Disclosures

• I have no commercial relationships to disclose
• I will not be discussing any unapproved uses of pharmaceuticals or devices

Objectives & Outline

• Describe key updates to the 2015 STD treatment guidelines
• Describe key updates to the 2016 contraception guidelines
STI Updates

1. Alternative treatment regimens to Neisseria gonorrhoeae
2. Rapid trichomonas test
3. Role of *Mycoplasma genitalium* in urethritis/cervicitis
4. Updated HPV vaccine recommendations and counseling messages

Gonorrhea: Epidemiology & Screening

- 2nd most commonly reported communicable disease
- **Annual screening** recommended for sexually active women <25 years old
  - **NAAT**: Superior sensitivity to culture, variable tests
  - **Culture**: Available for rectal, oropharyngeal, conjunctiva
    - Can provide antimicrobial susceptibility
  - Gram stain of urethral secretions: >99% specificity for diagnosis in males (does not rule out if negative)

Gonorrhea: Treatment

- **Ceftriaxone 250mg IM + Azithromycin 1mg PO**
  - Even if negative chlamydia test b/c ↓ susceptibility to cephalosporins (cefixime no longer 1st line)
  - Decreasing susceptibility expected → surveillance for resistance is crucial!
  - Azithromycin preferred over doxycycline
    - Single dose-compliance
    - Higher tetracycline than azithromycin resistance
  - Direct-observed tx in clinic
Gonorrhea: Alternative Regimens

• Cefixime 400mg PO + Azithromycin 1g PO
  • Limited efficacy for treating pharyngeal gonorrhea

• Azithromycin allergy
  • Substitute Doxycycline 100mg BID x 7 days

• Cephalosporin allergy
  • Gemifloxacin 320mg PO + Azithromycin 2g PO
  • Gentamicin 240mg IM + Azithromycin 2g PO

Gonorrhea: Follow-up

• No test-of-cure needed for uncomplicated infection
  • Culture ≥72 hours, NAAT ≥7 days
  • If symptoms persist >3-5 days → Culture with antimicrobial susceptibility testing

• Retest in 3 months for reinfection

• Partner treatment
  • Partners within 60 days of sx or dx OR last partner
  • No sex x 1 week after both treated

Trichomoniasis

• Most prevalent non-viral STI in US
• 3.7 million infections
• 70-85% of infected persons asymptomatic
• Associated with 2-3x increased risk of HIV

Trichomoniasis: Diagnosis

• NAAT
  • Sensitivity: 95-100%
  • Source: Vaginal, endocervical, urine, urethral (depending on test used)
  • Detects trich 3-5 times more than wet-mount microscopy (51-65% sensitivity, lower in men)

• Trichomonas Rapid Test
  • Antigen-detection test at pt of care
  • 10-45 min
  • Self-testing future option
  • >99% 14-22 yr old women correctly performed & interpreted
Trichomoniasis: Treatment

- **Metronidazole 2g PO in single dose**
  - 84-98% cure rates
  - Gel does not reach therapeutic levels, not recommended
- **Tinidazole 2g PO in single dose**
  - More expensive but 92-100% cure rate
- Alternative: Metronidazole 500mg PO BID x 7 days
- Avoid alcohol x 24hrs after completion of flagyl

Trichomoniasis: Follow-Up

- High rates of reinfection – 17% within 3 months
- Retest within 3 months following initial treatment
- Can use NAAT as soon as 2 weeks after treatment

Mycoplasma genitalium

- First identified in 1980s
- N. gonorrhoeae < M. genitalium < C. trachomatis
- Cause of male urethritis and prostatitis
  - Accounts for 15-25% of non-gonococcal urethritis in US
- Also found in women
  - 10-30% with clinical cervicitis
  - 2-22% of PID cases

Mycoplasma genitalium: Diagnosis & Treatment

- No FDA-approved tests
- Slow-growing organism
  - Culture takes up to 6 months
- NAAT used in research settings or large centers
- Suspect in cases of persistent or recurrent urethritis
- Azithromycin 1gm PO single dose (rising resistance)
  - Doxycycline 7 days NOT effective
  - Moxifloxacin 400mg PO daily x 7 days
HPV Vaccines Licensed in the US

