The Reproductive System and Development

This section considers applied topics related to the continuation of the species and the life histories of individuals. In the process we will consider aspects of the male and female reproductive systems, pregnancy, development, aging, and death.

THE PHYSICAL EXAMINATION AND THE REPRODUCTIVE SYSTEM

The male reproductive system includes the gonads (testes), a series of specialized ducts (the epididymis, ductus deferens, ejaculatory duct, and urethra), accessory glands (the seminal vesicles, prostate, and bulbourethral glands), and the external genitalia (penis and scrotum).

The female reproductive system includes the gonads (ovaries), derivatives of an embryonic system of ducts (the uterine tubes, uterus, and vagina), accessory glands (the greater and lesser vestibular glands), the external genitalia (the clitoris, labia majora and labia minora), and secondary sexual organs, the mammary glands of the breasts.

Assessment of the Male Reproductive System

An assessment of the male reproductive system begins with a physical examination. Common signs and symptoms of male reproductive disorders include:

- **Testicular pain** may result from a variety of infections, including gonorrhea or other sexually transmitted diseases (p. 170), and mumps (EAP p. 492). Testicular pain can also result from testicular torsion, testicular cancer, cryptorchidism (EAP p. 584), or the presence of a hernia (p. 67). The pain may also originate elsewhere along the reproductive tract, such as along the ductus deferens or within the prostate, or in other systems, as in appendicitis (p. 122) or a urinary obstruction.

- **Urethral discharge** and dysuria are often associated with sexually transmitted diseases. These symptoms also accompany disorders, such as epididymitis or prostatitis, that may be infectious or noninfectious.

- **Impotence** is an inability to achieve or maintain an erection. It may occur as the result of psychological factors, such as fear or anxiety, medications, or alcohol abuse. It may also develop secondary to cardiovascular or nervous system problems that affect blood pressure or blood flow to the penile arteries.

- **Male infertility** may be caused by a low sperm count, abnormally shaped sperm, or abnormal semen composition. Analysis of the semen can often yield important diagnostic information.

Inspection of the male reproductive system usually involves the examination of the external genitalia and palpation of the prostate gland. Inspection of the external genitalia entails the following observational steps:

1. Inspection of the penis and scrotum for skin lesions such as vesicles, chancres, warts, and condylomas (wartlike growths). For example, painful vesicles often appear in clusters following infection with the herpes simplex (type 2) virus. A chancre is a painless ulceration often associated with early-stage syphilis (p. 170). These skin lesions usually indicate the presence of sexually transmitted diseases (p. 170). In the course of the examination of uncircumcised males, the foreskin is retracted to observe the preputial lining. **Phimosis**, an inability to retract the foreskin in an uncircumcised male, usually indicates inflammation of the prepuce and adjacent tissues.

2. Palpation of each testis, epididymis, and ductus deferens to detect the presence of abnormal masses, swelling, or tumors. Possible abnormal findings include:

   - **Scrotal swelling** due to distortion of the scrotal cavity by blood (a hematocele), lymph (a chylocele), or serous fluid (a hydrocele).

   - **Testicular swelling** due to enlargement of the testis or formation of a nodular mass. **Orchitis** is a general term for inflammation of the testis. This can be the result of an infection, such as syphilis (p. 170), mumps, or tuberculosis (p. 137). Testicular swelling may also accompany testicular cancer.

   - **Epididymal swelling** due to cyst formation (spermatocele), tumor formation, or infection. **Epididymitis** is an acute inflammation of the epididymis that may indicate an infection of the reproductive or urinary tracts. This condition may also develop due to irritation caused by the backflow, or reflux, of urine into the ductus deferens.

   - **Swelling of the spermatic cord** may indicate (1) inflammation of the ductus deferens (deferentitis), (2) serous fluid accumulation in a pocket of the peritoneal cavity (a hydrocele), (3) bleeding within the spermatic cord, (4) testicular torsion, or (5) the formation of varicose veins (p. 112) within the testicular venous network—a condition known as a varicocele.

3. A **digital rectal examination (DRE)** is usually performed as a screening test for prostatitis or inflammation of the seminal vesicles. In this procedure, a gloved finger is inserted into the rectum and pressed against the anterior rectal
wall to palpate the posterior walls of the prostate gland and seminal vesicles.

If urethral discharge is present or if discharge occurs in the course of any of these procedures, the fluid can be cultured to check for the presence of pathogenic microorganisms.

**Assessment of the Female Reproductive System**

Important signs and symptoms of female reproductive disorders include the following:

- **Acute pelvic pain** is a symptom that may accompany a variety of different disorders. For example, it may be associated with pelvic inflammatory disease (PID), ruptured tubal pregnancy, a ruptured ovarian cyst, or inflammation of the uterine tubes (salpingitis).

- Bleeding between menstrual cycles can result from oral contraceptive use, hormonal fluctuation, pelvic inflammatory disease (EAP p. 594), or endometriosis.

- **Amenorrhea** (EAP p. 595) may occur in women with anorexia nervosa (p. 149), women who overexercise and are underweight, in extremely obese women, and in post-menopausal women.

- **Abnormal vaginal discharge** may be the result of a bacterial infection, such as an STD.

- Although the female reproductive and urinary tracts are distinct, dysuria may accompany an infection of the reproductive system due to migration of the pathogen to the urethral entrance.

- Infertility may be related to hormonal disturbances, a variety of ovarian disorders, or anatomical problems along the reproductive tract.

A physical examination usually includes the following steps:

1. **Inspection of the external genitalia** for skin lesions, trauma, or related abnormalities. Swelling of the labia majora may result from (a) regional lymphedema, (b) a labioinguinal hernia (rare), (c) bleeding within the labia, as the result of local trauma or cellulitis, or (4) Bartholinitis, an abscess within one of the greater vestibular glands (Bartholin’s glands).

2. **Inspection and/or palpation of the perineum**, vaginal opening, labia, clitoris, urethral meatus, and vestibule to detect lesions, abnormal masses, or discharge from the vagina or urethra. Samples of any discharge present can be cultured to detect and identify any pathogens involved.

3. **Inspection of the vagina and cervix** can be performed with a speculum, an instrument that retracts the vaginal walls to permit direct visual inspection. Changes in the color of the vaginal wall may be important diagnostic clues. For example:

   - **Cyanosis of the vaginal mucosa** normally occurs during pregnancy (see below), but it may also occur when a pelvic tumor exists or in persons with congestive heart failure.

