Reproductive Endocrinology

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A 3-hormone chain of command controls reproduction with the brain being the primary regulator.

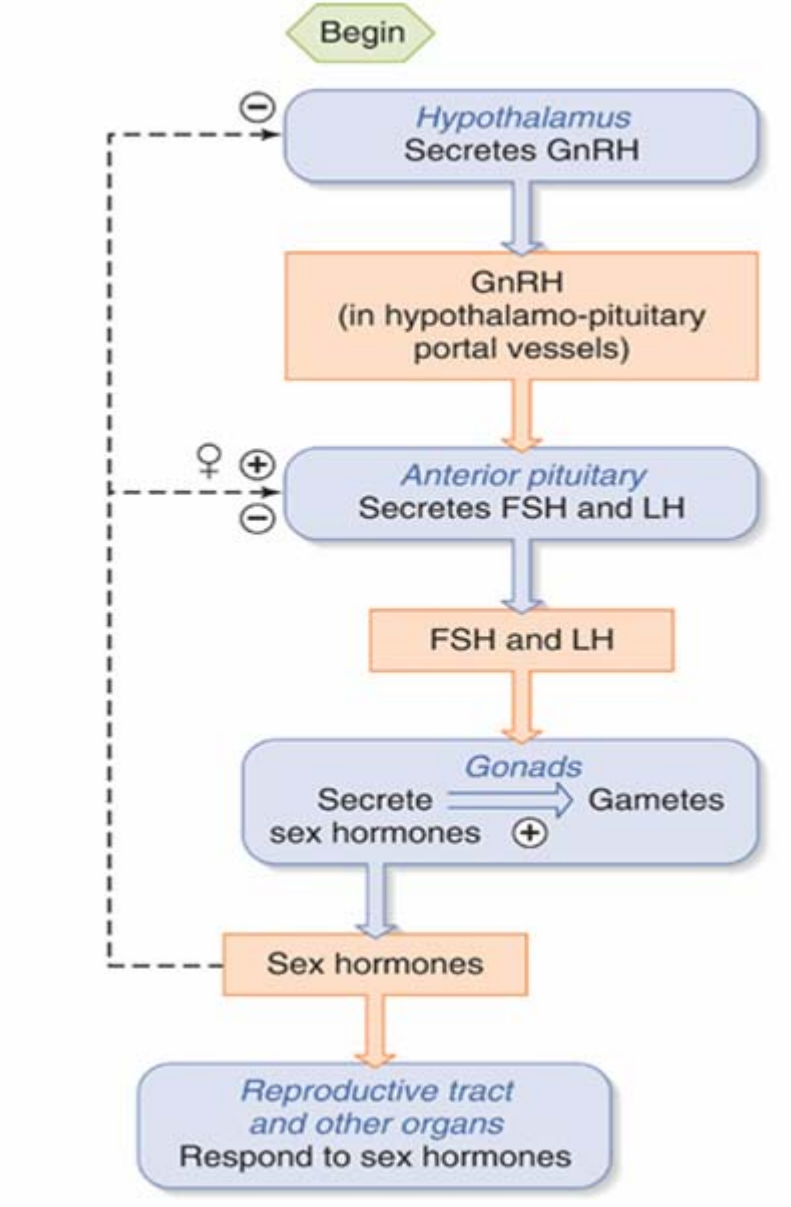


TABLE 17–1 Stages in the Control of Reproductive Function

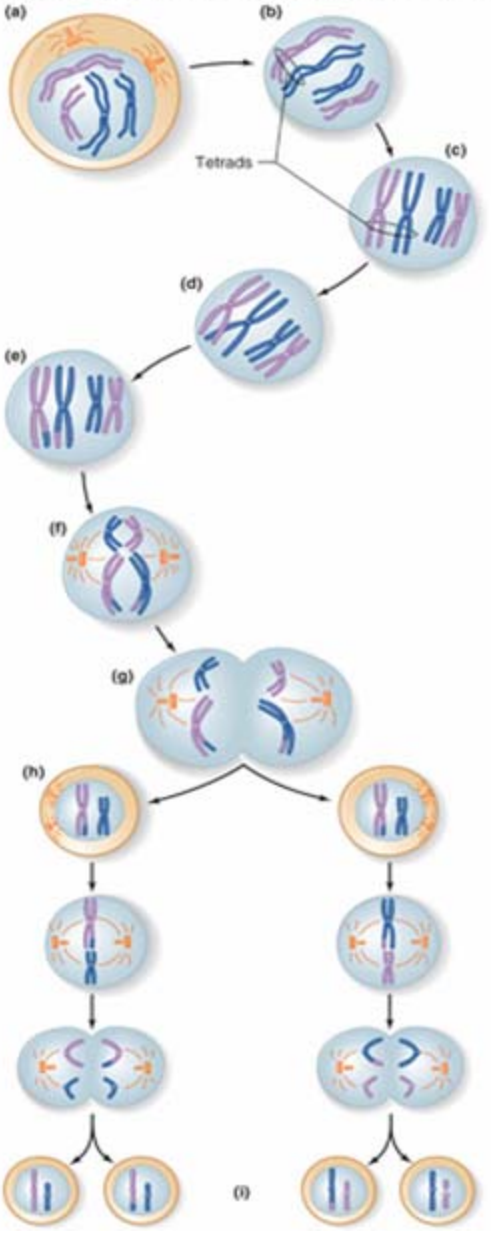
1. During the initial stage, which begins during fetal life and ends in the first year of life (infancy), GnRH, the gonadotropins, and gonadal sex hormones are secreted at relatively high levels.
2. From infancy to puberty, the secretion rates of these hormones are very low, and reproductive function is quiescent.
3. Beginning at puberty, hormonal secretion rates increase markedly, showing large cyclical variations in women during the menstrual cycle. This ushers in the period of active reproduction.
4. Finally, reproductive function diminishes later in life, largely because the gonads become less responsive to the gonadotropins. The ability to reproduce ceases entirely in women.

Figure 17-2

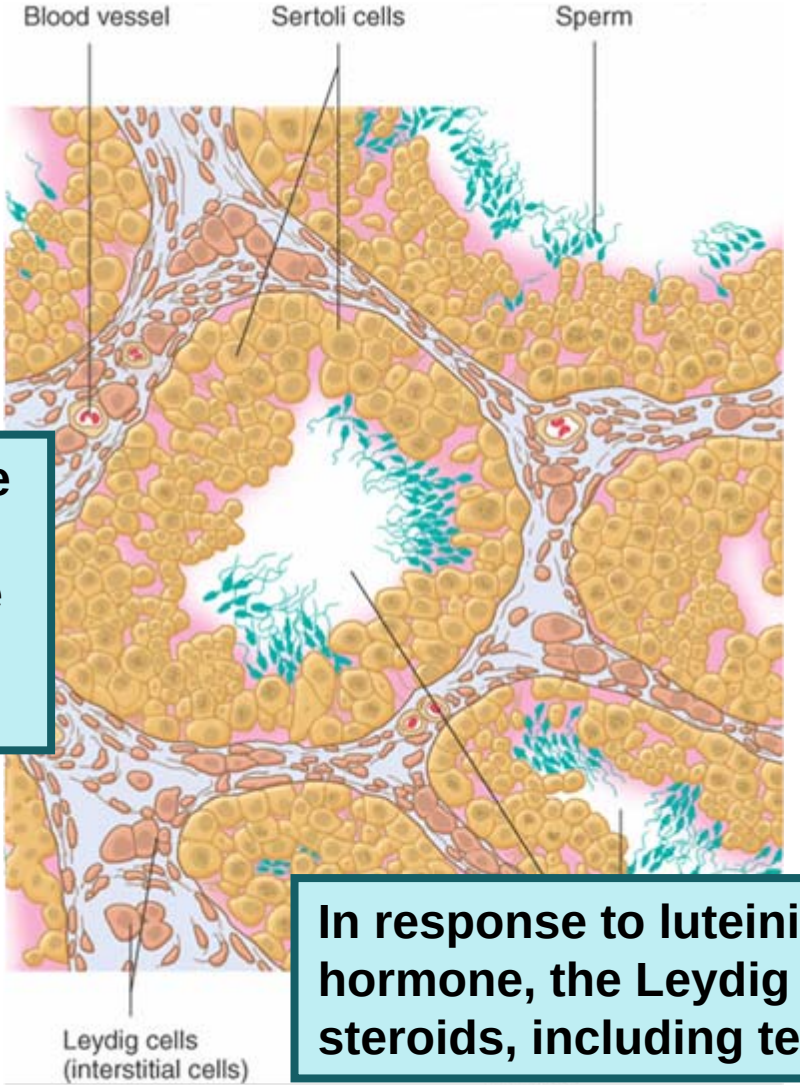
Meiosis is the process of producing gametes (sperm and eggs) that have only one chromosome instead of a pair.

This picture represents a hypothetical case for a species with 4 chromosomes (2 pairs; humans have 23 pairs of chromosomes).

Blue and red colors indicate the parental origin of chromosomes; note that two of the gametes formed represent new combinations of genetic information.



A representative cross-section of the seminiferous tubules in the testis is sketched here.



In response to follicle stimulating hormone and testosterone, the Sertoli cells support spermatogenesis.

In response to luteinizing hormone, the Leydig cells produce steroids, including testosterone.

The seminiferous tubules in this testis are apparent in the area that has been cut away. Spermatozoa move from the tubules into the rete testis, and then into the epididymis, first into the efferent ductules, and then into the vas deferens.

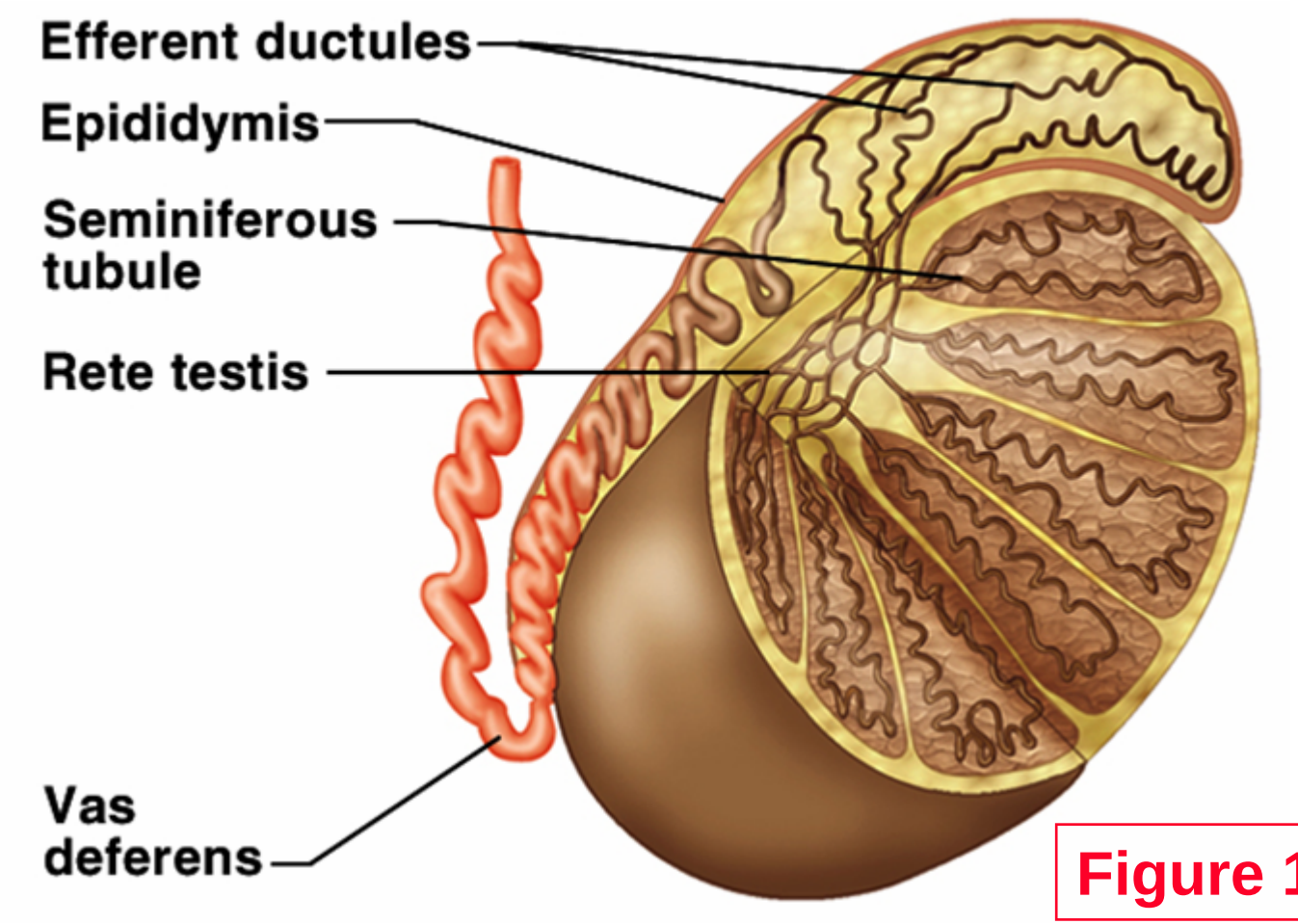


Figure 17-5

Semen is composed of spermatozoa and fluids from the testes, the epididymis, the seminal vesicles, and the bulbourethral and prostate glands; enlargement of the latter can block urine flow.

