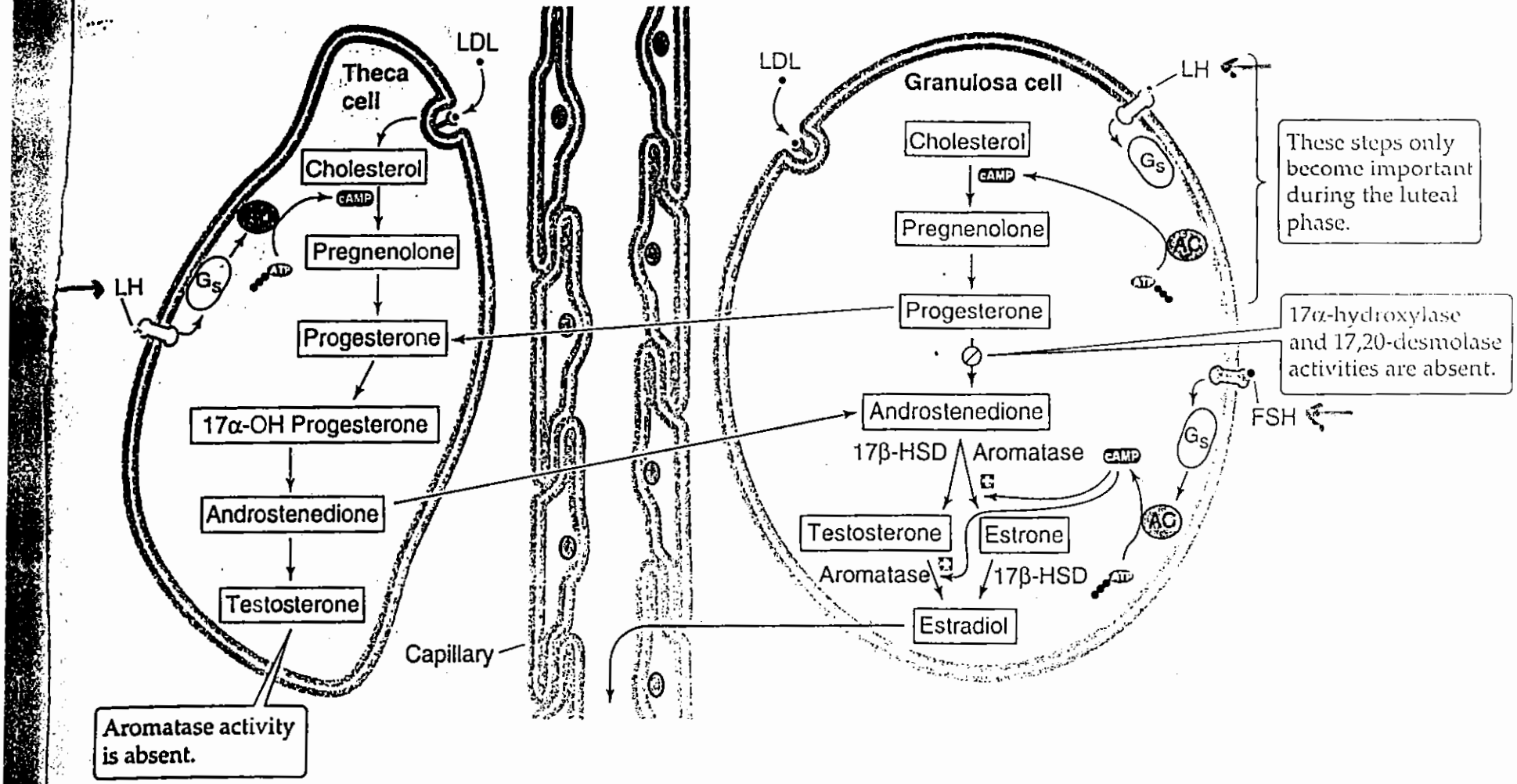


FIGURE 54–10. Two-cell, two-gonadotropin model. During the follicular phase, the major product of the follicle is estradiol, whereas during the luteal phase, the major products of the corpus luteum are the progestins, although estradiol synthesis is still substantial. In the follicular phase, LH primes the theca cell to convert cholesterol to androstenedione. Because the theca cell lacks aromatase, it cannot generate estradiol from this androstenedione. Instead, the androstenedione diffuses to the granulosa cell, whose aromatase activity has been stimulated by FSH. The aromatase converts the androstenedione to estradiol. In the luteal phase, the vascularization of the corpus luteum makes LDL available to the granulosa-lutein cells. Thus, both the theca-lutein and the granulosa-lutein cells can produce progesterone, the major product of the corpus luteum. For production of 17α-hydroxyprogesterone (17α-OH progesterone), some of the progesterone diffuses into the theca-lutein cell, which has the 17α-hydroxylase activity needed for converting the progesterone to 17α-hydroxyprogesterone. The theca-lutein cell can also generate the androstenedione, which diffuses into the granulosa-lutein cell for estradiol synthesis. AC, adenylyl cyclase; ATP, adenosine triphosphate; cAMP, cyclic adenosine monophosphate; FSH, follicle stimulating hormone; HSD, hydroxysteroid dehydrogenase; LDL, low density lipoprotein; LH, luteinizing hormone.

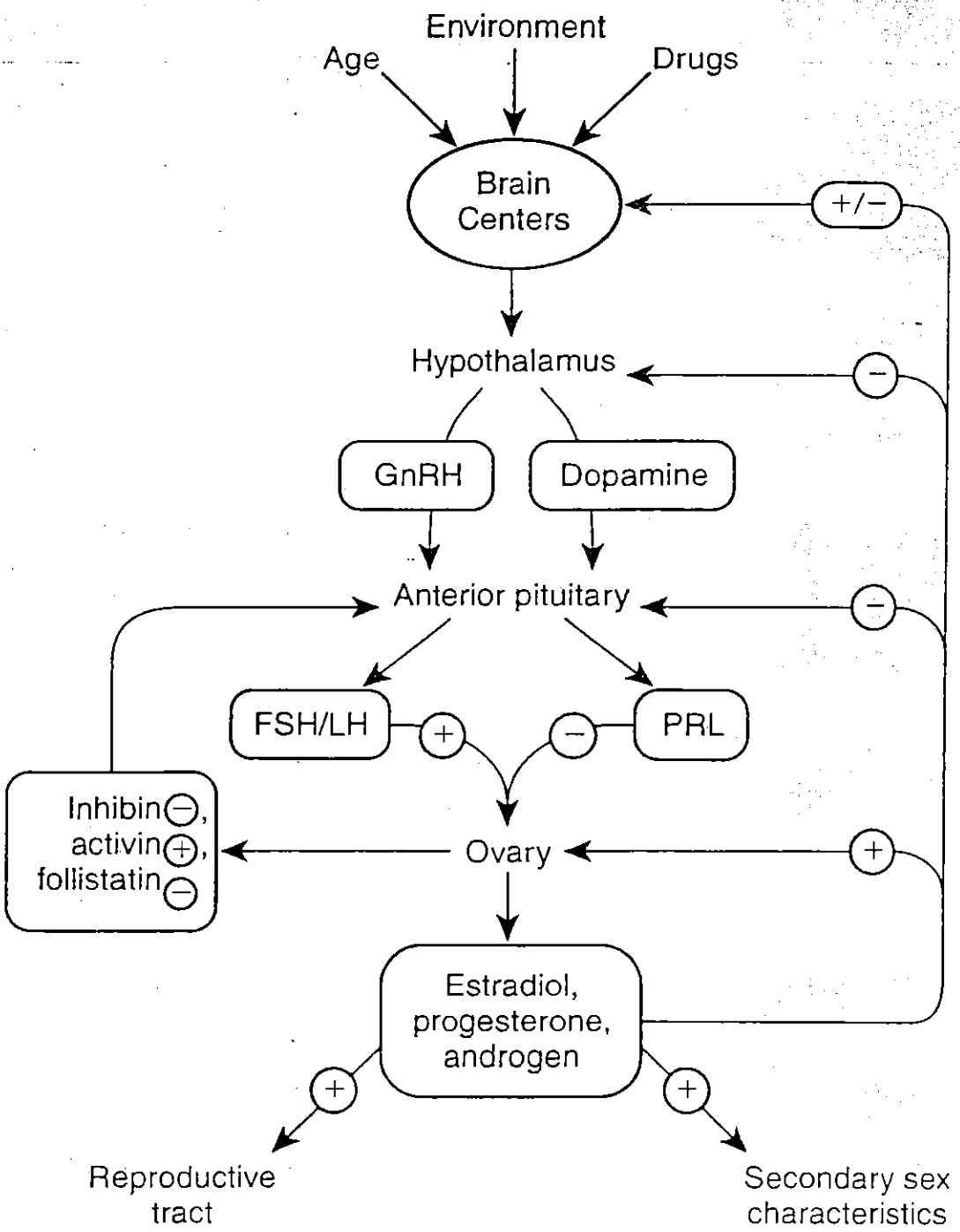


FIGURE 38.1 Regulation of the reproductive tract in the female. The main reproductive hormones are shown in boxes. Positive and negative regulations are depicted by plus and minus signs.

