- XXYY Project: xxyysyndrome.org/main [http://xxyysyndrome.org/main]

Outlook (Prognosis)

Please see information on the individual conditions. The prognosis depends on the specific cause of intersex. With understanding, support, and appropriate treatment, overall outlook is excellent.

When to Contact a Medical Professional

If you notice that your child has unusual genitalia or sexual development, discuss this with your health care provider.

Alternative Names

Disorders of sex development; DSDs; Pseudohermaphroditism; Hermaphroditism; Hermaphrodite

References

Donohoue PA. Disorders of sex development. In: Kliegman RM, Stanton BF, St Geme JW III, Schor NF, eds. *Nelson Textbook of Pediatrics*. 20th ed. Philadelphia, PA: Elsevier; 2016:chap 588.

Wherrett DK. Approach to the infant with a suspected disorder of sex development. *Pediatr Clin North Am*. 2015;62(4):983-99. PMID: 26210628 www.ncbi.nlm.nih.gov/pubmed/26210628 [https://www.ncbi.nlm.nih.gov/pubmed/26210628].

Review Date 7/10/2015

Updated by: Neil K. Kaneshiro, MD, MHA, Clinical Assistant Professor of Pediatrics, University of Washington School of Medicine, Seattle, WA. Also reviewed by David Zieve, MD, MHA, Isla Ogilvie, PhD, and the A.D.A.M. Editorial team.

A.D.A.M., Inc. is accredited by URAC, also known as the American Accreditation HealthCare Commission (www.urac.org). URAC's accreditation program is an independent audit to verify that A.D.A.M. follows rigorous standards of quality and accountability. A.D.A.M. is among the first to achieve this important distinction for online health information and services. Learn more about A.D.A.M.'s editorial policy, editorial process and privacy policy. A.D.A.M. is also a founding member of Hi-Ethics and subscribes to the principles of the Health on the Net Foundation (www.hon.ch).

The information provided herein should not be used during any medical emergency or for the diagnosis or treatment of any medical condition. A licensed physician should be consulted for diagnosis and treatment of any and all medical conditions. Call 911 for all medical emergencies. Links to other sites are provided for information only -- they do not constitute endorsements of those other sites. Copyright 1997-2017, A.D.A.M., Inc. Duplication for commercial use must be authorized in writing by ADAM Health Solutions.

U.S. National Library of Medicine 8600 Rockville Pike, Bethesda, MD 20894

U.S. Department of Health and Human Services National Institutes of Health

Page last updated: 04 April 2017

FACT SHEET

Intersex

FREE & EQUAL
UNITED NATIONS FOR LGBT EQUALITY

What does 'intersex' mean?

Intersex people are born with sex characteristics (including genitals, gonads and chromosome patterns) that do not fit typical binary notions of male or female bodies.

Intersex is an umbrella term used to describe a wide range of natural bodily variations. In some cases, intersex traits are visible at birth while in others, they are not apparent until puberty. Some chromosomal intersex variations may not be physically apparent at all.

According to experts, between 0.05% and 1.7% of the population is born with intersex traits – the upper estimate is similar to the number of red haired people.

Being intersex relates to biological sex characteristics, and is distinct from a person's sexual orientation or gender identity. An intersex person may be straight, gay, lesbian, bisexual or asexual, and may identify as female, male, both or neither.

Because their bodies are seen as different, intersex children and adults are often stigmatized and subjected to multiple human rights violations, including violations of their rights to health and physical integrity, to be free from torture and ill-treatment, and to equality and non-discrimination.

Physical integrity

It has become common practice to subject intersex children to unnecessary surgical and other procedures for the purpose of trying to make their appearance conform to binary sex stereotypes.

These often irreversible procedures can cause permanent infertility, pain, incontinence, loss of sexual sensation, and lifelong mental suffering, including depression. Regularly performed without the full, free and informed consent of the person concerned, who is frequently too young to be part of the decision-making, these procedures may violate their rights to physical integrity, to be free from torture and ill-treatment, and to live free from harmful practices.

Such procedures are frequently justified on the basis of cultural and gender norms and discriminatory beliefs about intersex people and their integration into society.

Discriminatory attitudes can never justify human rights violations, including forced treatment and violations of the right to physical integrity. States have a duty to combat harmful stereotypes and discrimination, rather than reinforcing them. Such procedures may sometimes also be justified on the basis of alleged health benefits, but these are often proposed on the basis of weak evidence and without discussing alternative solutions that protect physical integrity and respect autonomy.

Unfortunately, such beliefs and societal pressures are often reflected by doctors, as well as parents of intersex children, who may encourage and/or give their agreement to such procedures, despite the lack of medical indication, necessity or urgency, and despite the fact that such procedures may violate human rights standards. Agreement is frequently given in absence of information on the short and long-term consequences of such surgery and lack of contact with peers, including intersex adults and their families.

Many intersex adults exposed to such surgery as children emphasize the shame and stigma linked to attempts to erase their intersex traits, as well as significant physical and mental suffering, including as a result of extensive and painful scarring. Many also feel that they were forced into sex and gender categories that do not fit them.

Given their irreversible nature and impact on physical integrity and autonomy, such medically unnecessary, unsolicited surgery or treatment should be prohibited. Intersex children and their families should receive adequate counselling and support, including from peers.

Discrimination

Intersex persons are often subjected to discrimination and abuse if it becomes known that they are intersex, or if they are perceived not to conform to gender norms. Anti-discrimination laws do not typically ban discrimination against intersex persons, leaving them vulnerable to discriminatory practices in a range of settings, including access to health services, education, public services, employment and sports.

UNITED NATIONS HUMAN RIGHTS
OFFICE OF THE HIGH COMMISSIONER

Health-care professionals often lack the needed training, knowledge and understanding to take into account the specific health needs of intersex persons, provide appropriate healthcare, and respect the autonomy and rights of intersex persons to physical integrity and health.

Some intersex people also face barriers and discrimination if they wish to or need to amend sex markers on birth certificates and official documents.

Intersex athletes face a specific set of obstacles. There have been several cases of female intersex athletes who have been disqualified from sports competitions on the basis of their intersex traits. However, being intersex of itself does not entail better performance, whereas other physical variations that do affect performance, such as height and muscle development, are not subjected to such scrutiny and restrictions.

Protection and Remedy

Intersex people should be protected from violations of their rights. Whenever such violations occur, they should be investigated and alleged perpetrators prosecuted. Victims should have access to effective remedy, including redress and compensation.

Intersex people should also be consulted in the development of legislation and policies that impact on their rights.

Positive developments

In 2013, Australia adopted the Sex Discrimination Amendment (Sexual Orientation, Gender Identity and Intersex Status) Act – the first law to include intersex status as a stand-alone prohibited ground of discrimination. The Australian Senate has also carried out an official inquiry into the involuntary or coerced sterilization of intersex people.

In 2015, Malta adopted the Gender Identity, Gender Expression and Sex Characteristics Act – the first law to prohibit surgery and treatment on the sex characteristics of minors without informed consent. It also prohibits discrimination on the basis of sex characteristics.

Action points

States:

» Prohibit medically unnecessary surgery and procedures on the sex characteristics of intersex children, protect their physical integrity and respect their autonomy.
» Ensure that intersex people and their families receive adequate counselling and support, including from peers.
» Prohibit discrimination on the basis of intersex traits, characteristics or status, including in education, health care, employment, sports and access to public services, and address such discrimination through relevant anti-discrimination initiatives.
» Ensure that human rights violations against intersex people are investigated and alleged perpetrators prosecuted, and that victims of such violations have access to effective remedy, including redress and compensation.
» National human rights bodies should research and monitor the human rights situation of intersex people.
» Enact laws to provide for facilitated procedures to amend sex markers on the birth certificates and official documents of intersex people.
» Provide health care personnel with training on the health needs and human rights of intersex people and the appropriate advice and care to give to parents and intersex children, being respectful of the intersex person's autonomy, physical integrity and sex characteristics.
» Ensure that members of the judiciary, immigration officers, law enforcement, healthcare, education and other officials and personnel are trained to respect and provide equal treatment to intersex persons.
» Ensure that intersex people and organizations are consulted and participate in the development of research, legislation and policies that impact on their rights.

