Organ Systems

A Brief Introduction into Organ System Development from Gamete to Newborn

with

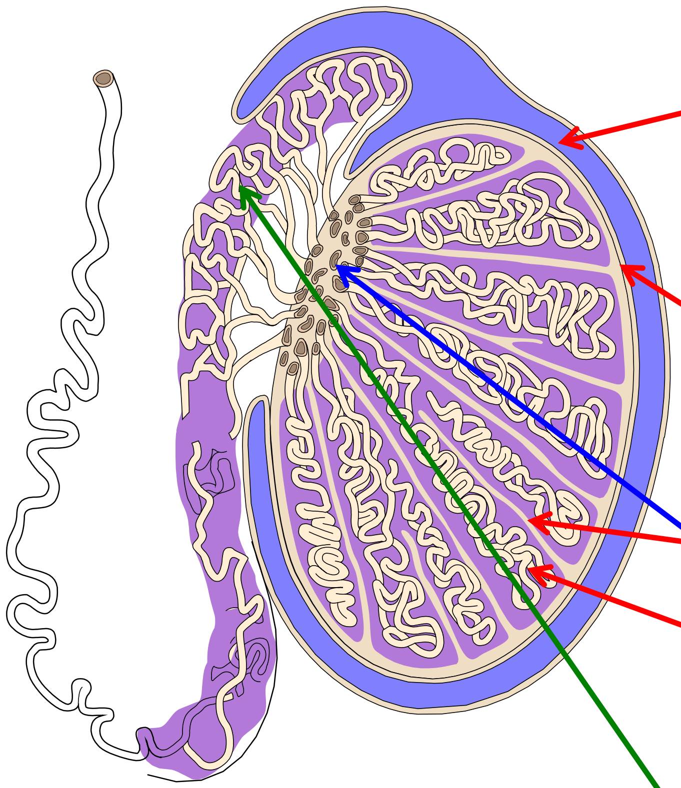
Elementary, Illustrative, Pathology

DISCLAIMER!

- This lecture is a clinically and scientifically frank **ADULT** discussion about a portion of the human reproductive system focusing on illustrative organ system development with **ADULT** students who are studying to go into fields of health care and need a fundamental knowledge of:
  - The anatomy and physiology of the human reproductive system, and
  - Embryogenesis and fetal development.
- If you feel uncomfortable with and/or about this[these] topic[s], it is quite likely that you're probably not going into an appropriate field of study for your future and may wish to reconsider your career path.

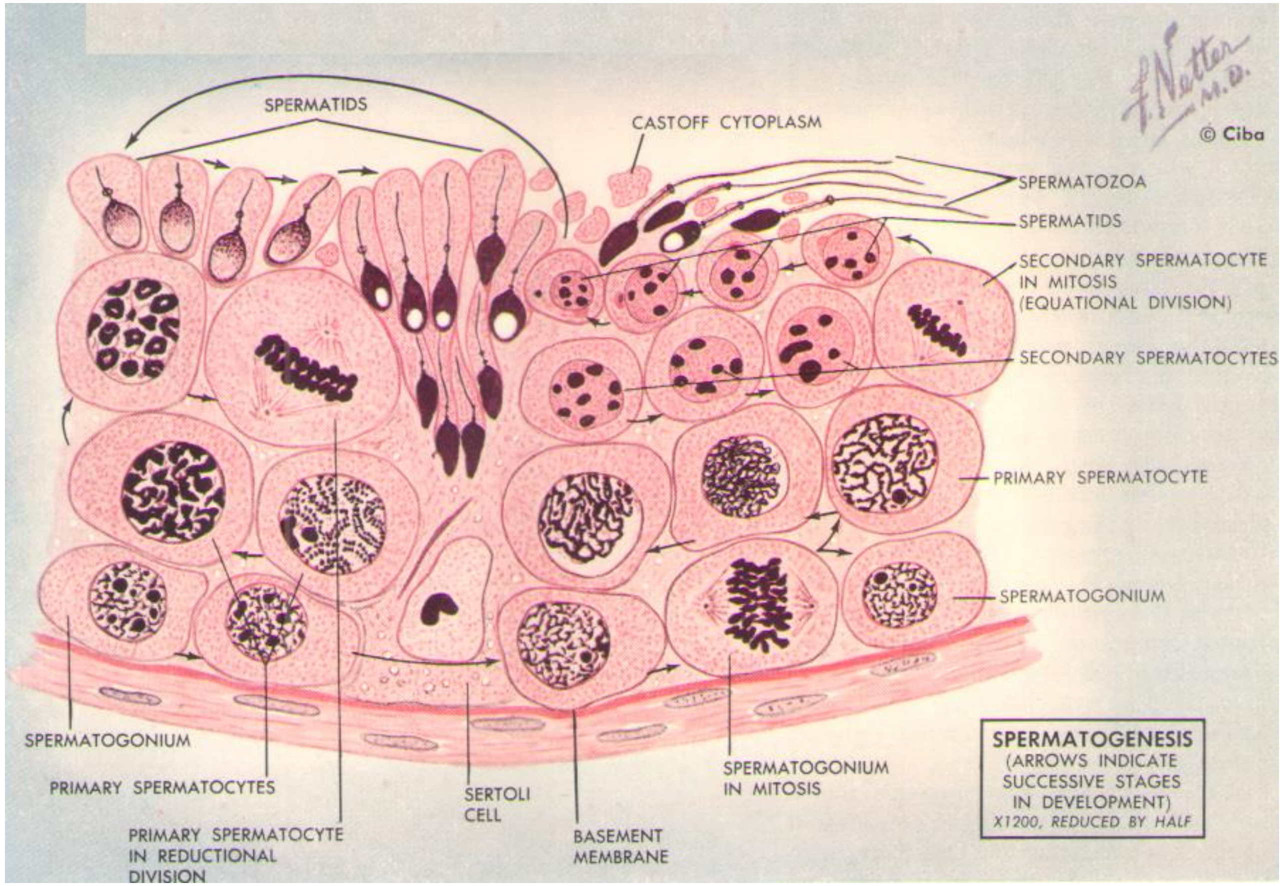
You've been forewarned.

Testis



- The outer coating of the testis (the tunica albuginea) is eventually surrounded by the tunica vaginalis (this is from "vaginal“ growth during embryological differentiation).
- At 7 months, the tunica vaginalis "drops" into the scrotum; at 8 months, it is in the scrotum anterior to the testis.
- By one month of post-natal age, it is called the tunica vaginalis.
- The tunica albuginea give rise to the septa in the testes, which separate the tissue into lobules.
- The lobules consist of the seminiferous tubules (where the sperm are synthesized).
- ALL seminiferous tubules converge on the rete testis and the epididymis.

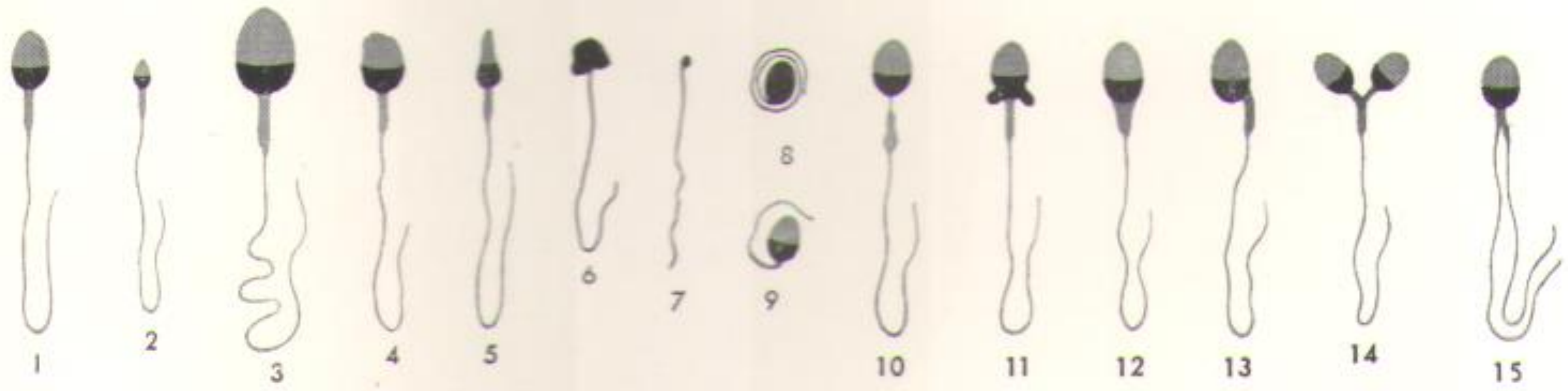
Spermatogenesis



- Note that the synthesis of sperm occurs in the seminiferous tubules which enclose the Sertoli (or sustentacular or nurse) cells, which is the ultimate source of the sperm.

