Lecture 6

Sex Determination

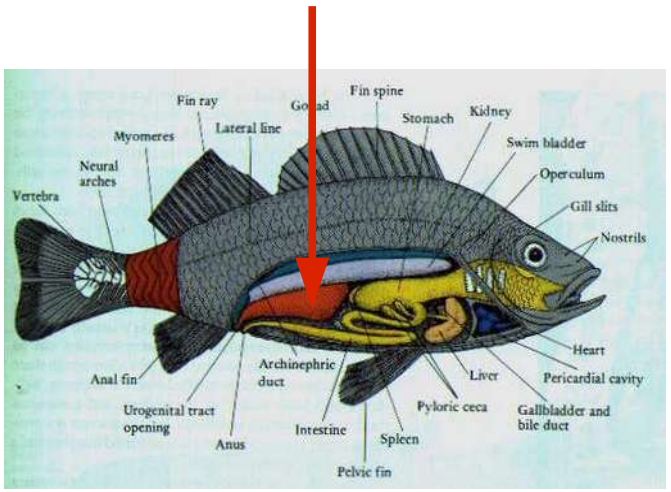
The embryos of males and females begin developing the same way, making the foundations for both sexes.

By the time they start making gonads, they have to decide.

Your gonads developed in the trunk of your body, about half way between shoulder and pelvis (whatever sex you are).

This makes sense if you consider where gonads still are in a fish

testis



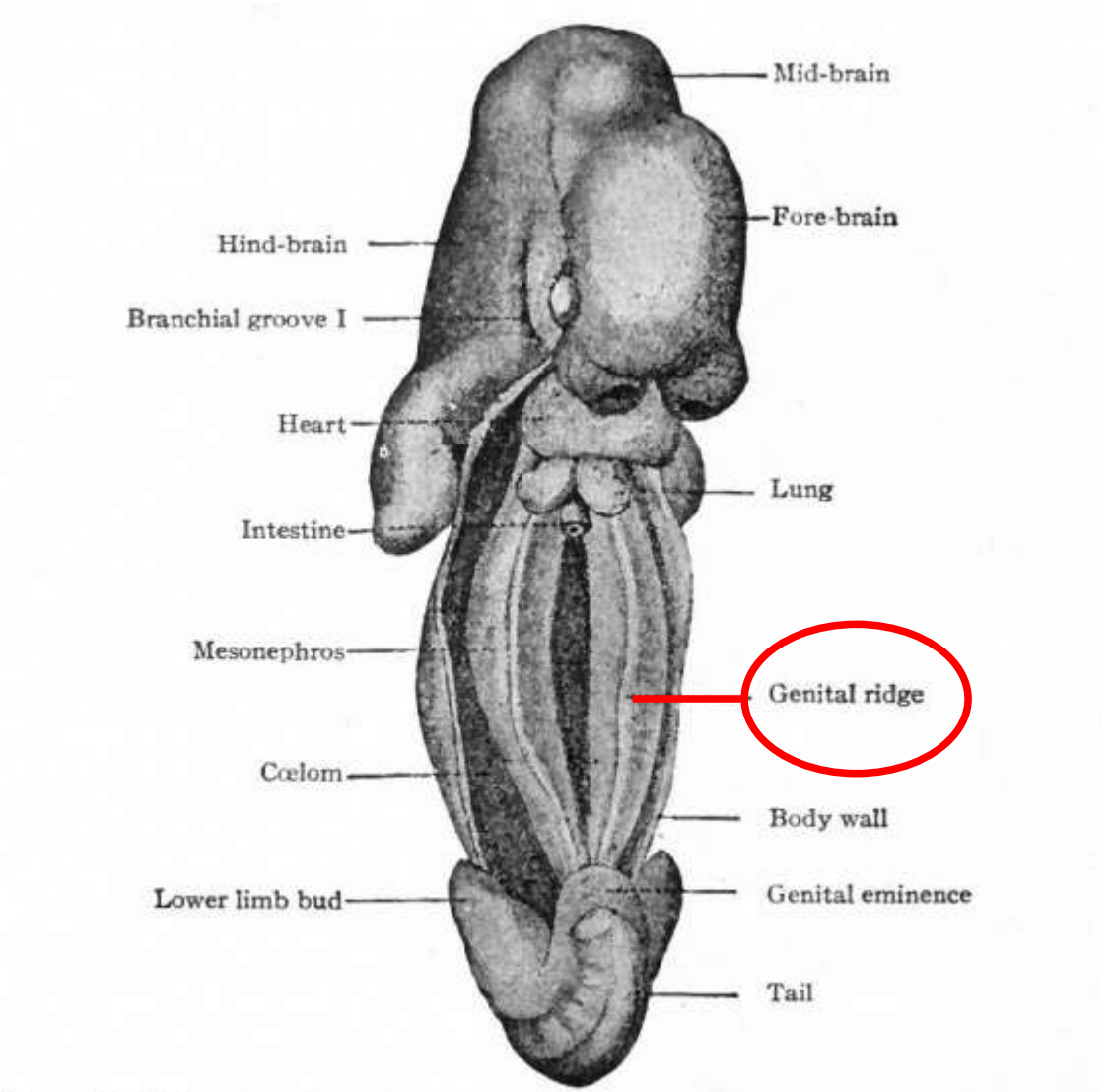
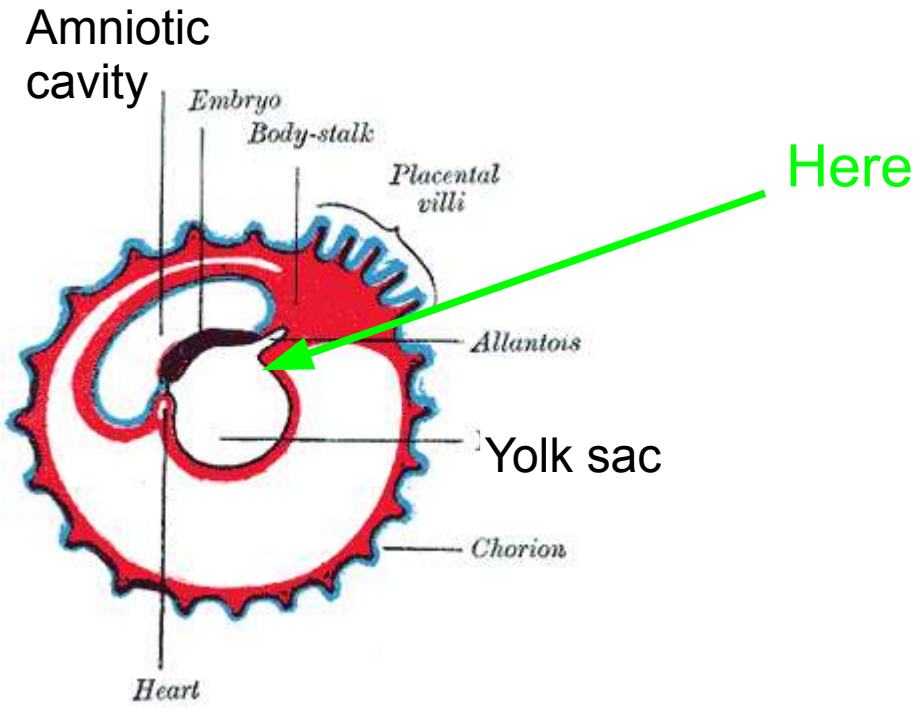


