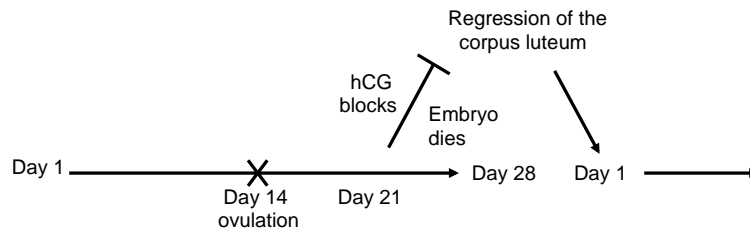


**ANA 301H1
EMBRYOLOGY LECTURE #4**

INFERTILITY

Early Pregnancy Loss not same as infertility



Infertility

- 1 in 4 couples experience difficulty achieving natural pregnancy.
- Infertility = failure to achieve pregnancy after 1 year of regular unprotected intercourse. but it seems many more couples (~90%) are able to get pregnant within 2 years
- 15 % of couples are infertile.
25% of time something wrong w/ male; 35% of time F; 25% of time both; 15% unsure of cause

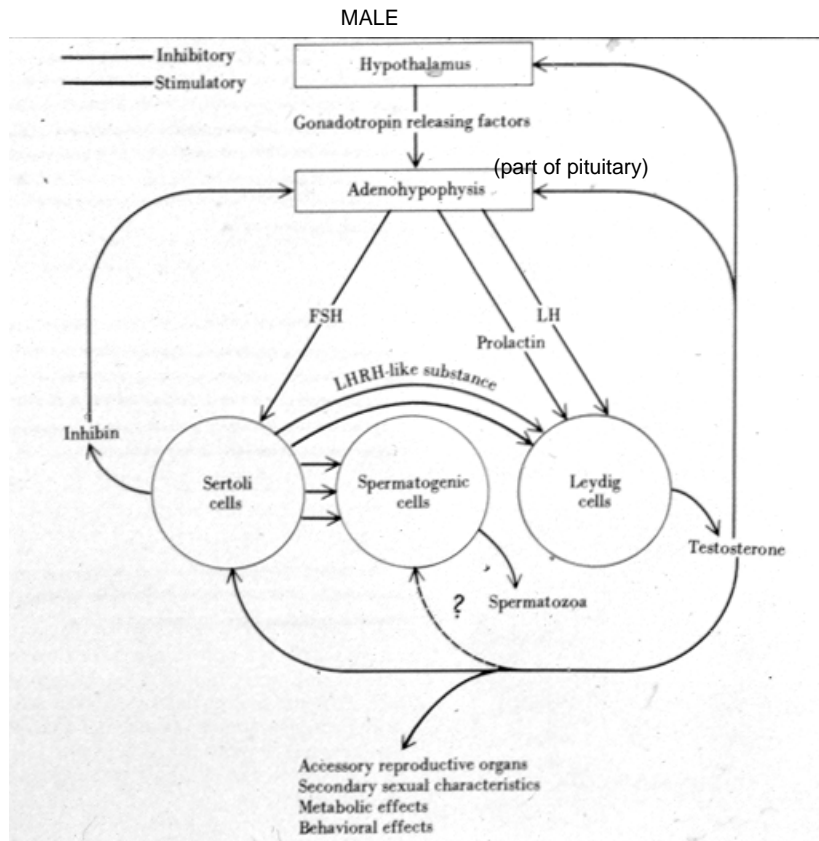
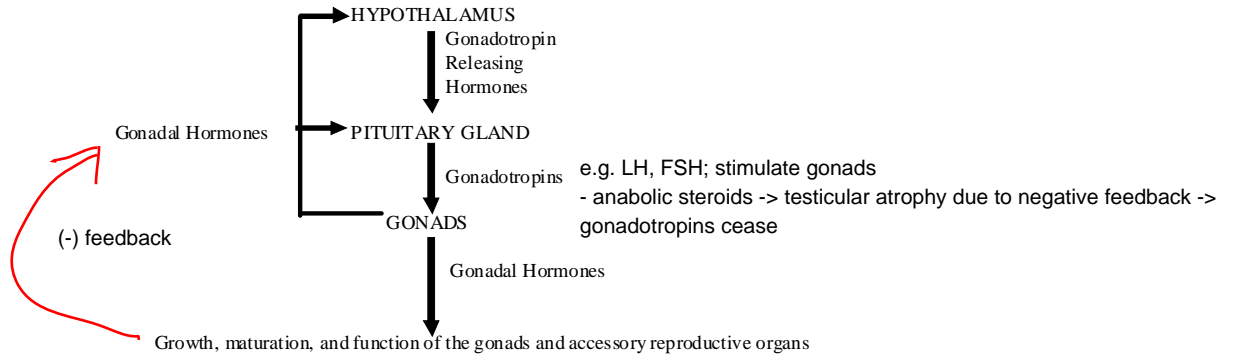
The Factors that Affect Fertility

