CONTRACEPTION:
OLD METHODS
NEW APPROACHES

CECE NORTON MSN, APRN-CNM

DISCLOSURES

• Merck- Speaker/Trainer - Nexplanon
CONTRACEPTIVE COUNSELING

• Considerations
  • Age of the patient
  • Desire for future fertility
  • Personal and cultural values
  • Literacy
  • Capacity for behavior change
  • Informed consent
  • Non-contraceptive benefits
  • Cost

Burlington, MA: Jones and Bartlett Learning

CONTRACEPTIVE COUNSELING

• Efficacy- Perfect use
  • Likelihood that an unintended pregnancy will occur when the method is used consistently as prescribed

• Effectiveness- Typical use
  • How well it will work in actual practice

Burlington, MA: Jones and Bartlett Learning
NON-HORMONAL

CONTRACEPTION

CONDOMS
WITHDRAWAL

DIAPHRAGM
DIAPHRAGM

Retrieved from: www.caya.us.com

CAYA DIAPHRAGM

• One size fits most
• Available by prescription
• Non-latex
• Non-hormonal
• Typical use 86%
• www.caya.us.com
HORMONAL CONTRACEPTION

COMBINED ORAL CONTRACEPTION

ORAL CONTRACEPTIVE PILLS
COMBINED ORAL CONTRACEPTIVES

- Factors in choosing an oral contraceptive pill
  - Insurance - formulary may decide for you
  - Cost - brand names expensive
  - Prior use of OCPs - what worked/what didn’t
  - Estrogen sensitivity
  - Age
  - Non-contraceptive benefits
  - Comorbidities

COMBINED ORAL CONTRACEPTION

- **Mechanism of Action**
  - Estrogen and progesterone
  - Prevent pregnancy by suppressing ovulation
  - Added estrogen mimics changes in pregnancy
  - Blocks GnRH from the hypothalamus
  - No release of FSH and LH from the pituitary gland
  - Endometrium is altered, edematous
  - Corpus luteum degenerates
  - Cervical mucous thickens
  - Progesterone inhibits ovulation


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COMBINED ORAL CONTRACEPTION

- **Estrogen**
  - Suppresses the FSH surge
  - Estrogen stabilizes the endometrium
  - Reduces breakthrough bleeding
  - Cycle control

- **Progesterone**
  - Inhibits ovulation
  - Blocks GnRH suppressing the LH surge

COMBINED ORAL CONTRACEPTIVES

- Estrogen
  - Ethinyl estradiol (EE)
  - Estradiol valerate
- Pills less than 35 mcg are considered “low dose”
- Dosing above 50 mcg increases risk of stroke and blood clots
- Dosage ranges from 10 mcg to 50 mcg EE
- Metabolism of estrogen varies with each individual


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REDUCTION IN ETHINYL ESTRADIOL (EE) DOSAGE IN ORAL CONTRACEPTIVE PRODUCTS OVER TIME

Estrogen dosing has gradually declined over the years to potentially improve the safety profile (reducing hypercoagulability and cardiovascular adverse events) without a reduction in contraceptive efficacy or cycle control


18
COMBINED ORAL CONTRACEPTIVES

• Progestins
  • All except drospirenone are derived from 19-nortestosterone
  • Many different derivatives
    • Levonorgestrel
    • Norethindrone
    • Norgestimate
    • Drospirenone - analogue of spironolactone


PHARMACOLOGY

First generation COCs
• EE 50mcg or higher
• Norethindrone

Second generation COC
• Low dose EE 35mcg
• Levonorgestrel
• Norgestimate
• Norgestrel
  • High bioavailability
  • Increased potency
  • Higher androgenic effects

PHARMACOLOGY

Third-generation COC

- Ethinyl estradiol less than 35mcg
- Third-generation progestins
  - Desogestrel and gestodine
  - Fewer androgenic side effects
  - Controversy over concern for increased thrombotic risk


PHARMACOLOGY

- Fourth generation COCs

- Same Ethinyl Estradiol 20-30mcg
- Progestins
  - Drospirenone
  - Dienogest
  - Low androgenic effects-decreased hirsutism, acne
  - Antimineralocorticoid activity-reduced water retention and weight gain

PHARMACOLOGY

- Next generation
- Estradiol Valerate (E2V)
  - Natural estrogen
  - Fewer side effects
  - Poorly absorbed
  - Used for non-contraceptive benefit: endometriosis and dysmenorrhea
  - Quadraphasic
  - 26/2 regimen
  - EV2/Dienogest- Natazia
    - 3mg E2V x 3 days
    - 2mg E2V + 2 mg DNG x 5 days
    - 2mg E2V + 3 mg DNG x 17 days
    - 1mg E2V x 2 days
    - Placebo x 2 days

De Leo, V. et. al., Hormonal contraceptives: Pharmacology tailored to women’s health, Human Reproduction Update, 22(5), 634-646.

