From the desk of

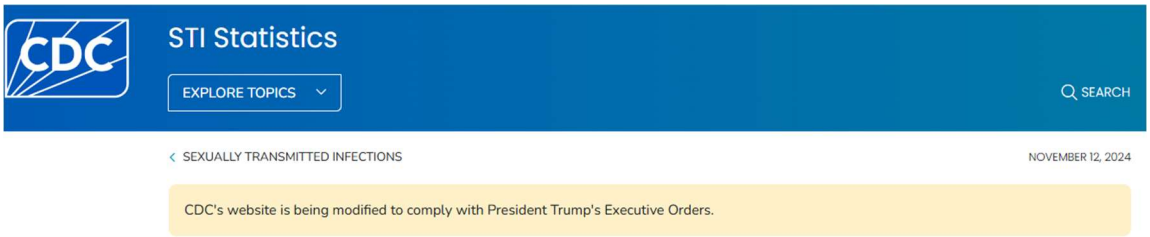
Mrs. Melanie Marshall

Part I - Notes for school board discussion about condoms at GHS.

I made 9 figures and found 3 documents that I will use to help inform my vote. Helpful links, in case I need them.

- **National Youth Sexual Risk data from the CDC:** https://www.cdc.gov/healthyyouth/data/yrbs/reports_factsheet_publications.htm#anchor_1596724918
- **National Youth STI data from the CDC:** https://www.cdc.gov/sti-statistics/?CDC_AAref_Val=https://www.cdc.gov/std/statistics/2020/figures.htm
- **US Teen Pregnancy Information:** https://opa.hhs.gov/adolescent-health/reproductive-health-and-teen-pregnancy/trends-teen-pregnancy-and-childbearing
- **CDC Sexually Risky Behaviors in Youth:** https://www.cdc.gov/youth-behavior/risk-behaviors/sexual-risk-behaviors.html?CDC_AAref_Val=https://www.cdc.gov/healthyyouth/sexualbehaviors/
- **Collaborative review on effective interventions for preventing teen pregnancy:** https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD005215.pub3/full#CD005215-abs-0003
- **Teen Birth Rates by US County:** https://www.cdc.gov/teenpregnancy/about/alt-text/map-county-text.htm - *This website has been pulled, but this replacement site has some good information: https://www.congress.gov/crs-product/R45184*

Interestingly, some of the information I was looking for (and had previously bookmarked on my computer when I was researching something from the news about teen pregnancies) has been removed by the current White House administration. The removal and restructuring of information have occurred sometime between fall of 2024 and now (spring of 2025).



When looking at CDC data for youth risk, I saw the disclaimer below.

> Per a court order, HHS is required to restore this website as of 11:59PM ET, February 11, 2025. Any information on this page promoting gender ideology is extremely inaccurate and disconnected from the immutable biological reality that there are two sexes, male and female. The Trump Administration rejects gender ideology and condemns the harms it causes to children, by promoting their chemical and surgical mutilation, and to women, by depriving them of their dignity, safety, well-being, and opportunities. This page does not reflect biological reality and therefore the Administration and this Department rejects it.

It is unclear to me exactly what this disclaimer is for. However, this dataset contains information on LGBTQ+ students. I am now curious about this biological claim of two sexes. Given the Presidential Executive Order (Jan 20, 2025) and our state Governor's corresponding (Jan 30, 2025) directive about sex and gender, I wonder if this topic will come up during our next meeting? Also, there is a current Texas Senate bill about restroom use (SB240), so we may need to talk about this. Just in case, I'll take some notes after I'm done here.

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Mrs. Melanie Marshall

Notes for condom access program:

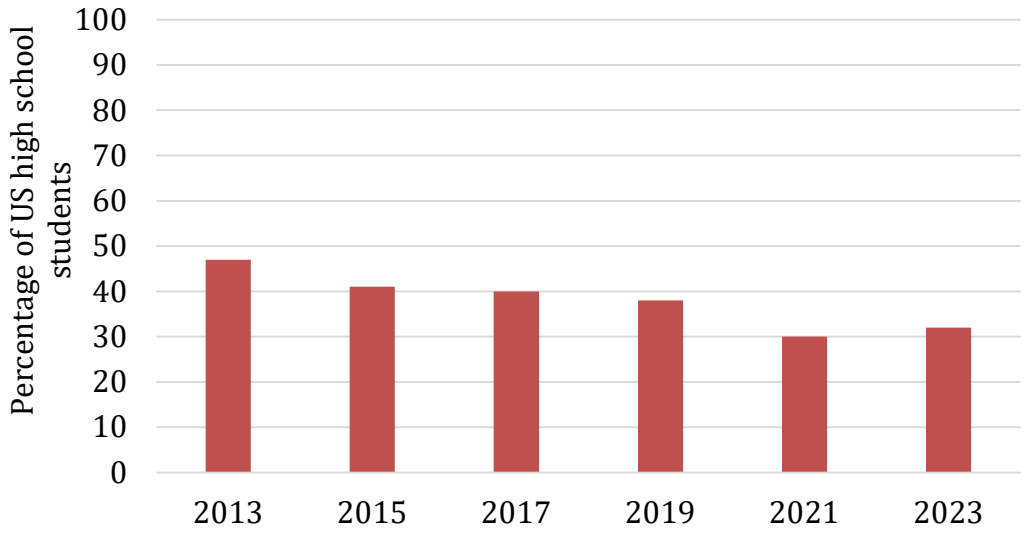

Figure 1. Percentage of US high school students who have ever engaged in sexual intercourse (data from CDC National Youth Risk Behavior Surveys, 2013 - 2023).

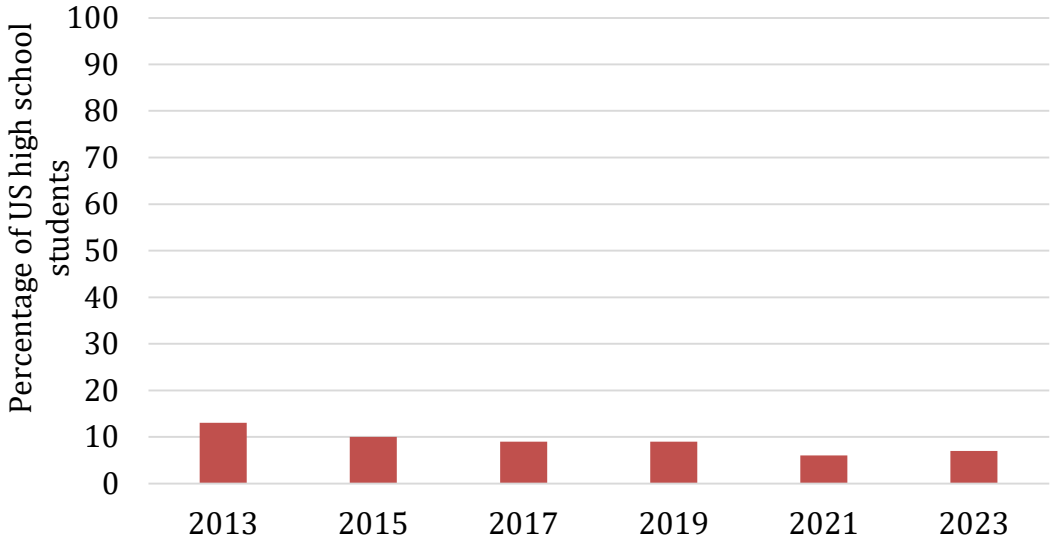

Figure 2. Percentage of US high school students who were tested for HIV and/or other STIs during the last year (data from CDC National Youth Risk Behavior Survey, 2013-2023; note the questions about STI testing changed throughout the years, this is a general summary).

From the desk of
Mrs. Melanie Marshall

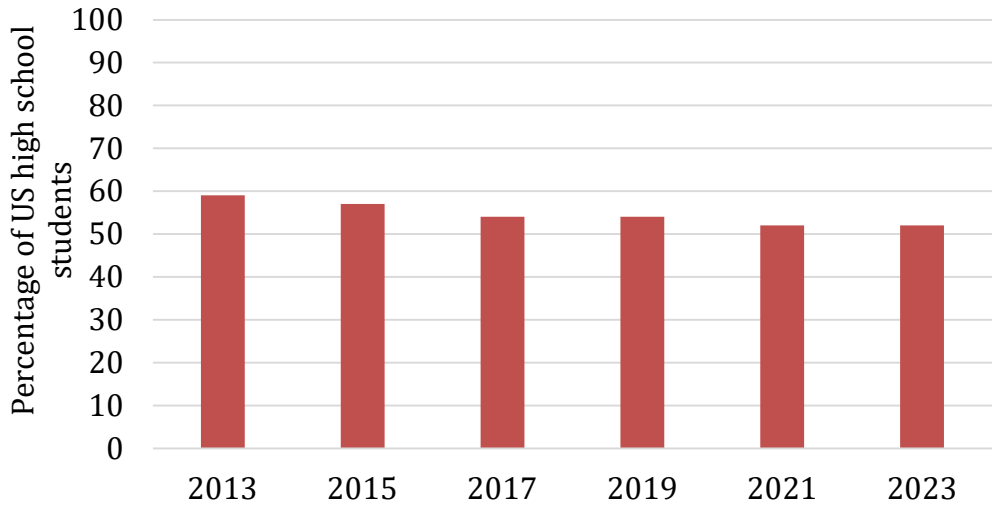

Figure 3. Percentage of US high school students who used a condom during last sexual intercourse (data from CDC National Youth Risk Behavior Survey, 2013-2023).