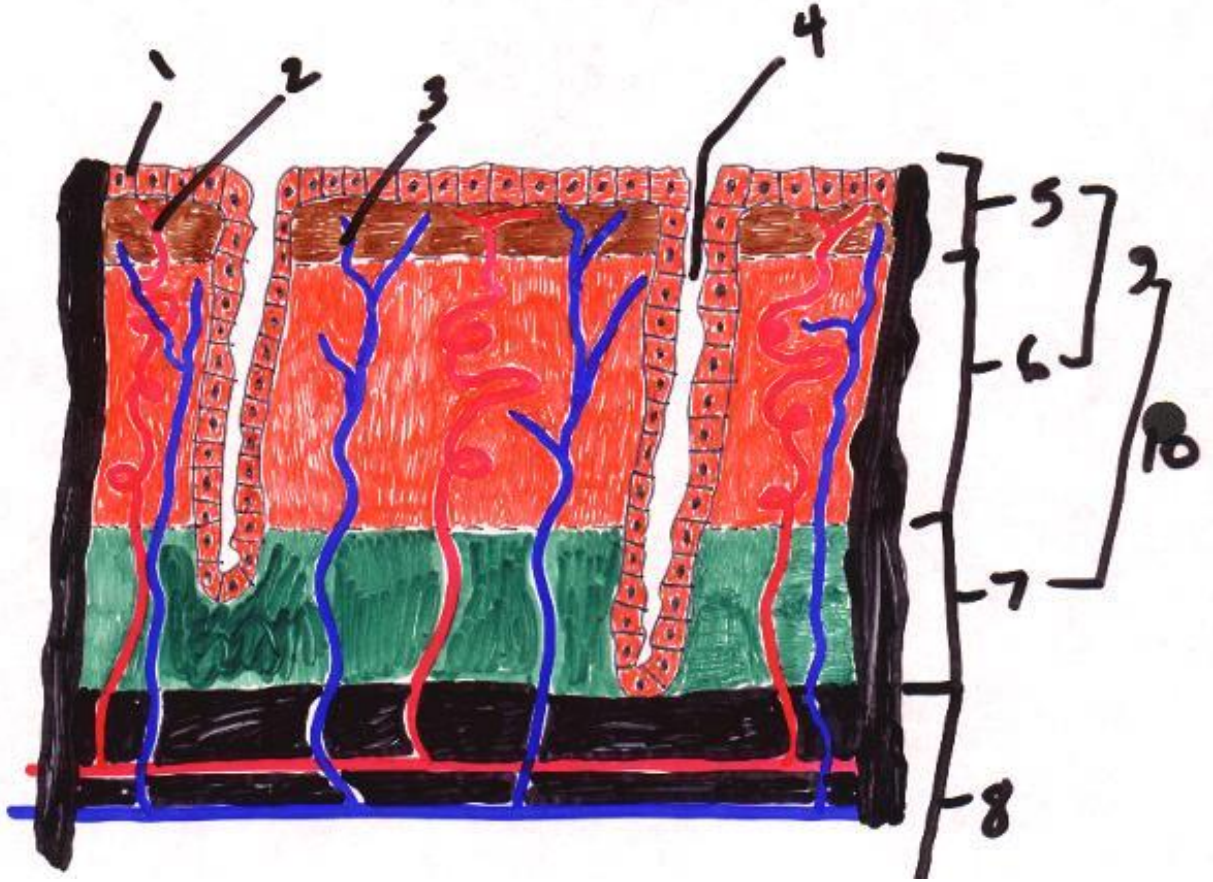
Sperm Morphologies

SEMEN ANALYSIS
SOME ABNORMAL FORMS OF HUMAN SPERMATOZOA COMPARED
WITH THE NORMAL (1)



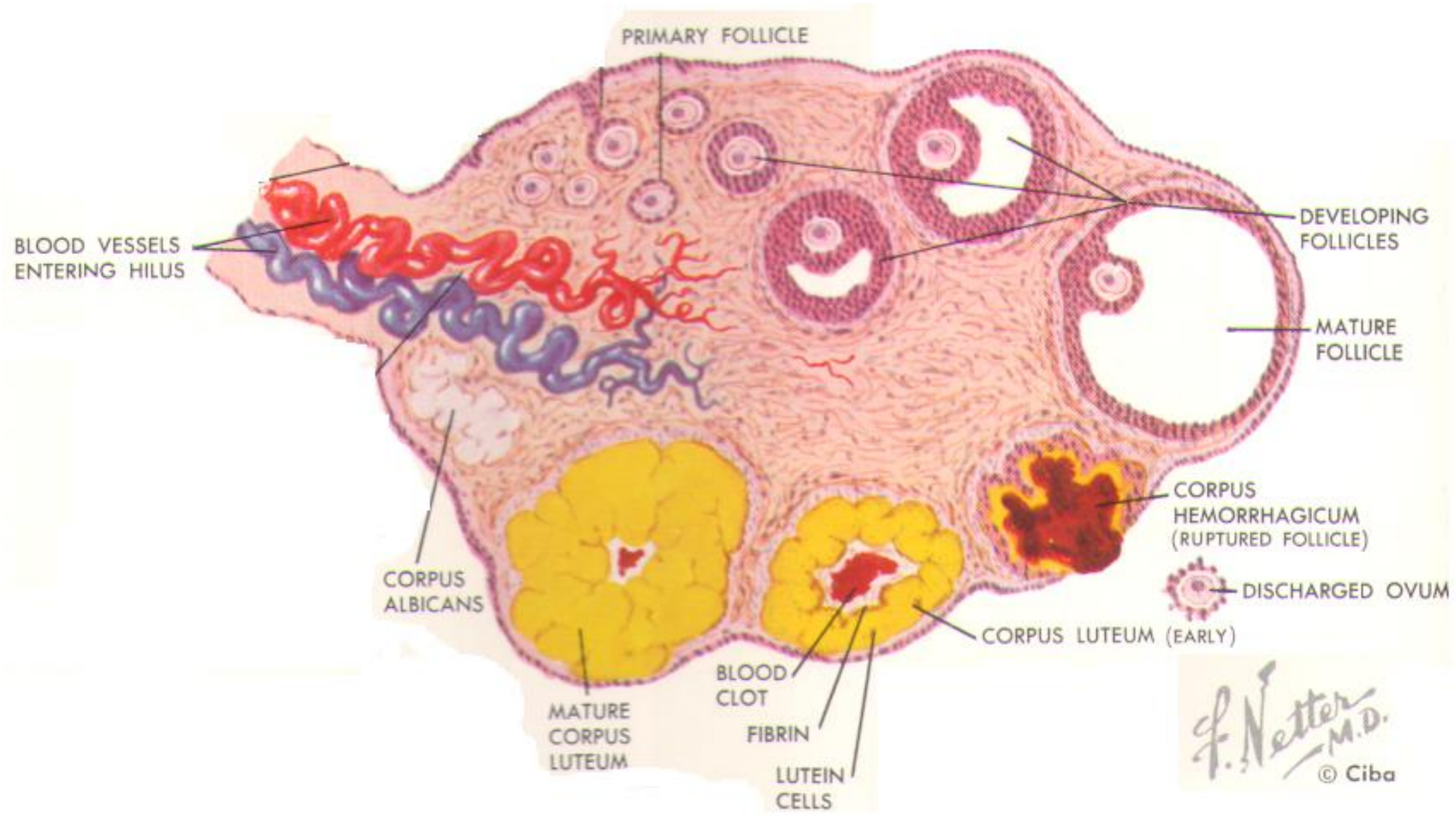
1. Normal; 2. Microsperm; 3. Megalosperm; 4. Roughened head membrane; 5. Elongated forepart of head; 6. Irregular, solid staining head; 7. Aplastic head, absent body; 8. Solid staining head, tail curled around body; 9. Arrested development of tail; 10. Filiform segment between head and body, and swelling of posterior part of body; 11. Cytoplasmic extrusions at posterior end of head; 12. Cone-shaped body; 13. Abaxial implantation of body; 14. Double head; 15. Double body.

Uterine Wall Anatomy



1. Endometrial endothelium
2. Spiral artery
3. Vein
4. Uterine gland
5. Compact layer
6. Spongy layer
7. Basal layer
8. Myometrium
9. Functional layer (layer sloughed off during menstruation)
10. Endometrium

