Updates on Contraception

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Disclosures

I have no conflicts of interest.

Key Question: "Would you like to become pregnant in the next year?"

- New Oregon initiative: ask during each medical visit
- "Yes": offer counseling, resources
- "No": contraception discussion
- Prelim data:
  - Increase in preconception care
  - Increase in contraception

www.slate.com 7/2014

Contraception: Learning objectives

1. Choosing a method
2. Long-acting reversible options
3. Injectables
4. Combined hormonal contraception
5. Progestin only pills
6. Emergency contraception

What is the “best” contraceptive method for your patient?

Best answer is:

1. Medically appropriate
2. Used every time
3. Effective
4. Patient is happy with it
5. All of the above

Contraceptive Method	% Women with Unintended Pregnancy in 1st Yr
Highly effective	**Typical use**
Sterilization	0.15-0.5
IUD	0.1-0.8
Implant	0.2
DMPA	5.0
Moderately effective	
Pills: COCs, POPs	9.0
Ring	8.0
Patch	8.0

Contraceptive Method	% Women with Unintended Pregnancy in 1st Yr
Slightly effective	**Typical use**
Male condoms	18.00
Diaphragm	11.5
Cap	16 – 32
Spermicides	28
Withdrawal	28
Natural family planning: calendar, temp., mucus	25
No method	85

NEW: The Quick Start for all methods and everyone

- Start contraceptive method on the day the patient sees you
- Now recommended for all methods: pills, patch, ring, injections, implants, IUDs
- Need to be certain that patient is not pregnant

Zieman M, et al. Managing Contraception 2015-2016

How to be certain that a woman is not pregnant

1. No intercourse since last menses
2. Using reliable method consistently
3. ≤ 7 days after start of menses
4. Within 4 weeks postpartum
5. ≤ 7 days post abortion or miscarriage
6. Fully/nearly fully breastfeeding, no menses and < 3 months postpartum

When is back-up contraception needed?

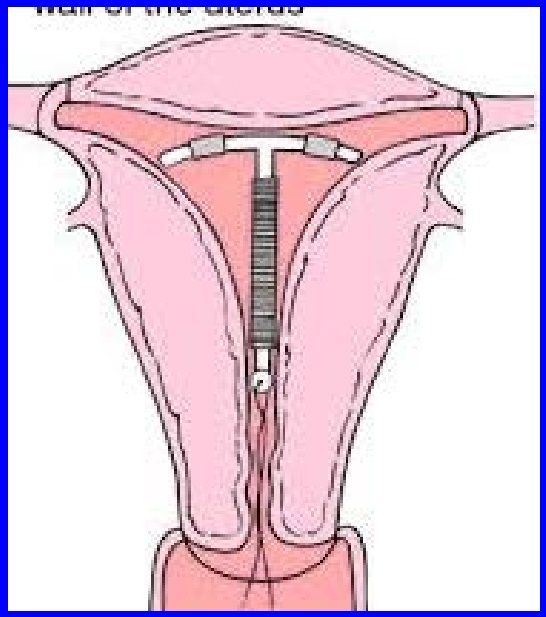
- Copper IUD: not needed

- Levonorgestrel IUD, implant, injectable, COC and POPs:
  - If > 5 days after menses started
  - Back-up: condoms for 7 days OR abstain for 7 days

Case 1: Alice

- Alice is a 20 yo single woman in a monogamous relationship who wants to avoid pregnancy. She describes herself as “not very well organized.”
- What contraceptive might be a good choice?
  1. An IUD
  2. The implant
  3. A birth control pill
  4. Either 1. or 2.

