Caring for the Pregnant Patient

Caroline B. Pate, OD, FAAO
Associate Professor
UAB School of Optometry
Birmingham, AL
cbeesley@uab.edu

Another Baby “boom”?
- 6.5 million pregnancies in the US each year
- 1 out of 10 women of childbearing age is pregnant each year
- How do you identify these patients in your practice?

Still newsworthy?
- Feb 1, 2016, the WHO declares “a public health emergency of international concern”
- Symptoms: joint pain, fever, rash, headache, conjunctivitis

Zika virus transmission in pregnant women linked to microcephaly
- July 22, 2016 – 1st baby in US born with zika-related microcephaly

What we want to know...
- If a woman is infected during pregnancy, how likely is it that the virus will affect her or her pregnancy?
- How likely is it that the virus will be passed to the fetus?
- How likely is it that the fetus, if infected, will have birth defects?
- When in pregnancy the infection might harm the fetus?

CDC Report, 2017
- In the US states, 2 in 25 (8%), pregnant women with symptoms of Zika virus infection had a baby with Zika-associated birth defects, compared with 3 in 25 (12%) pregnant women without symptoms of Zika virus infection.
- In US states, about 4 in 25 (15%) pregnant women with confirmed Zika virus infection in the first trimester had babies with Zika-associated birth defects.
2016 - 5,102 symptomatic Zika cases reported in US
2017 - 278 symptomatic Zika cases reported in US
2018 - 21 symptomatic Zika cases reported in US, all from travelers returning to US from affected areas
From 2015-2018...Pregnant women in US with lab evidence of Zika: 2,441

What pregnant patients need to know....
1. Greatest risk is in the first trimester of pregnancy
2. Pregnant patients should consider avoiding/postponing travel to affected areas
3. Take proper precautions to prevent mosquito bites
4. Zika can be sexually transmitted via infected partners
5. There is no vaccine or medicine for Zika

Ocular abnormalities reported in babies born to Zika-infected mothers
- Focal pigment mottling of the retina
- Optic nerve abnormalities
- Chorioretinal atrophy
- Optic nerve atrophy
- Cataract
- Lens subluxation
- Iris coloboma
- Asymmetrical eye size
- Intraretinal calcifications
- Foveal reflex loss
- Severe ONH cupping
- Optic nerve hypoplasia/double ring sign
- Vascular changes
- Retinal hemorrhages

Pregnancy and the Eye
- Physiologic and pathologic changes
  - Most often transient, but some can be permanent
  - Can develop new conditions, or exacerbate pre-existing conditions
- Pharmacologic considerations for the pregnant patient
Physiologic Changes

Lid/External

- **Ptosis**
  - Can be unilateral
  - Must rule-out underlying neurologic entity
  - Due to fluid retention — advise to sleep in propped up position

- **Chloasma**
  - “Mask of Pregnancy”
  - Hormone mediated - steep rise in estrogen levels stimulates melanocytes
  - Generally fades post-partum

Skin cancer more deadly when caught during pregnancy...

Corneal Changes

- **Krukenberg spindle**
  - 3%
  - No other signs of pigment dispersion
  - No iris transillumination
  - Normal angle pigmentation
  - Decrease in size during the 3rd trimester and postpartum

Skin cancer more deadly when caught during pregnancy...

Corneal Changes

- ↑ thickness
- ↑ curvature
- ↓ sensitivity
- ↓ tear production
  - Upwards of 80% of pregnant patients report dry eye symptoms
  = temporary refractive changes & contact lens intolerance

Refractive Changes

- Transient – typically returns to normal within the first few months postpartum
- Due to hormonal changes and water retention in cornea and lens
- Typically myopic shift ~1D or less
- Most common complaint: difficulty driving at night
- Refractive surgery contraindicated
- Accommodative changes also possible
Intraocular Pressure

- Decreased IOP, particularly during the second half of pregnancy
  - Normals ↓ 19.6%
  - Ocular Hypertensives ↓ 24.4%
  - Persists several months postpartum
- Influenced by hormones
  - Increased uveoscleral outflow
  - Decreased episcleral venous pressure

