A “Boy” Named Tina? The Past and Present of Congenital Adrenal Hyperplasia

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My paternal grandfather, Norman Ricker, born in 1897, was the second of four children. His youngest sibling, born in 1900, was identified on the birth certificate as an unnamed male. One month later, a census taker visited the Ricker household just outside of Boston. The entry included my great-grandparents and their four sons: Leon, Norman, Allan, and a still-unnamed newborn male.

This child died less than five years later. The 1905 death certificate again identified the child as a male, but now with the given name of Tina! What was going on here? Was the child a girl or a boy?

The Continuum of Biological Sex

The first question people usually ask about a newborn is , “Is it a boy or a girl ?” Most of us believe that a quick glance between the legs will settle the matter. We assume that biological sex is the result of two separate and nonoverlapping pathways, male and female. This assumption, however, is incorrect. In fact, when we look at all the biological features associated with sex, we find that each of us can be placed somewhere between an “ideal female” at one extreme and an “ideal male” at the other (Ainsworth, 2015). In other words, we all can be located somewhere on a sex continuum. For many of us, most of these biological features cluster near one extreme or the other, but with some features closer to those of the opposite extreme.

For instance, during puberty, many boys show the beginnings of breast development—a condition called “gynecomastia” (Braunstein & Anawalt, 2021). Hormonal changes during early puberty may cause a “breast bud” to develop. Levels of the female hormone, estrogen, may increase for a time relative to levels of male hormones (i.e., androgens such as testosterone). This departure from male-typical development is only temporary. The breast bud usually disappears within two years.

Occasionally, however, large and lifelong departures from typical sex development occur. For example, people sometimes inherit an atypical number of the so-called sex chromosomes—the X and Y chromosomes. Females typically inherit one X chromosome from each parent, whereas males typically inherit an X chromosome from their mothers and a Y chromosome from their fathers (Carey et al., 2022). Thus, the bodies of females typically consist of XX cells, whereas the bodies of males typically consist of XY cells. But clinicians have reported rare cases of people with both types of cells:

A 46-year-old woman pregnant with her third child underwent amniocentesis to rule out chromosomal abnormalities in the fetus…. But the only chromosomal abnormalities found were in the mother’s body…. One set of cells carried two X chromosomes…; the other had an X and a Y. (Ainsworth, 2015, p. 288)

This woman's body likely developed from the merging of twin embryos, one male and one female. Thus, some parts of her body, such as her reproductive system, consisted of female (XX) cells, whereas other parts of her body consisted of male (XY) cells.

Some departures from typical sex development result in significant problems in biological functioning, such as sterility or life-threatening medical problems. These problematic departures make up a large part of the category known as "Disorders of Sex Development" (DSDs; Chan & Levitsky, 2022). In general, DSDs are a collection of congenital (i.e., inborn) conditions involving an atypical sexual anatomy or an atypical number/combination of sex chromosomes (Hughes et al., 2006; Witchel, 2018).

The most common DSDs include conditions in which people develop an atypical genital appearance, sometimes called "ambiguous genitalia" (Chan & Levitsky, 2022; Eder, 2022). In these conditions, the external genitalia may appear to be neither fully male nor fully female, or they may have other structural differences from typical genitalia.

In some other types of DSDs, people develop a typically male or female external appearance that conflicts with other sexual features. For example, people with a condition known as "*complete androgen insensitivity syndrome"* (CAIS), develop a female-typical external appearance (e.g., have a vulva and breasts) but inherit the typical male chromosomal complement of XY (Ainsworth, 2015; Hiort, 2022). Thus, based only on their external appearance, no one would question the female sex assigned to them at birth.