Long-acting reversible contraception (LARC): IUD and implant



American Academy of Pediatrics Policy Statement

- Long-acting reversible contraceptive options – implants and IUDs – should be considered 1st line contraceptive choices for adolescents
  - advantages: efficacy, safety, ease of use

Pediatrics , October 2014,134, published online 9/29/2014

Accessing IUDs or implants remains a problem

- Multiple studies in 2014:
  - Many women, especially those served by federally qualified health centers (FQHCs), still face challenges in obtaining IUDs, implants
  - Barriers: staff training, cost of supplies, poor reimbursement, costs to patients

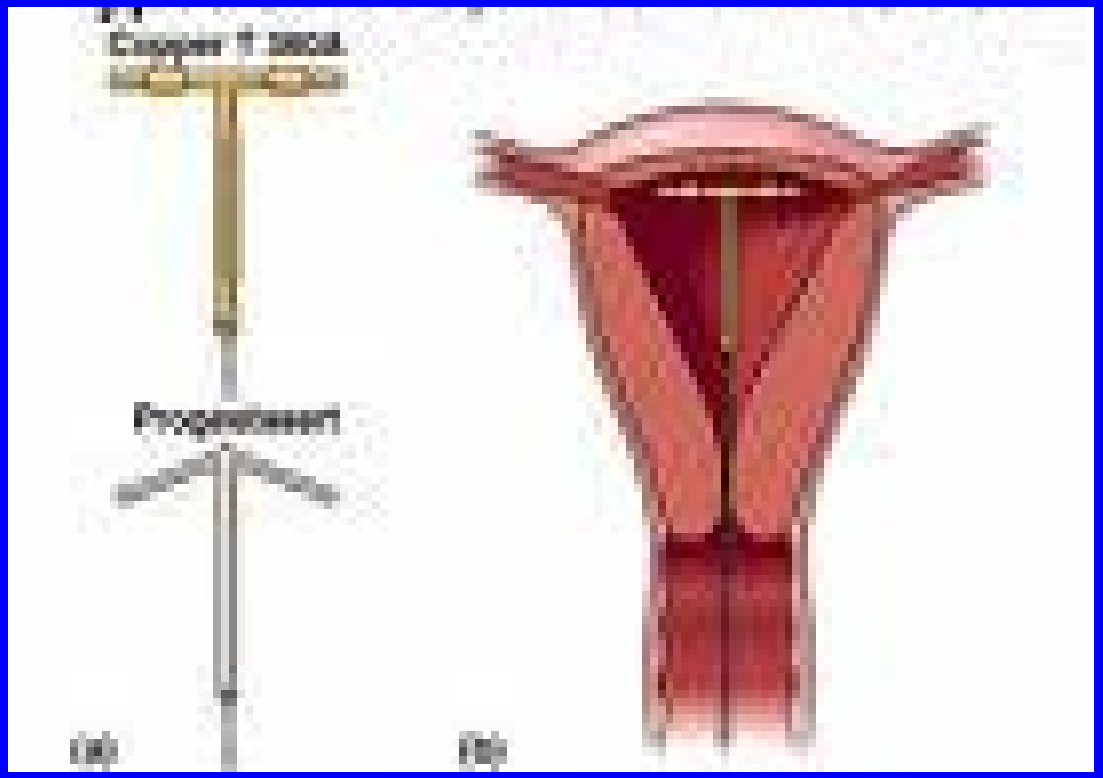
Contraception 2014 Feb;89:85 and 91

Removing the barriers to LARC leads to increased use, decreased pregnancy

- CHOICE project: 2-3 yr prospective study of 1404 girls ages 15-19
- Education and free, available contraception
- 72% chose LARC method, 28% other
- Rates of pregnancy, birth, abortion much lower than national rates

N Engl J Med 2014;371:1316

IUDs



Intrauterine devices (IUDs): advantages

1. Safe for all ages
   - Slightly increased risk of PID within 1st 20 days (1/1000)
   - NO increased risk of tubal infertility
2. Effective for all ages
3. Long lasting
4. Reversible: easily removed
5. AND highest level of user satisfaction (99%) !

