Use of Ophthalmic Medications in Pregnancy

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Diagnostic and Therapeutic Ophthalmic Drugs

- The benefit to the mother must be weighed against the side effects to the fetus
- Potential risk to fetus caused by teratogens (Agents during the embryonic or fetal period that produce morphologic or functional malformations that become apparent postnatal)
    - Structural or visceral abnormalities to the fetus
    - Altered physiological function of a nursing baby

Medication Use In Pregnancy- Categorized by the FDA

Category A	Adequate and well controlled studies have failed to demonstrate a risk to the fetus in the first trimester of pregnancy (and there is no evidence of risk in later trimesters).
Category B	Animal reproduction studies have failed to demonstrate a risk to the fetus and there are no adequate and well-controlled studies in pregnant women.
Category C	Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.
Category D	There is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience or studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.
Category X	Studies in animals or humans have demonstrated fetal abnormalities and/or there is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience, and the risks involved in use of the drug in pregnant women clearly outweigh potential benefits.

Medications Used For Diagnostic Measures

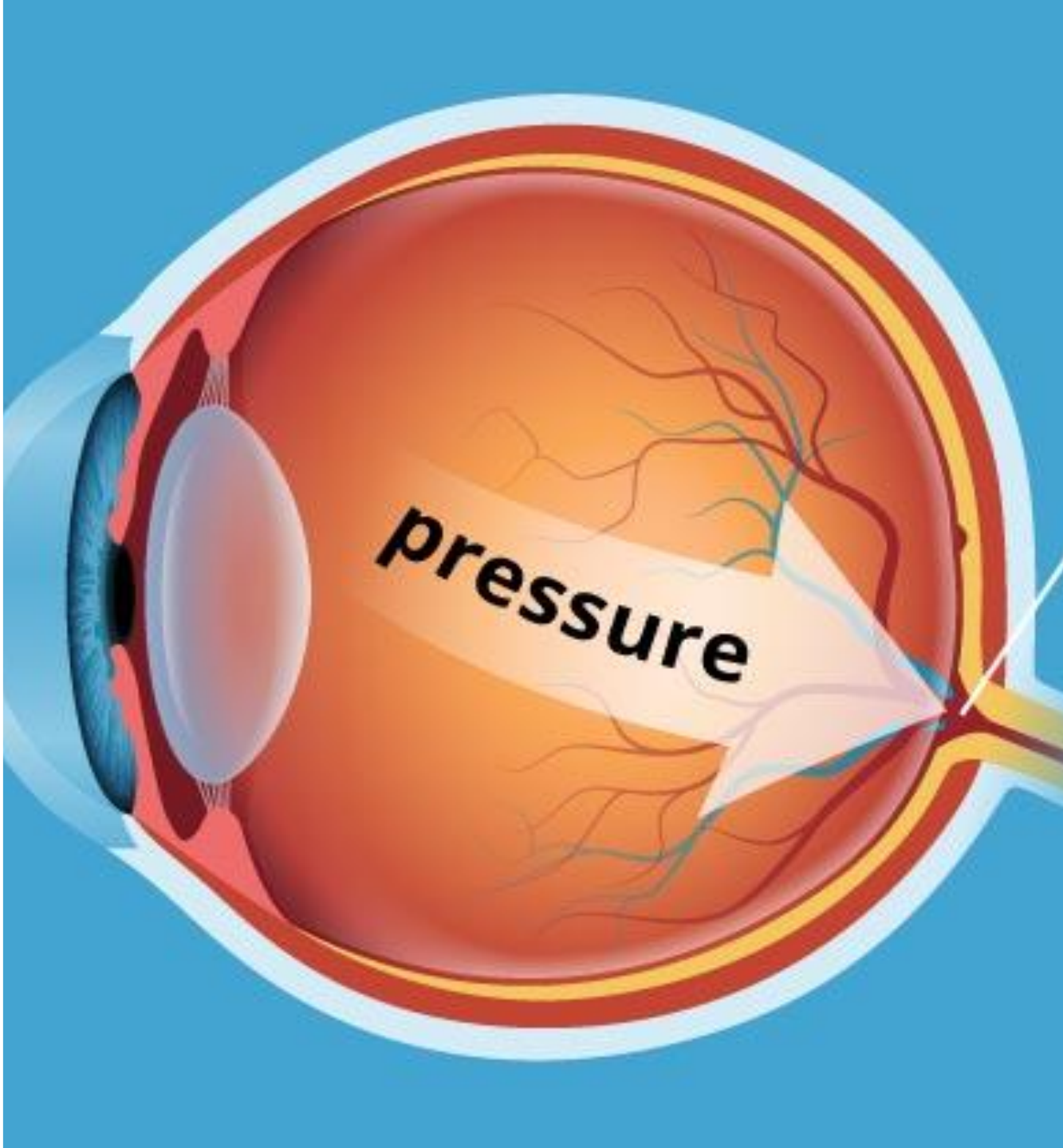
- **Topical Anesthetics**
  - NO teratogenic effects
    - Category B
- **Indocyanine Green Dye**
  - No adverse effects on mother or fetus (will not cross the placental barrier)
  - However, it is yet determined if it is present in breast milk
    - Can be used non-ophthalmically to measure hepatic blood flow in pregnant women
    - Category C (use only if clearly indicated)