Media:

» Include the voices of intersex people and groups in newspaper, TV and radio coverage.
» Give an objective and balanced picture of intersex people and their human rights concerns.
» Do not make assumptions about the sexual orientation or gender identity of intersex people.

You, your friends and other individuals can make a difference too:

» Speak out when you see any form of discrimination or violence against intersex people.
» Remember that intersex people may have any sexual orientation and gender identity.

UNITED NATIONS HUMAN RIGHTS OFFICE OF THE HIGH COMMISSIONER

www.ohchr.org www.unfe.org

How common is intersex?

To answer this question in an uncontroversial way, you'd have to first get everyone to agree on **what counts as intersex** —and also to agree on what should count as strictly male or strictly female. That's hard to do. How small does a penis have to be before it counts as intersex? Do you count "sex chromosome" anomalies as intersex if there's no apparent external sexual ambiguity?[1] (Alice Dreger explores this question in greater depth in her book **Hermaphrodites and the Medical Invention of Sex**.)

Here's what we do know: If you ask experts at medical centers how often a child is born so noticeably atypical in terms of genitalia that a specialist in sex differentiation is called in, the number comes out to about 1 in 1500 to 1 in 2000 births. But a lot more people than that are born with subtler forms of sex anatomy variations, some of which won't show up until later in life.

Below we provide a summary of statistics drawn from an article by Brown University researcher Anne Fausto-Sterling.[2] The basis for that article was an extensive review of the medical literature from 1955 to 1998 aimed at producing numeric estimates for the frequency of sex variations. Note that the frequency of some of these conditions, such as congenital adrenal hyperplasia, differs for different populations. These statistics are approximations.

Not XX and not XY	one in 1,666 births
Klinefelter (XXY)	one in 1,000 births
Androgen insensitivity syndrome	one in 13,000 births
Partial androgen insensitivity syndrome	one in 130,000 births
Classical congenital adrenal hyperplasia	one in 13,000 births
Late onset adrenal hyperplasia	one in 66 individuals
Vaginal agenesis	one in 6,000 births
Ovotestes	one in 83,000 births
Idiopathic (no discernable medical cause)	one in 110,000 births
Iatrogenic (caused by medical treatment, for instance progestin administered to pregnant mother)	no estimate
5 alpha reductase deficiency	no estimate
Mixed gonadal dysgenesis	no estimate
Complete gonadal dysgenesis	one in 150,000 births
Hypospadias (urethral opening in perineum or along penile shaft)	one in 2,000 births
Hypospadias (urethral opening between corona and tip of glans penis)	one in 770 births
Total number of people whose bodies differ from standard male or female	one in 100 births
Total number of people receiving surgery to "normalize" genital appearance	one or two in 1,000 births

[1] Dreger, Alice Domurat. 1998. **Ambiguous Sex—or Ambivalent Medicine? Ethical Issues in the Treatment of Intersexuality**. Hastings Center Report, 28, 3: 24-35.

[2] Blackless, Melanie, Anthony Charuvastra, Amanda Derryck, Anne Fausto-Sterling, Karl Lauzanne, and Ellen Lee. 2000. **How sexually dimorphic are we? Review and synthesis.** *American Journal of Human Biology* 12:151-166.

We were recently asked to update these frequency figures, and a lively **discussion** arose between two staff members.

What is intersex? Intersex conditions

CULTURE

This is What Intersex Means

Katy Steinmetz
Nov 21, 2014

A longer version of LGBT is LGBTQQIA, which stands for lesbian, gay, bisexual, transgender, queer, questioning, intersex and allies. The last few letters tend to get far less attention than the first, but a woman who claimed she was dating the Olympic swimmer Michael Phelps at the time of his DUI recently has raised interest in the "I."

"The truth is I have been living with secrets my whole life," Taylor Lianne Chandler wrote on Facebook on Nov. 13. "I was born intersex and named David Roy Fitch at birth."

Intersex is a term that refers to someone whose anatomy or genetics at birth—the X and Y chromosomes that are usually XX for women and XY for men—do not correspond to the typical expectations for either sex. The "I" is distinct from the "T" for transgender people, who are typically born with a biological sex that fits the norm for male or female and then grow up to identify with the opposite gender. Intersex babies are not obviously male or female to begin with, according to society's general rules about what one's physical characteristics and chromosomal makeup are supposed to signify.

As University of Oregon professor and intersex expert Elizabeth Reis writes in her book *Bodies in Doubt*, "In the United States and most other places, humans are men or they are women; they may not be neither or both. Yet not all bodies are clearly male or female." That may mean a child has typical female chromosomes and ovaries but external bodies parts of a male. Or it could mean the body parts that a doctor typically looks to when declaring a baby to be a girl or boy are incompletely formed, or ambiguous. Sometimes it's clear in the delivery room, sometimes intersex people don't become aware of their status until they are teenagers and puberty doesn't happen as expected.

Performing surgery on an intersex baby is controversial. In South Carolina, the parents of an adopted intersex child are suing a hospital and its employees for surgically assigning "M.C.'s" sex as female at 16-months-old. Now around 10 years old, the child identifies as a boy. "Genital 'normalizing' surgery does not create or cement a gender identity; it just takes tissue away that the patient may want later," writes the Intersex Society of North America in their position statement. Some in the intersex community choose not to have any

medically unnecessary surgeries to change how they were born, even after they are old enough to identify their own gender and sexual orientation.

Though it's hard to say exactly how common being intersex is (since it's debatable which people belong under that umbrella term), medical experts say that genital anomalies occur in about 1 in 2,000 babies.

It's worth noting that the word *hermaphrodite* is considered insensitive and stigmatizing by many who see it as "vague, demeaning, and sensationalistic, conjuring mythic images of monsters and freaks," as Reis writes. Some parents have also balked at the word *intersex*, pushed by activists in the 1990s, feeling it suggests their child has a third gender and can not be a girl or a boy. In the medical establishment, the wide variety of conditions that might be referred to as *intersex* are typically referred to as *disorders of sex development*. Reis has advocated shifting that to *divergence of sex development*, to avoid the connotations of *disorder*, much as *gender identity disorder* was rebranded *gender dysphoria* by medical professionals addressing transgender people.

NEWS FEATURE

SEX REDEFINED

THE IDEA OF TWO SEXES IS SIMPLISTIC. BIOLOGISTS NOW THINK THERE IS A WIDER SPECTRUM THAN THAT.

BY CLAIRE AINSWORTH

As a clinical geneticist, Paul James is accustomed to discussing some of the most delicate issues with his patients. But in early 2010, he found himself having a particularly awkward conversation about sex.

A 46-year-old pregnant woman had visited his clinic at the Royal Melbourne Hospital in Australia to hear the results of an amniocentesis test to screen her baby's chromosomes for abnormalities. The baby was fine — but follow-up tests had revealed something astonishing about the mother. Her body was built of cells from two individuals, probably from twin embryos that had merged in her own mother's womb. And there was more. One set of cells carried two X chromosomes, the complement that typically makes a person female; the other had an X and a Y. Halfway through her fifth decade and pregnant with her third child, the woman learned for the first time that a large part of her body was chromosomally male[1]. "That's kind of science-fiction material for someone who just came in for an amniocentesis," says James.

Sex can be much more complicated than it at first seems. According to the simple scenario, the presence or absence of a Y chromosome is what counts: with it, you are male, and without it, you are female. But doctors have long known that some people straddle the boundary — their sex chromosomes say one thing, but their gonads (ovaries or testes) or sexual anatomy say another. Parents of children with these kinds of conditions — known as intersex conditions, or differences or disorders of sex development (DSDs) — often face difficult decisions about whether to bring up their child as a boy or a girl. Some researchers now say that as many as 1 person in 100 has some form of DSD[2].