<table>
<thead>
<tr>
<th></th>
<th>Bivalent 2vHPV (Cervarix)</th>
<th>Quadrivalent 4vHPV (Gardasil)</th>
<th>9-valent 9vHPV (Gardasil 9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>VLP types</td>
<td>16, 18</td>
<td>6, 11, 16, 18</td>
<td>6, 11, 16, 18, 31, 33, 45, 52, 58</td>
</tr>
<tr>
<td>Adjuvant</td>
<td>AS04</td>
<td>AAHS</td>
<td>AAHS</td>
</tr>
<tr>
<td>FDA Licensed</td>
<td>2009</td>
<td>2006</td>
<td>2014</td>
</tr>
<tr>
<td>Sex / age groups</td>
<td>Females 9-25</td>
<td>Females and males 9-26</td>
<td>Females and males 9-26</td>
</tr>
<tr>
<td>Schedule</td>
<td>3 doses (0, 1-6 months)</td>
<td>3 doses (0, 2-6 months)</td>
<td>3 doses (0, 2-6 months)</td>
</tr>
</tbody>
</table>

HPV Vaccine Dosing Schedule

- Initiating before 15th birthday, recommend **2 doses**
  - Second dose 6-12 months after first dose
  - Minimum interval is **5 months**
- Initiating after 15th birthday, recommended **3 doses**
  - Second dose 1-2 months after first dose, and third dose 6 months after first dose (0, 1-2, 6 month schedule)
- 3 doses for immunocompromising conditions
  - HIV infection, malignant neoplasm, immunosuppressive tx

Immunologic basis of HPV Vaccination Schedules

- **3-dose schedule** (0, 1-2, 6 months)
  - Considered “prime-prime-boost”
- **2-dose schedule** (0, 6 months)
  - Considered “prime-boost”

- Memory B cells require at least 4-6 months to mature and differentiate into high-affinity B cells
  - ~6 month interval between first and last dose allows last dose to efficiently reactivate memory B cells
STI Updates Summary

- **Gonorrhea**: Ceftriaxone + Azithromycin  
  • Retest in 3 months for reinfection
- **Trichomonas**: Use NAAT or rapid test for diagnosis  
  (much better than wet mount)
- **Mycoplasma genitalium**: Rising cause of male urethritis, Azithromycin 1gm PO (but ↑ resistance)
- **HPV vaccine**: 2-dose schedule (0,6 mo) if initiate before 15th birthday because of higher immunogenicity at younger ages
Contraceptive Updates

- Some basic reminders
- Emergency contraception recommendations
- Contraception for women using psychotropic meds
- LARC Overview

### When to start contraception

<table>
<thead>
<tr>
<th>Method</th>
<th>When to start, if provider is reasonably certain woman is not pregnant</th>
<th>Additional contraception needed for back-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Copper IUD</td>
<td>Any time</td>
<td>Not needed</td>
</tr>
<tr>
<td>LNG IUD</td>
<td>Any time</td>
<td>If &gt; 7 days after menses started, use back-up method or abstain for 7 days</td>
</tr>
<tr>
<td>Arm Implant</td>
<td>Any time</td>
<td>If &gt; 5 days after menses started, use back-up method or abstain for 7 days</td>
</tr>
<tr>
<td>Injectable</td>
<td>Any time</td>
<td>If &gt; 7 days after menses started, use back-up method or abstain for 7 days</td>
</tr>
<tr>
<td>Combined hormonal (pill, ring, patch)</td>
<td>Any time</td>
<td>If &gt; 5 days after menses started, use back-up method or abstain for 7 days</td>
</tr>
<tr>
<td>Progestin-only pill</td>
<td>Any time</td>
<td>If &gt; 5 days after menses started, use back-up method or abstain for 2 days</td>
</tr>
</tbody>
</table>

Adapted from U.S. SPR for Contraceptive Use, 2016, Appendix B
When to start contraception

- **Barriers to starting**
  - Waiting for menses
  - Waiting for test results
  - Coming back for a second (or more) visit

- **“Quick start”: Starting when a young woman requests contraception**
  - Sooner to become effective
  - Minimize barriers
  - Risk that teen is already pregnant

---

**Routine Follow-Up After Contraception Initiation**

<table>
<thead>
<tr>
<th></th>
<th>IUD</th>
<th>Implant</th>
<th>Depo</th>
<th>COCs</th>
<th>POPs</th>
</tr>
</thead>
<tbody>
<tr>
<td>General follow-up</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Satisfaction with current method</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Changes in health status (medications that might affect contraception)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Consider exam to check IUD string</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Consider assessing weight changes &amp; counseling</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Measure blood pressure</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

---

**Weight Changes Associated with Contraceptive Methods**

- **Depo**
- **Implant**
- **Mirena IUD**
- **Combined OCs**
- **Paraguard**

---

**US Medical Eligibility Criteria & Selected Practice Recommendations for Contraceptive Use - App**

- **US MEC**
- **US SPR**

---

Case 1

- 16 year old female
- History of migraines with aura
- Interested in starting combined hormonal contraceptive (CHC) method
Case 1

• What do you tell your resident?