- Pre-gonadal ... ^{largely} endocrine. (upstream from gonads)
- Gonadal.
- Post-gonadal. (downstream from gonads)

1. Pre-gonadal factors

Pre-gonadal factors

- Mainly endocrine



2. Gonadal Factors/Gonadal Failure:

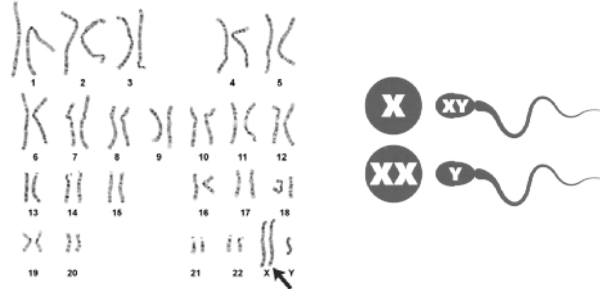
A) Abnormalities in the numbers of sex chromosomes.

aneuploidy of sex chromosomes -> gonadal failure

- eg.) Klinefelter's syndrome (47 XXY), Turner's syndrome (45 XO)
- Abnormalities in the numbers of autosomes are most frequently lethal in utero with a few exceptions (eg Down's syndrome -21 trisomy; Patau's syndrome – 13 trisomy; Edward's syndrome – 18 trisomy). Monosomy of the autosomes is typically lethal in utero.
- Most embryos with Turner's syndrome die in utero. Those that survive, and those who have Klinefelter's syndrome are **typically sterile**.

Abnormal Sex Chromosome Number

Karyotype from a male with Klinefelter syndrome (47,XXY)



Klinefelter's
(XXY)

individual is male but has extra X chromosome

- either nondisjxn in spermatogenesis or nondisjxn in oogenesis
- phenotype: tall, skinny, underdeveloped 2^o sex characters; lower intel

Abnormal Sex Chromosome Number



Turner's
(XO)

- 45 XO

- phenotype: webbing in neck; wide chest; ovaries infertile; not obvious 2^o sex characters