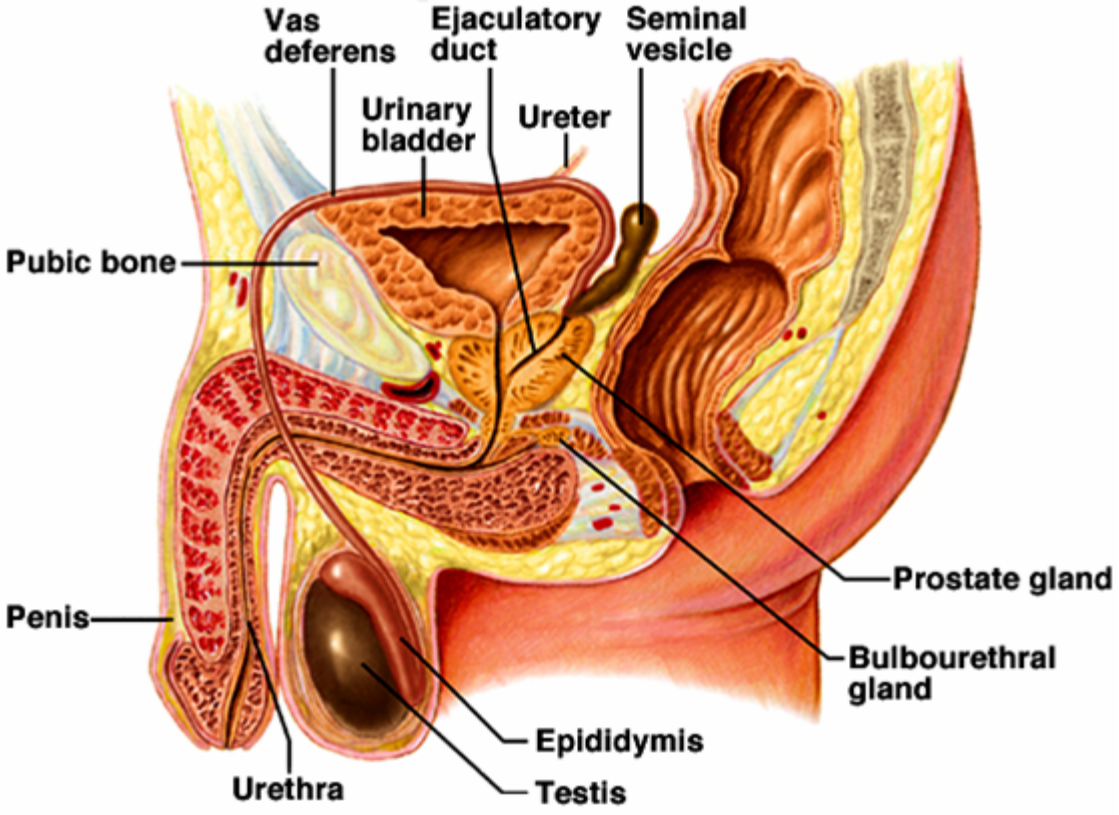
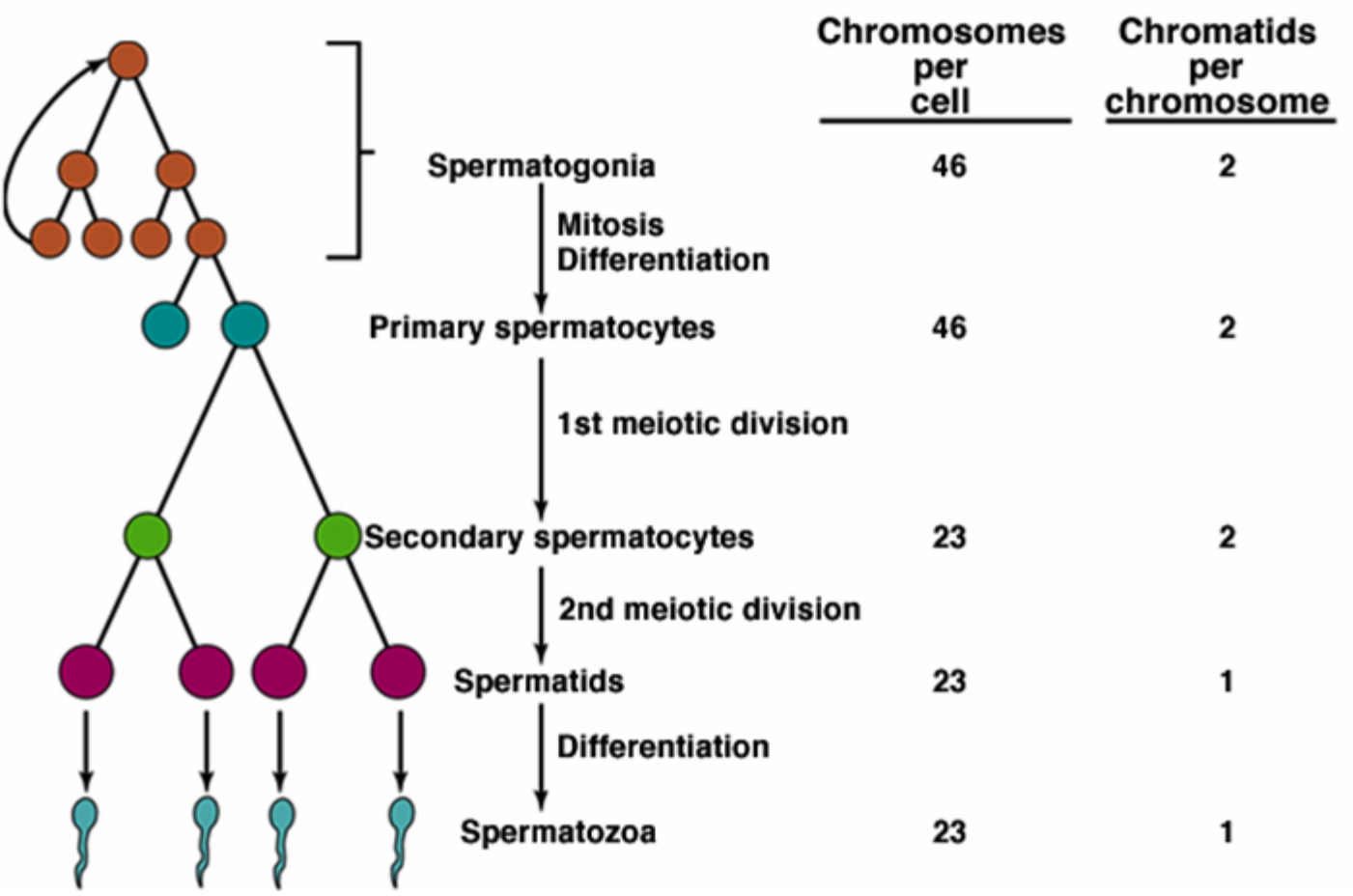


Figure 17-6

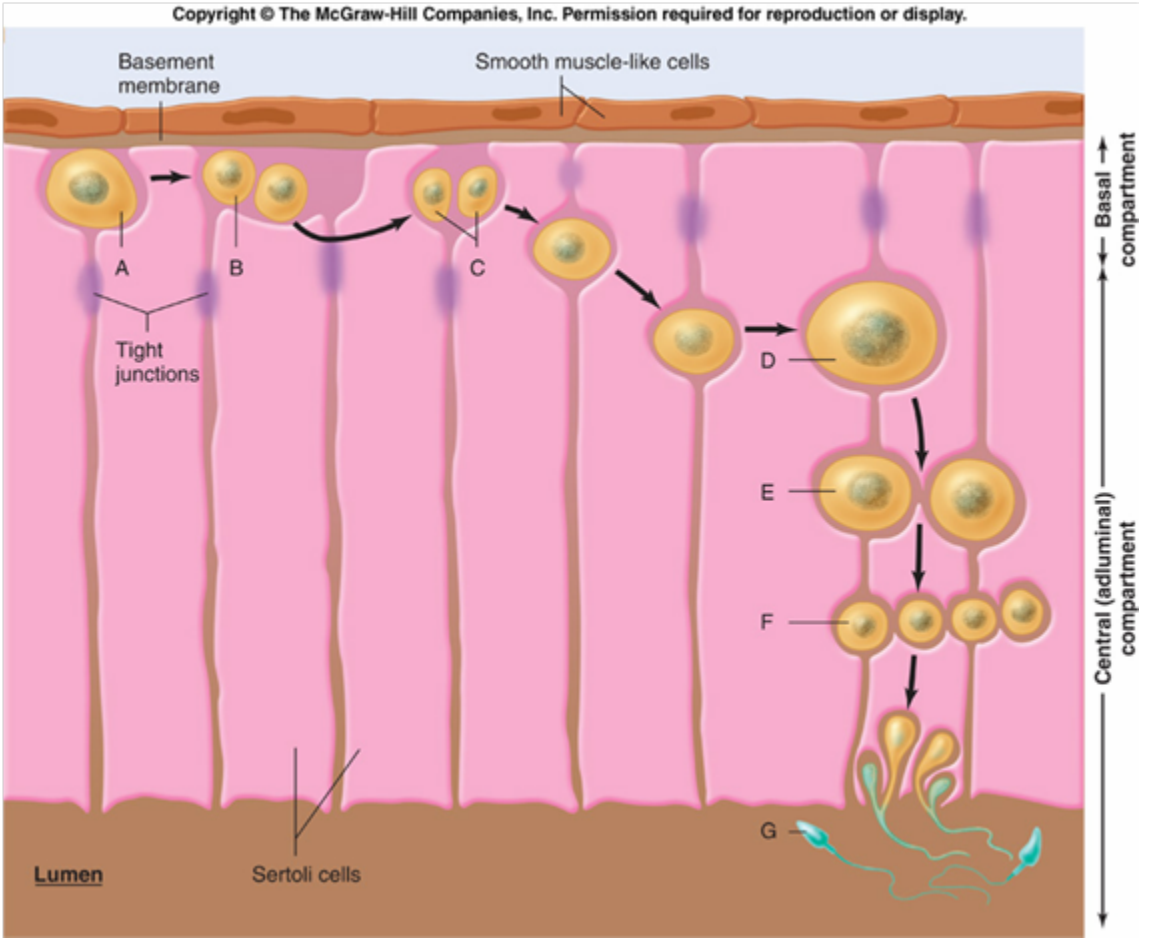


Spermatogenesis is the testicular process in adult males that generates haploid gametes capable of fertilizing ova.

The overall result is that the set of 23 pairs of homologous chromosomes is reduced to a set of 23 chromosomes per sperm–the corresponding 23 pairs are present in ova.

Click here to play the Spermatogenesis Flash Animation

Figure 17-9



Sertoli cells support spermatogenesis in the seminiferous tubules in response to testosterone and FSH.

After its release in the female reproductive tract, a spermatozoan is propelled by the thrashing movements of its flagellum.

At the time of fertilization, the acrosome at the head of an individual spermatozoan releases enzymes that allow it to gain access to the interior of the ova and accomplish the union of genetic material.

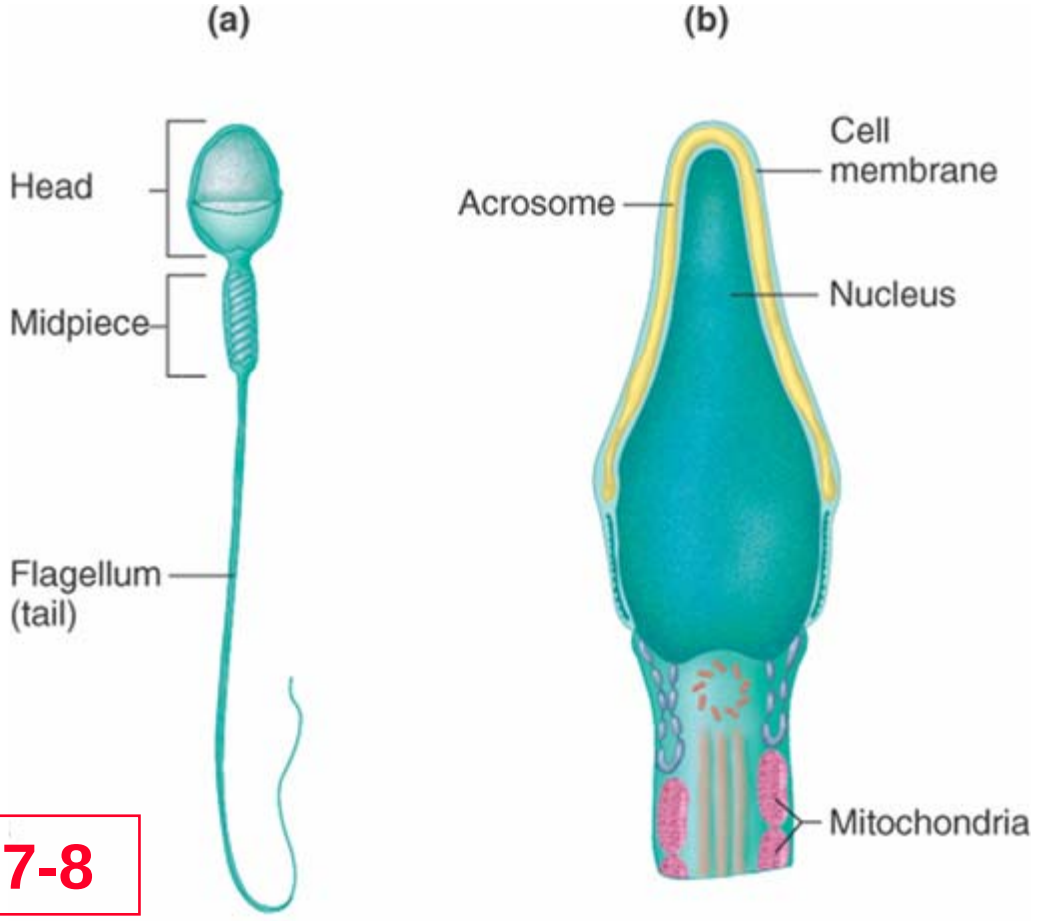
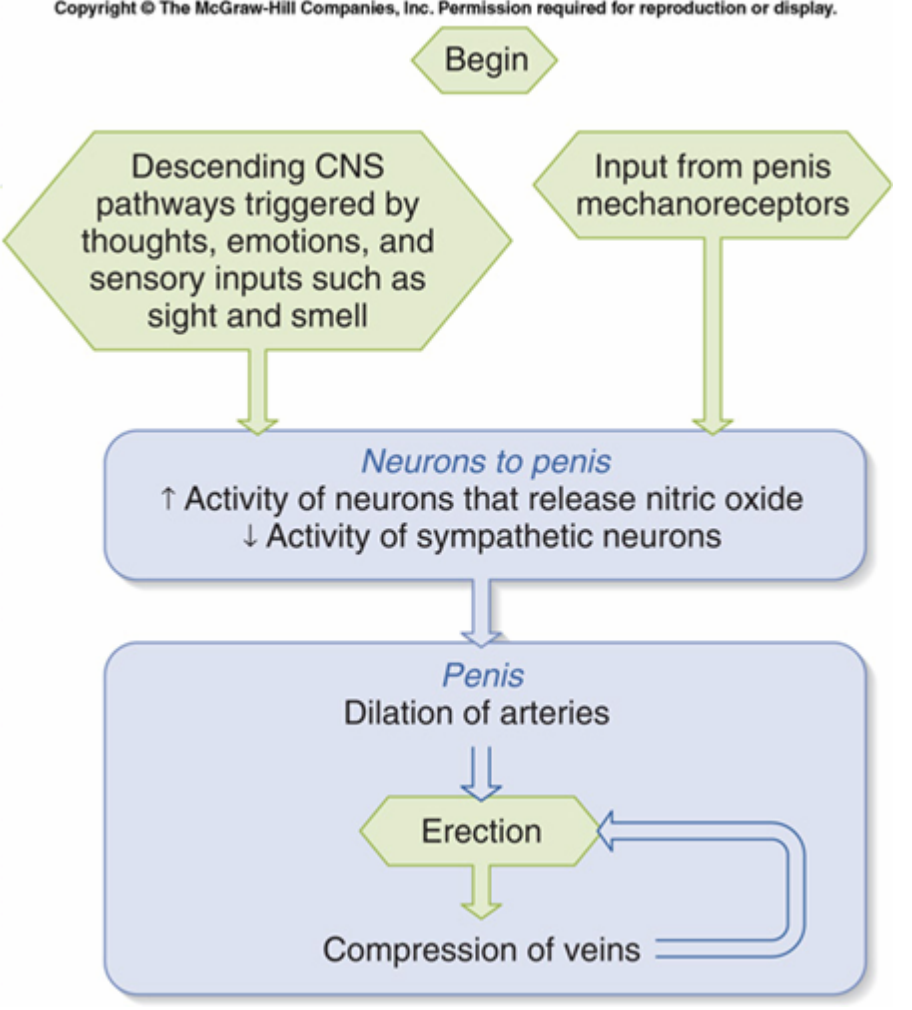