When genetics is taken into consideration, the boundary between the sexes becomes even blurrier. Scientists have identified many of the genes involved in the main forms of DSD, and have uncovered variations in these genes that have subtle effects on a person's anatomical or physiological sex. What's more, new technologies in DNA sequencing and cell biology are revealing that almost everyone is, to varying degrees, a patchwork of genetically distinct cells, some with a sex that might not match that of the rest of their body. Some studies even suggest that the sex of each cell drives its behaviour, through a complicated network of molecular interactions. "I think there's much greater diversity within male or female, and there is certainly an area of overlap where some people can't easily define themselves within the binary structure," says John Achermann, who studies sex development and endocrinology at University College London's Institute of Child Health.

These discoveries do not sit well in a world in which sex is still defined in binary terms. Few legal systems allow for any ambiguity in biological sex, and a person's legal rights and social status can be heavily influenced by whether their birth certificate says male or female.

"The main problem with a strong dichotomy is that there are intermediate cases that push the limits and ask us to figure out exactly where the dividing line is between males and females," says Arthur Arnold at the University of California, Los Angeles, who studies biological sex differences. "And that's often a very difficult problem, because sex can be defined a number of ways."

THE START OF SEX

That the two sexes are physically different is obvious, but at the start of life, it is not. Five weeks into development, a human embryo has the potential to form both male and female anatomy. Next to the developing kidneys, two bulges known as the gonadal ridges emerge alongside two pairs of

© 2015 Macmillan Publishers Limited. All rights reserved

Zzyym v. Tillerson - AR 0610

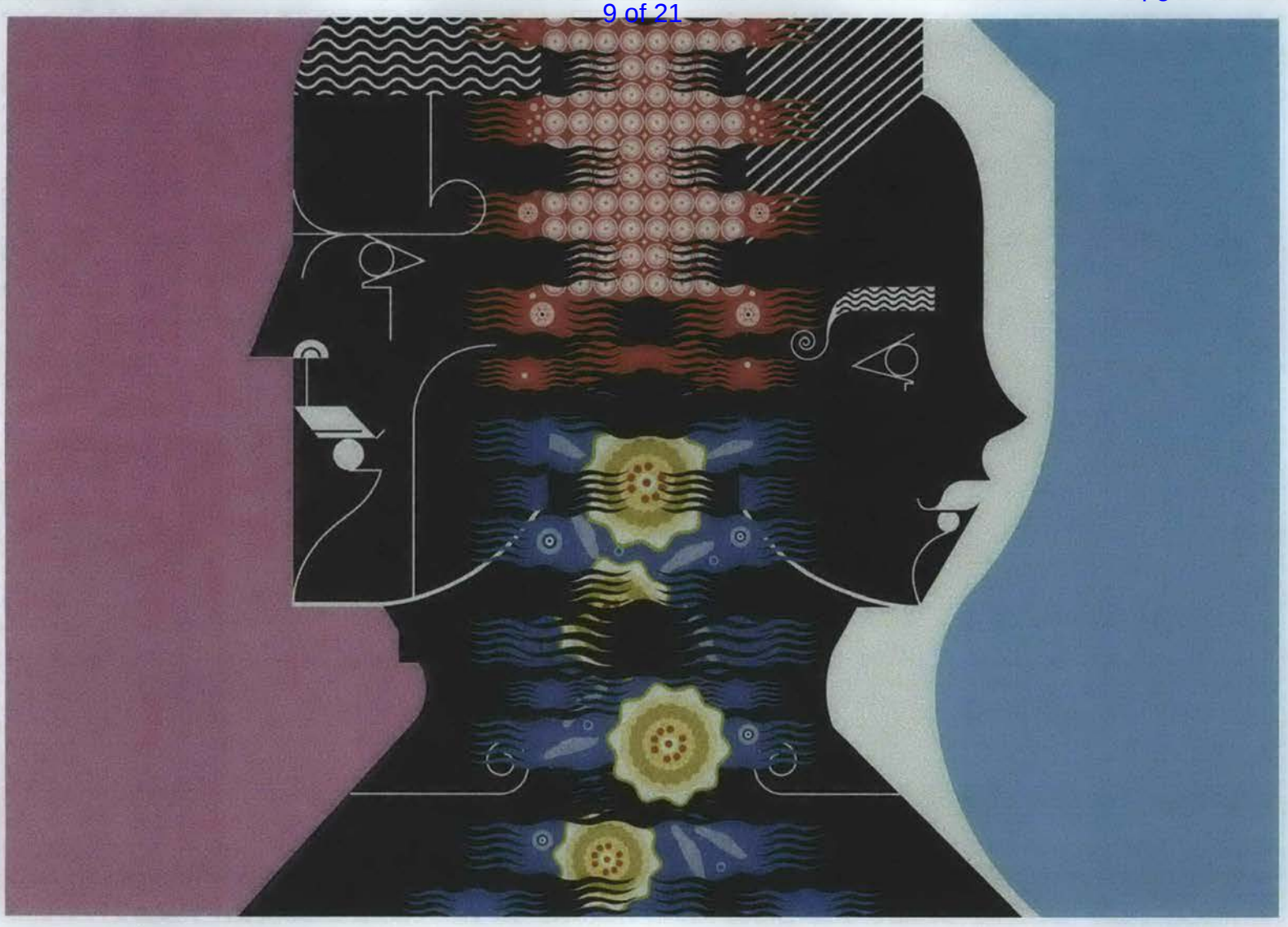


ILLUSTRATION BY JONNY WAN

ducts, one of which can form the uterus and Fallopian tubes, and the other the male internal genital plumbing: the epididymes, vas deferentia and seminal vesicles. At six weeks, the gonad switches on the developmental pathway to become an ovary or a testis. If a testis develops, it secretes testosterone, which supports the development of the male ducts. It also makes other hormones that force the presumptive uterus and Fallopian tubes to shrink away. If the gonad becomes an ovary, it makes oestrogen, and the lack of testosterone causes the male plumbing to wither. The sex hormones also dictate the development of the external genitalia, and they come into play once more at puberty, triggering the development of secondary sexual characteristics such as breasts or facial hair.

Changes to any of these processes can have dramatic effects on an individual's sex. Gene mutations affecting gonad development can result in a person with XY chromosomes developing typically female characteristics, whereas alterations in hormone signalling can cause XX individuals to develop along male lines.

For many years, scientists believed that female development was the default programme, and that male development was actively switched on by the presence of a particular gene on the Y chromosome. In 1990, researchers made headlines when they uncovered the identity of this gene[3,4], which they called *SRY*. Just by itself, this gene can switch the gonad from ovarian to testicular development. For example, XX individuals who carry a fragment of the Y chromosome that contains *SRY* develop as males.

By the turn of the millennium, however, the idea of femaleness being a passive default option had been toppled by the discovery of genes that actively promote ovarian development and suppress the testicular programme — such as one called *WNT4*.

NATURE.COM
For a podcast on the sex spectrum, see:
go.nature.com/xowzq5

XY individuals with extra copies of this gene can develop atypical genitals and gonads, and a rudimentary uterus and Fallopian tubes[5]. In 2011, researchers showed[6] that if another key ovarian gene, *RSPO1*, is not working normally, it causes XX people to develop an ovotestis — a gonad with areas of both ovarian and testicular development.

These discoveries have pointed to a complex process of sex determination, in which the identity of the gonad emerges from a contest between two opposing networks of gene activity. Changes in the activity or amounts of molecules (such as WNT4) in the networks can tip the balance towards or away from the sex seemingly spelled out by the chromosomes. "It has been, in a sense, a philosophical change in our way of looking at sex; that it's a balance," says Eric Vilain, a clinician and the director of the Center for Gender-Based Biology at the University of California, Los Angeles. "It's more of a systems-biology view of the world of sex."

