Contraceptive Risk Analysis

- Define the risk of pregnancy
- Define the risk of the method
  - The intrinsic safety risks of the method
  - That the method will make the disease worse
  - That the method won’t work, including reduced efficacy due to drug interactions
  - That the method will not be used effectively
  - That EC or abortion won’t be used as backup

WHO Medical Eligibility Criteria

- Unique contributions
  - Evidence based
  - Comprehensive, up-to-date
  - Only “accepted” guideline of its kind
- Considerations for use in US
  - WHO Criteria were written to include “lowest common denominator” health systems
  - Conservative for use in the US
  - Consider as “tools not rules”
WHO Medical Eligibility Criteria

- **Combined hormonal contraceptives (CHC)**
  - COC: Combined oral contraceptives
  - CIC: Combined injectable contraceptives
  - P/R: Patch and Vaginal Ring
- **Progestin only contraceptives**
  - POP: Progestin only pills
  - DMPA: Depo-MPA
  - IMPLT: Implanon contraceptive implant
- **Intrauterine contraceptives**
  - Cu-IUD: Copper T-380 IUD
  - LNG-IUD: Levonorgestrel IUS

### WHO Medical Eligibility Criteria

<table>
<thead>
<tr>
<th>WHO Category</th>
<th>Definition</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No restriction in contraceptive use</td>
<td>Use the method</td>
</tr>
<tr>
<td>2</td>
<td>Advantages generally outweigh theoretical or proven risks</td>
<td>More than usual follow-up needed</td>
</tr>
<tr>
<td>3</td>
<td>Theoretical or proven risks outweigh advantages of the method</td>
<td>Clinical judgment that this patient can safely use</td>
</tr>
<tr>
<td>4</td>
<td>The condition represents an unacceptable health risk if the method is used</td>
<td>Do not use the method</td>
</tr>
</tbody>
</table>

**Is there a Need for “Routine” Screening of Hormonal Contraceptive Users?**

- **2004 WHO Selected Practice Recommendations for Contraceptive Use**
  - Blood pressure measurement before initiation of
    - COC, P/R, POP, DMPA, and implants
  - *Not recommended* as “contributing substantially to safe and effective use of contraceptive method”
    - Breast or genital tract examination
    - Cervical cancer screening
    - STI assessment or lab test screening
    - Hemoglobin determination
    - Other routine lab tests
Case Study: History of Stroke

- 35 year old Latina woman G₂ P₂ seeks DMPA
- She is 6 months post-partum after uncomplicated NSVD
- History of “stroke” which occurred in Guatemala when she was 20 years old
- Slow to regain use of right arm; slight residual weakness
- Was advised not to take OCs in the future

Stroke (CVA) and Contraception

- “Stroke” does not suggest actual cause
  - Thrombotic (ischemic) stroke
  - AVM or aneurysm (hemorrhagic stroke)
  - Cocaine induced arteriospasm
  - Infectious meningitis
- Stroke risk factors
  - HTN, smoking, diabetes, ▲ body weight
  - Migraine headache with aura, focal neuro signs
- Thrombotic stroke (but not other CVA types) is associated with estrogen dose, but not progestin

WHO MEC 2004: Stroke

History of thrombotic stroke
- WHO-4: COC, P/R
- WHO-3: DMPA
  POP, IMPLT continuation
- WHO-2: LNG-IUD;
  POP, IMPLT initiation
- WHO-1: Cu-IUD

Stroke and Contraception: Management

- Document of thrombotic stroke vs. other types
- Combined hormonal contraceptives
  - Evaluate CV risk profile
  - Use low estrogen effect product
  - Co-manage with PCP, neurologist, or neurosurgeon
- Progestin only methods
  - DMPA may reduce seizure frequency
  - Does not increase risk of arterial thrombosis
- IUCs are safe and effective choice
**Case Study: Headaches**

- Ms. K is a married 22 year old G3 P0 TAB3 woman who requests OCs
- Her first two pregnancies were at 17 and 19 years old and occurred while using condoms
- States that she had experienced occasional "sick headaches" over the past 9 months, and mentioned that two episodes had been so severe that she had to go home from work

**Headaches and Contraception**

- **Tension headache** is most common type
  - Muscle tightening and pain in neck, scalp
  - Improved with sleep, analgesics, relaxation
  - No interaction with hormones
- **Common (or simple) migraine headaches**
  - Unilateral or bilateral temporal pain
  - Nausea, vomiting, visual spots/ flashing
  - Sonophobia (worse pain with sound)
  - Photophobia (worse pain with light)
  - No aura or focal neurologic symptoms

