3

Sex Differences in Behavior

SEX DETERMINATION AND DIFFERENTIATION

Girls and boys are different. Humans, like many other animals, are sexually dimorphic (*di*, "two"; *morph*, "type") in the size and shape of their bodies, their physiology, and their behavior. The behavior of boys and girls differs in many ways. Girls generally excel in verbal abilities relative to boys; boys are nearly twice as likely as girls to suffer from dyslexia (reading difficulties) and stuttering. Boys are generally better than girls at tasks that require visuospatial abilities. Girls engage in nurturing behaviors more frequently than boys. Over 90% of all anorexia nervosa cases involve young women. Young men are twice as likely to suffer from schizophrenia as young women. Boys are much more aggressive and generally engage in more rough-and-tumble play than girls (Hines, 2004; Ruble and Martin, 1998). Many sex differences, such as the difference in aggressiveness, persist throughout adulthood. For example, there are many more men than women serving prison sentences for violent behavior. What accounts for these sex differences?

Behavioral endocrinologists, like most people, are interested in these and other behavioral sex differences. What are the proximate causes of behavioral sex differences? This question is one version of the enduring nature-versus-nurture question. As you probably already know, all behavior results from an interaction between environmental factors, including learning and cultural influences ("nurture"), and biological factors, including genes and physiological influences ("nature"). Students of behavioral endocrinology try to discern how the behavioral differences between

males and females are mediated by environmental influences, including social interactions, and the extent to which they are mediated by physiological factors, especially hormones. Trying to separate these influences can be difficult, if not impossible. Sex differences in some behaviors, such as snoring, are probably due exclusively to biological factors, whereas other behaviors, such as choosing a style of clothing or haircut, appear to reflect only cultural influences. But what about the pattern of play behavior? Is the difference in the frequency of rough-and-tumble play between boys and girls due to biological factors associated with being male or female, or due to cultural expectations and learning? If there is a combination of biological and cultural influences mediating the frequency of rough-and-tumble play, then what proportion of the variation between the sexes is due to biological factors and what proportion is due to social influences?

It is easy to speculate on these questions in a casual manner. Visit any preschool and watch 3- or 4-year-old children at play. Even when gender-neutral toys are provided, boys tend to play aggressive, rowdy games, whereas girls tend to engage in play activities in which cooperation is valued (Figure 3.1). Again, are these differences mediated by biological influences, or are they due to cultural influences? Perhaps children learn sexually dimorphic modes of behavior from TV or from their friends at nursery school—boys play with guns and trucks and girls play with dolls and tea sets. Of course, it is easy to produce examples of girls who enjoy rough-and-tumble play and boys who enjoy playing nurturing roles.

(A)

(B)

3.1 Patterns of play behavior. The play behavior of boys and girls is different from a very early age. (A) Girls tend to play games that involve groups and verbal cooperation. (B) Boys tend to play with toys that move through space, such as vehicles and balls. These patterns of play behavior probably reflect both socialization and biological differences that may involve hormones. (A) © Stock Connection/Alamy Images; (B) © Painet, Inc.

However, producing examples to support one's contentions is not the most effective way to determine the causes of a particular phenomenon. In order to ascertain the true causes underlying behavior, all biases must be eliminated from the data-gathering process. The most effective manner of obtaining information about an adequately described phenomenon is via the experimental method, primarily through the use of inductive reasoning (Platt, 1964).

Behavioral endocrinologists are particularly interested in the extent to which hormones mediate behavioral sex differences because it is known that steroid hormone concentrations differ between males and females from almost the first trimester of gestation. However, it is extremely difficult to ascertain the proximate factors underlying sex differences in human behavior experimentally. Although the critical experiments can be designed, they cannot ethically be performed on humans. Tracking hormone concentrations during sexual differentiation in utero could jeopardize the well-being of the fetus. To assess the role of hormones in rough-and-tumble play, children would have to be castrated and receive hormone replacement therapy. Other children would have to be reared in social isolation to assess the contribution of social factors to aggressive play. Obviously, such studies are not possible. However, indirect evidence has been obtained from several converging sources that can help us to understand the behavioral differences between human males and females.

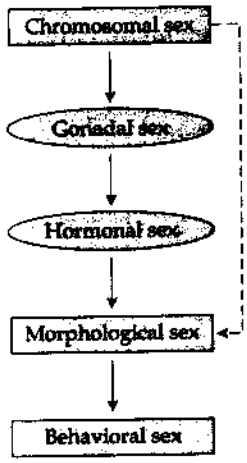
Three strategies that do not require experimentation on humans have been used to explore questions about the origin of human behavioral sex differences. First, animal models have been used to study **sexual differentiation**, the developmental process of becoming male or female, which occurs before or immediately after birth or hatching. The study of nonhuman mammals has established that hormone concentrations during sexual differentiation guide the development of many physiological, morphological, and behavioral characteristics that are displayed later in life (Figure 3.2). The second strategy has involved studies of people

3.2 Rough-and-tumble play in nonhuman primates. Although it is often difficult to account for behavioral sex differences in humans, studies of nonhuman animals can often provide insights. For example, strong sex differences in rough-and-tumble play are observed in humans, as well as nonhuman primates, and these sex differences appear to be modulated by early exposure to hormones. Photo © Craig Lovell/Eagle Visions Phototgraphy/Alamy Images.

or nonhuman animals that have undergone anomalous sexual differentiation. For example, studying the behavior of girls who were exposed to a male-typical hormonal milieu in utero helps to separate the contribution of rearing conditions from the hormonal factors that may underlie behavioral sex differences. Finally, because child-rearing practices vary so greatly among different cultures, anthropologists, psychologists, and sociologists have looked for universal commonalities in the behavior of all children. Studies of sex differences in behavior that emerge consistently regardless of rearing conditions suggest that some such differences—in aggressive behavior, for example—are mediated by biological factors (Hines, 1982, 2004). Although this third approach will not be reviewed in great depth here, such behavioral surveys have indicated that several behaviors in humans may have significant biological bases that could override social effects. Of course, one could argue that human parents may universally treat their sons differently from their daughters and induce the sex differences in emitted behaviors. This argument is hard to refute because experimental controls are infrequent in long-term developmental studies of human behavior. Consequently, nonhuman animal studies have generally proven to be superior to human studies for understanding the sex differences underlying behavior because of the possibility for greater experimental control.

Sex Determination and Differentiation

What is sex? What makes you male or female? There are several different ways to answer this very basic question (Figure 3.3). First, there is **chromosomal sex**, determined by the sex chromosomes the individual receives at fertilization. In mammals, the homogametic sex is female (XX), whereas the heterogametic sex is male (XY). Chromosomal sex is fundamental during the process of sexual differentiation, and determines **gonadal sex**: the possession of either ovaries or testes. Females have ovaries, whereas males have testes. Gonadal sex is related to **gametic sex**: the ovaries of females produce large, immobile, resource-rich gametes called ova or eggs, whereas the testes of males produce small, mobile gametes called sperm. Females and males also differ on the basis of **hormonal sex**. Females of most vertebrate species tend to have high estrogen-to-



3.3 Levels of sex determination. Chromosomal sex, which is determined at conception, determines which gonads form in the embryonic individual. Gonadal sex determines the hormonal environment in which the fetus develops, and steers morphological development in a male or female direction. The resulting sex differences in the central nervous system and in some effector organs lead to the behavioral sex differences observed in later life. There is some evidence that chromosomes may also directly influence specific sexually dimorphic brain anatomy and function.

androgen ratios of circulating steroid hormone concentrations; males have the opposite pattern. **Morphological sex** refers to the differences in body type between males and females. Male mammals are typically larger than females and possess different external genitalia. In addition, males of many species differ from females in coloration, the presence of horns, antlers, and other ornamentation, and body shape. **Behavioral sex** can be discriminated on the basis of male-typical and female-typical behaviors. For example, females of many species often care for young, whereas males, especially male mammals, rarely provide parental care (see Chapter 7). Male and female birds of many species share equally in parental care, but they display other types of behavioral sex differences. For example, males of many avian species sing, but their female conspecifics do not.