- Both LH and FSH regulate follicular steroidogenesis and androgen and estradiol secretion, and LH regulates the secretion of progesterone from the corpus luteum.
- **Inhibin** suppresses the secretion of FSH. **Activin** (an inhibin-binding protein) increases the secretion of FSH, and **follistatin** (an activin-binding protein) reduces the secretion of FSH.

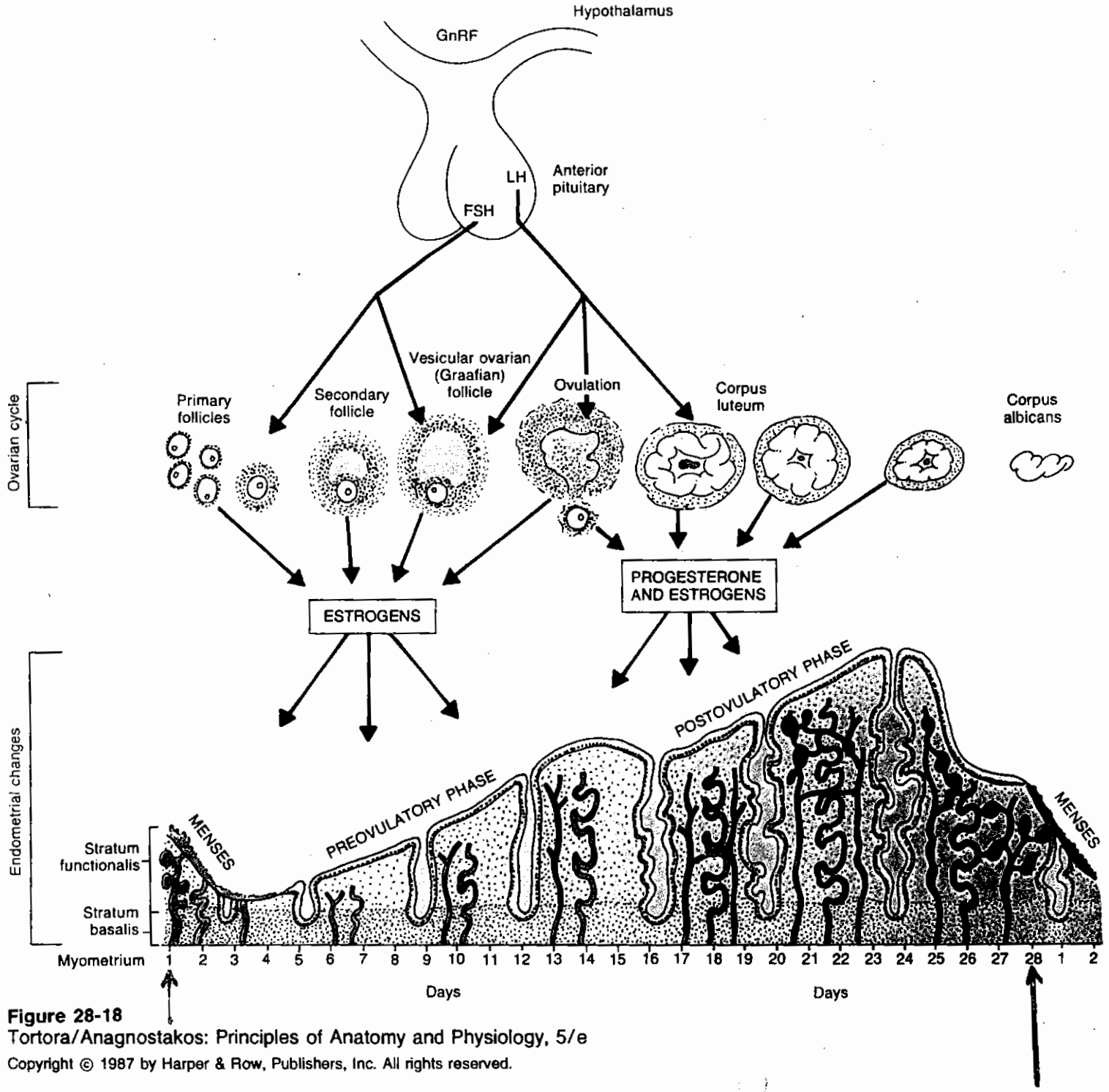
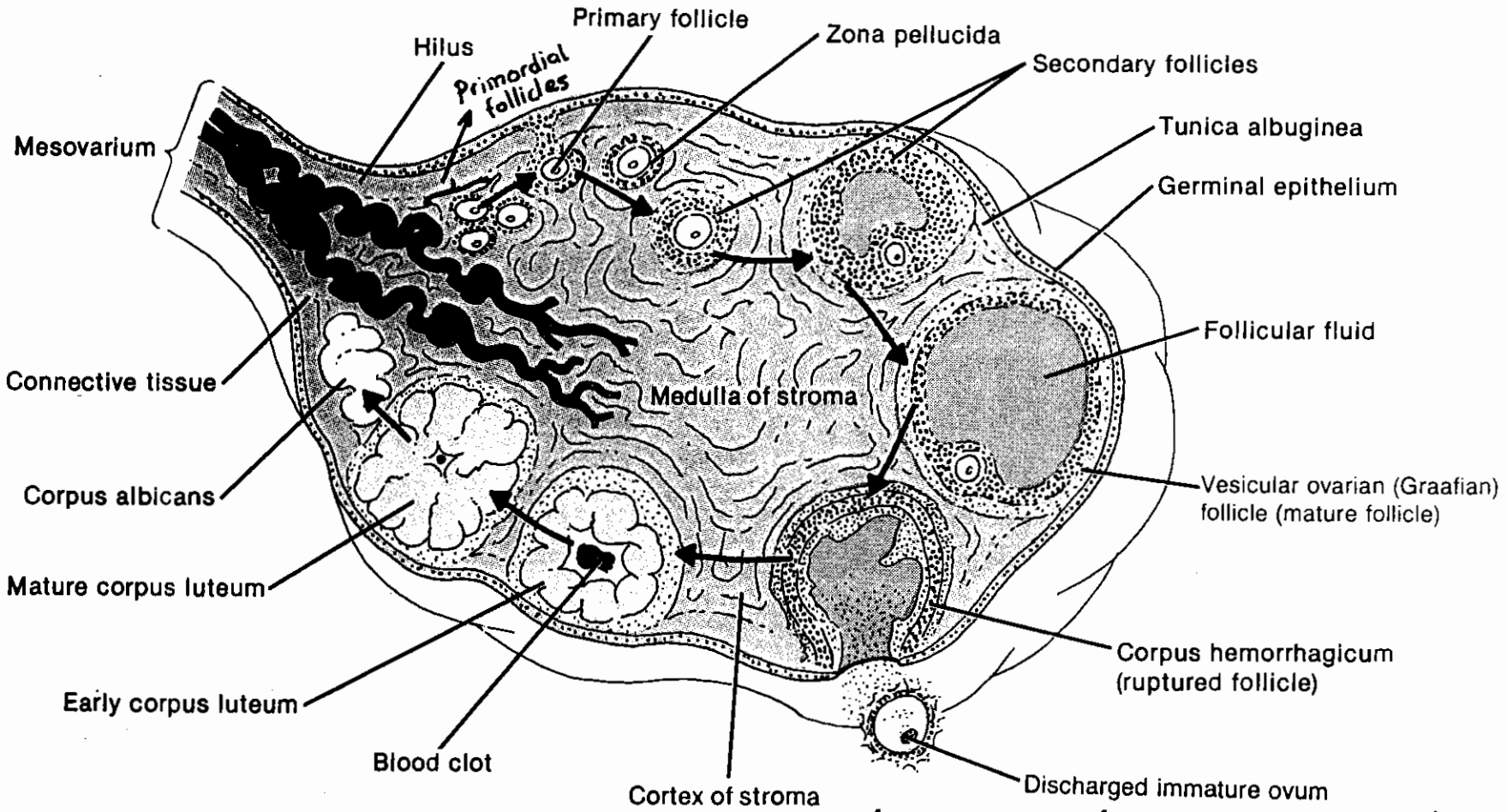


Figure 28-18
Tortora/Anagnostakos: Principles of Anatomy and Physiology, 5/e



(a)

Figure 28-13a
Tortora/Anagnostakos: Principles of Anatomy and Physiology, 5/e

1) At the 30th week of gestation 7 million ova are present in the two ovaries.
2) 2 million at birth. The others degenerated.
3) Only 300,000 – 400,000 reach puberty
4) During all reproductive years (13 – 50) about 450 of these follicles develop to expel ova, one each month, the 2 ovaries alternate.