Obstet Gynecol 2014;123:585

Contraindication to IUD insertion: active pelvic infection

- Active infection
  - Foreign body may impede resolution of infection
  - Wait ≥ 3 months post-treatment
- If asymptomatic, unknown STD status
  - Test for gc/chlamydia; can insert IUD
  - Positive test: treat, don't remove IUD
  - Retest after ≥ 3 weeks

Copper IUD (ParaGard)

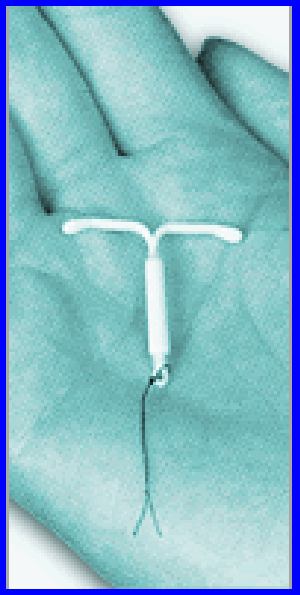
- Mechanism: causes sterile inflammation toxic to sperm and egg, impairs implantation
- Increases menstrual blood loss
- May increase dysmenorrhea

Copper IUD (ParaGard): Update on duration of action

- Initially approved for 10 years
- Now:
  - Women between 25-34: 12 years
  - Women ≥ 35 years old at time of placement: can leave IUD in place till menopause

Contraception 2014;89:495

Levonorgestrel IUD (Mirena)



- Releases 20 mcg/day of levonorgestrel (progestin)
- Contraception for 5 years
- Mechanism
  - thickens cervical mucus
  - causes endometrial atrophy with decreased blood loss, 20% incidence of amenorrhea by 1 year

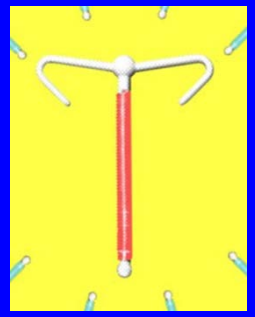
Contraception 2011;83:48

NEW: low-dose levonorgestrel IUD (Skyla)

- Releases 14 mcg/day initially with gradual decrease to 5 mcg/day
- Contraception for 3 years
- Smallest IUD: possible advantage in nulliparous women
- By 1 year, 6% of users have amenorrhea