Additional categories of sex classification exist among humans. For example, **gender identity** reflects the sex, or gender, that individuals feel themselves to be; gender identity usually corresponds to the expression of a **gender role**, a culturally based summary of sex-specific behaviors. **Sexual orientation** or **sexual preference** can also categorize males and females: males generally prefer female sexual partners, whereas females generally prefer male sexual partners. Finally, there is **legal sex**. You are recognized by governmental agencies as male or female because of an "M" or "F" on your birth certificate, driver's license, or some other official document. If individuals sporting "M" identification documents enter a women's rest room, they can be arrested in most parts of North America, even if they are exhibiting female-typical behavior (for example, wearing a silk evening gown). Sex differences occur at each of these systematic levels.

Ultimate Causes of Sex Differences

Most of the animals with which you are familiar engage in sexual reproduction. In fact, most animal species currently on the planet engage in sexual reproduction. However, a survey of the entire animal kingdom reveals that a number of animals, especially insect species, breed asexually. There are several forms of asexual reproduction. Among vertebrate animals, the process of asexual reproduction is called **parthenogenesis**. In parthenogenetic vertebrates, there is only one sex: female. Parthenogenetic females produce genetically identical eggs that develop into female offspring that are all genetically identical to their mother.

From the Darwinian perspective, reproductive success reflects the amount of genetic material an individual contributes to subsequent generations. Thus, asexual reproduction may seem like an extremely efficient system. This mode of breeding must have some distinct disadvantages, however, if so many animals breed sexually. One hypothesis about why asexual reproduction is rare among vertebrates is that asexual individuals, because they have such similar genotypes, provide little variation on which natural selection can act. Thus, if the conditions of its environment change, an asexual species could become extinct. Sexual reproduction, through the separation of chromosome pairs into haploid gametes and their recombination in each offspring, provides genetic variability and hence evolutionary flexibility (Howard and Lively, 1994). Those animals and plants that have the option of either sexual or asexual reproduction usually opt for sexual repro-

duction when the environment becomes unstable. By analogy, would you rather have 100 lottery tickets with the same number or 50 tickets, each with a slightly different number? Another problem that can burden asexual species is the likelihood that pathogens may become specialized to exploit a single genotype (Ewald, 1994). Because pathogens reproduce faster than their hosts, they can rapidly evolve ways to override the immunological defenses of their hosts (Judson, 1997; Ladle et al., 1993). By shuffling their genetic material, host species reduce the odds that pathogens will be preadapted to exploit their offspring. Why sex evolved remains a question that is far from settled among evolutionary biologists.

Sexually reproducing species have two sexes: male and female. Why do the two sexes differ in appearance and behavior? In other words, what are the ultimate causes of the behavioral differences between males and females? We cannot travel back in time to watch the slow evolution of sexual dimorphism in a given species and note the ecological or social factors associated with the development of sex differences. But we can address these "why questions" by examining present-day species that show little or no sexual dimorphism and comparing them with species that are sexually dimorphic. When these comparisons are made, a striking relationship between sexual dimorphism and mating system becomes obvious. Species that are **monogamous** (have a single mating partner) display

BOX 3.1 Behavioral Sex Role Reversals

In virtually every mammalian and avian species studied, males are more aggressive than their female conspecifics. They also tend to weigh more, and are (particularly among mammals) more likely to establish and defend breeding territories and less likely to provide parental care to the young. There are several notable exceptions to this dogma, however, and the study of these unusual cases is useful for shedding light on the more typical situation as well as for understanding how reliable the "generalities" of the interaction between hormones and behavior are.

Female spotted hyenas (*Crocuta crocuta*) are socially dominant: in addition to eliciting submissive postures and vocalizations from males, they are also allowed first access to food (Frank, 1986; Kruuk, 1972). In addition to their masculinized behavior, these females have masculinized external genitalia. Indeed, the species was once thought to be hermaphroditic because all individuals, even nursing mothers, possess scrota and penis-like structures. The photographs in this box show the external genitalia of male (left) and female (right)

Photographs courtesy of Stephen Glickman.

less sexual dimorphism than species that are **polygamous** (have multiple mating partners) (Trivers, 1972). In polygamous species, in which members of one sex compete to mate with the other sex, sexual selection may act to favor certain behavioral or morphological traits in the competing sex (Andersson, 1994).

Sexual selection is a subcategory of natural selection (Andersson, 1994; Trivers, 1972). Generally, the rule among animal species is that males compete and females choose. For instance, female deer choose to mate with bucks that control the largest feeding areas (intersexual selection). Bucks obtain feeding areas prior to the breeding season by fighting among themselves and establishing a social hierarchy (intrasexual selection). The largest bucks usually have the largest antlers, and they typically win the most fights, move to the top of the hierarchy, and control the best feeding areas. Thus, they are able to mate with the most females and pass on their genes to the most offspring (Lincoln et al., 1972). Consequently, females indirectly select for males with large body and antler size, as well as for aggressive behavior. Because males typically compete for females, they are usually bigger, more colorful, and more aggressive than females. In species in which the sex roles are reversed and females compete with one another for males (Box 3.1), the females are typically larger and more colorful than their male conspecifics (Trivers, 1972). Thus, sexual selection favors

hyenas. The vaginal labia in spotted hyenas are fused to form a fat-filled pseudoscrotum. The clitoris develops into a pseudopenis through which the urogenital tract passes. Females urinate, copulate, and deliver young through the urogenital tract. The pseudopenis possesses full erectile function, and both males and females routinely display erections as part of their social interactions (Glickman et al., 1987). Erectile function in both sexes is observed from infancy.

The extreme masculinization of female behavior and morphology appears to be organized by high concentrations of ovarian androstenedione in pregnant females, which is converted to testosterone by the placenta (Glickman et al., 1987, 1992). However, exposure to anti-androgens in utero does not block the development of a pseudopenis in female hyenas (Drea et al., 1998). It is possible that some other factor stimulates the androgen receptors, leading to external masculinization, but the androgen receptors themselves appear relatively unaltered (Catalano et al., 2002). Adult males exhibit higher androgen concentrations than adult females. Thus, adult concentrations of androgens do not appear to account for the difference in social dominance (see Chapter 10).

Spotted sandpipers (*Actitis macularia*) are birds that display atypical sex roles. Females establish and defend a feeding territory and compete with other females for access to males (Fivizzani and Oring, 1986). Males incubate the eggs and brood the young with little or no assistance from the females. Prior to incubation, blood plasma concentrations of testosterone and dihydrotestosterone are substantially higher in males than in females. As incubation proceeds, testosterone levels in males plummet 25-fold. Mated females exhibit testosterone concentrations that are 7-fold higher than those of unmated females (Fivizzani and Oring, 1986). These hormone profiles are similar to those of other avian species in which males assist with care of the young. Thus, the reversal of sex roles in spotted sandpipers appears to be unrelated to adult hormonal effects.

sexual dimorphisms, and probably amplifies them over time (Zahavi and Zahavi, 1997).

Although monogamy is asserted to be the most common mating system practiced by humans (*Homo sapiens*) in Western societies, examination of many societies suggests that humans are mildly to strongly polygynous; that is, each male may mate with more than one female (Alexander et al., 1979; Daly and Wilson, 1983; Martin and May, 1981; Murdock, 1967). Approximately 700 out of 850 human societies described in an extensive ethnographic catalog practiced polygyny (Murdock, 1967). Furthermore, as noted above, the sex differences observed among humans are atypical for monogamous animals, but are common in polygynous and promiscuous species. Human sexual dimorphisms include increased body size and strength (Alexander et al., 1979), later puberty (Bronson, 1988; Tanner, 1962), and higher mortality rates (Shapiro et al., 1968) in men than in women. Importantly, cross-cultural studies of humans have revealed behavioral sexual dimorphisms that are also consistent with those of other polygynous species, including increased courtship activity (Daly and Wilson, 1983), higher levels of aggression (Moyer, 1976), and reduced parental care (Clutton-Brock, 1991) in males than in females. Thus, the morphological, physiological, and behavioral differences between men and women may reflect the evolutionary history of the species' most common mating pattern, namely, polygyny.

