A biologist looks at sex and gender

Michael J. Reiss

When I was a secondary biology teacher, teaching about sex was pretty straightforward. In mammals, males had one X chromosome and one Y chromosome in each of their diploid cells, and females two X chromosomes. At A-level, one would teach briefly about sex chromosome abnormalities – for example, Klinefelter syndrome where males have an additional X chromosome and so are XXY, with a total of 47 chromosomes rather than the usual 46. But I wasn't aware of knowing anyone who wasn't either XX or XY and no one talked about sex being 'assigned' at birth.

Fast forward the considerable period of time since I left the classroom and it all seems to have got more complicated. So, what can a biological perspective on sex and gender say that might be useful for science teachers?

Sex determination – in humans and other species

There is an extraordinary range of ways in which sex is determined in different species. For a start, many species, including most flowering plants and about 5% of all animals, are hermaphrodites, so that an individual can produce both female and male gametes. The clownfish that star in *Finding Nemo*, and which I used to keep in a marine tank in the last school in which I taught, are (in nature, not in the film) sequential hermaphrodites. Individuals start off as males and then the largest in the group becomes a female. If this female dies, its male mate changes sex so that it becomes the dominant female, and the next largest male becomes its mate. Nemo's dad, Marlin, should have changed into a female soon after the start of the film when his 'wife' Coral (along with all other offspring except Nemo) got eaten by barracuda.

Back to humans. The Y chromosome is unusual in that it has far fewer genes than our other chromosomes, probably only about 50-60, compared to an average of about 1000 for each of the others. Unsurprisingly, as only males have Y chromosomes, the genes that are on the Y chromosome tend to play roles in male sex determination and development. One of the most important of these genes is the SRY (Sex-determining Region Y) gene. The DNA of this gene, early in development, produces a protein called TDF (testis-determining factor). Classic research by Robin Lovell-Badge and his colleagues showed that when mice SRY gene sequences were injected into XX (female) mice early in development, the resulting mice looked male.

Until the developing human embryo is about seven weeks old (post-conception), there is no visible sexual differentiation. Individuals with XX chromosomes look the same as individuals with XY chromosomes. Then, at about the same time that the embryo starts to be called a fetus, sexual differentiation begins. The TDF protein does several crucial things. For one thing, it begins to act on certain tissues, turning them into what will become the testes. At the same time, it stops the same tissues from developing into ovaries, fallopian tubes and the upper vagina. And, again at the same time, it turns on genes on other, non-sex chromosomes. The net result is that, in an XY fetus from about seven weeks of age, levels of the hormone testosterone (which promotes development of the testes) and anti-Müllerian hormone (which stops the ovaries, fallopian tubes and the upper vagina from developing) are substantially higher than in an XX fetus. In the large majority of cases, such development results in the birth of individuals that are unambiguously females or males.

But sometimes it doesn't. For example, occasionally, during meiosis (the type of cell division that occurs in the production of sperm and eggs), the SRY gene ends up on the X chromosome. If this chromosome is in the sperm that gives rise to a fertilised egg and then a baby, the resulting individual ends up with what is called 'XX male syndrome'. As the term suggests, the individual has two X chromosomes in each of their cells, but looks male. Of course, while these X chromosomes look under a light microscope like X chromosomes, the point is that one of them in each cell has the SRY gene on it, so these chromosomes differ from the usual X chromosomes.

XX male syndrome is only one of a large number of conditions where individuals don't fit unambiguously into the binary classification of 'male' and 'female' on grounds of appearance. For such a classification of sex to work, one needs a clear-cut alignment of sex chromosomes, sex hormones (such as testosterone and oestrogen) and development. An example where these do not align is congenital adrenal hyperplasia. This condition results from a number of different causes but, in all cases, entails either excessive or deficient production of the hormone androgen by the adrenal glands. Importantly, the gene responsible for the production of this hormone is located on an 'ordinary' (autosomal) chromosome, i.e. not the X or Y chromosomes. This means that congenital adrenal hyperplasia can affect individuals who are XX ***and*** it can affect individuals who are XY.