Figure 17-8

TABLE 17–2 Functions of Sertoli Cells

1. Provide Sertoli cell barrier to chemicals in the plasma
2. Nourish developing sperm
3. Secrete luminal fluid, including androgen-binding protein
4. Respond to stimulation by testosterone and FSH to secrete paracrine agents that stimulate sperm proliferation and differentiation
5. Secrete the protein hormone inhibin, which inhibits FSH secretion from the pituitary
6. Secrete paracrine agents that influence the function of Leydig cells
7. Phagocytize defective sperm
8. Secrete, during embryonic life, Müllerian inhibiting substance (MIS), which causes the primordial female duct system to regress



Engorgement of the penis during sexual excitement is due to activation of the reflex pathways for erection. Nitric oxide is an important vasodilator in this reflex.

Summary of hormonal control of Male reproductive function.

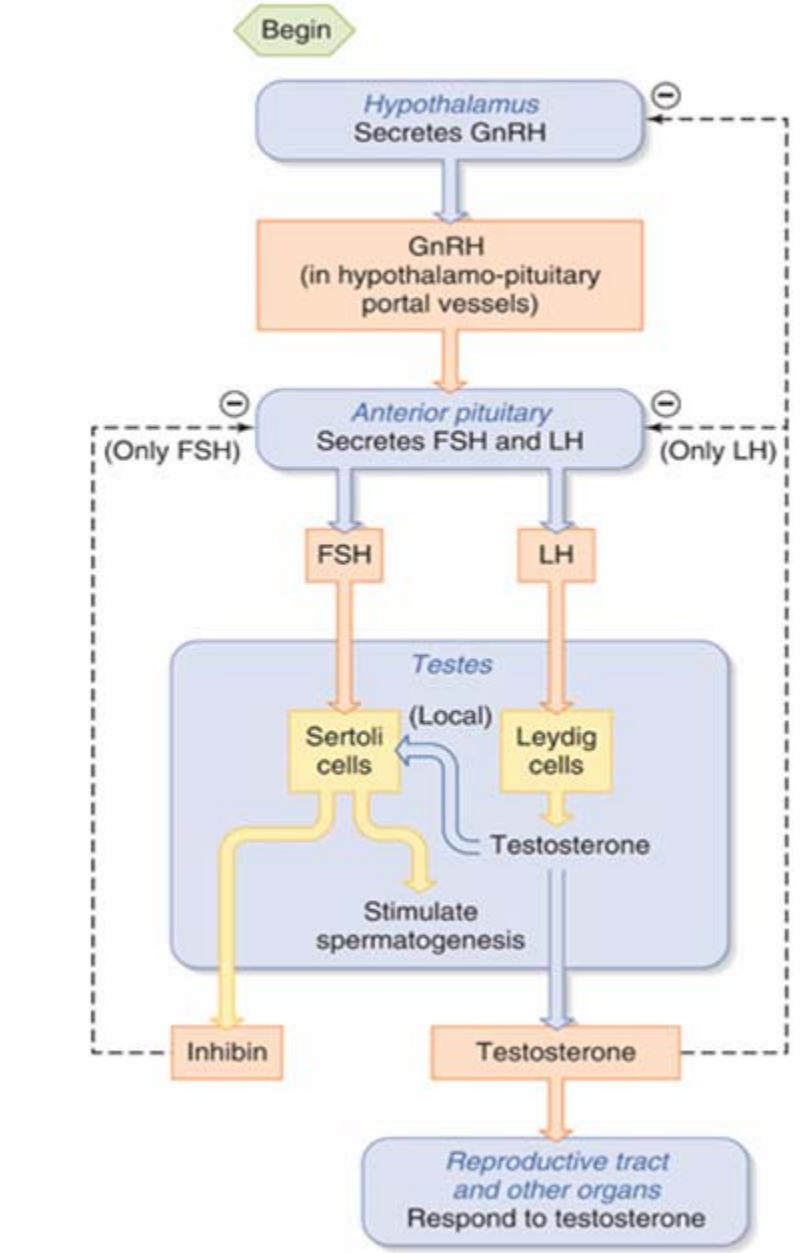
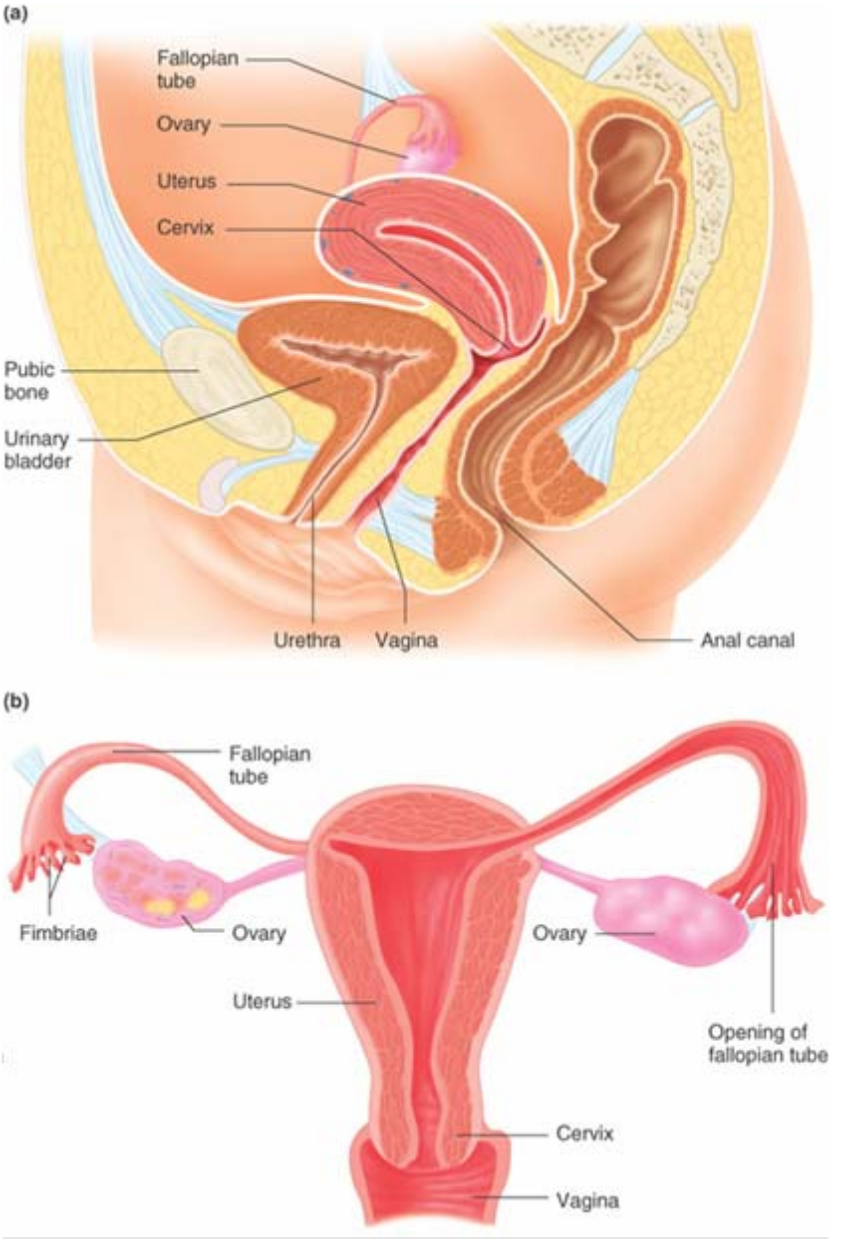
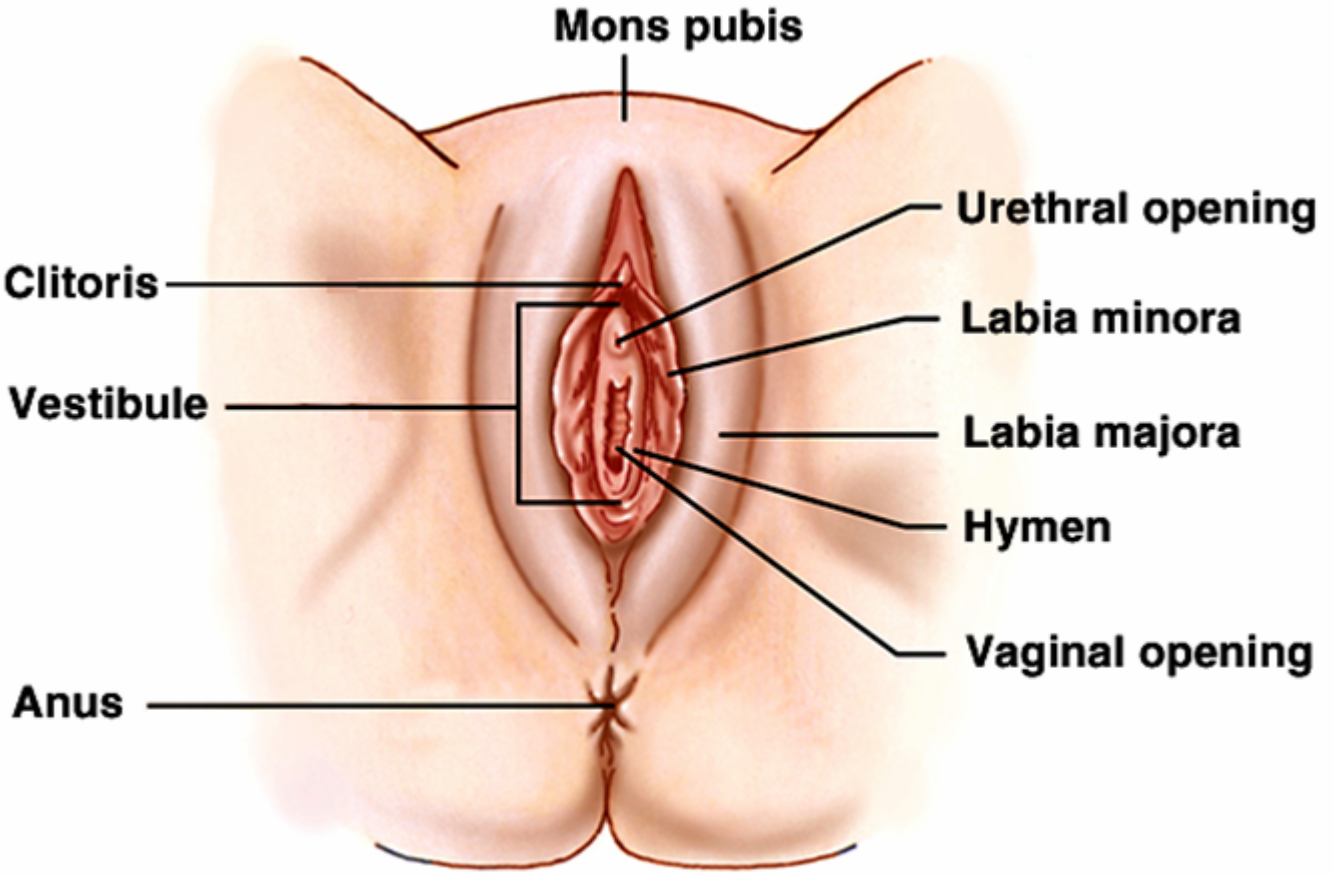