   - **Reddening of the vaginal walls occurs in vaginitis**, bacterial infections, such as gonorrhea, protozoan infection by *Trichomonas vaginalis*, and yeast infections. It can also appear postmenopausically in some women (a condition known as *atrophic vaginitis*).

   The cervix is inspected to detect lacerations, ulceration, polyps, or cervical discharge. A spatula or brush is then used to collect cells from the cervical os and transfer them to a glass slide. After fixation by a chemical spray, cytological examination is performed. This is the best-known example of a *Papanicolaou (Pap) test* (see Cytology tests in Table A-4, p. 15), and the process is commonly called a Pap smear. A Pap smear is a screening test for the presence of cervical cancer.

4. **A bimanual examination** is a method for the palpation of the uterus, uterine tubes, and ovaries. The physician inserts two fingers vaginally and places the other hand against the lower abdomen to palpate the uterus and surrounding structures. The contour, shape, size, and location of the uterus can be determined, and any swellings or masses will be apparent. Abnormalities in other reproductive organs, such as ovarian cysts, endometrial growths, or tubal masses, can also be detected in this way.

**Normal and Abnormal Signs Associated with Pregnancy**

Pregnancy imposes a number of stresses on the maternal body systems. The major physiological changes are discussed in Chapter 20 (EAP p. 626). Several clinical signs may be apparent in the course of a physical examination:

- **Chadwick’s sign** is a normal cyanosis of the vaginal wall and cervix during pregnancy.

- The size of the uterus changes drastically during pregnancy; at full-term the uterus extends almost to the level of the xiphoid process.

- Significant uterine bleeding, causing vaginal discharge of blood, most often occurs in placenta previa (p. 174), in which the placenta forms near the cervix. Subsequent cervical stretching leads to tearing and bleeding of the vascular channels of the placenta. Vaginal bleeding may also occur prior to miscarriage.

- Nausea and vomiting often occur in pregnancy, especially during the first 3 months.

- Edema of the extremities, especially the legs, often occurs due to increased blood volume and weight of the uterus compressing the inferior
vena cava and its tributaries. As venous pressures rise in the lower limbs and inferior trunk, varicose veins and hemorrhoids (p. 112) may develop.

- Back pain due to increased stress on muscles of the lower back is common. These muscles balance the weight of the uterus over the lower limbs by accentuating the lumbar curvature.
- A weight gain of 10-12.5 kg (22–27.5 lb) is now considered desirable, although 20 years ago weight increases of 20-25 kg (44–55 lb) were considered acceptable. Failure to gain adequate weight during a pregnancy can indicate serious problems.
- In some cases, a dangerous combination of hypertension, proteinuria, edema, and seizures may occur. This condition, called preeclampsia, is considered in a later section (p. 175).

**DISORDERS OF THE REPRODUCTIVE SYSTEM**

Representative disorders of the reproductive system are diagrammed in Figure A-56.

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**Prostatitis, Prostatic Hypertrophy, and Prostate Cancer**

Prostatic inflammation, or prostatitis (pros-ta-Ti-tis), can occur at any age, but it most often afflicts older men. Prostatitis may result from bacterial infections, but the condition may also develop in the apparent absence of pathogens. Individuals with prostatitis complain of pain in the lower back, perineum, or rectum, sometimes accompanied by painful urination and the discharge of mucous secretions from the urethral meatus. Antibiotic therapy is usually effective in treating cases resulting from bacterial infection, but in other cases antibiotics may not provide relief. Prostatitis is taken seriously because the symptoms can resemble those of prostate cancer.

Prostatic enlargement, or benign prostatic hypertrophy (BPH), usually occurs spontaneously in men over age 50. The increase in size occurs at the same time that hormonal changes are under way within the testes. Androgen production by the interstitial cells decreases over this period, and at the same time these endocrine cells begin releasing small quantities of estrogens into the circulation. The combination of lower testosterone levels and...
the presence of estrogen probably stimulates prostatic growth. In severe cases, prostatic swelling can constrict and block the urethra and even the rectum. The urinary obstruction can cause permanent kidney damage if not corrected. Partial surgical removal is the most effective treatment at present. In the procedure known as a TURP (transurethral prostatectomy), an instrument pushed along the urethra restores normal function by cutting away the swollen prostatic tissue. Most of the prostate remains in place, and there are no external scars.

**Prostate cancer** is the most common cancer in men, and it is the second most common cause of cancer deaths in males. In 2001 approximately 198,100 new cases of prostate cancer were diagnosed in the United States, and there were approximately 31,500 deaths. Most patients are elderly (average age 72 at diagnosis). There are racial differences in susceptibility that are poorly understood. At age 50–54 the prostate cancer rates are twice as high for African Americans as for Caucasian Americans. (The rates at all ages are about one-third higher for African Americans.) The prostate cancer rates for Asian males are relatively low compared with either Caucasian Americans or African Americans. For all age groups and all races, the rates of prostate cancer increased between 1988 and 1992, dropped between 1992 and 1995, and leveled off after 1996, probably related to improved detection and earlier diagnosis.

Prostate cancer usually originates in one of the secretory glands, and as it progresses, it produces a nodular lump or swelling on the prostatic surface. Palpation of the prostate gland through the rectal wall, a procedure known as a digital rectal exam, or DRE, is the easiest diagnostic screening procedure. Transrectal prostatic ultrasound (TRUS) can be used to obtain more detailed information about the status of the prostate, but at significantly higher cost to the patient.

If the condition is detected before the cancer cells have spread to other organs, the usual treatment is either localized radiation or the surgical removal of the prostate gland. This operation, called a prostatectomy (pros-ta-TEK-to-mē), is often effective in controlling the condition, but undesirable side effects may include a loss of sexual function and urinary incontinence. Modified surgical procedures can reduce these risks and maintain normal sexual function in perhaps 3 out of 4 patients.

One common screening method involves a blood test for prostate-specific antigen (PSA). Elevated levels of this antigen, normally present in low concentrations, may indicate the presence of prostate cancer. This test is more sensitive than the serum enzyme assay previously used for screening purposes. That enzyme test, which checks levels of the isozyme prostatic acid phosphatase, detects prostate cancer in comparatively late stages of development. Screening with periodic PSA tests is now being recommended for men over age 50.

