to penicillin.

https://www.cdc.gov/std/syphilis/stdfact-syphilis-detailed.htm

Transmission of Syphilis to Fetus

- Infection results from transplacental migration of the organism to the fetus.
  - can occur at any stage of maternal infection and at any gestational age.
    - It is believed that transplacental infection must be close to 100% during the early stages of maternal disease because of the known hematogenous spread, with rates of transmission falling to 10% as bacteremia abates with the subsequent mounting of the maternal immunologic response during late latent disease.
  - Disease early in gestation incites little response because the fetal immune system functions little until mid-gestation.
  - After mid-gestation, the fetus is able to mount a vigorous response with marked endarteritis and end-organ involvement.
  - The risk for adverse pregnancy outcome in pregnant women with syphilis that was untreated is approximately 52%.
  - The specific risks include a higher risk for:
    - miscarriage or stillbirth - 21%
    - neonatal death - 9.3%
    - premature birth or low birthweight - 5.8%
    - clinical evidence of congenital infection - 15%

Recommended Treatment Regimens for Treponema pallidum Infections*
(The CDC recommends penicillin as the treatment of choice in individuals with syphilis.)

Primary, Secondary, Early Latent Disease	Benzathine penicillin G, 2.4 million U IM as a single dose
Late Latent and Latent Disease of Unknown Duration	Benzathine penicillin G, 2.4 miU IM weekly for three doses (7.2 miU total)
Tertiary Disease With Neurosyphilis	•Aqueous crystalline penicillin G, 18 to 24 miU/day IV (3 to 4 miU every 4 hours or continuous infusion) for 10 to 14 days or •Procaine penicillin G, 2.4 miU IM once daily with probenecid 500 mg PO four times a day for 10 to 14 days if compliance can be ensured
Tertiary Disease Without Neurosyphilis	Benzathine penicillin G, 2.4 miU IM weekly for 3 weeks (7.2 miU total)
Penicillin Allergy (Documented) In Pregnancy	Without Neurosyphilis •Desensitization and penicillin therapy as above IM, intramuscularly; IV, intravenously; miU, million units; PO, per os.

Box 52-3: Modified from Workowski KA, Bolan GA; Centers for Disease Control and Prevention (CDC): Sexually transmitted diseases treatment guidelines, 2015. *MMWR Morb Mortal Wkly Rep.* 2015;64(RR-03):1-137.

Gabbe, et al. OBSTETRICS: NORMAL AND PROBLEM PREGNANCIES, 7th Ed 2017 by Elsevier, Inc.

Other Management Considerations

- Some evidence suggests that additional therapy is beneficial for pregnant women.
  - For women who have primary, secondary, or early latent syphilis, a second dose of benzathine penicillin 2.4 million units IM can be administered 1 week after the initial dose
- When syphilis is diagnosed during the second half of pregnancy, management should include a sonographic fetal evaluation for congenital syphilis.
  - Ultrasound evaluation should not delay therapy.
  - Sonographic signs of fetal or placental syphilis (i.e., hepatomegaly, ascites, hydrops, fetal anemia, or a thickened placenta) indicate a greater risk for fetal treatment failure; cases accompanied by these signs should be managed in consultation with obstetric specialists. Evidence is insufficient to recommend specific regimens for these situations.
- Women treated for syphilis during the second half of pregnancy are at risk for premature labor and/or fetal distress
  - These women should be advised to seek obstetric attention after treatment if they notice any fever, contractions, or decrease in fetal movements.
  - Stillbirth is a rare complication of treatment, but concern for this complication should not delay necessary treatment. No data are available to suggest that corticosteroid treatment alters the risk for treatment-related complications in pregnancy.
- Missed doses are not acceptable for pregnant women receiving therapy for late latent syphilis (423). Pregnant women who miss any dose of therapy must repeat the full course of therapy.
- All women who have syphilis should be offered testing for HIV infection.
- Follow-Up
  - Coordinated prenatal care and treatment are vital.
  - At a minimum, serologic titers should be repeated at 28–32 weeks' gestation and at delivery.
  - Serologic titers can be checked monthly in women at high risk for reinfection or in geographic areas in which the prevalence of syphilis is high.
  - Providers should ensure that the clinical and antibody responses are appropriate for the patient's stage of disease, although most women will deliver before their serologic response to treatment can be assessed definitively. Inadequate maternal treatment is likely if delivery occurs within 30 days of therapy, clinical signs of infection are present at delivery, or the maternal antibody titer at delivery is fourfold higher than the pretreatment titer.

https://www.cdc.gov/std/tg2015/syphilis-pregnancy.htm

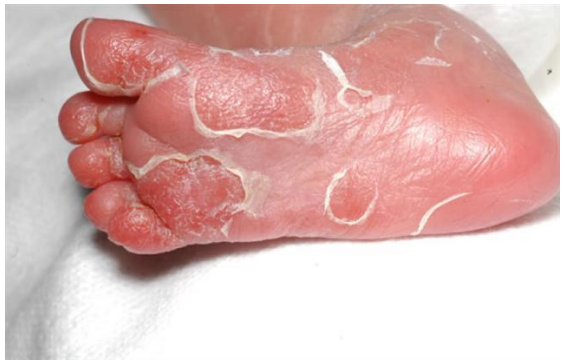
Congenital Syphilis

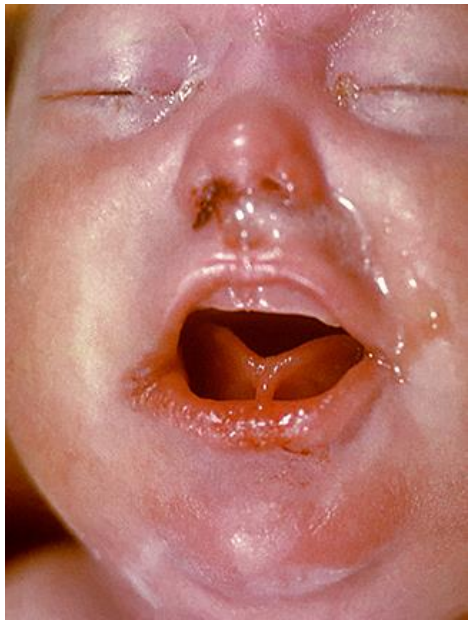
- Congenital syphilis occurs when the spirochete Treponema pallidum is transmitted across the placenta and are able to pass through the chorionic layers of the amniotic sac and infiltrate the developing fetus.
- Congenital syphilis can be acquired at any time during pregnancy or birth, transplacental transmission commonly occurs during the early fetal period of development (14-16 weeks gestation).
- Vertical transmission occurs when the mother transmits the bacteria to the infant during birth; although less common, transmission is possible if the infant comes in contact with an infected lesion when passing through the birth canal.

Image: https://slideplayer.com/slide/1703198/

Congenital Syphilis

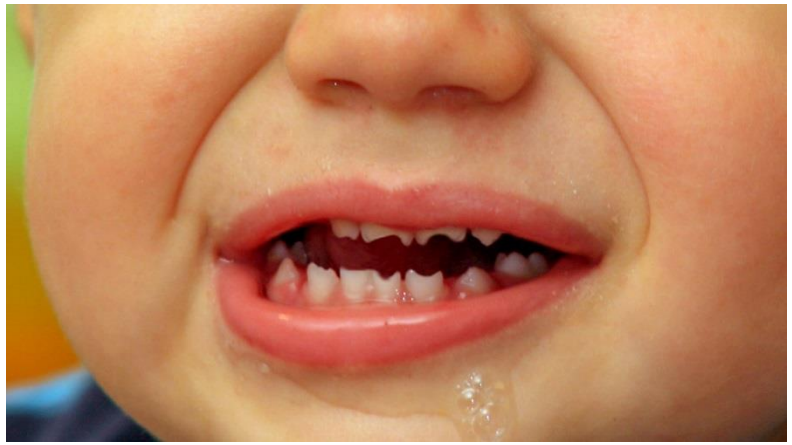
- Infants may have typical signs and symptoms or they may be asymptomatic. The stage of maternal syphilis, prenatal treatment, fetal immunological response, and gestational age influence the degree of clinical manifestations. The disease may manifest in 2 categories: Early Congenital Syphilis and Late Congenital Syphilis.
- **Early Congenital Syphilis** is usually identified by 3 months of age but symptoms may present as late as two years of age.
- Hepatomegaly is the most common physical finding and reported in almost 100% of cases of symptomatic infants
- Skin rash/copper-red maculopapular lesions on the body, with the hands and feet being the most likely and most severely affected areas. Mucocutaneous involvement may be present at birth or within the first few weeks of life.
- Rhinitis with bloody mucus discharge may be present during the first week of life or as late as 3 months of age





Congenital Syphilis

- **Late Congenital Syphilis:** Approximately 40% of untreated early congenital syphilis may lead to late congenital syphilis. Diagnoses is typically any time after two years of age; symptoms include syphilitic rhinitis, syphilitic vasculitis, interstitial keratitis, and neurological and musculoskeletal abnormalities.
- Syphilitic vasculitis is responsible for dental abnormalities such as peg-shaped, wide-spaced teeth known as Hutchinson's teeth



Advances in Neonatal Care; Dec 2018

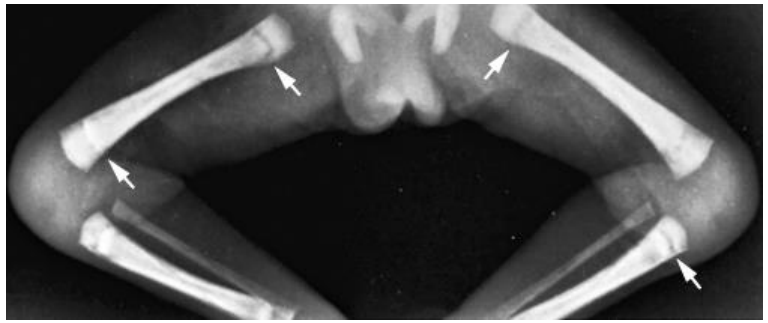
Congenital Syphilis

- Interstitial keratitis is usually manifested as secondary glaucoma or corneal clouding and may not be present until second decade of life
- Neurological involvement can result in hydrocephalus, seizure disorders , developmental delays, deafness, blindness.
- If unidentified and left untreated, the disease can progress to organ damage, including heart failure, brain damage and infections, which can result in seizures and paralysis; and deformities of the arms and legs resulting in immobility

Diagnosing Congenital Syphilis

- All neonates born to women who have a reactive serologic tests for syphilis should be examined thoroughly for evidence of congenital syphilis
- Abnormal long-bone radiographs are a common manifestation of early congenital syphilis, occurring in 60-80% and may be the sole manifestation in infants born to mothers with untreated syphilis. The radiographic changes usually are present at birth but may appear in the first few weeks of life

Lucent Metaphyseal Bands



Diagnosing/Treatment Congenital Syphilis

- Laboratory Abnormalities
  - Serum RPR or VDRL
  - CSF abnormalities
    - Reactive CSF VDRL
- CDC Policy States
  - No newborn should leave a hospital without documentation of the mother's serologic status at least once during the pregnancy
- Treatment Decisions are made on the basis of:
  - Identification of syphilis in the mother
  - Adequacy of maternal treatment
  - Presence of clinical, laboratory, or radiographic evidence of syphilis in the neonate
  - Comparison of maternal (at delivery) and neonatal serologic titers using the same test
  - Any infant at risk for congenital syphilis should receive a full evaluation and testing for HIV infection

http://www.cdc.gov/std/tg2015/congenital.htm

Congenital Syphilis Treatment

- CDC Recommendations for treatment of congenital syphilis
  - Proven or highly probable congenital syphilis
    - Aqueous crystalline Penicillin G: 100,000-150,000 units/kg/day, administered as 50,000 units/kg/dose IV every 12 hours during the first 7 days of life and every 8 hours thereafter for a total of 10 days OR
    - Procaine Penicillin G: 50,000 units/kg/dose IM in a single daily dose for 10 days
  - Possible Congenital Syphilis
    - Aqueous crystalline Penicillin G 100,000-150,000 units/kg/day, administered as 50,000 units/kg/dose IV every 12 hours during the first 7 days of life and every 8 hours thereafter for a total of 10 days OR
    - Benzathine Penicillin G: 50,000 units/kg/dose IM in a single dose
  - Congenital Syphilis less likely
    - Benzathine Penicillin G: 50,000 units/kg/dose IM in a single dose
  - Congenital Syphilis unlikely
    - No treatment required but infants with reactive nontreponemal tests should be followed serologically to ensure the nontreponemal test returns to negative. Benzathine Penicillin G 50,000 units/kg as a single IM injection may be considered.
- Note: To review full details of the above scenarios , please visit: https://www.cdc.gov/std/tg2015/congenital.htm

Bacterial Infections

Mom – Group B Streptoccus

- GBS is a β-hemolytic, gram-positive coccus that asymptomatically colonizes the lower genital and gastrointestinal tracts but is an invasive pathogen in other host niches.
- On average, about 20% to 25% of pregnant women in the United States harbor this group B Streptococcus (GBS) in their lower genital tract and rectum.
- GBS is one of the most important causes of early-onset neonatal infection.
- The prevalence of neonatal GBS infection now is about 0.5 per 1000 live births, and about 10,000 cases of neonatal streptococcal septicemia occur each year in the United States.