Throughout reproductive life, 90% to 95% of all follicles are primordial follicles (Nongrowing).
In fetal life and childhood, some primordial follicles

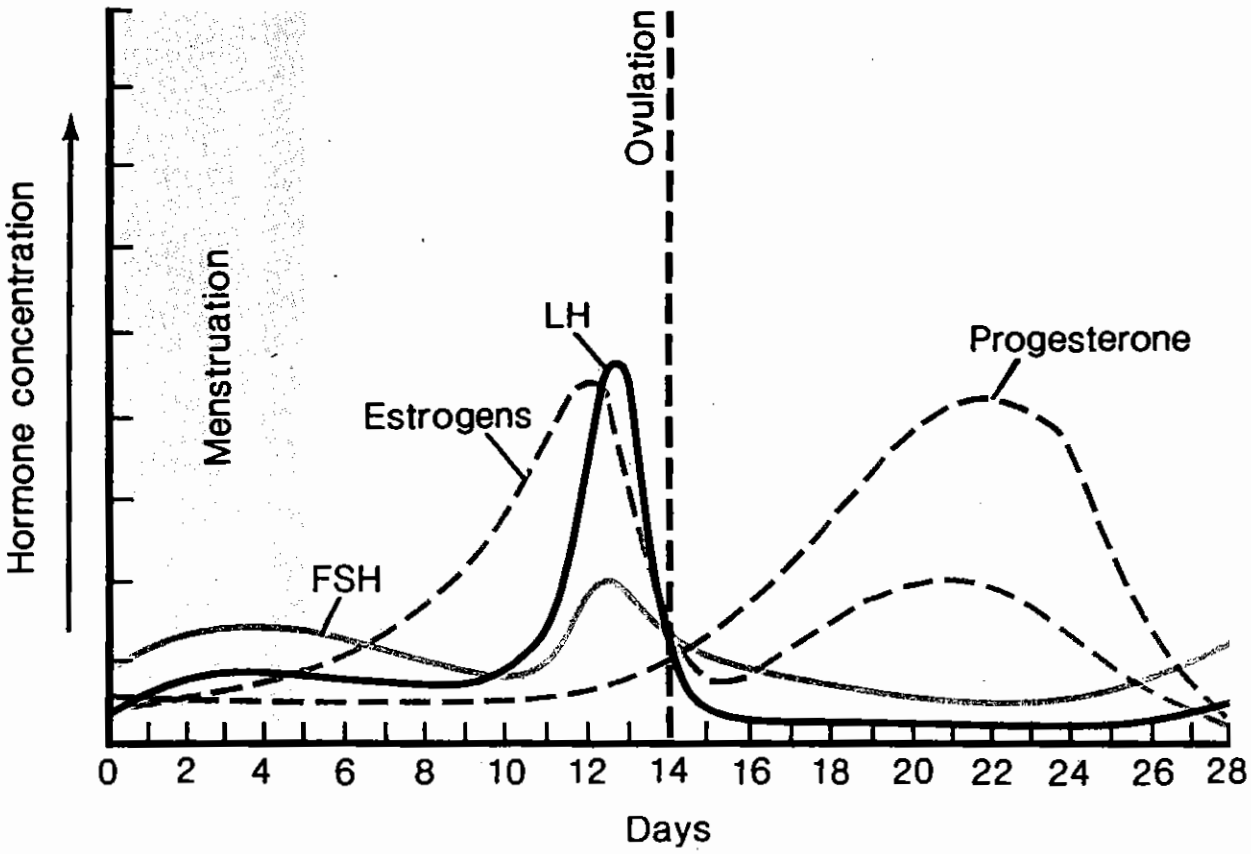
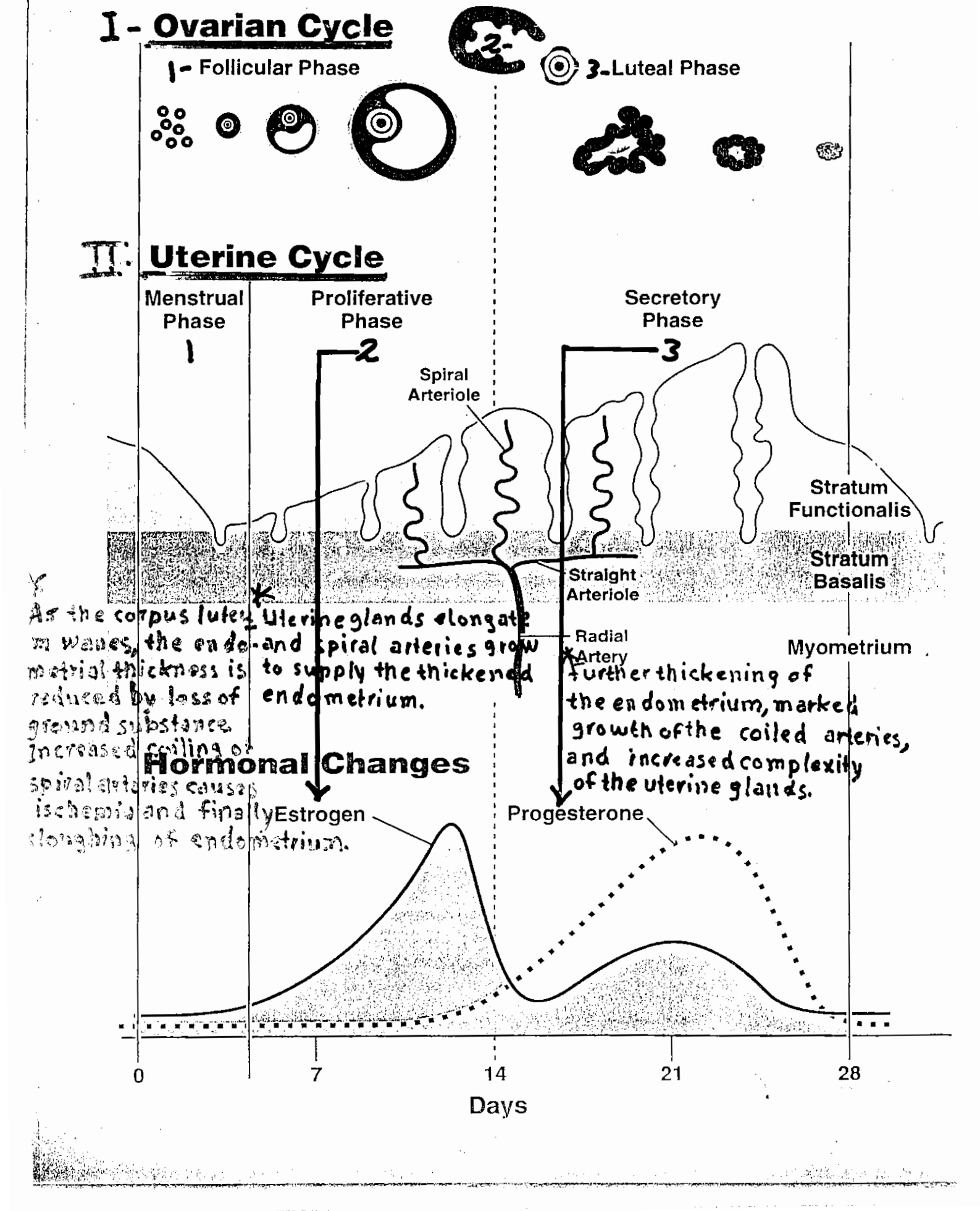


Figure 28-19
Tortora/Anagnostakos: Principles of Anatomy and Physiology, 5/e

FEMALE REPRODUCTIVE CYCLE



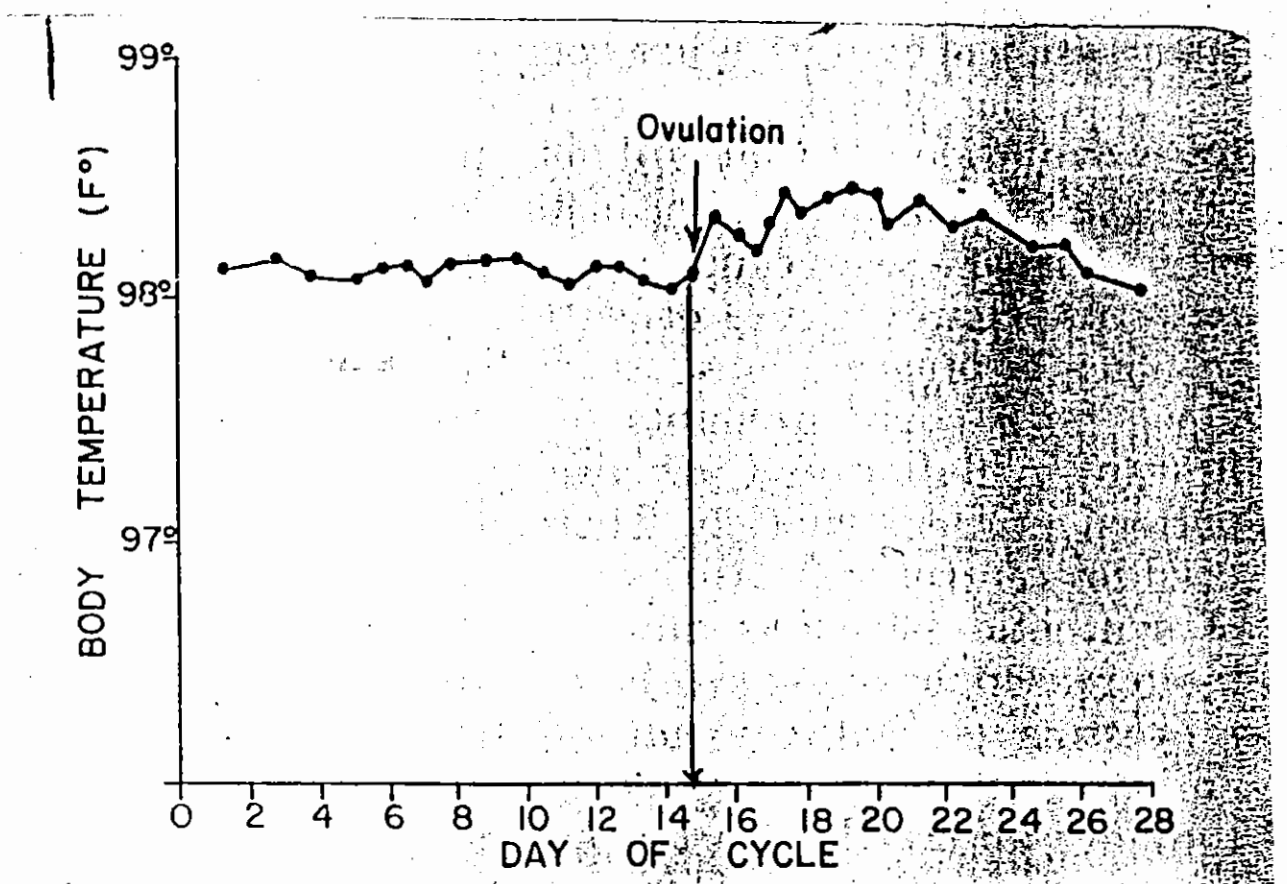


Figure 81–9. Elevation in body temperature shortly after ovulation.

