

#### **Financial Disclosures**

None to disclose

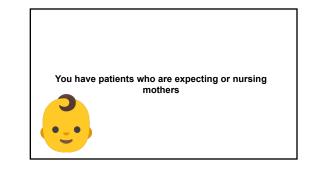
#### Learning Objectives

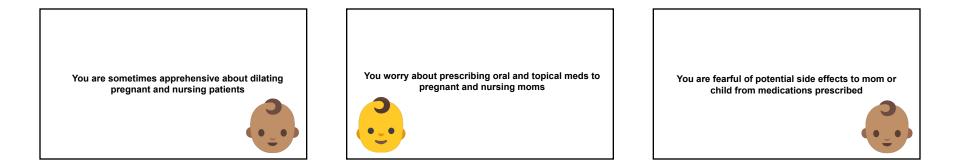
- <u>Discuss</u> general considerations for safely prescribing to pregnant and lactating patients
- Review pharmacological mechanisms of action and drugs deliveries to fetus and babies
- Discuss the FDA Pregnancy Risk Categories
- Review ophthalmic considerations when prescribing medications to pregnant and postpartum patients











Expecting and nursing moms often ask questions about how topical and oral meds used in clinic or prescribed might affect their child

Why is this topic important?

Importance of Safely Treating & Managing Pregnant and Lactating Patients

- There are <u>approximately 6 million pregnancies</u> in the U.S. each year
  - Not all pregnancies are planned or known
- Many women <u>need to take medicines</u> when they are pregnant.
  - <u>>50%</u> of pregnant women report that they take at least one medicine.
- Some women take medicines for health problems, like diabetes, morning sickness or hypertension, that can start or worsen with pregnancy.



Did you know?

## Did you know that.....

Over **80%** of physicians are apprehensive about prescribing medicine to or treating pregnant and postpartum nursing women

(Pregnancy & Medicine Initiative, 2014)

Additionally.....



Over **80%** of mothers fear taking medications during pregnancy and nursing

(Pregnancy & Medicine Initiative, 2014)

What are mothers and doctors afraid of?

## **TERATOGENS!!!!!**



Principles of Teratology



- Any environmental agent that may potentially alter normal embryological or fetal development
- Examples:

Definition

- o medicines, recreational drugs, chemicals, metals, infections, systemic diseases
- Risk of birth defects increases with certain categories and classes of medications
- · Especially when teratogenic medications are taken during early embryonic development



- Teratology Adverse Effects Cont'd
- Problems for you before and during pregnancy, including
  - Not being able to get pregnant. This is called infertility.
  - Problems with the placenta. The placenta grows in your uterus and supplies your baby with food and oxygen through the umbilical cord.
  - Preterm labor. This is labor that happens before 37 weeks of pregnancy.
  - Miscarriage. This is when a baby dies in the womb before 20 weeks of pregnancy.
  - Stillbirth. This is when a baby dies in the womb after 20 weeks of pregnancy.

#### Teratogenic Drugs → Birth Defects

Each of the following drugs or drug groups may cause birth defects in a developing fetus:

- some anticonvulsant medications
   some cancer-fighting medications alcohol cocaine
- some drugs for certain rheumatic conditions
   high doses of vitamin A lithium
- some thyroid medications
- thalidomide
- the blood-thinning drug warfarin
  the hormone diethylstilbestrol (DES)
- ACE inhibitors
- angiotensin II antagonist
- isotretinoin (an acne drug)
- abnormalities in the child male hormones · Alcohol passes easily across the some antibiotics placental barrier
  - It is broken down more slowly in the immature body of the fetus than in the body of an adult.