**Migraine Headache**

- **Classic** migraine headaches
  - Aura, before onset of migraine headache
  - Transient hemianopsia (unilateral loss of vision)
  - Unilateral paresthesias (sensory defects)
  - Hemiparesis (weakness or paralysis)
  - Aphasia (speech defects)

**Migraine Headaches**

**Pre-migraine aura**

- Associated with increased risk of stroke
- Symptom pattern
  - Occurs 6-60 minutes before headache
  - Flickering zig-zag line moves toward periphery
  - Scotomata (loss of vision)
WHO MEC 2004: Headaches

• Non-migrainous headaches
  – WHO-1: all methods
• Migraines, < 35 years old, no aura or neuro symptoms
  – WHO 2: COC, P/R, progestin only methods
  – WHO 1: POP, Cu-IUC
• Migraines, ≥ 35 years old, no aura or neuro symptoms
  – WHO-3: COC, P/R
  – WHO-2: All others
  – WHO-1: POP, Cu-IUC

WHO MEC 2004: Headaches

• Migraines, *with aura or* neurologic symptoms
  – WHO-4: COC, P/R (at any age)
  – WHO-2: POP, DMPA, LNG-IUD
  – WHO-1: Cu-IUD

Headaches and Contraception: Management

• Differentiate migraine from non-migraine headaches; obtain neurologist consultation if necessary
• If catamenial (menstrual) headaches, suggest OCs or NuvaRing in extended regimen
• CHC in women with common migraines
  – Use low estrogen effect product
  – Recommend frequent follow-up visits
  – If HA worsening frequency or severity, or new neurological symptoms, CHC must be discontinued
• Progestin-only methods, IUC are safe and effective

Case Study: Liver Disease

• 24 year old G₂ P₀ TAB₂ woman would like to use “the Pill” or OrthoEVRA patch
• Previous history of IV drug use, but now clean
• Has 4 or 5 sexual partners per year
• Tested positive for hepatitis B virus (HBsAg+) 2 years ago; liver enzymes are mildly elevated
• Tested negative for hepatitis C and HIV
• Occasional drinker; no longer smokes
**WHO MEC 2004: Liver Disease**

- **Hepatitis carrier:** all methods are WHO-1
- **Mild cirrhosis:** CHC-3; others-2, Cu IUD-1
- **Severe cirrhosis:** or
- **Active hepatitis:** or
- **Benign liver tumor (adenoma):** or
- **Malignant liver tumor (hepatoma):**
- **Cholestatic jaundice in pregnancy (not in MEC):**
  - WHO-4: OC, P/R
  - WHO-3: all others
  - WHO-1: Cu IUC

**Liver Disease and Contraception: Management**

- Few studies of CHC and liver disease
- Combined hormonal contraceptives, P/R
  - Determine the specific diagnosis
  - Order/review liver function tests
  - If no/ minimal ▲: OK to start; repeat LFTs in 2-3 months
- Progestin only methods have no effect on liver disease
- IUCs are safe and effective choice

**Case Study: Breast Lump in OC User**

- 41 year old G_2_ P_2_ lawyer using OC's for 9 years
- Regular withdrawal bleeds; wants to continue
- Past history is unremarkable
- Breasts nodular; 3 x 3 cm "prominence" R-UOQ
  - No fixation; no nipple discharge
- At breast clinic, told that biopsy not needed
  - Plan to "observe" over the next 3 months
  - "Up to the gynecologist" to decide whether to continue on OC's

**WHO MEC 2004: Breast Disease**

- **Benign breast disease (or)**
- **Family history of breast cancer**
  - All methods are WHO-1
- **Undiagnosed breast mass**
  - WHO-2: COC, P/R, POP, DMPA, LN-IUD, IMPLT
  - WHO-1: Cu-IUD
- **Past breast cancer and NED for ≥ 5 years**
  - WHO-3: COC, P/R, POP, DMPA, LN-IUD, IMPLT
  - WHO-1: Cu-IUD
- **Breast cancer treatment within 5 years**
  - WHO-1: Cu-IUD; all others are WHO-4
Breast Conditions and Contraception

- OCs are an effective treatment of cyclic mastadynia and prevents breast cysts (advise extended regimen)
- Women with (biopsy-proven) fibroadenoma may use hormonal contraceptive methods
- CHC users with abnormal breast findings
  - Guidelines recommend continuation of CHC until diagnosis is made; inform client of risks/ benefits
  - Non-suspicious findings: plan follow-up exam
  - Suspicious findings: specialist referral for diagnostic mammogram and FNAC

Breast Lump and Contraception Management

- Based on WHO-MEC criteria (2), continue OCs during observation period
- Considering age and breast findings, order diagnostic mammogram
- Management plan explained to the patient...she was willing to follow this plan
- Reference algorithms for breast abnormalities
  - http://qap.sdsu.edu/screening/breastcancer/bd a/index.html

