

DISORDERS: HOMEOSTATIC IMBALANCES

SEXUALLY TRANSMITTED DISEASES

The general term **sexually transmitted disease (STD)** is applied to any of the large group of diseases that can be spread by sexual contact. The group includes conditions traditionally specified as **venereal diseases (VD)** (from Venus, goddess of love), such as gonorrhea, syphilis, and genital herpes. In most developed countries of the world, such as those of the European Community, Japan, Australia, and New Zealand, the incidence of STDs has declined markedly during the past 20 years. In the U.S. by contrast, STDs have been rising to near epidemic proportions, especially among urban populations. AIDS, which is a sexually transmitted disease that may also be contracted in other ways, is discussed on page 712.

Gonorrhea

Gonorrhea (or "clap") is an infectious sexually transmitted disease that affects primarily the mucous membrane of the urogenital tract, the rectum, and occasionally the eyes. The disease is caused by the bacterium *Neisseria gonorrhoeae*. In the U.S. there are an estimated one to two million new cases of gonorrhea each year. Most cases are in the 15- to 24-year-old age group. Discharges from the involved mucous membranes are the source of infection, and the bacteria are transmitted by direct contact, usually sexual, or during passage of a newborn through the birth canal.

Males usually suffer inflammation of the urethra with pus and painful urination. There also may be involvement of the epididymis and prostate gland. In females, infection may occur in the urethra, vagina, and cervix, often with a discharge of pus. However, infected females may harbor the disease without any symptoms until it has progressed to a more advanced stage. If the uterine (Fallopian) tubes become involved, pelvic inflammation may follow. Peritonitis, or inflammation of the peritoneum, is a life-threatening disorder. The infection should be treated and controlled immediately because, if neglected, sterility or death may result. Although antibiotics have greatly reduced the mortality rate of acute peritonitis, it is estimated that between 50,000 and 80,000 women are made sterile by gonorrhea every year as a result of scar tissue formation that closes the uterine tubes. If the bacteria are transmitted to the eyes of a newborn in the birth canal, blindness can result.

Administration of a 1% silver nitrate solution in the infant's eyes prevents infection. For many years, penicillin and tetracycline were the drugs of choice for the treatment of gonorrhea in adults. Until 1976, all cases of gonorrhea could be effectively treated with penicillin. However, bacterial strains resistant to these antibiotics have become very prevalent since the mid-1980s. Currently, ceftriaxone is the antibiotic that most effectively attacks the majority of gonorrhea bacteria.

Syphilis

Syphilis is a sexually transmitted disease caused by the bacterium *Treponema pallidum*. In the U.S. there are about 100,000 new cases per year. Although the incidence among male homosexuals is 25 to 30% higher than in the general population, significant increases in reported cases among heterosexuals have been observed since 1985. The highest incidence is in the 20- to 39-year-old age group. It is acquired through sexual contact or transmitted through the placenta to a fetus. The disease progresses through several stages. During the **primary stage**, the chief symptom is an open sore,

called a **chancre** (SHANKG-ker), at the point of contact. The chancre heals within one to five weeks. From 6 to 24 weeks later, symptoms such as a skin rash, fever, and aches in the joints and muscles usher in the **secondary stage**. These symptoms also eventually disappear (in about 4 to 12 weeks), and the disease ceases to be infectious, but a blood test for the presence of the bacteria generally remains positive. During this "symptomless" period, called the **latent stage**, the bacteria may invade body organs. When signs of organ degeneration appear, the disease is said to be in the **tertiary stage**.

If the organs of the nervous system become involved, the tertiary stage is called **neurosyphilis**. Neurosyphilis may take different forms, depending on the tissue involved. Cerebellar damage is manifested by uncoordinated movements in such activities as writing. As the motor areas become extensively damaged, victims may be unable to control urine and bowel movements. Eventually, they may become bedridden, unable even to feed themselves. Damage to the cerebral cortex produces memory loss and personality changes that range from irritability to hallucinations. AIDS may speed the progression of neurosyphilis, possibly by impairing macrophages and antibody production.