However, people with CAIS have no ovaries, uterus, or other internal female-typical reproductive structures (Ainsworth, 2015; Hiort, 2022). These structures fail to develop because of a gene on the Y chromosome called "SRY." The SRY gene triggers the development of testes, which, in those with CAIS, usually remain in the body (i.e., undescended testes). The testes release the primary male hormone, testosterone, which prevents the development of internal female reproductive structures. Testosterone also usually triggers the development of male-typical external sex characteristics. The cells of CAIS fetuses, however, do not respond to testosterone. Because testosterone has no effect, genes associated with female sex development steer external physical development into a female form.

Because of their female-typical external appearance, people with CAIS may not know that their internal anatomy is atypical until they fail to menstruate, try to get pregnant, or develop hernias caused by the prenatal development of testes (Hiort, 2022; Hughes et al., 2012). Females with CAIS are at risk for certain medical problems (e.g., gonadal tumors) and impaired sexual functioning (e.g., low sex drive and a narrow/shortened vagina). They also may require counseling to deal with distress about infertility and relationship issues. Overall, however, females with CAIS are as psychologically normal, on average, as XX females.

Because conditions like CAIS are not associated with chronic medical or psychological illnesses, many patients and their families, clinicians, and advocacy groups argue that the DSD category should be either eliminated or renamed "Differences/variations of Sex Development" (Alderson et al., 2022; Houk et al., 2021).

What About Tina?

It seems likely that my great-aunt Tina had what today would be classified as a DSD. But which one? I have only her 1900 birth certificate, her entry in the 1900 Federal Census, her 1905 death Certificate, and records of her burial later in 1905. But these documents provide a few clues:

1. She was assigned the biological sex of a male at birth.
2. She was still unnamed one month after her birth.
3. She died just before her fifth birthday of heart failure due to diphtheria.
4. Her remains were buried several months after her death in a cemetery different from the one used for other family members

We can infer from the first two clues that Tina was born with mildly to moderately masculinized genitalia. The most likely cause would have been prenatal exposure to high levels of androgens (Chan & Levitsky, 2023 ; Houk et al., 2021; Merke & Auchus, 2021; Speiser et al., 1991; White & Speiser, 2000). Masculinized genitalia most often occurs in female newborns with “congenital adrenal hyperplasia" (CAH). About 95% of CAH newborns have classic CAH. Classic CAH is a severe form of CAH often featuring repeated life-threatening crises (see below) that begin soon after birth.

The third and fourth clues also support the diagnosis of classic CAH: diphtheria may have triggered a severe crisis that caused her to go into shock Lousada et al., 2021). I can only speculate about the reason why my great-grandparents decided to bury Tina in a site separate from other family members. But given that feelings of shame and guilt in parents of children with classic CAH are not uncommon even today, I wonder if they wanted to keep secret her relationship to them. Perhaps they feared the appearance of a “hereditary taint.”

And in fact, heredity is central to understanding Tina’s condition. The development of classic CAH is associated with recessive genes located on chromosome 6 (Merke & Auchus, 2021; Yau et al., 2022). To develop classic CAH, one must inherit two copies of the gene. Each of my great-grandparents, therefore, must have had one copy of the gene. The probability that any of their children would inherit two copies was 25%. In other words, we would expect that, on average, one of their four children would develop classic CAH, which is exactly what happened.

What is Congenital Adrenal Hyperplasia

The primary problem in classic CAH is the virtual absence of the hormone, cortisol (Merke & Auchus, 2021; Yau et al., 2022). Cortisol is produced by the adrenal glands, which sit atop the kidneys. The virtual absence of cortisol (concentrations of 0- 2% of normal) causes the adrenals to produce high levels of androgens (Kurtoğlu & Hatipoğlu, 2017).

Cortisol is the final product of a pathway consisting of five major steps (Yau et al., 2022). Cortisol production depends on the action of several enzymes, which are molecules that increase the rates of biochemical reactions. Enzymes specific to each step make possible the production of the biochemical precursors of cortisol. The presence of a faulty enzyme in a step blocks the production of that step’s biochemical precursor.

