Complex Medical Problems?  
Complex Contraception  
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Objectives  
• Identify contraceptive options for an adolescent with  
  – Thrombophilia  
  – Diabetes  
  – SLE  
  – Migraines  
  – Epilepsy  
• Effectively counsel a patient on the use of progestin only methods of contraception in these specific situations  

Contraception for a Female with a Thrombophilia  
A 18 year old female presents to your office requesting birth control.  
On history she states that her mother recently had a pulmonary embolism and her aunt had a DVT. She would like to know what she can use for birth control.  
She has been on the combined oral contraceptive pill in the past and would like to go back on this.
Risk of VTE

- Heterozygous prothrombin gene mutation:
  - 2-3x increase risk
- Factor V Leiden
  - Heterozygous Factor V Leiden (FVL):
    - 5-7x increase risk (5.7/10,000/year)
  - FVL + COC: 15-30X (28.5/10,000/yr)

Key Point

- Having a known thrombophilia increases the risk of developing a VTE
- Certain thrombophilias have a greater risk of VTE
- Being on the COC may further increase the risk of VTE in patients with a known thrombophilia (15-30X risk if FVL + COC)


Key Point

- Thrombophilia screening is indicated in women with a personal or family history of VTE
- Screening of asymptomatic women is not recommended because it is not cost effective
  - Screen 20,000 women → prevents 1 episode VTE
  - Screen 2 million women → prevents one death from pulmonary embolism

Fertility and Sterility 1999;72(4): 646-651
BMJ 1996; 313(7065):1127-1130
**Thrombophilia Screen**

- Factor V Leiden
- Prothrombin gene mutation
- Protein C
- Protein S
- Antiphospholipid antibodies: Lupus anticoagulant + anticardiolipin antibodies
- Homocysteine
- Antithrombin III
- Factor VIII
- Consult your local hematologist

**Key Point**

- Progestin only methods (DMPA, POP) do not appear to increase the risk of VTE
- Whether the use of progestin-only methods in women with a proven thrombophilia alters the risk of VTE is not known
- Other options include the intrauterine device, barrier methods, spermicides.

**Risk of VTE**

<table>
<thead>
<tr>
<th>Population</th>
<th>Risk of VTE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(per 100,000 women/year)</td>
</tr>
<tr>
<td>General population</td>
<td>5</td>
</tr>
<tr>
<td>Age 20-24</td>
<td>3</td>
</tr>
<tr>
<td>Age 45+</td>
<td>6</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>60</td>
</tr>
<tr>
<td>Pregnancy + Post-partum</td>
<td>1/10,000 deliveries</td>
</tr>
<tr>
<td>OC</td>
<td>15-20</td>
</tr>
</tbody>
</table>


Contraception for a Female with Epilepsy

A 13 year old female presents to your office with her family. On history, she has a long standing history of seizures and is on Gabapentin. Her mom would like to suppress her periods as they are interfering with her ADL.

Contraception and Epilepsy

- Some anti-epileptic drugs
  - Induce hepatic microsomal enzymes
  - Increase estrogen metabolism and progesterone’s protein binding
  - Decreased hormone concentration and decreased efficacy
  - The 3 P’s: Phenytoin, Primidone, Phenytoin
- Concurrent use of hormonal contraception and AEDs doesn’t adversely affect seizure control

AEDs and Contraception

- Enzyme inducing AEDs
  - Carbamazepine, felbamate, oxcarbazepine
  - Phenobarbital, phenytoin, primidone, topiramate
- Enzyme inhibiting AEDs
  - VPA, zonisamide
- AEDs that have no effect
  - Gabapentin, lamotrigine, levetiracetam, pregabalin
  - Tiagabine, vigabatrin
Contraceptive Options for Epilepsy

- Combined hormonal contraception (pill, patch, ring)
  - If she is taking an AED that induces hepatic enzymes, consider 50 mcg OC
- Depot Medroxyprogesterone Acetate (DMPA)
  - May reduce seizure frequency
  - May need to decrease dosing interval if she is taking an AED that induces hepatic enzymes
- Condoms
- Folic acid supplements