Early detection is important because metastasis from the prostate soon involves the lymphatic system, lungs, bone marrow, liver, or adrenal glands. The survival rates at this stage become relatively low. Potential treatments for metastatic prostate cancer include more intensive radiation dosage, hormonal manipulation, lymph node removal, and aggressive chemotherapy. Because the cancer cells are stimulated by testosterone, treatment may involve castration or hormones that depress GnRH or LH production. Until recently the usual hormone selected was diethylstilbestrol (DES), an estrogen. There are now two other options: (1) Drugs that mimic GnRH: These drugs are given in high doses, producing a surge in LH production followed by a sharp decline to very low levels, presumably as the endocrine cells adapt to the excessive stimulation. (2) Drugs that block the action of androgens: Several new drugs, including flutamide and finasteride, prevent stimulation of the cancer cells by testosterone. Despite these interesting advances in treatment, however, the average survival time for patients diagnosed with advanced prostatic cancer is only 2.5 years.

**Ovarian Cancer**

A woman in the United States has a lifetime risk of 1 chance in 70 of developing ovarian cancer. In 2001 there were an estimated 23,400 ovarian cancers diagnosed, and an estimated 13,400 deaths from this condition. Although ovarian cancer is the third most common reproductive cancer among women, it is the most dangerous because ovarian cancer is seldom diagnosed in its early stages. The prognosis is relatively good for cancers that originate in the general ovarian tissues or from abnormal oocytes. These cancers respond well to some combination of chemotherapy, radiation, and surgery. However, most ovarian cancers (85 percent) develop from epithelial cells, and sustained remission can be obtained in only about one-third of these patients. Early diagnosis would greatly improve the chances for successful treatment, but as yet there is no standardized screening procedure. (Transvaginal sonography can detect ovarian cancer at Stage I or Stage II, but there is a high incidence of false positive results.)

The minimal treatment of Stage I or Stage II involves unilateral removal of an ovary and uterine tube (a salpingo-oophorectomy), or, in some cases, bilateral salpingo-oophorectomy (BSO) and total hysterectomy (removal of the uterus). Treatment of more dangerous forms of early stage ovarian cancer includes radiation and chemotherapy in addition to surgery.

Treatment of Stage III or Stage IV ovarian cancer often involves removal of the omentum, in addition to a BSO and total hysterectomy and aggressive chemotherapy. Bone marrow transplantation may
be required, due to destruction of stem cells in the bone marrow by these chemicals. Some chemotherapy agents may be introduced into the peritoneal cavity, because higher concentrations can be administered without the systemic effects that would accompany infusion of the drugs into the bloodstream. This procedure is called intraperitoneal therapy.

**Uterine Tumors and Cancers**

EAP p. 594

Uterine tumors are the most common tumors in women. It has been estimated that 40 percent of women over age 50 have benign uterine tumors involving smooth muscle and connective tissue cells. If small, these leiomyomas (le-ô-mi-ô-maz), or fibroids, generally cause no problems. If stimulated by estrogens, they can grow quite large, reaching weights as great as 13.6 kg (30 lb). Occlusion of the uterine tubes, distortion of adjacent organs, and compression of blood vessels may then lead to a variety of complications. In symptomatic young women, observation or conservative treatment with drugs or restricted surgery may be utilized to preserve fertility. In older women, a decision may be made to remove the uterus, a procedure called a hysterectomy (his-ter-EK-to-mé).

Benign epithelial tumors in the uterus are called endometrial polyps. Roughly 10 percent of women probably have polyps, but because the polyps tend to be small and cause no symptoms, the condition passes unnoticed. If bleeding occurs, if the polyps become excessively enlarged, or if they protrude through the cervical os, they can be surgically removed.

Uterine cancers are less common, affecting approximately 11.9 per 100,000 women. In 2001, roughly 51,200 new cases were reported in the United States, and approximately 11,000 women died from the disease. There are two types of uterine cancers, (1) endometrial and (2) cervical.

**Endometrial cancer** is an invasive cancer of the endometrial lining. About 38,300 cases are reported each year in the United States, with approximately 6600 deaths. The condition most commonly affects women age 50–70. Estrogen therapy, used to treat osteoporosis in postmenopausal women, increases the risk of endometrial cancer by 2–10 times. Adding progesterone therapy to the estrogen treatment seems to reduce this risk.

Cervical cancer is the most common reproductive system cancer in women age 15–34. Roughly 12,900 new cases of invasive cervical cancer are diagnosed each year in the United States, and approximately 33 percent of them will eventually die of this condition. Another 33,500 patients are diagnosed with less-aggressive forms of cervical cancer.

Most women with cervical cancer fail to develop symptoms until late in the disease. At that stage, vaginal bleeding, especially after intercourse, pelvic pain, and vaginal discharge may appear. Early detection is the key to reducing the mortality rate for cervical cancer. The standard screening test is the Pap smear, named for Dr. George Papanicolaou, an anatomist and cytologist. The cervical epithelium normally sheds its superficial cells, and a sample of cells scraped or brushed from the epithelial surface can be examined for abnormal or cancerous cells. The American Cancer Society recommends yearly Pap tests at ages 20 and 21, followed by smears at 1-year to 3-year intervals until age 65.

The primary risk factor of cervical cancer is a history of multiple sexual partners. It appears likely that these cancers develop after viral infection by one of several different human papilloma viruses (HPV) that can be transmitted through sexual contact.

Early treatment of abnormal but not cancerous lesions detected by mildly abnormal Pap smears may prevent progression to cancer formation. The treatment of localized, noninvasive cervical cancer involves the removal of the affected portion of the cervix. Treatment of more-advanced cancers typically involves a combination of radiation therapy, hysterectomy, lymph node removal, and chemotherapy.

**Endometriosis**

EAP p. 594

In endometriosis (en-dô-mé-trê-Ô-sis), an area of endometrial tissue begins to grow outside the uterus. The severity of the condition depends on the size of the abnormal mass and its location. Abdominal pain, bleeding, pressure on adjacent structures, and infertility are common symptoms. As the island of endometrial tissue enlarges, the symptoms become more severe.

Diagnosis can usually be made by using a laparoscope inserted through a small opening in the abdominal wall. Using this device, a physician can inspect the outer surfaces of the uterus and uterine tubes, the ovaries, and the lining of the pelvic cavity. Treatment of endometriosis may involve hormonal therapy or surgical removal of the endometrial mass. If the condition is widespread, a hysterectomy or oophorectomy (removal of the ovaries) may be required.

**Vaginitis**

EAP p. 595

There are several different forms of vaginitis, and minor cases are relatively common. Candidiasis (kan-di-DI-a-sis) results from a fungal (yeast) infec-
Early detection of breast cancer is the key to reducing mortalities. Most breast cancers are found through self-examination, but the use of clinical screening techniques has increased in recent years. Mammography involves the use of X-rays to examine breast tissues; the radiation dosage can be restricted because only soft tissues must be penetrated. This procedure gives the clearest picture of conditions within the breast tissues, especially after menopause. Ultrasound can provide some information, but the images lack the detail of standard mammograms. Thermography maps the surface temperatures on the skin of the breasts. Because cancer cells have abnormally high metabolic rates and increased vascularization, tumors are significantly warmer than the surrounding tissues. The heat can be detected with this technique, but unfortunately, the results are subject to considerable variation.