3

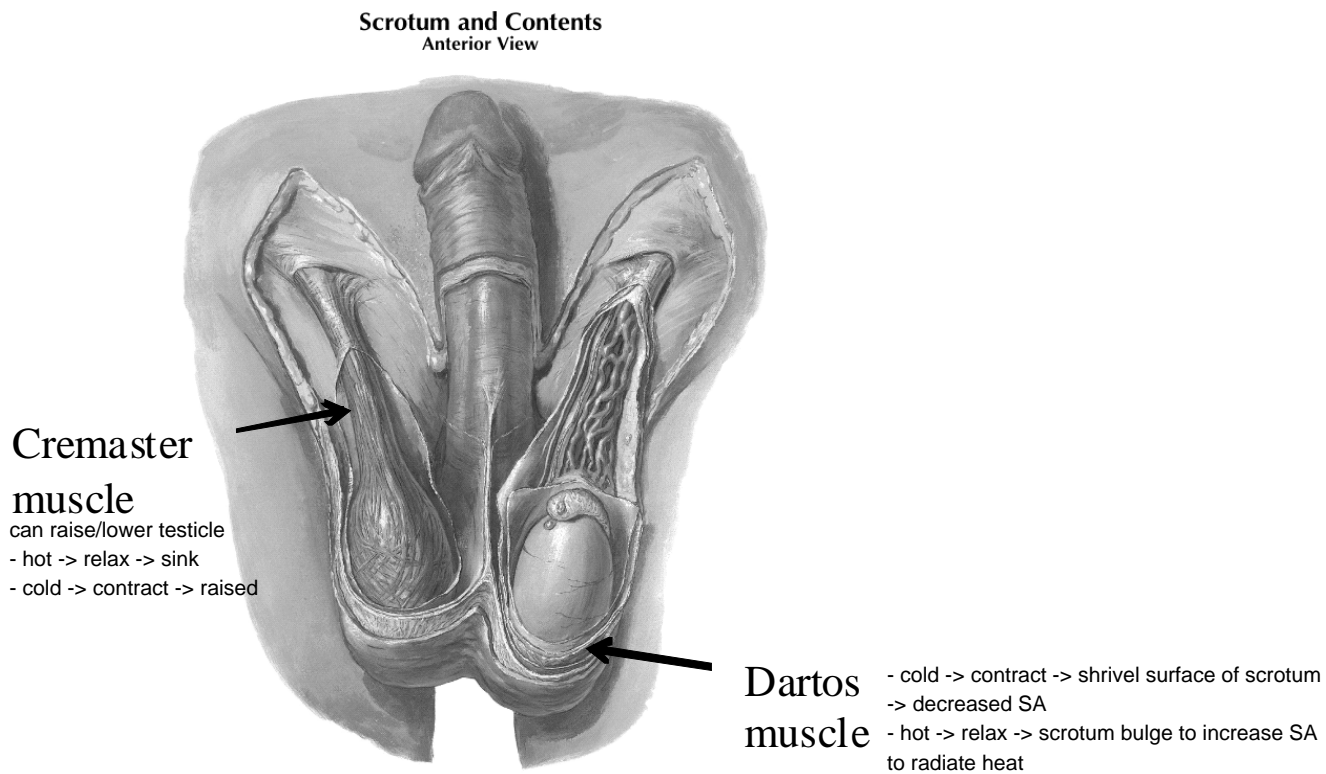
- 2^o sex characters can be gotten w/ hormones though

B) Space occupying lesions that take up volume normally occupied by functional gonadal tissue. (eg. cysts, tumours and scars). blocks gametes -> infertility

C) Certain environmental agents (eg. lead, alcohol and nicotine), although the mechanisms are not clear. heavy metal; gonadotoxins

D) *In the testicles*, decreased function may also be linked to increases in the temperature of the testicles. Spermatogenesis is optimal at a temperature about 2° lower than core body temperature. ~~A number of adaptations have developed to help maintain the temperature of the testicles within a narrow optimum range. e.g.)~~

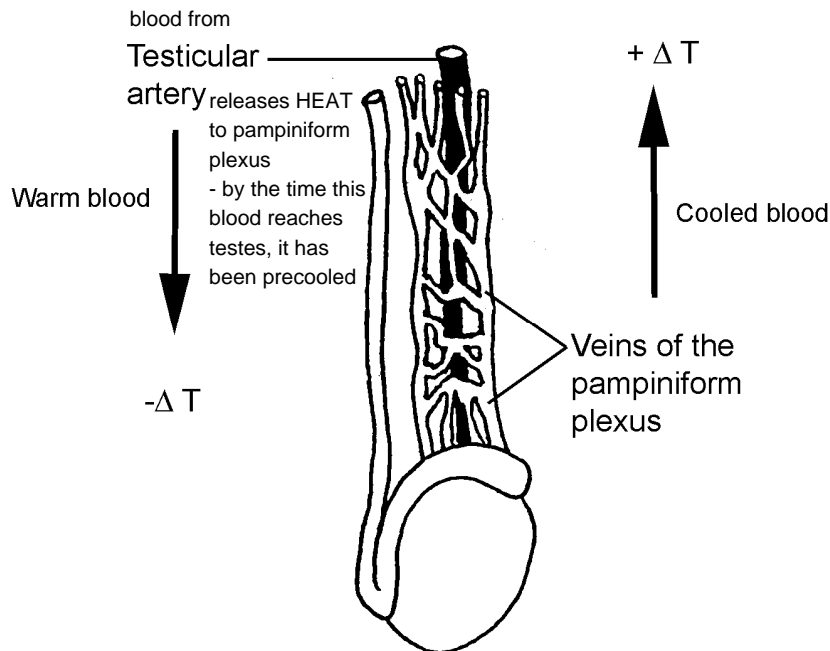
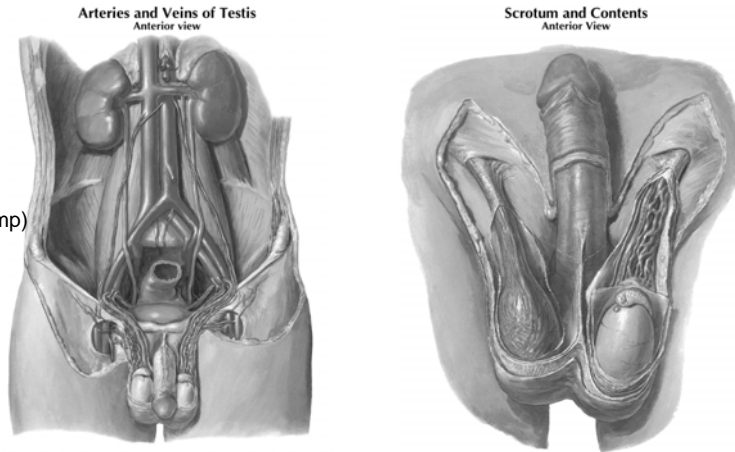
- migration from the abdominal cavity into the scrotum.
- the cremaster reflex.
- the dartos reflex.