TABLE 17–3 Effects of Testosterone in the Male

1. Required for initiation and maintenance of spermatogenesis (acts via Sertoli cells)
2. Decreases GnRH secretion via an action on the hypothalamus
3. Inhibits LH secretion via a direct action on the anterior pituitary
4. Induces differentiation of male accessory reproductive organs and maintains their function
5. Induces male secondary sex characteristics; opposes action of estrogen on breast growth
6. Stimulates protein anabolism, bone growth, and cessation of bone growth
7. Required for sex drive and may enhance aggressive behavior
8. Stimulates erythropoietin secretion by the kidneys

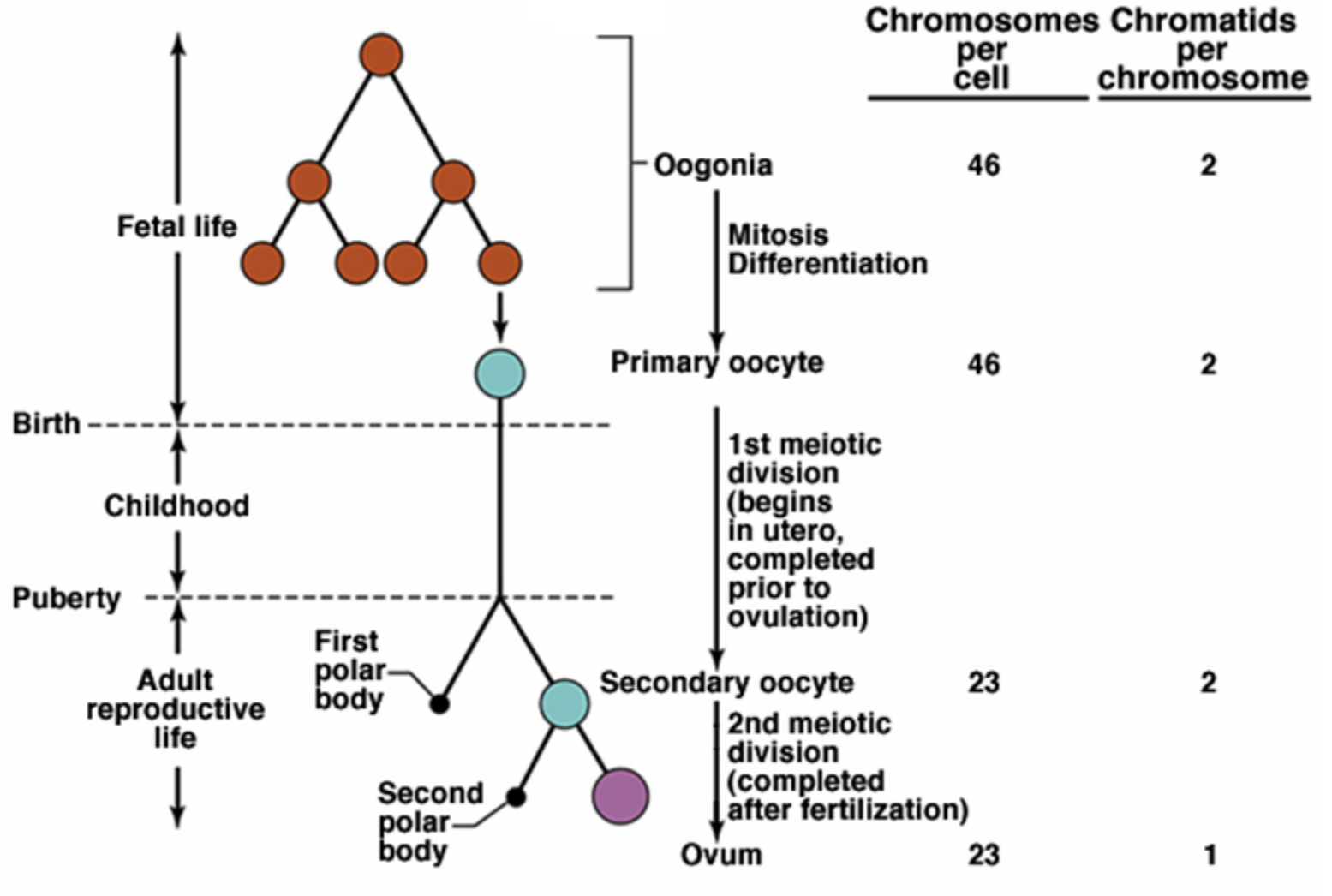
A spermatozoan ejaculated into the female reproductive tract must move through the cervix and uterus before it can fertilize an ovulated egg that has been moved from the ovaries into the uterine tube by the combined actions of fimbrial contractions and the oviduct's "ciliary escalator."

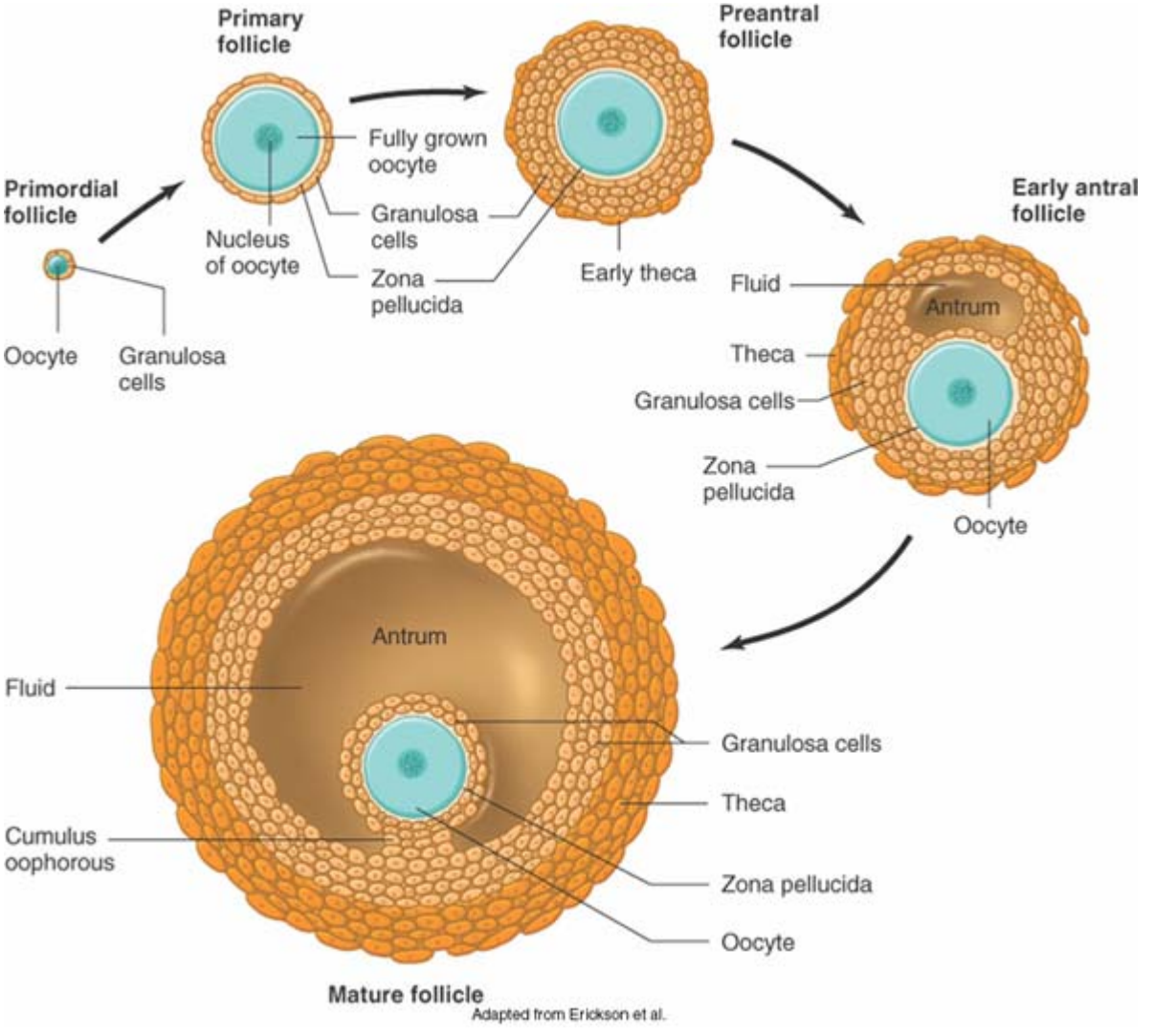




The external genitalia of the female accommodate the reproductive processes at the time of sexual intercourse and at the time of birth. The tract is somewhat protected from invasion by pathogenic organisms by an acidic mucus.

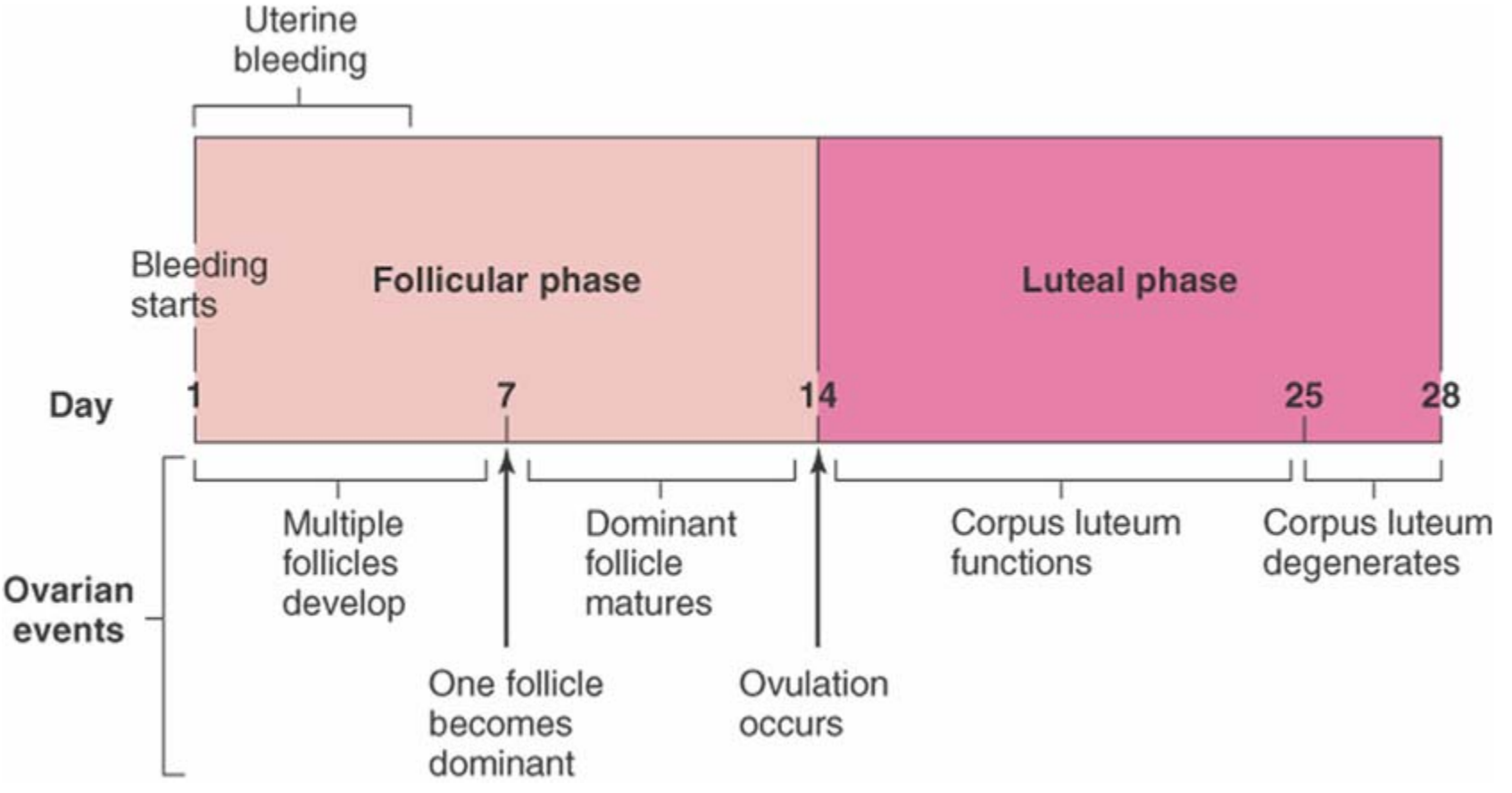
Production of haploid gametes in females is called oogenesis. The full sequence of meiosis is not completed until fertilization.





The development of an ovarian follicle and oocyte. The fully mature follicle is 1.5 cm in diameter.

Click here to play the Maturation of the Follicle and Oocyte Flash Animation



The ovarian cycle of changes in steroid production drives the rest of the changes that characterize the menstrual cycle of adult females. The follicular phase is marked by increasing levels of estrogens whereas the luteal phase is one of increased progesterone levels; the transition between the two is ovulation.

Ovulation is provoked by a surge in LH and marks the transition to the luteal phase of the cycle,
characterized by high levels of progesterone. (8-14).

Eventually, (15) a decrease in LH leads to luteolysis, and the withdrawal of steroid support for a thick, active uterus.

Small increases in the secretion of gonadotropins (LH & FSH) lead to follicular maturation, including an increase in the synthesis and secretion of ovarian steroid hormones (1-7).

