CONTRACEPTIVE UPDATES AND PEARLS FOR PRIMARY CARE



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Objectives

- Describe mechanism of action for 2 components of combination hormona contraceptives.
- List 2 non-contraceptive benefits of hormonal contraceptives
- Describe 1 contraceptive prescribing resource for the medically complicated patient.
- ✓ Identify 2 non hormonal contraceptive options.
- ✓ Identify 2 new contraceptive therapies.

Overview

- Historical perspective & fun facts
- Oral contraceptives
- Transdermal and Injectables
- LARCs Old & New
- Barriers
- Useful Apps and advice
- Male contraceptives
- In the Pipeline and On the Horizon



They put what....where?

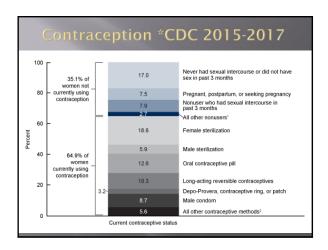
- Ancestors used about anything to avoid pregnancy... Including animal feces, wooden objects, stones!
- Chinese women drank lead and mercury to induce sterility! Serious consequences ...
- Savin & Pennyroyal douches (abortifacients)
- Soranus, greek GYN, encouraged jumping backwards 7 X after sex and drink water of blacksmiths (metal)
- 1800s: Chastity Belts advertised as protection against rape and encouraged by men to prevent masturbation and cheating.

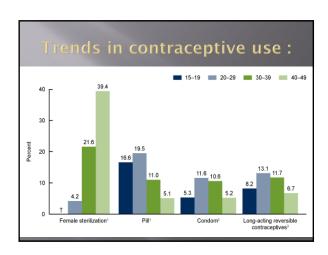


□ 1985: Harvard study on soda "Share a Coke!"









Keys to successful OC prescribing and pt use:

- Knowledge of the contraindications to OC use, both absolute and relative
- Knowledge of the causes of common side effects
- The ability to recognize potentially serious illness ASAP
- Access to accurate info re: biological activity differences among OCs

Contraceptive counseling pearls

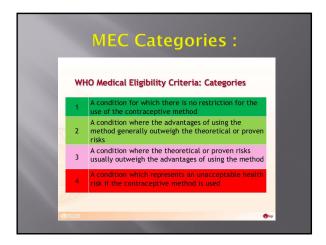
- Identify patients lifetime family planning goals
- Clearly identify contraindications
- Prescribe a 1 year supply
- Quick Start
- Not always a pelvic
- Avoid "hormone breaks"
- Prescribe Emergency Contraception (EC)
- Don't hold contraception hostage to the Pap
- Don't cause " Iatrogenic " pregnancy!

Medical Eligibility Criteria (MEC)



- Published in 2010, updated in 2016
- Evidence-based guidance for the use of contraceptive methods by women with specific medical conditions or characteristics
- Based upon WHO guidelines, adapted by CDC

Examples: obesity, hypertension, history of stroke, breast cancer HIV



Selected Practice Recommendations (SPR)

Evidence-based guidance for initiation & use of specific contraceptive methods.

US SPR

- How long to use back up methods?
- How to manage any side effects?
- What screening to do before starting a method?
- What to do about missed pills

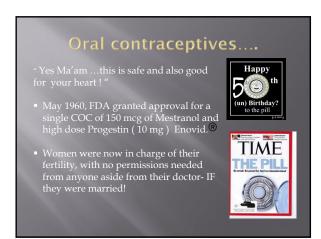
Ex: "How to be reasonably be sure a woman is not pregnant "

" A health care provider can be reasonably certain that a woman is not pregnant if she has no symptoms or signs of pregnancy and meets any one of the following criteria ":

- Is ≤7 days after the start of normal menses
 Has not had sexual intercourse since the start of last
 normal menses
 Has been correctly and consistently using a reliable
 method of contraception
 Is ≤7 days after spontaneous or induced abortion
 Is within 4 weeks postpartum
 Is fully or nearly fully breastfeeding (exclusively
 breastfeeding or the vast majority [≥85%] of feeds are
 breastfeeds), amenorrheic, and <6 months postpartum







