CONTRACEPTIVE TECHNOLOGY: SIMPLEX, COMPLEX, COMPLICATED?

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DISCLOSURES

I do not receive any financial or other payments from drug or device companies.

I received no compensation to develop this presentation.

CONTRACEPTIVE TECHNOLOGY: SIMPLEX, COMPLEX, COMPLICATED?

Goals:

- To discuss contraceptive methods
- To understand mechanisms of actions of non-hormonal hormonal (NHC) and hormonal contraception (HC)
- To understand medical ethical, and theological considerations that arise in the context of women's use of contraceptive technology

CONTRACEPTIVE METHODS AND THEIR MECHANISMS OF ACTION

This information relates not only to policy but to practice

- Clinicians
- Patients
- Policymakers
- Faculty, staff and students

CONTRACEPTIVE METHODS AND THEIR MECHANISMS OF ACTION

Review reproductive physiology

Review specific types of contraception and their mechanisms of action

Discuss how contraception may affect embryo survival

Discuss theological and ethical issues

Discuss some potential future concerns regarding the use of hormonal contraception

OVERVIEW

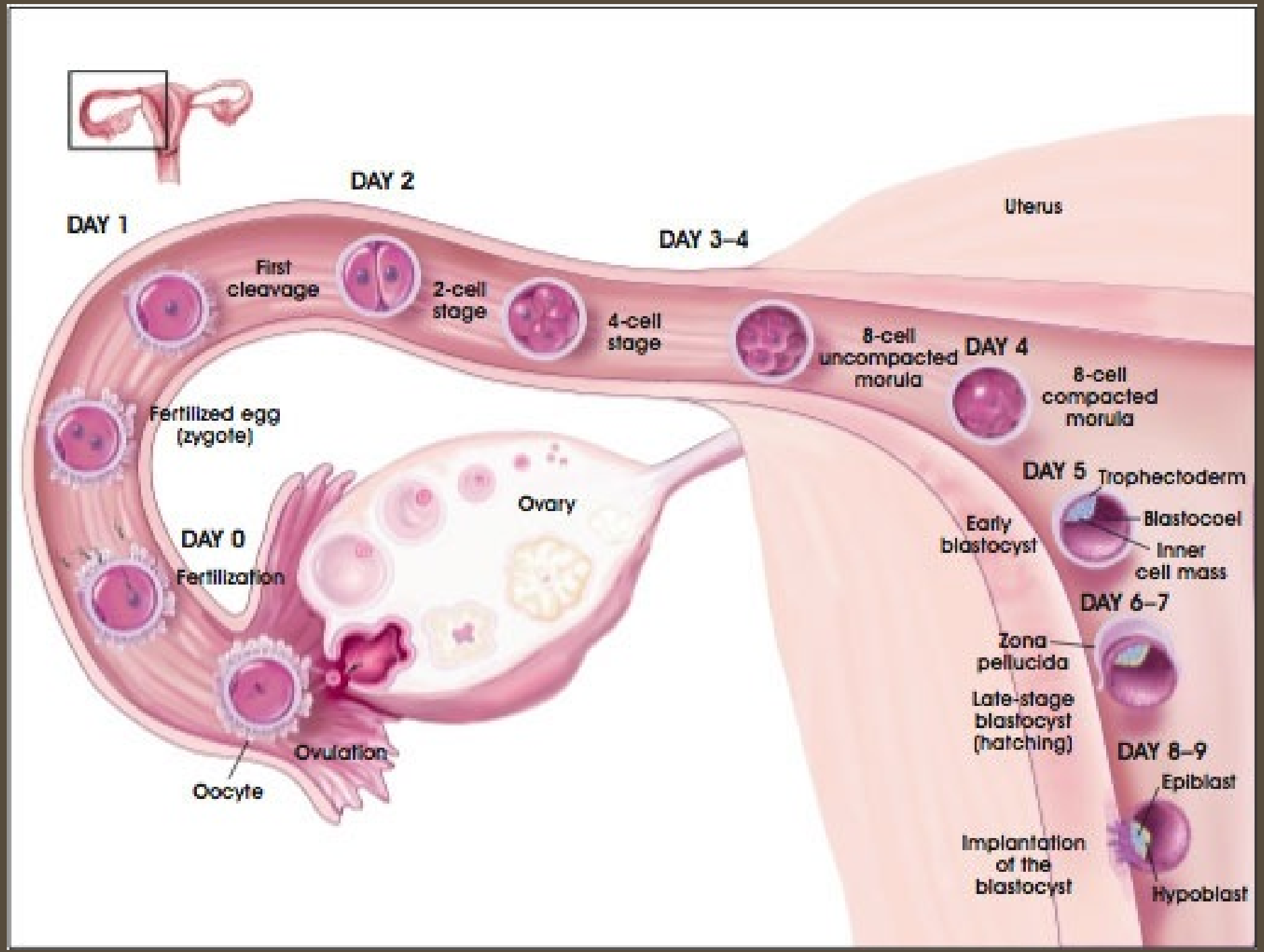
We will discuss 2 potential contraceptive mechanisms of action related to embryo survival, that are of concern with use of HC

- Embryo formation followed by embryo death due to inadequate hormonal (progesterone) support
- Changes in the uterine lining that make it inhospitable to implantation

OVERVIEW

Additional issues for discussion

- Theological and ethical perspectives
- Possible long-term effects of HC on the human egg


DAY 1
DAY 2
DAY 3–4
DAY 4
DAY 5
DAY 6–7
DAY 8–9
DAY 0
Uterus
First cleavage
2-cell stage
4-cell stage
8-cell uncompacted morula
8-cell compacted morula
Fertilized egg (zygote)
Ovary
Fertilization
Ovulation
Oocyte
Trophectoderm
Blastocoel
Early blastocyst
Inner cell mass
Zona pellucida
Late-stage blastocyst (hatching)
Epiblast
Implantation of the blastocyst
Hypoblast

CONTRACEPTIVE TECHNOLOGY

Specific types of contraceptives to be considered:

