Deciphering the Genetic Language of Sex
David C. Page, M.D.

http://www.hhmi.org/biointeractive/gender/index.html

"It's a boy!" "It's a girl!" shout the banners and balloons that usually herald the arrival of a new baby. They're expressions of welcome and joy, but what do these exclamations really tell us? Just what is a male? What is a female? The questions may seem stunningly simple, but they're actually rather complex. Sex, it turns out, can be defined on a number of different levels, from anatomical to psychological. So before we can discuss-or study scientifically—how we come to be one sex or the other, we need to think more carefully about what we mean by male and female. Examining the distinctions will lead us to the heart of sex determination.

First and foremost, males and females sport obvious differences in external genitalia-penis versus clitoris, for one. Taking note of anatomy is a time-honored method for telling male from female: it's the way an obstetrician traditionally determines the sex of a newborn baby.

Of course there's more to sex than external anatomy. Men and women have different gonads, testes, or ovaries, and produce different gametes, sperm versus eggs. Even their chromosomal complement is different: Females have two X chromosomes, and males have an X and a Y.

How do these differences arise? In one sense, the sex of a baby is determined at the moment of conception. The egg, which always carries an X chromosome, will either be fertilized by a sperm bearing another X-generating a female—or a sperm bearing a Y-generating a male. Other than that single chromosome difference, human male embryos and female embryos are identical until the seventh week of development. At that point, a sex-determining gene on the Y chromosome—if it's present—sets in motion a cascade of biological activity that results in the development of a male. This genetic trigger directs the bipotential gonad—the primitive tissue from which both male and female sex organs derive—to turn into testes rather than ovaries. The testes then produce the hormones, including testosterone, that prompt the development of all other male-specific characteristics, including the external genitalia and, later, secondary characteristics such as facial hair and a deep voice. In the absence of a Y chromosome, the embryo will develop female structures.

But the process is not flawless. Once in a while, an XY embryo will develop as a female, complete with ovarian tissue instead of testes; likewise, an XX embryo will sometimes develop as a male. Such sex-reversed individuals, unaware of the chromosomal mismatch, often show up at the clinic when they experience problems with infertility. As it turns out, most XX males actually harbor a small piece of the Y chromosome, which has gotten stuck onto the end of one of their Xs; and some XY females are missing the corresponding small fragment from the tip of their Y.

This discovery suggested to researchers that the part of the Y chromosome that directs the development of a male lies in that small region, which is lost or gained in sex-reversed individuals. A genetic manhunt subsequently turned up SRY (sex determining region Y), the gene that acts as the master switch controlling male development in all mammals, including humans.

Why sex chromosomes evolved is still a mystery. Many reptiles, including alligators and certain turtles, develop as male or female depending on the environment. Their sex is determined by the ambient, or surrounding, temperature. Such a system might seem simpler than maintaining special sex chromosomes, but it, too, has its shortcomings. Perhaps some years the climate will foster the development of many more males than females. Such a situation could hinder reproduction and survival of the species. At least sex chromosomes help to keep the sex ratios relatively stable-two chromosomes, two sexes, usually present in about a 50:50 split.

That raises another interesting question: Why do we need two sexes in the first place? Seems a bit of a waste, really. What if there were only one sex, and each one of those individuals could reproduce an exact replica of itself? In that case, if the population needed to expand in a hurry, every single individual could produce a clone—or a handful of clones. In a way, having two sexes—only one of which can bear young—cuts the reproductive capability of a population in half. So why have males at all?
Further, why have sex at all? One oft-cited benefit of sexual reproduction is that it allows a population to be adaptable, as it promotes the generation of new combinations of genes. But what are the costs—to the organism and to the species? Do the benefits of sex really outweigh the costs? These seemingly simple questions remain hotly debated and enthusiastically explored.

Key Concepts

- Most animals come in two readily distinguishable forms, a property called sexual dimorphism. In mammals, including humans, these two sexes are male and female.
- The sex of an individual can be classified on a number of levels, taking into account, for example, external and internal anatomy, chromosomal makeup, and the type of gametes he or she produces.
- Generally speaking, the male comes equipped with a penis, scrotum, and testes; he produces sperm and has both an X and a Y chromosome. The female, on the other hand, has a clitoris, labia, and ovaries; she makes eggs and has two X chromosomes.
- Aside from the chromosomal differences, in humans male and female embryos are identical until the seventh week of development.
- Sexual differentiation begins when a sex-determining gene on the Y chromosome directs the bipotential gonad-the primitive tissue from which both male and female sex organs derive—to turn into testes rather than ovaries.
- Hormones produced by the testes or ovaries subsequently shape the development of other sexually dimorphic structures, including the external genitalia, and, eventually, the secondary characteristics—facial hair for males, breasts for females.
- In the absence of a Y chromosome, the embryo will develop female structures.

- The process of sexual differentiation is disrupted in sex-reversed individuals, people whose outward appearance contradicts their genetic makeup. One in 20,000 males lacks a Y chromosome; these XX males are genetically female but have a penis and testes. Similarly, one in 20,000 females has a Y chromosome; these XY females are genetically male but have ovaries and appear to be female.
- Study of such sex-reversed individuals led researchers to discover the part of the Y chromosome that directs male development. Most XX males, it turns out, harbor a tiny piece of the Y chromosome—inherited from their fathers—stuck on the end of one of their Xs. And some XY females are missing this same small piece from their Y.
- Genetic dissection of that fragment of the Y chromosome led to the identification of SRY (sex determining region Y), the gene that acts as the master switch controlling male development in all mammals, including humans.
- Why the sex chromosomes evolved is still something of a mystery. Reptiles, including alligators and turtles, have no sex chromosomes and rely instead on ambient temperature to dictate the sex of their offspring.
- Although all mammals come in two sexes, the benefits of this arrangement remain arguable. Why we have sex—and why we need two sexes—are topics that continue to be debated and explored.