

The Ocular Effects of Pregnancy:

- Physiologic changes
- Pathologic changes
- Modifications of pre-existing conditions

Approximate breakdown of a weight gain of 29 pounds:

Baby	8 pounds	Generally, little weight gained during the first trimester of pregnancy <u>~4 lbs</u>
Fat	7 pounds	
Retained H2O	4 pounds	Most of the weight is gained in the second trimester of pregnancy <u>~15 lbs</u>
Blood	3 pounds	
Breasts	2 pounds	
Womb	2 pounds	During the third trimester usually about <u>10 lbs</u> is added
Amniotic fluid	2 pounds	
Placenta	1 pound	

Blood Pressure – May spike, along with Proteinuria

= Pre-eclampsia (~ 8%)

Baby may not gain weight properly, placenta may separate from the wall of the uterus, the mother may be prone to stroke, liver dysfunction, etc.

Urine test – Checks for protein, sugar and bacteria (UTI)

Detailed physical History

- Prenatal blood work CBC
- RPR
- Hepatitis Screen
- Rh
- Sickle Cell
- Immune status for Rubella
- Urinalysis

Pregnancy Hormones and their effects:

- “ Human Placental Lactogen (HPL)
- “ Human Chorionic Gonadotropin
 - “ Estrogen
 - “ Progesterone

Physiologic changes

Intraocular pressure – Decreases in the second half of pregnancy - Weinreb et al described a decrease of 10%

Increase in trabecular meshwork system

Increase in uveoscleral outflow

Decrease in the episcleral venous pressure

The IOP goes back to prepregnancy reading ~ 2 mo postpartum

Physiologic changes

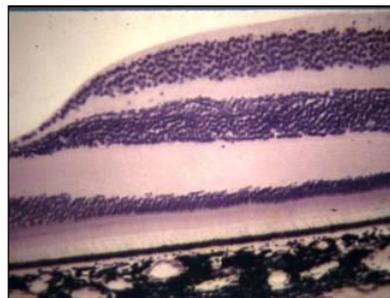
Cornea –

- Decrease corneal sensitivity
- Increase in corneal curvature
- Increase in corneal thickness
- Spectacles should be given after ~ 4 weeks postpartum

Physiologic changes

Refractive Error – Should remain stable during pregnancy

- May see a myopic shift in the last trimester
- Accommodation – may decrease in last trimester
- Night vision changes – may occur if Vitamin A decreased
- Myopia may progress during pregnancy and may present as a worsening of night vision, particularly when driving. Rx returns to normal postpartum



Retina = Blood vessels under Autoregulation

Choroid = Blood vessels under Sympathetic Nervous System

Cardiovascular Changes During Pregnancy:

- Increase in maternal heart rate ~ 20%
- Increase in cardiac output (the product of heart rate and stroke volume) of 30- 50%
- Increase in intravascular volume ~ 50% increase in plasma volume

Pregnancy Induced Hypertension

- Occurs in ~ 5 – 10 % of pregnancies
- Includes both Pre-eclampsia and Eclampsia
- Blood pressure > 140 / 90 or > 160 / 110 after 20 weeks
- Runs in families (3X if mom had it and 2X if mother in law had it)
- Immunological response to the placenta. Woman allergic to placenta
- Risk factors: AA, < 20 or > 40 years of age, multifetal pregnancy

Pre-eclampsia = Hypertension, peripheral edema and proteinuria

Eclampsia = Seizures / coma + pre-eclampsia

Selected Antihypertensive Medications in Pregnancy

- | | |
|-----------------------------------|--|
| • Antiadrenergics | Prazosin HCL (Minipress) |
| • Beta blockers | Propranolol (Inderal)
Atenolol (Tenormin) |
| • Vasodilators | Hydralazine HCL (Apresoline) |
| • Calcium Channel blockers | Nifedipine (Adalat) |
| • Diuretics | HCTZ |
| • ACE inhibitors | Captopril |

Ocular Manifestations Pregnancy Induced Hypertension

- Choroidal ischemia – secondary to the rise in blood pressure
- Serous retinal detachments – linked to elevated serum cortisol
- Acute ischemic optic neuropathy
- Central retinal artery occlusion
- Cortical blindness – most common (15%) lasting 4 hrs – 8 days