Syphilis can be treated with antibiotics (penicillin) during the primary, secondary, and latent periods. Certain forms of neurosyphilis may also be successfully treated, but the prognosis for others is very poor. Noticeable symptoms do not always appear during the first two stages of the disease. Syphilis, however, is usually diagnosed through a blood test whether noticeable symptoms appear or not. The importance of these blood tests and follow-up treatments cannot be overemphasized.

Genital Herpes

Another sexually transmitted disease, **genital herpes**, is common in the U.S. Each year, between 400,000 and 600,000 new cases are reported. The sexual transmission of the herpes simplex virus, the causative agent of genital herpes, is well established. Unlike syphilis and gonorrhea, which are caused by bacteria and treatable with antibiotics, genital herpes is incurable. Type I herpes simplex virus is the virus that causes the majority of infections above the waist such as cold sores. Type II herpes simplex virus causes most infections below the waist such as painful genital blisters on the prepuce, glans penis, and penile shaft in males and on the vulva or sometimes high up in the vagina in females. The blisters disappear and reappear in most patients, but the virus itself remains in the body.

Treatment of the symptoms involves pain medication, saline compresses, sexual abstinence for the duration of the eruption, and use of an oral drug called acyclovir (Zovirax). This drug interferes with viral DNA replication but not with host cell DNA replication. Acyclovir speeds the healing and sometimes reduces the pain of initial genital herpes infections and shortens the duration of lesions in patients with recurrent genital herpes. A topically applied ointment that contains Inter Vir-A (Immuvir), an antiviral substance, is another drug used to treat genital herpes. Inter Vir-A provides rapid relief for the pain, itching, and burning associated with genital herpes. An experimental genital herpes vaccine will involve human testing shortly.

Chlamydia

Chlamydia (kla-MID-ē-a) is a sexually transmitted disease

caused by the bacterium *Chlamydia trachomatis* (*chlamys* = cloak). This unusual bacterium cannot grow outside the body; it cloaks itself inside cells to divide. At present, chlamydia is the most prevalent and one of the most damaging of the sexually transmitted diseases. It affects between three and five million persons annually in the U.S. Unlike gonorrhea, chlamydia afflicts all socioeconomic groups. For example, it is found in up to 5% of female college students and 10% of young men in the military.

In males, urethritis is the principal result. It is characterized by burning on urination, frequency of urination, painful urination, and low back pain. In females, urethritis may spread through the reproductive tract and develop into inflammation of the uterine tubes, which increases the risk of ectopic pregnancy (implantation of a fertilized ovum outside the uterus) and sterility. As in gonorrhea, the organism may be passed from mother to infant during childbirth, infecting the eyes. Treatment consists of the administration of tetracycline or doxycycline.

Trichomoniasis

The microorganism *Trichomonas vaginalis*, a flagellated protozoan (one-celled animal), causes **trichomoniasis**, an inflammation of the mucous membrane of the vagina in females and the urethra in males. *T. vaginalis* is a common inhabitant of the vagina of females and urethra of males. If the normal acidity of the vagina is disrupted, the protozoan may overgrow the normal microbial population and cause trichomoniasis. Symptoms include a yellow vaginal discharge with a particularly offensive odor and severe vaginal itch in women. Men can have it without overt symptoms but can nevertheless transmit it to women. Sexual partners must be treated simultaneously. The drug of choice is metronidazole.

Genital Warts

Warts are an infectious disease caused by viruses. Sexual transmission of **genital warts** is common and is caused by the *human papillomavirus* (HPV). It is estimated that nearly one million persons a year develop genital warts in the U.S. Patients with a history of genital warts may be at increased risk for certain types of cancer (cervical, vaginal, anal, vulval, and penile). There is no cure for genital warts. Treatment consists of cryotherapy with liquid nitrogen; electrocautery, excision, laser surgery, and topical application of podophyllin in tincture of benzoin. Alpha interferon is also used to treat genital warts.