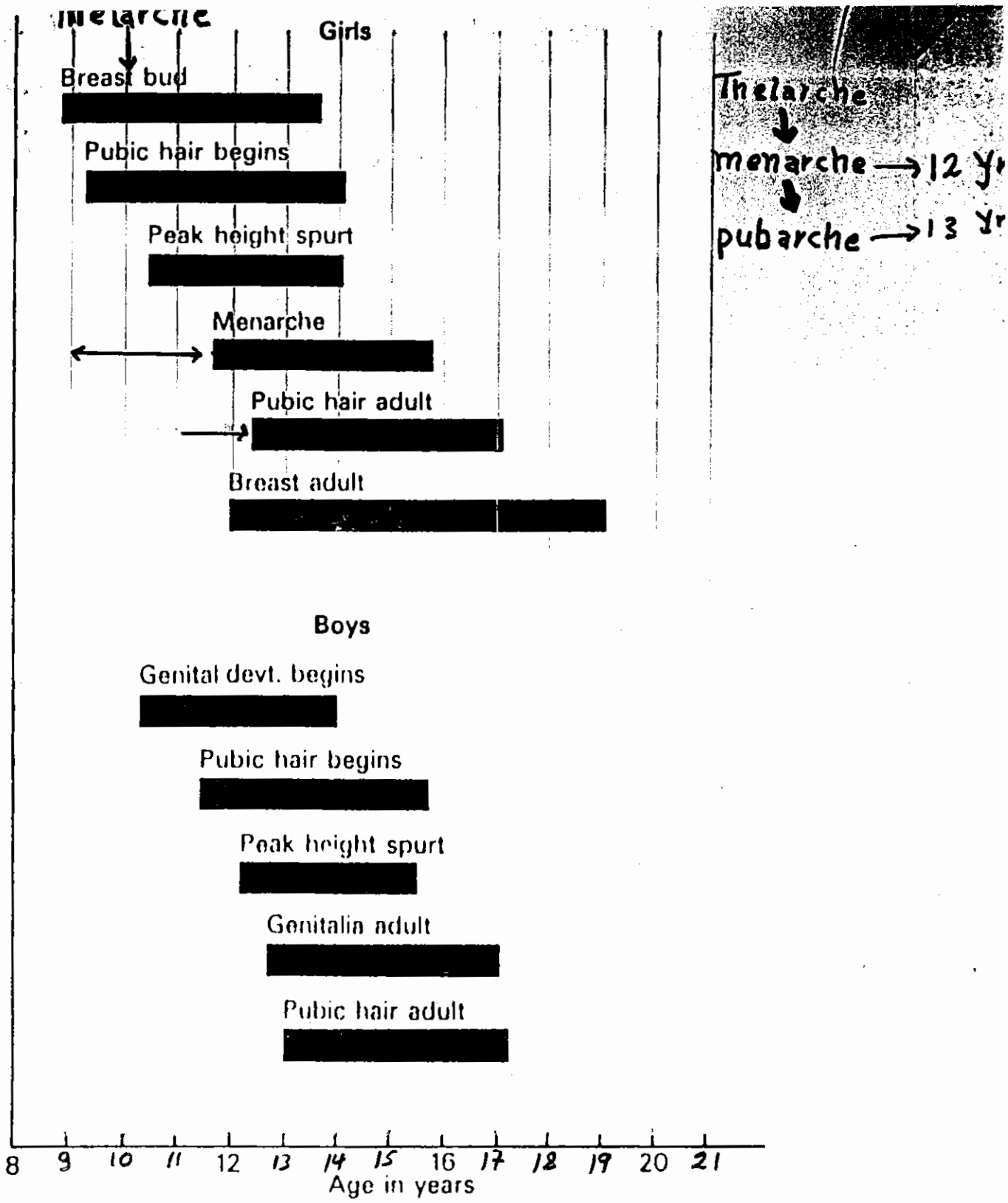


FIG. XI.21. Time of development of the different physical manifestations of puberty in boys and girls.
(Redrawn from Sadow, J. I. D. *et al.* (1980). *Human reproduction*. Croom Helm, London.)

Thelarche
menarche → 12 Yr
pubarche → 13 Yr

*The adrenal androgens are responsible in part for pubarche.

Adrenarche

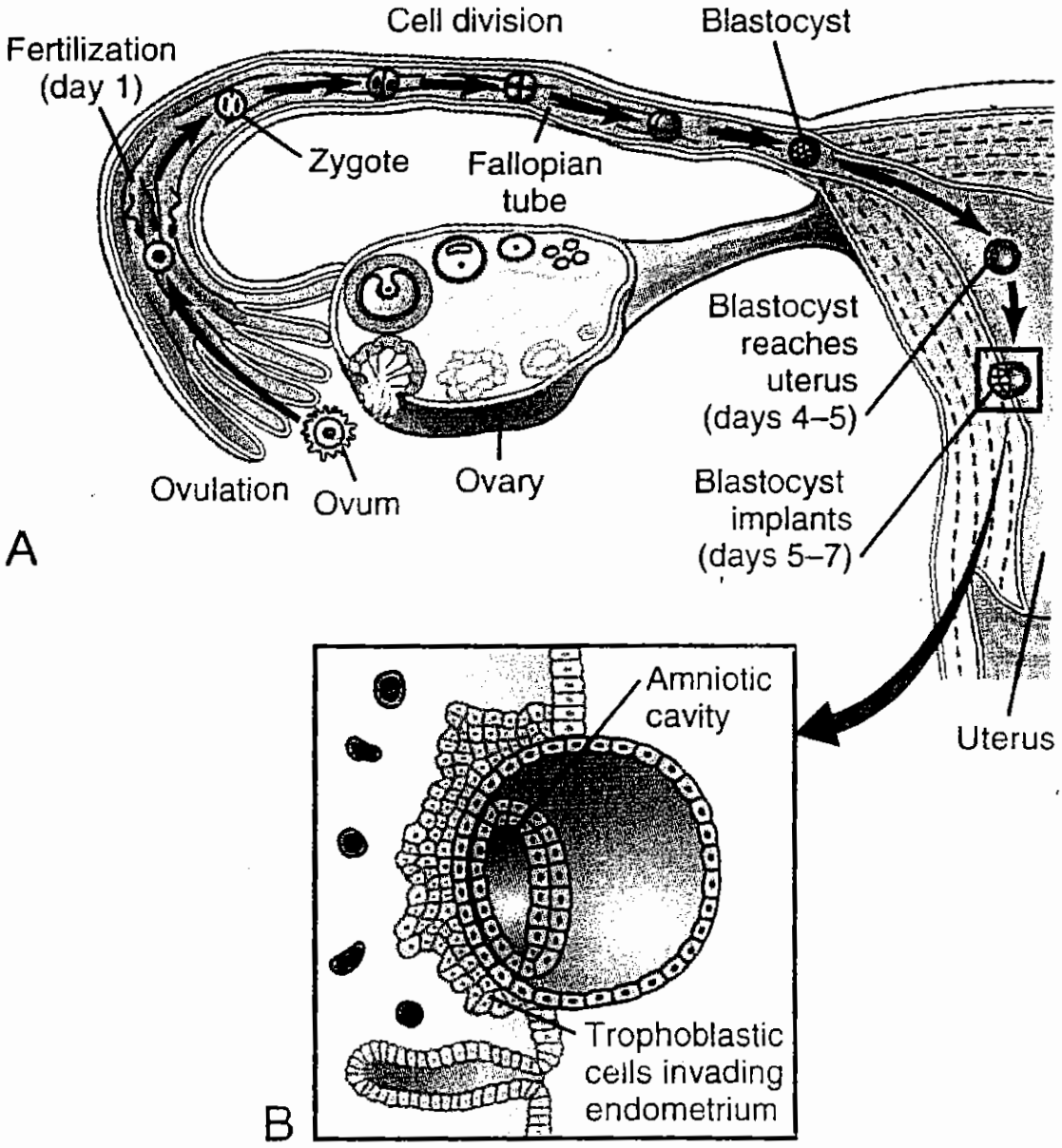


Figure 82-2 *A*, Ovulation, fertilization of the ovum in the fallopian tube, and implantation of the blastocyst in the uterus. *B*, Action of trophoblast cells in implantation of the blastocyst in the uterine endometrium.