The faulty enzyme responsible for over 90% of all cases of classic CAH is 21-hydroxylase (Merke & Auchus, 2021; White and Speiser, 2000; Yau et al., 2022). This enzyme converts the hormone 17-hydroxyprogesterone, into the hormone, 11-deoxycortisol. The result is:

- The unconverted 17-hydroxyprogesterone builds up in cells.
- No other biochemical reaction beyond this one in the cortisol pathway can occur.
- Thus, little or no cortisol is produced.

Low levels of cortisol cause the pituitary gland to release Adrenocorticotropic hormone (ACTH). ACTH activates the adrenal glands. Activation of the adrenals triggers cortisol production in those with functional enzymes. But because functional 21-hydroxylase is absent, no cortisol is produced. Thus, the pituitary continues to release ACTH, which continuously activates the adrenals.

The continuous activation of the adrenals has several effects (Yau et al., 2022):

- The adrenal glands enlarge over time (i.e., they become hyperplasic).
- The unconverted 17-hydroxyprogesterone is shunted into a different pathway, where it is used to produce large amounts of the androgen, Δ4-androstenedione.
- The excess Δ4-androstenedione masculinizes the external genitalia of female fetuses.

The excess androgen, however, affects only the external genitalia. The hormone has no effect on the internal reproductive anatomy, which develops in a female-typical pattern. Thus, females are born with ovaries, a uterus, Fallopian tubes, etc. In fact, the individual may be capable of pregnancy upon reaching reproductive age.

Another hormone important for the development of classic CAH is aldosterone, which is an adrenal hormone that regulates blood volume and blood pressure (Speiser et al., 1991; Yau et al., 2022). Aldosterone regulates these processes by controlling the amount of sodium (salt) and water released into the blood stream. When cortisol levels are less than about 1% of normal, the production of aldosterone is not sufficient to prevent the excess release of sodium. When sodium is released at high levels, an adrenal crisis usually occurs within a few weeks after birth (Lousada et al., 2021; Merke & Auchus, 2021). The symptoms of an adrenal crisis include Dehydration, High fever, Low blood pressure, Low blood sugar, vomiting, Rapid heart rate, and rapid breathing. If blood pressure drops suddenly, a person may go into shock. Shock can be life-threatening because bodily organs do not get enough blood and oxygen.

Adrenal crises continue to occur if CAH is not treated (Yau et al., 2022). No effective treatments for CAH existed in Tina's time (Dreger, 1998; Eder, 2022; Reiss, 2021). Her death before her fifth birthday may have been due to an adrenal crisis triggered by a diphtheria infection.

How did Tina and my great-grandparents cope with what was, in 1900, a mysterious illness? I know nothing beyond the records mentioned above. But we may gain some insight into their experiences by looking at a case study published only 35 years before Tina's birth.

What About Giuseppe ?

In 1865, Luigi De Crecchio published one of the first case reports of congenital adrenal hyperplasia. De Crecchio was a professor of forensic medicine at the University of Naples (Delle Piane et al., 2015). The report described the life history and autopsy of Giuseppe Marzo, who was born in 1820 with ambiguous genitalia. A midwife declared Marzo to be a female on the birth certificate. The newborn was baptized as Maria Giuseppa Margharita Marzo and raised as a girl.

Before effective treatments for CAH existed, excess androgens would continue to be released after birth, which would continue to masculinize the body (Eder, 2022). Thus, Marzo's body probably looked increasingly like a boy's over the next few years. When Maria Giuseppa was four years old, her parents consulted a surgeon who concluded that the child was a boy with undescended testes (Delle Piane et al., 2015). Maria Giuseppa was renamed Giuseppe and his family raised him as a boy. He lived as a male until his death in December 1864, at the age of 44 years.

Two weeks after his death, , Giuseppe's body was removed from his grave, probably without his family's consent, and taken to the university of Naples for autopsy (Delle Piane et al., 2015). The autopsy revealed genital abnormalities: his penis was curved and much shorter than average, and the urethral opening was under the tip of the penis. His internal anatomy, on the other hand, was female-typical. And he had ovaries, not testes.