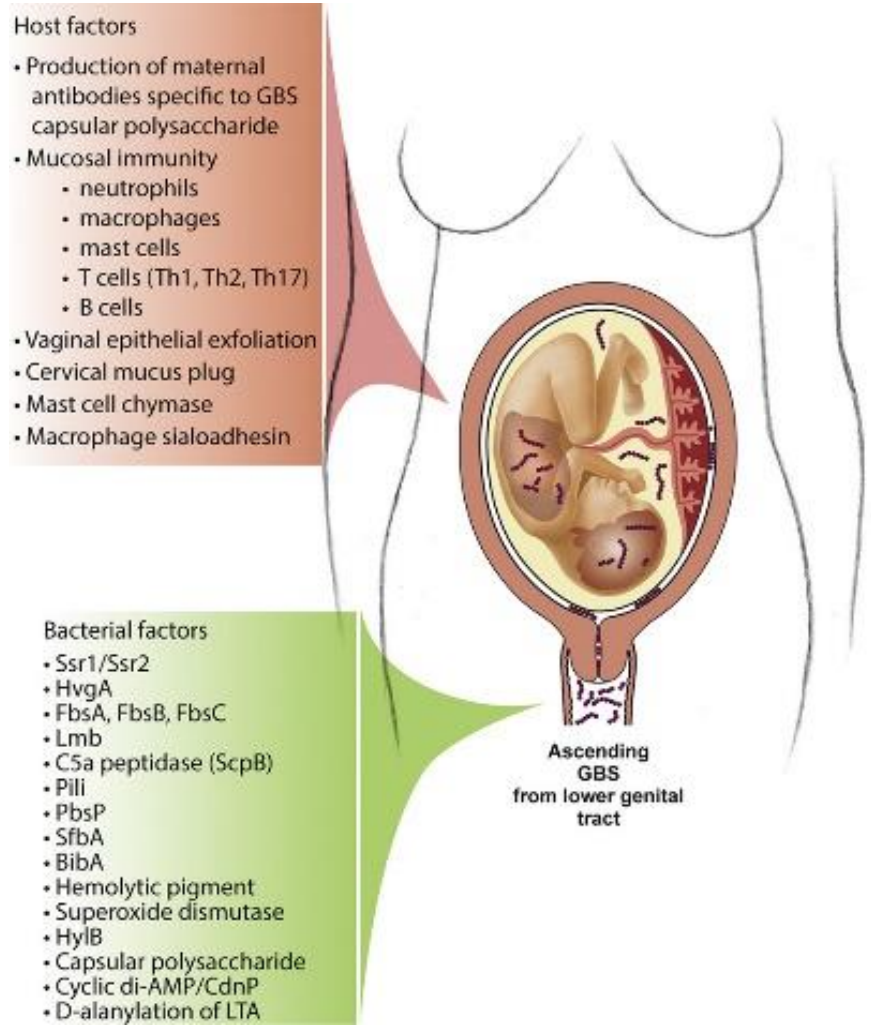


Fig. 2. Host and bacterial factors that contribute to GBS's status as either an asymptomatic colonizer or an invasive pathogen. GBS typically colonizes the gastrointestinal/vaginal tract asymptomatically but is highly pathogenic in other host compartments. The host responses to GBS are multifaceted and can promote asymptomatic colonization and clearance or alternatively permit invasive infection and disease. Many of the bacterial factors that promote colonization are also involved in dissemination and tissue damage. GBS tightly regulates the expression of these factors using signal transduction systems, which sense and respond to variations in the external environment.

- Gabbe, et al. OBSTETRICS: NORMAL AND PROBLEM PREGNANCIES, 7th Ed 2017 by Elsevier, Inc.
- Armistead, B, et al. The Double Life of Group B Streptococcus: Asymptomatic Colonizer and Potent Pathogen. Journal of Molecular Biology (2019) 431, 2914-2931

ACOG Committee Opinion - Number 782. "Prevention of Early-Onset Group B Streptococcal Disease in Newborns"

Table 1. Indications for Intrapartum Antibiotic Prophylaxis to Prevent Neonatal Group B Streptococcal Early-Onset Disease*

Intrapartum GBS Prophylaxis Indicated	Intrapartum GBS Prophylaxis Not Indicated
Maternal history	
Previous neonate with invasive GBS disease	Colonization with GBS during a previous pregnancy (unless colonization status in current pregnancy is unknown at onset of labor at term)
Current pregnancy	
Positive GBS culture obtained at 36 0/7 weeks of gestation or more during current pregnancy (unless a cesarean birth is performed before onset of labor for a woman with intact amniotic membranes)	Negative vaginal–rectal GBS culture obtained at 36 0/7 weeks of gestation or more during the current pregnancy
GBS bacteriuria during any trimester of the current pregnancy	Cesarean birth performed before onset of labor on a woman with intact amniotic membranes, regardless of GBS colonization status or gestational age
Intrapartum	
Unknown GBS status at the onset of labor (culture not done or results unknown) and any of the following: Birth at less than 37 0/7 weeks of gestation Amniotic membrane rupture 18 hours or more Intrapartum temperature 100.4°F (38.0°C) or higher* Intrapartum NAAT result positive for GBS Intrapartum NAAT result negative but risk factors develop (ie, less than 37 0/7 weeks of gestation, amniotic membrane rupture 18 hours or more, or maternal temperature 100.4°F (38.0°C) or higher Known GBS positive status in a previous pregnancy	Negative vaginal–rectal GBS culture obtained at 36 0/7 weeks of gestation or more during the current pregnancy, regardless of intrapartum risk factors Unknown GBS status at onset of labor, NAAT result negative and no intrapartum risk factors present (ie, less than 37 0/7 weeks of gestation, amniotic membrane rupture 18 hours or more, or maternal temperature 100.4°F (38°C) or higher

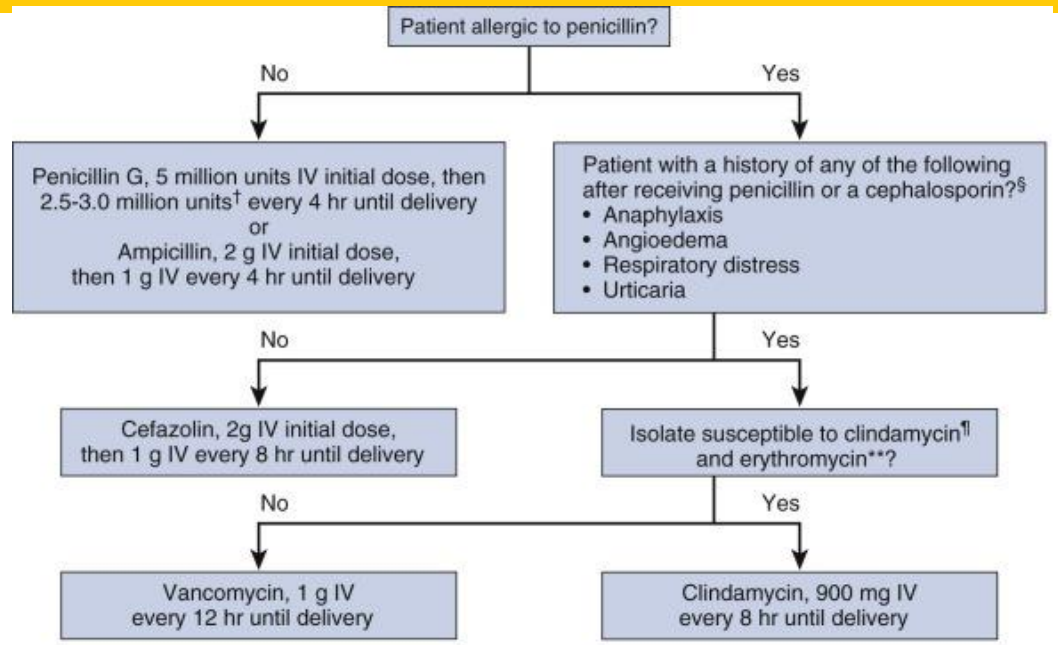
Abbreviations: GBS, group B streptococcus; NAAT, nucleic acid amplification test.

*If intraamniotic infection is suspected, broad-spectrum antibiotic therapy that includes an agent known to be active against GBS should replace GBS prophylaxis.

Modified from Verani JR, McGee L, Schrag SJ. Prevention of perinatal group B streptococcal disease: revised guidelines from CDC, 2010. Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention (CDC). MMWR Recomm Rep 2010;59(RR-10):1–36. (This Committee Opinion, including Table 1, Box 2, and Figures 1–3, updates and replaces the obstetric components of the CDC 2010 guidelines, "Prevention of Perinatal Group B Streptococcal Disease: Revised Guidelines From CDC, 2010.")

GBS Treatment

- 2010 CDC Recommendations:
  - Universal cultures in all patients as the optimal method of prevention.
    - Cultures should be performed at 35 to 37 weeks' gestation.
  - All patients who test positive should receive intrapartum antibiotic prophylaxis with one of the regimens
  - Ideally, antibiotics should be administered at least 4 hours before delivery.
    - Studies have shown that the rate of neonatal GBS infection was reduced significantly when patients were treated for at least 4 hours before delivery
    - Subsequent studies showed that mean vaginal GBS counts decreased fivefold within 2 hours of antibiotic administration, fiftyfold within 4 hours, and almost a thousand fold within 6 hours.



* Broader spectrum agents, including an agent active against GBS, might be necessary for treatment of chorioamnionitis.

† Doses ranging from 2.5 to 3.0 million units are acceptable for the doses administered every 4 hours following the initial dose. The choice of dose within that range should be guided by which formulations of penicillin G are readily available to reduce the need for pharmacies to specially prepare doses.

§ Penicillin-allergic patients with a history of anaphylaxis, angioedema, respiratory distress, or urticaria following administration of penicillin or a cephalosporin are considered to be at high risk for anaphylaxis and should not receive penicillin, ampicillin, or cefazolin for GBS intrapartum prophylaxis. For penicillin-allergic patients who do not have a history of those reactions, cefazolin is the preferred agent because pharmacologic data suggest it achieves effective intraamniotic concentrations. Vancomycin and clindamycin should be reserved for penicillin-allergic women at high risk for anaphylaxis.

¶ If laboratory facilities are adequate, clindamycin and erythromycin susceptibility testing should be performed on prenatal GBS isolates from penicillin-allergic women at high risk for anaphylaxis. If no susceptibility testing is performed, or the results are not available at the time of labor, vancomycin is the preferred agent for GBS intrapartum prophylaxis for penicillin-allergic women at high risk for anaphylaxis.

** Resistance to erythromycin is often but not always associated with clindamycin resistance. If an isolate is resistant to erythromycin, it might have inducible resistance to clindamycin, even if it appears susceptible to clindamycin. If a GBS isolate is susceptible to clindamycin, resistant to erythromycin, and testing for inducible clindamycin resistance has been performed and is negative (no inducible resistance), then clindamycin can be used for GBS intrapartum prophylaxis instead of vancomycin.

Gabbe, et al. OBSTETRICS: NORMAL AND PROBLEM PREGNANCIES, 7th Ed 2017 by Elsevier, Inc.

GBS Infection in Mom

- Several obstetric complications occur with increased frequency in pregnant women who are colonized with GBS.
  - The organism is one of the major causes of chorioamnionitis and postpartum endometritis .
  - It may cause post-cesarean delivery wound infection , usually in conjunction with other aerobic and anaerobic bacilli and staphylococci.
  - The organism also is responsible for approximately 2% to 3% of lower urinary tract infections in pregnant women.
    - GBS urinary tract infection, in turn, is a risk factor for preterm PROM and preterm labor.
  - Other investigations have confirmed the association between GBS colonization and preterm labor and preterm PROM.
    - Women with the latter complication who are colonized with GBS tend to have a shorter latent period and higher frequency of chorioamnionitis and puerperal endometritis compared with non-colonized women.

Gabbe, et al. OBSTETRICS: NORMAL AND PROBLEM PREGNANCIES, 7th Ed 2017 by Elsevier, Inc.