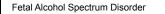
Resultant of prenatal exposure to

Alcohol Use While Pregnant

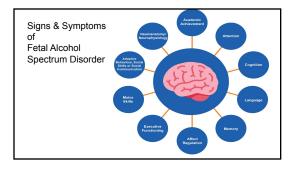
alcohol which causes

Fetal Alcohol Spectrum

Disorder(FASD)



- Dysmorphic Features of FAS • FASD is characterized by facial and cranial deformities, intellectual disability and Low nasal bride behavioral problems such as Epicanthal folds hyperactivity • The risk of infertility,
- miscarriage, stillbirth, and Cardinal features in blue sudden infant death syndrome (SIDS) increases with alcohol consumption



#### Substance Abuse & Pregnancy

#### Marijuana

- · More women are using it to alleviate morning sickness and reduce stress.
- o The American College of Obstetricians and Gynecologists recommends against using marijuana both prenatally and while breastfeeding Can lead to preterm birth or stillbirth
  - Babies may also face growth and development issues as they get older
- Cocaine
  - · Declines in cognitive performance, information processing, and attention span are common in children and into adulthood
- Benzodiazepines
- I.e. Xanax, Ativan, Valium or Klonopin
- can lead to toxicity in newborns → reduced muscle tone, breathing problems, and sedation ■ May suffer from withdrawal → sleep disturbances, irritability, and even seizures
  - Preterm birth and low birth weight are also more likely to occur

#### **Opioid Abuse & Pregnancy**

- Opioid exposure during pregnancy negatively impacts the fetus as well Associated with
  - preterm birth, congenital disabilities, poor fetal growth, and even stillbirth
- There's also a chance of neonatal abstinence syndrome (also known as neonatal opioid withdrawal syndrome),

Narcan (Naloxone HCI) Use for opiates, heroin, fentanyl cases

- · A condition that causes tremors, sleep difficulties, vomiting, dehydration, hyperactive reflexes, seizures, · First OTC FDA approved drug for opioid overdose,

NASAL SPE

#### Teratologic Mechanism

- Medical science cannot always predict how exposure to a teratogenic drug will affect a fetus. The potential for harm depends on a range of factors including:
  - the type of drug
  - the size of the dose
  - how often it's taken
  - the stage of fetal development (gestational age) at the time of drug exposure
  - the individual response of the fetus to the drug
  - other factors, such as maternal diet or illness.

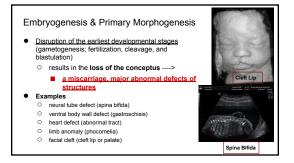




#### First Trimester: Embryogenesis & Primary Morphogenesis

- Blastocyst embeds within uterine lining
  First 14-16 days = formation of an
- embryoHistiotrophic nutrition relies on uterine
- Institution relies on uternite secretions for oxygen and metabolic substrates
- Establishment of the Placenta

   Digestion of maternal tissue to release metabolic substrates
- Primary Decidualization Reaction
   Weeks 1-12
- 23



## Second & Third Trimesters: Fetal Development & Organogenesis

- Involves the growth and differentiation of precursor cells and tissues contained within each of the organ rudiments formed during primary morphogenesis.
- Organogenesis occurs over the longest period of time, extending from about four weeks of development (during the period of the embryo), throughout the fetal period, and for some organ systems even continuing postnatally.

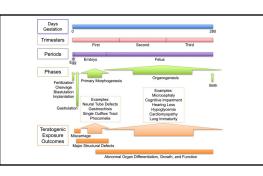




## Second & Third Trimesters: Fetal Development & Organogenesis

- Disruption during the late embryonic and fetal period generally results in abnormal organ differentiation, growth, and function
  - I.e cognitive impairment, hearing loss, neonatal hypoglycemia, lung immaturity).
  - the most likely teratogenic outcomes are microcephaly, preterm birth, low birth weight, organ abnormalities/defects, and intellectual disability

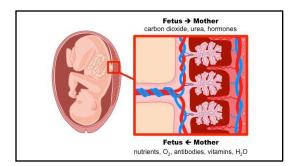


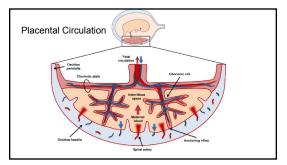


#### Placenta

- Transports oxygen to fetal bloodstream
- Removes carbon dioxide
- Carries in nutrients
- Eliminates waste products to mother for disposal
- Barrier against noxious agents circulating in maternal blood
  - BLOOD PLACENTA BARRIER