De Crecchio stated that the adrenals were "extraordinarily large" (cited in Delle Piane et al, 2015, p. 168). He mistakenly believed that the hyperplasic adrenals were unrelated to the atypical genitalia. In 1865, physicians knew nothing about the role of the adrenals in sex development.

In fact, virtually nothing was known about the causes of sex development until after 1900. For example, it was not until 1905 that the chromosomal researcher, Nettie Stevens, identified the role of the Y chromosome in determining male sex in mealworms (Carey et al., 2022; Sturtevant, 1965). Soon thereafter, Stevens and other researchers extended these findings to other species, including humans. And although the role of the testes in determining male physical and behavioral development had been known for centuries, hormone researchers did not isolate testosterone until the 1930s (Eder, 2022; Nieschlag & Nieschlag, 2019; Tomlinson, 2012). Researchers identified other hormones, such as progesterone and cortisol, around the same time.

The 1865 report described some fascinating details of Giuseppe's life that reflect the experiences of those with CAH even today. Of most importance for our discussion are the details about Giuseppe's experience of himself as a male, what might be called his "psychological sex" (Eder, 2022). The sense of ourselves as male, female, both, or neither is a basic part of our personal identities. Personal identity comprises a set of beliefs about the characteristics that define us as individuals and distinguish us from other individuals (see Olson, 2022, for this and other meanings of the term). In those with CAH, the experience of psychological sex comes to the forefront because, as in the case of Giuseppe, their atypical physical development distinguishes them from others (Forcier & Olson-Kennedy, 2022).

Although raised as a girl for the first four years of life, Giuseppe thought of himself as a male (Delle Piane et al., 2015). Today, we would call Marzo a man because that is how he saw himself. But the title of De Crecchio's 1865 article is, "*Sopra un Caso di Apparenze Virili in una Donna*" ["A Case Report of Masculine Appearance in a Woman"].

The issue of identity is at the heart of controversies surrounding DSDs today. Let's look more closely at this issue.

Personal Identity and DSDs

Clinicians, researchers, scholars, and advocacy groups have proposed a dizzying variety of terms related to sex, gender, and sexuality (Alderson et al., 2022; Dreger, 1998; Eder, 2022; Feder & Karkazis,

2008; Forcier & Olson-Kennedy, 2022; Hughes et al., 2006; Reis, 2021). I will simplify the discussion by defining only two terms: sexual identity and gender identity.

I define "sexual identity" as the biological sex assigned at birth. A person's sexual identity usually is based on the appearance of the external genitalia. However, in newborns with a DSD, especially those with an atypical genital appearance, clinicians often consider additional features. In the late-nineteenth and early-twentieth centuries, physicians in the United States and several European countries defined males as people with testes and females as people with ovaries, regardless of external appearance (Dreger, 1998; Eder, 2022; Reis, 2021). Using this definition, physicians of that time would have identified CAIS females as males because of their undescended testes. Marzo had ovaries and, therefore, the pathologists performing his autopsy identified him as a female. That is why De Crecchio referred to him as a woman in the title of the 1865 paper.

Assuming that Tina had classic CAH, she would have had ovaries. If the ovaries had been detected at birth, Tina would have been assigned a sexual identity of a female rather than a male. Eventually, her family decided that she was a girl. Yet, her death certificate still identified her as a male. The reason is that the sex entered on the birth certificate is the official sex for legal purposes (Houk et al., 2021).

Although physicians in Giuseppe's time identified him as a woman, he identified himself as a man. This self-identification is called "gender identity," which is the inner experience of being male, female, both, or neither (Forcier & Olson-Kennedy, 2022). Children usually have a basic sense of themselves as male or female by about three years of age (Perri et al., 2019). Marzo apparently thought of himself as a boy by age four. Today, we identify a person as their experienced (or perceived) gender. Thus, people with CAIS are identified as female, male, both, or neither depending on how they experience themselves.