BATTLE OF THE SEXES

According to some scientists, that balance can shift long after development is over. Studies in mice suggest that the gonad teeters between being male and female throughout life, its identity requiring constant maintenance. In 2009, researchers reported[7] deactivating an ovarian gene called *Foxl2* in adult female mice; they found that the granulosa cells that support the development of eggs transformed into Sertoli cells, which support sperm development. Two years later, a separate team showed[8] the opposite: that inactivating a gene called *Dmrt1* could turn adult testicular cells into ovarian ones. "That was the big shock, the fact that it was going on post-natally," says Vincent Harley, a geneticist who studies gonad development at the MIMR-PHI Institute for Medical Research in Melbourne.

The gonad is not the only source of diversity in sex. A number of DSDs are caused by changes in the machinery that responds to hormonal

© 2015 Macmillan Publishers Limited. All rights reserved

THE SEX SPECTRUM

A typical male has XY chromosomes, and a typical female has XX. But owing to genetic variation or chance events in development, some people do not fit neatly into either category. Some are classed as having differences or disorders of sex development (DSDs), in which their sex chromosomes do not match their sexual anatomy.

	Typical male	Subtle variations	Moderate variations	46,XY DSD
Chromosomes	XY	XY	XY	XY
Gonads	Testes	Testes	Testes	Testes
Genitals	Male internal and external genitals	Male internal and external genitals	Male external genitals with anatomical variations such as urethral opening on underside of penis.	Often ambiguous
Other characteristics/ examples	Male secondary sexual characteristics	Subtle differences such as low sperm production. Some caused by variation in sex-development genes.	Affects 1 in 250–400 births.	The hormonal disorder persistent Müllerian duct syndrome results in male external genitals and testes, but also a womb and Fallopian tubes.

signals from the gonads and other glands. Complete androgen insensitivity syndrome, or CAIS, for example, arises when a person's cells are deaf to male sex hormones, usually because the receptors that respond to the hormones are not working. People with CAIS have Y chromosomes and internal testes, but their external genitalia are female, and they develop as females at puberty.

Conditions such as these meet the medical definition of DSDs, in which an individual's anatomical sex seems to be at odds with their chromosomal or gonadal sex. But they are rare — affecting about 1 in 4,500 people[9]. Some researchers now say that the definition should be widened to include subtle variations of anatomy such as mild hypospadias, in which a man's urethral opening is on the underside of his penis rather than at the tip. The most inclusive definitions point to the figure of 1 in 100 people having some form of DSD, says Vilain (see 'The sex spectrum').

But beyond this, there could be even more variation. Since the 1990s, researchers have identified more than 25 genes involved in DSDs, and next-generation DNA sequencing in the past few years has uncovered a wide range of variations in these genes that have mild effects on individuals, rather than causing DSDs. "Biologically, it's a spectrum," says Vilain.

A DSD called congenital adrenal hyperplasia (CAH), for example, causes the body to produce excessive amounts of male sex hormones; XX individuals with this condition are born with ambiguous genitalia (an enlarged clitoris and fused labia that resemble a scrotum). It is usually caused by a severe deficiency in an enzyme called 21-hydroxylase. But women carrying mutations that result in a milder deficiency develop a 'non-classical' form of CAH, which affects about 1 in 1,000 individuals; they may have male-like facial and body hair, irregular periods or fertility problems — or they might have no obvious symptoms at all. Another gene, *NR5A1*, is currently fascinating researchers because variations in it cause a wide range of effects[10], from underdeveloped gonads to mild hypospadias in men, and premature menopause in women.

SURGEONS DISCOVERED THAT THE MAN HAD A WOMB. HE WAS 70.

Many people never discover their condition unless they seek help for infertility, or discover it through some other brush with medicine. Last year, for example, surgeons reported that they had been operating on a hernia in a man, when they discovered that he had a womb[11]. The man was 70, and had fathered four children.

CELLULAR SEX

Studies of DSDs have shown that sex is no simple dichotomy. But things become even more complex when scientists zoom in to look at individual cells. The common assumption that every cell contains the same set of genes is untrue. Some people have mosaicism: they develop from a single fertilized egg but become a patchwork of cells with different genetic make-ups. This can happen when sex chromosomes are doled out unevenly between dividing cells during early embryonic development. For example, an embryo that starts off as XY can lose a Y chromosome from a subset of its cells. If most cells end up as XY, the result is a physically typical male, but if most cells are X, the result is a female with a condition called Turner's syndrome, which tends to result in restricted height and underdeveloped ovaries. This kind of mosaicism is rare, affecting about 1 in 15,000 people.

The effects of sex-chromosome mosaicism range from the prosaic to the extraordinary. A few cases have been documented in which a mosaic XXY embryo became a mix of two cell types — some with two X chromosomes and some with two Xs and a Y — and then split early in development[12]. This results in 'identical' twins of different sexes.

There is a second way in which a person can end up with cells of different chromosomal sexes. James's patient was a chimaera: a person who develops from a mixture of two fertilized eggs, usually owing to a merger between embryonic twins in the womb. This kind of chimaerism resulting in a DSD is extremely rare, representing about 1% of all DSD cases.

Another form of chimaerism, however, is now known to be widespread. Termed microchimaerism, it happens when stem cells from a fetus cross the placenta into the mother's body, and vice versa. It was first identified in the early 1970s — but the big surprise came more than two decades later, when researchers discovered how long these crossover cells survive, even though they are foreign tissue that the body should, in theory, reject. A study in 1996 recorded women with fetal cells in their blood as many as 27 years after giving birth[13]; another found that maternal cells remain in children up to adulthood[14]. This type of work has further blurred the sex divide, because it means that men often carry cells from their mothers, and women who have been pregnant with a male fetus can carry a smattering of its discarded cells.

Microchimaeric cells have been found in many tissues. In 2012, for example, immunologist Lee Nelson and her team at the University of Washington in Seattle found XY cells in post-mortem samples of women's brains[15]. The oldest woman carrying male DNA was 94 years old. Other studies have shown that these immigrant cells are not idle; they integrate into their new environment and acquire specialized functions, including (in mice at least) forming neurons in the brain[16]. But what is not known is how a peppering of male cells in a female, or vice versa, affects the health or characteristics of a tissue — for example, whether it makes the tissue more susceptible to diseases more common in the opposite sex. "I think that's a great question," says Nelson, "and it is essentially entirely unaddressed." In terms of human behaviour, the consensus is that a few male microchimaeric cells in the brain seem unlikely to have a major effect on a woman.

Scientists are now finding that XX and XY cells behave in different ways, and that this can be independent of the action of sex hormones. "To tell you the truth, it's actually kind of surprising how big an effect of sex chromosomes we've been able to see," says Arnold. He and his colleagues have shown[17] that the dose of X chromosomes in a mouse's body can affect its metabolism, and studies in a lab dish suggest[18] that XX and XY cells behave differently on a molecular level, for example with different metabolic responses to stress. The next challenge, says

© 2015 Macmillan Publishers Limited. All rights reserved

Zzyym v. Tillerson - AR 0612

	Ovotesticular DSD	46,XX testicular DSD	Moderate variations	Subtle variations	Typical female
Chromosomes	XX, XY or mix of both	XX	XX	XX	XX
Gonads	Both ovarian and testicular tissue	Small testes	Ovaries	Ovaries	Ovaries
Genitals	Ambiguous	Male external genitals	Female internal and external genitals	Female internal and external genitals	Female internal and external genitals
Other characteristics/ examples	Rare reports of predominantly XY people conceiving and bearing a healthy child.	Usually caused by presence of male sex-determining gene *SRY*.	Variations in sex development such as premature shutdown of ovaries. Some caused by variation in sex-development genes.	Subtle differences such as excess male sex hormones or polycystic ovaries.	Female secondary sexual characteristics

Arnold, is to uncover the mechanisms. His team is studying the handful of X-chromosome genes now known to be more active in females than in males. "I actually think that there are more sex differences than we know of," says Arnold.

