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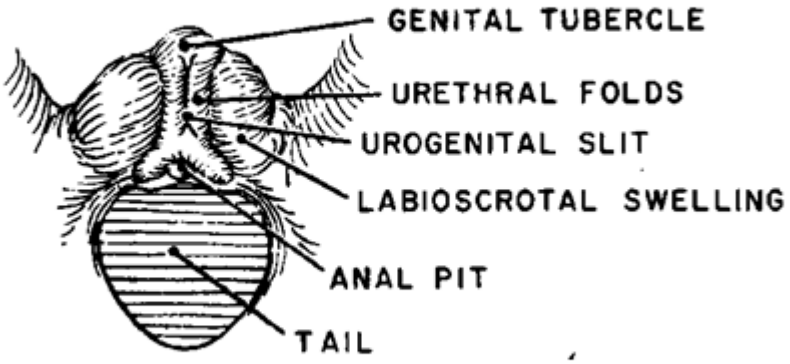
The Biological Basis of Gender



By William Patton, MD

Assembly Room, A. K. Smiley Public Library

SUMMARY: The Biological Basis of Gender

Bill Patton, MD

Sex, the presence of sexual organs allowing for sexual reproduction, is usually clearly male or female, and is generally determined at birth by inspection of the external genitals of the newborn. It is the result of a complex developmental sequence involving genetic sex, gonadal sex, and embryonic development of external and internal genital structures.

Gender, on the other hand, is a behavioral category, usually masculine or feminine, that reflects social and cultural norms and experience.

Gender identity, the deeply held innate personal sense of being male or female (or perhaps some alternative gender) is a result of genetic and epigenetic factors, cultural values and learning.

This paper reviews some of what is known and not known about how this all comes about. Embryonic development is detailed and the development of gender identity is described. Disorders of sexual organ development provide insights into the causes of gender dysphoria--distress experienced if gender identity and gender assignment are not congruent.

The fact that transgender issues and homosexuality have essentially nothing in common requires emphasis.

The options for resolution of gender dysphoria with development of a well-adjusted transgender person include family and societal support, suppression of puberty, sex hormone treatments, and surgical alteration of genital structures. All these involve issues of timing and risks.

Reproduction, contraception, military service, and athletic competition in transgender persons are discussed as well.

Bill Patton, MD

Bio information for Fortnightly Club meeting #1944

The Biological Basis of Gender

Born in Omaha in 1944 (today's Fortnightly Club meeting's "year"), where his father worked for Martin Aviation building B-29's during WWII.

Grew up in Merna, a central Nebraska town of 350, graduating from high school in 1961.

B.A. in Chemistry from Union College, Lincoln, Nebraska, 1965.

M.D. from Loma Linda University School of Medicine, 1969. Alpha Omega Alpha.

Internship in Internal Medicine and residency in Ob/Gyn, both at Loma Linda University, 1969 to 1973.

Fellowship in Reproductive Endocrinology and Infertility at Peter Bent Brigham Hospital, Harvard Medical School, Boston, 1973 to 1975.

Dual Board Certified in Ob/Gyn and Reproductive Endocrinology and Infertility.

Faculty member at Loma Linda University School of Medicine since 1973. Current rank, Professor of Ob/Gyn.

Served as Chief of Reproductive Endocrinology and Director of IVF for 15 years and Chairman of the department of Ob/Gyn for 6 years.

Retired from practice in 2010. Continues to teach medical students, residents, and faculty voluntarily one to two days a week.

Enjoys rowing, sailing, cycling, and astronomy.

Has lived in Redlands since 1975, where he and his wife, Julie, have raised two sons.

The Biological Basis of Gender

Bill Patton, MD

Introduction

Perhaps the best introduction to this topic is simply to define some terms.

Sex—sexual organs, usually male or female indicating the ability to reproduce sexually, generally determined at birth by inspection of the external genitalia.

Gender—Behavioral category, usually masculine or feminine, determined by culture; contains tasks, rules, and norms.

Gender expression—External manifestations of gender, name, pronouns, clothing, haircut, behavior, voice, body characteristics.

Gender identity—internal, intrinsic, deeply held sense of being male, female, or an alternative (boygirl, girlboy, transgender, gender queer, eunuch).

Gender incongruence—Gender identity or gender expression differs from what is typically associated with the assigned gender.

Gender dysphoria—Distress experienced if gender identity and gender assignment are not congruent.

Transgender male--a person who was assigned female sex early in life, but feels they are a male.

Cisgender male—a person who was assigned male sex and feels they are a male.

Transgender female—a person who was assigned male sex early in life, but feels they are a female.