- the counter - current heat exchange ~~between the testicular artery and the pampiniform plexus of veins.~~

The pampiniform plexus draws heat from the testicular artery and pre-cools the arterial blood entering the testicle

- in embryo, testes developed up near kidney; blood supply to testes hence comes from aorta
- this blood is too warm (core body temp)



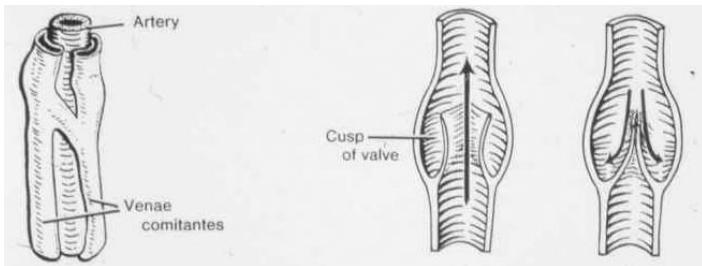
Increased testicular temperatures are associated with:

- decreased sperm motility.
 - decreased sperm numbers
 - increased numbers of abnormal sperm
- } decreased fertility

• Increased temperatures in the testicles may be due to:

- Cryptorchid(undescended) testicles
 - hormonal treatment, surgery or removal (if vas or testicular artery too short for e.g.)
 - must remove b/c likely to develop malign tumor
- Environmental factors (eg. clothing, occupation)
- Varicocele – A dilatation of the veins in the pampiniform plexus. As the veins stretch, the venous valves cease to function. This leads to **venous stasis**, breakdown of the counter-current heat exchange, elevated testicular temperatures, deterioration of sperm factors (reduced number, loss of motility, increased abnormal forms) and reduced fertility.
 - treatment improves fertility factors but not to 100%

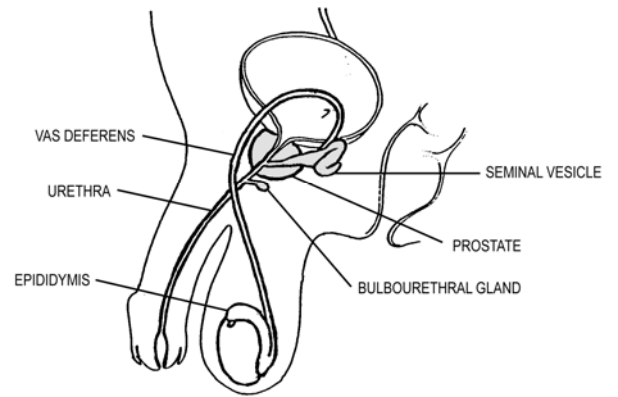
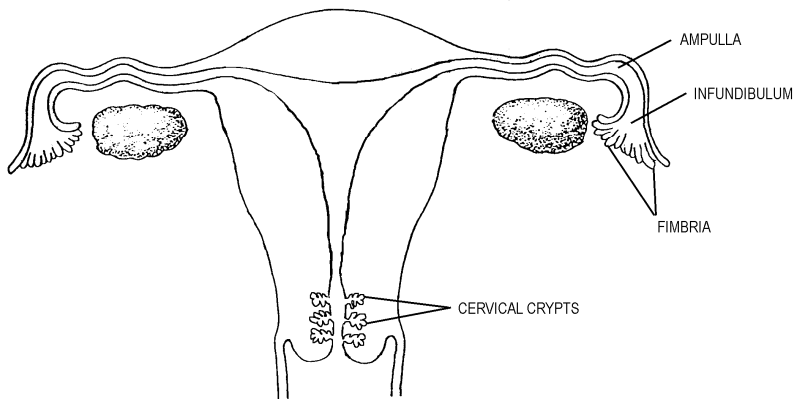
Veins and Venous Valves