Again, we cannot go back in time to test these ultimate hypotheses, but we can use them to make predictions about current behaviors, and we can conduct animal experiments designed to test our predictions. For example, males of polygynous species typically move around over larger areas than conspecific females or males of monogamous species, presumably because wandering around increases their chances of finding additional mates. One might predict that females and males of monogamous species will have poorer direction-finding skills or spatial aptitude in general than males of these wide-ranging polygynous species. This prediction appears to be true when tested. Males of polygynous species, including rats, mice, meadow voles (a small field rodent; *Microtus pennsylvanicus*), and humans, are superior in spatial aptitudes to females of the same species (see the next section). Moreover, male meadow voles are superior in spatial abilities (navigating a maze) to male pine voles (*Microtus pinetorum*), a monogamous species of the same genus (Gaulin and FitzGerald, 1986).

The ultimate level of explanation is useful for guiding predictions about the proximate mechanisms that cause males and females to behave differently. The remainder of this chapter will review the proximate processes of sex determination and sexual differentiation. In other words, it will look at how sexually dimorphic behaviors arise.

Proximate Causes of Sex Differences

Because behavioral sex differences are so ubiquitous among animals, behavioral endocrinologists have focused significant effort on studying this phenomenon. One very important concept developed to guide this effort is the so-called **organizational/activational hypothesis.** This fundamental hypothesis on how hormones guide

behavioral sex differences will be presented within its historical context. Basically, the organizational/activational hypothesis suggests that behavioral sex differences result from (1) differential exposure to hormones that act early in development to organize the neural circuitry underlying sexually dimorphic behaviors and (2) differential exposure to sex steroid hormones later in life that activate the neural circuitry previously organized. The workings of this process in several animal models commonly used to study behavioral sex differences will be described in detail in the next section. Sex differences in brain structures, how these differences arise, and how these differences might mediate behavioral differences between males and females will also be reviewed in this chapter, as well as in Chapter 4.

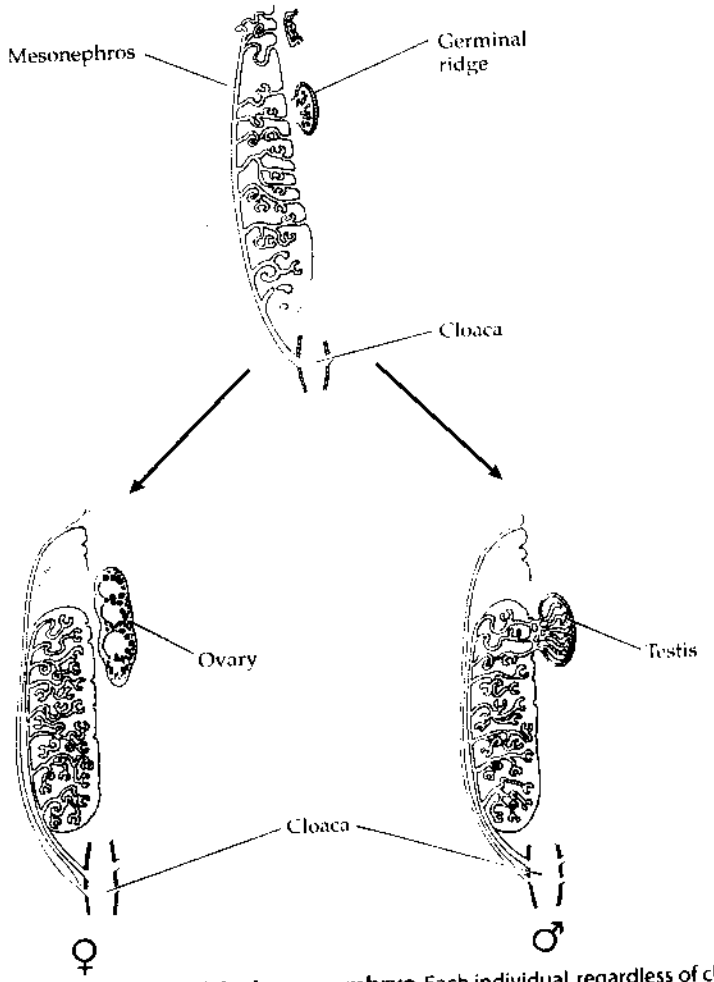
A number of clinical syndromes exist among humans and nonhuman animals that cause anomalies in the process of sexual differentiation. Many of these syndromes are congenital; others are the result of endocrine treatment during gestation. The behavioral consequences resulting from these developmental irregularities in humans, as well as from animal studies in which these clinical syndromes are simulated, will be presented in this chapter. Issues of gender, sex role, and sexual orientation among humans, as well as cognitive sex differences, will be explored in Chapter 4.

There are real and substantial differences between males and females. Some of these sex differences may be apparent at birth; others appear later in development. Our goal is to understand how behavioral sex differences are mediated. But in order to do this, it is necessary to understand sexual differentiation in general. If we limit our discussion to mammals and birds, then basically, chromosomal sex determines gonadal sex, and all subsequent sexual differentiation is normally the result of differential exposure to gonadal steroid hormones. Thus, gonadal sex determines hormonal sex, which in turn influences morphological sex. Morphological differences in the central nervous system, as well as in some effector organs, lead to behavioral sex differences (see Figure 3.3). To understand the specifics of how sexually dimorphic behaviors arise, a discussion of embryology is necessary. This discussion will yield a rationale for the principles underlying behavioral sex differences.

Mammalian Sexual Differentiation

The primary step in the process of mammalian sexual differentiation occurs at fertilization. An ovum can be fertilized by a sperm bearing either an X or a Y chromosome. This event, called **sex determination**, has far-reaching consequences for the differentiation of the embryonic gonads, as well as subsequent behavioral differences.

Each individual embryonic mammal, whether XX or XY, exhibits a thickened ridge of tissue on the ventromedial surface of each mesonephros (protokidney), known as the **germinal ridge** (Figure 3.4; Jost, 1979). At this stage, this primordial gonad is said to be *indifferent* or *bipotential*. In most mammals studied to date, whether the germinal ridge will develop into a testis or an ovary is determined by the cellular expression of the **testis determination factor** (TDF)—a protein encoded



3.4 Gonadal development of the human embryo. Each individual, regardless of chromosomal sex, develops a thickening called the germinal ridge on the ventromedial surface of each mesonephros (protokidney). The germinal ridge is a bipotential primordial gonad; it can become either an ovary or a testis. If the *SRY* gene is expressed and the testis determination factor protein is present, the medulla of the germinal ridge develops, forming a testis. If the *SRY* gene is not expressed, the cortex of the germinal ridge develops, and an ovary is formed.