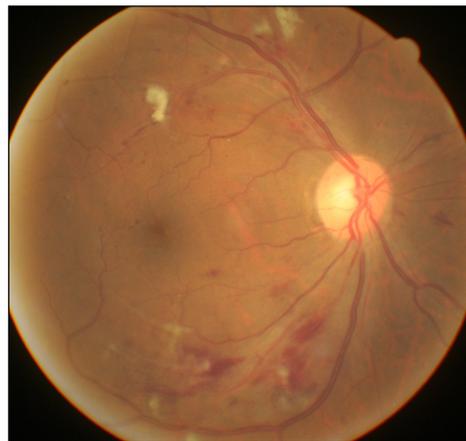
Symptoms of PIH

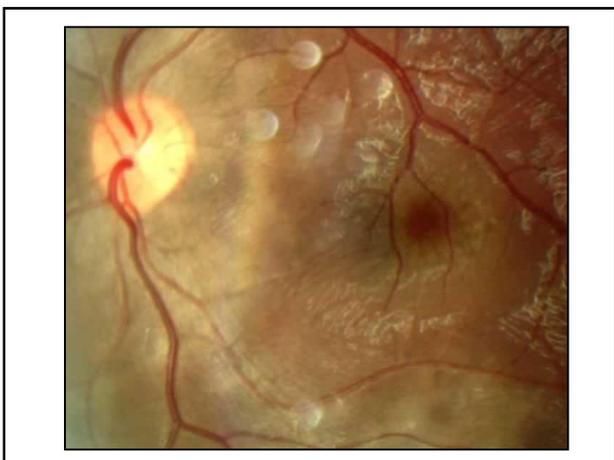
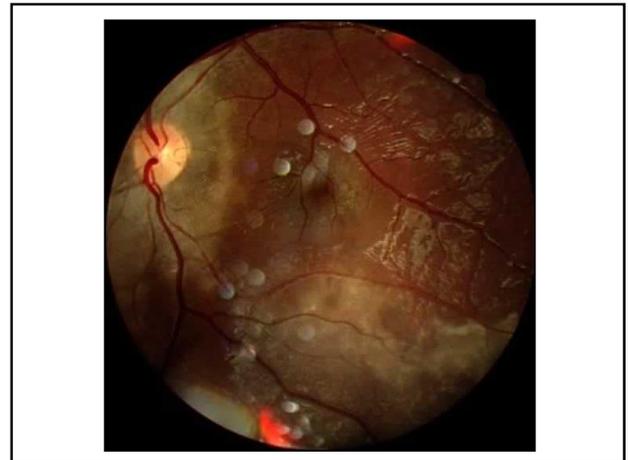
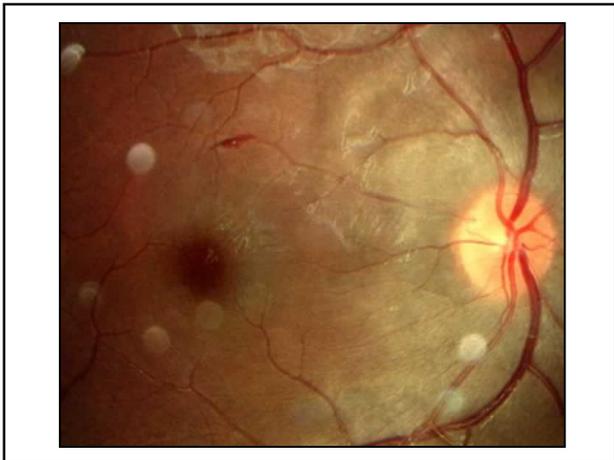
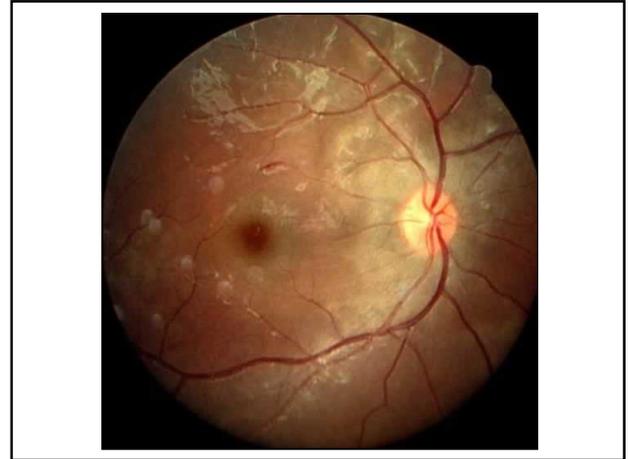
- Blurred vision, photopsia, scotomas