Depot Medroxyprogesterone Acetate (DMPA)

- Used since 1967 as a contraceptive agent
- MPA 150 mg intramuscularly every 12 weeks
- Mechanism of action:
  - Inhibits ovulation
  - Increases viscosity of cervical mucus
  - Endometrial atrophy
- Efficacy:
  - Typical use = (approx) Perfect use
  - As effective as female sterilization

Injectable Progestins: Non contraceptive Benefits

- Estrogen free
- Scanty menses or amenorrhea
- Decreased menstrual cramps
- Suppression of mitschmext
- Decreased risk of endometrial cancer
- Management of endometriosis associated pain
- Improvement in luteal phase disorders
- Heightens seizure threshold
DMPA

• Contraindications
  • Pregnancy
  • Liver dysfunction
  • Breast cancer

• Advantages:
  • No estrogen
  • Less compliance demanding
  • Amenorrhea (may be desirable state)
  • Decreased risk of endometrial cancer
  • Fewer seizures

DMPA: Concerns

• Irregular bleeding
  • Frequent in first 3-6 months
  • 55% amenorrheic at 12 months
  • 70% amenorrheic at 24 months

• Return to fertility
  • 9 month delay in restoration to full fertility

• Weight
  • Average weight gain at one year = 5 pounds

• Bone density

Key Point

• Menstrual irregularities are a common side-effect of DMPA use
• No proven effective management strategy other than time
• Rates of amenorrhea are high:
  • 55% after 12 months
  • 68% after 24 months
  • >75% of long term users are amenorrheic
DMPA: Bone Density

<table>
<thead>
<tr>
<th>Type of Study</th>
<th>Authors, Year</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level I</td>
<td>Berenson, 2001</td>
<td>Decrease (-2.74%)</td>
</tr>
<tr>
<td>Level II-1</td>
<td>Naessen et al, 1995</td>
<td>No effect</td>
</tr>
<tr>
<td></td>
<td>Blair et al, 1995</td>
<td>Decrease</td>
</tr>
<tr>
<td></td>
<td>Cromer et al, 1996</td>
<td>Decrease</td>
</tr>
<tr>
<td></td>
<td>Scholes et al, 2005</td>
<td>Decrease BMD effects reversible</td>
</tr>
</tbody>
</table>

Level II-2

<table>
<thead>
<tr>
<th>Type of Study</th>
<th>Authors, Year</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cohort or Case Control</td>
<td>Scholes, 2002</td>
<td>- Decrease (0.87-1.12%)&lt;br&gt;- Reversed when discontinued</td>
</tr>
<tr>
<td></td>
<td>Busen, 2003</td>
<td>- Decrease (0.25%)</td>
</tr>
<tr>
<td></td>
<td>Lara-Torre, 2004</td>
<td>- Decrease (3.01-6.81%)</td>
</tr>
<tr>
<td>Cross Sectional</td>
<td>Cundy et al, 1991</td>
<td>- Decrease (6.6-7.5%)</td>
</tr>
<tr>
<td></td>
<td>Vitaranasen, 1994</td>
<td>- No change</td>
</tr>
<tr>
<td></td>
<td>Cundy et al, 1996</td>
<td>- No change</td>
</tr>
<tr>
<td></td>
<td>Paiva et al, 1998</td>
<td>- Decrease (4.9%-7.4%)</td>
</tr>
<tr>
<td></td>
<td>Scholes et al, 1999</td>
<td>- Decrease (3.1-3.3%)</td>
</tr>
<tr>
<td></td>
<td>Tang et al, 1999</td>
<td>- Decrease (0.8%-2.3%)</td>
</tr>
<tr>
<td></td>
<td>Scholes et al, 2004</td>
<td>- No significant difference</td>
</tr>
</tbody>
</table>

Bone Density

- FDA Warning 2004
- Unpublished data submitted to FDA
- Prospective controlled study
  - Adult Woman
    - Spine and hip BMD decreases of 5-6%
    - Decline most pronounced in first 2 years
    - Partial recovery of BMD when DMPA stopped
  - Adolescent Women
    - Spine and hip BMD decrease of 4.7%
    - 153 women at 1 year, 9 women at 5 years
    - Partial recovery of BMD in 2 years post-use
SOGC: Key Recommendations

• Healthcare providers should inform patients of the potential effects of Depo-Provera™ on bone-mineral density and counsel them on “bone health”, including calcium and vitamin D supplements, smoking cessation, weight-bearing exercise, and decreased alcohol and caffeine consumption.