Cisgender female—a person who was assigned female sex and feels they are a female.

Gender queer (non-binary)—Spectrum of gender identities that are not exclusively masculine or feminine. May have variety of sexual orientations, just as cisgender people do.

Questioning—Unsure of congruent gender and/or sexual orientation

Queer—Not heterosexual or not cisgender. (Perjorative term developed in the late 19th century used against those with same-sex desires or relationships).

LGBTQ…Lesbian, Gay, Bisexual, Transgender, Queer-- Includes two general categories--sexual orientation and gender identity which do not share the same genetic and environmental determinants. Three terms, LGB, pertain to sexual orientation to another person of the same sex or to both sexes. One term, T, pertains to gender identity, the self-described gender of an individual. One term, Q, pertains to persons who are not heterosexual and/or not cisgender, thus including both sexual orientation and gender identity. These groups are likely combined in the LGBTQ designation to unite groups of individuals in a common quest against the discrimination associated with both.

Sexual orientation—An individual's enduring physical and emotional sexual attraction to another person.

Homosexuality—Sexual orientation toward a person of the same sex or gender.

Heterosexuality—Sexual orientation toward a person of the opposite sex or gender.

Today's paper will attempt to clarify what is known and what is not known about sexual and gender development. I will leave sexual orientation to others, or perhaps to another paper.

Sexual Differentiation in the Embryo and Fetus

Genetic Sex

At the moment of fertilization, the potential mother's egg contributes one sex chromosome (always an X, but an X that may be inherited from her mother or her father), and the potential father's sperm contributes one sex chromosome (either an X inherited from his mother, or a Y inherited from his father).

Gonadal Sex

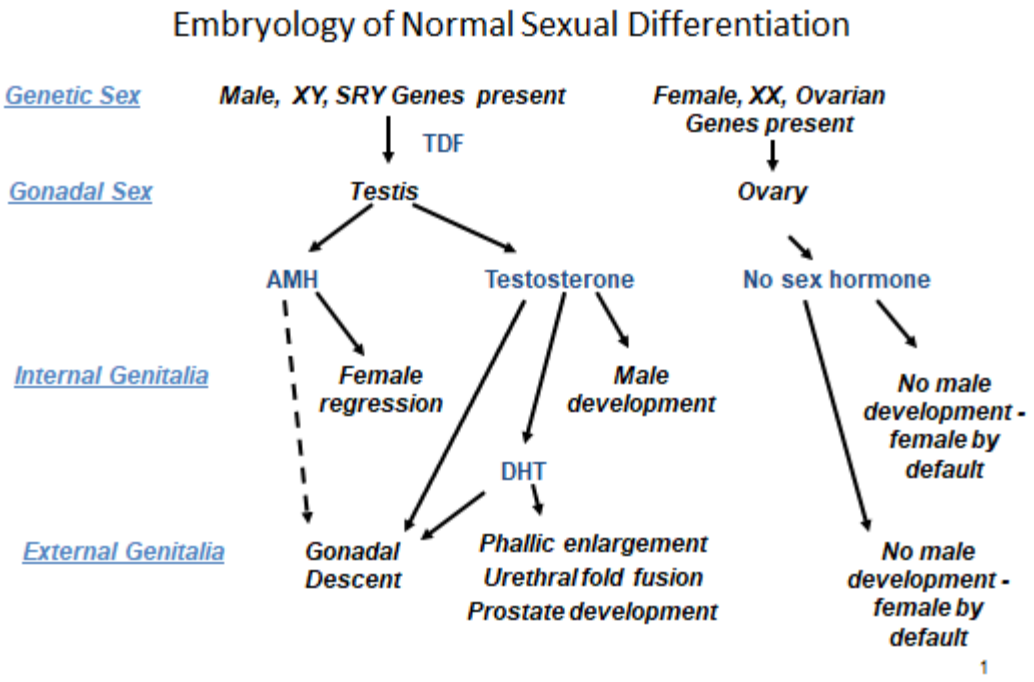
The Y chromosome contains a small region of genes called the SRY (Sex-determining Region of the Y chromosome). The expression of these genes (Testis Determining Factors, TDF's) results in the formation of fetal testes very early in embryonic life. If these genes are absent, the embryo will form ovaries if a full complement of ovarian determining genes on both X chromosomes are present, or undeveloped streak gonads if the genes are incomplete (such as XO, inheritance of only one X chromosome).

The fetal testes produce several hormones and proteins, but two are essential to the formation of a normal male fetus--testosterone (T) and Anti-Mullerian Hormone (AMH). The fetal ovaries don't appear to produce any hormones that are germane to sexual development.