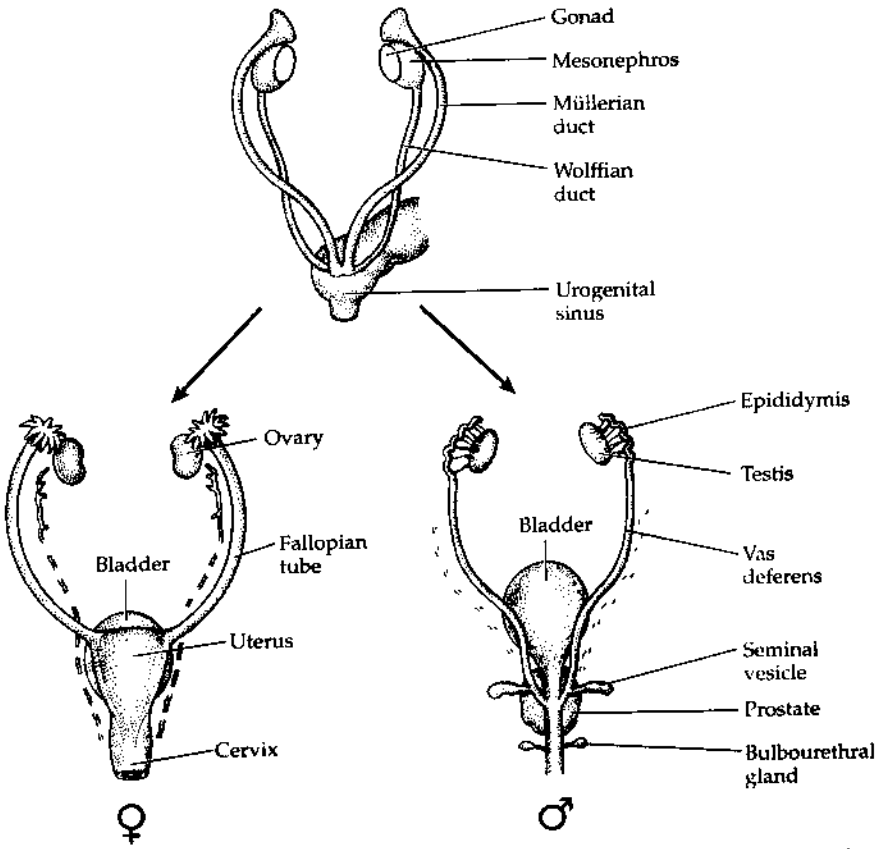
by a gene known as *SRY* (sex-determining region on the *Y* chromosome) (Berta et al., 1990). When the *SRY* gene is expressed in the indifferent gonads, the testis determination factor, binds to a specific hormone response element in the promoter region of other genes that it regulates (Harley and Goodfellow, 1995). When the protein products of these genes are produced, the middle (medulla) of the germinal ridge develops, and a testis forms (Berta et al., 1990). If the *SRY* gene is not

expressed, then the outer part of the germinal ridge (the cortex) develops, and an ovary is formed. It is possible for the *SRY* gene to be expressed in one gonad but not in the other, which leads to unilateral differentiation: in other words, a testis develops on one side while an ovary develops on the other side, suggesting that the testis determination factor functions only locally and is not a blood-borne agent. Partial expression of the *SRY* gene can lead to incomplete gonadal differentiation, yielding an ovotestis. Mice that are chromosomal XY males but do not have the *SRY* gene develop ovaries; similarly, XX transgenic mice into which an *SRY* gene has been inserted develop testes (Goodfellow and Lovell-Badge, 1993; McElreavey et al., 1995). In non-mammalian vertebrates, *SRY* is not a testis-determining gene.

Hormonal secretions from the developing gonads determine whether the individual develops in a male or female manner. The mammalian embryonic testes produce androgens, as well as peptide hormones, that steer the development of the body, central nervous system, and subsequent behavior in a male direction. The embryonic ovaries of mammals are virtually quiescent and do not secrete high concentrations of hormones (but see Arnold and Breedlove, 1985; Döhler et al., 1982). In the presence of ovaries, or in the complete absence of any gonads, morphological, neural, and later, behavioral development follows a female pathway. (As we will see, however, low estrogen concentrations are probably required for normal female neural and behavioral development.) Thus, the prevailing hypothesis about the initiation of sexual differentiation indicates that the gonads are differentiated by genetic influences (*SRY*), and that all other sexual differentiation reflects hormonal mediation.

It is possible, however, that some sex differences in brain and behavior might be mediated directly by gene expression in nongonadal tissue (Arnold, 2002), without the involvement of hormones. For example, the *SRY* gene is transcribed in the hypothalamus and midbrain of adult male mice (Lahr et al., 1995). Indeed, sexually dimorphic transcription of over 50 genes was observed in the brains of mice 10.5 days post-conception, before the gonads had developed (Dewing et al., 2003). Because only genetic males possess a Y chromosome, any gene located on the Y chromosome that is involved in neural development is a candidate to mediate sex differences in brain and behavior directly, without invoking hormones. Mice can be genetically engineered to differ in their sex chromosomes (i.e., XX or XY) but possess the same type of gonads (i.e., ovaries or testes). Such mice show subtle differences in certain brain cell types but most sex differences in these mice appear to rely on hormonal signals regardless of genotype. For example, mice with ovaries, regardless of sex chromosomes, have fewer cells expressing tyrosine hydroxylase in the anteroventral periventricular nucleus of the preoptic area than mice with testes (Arnold et al., 2004). Sex chromosomes also appear to influence the density of vasopressin-containing fibers in the lateral septum, a part of the limbic system located just below the lateral ventricles (DeVries et al., 2002). Additional work is required to determine the importance of all of these factors in the development and expression of sexually dimorphic behaviors.

In contrast to the single, bipotential primordial gonad, dual **anlagen** (primordia) for the accessory sex organs are present early during ontogeny (Figure 3.5). The



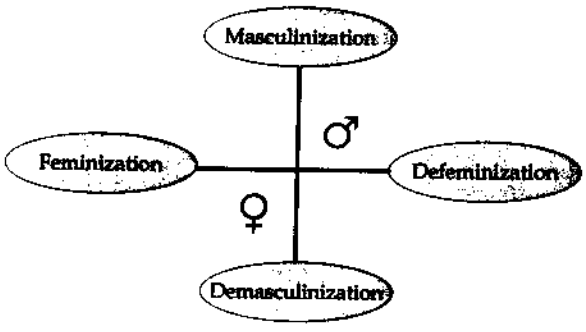
3.5 The Müllerian and Wolffian duct systems are normally both present early in embryonic development. In the absence of testicular hormones, the Müllerian duct system develops into the fallopian tubes, uterus, and, the Wolffian ducts regress. This is the normal course of events in female mammals. When testicular hormones are present, as is normally the case in male mammals, the Wolffian ducts eventually develop into the seminal vesicles and vas deferens, and the Müllerian ducts regress. Because anlagen for each of these duct systems are initially present in the embryo, it is possible in some circumstances for both systems to develop in a single individual.

accessory sex organs connect the gonads to the outside environment. The **Müllerian duct system** develops into the female accessory sex organs: the fallopian tubes, uterus, and cervix. The **Wolffian duct system** develops into the male accessory sex organs, which connect the testes to the outside environment via the penis. Later-developing components of the Wolffian duct system include the seminal vesicles and vas deferens. During normal sexual differentiation, the Wolffian duct system develops in males, whereas the Müllerian duct system regresses. Conversely, in females, the Müllerian duct system develops, whereas the Wolffian duct system regresses. In humans, this process occurs during the first trimester of gestation.

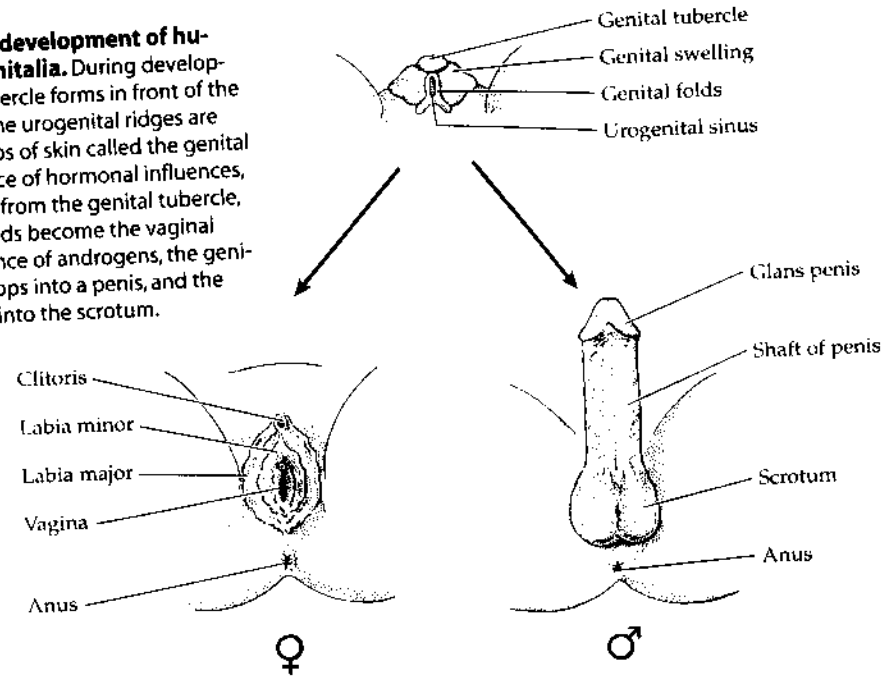
In the presence of ovaries or in the complete absence of gonads, normal development of the Müllerian ducts is accompanied by complete regression of the Wolffian duct system. Again, no hormones are necessary to permit normal female development among mammals. Male development of the accessory sex organs requires two products from the embryonic testes: testosterone and a peptide hormone called **Müllerian inhibitory hormone (MIH)**. Testosterone is necessary to stimulate Wolffian duct development. Müllerian inhibitory hormone, as its name implies, causes the regression of the Müllerian duct system. If testosterone is absent early in development, then Wolffian duct development fails to occur. If MIH is not secreted at the proper time, then the Müllerian duct system develops. Because of the twin anlagen, it is possible for both systems to develop in a single individual.