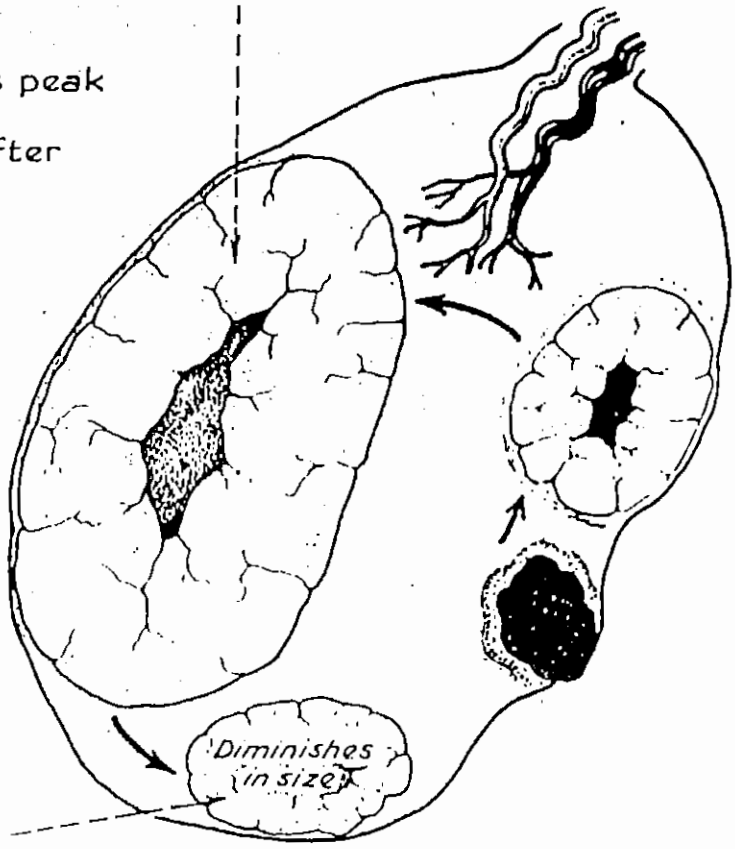
*The oviducts transport the germ cells in two directions: sperm ascend toward the ampulla and the zygote descends toward the uterus. This requires coordination between smooth muscle contraction, ciliary movement, and fluid secretion, all of which are under hormonal and neuronal control.

OVARY in PREGNANCY

* When pregnancy occurs the ordinary ovarian cycle is suspended.
* After the first 14 days the developing placenta secretes a LUTEINIZING HORMONE (chorionic gonadotrophin).
* Under its influence the CORPUS LUTEUM continues to grow until it may come to occupy 30% to 50% of the total volume of the OVARY.

* The large amount of PROGESTERONE
  - helps to maintain the PREGNANCY in its early stages and is essential for development of the PLACENTA – the special structure through which the child receives its nourishment from the mother.
  - It also produces PROGESTERONE which gradually takes over from the

* reaches its peak at about 6 weeks after conception
  - falls off about 2nd. month



* CORPUS LUTEUM —— ceases to be active about 4th. month

* PLACENTAL PROGESTERONE —— takes over to maintain the PREGNANCY, and to help to prepare the mammary glands for Lactation.

TABLE 55–2

SUBSTANCES SECRETED BY THE BLASTOCYST

Immunosuppressive agents
- Platelet-activating factor (PAF)
- Human chorionic gonadotropin (hCG)
- Early pregnancy factor
- Immunosuppressive factor
- Prostaglandin E_2
- Interleukins 1α and 6
- Interferon-α
- Leukemia inhibitory factor
- Colony-stimulating factor

Metalloproteases (facilitate invasion of trophoblast into the endometrium)
- Collagenases: digest collagen types I, II, III, VII, and X
- Gelatinases: 2 forms, digest collagen type IV and gelatin
- Stromelysins: digest fibronectin, laminin, and collagens IV, V, and VII

Serine proteases (facilitate invasion of trophoblast into the endometrium)

Other factors or actions
- Ovum factor
- Early pregnancy factor
- Embryo-derived histamine-releasing factor
- hCG: autocrine growth factor
- Plasminogen activator and its inhibitors
- Insulin-like growth factor type II (IGF-II): promotes trophoblast invasiveness
- Estradiol
- β_1 Integrin
- Fibroblast growth factor (FGF)
- Transforming growth factor-α (TGF-α)
- Inhibins

hCG is one of the most important of the factors secreted by the trophoblast of the blastocyst, both preimplantation and postimplantation. Besides rescuing the corpus luteum, hCG acts as an immunosuppressive agent, has growth-promoting activity, and acts as an autocrine growth factor that promotes trophoblast growth and placental development. Thus, hCG may have a role in the adhesion of the trophoblast to the epithelia of the endometrium. hCG has protease activity, and hCG levels are high in the area where the trophoblast faces the endometrium.

TABLE 55–4

HORMONES MADE BY THE PLACENTA

Peptide Hormones and Neuropeptides

Human chorionic gonadotropin (hCG)

Thyrotropin (thyroid-stimulating hormone [TSH])

Placental-variant growth hormone

Human chorionic somatomammotropins 1 and 2 (hCS1 and hCS2), also known as human placental lactogen (hPL: hPL1 and hPL2)

Placental proteins PP12 and PP14

Thyrotropin-releasing hormone (TRH)

Corticotropin-releasing hormone (CRH)

Growth hormone–releasing hormone (GHRH)

Gonadotropin-releasing hormone (GnRH)

Substance P

Neurotensin

Somatostatin

Neuropeptide Y

(ACTH)-related peptide

The inhibins

Steroid Hormones

Progesterone

Estrone

Estradiol

Estriol

The most important of the placental peptide hormones is **hCG**. In the developing blastocyst, and later in the mature placenta, it is the syncytiotrophoblast cells that synthesize hCG, perhaps under the direction of progesterone and estrogens. The placenta also produces two **human chorionic somatomammotropins,** hCS 1 and hCS 2, also called *human placental lactogen* (hPL). hCS 1 and 2 are polypeptide hormones that are structurally related to growth hormone and placental-variant growth hormone, as well as to prolactin (see Table 47–1). They play a role in the conversion of glucose to fatty acids and ketones, thus coordinating the fuel economy of the fetoplacental unit. The fetus and placenta use fatty acids and ketones as energy sources and store them as fuels in preparation for the early neonatal period, when a considerable reservoir of energy is necessary for the transition from intrauterine life to life outside the uterus. hCS 1 and 2 also promote development of maternal mammary glands during pregnancy.

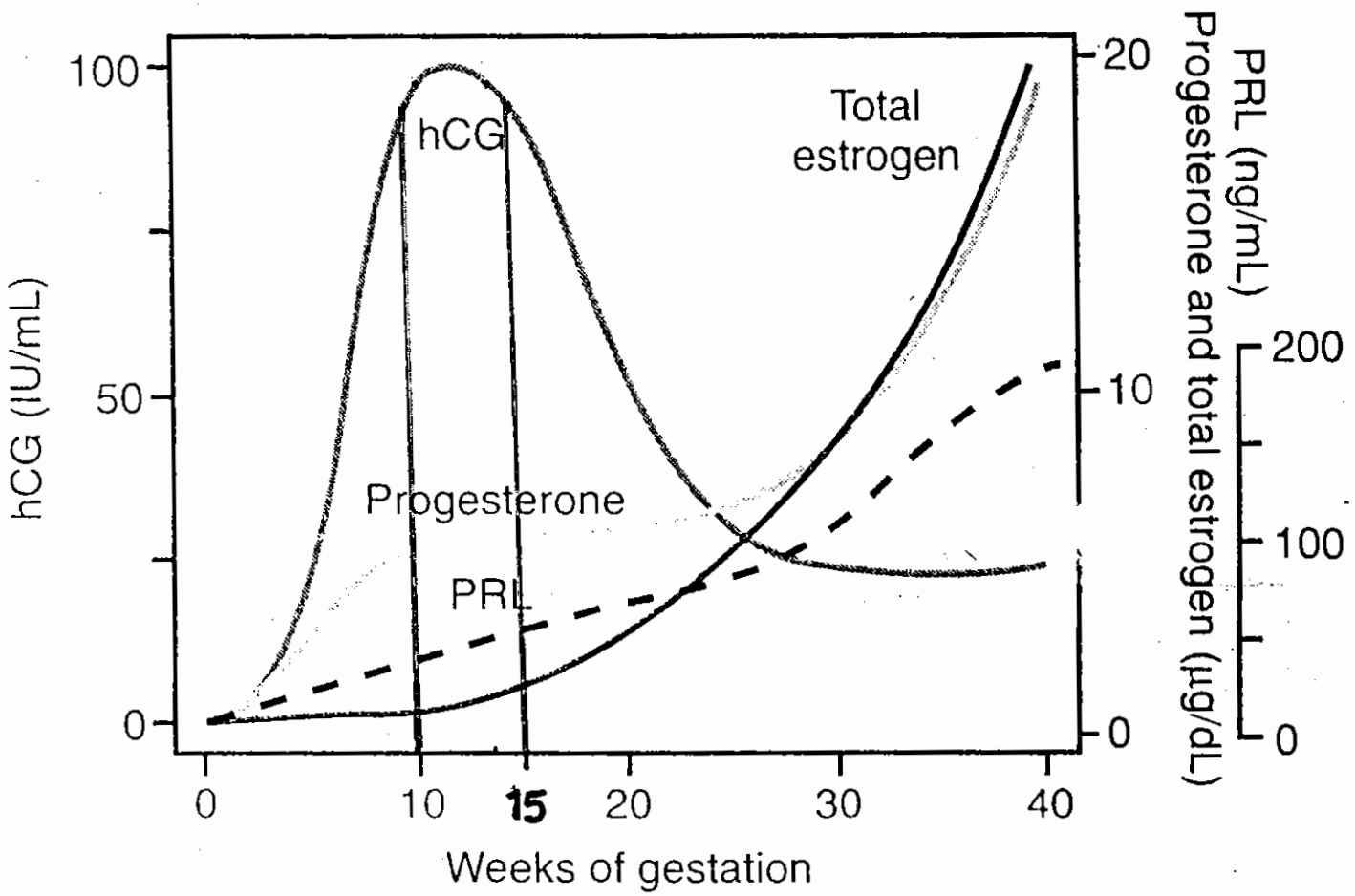


FIGURE 39.6 Profiles of hCG, progesterone, total estrogens, and PRL in the maternal blood throughout gestation.