For treatment to be successful the cancer must be identified while it is still relatively small and localized. Once it has grown larger than 2 cm (0.78 in.), the chances for long-term survival worsen. A poor prognosis also follows if the cancer cells have spread through the lymphatic system to the axillary lymph nodes. If the nodes are not yet involved, the chances of 5-year survival are about 82 percent, but if four or more nodes are involved, the survival rate drops to 21 percent.

Treatment of breast cancer begins with the removal of the tumor. Because the cancer cells usually begin spreading before the condition is diagnosed, surgical treatment involves the removal of part or all of the affected breast:

- In a segmental mastectomy, or “lumpectomy,” only a portion of the breast is removed.
- In a total mastectomy the entire breast is removed, but other tissues are left intact.
- In a modified radical mastectomy, the most common operation, the breast and axillary lymph nodes are removed but the muscular tissue remains intact.

A combination of chemotherapy, radiation treatments, and hormone treatments may be used to supplement the surgical procedures. Tamoxifen is an estrogen blocking drug that may be used to treat breast cancer. It is more effective than conventional chemotherapy for treating breast cancer in women over 50, and it has fewer unpleasant side effects. It can also be used in addition to regular chemotherapy when treating advanced-stage disease. As an added bonus, tamoxifen prevents and even reverses the osteoporosis of aging. There are down sides, however. When given to premenopausal women, tamoxifen can cause amenorrhea and hot flashes similar to those of menopause. Tamoxifen has also been linked to an increased risk of endometrial cancer and perhaps liver cancer as well. For high-risk women, this drug may be used to prevent breast cancer, rather than treat it.
New treatment options are also under development. For example, a tumor-suppressor gene that inhibits breast cancer development has been isolated from normal breast tissue. The protein has been identified, and researchers are now experimenting to see if the activity of the gene can be stimulated to fight existing breast cancers.

**Sexually Transmitted Diseases**

Sexually transmitted diseases, or STDs, are transferred from individual to individual, usually or exclusively by sexual intercourse. A variety of bacterial, viral, and fungal infections are included in this category. At least two dozen different STDs are currently recognized, and roughly 15 million people become infected each year in the United States. All STDs are unpleasant, and some are deadly. Here we will discuss four of the most common sexually transmitted diseases: gonorrhea, syphilis, herpes, and chancroid.

**GONORRHEA.** The bacterium *Neisseria gonorrhoeae* is responsible for gonorrhea, one of the most common sexually transmitted diseases in the United States. Nearly 2 million cases were reported in the early 1970s; roughly 400,000 cases were expected to be reported in 2000. These bacteria usually invade epithelial cells lining the male or female reproductive tracts. In relatively rare cases they will also colonize the pharyngeal or rectal epithelium.

The symptoms of genital infection vary, depending on the sex of the individual concerned. It has been estimated that up to 80 percent of women infected with gonorrhea experience no symptoms, or symptoms so minor that medical treatment is thought to be unnecessary. As a result these individuals act as carriers, spreading the infection through their sexual contacts. An estimated 10–15 percent of women infected with gonorrhea experience more acute symptoms because the bacteria invade the epithelia of the uterine tubes. This probably accounts for many of the cases of pelvic inflammatory disease (PID) in the U.S. population; as many as 80,000 women may become infertile each year as the result of scar tissue formation along the uterine tubes after gonorrhea infections.

Seventy to eighty percent of infected males develop symptoms painful enough to make them seek antibiotic treatment. The asymptomatic 20–30 percent are male carriers who unknowingly spread the disease. The urethral invasion is accompanied by pain on urination (*dysuria*) and often a viscous urethral discharge. A sample of the discharge can be cultured to permit positive identification of the organism involved.

**SYPHILIS.** Syphilis (SIF-i-lis) results from infection by the bacterium *Treponema pallidum*. The first reported syphilis epidemics occurred in Europe during the sixteenth century, possibly introduced by early explorers returning from the New World. The death rate from the “Great Pox” was appalling, far greater than today, even after taking into account the absence of antibiotic therapies at that time. It appears likely that the syphilis organism has mutated since those times. These changes have reduced the mortality rate but prolonged the period of illness and increased the likelihood of successful transmission. Despite these relative improvements, syphilis still remains a life-threatening disease. Untreated syphilis can cause serious cardiovascular and neurologic illness years after infection, or it can be spread to the fetus during pregnancy producing congenital malformations. The annual reported incidence of this disease has declined from 20.3 cases to 2.5 cases per 100,000 population. An equivalent or greater number probably went unrecognized or unreported.

Primary syphilis begins as the bacteria cross the mucous epithelium and enter the lymphatic vessels and bloodstream. At the invasion site the bacteria multiply, and after an incubation period ranging from 1.5–6 weeks their activities produce a painless raised lesion, or chancre (SHANG-ker) (Figure A-57). This lesion remains for several weeks before fading away, even without treatment. In heterosexual men the chancre usually appears on the penis; in women it may develop on the labia, vagina, or cervix. Lymph nodes in the region usually enlarge and remain swollen even after the chancre has disappeared.

Symptoms of secondary syphilis appear roughly 6 weeks later. Secondary syphilis is also infectious. Secondary syphilis usually involves a diffuse, reddish skin rash. Like the chancre, the rash fades over a period of 2–6 weeks. These symptoms may be accompanied by fever, headaches, and uneasiness. The combination is so vague that the disease may easily be overlooked or diagnosed as something else entirely. In a few instances more serious complications such as meningitis (p. 74), hepatitis (p. 144), or arthritis (p. 59) may develop.

The individual then enters the latent phase which is noninfectious. The duration of the latent phase varies widely. Fifty to 70 percent of untreated individuals with latent syphilis fail to develop the symptoms of tertiary syphilis, or late syphilis, although the bacterial pathogens remain within
their tissues. Those destined to develop tertiary syphilis may do so 10 or more years after infection.

The most severe symptoms of tertiary syphilis involve the CNS and the cardiovascular system. **Neurosyphilis** may result from bacterial infection of the meninges or the tissues of the brain and/or spinal cord. **Tabes dorsalis** (TA-bez dor-SAL-is) results from the invasion and demyelination of the posterior columns of the spinal cord and the sensory ganglia and nerves. In the cardiovascular system the disease affects the major vessels, leading to aortic stenosis (p. 105), aneurysms (p. 109), or focal calcification (p. 110).