Pregnancy Induced Hypertension (PIH)

Treatment

- Delivery of the baby and management of the Hypertension
- Delivery dependent on gestational age and severity of disease

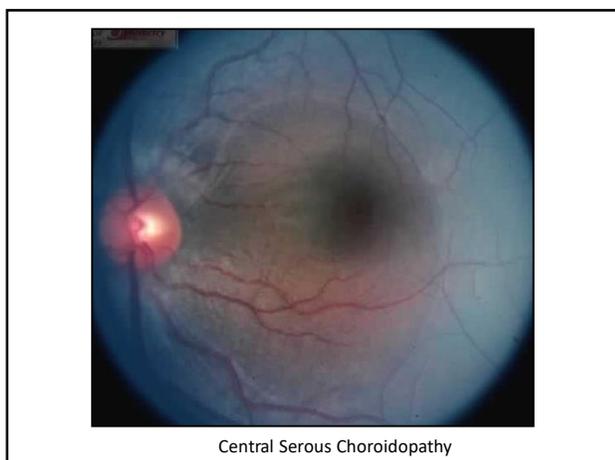
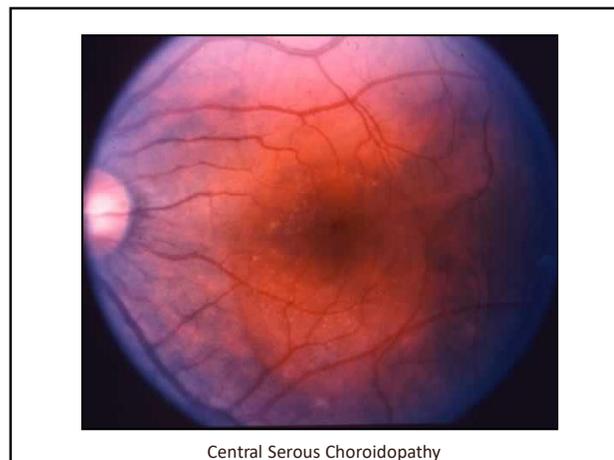
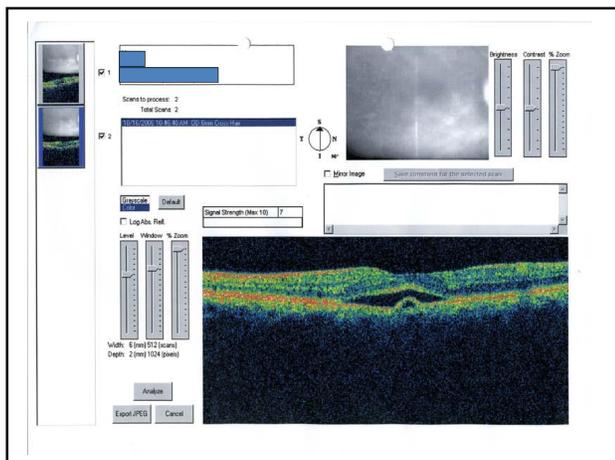
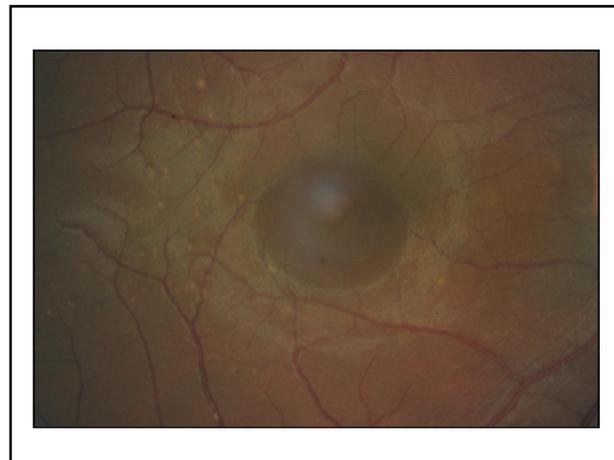
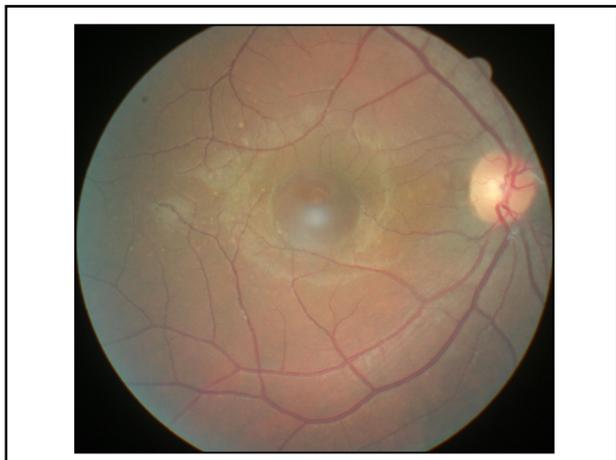