If a normal Y chromosome is present, fetal testes will result and they will **actively** promote the formation of a male newborn. If a Y chromosome is not present, and fetal testes don't develop, the newborn will become female by **default**.

Development of the Internal Genitalia

The internal and external genitalia of the early embryo are indifferent, that is to say, they can differentiate to either male or female structures. The female internal genitalia are the Fallopian tubes, uterus, cervix, and the upper part of the vagina. The male internal genitalia are the duct systems that manufacture seminal fluid and convey sperm from the testes to the urethra.

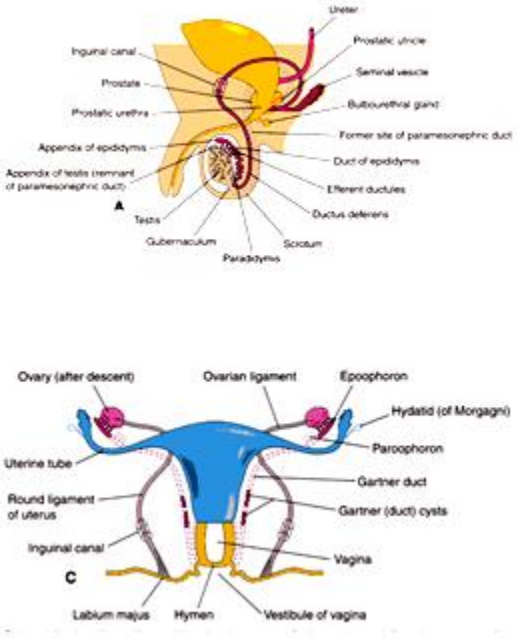


If a fetal testis is present, it will produce testosterone, which will cause the male structures to develop, and the Anti-Mullerian Hormone, which will cause the female structures to regress. If no fetal testis is present, regardless of whether an ovary is present or not, the female structures will develop— male by action, female by default.

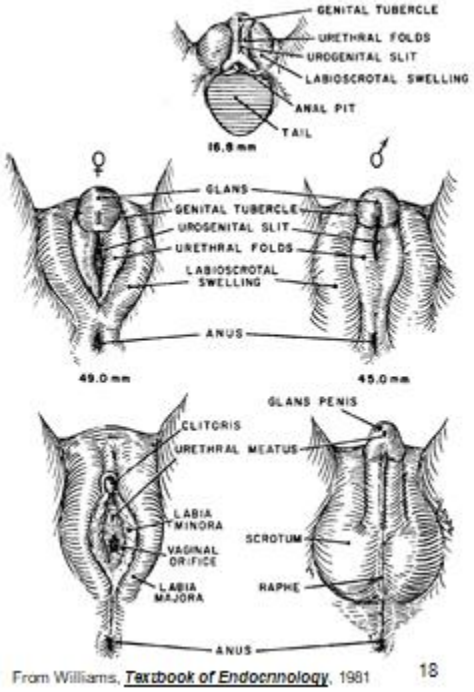
Development of the External Genitalia

The external genitalia are also indifferent early in embryonic life, and are described by a potential phallus, paired urethral folds, and paired labio-scrotal swellings. In the absence of fetal testosterone (T) and its more potent conversion product, dihydrotestosterone (DHT), the phallus will not elongate and will form a clitoris, the paired urethral folds will not fuse and will form the inner labia (lips) and vaginal opening, and the paired labio-scrotal swellings will not fuse and will form the outer labia. If DHT is present, the phallus will elongate to form a penis, the inner paired urethral folds will fuse to form the penile urethra which will open at the tip of the penis, and the outer paired labio-scrotal swellings will fuse to form the scrotum. Again, without DHT, the default structures are female, with it, the active structures are male.

Another embryonic structure is the urogenital sinus. If dihydrotestosterone (DHT) is present in a male this will form the part of the urethra that goes through the prostate gland, and also the prostate gland itself. If DHT is not present, the urogenital sinus will form the urethra, hymen, and lower vagina in the female. Female by default, male by action.



From Moore and Persaud, ***The Developing Human***, 1998



From Williams, Textbook of Endocrinology, 1981

It is likely that T, DHT, and AMH are all required for final migration of the testes through the inguinal (groin) canals into the scrotum. Without these hormones, the gonads will be undescended and remain within the abdominal cavity, the normal position of the ovaries. Again, active action to form the male, default for the female.

Gender Identity

The final aspect of sexual differentiation is gender identity, an individual's internal deeply held sense of gender, the gender that a person "identifies" with or feels themselves to be. Once gender assignment has taken place at birth, or very soon after, the overwhelming majority of males and females will be comfortable with that assignment and will establish gender identity by age 2-3.