Medications Used For Diagnostic Measures

- **Fluorescein Dye (Topical & IV)**
  - Crosses the placental barrier
  - However, no adverse effects have been reported in humans
    - Category C (Avoid angiography on pregnant patients, especially in the first trimester)
- **All Mydriatic/Cycloplegic Drops**
  - Avoid unless absolutely necessary
  - Relatively contraindicated due to fetal hypoxia in late pregnancy and delivery
    - Category C

GLAUCOMA MEDICATIONS

- **Incidence of Glaucoma**
  - Low in women of child-bearing age
- **Disease Severity**
  - Mothers can tolerate mild increases in IOP during pregnancy
  - If IOP is dangeruosly high, consider Selective Laser Trabeculoplasty (SLT) to limit risk to fetus



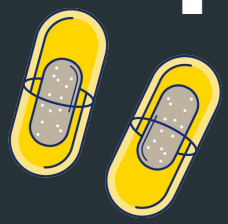
Beta-Adrenergic Antagonists

(Timolol, levobunolol, betaxolol, carteolol)

- **Systemic Side Effects**
  - Respiratory distress, bradycardia, heart failure, fatigue, depression
- **Effects in Pregnancy**
  - Apnea, intrauterine growth retardation, neonatal depression at birth (Low APGAR), postnatal hypoglycemia, bradycardia
- **Breastfeeding**
  - Secreted and concentrated in breast milk
  - Category C (Can cause serious adverse side effects)
    - Example: Apnea in 18 month old child being breastfed
  - Discontinue nursing or discontinue drug

Carbonic Anhydrase Inhibitors

- **Topical Agents (Dorzolamide and Brinzolamide)**
  - Published reports are limited, but no adverse effects have been reported
  - It is still unknown if they are excreted through breast milk
  - Category C
    - Discontinue nursing or discontinue drug
- **Oral Agents (Acetazolamide)**
  - Malformations and electrolyte imbalances have been studied in experiments with animals
  - Hepatic and renal symptoms have occured in infants being breastfed
    - National Collaborative Perinatal Project
    - No incidence in major or minor fetal abnormalities in infants with mothers who took medication at various stages of pregnancy. However, the study size considered too small



Prostaglandin Analogues

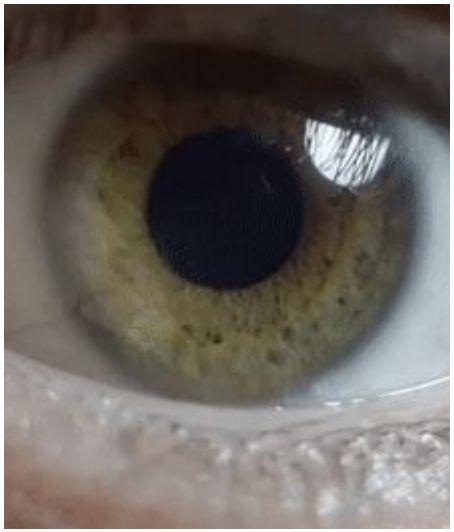
(Latanoprost, Bimatoprost, Travoprost)