COMBINED ORAL CONTRACEPTIVES

- Types of pill packaging
  - Monophasic- same dose of estrogen and progesterone throughout the cycle
  - Multiphasic- levels of estrogen and progesterone change during the cycle
    - Designed to minimize side effects
    - Reduce total dose of steroids
    - Mimic menstrual cycle
    - No evidence of clinical advantage
  - Extended cycle- Shortened hormone free interval

De Leo, V., et. al., Hormonal contraceptives: Pharmacology tailored to women’s health, Human Reproduction Update, 22(5), 634-646.
EXTENDED ACTIVE HORMONE TREATMENT FOR COCs

- May decrease breakthrough bleeding and decrease discontinuations associated with lower-estrogen COCs1-4

A 2016 review of contraceptive use by the U.S. SPR showed studies comparing 7-day hormone-free intervals with shorter hormone-free intervals5:

- Ten studies reported lower rate of pregnancy and significantly greater suppression of ovulation among women with shorter intervals
- One study found no difference
- The review did not discuss differences in adverse event rates


EXTENDED ACTIVE HORMONE TREATMENT

STANDARD DOSAGE REGIMEN

Active Hormone Treatment: Days on Estrogen and Progestin

21

Hormone-Free Interval: Days on Placebo

7

EXTENDED ACTIVE TREATMENT REGIMEN

Active Hormone Treatment: Days on Estrogen and Progestin

24 - 26

Hormone-Free Interval: Days on Placebo

2-4

A 2016 review of contraceptive use by the U.S. SPR showed studies comparing 7-day hormone-free intervals with shorter hormone-free intervals5:

- Ten studies reported lower rate of pregnancy and significantly greater suppression of ovulation among women with shorter intervals
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SHORTER HORMONE FREE INTERVALS (HFI) WITH COCs

EXTENDING THE ACTIVE REGIMEN AND DECREASING THE ‘PILL-FREE’ INTERVAL FROM THE TRADITIONAL 7 DAYS

<table>
<thead>
<tr>
<th>Study</th>
<th>Study objective</th>
<th>Study results</th>
<th>Safety results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Double-blind, randomized trial, Spona J, et al.1 (n = 60)</td>
<td>Determine the suppressive effect on ovarian activity of a COC* administered for 21 or 23 days (Shortening of the HFI from 7 days to 5 days)</td>
<td>Suppression of ovarian activity was more pronounced by the 23-day regimen • 17β-estradiol serum levels during the last six days of a cycle and during the first six days of the next cycle were less (p &lt; 0.05) in the 23-day regimen</td>
<td>Most frequent AEs which were reported in both groups were breast tension, vomiting, nausea, and acne</td>
</tr>
<tr>
<td>Prospective trial, Wits SA, et al.2 (n = 12)</td>
<td>Evaluate the serum levels of four reproductive hormones during the HFI to determine whether the pituitary-ovarian response can be blunted by decreasing the HFI from 7 days to 3 or 4 days†</td>
<td>Greater pituitary and ovarian suppression for FSH, LH, estradiol and inhibin-B (p &lt; 0.001) was seen with the shortened HFI • Greater pituitary-ovarian inhibition may reduce the risk of ovulation, cyst formation and, potentially, common hormone withdrawal symptoms</td>
<td>AEs were not reported</td>
</tr>
<tr>
<td>Open-label, randomized, active-controlled trial, Nakajima ST, et al.3 (n = 705)</td>
<td>Assess the efficacy of a COC‡ administered for 21 or 24 days over 6 months (Shortening of the HFI from 7 days to 4 days)</td>
<td>The 24-day regimen, vs. 21-day, was associated with: • Lower pregnancy rate (Pearl Index) 1.82 vs. 2.98 pregnancies per 100 women-years • Fewer intracyclic bleeding days 0.95 vs. 1.63; p = 0.005 • Fewer days of withdrawal bleeding 2.66 vs. 3.88; p &lt; 0.001 • Fewer total bleeding/spotting days for Cycles 2-6 18.6 vs. 23.2; p &lt; 0.001</td>
<td>Most commonly reported AEs in both groups were headache, vaginal candidiasis and upper respiratory tract infection</td>
</tr>
</tbody>
</table>

AF = adverse event. COC = combined oral contraceptives. EE = ethinyl estradiol. FSH = follicle-stimulating hormone. LH = luteinizing hormone. *20 mcg EE plus 75 mcg gestodene. †30 mcg EE plus 3 mg drospirenone. ‡20 mcg EE plus 1 mg norethindrone acetate.