But throughout history some men and women have experienced confusion and anguish, feeling that they are "trapped" in the wrong body. This distress is now called gender dysphoria, and it is part of the spectrum of transgender.

Estimates based on surveys suggest that about 0.6% of Americans identify themselves as transgender from a low of 0.30% in North Dakota to a high of 0.78% in Hawaii. It is likely that this is an underestimation. A commonly used estimate is a number somewhat greater than 1%. This represents 2-3 million persons or more in the US.

Disorders of Sexual Differentiation (DSD)

Before ultrasound and genetic testing were available to tell us the sex of fetuses before birth, the first question most parents would ask when a baby was born was "is it a boy or a girl?", and the person delivering the baby would be able to answer unequivocally "boy" or "girl" in almost all cases. But occasionally, there would be an awkward pause, and the answer might be "It's not clear for sure, but we will do some tests to find out." Sex assignment is thus usually easily made very early in life, with occasional cases of ambiguous genitalia causing some difficulties and chances for error.

Cases of abnormal sexual differentiation provide confirmation of how the normal mechanisms of sexual development occur, and also potentially shed light on how gender identity might result in humans. Much of the early research on gender identity was based on studies of this group.

Is a newborn a *tabula rosa* (Latin for scraped tablet), a "clean slate," with all behavior and knowledge gained by experience after birth? Is gender identity "baked into the cake" (determined genetically)? Is gender identity altered by brain exposure to testosterone the same way that testosterone affects other aspects of physical sex organ development—male by action, female by default?

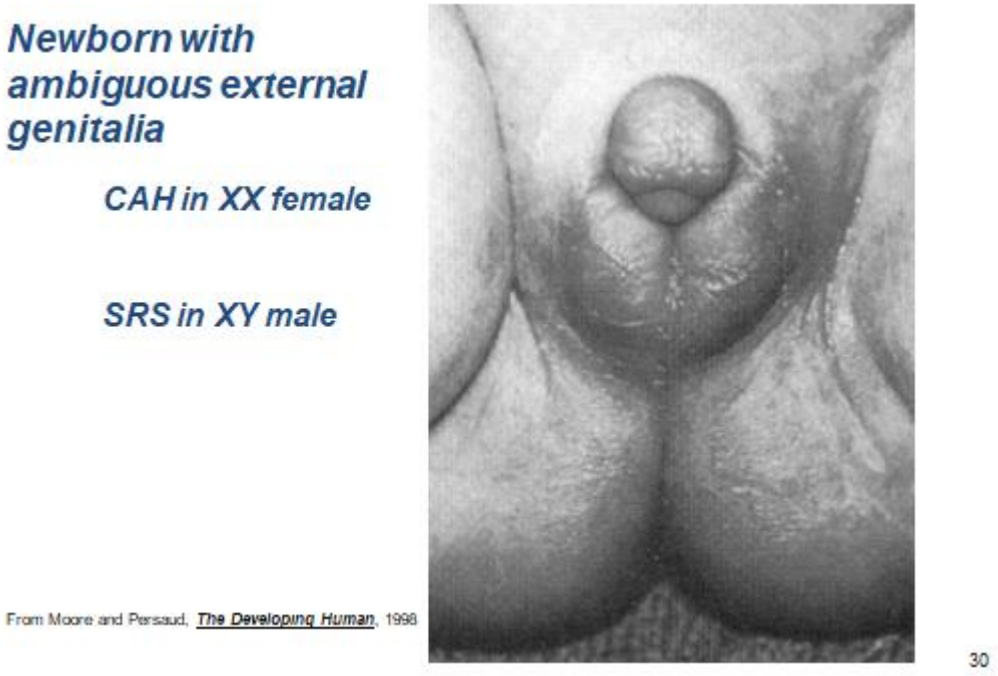
Do epigenetic mechanisms, other hormones, proteins, chemicals, infections, etc. act during embryonic life in ways that determine or alter gender identity? Is the timing of these exposures critical?

When a baby is born with ambiguous genitalia, the cause fundamentally has one of two explanations. Either the baby is a male that received incomplete actions of androgens (T, DHT) and AMH so the male structures are not fully developed, or it is a female that was exposed to some of the actions of male hormones (androgens) thus preventing the default development of the normal female by introducing some male features.

I will discuss three such abnormalities: Congenital Adrenal Hyperplasia (CAH), the so-called Sex Reversal Syndrome (SRS), and Androgen Insensitivity Syndrome (AIS). How is gender identity affected in these children?