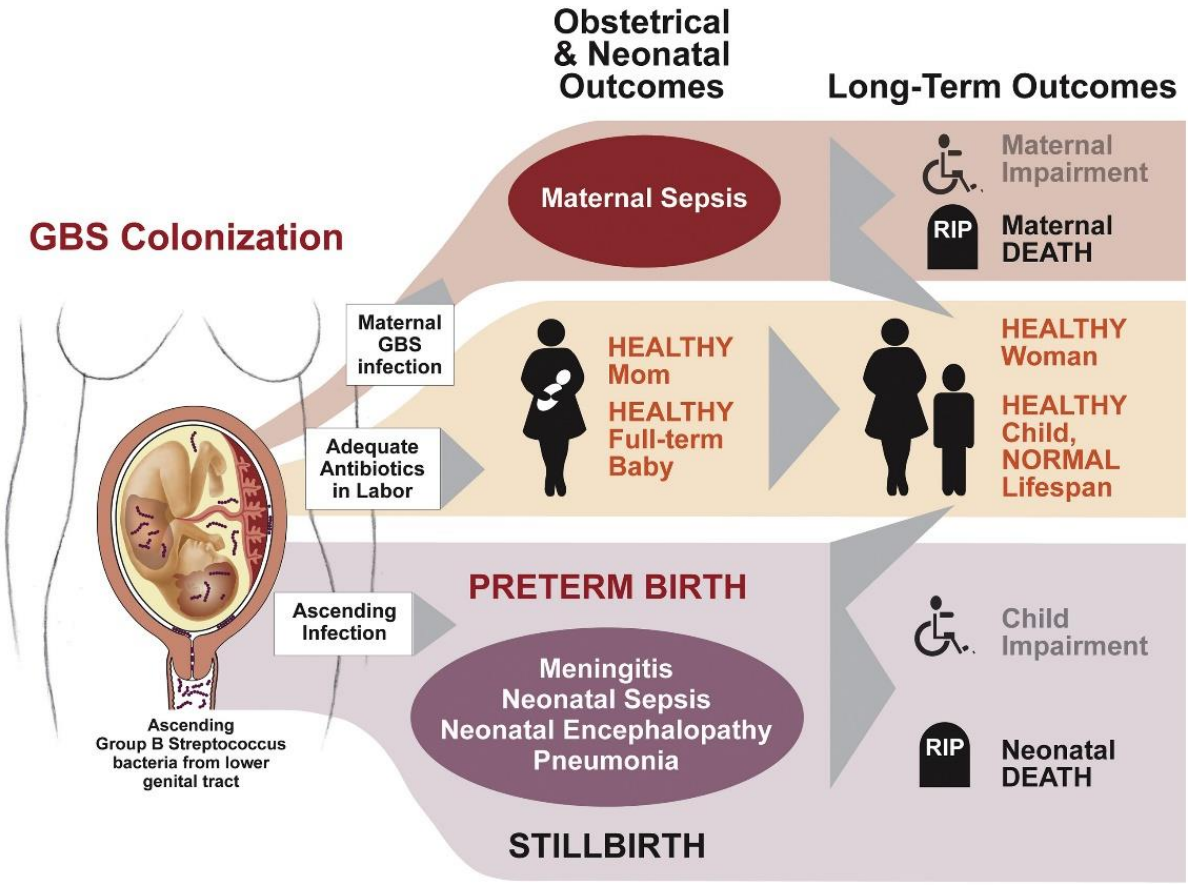


Fig. 1. Clinical pathways in maternal GBS colonization. GBS is associated with several perinatal outcomes. In the case of adequate prophylaxis, most mothers and babies are healthy with normal life span. Virulent ascending GBS is associated with significant morbidity and mortality, some of which is not preventable with intrapartum prophylaxis. With adequate treatment of ascending infection, normal and healthy outcomes may be achieved. Figure adapted from Lawn et al.

Image from: Armistead, B, et al. The Double Life of Group B Streptococcus: Asymptomatic Colonizer and Potent Pathogen. Journal of Molecular Biology (2019) 431, 2914-2931

Diagnosis of GBS

- The gold standard for the diagnosis of GBS infection is bacteriologic culture.
- Specimens for culture should be obtained from the lower vagina, perineum, and perianal area using a simple cotton swab.
- These authors noted that, although the rapid diagnostic tests had reasonable sensitivity in identifying heavily colonized patients, they had poor sensitivity in identifying lightly and moderately colonized patients.

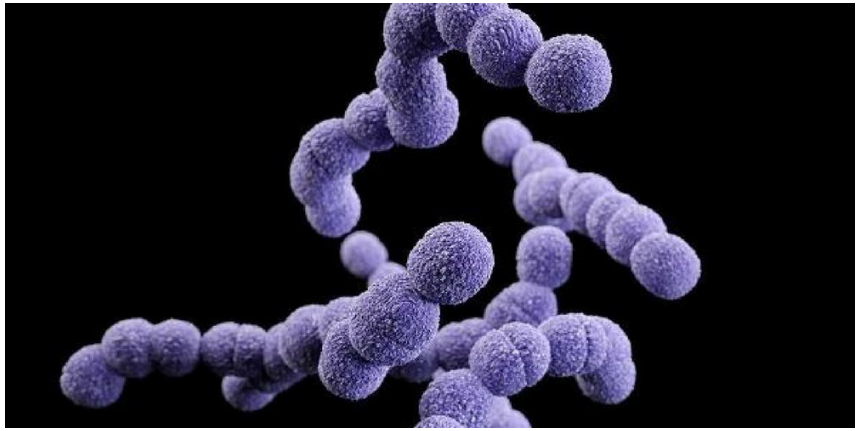


Image from: https://gbss.org.uk/info-support/group-b-strep-infection/gbs-infection-in-adults/

Neonatal Group B Streptococcal Infection

- Group B Strep remains the most common cause of neonatal early-onset sepsis and a significant cause of late-onset sepsis. GBS early-onset disease is defined as isolation of group B Streptococcus organisms from blood, cerebrospinal fluid, or another normally sterile site from birth through 6 days of age. Majority of infants become symptomatic by 12 to 24 hours of age.
- The most common pathogenesis of GBS early-onset sepsis is that of ascending colonization of the uterine compartment with group B streptococci that are present in the maternal gastrointestinal and genitourinary flora. Infection occurs with subsequent colonization and invasive infection of the fetus and/or fetal aspiration of infected amniotic fluid. The pathogenesis primarily occurs during labor for term infants, but timing is less certain among preterm infants. Intraamniotic infection may be the cause of PROM and/or preterm labor

https://pediatrics.aappublications.org/content/144/2/e20191881

Late Onset Group B Streptococcus

- Late onset Group B Streptococcus is defined as isolation of group B strep from a normally sterile site from 7 to 89 days of age. There is no epidemiological evidence to suggest a protective effect of GBS intrapartum antibiotic prophylaxis for the prevention of late onset group B streptococcus. Evaluation for late onset GBS disease should be based on clinical signs of illness in the infant. Diagnosis is based on the isolation of group B streptococci from blood, CSF, or other normally sterile sites. Late onset GBS disease occurs among infants born to mothers who had positive GBS screen results as well as those who had negative screen results during pregnancy. Again, adequate intrapartum antibiotic prophylaxis does not protect infants from the late onset group B step disease.

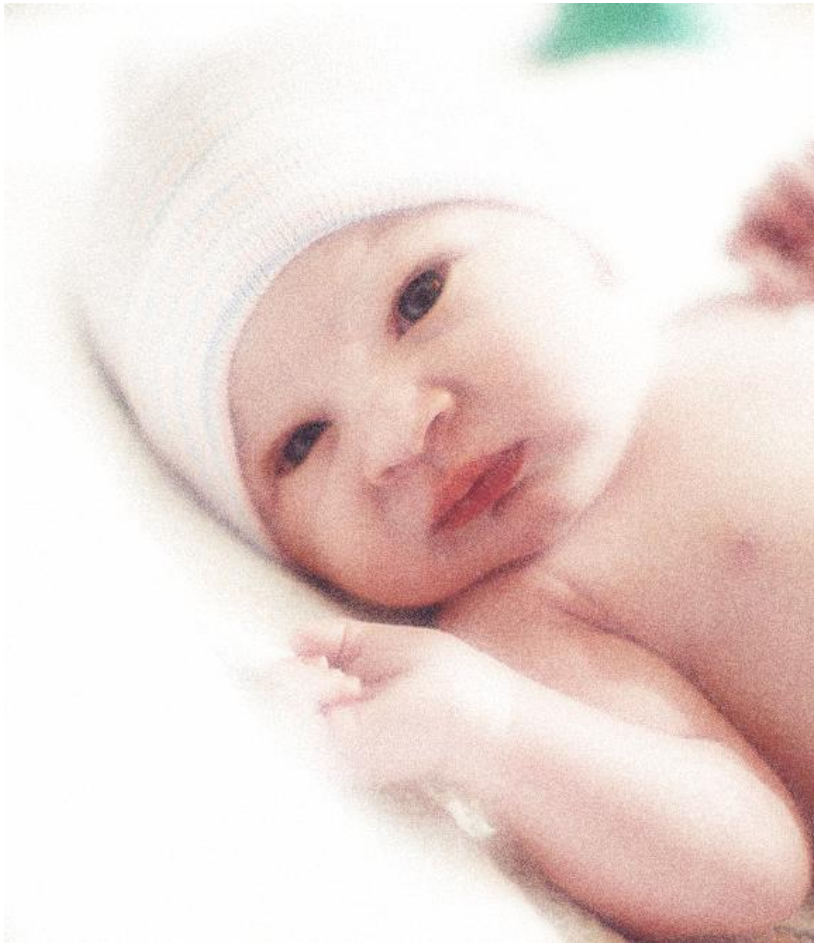
https://pediatrics.aappublications.org/content/144/2/e20191881

Neonatal Group B Streptococcal Infection Management

- Next we will discuss the current AAP clinical reports on management of neonates with suspected or proven early-onset bacterial sepsis:
- There are 3 Current Approaches to Risk Assessment Among Infants Born at ≥35 Weeks Gestation:
- For further information refer to:
  - https://pediatrics.aappublications.org/content/144/2/e20191881

Early Onset Sepsis Calculator

Early Onset Sepsis (EOS):
The new approach in the Newborn Setting for Neonates ≥35 Weeks Gestation



Early Onset Sepsis

- Defined as a blood or CSF culture obtained within 72 hours after birth growing a pathogenic bacterial species
- EOS is a serious and potentially fatal complication of birth
- Assessing term and late preterm infant at risk is one of the most common clinical tasks by providers
- Concern's for providers
  - Well-appearing infant's with identified risk factors for EOS, fear of missing opportunity to intervene before infants become critically ill
  - Steps they are thinking about
    - Assess the newborn infant at risk for EOS
    - Determine what to do? Start empirical, broad-spectrum antibiotics
    - Once the antibiotics are started, when should they be discontinued?
- These are important decisions made daily by doctors caring for neonates

Current Incidence and Mortality of EOS

- Before recommended intrapartum antibiotic prophylaxis to prevent GBS disease, the overall incidence of EOS in the US
  - 3 to 4 cases per 1000 live births
- Currently Incidence of early onset sepsis:
  - 0.5/1000 live births (Term infants)
  - 1/1000 live births (Late-Preterm infants)
- Morbidity from EOS
  - 60% of term infants with EOS require NICU for respiratory distress and/or blood pressure support
- Mortality from EOS
  - 2% to 3% infants with EOS born ≥35 weeks

https://pediatrics.aappublications.org/content/142/6/e20182894

Most Recent EOS Guidelines for Neonates

Pediatrics
December 2018, VOLUME 142 / ISSUE 6
From the American Academy of Pediatrics
Clinical Report

Management of Neonates Born at ≥35 0/7 Weeks' Gestation With Suspected or Proven Early-Onset Bacterial Sepsis

Karen M. Puopolo, William E. Benitz, Theoklis E. Zaoutis, COMMITTEE ON FETUS AND NEWBORN, COMMITTEE ON INFECTIOUS DISEASES

- Incidence of neonatal EOS has declined over the last 20 years
  - Implementation of intrapartum antimicrobial therapy
- Laboratory tests alone are neither sensitive nor specific enough to guide EOS management decisions
- Three approaches exist for the use of risk factors to identify infants who are at increased risk of EOS
  - Categorical Risk Factor
  - Multivariate Risk Assessment
  - Risk Assessment Primarily Based on Newborn Clinical Condition

Three Approaches for Identification of Early Onset Sepsis

Categorical Risk Factor Assessment

- Algorithms for management of GBS-specific EOS are used as a general framework for the prevention of all EOS
  - Different versions published since 1996
- Advantage:
  - Larges amounts of data have been reported that are used to address the effects on GBS-specific disease and on the frequency of neonatal EOS evaluation
- Limitations:
  - Lack of clear definitions for newborn clinical illness
  - Difficulties in establishing the clinical diagnosis of maternal chorioamnionitis
  - Inconsistent consideration of intrapartum antibiotics
  - Absence of guidance on what is used to define abnormal lab test results in the newborn period

Multivariate Risk Assessment

- Individualized synthesis of established risk factors and the newborn clinical condition to estimate each infant's risk of EOS ("EOS Calculator")
- Based on a cohort of 608,000 newborn infants which were used to develop predictive models for culture-confirmed EOS based on objective data that are known at the moment of birth and the evolving newborn condition during the first 6-12 hours after birth
- Objective Data:
  - Gestational age
  - Highest maternal intrapartum temperature
  - Maternal GBS colonization status
  - Duration of ROM
  - Type and duration of intrapartum antibiotic therapies
- Advantages:
  - Used to provide differential information on an individual infant's risk rather than place infants in categories with a wide range of risk
  - Includes only objective data (not maternal chorioamnionitis)
  - Results in relatively few well –appearing newborn infants being treated empirically with antibiotic agents
- Concerns:
  - Requires increased clinical surveillance for some infants in the NBN
  - Classification of infants (ill, equivocal or well appearing) requires ongoing clinical assessment over the first 12 hours after birth

