

Are Oral Contraceptives Safe for Women?

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History

Hormones

Hypothalamus and Pituitary Hormones

- Progestin and estrogen have (-) feedback GnRH at hypothalamus.
- FSH has an estrogen effect and LH has the progestin effect at the pituitary.

Types of Oral Contraceptives

Combined Oral Contraceptive (COC)

Progestin-Only Oral Contraceptive (Minipill/POC)

Hormones Involved in Combined Oral Contraceptives (COCs)

• Estradiol

– Synthetic

• Estrogen

• Progesterone

– Anti-estrogen effects

– Synthetic

• Progestin

Combined Oral Contraceptive Generations

Progestin Derivatives

– 1st Generation

– 2nd Generation

– 3rd Generation

• Estrogen Derivatives

– Mestranol

– Ethinyl Estradiol

Estrogen and Progestin

• Binding Affinity

– Differs by progestin

• Half-Life

• Peak serum concentrations

• Combination Oral Contraceptive (COC)

– Ethinylestradiol

Dose - 20 - 40 micrograms

– 2nd and 3rd generation progestins

• Progestin component

• Dose - 0.15-1.5 mg

- Normal schedule is 21d on COC with a 7d gap.

Current COCs

- Lower Estrogen dose than 1960's
- 50-150 µg vs. 20-40µg of estrogen
- New 2nd and 3rd generation progestins
- 10mg vs. 0.15-1.5mg
- Occurrence of serious side effects decreased due to lower dose of estrogen and progestin.

COCs Prevent Pregnancy

- Prevent ovulation
- Progestin effects:
 - Suppresses LH secretion
 - Thickens cervical mucus preventing/hindering sperm transport
 - Thins endometrium preventing ovum implantation
 - Interferes with secretory/peristaltic function inside fallopian tubes
- Estrogenic effects
 - Inhibits ovulation by suppressing FSH and LH
 - Alters endometrium secretions

Progestin-only Oral Contraceptive

- “Minipills”/POC- lower dose of progestin
 - 28 day active hormone cycle
 - Does not always suppress GnRH.
 - Ovulation can occur
 - Efficacy dependent on cervical mucus and endometrial effects
 - 6-10% ectopic pregnancies among users
 - Not as common

Risk Factors...

Venous Thromboembolism(VTE) -

- Highest risk in first year of use
- Highest risk with 3rd generation progestins
- 50 fold increase of VTE if individual is a carrier for coagulation Factor V. Leiden mutation when using 3rd generation COCs
- Duration of Use
- VTE risk decreased with decreasing estrogen dose
- 2nd generation safer than 3rd generation
 - Translates 1-2 additional cases/yr/10,000 users
 - Highest risk associated with 1st generation users.

Myocardial Infarction (MI)/ Stroke

- 2 fold increased risk of Ischemic Stroke with any COC.
- COCs with dose greater than 50µg Ethinyl estadiol have greatest risk.
- Conflicting results between risks with 2nd or 3rd generation COCS

- Carriers of Factor V. Leiden mutation had 13 fold increase risk.

Additional Risk Factors for MI/Stroke

- Increased Risks with COCs:
 - Smoking
 - Age >30 (2-3 fold)
 - Hypertension (10 fold)
 - Estrogen Level (>30 μ g)
 - Hypercholesterolemia
 - Obesity
 - Migraines if over 35y

- POCs do not cause a risk of myocardial infarction or stroke.

Migraine

- Estrogens are vasodilators causing migraines in some women.
- Migraines are thought to be associated with estrogen withdrawal period.
- Dose and progestin generation does not influence migraines.
- Occurrence highest in women >35y.
- Migraines are linked to a stroke.

Bone Mass

- COC users <18y may gain less BMD.
- Decreased estrogen exposure.
- Loss of bone mineral content.
- Increases risk of fracture.
- Limited studies in women under 30.

Gall Bladder Disease

- Oral contraceptives have little effect on development of gallbladder disease.
- Use of COCs can cause gall bladder attacks
- COC association is unknown
 - Hormones may increase cholesterol saturation and decrease gall bladder motility
 - Decreased motility causes gallstone formation

Risk of Breast Cancer

- Increased risk if used <45y (20-40x)?
- Increased risk if 20-29 or <35?
- Greatest risk is in women <35 with recent COCs
- Increased risk if used >35y
 - due to increase risk of breast cancer with age
- Conflicting results for type or generation of progestin.
- 50x higher risk with >35 μ g estrogen dose.
- With breast cancer, COC users have increased rate of tumor growth
- POCs have lower risk.

Fertility

- Fertility Problems
 - 58% 1st cycles are ovulatory
 - Cycles can take up to one year to normalize.
- Oral contraceptives do not cause permanent infertility.

Benefits

- Prevention of:
 - Bone loss
 - 12% increase in BMD vs. control >18y
 - Greatest protection with ≥10 yrs use
 - Due to estrogen dose
 - 25µg
- Treatment of:
 - Acne
 - Hirsutism
- COC regulate:
 - Irregular cycles
 - Dysmenorrhea
 - Menorrhagia
 - Amenorrhea

Pelvic inflammatory disease (PID)

- COCs increasing the thickness of cervical mucus.
- Preventing bacteria from moving up the reproductive system.
- Decreasing menstrual flow, limiting the opportunity for bacteria to grow in the upper reproductive tract.

–Ectopic pregnancy

- Less likely
- High contraceptive efficacy

Ovarian cancer

- 10 to 12 percent decrease in risk after 1 year of use
- 50 percent decrease after 5 years of use
- Regardless of generation or dose

Endometrial Cancer

- Decreases with length of use
- Protection continues after discontinuation

Breast Cancer Benefits

- Long term COC use reduces:
 - Benign breast disease