Ovary



PRIMARY FOLLICLE
DEVELOPING FOLLICLES
BLOOD VESSELS ENTERING HILUS
MATURE FOLLICLE
CORPUS HEMORRHAGICUM (RUPTURED FOLLICLE)
DISCHARGED OVUM
CORPUS ALBICANS
CORPUS LUTEUM (EARLY)
BLOOD CLOT
FIBRIN
LUTEIN CELLS
MATURE CORPUS LUTEUM
F. Netter M.D.
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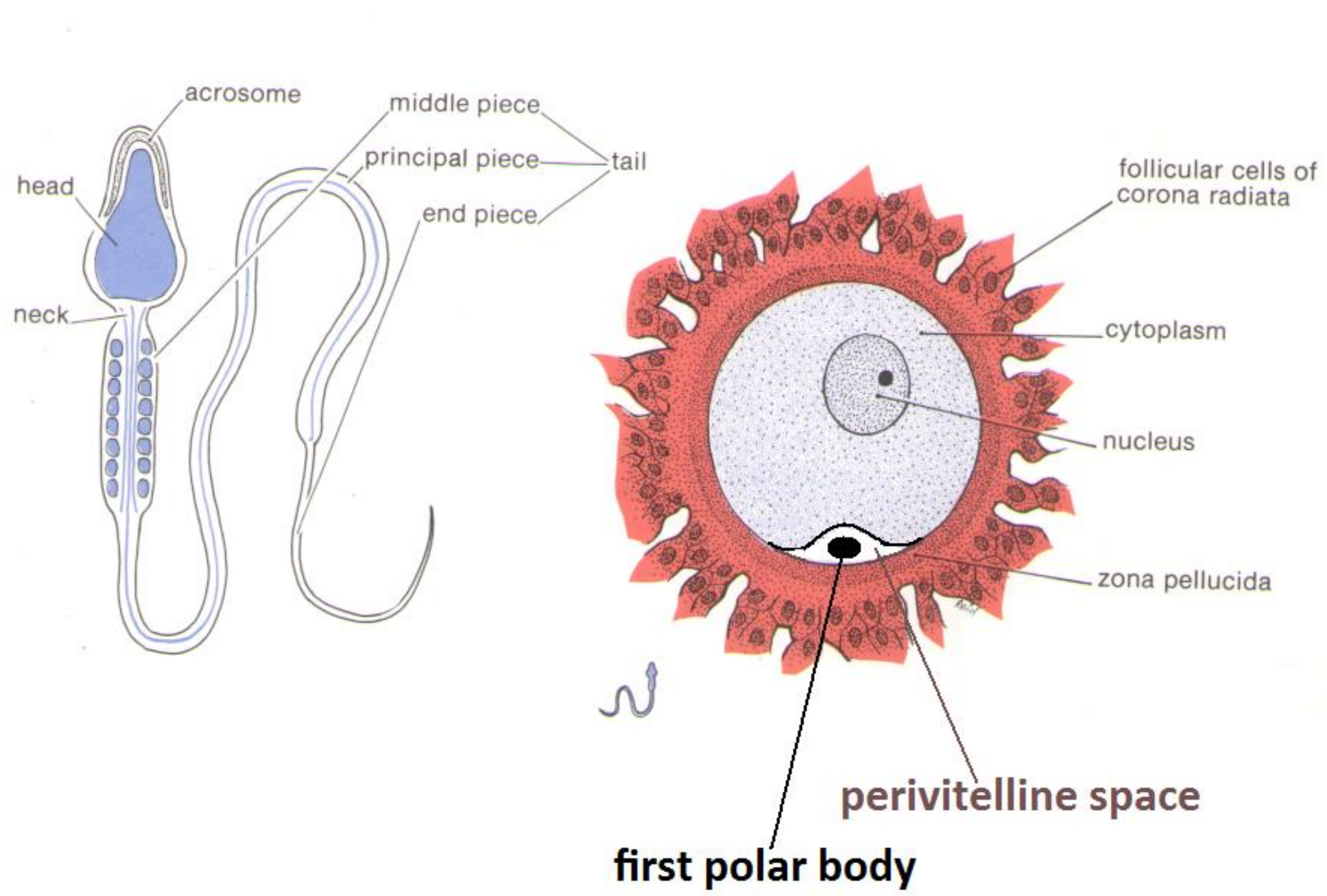
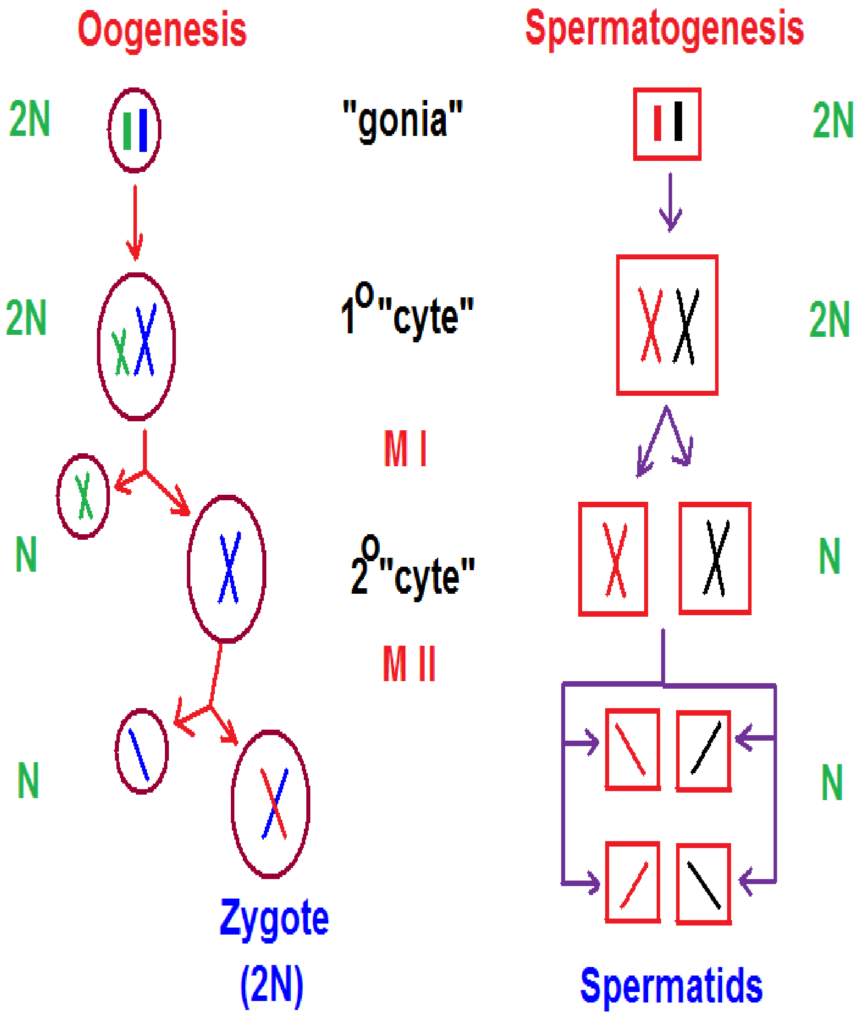
Gametogenesis – More or Less