MALE DISORDERS

Testicular Cancer

Testicular cancer occurs most often between the ages of 15 and 34 and is one of the most common cancers seen in young males. Although the cause is unknown, the condition is associated with males who have a history of undescended testes or late-descended testes. Most testicular cancers arise from the sperm-producing cells. An early sign of testicular cancer is a mass in the testis, often associated with pain or discomfort. All males should perform regular testicular self-exams. Treatment involves removal of the diseased testis.

Prostate Disorders

Because the prostate surrounds the urethra, any infection, enlargement, or tumor can obstruct the flow of urine. Prolonged obstruction may result in serious changes in the urinary bladder, ureters, and kidneys and may perpetuate urinary tract infections. One treatment consists of widening a

narrowed urethra with a balloon catheter (balloon urethroplasty). If the obstruction cannot be relieved by other means, the gland may be partially or completely removed. The surgical procedure is called **prostatectomy** (pros'-ta-TEK-tō-mē).

Acute and chronic infections of the prostate gland are common in postpubescent males, often in association with inflammation of the urethra. In **acute prostatitis**, the prostate gland becomes swollen and tender. Appropriate antibiotic therapy, bed rest, and above-normal fluid intake are effective treatment.

Chronic prostatitis is one of the most common chronic infections in men of the middle and later years. On examination, the prostate gland feels enlarged, soft, and very tender, and its surface outline is irregular. This disease often produces no symptoms, but the prostate is believed to harbor infectious microorganisms responsible for some allergic conditions, arthritis, and inflammation of nerves (neuritis), muscles (myositis), and the iris (iritis).

An enlarged prostate gland, two to four times the normal size, occurs in approximately one-third of all males over age 60. The condition is called **benign prostatic hyperplasia** (BPH) and is characterized by nocturia (bed-wetting), hesitancy in urination, decreased force of urinary stream, postvoiding dribbling, and a sensation of incomplete emptying. Surgical correction is possible by a procedure called **transurethral resection of the prostate (TURP)**, in which pieces of the gland are removed using a special cystoscope inserted into the urethra. Enlargement usually can be detected by a **digital rectal exam**, in which the physician palpates the prostate through the rectum with the fingers (digits).

Prostate cancer is the leading cause of death from cancer in men in the U.S. (having surpassed lung cancer in 1991) and it is responsible for about 32,000 deaths annually. Both benign and malignant growths are common in elderly men. Both types of tumors put pressure on the urethra, making urination painful and difficult. At times, the excessive back pressure destroys kidney tissue and increases susceptibility to infection. Therefore, even when the tumor is benign, surgery is indicated. Prostate cancer may be detected by digital rectal examination and fine-needle aspiration. A procedure called **transrectal ultrasonography** can detect tumors as small as a grain of rice. In the procedure, a rectal probe is used to bounce sound waves off the prostate gland. The returning echoes are converted into an image that can be viewed on a monitor and printed on paper. Treatment for prostate cancer may involve surgery, radiation, hormonal therapy, and chemotherapy.

Sexual Functional Abnormalities

Impotence (*impotencia* = lack of strength) is the inability of an adult male to ejaculate or to attain or hold an erection long enough for sexual intercourse. Most cases of impotence are thought to be caused by insufficient release of nitric oxide. Other causes include diabetes mellitus, physical abnormalities of the penis, systemic disorders such as syphilis, vascular disturbances (arterial or venous obstructions), neurological disorders, testosterone deficiency, or drugs (alcohol, antidepressants, antihistamines, antihypertensives, narcotics, nicotine, and tranquilizers). Psychic factors such as fear of causing pregnancy, fear of sexually transmitted diseases, religious inhibitions, and emotional immaturity may also cause impotence.