“Let’s see what the MEC says about migraines with aura and CHCs”

CDC MEC Table

<table>
<thead>
<tr>
<th>Condition</th>
<th>Sub-condition</th>
<th>CHC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>Migraine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1) Without aura</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>2) With Aura</td>
<td>4</td>
</tr>
</tbody>
</table>

Key:
1. No restriction
2. Advantages outweigh theoretical or proven risks
3. Theoretical or proven risks outweigh advantages
4. Unacceptable health risk
Migraine with Aura
Diagnostic Criteria

• Characteristics (at least two)
  • One aura symptom ≥ 5 minutes or ≥ 2 symptoms occur in succession
  • Each aura lasts 5-10 minutes
  • Aura is unilateral
  • Aura accompanied or followed within 60 minutes by headache

Migraines with Aura, Stroke & CHCs (Combined Hormonal Contraceptive)

<table>
<thead>
<tr>
<th></th>
<th>Odds of Ischemic Stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>Migraine with aura &amp; CHC use</td>
<td>6.0</td>
</tr>
<tr>
<td>Migraine without aura &amp; CHC use</td>
<td>1.8</td>
</tr>
<tr>
<td>No migraine and CHC use</td>
<td>1.4</td>
</tr>
</tbody>
</table>

Migraines & Hormones DON'T PLAY WELL TOGETHER

Especially if you have an aura!

Case 1
Patient Contraception Options

• Non-estrogen contraceptive options
  • Contraceptive injection (Depo-Provera)
  • Contraceptive implant (Nexplanon)
  • Progestin intrauterine device (Mirena)
Emergency Contraception

**Emergency Contraception**

- **LNG Pills (Brand)**
  - Plan B® One Step: One 1.5mg LNG pill
  - Next Choice One Dose™: One 1.5mg LNG pill
  - My Way™: One 1.5mg LNG pill
  - LNG tablets: Two 0.75mg LNG pills

- **Ulipristal acetate**
  - ella®: One 30 mg ulipristal acetate pill

- **Copper T IUD**
  - Highly effective method of EC
  - Can be used as an ongoing contraception for 10 years


Ulipristal acetate (ella)

- Effectiveness does not decline with delay in treatment
- Only emergency contraception product labeled for use in the 73-120 hr window after sex

Case 2

- 18 year old female
- History of depression with prior suicide attempt
  - Was told by current mental health provider to avoid hormonal methods
Case 2

• “So I talked about non-hormonal methods. She’s not interested in a copper IUD, so I guess we’re stuck with condoms?”

Case 2 (continued)

• No prior history of hormonal contraception use
• Symptoms well-controlled on fluoxetine 40 mg daily

Contraception for women taking SSRIs

• All types of contraception are considered safe for use

• The frequency of psychiatric hospitalizations for women with BPD or depression did not differ significantly among women using Depo, IUD or sterilization

Drug Interactions

Psychotropic medications

<table>
<thead>
<tr>
<th>Drug</th>
<th>SSRI</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oscillatory movement</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serotonin syndrome</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe dysmenorrhea</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe nausea/vomiting</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe weight gain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe extrapyramidal symptoms</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Comment

For many women, psychiatric agents lead to increased levels of adverse reactions, most of them being infection-related. This suggests that any SSRIs might be balanced with certain SSRIs and may cause less severe reactions than when compared with women not taking neuroleptic agents.
Case 2 – Lots of options!

Nexplanon

You’re like my birth control implant... I’ve got you under my skin!

Nexplanon Basics

- Single rod
- Progestin-only subdermal implant
- Effective for up to 3 years
- Safety and effectiveness demonstrated in clinical trials in >17 countries, including U.S.