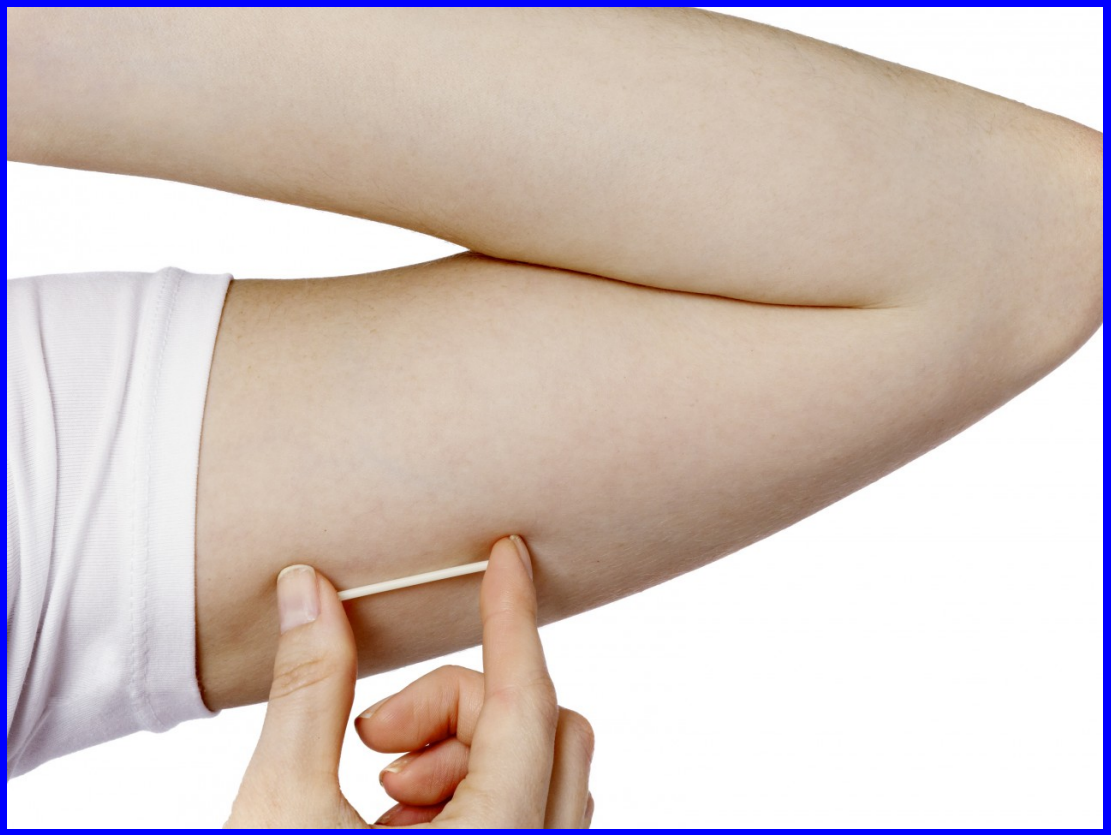
Medical Letter 2013;55:21

NEWEST: potentially cheaper levonorgestrel IUD (Liletta)



- Approved by the FDA 2/27/2015
- Partnership of Medicines360, nonprofit women's health pharmaceutical company, with Actavis, a global pharmaceutical company
- Average release of 15.6 mcg/day of levonorgestrel over 3 yrs
- By 1 year, 19% of users had amenorrhea

Implant



Implant: Nexplanon

- Single radio-opaque etonogestrel implant 4 cm long, 2 mm in diameter
- Inserted in upper arm
- Effective for at least 3 years
- Mechanism:
  - thickens cervical mucus
  - atrophic endometrium
  - inhibits ovulation

Nexplanon

- Pros:
  - Long-lasting
  - High continuation rate
  - Rapid return to fertility: 94% ovulate within 3-6 weeks of removal
- Cons:
  - Requires insertion and removal
  - Irregular bleeding
  - Anticonvulsants lower its effectiveness: phenytoin, carbamazepine, topiramate

Case #2: Betty

- Betty is a sexually active 18 yo woman with sickle cell disease and a seizure disorder. She does not want an IUD.
- Best method for her is:
    1. OCP
    2. Depot medroxyprogesterone acetate (DMPA)

DMPA: benefits for women with medical problems

- Sickle cell: may reduce acute sickle cell crises
- Seizure disorder:
  - may decrease seizures
  - anticonvulsants don't decrease its effectiveness

Cochrane Fertility Regulation Group, 31 Oct. 2011.
Contraception 2003;68:75

DMPA: other advantages

- High efficacy
- Teens less likely to become pregnant than teens on OCP or patch
- Decreased blood loss: amenorrhea in 50% after 1 yr
- Decreased dysmenorrhea (off-label indication)

J Ped Adol Gyn 2007;20:61

DMPA: Disadvantages

- Irregular bleeding
- Weight gain
- Delayed return of fertility
- Mood changes
- Decrease in bone density BUT complete recovery after cessation and no increased risk of fractures

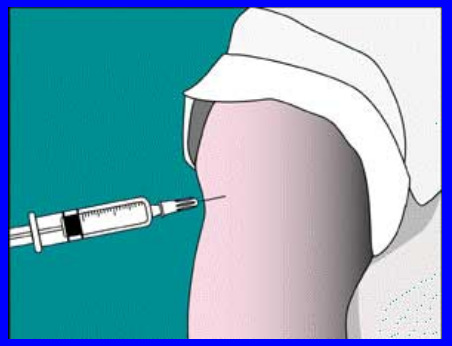
Contraception 2007;76:425. Obstet Gynecol 2013 Mar;121:593