Central serous retinopathy (CSR):

• Can occur at any trimester of pregnancy – more common in 3rd trimester

- The etiology is unknown in pregnancy – hormones may play a role
- Subretinal exudates are more often seen in CSR with pregnancy
- The exudate is fibrin in the subretinal space
- The CSR and fibrin exudate resolve postpartum (1-2 months)
- If CSR episode occurs during pregnancy - may have recurrence after pregnancy or during another pregnancy



Occlusive vascular disorders

- **Amniotic fluid embolism**
 - Occurs during labor, delivery or immediately postpartum
 - Cardiopulmonary, cerebral failure
 - CRAO
- **Disseminated intravascular coagulation**
 - Can occur in pre-eclampsia
 - Widespread thrombus formation
 - Choroid is the most common structure involved
 - Serous retinal detachment
 - RPE changes may occur after resolution of RD
- **Thrombotic thrombocytopenic purpura (TTP)**
 - Thrombus formation, hemolytic anemia, fever and renal dysfunction
 - Retinal vascular occlusions, retinal hemorrhages, serous RD

Pregnancy Complications

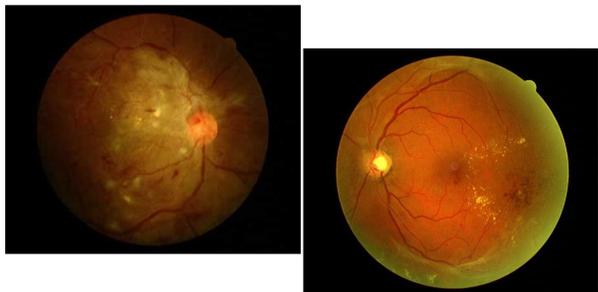
Central Retinal Artery Occlusion



Other Complications:

- HELPP syndrome
- 10% of patients with PIH - HELPP syndrome occurs
- Hemolysis
- Elevated liver enzymes
- Low platelets
- Bilateral serous retinal detachments - yellow white subretinal opacities
- Cortical blindness
- Vitreous hemorrhage
- Poor maternal and fetal outcome

Pre-existing conditions: Pregnancy and Diabetes



- É Follow every 3 months if the patient is diabetic before pregnancy
- Gestational diabetes unlikely to get retinopathy

The Diabetes in Early Pregnancy Study (DIEP)

Women with the greatest reduction in their Hb A1C during the 1st trimester were at increased risk for progression of diabetic retinopathy.

Poor metabolic control at baseline and the largest improvement of Hb A1C = retinopathy was most likely to progress

DIEP showed longer duration of diabetes (> 15 yrs) = Increased risk of PDR

Non proliferative diabetic retinopathy at conception = Increased risk of PDR

All diabetic patients should have a baseline retinal exam during their first trimester

Pregnancy and Diabetes

É Diabetic retinopathy frequently progresses during pregnancy but frequently returns to prepartum status after delivery.