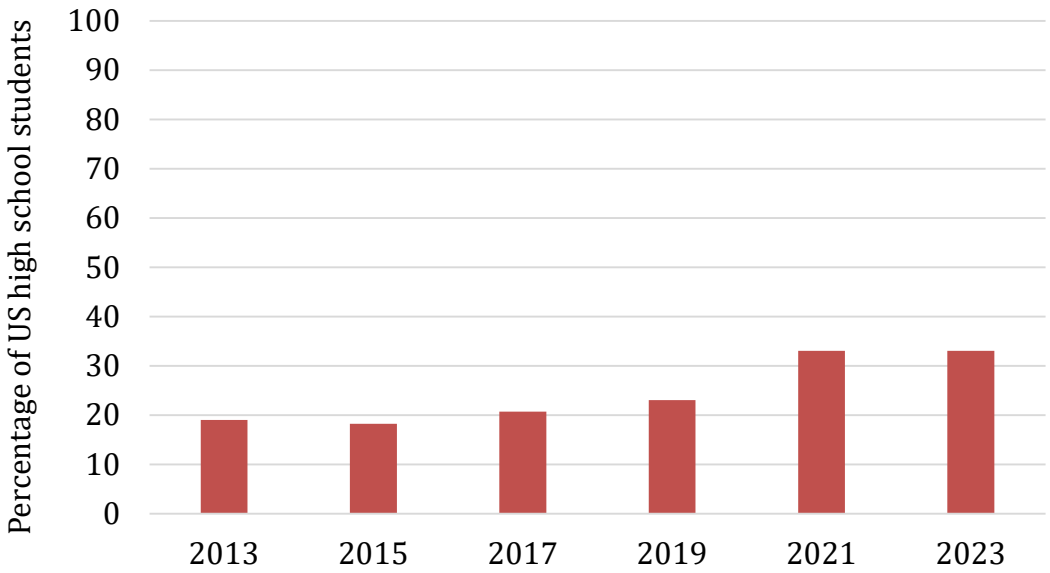

Figure 4. Percentage of US high school students who used hormonal birth control pills before last sexual intercourse (data from CDC National Youth Risk Behavior Survey, 2013 - 2023).

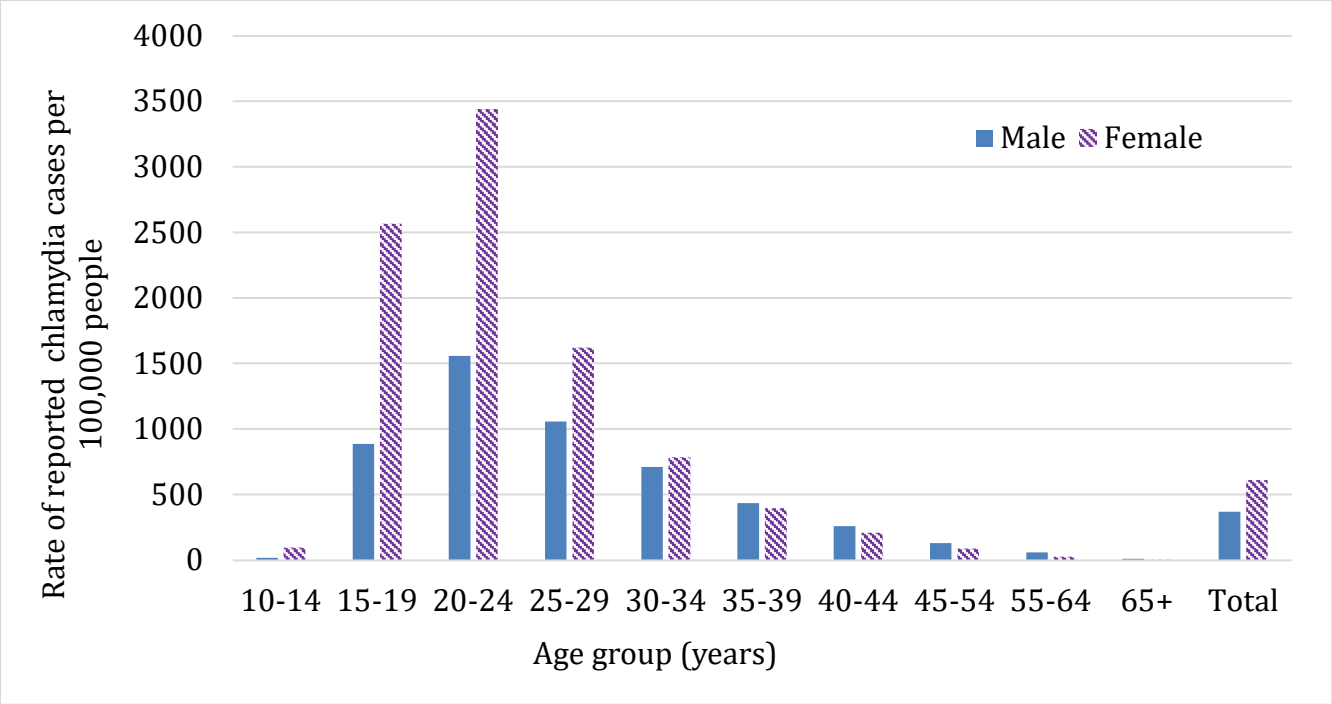

Figure 5. Reported cases of chlamydia, per 100,000 people, by age and sex in the US in 2023. Data from the CDC. https://www.cdc.gov/sti-statistics/annual/slides.html

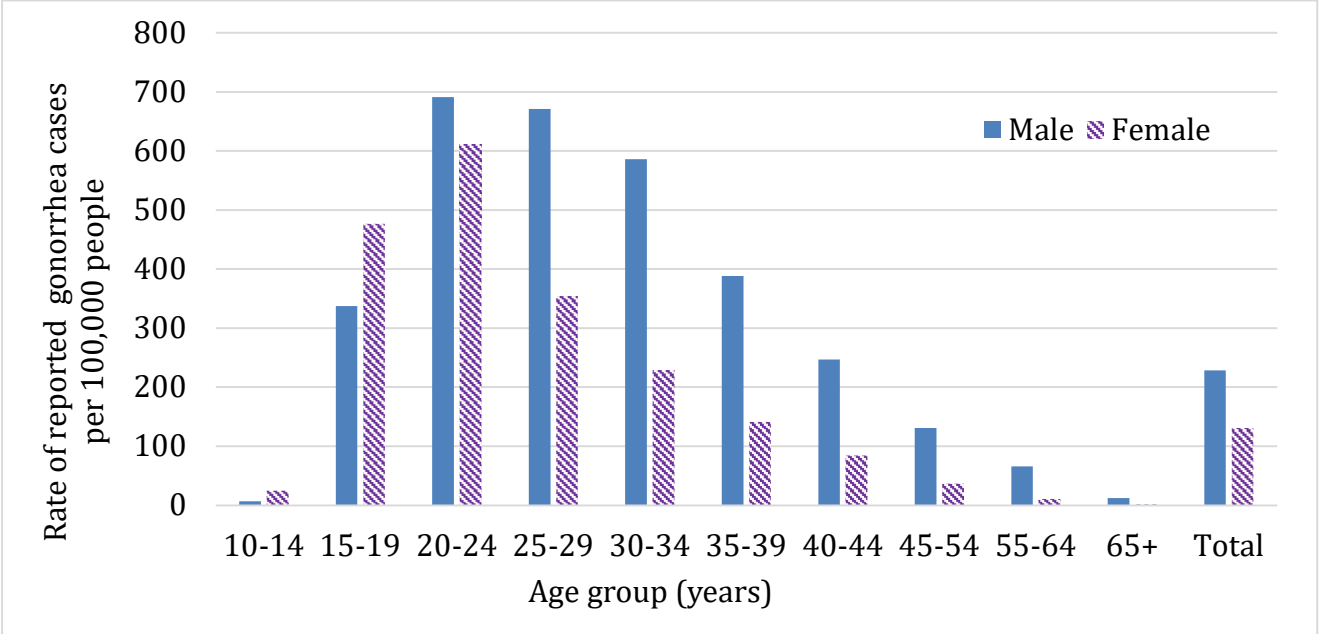

Figure 6. Reported cases of gonorrhea, per 100,000 people, by age and sex in the US in 2023. Data from the CDC. https://www.cdc.gov/sti-statistics/annual/slides.html

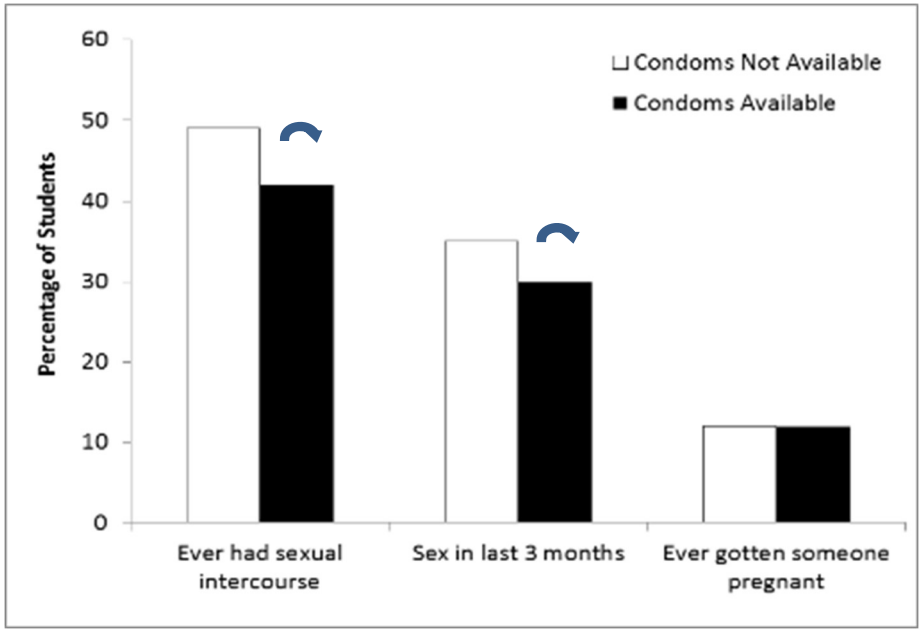

Figure 7. Data from adolescents in schools that made condoms available compared to schools that did not have condoms available. There was no difference between the percentage of students who got another person pregnant. The symbols mean the groups are statistically different from one another (redrawn from data in Blake et al., 2003).