Case Study: Type 2 Diabetes

- 33 year old G₃P₃ woman with gestational diabetes diagnosed in 2nd pregnancy
- No insulin between 2nd and 3rd pregnancies, required insulin during third pregnancy, which ended 2 years ago
- Now on metformin for type 2 diabetes; considering switch to insulin due to poor control
- Would like to use a hormonal method of contraception, if possible

Diabetes and Contraception

- Progestins may increase insulin resistance, but not usually to the point of clinically significant ▲ blood glucose
- Estrogen increases risk of thrombosis in vessels damaged by diabetic vascular disease
- CHC may be used in diabetics in the absence of clinically-manifest vascular disease, including
  - Retinopathy, nephropathy
  - Peripheral vascular disease, heart disease
WHO MEC 2004: Diabetes

- DM without vascular disease (+ insulin)
  - WHO-1: Cu-IUD
  - WHO-2: All others
- DM with vascular disease or DM > 20 years
  - WHO-3: OC, P/R, DMPA
  - WHO-2: POP, IMPLT, LNG-IUD
  - WHO-1: Cu-IUD
- History of gestational diabetes: all are WHO-1

Diabetes and Contraception: Management

- Adjust insulin or oral hypoglycemic as necessary
- Combined hormonal contraceptives
  - Evaluate CV risk profile
  - Use low E (thrombosis) + low P (glucose control)
  - If possible, co-manage with primary care provider
- Progestin only methods
  - May cause insulin resistance and ▲ blood glucose, but usually clinically insignificant
  - Do not increase risk of arterial thrombosis
- IUCs are safe and effective choice
- Discuss preconception care with all diabetic women

Contraception and Gestational Diabetes Mellitus (GDM)

- Older studies showed that OC may hasten insulin dependence; newer studies do not
- If GDM, ADA and ACOG recommend
  - 2 hour PGL (75 gm) 6 weeks postpartum
  - Given >50% chance of Type 2 DM in next 10 years, repeat diabetes screening annually, irrespective of contraceptive method
- GDMs who become frankly diabetic may continue combined hormonal contraceptives

ADA: Contraception After GDM
Damm P, Diabetes Care 2007; 30(S2):S236-241

<table>
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<tr>
<th>Method</th>
<th>OC</th>
<th>P/R</th>
<th>POP BF</th>
<th>POP Not BF</th>
<th>DMPA, Implants</th>
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</table>

- POPs are “first line” in T1 diabetics, non-lactating GDMs
- DMPA, implants are first line if compliance with a daily method is a problem or methods with estrogen are contraindicated
- Avoid OC, patch, and ring if cardiovascular disease or risk factors
Case Study: Type 2 Diabetes

- Check lipid profile
- If given progestin-containing method, monitor blood glucose levels closely
- Preferred methods
  - IUCs
  - Progestin only method
- Acceptable methods
  - OC (low E, low P), Patch, Ring
- Unacceptable risk
  - None

Case Study: History of Deep Vein Thrombosis

- 24 year old G₁P₀ woman presents with a request for either the Pill or the Patch
- History of deep vein thrombosis in her right calf at 18 years old
- Hospitalized for 1 week: had “shots” for 5 days; then switched to “pills” for 3 months
- Mother “had a blood clot go to her lungs” during pregnancy
- Healthy non-smoker; stable relationship; intercourse once or twice a week

Risk Factors for DVT and VTE

- Age (especially >40 years old)
- Pregnancy, post-partum period (< 3-4 weeks)
- Obesity
- Immobilization with venous stasis
- Personal history of DVT or VTE
- Family history (inherited clotting disorder)
  - Factor V Leiden mutation (Protein C resistance)
  - Protein S, Protein C deficiency

Venous Thrombosis and CHC

- ▲DVT rates with increasing dose of estrogen
- OC and OrthoEvra have similar DVT risk (Jick, 2006)
  - NGM OCs: 4.2/10,000 women/year
  - Patch: 5.3/10,000 women/year
  - Age-adj RR: 1.1 (95% CI: 0.7-1.8)
- DVT risk declines with increasing duration of use
- Progestin type, dose have no (or minimal) impact
- No attributable risk of fatal PTE in OC users
- Smoking, HTN, hypercholesterolemia, and diabetes not risk factors for venous disease
Comparative Risks of VTE

Prior Venous Thrombosis and CHC

Conventional wisdom
- If a woman has a history an idiopathic or post-partum DVT or VTE, she may be predisposed to recurrence if given exogenous estrogen
  - Hence, avoid E-containing contraceptives
- If the DVT was related to another condition (e.g., immobilization, trauma), without a history of recurrence, E-containing contraceptives may be considered