LO LOESTRIN FE: DOSAGE
Consists of 28 tablets

- Order:
  - 24 blue tablets (Active)
    - Each containing 1 mg norethindrone acetate and 10 mcg ethinyl estradiol
  - 2 white tablets (Active)
    - Each containing 10 mcg ethinyl estradiol
  - 2 brown tablets (Nonhormonal placebo - Do not serve any therapeutic purpose)
    - Each containing 75 mg ferrous fumarate

COMBINED ORAL CONTRACEPTIVES

- Continuous cycle dosing
  - 21/7 designed to mimic normal menstrual cycle
  - Reassure women of no pregnancy
  - Not interfere with “normal” menstruation
  - Artifact of an earlier era rather than evidence
- CC dosing
  - Treat menstrual disorders
  - Chronic pelvic pain
  - Bleeding disorders
  - Perimenopause
  - PMDD/PMS
  - Reduce ovarian and endometrial cancer
- Not dependent on packaging
- May be used with any monophasic pill

COMBINED ORAL CONTRACEPTIVES

• What to prescribe?
• Biological activity
  • How estrogen and progesterone interact with each other rather than dose
  • Estrogenic activity
  • Progestational activity
  • Androgenic activity
  • Endometrial activity- spotting
  • Effect on serum lipoproteins


ESTROGEN EXCESS

• Heavy periods-menorrhagia
• Dysmenorrhea
• Increased breast size
• Increased vaginal discharge
• Cystic breast changes
• Breast tenderness
• PMS symptoms

ESTROGEN DEFICIENCY

• Absence of withdrawal bleeding-hormone free week
• Bleeding and spotting during the first week of pill pack
• Continuous bleeding and spotting
• Decreased flow
• Atrophic vaginitis


PROGESTERONE EXCESS

• Decreased length of flow
• Increased appetite-weight gain
• Mood changes
• Depression
• Fatigue
• Decreased libido

PROGESTERONE DEFICIENCY

- Breakthrough bleeding days 10 to 21 of pill pack
- Delayed withdrawal bleeding
- Dysmenorrhea
- Heavy flow and clots-menorrhagia


ANDROGEN EXCESS

- Acne
- Hirsutism
- Libido increase
- Oily skin and scalp
- Rash and pruritus
- Edema

ANDROGEN DEFICIENCY

• Decrease in libido

• COC bind with Sex Hormone Binding Globulin (SHBG)

• Potential to impact libido

BIOLOGIC ACTIVITY

- Norethindrone acetate/EE-10-30
  - Activity
    - Endometrial- low
    - Progestational- intermediate/high
    - Androgenic- intermediate/high
- Drospirenone/EE 20-30
  - Activity
    - Endometrial – intermediate
    - Progestational- high
    - Androgenic- low

COMBINED ORAL CONTRACEPTIVES

- Contraindications to OCPs
- Risks for blood clots
  - Hx of thrombophlebitis
  - Hx of thromboembolic disorders
  - Cerebrovascular disease
  - Coronary occlusion
ABSOLUTE CONTRAINDICATIONS

- Thrombophlebitis or thromboembolic disorders
- Cerebrovascular or coronary artery disease
- Cancer of the breast
- Undiagnosed abnormal vaginal bleeding
- Known or suspected pregnancy
- Benign or malignant liver tumor
- Uncontrolled hypertension

RISK OF THROMBOTIC STROKE AND MYOCARDIAL INFARCTION (MI) WITH HORMONAL CONTRACEPTION

Study Design

Danish 15-year cohort study to assess risks of thrombotic stroke and MI associated with use of hormonal contraception
- Data obtained from Statistics Denmark, the National Registry of Patient, the Register of Causes of Death and the National Registry of Patients for use of hormonal contraception, clinical end points, and potential confounders
- Women hormonal contraceptive users* and nonusers between 15 to 49 years of age (1995 through 2009)
- Total of 1,626,158 women contributed 14,251,063 person-years of observation

Results

- Risk of arterial thrombosis increased by:
  - A factor of 1.3 to 2.3 with OCs that included ethinyl estradiol (EE) 30 to 40 mcg
  - A factor of 0.9 to 1.7 with OCs that included EE 20 mcg