CAH (Congenital Adrenal Hyperplasia)

The most common cause of ambiguous genitalia in a newborn is Congenital Adrenal Hyperplasia (CAH). There is a defect in an enzyme required for the baby's adrenal glands to produce cortisol. The net effect is that, in trying to make enough cortisol, which is vital to life, the adrenal is forced to make too much male hormone, and so an otherwise normal XX female fetus is partially masculinized. The male hormones produced are less potent than testosterone, so the masculinization is usually not severe. Presently, virtually all such females would be assigned female gender, but in the past some have been raised as males.



If exposure of the fetal brain to androgen has an influence on gender identity, one might expect that a disproportionate number of these girls would have gender dysphoria and would become transgender males. But the medical literature is inconclusive on this matter, with gender

dysphoria varying from <1% (the normal population rate) to as high as 10% in reported studies of these girls.

SRS (Sex Reversal Syndrome)

These genetic XY males with testes have ambiguous external genitalia at birth with varying degrees of masculinization (like CAH) because they have a deficiency of the enzyme 5-alpha-reductase, and thus cannot produce enough dihydrotestosterone to fully masculinize the external genitalia. The fetal testosterone levels are high enough, however, to cause some masculinizing of the external genitalia, making them ambiguous. Internal structures are normal male, and no female internal structures persist.

These XY males have often been assigned female sex at birth, but at puberty, when their testes begin to produce large amounts of testosterone, they will virilize. Even without DHT, the very high testosterone levels of puberty will cause some elongation of their phallus—in effect, a clitoris becoming a penis—hence the term Sex Reversal Syndrome. These sudden pubertal changes cause some of them to experience gender dysphoria, and about 60% of them become transgender males. Even when they have had testicular removal and female sex hormone therapy, they often will still identify as males, sometimes even quite late in life. A number have married women, and a few have fathered children in the usual way. This suggests that prenatal exposure to testosterone tends at least to facilitate male gender identity in spite of female sex assignment and rearing. But, the fact that nearly half of these girls retain their female gender identity suggests that cultural and educational factors may also be in play.

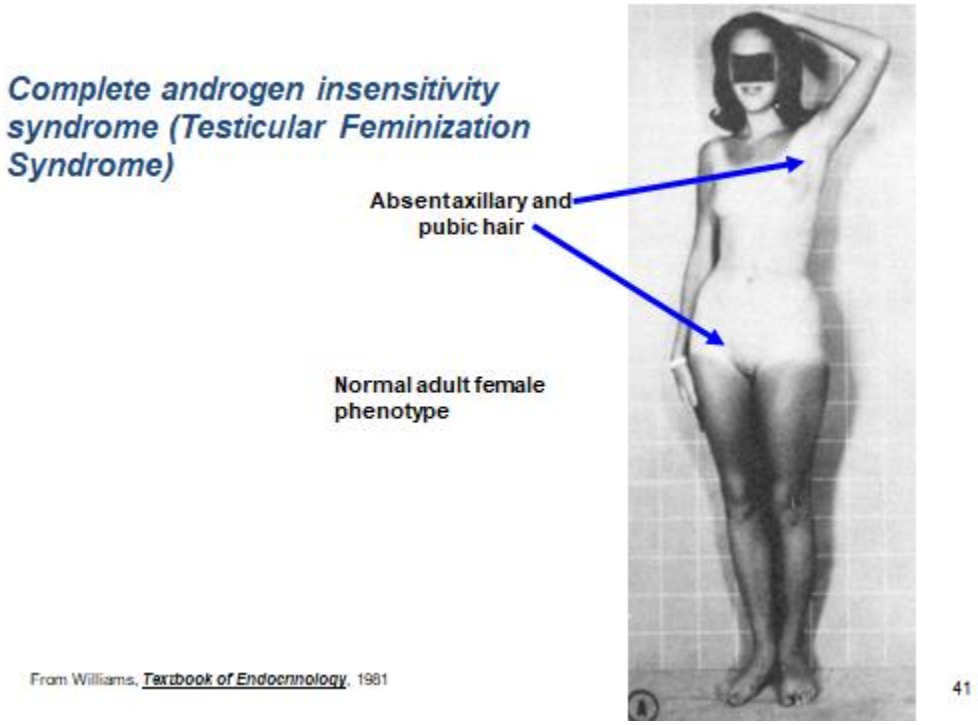
AIS (Androgen Insensitivity Syndrome)

These are genetic XY males with normal testes that do not descend. There are no cellular receptors for androgens (T and DHT), so there is no action of any male hormone, even though the levels of T and DHT are normal in this male fetus. The internal female structures regress and internal and external male structures do not develop, so the baby is born looking like a completely normal female, and is assigned female sex at birth.

