

Defining Male And Female -- Research Casts Further Doubt On Newborn Sex-assignment Surgeries

ScienceDaily (Feb. 28, 2005) — WASHINGTON, DC -- Gender, often said to depend solely upon anatomy or hormones, may depend also on hard-wired genetics, according to new research that could help doctors and lawyers better understand the one in 4,000 babies born with both male and female traits.

"The biology of gender is far more complicated than XX or XY chromosomes and may rely more on the brain's very early development than we ever imagined," researcher Eric Vilain, M.D., reported today at the American Association for the Advancement of Science (AAAS) Annual Meeting in Washington, D.C.

"Surgical sex assignment of newborns with no capacity to consent should never be performed for cosmetic reasons, in my opinion," said Vilain, an associate professor of human genetics who also serves as a chief of medical genetics and director of research in urology and sexual medicine within the David Geffen School of Medicine at the University of California, Los Angeles. "We simply don't know enough yet about gender to be making surgical or legal assumptions."

Another AAAS speaker, William G. Reiner, M.D., agreed. "The most important sex organ is the brain," said Reiner, a psychiatrist and associate professor in the Department of Urology, Oklahoma University Health Science Center. "We have to let these children tell us their gender at the appropriate time."

An estimated 1 in 4,000 to 1 in 5,000 babies may be classified as "gender ambiguous" because intersex conditions affecting their genitalia, reproductive systems or sex chromosomes make an immediate assessment impossible, Reiner explained.

Yet, many laws -- including U.S. marriage laws -- assume that everyone is clearly male or female, a concept known in legal circles as sexual dimorphism, or binary law, legal expert Susan Becker of the Cleveland State University explained at the AAAS Meeting. At the same time, children with ambiguous genitalia continue to undergo surgical sex assignment. Baby girls with a condition called congenital adrenal hyperplasia (CAH), for example, may undergo clitoroplasty to reduce male-looking anatomy, as well as vaginoplasty if the labia are fused together.

"The U.S. Constitution promises equality, rights and benefits for all citizens," Becker noted. "But, as the Constitution is structured and interpreted, individuals who do not meet the binary definition for male versus female don't have the same benefits and aren't completely protected from discrimination."

Children may be particularly vulnerable to negative consequences resulting from binary or gender-based laws, Becker added. If one partner in a same-sex union dies, for example, the surviving partner may face a legal battle to retain custody of the children, thus inflicting a second major trauma on the grieving children. A host of legal documents that convey rights and benefits, from birth certificates to passports and drivers' licenses, require declaration of one gender or the other, which may be impossible for some people.

Various conditions can cause genital ambiguity. For example, a condition called Congenital Adrenal Hyperplasia (CAH) in genetic girls (XX chromosomal makeup) results in prenatal exposure to androgen, the steroid that triggers male development. Genital features of girls born with CAH may appear to be male. In other cases, collectively known as Androgen Insensitivity Syndrome (AIS), genetic males (46 XY chromosomal makeup) may have female characteristics when a mutation of the gene that encodes for the androgen receptor results in resistance to androgen's masculinizing effects during development. Depending upon the timing of exposure to androgens in the uterus, a host of other conditions may result in ambiguous genitalia.

Through his clinical work with some 100 patients, Reiner said, those who are genetically male, with the 46 XY makeup, will tend to identify themselves as boys if they can react and respond to male hormone, and even if they are born without a penis, underwent surgical reassignment and were raised as girls. "These children know who they are," Reiner said. "It's encouraging that many more surgeons today are choosing to postpone surgical gender assignment until the patient is mature enough to take that step. Of course, social and legal gender assignment still must be carried out at birth."

Scientific evidence on gender is revealing an increasingly complex picture. For example, conventional wisdom has held that gonadal hormones dictate whether the brain becomes masculine or feminine during development.

But, even before hormonal influence, Vilain has reported, embryonic mouse brains show clear gender-specific differences. Building on his previous discovery, Vilain said, he and colleagues have since identified 54 genes that were differentially expressed in the brains of male and female embryonic mice just 10 days after conception, prior to hormonal exposure.

"Differences of gene expression between male and female brains, very early on, suggest that our brains may be hard-wired at a very early stage to become male or female," according to Vilain.

Biological differences have clear implications for laws related to sexually dimorphic traits, including sexual preferences, Vilain said. Understanding male versus female development also could help provide new clues to diseases such as autism, which occurs most often among males, or depression, an illness that is more common among females. In fact, Vilain said, his group already is investigating a specific region of the brain, the substantia nigra, which is damaged more often in men with Parkinson's disease.

Becker, the legal expert, said that straight-forward public discourse on gender will be essential for developing improved public policy: "In U.S. society, sex, sexuality and sex appeal is used to sell everything from toothpaste to cars," Becker commented. "It seems that we can handle sexual caricatures in the media and sexually explicit movies, but we aren't equipped to have open, honest discussions regarding sexuality and gender. The time has come to move beyond our discomfort to engage in more product dialogue, informed by the best possible scientific information."

Becker's sentiments were echoed by Rochelle Diamond of the National Organization of Gay and Lesbian Scientists and Technical Professionals, co-organizer of the AAAS session, with Mark Tumeo of Cleveland State University. "Policymakers, surgeons, parents and patients all need to know more about gender ambiguity from the scientists' viewpoint," she said.

The AAAS session also was expected to include Mara Keisling of the National Center for Transgender Equality; James P. McGovern of the U.S. House of Representatives (D-MA); and Stephanie J. Bird of Massachusetts Institute of Technology.

The session and related news briefing were held today in memory of David Reimer. A man raised as a girl after a botched circumcision, Reimer played a key role in raising public awareness of gender ambiguity. He took his life in May 2004 at the age of 38.

Adapted from materials provided by [American Association For The Advancement Of Science](http://www.aas.org).