Oral contraceptives



- 20-35 mcg of 2 primary synthetic
- Low dose but higher activity of 12 progestins

Menstrual cyclecollective groan! 1 ² 3 ⁴ 5 ⁶ 7 ⁸ 9 ¹⁰ 11 ¹² 13 ¹⁴ 15 ¹⁶ 17 ¹⁸ 19 ²⁰ 21 ²² 23 ²⁴ 25 ²⁶ 27 Day of Cycle

Combination Oral Contraceptives

- 2 primary synthetic estrogens
- Synthetic progestins: Primary mechanism for contraception
 Testosterone or C21 derivatives
 4-5 generations (Norethindrone, Norgestimate, Levonorgesterel, Desogesterol, Drospironone)

 - ** Newer progestins can use a lower does, but move toward less androgenicity BUT MORE thrombophilia !



Contraindications -**ABSOLUTE**

- PREGNANCY !!!
- Thrombophilias
- Hx VTE/T.hlebitis
- Cerebral vascular/CAD
- Known OR suspected cancer of breast, endometrium or ANY estrogen-dependent neoplasm
- Migraine WITH aura



- Undiagnosed AUB
- Liver cancer or tumor, even if benign
- Signif. Abnl. LFTs
- Factor V Leiden
- □ Type II
- Hyperlipidemia



Contraindications -Relative

- Cardiac / Renal prob.
- Diabetes/GDM/IGT
- HTN or DBP > 90
- Major depression
- Sickle cell / Hbg C
- Over 35 AND smoker
- Ulcerative Colitis
- Varicose veins
- Cholestatic jaundice of pregnancy
- Worsening of any chronic condition during pregnancy
- □ 1st degree FHx HD before age 50
- Drugs known to interact with COCs.

Serious symptoms

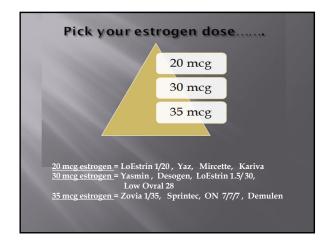
- Chest, arm/neck pain Hot,red,cord/edema

- HemoptysisSlurred speechHepatic mass, tender
- Absence of menses
- Retinal artery thromb
- Thromb/Hem stroke
- VTE
- Stroke
- Hepatic neoplasm
- PREGNANCY
 - Vascular spasms-precedes stroke

Non-contraceptive Benefits Reduce anemia Lessen PMS/PMDD Reduce endometrial ca Reduce ovarian ca risk Decrease colorectal ca Treat ovarian cysts Decrease PID / FCBS Treat endometriosis/adeno Treat uterine fibroids Treat menstrual migraines Treat dysmenorrhea Improve BMD

How to choose an Oral Contraceptive Choose Combination vs Progesterone Only pill Choose your estrogen dose Pick your progestin Pick your " phases "

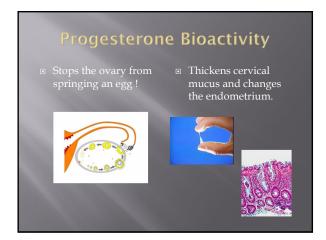
COC Composition ... does it matter? 21, 24, 28, 84 day brands Doses and ratios of EE and Progestins vary Some brands add FESO4 Typical is 21 days active, 7 placebo Continuous use requires 9 weeks extra dosing – longer RX!

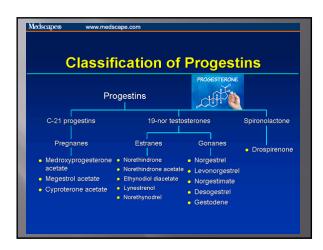


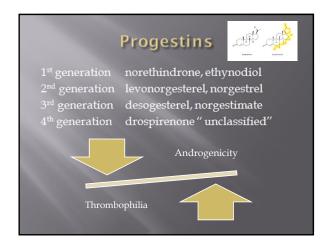
Estrogen Bioactivity Added to COCs to help control bleeding Noted a significant increase in VTE - slowly decreased EE content in OCs. Primarily endometrial activity How the Bioactivity Increases T4, TBG, Total lipids / TGR, Prolactin, FSH, Fibrinogen Decreases B-complex Decreases Insulin, PT, total chol. /HDL, T3 uptake