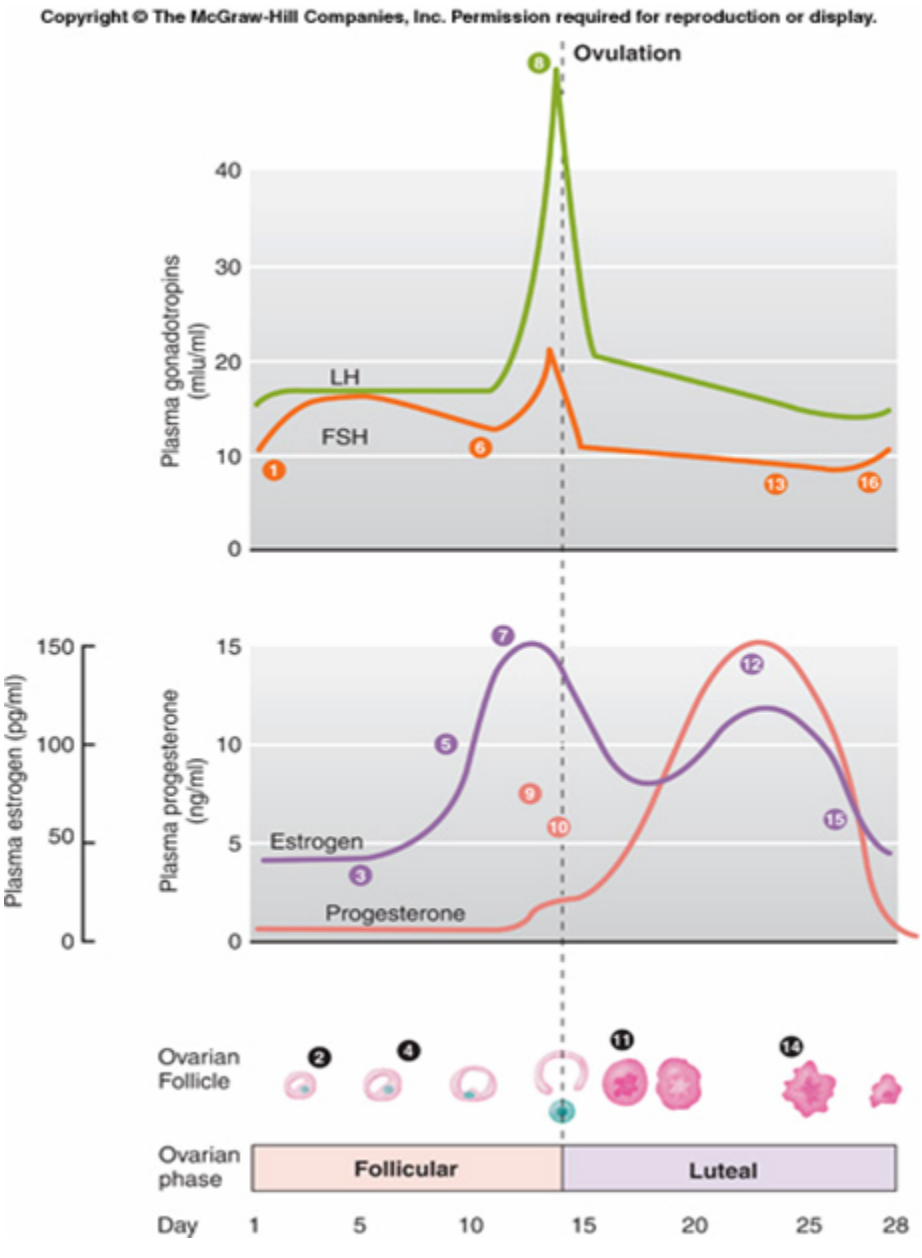


TABLE 17–4 Summary of Major Feedback Effects of Estrogen, Progesterone, and Inhibin

1. **Estrogen,** in **low plasma concentrations,** causes the anterior pituitary to secrete less FSH and LH in response to GnRH and also may inhibit the hypothalamic neurons that secrete GnRH.

   Result: Negative feedback inhibition of FSH and LH secretion during the early and middle follicular phase.

2. **Inhibin** acts on the pituitary to inhibit the secretion of FSH.

   Result: Negative feedback inhibition of FSH secretion throughout the cycle.

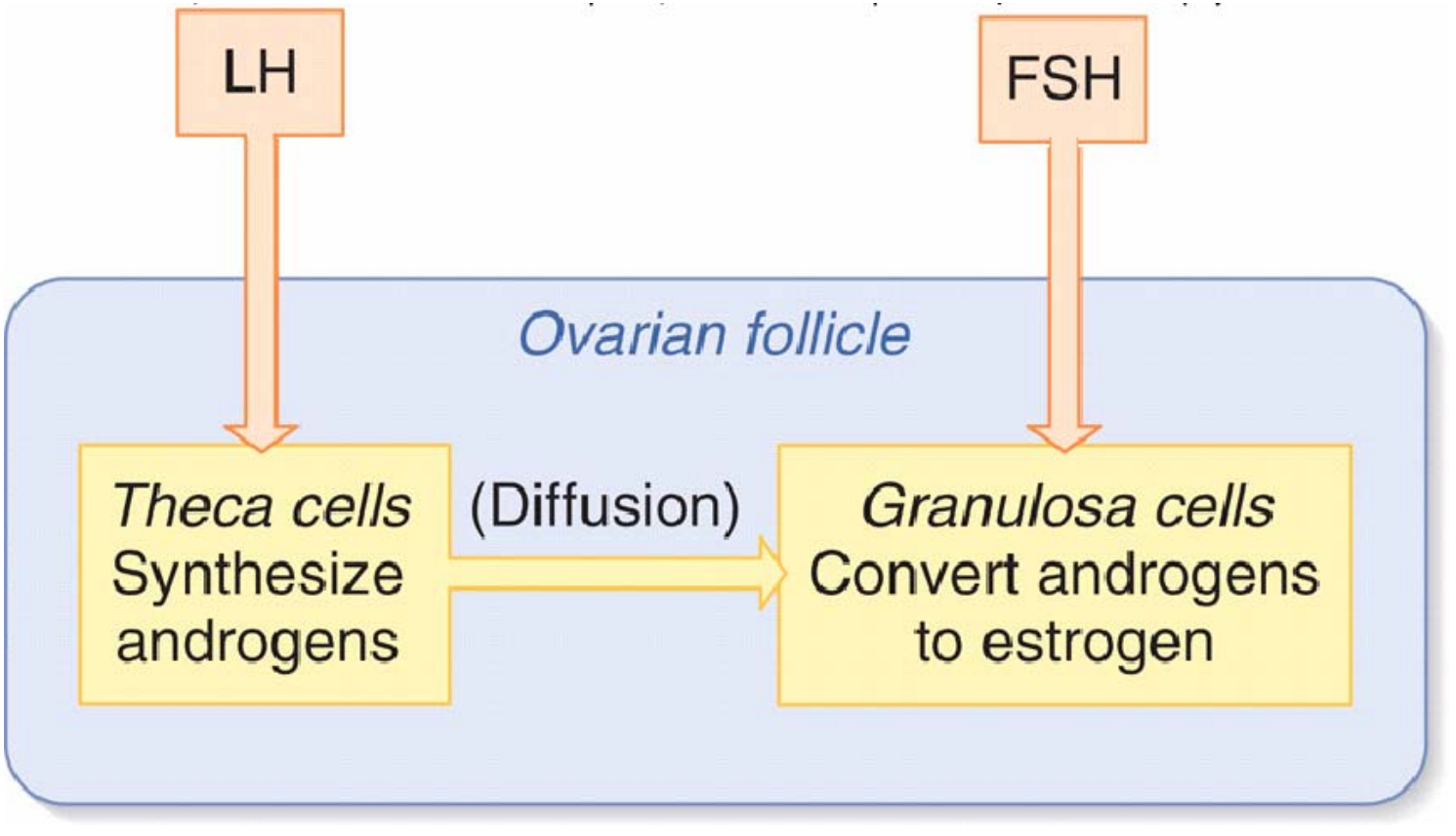
3. **Estrogen, when increasing dramatically,** causes anterior pituitary cells to secrete more LH (and FSH) in response to GnRH and also stimulate the hypothalamic neurons that secrete GnRH.

   Result: Positive feedback stimulation of the LH surge, which triggers ovulation.

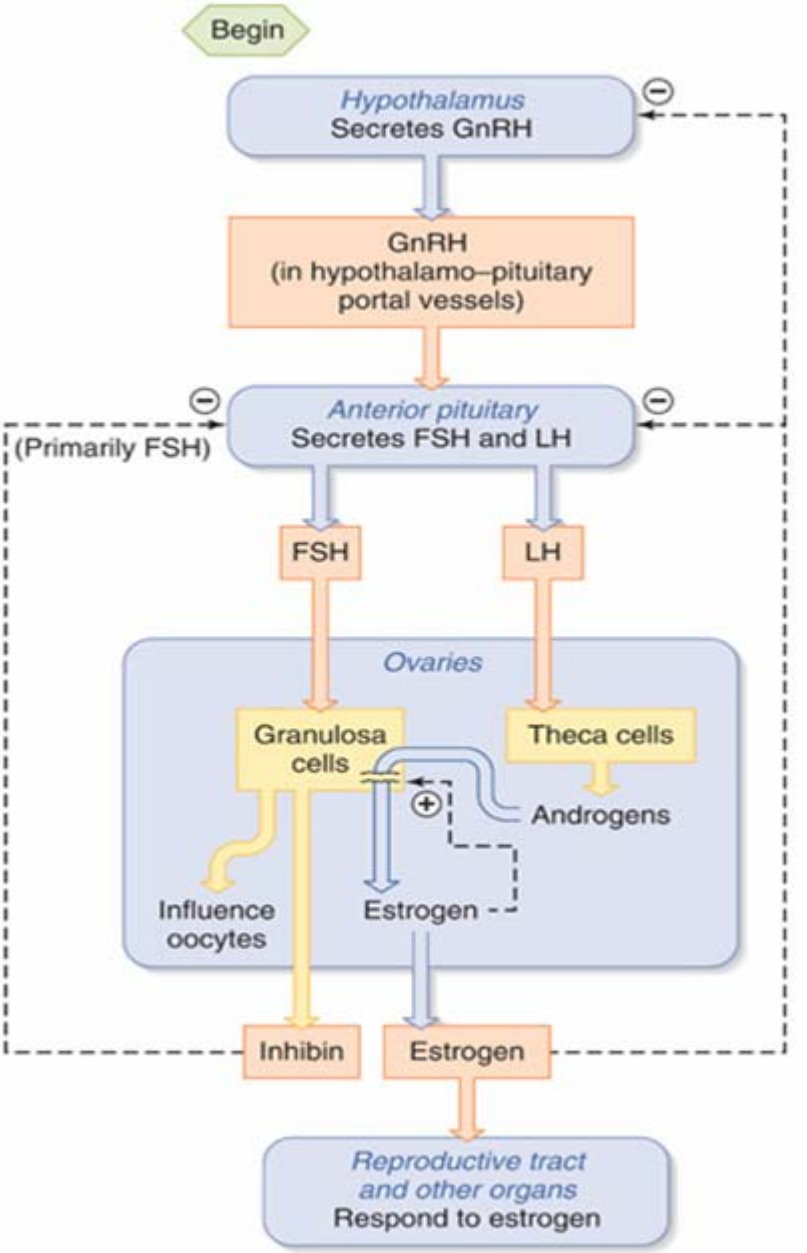
4. High plasma concentrations of **progesterone,** in the presence of estrogen, inhibit the hypothalamic neurons that secrete GnRH.

   Result: Negative feedback inhibition of FSH and LH secretion and prevention of LH surges during the luteal phase and pregnancy.

The two-stage model of estrogen synthesis holds that androgen precursors are synthesized in the outer layer (theca cells) of the ovarian follicles and diffuse to the inner layer (granulosa cells) for conversion to estrogens; LH drives the former, FSH the latter.



Summary of the hormonal control of ovarian function during the follicular phase.



The feedback relationship between the ovarian steroid hormones and secretion from the hypothalamus/anterior pituitary gland reverses in mid-cycle, eliciting the large, ovulatory surge in LH.