• Endorse the World Health Organization recommendation that “there should be no restriction on the use of DMPA; including no restriction on the duration of use, among women aged 18 to 45 who are otherwise eligible to use the method”.

SOGC: Key Recommendations

• The overall risks and benefits of continuing DMPA use should be discussed with DMPA users at intervals throughout the course of treatment.

• Current evidence does not support performing routine BMD testing in DMPA users.

Key Point

• DMPA use is associated with a decrease in bone mineral density (BMD) (Level I to II-3)

• This decrease appears to be reversible once DMPA is discontinued (Level II-2)

• Supplemental calcium or estrogen may help to attenuate the loss in BMD (Level I)

• Risks of decrease in BMD must be weighed against risk of unintended pregnancy.
DMPA: How to manage bleeding

- First 6:
  - Reassurance
  - Patience
- At 6 months:
  - Rule out medical conditions
  - Increase dose to 225-300 mg IM for 2-3 injections
  - Decrease dosing interval
  - Estrogen orally:
    - Premarin 0.625 - 1.25 mg PO x 28 days
    - Estrace 1-2 mg PO x 28 days
  - Estrogen patch
    - 17 beta-estradiol 50-100 mg x 25 days
  - NSAIDs
    - Ibuprofen 400-800 mg bid for 10 days, repeat prn

DMPA: Late for Injection

- <14 weeks:
  - Give the injection
- >14 weeks:
  - If no intercourse within the last 10 days:
    - bHCG
    - Give injection if bHCG is negative
    - Back-up method for 2 weeks
  - If intercourse within the last 10 days:
    - bHCG
    - Give injection if bHCG is negative (not teratogenic!)
    - Back-up method for 2 weeks
    - Repeat bHCG in 2 weeks

An adolescent with headaches

A 17 year old female presents to your office for birth control. She complains of occasional headaches on a monthly basis.

She has been in a relationship for the last 3 months and they are using condoms.
Characterize the headache

- Tension Headache
- Migraine Headache
- Menstrual Migraine

Menstrual Migraines

- 2-3 days pre menstrual
- Lasting through period
- NO other times of the month
- Occurs in 7-8% of all migraine sufferers
- 35% of current migraine sufferers report increase intensity during menstruation

Migraines

- Occurs frequently in adolescent females
- Focal neurological symptoms can be present
- Triggers include:
  - hormonal changes
  - stress
  - food, beverage
  - scents, fumes
  - fatigue
  - hunger
  - trauma

<table>
<thead>
<tr>
<th>Atypical aura</th>
<th>Typical aura</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Onset and progression</strong></td>
<td></td>
</tr>
<tr>
<td>Sudden, unilateral</td>
<td>Slow, progressive over a few minutes</td>
</tr>
<tr>
<td><strong>Duration</strong></td>
<td></td>
</tr>
<tr>
<td>&gt; 30 to 60 minutes</td>
<td>&lt; 30 to 60 minutes</td>
</tr>
<tr>
<td><strong>Headache</strong></td>
<td></td>
</tr>
<tr>
<td>Present or absent</td>
<td>Aura precedes migraine</td>
</tr>
<tr>
<td><strong>Visual symptoms</strong></td>
<td></td>
</tr>
<tr>
<td>Negative:</td>
<td>Positive:</td>
</tr>
<tr>
<td>- loss of vision</td>
<td>- Bilateral scintillating scotoma</td>
</tr>
<tr>
<td>- amaurosis fugax</td>
<td>- Fortification spectra</td>
</tr>
<tr>
<td>- visual field anomaly</td>
<td>- Blurred vision</td>
</tr>
<tr>
<td><strong>Sensory and motor symptoms</strong></td>
<td></td>
</tr>
<tr>
<td>including lower limbs, anesthesis, hypoesthesia</td>
<td>Often related to visual symptoms</td>
</tr>
<tr>
<td></td>
<td>Upper limbs, mouth, tongue</td>
</tr>
<tr>
<td></td>
<td>Tingling, pinching</td>
</tr>
</tbody>
</table>