Venous Thrombosis and CHC

Factor V Leiden mutation, DVT risk, and OCs
- Individuals with the FVLM have activated Protein C resistance and hypercoagulability
- Present in 70-90% of inherited thrombophilias
  - 20-40% of patients having a first DVT
  - 50% of those with > 1 episode of DVT
- Present in 1-5% of US population; 5% of Europeans; up to 15% of Scandinavians
- OC users with FVLM who use have a 30-fold increased risk of DVT (Lancet 1994:344:1453)

Venous Thrombosis and CHC

- Best indicator of inherited clotting disorders is personal or close family history of DVT
- If no personal or family history of DVT, tests for (low) AT III, proteins C and S are unlikely to be positive and are poor predictors of DVT
- If personal or family history of DVT and considering CHC use or pregnancy, best screening test is an activated Protein C ($100)
  - If abnormal, follow with PCR test for the Leiden mutation
**Venous Thrombosis and CHC**

- Superficial varicose veins do not increase the risk of DVT or VTE, regardless method.
- Women who are about to undergo major surgery should discontinue OC’s 30 days before the procedure is scheduled.
- Not necessary to interrupt OC’s before short operative procedures with early physical activity.

**WHO MEC 2004: Venous Thrombosis**

- Known thrombogenic mutation (or)
- Past thromboembolic disorder
  - WHO-4: COC, P/R
  - WHO-2: POP, DMPA, IMPLT, LNG-IUD
  - WHO-1: Cu-IUD
- Varicose veins: all methods are WHO-1
- Superficial thrombophlebitis
  - WHO-2: OC, P/R
  - WHO-1: all others

**Venous Thrombosis and Contraception: Management**

- **Combined Hormonal Contraceptives**
  - OCs: use 20 ug dose of ethinyl estradiol (EE)
  - Patch
    - Systemic EE uptake → no liver first pass (good)
    - Higher EE exposure than OC (bad)
  - Ring: systemic uptake of EE + low EE exposure
- **Progestin only methods** and IUCs do not increase risk of venous thrombosis and are a safe and effective choice.

**Case Study: Prior DVT**

- Recommend coagulation studies, since may affect contraceptive choice and pregnancy management.
- **Preferred methods**
  - Cu-IUD
- **Acceptable methods**
  - POP, DMPA, IMPLT, LNG-IUD
- **Unacceptable risk**
  - COC, patch, ring
Case Study: A History of Depression

• 28 year old G₀ P₀ woman using 20 ug EE monophasic OC for 2 years; no problems
• Feeling sad over the past 3 months, so tried St John’s Wort tablets with no effect
• Her family medicine clinician recommended that she try fluoxetine
• Is the Pill making her depression worse?
• Will anti-depressants reduce OC efficacy?

Do Hormonal Contraceptives Cause or Worsen Depression?

• Older studies suggested that progestins could
  – Make pre-existing depression worse
  – Cause depression in a small % of users
  – “More likely” with progestin-only methods
• Newer (and better) studies show that none of these assertions is correct
• 2004 WHO Medical Eligibility Criteria
  – In depressed women, all methods are categorized as “WHO 1”

St John’s Wort and OC Use

• St John’s Wort widely used for depression
• Many studies show induction of CYP450 (3A4)
  – “Comparable to rifampin and carbamazepine when given for >10 days” (Markowitz, NEJM 2003)
• Studies of SJW in OC users

<table>
<thead>
<tr>
<th>Study</th>
<th>Hormone level</th>
<th>Ovulation</th>
<th>Follicle growth</th>
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<tbody>
<tr>
<td>Hall 2003</td>
<td>P, E ▼</td>
<td>no</td>
<td>NA</td>
</tr>
<tr>
<td>Pfrunder 2003</td>
<td>P ▼42%</td>
<td>no</td>
<td>no</td>
</tr>
<tr>
<td>Murphy 2006</td>
<td>P ▼15%</td>
<td>probable 38%</td>
<td>yes</td>
</tr>
</tbody>
</table>

“Caution patients that OC effectiveness may be reduced”

OCs and Treatment of Depression and Bipolar Disorder

• Depression
  – Possible effect: St John’s Wort
  – No effect
    • SSRIs (fluoxetine), SNRIs (venlafaxine)
    • Tricyclics (imipramine, amitryptaline)
• Bipolar Disorder
  – Enzyme-inducing anti-epileptic drugs (WHO-3)
    • Carbamazepine, Oxcarbazine, Lamotrigine, Topiramate
  – No effect
    • Lithium, Aripiprazole, Valproate
Case Study: Depression

- If started on OCs (or patch, ring) and St John’s wort continued, counsel regarding possibility of reduced method effectiveness
- **Acceptable methods:** all
- **Unacceptable risk:** none