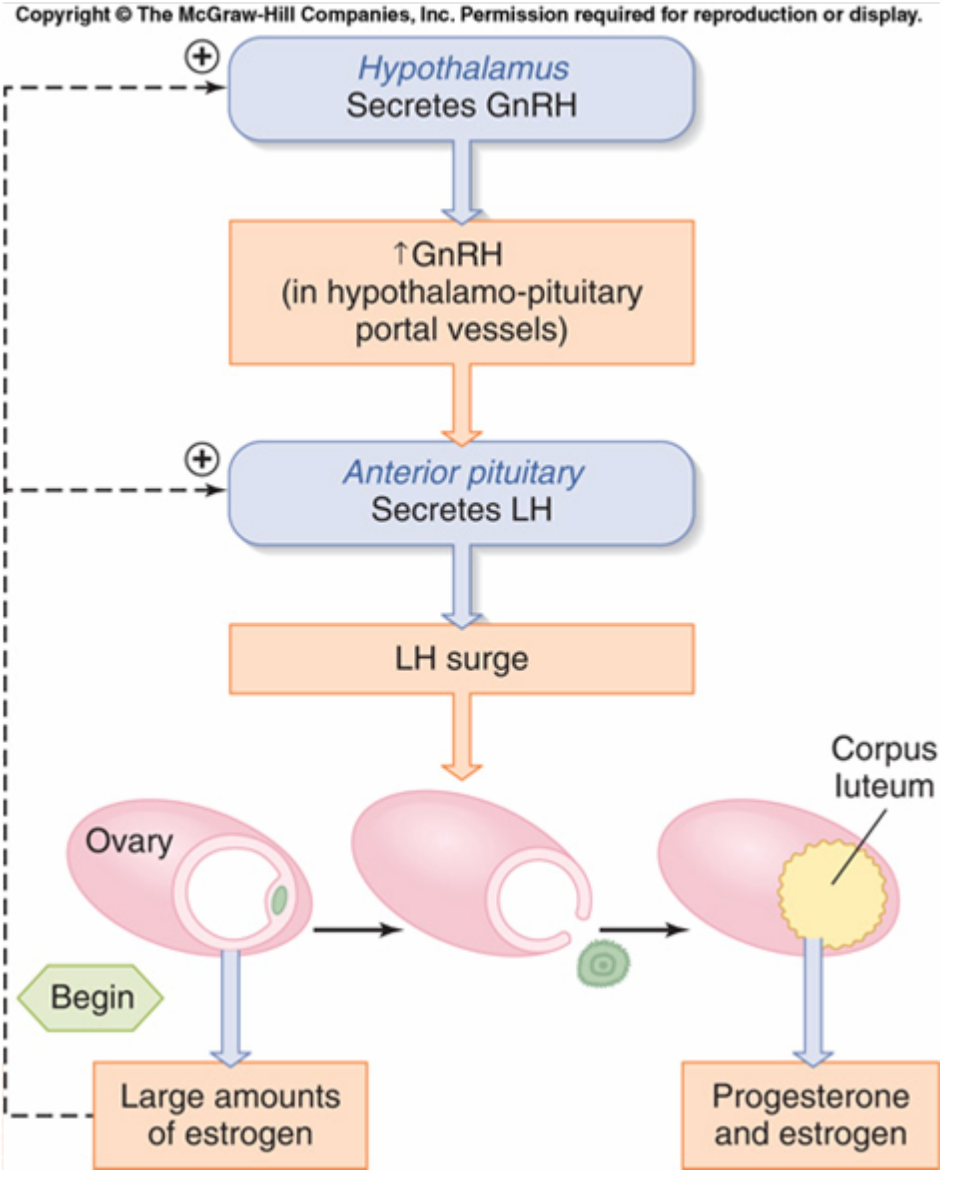
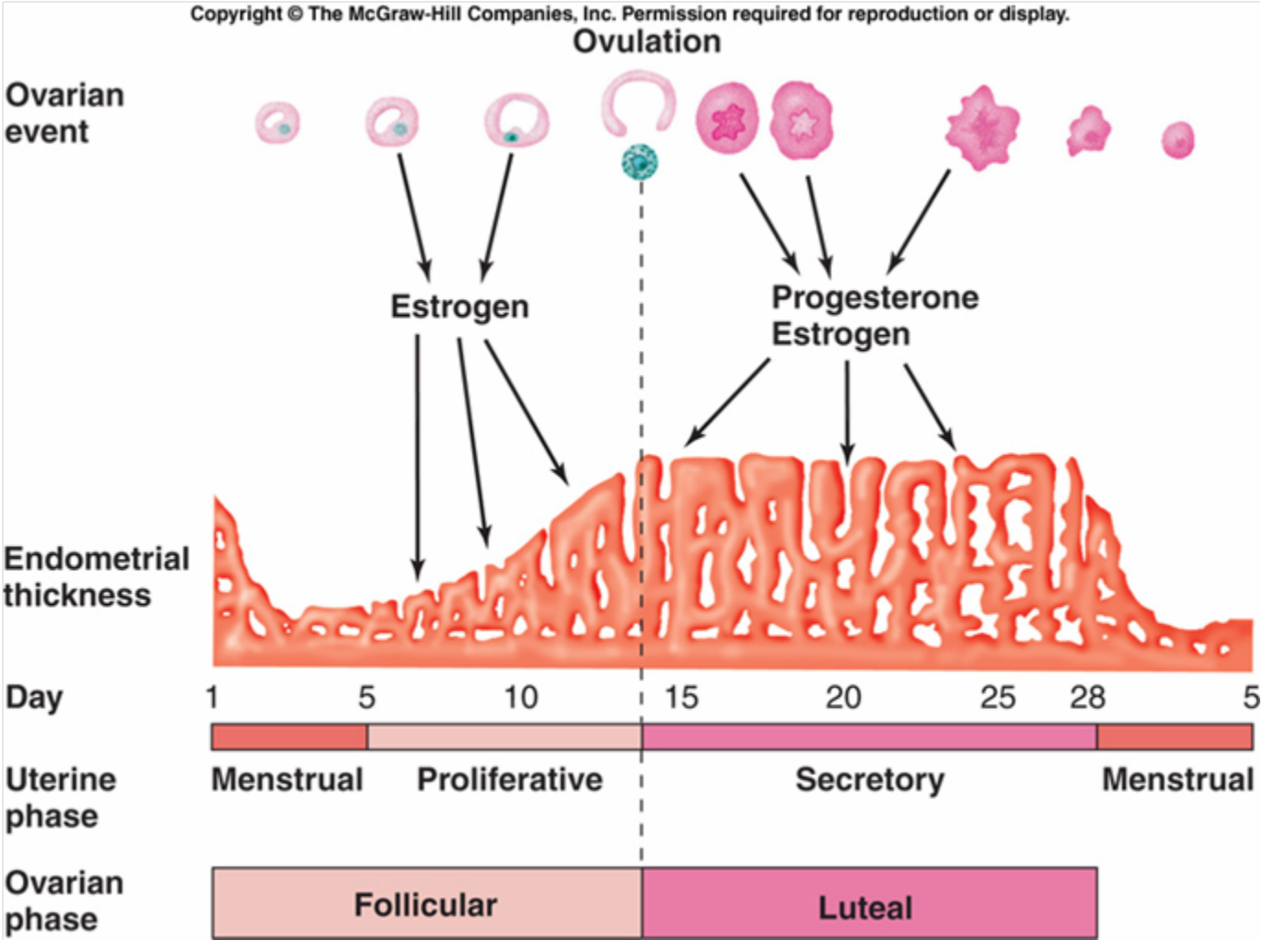


TABLE 17–5 Effects of the LH Surge on Ovarian Function

1. The primary oocyte completes its first meiotic division and undergoes cytoplasmic changes that prepare the ovum for implantation should fertilization occur. These LH effects on the oocyte are mediated by messengers released from the granulosa cells in response to LH.
2. Antrum size (fluid volume) and blood flow to the follicle increase markedly.
3. The granulosa cells begin releasing progesterone and decrease the release of estrogen, which accounts for the midcycle decrease in plasma estrogen concentration and the small rise in plasma progesterone just before ovulation.
4. Enzymes and prostaglandins, synthesized by the granulosa cells, break down the follicular-ovarian membranes. These weakened membranes rupture, allowing the oocyte and its surrounding granulosa cells to be carried out onto the surface of the ovary.
5. The remaining granulosa cells of the ruptured follicle (along with the theca cells of that follicle) are transformed into the corpus luteum, which begins to release progesterone and estrogen.

TABLE 17–6 Functions of Granulosa Cells

1. Nourish oocyte
2. Secrete chemical messengers that influence the oocyte and the theca cells
3. Secrete antral fluid
4. Are the site of action for estrogen and FSH in the control of follicle development during early and middle follicular phases
5. Express aromatase, which converts androgen (from theca cells) to estrogen
6. Secrete inhibin, which inhibits FSH secretion via an action on the pituitary
7. Are the site of action for LH induction of changes in the oocyte and follicle culminating in ovulation and formation of the corpus luteum



Estrogens are the predominant steroid hormones prior to ovulation; progesterone predominate after ovulation.

TABLE 17–7 Summary of the Menstrual Cycle

DAY(S)	MAJOR EVENTS
1–5	Estrogen and progesterone are low because the previous corpus luteum is regressing. *Therefore:* (a) Endometrial lining sloughs. (b) Secretion of FSH and LH is released from inhibition, and their plasma concentrations increase. *Therefore:* Several growing follicles are stimulated to mature.
7	A single follicle (usually) becomes dominant.
7–12	Plasma estrogen increases because of secretion by the dominant follicle. *Therefore:* Endometrium is stimulated to proliferate.
7–12	LH and FSH decrease due to estrogen and inhibin negative feedback. *Therefore:* Degeneration (atresia) of nondominant follicles occurs.
12–13	LH surge is induced by increasing plasma estrogen. *Therefore:* (a) Oocyte is induced to complete its first meiotic division and undergo cytoplasmic maturation. (b) Follicle is stimulated to secrete digestive enzymes and prostaglandins.
14	Ovulation is mediated by follicular enzymes and prostaglandins.
15–25	Corpus luteum forms and, under the influence of low but adequate levels of LH, secretes estrogen and progesterone, and so plasma concentrations of these hormones increase. *Therefore:* (a) Secretory endometrium develops. (b) Secretion of FSH and LH is inhibited, lowering their plasma concentrations. *Therefore:* No new follicles develop.
25–28	Corpus luteum degenerates (if egg is not fertilized). *Therefore:* Plasma estrogen and progesterone concentrations decrease. *Therefore:* Endometrium begins to slough at conclusion of day 28, and a new cycle begins.

TABLE 17–8 Some Effects of Female Sex Steroids

Estrogen

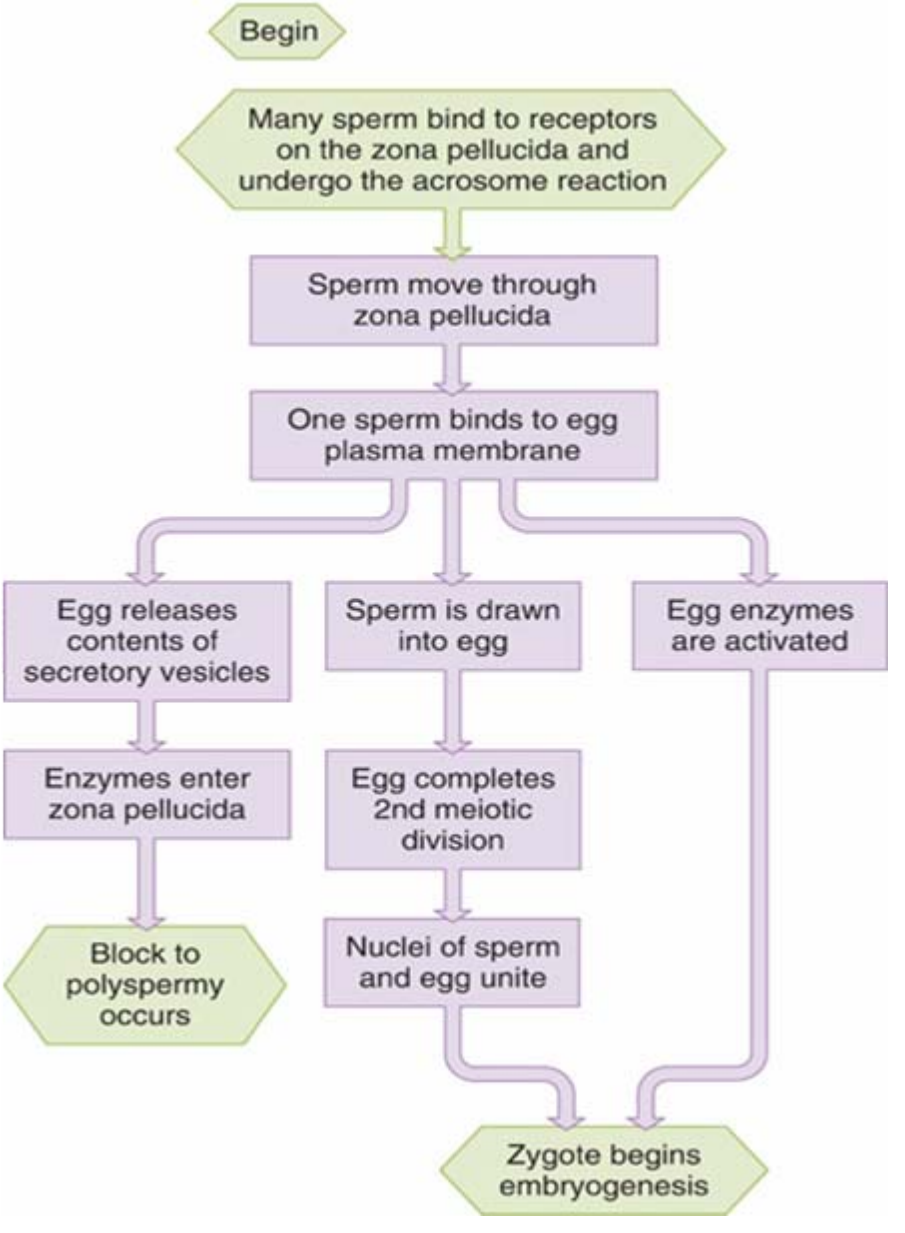
1. Stimulates growth of ovary and follicles (local effects)
2. Stimulates growth of smooth muscle and proliferation of epithelial linings of reproductive tract. In addition:
   a. Fallopian tubes: Increases contractions and ciliary activity.
   b. Uterus: Increases myometrial contractions and responsiveness to oxytocin. Stimulates secretion of abundant, fluid cervical mucus. Prepares endometrium for progesterone's actions by inducing progesterone receptors.
   c. Vagina: Increases layering of epithelial cells.
3. Stimulates external genitalia growth, particularly during puberty
4. Stimulates breast growth, particularly ducts and fat deposition during puberty
5. Stimulates female body configuration development during puberty: narrow shoulders, broad hips, female fat distribution (deposition on hips and breasts)
6. Stimulates a more-fluid secretion from lipid (sebum)-producing skin glands (sebaceous glands); (This "anti-acne" effect opposes the acne-producing effects of androgen.)
7. Stimulates bone growth and ultimate cessation of bone growth (closure of epiphyseal plates); protects against osteoporosis; does not have an anabolic effect on skeletal muscle
8. Vascular effects (deficiency produces "hot flashes")
9. Has feedback effects on hypothalamus and anterior pituitary (see Table 17–4)
10. Stimulates prolactin secretion but inhibits prolactin's milk-inducing action on the breasts
11. Protects against atherosclerosis by effects on plasma cholesterol (Chapter 16), blood vessels, and blood clotting (Chapter 12)