Gender identity continues to develop through childhood and adolescence (Forcier & Olson-Kennedy, 2022; Hines et al., 2004; Steensma et al., 2013). And similar to biological sex, gender identity exists on a continuum between an "extreme woman/girl" and an "extreme man/boy".

Because gender identity takes years to develop and stabilize, the gender identity that eventually develops may not match the sexual identity assigned at birth. The possibility that gender and sexual identities may not match is a major concern when making decisions about children with DSDs. This concern is why, in much of the United States today, birth certificates contain a "gender neutral" category: if the sex at birth is uncertain, clinicians can choose the neutral category. When gender identity has stabilized, the identification can be changed (Houk et al., 2021).

If the sexual and gender identities differ, psychological distress may develop (American Psychiatric Association, 2022). Sometimes, the distress become so severe that chronic depression develops. Gender dysphoria is diagnosed when the depression is coupled with a strong desire to change one's appearance to better match gender identity. When gender dysphoria is severe, the person is at greatest risk for self-harm, including self-mutilation and suicidal behavior (Forcier & Olson-Kennedy, 2022). When assigning a sexual identity to a newborn with a DSD whose biological sex is uncertain, clinicians can use the following biological features together with what is known about the DSD to predict the eventual gender identity (American Psychological Association, 2006):

- internal reproductive organs: in females, structures such as an internal clitoris, ovaries, and uterus; in males, features such as testes and seminal vesicles
- sex chromosomes: XX in females and XY in males
- sex hormones: in females, greater concentrations of female-typical hormones such as estrogen; in males, greater concentrations of testosterone and other androgens.

If, for instance, a newborn has two X chromosomes, high levels of androgens, and primarily male-typical internal structures, the clinician might conclude that the child will eventually develop a male gender identity. This prediction should inform the clinician's decision about sex assignment.

most clinicians and researchers believe that the development of gender identity is primarily innate (Forcier & Olson-Kennedy, 2022; Houk, et al. 2021). The claim that gender identity is innate usually means that a particular gender identity is likely to develop regardless of how a child is raised. The case of Giuseppe Marzo provides some evidence for this claim: he was raised as a girl for the first four years of life but still experienced himself as a male. But better evidence for the claim comes from the next case study.

Bruce Begat Brenda Begat David

In 1965, Janet and Ron Reimer had identical-twin boys, Bruce and Brian (Colapinto, 2006). Because of a medical condition that interfered with urination, doctors recommended circumcision for the boys. At about seven months of age, Bruce underwent an unconventional circumcision procedure. Instead of using a scalpel, the doctor cauterized the foreskin with an electric current. The current destroyed his penis. (Surgery was canceled for Brian.)

Bruce's parents consulted experts, who told them that no reconstructive surgery could repair his damaged penis (Colapinto, 2006). They gave up hope until meeting John Money, a psychologist who recently had cofounded the *Gender Identity Clinic* at Johns Hopkins University. Money had long argued for a social learning theory of gender-identity development. He believed that any child, regardless of biological sex, could develop a male or female gender identity. Parents needed only to raise the child as that sex.

Money recommended sex reassignment for Bruce (Colapinto, 2006). He assured the Reimers that Bruce could become a normal girl. The reassignment process, he explained, involved surgeries to construct a vulva and, at puberty, hormone treatments to produce female secondary sex characteristics. Money warned the Reimers that the success of the intervention required that they never tell Bruce that he was born a male.

The Reimers renamed the infant "Brenda" (Colapinto, 2006). At almost two years of age, the Clinic's surgeons removed what remained of Brenda's damaged penis and began to construct a primitive vulva, which they planned to finish at a later date. The parents encouraged Brenda to play with dolls, dress as a girl, and behave in other female-stereotypic ways.