At puberty, her testes produce much more testosterone, and enough of this testosterone can be converted in the body fat to estrogen so as to make her go through normal female pubertal changes. The condition is usually discovered because no menses occur during puberty, since the uterus has disappeared. An additional consequence of no male hormone action is total lack of sexual hair, even that which would be normal for a female.

These girls and women invariably have female gender identity, and only a few cases have been reported where conversion to a transgender male occurred. This would suggest that any effect

of androgen on gender identity is likely mediated through the action of androgen on its androgen receptor.



<u>Mechanisms for Establishing Gender Identity</u>

Since the mid-20th century the old debate about whether ***<u>nature or nurture</u>*** is the cause of various human behaviors has been largely resolved by scientific discoveries that show that many complex behavioral phenomena are a result of the interaction of multiple factors involving genetics, epigenetics, cultural values, and learning, so that nature vs nurture is a false dichotomy that also represents a gross oversimplification.

Genetics

Heritability of traits is usually assessed by twin studies, comparing the behavior of one twin member with the other. Such behavior is not expected to be influenced by rearing in identical twins. In the case of identical (monozygotic) twins, inherited genetic DNA is identical. In fraternal (dizygotic) twins, shared genes are much more common that in the population at large.

When one member of an identical twin pair is transgender, the other member of the pair will be transgender about 50% of the time. Similar concordance is found in the small number of identical twin pairs that were separated at birth and did not share the same family and social dynamics.

When one member of a set of fraternal twins of the same sex is transgender, about 1% of the other pair members is transgender--not different from the general population. One would expect some increase because these twins do share more genes than two random pairs in the general population. A possible explanation is that a threshold number of multiple genes are required to create the genetic climate for transgender behavior, and this is not reached in most fraternal twins, nor in random members of the population.

Studies have shown that several brain structures in transgender persons differ from control males and females, but there is not a complete reversal of structure. Transgender persons are less right-handed, and the prevalence of autism spectrum disorders, and attention-deficit/hyperactivity disorder (ADHD) appears to be higher in children referred for gender dysphoria than in the general population of children.

All these findings and observations would suggest that genes are involved in transgender development.

Research comparing individual genes and groups of genes between transgender and cisgender individuals has found differences, but so far the numbers of genes and persons are too small to draw clear conclusions. Whole genome studies on larger populations are in progress.

Epigenetics

Epigenetics is the study of changes in organisms caused by modification of gene structure and expression but not in alteration of the actual DNA sequence. It is increasingly likely that epigenetic mechanisms provide a major link between genetics and behavior in transgender individuals.

A variety of chemical compounds can be attached to genes that change the structure of their DNA bases to regulate the expression of affected genes without changing their actual DNA sequences. These compounds can be created from transcription of what used to be called "junk DNA" or from environmental exposures such as diet, pollution, or infections. They are thus "epi" genetic (epi means above in Greek), and can be viewed in an oversimplified fashion as "switches" that facilitate or repress gene expression. These epigenetic modifications remain as cells divide during the life of the individual, and in some cases can even be transmitted to subsequent generations.

It has long been realized that traits of identical twins are not completely identical even though they have the exact same DNA sequences. Recall that expression of transgender behavior is only about 50% concordant in identical twins. It is likely that epigenetic unblocking of genes that tend to favor expression of transgender is required for such expression, and such unblocking may occur in one twin and not the other.

In a very early embryo most of the switches are "on", but as the embryo develops different types of cells and tissues, some of the genes in any given cell are switched "off". This allows a muscle cell to develop and function differently from a nerve cell, even though they both contain the same overall DNA sequence. Use of embryonic stem cells to repair damaged tissues is based on their ability to differentiate in any direction because they have not yet been much modified by epigenetics.

We each receive one set of DNA from each of our parents. Any given gene, therefore, has two copies and most of the time both are used for transcription. But sometimes only one or the other may be activated or inactivated by an epigenetic mechanism called imprinting. This may also be part of the explanation of why identical twins do not turn out to be exactly identical.

Cultural Values and Learning

Following societal norms of gender assignment at birth most children learn to dress and comport themselves in their congruent gender (early gender learning) by age 2 or 3. This is accomplished by multiple learning experiences such as parental instruction, seeing others who are similarly dressed, and by behavior imitation. Learning about sex, in contrast, takes place later in development, well after gender identity has formed.

The Onset and Resolution of Gender Dysphoria

Transgender Behavior

Transgender behavior usually first appears between the ages of 4-6 with the child's assertions that he or she is really of the opposite gender. Depending on parental attitudes and responses, such a child may express and/or act on these feelings or keep them secret.