- Monitor these diabetic pregnant patients closely
- American Academy of Ophthalmology guidelines suggest an examination prior to the planning of becoming pregnant
- Exam should then be in the first trimester with monitoring then based on severity of exam findings

Intraocular / intracranial tumors – grow during pregnancy

- Uveal melanoma
- Pituitary adenoma
- Choroidal osteoma
- Meningioma – They may enlarge in the 3rd trimester (hormonal changes)

Pseudotumor Cerebri – May occur at any time during pregnancy
Oral diamox used only after 20 weeks of gestation

Multiple Sclerosis – Attacks decrease during pregnancy
Attacks during pregnancy are less severe than relapses

Ptosis – levator edema induced by estrogen? Will resolve

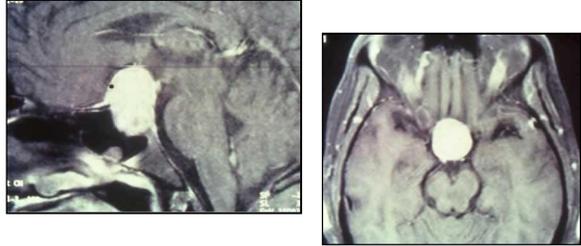
Facial palsy – Viral induced? Third trimester and 2 wks pp

High Myopia - during pregnancy and labor / delivery does not appear to be a risk factor for retinal detachment in patients with peripheral retinal degenerations (lattice, cystic retinal tufts)

Migraine headaches – tend to improve during pregnancy. They tend to return after delivery or during menses post-partum

Pituitary Adenoma

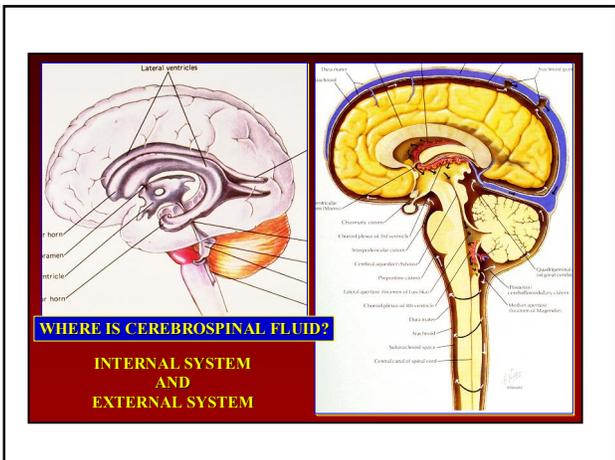
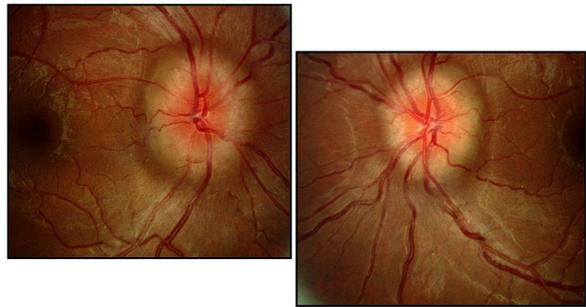
During pregnancy the size of the normal pituitary gland increases up to 136%. Maximum size is after delivery



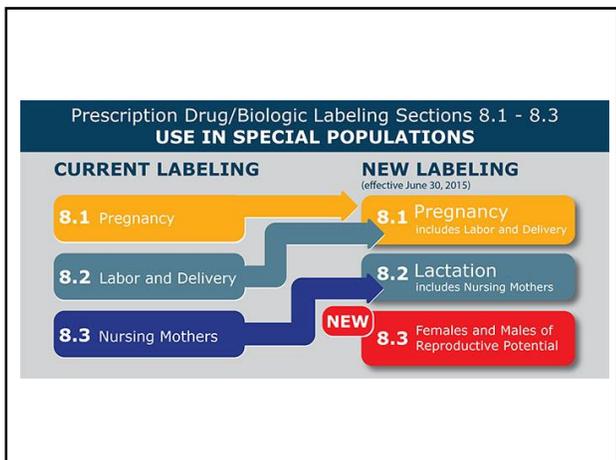
Pseudotumor Cerebri



Pseudotumor Cerebri



- Medications**
- A Adequate, well-controlled studies in pregnant women have not shown an increased risk of fetal abnormalities to the fetus in any trimester of pregnancy.
 - B Animal studies have revealed no evidence of harm to the fetus OR well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus in any trimester.
 - C Animal studies have shown an adverse effect and there are no adequate and well-controlled studies in pregnant women.
 - D Adequate well-controlled or observational studies in pregnant women have demonstrated a risk to the fetus.
 - X The use of the product is contraindicated in women who are or may become pregnant



Medications During Pregnancy

Antibiotics

- Glaucoma meds
- Steroids
- Viral meds
- Diagnostic meds – Avoid during pregnancy