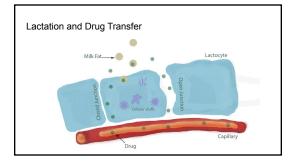


#### Lactation (Breast Feeding)

- Describes the production of breast milk and its secretion from mammary glands after delivery
- Most drugs enter milk at very low levels and are safe
- There are exceptions, though, in which drugs can become concentrated in breast milk.



## Lactation and Drug Transfer AUEOLI Capillary Autocytes Transfer of oxygen and nutrients to the Lactocytes needs to be extremely rapid 1-2 layer cell separation between blood capillaries and alveolar cells (cluster of lactocytes) Easy passage!





#### Lactating Clinical Pearls

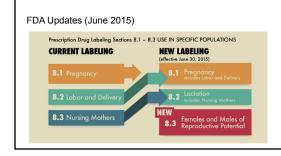
- A drug considered safe for patients who are pregnant may not be safe for patients who are nursing.
- Mothers with medically fragile infants may need different dosing to minimize drug accumulation and toxicity in the infant
- Consult with their lactation
   specialist



Drug Categories

# FDA Pharmaceutical Labeling FDA Pregnancy Risk Factor Categories <u>Category R</u> Safest to take during pregnancy <u>Category R</u> Showing no risk in animal studies but a lack of controlled studies on pregnant women <u>Category C</u> Animal studies showed risk to the fetus but no human studies have been performed or unavailable <u>Category D</u> Exhibited positive evidence of potential fetal risk but benefits for pregnant

- Exhibited positive evidence of potential fetal risk but benefits for pregnant women may be acceptable despite the risk
- <u>Category X</u>
  - Contraindicated in women who are pregnant or may become pregnant because of known fetal risk and abnormalities



Most ophthalmic medications are safe......

### Many are CATEGORIES B & C

The risk of birth defects resulting from topically-applied medications is <u>extremely low</u>, suggesting that, although prescribing for the pregnant patient requires an increased level of caution, especially in gestational weeks two through 10, <u>there are a variety of relatively safe options available for</u> <u>most occular disease conditions</u>.



#### Physiological Changes in Pregnancy

- Decreased intraocular pressure
- Fluctuations in refractive error
- Dry eye symptoms
- Subconjunctival hemorrhages
- Decreased corneal sensitivity
- Ptosis
- Lenticular Changes



Is it safe to Dilate My Pregnant or Nursing Patient During A Routine Eye Exam?





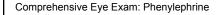
## Comprehensive Eye Exam: Dilation Benefits>Risks Ccassional dilation is acceptable Caution against <u>repeated dilation</u> Topical Tropicamide 0.5% vs. 1% (Category C) Punctal Occlusion Pecreases systemic absorption Reduces amount of drug excreted into the breast milk

- Use manual or temporary plugs
- Long-term use in lactating mothers
- May inhibit lactation and result in slow weight gain,

#### Comprehensive Eye Exam: Dilation

- Evidence is <u>unknown</u> if cycloplegics and mydriatics cross the placenta or excreted into human breast milk
- Avoid the use of longer duration and increased half life parasympatholytics such as
  - atropine, scopolamine and homatropine
- The <u>shorter acting agents</u> such as tropicamide or cyclopentolate are considered safer for use in pregnancy and lactation.





