

Is transgender identity inherited?

March 3 2017, by Ricki Lewis, Phd



The recent return of the ["which bathroom?" issue](#) regarding transgender individuals' use of public restrooms has made me think about how I've handled sex and gender in my [human genetics textbook](#). Over the editions, the two topics have diverged. And that's at the crux of misunderstanding.

Sex and gender through the editions

When I wrote the first edition in 1993, coverage of the X and Y

chromosomes that make us female or male (sex determination) was squished into a chapter on genetic linkage. I didn't mention [gender identity](#) at all.

By the second edition, "Matters of Sex" was its own chapter, starting with a table called "Sexual Identity." The last entry was "gender identity," defined as "Strong feelings of being male or female, from childhood."

In early 1998, while writing the third edition, I read John Colapinto's unforgettable article in Rolling Stone (summarized by Colapinto here) about David Reimer (1965-2004). After David's penis was removed following a botched circumcision, his parents were pressured into raising him as a girl, and the infant underwent the first "sex reassignment" surgery performed on an anatomically normal individual. It's a complex tale. The physician regarded David (then named Brenda) as part of a science experiment of sorts by comparing her to his identical twin Brian.

Brenda/David, however, always knew he was a he, preferring boys' games and attire, even peeing standing up without knowing why. When a psychiatrist finally told him of his beginnings at age 14, David sought surgery to return to his male origin.

With David's help, Colapinto published ["As Nature Made Him: The Boy Who Was Raised As A Girl"](#) in 2000. About that time, I wrote an article, "Reevaluating Sex Reassignment", for [The Scientist](#), concluding from interviewing experts that "Both clinical trials and case reports powerfully argue for nature over nurture in establishing gender identity." On the surface, that statement could mean that a baby with a penis becomes a man and a baby with a vagina becomes a woman, no matter what. But it also argues for the power of knowing one's gender, whether one has the corresponding anatomy or not.

David Reimer's sad story entered my textbook with the third edition. The next leap in my coverage of gender happened after I met [Jennifer Finney Boylan](#), who was born James.

My daughter Heather and I met Jennifer at a bookstore in 2003, just before publication of Jennifer's book [She's Not There: A Life in Two Genders](#). Today she's an outspoken transgender author who predicted in a *New York Times* op-ed just after the election that the new president would throw out President Obama's protection of the right of transgender students to use school bathrooms matching their gender identity. Sadly she was right, even though just last April candidate Trump said that people should ["use the bathroom they feel is appropriate."](#)

At the bookstore all those years ago, Jennifer stayed afterwards to talk with Heather, who was at the time contemplating her future career as a social worker. Jennifer's bravery and kindness impressed both of us. No one would go through what she did for something trivial, for just a feeling.

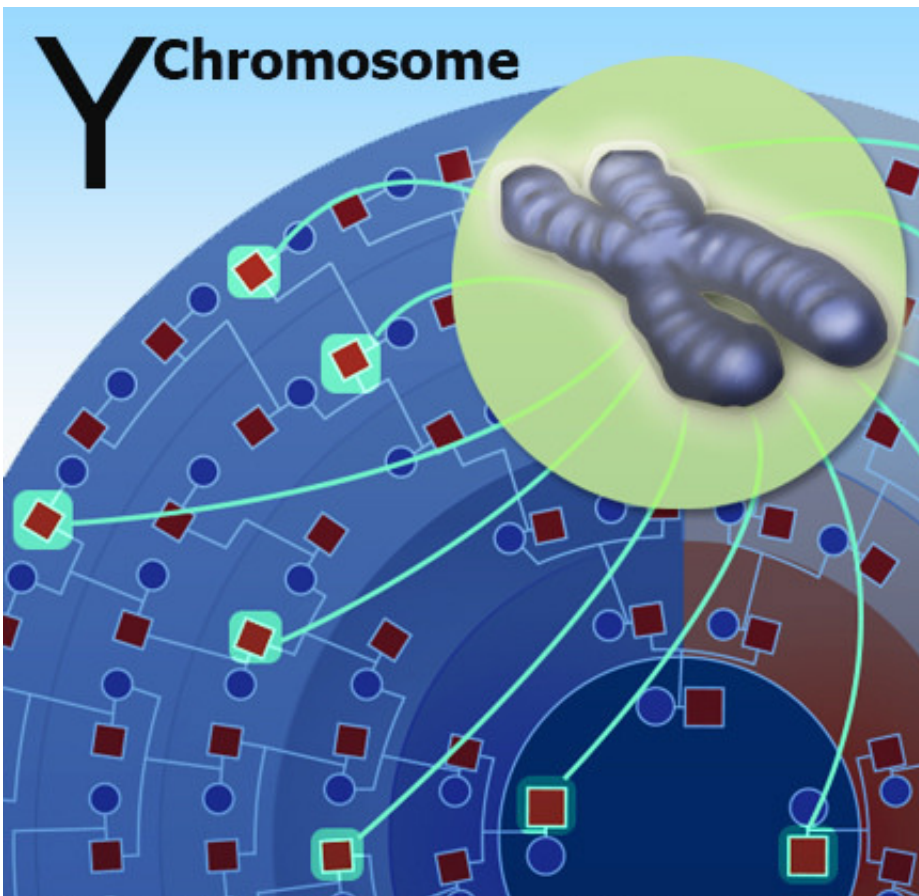
So my next textbook edition included this paragraph:

"Transgender is a poorly understood condition related to [sexual identity](#). A transgendered individual has the phenotype and sex chromosomes of one gender, but identifies extremely strongly with the opposite gender. It is a much more profound condition than transvestitism, which refers to a male who prefers women's clothing. The genetic or physical basis of transgender is not known. Some affected individuals have surgery to better match their physical selves with the gender that they feel certain they are."