Optic Nerve/Pathway

- Normal pituitary gland enlargement during pregnancy
  - Weight increases by 30%, 2x volume
  - Can cause visual field changes, many asymptomatic
  - Returns to normal 1-2 weeks postpartum
- Prolactinoma – most common functioning tumor in pregnant patient
  - Macroadenomas (>10mm) more likely to have clinically significant tumor growth during pregnancy as compared to microadenomas (<10mm)
  - Monthly VF needed to monitor for changes

Pathological Changes

- Central Serous Retinopathy
  - Although 10x more common in males, CSR has a strong association with pregnancy
  - Current or past pregnancy increases risk of developing CSR by 7x in females
  - More often associated with subretinal fibrinous exudates (90%) than in non-pregnancy related CSR (17% males, 0% non-pregnant females)
  - Can occur during any trimester
- Tx: observation
  - Typically resolves on own 1-2 months after delivery

32 yo AA F
7 months pregnant
CC: 3 day history of blurring with greenish discoloration of her central vision OS
VA OS: 20/70

New Eng J Med 2005
### Pregnancy-induced Hypertension (PIH)

- 5% of all pregnancies
- Typically occurs after 20th week of pregnancy
- Can be life threatening to both mother and child
- Symptoms: Headache, sudden weight gain, stomach pain/vomiting, visual disturbances
  - Blur, photophobia, scotoma, diplopia
- Pre-eclampsia = Hypertension (>140/>90) + proteinuria (>300mg/day)
- Eclampsia = Pre-eclampsia + seizures

### Risk factors for pre-eclampsia

- 1st pregnancy
- Young/old maternal age
- Multi-fetal pregnancy
- Pre-existing vascular disease (e.g., diabetes)

### Ocular manifestations of PIH

- PIH can cause hypertensive retinopathy
  - 60% of patients
- Most common retinal abnormality seen in preeclampsia is focal arteriolar narrowing
- Serous retinal detachments (1% pre-eclampsia; 10% eclampsia)
- Cortical blindness (up to 15%)

### Ocular manifestations of PIH

- Vision loss should be considered a symptom of impending eclampsia in patients with pre-eclampsia
  - Especially if preceded by severe headache
  - Immediate referral to OBGYN/PCP
- Most ocular abnormalities improve with medical management of PIH or with delivery of the fetus

### How Does Diabetes Affect the Pregnant Patient?

- Increased risk of miscarriage, birth defects
- Increased size/weight of infant
- Higher risk of complications during/after delivery

- Blood sugar goals (ADA):
  - Pre-prandial/Overnight: 60-99mg/dl
  - Post-prandial: 100-129 mg/dl
  - A1C: <6%
- Monitor blood pressure closely

Diabetes

- Progression of diabetic retinopathy is influenced by:
  - Duration of diabetes (Type I vs. Type II)
  - Metabolic control before and during pregnancy
  - Coexisting hypertension or preeclampsia
  - Severity of retinopathy at conception

- Gestational diabetes does not increase the risk of diabetic retinopathy during pregnancy
  - 35% risk of developing Type 2 diabetes within 5 years

How Does Diabetes Affect the Pregnant Patient?

- Increased risk of development or progression of diabetic retinopathy
  - Exact mechanism unknown
  - Usually mild, temporary
  - Regression to normal several months post-delivery
  - Grading is the same as for non-pregnant patients

- Increased risk of macular edema
  - With or without proliferative retinopathy
  - Postpartum regression
  - May not resolve
  - Possible long-term vision loss

Severity of diabetic retinopathy at conception matters....

- Diabetes in Early Pregnancy Study
  - Chew EY et al. Diabetes Care 1995

<table>
<thead>
<tr>
<th>Level of retinopathy at baseline</th>
<th>Disease progression during pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Retinopathy</td>
<td>10.3%</td>
</tr>
<tr>
<td>Microaneurysms only</td>
<td>21.1%</td>
</tr>
<tr>
<td>Mild NPDR</td>
<td>18.8% (6.3% to proliferative)</td>
</tr>
<tr>
<td>Moderate NPDR</td>
<td>54.8% (29% to proliferative)</td>
</tr>
</tbody>
</table>

Treatment

- Based on same criteria as non-pregnant patients
- Diabetic macular edema is often observed – regression is common post-partum
- Insufficient information on safety of anti-VEGF use for proliferative changes in pregnancy
  - Benefits vs. Risks
  - Increased risk for progression continues up to 1 year post-partum \(\rightarrow\) careful monitoring important!