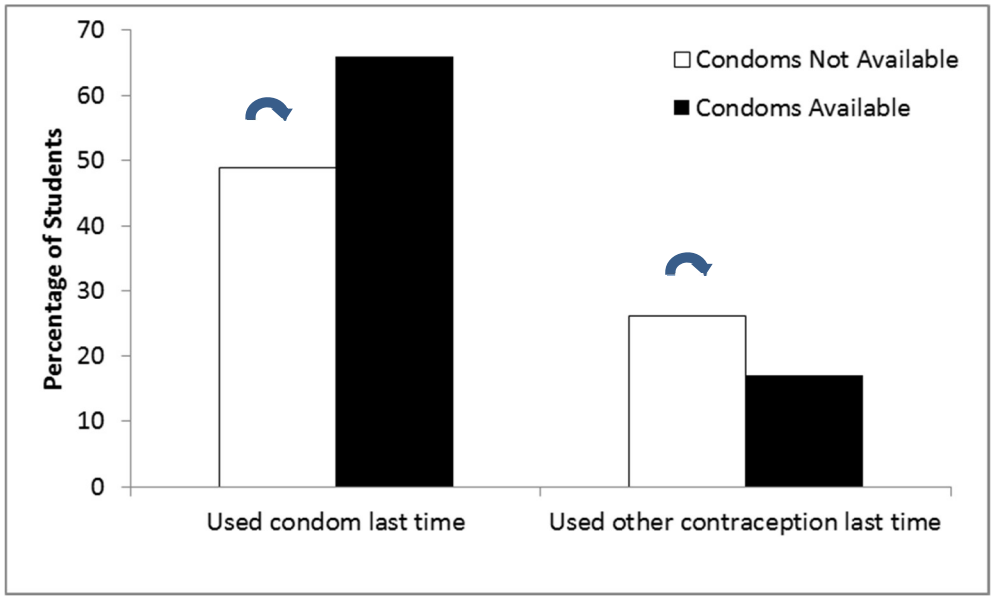

Figure 8. Data from adolescents in schools that made condoms available compared to schools that did not have condoms available. When condoms were available students were more likely to have used a condom during their most recent sexual encounter and less likely to have used other contraceptive methods (redrawn from data in Blake et al., 2003).

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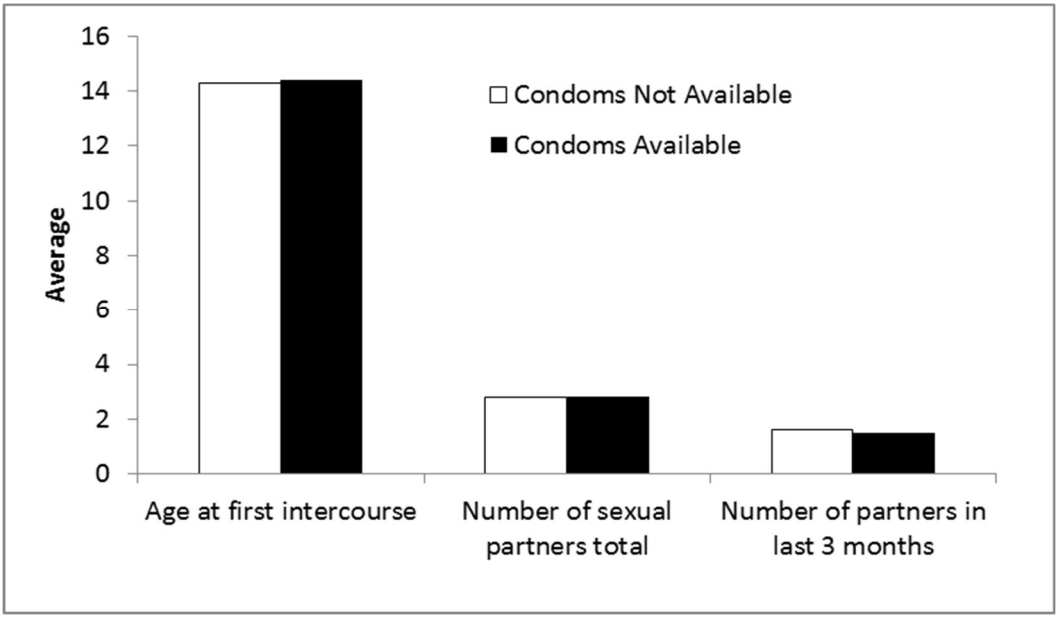

Figure 9. Data from adolescents in schools that made condoms available compared to schools that did not have condoms available. Adolescents in the two schools did not differ in age at first intercourse, number of sexual partners in their lifetime, or number of sexual partners in the last 3 months (redrawn from data in Blake et al., 2003).

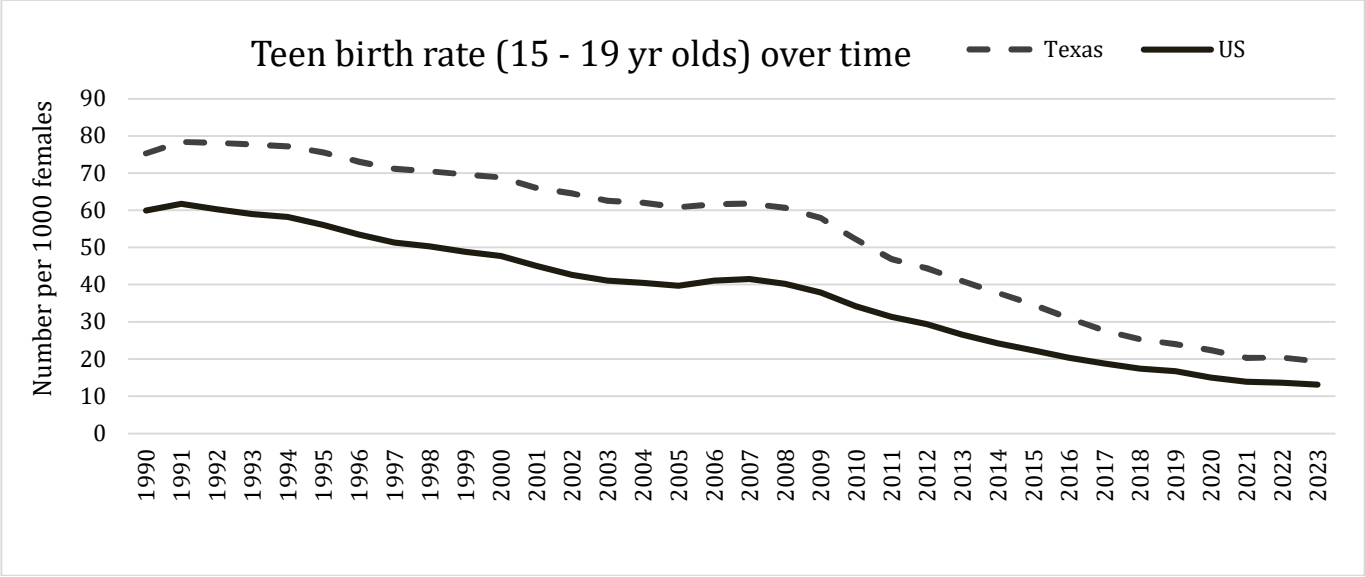

Figure 10. Teen birth rate, defined as number of births per 1000 females aged 15-19 from 1990 - 2023 for the US as a whole and for Texas (where the Marshalls live).

If f you'd like to compare to your state data, or look at US trends from 1940- 2023, see here: https://www.congress.gov/crs_external_products/R/HTML/R45184.web.html#_Ref195711450 and this interactive graph https://www.congress.gov/crs-product/R45184)

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Document 1 - Summary of condoms and STI prevention. Based on a meta-analysis (an analysis of multiple studies) that analyzed 45 different studies that investigated this topic. The conclusion from that paper is as follows: "*Condom use was associated with reduced risk of gonorrhea and chlamydia in men and women in most studies, despite methodological limitations that likely underestimate condom effectiveness.*" (Warner et al., 2006).

Condoms also significantly reduce the chances of contracting HIV from a partner during sexual activity. *"Sexual intercourse and contact with contaminated blood products (e.g., intravenous drug use) account for the majority of HIV infections. The wearing of condoms during sexual intercourse has been promoted to reduce the infection and spread of sexually transmitted infections (STIs) such as HIV. The review of studies found that condoms, when used consistently, substantially reduced HIV infection but did not totally eliminate the risk of infection."* (Weller and Davis-Beaty, 2002).