3. Post-Gonadal/Pelvic Factors

- ~~Pelvic factor infertility refers to a wide range of male and female disorders that can prevent the sperm and the egg from meeting in the uterine tube.~~

1. Altered Anatomy of the accessory reproductive ducts.

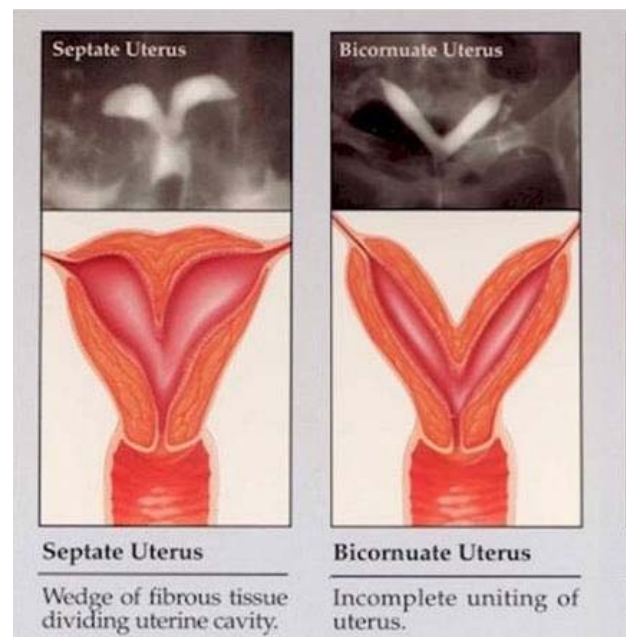


- Can be congenital or acquired.

egs) Congenital

- a) Congenital absence of the vas
- b) Mullerian agenesis absence of uterus
- c) Tubal and/or uterine malformation

Divided Uterus



egs) Acquired

- a) ~~Space occupying lesions in the walls of the reproductive tubes may occlude them. Space occupying lesions in adjacent structures may block the tubes by compressing them.~~

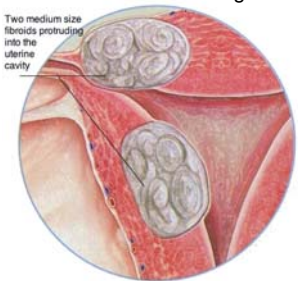
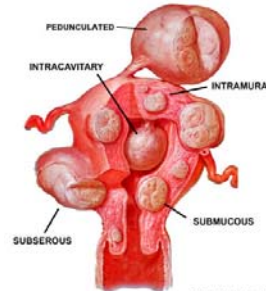
Space Occupying Lesions

- Internal occlusion (within tube; left)
- External compression (outside tube; right)



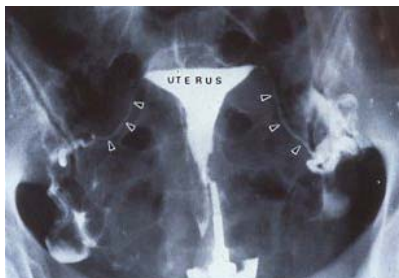
~~Scars can distort normal anatomy and function.~~

Space Occupying Lesions - eg) **Fibroids**
= benign tumors of uterus; can be acquired via inflam -> scarring