FIG. 308.—Human embryo of 5 weeks. The ventral body wall has been removed to disclose the mesonephroi. *Kollmann.*

The germ line comes from epiblast cells that were removed from the body around the time of gastrulation. It therefore ends up outside the body, in the yolk sac.

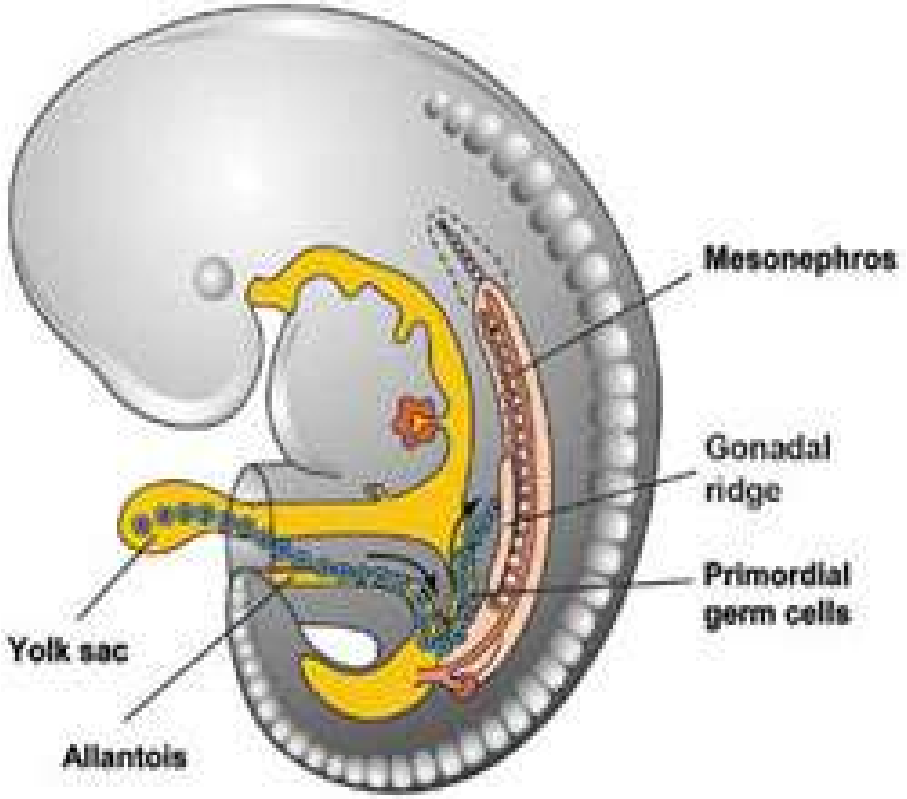


This is a problem, because obviously the germ line needs to be in the gonads.

Image: Gray's Anatomy (now public domain)

The primordial germ cells use this connection, and the gut and its mesentery, as a way to invade the body;

(the sheet-like connection between gut and the rest of the body)



When they reach the level of the developing gonads, they move up the mesentery and then move across to enter the gonads themselves:

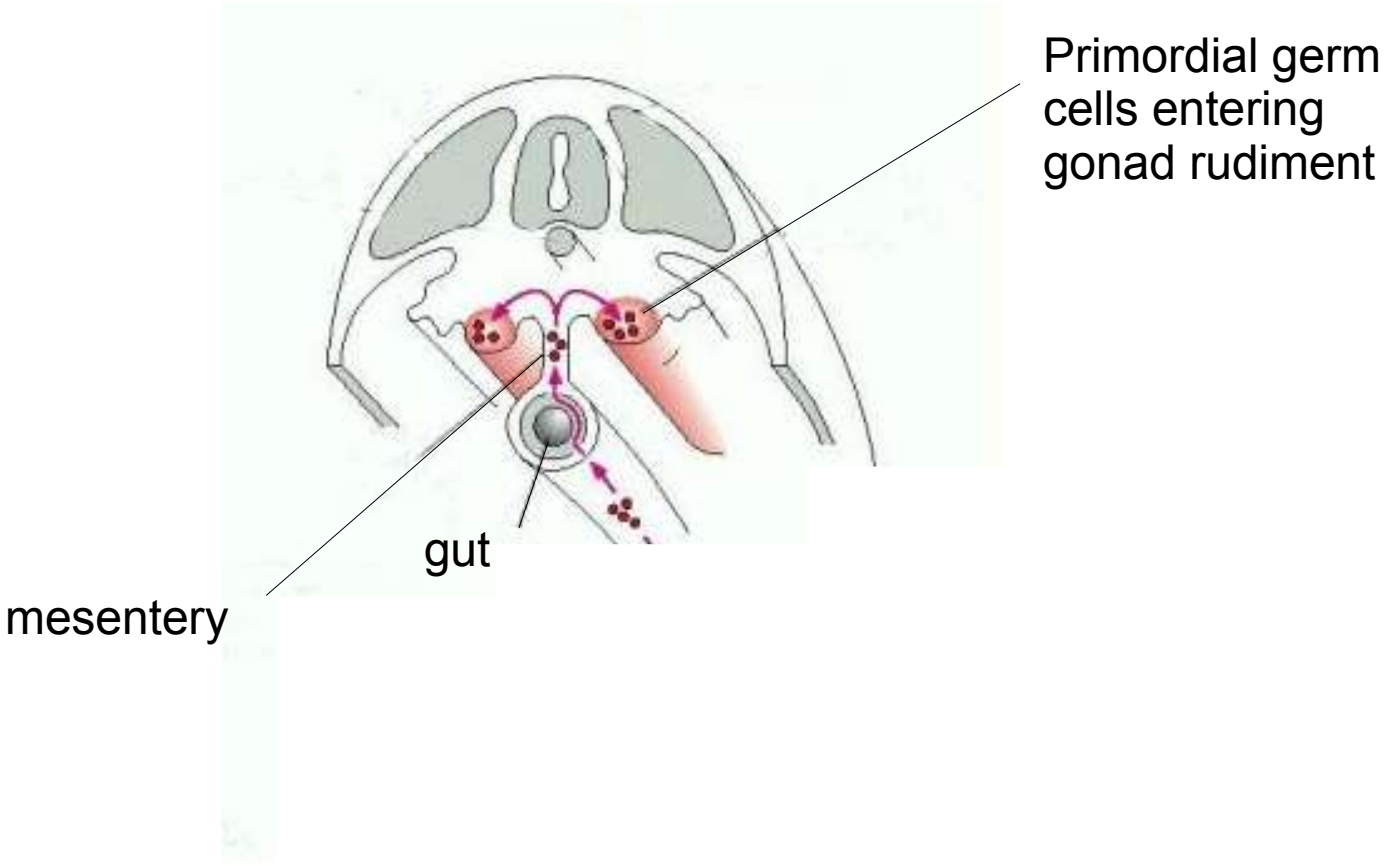


Figure based on one in Alberts et al. *Molecular Biology of the Cell*

Around this time, the gonad has to make a decision about whether to develop into a testis or an ovary

Males and females have a different chromosome constitution;