Congenital adrenal hyperplasia results in alteration to either the primary (genitalia) or secondary sexual characteristics. Our secondary sexual characteristics develop at puberty, so include growth of pubic hair and, in females, widening of the hips and growth of breasts and, in males, broadening of the shoulders and enlargement of the larynx. With congenital adrenal hyperplasia, there can be ambiguous genitalia resulting from *in utero* exposure to unusual levels of sex hormones.

Intersex issues

The term 'intersex' is widely used to identify individuals who can't unambiguously be assigned as male or female. While some intersex individuals find the term helpful, others don't. It can be read as reifying the notion of two 'correct' sexes with 'intersex' stuck in between in a sort of no-man's (!) land.

XX male syndrome and congenital adrenal hyperplasia are each a cause of someone being intersex. As mentioned above, XX male syndrome results from a tiny, but crucial, piece of DNA that would normally be on the Y chromosome ending up on the X chromosome. The result is that, while the person looks male, their chromosomes look XX. The reason why this matters is that, for a person with XX male syndrome, their X chromosomes lack a number of the genes that are normally found on a Y chromosome. Although individuals with XX male syndrome have normal male genitalia and can ejaculate, they are infertile.

Other causes of being intersex include being XX but one's mother having unusually high levels of testosterone (for example, because of an ovarian tumour), and being XY but the receptors to the male hormones not working properly (over 150 different problems with these receptors not working are known, each sometimes called 'testicular feminisation'). Some individuals have both ovarian and testicular tissue; this used to be called 'true hermaphroditism' and the cause is usually unknown, though in some non-human animal research it has been linked to exposure to high levels of certain agricultural pesticides.

There are many types of intersexuality and it is difficult to determine its overall extent. If one includes conditions like Klinefelter syndrome, Turner syndrome (women with 45 chromosomes as they have only one X chromosome) and late-onset adrenal hyperplasia, a figure of 1.7% has been calculated. Adopting much narrower criteria, a figure of 0.02% has been calculated. A recent review noted that, if we use a definition of intersexuality that focuses on genitalia that make classification at birth as a boy or girl difficult, a figure of about 0.6% is reasonable.

But how precisely does a midwife or doctor tell if a newborn is a boy or a girl? A quick inspection of the genital region usually suffices, but things are not always so straightforward. The Phall-O-Meter (Figure 1) is a semi-satirical device devised by Kiira Triea, one of the founders of the intersex movement, based on a book by Suzanne Kessler in which she summarised existing views on what were considered medically acceptable infant penis and clitoris sizes.