Equally disturbing are the effects of transmission from mother to fetus across the placenta. These cases of congenital syphilis are marked by infections of the developing bones and cartilages of the skeleton and progressive damage to the spleen, liver, bone marrow, and kidneys. The risk of transmission may be as high as 95 percent, so maternal blood testing is recommended early in pregnancy. The treatment of syphilis involves the administration of penicillin or other antibiotics.

**HERPES.** Genital herpes results from infection by herpes viruses. Two different viruses are involved. Eighty to 90 percent of genital herpes cases are caused by the virus known as HSV-2 (herpes simplex virus Type 2), which is usually associated with the external genitalia. The remaining cases are caused by HSV-1, the virus that is also responsible for cold sores on the mouth. Typically within a week of the initial infection the individual develops a number of painful, ulcerated lesions on the external genitalia. In women, ulcers may also appear on the cervix. These ulcerations gradually heal over the next 2–3 weeks. Recurring lesions are common, although subsequent incidents are less severe.

Infection of the newborn infant during delivery with herpes viruses present in the vagina can lead to serious illness, because the infant has few immunological defenses. Recent development of the antiviral agent acyclovir has helped in treating initial infections and in reducing recurrences.

**CHANCROID.** Chancroid is an STD caused by the bacterium *Haemophilus ducreyi*. Chancroid cases were rarely seen inside the United States before 1984, but since then the number of cases has risen dramatically, reaching 4000–5000 cases per year in 1987. Only 143 cases were reported in 1999, but chancroid is difficult to detect and may be underdiagnosed. The primary sign of this disease is the development of soft chancre, soft lesions otherwise resembling those of syphilis. The majority of chancroid patients also develop prominent inguinal lymphadenopathy.

### Experimental Contraceptive Methods

A number of experimental contraceptive methods are being investigated. For example, researchers are attempting to determine whether low doses of inhibin will suppress GnRH release and prevent ovulation. Another approach is to develop a method of blocking human chorionic gonadotropin (hCG) receptors at the corpus luteum. HCG, produced by the placenta, maintains the corpus luteum for the first three months of pregnancy. If the corpus luteum were unable to respond to hCG, normal menses would occur despite implantation of a blastocyst.

Male contraceptives are also being developed:

- **Gossypol**, a yellow pigment extracted from cottonseed oil, produces a dramatic decline in sperm count and sperm motility after 2 months. Fertility returns within a year after treatment is discontinued, but permanent sterility (around 10 percent) occurs, making it unacceptable to the World Health Organization.
- Weekly doses of testosterone suppress GnRH secretion over a period of 5 months. The result is a drastic reduction in the sperm count. The combination of a testosterone implant, comparable to that used in the Norplant® system, with a GnRH antagonist, cetorelix, effectively suppresses spermatogenesis. A new synthetic form of testosterone, alpha-methyl-noretestosterone (MENT), appears even more effective than testosterone in suppressing GnRH production.

If contraceptive methods fail, options exist to either prevent implantation or terminate the pregnancy. The “emergency contraceptive” or “morning-after pills” contain estrogens and/or progestins. They may be taken within 72 hours of intercourse, and they appear to act by altering the transport of the zygote or preventing its attachment to the uterine wall. The drug known as RU-486 (Mifepristone) blocks the action of progesterone at the endometrial lining. The result is a normal menses and the degeneration of the endometrium regardless of whether or not a pregnancy has occurred.

### Technology and the Treatment of Infertility

An infertile, or sterile, woman is unable to produce functional eggs or support a developing embryo. An infertile man is incapable of providing a sufficient number of motile sperm for successful fertilization. Because sterility of either sexual partner will have the same result, diagnosis and treatment of infertility must involve evaluation of both sexual partners. Approximately 60 percent of infertility cases can be attributed to problems with the female reproductive system.

Recent advances in our understanding of reproductive physiology are providing new solutions to fertility problems. These approaches, called assisted reproductive technologies (ART), are diagrammed in Figure A-58:

- **Low sperm count.** In cases of male infertility due to low sperm counts, semen from several ejaculates can be pooled, concentrated, and introduced into the female reproductive tract.
This technique, known as artificial insemination, may lead to normal fertilization and pregnancy. In special cases, where an individual’s spermatozoa are unable to accomplish oocyte penetration, single-sperm fertilization has been accomplished with micromanipulation of the oocyte and corona radiata.

- **Abnormal spermatozoa.** If the man cannot produce functional sperm, sperm can be obtained from a “sperm bank” that stores donor sperm.

- **Hormonal problems.** If the problem involves the woman’s inability to ovulate due to low gonadotropin or estrogen levels, or to maintain adequate progesterone levels after ovulation, these hormones can be provided.

  **Fertility drugs**, such as clomiphene (Clomid®), stimulate ovarian egg production. Clomiphene works by blocking the feedback inhibition of estrogen on the hypothalamus and pituitary gland. As a result, circulating FSH levels rise, and more follicles are stimulated to complete their development. The chance of a single egg being fertilized through normal sexual intercourse is around 1 in 3. Increasing the number of eggs released increases the odds of a pregnancy. Unfortunately, it is not easy to determine just how much ovarian stimulation will be needed, so multiple births have often resulted from treatment with fertility drugs.

- **Problems with oocyte transport.** When there are problems with the transport of the egg from the ovary to the uterine tube, due to scarring of the fimbriae or other problems, a procedure called GIFT can be used. GIFT is short for *gamete intrafallopian tube transfer*. (*Fallopian tube* is another name for the uterine tube or oviduct.) In this procedure, the ovaries are stimulated with injected hormones, and a large “crop” of mature oocytes is removed from tertiary follicles. Then the individual eggs are examined for defects, inserted into the uterine tubes, and exposed to high concentrations of sperm from the husband or donor. The success rate for this procedure is less than that of nat-
atural fertilization (33 percent), and not every pregnancy produces an infant. The cost of a single procedure (successful or not) averages $5000.

- **Blocked uterine tubes.** In the GIFT procedure, fertilization occurs in its normal location, within the uterine tube. This site is not essential, and fertilization can also take place in a test tube or petri dish. This process is called *in vitro fertilization* (*vitro*, glass). If a carefully controlled fluid environment is provided, early development will proceed normally. One variation on the GIFT procedure, called ZIFT (*zygote intrafallopian tube transfer*), exposes selected eggs to sperm outside the body and inserts zygotes or early cleavage-stage embryos, rather than oocytes, into the uterine tubes. If multiple zygotes are available, some can be frozen and stored for later insertion in case the initial procedure fails to produce a successful pregnancy. The cost for a single ZIFT procedure ranges between $8000 and $10,000.

