Instructor's Answer Key

Chapter 20: Reproduction

Answers to Test Your Understanding of Concepts and Principles

1. In the brain and some other accessory organs, testosterone can be converted by the enzyme aromatase into estradiol-17β, or it can be converted by the enzyme 5α-reductase to dihydrotestosterone (DHT). The DHT, in turn, may be converted into other 5α-reduced androgens, including two whose names are shortened to 3-alpha and 3-beta diol. In the brain, testosterone may be converted to estradiol-17β that is involved in negative feedback control of LH secretion. In the prostate, DHT stimulates the function and maintains the structure of this gland. In the seminiferous tubules, the 5α-reduced derivatives of testosterone are needed for the production of sperm. [Note: This question is also answered in the Student Study Guide.]

2. During spermatogenesis, spermatozoa are produced by meiosis of the germinal epithelium of the seminiferous tubules, which comprise about 90% of the mass of each testis. The interstitial tissue, by contrast, contains Leydig cells, found within a thin web of connective tissue between convolutions of the tubules. Whereas the tubules produce sperm (exocrine), the Leydig cells produce testosterone (endocrine). Receptors for FSH are localized to the tubules, while receptors for LH are localized to the Leydig cells. FSH thus specifically stimulates the tubules while LH specifically stimulates the Leydig cells. Testosterone from the Leydig cells, however, stimulates the seminiferous tubules and is needed for sperm production. Products from the tubules, in turn, may have some regulatory role in the Leydig cells. This is suggested by the observation that, during the beginning of puberty, FSH in some permissive way increases the responsiveness of the testes to later stimulation by LH.

3. Sertoli cells span the width of the seminiferous tubules from the basement membrane to the lumen with cup-shaped processes that engulf the spermatids, as they undergo meiosis and are changed to spermatozoa. As nongerminal cells, Sertoli cells form a continuous layer connected by tight junctions around the tubule circumference. In this way, Sertoli cells form a blood-testes barrier that prevents the immune system from exposure to developing sperm antigens and possible autoimmune destruction of the sperm. This helps make the seminiferous tubules form an immunologically privileged site. Sertoli cells produce FAS ligand, which binds to FAS receptors on the T lymphocyte surface and trigger their apoptosis. Sertoli cells may also aid the developing sperm cells metabolically; as shown by the observations that: (1) FSH specifically stimulates receptors on the Sertoli cells and in this way indirectly mediates spermatogenesis and spermiogenesis; (2) the X chromosome of the developing spermatocyte is inactive, and so essential molecules coded by genes on this chromosome appear to be supplied by the Sertoli cells during development; and (3) autocrine interactions between Sertoli cells and Leydig cells may involve androgen-binding protein (ABP), secreted by Sertoli cells.

4. Primary spermatocytes enter into early prophase I during embryonic development and stop progress until puberty. At the beginning of puberty, testosterone acts as a paracrine regulator by stimulating the completion of the meiotic division of the primary spermatocyte, converting these cells to secondary spermatocyte and spermatids; while FSH enhances (but is not required for) the maturation of spermatids to spermatozoa. Without FSH, spermatogenesis would commence later in puberty. In the mature adult testes, maintenance of spermatogenesis requires only testosterone. FSH, through its stimulation of Sertoli cells and subsequent release of paracrine regulators, is required for maximal sperm production and optimal fertility.

5. The primary ovarian follicles develop under stimulation by FSH. This development entails the maturation of the oocyte as the follicle gets larger and becomes a secondary follicle. The secondary follicle completes meiosis I and begins the second meiotic division, where it is arrested at metaphase II. As the follicle increases in size there are more and more active granulosa cells, FSH stimulates an increasing amount of estradiol secretion by the granulosa cells. The blood levels of estradiol thus increase in correspondence to the increased maturation of the ovum and size of the follicle. When the graafian follicle is ready to ovulate, the blood levels of estradiol have increased sufficiently to stimulate the anterior pituitary to secrete a surge of LH secretion, which causes rupture of the follicle and ovulation at about day 14.

6. Menstrual bleeding occurs during the first few days of the menstrual cycle as the endometrium is shed. The shedding of the endometrium with accompanying bleeding occurs as a result of the rapid declines in the blood levels of estradiol and progesterone that occur at the end of the luteal phase of the previous cycle. By contrast, the bleeding that occurs during the estrous cycle of a dog occurs at about the middle of its cycle, does not accompany the shedding of the endometrium, and is not caused by a decrease in the secretion of ovarian steroids. Instead, a high secretion of estradiol from the dog ovaries at about the time of ovulation causes this bleeding.

7. During pregnancy there is a continued high secretion of ovarian steroids—estrogen and progesterone—first from the corpus luteum of the mother's ovary and then from the placenta. The high blood levels of estradiol and progesterone during pregnancy inhibit the secretion of FSH and LH from the anterior pituitary; this negative feedback inhibition assures that a pregnant woman cannot ovulate during her pregnancy. Since the contraceptive pill contains derivatives of estrogen and progesterone, a woman who takes this pill daily will have steroid hormone levels in her blood that mimic pregnancy and will exhibit the same negative feedback inhibition of FSH and LH secretion. Ovulation therefore will not occur and conception is prevented.