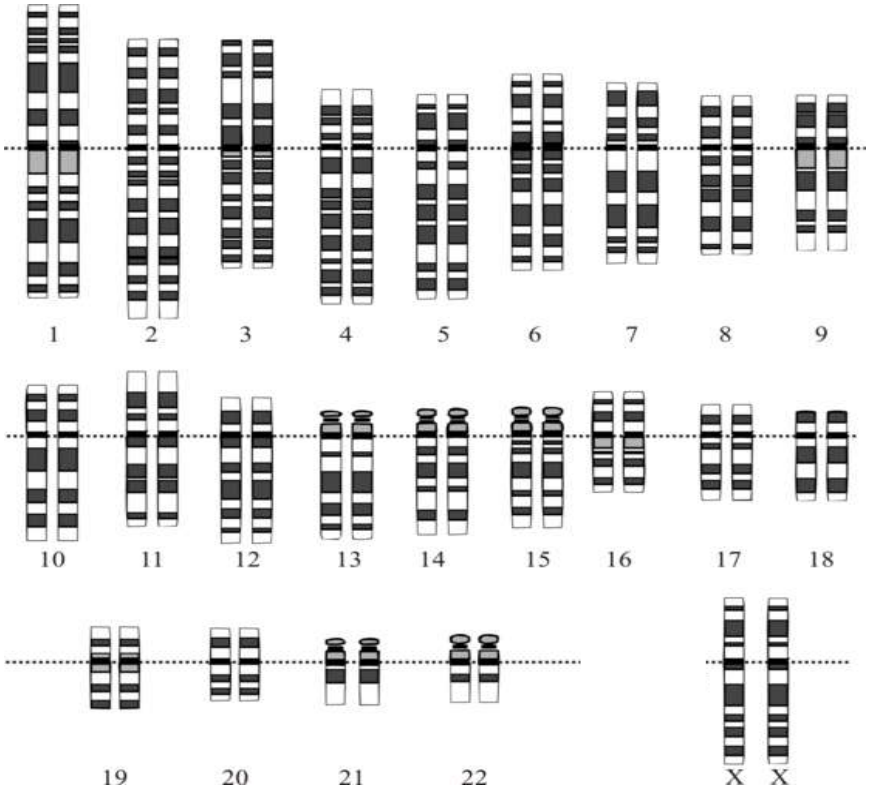
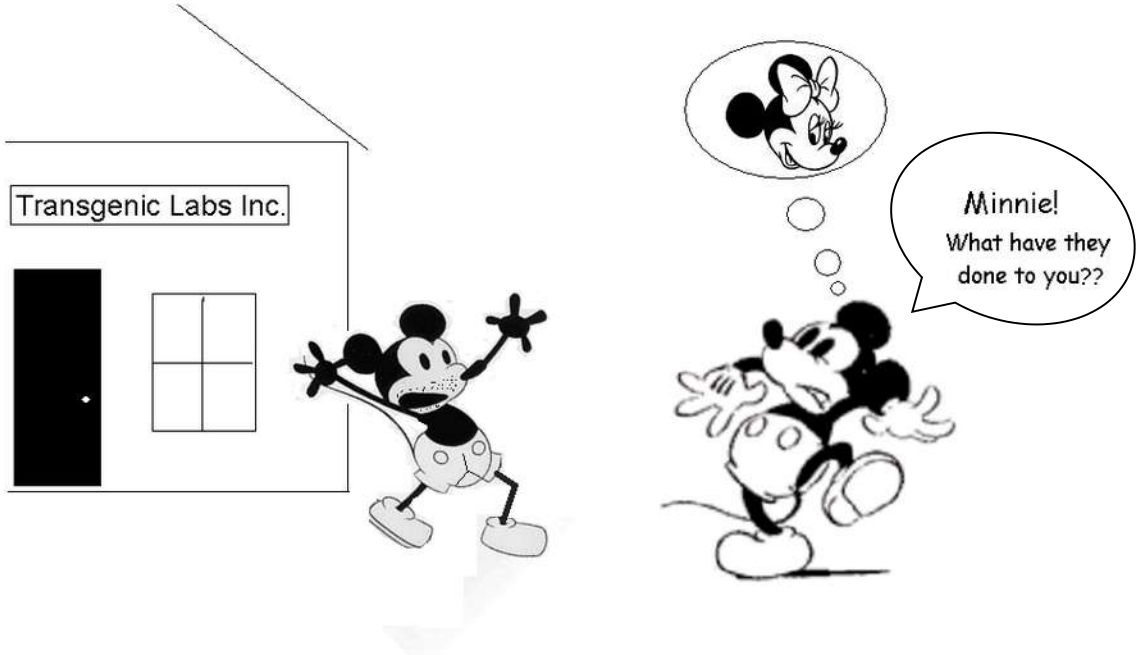


Image credit: NIH (Creative Commons)

A gene on the Y chromosome (SRY) determines sex;

If you force an XX mouse to express SRY, by genetic engineering….

….a male mouse develops



How does SRY act?

How does SRY act?

- Primitive gonads consist of somatic cells and germ line cells
- *Somatic* cells express SRY (if it is present)
- SRY forces somatic cells to develop into testis cells (otherwise they form ovary cells).

Sex determination outside the gonad

In Eutherian Mammals*, the rest of the body pays no attention at all to whether it has a Y chromsome.

It has to take its cue from the testis

The testis communicates with the rest of the body by excreting androgenic hormones.

* in many other animal types, even birds, body cells make their own decisions about male-female according to their chromosomes. In yet other types (Alligators), everything is decided by environmental temperature.

'Indifferent' Gonad

Indifferent soma

Testosterone + AMH production

Female

Male

Image from *The Creation of Adam* (Michelangelo)

The most obvious somatic differences are in the reproductive system itself:

Mullerian ducts make oviducts, uterus, cervix uteri and upper vagina	Mullerian ducts disappear (AMH = anti-Mullerian hormone)
Wolffian ducts disappear	Wolffian ducts become vas deferens
Cloaca makes lower vagina (see year 2)	Cloaca does not become vagina
Phallus develops into clitoris	Phallus develops into penis
Labioscrotal folds remain separate and develop into labia	Labioscrotal folds fuse to become scrotum
Gonads remain internal	Gonads descend into scrotum

You do not need to know the details of genital formation until year 2: I just mention the above so that you can see how many differences there are.

Sexual dimorphism in humans:

Externally obvious differences in:

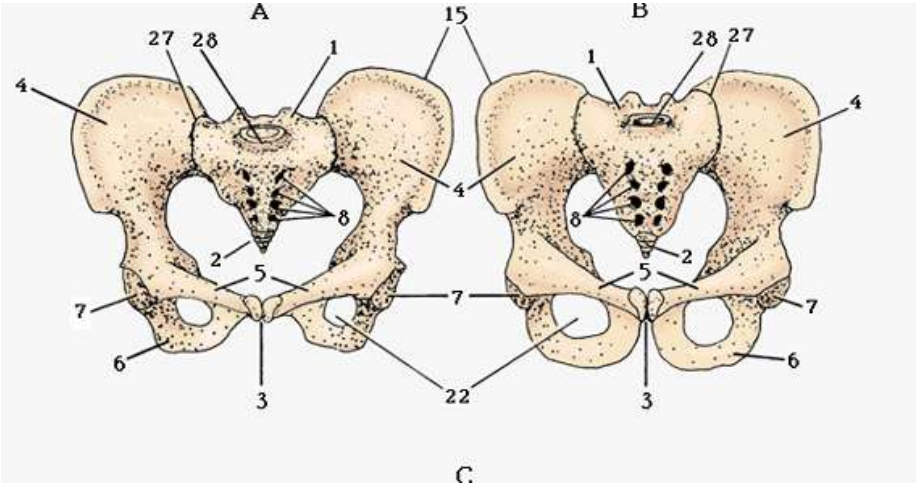
* *average* height & mass
* body shape
* development of external genitalia
* development of mammary glands
* body hair pattern (extent varies with race)

Sexual dimorphism in humans:

M

F

Also brain (eg gender-specific sexual behaviour), although it is difficult to research anything about sex differences in brain without attracting masses of protest from some group or other.