- <u>Avoid phenylephrine</u>
- Topical vs. Oral
- MOA: vasoconstriction
  - → reduces the blood flow to the placenta
     Possible risk for fetal malformations, fetal hypoxia, and bradycardia during early embryonic development
- Evidence of systemic hypertension in low birth weight babies when phenylephrine 2.5% or 10% is used



#### OTC Phenylephrine

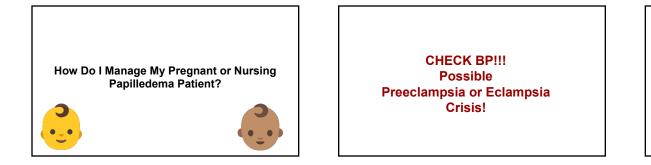
- Oral decongestants (Category C)
   may also result in vasoconstriction
   —induce maternal hypertension
  - →impaired blood flow to the fetus
- The decongestants pseudoephedrine and phenylephrine are generally not recommended during the first 13 weeks

#### of pregnancy

Benefits>Risks

- → potential increased risk of gastroschisis (an abdominal wall defect)
- After the first trimester, caution should be use





#### Preeclamosia

- · Preeclampsia is a pregnancy complication characterized primarily by high blood pressure, edema, and protein spillage in the urine
- Occurring frequently after the 20th week of pregnancy or after giving birth (postpartum preeclampsia).
- Most pregnant women with preeclampsia have healthy babies.
  - If not treated, it can cause serious problems, like premature birth and even death.



- Eclamosia Eclamosia is seizures that occur in pregnant people with preeclampsia
- Symptoms of eclampsia
  - High blood pressure
  - Headaches Blurry vision
  - Convulsions
- Eclampsia is rare affects less than 3% of people with preeclampsia
- Serious condition that occurs in the second half of pregnancy



- Warning Signs of Preeclampsia & Eclampsia

  Many people will have warning signs before having a seizure caused by
  - eclampsia.
  - Severe headaches
  - Difficulty breathing
  - Nausea or vomiting
  - o Trouble urinating or not urinating often Abdominal pain
- Blurred vision, seeing double or loss of vision • Swelling of the hands, face or ankles
- Seizures
- Distress or Confusion
- Loss of consciousness
- Ŧ protein arterial



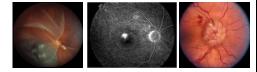
Preeclampsia & Eclampsia Ocular Manifestations

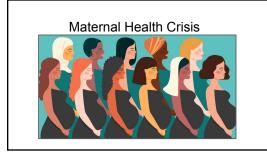
- Visible retinal vascular changes in 40-100% of preeclamptic patients
  - Visual symptoms in 25-50%
  - Blurred or decreased vision, scotoma, photopsia, diplopia, VF defects, reduced vision/blindness
- · Most common: constriction or spasm of retinal arterioles with decreased retinal artery to vein ratio
  - If severe, changes associated with hypertensive retinopathy may occur



#### Preeclampsia & Eclampsia Ocular Manifestations

- Exudative Retinal Detachment
- Cortical Blindness
- Visual Field Defects
- Central Serous Chorioretinopathy (CSR)







## 7 minutes

My Preeclampsia Story

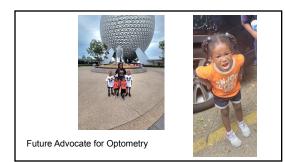


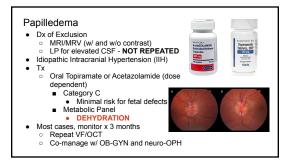














Gestational Diabetes

- Gestational diabetes is a type of diabetes that can develop during pregnancy in women who don't already have diabetes.
- Gestational diabetes occurs when your body can't make enough insulin during your pregnancy.
- Every year, 2% to 10% of pregnancies in the United States are affected by gestational diabetes.
- About 50% of women with gestational diabetes go on to develop type 2 diabetes
- Managing gestational diabetes will help make sure you have a healthy pregnancy and a healthy baby

#### Diabetic Retinopathy

- If a pregnant patient presents initially with <u>mild to moderate DME</u>, then it's reasonable to recommend close observation with an emphasis on blood glucose control.
- In severe cases, if DME does not improve after a period of observation, the first treatment option should be laser, grid or focal for CSME per Early Treatment Diabetic Retinopathy Study (ETDRS)