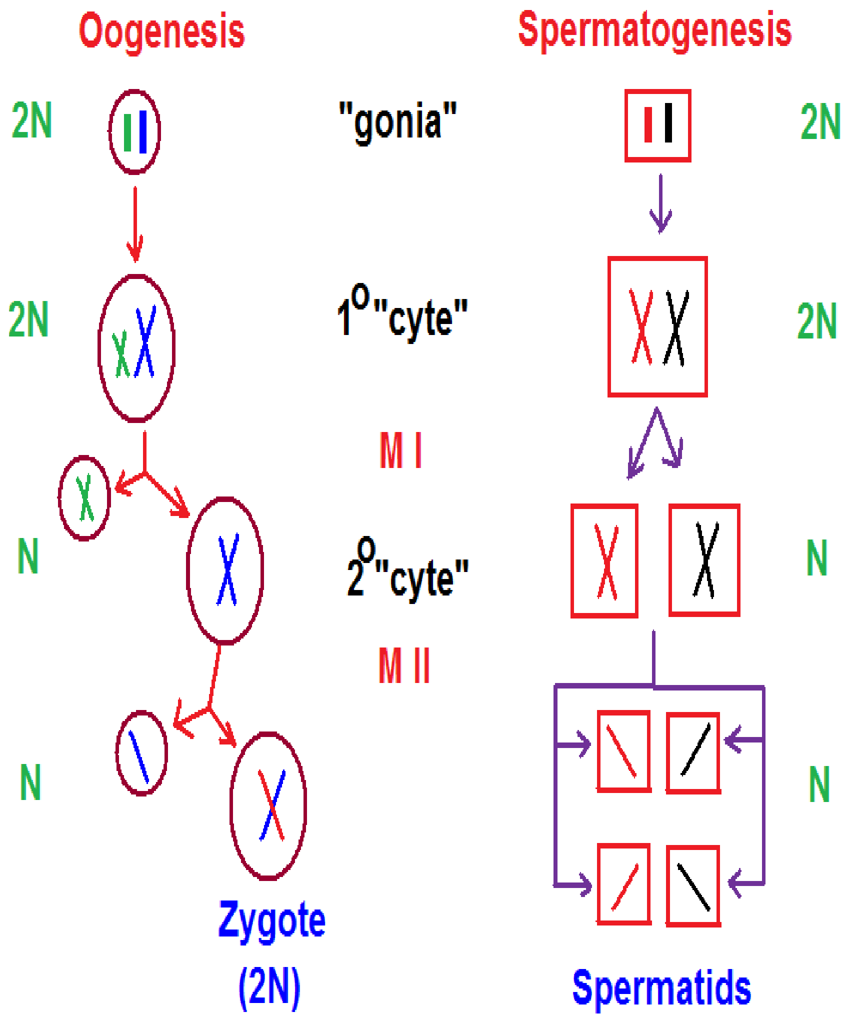
Gametes -- Anatomy

Where Gametes Come from



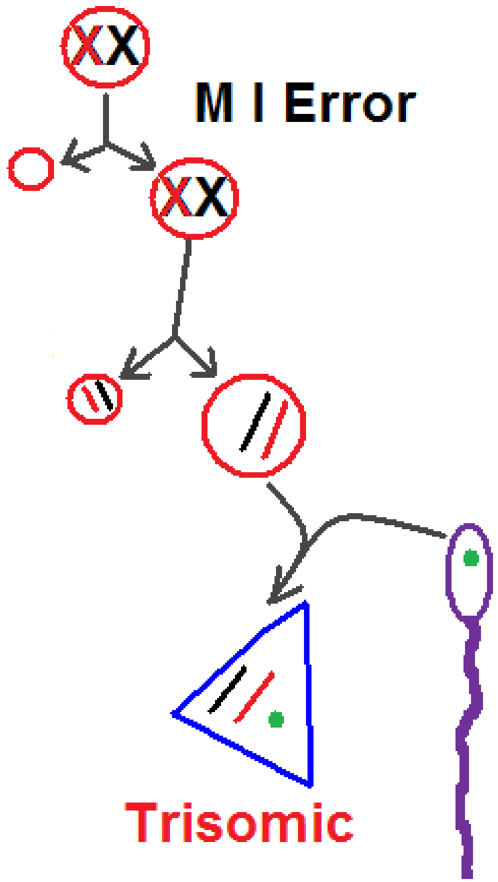
- In **spermatogenesis**, a 2N spermatogonium (stem cell before birth) undergoes mitosis to form a primary spermatocyte and is arrested in prophase I at birth.
- When puberty kicks in, this 2N cell undergoes meiosis I to form two secondary spermatocytes.
- These cells then undergo meiosis II to form four early spermatids which mature to late spermatids, then to spermatozoa.
- From the formation of the secondary spermatocytes on, the cells are N cells, i.e., have 23 chromosomes.

Where Gametes Come from



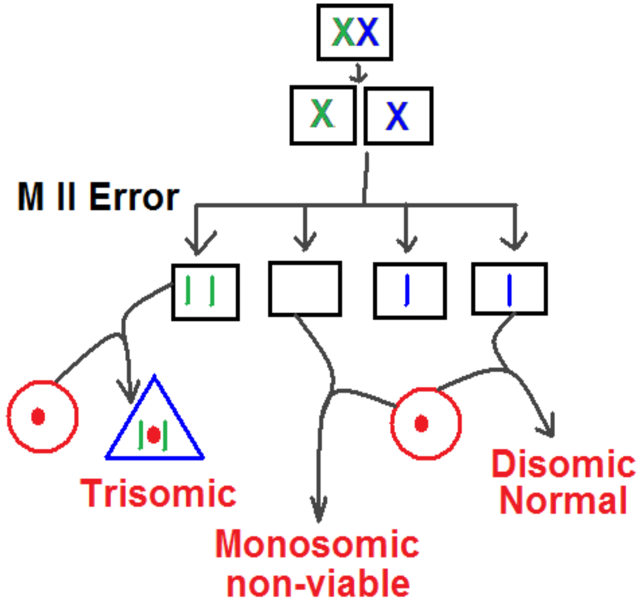
- In **oogenesis**, the 2N cells (oogonium/stem cells before birth) are arrested as primary oocytes in prophase I at birth.
- When puberty kicks in, the primary oocyte (primary follicle) grows and undergoes meiosis I to form a polar body and a secondary oocyte (the mature Graafian follicle).
- Once the Graafian follicle is ovulated, it must be fertilized by a sperm BEFORE it can undergo meiosis II.
- If that happens, then a zygote is formed that will differentiate into an embryo and then into a fetus.

Non-dysjunction – Meiosis I



- What happens, though, when non-dysjunction (non-separation during meiosis I or II) occurs?
- Specifically, non-dysjunction is the failure of a pair of chromosomes to separate at meiosis.
- Errors may occur in either meiosis I or II.
- In the case of meiosis I non-dysjunction, this may result in a trisomic zygote.

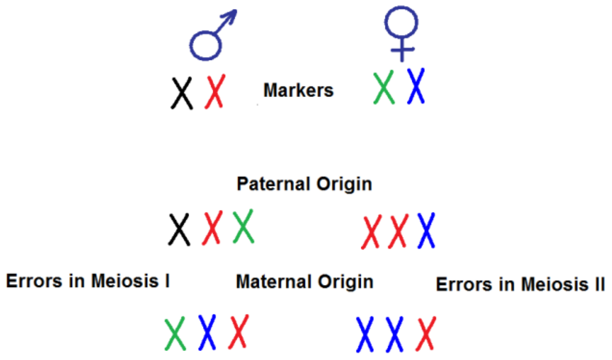
Non-dysjunction – Meiosis II

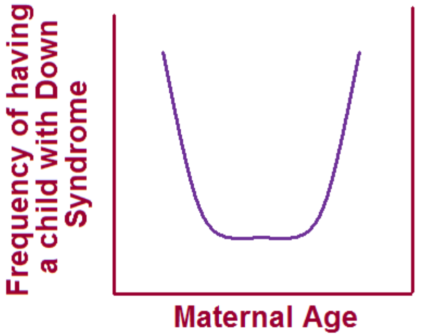


- What happens, though, when non-dysjunction (non-separation during meiosis I or II) occurs? Specifically, non-dysjunction is the failure of a pair of chromosomes to separate at meiosis. Errors may occur in either meiosis I or II.
- If it were to happen in the case of meiosis II in spermatogenesis, the resulting zygote could be monosomic, normal or trisomic.
- The monosomic zygote is not viable.
- In the case of trisomic zygotes that are carried to term, it is possible to determine the origin of the extra chromosome by using stains or fluorescent antibody techniques.
- By walking through the errors, above, in either stage of meiosis, you can see how the following illustration (next 2 slides) takes advantage of these errors by the color coding of the extra chromosome using trisomy 21 as an example.

Trisomy 21 – Down Symdrome

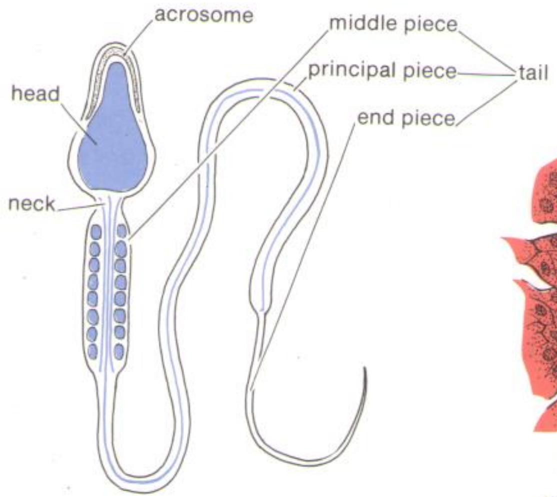
- Did you note in the bottom of the graphic that the frequency of a woman having a child with trisomy 21 follows a "U-shaped" curve: the very young mother and the very old mother have the highest risks of having a child with Down Syndrome.
- Keep in mind that research is showing that at least a third of all cases of children with Down Syndrome are paternal in origin.
- I expect that will level out at 50% in the next 30-50 years.