Risk Assessment Primarily Based on Newborn Clinical Condition

- Relies on clinical signs of illness to identify infants with EOS
- Infants who appear ill at birth or those who develop signs of illness over the first 48 hours after birth
  - Further evaluated by lab screening or
  - Treated with empiric antimicrobials
- Infants born to mom with Triple I (Chorioamnionitis) are flagged but evaluation primarily relies on clinical observation alone for well-appearing term and late-preterm infants
- Advantage:
  - Significant reduction in the rate of antibiotic use
- Disadvantages:
  - Can require significant changes to newborn care
    - Establishment of processes to ensure universal serial, structured, documented examinations
    - Development of clear criteria for additional evaluation and empirical antibiotic administration
  - Families must understand that the identification of initially well-appearing infants who develop illness is not a failure of care

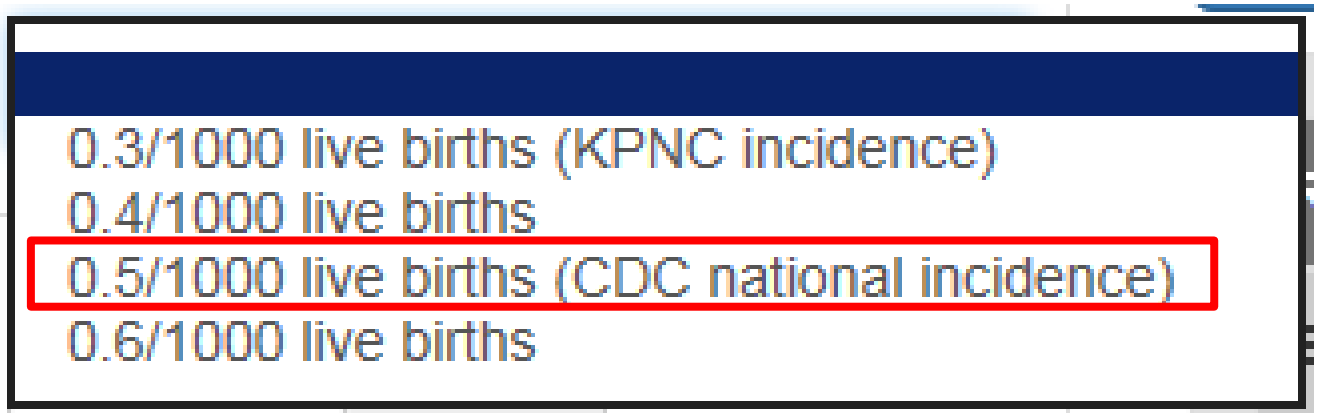
Puopolo, Pediatrics, 2018, https://pediatrics.aappublications.org/content/142/6/e20182894

Using the Kaiser Permanente EOS Calculator for >= 35 Weeks

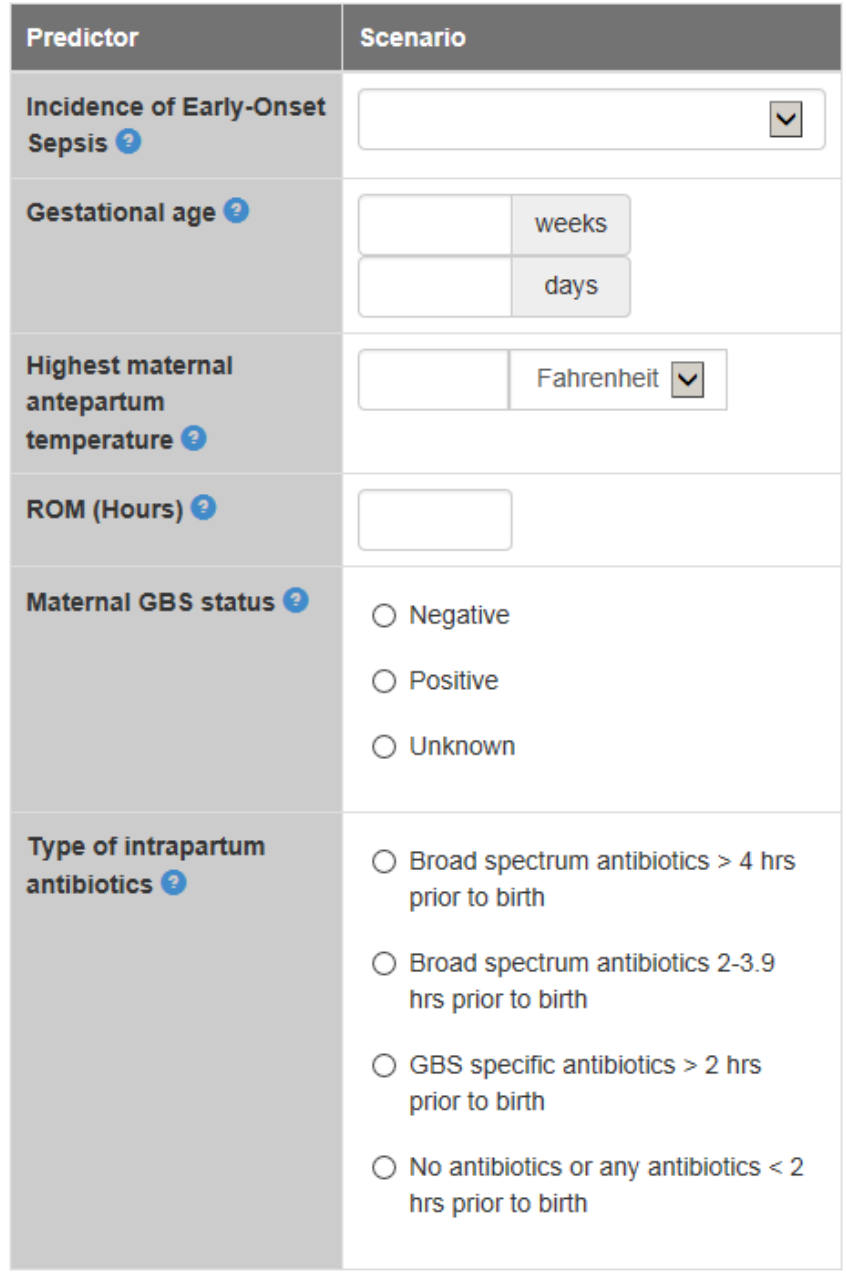
- Estimating the probability of neonatal early-onset infection on the basis of maternal risk factors
- Two Parts to the Calculator:
  - Clinical Presentation of the neonate who is >= 35 Weeks Gestation
  - Sepsis Risk at birth estimated from maternal risk factors
    - Highest antepartum temperature
    - Gestational age
    - Duration of ruptured membranes
    - Duration of intrapartum antibiotics
    - Maternal GBS status
  - https://neonatalsepsiscalculator.kaiserpermanente.org/

How do you use the calculator?

- When selecting the "incidence of early-onset sepsis" always choose the CDC national incidence or 0.5/1000 live births



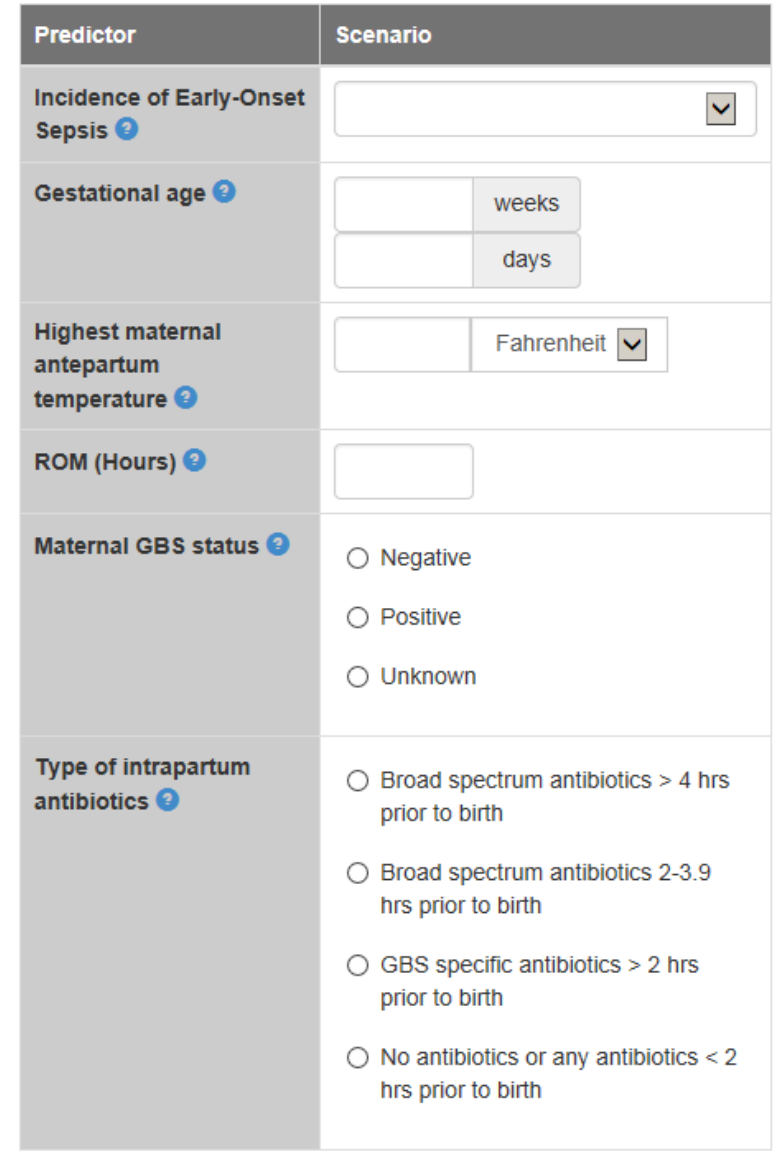
The calculator can be found:
https://neonatalsepsiscalculator.kaiserpermanente.org/



How do you use the calculator?

- Enter the exact gestational age at delivery
- Enter the highest maternal antepartum temperature obtained prior to delivery
- Enter the number of hours of ruptured membranes
- Enter the maternal GBS status
- Enter the type of intrapartum antibiotics used, if any, and the appropriate time frame
  - Broad spectrum antibiotics= gentamicin, cefoxitin, metronidazole, piperacillin/tazobactam
  - GBS specific antibiotics= penicillin G, cefazolin, ampicillin, vancomycin, clindamycin
  - **if both classes of abx are administered, utilize the timing of the broad spectrum

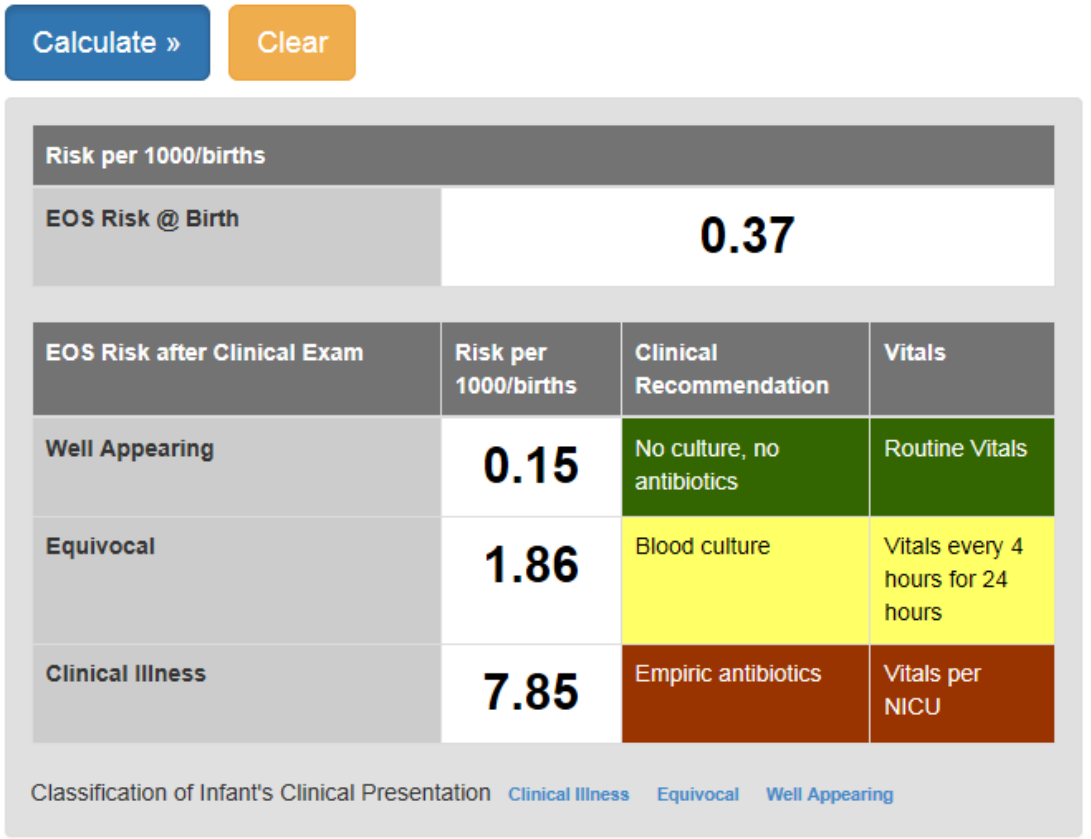
- This completes part 1 of the calculator



The calculator can be found: https://neonatalsepsiscalculator.kaiserpermanente.org/

How do you use the calculator?