BEYOND THE BINARY

Biologists may have been building a more nuanced view of sex, but society has yet to catch up. True, more than half a century of activism from members of the lesbian, gay, bisexual and transgender community has softened social attitudes to sexual orientation and gender. Many societies are now comfortable with men and women crossing conventional societal boundaries in their choice of appearance, career and sexual partner. But when it comes to sex, there is still intense social pressure to conform to the binary model.

This pressure has meant that people born with clear DSDs often undergo surgery to 'normalize' their genitals. Such surgery is controversial because it is usually performed on babies, who are too young to consent, and risks assigning a sex at odds with the child's ultimate gender identity — their sense of their own gender. Intersex advocacy groups have therefore argued that doctors and parents should at least wait until a child is old enough to communicate their gender identity, which typically manifests around the age of three, or old enough to decide whether they want surgery at all.

This issue was brought into focus by a lawsuit filed in South Carolina in May 2013 by the adoptive parents of a child known as MC, who was born with ovotesticular DSD, a condition that produces ambiguous genitalia and gonads with both ovarian and testicular tissue. When MC was 16 months old, doctors performed surgery to assign the child as female — but MC, who is now eight years old, went on to develop a male gender identity. Because he was in state care at the time of his treatment, the lawsuit alleged not only that the surgery constituted medical malpractice, but also that the state denied him his constitutional right to bodily integrity and his right to reproduce. Last month, a court decision prevented the federal case from going to trial, but a state case is ongoing.

"This is potentially a critically important decision for children born with intersex traits," says Julie Greenberg, a specialist in legal issues relating to gender and sex at Thomas Jefferson School of Law in San Diego, California. The suit will hopefully encourage doctors in the United States to refrain from performing operations on infants with DSDs when there are questions about their medical necessity, she says. It could raise awareness about "the emotional and physical struggles intersex people are forced to endure because doctors wanted to 'help' us fit in," says Georgiann Davis, a sociologist who studies issues surrounding intersex traits and gender at the University of Nevada, Las Vegas, who was born with CAIS.

Doctors and scientists are sympathetic to these concerns, but the MC case also makes some uneasy — because they know how much is still to be learned about the biology of sex[19]. They think that changing medical practice by legal ruling is not ideal, and would like to see more data collected on outcomes such as quality of life and sexual function to help decide the best course of action for people with DSDs — something that researchers are starting to do.

Diagnoses of DSDs once relied on hormone tests, anatomical inspections and imaging, followed by painstaking tests of one gene at a time. Now, advances in genetic techniques mean that teams can analyse multiple genes at once, aiming straight for a genetic diagnosis and making the process less stressful for families. Vilain, for example, is using whole-exome sequencing — which sequences the protein-coding regions of a person's entire genome — on XY people with DSDs. Last year, his team showed[20] that exome sequencing could offer a probable diagnosis in 35% of the study participants whose genetic cause had been unknown.

Vilain, Harley and Achermann say that doctors are taking an increasingly circumspect attitude to genital surgery. Children with DSDs are treated by multidisciplinary teams that aim to tailor management and support to each individual and their family, but this usually involves raising a child as male or female even if no surgery is done. Scientists and advocacy groups mostly agree on this, says Vilain: "It might be difficult for children to be raised in a gender that just does not exist out there." In most countries, it is legally impossible to be anything but male or female.

Yet if biologists continue to show that sex is a spectrum, then society and state will have to grapple with the consequences, and work out where and how to draw the line. Many transgender and intersex activists dream of a world where a person's sex or gender is irrelevant. Although some governments are moving in this direction, Greenberg is pessimistic about the prospects of realizing this dream — in the United States, at least. "I think to get rid of gender markers altogether or to allow a third, indeterminate marker, is going to be difficult."

So if the law requires that a person is male or female, should that sex be assigned by anatomy, hormones, cells or chromosomes, and what should be done if they clash? "My feeling is that since there is not one biological parameter that takes over every other parameter, at the end of the day, gender identity seems to be the most reasonable parameter," says Vilain. In other words, if you want to know whether someone is male or female, it may be best just to ask. ■

Claire Ainsworth *is a freelance writer based in Hampshire, UK.*

1. James, P. A., Rose, K., Francis, D. & Norris, F. *Am. J. Med. Genet. A* **155,** 2484–2488 (2011).
2. Arboleda, V. A., Sandberg, D. E. & Vilain, E. *Nature Rev. Endocrinol.* **10,** 603–615 (2014).
3. Sinclair, A. H. *et al. Nature* **346,** 240–244 (1990).
4. Berta, P. *et al. Nature* **348,** 448–450 (1990).
5. Jordan, B. K. *et al. Am. J. Hum. Genet.* **68,** 1102–1109 (2001).
6. Tomaselli, S. *et al. PLoS ONE* **6,** e16366 (2011).
7. Uhlenhaut, N. H. *et al. Cell* **139,** 1130–1142 (2009).
8. Matson, C. K. *et al. Nature* **476,** 101–104 (2011).
9. Hughes, I. A., Houk, C., Ahmed, S. F., Lee, P. A. & LWPES1/ESPE2 Consensus Group *Arch. Dis. Child.* **91,** 554–563 (2006).
10. El-Khairi, R. & Achermann, J. C. *Semin. Reprod. Med.* **30,** 374–381 (2012).
11. Sherwani, A. Y. *et al. Int. J. Surg. Case Rep.* **5,** 1285–1287 (2014).
12. Tachon, G. *et al. Hum. Reprod.* **29,** 2814–2820 (2014).
13. Bianchi, D. W., Zickwolf, G. K., Weil, G. J., Sylvester, S. & DeMaria, M. A. *Proc. Natl Acad. Sci. USA* **93,** 705–708 (1996).
14. Maloney, S. *et al. J. Clin. Invest.* **104,** 41–47 (1999).
15. Chan, W. F. N. *et al. PLoS ONE* **7,** e45592 (2012).
16. Zeng, X. X. *et al. Stem Cells Dev.* **19,** 1819–1830 (2010.
17. Link, J. C., Chen, X., Arnold, A. P. & Reue, K. *Adipocyte* **2,** 74–79 (2013).
18. Penaloza, C. *et al. FASEB J.* **23,** 1869–1879 (2009).
19. Warne, G. L. *Sex Dev.* **2,** 268–277 (2008).
20. Baxter, R. M. *et al. J. Clin. Endocrinol. Metab.* **100,** E333–E344 (2014).

© 2015 Macmillan Publishers Limited. All rights reserved

Zzyym v. Tillerson - AR 0613

The Harry Benjamin International Gender Dysphoria Association's Standards Of Care For Gender Identity Disorders, Sixth Version

February, 2001

Committee Members: Walter Meyer III M.D. (Chairperson), Walter O. Bockting Ph.D., Peggy Cohen-Kettenis Ph.D., Eli Coleman Ph.D., Domenico DiCeglie M.D., Holly Devor Ph.D., Louis Gooren M.D., Ph.D., J. Joris Hage M.D., Sheila Kirk M.D., Bram Kuiper Ph.D., Donald Laub M.D., Anne Lawrence M.D., Yvon Menard M.D., Stan Monstrey M.D., Jude Patton PA-C, Leah Schaefer Ed.D., Alice Webb D.H.S., Connie Christine Wheeler Ph.D.

This is the sixth version of the Standards of Care since the original 1979 document.
Previous revisions were in 1980, 1981, 1990, and 1998.