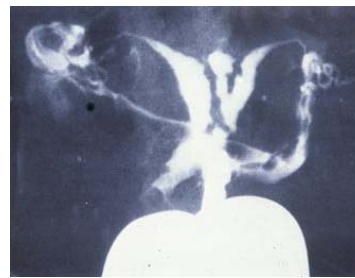


- Surgery eg) Asherman's syndrome

Asherman's Syndrome



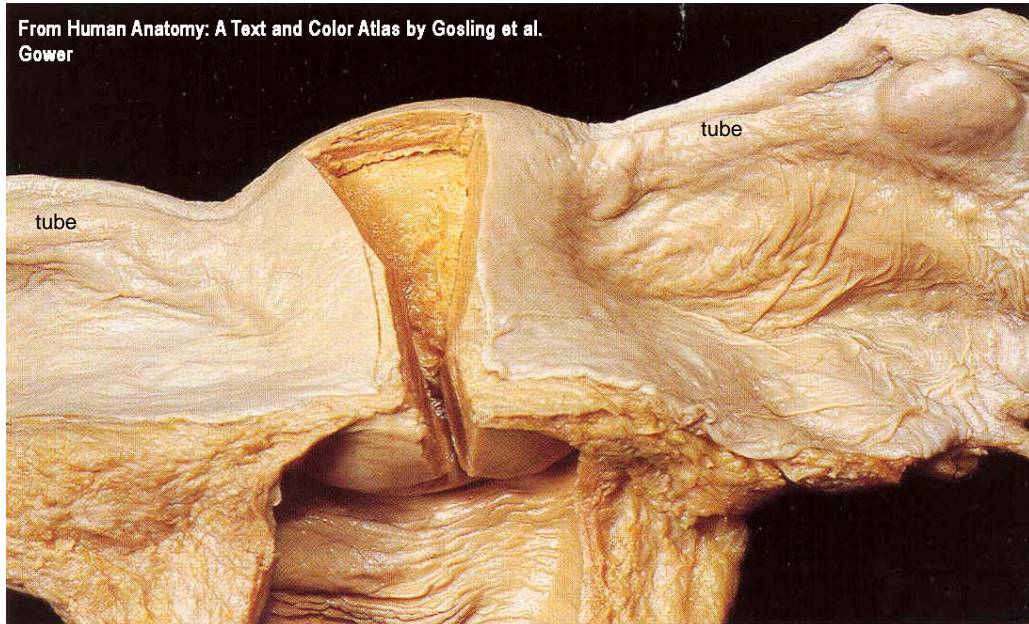
Normal



Asherman's Syndrome = front wall of uterus stuck to back wall of uterus

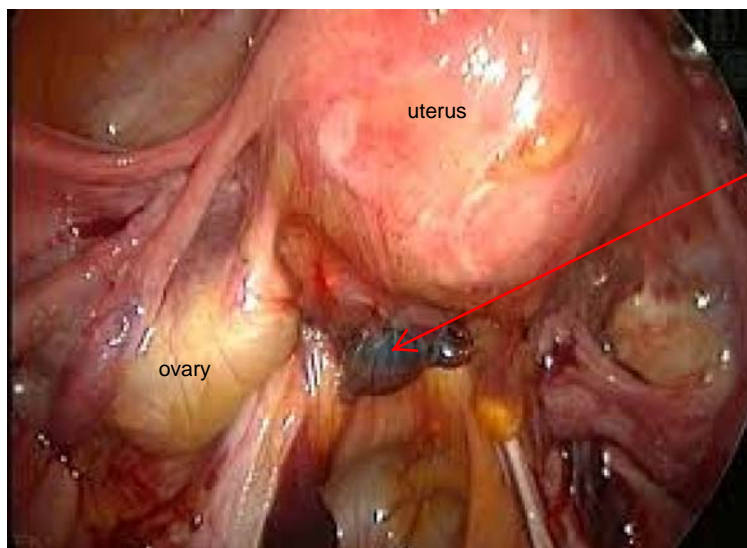
- **Infection** eg) Ruptured Appendix, U.T.I., P.I.D. = pelvic inflam disease = scarring of uterine tube
-> inflam -> scarring
- e.g. dirty catheter in urinary bladder -> infection -> spread to vas and scar
- **Endometriosis** – the presence of endometrial tissue outside of the uterus, Typically on pelvic organs where lesions can cause pain and scarring.
- tissues fibrose, scar, distort anatomy, difficulty conceiving