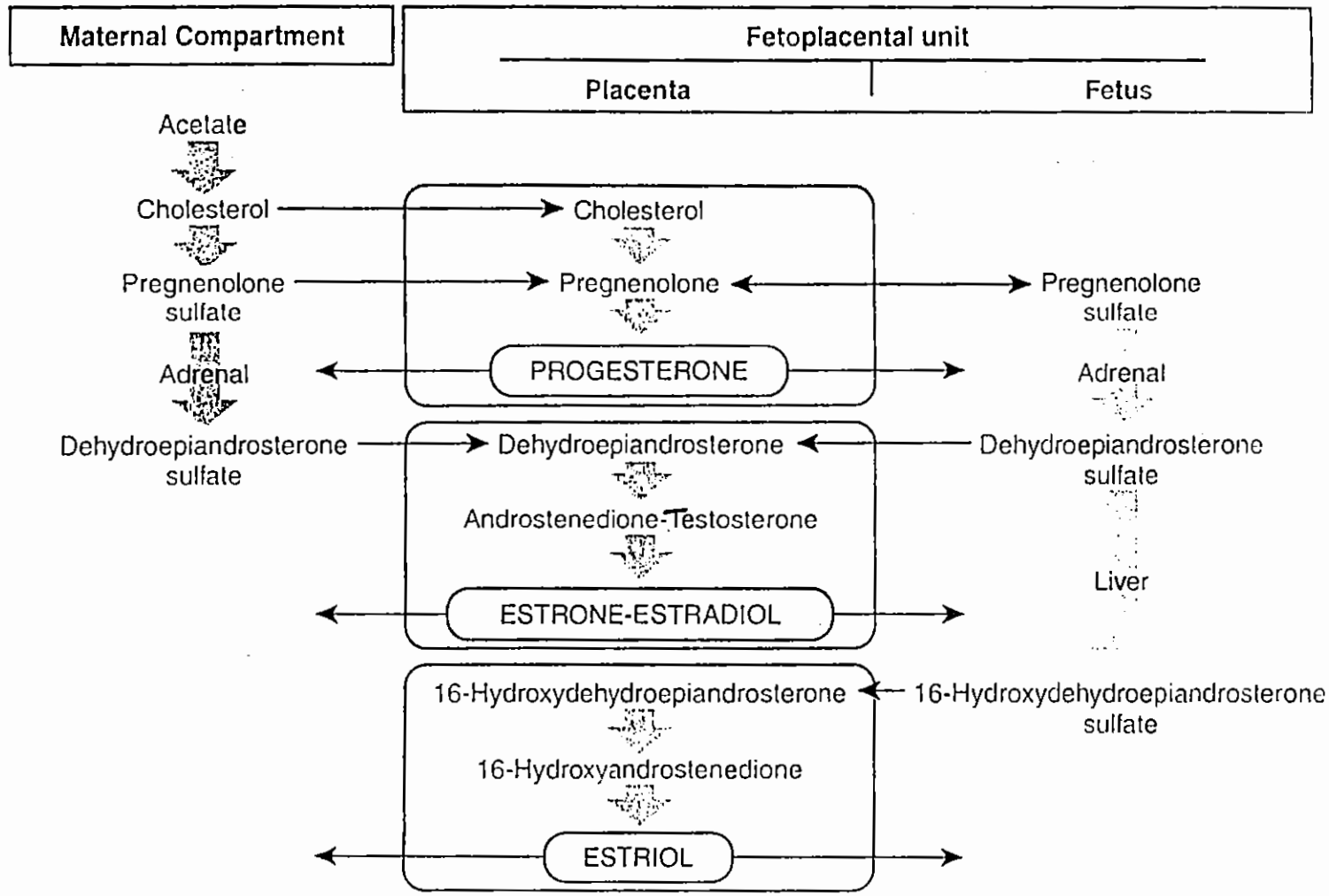


FIGURE 38.7 **The fetoplacental unit and steroidogenesis.** Note that estriol is the product of reactions occurring in the fetal adrenal, fetal liver, and placenta. (Modified from Goodman HM. Basic Medical Endocrinology. New York: Raven, 1988.)

* The levels of estriol in plasma, amniotic fluid, or urine are used as an index of fetal well-being. Low levels of estriol would indicate potential fetal distress, although rare inherited sulfatase deficiencies can also lead to low estriol.

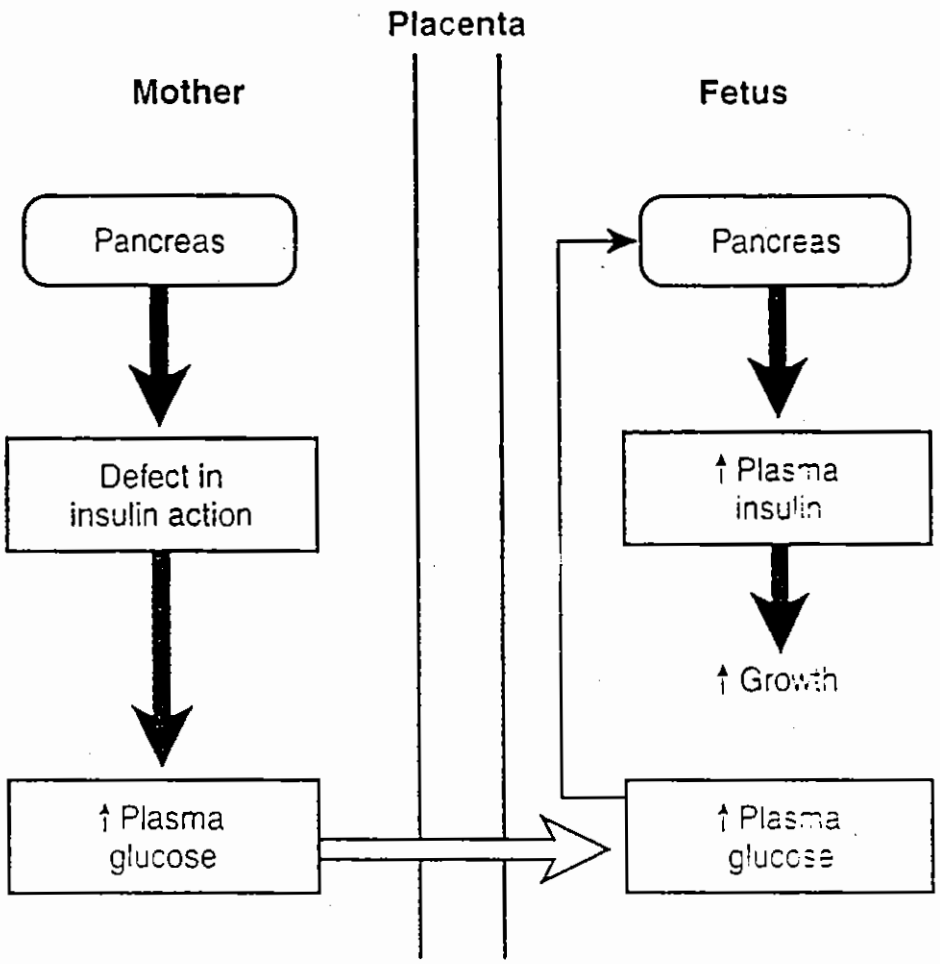


FIGURE 38.8 Effects of maternal diabetes on fetal growth.