- Oral contraceptive pills
- Contraceptive ring (NuvaRing)
- Contraceptive patch (OrthoEvra) - black box warning
- Injectable contraceptive (DepoProvera) – black box warning
- Intrauterine devices (Mirena)
- Contraceptive implants (Nexplanon, Implanon)

CONTRACEPTIVE METHOD CHOICE

Most effective method used in the past month by U.S. women, 2012

METHOD	No. of users	% of women aged 15–44	% of women at risk of unintended pregnancy	% of contraceptive users
Pill	9,720,000	16.0	23.3	25.9
Tubal (female) sterilization	9,443,000	15.5	22.6	25.1
Male condom	5,739,000	9.4	13.7	15.3
IUD	3,884,000	6.4	9.3	10.3
Vasectomy (male sterilization)	3,084,000	5.1	7.4	8.2
Withdrawal	1,817,000	3.0	4.4	4.8
Injectable	1,697,000	2.8	4.1	4.5
Vaginal ring	759,000	1.2	1.8	2.0
Fertility awareness-based methods	509,000	0.8	1.2	1.4
Implant	492,000	0.8	1.2	1.3
Patch	217,000	0.4	0.5	0.6
Emergency contraception	91,000	0.2	0.2	0.2
Other methods*	133,000	0.2	0.3	0.4
No method, at risk of unintended pregnancy	4,175,000	6.9	10.0	na
No method, not at risk	19,126,000	31.4	na	na
Total	60,887,000	100.0	100.0	100.0

NOTE: "At risk" refers to women who are sexually active; not pregnant, seeking to become pregnant, or postpartum; and not noncontraceptively sterile. na=not applicable. *Includes diaphragm, female condom, foam, cervical cap, sponge, suppository, jelly/cream and other methods.

CONTRACEPTIVE TECHNOLOGY: SIMPLEX, COMPLEX, COMPLICATED

Simplex:

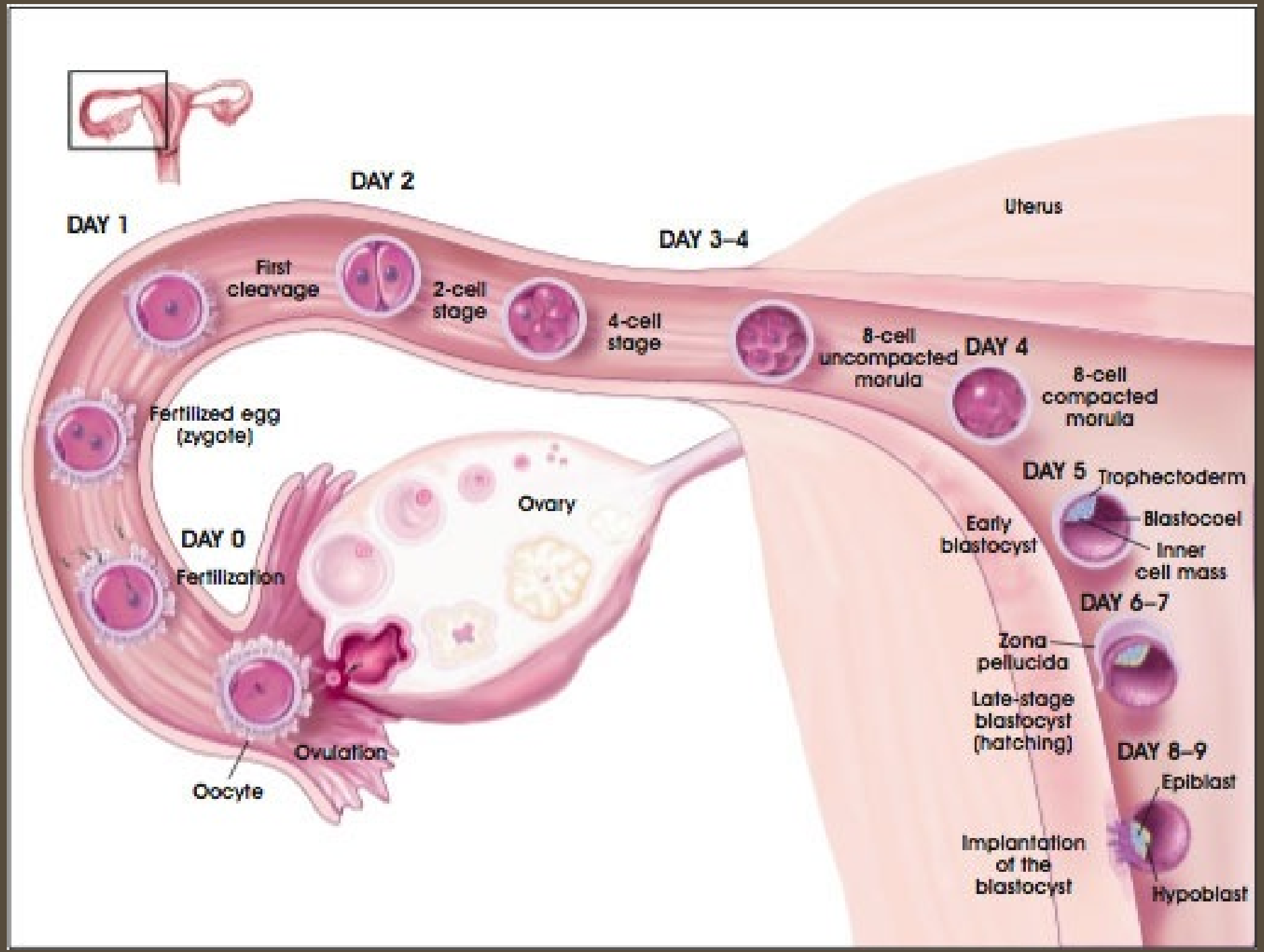
- Contraceptive technology with 1presumptive mechanism of action

Complex:

- Contraceptive technology with >1 presumptive mechanism of action

Complicated:

- Contraceptive technology, for which there are theological and ethical concerns or ramifications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CONTRACEPTIVE TECHNOLOGY: SIMPLEX

Simplex (1):

- Contraceptive technology with presumptive mechanism of action = prevention of conception
- Prevent union of egg and sperm
  - Condoms (male and female)
  - Diaphragms, sponge, cervical cap

CONTRACEPTIVE TECHNOLOGY: SIMPLEX

Simplex(2):

- Contraceptive technology with presumptive mechanism = gametocidal action
- Kills egg or sperm
  - Spermicides (jelly, cream, foam, vaginal contraceptive film)
  - Copper IUD – appears to be possibly embryocidal

What about HC?