ACOG and WHO: advantages of DMPA outweigh risks

- Choose patients appropriately
- Advise adequate calcium, vitamin D and daily exercise
- Don’t check bone density
- Can continue DMPA for decades

Obstet Gynecol 2006;107:1453. www.who.int

DMPA: dose



- Standard: 150 mg DMPA IM every 3 months
- New low dose: 104 mg SC, available in prefilled syringes
  - Potential for self-administration, NOT yet FDA approved
  - Compared to 150 mg dose: lower peak levels, less weight gain, more expensive

Contraception 2012;85:453 and 458

Case #3: Corinne

- Corinne is a sexually active 30 yo lawyer with PCOS and anovulatory bleeding. Her mother died from endometrial cancer.
- Good contraceptive choice?
    1. Copper IUD
    2. Combined oral contraceptive pill (COC): pill containing estrogen and progestin

Combined oral contraceptive (COC) pill: advantages for women with PCOS and anovulatory bleeding

- Can prevent endometrial hyperplasia by providing progestin and regulating menses
- Can prevent endometrial cancer

New data on oral contraceptives (OCPs) decreasing the risk of endometrial cancer

- Background: OCPs known to reduce rate of endometrial cancer but uncertain how long this effect lasts after OCP use ceases
- Methods: Meta-analysis of 27, 276 women with endometrial cancer and 115,743 controls from 36 epidemiological studies

www.thelancet.com/oncology; pub online 8/5/2015

OCPs and endometrial cancer: findings

- The longer the women had used OCPs, the greater the reduction in risk
  - 10 yrs use was estimated to reduce absolute risk of endometrial cancer by age 75 from 2.3 to 1.3 per 100 women
- Reduction in risk persisted for more than 30 yrs after OCP use had ceased

www.thelancet.com/oncology; published online 8/5/2015

OCPs and endometrial cancer: conclusions

- Use of OCPs gives long-term protection against endometrial cancer.
- Results suggest:
  - about 400,000 cases of endometrial cancer before age 75 have been prevented over the past 50 years
  - 200,000 cases prevented in past decade

www.thelancet.com/oncology; published online 8/5/2015

Combined oral contraceptives and risk of venous thromboembolism (VTE)

- Background: COCs are associated with increased risk for VTE but controversy persists about relative risks of specific progestins
- Method: Two large UK case-control studies: women aged 15-49 with 1st dx of VTE in 2001-13, each matched with up to 5 controls

BMJ 2015;350:h2135

COCs and VTE risk: results

COC	Risk of VTE: Odds ratio
Any COC pill	2.97
Desogestrel	**4.28**
Drospirenone	**4.12**
Norgestimate	2.53
Levonorgestrel	2.38

BMJ 2015;350:h2135

Number of extra cases of VTE per year per 10,000 treated women

Progestin	# Extra cases per year
Levonorgestrel	6
Norgestimate	6
Desogestrel	14

BMJ 2015;350:h2135

COCs and risk of VTE: conclusions

- This is the 1st study with sufficient power to provide reliable findings for different formulations of COCs
- Results similar to 2011 Danish national study
- Recommendation: Prescribe COCs with progestins associated with lowest risk for VTE

Good choice: generic pill with 20 mcg ethinyl estradiol, 0.1 mg levonorgestrel

- Generics are fine
- Use lowest dose of estrogen
- Use monophasic pills
  - same daily dose of estrogen and progestin
  - can be used continuously if she wishes to eliminate menses

Use continuous active COCs to eliminate menses

- Take active pill every day
- Monophasic pills recommended
- May have increased spotting, which decreases over time

Continuous COC Use: Indications

- Patient convenience
- Menstrual migraines
- Dysmenorrhea
- Endometriosis
- PCOS

Obstet Gynecol 2012;119:1143

Continuous COC use: safety

- Year-long continuous use:
  - Menses or pregnancy in 99% users within 90 days of stopping pill
- Progestin effect predominates:
  - Endometrial atrophy, not hyperplasia