8. Menstruation normally occurs as a result of the lowering of estradiol and progesterone secretion that occurs at the end of a luteal phase. Anything that prevents the lowering of the levels of estradiol and progesterone will prevent menstruation. This can occur if the corpus luteum of the newly pregnant mother does not regress at the end of a cycle due to stimulation by hCG from her implanted blastocyst. Also, a woman who continues to take contraceptive pills daily likewise will not menstruate, as the blood levels of estrogen and progesterone will remain high.

9. The stimulus of a baby suckling elicits a neuroendocrine reflex relayed to the hypothalamus by sensory neurons and inhibits PIH (believed to be dopamine) secretion, thus resulting in an increase in the secretion of prolactin from the anterior pituitary. (Although controversial, prolactin secretion may also be increased during suckling by reflex secretion of a prolactin-releasing hormone from the posterior pituitary.) Increased secretion of prolactin, in turn, stimulates the increased production of milk by the mammary glands. The stimulus of suckling also results in the reflex secretion of oxytocin from the posterior pituitary. Oxytocin stimulates contraction of the lactiferous ducts, resulting in the milk-ejection reflex. The sound of the baby crying may initiate the secretion of oxytocin through the integration of sensory function performed by the central nervous system due to conditioning of the mother by the auditory cue (crying child).

10. Primordial follicles in the ovary contain primary oocytes that have become arrested at prophase of the first meiotic division; the number of these is maximal at birth and declines thereafter. A small number of oocytes in each cycle are stimulated to complete their first meiotic division and become secondary oocytes arrested in metaphase II. At the completion of the first meiotic division, the secondary oocyte is the only complete cell formed; the other product of this division is a tiny polar body, which disintegrates. One of the secondary follicles grows very large, becomes a graafian follicle, and on day 14 ovulates a secondary oocyte. Upon ovulation, the secondary oocyte is extruded from the ovary, but does not complete the second meiotic division unless it becomes fertilized. Polar bodies are produced so that the chromosome number is reduced and so the selected oocyte will be large enough to become a viable embryo should fertilization occur.

11. The placenta secretes chorionic gonadotropin (hCG), chorionic somatomammotropin (hCS), progesterone, and estrogens. The placenta is considered an incomplete endocrine gland because it cannot produce estrogen and progesterone without the aid of precursors supplied to it by both the mother and the fetus.

12. At the menopause, the ovaries are depleted in follicles, which cease secreting estradiol and inhibin. FSH and LH secretion by the pituitary is therefore elevated due to the absence of negative feedback inhibition from estradiol and inhibin. It is the withdrawal of estradiol secretion from the ovaries that is most responsible for the many debilitating symptoms of menopause, and many of these symptoms can be reversed by exogenous estrogen treatment, or estrogen replacement therapy (ERT). Furthermore, ERT helps to prevent bone loss and reduce other symptoms of menopause. However, like all drug treatment, ERT has adverse effects that include increased risks of certain forms of cancer and cardiovascular disease.

13. In the presence of a Y chromosome, testes develop. The testes then produce testosterone, which causes the development of the male sex accessory organs, the prostate, and the penis and scrotum, and müllerian inhibition hormone (MIH), which causes the paramesonephric duct to degenerate. Testosterone and MIH cause the development of the male accessory sex organs and external genitalia. If a male embryo lacks receptor proteins for testosterone, he is considered a male pseudohermaphrodite, with testicular feminization syndrome. Embryonic tissues cannot respond to testosterone in the absence of receptor proteins, and so female genitalia develop, even though he has testes. A male embryo lacking the enzyme 5α-reductase is also a male pseudohermaphrodite, with 5α-reductase deficiency. These individuals have normal wolffian duct derivatives (epididymis, vas deferens, seminal vesicles, and ejaculatory duct) because the development of these structures is stimulated by testosterone directly. But they do not have male genitalia, because the development of male genitalia requires the action of DHT, which cannot be produced from testosterone in the absence of 5α-reductase.

14. The timing of the onset of parturition (labor) in sheep (as in all mammals) is regulated primarily by the fetal adrenal cortex. Rising fetal adrenal corticosteroids due to increased CRH and ACTH secretion from the fetal hypothalamus and anterior pituitary gland, respectively, stimulate production of placental enzymes. These enzymes convert progesterone to estrogen and subsequently cause a decrease in circulating progesterone and an increase in circulating estrogen. This change in circulating hormones causes increased myometrial contractility. In humans and other primates, progesterone levels do not fall and it appears that the placenta produces the increased corticotropin-releasing hormone (CRH) necessary to increase fetal adrenal cortical activity. In response to stimulation the inner part of the fetal adrenal gland, called the fetal adrenal zone, secretes the androgen dehydroepiandrosterone sulfate (DHEAS), which the placenta converts to estrogens. The increased circulating estrogens (mostly estriol) stimulate the uterus to (1) produce oxytocin receptors, (2) produce prostaglandin receptors, and (3) produce gap junctions between myometrial cells in the uterus. Parturition in animals (pigs, rats, and guinea pigs) is aided by the hormone relaxin, which softens the pubic symphysis and relaxes the cervix. Relaxin in humans however, does not seem to be required for parturition but rather is involved in the formation of the placenta early in pregnancy.