- Latanoprost, Bimatoprost, Travoprost
  - Prostaglandins cause uterine smooth muscle contractions
- Animal studies (systemic prostaglandins)
  - Increase the risk of abortion or premature delivery
  - Positive excretion in breast milk
- Human studies (topical prostaglandins)
  - Case studies: No adverse effect on pregnancy nor neonatal outcomes
  - Unknown excretion in breast milk
- Category C
  - Due to potential causation of uterine muscle contractions
  - Should be avoided in pregnant women and women planning on becoming pregnant

Sympathomimetics

Epinephrine	Dipivefrin Hydrochloride	Apraclonidine & Hydrochloride
Used in anesthesthesia during cataract surgery Stimulates alpha and beta adrenergic receptors Human Studies: Systemic Use in First Trimester Associated with Minor and Major Anomalies-- Inguinal Hernias Category C	Prodrug of Epinephrine Converted by corneal enzymes Animal Studies: Negative for side effects Unknown if excreted in breastmilk Category B	Selective Alpha-2 adrenergic agonists Case Reports: No adverse side effects during pregnancy Unknown if excreted in breastmilk Apraclonidine – Category B Hydrochloride – Category C

Miotics



- Parasympathomimetic Agents
  - Includes direct acting cholinergic agents (Pilocarpine, Carbachol)
  - Animal Studies
    - Pilocarpine caused limb abnormalities
    - Carbachol caused cervical vertebrae abnormalities
  - Human Study (Systemic pilocarpine)
    - No side effects in the first four months of gestation
    - Side effects of the near term included neonatal hyperthermia, seizures, and restlessness
  - Category C

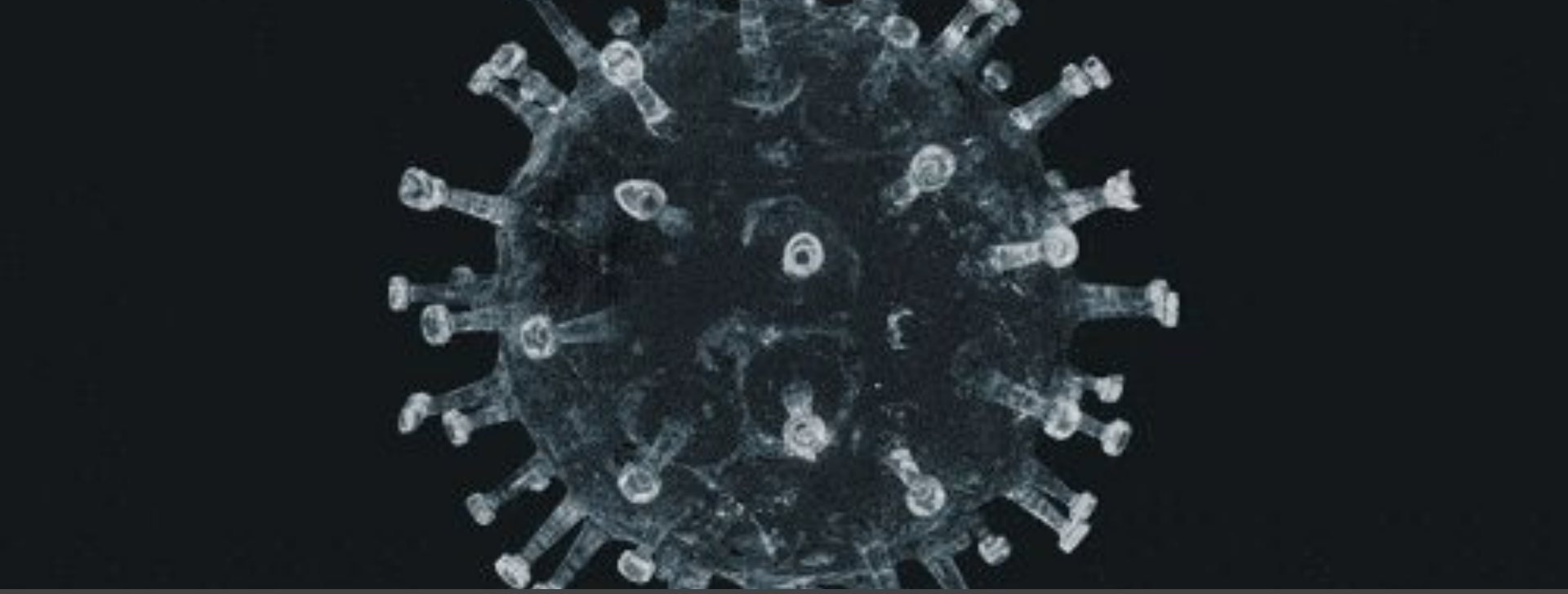
CORTICOSTEROIDS

- Systemic Corticosteroids
  - Increased risk of stillbirth
  - Intrauterine growth retardation and adrenal insufficiencies
  - Excreted in breast milk
    - Suppressed growth or interfered with endogenous productions
- Topical Corticosteroids
  - Animal studies:
    - Developmental and teratogenic effects including cleft lip, cleft palate & sex organ abnormalities in mice
    - Unknown if secreted in breast milk
- Category C (Avoid use when nursing)