Intravitreal Anti-VEGF in Pregnancy

- Based on same criteria as non-pregnant patients
- Diabetic macular edema is often observed – regression is common post-partum
- Insufficient information on safety of anti-VEGF use for proliferative changes in pregnancy
  - Benefits vs. Risks
  - Increased risk for progression continues up to 1 year post-partum \(\rightarrow\) careful monitoring important!

The unfortunate combination

26yo AAF, LEE 2 years ago, 34 weeks pregnant
Pre-eclampsia x 4 months. Hospitalized with BP 200/110
Type I DM since age 7. Prior to hospitalization, BS 300-400's.
Macular edema is more common in women with diabetes AND preeclampsia.

When to dilate a pregnant diabetic?

- Updated AOA Clinical Practice Guidelines
- Ideally – dilated exam before conception to establish baseline/risk
- Once per trimester if minimal - no retinopathy
  - Mild-moderate retinopathy – every 4-6 weeks, if progression noted, then every 2 weeks
- Fundus photography
- Refer for treatment of proliferative retinopathy or macular edema
- Retinopathy counseling

25yo AAF, 24 weeks pregnant

- CC: blur and headaches (taking Tylenol 4x/day)
- Type 1 DM x 14 years (HbA1c 7.5%)
- BCVA: 20/25 OD; 20/30 OS
  - 1D myopic shift noted OU
- BP: 124/74
- SLE: 1+ diffuse SPK, TBUT 2 seconds

ICD-10

- Supervision of pregnancy with poor obstetric history
  - O09.291 – 1st trimester
  - O09.292 – 2nd trimester
  - O09.293 – 3rd trimester
- Unspecified pre-existing DM in pregnancy
  - O24.311 – 1st trimester
  - O24.312 – 2nd trimester
  - O24.313 – 3rd trimester
  - O24.319 – unspecified trimester
- Gestational diabetes mellitus in pregnancy
  - O24.410 – diet controlled
  - O24.414 – insulin controlled
Prescribing for the Pregnant Patient

When needing to prescribe during pregnancy

- **Choosing a medication**
  - Try to select medication that is category A or B if possible
  - Category C if benefit outweighs the risk
  - Avoid categories D and X

- **Dosage of medication**
  - Shortest treatment course necessary to take care of patient’s problem
  - Prefer topical therapy vs. oral therapy when possible
  - Utilize/teach punctal occlusion

FDA Safety Categories (1979-2015)

- **Category A** – strong evidence of safety based on human studies
- **Category B** – no fetal risk in animal trials, but no adequate studies have confirmed or denied risk in humans; generally accepted as safe
- **Category C** – evidence of risk in animals, but few to no studies available in humans; prescribed when benefit justifies the potential of risk
- **Category D** – evidence of risk to human fetus shown in studies; only used in severe disease where safer drugs cannot be used or have not been effective
- **Category X** – strong evidence of birth defects in humans; risks outweigh benefits; DO NOT prescribe
FDA Update – Effective June 30, 2015

Pregnancy and Lactation Labeling Rule (PLLR)
- Required for prescription drugs submitted after June 30, 2015
- Gradual phase-in of prescription drugs approved on or after June 30, 2001
- Advantages:
  - Will make the prescriber and the patient more informed
  - Addresses timing of exposure during specific trimesters
  - Addresses the lack of widespread data on many medications
  - Will not become dated as new data is discovered
  - Pregnancy Exposure Registries

BromSite®
- Approved 4/11/2016
- Sun Pharma
- 0.075% bromfenac
- BID
- Vehicle: Durasite
- BAK
- Rx: to prevent pain and treat inflammation in cataract surgery

LactMed
- US National Library of Medicine
Keep in mind….