CONTRACEPTIVE TECHNOLOGY: SIMPLEX?

Simplex:

- Theoretically, hormonal contraceptive (HC) technology would be simplex if its presumptive mechanism = prevention of ovulation
- HC suppresses LH and FSH surge at midcycle; includes
  - Oral contraceptive pills
  - Contraceptive ring (NuvaRing)
  - Contraceptive patch (Ortho-Evra)
  - Contraceptive injection (DepoProvera)
  - Contraceptive implants (Nexplanon, Implanon)

CONTRACEPTIVE TECHNOLOGY: COMPLEX

- If HCs worked by consistent suppression of ovulation, they would be similar to barrier and gametocidal methods in that (1) They would have only 1 mechanism of action and (2) With their use, there would be decreased fertilization potential
  - Barrier and gametocidal methods: no union of sperm and egg = decreased fertilization potential
  - HCs: No ovulation, no egg = decreased fertilization potential

CONTRACEPTIVE TECHNOLOGY: COMPLEX

- Moreover, if fertilization and embryo formation did occur, there would be no barrier to embryo survival and implantation

CONTRACEPTIVE TECHNOLOGY: COMPLEX

- However, despite perceptions that HCs only act to suppress ovulation, there is abundant evidence for additional mechanisms of action which are of concern to those with pro-life convictions, especially Christians.
- Thus these methods have > 1 mechanism of action and are <u>complex</u>

CONTRACEPTIVE TECHNOLOGY: COMPLEX

Complex: Contraceptive technology with > 1 mechanism of action

- Oral contraceptive pills
- Contraceptive ring (NuvaRing)
- Contraceptive patch
- Injectable contraceptives (DepoProvera)
- Contraceptive implants (Nexplanon, Implanon)
- **Emergency contraception (Plan-B, Ella)**

CONTRACEPTIVE TECHNOLOGY: COMPLEX

Complex: Contraceptive technology with > 1 mechanism of action

- Prevents ovulation by suppression of the LH and FSH surges at midcycle
- Decreases endometrial receptivity
- Decreases embryo (blastocyst) survival

CONTRACEPTIVE TECHNOLOGY: COMPLEX

Complex: Contraceptive technology with > 1 mechanism of action

- Prevention of ovulation by suppression of the LH and FSH surges at midcycle
- Decreases endometrial receptivity
- Decreases embryo (blastocyst) survival, therefore indirectly embryocidal