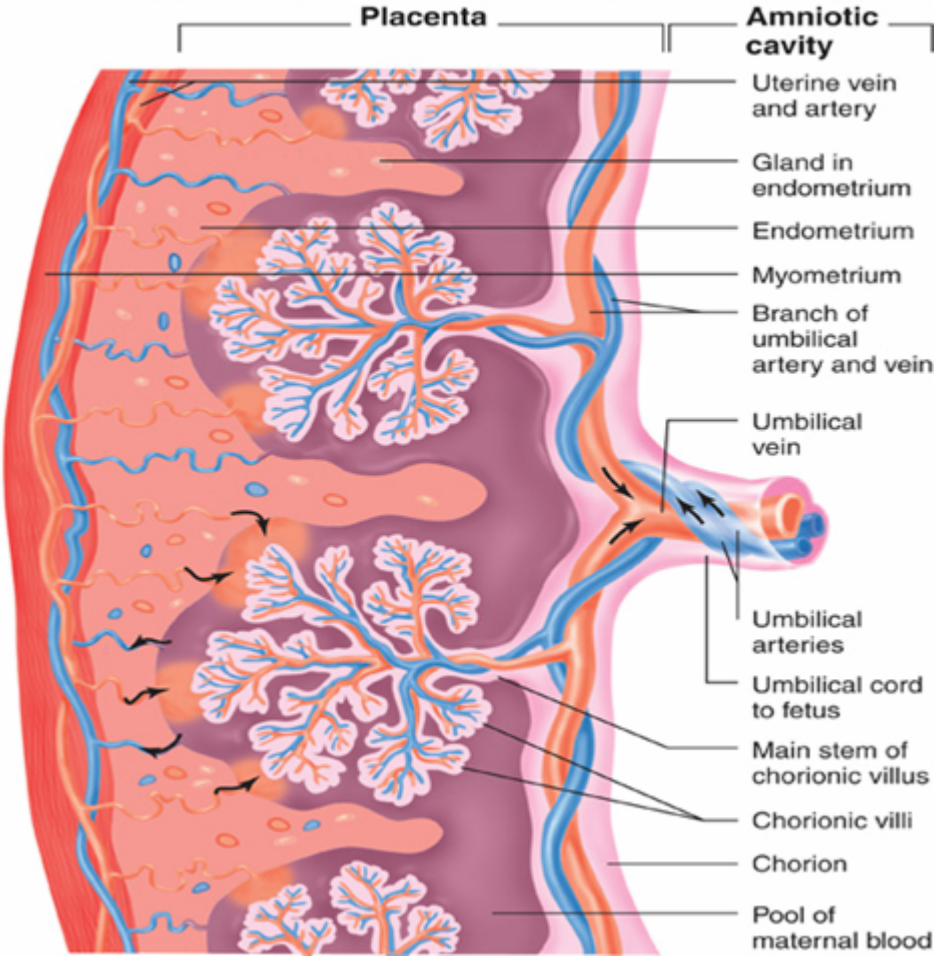
Progesterone

1. Converts the estrogen-primed endometrium to an actively secreting tissue suitable for implantation of an embryo
2. Induces thick, sticky cervical mucus
3. Decreases contractions of fallopian tubes and myometrium
4. Decreases proliferation of vaginal epithelial cells
5. Stimulates breast growth, particularly glandular tissue
6. Inhibits milk-inducing effects of prolactin
7. Has feedback effects on hypothalamus and anterior pituitary (see Table 17–4)
8. Increases body temperature

Only a single spermatozoan gains access to the ovum at the time of fertilization due to a biochemical block; sperm penetration also triggers the completion of meiosis in the ovum so that fertilization can occur.

The fertilized egg is called a zygote.

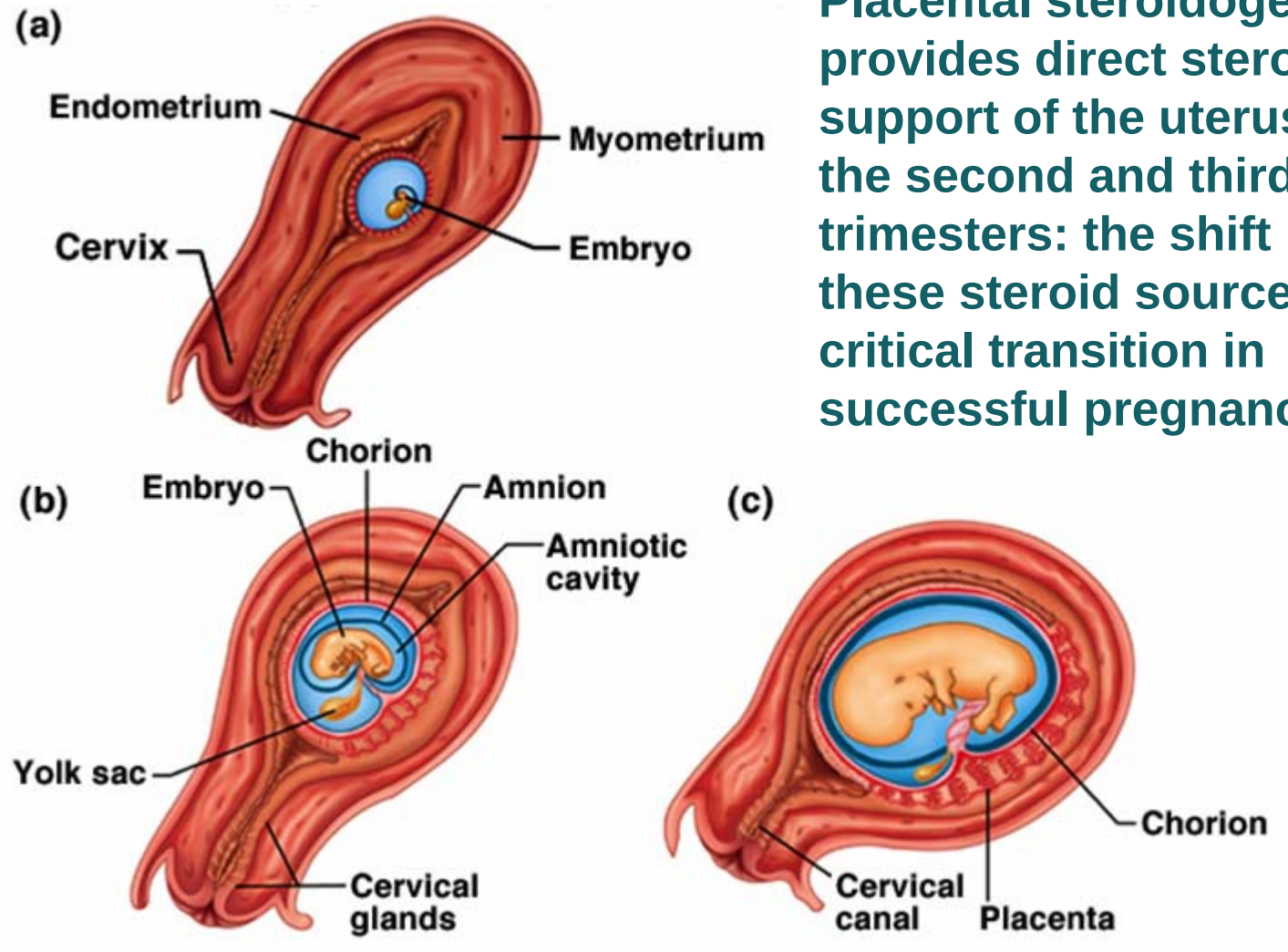


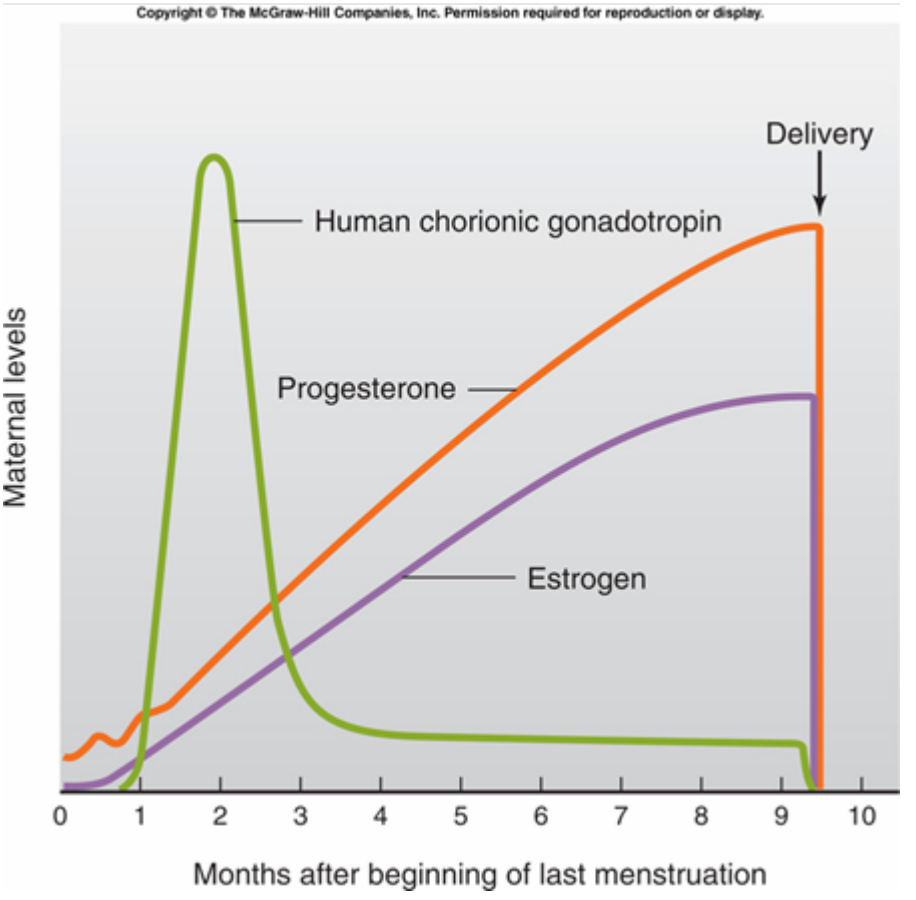


After the end of the first trimester, the placenta is more fully developed, including its nutritive/exchange relationship between the maternal and fetal circulations, and its steroid products provide hormonal support for the uterus .

During the first trimester, the chorion is the source of a gonadotropin hormone that maintains steroid production by the corpus luteum in the ovary.

Placental steroidogenesis provides direct steroidal support of the uterus during the second and third trimesters: the shift between these steroid sources is a critical transition in successful pregnancy.





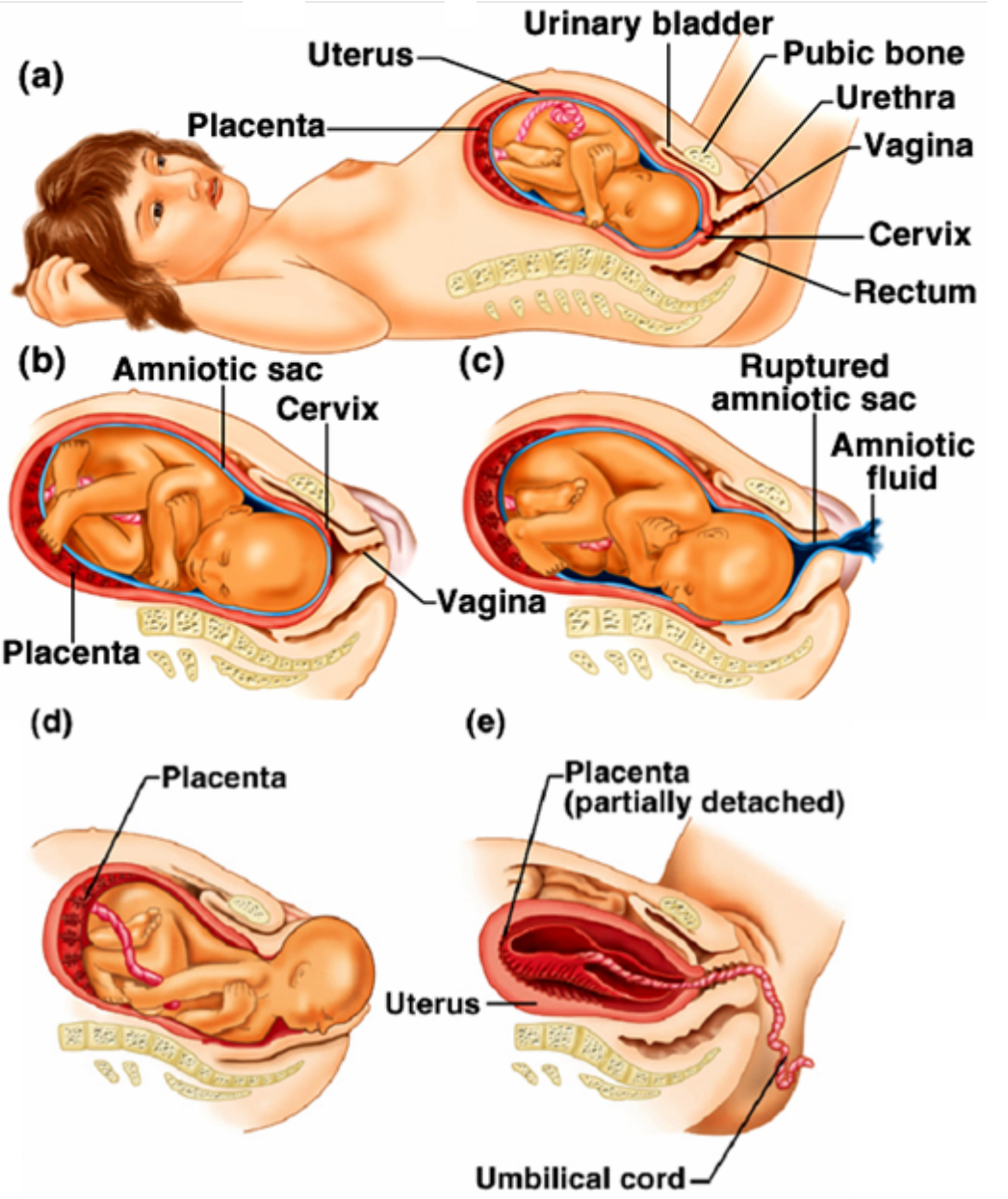
Metabolites of chorionic gonadotropin in the urine are an "early indicator" that pregnancy is underway. The critical transition between uterine dependence on ovarian versus placental steroids occurs at the end of the first trimester, an interval with the greatest likelihood of miscarriage.