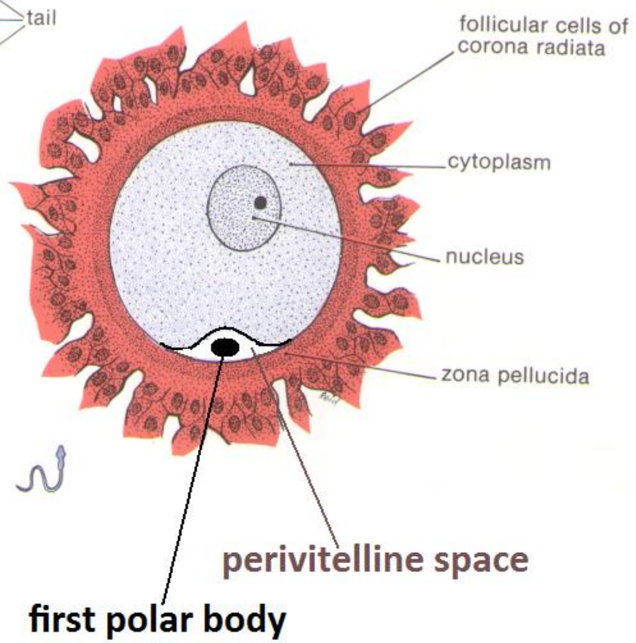




Zygogenesis – More or Less

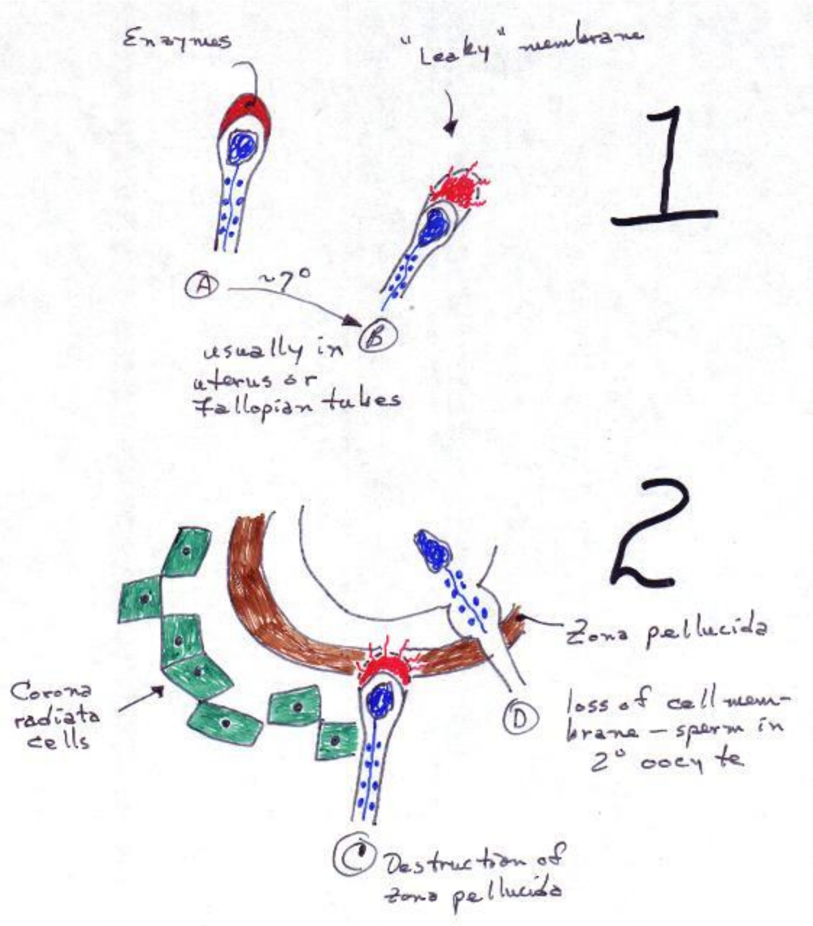
Note: Study the Cellular Physiology and Mendelian Genetics Experiment from BIOL 190 Ahead of Time (http://www.drcarman.info/bio223lb/223lab05.pdf)





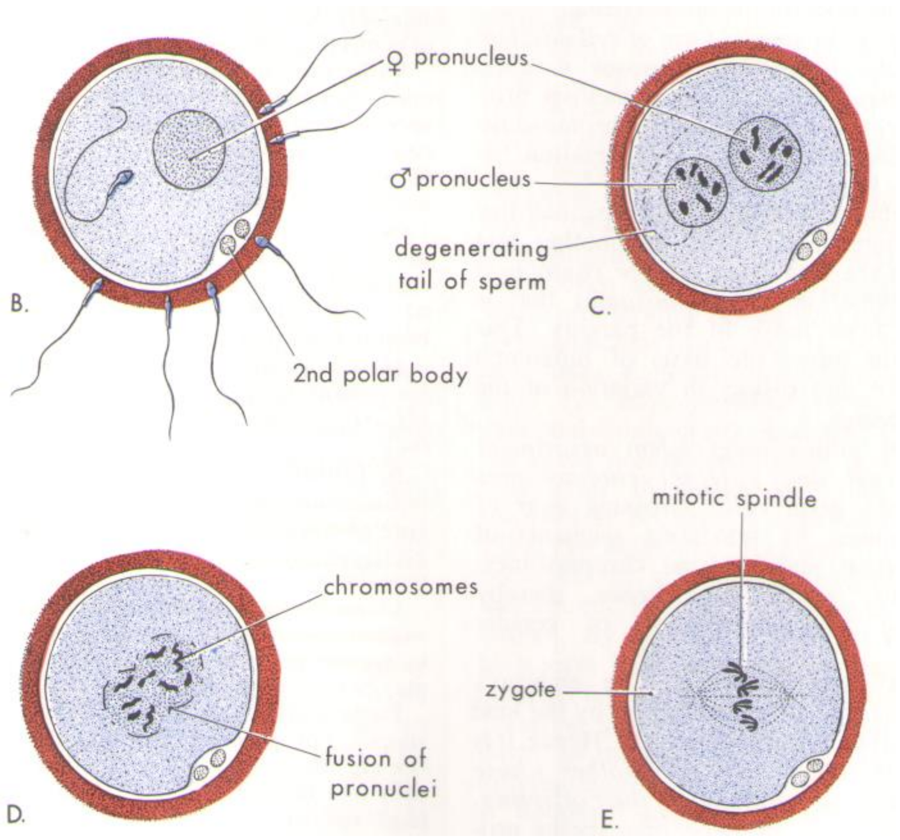
Gametes -- Anatomy

Capacitation and Fertilization



- In order for a sperm to fertilize a Graafian follicle, the sperm must undergo the process of capacitation:
- Capacitation is a process that causes the acrosome of the sperm to become "leaky" (#1, above) so it can release enzymes that will destroy the zona pellucida around the Graafian follicle and permit fertilization (#2, above) to occur.
- Capacitation takes about 7 hours or so and generally occurs in the fallopian tubule or uterus.
- 04/18/2003 -- I was just reading a recent text on Human Reproductive Biology that has changed some of the dogma regarding fertilization – the biggest change is that after capacitation, the sperm does not "attach" head-first.
- It "attaches" to the secondary oocyte SIDEWAYS.

Once the sperm has invaded the Graafian follicle, meiosis II occurs and the two haploid cells unite (fuse) to initiate zygogenesis



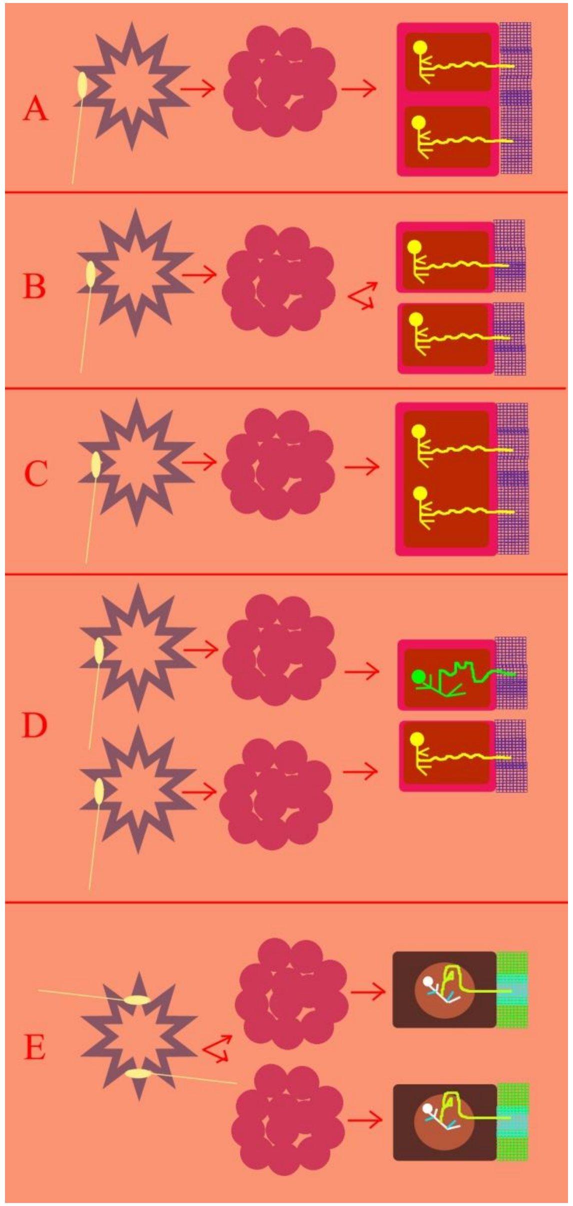
- NOTE: In a period of ONLY 24 hours, the sperm and ovum create two pro-nuclei (C) that will fuse into one nucleus (D) with 2N chromosomes and undergo mitosis to initiate further cell reproduction for zygogenesis (E).

Twins – Identical and Fraternal

- Identical Twins = monozygotic twins; one ovum, one sperm
- Fraternal Twins = dizygotic twins; 2 ova, 2 sperm