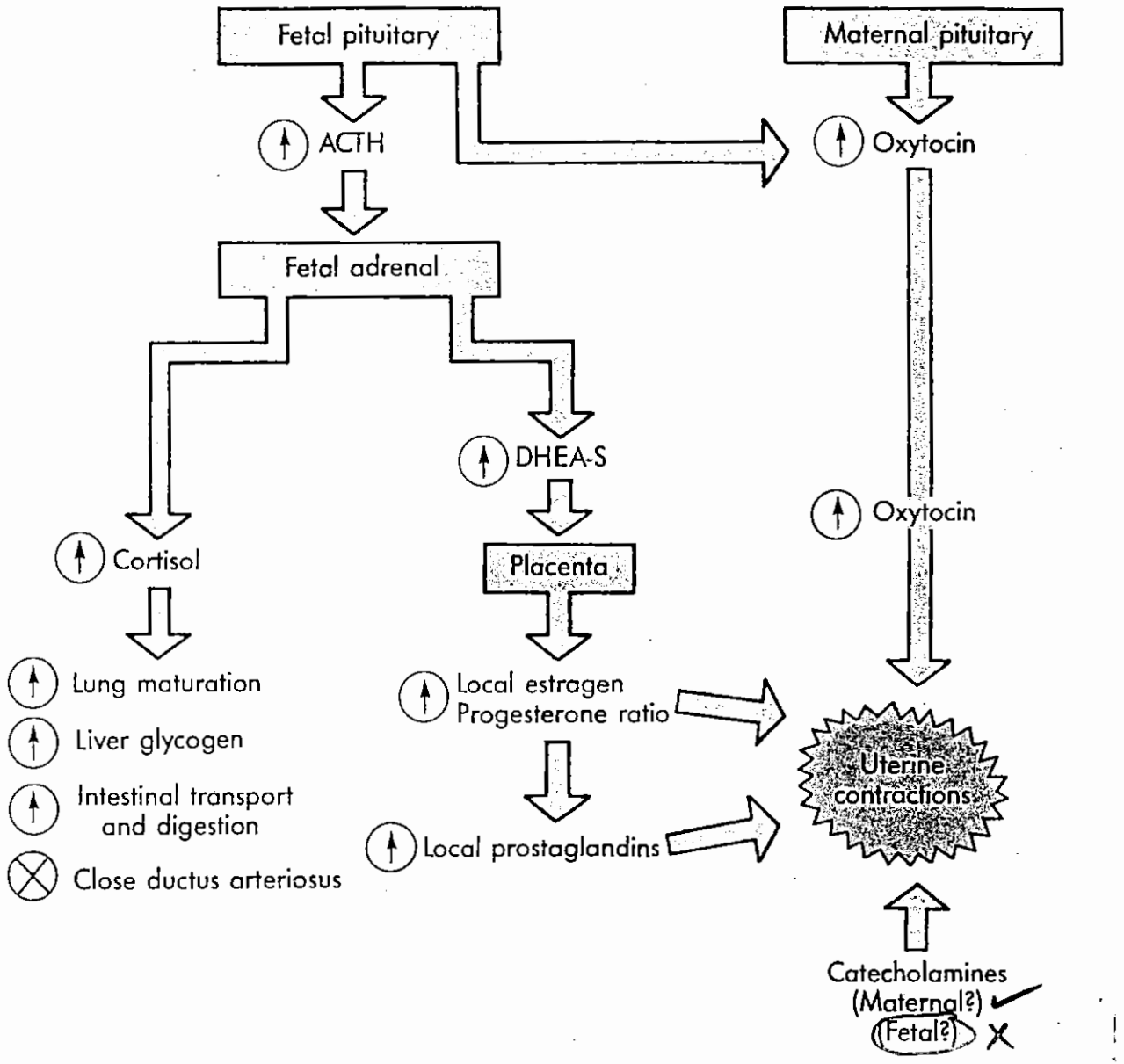


Fig. 51-30 Endocrine regulation of parturition. The fetal pituitary-adrenal axis initiates signals that decrease the ratio of effective progesterone to estrogen in the myometrium. This leads to uterine contractions, which are mediated by prostaglandins. Oxytocin may contribute to labor but is not essential. However, oxytocin sustains uterine contractions after expulsion of the fetus so as to minimize maternal loss of blood. Cortisol prepares the fetus to adapt to extrauterine life successfully. *ACTH*, Adrenocorticotropic hormone; *DHEA-S*, dehydroepiandrosterone sulfate.

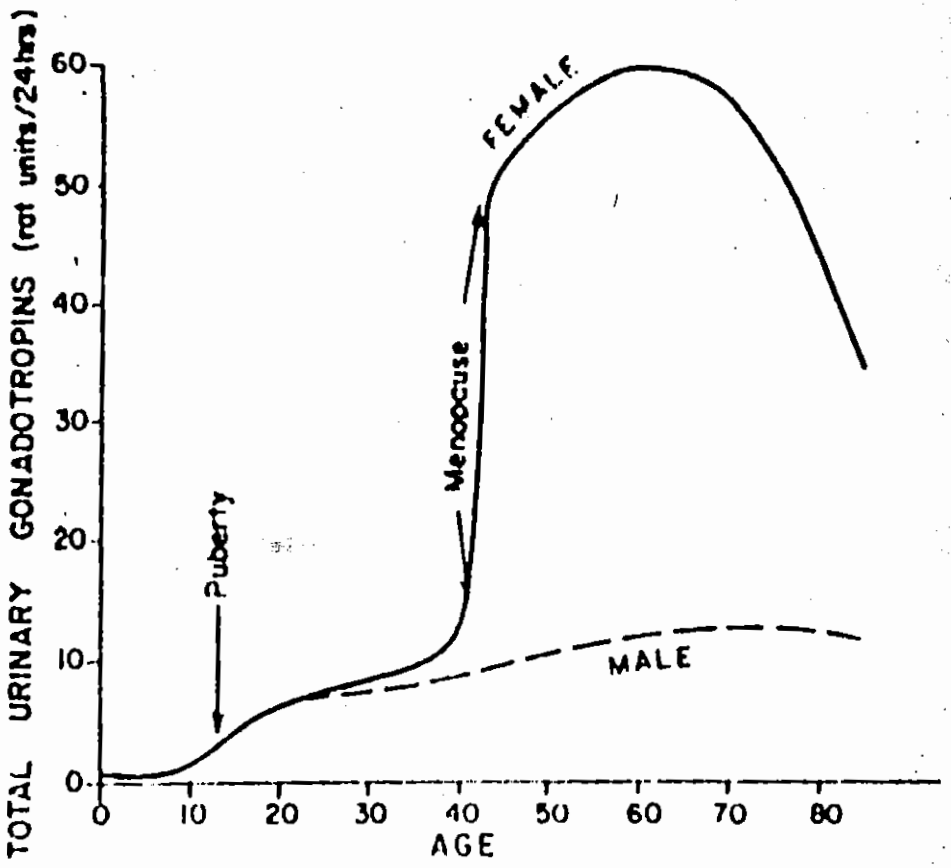


Figure 81–7. Total rates of secretion of gonadotropic hormones throughout the sexual lives of females and males, showing an especially abrupt increase in gonadotropic hormones at the menopause in the female.

TABLE 39.A Contraceptive Use and Efficacy Rates in the United States

Method	Estimated Use (%)	Accidental Pregnancy in Year 1 (%)
Pill	32	3
Female sterilization	19	0.4
Condom	17	12
Male sterilization	14	0.15
Diaphragm	4–6	2–23
Spermicides	5	20
Rhythm	4	20
Intrauterine device	3	6

From Developing New Contraceptives: Obstacles and Opportunities. Washington, DC: National Academy Press, 1990.

BIRTH CONTROL

Methods	Examples	Comments
Hormones	Norplant Oral Contraceptive ("The Pill")	Estrogen and progesterone prevent follicle development and ovulation.
Barriers	Cervical Cap Condom Diaphragm Vaginal Pouch	Sperm are prevented from entering the uterine cavity. Male condoms protect against sexually transmitted diseases.
Spermicides	Contraceptive Sponge Creams Douches Foams Jellies Suppositories	These methods depend upon sperm-killing chemicals. The contraceptive sponge releases spermicide for up to 24 hours.
Timing	Rhythm Method Sympto–thermal Method	The avoidance of sexual intercourse for about 7 days (while a viable ovum is in the uterine tube).
Sterilization	Vasectomy (male) Tubal Ligation (female)	The severing of each ductus deferens in the male and both uterine tubes in the female.
Intrauterine Device (IUD)		An object placed in the uterine cavity prevents implantation.
Withdrawal (Coitus Interruptus)		The penis is withdrawn from the vagina before ejaculation occurs.
Abortion		Surgical or drug-induced removal of the embryo.

Types of hormonal contraceptive

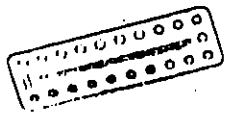
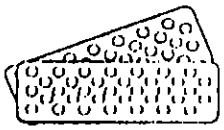
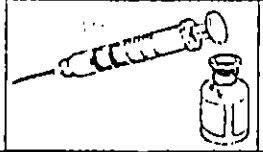
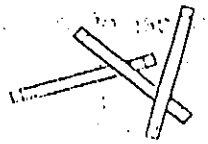
	Combined oral contraceptive pill (COCP)	Progestogen-only pill (POP)	Emergency pill	Depot (contraceptive injection)	Implants
					
Composition	synthetic oestrogens and progestogens	synthetic progestogens	high dose of synthetic oestrogens and progestogens	synthetic progestogens (medroxyprogesterone)	synthetic progestogens
Administration	oral, daily for 21 days with a 7-day gap before the next course of pills (during the 7 day gap a withdrawal bleed occurs)	oral, daily without a break between packs, and must be taken at the same time every day	oral, must be taken within 72 h of coitus if no other contraception was used	intramuscular injection, lasts 8–12 weeks	small soft tubes inserted under the skin, lasts up to 5 years
Mode of action	principal action = suppression of ovulation	does not reliably suppress ovulation	inhibits implantation	does not reliably suppress ovulation	prevents ovulation
Effectiveness if taken/ applied according to instructions	>99%	99% (less effective in young women and if >70 kg)	>95%	>99%	>99%
Advantages	often decreases menstrual bleeding, pain, premenstrual tension, and acne, and may protect against ovarian cancer	useful for women who cannot use the COCP (because POP contains no oestrogen)	postcoital contraceptive	do not have to remember to take pills, may protect against endometrial cancer	same as for depot
Disadvantages	increased risk of thromboembolic disease (e.g. deep vein thrombosis, pulmonary embolism, cerebral thrombosis), dyslipidaemia, hypertension	side effects include: irregular uterine bleeding ('breakthrough bleeding' or amenorrhoea), breast discomfort, premenstrual tension, skin reactions, increased risk of ectopic pregnancy	same as for COCP, although risk is increased owing to high dose of oestrogen, often cause nausea and vomiting	side effects are same as for POP, plus: weight gain, loss of bone density	some as for depot, plus: often difficult to remove owing to fibrosis
Comments	not reliable if taken >12 h late, or after vomiting/ diarrhoea	not reliable if taken >3 h late, or after vomiting/ diarrhoea	should not be used as a regular form of contraception	not immediately reversible	

Fig.11.4 Types of hormonal contraceptive.