Answers to Test Your Ability to Analyze and Apply Your Knowledge

1. I do not agree. To be effective, a male contraceptive pill would have to suppress the hypothalamus and/or anterior pituitary secretion of hormones that will ultimately interrupt/cease sperm production. Attempts have been made to develop new methods of male contraception. Specifically, these new drugs have generally involved compounds that suppress gonadotropin secretion, such as testosterone or a combination of progesterone and a GnRH antagonist. Another compound, gossypol, which interferes with sperm development, has also been tried. These drugs can be effective but have unacceptable side effects.

2. GnRH and the gonadotropins are normally secreted in a pulsatile fashion. In benign prostatic hyperplasia (BPH) the enlarged prostate is caused by testosterone stimulating and supporting the abnormal glandular growth. Administration of estrogen to elderly males with BPH would supply continuous negative feedback that would tonically suppress both GnRH release from the hypothalamus and gonadotropin secretion from the anterior pituitary. The decrease in LH would produce a fall in testosterone secretion from the Leydig cells of the testes, causing the prostate (and other reproductive structures) to shrink. Concomitantly, the fall in FSH would reduce spermatogenesis as well. In elderly males the relief from urination difficulties should outweigh the other adverse effects of estrogen treatment. Other drugs used to treat BPH include α_1-adrenergic receptor blockers, which decrease the muscle tone of the prostate and bladder neck thus making urination easier; and 5α-reductase inhibitors, which inhibit the enzyme needed to convert testosterone into its active form, dihydrotestosterone (DHT). A reduction in DHT may help to reduce prostate size.

3. The female *embryonic* ovaries contain approximately 6 to 7 million oogonia. Most of these oogonia die prenatally through apoptosis. No new oogonia will be made during the life of this female. Meiosis will begin toward the end of gestation with an arrest made in prophase I of the first meiotic division (as in males) until puberty. The ovaries of a newborn girl will have reduced the total number of oogonia to about 2 million, each within an ovarian follicle. At the time of puberty, the number of oocytes within follicles has been reduced to 400,000. During her lifetime, a female will ovulate about 400 of these oocytes and the rest will die by apoptosis. After puberty, FSH hormone released from the anterior pituitary during normal menstrual cycles will select one graafian follicle for ovulation; and the other secondary follicles during that cycle will regress and become atretic, or "without opening." Follicle atresia, or degeneration, is a type of apoptosis that results from a complex interplay of hormones and paracrine regulators. The gonadotropins (FSH and LH), as well as various paracrine regulators, and estrogen act to protect follicles from atresia. By contrast, paracrine regulators that include androgens and FAS ligand promote atresia of the follicles.

4. Not true. There are many examples of hormonal crossover between males and females. In females, the granulosa cells of the ovarian follicle produce estrogen from its precursor molecule, testosterone. Androgens in the ovary are involved in the atresia of follicles. In the pregnant female, the placenta depends upon the fetus to deliver androgen hormones for conversion into estrogens that support and maintain the pregnancy. In this way, the fetal adrenal gland secretes the androgen dehydroepiandrosterone sulfate (DHEAS) that travels to the placenta for the conversion to estrogens. Within the male brain, testosterone may be converted to estradiol-17β by an aromatization reaction; and is required for the negative feedback effects of testosterone on LH secretion. Furthermore, there is evidence that receptors for estradiol are found in Sertoli and Leydig cells of the male testes, as well as cells lining the male reproductive tract (efferent ductules and epididymis) and accessory sex organs (prostate and seminal vesicles). Estrogen receptors have also been located in the developing sperm cells (spermatocytes and spermatids), suggesting a role for estrogens in spermatogenesis. Indeed, knockout mice missing an estrogen receptor gene are infertile. Also, males genetically deficient in aromatase enzymes that convert androgens to estrogens are infertile. Estrogen may be responsible for sealing of the epiphyseal plates of cartilage, thereby "sealing" the discs and stopping bone growth in length.

5. Ovariectomy precipitates menstruation in humans because the endometrium lining of the uterus is no longer nourished and supported by the trophic action of estrogen and progesterone hormones that were secreted by the intact ovaries. On day 1 of the normal human menstrual cycle, the sudden loss of these hormones causes the interruption in blood flow to the endometrium that results in the loss of blood with the loss of tissue, known as menstrual flow. Dogs and cats, however, are nonprimate and are sexually receptive only at a particular time in their cycle of estrus or "heat." Bleeding occurs in dogs and cats during estrous cycles shortly before they permit coitus as a result of high blood estrogen levels. Therefore, ovariectomy in dogs or cats is not associated with shedding of the endometrium and would not cause the discharge of uterine blood in these animals following surgery.