But Brenda's opposition to this plan erupted almost immediately. She forcefully refused to act like a traditional girl. She usually behaved in stereotypically male ways and identified more with males than females:

> Brenda frequently rejected girls' toys, activities, and clothing. She would also mimic her father's behaviors (e.g., shaving) as opposed to her mother's behaviors (e.g., applying makeup).... As she

> grew older, Brenda complained that she felt like a boy and viewed her physical characteristics as more masculine than feminine. (Colapinto, 2006, p. 57)

Throughout elementary and middle school, children and adults constantly criticized, and even ridiculed, Brenda's masculine appearance and boyish behavior.

After Brenda turned twelve, Money started her on estrogen to begin the development of breasts and other female secondary sex characteristics (Colapinto, 2006). He also repeatedly pressured her to undergo the surgeries needed to construct a realistic-looking vulva. But Brenda refused the surgeries.

By the time she was 14, Brenda had had enough. She had developed severe gender dysphoria and attempted suicide several times (Colapinto, 2006). Her parents decided to tell Brenda the truth about her history. The revelation came as a relief. She quickly decided to begin living as a boy. Brenda became David. He had a double mastectomy and took testosterone to develop male secondary sex characteristics.

As an adult, David married a woman and, for many years, their marriage was a happy one (Colapinto, 2006). Eventually, however, David's life circumstances changed in ways that led to marital difficulties and severe depression. He committed suicide at the age of 38.

David's case supports the claim that gender identity is innate: he thought of himself as a male even though his parents strongly encouraged him to think of himself as a female. But David also was raised as a boy for the first 18 months of his life. This early experience may have nudged him towards a male gender identity.

The Development of Gender Identity in CAH

Prenatal exposure to sex hormones is important for the development of the fetal brain (Kolb & Whishaw, 2021; Yau et al., 2022). Brain development determines our experience of, and responses to, the world around us. Brain development also influences how we experience ourselves, including our self-experience of gender (de Jesus et al., 2019; Hines et al., 2004; Houk et al., 2021). For example, XX females with CAH are more likely than those without CAH to:

- engage in male-typical play behavior during childhood
- prefer a male-typical appearance (e.g., hair styles and clothing)
- be sexually oriented to other females

In short, XX females with CAH are more likely than those without CAH to experience male-typical interests, motivations, and desires.

The major hypothesis for the increased male-stereotypic behaviors in XX individuals with classic CAH is prenatal exposure to high levels of androgens. The exposure to excess androgens is thought to masculinize the brain as well as the genitalia (Yau et al., 2022). The vast majority of these individuals are assigned a female sexual identity at birth or soon thereafter. And although they are more likely to develop stereotypically male interests, desires, and motivations, about 90% experience themselves as females (i.e., have a female gender identity). This number is only slightly lower than the percentage of XX females without CAH who report a female gender identity. The small difference in gender identity

between those with and without CAH is the reason why treatment guidelines for classic CAH recommend that newborns receive a female sex assignment (Houk et al., 2021)

But the research that gave rise to this recommendation has significant limitations (de Jesus et al., 2019). First, because classic CAH is rare, researchers usually observe groups with small sample sizes. The problem is that these small groups may differ from most people with CAH.

Second, in classic CAH, gender dysphoria usually does not emerge until late adolescence or early adulthood. However, researchers often end their observations during childhood or adolescence, or they observe mixed groups of children, adolescents, and adults. These procedures tend to overestimate the number who develop a female gender identity and underestimate the number who develop gender dysphoria.

Lastly, when CAH is not adequately treated, masculinization continues after birth. The individuals who receive inadequate treatment may be more likely to develop a nonfemale gender identity. In other words, both prenatal and postnatal exposure to excess androgens may require a delay in assigning asexual identity.

Social and cultural factors also may affect the likelihood that XX individuals with CAH will become dissatisfied with their female sexual identity or develop gender dysphoria. Of most importance are social and cultural factors that influence decisions about the sex of rearing (de Jesus et al., 2019; Gardner & Sandberg, 2018). In the past, simplistic definitions of biological sex (e.g., ovaries define females and testes define males) guided decision-making about sex assignment at birth. The modern view that biological sex is best represented as a continuum characterized by several biological features lessens the likelihood that clinicians will assign an inappropriate sexual identity.