Document 2 – Data from the *Teen Births in the United States: Overview and Recent Trends congressional report*, dated 4/17/2025. https://www.congress.gov/crs-product/R45184

> "Adolescent childbearing is associated with significant social, health, and financial risks for teens, their families, and society more broadly. Data from the National Center for Health Statistics (NCHS), within the Centers for Disease Control and Prevention (CDC), indicate that the teen birth rate has decreased steadily over time. However, the United States continues to have one of the highest rates of teen births among other industrialized countries.
>
> This report focuses on teen birth rates—and the marked decline in recent years. The teen birth rate is defined as the number of live births per 1,000 females aged 15 to 19 each year. The earliest NCHS estimate of the teen birth rate (in 1940) was 54.1, which later peaked in 1957 at 96.3. It then decreased in most years from the 1960s through the 1980s, with a low of 50.2 in 1986. The birth rate increased over the next few years, to 61.8 in 1991. From 1992 onward, the teen birth rate declined except in two years, 2006 and 2007. From 2007 to 2023, the rate declined by approximately 68%, to a historical low in 2023 of 13.1.
>
> Research suggests that multiple factors have led to lower teen birth rates in the United States. From the 1990s through 2019, the risk of teen pregnancy decreased primarily because of improved contraceptive use, including an increase in the use of more effective contraceptive methods (e.g., long-acting and reversible methods) and an increase in the use of multiple methods of contraception. During this period, some of the risk of pregnancy among younger teens declined because of decreased sexual activity; however, general trends in adolescent sexual activity have remained relatively stable. Broad economic and social variables may also influence teen behaviors, such as expanded educational or labor opportunities.
>
> Teen pregnancy has high costs for teen parents, their children, and society more

generally. Teenage mothers and fathers tend to have less education and are more likely to have lower incomes than their peers who are not parents. Moreover, lower levels of education reduce teen parents' potential for economic self-sufficiency. Children of adolescent parents are also more likely to face certain adverse health and social outcomes, such as preterm birth and other child morbidities.

This report accompanies CRS Report R45183, Adolescent Pregnancy: Federal Prevention Programs, which discusses federal support for programs that seek to prevent pregnancy among adolescents, and CRS In Focus IF10877, Federal Adolescent Pregnancy Prevention Programs, which includes summary information about the programs."

Document 3 – This is a great study! It provides data from 29 articles published with data from 6 countries on condom availability programs (CAPs) in high schools. There are a lot of tables and charts in this paper, but the authors' summary of the paper is here: *"We found that CAP does not increase sexual activity nor lead to a greater number of sexual partners. It also does not lower the age of sexual initiation. A majority of the studies reported an increase in condom uptake and use at last sex among students with CAP. All the studies that examined STI found a decrease of STI symptoms and rates for students with CAP compared with the control group. The data on HIV rates was inconclusive. There was no difference in pregnancy rates associated with participation in CAP programs." (Algu et al., 2019).*

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From the desk of
Mrs. Melanie Marshall

Part II – Notes on Sex, Gender, Biology, and Policy

I know I have my own feelings about sex and sexuality, and it seems those in government do, too. The removal of information from federal agency websites concerns me as a citizen. I want to know more.

In January, President Trump issued an Executive Order (EO) defining sex. Later that month, Governor Abbott sent a letter echoing Trump's EO. Parts of Trump's EO and all of Abbott's letter are copied below so I can easily access them.

EO: https://www.whitehouse.gov/presidential-actions/2025/01/defending-women-from-gender-ideology-extremism-and-restoring-biological-truth-to-the-federal-government/
Letter: https://gov.texas.gov/news/post/governor-abbott-directs-texas-state-agencies-to-reject-woke-gender-ideologies

PRESIDENT DONALD J. TRUMP — The WHITE HOUSE

Released by the White House on January 20, 2025

Section 1. Purpose. Across the country, ideologues who deny the biological reality of sex have increasingly used legal and other socially coercive means to permit men to self-identify as women and gain access to intimate single-sex spaces and activities designed for women, from women's domestic abuse shelters to women's workplace showers. This is wrong. Efforts to eradicate the biological reality of sex fundamentally attack women by depriving them of their dignity, safety, and well-being. The erasure of sex in language and policy has a corrosive impact not just on women but on the validity of the entire American system. Basing Federal policy on truth is critical to scientific inquiry, public safety, morale, and trust in government itself.

This unhealthy road is paved by an ongoing and purposeful attack against the ordinary and longstanding use and understanding of biological and scientific terms, replacing the immutable biological reality of sex with an internal, fluid, and subjective sense of self unmoored from biological facts. Invalidating the true and biological category of "woman" improperly transforms laws and policies designed to protect sex-based opportunities into laws and policies that undermine them, replacing longstanding, cherished legal rights and values with an identity-based, inchoate social concept.

Accordingly, my Administration will defend women's rights and protect freedom of conscience by using clear and accurate language and policies that recognize women are biologically female, and men are biologically male.

From the desk of

Mrs. Melanie Marshall

Sec. 2. Policy and Definitions. It is the policy of the United States to recognize two sexes, male and female. These sexes are not changeable and are grounded in fundamental and incontrovertible reality. Under my direction, the Executive Branch will enforce all sex-protective laws to promote this reality, and the following definitions shall govern all Executive interpretation of and application of Federal law and administration policy:

(a) "Sex" shall refer to an individual's immutable biological classification as either male or female. "Sex" is not a synonym for and does not include the concept of "gender identity."

(b) "Women" or "woman" and "girls" or "girl" shall mean adult and juvenile human females, respectively.

(c) "Men" or "man" and "boys" or "boy" shall mean adult and juvenile human males, respectively.

(d) "Female" means a person belonging, at conception, to the sex that produces the large reproductive cell.

(e) "Male" means a person belonging, at conception, to the sex that produces the small reproductive cell.

(f) "Gender ideology" replaces the biological category of sex with an ever-shifting concept of self-assessed gender identity, permitting the false claim that males can identify as and thus become women and vice versa, and requiring all institutions of society to regard this false claim as true. Gender ideology includes the idea that there is a vast spectrum of genders that are disconnected from one's sex. Gender ideology is internally inconsistent, in that it diminishes sex as an identifiable or useful category but nevertheless maintains that it is possible for a person to be born in the wrong sexed body.

From the desk of
Mrs. Melanie Marshall

The Texas Governor, Greg Abbott, followed suit and issued his own letter 10 days later.

GOVERNOR GREG ABBOTT

January 30, 2025

Dear Chairmen and Executive Directors:

This office has consistently reiterated a simple truth: The State of Texas recognizes only two sexes—male and female—and sex discrimination consists in treating a member of one sex less favorably than the other, absent some pertinent difference.[1]

Others have sought to distort the guarantee that men and women must be treated equally in order to impose mandates concerning sexual orientation and gender identity. For example, Travis County courts purported to instruct state agencies to change an individual's "sex" designation on birth certificates and driver's licenses to reflect supposed gender identity. These instructions were not grounded in any recognized state cause of action, were issued in proceedings where no agency was a party, and contradicted both statutory law and biological reality. Consistent with state law, the Texas Department of Public Safety (DPS) and Department of State Health Services (DSHS) have rightly refused to observe these lawless pronouncements.

On January 20, 2025, President Donald Trump issued an Executive Order, *Defending Women from Gender Ideology Extremism and Restoring Biological Truth to the Federal Government*, rejecting similar efforts by the Biden-Harris Administration to distort commonsense notions of biological sex. Section 2 of the President's Executive Order provides that "[i]t is the policy of the United States to recognize two sexes, male and female. These sexes are not changeable and are grounded in fundamental and incontrovertible reality." This understanding "shall govern all … application of Federal law." And it confirms what my office has repeatedly stressed before.

As the Chief Executive Officer of the State, I direct you to follow state and federal law. All Texas agencies must ensure that agency rules, internal policies, employment practices, and other actions comply with the law and the biological reality that there are only two sexes—male and female.