It was a start. I should have replaced "feel" with "are." To my astonishment, when drafts of that edition were reviewed, instructors

asked that the paragraph be removed, because they felt identifying as transgender had nothing to do with genetics.

I refused. We can't say a characteristic isn't genetic just because we don't yet have any evidence. But in the next few editions, I fielded the same request, and again ignored it. Writing a textbook brings an authority beyond a mere article or blog post, and I wanted people wondering about the role of genetics in transgender identities, and taking a course in human genetics to at least find a definition in their textbook.



Meanwhile, I started to wonder if certain genotypes in some way contribute to the overwhelming sense that gender doesn't match genes, chromosomes, or gonads.

Here's what we know: Bio 101

Sex is set, or "determined," when an X chromosome from an egg finds itself in a nucleus with an X or a Y from a sperm. XX=female:
XY=male.

For six weeks, the embryo unfurls two sets of "indifferent" gonads, with two sets of plumbing. At week 6, a gene on the Y called SRY, for "sex determining region of the Y," turns on and the fledgling female parts shrivel away. Without SRY, and under guidance of other genes, the male structures vanish instead. So anatomically we all start out with a bit of both.

Mess with the genes and chromosomes behind our sexuality, and mismatches arise. A mutation in a gene called Wnt4, for example, disables the switch to femaleness, and an XX embryo drowns in testosterone. Vagina, cervix, and uterus never develop. In fact, SRY was [discovered](#) in people who looked female but were XYs missing SRY, and people who looked male but were XXs with an SRY gene plunked onto one of the X's. Another type of female with XY chromosomes has [androgen insensitivity syndrome](#), lacking receptors on cells that bind testosterone, cutting off the hormonal signals necessary for maleness. Several historical figures supposedly had this condition.

Most fascinating is 5-alpha reductase deficiency, in which life begins as a girl, based on appearance. The enzyme to convert testosterone into the form needed to sculpt a penis isn't there, and so external male structures don't develop early on, although interior structures are male. At puberty, the adrenal glands release testosterone, as they normally do, and then the

voice deepens, facial hair grows, muscles become leaner, and instead of developing breasts and menstruating, the clitoris swells into a penis and sperm are produced.

In the Dominican Republic, where 5-alpha reductase deficiency is more common due to relatives marrying relatives awhile back, these special adolescents are given their own gender name— guevedoces, for "penis at age 12" – and are fully accepted as whatever they want to be. Most become fertile males. Discovery of the fact that guevedoces have small prostates led to development of the drug [finasteride](#), which inhibits 5-alpha reductase and is used to treat enlarged prostate. The Pulitzer-prize-winning novel [Middlesex](#), by Jeffrey Eugenides, tells the story of a young man with the condition. It's one of my all-time favorite books.

So the X and Y chromosomes determine sex, unless a single-gene mutation intervenes and then they don't. Could gene variants, perhaps specific sets of them, somehow set the stage for the gestation of a transgender individual? For the upcoming twelfth edition of my textbook, I took a look.

Scant evidence for transgender genes

A genome-wide association study (GWAS) might be the way to go to identify genes that have variants that affect gender identity. Scan the genomes of a few hundred or thousand transgender individuals and a similar number of controls, perhaps their cisgender siblings, for a few million SNPs (single nucleotide polymorphisms; places in the genome where a DNA base varies in a population). Identify gene variants shared only among the trans. Then look in those genome regions for genes whose functions make sense – this might be more objective than rounding up the usual suspects, such as hormone receptors and enzymes needed to synthesize steroids.

Here's what I found:

23andme indeed conducted a GWAS in 2005, but on [sexual orientation](#) — hetero, homo, and bi. Not the same thing.

A 2008 study found a SNP in [CYP17](#), making it a "candidate" gene for transgender individuals. Trans men were more likely to have the variant than cis women. The gene controls sex hormone production.

A just-completed [clinical trial](#) ruled out the 5-alpha reductase penis-at-12 gene (SRD5A2) as a candidate.

That's it. Or at least all I could find. Although clinicaltrials.gov lists 58 studies under "transgender," nothing much comes up in the way of genetics. The closest was the "[exploration of the neovagina](#)" study to investigate ways to entice a [vaginal microbiome](#) to flourish in a surgically created organ.

A genomewide SNP screen, or even genome sequencing, might one day identify a genetic "signature" for individuals more likely to identify as transgender. Should we even go there? I don't think so. What good could it do? People who identify as [transgender](#) already know it — it's certain others who have a problem with it. And imagine new parents of a girl told she will identify as a boy, or vice versa. What would they do? I'd say just wait and see. Let it be.

I'm not a psychologist and clearly out of my depth when matters get beyond genes and [chromosomes](#). Comments welcome! (Are any other nerds glad to hear cis and trans outside of the context of rotation around a double carbon bond or the orientation of allele pairs?)

More information: Teenus Paramel Jayaprakash et al. High Diversity and Variability in the Vaginal Microbiome in Women following Preterm

Premature Rupture of Membranes (PPROM): A Prospective Cohort Study, *PLOS ONE* (2016). [DOI: 10.1371/journal.pone.0166794](https://doi.org/10.1371/journal.pone.0166794)

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