But other cultural factors may increase the likelihood that gender dissatisfaction or gender dysphoria will develop. For example, in some cultures, male children are preferred over female children. In these cultures, if the biological sex of a newborn is uncertain, the family may push for a male sex assignment. This possibility is greatest in underdeveloped countries where resources for medical and psychological assistance in decision-making are scarce (de Jesus et al., 2019; Gardner & Sandberg, 2018).

In conclusion, the limited evidence available suggests that prenatal exposure to excess androgens has a minimal effect on the development of gender identity and gender dysphoria in XX individuals with classic CAH. But this conclusion rests on an unstable research foundation. Many questions remain to be answered. In order to answer them, researchers need to perform studies with larger sample sizes and better controls.

If Tina Were Born Today…

If Tina had been born in Boston in 2000 rather than 1900, she probably would have lived well beyond her fifth year. First, she would have had a mandatory blood test within a few days after birth (Chan & Levitsky, 2023 ; Merke, 2021). Clinicians would have quickly diagnosed her with congenital adrenal hyperplasia due to 21-hydroxylase deficiency. The recommended treatment for children with this disorder is hydrocortisone, which substitutes for the absent cortisol (Whittle & Falhammar, 2019). Hydrocortisone has physiologic effects similar to cortisol, including suppressing the release of ACTH. Suppression of ACTH ends the overactivation of the adrenals and the excess production of androgens.

In the majority of cases of classic CAH, low levels of aldosterone result in adrenal crises. These crises are the main cause of death during infancy and childhood. They can be prevented with fludrocortisone and salt supplements (Padidela & Hindmarsh, 2010).

A more difficult and vexed set of decisions involves surgery to modify genital appearance and to increase sexual/reproductive functioning. This topic is fraught with controversy and, therefore, requires an in-depth and nuanced consideration of many issues. Such a discussion goes beyond the scope of this article. For reviews of the various arguments and counterarguments. See the following articles, books, and references therein: Dreger (1998), Eder (2022), Gardner and Sandberg (2018), Houk et al. (2021), Hughes et al. (2006), Reiss (2021).

Conclusion

In this article, I compared what clinicians knew about congenital adrenal hyperplasia circa 1900 and what they know today. I also touched upon the experiences of people with CAH and their families. I quickly discovered that, although physicians in 1900 knew that people sometimes were born with ambiguous genitalia, they had no idea why. They knew virtually nothing about the causes of atypical sex development.

In 1900, the families of children with what today is called classic CAH must have suffered much when confronted with this mysterious illness. They could not even answer the first question others asked: is it a boy or a girl? And then, soon after birth, the newborn experienced a life-or-death crisis that had no effective treatment.

I wondered about my great-grandparents decision to bury Tina several months after her death in a cemetery separate from other family members. Was this action an attempt to deny that Tina had been their child? Regardless of the reason for their decision, it seems undeniable that sex and gender are central to how we view ourselves and others. And in1905, anyone who knew the specifics of Tina's case might have wondered about a "hereditary weakness" in the family (see, for example, Kevles, 1995).

The history of treatments for CAH raise the issue of cultural views on what makes a life worth living. These views informed surgical interventions designed to "correct" what seemed to generations of clinicians to be mistakes of nature. For example, from the late-nineteenth to the mid-twentieth centuries, surgeons often amputated the enlarged (penis-like) clitoris to create "normal-looking" genitalia (Eder, 2022). They had decided that the positive reaction of a future husband to the appearance of his wife's genitals was more important than her loss of sexual pleasure.

In recent decades, attitudes have begun to change due to the efforts of people with DSDs, their families, clinicians, and advocacy groups. But given cultural and societal attitudes about these core aspects of personal identity, the journey is still, and perhaps always will be, difficult for those with differences of sex development.

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