**Migraines with Aura**

Can be
- visual
- sensory – tingling or numbness
- motor – parasthesia
- reflective of brainstem involvement
  - vertigo, diplopia
- cerebral cortex (aphasia) involvement

**Migraines**

The following DO NOT constitute AURA:
- Photophobia
- Phonophobia
- Nausea, vomiting
- Visual blurring
- Generalized visual spots/flashing lights

ACOG Practice bulletin, clinical management guidelines for Obstetricians-Gynecologists, 115(6), June 2006; 1453-1460.
Biller, J et al. Practical Neurology. 2002
Women with Migraines with Aura: Increased Risk of CVA

- Most studies have noted a higher risk of strokes in women who have migraine with aura than in those who have migraine without aura
- Migraine history + OC use + smoking synergistic re stroke risk

Migraines and contraception
- No contraindication to using a progestin alone
  - Mirena®
  - Depo-Provera®
- Typical aura less than 1 hour is a relative contraindication to CHC

Contraceptive Options
- Migraines without aura
  - OC, patch, ring
  - DMPA
  - IUD or LNG-IUS
  - Condoms
- Migraines with aura
  - Combined hormonal contraception usually contraindicated
  - Exception: visual scintillations <1 hour
- Migraines during pill free interval
  - Extended cycle use
  - Add-back estrogen during pill free week
### Migraines and COCs

<table>
<thead>
<tr>
<th>Study</th>
<th>Migraine alone OR (95% CI)</th>
<th>Migraine + COC OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CGSS (1975)</td>
<td>2.0 (1.2-3.3)</td>
<td>5.9 (2.5-12.2)</td>
</tr>
<tr>
<td>Tzourio (1995)</td>
<td>3.0 (1.5-5.6) without aura</td>
<td>13.9 (5.5-35.1) with and without aura</td>
</tr>
<tr>
<td></td>
<td>6.2 (2.1-18.6) with aura</td>
<td></td>
</tr>
<tr>
<td>Lidegaard (1995)</td>
<td>2.8 (N/A)</td>
<td>5 (N/A)</td>
</tr>
<tr>
<td>Carolei (1996)</td>
<td>1.0 (0.5-2.0) without aura</td>
<td>No data</td>
</tr>
<tr>
<td></td>
<td>8.6 (1.7-75) with aura</td>
<td></td>
</tr>
<tr>
<td>Chang (1999)</td>
<td>2.97 (0.7-13.5) without aura</td>
<td>6.59 (0.79-54.8)</td>
</tr>
<tr>
<td></td>
<td>3.8 (1.3-11.5) with aura</td>
<td></td>
</tr>
</tbody>
</table>

### Migraines and Risk of CVA

<table>
<thead>
<tr>
<th>Population</th>
<th>Rate per 100,000 women yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>General population (&lt;age 45)</td>
<td>5-10</td>
</tr>
<tr>
<td>Migraine</td>
<td>17-19</td>
</tr>
<tr>
<td>Migraine + COC + smoking</td>
<td>45 x increase</td>
</tr>
</tbody>
</table>

### Key Point
- In the absence of other contraindications, low dose COCs are safe for women with migraines without aura or with aura lasting less than one hour.
- Risk of CVA is increased in migraineurs.
- Consider other risk factors (e.g., smoking, hypertension, diabetes, CAD, age, family history, hyperlipidemia, obesity) when prescribing contraception.