ANTI-INFLAMMATORY DRUGS

- **Cyclosporine**
  - Immunomodulator
  - Animal Studies: No abnormalities
  - Excreted in breast milk when used systemically
- **NSAIDS**
  - Flurbiprofen
    - Animal studies: Embryocidal, prolonged gestation, retarded growth
- **Diclofenac**
  - Animal studies: Crosses placenta
- **Nepafenac**
  - Animal studies: Crosses placenta
  - Found in breast milk
- **Bromfenac**
- **Ketorolac**

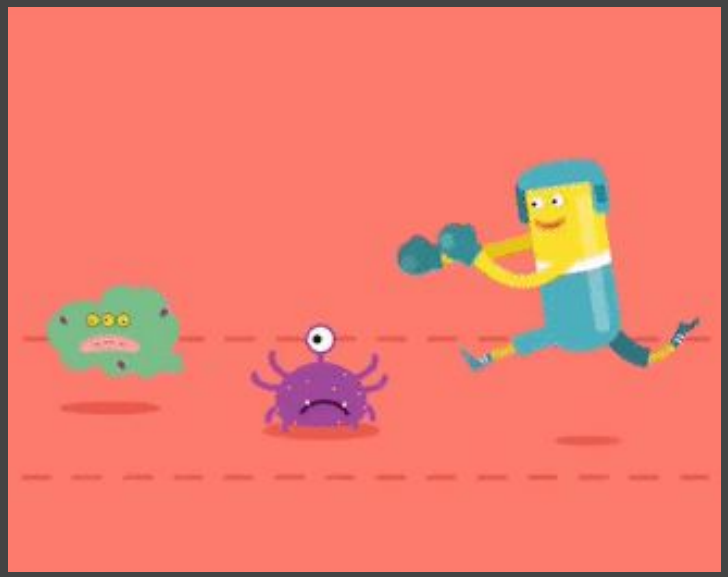
- All NSAIDS : Category C (Affects fetal cardiovascular system)



ANTIVIRALS

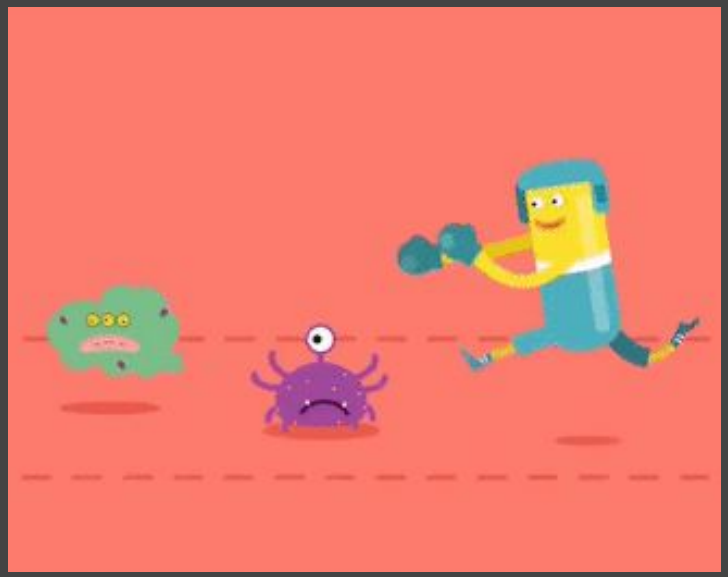
- Topical (Trifluridine & Vidarabine)
  - For the treatment of HSV keratitis
  - Category C (Avoid in pregnancy due to the teratogenic and tumorigenicity effect)
- Oral (Acyclovir & Valacyclovir)
  - For treatment of epithelial corneal diseases
  - Category B (Safer than topicals)