Medications During Pregnancy

Ócular medication during pregnancy is a complicated area

- Most commonly used eye drops are category C drugs and should be avoided during pregnancy
- When drops are given, punctal occlusion is strongly recommended
- Doctors must carefully weigh the risks of discontinuing meds vs. the risk to the fetus if medication use continues

Dr. Trad's guide to using ophthalmic agents during pregnancy and lactation

Category	FDA rating	Use during lactation, other comments
TOPICAL AGENTS		
Anesthetics	C	Use with caution
Diphenhydramine	C	Use with caution
Mydriatic reversal agent: epinephrine	B	Unnecessary to use
Mydriatics/cycloplegics: tropicamide, cyclopentolate, atropine, hydroxyamphetamine/tropicamide	C	Use with caution/routine dilation not advised
Hypertensive agents	C	Use with caution
Antibiotics: gentamicin, moxifloxacin, levofloxacin, ofloxacin, norfloxacin, ciprofloxacin, gentamicin, sulfacetamide, trimethoprim/polymyxin B, bacitracin, neomycin	C	Discontinue drug or nursing
Antibiotics: erythromycin	B	Use with caution/Good safety profile in pregnancy
Antibiotics: tetracycline	D	Discontinue drug or nursing/Do not use in pregnant women
Allergy medications: antazoline, naphazoline, pheniramine, oxymetazoline, tetrahydrozoline, zinc sulfate, olopatadine, pemirolast, ketotifen, epinephrine, naphazoline	C	Use with caution
Allergy medications: emedastine, lodoxamide, nedocromil, cromolyn	B	Use with caution
Antifungals: natamycin	C	Use with caution/Infant risk cannot be ruled out
NSAIDs: ketorolac, bromphenamine, diclofenac, diclofenac (regalac, 0.1% Alcon), ibuprofen (bromphenac 0.09%, Ista)	C	Use with caution/avoid during late pregnancy (third trimester) due to potential effects on fetal cardiovascular system
Antivirals: trifluridine	C	Discontinue drug or nursing
Antivirals (off-label): povidone-iodine	C	Use with caution/Potential off-label use for acute adenoviral infection
Dry eye: cyclosporine	C	Use with caution
Steroids: rimexolone, loteprednol, prednisolone, fluorometholone, dexamethasone	C	Use with caution/Best to discontinue drug or nursing
Glaucoma: brimonidine	B	Discontinue drug or nursing
Glaucoma (beta-blockers): timolol, betaxolol, levobunolol	C	Use with caution/It is best to avoid beta-blockers during the first trimester. If necessary during the last two trimesters, use a 0.25% concentration. Beta-blockers should be discontinued at least 48 to 72 hours prior to delivery. Infants of nursing mothers must be observed for signs of beta-blockade (apnea, bradycardia).
Glaucoma: latanoprost, travoprost, bimatoprost	C	Use with caution
Glaucoma: pilocarpine	C	Use with caution
Glaucoma: dorzolamide, brinzolamide	C	Use with caution

Medications used in pregnancy and lactation must be given with extreme caution. Contact PCP or Ob-Gyn.

- Tropicamide – agent of choice for routine dilation during pregnancy
- Phenylephrine – avoid
- Homatropine – avoid
- Scopolamine – avoid
- Atropine – avoid
- Proparacaine / tetracaine - avoid

Medications

Category	FDA rating	Use during lactation, other comments
ORAL AGENTS		
Antibiotics: erythromycin, azithromycin, cefadroxil, amoxicillin, amoxicillin/clavulanate, cephalexin, cefaclor	B	Use with caution/Infant risk cannot be ruled out
Antibiotics: levofloxacin, clarithromycin	C	Use with caution/Infant risk cannot be ruled out
Antibiotics: sulfamethoxazole/trimethoprim	C	Not recommended for use as potentially nephrotoxic
Antibiotics: tetracycline	Unknown	Contraindicated in pregnant and nursing mothers due to abnormal bone development in the fetus and infant
Antibiotics: doxycycline	D	See "tetracycline"
Analgesics: acetaminophen	Unknown	Risk cannot be ruled out, although found to be largely compatible with lactation
Analgesics: ibuprofen, aspirin	D	Avoid use in nursing mothers/Infant risk cannot be ruled out
Antivirals: acyclovir, famciclovir, valacyclovir	B	Infant risk appears minimal
Steroids: prednisone, methylprednisolone	Unknown	Use with caution/Infant risk cannot be ruled out
Carbonic anhydrase inhibitors: acetazolamide	C	Use with caution/Infant risk cannot be ruled out