In order for normal female morphological development of the accessory sex organs to occur, the embryo must become feminized (Müllerian duct development), as well as demasculinized (Wolffian duct regression). Normal male development requires both masculinization (Wolffian duct development) and defeminization (Müllerian duct regression). In other words, sexual differentiation of the accessory sex organs proceeds along two continua: (1) a masculinization–demasculinization scale and (2) a feminization–defeminization scale (Figure 3.6). **Masculinization** is the induction of male traits; **feminization** is the induction of female traits. **Demasculinization** is the removal of the potential for male traits, whereas **defeminization** is the removal of the potential for female traits. This nomenclature will be important for describing the development of behavioral sex differences as well as morphological ones.

The difference in external genitalia is the most obvious difference between the sexes at birth and has been used for generations to assign the sex of humans. During embryological development, the urogenital sinus is surrounded on both sides by long, thickened urogenital ridges, which are flanked by two flaps of skin called the **genital folds** (Figure 3.7). In front of (anteroventral to) the urogenital opening, the two ridges meet to form a median outgrowth called the **genital tubercle**. The genital tubercle and folds are common to both sexes and develop into the external genitalia. Female humans, as well as many other species of mammals, possess a clitoris and vaginal labia, which develop from the genital tubercle



3.6 Normal development of the accessory sex organs occurs along two dimensions. Normal females must become feminized (Müllerian duct development) as well as demasculinized (Wolffian duct regression). Normal males must become masculinized (Wolffian duct development) as well as defeminized (Müllerian duct regression). Thus, sexual dimorphism in accessory sex organs, as well as in many behaviors, requires development along two separate continua, a masculinization–demasculinization continuum and a feminization–defeminization continuum. Male-typical behavior should be masculinized and defeminized.



3.7 Embryonic development of human external genitalia. During development, a genital tubercle forms in front of the urogenital sinus. The urogenital ridges are flanked by two flaps of skin called the genital folds. In the absence of hormonal influences, a clitoris develops from the genital tubercle, and the genital folds become the vaginal labia. In the presence of androgens, the genital tubercle develops into a penis, and the genital folds fuse into the scrotum.

and genital folds, respectively. Males possess a penis, which develops from the genital tubercle, and a scrotal sac, which results from the fusing of the genital folds and eventually contains the testes. Consequently, development of one type of genitalia occurs at the expense of the other type. In other words, a single continuum of feminine to masculine external genital development exists (Figure 3.8).

Androgens are responsible for the differentiation of the external genitalia. In the absence of sex steroid hormones, a clitoris develops from the genital tubercle and the vaginal labia develop from the genital folds. In the presence of androgens, the urethral groove fuses, the genital tubercle develops into a penis, and the genital folds fuse into the scrotum (Wilson et al., 1981). One of the androgenic metabolites of testosterone, 5α-dihydrotestosterone (DHT), is critical for this process of genital fusing. Testosterone is converted to DHT by an enzyme called **5α-reductase**, which is locally abundant in the embryonic genital skin of both females and males (Wilson et al., 1981). If unusually high concentrations of androgens are available to a female fetus, they are converted to DHT in the genital skin,

3.8 Normal development of the external genitalia proceeds along a single masculinization–feminization continuum. Because there is a single anlage for female and male external genitalia, the development of one type of genitalia precludes the development of the other.

and the deve
genitally lacl
genitalia anc
lack 5α-redu
development

Anomalou

The process
(MacLaughli

Chromosomal

SRY

Testis determir
factor?

Gonadal
differentiation

Gonadal
development

Local testoster
secreted?

Wolffian duct
development?

Müllerian
inhibitory horr

Development c
uterus and fall
tubes?

Blood-borne
testosterone?

5α-reductase ir
genital skin?

External genita

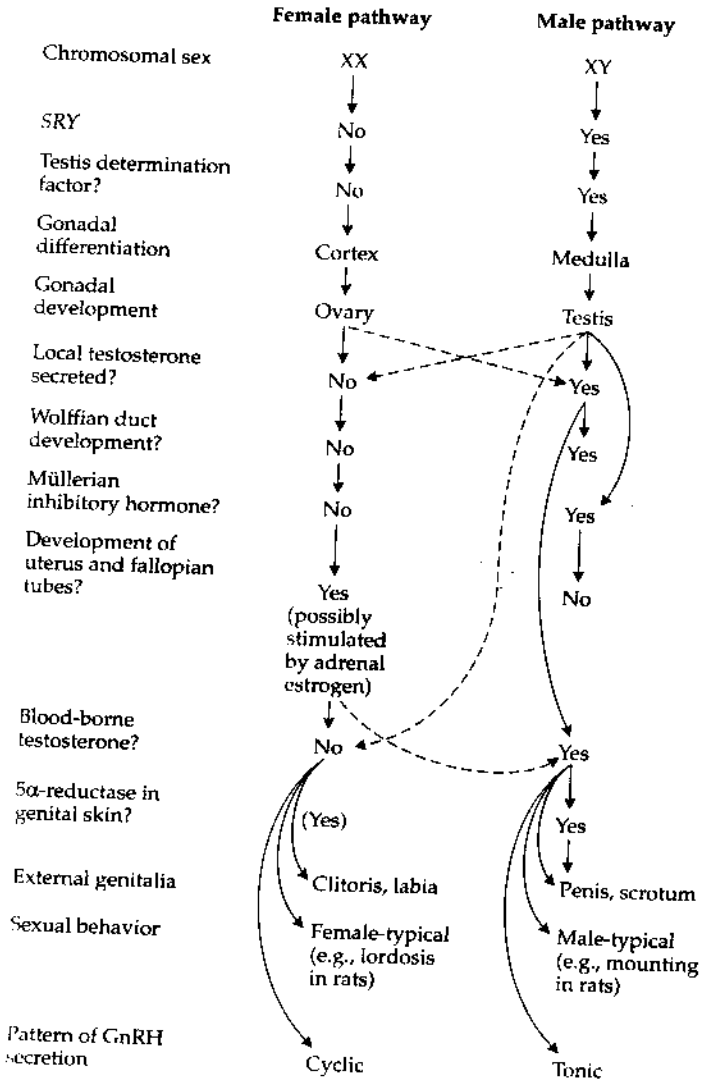
Sexual behavio

Pattern of GnR
secretion

and the development of male-typical external genitalia proceeds. Males that congenitally lack 5α-reductase undergo incomplete differentiation of the external genitalia and may be considered female at birth (see Figure 3.13). Females that lack 5α-reductase suffer no grave consequences, because normal female genital development occurs in the absence of sex steroid hormones.