<table>
<thead>
<tr>
<th>Type</th>
<th>Thrombotic Stroke</th>
<th>Myocardial Infarction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Relative Riska</td>
<td>95% CI</td>
</tr>
<tr>
<td>20 mcg</td>
<td>1.60</td>
<td>1.37 to 1.86</td>
</tr>
<tr>
<td>30 to 40 mcg</td>
<td>1.75</td>
<td>1.61 to 1.92</td>
</tr>
<tr>
<td>50 mcg</td>
<td>1.97</td>
<td>1.45 to 2.66</td>
</tr>
</tbody>
</table>

*Included oral contraceptives, intrauterine devices, patches and rings.
+Ethinyl estradiol 10 mcg was not studied.
*Analysis adjusted for differences in progestin type, age, and calendar year.
COC AND EFFICACY

- Unexpected breakthrough bleeding or spotting
  - May indicate interaction
- Barbiturates
- Anticonvulsants
- Hypnotics
- Antibiotics
- Cholesterol lowering agents
- OTC supplements- St John’s Wort

COMBINED ORAL CONTRACEPTIVES

- Indications- Non-Contraceptive Benefits
  - Dysfunctional uterine bleeding
  - Dysmenorrhea
  - Endometriosis/Adenomyosis
  - Polycystic Ovary Syndrome
  - Acne
  - Peri-menopausal symptoms
  - Blood disorders- Von Willebrand Disease
  - PMDD/PMS

## AGE AND COC

- **Adolescents**
  - Immature HPO axis, bone mass, sex characteristics
  - 30mcg EE preferred
  - Delay until 1-2 years after menarche

- **Perimenopause**
  - High unintended pregnancy rate
  - Relief of perimenopausal symptoms
  - No association with increased risk of breast cancer
  - Prevention of endometrial, ovarian, and colon cancer
  - Decreases osteoporosis risk
  - Safe without comorbid conditions


## EMERGENCY CONTRACEPTION

- Safe
- Not an abortifacient
- Not a teratogen
- Will not harm an early pregnancy
- Will not cause a miscarriage
- Pregnancy testing is not required before starting
- **NOT** RU-486- mifepristone used in combination with misoprostol
EMERGENCY CONTRACEPTION

• Plan B, Plan B® One-Step®, Next Choice, ella™
• Plan B, Plan B One-Step, Next Choice
  • Contain levonorgestrel
  • Most effective if taken with 72 hours
  • Reduces pregnancy risk by 52-94%
• Ella™
  • Ulipristal acetate-progesterone agonist/antagonist
  • Works up to 120 hours (5days)
  • Reduces risk by 62-85%
  • Prescription only
• Copper IUD
  • Placement within 120 hours
  • Reduces risk by 99%

LONG ACTING REVERSIBLE CONTRACEPTION
Unintended Pregnancy in the United States

6.7 million pregnancies over 1 year

Intended: 51%
Unintended 49%

Unintended births

23%
21%
5%

Elective abortions
Fetal losses


Unintended Pregnancy in First Year of Contraceptive Use (Typical Use)*

Male sterilization 0.15
Female sterilization 0.5
Implant 0.05
LNG IUD 20 µg/24 h 0.2
IUD copper T 0.8
Injection 0.6
Vaginal ring/patch/condom 0.9
Male condom 18
Female condom 21
Withdrawal 22
Fertility awareness 24
Spermicides 28
None 85

*From the 1995 and 2002 National Survey of Family Growth
Trussel J. Contraception. 2011;83:397-404.[13]
**CHOICE Study: Contraceptive Failure**

- LARC
- DMPA
- PPR

![Graph showing contraceptive failure rates](image)

*The LARC methods were 22 times more effective than pills, patch, or ring (PPR)*

*Hazard ratio after adjustment for age, educational level, and history with respect to unintended pregnancy, 21.8; 95% confidence interval, 13.7 to 34.9; efficacy of DMPA injection was similar to LARC, but failures for DMPA were counted only in users who returned for injections, so this failure rate was underestimated.*


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**Types of LARCs**

<table>
<thead>
<tr>
<th>Generic</th>
<th>Brand</th>
<th>Reservoir</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>ENG implant</td>
<td>Nexplanon</td>
<td>68 mg ENG</td>
<td>Up to 3 years</td>
</tr>
<tr>
<td>LNG IUD 20 µg/24 h</td>
<td>Mirena</td>
<td>52 mg LNG</td>
<td>Up to 5 years</td>
</tr>
<tr>
<td>LNG IUD 13.5 mg</td>
<td>Skyla</td>
<td>13.5 mg LNG</td>
<td>Up to 3 years</td>
</tr>
<tr>
<td>T380A Copper IUD</td>
<td>ParaGard</td>
<td>380 mm²</td>
<td>Up to 10 years</td>
</tr>
<tr>
<td>LNG IUD</td>
<td>Liletta</td>
<td>52 mg LNG</td>
<td>Up to 5 years</td>
</tr>
<tr>
<td>LNG IUD</td>
<td>Kyleena</td>
<td>19.5 mg LNG</td>
<td>Up to 5 years</td>
</tr>
</tbody>
</table>