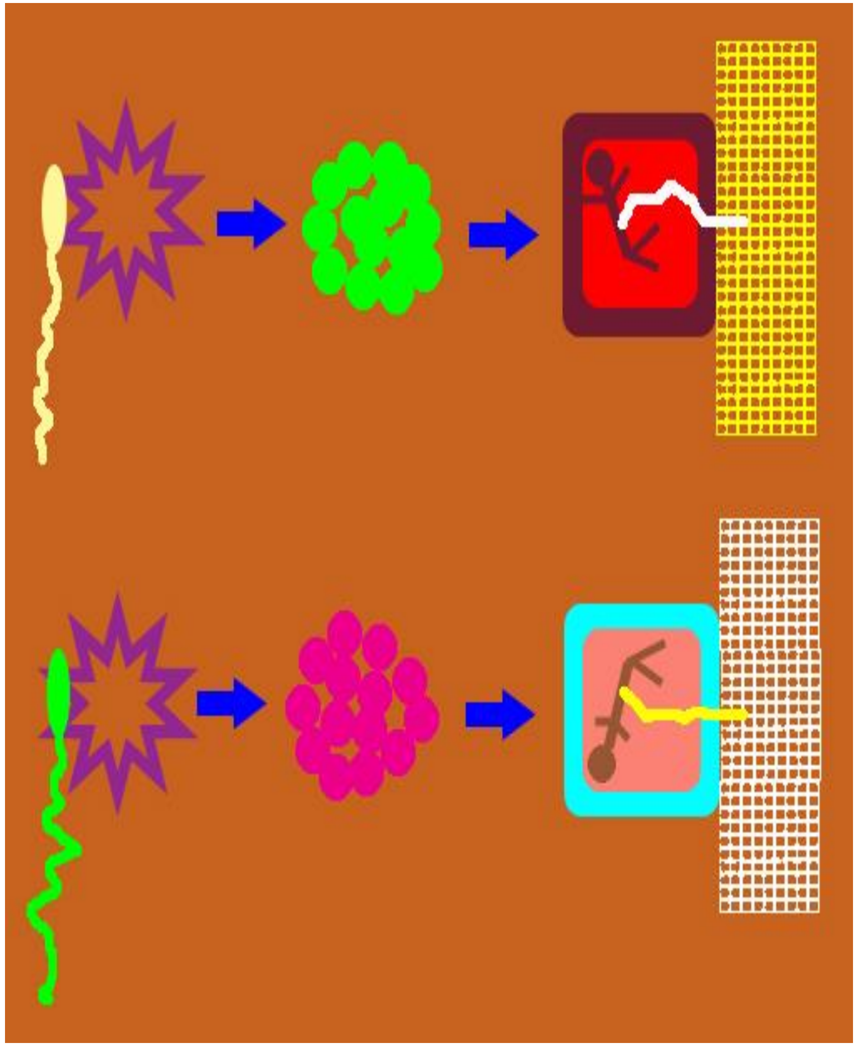
A New Kind of Twin – Spring 2007

- ✓ A. Identical Twins -- 70-75% of the time – monochorionic , diamniotic, same gender, mono-placental
- ✓ B. Identical Twins – ca 25-30% of the time– dichorionic, diamniotic, same gender, di-placental
- ✓ C. Identical Twins – ca 1% of the time – Monochorionic, monoamniotic, monoplacental, same gender, mono-placental
- ✓ D. Fraternal Twins – dichorionic, diamniotic, diplacental, not necessarily same gender
- ✓ E. **Semi-identical Twins** – **dichorionic, diamniotic, not necessarily same gender; maternal genes identical; share only half of their genes from dad; di-placental**

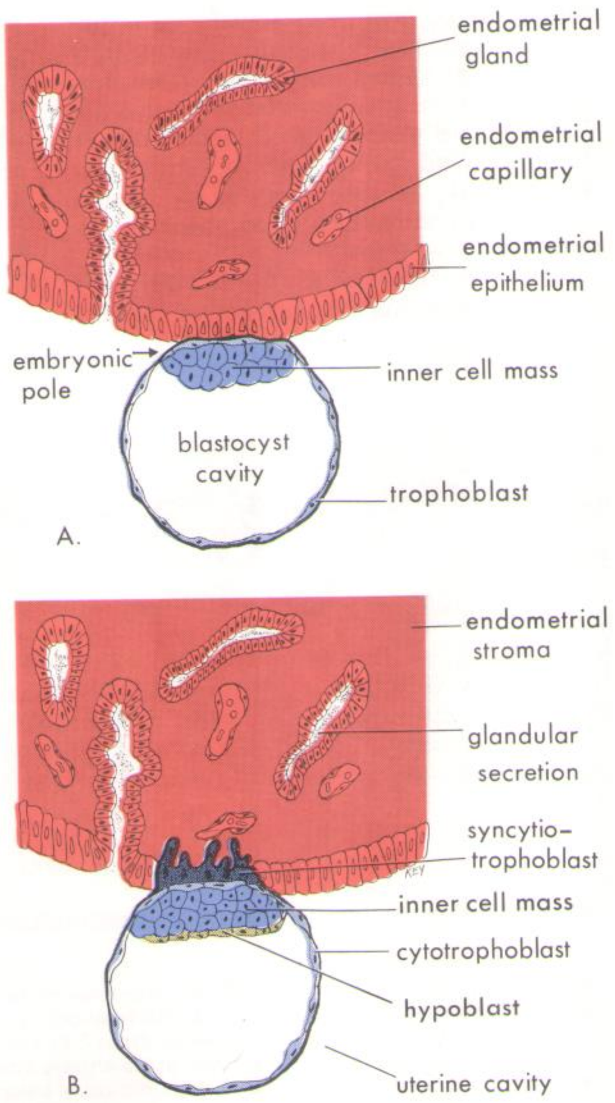


Super-fecundation

- While we're on the topic of twins, we need to discuss a phenomenon that happens all the time in dogs, in humans on fertility drugs and/or rarely in humans naturally.
- This phenomenon is called super-fecundation.
- This is successive fertilization by 2 or more separate instances of intercourse of 2 or more ova formed during the same menstrual cycle.
- Fertilization may be by the same male or by two different males.
- These babies are dizygotic, dichorionic, diamniotic, not necessarily identically sexed and their genetics are not identical.

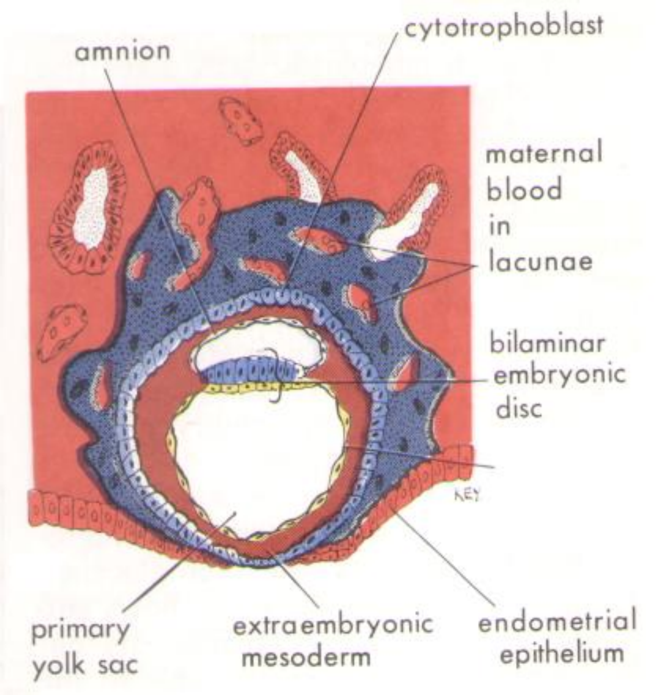


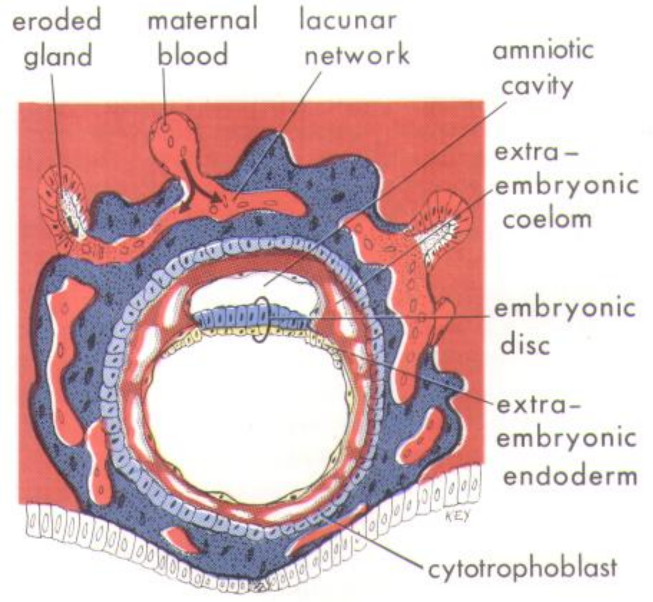
Implantation



- The graphic, at upper left, illustrates what happens between the 6th and 7th days following conception.
- Note that the syncytiotrophoblast (the precursor to the placenta) has already begun invading the endometrial tissue within 7 days of fertilization (lower left).