#### **Diabetic Retinopathy**

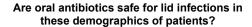
- If laser therapy yield poor results, intravitreal steroids are thought to be a safe option during pregnancy.
- the systemic absorption of intravitreal triamcinolone has been shown to be minimal compared to topical and systemic steroids



Proliferative Diabetic Retinopathy

- The use of anti-VEGF drugs during pregnancy is <u>controversial</u> because they may potentially cause systemic side effects in the mother and fetal harm, as spontaneous miscarriage, defective embryogenesis and/or precelampsia
  - <u>VEGF contributes to fetal and</u> <u>placental vasculature</u>







- Soft Tissue & Gland Infections

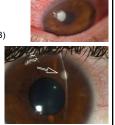
  Preseptal, MGD, Lid Edema, Hordeolum
  TX:

  Category B
  - Oral Penicillins
    - (Augmentin 875 mg BID/ Amoxicillin 875mg X BID)
       Oral Cephalosporins
  - Oral Cephalosporins (Cephalexin 500 mg x BID)
     Oral Azithromycin (500 mg/
  - Zpak)
  - Oral Erythromycin (500 mg x BID)



#### Corneal Bacterial Keratitis

- Tx
  - Topical Antibiotics (Category B)
    - Tobramycin Polymyxin B
    - Erythromycin
    - Azithromycin
  - Severe cases → Fortified cephalosporins



#### Infectious Microbial Keratitis

- Fortified Therapies have an excellent safety profile for severe bacterial keratitis
  - Topical cephalosporin antibiotics,
  - such as cefazolin and ceftazidime
  - Topical tobramycin antibiotics



#### **Topical Fluoroquinolones**

- The use of topical fluoroquinolones during pregnancy has not been well studied;
  - however, because of their undisputed efficacy in the treatment of corneal ulcers,
    - necessary if the benefits outweigh the potential risk to the developing fetus.



these medications may be

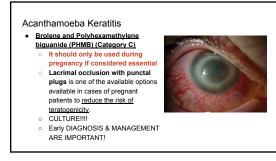


#### Fungal Keratitis

- Topical administration of amphotericin and voriconazole is not considered to be harmful in pregnant and lactating women.
  - Econazole should be avoided during the first trimester and used sparingly during 2nd and 3rd trimester. For antifungal medications,
  - clotrimazole, miconazole and nystatin are considered first-line agents.
- There are however contraindications to the use of systemic antifungal therapy in pregnancy and lactation.







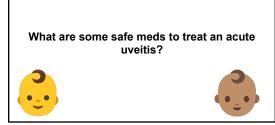
Systemic Medications to Avoid Oral Antibiotics • **Category D** $\rightarrow$  increased risk of pregnancy complications and congenital malformations Doxycycline Sulfonamides Trimethoprim Neomycin Fluoroquinolones Tetracyclines

#### Systemic Meds to Avoid

 It is prudent to avoid <u>tetracycline and fluoroquinolone derivatives</u> when treating pregnant and lactating patients,

Increased risks to the developing fetus or infant.

- Tetracycline and its derivatives
- including <u>doxycycline and minocycline</u>—have been known to cause discoloration of teeth and maternal liver toxicity.
- Fluoroquinolone derivatives
- such as <u>oral ciprofloxacin moxifloxacin or levofloxacin</u> have been associated with lab animal fetal cartilage-forming defects, and their use in pregnant patients is controversial despite data to suggest relative safety



#### Anterior Uveitis (G/NG)

#### • Tx

- Topical Corticosteroids(Category C)
  - Topical Prednisolone 1%
     Penetrates poorly into breastmilk
  - Safe for short-term use
  - Punctal occlusion
- Topical Cycloplegics/Mydriatics
  - Topical Cyclopentolate
     Punctal Occlusion recommended





#### **Oral Corticosteroids**

- <u>Systemic</u> corticosteroids have been associated with neonatal abnormalities and pregnancy complications.
- Caution with use!