- After entering all of the data in part 1, click on the blue calculate button
- The EOS risk @ birth will automatically populate in the top box
- Determine the EOS Risk after Clinical Exam using the classification chart hyperlinked under the table



The calculator can be found: https://neonatalsepsiscalculator.kaiserpermanente.org/

Classification of Clinical Signs

TABLE 1 Hierarchical Classification of Clinical Signs[a]

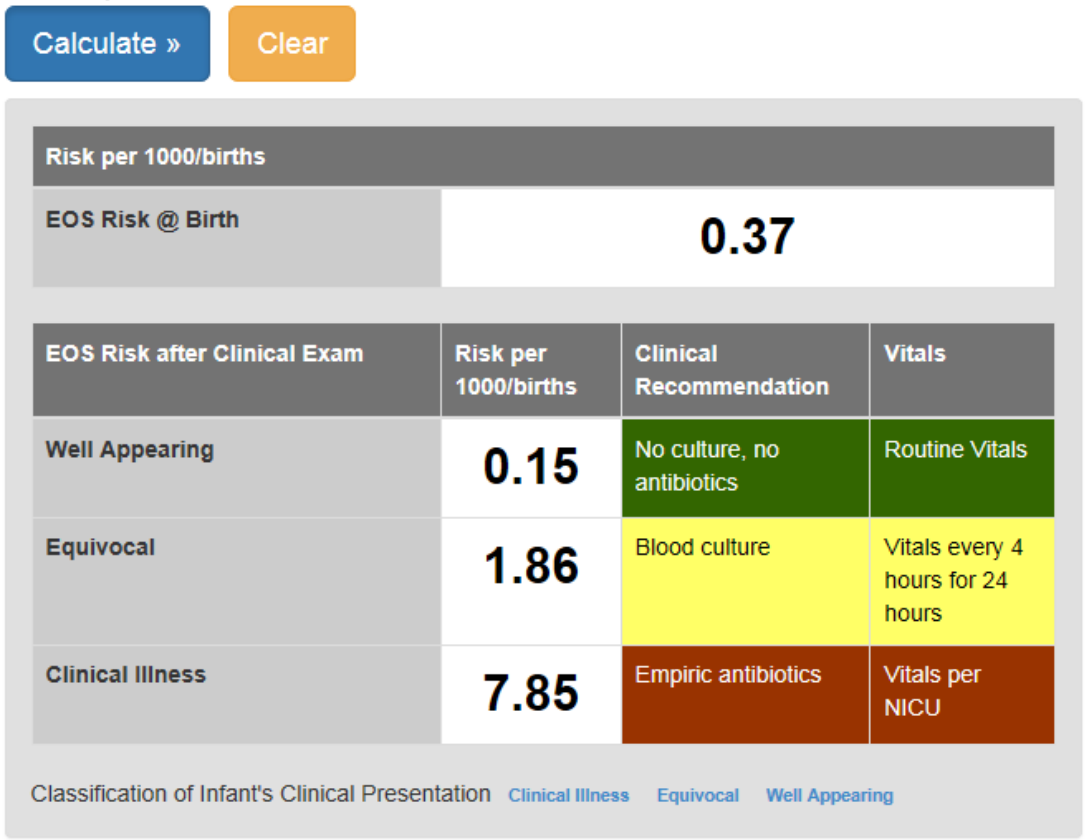
Clinical Presentation[b]	Description
Clinical illness	In the first 12 h of age, the infant had a 5-min Apgar <5; received nasal continuous positive airway pressure or mechanical ventilation; received continuous infusion of vasoactive drugs; had a clinical seizure; or had significant respiratory distress (nasal flaring, grunting, or retractions were present and the infant received supplemental oxygen within the first 6 h)
Equivocal presentation	In the first 12 h of age, the infant experienced at least 2 instances of 1 of the following, with "instance"[c] meaning that there were ≥2 measurements ≥2 h apart: Heart rate ≥160 Respiratory rate ≥60 Temperature ≥100.4°F or <97.5°F Respiratory distress (grunting, flaring, or retracting)
Well appearing	The infant did not fall into one of the above 2 groups in the first 12 h of age

- Some newborns will demonstrate physiologic abnormalities while transitioning to extra uterine life
- It is important to observe for intermittent and persistent trends after the 2 hour window

Escobar. Pediatrics, 2014

How do you use the calculator?

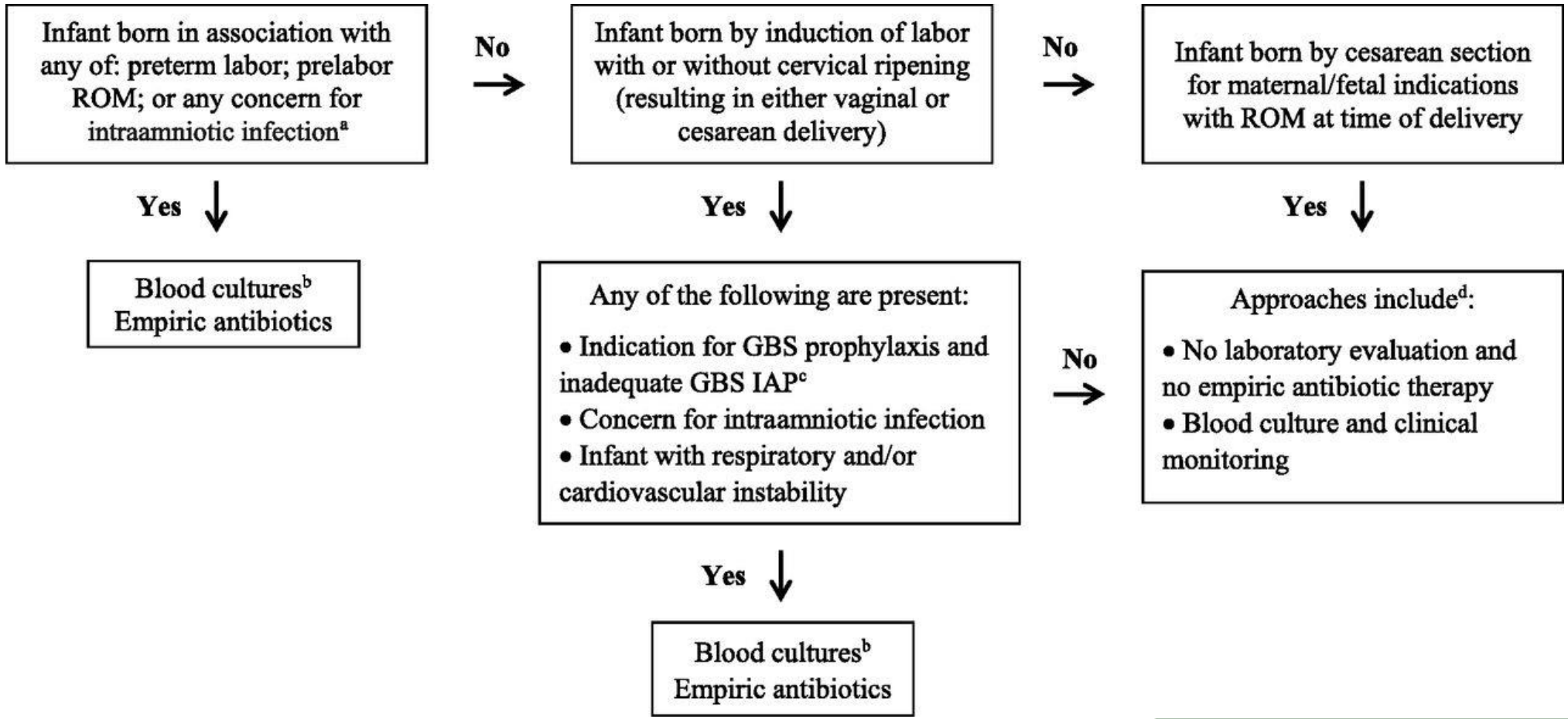
- After the clinical exam is completed on or around 2 hours of life and the newborn is determined to be well appearing, equivocal, or clinically ill, review the clinical recommendations that correspond with the exam
- These recommendations will be used to determine the newborn's plan of care
- Risk scores of <1 will receive no blood culture or no antibiotics
- Risk scores of 1.0-2.9 will have the blood culture drawn on the appropriate unit and then may be observed with q4hr vitals in the level I nursery, per the recommendations
- Newborns with risk scores of >= 3.0 should be transferred to a higher level of care, i.e. SCN or NICU, per the recommendations
- As you perform your scheduled assessments and VS the classification may change based on the clinical exam, but the EOS Risk score will remain the same



Management of Neonates Born ≤34 6/7 Weeks Gestation With Suspected of Proven Early Onset Bacterial Sepsis

- In evaluating the risk for GBS infection in newborns, separate consideration should be given to infants born at 35 0/7 weeks or older gestation and those born at 34 6/7 weeks or younger gestation. Infants born at or less than 34 6/7 weeks gestation are at highest risk for early onset infection from all causes, including Group B Streptococci
- Infants born at ≤34 6/7 weeks gestation can be categorized by level of risk for EOS by the circumstances of their preterm birth.
- The next slide will explain the level of risk for EOS and management by the circumstances of their preterm birth

EOS risk assessment among infants born ≤34 weeks' gestation. a Intraamniotic infection should be considered when a pregnant woman presents with unexplained decreased fetal movement and/or there is sudden and unexplained poor fetal testing. b Lumbar puncture...



Karen M. Puopolo et al. Pediatrics 2019;144:e20191881

PEDIATRICS®

Management of Neonates Born at ≤34 6/7 Weeks Gestation With Suspected of Proven Early Onset Bacterial Sepsis

- The diagnosis of EOS is made by blood or CSF culture. EOS cannot be diagnosed by laboratory tests alone, such as CBC or CRP
- The combination of ampicillin and gentamicin is the most appropriate empirical antibiotic regimen for infants at risk for EOS. Empirical administration of additional broad-spectrum antibiotics may be indicated in preterm infants who are severely ill and at a high risk for EOS

Maternal Bacterial Infection: Bacterial Vaginosis (BV)

- From the CDC:
  - Bacterial vaginosis is a condition that happens when there is too much of certain bacteria in the vagina. This changes the normal balance of bacteria in the vagina.
  - Researchers do not know the cause of BV or how some women get it. We do know that the infection typically occurs in sexually active women.
  - BV is linked to an imbalance of "good" and "harmful" bacteria that are normally found in a woman's vagina.
  - Having a new sex partner or multiple sex partners, as well as douching, can upset the balance of bacteria in the vagina. This places a woman at increased risk for getting BV.
  - Unsure how sex contributes to BV. There is no research to show that treating a sex partner affects whether or not a woman gets BV. Having BV can increase your chances of getting other STDs.
    - BV rarely affects women who have never had sex.

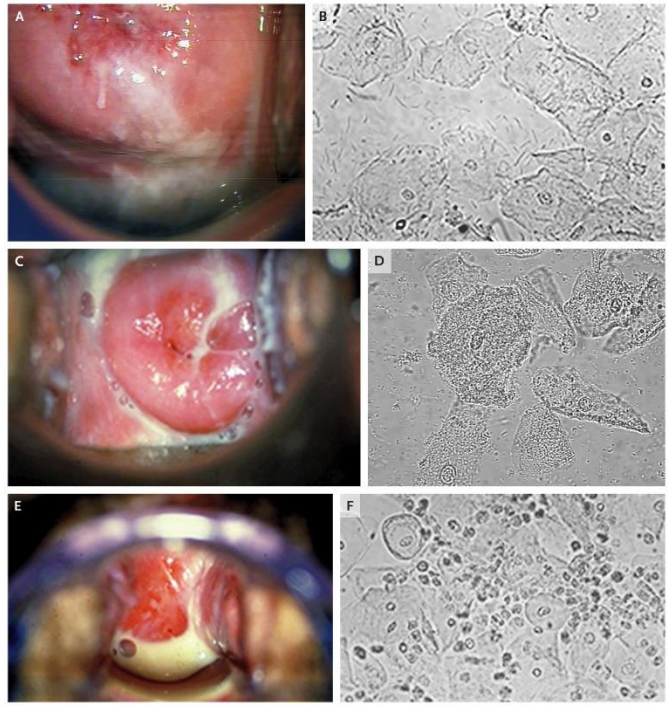


Figure 1. Features of Healthy Vaginal Flora, Bacterial Vaginosis, and Desquamative Inflammatory Vaginitis. Panel A shows healthy cervicovaginal mucosa and a small amount of vaginal discharge, findings that are consistent with a predominance of lactobacilli. Physiological cervical ectopy and clear cervical mucus are evident. In Panel B, microscopic examination of a wet-mount preparation shows rodlike bacteria, which are consistent with lactobacilli. No leukocytes are present. Panels C and D show the features of bacterial vaginosis: heavy, milky, homogeneous vaginal discharge with bubbles (Panel C), which are consistent with gaseous by-products of anaerobic bacteria, and vaginal epithelial cells covered by coccobacilli on microscopic examination (Panel D), a feature of clue cells. No leukocytes are present. Panels E and F show the features of desquamative inflammatory vaginitis: heavy, yellowish vaginal discharge and inflamed cervicovaginal mucosa (Panel E), with microscopic examination showing a high number of leukocytes (with a predominance of mononuclear leukocytes) and round parabasal cells (Panel F), findings that are consistent with inflammation.

https://www.cdc.gov/std/bv/stdfact-bacterial-vaginosis.htm
Image: J Paavonen, RC Brunham. N Engl J Med 2018;379:2246-2254.