In some impotent men, penile implants may be helpful. Penile injections of papaverine (Pavabid), a vasodilator, and

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phentolamine mesylate (Regitine), an alpha-adrenergic blocker, can produce excellent effects in overcoming both physical and psychological impotence.

Male infertility (sterility) is an inability to fertilize a secondary oocyte. It does not imply impotence. Male fertility requires production of adequate quantities of viable, normal spermatozoa by the testes, unobstructed transportation of sperm through the ducts, and satisfactory deposition in the vagina. The tubules of the testes are sensitive to many factors—x-rays, infections, toxins, malnutrition, and significantly higher-than-normal scrotal temperatures—that may cause degenerative changes and produce male sterility. If inadequate sperm production is suspected, a sperm analysis should be performed.

FEMALE DISORDERS

Menstrual Abnormalities

Because menstruation reflects not only the health of the uterus but also the health of the endocrine glands that control it, the ovaries and the pituitary gland, disorders of the female reproductive system often involve menstrual disorders.

Amenorrhea (ā-men'ō-RĒ-a; *a* = without; *men* = month; *rhein* = to flow) is the absence of menstruation. If a woman has never menstruated, the condition is called **primary amenorrhea**. Primary amenorrhea can be caused by endocrine disorders, most often in the pituitary gland and hypothalamus, or by a genetically caused abnormal development of the ovaries or uterus. **Secondary amenorrhea**, the skipping of one or more periods, is commonly experienced by women at some time during their lives. Changes in body weight, either gains or losses, often cause amenorrhea. Obesity may disturb ovarian function. Similarly, extreme weight loss, for example, in anorexia nervosa, often leads to a suspension of menstrual flow. When amenorrhea is unrelated to weight, analysis of levels of estrogens often reveals deficiencies of pituitary and ovarian hormones. Amenorrhea may also be caused by rigorous athletic training.

Dysmenorrhea (dis'men'ō-RĒ-a; *dys* = difficult) refers to pain associated with menstruation and is usually reserved to describe an individual with menstrual symptoms that are severe enough to prevent her from functioning normally for one or more days each month. **Primary dysmenorrhea** is painful menstruation with no detectable organic disease. The pain of primary dysmenorrhea is thought to result from uterine contractions, probably associated with uterine muscle ischemia and prostaglandins produced by the uterus.

Prostaglandins are known to stimulate uterine contractions, but they cannot do so in the presence of high levels of progesterone. As we have noted earlier, progesterone levels are high during the last half of the menstrual cycle. During this time, prostaglandins are apparently inhibited by progesterone from producing uterine contractions. However, if pregnancy does not occur, progesterone levels drop rapidly and prostaglandin production increases. This causes the uterus to contract and slough off its lining and may result in dysmenorrhea. Besides pain, other signs and symptoms may include headache, nausea, diarrhea or constipation, and urinary frequency. Primary dysmenorrhea is less of a problem after pregnancy and vaginal delivery, perhaps because of enlargement of the cervical canal. Drugs that inhibit prostaglandin synthesis (naproxen and ibuprofen) are used to treat primary dysmenorrhea.

Secondary dysmenorrhea is painful menstruation that is

frequently associated with a pelvic pathology. Some cases are caused by uterine tumors, ovarian cysts, pelvic inflammatory disease (PID), endometriosis, and intrauterine devices (IUDs). Treatment is aimed at correction of the underlying cause.

Abnormal uterine bleeding includes menstruation of excessive duration or excessive amount, diminished menstrual flow, too frequent menstruation, intermenstrual bleeding, and postmenopausal bleeding. These abnormalities may be caused by disordered hormonal regulation, emotional factors, fibroid tumors of the uterus, and systemic diseases.