Estrogen Side Effects Estrogen Excess Mastalgia, FCBC, cervical extropy, menorrhagia, excess flow, mucorrhea Fibroid growth, chloasma, UTI, rhinitis N/V Increased breast size VTE, dizziness, leg cramps, wt gain (cyclic) Capillary fragility Estrogen Deficiency No withdrawl bleeding Bleeding/spotting, BTB days 1-9 Continual BTB Hypo/oligo menor. Atrophic vaginitis Pelvic Relaxation Vasomotor symptoms/nervousness









Progesterone Profile ...

- Flow length decrease
- Increased appetite
 Depression/Fatigue
 HTN, Varicose Veins
 Libido decreased

- S/S hypoglycemia

Progestin Deficiency

- > BTB days 10-21
- Delayed W/D bleeding Dysmenorrhea (or EE excess)
- Heavy flow and cramps (can also be EE excess)
- PMS S/S (or EE excess)
- Bloating, HA, leg cramp, N/V, mood changes, syncope, wt gain, edema

Last decision... Phases?

- Monophasic Fixed dose EE/progestin
- Endometriosis, menstrual migraines, EC, vaca!
- Yasmin(Yaz) Mircette, LoEst, Sprintec, Desogen®
- Biphasic Fixed dose EE, step up progestin
- Necon 10/11, ON 10/11,? Mircette
- <u>Triphasic</u>-mimic "natural cycle." 3 phases.
- _"(NO EC) * Estrostep®(BTB), Tri "__
- Quadriphasic "natural" hormones, HMB
- * Natazia (Bayer Pharmaceuticals) NOEC

Progesterone Only Pills

- MicroNor Nor QD ®
- CI -Breast Cancer, Liver Disease
- Sensitive to timing of ingestion
- Can be started 4 weeks after SVD if Breastfeeding.
- \$4.00 generic or w / GoodRx card. (\$30-\$35).

Allergies to OCs ???

- Women have allergies to the inactive ingredients & nonsteroidal components.
- Most common reaction is to LACTOSE!

What's new in OCs?

- MEC / SPR combo app from CDC
- Natazia quadriphasic / different estrogen
- Conflicting breast ca studies
- Danish studies: + 13 cases /100,000 women/yr
 ** There is likely a small Dx of BrCa in current/recent use
- Decreases endometrial and ovarian cancer rates
- Newer extended regimens safe, effective
- Quick start



OC Pipeline



- cMPTs Contraceptive Multipurpose Technologies *** Birth Control PLUS HIV PREP!
- Began enrolling in 2018 The Population Council
- Levonorgestrel (150 mcg) + Eth. Estradiol (30 mcg) **PLUS**
- ☐ Tenofovir disoproxyl fumarate (300 mg), and ☐ Emtric itabine (already approved in US for PREP!) "Many years away ..."

More OC updates:



- Drospirenone 4 mg Progestin Only Pill
- 24/4 dosing more forgiving, less AUB
- FDA NDA approved June 6th, 2019
- Expected release: Fall of 2019!
- Approved WITHOUT black box warning -OK for smokers, BMI > 30
- CI conditions predisposing to hyperkalemia

Emergency Contraception

- Approved products using birth control hormones to prevent preg after intercourse
- Lowers pregnancy risk by 58-94%
- Progestin EC available without Rx
- Will not interrupt an established preg or prevent implantation of a fertilized egg
- Efficacy decreases with time since intercourse

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Emergency Contraception (EC)

- Inhibits LH surge and prevents or delays ovulation:

 -Uses the time between IC & fertilization
 -Unruptured follicles documented on U/S

 International Consortium: "EC is effective only before the ovum is released form the ovary and before the sperm fertilizes the ovum."
- ACOG: "EC cannot prevent implantation of a fertilized egg," 2

1. http://www.cecinfo.org. 2. ACOG Committee Opinion 542 November 2012 Review article : Contraception 2010; 82 404-9.