Observations suggest that this transgender behavior will disappear by puberty in 80-85% of these children, but 15-20% will continue to express transgender behavior and/or develop gender dysphoria. A portion of this group with transgender behavior in childhood may actually be prehomosexual and will become homosexual after puberty. Homosexuality does not cause gender dysphoria, and homosexuals are comfortable with their assigned sex and gender.

Gender identity clarification often occurs with the onset of puberty and dysphoria is heightened. Gender dysphoria in adolescence is very likely to persist into adulthood and a high percentage of these individuals will go on to become permanently transgender.

Three general approaches to transgender behavior have been proposed and practiced.

The first idea is that transgender behavior is completely due to faulty "nurturing" of a *tabula rosa* human being. Therefore attempts should be made to undo and/or correct the faulty nurturing so that the natural state of being cisgender can be expressed. Such "reeducation" efforts originated in the early 20th century, and have included bullying, medications, electric shock, psychoanalysis and various forms of counterconditioning. All have been shown to be ineffective. Such "failure" likely increases the rejection by--and ejection from--families and society, increasing homelessness and suicide—two outcomes that are inordinately high in transgender individuals. These ideas and practices still continue, however, but are no longer considered ethical, and are currently illegal in a number of US states and other countries.

The second idea is that transgender behavior almost always resolves with age due to increasing maturity and the response to increasing pressure from cultural rejection. The resulting approach is one of "watchful waiting" without permitting or encouraging any social gender transitioning until the onset of puberty solidifies gender identity. This approach is becoming increasingly difficult to follow, however, since many parents and children don't want to wait until puberty to begin the changes. Many parents relent when they see positive changes in mood and self-worth in their children with social transition.

The third idea is an affirmative approach. This was first developed for adults who were encouraged to explore their transgender behavior and to create safe environments in families and society for so doing. Permanent changes might then be chosen or not.

This approach has more recently been extended to children with social transition starting as soon as it clear that the child is "consistent, insistent, and persistent" in their new preferred gender. A significant unknown is whether affirming, confirming, or even encouraging childhood transgender behavior influences whether or not such transgender behavior persists into and after puberty. Social transition to a different gender in childhood is a controversial issue, and current evidence is insufficient to predict long-term outcomes, or make strong recommendations.

A tolerant, supportive approach can help to minimize the tremendous psychological stress that such individuals experience. The attempted suicide rate reported in adolescents with gender dysphoria is about 40%.

Puberty Suppression

In either watchful waiting or transgender affirmation approaches, current recommended management is to consider initiation of hormonal puberty-blocking just after the onset of puberty to delay further pubertal changes until age 16. The occurrence of gender dysphoria with puberty onset has diagnostic value in predicting the likelihood of continuing transgender transitioning.

Puberty suppression gives adolescents additional time to explore sex reassignment options and to try living in their new gender role. It also makes eventual transition easier because it prevents development of secondary sex characteristics that will be more difficult to reverse. Puberty suppression itself is reversible and does not inevitably lead to social transition and or gender reassignment.

At age 16 gender appropriate hormone therapy can be initiated if more complete transition to a transgender person is desired, or puberty is allowed to resume if a cisgender outcome is preferred. Transgender genital plastic surgery (TGPS) is not offered until at least age 18.

Normal puberty is initiated by the onset of secretion of pulses of a small peptide hormone, gonadotropin releasing hormone (GnRH), which is made by a small group of neurons in the hypothalamus at the base of the brain. Drugs that block the action of GnRH will block further development of the pubertal sex hormone increases that cause adult sexual developmental changes.

Gender Affirming Hormone Therapy

Exposure of an adult female who wishes to become a transgender male to normal male testosterone levels will result in deepened voice, increased coarse facial and body hair, suppression of menses, increased libido, atrophy (but not disappearance) of breast tissue, increased muscle mass compared to body fat, and perhaps male pattern baldness. Such testosterone exposure will cause some clitoral enlargement, but not the development of a penis with a penile urethra that opens at its tip. These changes would occur with or without ovarian removal. Even if we could administer Anti-Mullerian Hormone (we can't), female internal reproductive organs (i.e. uterus and vagina) would not disappear.

Conversely, an adult male wishing to become a transgender female will need to have testicular removal or suppression, or androgen blocking because an adult male has active testosterone levels about 30 times that of a normal adult female and estrogen administration is insufficient to completely suppress testosterone production and action. Administration of estrogen will then result in breast growth, decreased erectile function and libido, decreased testicular size,

and increased body fat deposition compared to muscle mass. The penis, internal male ducts, and prostate will remain, but no vagina or other internal female genital structures will develop.