- 64% of women use at least 1 prescription drug during pregnancy
- Average of 3 prescription drugs during pregnancy
- Despite uncertain safety, nearly ½ of prescription drugs used during pregnancy are category C, D, and X (4.6%)


Majority of severe birth defects are not due to drug side effects but to genetic or chromosomal abnormalities
- Most teratogenic birth defects are due to alcohol, illicit drugs, or ineffective teratogens and not the use of OTC or FDA approved medications
- The risk of birth defects resulting from topically applied medications is extremely low
- Very little published data on use of topical ophthalmics on pregnant/nursing mothers


Dilation

- No literature against topical mydriatics supporting damage to the fetus/resulting in miscarriage
- Occasional dilation okay, repeated should be only when absolutely necessary
- Tropicamide/cyclopentolate safest options
- Avoid longer duration parasympathomimetics due to increased half-life (atropine, scopolamine, homatropine)
- Avoid phenylephrine unless unable to dilate with tropicamide alone
  - 2.5% preferred over 10%

Diagnostic Agents

- No known side effects of fluorescein or topical anesthetics
- IVFA
  - Dye crosses placenta and is present in breast milk for at least 76 hours after administration
  - Study of 105 pregnant patients that received IVFA → no increase in rate of birth anomalies or complications (Halperin et al)
  - Typically postponed unless absolutely necessary for sight-threatening condition

Oral Antibiotics

- Broad spectrum coverage for soft tissue infections of lid/adnexa
- Category B
  - Augmentin
  - Erythromycin
  - Azithromycin
  - Amoxicillin
- AVOID:
  - Tetracycline, Doxycycline
  - Fluoroquinolones

Topical Antibiotics

- Tobramycin – Category B
- For less severe infections or prophylaxis:
  - Erythromycin
  - Polymixin B
  - Azithromycin
- Use of topical fluoroquinolones has not been well studied
- Benefits >> Risks
- Fortified cephalosporin (cefazolin, ceftriaxone) good options for severe infections
38yo AAF, 12 weeks pregnant

- Overwear of RGP lenses (1 year without removal)

Image courtesy of Christopher Kruthoff, OD OMNI Eye Services of Atlanta

Pain Management

- AVOID Aspirin, NSAIDS
- Acetaminophen may or may not give necessary relief
  - Short term pain relief with:
    - TYLENOL #3 (acetaminophen + codeine) (category C)
    - Consult with patient’s OB/GYN during pregnancy
    - Not recommended when breastfeeding
    - Vidodin (acetaminophen + hydrocodone) (category C)
    - Consult with patient’s OB/GYN during pregnancy/breastfeeding

Antivirals

- Herpes Simplex recurrences during pregnancy more likely
- Orals often used in pregnant and lactating women to prevent genital outbreaks
  - Acyclovir
  - Valacyclovir
  - Famciclovir
  - Topicals – Category C
    - Viroptic
    - Zirgan

Dry Eye

- 80% of pregnant patients experience some form of dry eye symptoms
- Restasis – Category C
- Recommend increased non-preserved artificial tears, gels, ointments
- Punctal plugs
- Caution with flax/fish oils – discuss with OB/GYN

Ocular Allergies

- Up to 40% of US population at some point in their life will be affected by ocular allergies
- Non-Rx treatment options:
  - Cold Compresses
  - Avoidance of allergen
  - Preservative-free AT’s
- Category B:
  - Crolom/Opticrom
  - Alomide
  - Alciclair
  - Emadine
  - Lastacaft
- Category C:
  - Pataday
  - Patzoe

Ocular Steroids

- Typically have low systemic absorption when topically prescribed
- Benefits>>Risks
- Category C:
  - Lotemax
  - Alrex
  - Pred Forte
  - Durezol
- Check with OB/GYN prior to prescribing oral steroids
Glaucoma

- IOP typically decreases during pregnancy
- Brimonidine (Alphagan) is the only ocular hypotensive that is Category B
  - Should be avoided during lactation – can induce apnea and CNS depression in breastfed infants
- Oral CAI’s contraindicated
  - Topicals? - best to avoid
- Oral prostaglandins are used to induce labor
  - Topicals? – best to avoid
- Surgical options (SLT, ALT) if medications are not controlling IOP

In Summary

- Every pregnancy is unique and different
- Ask about pregnancy in patient history!
- Most ocular changes in pregnancy are physiologic and reversible
- Consider benefits vs. risks when exploring pharmaceutical treatment
  - Review with patient and document in record
  - Nasolacrimal duct occlusion
  - Consult OBGYN/PCP if uncertain