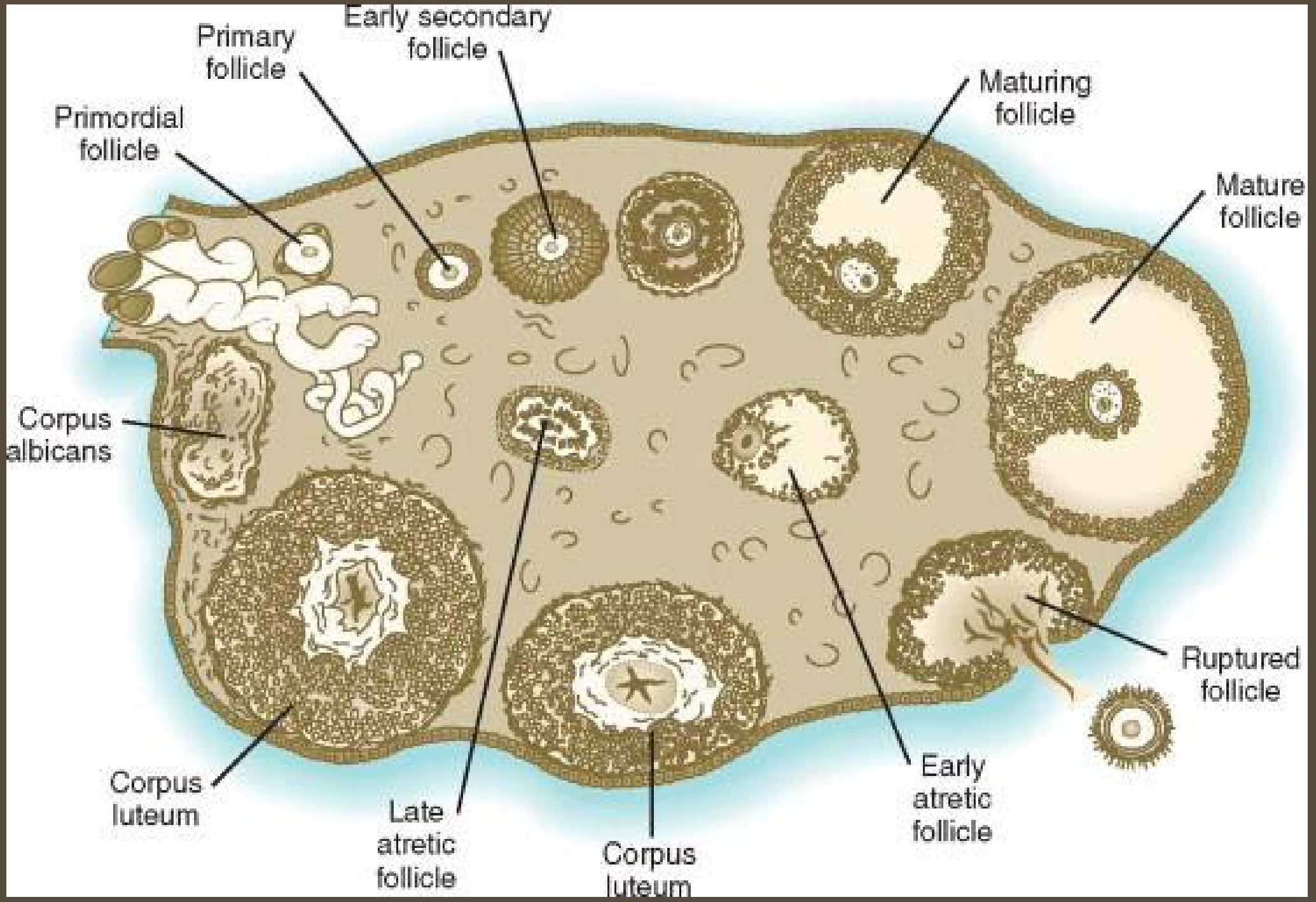
CONTRACEPTIVE TECHNOLOGY: COMPLEX

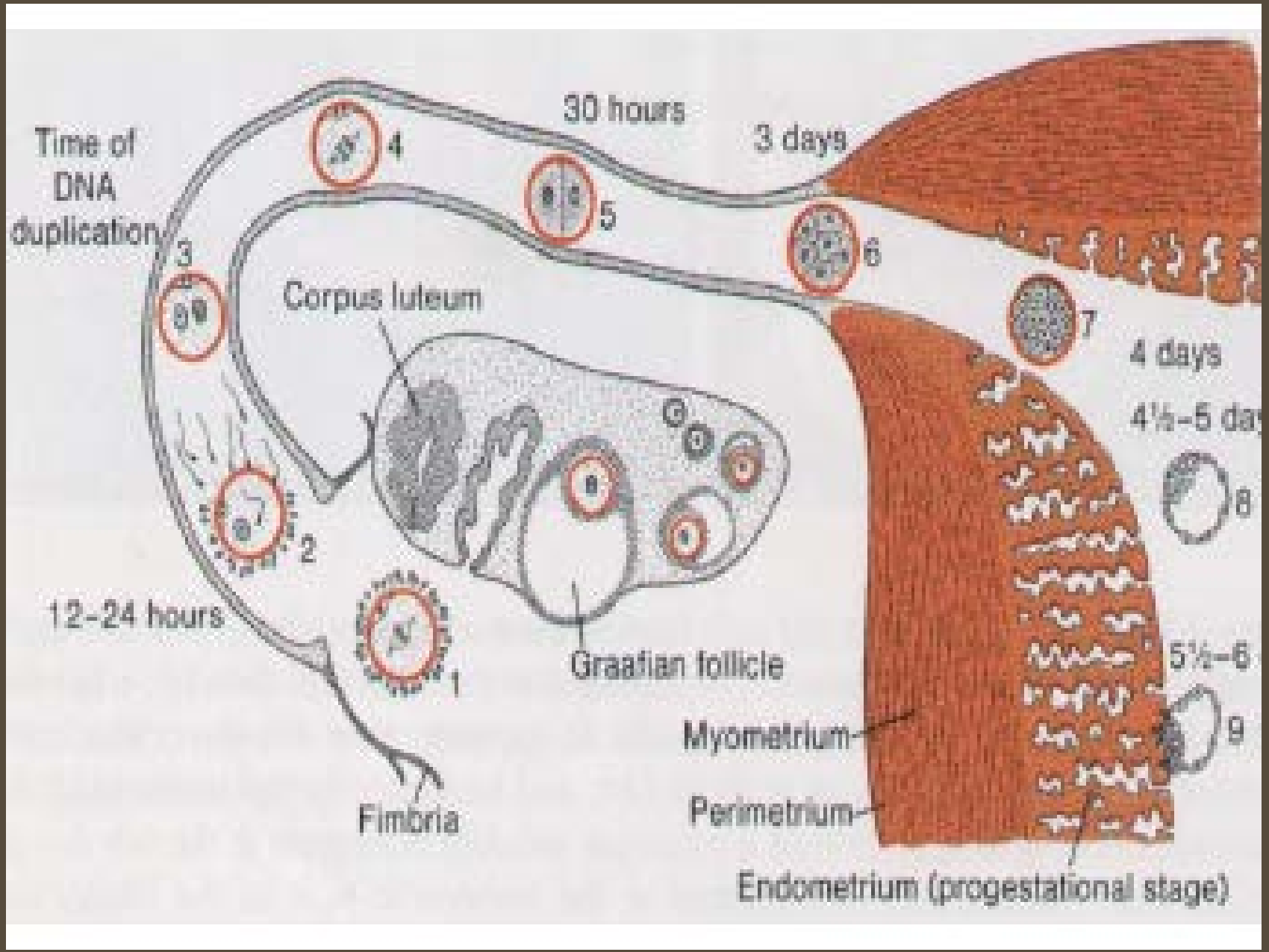
To understand this, return to consideration of conception, embryo transport and embryogenesis

Transport of Gametes and Fertilization

Ovulation :

- Mid point of menstrual cycle
- Under the influence LH and FSH→ primary oocyte complete Meiosis I (oocyte +1st polar body → Meiosis II→ arrested at metaphase II
- Ovary bulge locally→ stigma→ collagenase activity ↗→ local muscular contraction↗ → extrude oocyte, breaks free→ floats out of the ovary


Primary follicle
Early secondary follicle
Primordial follicle
Maturing follicle
Mature follicle
Corpus albicans
Ruptured follicle
Corpus luteum
Late atretic follicle
Corpus luteum
Early atretic follicle


Time of DNA duplication
30 hours
3 days
4 days
4½–5 day
5½–6
12–24 hours
Corpus luteum
Graafian follicle
Fimbria
Myometrium
Perimetrium
Endometrium (progestational stage)
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REPRODUCTIVE PHYSIOLOGY

Once ovulation has occurred, LH acts upon the cells (granulosa cells) lining the Graafian follicle, causing luteinization

- The granulosa cells synthesize progesterone

CONTRACEPTIVE TECHNOLOGY: COMPLEX

A brief review of the literature on HC's mechanism of action indicates that HC may not completely suppress ovulation. Why?