Implanon vs Nexplanon
NEXPLANON™

Core: 40% ethylene vinyl acetate (EVA)
60% etonogestrel (68 mg)
Rate-controlling membrane: (0.06 mm)
100% EVA

Release Rate: 60 μg/day to 70 μg/d initially then decreases to 25 μg/d to 30 μg/d by end of third year

Nexplanon Basics

- Supplied in a sterile and disposable preloaded applicator
- Inserted subdermally below groove between the biceps and triceps muscles

Nexplanon: Mechanisms of Action

- Primarily inhibits ovulation
  - No ovulation was observed for 30 months
  - Only 2 out of 31 (6.5%) subjects ovulated in year 3, with no resulting pregnancies

- Secondary
  - Increases viscosity of cervical mucus
  - Alter endometrium environment

Nexplanon Pharmacokinetics

Mean serum concentration-time profile of Etonogestrel during 2 years of IMPLANON™ use and after removal in 20 healthy women
Nexplanon Does Not Affect Estradiol

- IMPLANON™ n = 44
- Copper IUD n = 29


Nexplanon is Very Effective

- 6 pregnancies reported in 20,648 cycles
- Each conception was likely to have occurred shortly before or within two weeks after Nexplanon removal

Nexplanon Bleeding Profile

- Patients will most likely experience a vaginal bleeding pattern that:
  - Is different from their monthly cycle
  - Most likely will vary during the duration of use
  - Is not predictable
  - Some women may have a slight trend towards lighter and infrequent bleeding or no bleeding at all

Implant Discontinuation Rates (n=942)

<table>
<thead>
<tr>
<th>Reason for Discontinuation</th>
<th>Rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleeding irregularities*</td>
<td>11.0% (104/942)</td>
</tr>
<tr>
<td>Weight gain</td>
<td>2.3% (22/942)</td>
</tr>
<tr>
<td>Emotional lability</td>
<td>2.3% (22/942)</td>
</tr>
<tr>
<td>Headache</td>
<td>1.6% (15/942)</td>
</tr>
<tr>
<td>Acne</td>
<td>1.3% (12/942)</td>
</tr>
<tr>
<td>Depression</td>
<td>1.0% (9/942)</td>
</tr>
</tbody>
</table>

* includes frequent, heavy, prolonged, spotting and other patterns of bleeding irregularity

Contraception Summary

• Use a **good visual aid** when discussing options
• The **CDC MEC/SPR app** is money!
• You can start contraception **ANYTIME** (but may need to recommend back-up method)
• Ulipristal acetate (**ella**) is newer emergency contraception that works up to 5 days after sex
• Pts taking **SSRIs** can use any method
• **Nexplanon** – Safe, effective & easy insertion, main side effect is irregular bleeding

Questions? And Thank You!

• charlene.wong@duke.edu

EXTRA SLIDES

**Bonus Question**

LARC is ____ fold more effective in pregnancy prevention than the pill, patch, and ring.

a) 2  
b) 5  
c) 10  
d) 20
Bonus Question

LARC is **20 fold** more effective in pregnancy prevention than the pill, patch, and ring.

a) 2  
b) 5  
c) 10  
d) 20

Exams and tests before starting contraception

- **Class “A”**: essential and mandatory
- **Class “B”**: contributes substantially to safe and effective use, but implementation may be considered within the public health and/or service context
- **Class “C”**: does not contribute substantially to safe and effective use of the contraceptive method

### Exam or test

<table>
<thead>
<tr>
<th>CHC</th>
<th>Injectable</th>
<th>Implant</th>
<th>IUDs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood pressure</td>
<td>A</td>
<td>C</td>
<td>C</td>
</tr>
<tr>
<td>BMI</td>
<td>*</td>
<td>C</td>
<td>C</td>
</tr>
<tr>
<td>Breast exam</td>
<td>C</td>
<td>C</td>
<td>C</td>
</tr>
<tr>
<td>Bimanual exam</td>
<td>C</td>
<td>C</td>
<td>C</td>
</tr>
<tr>
<td>Glucose</td>
<td>C</td>
<td>C</td>
<td>C</td>
</tr>
<tr>
<td>Lipids</td>
<td>C</td>
<td>C</td>
<td>C</td>
</tr>
<tr>
<td>Liver enzymes</td>
<td>C</td>
<td>C</td>
<td>C</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>C</td>
<td>C</td>
<td>C</td>
</tr>
<tr>
<td>Pap smear</td>
<td>C</td>
<td>C</td>
<td>C</td>
</tr>
<tr>
<td>STD screen</td>
<td>C</td>
<td>C</td>
<td>C</td>
</tr>
<tr>
<td>HIV test</td>
<td>C</td>
<td>C</td>
<td>C</td>
</tr>
</tbody>
</table>

Adapted from U.S. Selected Practice Recommendations for Contraceptive Use, 2016, Appendix C
How well does Implant work in Overweight Women?

- No clinical trial data
- Women who weighed more than 130% ideal body weight were excluded from the clinical trials
- It is possible that with time IMPLANON™ may be less effective in overweight women
- Clinical judgment required