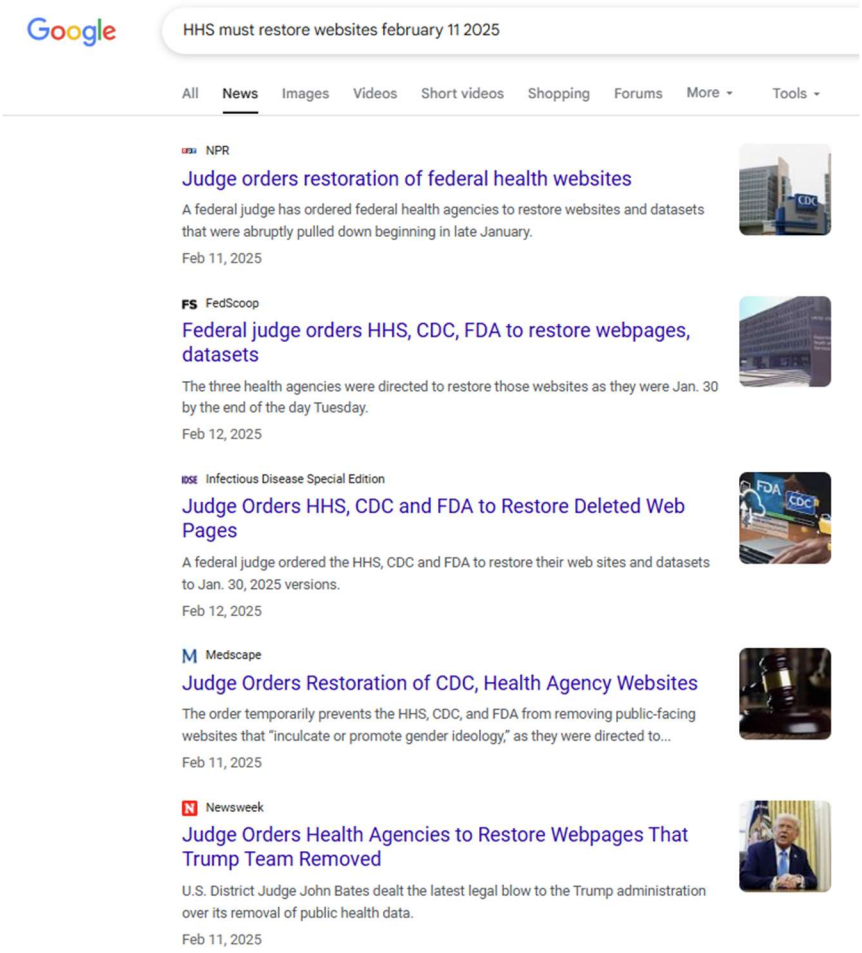
Sincerely,

Greg Abbott
Governor

It seems enforcement of the EO meant that multiple federal agencies had to amend or edit their information to align with the views posted in the EO. I went to Google to see what the court order mentioned in the disclaimer was all about. I got the below hits.

From the desk of

Mrs. Melanie Marshall



After perusing the articles, it seems that on January 29, 2025 the US Office of Personnel Management (OPM) sent out a memo to all Heads and Acting Heads of Departments and Agencies that they must comply with the new EO by taking several steps no later than 5 PM on January 31, 2025. Point 1, section d includes websites (1.d. "Take down all outward facing media (websites, social media accounts, etc.) that inculcate or promote gender ideology."). This is why the Centers for Disease Control, Health and Human Services, and other agencies were removing (censoring) information.

OPM memo can be found here:
https://chcoc.gov/sites/default/files/OPM%20Memo%20Initial%20Guidance%20Regarding%20Trump%20Executive%20Order%20Defending%20Women%201-29-2025%20FINAL.pdf

From the desk of
Mrs. Melanie Marshall

UNITED STATES OFFICE OF PERSONNEL MANAGEMENT
Washington, DC 20415

The Director

MEMORANDUM

TO:	Heads and Acting Heads of Departments and Agencies
FROM:	Charles Ezell, Acting Director, U.S. Office of Personnel Management
DATE:	January 29, 2025
RE:	Initial Guidance Regarding President Trump's Executive Order *Defending Women*.

Pursuant to its authority under 5 U.S.C. § 1103(a)(1) and (a)(5), the U.S. Office of Personnel Management (OPM) is providing the following initial guidance to agencies regarding the President's Executive Order entitled *Defending Women from Gender Ideology Extremism and Restoring Biological Truth to the Federal Government* (*Defending Women*).

Steps to End Federal Funding of Gender Ideology: In light of *Defending Women*, each agency should take prompt actions to end all agency programs that use taxpayer money to promote or reflect gender ideology as defined in Section 2(f) of *Defending Women*. Specifically, agency heads should take the following steps:

1. No later than **5:00 p.m. EST on Friday, January 31, 2025**

    a. Send an email to all agency employees announcing that the agency will be complying with *Defending Women* and this guidance.

    b. Review all agency programs, contracts, and grants, and terminate any that promote or inculcate gender ideology.

    c. Review all agency position descriptions and send a notification to all employees whose position description involves inculcating or promoting gender ideology that they are being placed on paid administrative leave effective immediately as the agency takes steps to close/end all initiatives, offices, and programs that inculcate or promote gender ideology.

    d. Take down all outward facing media (websites, social media accounts, etc.) that inculcate or promote gender ideology.

    e. Review agency email systems such as Outlook and turn off features that prompt users for their pronouns.

From the desk of
Mrs. Melanie Marshall

Removal of data caused multiple problems for medical personnel; Doctors for America sued. On February 11, 2025, Judge John Bates ruled that the websites must be restored. They were restored with the disclaimers.

Wow! I had no idea that all of this was so complex and connected. Now I want to really get a handle on what the terms sex and gender mean.

Definitions of relevant terms:

- Sex:
  - a combination of genetic, gonadal, gametic, hormonal, and other morphological characteristics used to categorize an individual along the male to female continuum. – *Harris et al., 2024 General and Comparative Endocrinology*
  - a set of biological attributes in humans and animals. It is primarily associated with physical and physiological features including chromosomes, gene expression, hormone levels and function, and reproductive/sexual anatomy. - *Canadian Institutes of Health Research*
  - is the biological trait that determines whether a sexually reproducing organism produces male or female gametes. – *Wikipedia*
    - *Note – I had to look this up. What are male and female gametes?*
      - *Gametes are sex or reproductive cells – sperm and egg. These are "sexed" based on size. This sizing is based on isogamy and anisogamy. In some species, gametes of different types are the same size (isogamous). In other species, including humans, the gametes of different types are different sized (anisogamous). By definition, those that produce the larger gamete are female and those that produce the smaller gamete are male.*
      - *This categorization works across the tree of life for sexually reproducing organisms because there are SO MANY variations on how organism become and maintain a sex. Interesting!!*
      - *I found great info here: https://open.lib.umn.edu/evolutionbiology/chapter/7-4-sex-its-about-the-gametes-2/*
  - Either of the two main categories (male and female) into which humans and most other living things are divided on the basis of their reproductive functions. – *Dictionary.com*
  - The National Institutes of Health defines biological sex ("assigned sex") as "a multidimensional biological construct based on anatomy, physiology, genetics, and hormones," also referred to by some as "sex traits." All animals, including humans, have a sex. – *American Society for Reproductive Medicine*
  - Biological sex is a label assigned by a medical professional at birth based on physical characteristics (genitalia) and other biological determinants. – *American Society for Reproductive Medicine*
    - *Note - in the US, our sex is assigned at birth and written on our birth certificates (and other legal documentation). The determination of sex is typically done via examination of the external genitalia. Sometimes, a blood test for genotype is done, but the primary means of assignment is visual inspection by the physician and delivery team.*
  - is a biological classification, encoded in our DNA. Males have XY chromosomes, and females have XX chromosomes. Sex makes us male or female. Every cell in

your body has a sex—making up tissues and organs, like your skin, brain, heart, and stomach. – *National Institutes of Health Office of Research on Women's Health*

- LGBTQ+ (also LGBTQiA+):
  - An acronym capturing sexual orientations, sexes, and genders
    - L = lesbian
    - G = gay
    - B = bisexual
    - T = transgender
    - Q = queer or questioning
    - i = intersex
    - A = asexual or ally
  - See more terms and definitions here: https://lgbtqia.ucdavis.edu/educated/glossary

- Gender:
  - a social construct incorporating psychological, social and cultural factors that shape attitudes, behaviors, and stereotypes. – *Harris et al., 2024 General and Comparative Endocrinology*
  - the socially constructed roles, behaviors, activities, and attributes that a given society considers appropriate for different genders. In a human context, the distinction between gender and sex reflects the usage of these terms: Sex refers to the biological status of being male, female, or intersex, whereas gender implies the psychological, behavioral, social, and cultural aspects of gender (i.e., masculinity, femininity, nonbinary, nonconforming, or other gender). – *American Psychological Association*
  - the range of social, psychological, cultural, and behavioral aspects of being a man (or boy), woman (or girl), or third gender. – *Wikipedia*
  - the male sex or the female sex, especially when considered with reference to social and cultural differences rather than biological ones, or one of a range of other identities that do not correspond to established ideas of male and female. – *Dictionary.com*
  - refers to the socially constructed roles, behaviors, expressions, and identities of girls, women, boys, men, and gender diverse people. It influences how people perceive themselves and each other, and how they act and interact. Gender is usually conceptualized as binary (girl/woman and boy/man), yet there is considerable diversity in how individuals and groups understand, experience, and express it. – *National Institutes of Health Office of Research on Women's Health*

- Sexual orientation:
  - An inherent or immutable enduring emotional, romantic or sexual attraction to other people. Note: an individual's sexual orientation is independent of their gender identity. – *Human Rights Campaign*
  - Sexual orientation is an enduring personal pattern of romantic attraction or sexual attraction (or a combination of these) to persons of the opposite sex or gender, the same sex or gender, or to both sexes or more than one gender. – *Wikipedia*

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Mrs. Melanie Marshall

- Intersex: Intersex people are born with a variety of differences in their sex traits and reproductive anatomy. There is a wide variety of difference among intersex variations, including differences in genitalia, chromosomes, gonads, internal sex organs, hormone production, hormone response, and/or secondary sex traits. -*Human Rights Campaign*

- Cisgender: denoting or relating to a person whose gender identity corresponds with the sex registered for them at birth; not transgender. – *Dictionary.com*

- Transgender: An umbrella term for people whose gender identity and/or expression is different from cultural expectations based on the sex they were assigned at birth. Being transgender does not imply any specific sexual orientation. Therefore, transgender people may identify as straight, gay, lesbian, bisexual, etc. – *Human Rights Campaign*

- Ideology: a system of ideas and ideals, especially one which forms the basis of economic or political theory and policy. – *Dictionary.com*

- Gender Norms or Gender Roles: the role or behavior considered to be appropriate to a particular gender as determined by prevailing cultural norms. – *Dictionary.com*

- Gender identity: a psychological sense of self; how individuals perceive themselves within specific cultures and contexts. Encompasses woman, man, and every option and combination in between, including agender. - *Harris et al., 2024 General and Comparative Endocrinology*

- Gender Expression: how individuals present their gender, e.g., via clothes, actions or other outward appearance, within specific cultures and contexts. Encompasses masculine, feminine, and every option and combination in between. - *Harris et al., 2024 General and Comparative Endocrinology*

There are so many nuances here! **Sex is not the same as gender. Gender identity is not related to sexual orientation**. All of these can be described as spectra.