Table of Contents:

I. **Introductory Concepts (p. 1)**
II. **Epidemiological Considerations (p. 2)**
III. **Diagnostic Nomenclature (p. 3)**
IV. **The Mental Health Professional (p. 6)**
V. **Assessment and Treatment of Children and Adolescents (p. 8)**
VI. **Psychotherapy with Adults (p. 11)**
VII. **Requirements for Hormone Therapy for Adults (p. 13)**
VIII. **Effects of Hormone Therapy in Adults (p. 14)**
IX. **The Real-life Experience (p. 17)**
X. **Surgery (p. 18)**
XI. **Breast Surgery (p. 19)**
XII. **Genital Surgery (p. 20)**
XIII. **Post-Transition Follow-up (p. 22)**

I. Introductory Concepts

The Purpose of the Standards of Care. The major purpose of the Standards of Care (SOC) is to articulate this international organization's professional consensus about the psychiatric, psychological, medical, and surgical management of gender identity disorders. Professionals may use this document to understand the parameters within which they may offer assistance to those with these conditions. Persons with gender identity disorders, their families, and social institutions may use the SOC to understand the current thinking of professionals. All readers should be aware of the limitations of knowledge in this area and of the hope that some of the clinical uncertainties will be resolved in the future through scientific investigation.

The Overarching Treatment Goal. The general goal of psychotherapeutic, endocrine, or surgical therapy for persons with gender identity disorders is lasting personal comfort with the gendered self in order to maximize overall psychological well-being and self-fulfillment.

The Standards of Care Are Clinical Guidelines. The SOC are intended to provide flexible directions for the treatment of persons with gender identity disorders. When eligibility

requirements are stated they are meant to be minimum requirements. Individual professionals and organized programs may modify them. Clinical departures from these guidelines may come about because of a patient's unique anatomic, social, or psychological situation, an experienced professional's evolving method of handling a common situation, or a research protocol. These departures should be recognized as such, explained to the patient, and documented both for legal protection and so that the short and long term results can be retrieved to help the field to evolve.

The Clinical Threshold. A clinical threshold is passed when concerns, uncertainties, and questions about gender identity persist during a person's development, become so intense as to seem to be the most important aspect of a person's life, or prevent the establishment of a relatively unconflicted gender identity. The person's struggles are then variously informally referred to as a gender identity problem, gender dysphoria, a gender problem, a gender concern, gender distress, gender conflict, or transsexualism. Such struggles are known to occur from the preschool years to old age and have many alternate forms. These reflect various degrees of personal dissatisfaction with sexual identity, sex and gender demarcating body characteristics, gender roles, gender identity, and the perceptions of others. When dissatisfied individuals meet specified criteria in one of two official nomenclatures--the International Classification of Diseases-10 (ICD-10) or the Diagnostic and Statistical Manual of Mental Disorders--Fourth Edition (DSM-IV)--they are formally designated as suffering from a gender identity disorder (GID). Some persons with GID exceed another threshold--they persistently possess a wish for surgical transformation of their bodies.

Two Primary Populations with GID Exist -- Biological Males and Biological Females. The sex of a patient always is a significant factor in the management of GID. Clinicians need to separately consider the biologic, social, psychological, and economic dilemmas of each sex. All patients, however, should follow the SOC.

II. Epidemiological Considerations

Prevalence. When the gender identity disorders first came to professional attention, clinical perspectives were largely focused on how to identify candidates for sex reassignment surgery. As the field matured, professionals recognized that some persons with bona fide gender identity disorders neither desired nor were candidates for sex reassignment surgery. The earliest estimates of prevalence for transsexualism in adults were 1 in 37,000 males and 1 in 107,000 females. The most recent prevalence information from the Netherlands for the transsexual end of the gender identity disorder spectrum is 1 in 11,900 males and 1 in 30,400 females. Four observations, not yet firmly supported by systematic study, increase the likelihood of an even higher prevalence: 1) unrecognized gender problems are occasionally diagnosed when patients are seen with anxiety, depression, bipolar disorder, conduct disorder, substance abuse, dissociative identity disorders, borderline personality disorder, other sexual disorders and intersexed conditions; 2) some nonpatient male transvestites, female impersonators, transgender people, and male and female homosexuals may have a form of gender identity disorder; 3) the intensity of some persons' gender identity disorders fluctuates below and above a clinical threshold; 4) gender variance among female-bodied individuals tends to be relatively invisible to the culture, particularly to mental health professionals and scientists.

Natural History of Gender Identity Disorders. Ideally, prospective data about the natural history of gender identity struggles would inform all treatment decisions. These are lacking, except for the demonstration that, without therapy, most boys and girls with gender identity disorders outgrow their wish to change sex and gender. After the diagnosis of GID is made the therapeutic approach usually includes three elements or phases (sometimes labeled triadic therapy): a real-life experience in the desired role, hormones of the desired gender, and surgery to change the genitalia and other sex characteristics. Five less firmly scientifically established observations prevent clinicians from prescribing the triadic therapy based on diagnosis alone: 1) some carefully diagnosed persons spontaneously change their aspirations; 2) others make more comfortable accommodations to their gender identities without medical interventions; 3) others give up their wish to follow the triadic sequence during psychotherapy; 4) some gender identity clinics have an unexplained high drop out rate; and 5) the percentage of persons who are not benefited from the triadic therapy varies significantly from study to study. Many persons with GID will desire all three elements of triadic therapy. Typically, triadic therapy takes place in the order of hormones = = > real-life experience = = > surgery, or sometimes: real-life experience = = > hormones = = > surgery. For some biologic females, the preferred sequence may be hormones = = > breast surgery = = > real-life experience. However, the diagnosis of GID invites the consideration of a variety of therapeutic options, only one of which is the complete therapeutic triad. Clinicians have increasingly become aware that not all persons with gender identity disorders need or want all three elements of triadic therapy.

Cultural Differences in Gender Identity Variance throughout the World. Even if epidemiological studies established that a similar base rate of gender identity disorders existed all over the world, it is likely that cultural differences from one country to another would alter the behavioral expressions of these conditions. Moreover, access to treatment, cost of treatment, the therapies offered and the social attitudes towards gender variant people and the professionals who deliver care differ broadly from place to place. While in most countries, crossing gender boundaries usually generates moral censure rather than compassion, there are striking examples in certain cultures of cross-gendered behaviors (e.g., in spiritual leaders) that are not stigmatized.

III. Diagnostic Nomenclature

The Five Elements of Clinical Work. Professional involvement with patients with gender identity disorders involves any of the following: diagnostic assessment, psychotherapy, real-life experience, hormone therapy, and surgical therapy. This section provides a background on diagnostic assessment.

The Development of a Nomenclature. The term *transexxual* emerged into professional and public usage in the 1950s as a means of designating a person who aspired to or actually lived in the anatomically contrary gender role, whether or not hormones had been administered or surgery had been performed. During the 1960s and 1970s, clinicians used the term *true transsexual*. The true transsexual was thought to be a person with a characteristic path of atypical gender identity development that predicted an improved life from a treatment sequence that culminated in genital surgery. True transsexuals were thought to have: 1) cross-gender identifications that were consistently expressed behaviorally in childhood, adolescence, and

adulthood; 2) minimal or no sexual arousal to cross-dressing; and 3) no heterosexual interest, relative to their anatomic sex. True transsexuals could be of either sex. True transsexual males were distinguished from males who arrived at the desire to change sex and gender via a reasonably masculine behavioral developmental pathway. Belief in the true transsexual concept for males dissipated when it was realized that such patients were rarely encountered, and thatsome of the original true transsexuals had falsified their histories to make their stories match the earliest theories about the disorder. The concept of true transsexual females never created diagnostic uncertainties, largely because patient histories were relatively consistent and gender variant behaviors such as female cross-dressing remained unseen by clinicians. The term "gender dysphoria syndrome" was later adopted to designate the presence of a gender problem in either sex until psychiatry developed an official nomenclature.

The diagnosis of Transsexualism was introduced in the DSM-III in 1980 for gender dysphoric individuals who demonstrated at least two years of continuous interest in transforming the sex of their bodies and their social gender status. Others with gender dysphoria could be diagnosed as Gender Identity Disorder of Adolescence or Adulthood, Nontranssexual Type; or Gender Identity Disorder Not Otherwise Specified (GIDNOS). These diagnostic terms were usually ignored by the media, which used the term transsexual for any person who wanted to change his/her sex and gender.