ANTIBIOTICS



- **Erythromycin & Polymyxin B**
  - No known congenital defects
  - Category B
- **Aminoglycosides (**Gentamycin, Streptomycin, Tobramycin, Neomycin)
  - Human studies (Used IV)
    - No teratogenic abnormalities
  - Animal studies: Hearing loss, nephrotoxicity
  - Category C
- **Sulfonamides**
  - Animal studies: Increase of cleft palates and other bone pathologies
  - Human case reports: Hyperbilirubinemia in infants (only when used during the third trimester of pregnancy)
  - Category C

ANTIBIOTICS



- **Fluoroquinolones**
  - Animal Studies of topical (ciprofloxacin, levofloxacin, moxifloxacin, and ofloxacin)
    - No teratogenic effects
  - Animal Studies with high doses
    - Decrease BMI, delayed skeletal development
  - Category C
- **Tetracycline**
  - Human case reports (systemic use)
    - Permanent discoloration of teeth in offspring
  - Category D

THERAPY FOR CHOROIDAL NEOVASCULARIZATION

Verteporfin	Pegaptanib	Bevacizumab	Ranibizumab	Aflibercept
Human Studies: None	Human Studies: None	Human Studies: None	Human Studies: None	Human Studies: None
Animal Studies: Increase anophthalmia and microphthalmia in rat fetuses	Animal Studies: No maternal or fetal abnormalities	Animal Studies: Disrupts angiogenesis in rabbits	Animal Studies: None	Animal Studies: Embryofetal toxicity at systemic exposures
Category C	Category B	Category C	Category C	Category C

Discussions with the Patient

- The clear indications for use
- Relative benefits versus potential risks
  - Birth defects occur in 2.0% or more of all neonates. Drugs used coincidently may be wrongly implicated as contributing to a birth defect
- Conversations must be held with the patient and obstetrician

DOSAGE

- Use the minimal effective dose
- Pick the shortest duration
- Limit systemic absorption of drops
  - Punctal occlusion
  - Eyelid closure
  - Absorb excess medication

OPHTHALMIC OINTMENTS

The safety profile differs from the drops and ointments create a reservoir of the active drug

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Prolonged absorption time

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Reduced serum level of the medication

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May create a lower therapeutic level within the eye

THERAPEUTIC AGENTS

- **Glaucoma Treatments**
  - Prostaglandins
    - Avoid due to effects on uterine contractility
  - Topical Beta Blockers
    - Reported positive and negative for fetal side effects
  - Topical Carbonic Anhydrase Inhibitors
    - Relatively safe after first trimester
  - Propine & Alphagan
    - Category B
    - Avoid use (Reports of apnea and somnolence in neonates)
- **Corticosteroids**
  - Use topically with caution

THERAPEUTIC AGENTS

- **Antibiotics**
  - Erythromycin— Relatively safe
  - Tetracycline—Avoid
  - Fluoroquinolones—Effects unknown
- **Antivirals**
  - Topical (Trifluridine & Vidarabine)
    - Avoid due to tumor formation and teratogenic effect
  - Oral (Acyclovir & Valacyclovir)
    - Relatively safe for treatment of epithelial keratitis
- **Anti-Inflammatory Drugs**
  - Cyclosporine ophthalmic emulsion – Use only if clearly needed
  - NSAIDS – Avoid use in late pregnancy due to cardiovascular system complications in fetuses

NURSING MOTHER

- Dilating Drops
  - Avoid due to infant systemic hypertension
- Fluorescein Dye
  - If the use is necessary, one should stop breastfeeding for hours/days
- Corticosteroids
  - Potentially serious side effects
- Antibiotics
  - American Academy of Pediatrics classified Erythromycin, Gentamycin, Tetracycline & Ciprofloxacin as “Maternal medications usually compatible with breastfeeding”

NURSING MOTHER

- Antivirals
  - Topicals
    - Avoid unless benefit outweighs risk
  - Orals
    - Found in breast milk (use with caution)
- Anti-Inflammatory Drugs
  - Cyclosporine ophthalmic emulsion & NSAIDS
    - Use with caution
- Glaucoma Treatment
  - Propine & Brimonidine
    - Unknown if excreted in breast milk
- Beta Blockers, CA Inhibitors, Pilocarpine, Carbachol, Epifrin, Iopidine, Prostaglandins
  - Discontinue nursing or discontinue drug