- There are lower doses of estrogen (ethinyl estradiol) in current oral contraceptive pill formulations, compared with earlier-generation pills, due to concerns for blood clots, vascular complications
- Phenomenon of escape ovulation
- Physical and pharmacogenetic differences between women

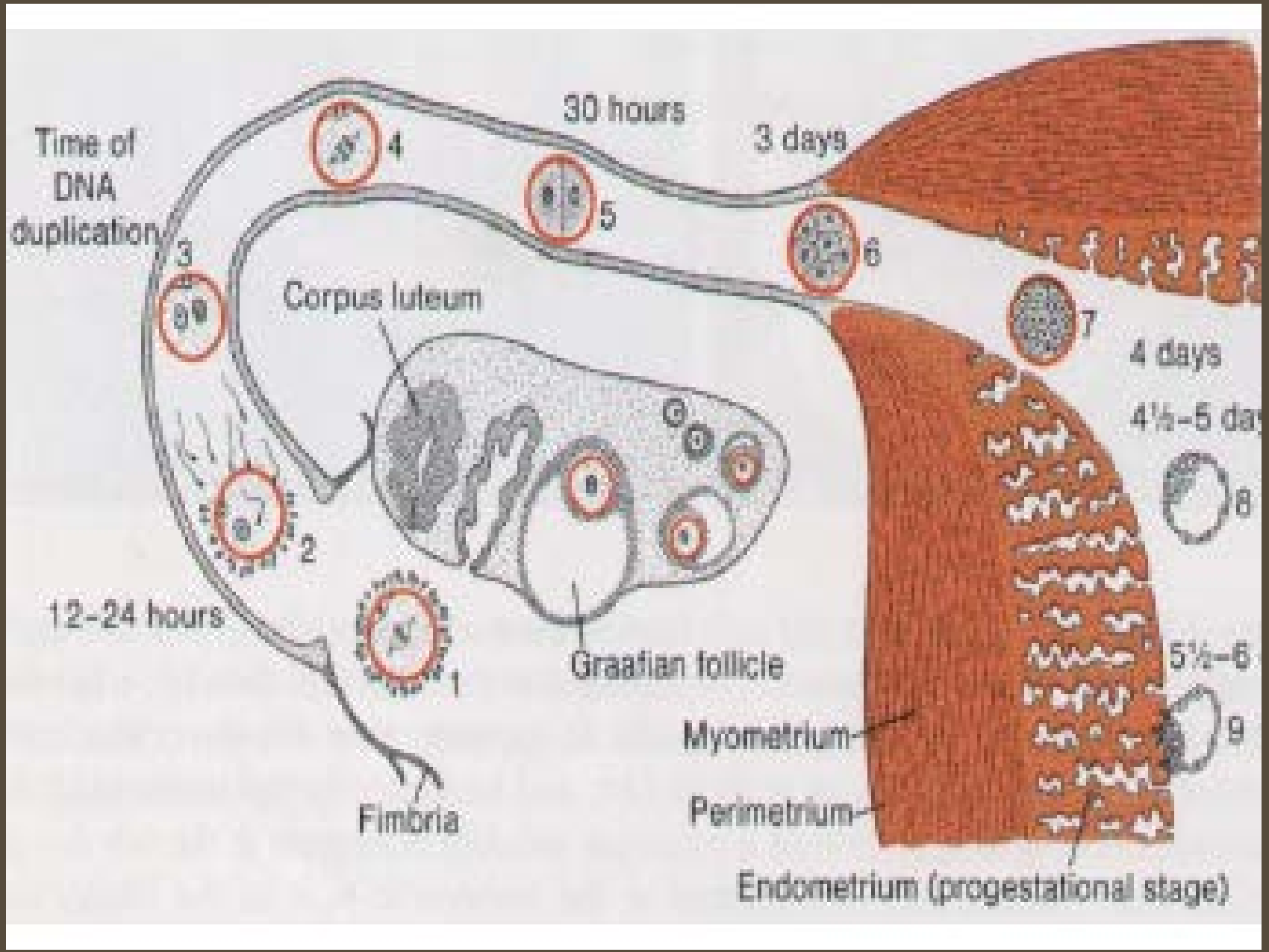
CONTRACEPTIVE TECHNOLOGY: LOWER ESTROGEN DOSES

- Lower doses of estrogen (ethinyl estradiol) in OCPs compared with early pills are now used due to concerns for blood clots, vascular complications
  - These lower doses do not suppress LH and FSH as effectively as higher doses

Transport of Gametes and Fertilization

Ovulation :

- Mid point of menstrual cycle
- Under the influence LH and FSH→ primary oocyte complete Meiosis I (oocyte +1st polar body → Meiosis II→ arrested at metaphase II
- Ovary bulge locally→ stigma→ collagenase activity ↗→ local muscular contraction↗ → extrude oocyte, breaks free→ floats out of the ovary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ESCAPE OVULATION

This occurs when there is insufficient suppression of the developing follicle, especially during the drug-free interval in a monthly oral contraceptive pill pack

Can also occur when pills are missed during the rest of the month

ESCAPE OVULATION

It is possible that if ovulation occurs, followed by pregnancy, that this may be a desired outcome

However, it is possible that this pregnancy might be "unwanted" and therefore at risk for abortion

In addition, when women who are using HCs do ovulate, the ovulatory process is likely to be abnormal

PHYSICAL AND PHARMACOGENETIC DIFFERENCES

- Obesity
- Genetic ability to metabolize estrogens – some women metabolize them more quickly, others more slowly
- This leads to variations in blood levels of estrogens