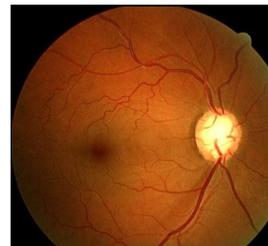
Author's disclosure: The author has attempted, to the best of his knowledge, to present the most accurate available information. However, the author assumes neither responsibility nor liability for incorrect information, changes in drug categorization or practitioner's prescribing habits. It is the responsibility of each prescriber to personally and independently verify any and all information. Source: MJ Trad

É Glaucoma and glaucoma suspects are being detected earlier due to the availability of new diagnostic tools and an increased awareness of the disease.

- The treatment of glaucoma during pregnancy is complicated by the patient's perception that the drugs controlling the IOP may be teratogenic
- Patients older than 35 are routinely informed that their age increases their baby's risk of birth defects and thus the patient may be more concerned about the topical IOP medication
- Most known teratogenic drugs increase the risk of major birth defects by only 1% to 3%

The studies mentioned earlier about IOP reduction during pregnancy did not include pregnant women who had glaucoma

No large studies have evaluated IOP in pregnant glaucoma patients

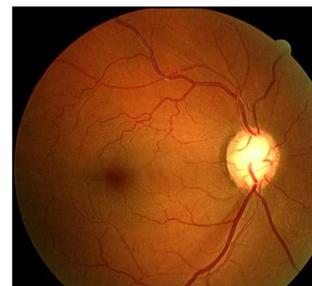


É Harvard Medical School retrospective case series reviewed 28 eyes of 15 pregnant women with preexisting glaucoma

- 13 of 15 patients used glaucoma medications while they were pregnant Beta blockers, alpha-agonists, CAI
- 57 % of the eyes had stable IOP's and visual fields during pregnancy
- 18 % of eyes experienced progressive visual field loss with stable or elevated IOP. 18 % IOP increased, VF stable
- No patients required surgical intervention only additional IOP meds

Conclusion:

- Glaucoma course during pregnancy is variable and close monitoring is needed (VF and IOP checks)



É The FDA has not classified any glaucoma meds as category A

- Because most glaucoma drugs are category C by the FDA physicians are limited to category B (brimonidine and dipivefrin)
- Category B shows no risk to the fetus
- Brimonidine is contraindicated in women who are near term it may cause bradycardia, apnea, and unreponsiveness in neonates and children
- Avoid Category C drugs unless the potential benefit for the pt. justifies the risk to the fetus

É A soft exception to this rule is the use of Beta-Blockers

- Ob-Gyn's use this med orally to control hypertension during pregnancy
- Topical timolol has been associated with fetal and neonatal bradycardia and arrhythmia
- Topical CAI may be used safely. The literature shows no reports of any adverse affects from this class of medications
- Oral CAI's however have shown sacrococcygeal teratoma and transient renal tubular acidosis

Prostaglandin analogues may be considered safe for the use during pregnancy

- Prostaglandins are usually avoided because this class of medication is similar to oxytocin, an agent used to induce labor
- One study observed 11 pregnant women exposed to latanoprost for various lengths of time.
- Investigators found no evidence that the drug posed a risk to the fetus or the course of the pregnancy.

- Physician's Desk Reference
- Web sites (Motherisk, teratogen information system, etc.)
- Obstetricians
- If advanced planning is possible, patients can undergo SLT
- Punctal occlusion to decrease the systemic absorption of the medication ... this may decrease the amount of the drug to which the fetus is exposed to

Neuro-Ophthalmic Conditions Related to Oral Contraceptives

- Pseudotumor Cerebri (rare)
- Hypercoaguable State (transient visual loss)
- Arterial Dissection
- Intracranial Occlusive Disease
- (BCP, HBP, Smoking, Migraines)

Smoking

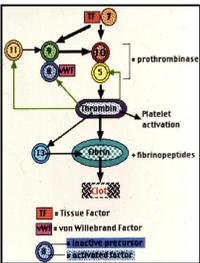
Smoking is a risk factor for proteinuria and increased blood pressure

- Nicotine increases blood platelet viscosity which can increase retinopathy
- Smoking also causes arterial wall damage and constriction




Hypercoaguable State:

- It is a risk factor for artery and venous occlusions
- Has an association with coronary artery disease
- Has an association with cerebral vascular accidents (CVA)
- Hypercoaguable state is associated with peripheral vascular disease



Hypercoaguable State:

During pregnancy many changes in hemostasis are brought about by the estrogen sensitive production of coagulation factors in the liver.