TABLE 17–9 Maternal Responses to Pregnancy

	RESPONSE
Placenta	Secretion of estrogen, progesterone, human chorionic gonadotropin, inhibin, human placental lactogen, and other hormones
Anterior pituitary	Increased secretion of prolactin Secretes very little FSH and LH
Adrenal cortex	Increased secretion of aldosterone
Posterior pituitary	Increased secretion of vasopressin
Parathyroids	Increased secretion of parathyroid hormone
Kidneys	Increased secretion of renin, erythropoietin, and 1,25-dihydroxyvitamin D Retention of salt and water. *Cause:* Increased aldosterone, vasopressin, and estrogen
Breasts	Enlarge and develop mature glandular structure *Cause:* Estrogen, progesterone, prolactin, and human placental lactogen
Blood volume	Increased. *Cause:* Total erythrocyte volume is increased by erythropoietin, and plasma volume by salt and water retention. However, plasma volume usually increases more than red cells, thereby leading to small decreases in hematocrit.
Bone turnover	Increased. *Cause:* Increased parathyroid hormone and 1,25-dihydroxyvitamin D
Body weight	Increased by average of 12.5 kg, 60 percent of which is water
Circulation	Cardiac output increases, total peripheral resistance decreases (vasodilation in uterus, skin, breasts, GI tract, and kidneys), and mean arterial pressure stays constant
Respiration	Hyperventilation occurs (arterial P_{CO_2} decreases) due to the effects of increased progesterone
Organic metabolism	Metabolic rate increases Plasma glucose, gluconeogenesis, and fatty acid mobilization all increase. *Cause:* Hyporesponsiveness to insulin due to insulin antagonism by human placental lactogen and cortisol
Appetite and thirst	Increased (particularly after the first trimester)
Nutritional RDAs	Increased

The onset of labor and delivery is typically heralded by the “breaking of the waters” in reference to the loss of amniotic fluid (c) through the ruptured amniotic sac.

Uterine contractions, coupled with the mother’s abdominal contractions, move the newborn into its own world.



Click here to play the Factors That Influence the Process of Parturition Flash Animation

A series of positive-feedback events involving neural and chemical cues promotes the cascade of uterine contractions (smooth muscle) that help to propel a neonate into the world.

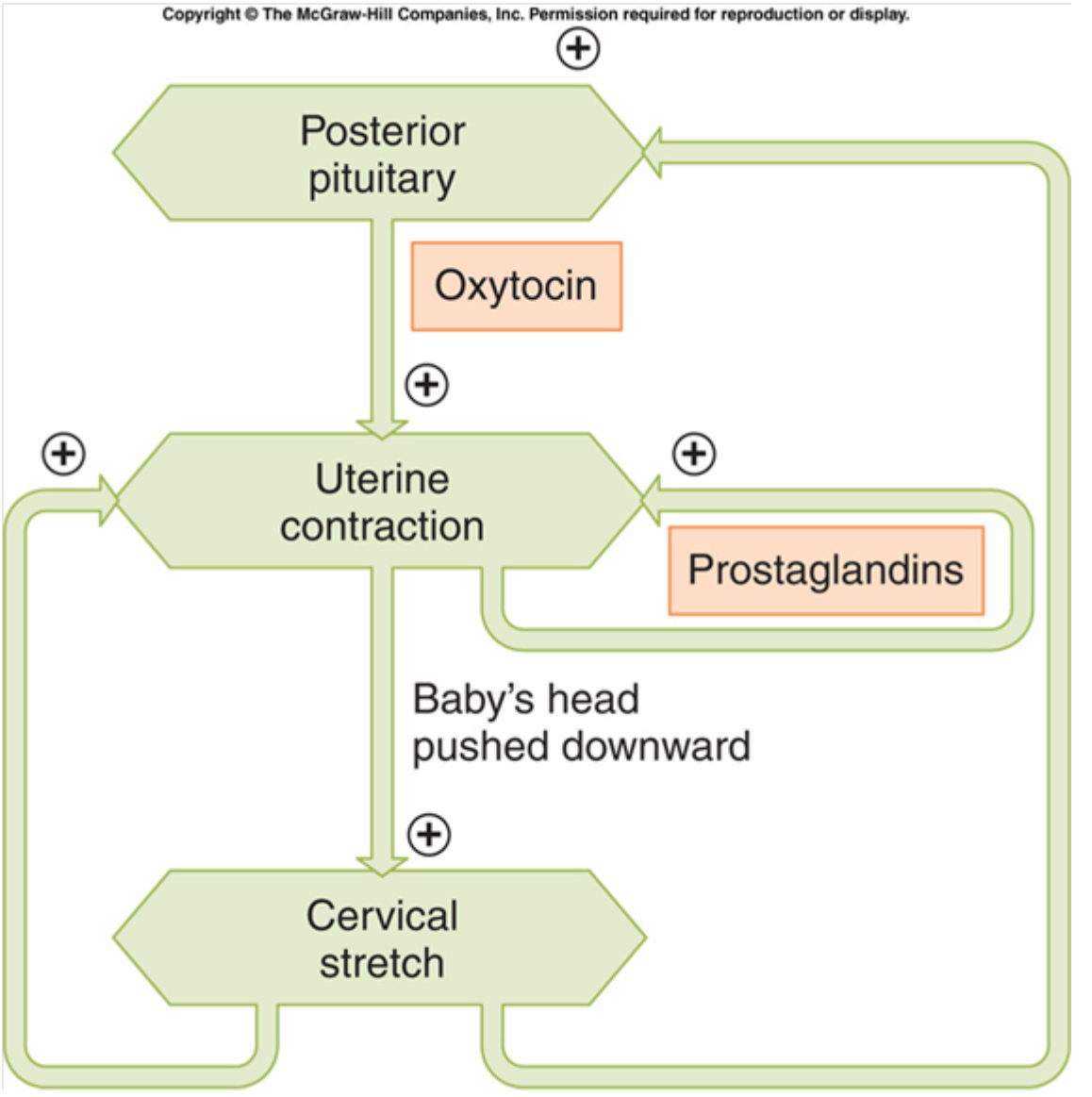
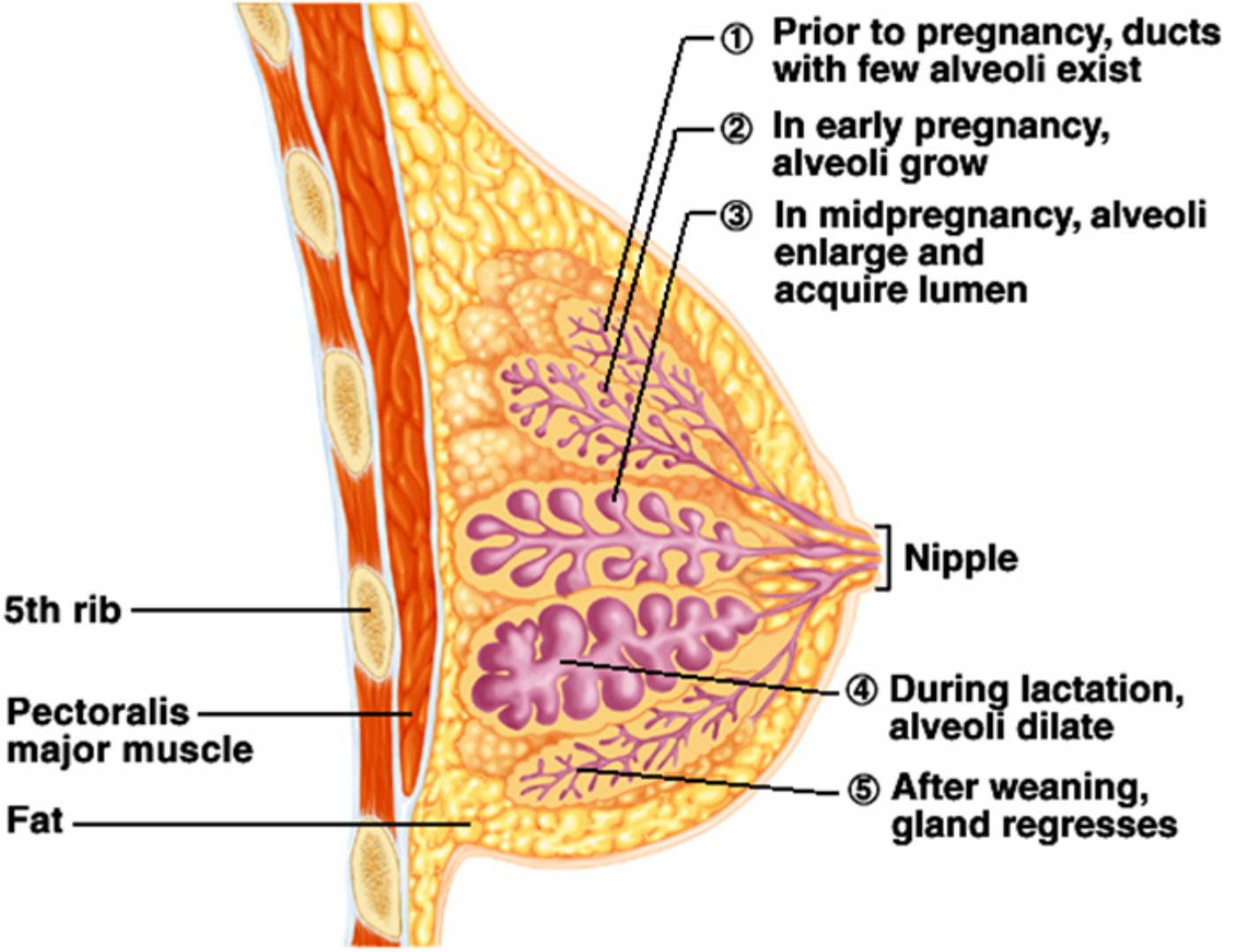


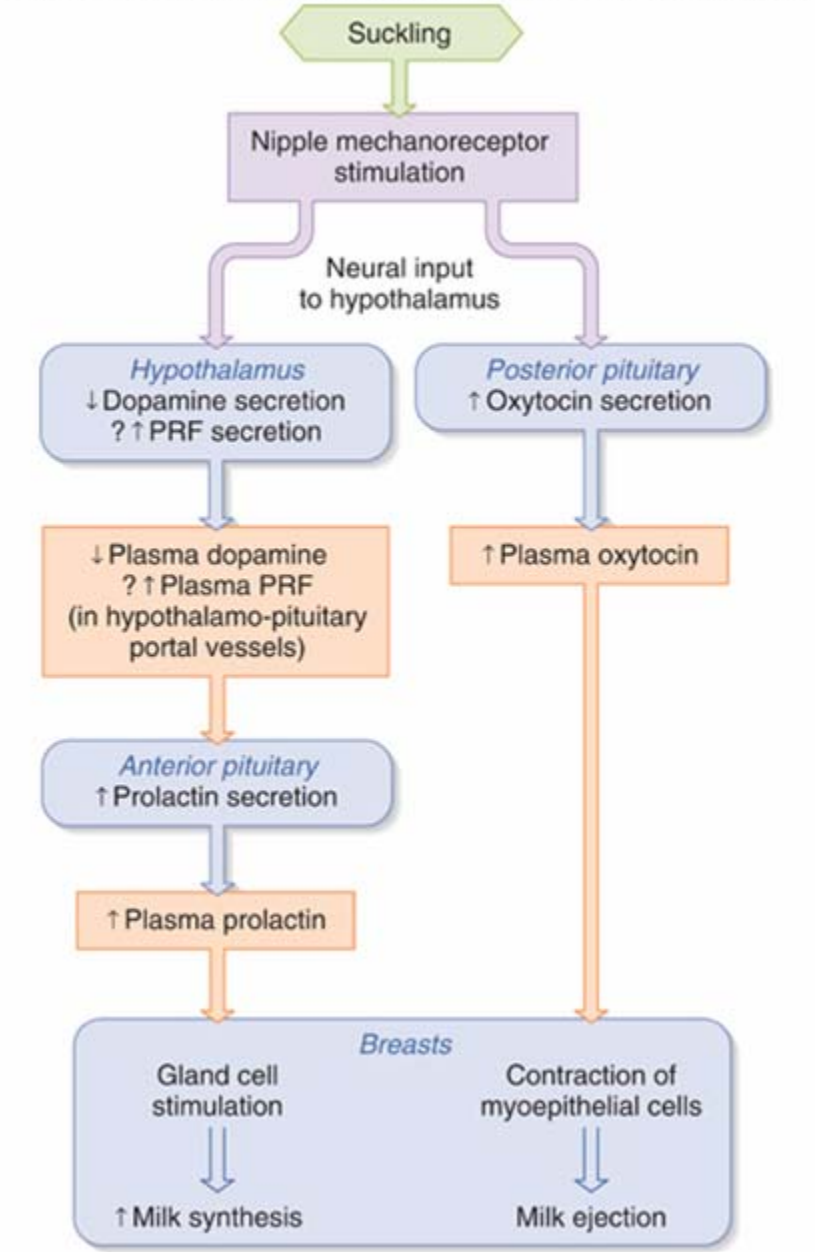
TABLE 17–10 Some Effects of Prostaglandins* on the Female Reproductive System

SITE OF PRODUCTION	ACTION	RESULT
Late-antral follicle	Stimulate production of digestive enzymes	Rupture of follicle
Corpus luteum	May interfere with hormone secretion and function	? Death of corpus luteum
Uterus	Constrict blood vessels in endometrium	Onset of menstruation
	Cause changes in endometrial blood vessels and cells early in pregnancy	Facilitate implantation
	Increase contraction of myometrium	Help initiate both menstruation and parturition
	Cause cervical "ripening"	Facilitate cervical dilation during parturition

*The term "prostaglandins" is used loosely here, as is customary in reproductive physiology, to include all the eicosanoids.



The hormones of pregnancy, including prolactin, estrogens, and progestins, stimulate development in the mammary glands.



Prolactin promotes the synthesis of milk; oxytocin promotes the ejection of milk from the nipple.