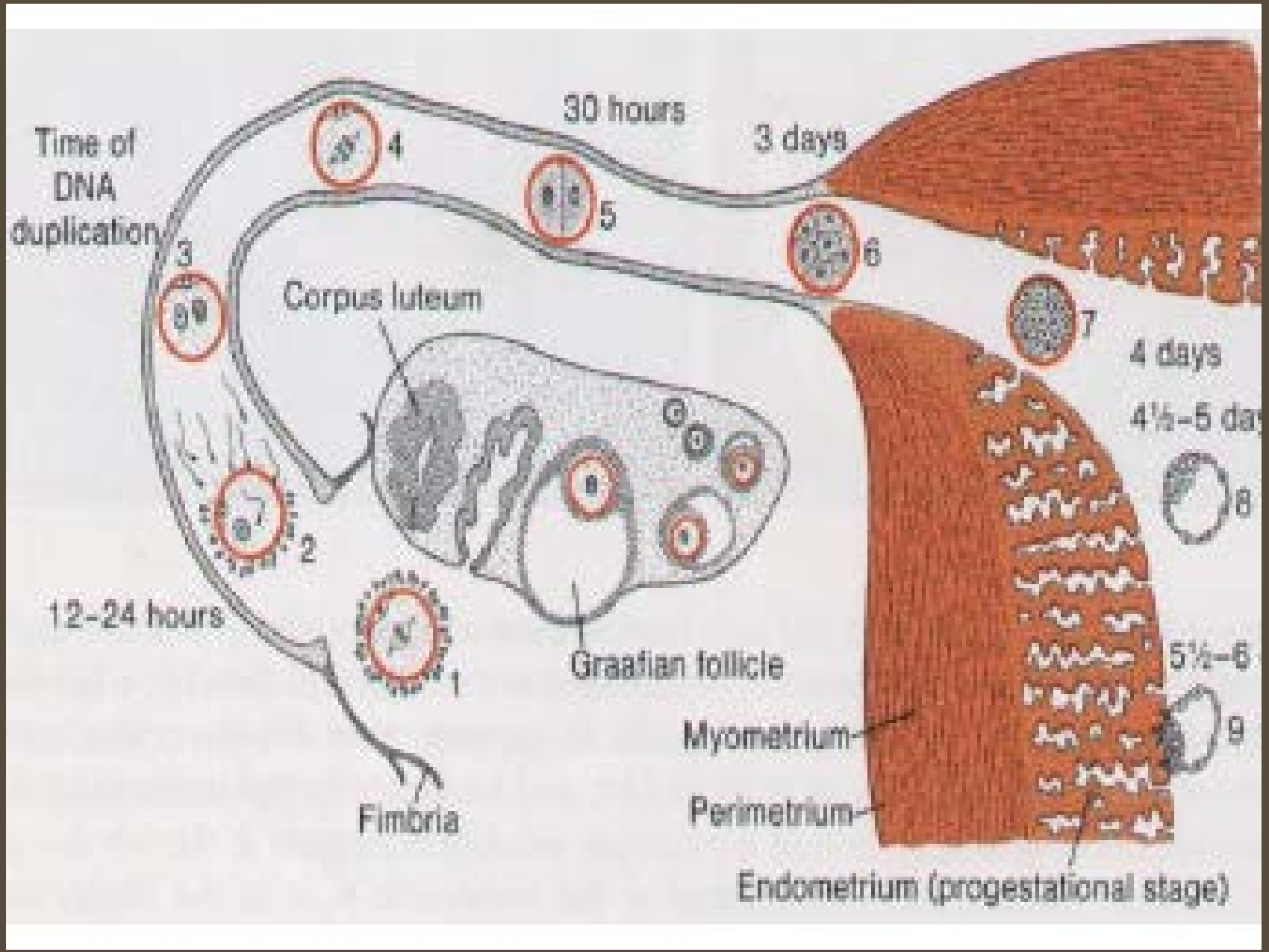
ABNORMAL OVULATION

Defined as follicle rupture with no or reduced LH surge prior to ovulation, and low progesterone after ovulation (Croxatto et al)

- Occurs as a result of high hormone levels (from HC) during the menstrual cycle

When abnormal ovulation occurs, it leads to low progesterone levels which are not sufficient to support the developing embryo; they are also not sufficient to induce changes in the uterine lining to make it conducive to implantation

Croxatto HB, Brache V, Pavez M, Cochon L, Forcelledo ML, Alverez F, Massai R, Faundes A, Salvatierra AM. Pituitary-ovarian function following a standard levonorgestreln emergency contraception dose or a single 0.75 mg dose given on the days preceding ovulation. Contraception 70 (2004) 442-450.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ABNORMAL OVULATION

Abnormal ovulation has been frequently seen with HCs

If and when it occurs, fertilization and embryo formation could also occur

- However, if embryo formation occurs, without sufficient progesterone levels to cause endometrial change and to support the embryo until placental function is sufficient, it is possible that the embryo might not survive.

Endrikat J, Parke S, Trummer D, Serrani M, Duijkers I, Klipping C. Pituitary, ovarian and additional contraceptive effects of an estradiol-based combined oral contraceptive: results of a randomized, open-label study Contraception 87 (2013) 227–234;Van Heusden AM, Coelingh Bennink HJ, Fauser BC FSH and ovarian response: spontaneous recovery of pituitary-ovarian activity during the pill-free period vs. exogenous recombinant FDS during high dose combined oral contraceptives. Clin Endocrinol (Oxf) 2002 Apr 56 (4); 509-17; Pierson RA, Archer DF, Moreau M, Shangold GA, Fisher AC, Creasy GW, (Ortho Evra™/Evra™ 008 Study Group) Fertility and Sterility Vol. 80, No. 1, July 2003; Seidman L, Kroll R, Howard B, Ricciotti N, Hsieh J, Weiss H. Contraception. 2015 Jun;91(6):495-502. doi: 10.1016/j.contraception.2015.03.001. Epub 2015 Mar 6.