Fertility and Sterility 2008;89:1059

COC use in peri-menopausal woman

- Advantages: controls cycle, treats hot flashes, provides contraception
- NEW very low dose pill:
  - 1 mg norethindrone acetate/10 mcg EE/ 75 mg ferrous fumarate
- Avoid in obese women: risk of DVT increases with age and BMI
- Stop by ~ age 51

The patch

- Brand name is off the market; generic is available
- Transdermal: 20 mcg EE +

  150 mcg norelgestromin: active metabolite of norgestimate
- Once-a-week x 3, on same day of week
- Rotate sites

The patch: pros and cons

- Pros
  - compliance
  - excellent for continuous use
- Cons
  - high serum estrogen levels: delivers about 60% more estrogen than a 35 mcg ethinyl estradiol pill
  - higher DVT risk than OCP

Vaginal ring: NuvaRing

- Flexible, soft ring
- 15 mcg EE and
  120 mcg etonogestrel qd
- Etonogestrel: active metabolite of desogestrel
- Use for 3 wks, remove for 1 wk

NuvaRing: pros and cons

- Pros - easy to use
  - great for compliance
  - great for continuous use
- Cons - possible higher DVT risk than OCP

www.nuvaring.com.

Vanity Fair, Jan. 2014

Absolute risks of DVT

	Absolute Risk of DVT/100,000 women per year
No COC	10
COC pill w LNG	50
COC pill w DG or drospirenone	100
Patch	97
Ring	78
Pregnancy	200

BMJ 2011;343:d6423. BMJ 2012;344:e2990

Breast cancer risk

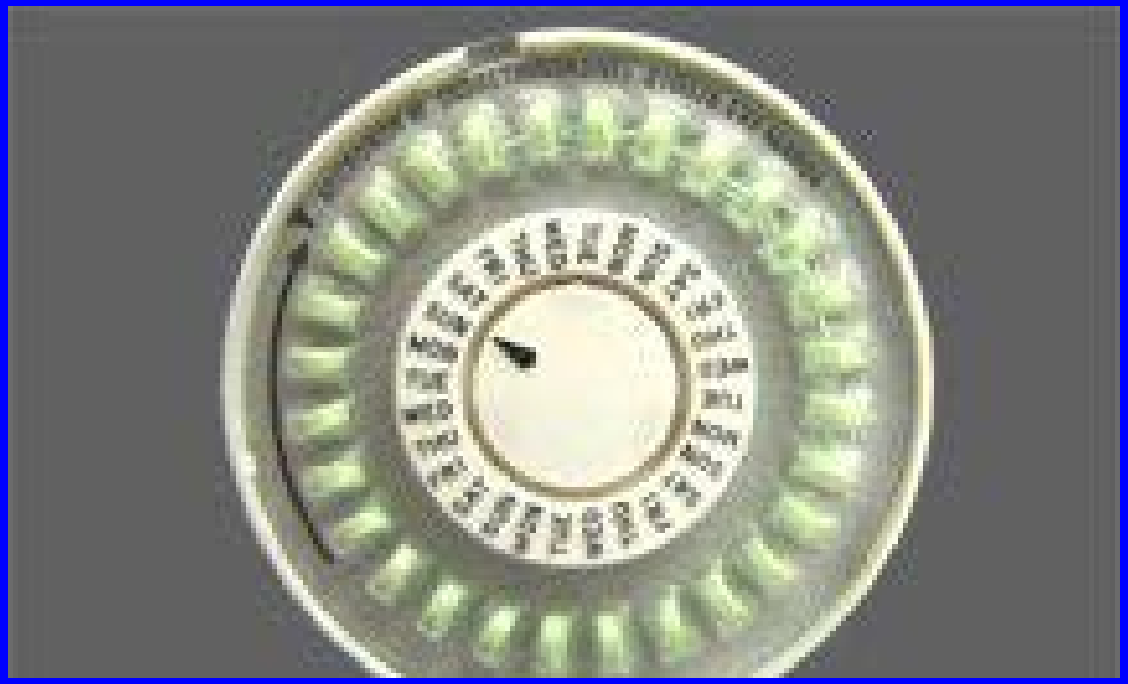
- More than 50 studies on COCs: no effect on risk of developing breast cancer
- WHO: ALL forms of hormonal contraception are category 1 (no restriction) for woman with FH breast ca
- COCs may be beneficial to patient with BRCA as reduce risk of ovarian cancer