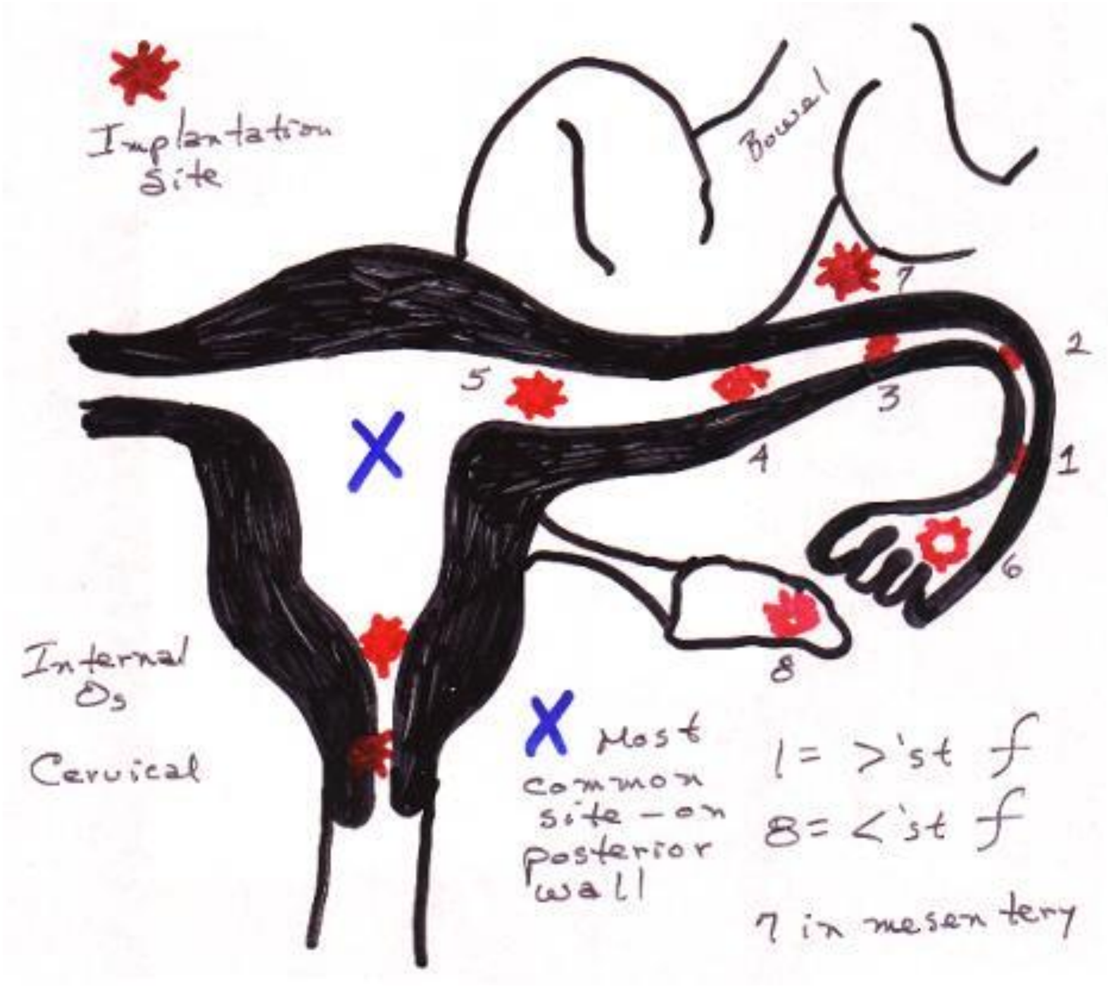
More Implantation





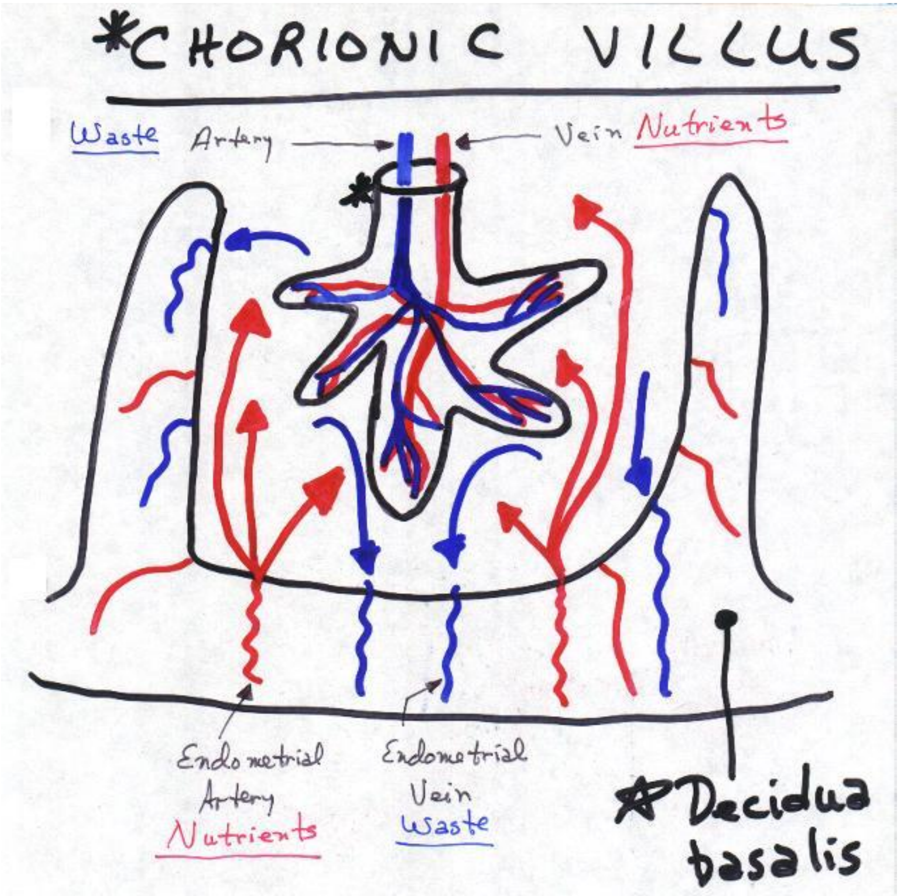
- The graphic, top left, illustrates the almost complete implantation of the blastocyst by 9 days of gestation.
- The graphic also illustrates the bilaminar disc (**hypoblast (upper)** and epiblast (lower) in top left and top right graphic).
- Top right graphic at 12 days gestation illustrating almost completed implantation and the bilaminar disc.

Uterine Implantation



- Should a pregnancy occur, implantation into the uterine wall occurs as illustrated, left.
- Site #1 is the most frequently implanted site all the way down to #8, which is the least frequently implanted site.
- The blue "X" marks the site most commonly implanted on the posterior wall.

Placenta

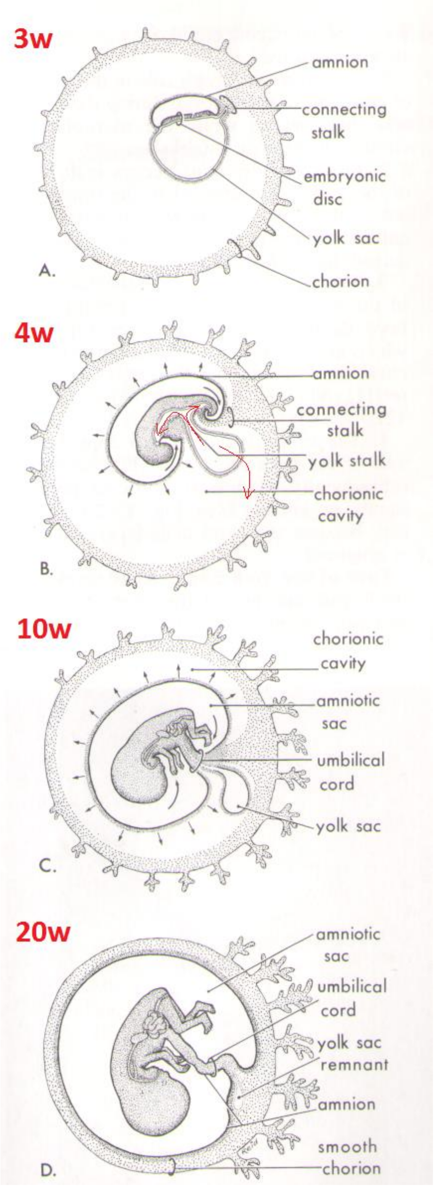


- The graphic at left illustrates a single chorionic villus (*).
- This is the fetal side of the placenta.
- It is continuously bathed in maternal blood.
- Indeed, this is the most important welfare factor on the development and health of the fetus.
- Note that the arterioles in the villus carry waste away from and the veins carry nutrients to the developing embryo/fetus.
- The decidua basalis (★) is the maternal portion of the placenta.
- Endometrial (spiral) arteries carry nutrients and the endometrial veins remove wastes from the regions around these chorionic villi.

Placental Physiology

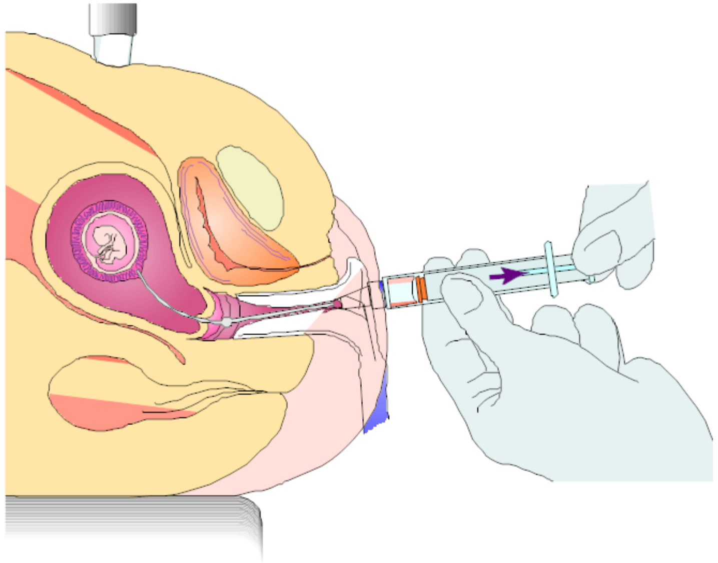
- The physiology of the placenta is complex.
- Nutrients (carbohydrates, proteins, amino acids, lipids, ad nauseum) are transported across the placenta from mother to embryo/fetus.
- IgG, varicella zoster virus (causes chicken pox), Toxoplasma gondii (causes toxoplasmosis), carbon monoxide and radioactive strontium cross the placenta from mother to embryo/fetus.
- On the other hand, bacteria, heparin, transferrin and IgM will NOT cross the placenta from mother to embryo/fetus.
- Wastes are transported from embryo/fetus to mother across the placenta.