Anomalous Mammalian Sexual Differentiation

The process of mammalian sexual differentiation is summarized in Figure 3.9 (MacLaughlin and Donahoe, 2004). This process is complex, and as the case of



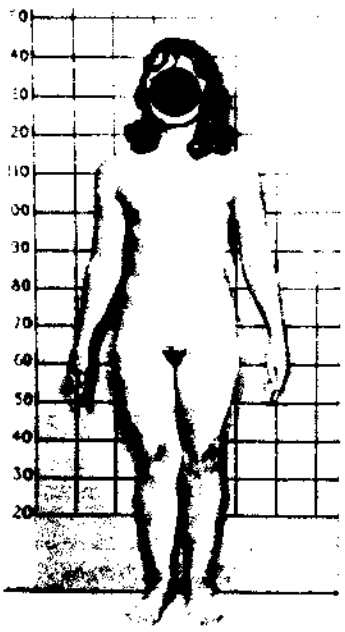
3.9 Sexual differentiation in humans is complex, and there are several stages where errors can occur. Chromosomal sex determination takes place when an egg is fertilized by a Y- or X-bearing sperm. The normal developmental pathways for females and males are indicated by the solid lines; common developmental errors are indicated by the dashed lines, which show where individuals can be "shunted" onto the developmental pathway of the opposite chromosomal sex.

5α-reductase deficiency shows, the potential for error is present. People and nonhuman animals that have undergone such anomalous sexual differentiation are of interest to behavioral endocrinologists because they can serve as "experiments of nature," and, as such, they can provide important information about the workings of the normal process of sexual differentiation.

Errors in sexual differentiation have been recognized by humans since early in their history. One very old idea was that male babies came from the right testis and females came from the left. **Hermaphrodites**, individuals who possess both ovaries and testes, were thought to arise when both testes simultaneously contributed to the offspring. All human babies born with ambiguous genital development used to be called hermaphrodites (Ellis, 1945), but they are now considered to be **pseudohermaphrodites**, because only one set of gonads is usually present. True hermaphrodites, with two sets of gonads, are extremely rare.

ANOMALIES IN FEMALES The female organization is basic among mammals. Because females are the so-called "neutral" or "default" sex, neither ovaries nor hormones are necessary for female development of the body prior to puberty. It is becoming increasingly clear, however, that low concentrations of estrogens are critical for normal female development of the brain (Döhler and Hancke, 1978; Döhler et al., 1982; Toran-Allerand, 1984). It has been hypothesized that females are the ancestral sex and that males are the derived sex (Crews, 1993).

One out of every 3000 live births in humans exhibits **Turner syndrome**, characterized by a congenital lack of, or damage to, the second X (or a Y) chromosome (XO) (Figure 3.10; Zinn et al., 1993). Individuals with Turner syndrome are unambiguously sexed as girls at birth. The gonads rarely develop completely, but they are clearly recognizable as ovaries. The dysgenic ovaries fail to produce steroid hormones, however, so girls with Turner syndrome must be treated with sex steroid hormones in their mid-teens to induce puberty. The consequences of missing a second sex chromosome are widespread and are not limited to sexual differentiation. Additional endocrine problems associated with Turner syndrome are reflected in the slow growth rates of afflicted girls. Both neural and non-neural tissues are also affected; hearing loss and mental retardation, as well as kidney dysfunction and webbing of the neck, are observed in some indi-



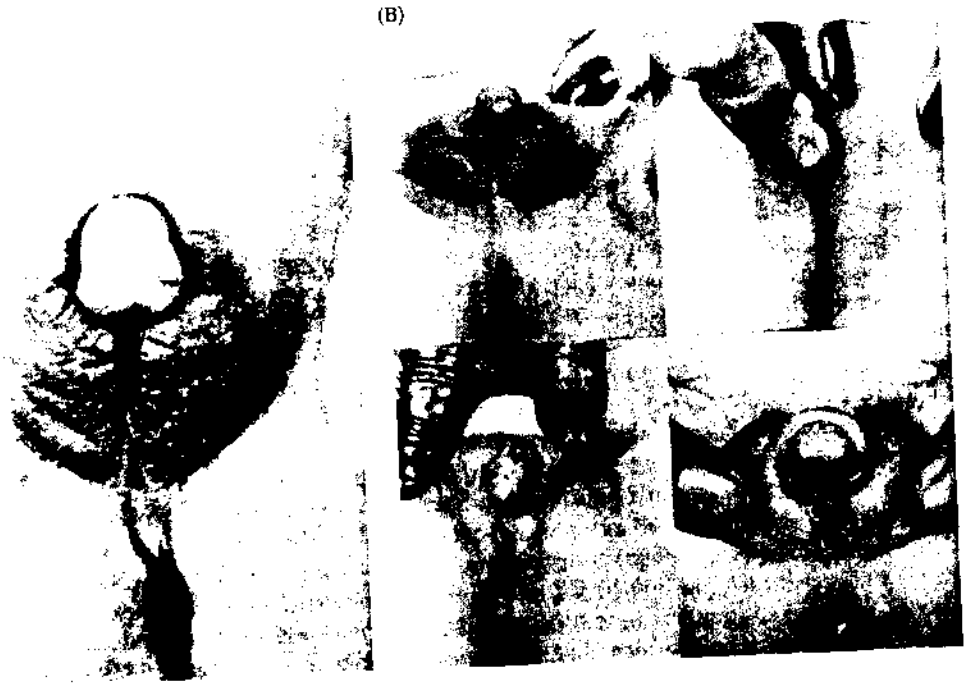
3.10 Turner syndrome results from a congenital absence of one of the X chromosomes. Without hormone therapy, these individuals do not undergo puberty. This 21-year-old XO woman is shown prior to estrogen therapy. She exhibits the short stature associated with the syndrome; however, she does not display other possible symptoms of Turner syndrome, such as webbed skin on the neck. Courtesy of John Money.

viduals born with Turner syndrome. These individuals are of interest to behavioral endocrinologists because they are not exposed to steroid hormones prenatally or postnatally until the age of 16 or 17, when exogenous hormonal treatments begin.

Recently, an intriguing study was conducted that examined the role of gene imprinting on behavior in girls with Turner syndrome. Because females normally inherit one X chromosome from their mother and another X chromosome from their father, one of the X chromosomes in each cell is usually disabled so that normal transcription can occur. The process of inactivating either maternal or paternal genes is called **gene imprinting**. Girls with Turner syndrome have only a single X chromosome, which is either maternal (X^m) or paternal (X^p). X^mO girls tend to suffer from neurodevelopmental disorders of social cognition (e.g., autism) more than X^pO girls (Skuse et al., 1997). Because the X chromosome of all males necessarily comes from the mother, these results suggest that the vulnerability of males to cognition and social adjustment problems is not necessarily due to the presence of specific genes on the Y chromosome, but could rather be due to genes on the maternal X chromosome (which presumably act independently of sex steroid hormones). Alternatively, it is possible that pieces of the Y chromosome might be expressed in neural tissue to cause these behavioral difficulties, because many individuals with Turner syndrome are so-called genetic mosaics (Henn and Zang, 1997), possessing cells with differing genetic contents. This issue will probably go unresolved for some time because it is virtually impossible to observe the chromosomal makeup of brain cells in living people (Skuse and Jacobs, 1997).

The most common reason for anomalous sexual differentiation in human females is prenatal exposure to androgens, either from exogenous or endogenous sources. Exogenous androgen exposure, or other steroid hormones that activate androgen receptors, most commonly occurs during treatment of the pregnant mother with steroid hormones to maintain the pregnancy. Exposure to the artificial steroid hormones diethylstilbestrol (DES) and medroxyprogesterone acetate (MPA), for instance, often causes masculinization of reproductive function and subsequent behavior in the exposed children (see Chapter 4). Endogenous androgens are most likely to come from one of two sources: the ovaries or the adrenal glands. For example, both males and females afflicted with **congenital adrenal hyperplasia (CAH)** possess fetal adrenal glands that produce high concentrations of androgens instead of cortisol. CAH does not cause sexual development problems in genetic males, but results in moderate to severe masculinization of the genitalia in afflicted females (Figure 3.11). The clitoris can be enlarged into a penis-sized structure, and the labia majora may be fused into a scrotum-like organ. The anomalous genitalia can be corrected at birth by surgery, and the endocrine disorder can be treated by lifelong cortisol treatments.