Emergency Contraceptive Options

- Paragard[®]T380-A- copper IUD: within 5 days
- Products containing Levonorgesterel * 1.5mg:
- Plan B , Plan B One-Step , Next Choice (generic)
 - Approved for use within 72 hours, but some efficacy up to 120 hours after intercourse
 - \$40-\$50 OTC. Less with generics and \$10-\$25.on-line

* BMI over 30 approx doubles the risk of pregnancy !!!

What's new in EC? Ulipristal (Ella®)



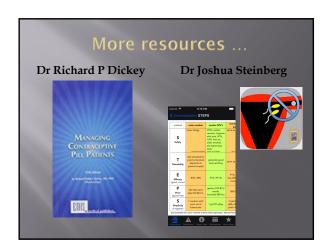
- Selective progesterone receptor modulator
- Higher efficacy than levonorgestrel
- More effective in overweight women
- Approved for up to 120 hours after UIC
- Side effect similar to progestin-only EC
- Prescription only: \$50-67. at pharmacy

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Ulipristal (UPA) 30 mg Updates :

- Start or resume HORMONAL contraception NO SOONER THAN 5 days after use of UPA (NEW!)
- Abstain from sexual intercourse or use barriers for next 7 days after sfter starting contraception or until NMP, whichever is first
- If vomits within 3 hours Repeat the dose
- Any non-hormonal method can be started immediately
- Pregnancy test if no withdrawl bleed in 3 wks





Contraceptive Ring "3 weeks in, 1 weeks out" • EE / Etonogestrel More convenient for many women – may improve adherence Similar to COC · Same contraindications as COCs

What's new in Ring Annovera ®



- FDA approval August 10th, 2018
- Combo of EE + Segesterone Acetate
- First reusable 1 year contraceptive vaginal ring
- Wear for 3 wks, wash, store in case 1wk, reinsert
- No fridge needed OK up to 86 * F
- 2-4 preg / 100 women in first year of use

Annovera®



- No estrogenic, androgenic, antimineralocortic.
- Slight affinity for glucocorticoid receptors.... (38% that of dexameth) but doesn't have glucocorticoid effects.

- □ Boxed warning for cigarette use / serious CV events
 □ CI = Hep C on combo drugs w / wo dasabuvir
 □ * " Not adeq. studied in women with BMI > 29."
 □ \$1800. \$2074. per ring (estimated , Good Rx)
 ****** Doesn't bind to SHBG!******
 □ Postmarketing surveillance: VTE, tampon use , CYP3A

Contraceptive Rings ... pipeline!

- Nuvaring © 2001, went off-patent in 4-8-2018
- Big patent law suits & the race is on!
- Generics were promised for fall 2019
- Mithra dba Mayne Parm : MyRing®
- Dr Reddy's Lab: generic delayed by FDA letter
- 6 ANDA FDA have been submitted

Wait for it but don't hold your breathe!



Depo Provera®

- DMPA

- 13-15 weeks

- Amenorrhea
- Weight gain
- Vaginal dryness
- Adverse lipid effect
- Prolonged pituitary suppression : median

time to preg = 9-10 months (18 is still nl)



DECREASE IN BMD

What's up with Depo Provera®

- Bone Mineral Density Black Box : Nov 2004
- 80% women have estradiol < 50 pg/ml at 1 yr
- Loss increases with prolonged use, ? Reversible
- "Use longer than 2 yrs only if other birth control methods are inadequate" (manufact)
- ACOG 2008 : " Concerns re: effect of DMPA should neither prevent practitioners from prescribing DMPA nor limit its use to 2 consecutive years." (CO # 415)

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Depo Provera[®]updates

- Discuss bone density
- Recommend calcium, Vit D, weight-bearing exercise
- Do not order BMD testing in young women

NEW Discuss possible increase risk for HIV infection and recommend condoms/testing



Nexplanon®



- One-rod subdermally administered, progestinonly hormonal contraceptive indicated for use by women to prevent pregnancy
- 68 mg etonogestrel (progestin-only LARC)
- Lasts 3 years
- Exclude pregnancy
- Non-breastfeeding: Insert 21-28 days PP*
- - * Use condoms or back up method X 7 days

Nexplanon®- Updates

- Required training updates for insertion & removal
- " insert in an area over the triceps muscle "
- New recs re: positioning the arm to avoid the ulnar nerve
- Reinsertion at the same site.