Premenstrual syndrome (PMS) refers to severe physical and emotional distress occurring late in the postovulatory phase of the menstrual cycle and sometimes overlapping with menstruation. Signs and symptoms usually increase in severity until the onset of menstruation and then dramatically disappear. Among the signs and symptoms are edema, weight gain, breast swelling and tenderness, abdominal distension, backache, joint pain, constipation, skin eruptions, fatigue and lethargy, greater need for sleep, depression or anxiety, irritability, mood swings, headache, poor coordination and clumsiness, and cravings for sweet or salty foods. The basic cause of PMS is unknown. Although PMS is related to the cyclic production of ovarian hormones, the symptoms are not directly due to changes in the levels of these hormones. Treatment is individualized, depending on the type and severity of symptoms, and may include dietary changes, exercise, over-the-counter drugs (aspirin or acetaminophen), psychoactive drugs (sedatives, tranquilizers, and antidepressants), prostaglandins (Ponstel), diuretics, hormone therapy (progesterone), and vitamin B₆. Management of PMS involves medical, psychological, and social support that may include education of the patient and her family; elimination of fears or inappropriate beliefs regarding the menstrual cycle; alteration in coping style; change in life style, occupation, or family relationships; and use of appropriate medications.

Toxic Shock Syndrome

Toxic shock syndrome (TSS), first described in 1978, is primarily a disease of previously healthy, young, menstruating females who use tampons. It is also recognized in males, children, and nonmenstruating females. Clinically, TSS is characterized by high fever up to 40.6°C (105°F), sore throat or very tender mouth, headache, fatigue, lethargy, memory loss, hypotension, irritability, muscle soreness and tenderness, conjunctivitis, diarrhea and vomiting, abdominal pain, vaginal irritation, and erythematous rash.

Toxin-producing strains of the bacterium *Staphylococcus aureus* are necessary for development of the disease. The risk is greatest in females who use highly absorbent tampons. TSS can also occur as a complication of influenza and influenza-like illness and use of contraceptive sponges. Initial therapy is directed at correcting all homeostatic imbalances as quickly as possible. Anti-staphylococcal antibiotics, such as penicillin or clindamycin, are also administered.

Ovarian Cysts

Ovarian cysts are fluid-containing sacs within the ovary. Follicular cysts may occur in the ovaries of elderly women, in ovaries that have inflammatory diseases, and in menstruating females. They have thin walls and contain a serous albuminous material. Cysts may also arise from the corpus luteum or the endometrium.

Endometriosis

Endometriosis (en'-dō-mē-trē-ō-sis; *endo* = within; *metri* = uterus; *osis* = condition) is characterized by the growth of endometrial tissue outside the uterus. The tissue enters the pelvic cavity via the open uterine tubes and may be found in any of several sites—on the ovaries, rectouterine pouch, surface of the uterus, sigmoid colon, pelvic and abdominal lymph nodes, cervix, abdominal wall, kidneys, and urinary bladder. One theory for the development of endometriosis is that there is regurgitation of menstrual flow through the uterine tubes. Another theory is that migrational events during embryonic development are somehow altered. Endometriosis is common in women 25 to 40 years of age who have not had children. Symptoms include premenstrual pain or unusual menstrual pain. The unusual pain is caused by the displaced tissue sloughing off at the same time the normal uterine endometrium is being shed during menstruation. Infertility can be a consequence. Treatment usually consists of hormone therapy, modified GnRH (nafarelin), videolaseroscopy (laparoscope with camera and laser), or conventional surgery. Endometriosis disappears at menopause or when the ovaries are removed.

Female Infertility

Female infertility, or the inability to conceive, occurs in about 10% of married females in the U.S. It may be caused by ovarian disease, tubal obstruction, and certain conditions of the uterus. An upset in hormone balance, so that the endometrium is not adequately prepared to receive the fertilized ovum, may also be the problem. Some research suggests that an autoimmune disease might underlie many cases of infertility. Infertility treatment may involve the use of fertility drugs, donor (artificial) insemination, or surgery. Gynecologists are now using a procedure called **transcervical balloon tuboplasty** to clear obstructions in the uterine tubes. The technique, borrowed from the cardiology procedure to unclog coronary arteries, consists of inserting a catheter through the cervix of the uterus and into the uterine tube. Then a balloon is inflated, compressing the obstruction.