Alternatively, the zygote can be maintained in an artificial environment through the first 2 to 3 days of development. This procedure is often selected if the uterine tubes are damaged or blocked. The cleavage-stage embryo is then placed directly into the uterus rather than into one of the uterine tubes. The cost of this procedure is comparable to that of ZIFT.

**Abnormal oocytes.** If the oocytes released by the ovaries are abnormal in some way, or if menopause has already occurred, viable oocytes can be obtained from a suitable donor. The donor may be anonymous or known; if anonymous, the donor usually receives a fee for the donation. After treatment with fertility drugs, the donor’s ovaries are stimulated to produce a large crop of oocytes. These are collected and fertilized in vitro, usually by the man’s sperm. After cleavage has begun, the pre-embryo is placed in the recipient’s uterus, which has been “primed” by progesterone therapy. The pregnancy rate for this procedure is roughly 33 percent for women over age 40, using oocytes donated by women in their early twenties. Oocyte donation has a much higher success rate for these women than ZIFT or GIFT, with either of which the odds of a successful pregnancy are only about 4 percent. This difference suggests that age-related changes in the characteristics and quality of the oocytes, rather than changes in hormone levels or uterine responsiveness, are often the primary cause of infertility in older women.

**Abnormal uterine environment.** If fertilization and transport occur normally but the uterus cannot maintain a pregnancy, the problem may involve low levels of progestin secretion by the corpus luteum. Hormone therapy may solve this problem. If the maternal uterus simply cannot support development, the zygote or cleavage-stage embryo can be introduced into the uterus of a substitute mother, or *surrogate mother*. If the embryo survives and makes contact with the endometrium, development will proceed normally even though the mother has no genetic relationship with the embryo.

Surrogate motherhood, which sounds relatively simple and straightforward, has proven to be one of the most explosive solutions in terms of ethics and legality. Since 1990, several court cases have resulted from disputes over surrogate motherhood and who merits legal custody of the infant. Legal battles have also broken out over a variety of complex questions, and some of them will take years to sort out. To understand the problem, consider the following questions:

- Do parents share property rights over frozen and stored zygotes? Can a husband have any of the stored zygotes implanted into the uterus of his second wife without the consent of his first wife, who provided the eggs?
- If both donor egg and donor sperm are used, do adoption laws apply?
- If the father provided the sperm that fertilized the egg of a donor who is not his wife, for implantation into a surrogate mother, can the wife, the surrogate mother, or the egg donor sue for custody of the child after a divorce?
- If you use your imagination, you can probably think of even more complex problems, many of which will probably be debated in a courtroom within the next decade.

**DISORDERS OF DEVELOPMENT**

Development is a complex process, and developmental disorders are extremely diverse. Figure A-59 surveys representative disorders of development.

**Ectopic Pregnancies**

Implantation usually occurs at the endometrial surface lining the uterine cavity. The precise location within the uterus varies, although most often implantation occurs in the body of the uterus. This is not an ironclad rule, and in an ectopic pregnancy implantation occurs somewhere other than within the uterus.

The incidence of ectopic pregnancies is approximately 0.6 percent. Women douching regularly have a 4.4 times higher risk of experiencing an ectopic pregnancy, presumably because the flushing action pushes the zygote away from the uterus. If the uterine tube has been scarred by a previous episode of pelvic inflammatory disease, there is also an increased risk of an ectopic pregnancy. Although implantation may occur within the peritoneal cavity, in the ovarian wall, or in the cervix, 95 percent of ectopic pregnancies involve implantation within a uterine tube. The tube cannot expand enough to accommodate the developing embryo, and it usually ruptures during the first trimester.
At this time the hemorrhaging that occurs in the peritoneal cavity may be severe enough to pose a threat to the woman’s life.

In a few instances, the ruptured uterine tube releases the embryo with an intact umbilical cord, and further development can occur. About 5 percent of these abdominal pregnancies actually complete full-term development; normal birth cannot occur, but the infant can be surgically removed from the abdominopelvic cavity. Because abdominal pregnancies are possible, it has been suggested that men as well as women could act as surrogate mothers if a zygote were surgically implanted in the peritoneal wall. It is not clear how the endocrine, cardiovascular, nervous, and other systems of a man would respond to the stresses of pregnancy. However, the procedure has been tried successfully in mice, and experiments continue.

Problems with Placentation

In a placenta previa (PRē-vē-uh: “in the way”), implantation occurs in or near the cervix. This condition causes problems as the growing placenta approaches the internal cervical orifice. In a total placenta previa the placenta actually extends across the internal orifice, while a partial placenta previa only partially blocks the os. The placenta is characterized by a rich fetal blood supply, and the erosion of maternal blood vessels within the endometrium. Where the placenta passes across the internal orifice the delicate complex hangs like an unsupported water balloon. As the pregnancy advances, even minor mechanical stresses can be enough to tear the placental tissues, leading to massive fetal and maternal hemorrhaging.

Most cases are not diagnosed until the seventh month of pregnancy, as the placenta reaches its full size. At this time the dilation of the cervical canal and the weight of the uterine contents are pushing against the placenta where it bridges the internal orifice. Minor, painless hemorrhaging usually appears as the first sign of the condition. The diagnosis can usually be confirmed by ultrasound scanning. Treatment in cases of total placenta previa usually involves bed rest for the mother until the fetus reaches a size at which cesarean delivery can be performed with a reasonable chance of neonatal (newborn) survival.

In an abruptio placentae (ab-RUP-shē-ō pla-SEN-tē) part or all of the placenta tears away from the uterine wall sometime after the fifth month of gestation. The bleeding into the uterine cavity and the pain that follows usually will be noted and reported, although in some cases the shifting placenta may block the passage of blood through the cervical canal. In severe cases the hemorrhaging leads to maternal anemia, shock, and kidney failure. Although maternal mortality is low, the fetal mortality rate from this condition ranges from 30 to 100 percent, depending on the severity of the hemorrhaging.