ENG = etonorgestrel; LNG = levonorgestrel.
LARC Continuation Rates Are the Highest of All Reversible Methods

1-year continuation rates

- Condom: 53%
- Injection: 56%
- OC + POP: 68%
- Copper T: 78%
- LNG-IUS: 80%
- Implant: 84%


LARCS

- Almost any woman of reproductive age
- Few contraindications
- Adolescents
- Nulliparous women
- Patients with contraindications to estrogen

### CDC Medical Eligibility Criteria

**CDC Medical Eligibility for Initiating Contraception**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Copper IUD</th>
<th>LNG IUS</th>
<th>Implant</th>
</tr>
</thead>
<tbody>
<tr>
<td>No restriction (method can be used)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Advantages generally outweigh theoretical or proven risks</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Theoretical or proven risks usually outweigh the advantages</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unacceptable health risk (method not to be used)</td>
<td>4</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


### Can a Woman Use a LARC When She Has High Blood Pressure?

**Yes, LARC is safe, even for women with uncontrolled hypertension**

**CDC Medical Eligibility for Initiating Contraception**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Copper IUD</th>
<th>LNG IUS</th>
<th>Implant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>During past pregnancy</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Systolic 140-159 &amp; diastolic 90-99</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Systolic &gt;160 &amp; diastolic &gt;100 or with vascular disease</td>
<td>1</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

ABSOLUTE CONTRAINDICATIONS

- Pregnancy
- Unexplained vaginal bleeding
- Sepsis (postpartum or post abortion)
- PID or acute cervicitis
- Breast cancer in the last 5 years
- Uterine malformations, fibroids
- Wilson disease (copper IUD)

COPPER IUDS

- Mechanism of action
  - Inhibits sperm migration via inflammatory reaction
- Caution with history of dysmenorrhea or menorrhagia
- Menstrual flow may increase 20-50%
- May increase cramping-5%
- Better candidates for patients with normal to light periods
- Bleeding may improve with NSAIDs

COMPLICATIONS OF INSERTION

- Uterine perforation
- IUD expulsion

- Use of misoprostol prior to insertion
  - no evidence to support
CONTRACEPTIVE IMPLANT

• Nexplanon
  • 3 years
  • Suppression of ovulation
  • Thickens cervical mucous
  • No non-contraceptive benefit
  • May cause breakthrough bleeding or amenorrhea
  • Rare contraindications
  • Rapidly reversible
  • FDA mandated training

CONTRACEPTIVE IMPLANT

• Bleeding profile
  • 1/5 amenorrhea
  • 3/5 unscheduled spotting
  • 1/5 frequent and/or prolonged bleeding
  • 10.8% discontinuation rate-frequent bleeding
  • 0.3% discontinuation rate-amenorrhea
  • Success is in the counseling

Merck, 2017
CONTRACEPTIVE IMPLANT

• Unscheduled bleeding
  • NSAIDs
  • Oral contraceptives
  • Estrogen
  • Doxycycline

• Tamoxiphen
• Ulipristal acetate


LONG ACTING REVERSIBLE CONTRACEPTION

• Highly effective methods >99%
• Lower risk than oral contraception
• Rapid return to fertility
• Eliminates typical use failures
• High rates of patient continuation
• Most are now covered under the ACA

LONG ACTING REVERSIBLE CONTRACEPTION

• LARC should be offered to all women as an option
• Low risk of infection -0.5%
• No risk of infertility
• Lower risk of absolute risk of ectopic pregnancy
  • However, if pregnancy occurs more likely to be ectopic
• Uterine perforation is rare- 1/1000 insertions
• May be used in adolescents and nulliparous women
• May be inserted immediately after delivery


CASE STUDY

• 20 year old on norethindrone acetate/EE 10mg (LoLoestrin FE) for the past 3 cycles presents for a follow up visit. She is concerned that her period has stopped. What do you do?
CASE STUDIES

• 15 year old female presents with painful menstruation and heavy menstrual bleeding
  • A. Levonorgestrel IUD
  • B. Drospirenone/EE COC
  • C. Etonogestrel Implant
  • D. Copper IUD

CASE STUDY

• 38 year old presents with heavy menstrual bleeding and c/o low libido
  • A. LNG IUD
  • B. Drospirenone/EE COC
  • C. Norethindrone acetate/EE COC
  • D. Copper IUD
REFERENCES