The DSM-IV. In 1994, the DSM-IV committee replaced the diagnosis of Transsexualism with Gender Identity Disorder. Depending on their age, those with a strong and persistent cross-gender identification and a persistent discomfort with their sex or a sense of inappropriateness in the gender role of that sex were to be diagnosed as Gender Identity Disorder of Childhood (302.6), Adolescence, or Adulthood (302.85). For persons who did not meet these criteria, Gender Identity Disorder Not Otherwise Specified (GIDNOS)(302.6) was to be used. This category included a variety of individuals, including those who desired only castration or penectomy without a desire to develop breasts, those who wished hormone therapy and mastectomy without genital reconstruction, those with a congenital intersex condition, those with transient stress-related cross-dressing, and those with considerable ambivalence about giving up their gender status. Patients diagnosed with GID and GIDNOS were to be subclassified according to the sexual orientation: attracted to males; attracted to females; attracted to both; or attracted to neither. This subclassification was intended to assist in determining, over time, whether individuals of one sexual orientation or another experienced better outcomes using particular therapeutic approaches; it was **not** intended to guide treatment decisions.

Between the publication of DSM-III and DSM-IV, the term "transgender" began to be used in various ways. Some employed it to refer to those with unusual gender identities in a value-free manner -- that is, without a connotation of psychopathology. Some people informally used the term to refer to any person with any type of gender identity issues. Transgender is not a formal diagnosis, but many professionals and members of the public found it easier to use informally than GIDNOS, which is a formal diagnosis.

The ICD-10. The ICD-10 now provides five diagnoses for the gender identity disorders (F64):

Transsexualism (F64.0) has three criteria:

1. The desire to live and be accepted as a member of the opposite sex, usually accompanied by the wish to make his or her body as congruent as possible with the preferred sex through surgery and hormone treatment;
2. The transsexual identity has been present persistently for at least two years;
3. The disorder is not a symptom of another mental disorder or a chromosomal abnormality.

Dual-role Transvestism (F64.1) has three criteria:
1. The individual wears clothes of the opposite sex in order to experience temporary membership in the opposite sex;
2. There is no sexual motivation for the cross-dressing;
3. The individual has no desire for a permanent change to the opposite sex.

Gender Identity Disorder of Childhood (64.2) has separate criteria for girls and for boys.
For girls:
1. The individual shows persistent and intense distress about being a girl, and has a stated desire to be a boy (not merely a desire for any perceived cultural advantages to being a boy) or insists that she is a boy;
2. Either of the following must be present:
    a. Persistent marked aversion to normative feminine clothing and insistence on wearing stereotypical masculine clothing;
    b. Persistent repudiation of female anatomical structures, as evidenced by at least one of the following:
        1. An assertion that she has, or will grow, a penis;
        2. Rejection of urination in a sitting position;
        3. Assertion that she does not want to grow breasts or menstruate.
3. The girl has not yet reached puberty;
4. The disorder must have been present for at least 6 months.

For boys:
1. The individual shows persistent and intense distress about being a boy, and has a desire to be a girl, or, more rarely, insists that he is a girl.
2. Either of the following must be present:
    a. Preoccupation with stereotypic female activities, as shown by a preference for either cross-dressing or simulating female attire, or by an intense desire to participate in the games and pastimes of girls and rejection of stereotypical male toys, games, and activities;
    b. Persistent repudiation of male anatomical structures, as evidenced by at least one of the following repeated assertions:
        1. That he will grow up to become a woman (not merely in the role);
        2. That his penis or testes are disgusting or will disappear;
        3. That it would be better not to have a penis or testes.
3. The boy has not yet reached puberty;
4. The disorder must have been present for at least 6 months.

Other Gender Identity Disorders (F64.8) has no specific criteria.

Gender Identity Disorder, Unspecified has no specific criteria.

Either of the previous two diagnoses could be used for those with an intersexed condition.

The purpose of the DSM-IV and ICD-10 is to guide treatment and research. Different professional groups created these nomenclatures through consensus processes at different times. There is an expectation that the differences between the systems will be eliminated in the future. At this point, the specific diagnoses are based more on clinical reasoning than on scientific investigation.

Are Gender Identity Disorders Mental Disorders? To qualify as a mental disorder, a behavioral pattern must result in a significant adaptive disadvantage to the person or cause personal mental suffering. The DSM-IV and ICD-10 have defined hundreds of mental disorders which vary in onset, duration, pathogenesis, functional disability, and treatability. The designation of gender identity disorders as mental disorders is not a license for stigmatization, or for the deprivation of gender patients' civil rights. The use of a formal diagnosis is often important in offering relief, providing health insurance coverage, and guiding research to provide more effective future treatments.

IV. The Mental Health Professional

The Ten Tasks of the Mental Health Professional. Mental health professionals (MHPs) who work with individuals with gender identity disorders may be regularly called upon to carry out many of these responsibilities:

1. To accurately diagnose the individual's gender disorder;
2. To accurately diagnose any co-morbid psychiatric conditions and see to their appropriate treatment;
3. To counsel the individual about the range of treatment options and their implications;
4. To engage in psychotherapy;
5. To ascertain eligibility and readiness for hormone and surgical therapy;
6. To make formal recommendations to medical and surgical colleagues;
7. To document their patient's relevant history in a letter of recommendation;
8. To be a colleague on a team of professionals with an interest in the gender identity disorders;
9. To educate family members, employers, and institutions about gender identity disorders;
10. To be available for follow-up of previously seen gender patients.

The Adult-Specialist. The education of the mental health professional who specializes in adult gender identity disorders rests upon basic general clinical competence in diagnosis and treatment of mental or emotional disorders. Clinical training may occur within any formally credentialing discipline -- for example, psychology, psychiatry, social work, counseling, or nursing. The following are the recommended minimal credentials for special competence with the gender identity disorders:

1. A master's degree or its equivalent in a clinical behavioral science field. This or a more advanced degree should be granted by an institution accredited by a recognized national

or regional accrediting board. The mental health professional should have documented credentials from a proper training facility and a licensing board.
2. Specialized training and competence in the assessment of the DSM-IV/ICD-10 Sexual Disorders (not simply gender identity disorders).
3. Documented supervised training and competence in psychotherapy.
4. Continuing education in the treatment of gender identity disorders, which may include attendance at professional meetings, workshops, or seminars or participating in research related to gender identity issues.

The Child-Specialist. The professional who evaluates and offers therapy for a child or early adolescent with GID should have been trained in childhood and adolescent developmental psychopathology. The professional should be competent in diagnosing and treating the ordinary problems of children and adolescents. These requirements are in addition to the adult-specialist requirement.

The Differences between Eligibility and Readiness. The SOC provide recommendations for eligibility requirements for hormones and surgery. Without first meeting these recommended eligibility requirements, the patient and the therapist should not request hormones or surgery. An example of an eligibility requirement is: a person must live full time in the preferred gender for twelve months prior to genital surgery. To meet this criterion, the professional needs to document that the real-life experience has occurred for this duration. Meeting readiness criteria -- further consolidation of the evolving gender identity or improving mental health in the new or confirmed gender role -- is more complicated, because it rests upon the clinician's and the patient's judgment.

The Mental Health Professional's Relationship to the Prescribing Physician and Surgeon. Mental health professionals who recommend hormonal and surgical therapy share the legal and ethical responsibility for that decision with the physician who undertakes the treatment. Hormonal treatment can often alleviate anxiety and depression in people without the use of additional psychotropic medications. Some individuals, however, need psychotropic medication prior to, or concurrent with, taking hormones or having surgery. The mental health professional is expected to make this assessment, and see that the appropriate psychotropic medications are offered to the patient. The presence of psychiatric co-morbidities does not necessarily preclude hormonal or surgical treatment, but some diagnoses pose difficult treatment dilemmas and may delay or preclude the use of either treatment.