Beyond binary

What if this system does not work?

'Indifferent' Gonad

Indifferent soma

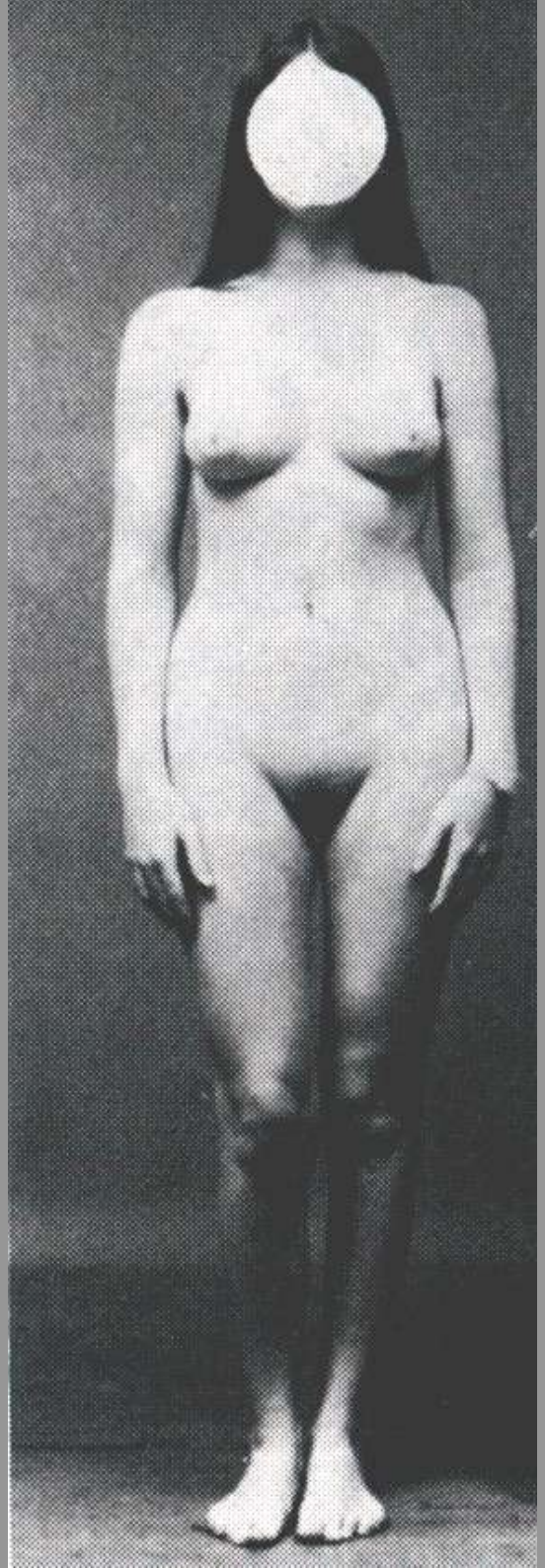
Testosterone + AMH production

Female

Male

Image from *The Creation of Adam* (Michelangelo)

Complete Androgen insensitivity – this person is XY.



{*Face is normal, but hidden for reasons of patient privacy*}

Image from Gilbert S "Developmental Biology"

“Women with AIS... who want AIS to be represented by real, proud people instead of stigmatizing pictures where the face has been removed”

Image credit: Ksaviano, Wikimedia commons

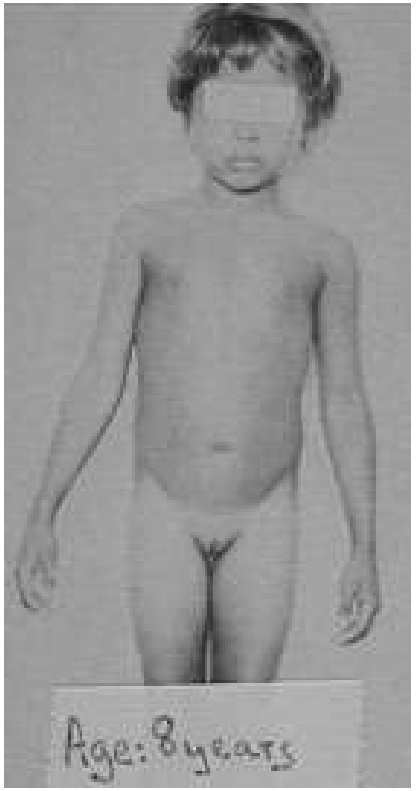
Testosterone itself is a relatively weak androgen