Uterus and Peritoneum



- endometriosis = when peritoneum starts to become like endometrium

Endometriosis

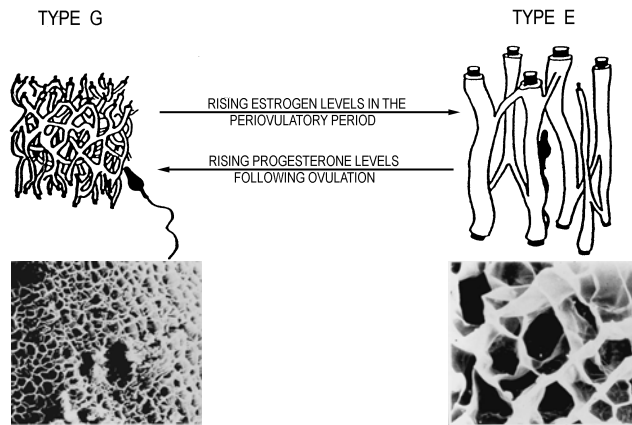


endometriotic tissue (trapped blood)

2. Hostile cervical mucous = when cerv mucous not cycling properly or chemistry too toxic to sperm

- cervical glands produce a mucin glycoprotein which alternates between a tightly structured fibrous form (type G) which is thought to be a barrier to microorganisms (and sperm) and a loosely structured, watery form (Type E) which allows passage of sperm into the uterus.

Cervical Mucous

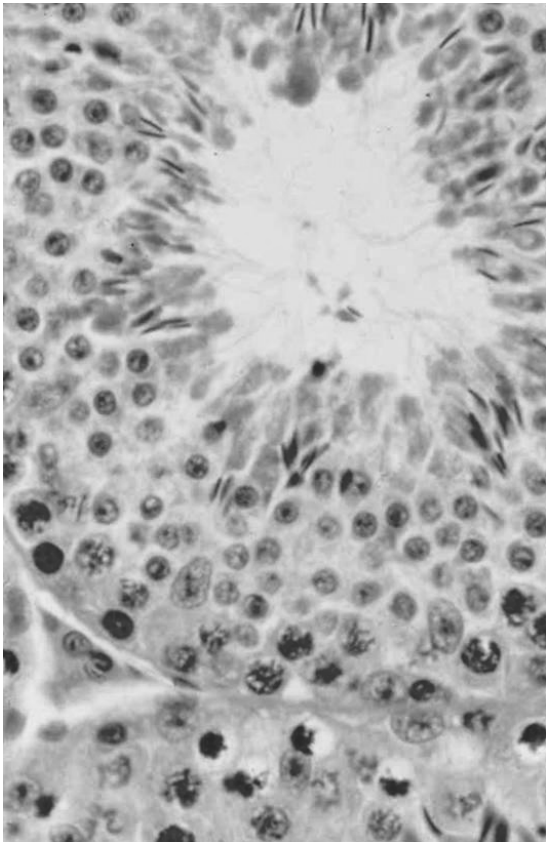
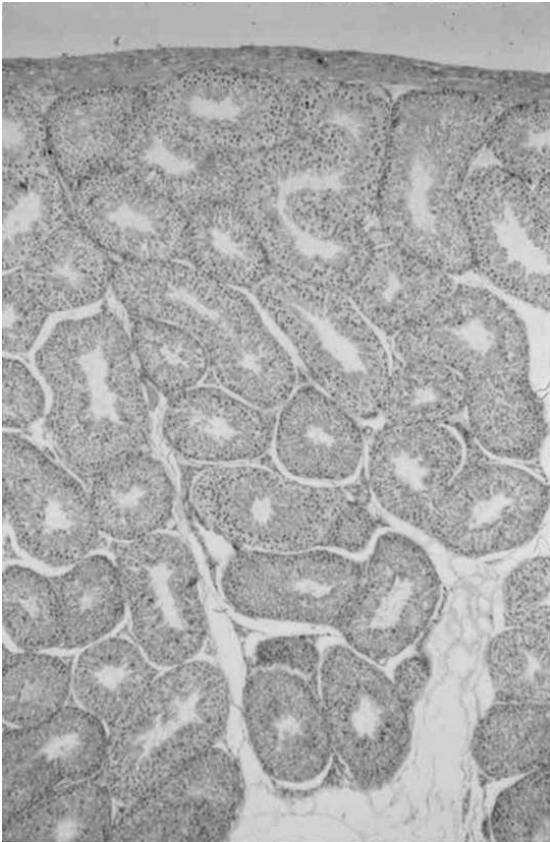