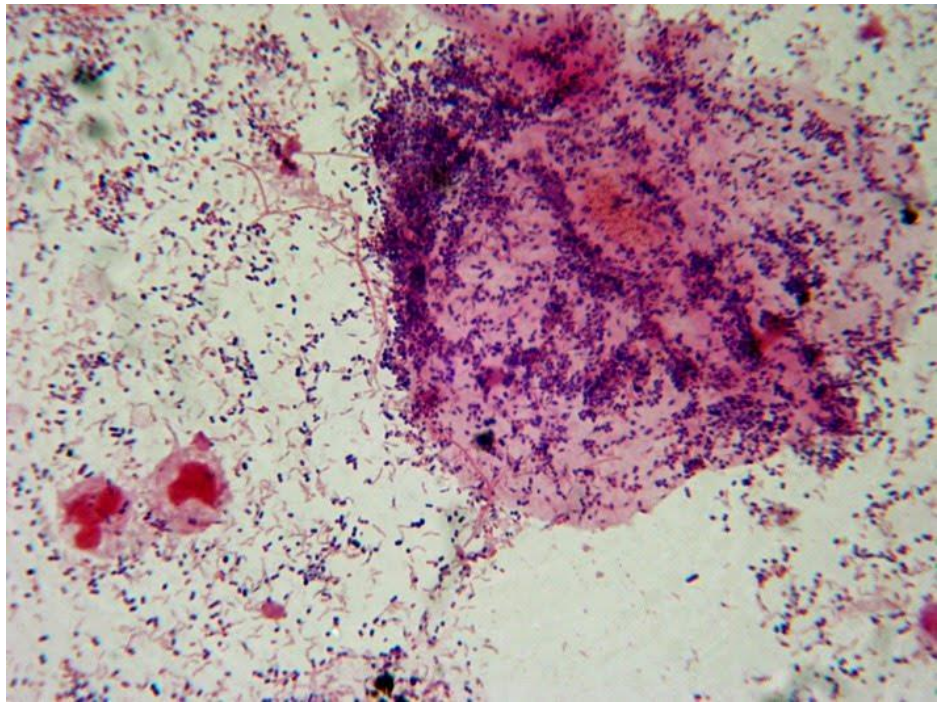
BV Notes from ACOG:

- Bacterial vaginosis is not a true infectious or inflammatory state.
- It represents a change in the normal microbiome of the vagina with an overgrowth of facultative anaerobic organisms
  - EX: G vaginalis, Bacteroides species, Peptostreptococcus species, Fusobacterium species, Prevotella species, and Atopobium vaginae) and a lack of hydrogen peroxide-producing lactobacilli.
- Bacterial vaginosis is the most common cause of abnormal vaginal discharge in patients of reproductive age
- has a higher prevalence in black, Hispanic, and Mexican American women compared with white non-Hispanic women
- In addition to race and ethnicity, age, douching, and sexual activity are associated with increased risk of bacterial vaginosis
- Although the occurrence of bacterial vaginosis is associated with sexual activity for both heterosexual and lesbian couples, and rarely occurs in patients who have never been sexually active, it is not directly caused by the sexual transmission of a single pathogen.
- Many patients with bacterial vaginosis are asymptomatic.
  - However, those who do have symptoms commonly report having an abnormal vaginal discharge and a fishy odor, particularly after vaginal intercourse and menses.

ACOG Practice Bulletin #215: Vaginitis in Nonpregnant Patients January 2020

Diagnosis:

- Clinical criteria
  - Amsel's Diagnostic Criteria
  - Gram stain
    - considered the gold standard laboratory method for diagnosing BV
    - determines the relative concentration of lactobacilli, Gram-negative and Gram-variable rods and cocci, and curved Gram-negative rods characteristic of BV.
  - Clinical criteria require three of the following symptoms or signs:
    - homogeneous, thin, white discharge that smoothly coats the vaginal walls;
    - clue cells (e.g., vaginal epithelial cells studded with adherent coccobacilli) on microscopic examination
    - pH of vaginal fluid >4.5
    - a fishy odor of vaginal discharge before or after addition of 10% KOH (i.e., the whiff test).



Treatment for BV in Pregnant Women

- All women with symptomatic BV should be treated to relieve bothersome symptoms. Oral treatment is effective and has not been associated with adverse fetal or obstetric effects .
  - Metronidazole 500 mg orally twice daily for seven days
  - Metronidazole 250 mg orally three times daily for seven days
  - Clindamycin 300 mg orally twice daily for seven days
  - As topical therapy is not inferior to oral therapy in effecting cure or preventing adverse pregnancy outcomes such as preterm birth, the CDC recommends either oral or topical therapy for treatment of symptomatic pregnant women.
    - The regimens are the same as for nonpregnant women. However, the author and other experts prefer oral therapy in pregnant women because some data indicate oral treatment is more effective against potential subclinical upper genital tract infection.
- Despite the association between BV and adverse outcome, screening and treatment of asymptomatic BV during pregnancy is controversial. Meta-analyses of randomized trials performed in general obstetric populations have generally found that treatment of asymptomatic infection does not reduce the incidence of preterm labor or delivery in the overall obstetric population

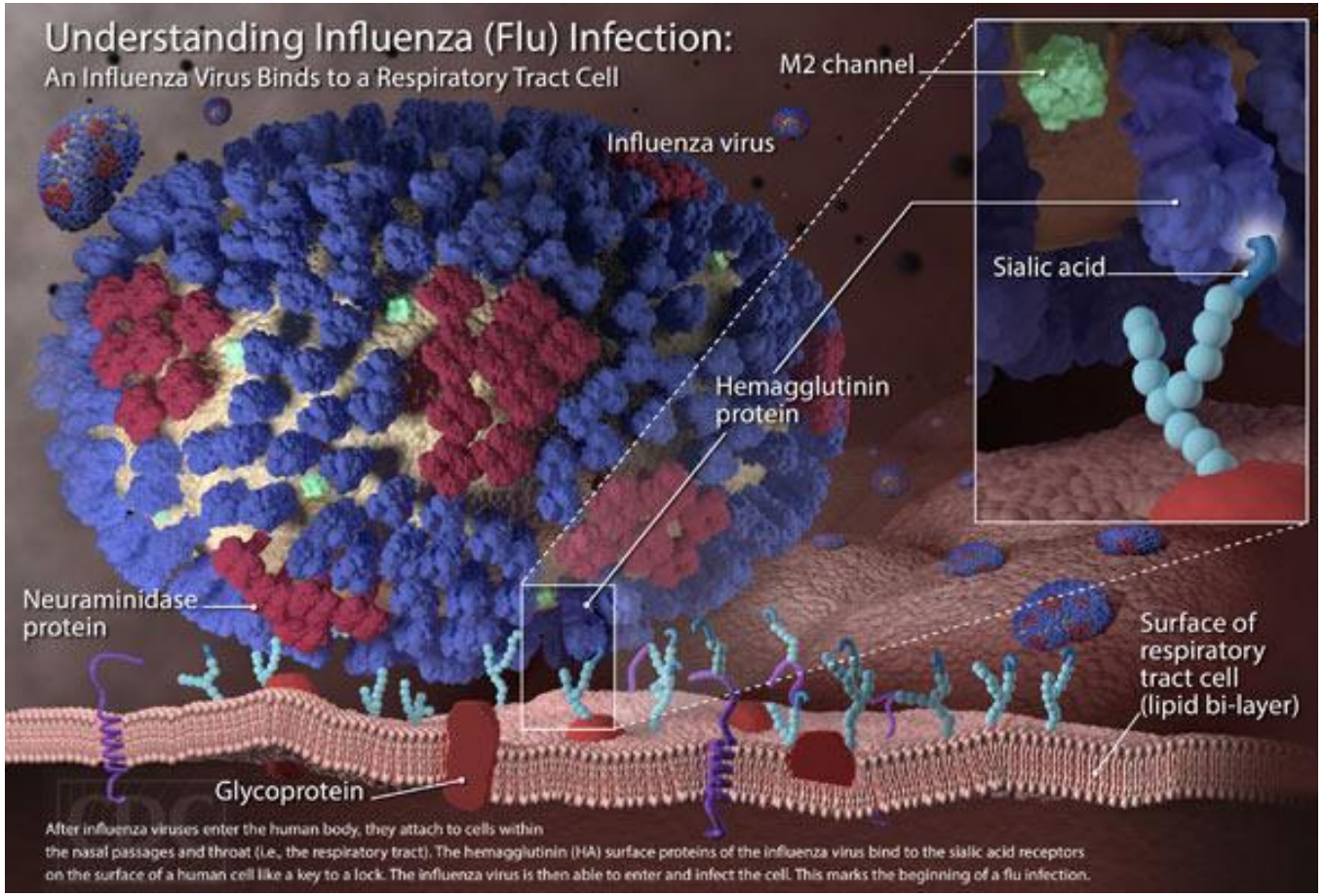
https://www.uptodate.com/contents/bacterial-vaginosis-treatment?search=bacterial%20vaginosis%20in%20pregnancy&source=search_result&selectedTitle=1~108&usage_type=default&display_rank=1

Viral

- We will focus on Influenza in this Section.

Influenza

- Influenza occurs in distinct outbreaks of varying extent every year. This epidemiologic pattern reflects the changing nature of the antigenic properties of influenza viruses, and their subsequent spread depends upon multiple factors, including transmissibility of the virus and the susceptibility of the population.
- Seasonal influenza is an acute respiratory illness caused by influenza A or B viruses



https://www.cdc.gov/flu/images/influenza-virus-fulltext.jpg

https://www.uptodate.com/contents/treatment-of-seasonal-influenza-in-adults?search=influenza&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1

Flu – PREVENTION

https://www.cdc.gov/flu/highrisk/pregnant.htm

- A Flu Vaccine is the Best Protection Against Flu
  - Getting an influenza flu vaccine is the first and most important step in protecting against flu.
  - Pregnant women should get a flu shot and not the nasal spray flu vaccine.
  - Flu shots given during pregnancy help protect both the mother and her baby from flu.
  - Vaccination has been shown to reduce the risk of flu-associated acute respiratory infection in pregnant women by about one-half.
    - A 2018 studyexternal icon showed that getting a flu shot reduced a pregnant woman's risk of being hospitalized with flu by an average of 40 percent.
  - Pregnant women who get a flu vaccine are also helping to protect their babies from flu illness for the first several months after their birth, when they are too young to get vaccinated.

Influenza: American College of Obstetricians and Gynecologists recommendations:

- The Centers for Disease Control and Prevention's (CDC) Advisory Committee on Immunization Practices and ACOG recommend that all adults receive an annual influenza vaccine and that women who are or will be pregnant during influenza (flu) season receive an inactivated influenza vaccine as soon as it is available. Any of the licensed, recommended, age-appropriate, inactivated influenza vaccines can be given safely during any trimester.
- Maternal influenza immunization is an essential component of prenatal care for women and their newborns. Obstetrician–gynecologists and other health care providers should counsel pregnant women about the safety and benefits of influenza immunization for themselves and their fetuses and advocate for the benefits of passive immunity from maternal immunization for their newborns.
- Obstetrician–gynecologists are encouraged to stock and administer the influenza vaccine to their pregnant patients in their offices, and should get the influenza vaccine themselves every season.
- If the influenza vaccine cannot be offered in a practice, obstetrician–gynecologists and obstetric care providers should refer patients to another health care provider, pharmacy, or community vaccination center.
- Obstetrician–gynecologists should strongly encourage their office staff to be vaccinated against influenza every season.