Disorders Involving the Breasts

The breasts of females are highly susceptible to cysts and tumors. Men are also susceptible to breast tumors, but breast cancers are 100 times more common in women.

In females, **fibrocystic disease** is the most common cause of a breast lump in which one or more cysts (fluid-filled sacs) and thickening of alveoli (clusters of milk-secreting glands) develop. The condition occurs mainly in females between the ages of 30 and 50 and is probably due to a hormonal imbalance; a relative excess of estrogens or deficiency of progesterone in the postovulatory (luteal) phase of the menstrual cycle may be responsible. Fibrocystic disease usually causes one or both breasts to become lumpy, swollen, and tender about a week or so before a menstrual cycle begins. The cysts may be aspirated to relieve the pain. Medical management may involve administration of progesterone, antiestrogens, prolactin inhibitors, and pituitary gonadotropin-inhibiting agents.

Benign **fibroadenoma** is a common tumor of the breast. It

occurs most often in young women. Fibroadenomas have a firm rubbery consistency and are easily moved about within the mammary tissue. The usual treatment is excision of the growth. The breast itself is not removed.

Breast cancer has one of the highest fatality rates of all cancers affecting women, but it is rare in men. In females, breast cancer is rarely seen before age 30, and its occurrence rises rapidly after menopause. Breast cancer is generally not painful until it becomes quite advanced, so often it is not discovered early or, if noted, is ignored. Any lump, no matter how small, should be reported to a physician at once. New evidence links some breast cancers to loss of protective anti-oncogenes.

Cervical Cancer

Another common disorder of the female reproductive tract is **cervical cancer**, carcinoma of the cervix of the uterus. The condition starts with **cervical dysplasia** (dis-PLĀ-sē-a), a change in the shape, growth, and number of the cervical cells. If the condition is minimal, the cells may regress to normal. If it is severe, it may progress to cancer. Cervical cancer may be detected in most cases in its earliest stages by a Pap smear. There is some evidence linking cervical cancer to penile virus (papillomavirus) infections of male sexual partners. Depending on the progress of the disease, treatment may consist of excision of lesions, radiotherapy, chemotherapy, and hysterectomy.

Pelvic Inflammatory Disease

Pelvic inflammatory disease (PID) is a collective term for any extensive bacterial infection (primarily involving *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Bacteroides*, *Peptostreptococcus*, and *Gardnerella vaginalis*) of the pelvic organs, especially the uterus, uterine tubes, or ovaries. A vaginal or uterine infection may spread into the uterine tube (**salpingitis**) or even farther into the abdominal cavity, where it infects the peritoneum (**peritonitis**). Diagnosis of PID depends on three findings: abdominal tenderness; cervical tenderness; and ovarian, uterine tube, and uterine ligament tenderness. In addition, diagnosis is based on at least one of the following: fever, leukocytosis, pelvic abscess or inflammation, purulent cervical discharge, and the presence of certain bacteria in smears. Early treatment with bed rest and antibiotics (cefoxitin, penicillin, tetracycline, doxycycline) can stop the spread of PID.

Vulvovaginal Candidiasis

Candida albicans is a yeastlike fungus that commonly grows on mucous membranes of the gastrointestinal and genitourinary tracts. The organism is responsible for **vulvovaginal candidiasis**, the most common form of vaginitis. It is characterized by severe itching; a thick, yellow, cheesy discharge; a yeasty odor; and pain. The disorder, experienced at least once by about 75% of females, is usually a result of proliferation of the fungus following antibiotic therapy for another condition. Predisposing conditions include use of oral contraceptives, cortisone-like medications, pregnancy, and diabetes. Treatment is by topical (clotrimazole) or oral (ketoconazole) antibiotics.