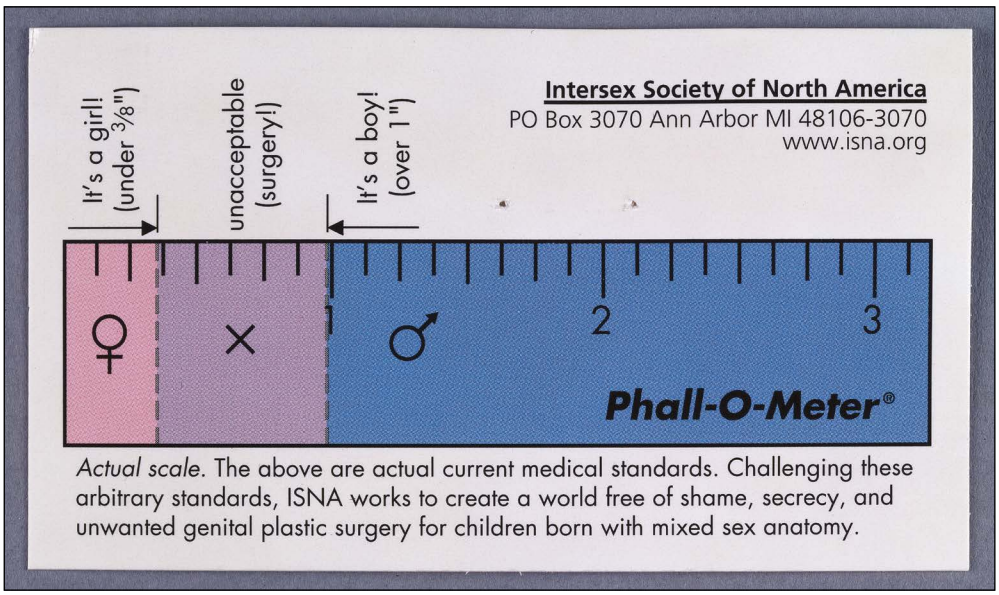

Figure 1. How to tell if a newborn is a boy or a girl. Source: Taken from https://en.wikipedia.org/wiki/Phall-O-Meter#/media/File:Phall-O-meter',_Intersex_Society_of_North_Wellcome_L0031936.jpg

What happens to newborns who cannot straightforwardly be classified as female or male? As the labelling on the Phall-O-Meter indicates, a common response has been surgery. Indeed, the incidence of 'corrective' genital surgery in the USA has been estimated to be about one to two per thousand births (0.1%-0.2%). There are two intertwined issues here – an ethical issue to do with consent (obviously, newborns cannot consent to such surgery) and a conceptual issue to do with what is deemed to be desirable.

There is a growing demand from the intersex movement that surgery should not be undertaken on newborns simply because they don't conform to general presumptions about what a baby should look like. The surgery required for intersex individuals is not straightforward. In the case of what are called 'feminising surgeries', what usually happens is clitoral reduction and vaginoplasty (construction or enlargement of a vagina). Vaginoplasty is not an easy surgical procedure, but 'masculinising surgeries' make it look relatively straightforward. The problem is building a conventional penis when you don't have that much to start with. It is difficult to draw firm conclusions about how successful these operations are. In many cases, data on satisfaction come predominantly either from follow-ups by doctors with former patients or from members of intersex support groups. Follow-ups by doctors with former patients often suggest that the surgery was welcomed; support group data point in the opposite direction. This may tell us as much about who goes to support groups and how easy it is for people to tell their doctors that the surgery was a failure as anything else.

Transgender issues

Someone is transgender if they identify with a gender other than that associated with the sex that they were assigned at birth. Iconically, this means someone who was presumed to be male at birth but, sometimes from an early age, feels (realises) that they are a girl, or being presumed to be female at birth but, from an early age, feels (realises) that they are a boy. Trans people often, to use medical language, manifest gender dysphoria – strong persistent feelings of discontent with one's assigned gender and identification with another (or no) gender, which result in significant distress and impairment.

Some trans people reject the term 'gender dysphoria', and the term 'gender diversity' is sometimes used more generally to reject a binary classification of people into female versus male, and instead describe the wide range of gender identifications outside conventional gender categories. At the present time, arguments about transgender and other gender diversity issues can be passionate to the point of violence. The arguments become especially heated when it is children who want to transition.

Trans issues are much in the news nowadays, but it is worth noting that many cultures have long rejected a binary classification of people in which everyone is either female or male. Examples of the many millions of people who do not fit into 'the standard gender model' include the Hijra of the Indian subcontinent (where they are officially recognised as third gender), 'two-spirit' people in some native American tribes (who sometimes reject the label), the *māhū* (meaning 'noble' or 'in-the-middle') on a number of Pacific Islands, including Hawaii and Tahiti, and the *mukhannathun* in pre-Islamic and early Islamic times.

Gender diversity illustrates a number of points. First, it does not fit with a narrow, essentialist reading of sex and gender in which there is a one-to-one correspondence between a person's sex (understood as a binary) and their gender (also understood as a binary). Secondly, it illustrates how, as humans, we are neither independent of our biological heritage nor reduced to it. Thirdly, it highlights how part of being human is to be able to exercise autonomy and live authentically.

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This piece is an abbreviated version of the argument in the chapter on 'Sex and Gender' in Reiss, M.J. & Ruse, M. (2023), *The New Biology: A Battle between Mechanism and Organicism*, Harvard University Press, Cambridge, Massachusetts, USA.

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