I found this website with a Genderbread Person to be really informative!
https://www.itspronouncedmetrosexual.com/2018/10/the-genderbread-person-v4/

I also really enjoyed this chapter. https://open.lib.umn.edu/evolutionbiology/part/chapter-8-sex-and-gender-2/

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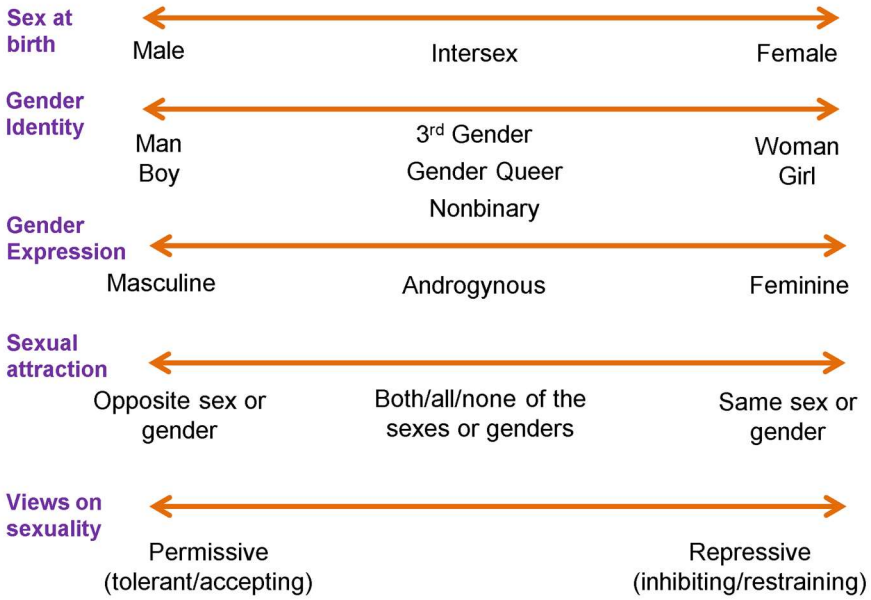
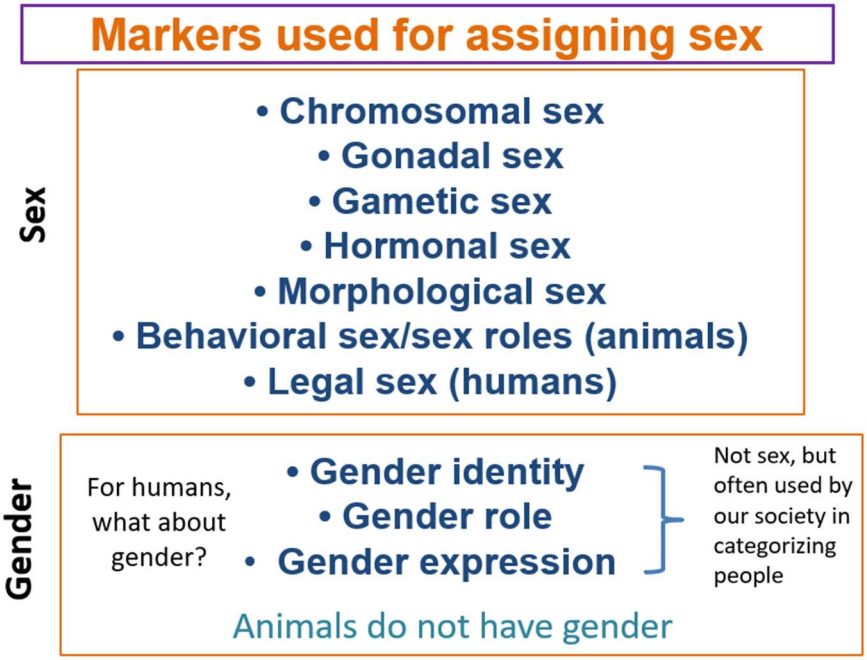
There are spectra associated with sex, gender, and sexuality!



Markers and terminology for classification of sex and gender:



<u>How does one become a sex? Via sex determination and differentiation.</u>

- <u>Sex determination:</u> The event that determines how an organism will develop along the sex continuum.
- <u>Sex differentiation:</u> The developmental processes that occur along the sex continuum.

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WOW! *not all organisms have a sex (e.g., fugus, slime mold) and some species are hermaphrodites (meaning they have both male and female reproductive parts; many plants, some invertebrates. Certain species are even sequential hermaphrodites! Meaning they change sexes!! See blue headed wrasse and clown fish). I now realize it is really hard to come up with a marker of sex that can apply across the tree of life!*

How the processes of becoming a sex happen in humans:

- *For humans, we use genetic sex determination. Note that this is not universal and there are multiple strategies across the tree of life for sex determination. Some species, like sea turtles and crocodiles, use temperature dependent sex determination.*
  - *Figure 4 in this paper is so cool!! https://pubmed.ncbi.nlm.nih.gov/24983465/*
- *The process of sex differentiation is complex, and science doesn't have all the answers. We are especially lacking information on processes in those who are XX.*
- *For humans, we know that genotype sets the process of differentiation in motion, but then various hormones and other cell signals are what drives the bipotential structures to differentiation into male-typical or female-typical parts.*
- *We have A LOT more information on what happens in XY than in XX*

What we do know:

- *When sperm and egg come together (conception), they define the genotype of the new organism. For humans, sperm and egg each have 23 chromosomes (or 1 full set each; they are haploid).*

- *CHROMOSOMES:*
  - *Chromosomes are thread-like structures located inside the nucleus of animal and plant cells. Each chromosome is made of protein and a single molecule of deoxyribonucleic acid (DNA).*
  - *The new cell, the zygote, typically has 46 chromosomes. 22 pairs of autosomes and 1 pair of sex chromosomes. Typically, the sperm provides either an X or a Y, the ovum provides an X.*
  - *The genotype refers to the entire genetic makeup of an individual.*
  - *Genotype also refers to the two alleles present at a specific locus in the genome. Genotype can contribute to an individual's observable traits, called the phenotype.*
  - *Genotype of the sex chromosomes matters in humans.*
    - *XX = genotypic female (46,XX)*
    - *XY = genotypic male (46, XY)*

- The zygote then beings to divide via mitosis. One cell becomes 2, 2 become 4, 4 become 8, 8 to 16, 16 to 32 and so on.
  - Zygote = new cell after conception
  - Morula = 16-32 cells
  - Blastocyst = about 5 days after conception, 50-150 cells with a hollow center full of fluid.
  - Implantation = when the blastocyst implants in the uterine lining. This is the medical definition of pregnancy. Typically occurs 6-10 days after conception.
  - An individual is now medically pregnant, and the ball of cells must continue to develop and differentiate to form all parts of the new human. All cells should have the same genotype as the initial zygote.
  - The initial cell is a zygote, after implantation, from weeks 3-8 after conception, the developing organism is called an embryo, and after the 8th week, it is called a fetus.
    - Embryology = the study of embryo and fetal development. I found the videos and images on this page very cool! https://embryology.med.unsw.edu.au/embryology/index.php/Main_Page
  - **Humans are initially undifferentiated and XX and XY fetuses look the same until about weeks 8-12 following conception!**

So, how does a new individual become phenotypically male or female?

- The Y chromosome contains the Sex-Determining Region of the Y (SRY gene). This was discovered in 1990.
- SRY codes for a protein, a transcription factor, call testis determining factor (TDF). TDF is expressed in the cells of the medulla of the bipotential gonad (a developmental structure that can become the ovary or the testis, depending on the developmental signals present! Wow!!).
- TDF turns on the expression of multiple other genes. We do not have all of the details worked out, but we know that expression of SOX9 is important for the development of testes.
- For a long time, it was assumed the XY development was the active process, and XX development was a passive/lack-of-action process. New data show this is not accurate and that both testis-determining and ovary-determining networks are active and complex processes.
- As of yet, we do not know of an ovary determining gene. But, there are multiple genes that are important in ovarian development, including RSPO1, WNT4, WT1, and FOXL2.
  - Note: I listened to a few really interesting podcasts about this! The RadioLab Gonads series is really good and I learned so much about what we know and don't know. https://radiolab.org/series/radiolab-presents-gonads/

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- *GAMETES*
  - Gametes are the sex cells or reproductive cells.
  - Interestingly, BEFORE the gonads differentiate, the primordial germ cells (precursors to gametes) begin to make their way to the bipotential gonad. These primordial germ cells are produced by the first few divisions of the zygote (the fertilized egg) and are totipotent – they can give rise to any type of body cell. The primordial germ cells are either XX or XY, but their differentiation is poorly understood. We do know that around 42 days after conception, they become spermatogonia or oogonia.
  - The oogonia go through mitosis to give rise to primary oocytes. These then undergo meiosis to give rise to millions of follicles (oocyte + surrounding support cells), which are arrested (paused) in meiosis II. XX individuals are born with all their ova!!
  - The spermatogonia go through mitosis to give rise to primary spermatogonium. These spermatogonia pause and wait until puberty to begin the process of meiosis.