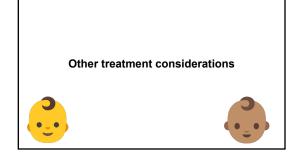


#### HSV

- Oral Antivirals (Category B)
- Acyclovir 400 mg 5x/day x 10 days
  - ONLY antiviral approved for use in lactating women
- Valacyclovir 250 mg tid x 7 days
- Famciclovir 500 mg tid x 7 days
- Topical Antivirals (Category C)
- Trifluridine Zirgan
- Stromal/AC Rxn Involvement
- Topical Prednisolone Acetate 1%
- Loteprednol 1%



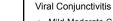
## HSV • H/O recurrence Prophylaxis (Category B): Oral therapy • Acyclovir 400 mg bid po Valacyclovir 250 mg bid po • Famciclovir 500 mg qd po



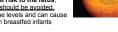
#### **Oral Pain Management**

- · Acetaminophen (Category B) safe in all three pregnancy trimesters
- Avoid OTC aspirin and ibuprofen (Category D) · Vicodin (acetaminophen and hydrocodone)- Category
- С
  - Safe in pregnancy and nursing
- Tylenol #3 (acetaminophen and codeine)- Category C
  - Safe in pregnancy (avoid prolonged use→risks) Avoid in nursing→ drug overdose in infant
  - Potential cause of CNS depression and

apnea in infants→ increased risk for SIDS



- Mild-Moderate Cases: AT's and monitor
- Severe: Topical Steroid
  - Prednisolone or Loteprednol 1% Presence of pseudomembranes and/or
- subepithelial infiltrates (SEIs) Betadine Therapy (EKC)
  - CAUTION
  - should be used during pregnancy only if the potential benefit to the mother justifies the potential risk to the fetus; non-prescription use should be avoided. increases breast milk iodine levels and can cause transient hypothyroidism in breastfed infants





#### Glaucoma

- Most anti-glaucoma topical therapeutics are <u>Category C</u>
- Alpha-agonist, Category B (safest option)
  - Increased risk for CNS depression and apnea Discontinue prior to breastfeeding
- Caution with
- Prostaglandins Increased risk for miscarriage and preterm labor Beta Blockers
- Risk for neonatal hypoglycemia and bradycardia ■ AVOID in 1st trimester→ Systemic HYPOtension
- o <u>CAls</u> Increased risk for hepatorenal abnormalities and teratogenic effects
- Rho-kinase inhibitors
   Limited clinical data regarding teratogenic effects · Surgical Options: MIGS or SLT may be considered



#### Dry Eye & Ocular Allergies



- Category C Caution due to risk of teratogenic and fetal abnormalities OTC AT's and Gels (safe)
- o OTC low dose Brimonidine
- LUMIFY has not been tested on pregnant or lactating women. If pregnant or breastfeeding, consult with OB-GYN prior to use.
- Ocular Allergies

• Dry Eye Syndrome

- Most topical antihistamines are Category B and safe to use → alcaftadine 0.25%
- However, Pataday and Pazeo are Category C (caution with use) Low dose topical steroid use: short term

Anti-inflammatory medication→ cyclosporine A

Omega 3 fish oil supplements are safe (fish oil allergies are RARE)

#### Safely Using & Prescribing

#### Medication Selection

- A & B Categories safest
- Benefits> Risks for Category C
- · Category D & X contraindicated use
- Medication Use
  - Short-term use
  - Topical > Oral if available→ limited systemic absorption
  - Punctal occlusion



#### Prescribing to Nursing Mothers

- · According to the AAP, health care providers should weigh the risks and benefits when prescribing medications to breastfeeding mothers by considering the following:
- a. Need for the drug by the mother
- b. Potential effects of the drug on milk production
- c. Amount of the drug excreted into human milk
- d. Extent of oral absorption by the breastfeeding infant e. Potential adverse effects on the breastfeeding infant
- f. Age of the infant
- g. Proportion of feedings that are breast milk







#### **Questions & Answers**

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