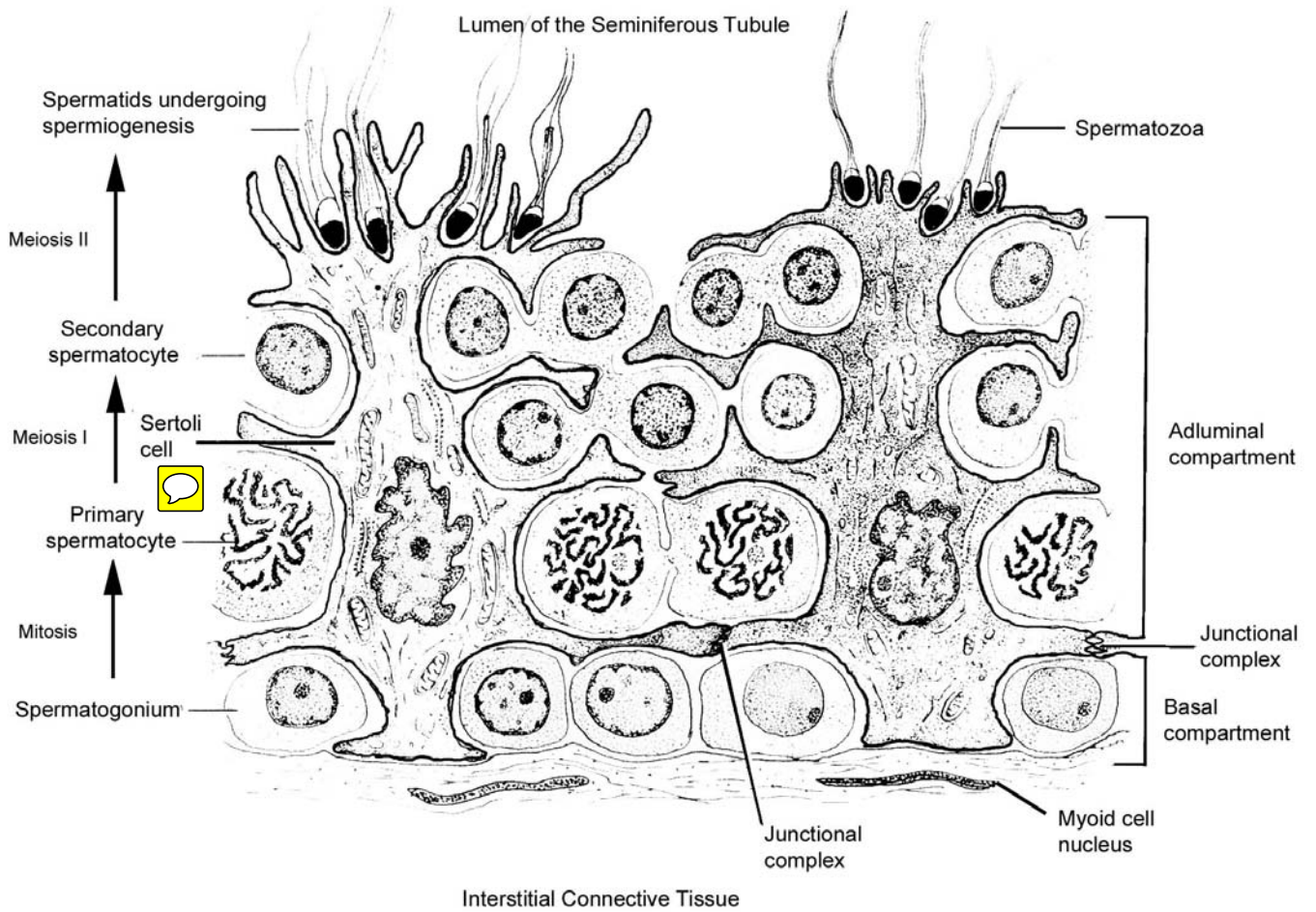
3. Antibodies to sperm antigens can cause:

- reduced motility
 - sperm agglutination
 - death of sperm cells
- } Reduced fertility

- **Isoimmunity** occurs when a woman develops antibodies to sperm cells. attack sperm antigens
- **Autoimmunity** occurs when a man develops antibodies to his own sperm cells. This is thought to arise when damage has been done to the 'blood - sperm barrier'. The blood - sperm barrier develops as a mechanism to isolate the cells that don't begin to develop until puberty with the onset of spermatogenesis from the rest of the body. For example, in the seminiferous tubules, the barrier consists of a series of continuous tight junctions that connect the Sertoli cells together.

Spermatogenesis





80/ from Krause and Cutts, Concise Textbook of Histology. Williams and Wilkins