WHO Medical eligibility criteria for contraceptive use. 4th ed, 2009.
Obstet Gynecol 2013 Jul;122:139

CDC contraindications to estrogen-containing contraception

- Smoker older than 35
- Uncontrolled hypertension: ≥ 160/100
- Hx of DVT or PE
- Known thrombogenic mutations
- Hx of CAD or stroke
- NEW: Migraine over age 35
- Migraine with aura
- Personal hx of breast cancer

Progestin-only pills



Progestin-only contraception

- WHO case-control study 1998: no increase in DVT, stroke, MI with progestin-only pills
- Safe in women with contraindications to estrogen

Progestin-only pills

- Have lower progestin doses than combined pills and no estrogen
  - each pill contains 0.35 mg norethindrone
- Taken daily with no hormone-free days
- Must take pill at same time each day

Progestin-only pills: mechanisms

1. Thicken cervical mucus
   - Happens 2-4 hours after pill is taken, lasts about 22 hours
   - If woman takes pill at 10 pm, has sex an hour before or after, pill not likely to be effective
   - Morning is best time to take pill if going to have sex at night

Zieman M, et al. Managing Contraception 2015-2016

Progestin-only pills: More mechanisms

2. Cause atrophy of endometrium
   - Leads to decreased menstrual blood loss, amenorrhea in 10% of women
3. Suppress ovulation
   - In only about 60% of women

Emergency contraception

New and best: Ulipristal ("Ella")

- Progestin receptor modulator: suppresses or delays ovulation
- One 30 mg pill: take no later than 5 days after intercourse
- More effective than levonorgestrel (Plan B)
- Very safe

Ann Pharmacother 2011;45:780.
Contraception 2014 May;89:431

Meta-analysis: ulipristal better than levonorgestrel

3242 women: ulipristal or levonorgestrel within 72 hours of intercourse

	Pregnancies	
	#	%
Ulipristal	22	1.4%
Levonorgestrel	35	2.2%

OR 0.58, CI 0.33-0.99, P=0.046

Lancet 2010;375:555

Levonorgestrel: Plan B

- One dose: levonorgestrel 1.5 mg
- Mechanism: inhibits ovulation
- Take ASAP but can be used up to 5 days after intercourse
- Brand name and generic now available OTC with no restrictions

Lancet 2002;360:1803. www.fda.gov

BMI affects efficacy of ulipristal (UPA) and levonorgestrel (LNG)

BMI	Pregnancy, %	
	UPA	LNG
Normal	1.1	1.3
Overweight	1.1	2.5
Obese	2.6	5.8

Overweight: ulipristal or IUD

Obese: IUD best, then ulipristal

Contraception 2011;84:363

Advance provision

- Recommend that patients have home supply of emergency contraceptives in addition to regular contraceptive method
  - available when/if needed
- Give prescription at annual exam

Copper IUD

- Insert up to 5 days after intercourse
- Mechanism: inflammation
  - toxic to sperm and egg
  - interferes with implantation

Emergency contraception: Efficacy

If 1000 women have intercourse…

Method	# pregnant	% reduction
No rx	80	-
COCs	20	75
Levonorg	10	88
Ulipristal	5	94
IUD	1	99

Take home points

1. Long-acting reversible methods are often the best choice
2. DMPA is excellent choice for teens
3. There are more effective options than combined hormonal contraception
4. Discuss emergency contraception and give your patient a Rx