ANOMALIES IN MALES There are more steps that require physiological intervention in male than in female sexual differentiation, and consequently, more clinical problems in male sexual development can occur. For example, some XY individuals look and act like males throughout their lives, but during surgery for abdominal cramps, a uterus and small fallopian tubes are discovered. These indi-



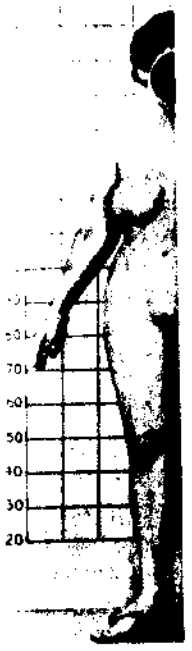
3.11 Partial masculinization of the external genitalia in genetic females can be caused by prenatal exposure to sufficient progestins to activate androgen receptors or by congenital adrenal hyperplasia (CAH). (A) The mother of this individual was treated with progestins to prevent miscarriage after suffering symptoms of premature labor. Note the enlarged clitoris and fusing of the vaginal labia majora. (B) Congenital adrenal hyperplasia, a condition in which the adrenal glands secrete high levels of androgens, can cause varying degrees of masculinization of the external genitalia in genetic females, including clitoral enlargement and fusing of the urethral groove. Courtesy of John Money.

viduals lack either Müllerian inhibitory hormone or the receptors that respond to this hormone; all other components of their sexual differentiation are male-typical. This sort of error in sexual differentiation does not have important consequences for male behavior, but in other cases anomalous sexual differentiation produces dramatic behavioral effects.

Anomalous sexual differentiation occurs in XY individuals afflicted with a condition known as **testicular feminization mutation (TFM)** in rodents and as **androgen insensitivity syndrome (AIS)** in humans. AIS can be complete (CAIS) or partial (PAIS). The tissues of individuals with CAIS do not possess functional androgen receptors. A genetic mutation on the X chromosome involving a single base pair substitution in the gene for the androgen receptor causes this insensitivity to androgens in rats (Yarbrough et al., 1990). In humans, there are several mutations that cause androgen insensitivity (Brinkmann et al., 1996). Genetic XX females

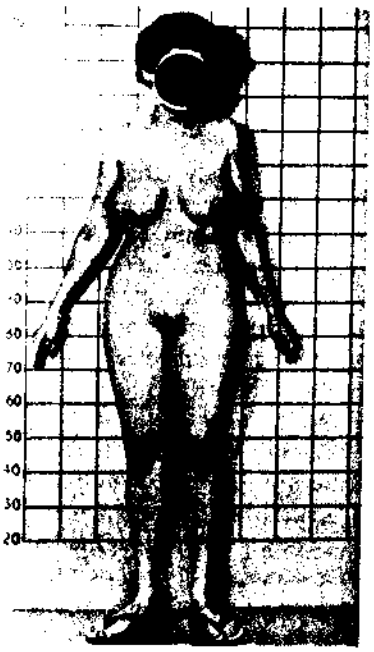
with such mut
for androgen r
because a Y chr
opment proce
secretion. The t
regression of th
stimulated to
with CAIS hav
sexed and rear
when menstru
reduced in leng
these individua
sterile. The test
ed, although th
received it. Ger
shapes and reg
(Figure 3.12).

Behavioral
ic defect has be
cattle, and chim
logical mechan
for, and normal



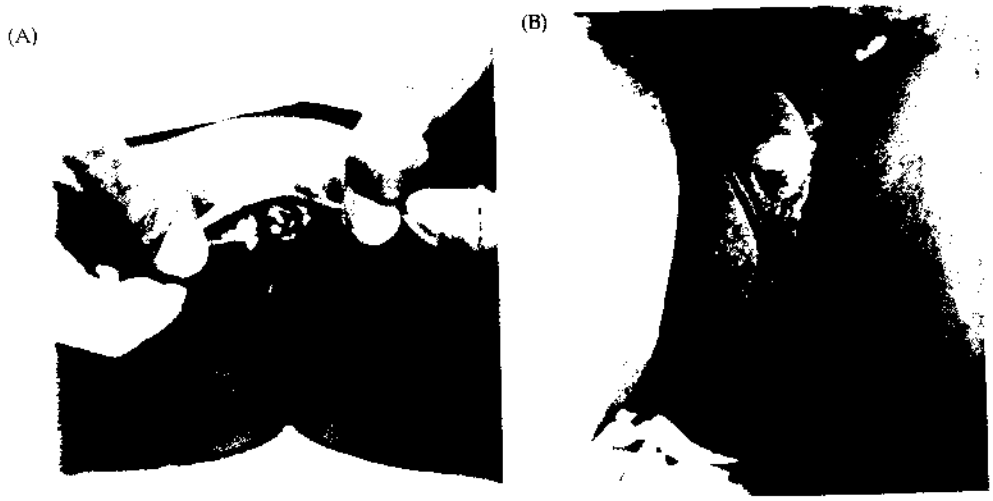
with such mutations have a second X chromosome that contains the normal gene for androgen receptors, so they suffer no ill effects. However, in genetic XY males, because a Y chromosome is present, the *SRY* gene is activated, and testicular development proceeds, accompanied by significant prenatal and postnatal androgen secretion. The testes also produce Müllerian inhibitory hormone, which causes the regression of the Müllerian duct system. However, the Wolffian duct system is not stimulated to develop, even in the presence of androgens. XY individuals born with CAIS have perfectly normal-appearing female external genitalia and are sexed and reared as girls. The condition is usually discovered during adolescence when menstruation fails to occur. Upon examination, the vagina is found to be reduced in length (blind vagina). Because the Müllerian ducts failed to develop in these individuals, there are no uteri or fallopian tubes, and unfortunately, they are sterile. The testes are usually removed surgically and estrogen treatment provided, although this treatment has been questioned by some individuals who have received it. Genetic male XY individuals with CAIS display normal female body shapes and regard themselves unequivocally as female (Wisniewski et al., 2000) (Figure 3.12).

Behavioral endocrinologists are interested in CAIS (TFM) because this genetic defect has been discovered in several nonhuman species, including rats, mice, cattle, and chimpanzees (Olsen, 1992), allowing experimental study of its physiological mechanisms. In addition, individuals with CAIS have normal receptors for, and normal concentrations of, the nonandrogenic hormones (such as estrogens) involved in sexual differentiation, and thus provide researchers with the ability to separate the contributions of these hormones from those of androgens to typical behavioral sexual differentiation.



As noted above, another genetic dysfunction that leads to anomalous sexual differentiation is 5α-reductase deficiency. Genetic males (XY) with 5α-reductase deficiency are born with ambiguous genitalia and small, undescended testes. They are usually considered females at birth and

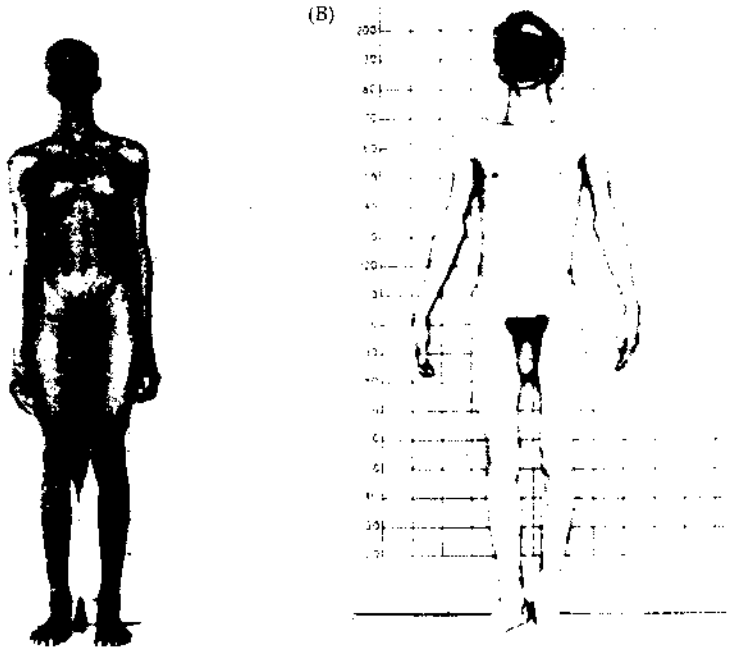
3.12 Complete androgen insensitivity syndrome (CAIS) is a condition caused by an absence of functional androgen receptors in genetic male (XY) individuals. Because individuals with CAIS completely lack androgen receptors, development of secondary sexual characteristics at puberty proceeds in a feminine direction. Although individuals with CAIS exhibit a normal female body morphology, the gonads are testes, and the accessory sex organs do not develop normally, resulting in sterility. Individuals may also display partial androgen insensitivity syndrome (PAIS). Courtesy of John Money.