We have seen that exposure of an embryo or fetus to testosterone and Anti-Mullerian Hormone causes development of male-specific internal and external genital structures and regression of female internal genital structures. At some point fairly early in development, however, epigenetic mechanisms cause these tissues to no longer respond to testosterone and AMH in the same way, or not at all. Thus androgen therapy doesn't cause complete female to male sexual transition.

Just as the adult form of men and women is quite variable with respect to many sexual characteristics (like breast or penis size, body shape, body hair, skin oiliness, beard, to name a few) depending on their genetic makeup, so it will be with a transitioning transgender person. In most cases the sexual changes produced by hormone therapy are very effective on external "public" body appearance. Hormone therapy is continued for life. Removal of gonads is often eventually done, and reduces the doses of hormone therapy required, with resulting reduction in the side-effects of such hormone therapy.

A simplified list of known risks for feminizing hormones given to transgender women is blood clots, gallstones, and weight gain, but no increase in breast cancer. For masculinizing hormones given to transgender men risks increase for polycythemia, weight gain, acne, balding, and sleep apnea, with no increase in risk of breast cancer.

Transgender Genital Plastic Surgery (TGPS)

During childhood and delayed puberty a transgender person may choose to simply dress, appear, and behave as a person of their comfort gender to be sure that they are comfortable in their new gender. Many transgender individuals find permanent comfort with just living their new gender role and the body changes that hormone therapy can induce without surgery, but others find that their gender dysphoria cannot be completely relieved without surgical modification of their genitalia and/or secondary sex characteristics via transgender genital plastic surgery (TGPS) to establish more complete congruence with their gender identity. Such surgery is not considered elective, but medically indicated. It has become very sophisticated and the results are excellent.

Surgery can also help transgender individuals feel more comfortable in the presence of sex partners, and in such places as swimming pools, health clubs, and doctors' offices. Surgery is used to create external and internal genital structures consistent with the gender identity of the individual.

For male to female (MtF) they include penectomy, orchiectomy (testicle removal), vulvar and vaginal construction, and perhaps breast implants (depending on the degree of breast development caused by female hormone administration).

For female to male (FtM) they includes phalloplasty (penis creation), scrotal construction, testicle implants (for appearance), penile implants (for erections), hysterectomy, removal of ovaries (oophorectomy), and perhaps mastectomy (depending on the degree of breast atrophy caused by male hormone administration.)

The surgical options and surgical results all depend, of course, on the person's individual hereditary potential for secondary sex characteristic development and how much puberty has been allowed to occur.

Reproduction

The availability of gamete (sperm and egg) freezing and gestational surrogates has opened up many additional options besides sexual intercourse for transgender individuals to reproduce using their own genes in their own sperm or eggs.

There is no evidence of any increased tendency for children of transgender parents to be transgender themselves, nor to be gay, lesbian, or bisexual.

Other Therapies

Voice and communication skill development can also be used to create comfort with a new gender role. Pitch, intonation, resonance, articulation, speech rate and phrasing, language including idiom use, loudness, voice quality, and non-verbal communication can be altered. Voice feminization surgery to pitch the voice higher by shortening the vocal cords is also an option for some male to female (MtF) transitioners.

Societal Issues

A significantly higher percentage of transgender persons join the US military compared to the rest of the population and it is estimated that there are 15,000 to 20,000 transgender service people in the military. Most of these individuals have completed gender transition, so gender dysphoria is not common. Being transgender has nothing to do with sexual orientation. The misconception that being transgender is somehow related to sexual arousal or is related to homosexuality causes some people to view transgender individuals as being sexually dangerous. Societal and parental rejection and even violence often occur toward transgender children and adults. These issues often have their origin in ignorance, misinformation, and cultural and ethnic attitudes.

There are also potentially confusing issues about the sex of athletes and whether, for example, a transgender woman would have an advantage over a cisgender woman. (She would). Chromosome tests can be confusing—recall the XY male who has a completely normal female body, or the XX female who was partially masculinized by Congenital Adrenal Hyperplasia and was raised as a male. Gonads have often been removed, and sex hormone therapy administered for medical reasons, creating more confusion. Governing athletic bodies have had to deal with all these questions, which probably pale in number compared to performance-altering drug use (another name for androgens).

In Conclusion

We have seen that gender development is a complex sequence involving genetic sex, gonadal sex, embryonic development of external and internal genital structures, sex assignment at birth, social and cultural norms and experience, genetic and epigenetic factors occasionally favoring gender dysphoria, and finally comfort with one's own personal gender identity. It's just not as simple as the age-old question: "Is it a boy or a girl." The truly correct answer to that question, perhaps with a bit of tongue-in-cheek, is "probably yes, but maybe not."

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