Problems with the Maintenance of a Pregnancy

The rate of maternal complications during pregnancy is relatively high. Pregnancy stresses maternal systems, and the stresses can overwhelm homeostatic mechanisms. The term toxemia (tok-SE-mē-uh) of pregnancy refers to disorders affecting the maternal cardiovascular system. Chronic hypertension is the most characteristic symptom, but fluid balance problems and CNS disturbances, leading to coma or convulsions, may also occur. Some degree of toxemia occurs in 6–7 percent of third-trimester pregnancies. Severe cases account for 20 percent of maternal deaths and contribute to an estimated 25,000 neonatal (newborn) deaths.
each year. Prenatal care involves monitoring the mother’s vital signs and urine to detect early signs of toxemia so that treatment can prevent further progression.

Toxemia of pregnancy includes preeclampsia (prē-ē-KLAMP-sē-uh) and eclampsia (ē-KLAMP-sē-uh). Preeclampsia most often occurs during a woman’s first pregnancy. Systolic and diastolic pressures become elevated, reaching levels as high as 180/110. Other symptoms include fluid retention and edema, along with CNS disturbances and alterations in kidney function. Roughly 4 percent of individuals with preeclampsia develop eclampsia.

Eclampsia, or pregnancy-induced hypertension (PIH), is heralded by the onset of severe convulsions lasting 1–2 minutes, followed by a variable period of coma. Other symptoms resemble those of preeclampsia, with additional evidence of liver and kidney damage. The mortality rate from eclampsia is approximately 5 percent; to save the mother the fetus must be delivered immediately. Once the period of coma. Other symptoms resemble those of convulsions lasting 1–2 minutes, followed by a variable period of coma. Other symptoms resemble those of preeclampsia, with additional evidence of liver and kidney damage. The mortality rate from eclampsia is approximately 5 percent; to save the mother the fetus must be delivered immediately. Once the period of coma.

Common Problems with Labor and Delivery EAP p. 628

There are many potential problems during labor and delivery. Two relatively common types of complications are forceps deliveries and breech births.

By the end of gestation, the fetus has usually rotated within the uterus so that it will enter the birth canal head first, with the face turned toward the sacrum. In around 6 percent of deliveries the fetus faces the pubis rather than the sacrum. Although these infants can eventually be delivered normally, risks to infant and mother increase the longer the fetus remains in the birth canal. Often the clinical response is the removal of the infant through a forceps delivery. The forceps used resemble a large, curved set of salad tongs that can be separated for insertion into the vaginal canal one side at a time. Once in place they are reunited and used to grasp the head of the infant. An intermittent pull is applied so that the forces on the head resemble those encountered during normal delivery.

In 3–4 percent of deliveries, the legs or buttocks of the fetus enter the vaginal canal first. Such deliveries are known as breech births. Risks to the infant are relatively higher in breech births because the umbilical cord may become constricted and placental circulation cut off. Because the head is normally the widest part of the fetus, the cervix may dilate enough to pass the legs and body but not the head. Entrapment of the fetal head compresses the umbilical cord, prolongs delivery, and subjects the fetus to severe distress and potential damage. If the fetus cannot be repositioned manually, a cesarian section is usually performed.

Monitoring Postnatal Development EAP p. 630

Each newborn infant is closely scrutinized after delivery. The maturity of the newborn may also be determined prior to delivery by means of ultrasound or amniocentesis. Immediately on delivery, the newborn is inspected and assigned an Apgar rating. This rating evaluates the heart rate, respiratory rate, muscle tone, response to stimulation, and color at 1 and 5 minutes after birth. In each category the infant receives a score ranging from 0 (poor) to 2 (excellent), and the scores are then totaled. An infant’s Apgar rating (0–10) has been shown to be an accurate predictor of newborn survival and of the presence of neurological damage. For example, newborn infants with cerebral palsy (EAP p. 262) usually have a low Apgar rating.

In the course of this examination, the breath sounds, the depth and rate of respirations, and the heart rate are noted. Both the respiratory rate and the heart rate are considerably higher in the infant than the adult (see Table A-3, p. 13). Later, a more complete physical examination of the newborn focuses on the status of vital systems. Inspection of the infant normally includes the following:

- The head of a newborn infant may be misshapen following vaginal delivery, but it generally assumes its normal shape over the next few days. However, the size of the head must be checked to detect hydrocephalus (p. 76).
- The eyes, nose, mouth, and ears are inspected for reflex responses and for obstruction.
- The abdomen is palpated to detect abnormalities of internal organs.
- The heart and lungs are auscultated to check for breath sounds and heart murmurs.
- The external genitalia are inspected. The scrotum of a male infant is checked for the presence of descended testes.
- Cyanosis of the hands and feet is normal in the newborn, but the rest of the body should be pink. A generalized cyanosis may indicate congenital circulatory disorders, such as erythroblastosis fetalis (EAP p. 354), or patent foramen ovale, ductus arteriosus, or tetralogy of Fallot (pp. 117-118; see Figure A-44).

Measurements of body length, head circumference, and body weight are taken. A weight loss in the first 48 hours is normal, due to fluid shifts that occur as the infant adapts to the change from weightlessness (floating in amniotic fluid) to normal gravity. (Comparable fluid shifts occur in astronauts returning to earth after extended periods in space.)

The neuromuscular system is assessed for normal reflexes and muscle tone. Reflexes commonly tested include the following:

- The Moro reflex is triggered when support for the head of a supine infant is suddenly
removed. The reflex response consists of trunk extension and a rapid cycle of extension-abduction and flexion-adduction of the limbs. This reflex normally disappears at an age of about 3 months.

- The stepping reflex consists of walking movements triggered by holding the infant upright, with a forward slant, and placing the soles of the feet against the ground. This reflex normally disappears at an age of around 6 weeks.

- The placing reflex can be triggered by holding the infant upright and drawing the top of one foot across the bottom edge of a table. The reflex response is to flex and then extend the leg on that side. This reflex also disappears at an age of around 6 weeks.

- The sucking reflex is triggered by stroking the lips. The associated rooting reflex is initiated by stroking the cheek, and the response is to turn the mouth toward the site of stimulation. These reflexes persist until age 4–7 months.

- The Babinski reflex is positive, with fanning of the toes in response to stroking of the side of the sole of the foot. This reflex disappears at around age 3, as descending motor pathways become established.

These procedures check for the presence of anatomical and physiological abnormalities. They also provide baseline information useful in assessing postnatal development. In addition, newborn infants are often screened for genetic and/or metabolic disorders, such as phenylketonuria (PKU) (p. 147), congenital hypothyroidism (p. 90), sickle cell anemia (p. 99), and galactosemia. Individuals with galactosemia lack the enzyme that converts galactose sugar in milk into glucose. Chronic high levels of galactose during childhood can cause abnormalities in nervous system development, jaundice, liver enlargement, and cataracts.