- *GONADS*
  - Gonads are the primary reproductive organs that produce gametes and hormones. In humans these are the ovaries and testes.
  - While the germ cells are following their processes (which we don't fully understand), the gonads differentiate.
  - SRY → TDF → SOX9 + others
    - This cascade causes the medulla of the bipotential gonad to develop into a testis. Leydig and Sertoli cells are formed.
    - Leydig cells produce androgens: testosterone (T) and dihydrotestosterone (DHT).
    - Sertoli cells produce anti-mullerian hormone (AMH; also called mullerian inhibiting hormone, MIH) and insulin-like factor 3 (Insl3)
  - We don't know what is going on to form the ovaries from the cortex of the bipotential gonad, but it is an active process. See here (females battle to suppress their inner male https://pubmed.ncbi.nlm.nih.gov/20005799/)

- *INTERNAL REPRODUCTIVE TRACTS*
  - Early during development, the mesonephros forms. This structure houses the primordial gonads and the precursors to the internal reproductive structures/ducts.
  - In the undifferentiated embryo there are two sets of ducts: the mesonephric (or Wolffian) ducts and the paramesonephric (or Mullerian) ducts. These ducts form Y shapes and each "arm" of the Y sits beside a primordial gonad.
  - As with gonadal development, we are still lacking a lot of information on the process in XX individuals, but we have a general process of

what happens.
    - In XY → SRY → TDF → testis develop → testes produce androgens and anti-mullerian hormone.
        - In the presence of testosterone the Wolffian ducts develop into the vasa deferentia, epididymis, and the seminal vesicles.
        - In the presence of anti-mullerian hormone, the Mullerian ducts regress.
    - In XX → no SRY, no TDF, no testes. Ovaries develop. The ovaries do not produce testosterone or AMH.
        - Without AMH, the Mullerian ducts develop ingo the fallopian tubes, the uterus, cervix, and upper portion of the vagina.
        - Without testosterone, the Wolffian ducts regress. However, new research suggests removal of the Wolffian ducts in XX individuals is an active process, with COUP-TFII playing a role. See here https://www.science.org/doi/10.1126/science.aao2630
- *GENITALIA*
    - The external genitalia are the reproductive organs
        - XX genitalia = vulva (which includes the clitoris, labia, and surrounding structures). Note it is not the vagina! The vagina is a specific canal leading from the uterus to outside the body (also known as the birth canal).
        - XY genitalia = penis and scrotum
    - During early development, the genital area looks the same as the bipotential genital tubercle and genital folds have not yet differentiated.
    - In XY → SRY → TDF → testis develop → testes produce androgens and anti-mullerian hormone.
        - The presence of strong androgens, mainly DHT, triggers the differentiation of the genital tubercle into the penis and the genital folds into the scrotum. (the testes descend between weeks 25-35 of pregnancy, driven by Insl3 and other hormones).
    - In XX → no SRY, no TDF, no testes. Ovaries develop. The ovaries do not produce testosterone.
        - The genital tubercle becomes the clitoris and the genital folds become the labia. We do not know what hormones or cell signals trigger this development. Sources seem to just say lack of androgens.

- SECONDARY SEX CHARACTERISTICS
    - Secondary sex characteristics are physical traits that are related to sex but are not directly involved in reproduction. Driven and maintained by "sex steroids"
    - In XX - Breasts, wider hips, thicker head hair, menstrual cycles, increased body fat
        - Happens at the onset of puberty. Regulated by estrogens and progestins and the hypothalamic-pituitary-gonadal axis.

- In XY - Facial and chest hair, increased body hair, pelvic build, upper body muscular build, Adam's apples
  - Happens at the onset of puberty. Regulated by androgens and the hypothalamic-pituitary-gonadal axis.

- INTERSEX
  - Sometimes, developmental processes do not occur as expected. This can be due to genetic anomalies, hormone alterations, or environmental exposure to hormones/drugs in utero.

    - Aneuploidy – one or more extra, or missing, chromosomes. When this happens with X and Y we can get:
      - XYY (47 chromosomes)
      - XXY (47 chromosomes)
      - XXX (47 chromosomes)
      - X0 (45 chromosomes)

    - Genetic mutations – changes in DNA sequence that can have various outcomes (e.g., nothing, alteration in protein production or function, etc.). Outcomes relevant to sex determination and differentiation:
      - Congenital adrenal hyperplasia
        - an enzyme in the pathway to produce cortisol, typically 21-hydroxylase, is not functional. The developing fetus makes too much androgens and not enough cortisol or aldosterone.
          - If XX, exposed to high levels of androgens during development. Born with ambiguous or masculinized external genitalia.
          - If XY, no noticeable impact on development.
          - Both need to be treated for lack of cortisol and aldosterone
      - Androgen Insensitivity Syndrome (AIS: aka Testicular Feminization or Morris Syndrome)
        - In this condition, the androgen receptor, responsible for binding all classes of androgens, does not work properly.
          - In complete AIS, the receptor cannot bind androgens.
          - In partial AIS, the receptor can bind androgens, but not fully. Thus, androgens do not have the same effects on the phenotype as they typically would.
          - XY individuals with this condition look phenotypically female.
      - 5-alpha reductase deficiency (aka Guevedoces)

    - In this condition, the enzyme that converts testosterone to dihydrotestosterone does not work.
        - XY individuals with this condition are born with female-typical external genitalia, but at puberty with the huge surge of testosterone, the penis and scrotum develop and the testes descend.
- SRY translocation – sometimes, during meiosis, cross over between two chromosomes happens. When this occurs with the X and Y, the SRY gene can end up moving from the Y to the X.
    - If the sperm containing the X with the SRY joins with an egg, the result will be XX with SRY. Testes develop.
    - If the sperm with the Y missing the SRY joins with an egg, the result will be XY without SRY, no tetes develop.
- SRY mutations and Swyer Syndrome
    - Various mutations or alteration of SRY can produce phenotypes that do not align with a typical XY genotype.

Holy cow!! That information was ***so*** interesting. I *NEVER* learned any of that in school (...hmmm, I wonder why?). I found this article and the graphic really useful! https://www.scientificamerican.com/article/beyond-xx-and-xy-the-extraordinary-complexity-of-sex-determination/. And the information in this one blew my mind, how could a man not know he had a womb!? https://www.nature.com/articles/518288a

We, as a society, learn about sex and sexuality from lots of places – family, friends, religion, culture, social norms, biology, medicine, etc. I was raised with very traditional gender norms and family values, and I felt sex education should be taught in a conservative manner. However, I also think we should all be allowed to access the full spectrum of ideas and information. I think we should all have access to accurate data and therefore be able to draw evidence-based conclusions about all aspects of sex education, sexuality, and reproductive health. We can then, as individuals, use aspects of information and experience to inform our personal views.

I've learned so much while compiling these notes. When discussing health and medicine, it is important to make sure we're looking at relevant biological and medical data.

From the desk of
Mrs. Melanie Marshall

For example, I had never thought about the fact that we all start from a single cell – that every part of our body had to come from that single entity. I also had no idea that we all – male, female, or interest - started from the same building blocks and parts. All the anatomy and physiology that seems to be so different are really very similar! Like, who would have guessed the clitoris and penis were homologous structures and come from the same developmental tissue!?! I also had NO IDEA that if individual development took a slightly different path, one could end up intersex. Intersex individuals can have XX, XY, XXY, XYY, XXX, or only 1 X chromosome!

I saw an ad for Every Body, a documentary about intersex individuals, and I really want to watch it. The Texas legislature is even included. Trailer here so I don't forget: https://youtu.be/SoNvk5N-MKo

I'm going to summarize information and then organize what I learned in the tables and bullet lists below.

Summary:
Multiple levels of sex in humans:

- Genetic sex – determined by sex chromosomes (in humans, those are X and Y)
- Gonadal sex – what gonads one has (genes play a role in driving gonadal development)
- Gametic sex – what gametes one makes (genes play a role in driving gamete development)
- Genital sex – what external genitalia one has (driven primarily by hormones)
- Internal system – what internal duct system one has (driven primarily by hormones)
- Hormonal sex – what gonadal steroids are produced in highest amounts, androgens or estrogens (and progestins)
- Phenotypic sex – usually influenced by gonadal steroid exposure with effects on morphology and physiology
- Alterations and variations can occur at all levels
    - E.g., Chromosome number; genetic variants; Body may not respond to certain hormones, etc.
- Gonadal steroid hormones from early development also influence the rest of the body, including the brain
- Intersex conditions are real and some of them occur fairly frequently! (for example some occur in 1 out of 1,500 or 1 out of 2000 births).