Influenza: American College of Obstetricians and Gynecologists recommendations Continued:

- Individuals with a history of egg allergy who have experienced only hives after exposure to egg can receive any licensed and recommended influenza vaccine that is otherwise appropriate for their age and health status.
- In the case of allergic symptoms more serious than hives, the vaccine should be administered in an inpatient or outpatient medical setting (including, but not necessarily limited to hospitals, clinics, health departments, and physician offices).
- Patients with flu-like illness should be treated with antiviral medications presumptively regardless of vaccination status. Health care providers should not rely on test results to initiate treatment and should treat patients presumptively based on clinical evaluation.
- Because of the high potential for morbidity, the CDC and ACOG recommend that postexposure antiviral chemoprophylaxis (75 mg of oseltamivir once daily for 10 days) be considered for pregnant women and women who are up to 2 weeks postpartum (including pregnancy loss) who have had close contact with someone likely to have been infected with influenza. If oseltamivir is unavailable, zanamiver can be substituted, two inhalations once daily for 10 days.

The American College of Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

Society for Maternal-Fetal Medicine
High-risk pregnancy experts

Assessment and Treatment for Pregnant Women With Suspected or Confirmed Influenza

Pregnant women are at high risk of serious complications of influenza (flu) infection such as intensive care unit admission, preterm delivery, and maternal death. Patients with suspected or confirmed influenza should be treated with antiviral medications presumptively regardless of vaccination status. Do not rely on test results to initiate treatment; treat presumptively based on clinical evaluation. The following algorithm is designed to aid practitioners in promptly assessing and treating suspected or confirmed influenza in pregnant women, and can be used for telephone triage.

Assess Patient's Symptoms

Influenza symptoms typically include fever ≥37.8°C (100.0°F) and one or more of the following:

- Cough
- Runny nose
- Fatigue
- Sore throat
- Headaches or body aches
- Difficulty breathing or shortness of breath

If a patient does not report fever but has abrupt onset of symptoms suggestive of influenza, proceed with the algorithm.

No → Routine Prenatal Care

Yes ↓

Conduct Illness Severity Assessment

- Does she have difficulty breathing or shortness of breath?
- Does she have new pain or pressure in the chest other than pain with coughing?
- Is she unable to keep liquids down?
- Does she show signs of dehydration such as dizziness when standing?
- Is she less responsive than normal or does she become confused when talking to her?
- Did she have influenza symptoms that improved but then returned or got worse?

Any Positive Answers → **Elevated Risk**
Recommend she immediately seek care in an emergency department or equivalent unit that treats pregnant women. When possible, send patient to a setting where she can be isolated. Consider admitting patient to critical care unit. Antiviral treatment should follow CDC guidelines.*†‡

No Positive Answers ↓

Assess Clinical and Social Risks

- Comorbidities (eg, HIV or asthma)
- Obstetric issues (eg, preterm labor)
- Inability to care for self or arrange follow-up if necessary

Any Positive Answers → **Moderate Risk**
See patient as soon as possible in an ambulatory setting with resources to determine severity of illness. When possible, send patient to a setting where she can be isolated. Clinical assessment for respiratory compromise includes physical examination and tests such as pulse oximetry, chest X-ray, or ABG as clinically indicated. Antiviral treatment should follow CDC guidelines.*†‡

No Positive Answers ↓

Low Risk
Begin antiviral treatment over the phone or in person following CDC guidelines.*†‡ Treatment via phone is acceptable to help reduce the spread of disease among other pregnant patients in the office. Plan for follow-up within 24–48 hours.

If no respiratory compromise or complications and able to follow-up with care ←

If yes to respiratory compromise or complications ↓
Admit patient for further evaluation and treatment.

Abbreviations: ABG, arterial blood gases; CDC, Centers for Disease Control and Prevention; HIV, human immunodeficiency virus.

*Oseltamivir (preferred) (75-mg orally twice daily for 5 days) or Zanamivir (two 5-mg inhalations [10 mg total] twice daily for 5 days).

†Check with institution to determine requirements for testing. Do not rely on test results to initiate treatment; treat presumptively based on clinical evaluation.

‡Treatment within 48 hours of the onset of symptoms is ideal but treatment should not be withheld if the ideal window is missed.

Because of the high potential for morbidity and mortality for pregnant and postpartum patients, the CDC advises that postexposure antiviral chemoprophylaxis can be considered for pregnant women and women who are up to 2 weeks postpartum (including after pregnancy loss) who have had close contact with infectious individuals. The chemoprophylaxis recommendation is oseltamivir 75 mg once daily for 7–10 days.

Influenza Algorithm

- **Assessment of Pregnant Women With Influenza**
  - Pregnant women with suspected influenza should be assessed based on a variety of symptoms
  - It is important to note that not all people infected with influenza will develop a fever; therefore, the absence of fever should not rule out an influenza diagnosis
  - Initial triage and treatment by telephone is acceptable to help reduce the spread of disease among other pregnant patients in the office.
- Management:
  - Pregnant women with suspected or confirmed influenza infection should receive antiviral treatment with oseltamivir and acetaminophen for treatment of fever.
    - Zanamivir and peramivir are alternative approved influenza antiviral options for treatment.
    - Pregnancy is not a contraindication to these antivirals.
    - Based on previous influenza seasons, oseltamivir is the preferred treatment for pregnant women (75 mg orally twice daily for 5 days)

CDC Posters for Patient Education – Influenza vaccine and Pregnancy

https://www.cdc.gov/flu/highrisk/pregnant.htm

Results of CDC's 2016-2017 Internet panel survey of pregnant women

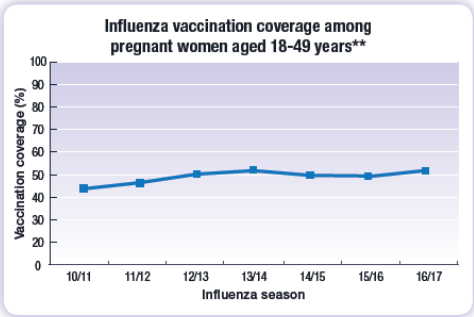
Half of pregnant women protect themselves and their babies against flu. Time to bump it up!

With only half of pregnant moms getting their flu shot, too many remain unprotected.

Flu shots help protect pregnant women and their babies from potentially serious flu illness during and after pregnancy.

During the 2016-2017 flu season, an estimated 50%* of pregnant women in the U.S. protected themselves and their babies from flu by getting a flu shot. While this is a significant improvement since the years before the 2009 pandemic, about half of pregnant women and their babies, still remain unprotected from influenza.

We can do better. All pregnant women need flu shots to protect themselves and their babies.



If you're pregnant, a flu shot:

- is recommended at any time during your pregnancy
- can reduce your risk of getting sick from flu
- can protect your baby from flu for several months after birth

Pregnant women also need a whooping cough (Tdap) shot. Talk to your doctor.

Get vaccinated to protect yourself and your baby.

www.cdc.gov/flu/protect/vaccine/pregnant.htm

NCIRDIg705 | 10/25/17

*https://www.cdc.gov/flu/fluvaxview/pregnant-women-nov2016.htm **Sources: 2007-2010 BRFSS, 2010-11-2016-17 Internet Panel Survey.

Pregnant? You Need a **Flu Shot!**

Information for pregnant women

Because you are pregnant, CDC and your ob-gyn or midwife recommend you get a flu shot to protect yourself and your baby from flu.

You should get vaccinated by the end of October, if possible. This timing can help ensure that you are protected before flu activity begins to increase. Talk to your ob-gyn or midwife about getting a flu shot.

The flu is a serious illness, especially when you are pregnant.

Getting the flu can cause serious problems when you are pregnant. Even if you are generally healthy, changes in immune, heart, and lung functions during pregnancy make you more likely to get severely ill from flu. Pregnant women who get flu are at high risk of developing serious illness, including being hospitalized.

Flu shots are the best available protection for you – and your baby.

When you get your flu shot, your body starts to make antibodies that help protect you against the flu. Antibodies also can be passed on to your developing baby, and help protect them for several months after birth. This is important because babies younger than 6 months of age are too young to get a flu vaccine. If you breastfeed your infant, antibodies also can be passed through breast milk. It takes about two weeks for your body to make antibodies after getting a flu vaccine. Talk to your doctor, nurse, or clinic about getting vaccinated by the end of October, if possible.

The flu shot is safe for pregnant and breastfeeding women and their infants.

You can get a flu shot at any time, during any trimester, while you are pregnant. Millions of pregnant women have gotten flu shots. Flu shots have a good safety record. There is a lot of evidence that flu vaccines can be given safely during pregnancy, though these data are limited for the first trimester.

If you deliver your baby before getting your flu shot, you still need to get vaccinated. The flu is spread from person to person. You, or others who care for your baby, may get the flu, and spread it to your baby. It is important that everyone who cares for your baby get a flu vaccine, including other household members, relatives, and babysitters.

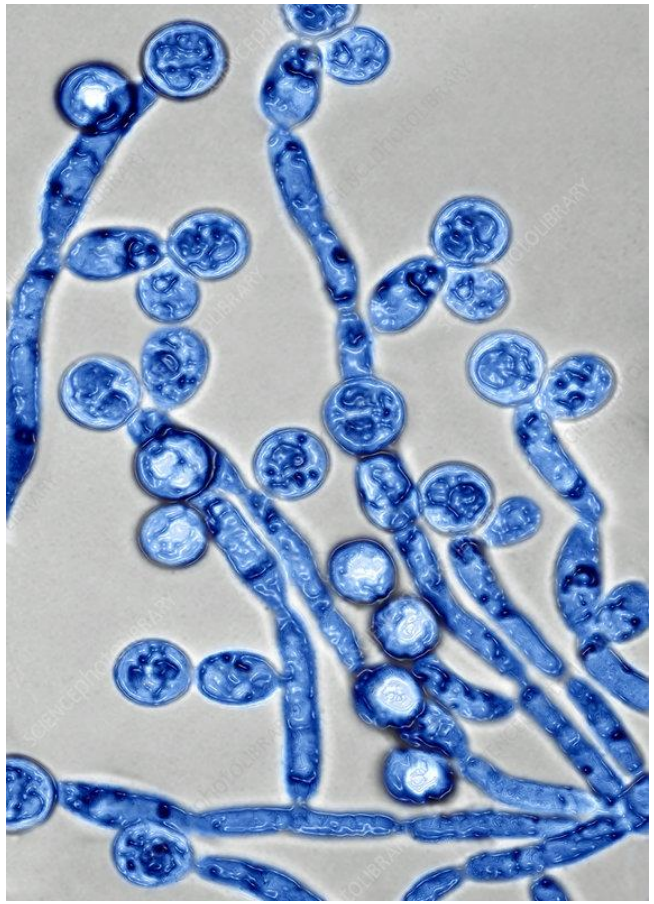
Common side effects of a flu vaccine are mild.

After getting your flu shot, you may experience some mild side effects. The most common side effects include soreness, tenderness, redness and/or swelling where the shot was given. Sometimes you might have a headache, muscle aches, fever, and nausea or feel tired.

Last Updated 12/27/2017

Fungal Infections

Candida Albicans Overview

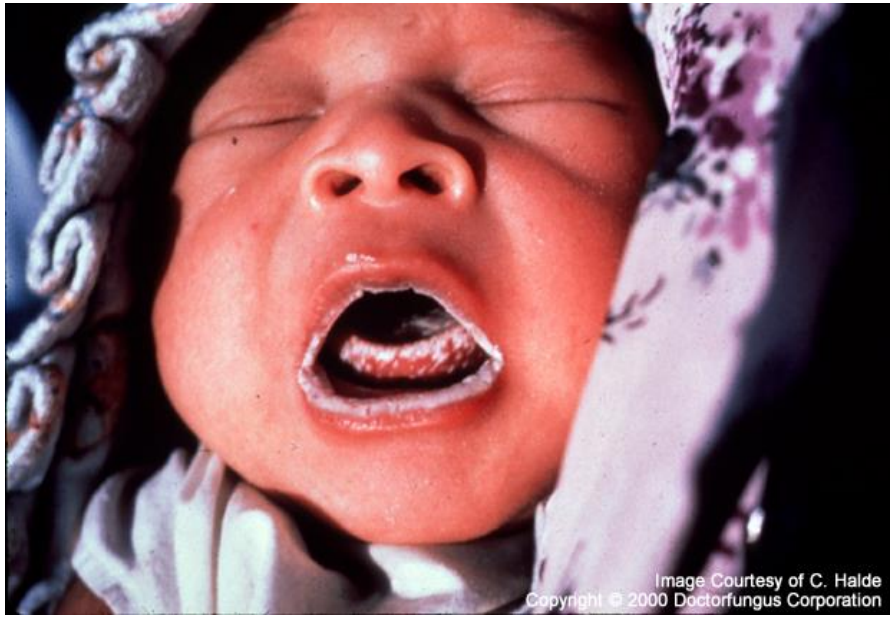


https://www.sciencephoto.com/media/515349/view/candida-albicans-yeast-tem

- Candida albicans is the most common cause of human candida infection. Albicans is the Latin word for "white". The yeast appears white when cultured on a plate. Candida albicans is part of our natural microflora and can be found in the mouth, GI tract and vagina. It is the most prevalent cause of fungal infections in people.