DECREASED ENDOMETRIAL RECEPTIVITY

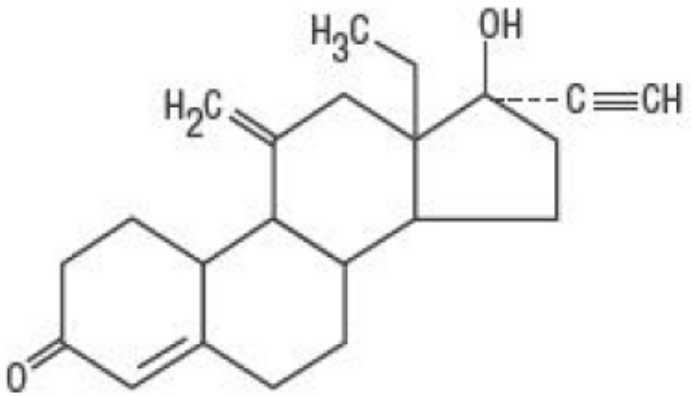
Several HCs have as part of their stated mechanism of action thinning of the endometrium (=decreased endometrial receptivity)

These include DepoProvera, Nexplanon, the Mirena IUD, and the vaginal ring

This effect is described in the manufacturers' prescribing information

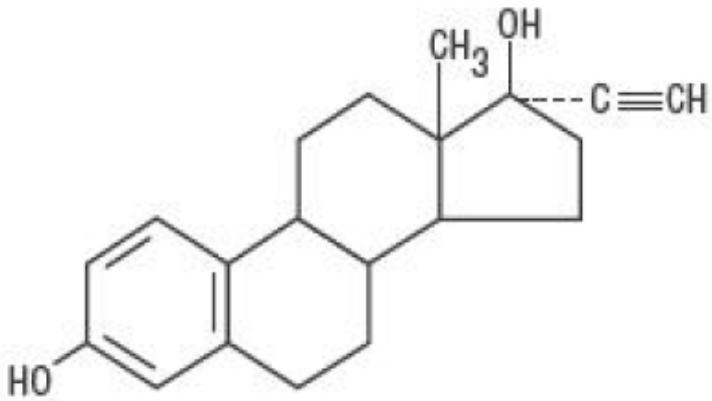
CONTRACEPTIVE RING (NUVARING) PRESCRIBING INFORMATION

ETONOGESTREL



$C_{22}H_{28}O_2$

ETHINYL ESTRADIOL



$C_{20}H_{24}O_2$

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Combination hormonal contraceptives act by suppression of gonadotropins. Although the primary effect of this action is inhibition of ovulation, other alterations include changes in the cervical mucus (which increase the difficulty of sperm entry into the uterus) and the endometrium (which reduce the likelihood of implantation).

COMPLICATED

If we consider the zygote and embryo to be human and that life begins at conception/fertilization, any contraceptive method that reduces embryo survival is embryocidal

- Implantation is necessary for blastocyst survival
- Prevention of implantation = decreased embryo survival

COMPLICATED

Based on the data, we must acknowledge that there is some likelihood that with HC methods, ovulation may occur, with subsequent embryo formation

Where abnormal ovulation has occurred due to HC use, embryo survival may be decreased due to inadequate hormonal support

Embryo survival may also be decreased due to inhospitable endometrium leading to failure of implantation

HISTORICAL, ETHICAL AND THEOLOGICAL ASPECTS

Contraception is not a modern issue, and it is not just a “Catholic issue”

- Though Catholics have been more faithful to uphold Christian tradition and teaching on contraception

HISTORICAL VIEWS

In Old Testament times, God's people were forbidden upon penalty of death to practice child sacrifice as the surrounding nations did (Lev 18:21; 20:5).

This is the context for considering the ethics of abortion, which Old Testament Judaism always forbade: life is a gift of God.

The preciousness of unborn human life is celebrated in Psalm 139, where David says, "For you formed my inward parts; you knitted me together in my mother's womb…I am fearfully and wonderfully made, … your eyes beheld my unformed substance; in your book were written, every one of them, the days that were formed for me, when as yet there was none of them." (Psalm 139: 13-14, 16).

HISTORICAL VIEWS

Even *in utero* at the earliest stages of development God recognizes the humanity of the embryo (see Genesis 20:18, 29:31, 30:2, 30:22; Judges 13:2-3; Ruth 4:13; 1 Samuel 1:6; Jeremiah 1:5; Luke 1: 13-15 and 1:24-25, 1:44).

In other words, life is sacred from the moment of conception.

HISTORICAL VIEWS

The historic position of all 3 branches of the church has always been emphatically against abortion. Not only this, but the Church has viewed contraception in a similar light.

Aristotle mentioned contraceptive methods, and many other cultures worldwide practiced contraception, abortion, or both. Abortion and contraception were very common in the Greco-Roman culture in which Christianity emerged, being approved at the highest levels of society even though induced abortion was often fatal for the mother.

SCRIPTURAL FOUNDATIONS

The Bible provides a framework for understanding family planning by describing the origin and sanctity of human life.

As the crowning act of His creation, God created humankind (male and female) uniquely in His own image.

A BIBLICAL FRAMEWORK FOR FAMILY PLANNING

God further dignified human life through the incarnation of Jesus Christ as a man and promises the resurrection of the physical body at the end of time.

Thus, all human life should be treated as a gift from God and worthy of respect

HISTORICAL VIEWS

Until the 20th century, the three major branches of Christianity (Roman Catholicism, Orthodoxy, and Protestantism) all condemned contraception.

THE CONTRACEPTIVE MENTALITY

"The contraceptive mentality," is deeply rooted in American and Western European culture. Dr. Donald DeMarco, drawing upon writings by Carl Jung, describes a mentality as existing in a society, "when enough people react automatically to a situation without thinking of the long-range consequences." Jesuit sociologist Stanislas de Lestapis was the first to draw attention to the "contraceptive mentality." Dr. Demarco states the following:

THE CONTRACEPTIVE MENTALITY

In his book, *La limitation des naissances*, published in 1960, de Lestapis provided sociological data that indicated the presence of what he termed a "contraceptive state of mind." “In England, for example, the Royal Commission on Population noted that in 1949 the number of procured abortions was 8.7 times higher among couples who habitually practiced contraception than among those who did not. In Sweden, after contraception had been fully sanctioned by law, legal abortions increased from 703 in 1943 to 6,328 in 1951. In Switzerland, where contraception was almost unrestricted, abortions were alleged to equal or outnumber live births by 1955, and so on. Such figures offered compelling evidence for the claim that more contraception does not reduce the incidence of abortion.