3.13 5α-reductase deficiency. (A) A lack of 5α-reductase, which converts testosterone into DHT, results in incomplete genital masculinization at birth. Note the incomplete fusing of the urogenital groove, the lack of penile development, and the presence of hypospadias, the opening of the urethra on the underside of the penis. Most individuals with 5α-reductase deficiency are sexed as girls at birth. (B) The same individual at puberty. Although DHT is still not present, high blood concentrations of other androgens at puberty can activate DHT receptors and cause delayed and partial masculinization of the external genitalia. Despite pubertal penile development, hypospadias remains, which contributes to infertility. Because these androgen-induced changes in the external genitalia are accompanied by a change to a male-typical body type, some individuals with 5α-reductase deficiency who have been raised as females may take on a male gender identity and gender role at puberty. Courtesy of Julianne Imperato-McGinley.

reared as females. At puberty, testosterone masculinizes the body, which develops male-typical musculature and axillary hair growth, and the genitalia develop to resemble a male-typical penis and scrotum (Figure 3.13). The urethra usually opens at the base of the penis; this condition, called **hypospadias**, substantially reduces fertility. Because these individuals are exposed to male-typical hormones pre- and postnatally, but are typically reared as females until puberty, behavioral endocrinologists have studied them in order to understand the contribution of hormones versus rearing to human behavioral sexual differentiation (see Chapter 4).

TRISOMIC ANOMALIES Occasionally, babies are born with extra chromosomes. Approximately one infant in every 600 live births is born with **Klinefelter syndrome** (Figure 3.14A; Nielsen and Wohlert, 1990). These individuals possess an extra X chromosome (XXY). The presence of the Y chromosome is sufficient for the *SRY* gene to be activated and masculinization to occur, and these individuals are sexed as males at birth. Although the testes develop sufficiently to cause masculinization, these individuals are usually sterile because of reduced sperm pro-



3.14 **Trisomic genetic anomalies.** (A) This 18-year-old XXY male shows the underdeveloped external genitalia, gynecomastia (breast development), and disproportionately long limbs characteristic of Klinefelter syndrome. (B) This young adult male with the XYY genotype is well over 2 meters tall. Like those with Klinefelter syndrome, XYY individuals are usually sterile. Other characteristic traits of the syndrome are above-average height and below-average intelligence. Courtesy of John Money.

dysfunction. Learning disabilities are also commonly observed among individuals with Klinefelter syndrome.

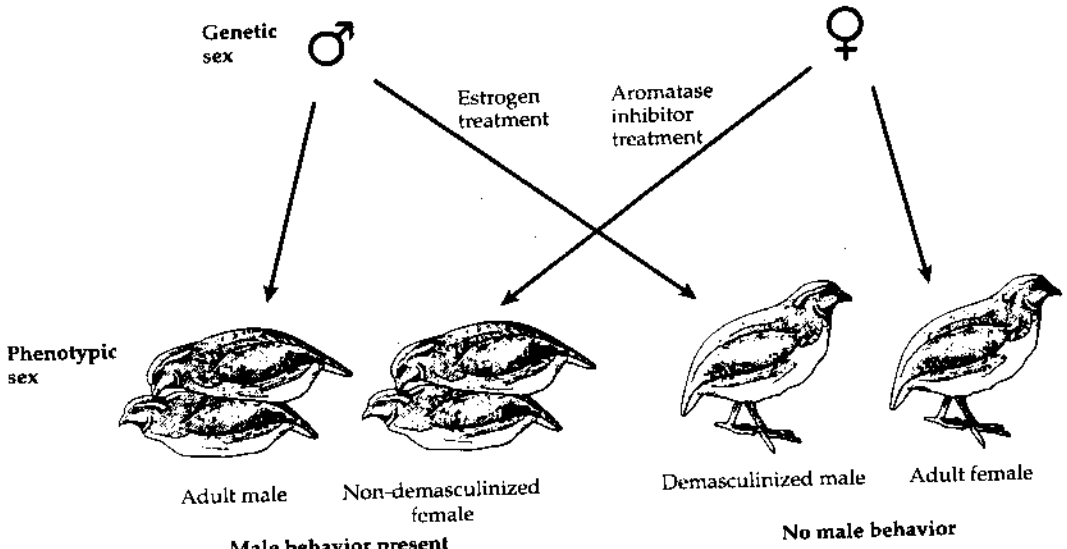
Approximately one infant in every 850 live births possesses an XYY genotype (Figure 3.14B; Nielsen and Wohlert, 1990). These individuals are considered male at birth, but in common with XXY individuals, XYY men may be sterile. The XYY genotype was once thought to result in increased aggressiveness because a survey of prison populations revealed that a disproportionately large number of these individuals were represented (Hook, 1973; Jacobs et al., 1965). It was proposed that the Y chromosome was responsible for aggressiveness in normal males; therefore, it was hypothesized that individuals with two Y chromosomes displayed increased aggression, which led to their imprisonment. Further analyses revealed that individuals with XYY genotypes were not necessarily more aggressive than XY males, but that they possessed two other traits that increased the likelihood of criminal prosecution: they were less intelligent than average and they were much taller than average. Thus, these individuals may not engage in

more criminal activities than average, but apparently they tend to be apprehended more readily (Witkin et al., 1976).

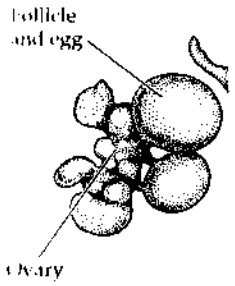
In sum, possession of a single Y chromosome sets off a chain reaction that leads to the differentiation of the testes. Hormonal secretions from the testes lead to masculinization and defeminization. In the absence of these hormonal events, feminization and demasculinization occur. In the following sections, the similarities and differences in the process of sexual differentiation among mammals, birds, and other animals will be presented.

Avian Sexual Differentiation

Studies of nonmammalian species offer intriguing insights into our own species by demonstrating alternative solutions to common problems of adaptation. The process of avian sexual differentiation is similar to that in mammals, but with several interesting differences. Among birds, females are the heterogametic sex (WZ), whereas males are the homogametic sex (ZZ). In the case of copulatory behavior, males are the default sex: in the absence of gonadal secretions, the masculine developmental track is followed, and the feminine pattern of development is attained by active hormonal secretion (Figure 3.15; Balthazart and Adkins-Regan



3.15 Development of female copulatory behavior requires active hormonal secretion. The genetic sex of birds in the egg is either male or female. If only the presence or absence of male copulatory behavior is considered, then males generally show masculine patterns and females generally show feminine patterns of copulatory behavior. If estrogen is given to a genetic male bird in the egg, he is demasculinized. If a genetic female bird is given an aromatase inhibitor in the egg, preventing the formation of estrogens, she is not demasculinized, and shows male copulatory behavior as an adult. After Balthazart and Ball, 1995.



1.16 Ovary and oviduct