- Thrombus formation is further increased by venous stasis in dependent limbs throughout pregnancy.

Primary Hypercoaguable States

- Protein C deficiency
- Protein S deficiency
- Antithrombin III
- Factor V Leiden
- Hyperhomocysteinemia
- Prothrombin 20210 mutation
- Antiphospholipid syndrome
(Lupus anticoagulant / Anti- cardiolipin antibody)

CBC c differential, Platelet count and PT / PTT

Clinical Features of the Antiphospholipid Syndrome.

Thromboembolism that may be either venous or arterial

- Deep vein thrombosis
- Pulmonary embolism
- Cerebral vascular accident

Autoimmune that is either “primary” or secondary

Hypercoaguable State: Important Note

- **Factor V Leiden** is the most common hereditary blood coagulation disorder in the United States ~10%
- **Prothrombin 20210** mutation is the second most common inherited clotting abnormality in the United States

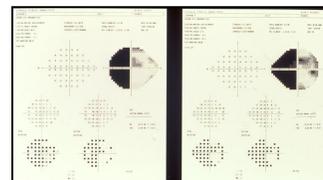
Ophthalmic Presentations:

- Central Retinal Artery Occlusion
- Branch Retinal Artery Occlusion
- Central Retinal Vein Occlusion



Hypercoaguable State: Treatment

- Monitor patient closely with Primary Care Physician
- Coumadin, Heparin, Aspirin therapy
- Treat ocular conditions accordingly



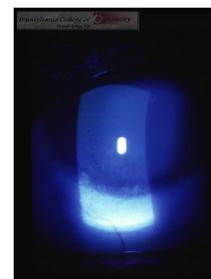
Secondary Hypercoaguable States:

- Pregnancy
- Malignancy
- Congestive Heart Failure
- Immobility

Dry Eye:

Functional Unit Components:

- Ocular surface
- Main lacrimal glands
- Meibomian glands



Neural Reflex Loop

Sensory (afferent) fibers from the cornea and conjunctiva travel along the ophthalmic branch of the trigeminal nerve. Efferent fibers then send messages via the facial nerve (CN 7) to the lacrimal gland

Tear Film

Lipid Layer - produced by the meibomian glands
 Aqueous Layer - made by the main and accessory lacrimal glands
 Mucous Layer - made by the goblet cells of the conjunctiva

Tears contain:

IgA, lactoferrin, lysozyme, and TGF-Beta
 Mucins (cornea) - defend against microtrauma
 Goblet cells (conjunctiva) - defend against microtrauma

Basal Tearing:

Results from continuous stimulation of the corneal surface

Lacrimal gland function:

Influenced by sex hormones. Androgens maintain normal glandular functions and suppress inflammation

Dry Eye:

Dry eye is multifactorial. A deficiency may occur in any one of the three tear film layers.

Autoimmune dry eye = lymphocytes and cytokines invade

Non-autoimmune dry eye = loss of neural tone leads to gland atrophy and immune response

Etiology:

- Idiopathic
- Collagen Vascular Disease (Sjogren's, RA, Lupus)
- Diabetes, Reduced levels of androgens (female patients, older age)
- Drugs (BCP, antihistamines, phenothiazines, antihypertensives)
- Lacrimal gland disease (sarcoidosis, lymphoma, tumor, etc.)
- Surgery (Lasik, PRK)
- Environmental (Low humidity, poor air quality, poor ventilation)
- Conjunctival scarring (chemical burn, Stevens-Johnson syndrome)

Dry Eye:

How Omega 3 Fatty Acids Benefit the Dry Eye Patient:

- Decrease inflammation
- Alter lipid tear layer
They produce lipid layer of tear film
- Stimulate Tear secretion
Prostaglandin E1 increases aqueous production

Sexually Transmitted Diseases

• Syphilis

- Chlamydia
- Cytomegalovirus
- Gonorrhea
- Hepatitis B
- Herpes (HSV / HZV)
- HIV