THE CONTRACEPTIVE MENTALITY

. In fact, the figures suggested that more contraception tends to establish a "contraceptive state of mind" which leads to absolving responsibility for children conceived which, in turn, leads to more abortion . . . Malcolm Potts, the former medical director of the International Planned Parenthood Federation, accurately predicted in 1973, ‘As people turn to contraception, there will be a rise, not a fall, in the abortion rate’.”

THE CONTRACEPTIVE MENTALITY

Lawrence Lader, whose influential 1966 book, *Abortion*, provided much of the scientific foundation for *Roe*, ratified this concept, lamenting that contraception,

…[has not] been scientifically perfected to meet every requirement of dependability, cost, and esthetic preference…until medical research discovers the final solution, abortion is the essential emergency measure, the inalienable right of all women in a free society…As long as a reasonable chance of contraceptive failure persists…abortion must be included as a part of birth control to insure every child's becoming a wanted child.

THE CONTRACEPTIVE MENTALITY

Lader quotes Garrett Hardin, professor of biology at University of California-Santa Barbara, as saying, "no matter how good a method of contraception is, we can never expect it to be perfect…Even one with a 1 percent failure rate produces a quarter of a million unwanted children a year [based on the US population at the time]…abortion is the much-needed backstop in the system of birth control." This explicit connection between contraception and induced abortion shows the fruit of the contraceptive mentality.

THE CONTRACEPTIVE MENTALITY

Existing as it does in a materialist and utilitarian ethical framework, the contraceptive mentality cannot help but lead couples to turn to abortion when contraception fails. George and Tollefson make the point that within any such utilitarian ethic, "there will always be human beings who are dispensable, who must be sacrificed for the greater good. Utilitarianism…treats the greater good, a mere aggregate of all the interests or pleasures or preferences of individuals, as the good of supreme worth and value, and demands that nothing stand in the way of its pursuit."

TOWARD A CHRISTIAN DEFINITION OF FAMILY PLANNING

Human beings cannot decide infallibly that they will or will not become pregnant when they want to. “Family planning” is a mirage which promotes the illusion that we have a degree of control over life that, as humans, we simply do not have. The Bible states that God has the ultimate power to open and shut the womb (Genesis 20:18, 29:31, 30:2, 30:22; Judges 13:2-3; Ruth 4:13; 1 Samuel 1:6; Luke 1:13-15, 1:24-25).

AVOIDING THE CONTRACEPTIVE MENTALITY

The argument can be made that the contraceptive mentality moves individuals and societies incrementally toward acceptance of induced abortion. This link was recognized by the Supreme Court in *Planned Parenthood v. Casey (1992)*, which stated:

[The *Roe v. Wade* decision] could not be repudiated without serious inequity to people who, for two decades of economic and social developments, have organized intimate relationships and made choices that define their views of themselves and their places in society, **in reliance on the availability of abortion in the event that contraception should fail…It should be recognized, moreover, that in some critical respects, the abortion decision is of the same character as the decision to use contraception**, to which *Griswold v. Connecticut, Eisenstadt v. Baird,* and *Carey v. Population Services International* afford constitutional protection.

AVOIDING THE CONTRACEPTIVE MENTALITY

Personally and societally people have tried to draw a strict boundary between contraception and abortion, but it can easily collapse. A further case can be made that the acceptance of contraception leads to other things that the Christian church has traditionally denounced. As Eberstadt notes, “If a church cannot tell its flock ‘what to do with my body’…with regard to contraception, then other uses of that body will quickly prove to be similarly off-limits to ecclesiastical authority.”

AVOIDING THE CONTRACEPTIVE MENTALITY

Like the “firewall” between contraception and abortion, the wall between contraception and sexual sin collapses because it is often built on a rejection of God’s authority.

CONCLUSION

A reflection on the Incarnation could help illuminate our thinking on this contentious subject. Jesus, the second member of the Trinity, could have come to earth as the Savior in any form he chose – as a spirit, as a fully-grown man – and bypassed the process of pregnancy. As God, He had the power to do so. But not only did he lay aside His position through the *κένωσις*, Jesus Himself became an embryo. As an embryo, He implanted in Mary's uterus and gestated. Like every other fetus, He grew and developed to the end of pregnancy, at which time Mary gave birth to Him. Was God's decision to send His son to become flesh and dwell among us, in the ultimate humility of conception, gestation and birth, random?

CONCLUSION

No. Through the beauty of the Incarnation God showed us that human reproduction is different from animal reproduction. God values and esteems human reproduction because, in His wisdom, He deemed the human frame, made from dust, as worthy to contain Christ, the fullness of the Godhead, the glory of God. In turn, Jesus submitted to the will of His Father and in so doing dignified conception, gestation, pregnancy, and women and mother In turn, Jesus submitted to the will of His Father and in so doing dignified conception, gestation, pregnancy, and women and motherhood. Further, God has given human beings the power, in cooperation with Him, through the act of marriage (sex) to create (קָנָה) immortal human life in His image and likeness (Genesis 4:1).

CONCLUSION

Our understanding of how to prevent pregnancy came to us after the Fall and is tainted by our fallen nature.

As fallen creatures, we need to exert the greatest caution in promoting the use of technology in a context that could not only damage or destroy the image of God in other human beings, but ultimately undermine society and culture.

Chireau Wubbenhorst M, Wubbenhorst J. Evangelical international organizations and family planning. Dignitas Summer 2017; 24(2):11-21.