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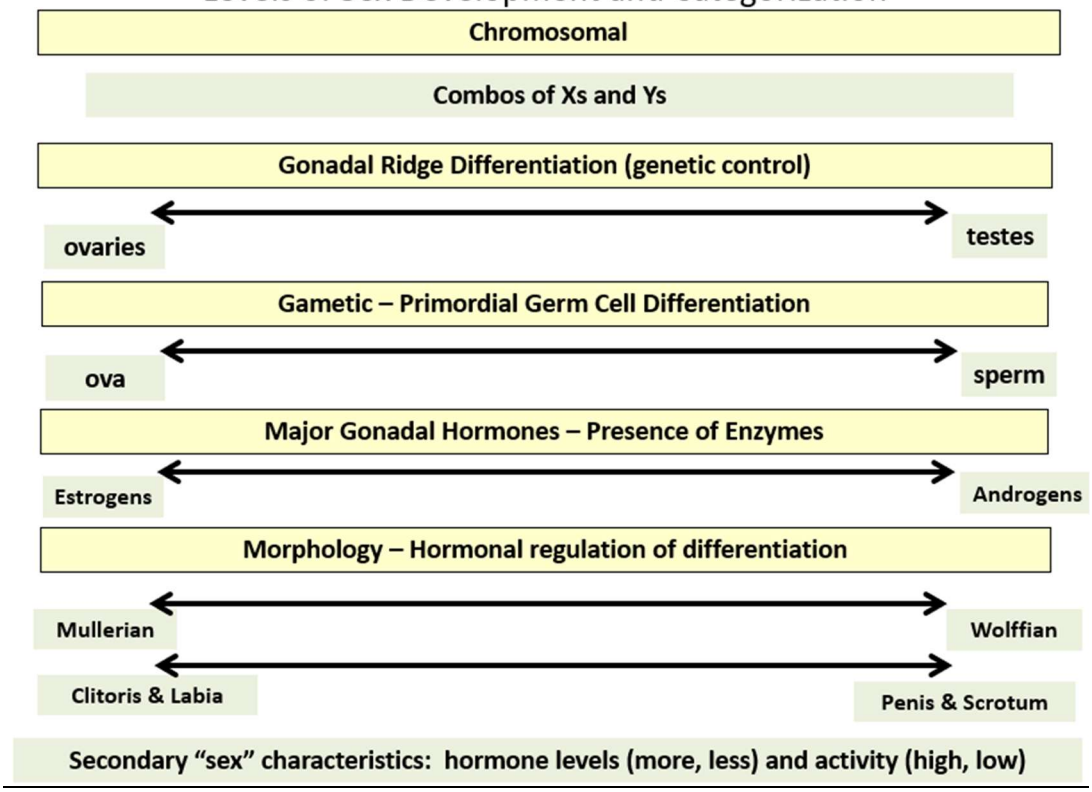
Levels of Sex Development and Categorization

Level	Outcomes	Developmental Substrate
Chromosomal	Combo of Xs and Ys	Chromosomes from zygote
Gonadal	Ovaries to testes	Gonadal/Germinal Ridge
Gametic	Meiotic products = gametes (ova or sperm)	Primordial Germ Cells
Hormonal	Androgens to Estrogens	Enzymes expressed in gonadal tissue
Morphological	Internal duct system	Bipotential duct system
	External genitalia	Genital tubercle and folds
	Secondary "sex" characteristics	Somatic and musculoskeletal structure

Levels of Sex Development and Categorization



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Sex differentiation and development:

Level of Analysis	Developmental precursor (substrate, origin)	Outcome of differentiation in those we assign female	Outcome of differentiation in those we assign male	Window of differentiation (when during fetal development do these changes happen?)
Chromosomes	Parental gametes (sperm and ovum; products of meiosis)	XX	XY	Genotype is set when the nuclei of sperm and egg fuse (at conception)
Gametic	Primordial Germ Cells	Ova	sperm	By ~35 days after conception, the primordial germ cells reach the undifferentiated gonadal ridge. At ~42 days, they differentiate in oogonia (ova precursors) or spermatogonia (sperm precursors)
Gonadal	The bipotential gonad (aka gonadal, germinal, or genital ridge)	The cortex of the bipotential gonads become the ovaries	The medulla of the bipotential gonads become the testes	At ~42 days, the gonads begin to differentiate into ovaries or testes, continues until ~70 days after conception
Internal tract anatomy	The bipotential duct system (mesonephric ducts)	The Mullerian ducts develop to become → Fallopian tubes, uterus, cervix, upper vagina. The Wolffian ducts regress	The Wolffian ducts develop to become → vasa deferentia, epididymis, seminal vesicles. The Mullerian ducts regress	Process is still not fully understood, especially in XX, but from ~56-70 days after conception the ducts differentiate
External genitalia anatomy	The genital tubercle and genital folds	Genital tubercle becomes the clitoris; genital folds become the labia	Genital tubercle becomes the penis; genital folds become the scrotum	At ~63-77 days after conception structures differentiate (presence of androgens is a big driver). Penis and clitoris are the same size until ~98 days
Gonadal steroid hormone(s)	Steroidogenic precursor cells	Theca cells that testosterone and granulosa cells that make the enzyme, aromatase, to convert testosterone to estradiol	Leydig cells that make testosterone and Sertoli cells that make the enzyme, 5-alpha reductase, to convert testosterone to dihydrotestosterone	The three types of cells in the primordial gonad (supporting; germ; steroidogenic) become granulosa, Sertoli; oogonium, spermatogonium; theca, Leydig in XX and XY, respectively. At ~50-60 days, the gonads start producing hormones. These hormones help drive other aspects of differentiation.

Great sources: https://www.ncbi.nlm.nih.gov/books/NBK279001/ and https://www.ncbi.nlm.nih.gov/books/NBK557601/ and https://www.ncbi.nlm.nih.gov/books/NBK26940/

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Intersex Table*

	Typical Female	Typical Male	SRY dysfunction	Translocation of SRY to X	Turner Syndrome	Klinefelter Syndrome	5 alpha reductase deficiency
Genotype	XX	XY	XY	XX	XO	XXY	XY
Gonads	Ovaries	Testes	Ovaries	Testes	(incomplete) Ovaries	(undescended) Testes	Testes (undescended initially)
Internal duct system	Mullerian	Wollfian	Mullerian	Wolffian	Mullerian (reduced development)	Wolffian	Wolffian
External genitalia	Clitoris and labia	Penis and scrotum	Clitoris and labia	Penis and scrotum	Clitoris and labia	Penis and scrotum	(Ambiguous) Penis and scrotum at puberty
Outward phenotype	Female	Male	Female	Male	Female	Male (but with some female traits)	Female then Male
Fertility	Typical	Typical	Reduced	Typical	Sterile (or in rare cases severely reduced)	Reduced or sterile	Reduced
Major gonadal sex steroid (T or E_2)	E_2	T	E_2	T	E_2	T	T

	XX with extra X	XY with extra Y	XY with CAH	XX with CAH	Complete AIS	Partial AIS	Mild AIS
Genotype	XXX	XYY	XY	XX	XY	XY	XY
Gonads	Ovaries	Testes	Testes	Ovaries	(undescended) Testes	(possibly undescended) Testes	Testes
Internal duct system	Mullerian	Wolffian	Wolffian	Mullerian	Neither	Wolffian (likely partial development)	Wolffian
External genitalia	Clitoris and labia	Penis and scrotum	Penis and scrotum	Masculinized clitoris and labia (sever to minor)	Clitoris and labia	Masculinized clitoris and labia (or micropenis or typical penis)	Penis and scrotum
Outward phenotype	Female	Male	Male	Female (can also be masculinized)	Female	Female or male	Male (with breasts at puberty)
Fertility	Typical	Typical	Reduced	Reduced	Sterile	Sterile or Reduced	Reduced
Major gonadal sex steroid (T or E_2)	E_2	T	T	E_2	T	T	T

**please note, this intersex table can also be found in the Optional Homework section of another case study by the same authors (Going for Gold: Sex, Gender, and Competition)*

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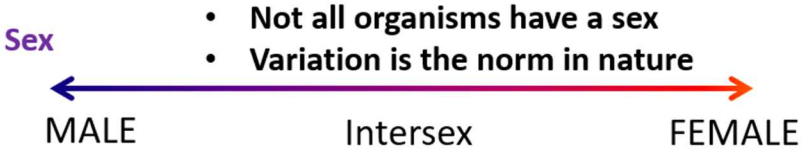
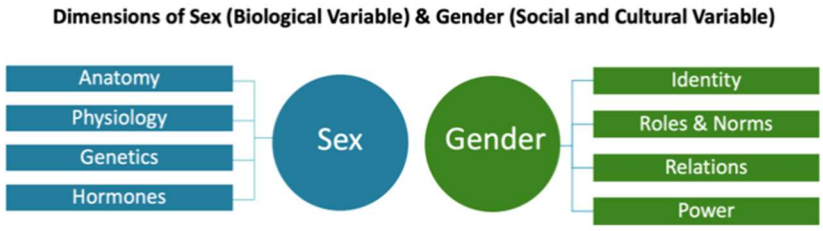
Summary:

- **Sex is not binary**
- **Sex is not black and white**
- **Sex is a spectrum**
- **Not all organisms have a sex**
- **Variation is the norm in nature**



- **Sex is a biological construct and can be defined at various biological levels**
- **Those biological levels do not necessarily fall on the same part of spectrum; can be a mosaic**
- **Sex and gender are different**
- **Gender is a social construct**

- **Gender is not binary**
- **Gender is not black and white**
- **Gender is a spectrum or mosaic**
- **Gender is not the same the as sex**
- **Variation is the norm in nature and falling anywhere on the mosaic of gender is okay!**
- **Gender is a social construct**
- **Gender matters in health, society, and policy**



Above image of sex and gender from the now removed webpage of the NIH Office of Research on Women's Health