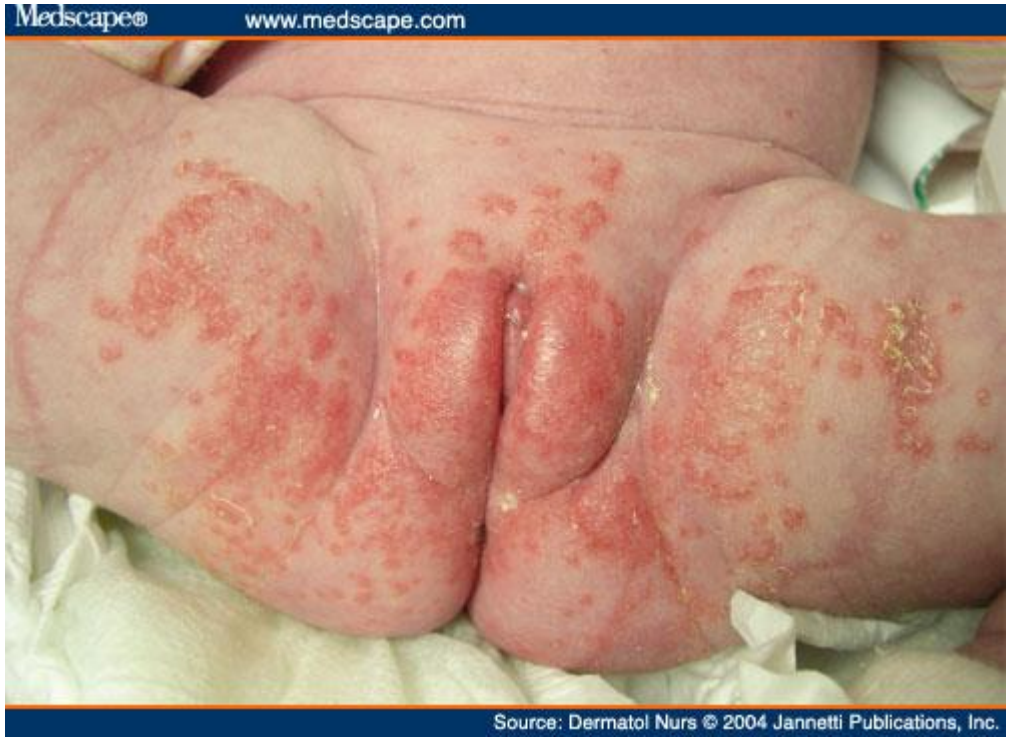
Thrush in Newborn

- Newborns can have symptoms of Candida at birth of soon after. Thrush often appears in the mouth in the first few weeks or months of life. Oral thrush may occur in infants because their immune system is not yet matured. Infant can present with white plaques in the mouth, lips, tongue, gums and palate. The plaque does not scrape off easily. Infants may experience pain, poor feeding, or fussiness. Oral thrush in infants often disappears within 2 weeks. If the infant is breastfeeding, the mother's nipples may need to be treated at the same time to prevent the infection passing back and forth.



Cutaneous Candidiasis

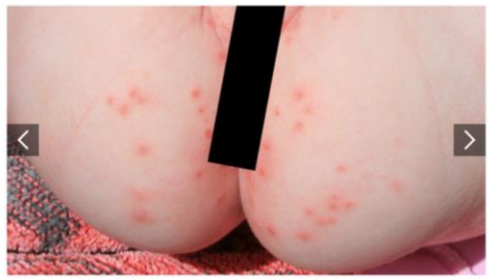
- Cutaneous candidiasis is a yeast infection of the skin. The skin is infected with candida fungi. This type of infection is fairly common and can involve almost any skin on the body, but most often it occurs in warm, moist, creased areas such as the groin. The fungus that most often causes cutaneous candidiasis is Candida albicans.



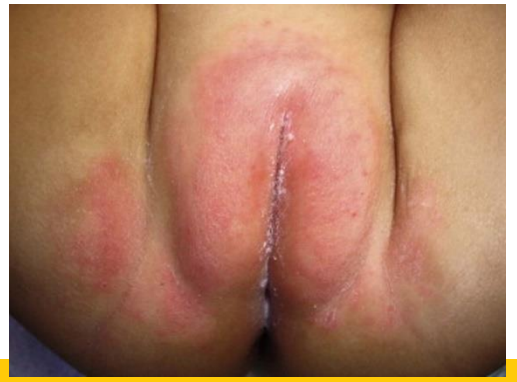
Yeast Diaper Rash vs Regular Diaper Rash

Yeast Diaper Rash Symptoms	Regular Diaper Rash Symptoms
Red skin with dots or pimples	Pink to reddish skin that's smooth or chapped
Rash doesn't respond to standard diaper cream and takes a while to treat	Rash responds to standard diaper creams and clears up in 2-3 days
Rash may occur more in the folds of legs, genitals or buttock	Rash may occur on smoother surfaces of the buttocks or on the vulvar
Rash may occur along with thrush infection	Rash doesn't usually occur with oral thrush
May have satellite spots of rash outside the border of the rest of the rash	Rash is localized in one area

https://www.healthline.com/health/parenting/yeast-diaper-rash#pictures



Mild diaper rash from yeast *(Candida)* infection



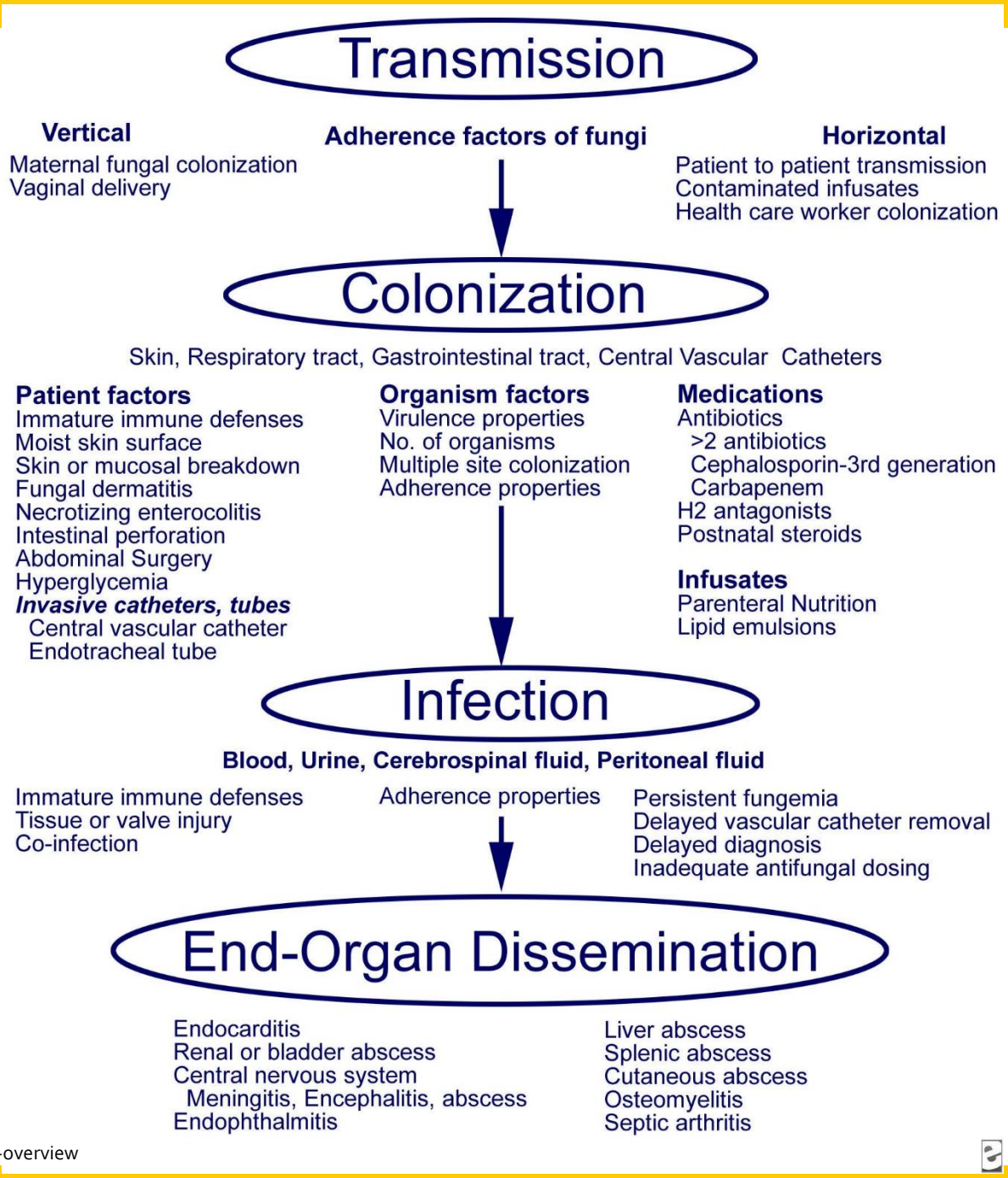
From Chayavichitsilp P et al: Diaper dermatitis. In: Lebwohl MG et al, eds: Treatment of Skin Disease: Comprehensive Therapeutic Strategies. 4th ed. Philadelphia, PA: Elsevier; 2014:188-9, Figure 1.

Fungal Infections In Preterm Infant

- The risk for invasive fungal infections is high in very low birth weight infants less than 1500 grams and highest for infants born at early gestational ages who survive past the immediate postnatal period.
- Most fungal infections in preterm neonates are due to Candida species. Candida species are organisms that colonize the skin and mucosal surfaces and adhere to catheter surfaces. Candida can invade the bloodstream and disseminate in these infants because of their immature immune system, complicated by the inevitable need to compromise their developing skin and mucosal membrane barrier defenses.

Kaufman, D, et al. Fungal Infections in Preterm Infants Jun 25, 2014 https://emedicine.medscape.com/article/980487-overview

Fungal Infections in the Infant

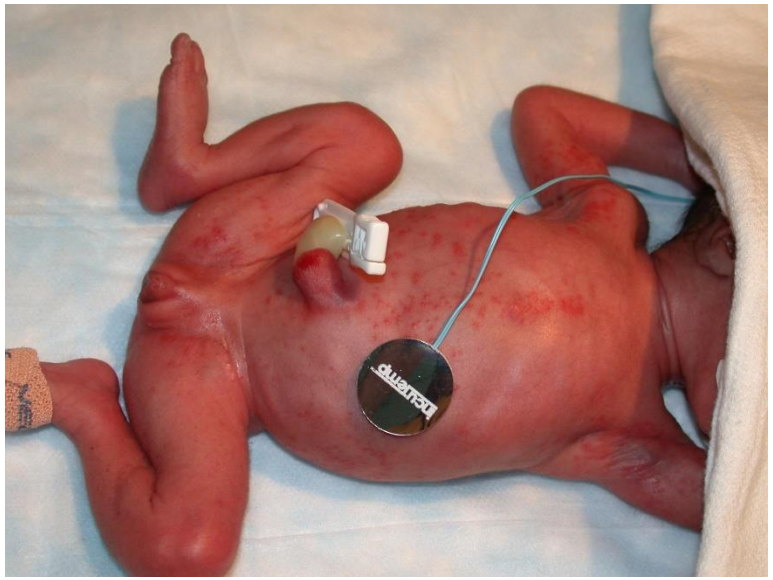


"The risk for invasive fungal infections is high in very low birth weight (VLBW) infants (< 1500 g) and highest for infants born at the youngest gestational ages who survive past the immediate postnatal period. [1, 2] These immunocompromised infants usually require invasive therapies, such as central vascular catheters and endotracheal tubes, and are exposed to broad-spectrum antibiotics and parenteral nutrition. In addition, they occasionally receive postnatal steroids and gastric acid inhibitors. All of these factors place them at high risk for fungal infection."

Kaufman, D, et al. Fungal Infections in Preterm Infants
Jun 25, 2014 https://emedicine.medscape.com/article/980487-overview

Fungal Treatment in Preterm Infants

- Fungal infections are often difficult to eradicate in the preterm infant. Because fluconazole prophylaxis is highly effective in preventing Candida albicans colonization and infection, today most neonatal intensive care units are routinely starting fluconazole prophylaxis in very low birth weight neonates.



Kaufman, D, et al. Fungal Infections in Preterm Infants Jun 25, 2014 https://emedicine.medscape.com/article/980487-overview

Congratulations! You have finished the module.

Last Step: Complete the Post-Test & Evaluation

- All participants must complete the Post-Test and Evaluation.
- Online Post-Test and Evaluation (Preferred Methods)
- Please click on the following link https://www.surveymonkey.com/r/FMW6PCZ or open your I-Phone Camera and scan the QR Code located to the right to access the online Post-Test and Module Evaluation
- Alternate option, please complete the paper version of the post-Test utilizing the Answer Sheet and Evaluation
  - Return Answer sheet/Evaluation Form to Perinatal Systems:
    - Fax: (803)434-4309
    - E-mail: PerinatalSystems@prismahealth.org
- Questions?
  Contact Cathy White (Cathy.White@prismahealth.org)
  or Michelle Flanagan (Michelle.Flanagan@prismahealth.org)