The Mental Health Professional's Documentation Letter for Hormone Therapy or Surgery Should Succinctly Specify:

1. The patient's general identifying characteristics;
2. The initial and evolving gender, sexual, and other psychiatric diagnoses;
3. The duration of their professional relationship including the type of psychotherapy or evaluation that the patient underwent;
4. The eligibility criteria that have been met and the mental health professional's rationale for hormone therapy or surgery;
5. The degree to which the patient has followed the Standards of Care to date and the likelihood of future compliance;
6. Whether the author of the report is part of a gender team;

7. That the sender welcomes a phone call to verify the fact that the mental health professional actually wrote the letter as described in this document.

The organization and completeness of these letters provide the hormone-prescribing physician and the surgeon an important degree of assurance that mental health professional is knowledgeable and competent concerning gender identity disorders.

One Letter is Required for Instituting Hormone Therapy, or for Breast Surgery. One letter from a mental health professional, including the above seven points, written to the physician who will be responsible for the patient's medical treatment, is sufficient for instituting hormone therapy or for a referral for breast surgery (e.g., mastectomy, chest reconstruction, or augmentation mammoplasty).

Two Letters are Generally Required for Genital Surgery. Genital surgery for biologic males may include orchiectomy, penectomy, clitoroplasty, labiaplasty or creation of a neovagina; for biologic females it may include hysterectomy, salpingo-oophorectomy, vaginectomy, metoidioplasty, scrotoplasty, urethroplasty, placement of testicular prostheses, or creation of a neophallus.

It is ideal if mental health professionals conduct their tasks and periodically report on these processes as part of a team of other mental health professionals and nonpsychiatric physicians. One letter to the physician performing genital surgery will generally suffice as long as two mental health professionals sign it.

More commonly, however, letters of recommendation are from mental health professionals who work alone without colleagues experienced with gender identity disorders. Because professionals working independently may not have the benefit of ongoing professional consultation on gender cases, two letters of recommendation are required prior to initiating genital surgery. If the first letter is from a person with a master's degree, the second letter should be from a psychiatrist or a Ph.D. clinical psychologist, who can be expected to adequately evaluate co-morbid psychiatric conditions. If the first letter is from the patient's psychotherapist, the second letter should be from a person who has only played an evaluative role for the patient. Each letter, however, is expected to cover the same topics. At least one of the letters should be an extensive report. The second letter writer, having read the first letter, may choose to offer a briefer summary and an agreement with the recommendation.

V. Assessment and Treatment of Children and Adolescents

Phenomenology. Gender identity disorders in children and adolescents are different from those seen in adults, in that a rapid and dramatic developmental process (physical, psychological and sexual) is involved. Gender identity disorders in children and adolescents are complex conditions. The young person may experience his or her phenotype sex as inconsistent with his or her own sense of gender identity. Intense distress is often experienced, particularly in adolescence, and there are frequently associated emotional and behavioral difficulties. There is greater fluidity and variability in outcomes, especially in pre-pubertal children. Only a few

gender variant youths become transsexual, although many eventually develop a homosexual orientation.

Commonly seen features of gender identity conflicts in children and adolescents include a stated desire to be the other sex; cross dressing; play with games and toys usually associated with the gender with which the child identifies; avoidance of the clothing, demeanor and play normally associated with the child's sex and gender of assignment; preference for playmates or friends of the sex and gender with which the child identifies; and dislike of bodily sex characteristics and functions. Gender identity disorders are more often diagnosed in boys.

Phenomenologically, there is a qualitative difference between the way children and adolescents present their sex and gender predicaments, and the presentation of delusions or other psychotic symptoms. Delusional beliefs about their body or gender can occur in psychotic conditions but they can be distinguished from the phenomenon of a gender identity disorder. Gender identity disorders in childhood are not equivalent to those in adulthood and the former do not inevitably lead to the latter. The younger the child the less certain and perhaps more malleable the outcome.

Psychological and Social Interventions. The task of the child-specialist mental health professional is to provide assessment and treatment that broadly conforms to the following guidelines:

1. The professional should recognize and accept the gender identity problem. Acceptance and removal of secrecy can bring considerable relief.
2. The assessment should explore the nature and characteristics of the child's or adolescent's gender identity. A complete psychodiagnostic and psychiatric assessment should be performed. A complete assessment should include a family evaluation, because other emotional and behavioral problems are very common, and unresolved issues in the child's environment are often present.
3. Therapy should focus on ameliorating any comorbid problems in the child's life, and on reducing distress the child experiences from his or her gender identity problem and other difficulties. The child and family should be supported in making difficult decisions regarding the extent to which to allow the child to assume a gender role consistent with his or her gender identity. This includes issues of whether to inform others of the child's situation, and how others in the child's life should respond; for example, whether the child should attend school using a name and clothing opposite to his or her sex of assignment. They should also be supported in tolerating uncertainty and anxiety in relation to the child's gender expression and how best to manage it. Professional network meetings can be very useful in finding appropriate solutions to these problems.

Physical Interventions. Before any physical intervention is considered, extensive exploration of psychological, family and social issues should be undertaken. Physical interventions should be addressed in the context of adolescent development. Adolescents' gender identity development can rapidly and unexpectedly evolve. An adolescent shift toward gender conformity can occur primarily to please the family, and may not persist or reflect a permanent change in gender identity. Identity beliefs in adolescents may become firmly held and strongly expressed, giving a false impression of irreversibility; more fluidity may return at a later stage. For these reasons, irreversible physical interventions should be delayed as long as is clinically appropriate. Pressure for physical interventions because of an adolescent's level of distress can be great and in such

circumstances a referral to a child and adolescent multi-disciplinary specialty service should be considered, in locations where these exist.

Physical interventions fall into three categories or stages:

1. Fully reversible interventions. These involve the use of LHRH agonists or medroxyprogesterone to suppress estrogen or testosterone production, and consequently to delay the physical changes of puberty.
2. Partially reversible interventions. These include hormonal interventions that masculinize or feminize the body, such as administration of testosterone to biologic females and estrogen to biologic males. Reversal may involve surgical intervention.
3. Irreversible interventions. These are surgical procedures.

A staged process is recommended to keep options open through the first two stages. Moving from one state to another should not occur until there has been adequate time for the young person and his/her family to assimilate fully the effects of earlier interventions.

Fully Reversible Interventions. Adolescents may be eligible for puberty-delaying hormones as soon as pubertal changes have begun. In order for the adolescent and his or her parents to make an informed decision about pubertal delay, it is recommended that the adolescent experience the onset of puberty in his or her biologic sex, at least to Tanner Stage Two. If for clinical reasons it is thought to be in the patient's interest to intervene earlier, this must be managed with pediatric endocrinological advice and more than one psychiatric opinion.

Two goals justify this intervention: a) to gain time to further explore the gender identity and other developmental issues in psychotherapy; and b) to make passing easier if the adolescent continues to pursue sex and gender change. In order to provide puberty delaying hormones to an adolescent, the following criteria must be met:

1. throughout childhood the adolescent has demonstrated an intense pattern of cross-sex and cross-gender identity and aversion to expected gender role behaviors;
2. sex and gender discomfort has significantly increased with the onset of puberty;
3. the family consents and participates in the therapy.

Biologic males should be treated with LHRH agonists (which stop LH secretion and therefore testosterone secretion), or with progestins or antiandrogens (which block testosterone secretion or neutralize testosterone action). Biologic females should be treated with LHRH agonists or with sufficient progestins (which stop the production of estrogens and progesterone) to stop menstruation.

Partially Reversible Interventions. Adolescents may be eligible to begin masculinizing or feminizing hormone therapy as early as age 16, preferably with parental consent. In many countries 16-year olds are legal adults for medical decision making, and do not require parental consent.

Mental health professional involvement is an eligibility requirement for triadic therapy during adolescence. For the implementation of the real-life experience or hormone therapy, the mental health professional should be involved with the patient and family for a minimum of six months. While the number of sessions during this six-month period rests upon the clinician's judgment,