* Now texts an illustrations fo & removal

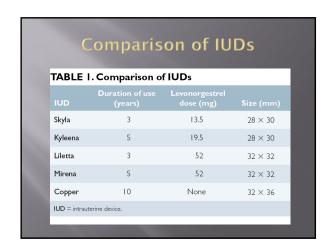
www.NexplanonTraining.com

Merck 1-877-888-4231

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Intraterine Contraceptives (IUCs)

- Mechanism of Action spermicidal, foreign body reaction in endometrium, and metal toxicity to sperm (T380A Copper IUD)
- LNG IUS thickens cervical mucus.
- Not abortifacient
- T380A Copper IUD can be used for up to 5 days after UPI for EC
- $\,\blacksquare\,$ Failure : copper 0.5 0.8% vs LNG IUS 0.1-0.4%

Intrauterine Contraceptives

- IUDS LARCs
- Affordable / covered / Title X
- Do NOT cause infertility
- Can be used in nulliparous women
- Risks
 - Perforation (1:1000 insertions) "migration"
 - Expulsion (10% at year 3)
 - Ectopic pregnancy: 1 out of 2 with LNG IUD **
 1 out of 16 with T380A copper

ACOG IUD Statement - 2017

- "IUDs offer safe, effective, long term contraception and should be considered for all
- " Providers should strongly encouraged young women who are appropriate candidates to use this method."
- "IUDs are safe to use among adolescents."
- " IUDs do not increase an adolescent's risk of infertility."

ACOG Practice Bulletin # 1866. November 201

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IUD pearls

- Ease the insertion with nitrous, misoprostol, NSAIDS, paracervical block, local lido, allis?
- Say "place," not insert
- Try music therapy!
- If no threads: GET TVS, and if no device seen GET AN XRAY!
- Skyla encourage pts to disclose before MRI

IUD "Migration "

LNG IUD Noncontraceptive benefits

- Lessens dysmenorrhea (off label)
- Can use as progesterone part of HRT (off label)
- Can decrease endometrial hyperplasia/Ca¹
- FDA-approved for tx of heavy menstrual
 - May work as well as endometrial ablation 2
 - More effective than medical therapy 3

1 Obstet Gynecol 2014; 124.292-9. 2 Am J Obstet Gynecol 2017; 217(5):574 3 N Engl J Med 2013; 368: 128-37







Male Contraceptive Options:

- Ejaculation 250 mil sperm vs 1-2 eggs/ mo? Prostaglandin effect
- Condoms, Pills, Gels, Injectables, Sterilization
- Not much funding and energy put into research
- Myths & folklore re: masculinity
- About 15 different methods in the Male Contraceptive Pipeline!





Updates in male contraception...

- Nesterone + Testosterone8 mg NES + 62 mg T (1.43%)
- Nesterone : segesterone acetate (SGA)
- Currently approved for birth control and endometriosis Tx
- 5 ml QD to shoulder/ upper arms

WWW.ClinicalTrials.Gov



** Doesn't bind to

NES/T Male Contraceptive Gel

- 2012 NIH studies found 90% of men had sperm suppression to < 1 million
- ☐ Initial studies: NES had SE of low libido / ED so they added Testost.
- Began enrolling 18-50 yo males, BMI
 33, N= 420 couples in 3-2018. Open label trial:

Suppression/ Efficacy/Recovery Phases

■ Est. completion date is 9-2021

Resources

- Apps: MEC/SPR, OCP Ref, STD2015 (CDC)
 i-Pill, Pillify, Period Tracker, Natural Cycles*
- <u>Websites</u>: OHIV.ORG, Bedsider.org
 <u>www.contraceptivetechnology.org</u>,
 WomensHealth.gov, www.CDC.gov/women
 <u>www.popcouncil.org</u>, www.healthfinder.gov
- Texts: Managing Contraceptive Pill Patients
 (Dickey), Managing Contraception (Hatcher)

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