- Testes secrete testosterone. This stimulates androgen receptors only weakly

- Tissues - 5α-reductase converts it to 5α-dihydrotestosterone

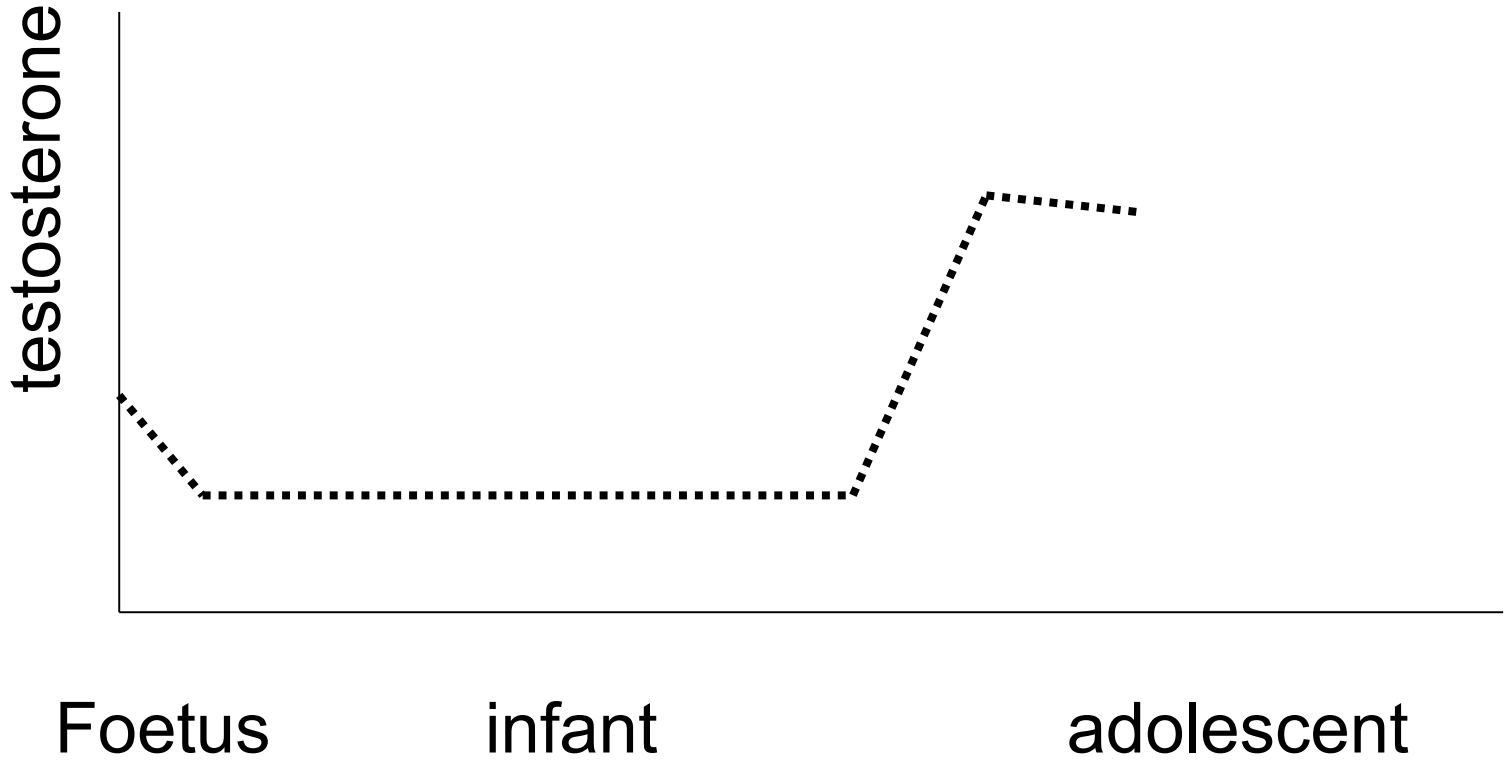
5α-dihydrotestosterone stimulates androgen receptors strongly

XY children with deficient 5α-reductase ('guevedoces') therefore make female bodies:

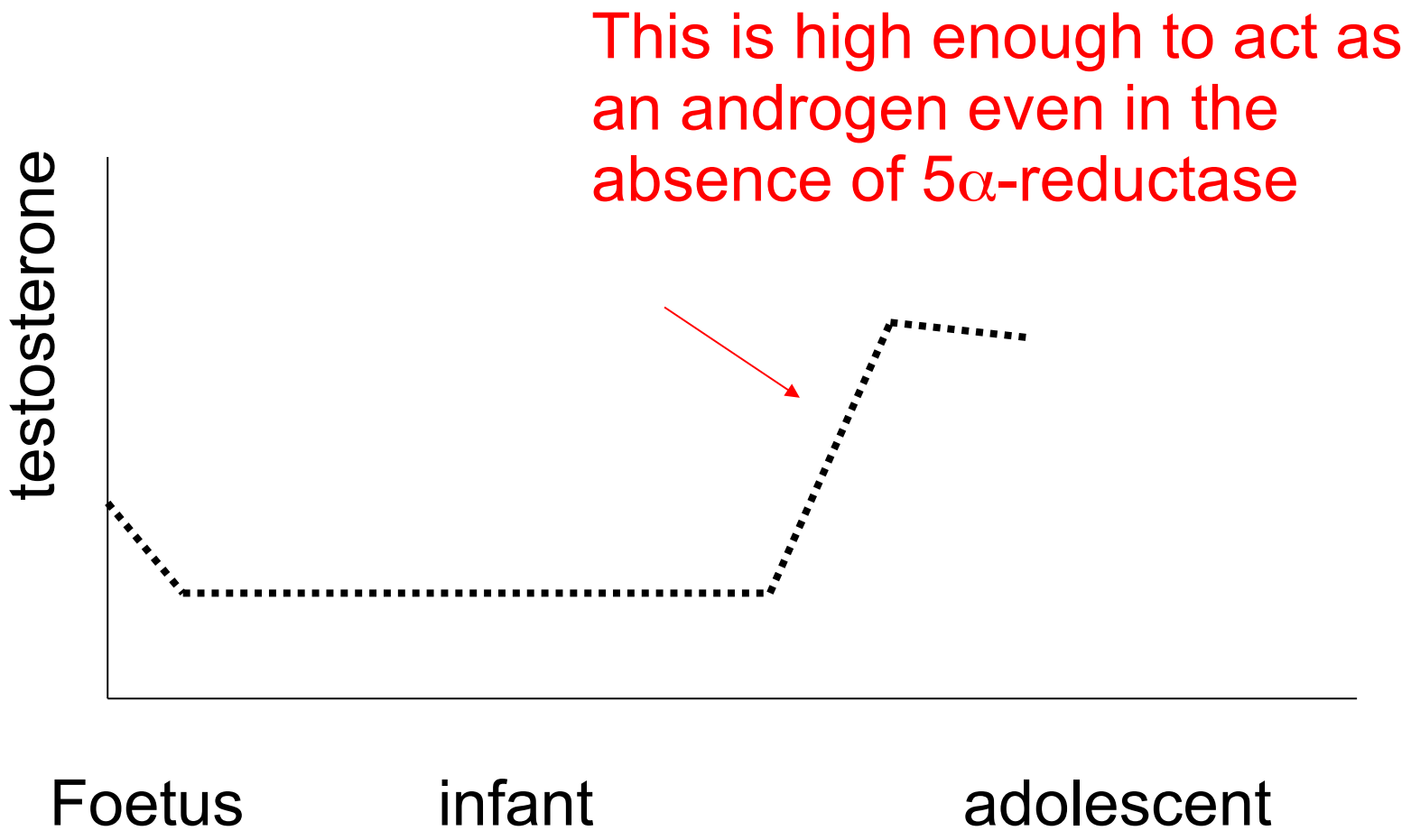


XY – 8 yrs old

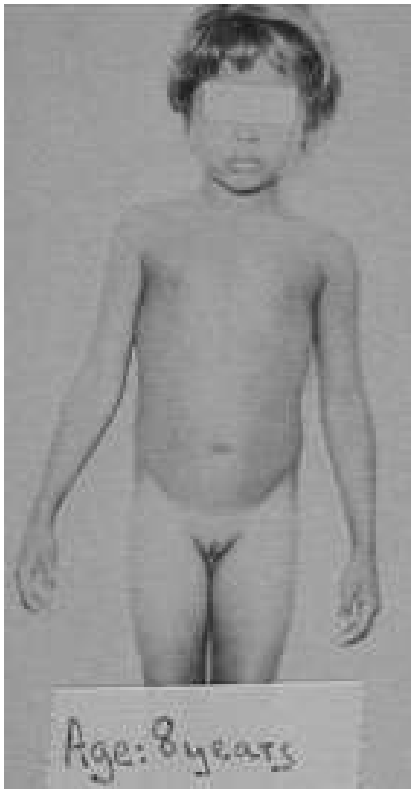
Testosterone rises at puberty

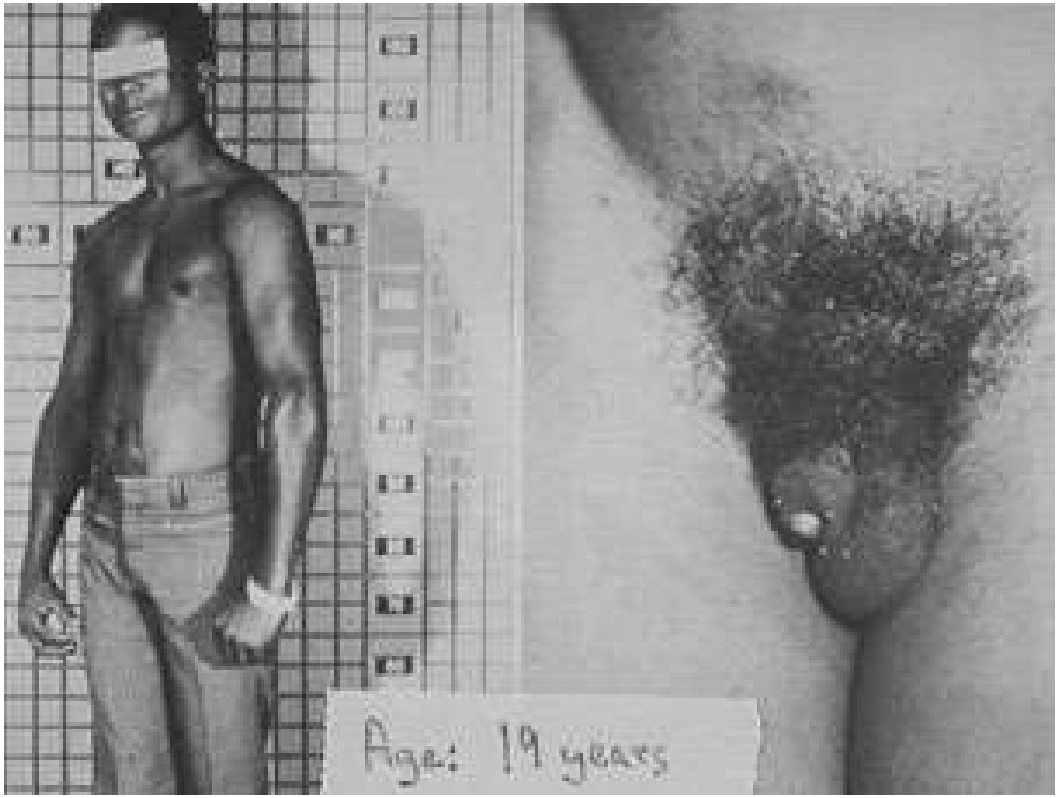


Testosterone rises at puberty



Guevedoces:





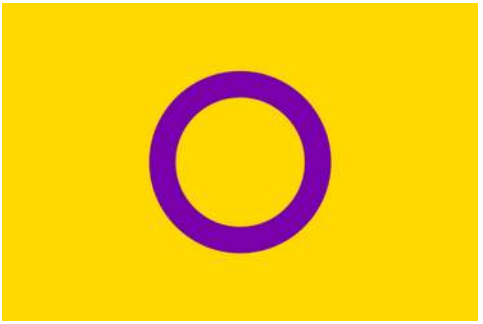
8 years old

19 years old

"Orlando in reverse"

Image credit: Charles Beresford (now public domain)

There is also a vast range of intersex phenotypes



(the intersex flag: non-gendered colours, circle symbolizing wholeness)

Generally, children born with them are subject to 'correction' so that they conform with society's expectation of belonging clearly to one binary sex or another.

Even if they are at no clinical risk from their phenotype.

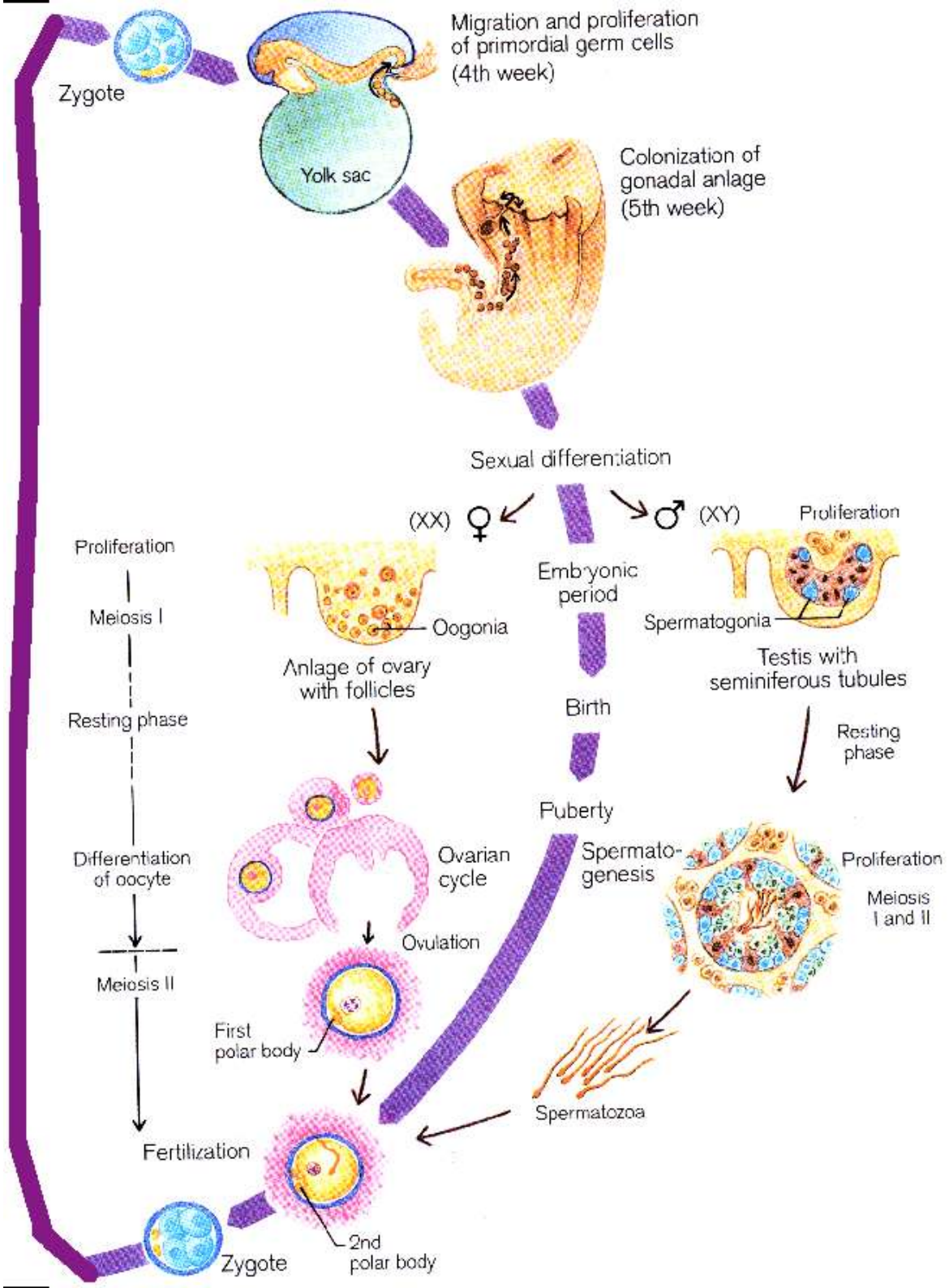
I will leave you to ponder the ethics of this.

And the end of all our exploring

Will be to arrive where we started

And know the place for the first time.

TS Elliot, *Little Gidding,* 1942



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