The excretory systems of the newborn infant are assessed by examination of the urine and feces. The first urination may have a pink coloration, due to the presence of urates. The first bowel movement consists of a mixture of epithelial cells and mucus. This meconium is greenish-black in color.

Pediatrics is a medical specialty focusing on postnatal development from infancy through adolescence. Because infants and young children cannot clearly describe the problems they are experiencing, pediatricians and parents must be skilled observers. Standardized testing procedures are also used to assess an individual’s developmental progress. In the Denver Developmental Screening Test (DDST), infants and children are checked repeatedly during their first 5 years. The test checks gross motor skills, such as sitting up or rolling over, language skills, fine motor coordination, and social interactions. The results are compared with normal values determined for individuals of similar age. These screening procedures assist in identifying children who may need special teaching and attention.

Too often parents tend to focus on a single ability or physical attribute, such as the age at first step or the rate of growth. This kind of one-track analysis has little practical value, and the parents may become overly concerned with how their infant compares with the norm. Normal values are statistical averages, not absolute realities. For example, most infants begin walking at 11 to 14 months of age. But around 25 percent start before then, and another 10 percent have not started walking by the fourteenth month. Walking early does not indicate true genius, and walking late does not mean that the infant will need physical therapy. The questions on such screening tests are intended to determine if there are patterns of developmental deficits. Such patterns appear only when a broad range of abilities and characteristics is considered.

Death and Dying

Despite exaggerated claims, few cases of individuals who have reached an age of 120 years have been substantiated. Estimates for the lifespan of individuals born in the United States during 1997 are 74 years for males and 80 years for females. Interestingly enough, the causes of death vary with age group. Consider the graphs shown in Figure A-60, indicating the mortality statistics for various age groups. Accidents are the major cause of death in young people, and cardiovascular diseases in those over 40–45. More specific information concerning the major causes of death can be found in Table A-25. Many of the characteristic differences in mortality figures result from changes in the functional capabilities of the individuals linked to development or senescence. These values would differ significantly if tabulated for countries and cultures with different genetic and environmental pressures.

The differences in mortality figures for male and female are related to differences in the accident rates for young people and in the rates of heart disease and cancer for older individuals. For instance, the upswing in female cancer rates reflects a rising breast cancer incidence for those over age 34, whereas lung cancer is the primary cancer killer of older men. Among women, the incidence of lung cancers and related killers, including pulmonary disease, heart disease, and pneumonia, has been steadily increasing as the number of women smokers has increased. This change has narrowed the difference between male and female life expectancies.

Experimental evidence and calculations suggest that the human lifespan has an upper limit of around 150 years. As medical advances continue, research must focus on two related issues: (1) extending the average lifespan toward that maximum and (2) improving the functional capabilities of long-lived individuals. The first objective may be the easiest from a technical standpoint. It
is already possible to reduce the number of deaths attributed to specific causes. For example, new treatments promote remission in a variety of cancer cases, and anticoagulant therapies may reduce the risks of death or permanent damage following a stroke or heart attack. Many defective organs can be replaced with functional transplants, and the use of controlled immunosuppressive drugs increases the success rates for these operations. Artificial hearts have been used with limited success thus far, and artificial kidneys and endocrine pancreases are under development.

The second objective poses more of a problem. Few people past their mid-90s lead active, stimulating lives, and most would find the prospect of living another 50 years rather horrifying unless the quality of their lives could be significantly improved. Our abilities to prolong life now involve making stopgap corrections in systems on the brink of complete failure. Reversing the process of senescence would entail manipulating the biochemical operations and genetic programming of virtually every organ system. Although investigations continue, breakthroughs cannot be expected in the immediate future.

Over the interim, we are left with some serious ethical and moral questions. If we could postpone the moment of death almost indefinitely with some combination of resuscitators and pharmacological support, how do we decide when it is appropriate to do so? How can medical and financial resources be fairly allocated? Who gets the limited number of organs, such as hearts, livers, kidneys, and corneas available for transplant? Who should be selected for experimental therapies of potential significance? Should we take into account that care of an infant or child may add decades to a lifespan, while the costly insertion of an artificial heart in a 60-year-old will add only months to years? How shall we allocate the costs for sophisticated procedures that may run to hundreds of thousands of dollars over the long run? Are these individual or family responsibilities? Will only the rich be able to survive into a second century of life? Should the government provide the funds? If yes, what will happen to tax rates as the baby boomers become elderly citizens? And what about the role of the individual involved? If you decline treatment, are you mentally and legally competent? Can your survivors bring suit if you were forced to survive or if you were allowed to die? These and other difficult questions will not go away. In the years to come we will have to find answers we are content to live and die with.

Table A–25 The Five Major Causes of Death in the U.S. Population

<table>
<thead>
<tr>
<th>Rank</th>
<th>Age 1–14</th>
<th>Age 15–44</th>
<th>Age 45–64</th>
<th>Age 64+</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Congenital anomalies</td>
<td>Accidents</td>
<td>Cancer</td>
<td>Heart disease</td>
</tr>
<tr>
<td>2</td>
<td>Accidents</td>
<td>Cancer</td>
<td>Heart disease</td>
<td>Cancer</td>
</tr>
<tr>
<td>3</td>
<td>Cancer</td>
<td>Heart disease</td>
<td>Accidents</td>
<td>Cerebrovascular disease</td>
</tr>
<tr>
<td>4</td>
<td>Homicide</td>
<td>Suicide</td>
<td>Cerebrovascular disease</td>
<td>COPD*</td>
</tr>
<tr>
<td>5</td>
<td>Pneumonia, influenza</td>
<td>Homicide</td>
<td>Pneumonia, influenza, COPD</td>
<td>Pneumonia, influenza</td>
</tr>
</tbody>
</table>

*COPD = chronic obstructive pulmonary disease
CRITICAL-THINKING QUESTIONS

11-1. Sally is an avid runner, and she trains incessantly. She has slimmed down so much that she is now underweight for her height and has very little fat tissue. Some of her laboratory values are below.

FSH: early cycle, 2 mIU/ml; midcycle, 3 mIU/ml
LH: early cycle, 2 mIU/ml; midcycle, 15 mIU/ml
Estrogen (serum): midcycle, 60 pg/ml

From this information you would expect Sally to
a. have heavy menstrual flows
b. double ovulate
c. be amenorrheic
d. have painful menstrual cramps

11-2. Many male athletes using anabolic steroids have low sperm counts and some feminizing characteristics, such as enlarged breasts. Why do these symptoms occur?

11-3. Diane has peritonitis, which she is told resulted from a urinary tract infection. Why does this occur in females but not males?