Types of non-hormonal contraceptive

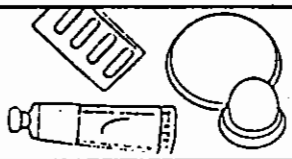
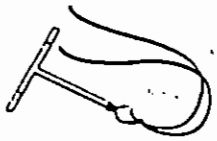
	Male condom	Diaphragm or cap with spermicide	Intrauterine contraceptive device (IUCD)	Natural (symptothermal) method
				
Description	rubber sheath, lubricated with spermicidal cream	flexible rubber device used with spermicide	small plastic or copper device (some contain progestogen)	avoid ovulation—unprotected sexual intercourse confined to the 'safe' infertile times of the menstrual cycle
Administration	put over the erect penis during intercourse	device is inserted into the vagina before intercourse and covers the cervix; it must stay in for at least 6 h after sex	inserted into the uterus and can stay there for 5 years	the fertile and infertile times of the menstrual cycle are identified by measuring monthly changes in body temperature and cervical mucus
Mode of action	prevents sperm from entering vagina	prevents sperm from entering uterus	inhibits sperm migration and prevents implantation	prevents sperm from encountering ovum
Effectiveness if taken/ applied according to instructions	98%	92–94% depending on the type of device used	98–99% depending on the type of device used	98% (although much lower if the menstrual cycle is irregular)
Advantages	may protect both partners from sexually transmitted diseases, and may protect female against cervical cancer	female is in control of contraception (important if male is not motivated); reusable	immediately effective, requires little follow-up; hormone-containing IUCD cause lighter periods	no side effects
Disadvantages	requires high motivation and may interrupt spontaneity and sensitivity	less protection against sexually transmitted disease	may cause heavy, prolonged, painful periods and predispose to pelvic inflammatory disease	need to use alternative method during fertile days; requires close attention to symptoms of cycle

Fig. 11.5 Types of non-hormonal contraceptive.

Hormonal Therapy for Ladies and Maintaining Beauty

Hormonal therapy for ladies is necessary through out all stages of life especially after the age of 50 specifically in these cases:

1. **To maintain the density of bones and stop osteoporosis. Here, I'd like to assure that taking calcium and vitamin D is no good to help maintain good posture if this is accompanied by the lack of Estrogen or Testosterone.**

2. **To maintain the beauty of complexion and prevent wrinkles I'd like to draw the attention that anti-wrinkles facial creams are no good for Estrogen is what creates collagen which is permanent unlike Botox which is temporary.**

3. **For the treatment of extreme facial and body hair.**

4. **For the low desire for sex compared to spouse.**

5. **For the maintaining of the size of breasts and preventing atrophy especially in menopause.**

6. **To prevent urine incontinence in ladies (unvoluntary)**

I'd like to make sure that hormonal treatment has many kinds and different dozes and is not given by the public. In the west women take the right hormones by the supervision of the doctor.

I'd like to add the Estrogen has proved special importance in the treatment of Zheimer and Amnesia.

Although pulsatile GnRH discharge elicits a corresponding pulsatile release of LH and FSH, *continuous* administration of GnRH—or intermittent administration of high doses of GnRH analogues—suppresses the release of gonadotropins.

A clinical application of this principle is in prostatic cancer, where the administration of GnRH analogues lowers LH and FSH levels, thus lowering testosterone production (i.e., chemical castration).

Leydig cells also contain receptors for **prolactin** (PRL). Hyperprolactinemia in men with pituitary tumors, usually microadenomas, is associated with decreased testosterone levels. This condition is a result of a direct effect of elevated circulating levels of PRL on Leydig cells, reducing the number of LH receptors or inhibiting downstream signaling events. In addition, hyperprolactinemia may decrease LH secretion by reducing the pulsatile nature of its release. Under nonpathological conditions, however, PRL may synergize with LH to stimulate testosterone production by increasing the number of LH receptors.

Once ejaculated into the female, the spermatozoa move up the uterus to the isthmus of the uterine tubes, where they slow down and undergo **capacitation.** This further maturation process involves two components: increasing the motility of the spermatozoa and facilitating their preparation for the acrosome reaction. However, the role of capacitation appears to be facilitatory rather than obligatory, because fertilization is readily produced in vitro.

In addition, spermatozoa express olfactory receptors, and ovaries produce odorant-like molecules. Recent evidence indicates that these molecules and their receptors interact, fostering movement of the spermatozoa toward the ovary (chemotaxis).

The ability to move forward (**progressive motility**), which is acquired in the epididymis, involves activation of a unique protein called **CatSper,** which is localized to the principal piece of the sperm tail. This protein appears to be a Ca^{2+} ion channel that permits cAMP-generalized Ca^{2+} influx.

Further Development of Spermatozoa

Spermatozoa leaving the testes are not fully mobile. They continue their maturation and acquire motility during their passage through the epididymis. Motility is obviously important in vivo, but fertilization occurs in vitro if an immotile spermatozoon from the head of the epididymis is microinjected directly into an ovum

→ In summary, three processes occur concurrently in the seminiferous epithelium: (1) an increase in the number of cells by mitosis, (2) a reduction in the number of chromosomes by meiosis, and (3) the production of mature sperm from spermatids by spermiogenesis. Thus, spermatogenesis is a regular, ordered, sequential process resulting in the production of mature male gametes.

If physical injury or infection ruptures the blood–testis barrier and sperm cells within the barrier are exposed to circulating immune cells, antibodies can develop to the sperm cells.

It appears that men with high levels of antisperm antibodies may exhibit some infertility problems.

men who have developed low or moderate levels of antisperm antibodies have normal fertility

in some cases, a high level of antisperm antibodies in men and women leads to infertility.

→ The time required to produce mature spermatozoa from the earliest stage of spermatogonia is 65 to 70 days.

Hormones can alter the number of spermatozoa, but they generally do not affect the duration of the cycle. Spermatogenesis occurs along the length of each seminiferous tubule in successive cycles. New cycles are initiated at regular time intervals (every 2 to 3 weeks) before the previous ones are completed.

Approximately 200 million spermatozoa are produced daily in the adult human testes.

Relation to Endocrine function

In nonprimate mammals :

1. Removal of the gonads leads eventually to decreased or absent sexual activity in both the male & the female - although the loss is slow to develop in the males of some species
2. Injections of gonadal hormones in castrated animals revive sexual activity .Testosterone in the male & estrogen in the female have the most marked effect.
3. Large doses of testosterone & other androgens in castrated females initiate female behavior and large doses of estrogens in castrated males trigger male mating responses. It is unsettled why responses appropriate to the sex of animal occur when the hormones of the opposite sex are injected.
4. In women , ovariectomy does not necessarily reduce libido (defined in this context as sexual interest and drive) or sexual ability.
5. Postmenopausal women continue to have sexual relations , often without much change in frequency from their premenopausal pattern
6. However , adrenal androgens are still present in these women

   Testosterone for example , increases libido in males , and so does estrogen used to treat diseases such as carcinoma of the prostate.
7. The behavioral pattern that was present before treatment is stimulated but not redirected.
8. Thus , administration of testosterone to homosexuals intensifies their homosexual drive but not convert it to a heterosexual drive.

Neural control in the female

1. In mammals , the sexual activity of the female is cyclic .
2. Most of the time , the female avoids the male and repulses his sexual advances.
3. Periodically , however there is an abrupt change in behavior and the female seeks out the male, attempting to mate

4. These short episodes of heat or estrus are so characteristic that the sexual cycle in mammalian species that do not menstruate is estrous cycle.

5. In captivity , monkeys and apes mate at any time ; but in the wild state , the females accept the male more frequently at the time of ovulation.

6. In women , sexual activity occurs throughout the menstrual cycle , but careful studies indicate that , as in other primates , there is more spontaneous female-initiated sexual activity at about the time of ovulation.

7. In female sheep , discrete anterior hypothalamic lesions abolish behavior heat without affecting the regular pituitary-ovarian cycle .

8. Implantation of minute amounts of estrogen in the anterior hypothalamus causes heat in ovariectomized rats . Implantation in other parts of the brain and outside the brain does not have this effect.