How Amnion Covers (Wraps Around) Cord;
How Yolk Sac Partially Incorporates as Primitive Gut



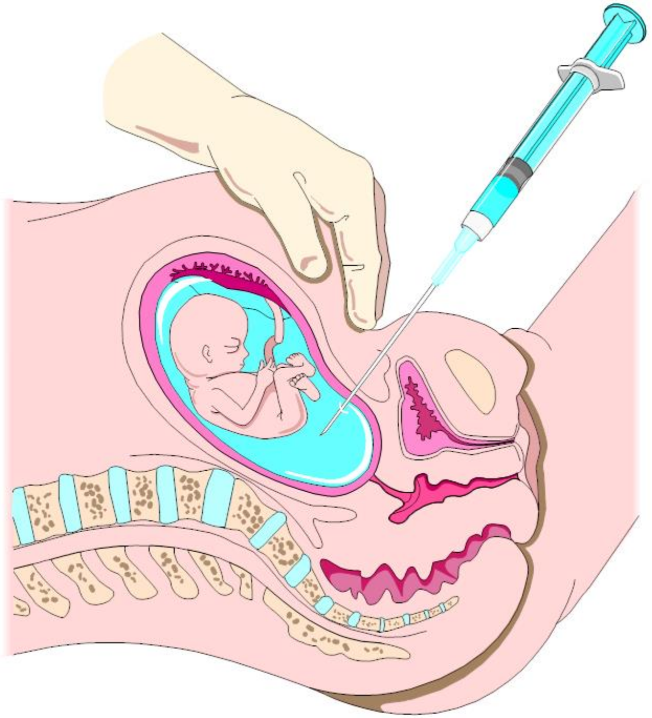
- Note at 10 weeks that the chorionic villi are migrating to one side to centralize the placenta by 20 weeks.

Chorionic Villus Sampling



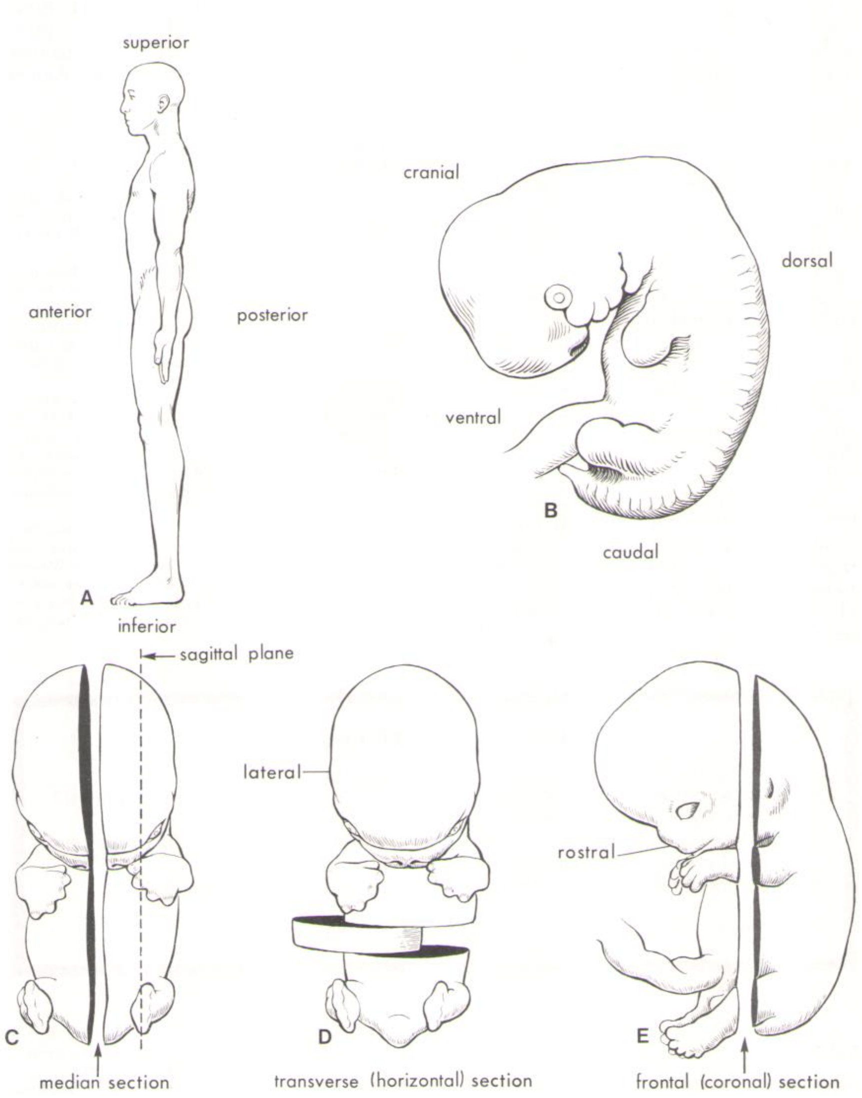
- The significance of these chorionic villi, besides fetal well-being, is that extra-placental villi samples may be obtained between 8-12 weeks of gestation.
- This is called chorionic villus sampling.
- The graphic at left shows the approximate procedure.
- An endoscope is inserted through the vagina into the cervix so that the aspiration needle may obtain a sample of these villi from the chorion.
- Although this is riskier to the fetus than amniocentesis, cells may be immediately karyotyped and anomalies detected sooner so that the parents may make decisions regarding the pregnancy.

Amniocentesis

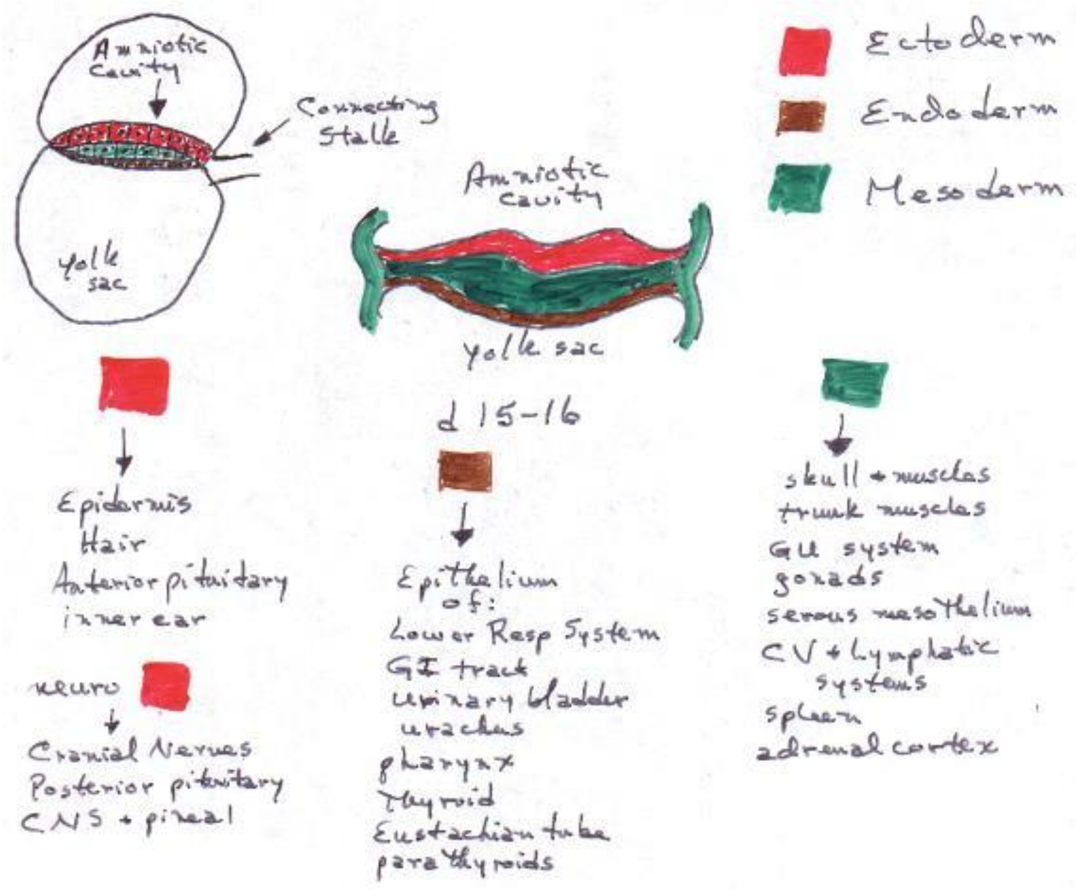


- The graphic at left illustrates amniocentesis: the removal of amniotic fluid for diagnostic purposes.
- In general, this is coupled with sonography for placental localization so that it is not inadvertently damaged.
- The needle and syringe are held at 90° to the abdominal wall and inserted into the amniotic sac.
- A sample is withdrawn for diagnostic studies.
- There is general agreement in the literature that 16 weeks of gestation is adequate for this procedure, although there are some references that indicate that amniocentesis may be performed at 14 weeks of gestation.
- The drawback to amniocentesis is that it takes several weeks to get back the results of karyotypes.

Embryological Anatomical Orientation

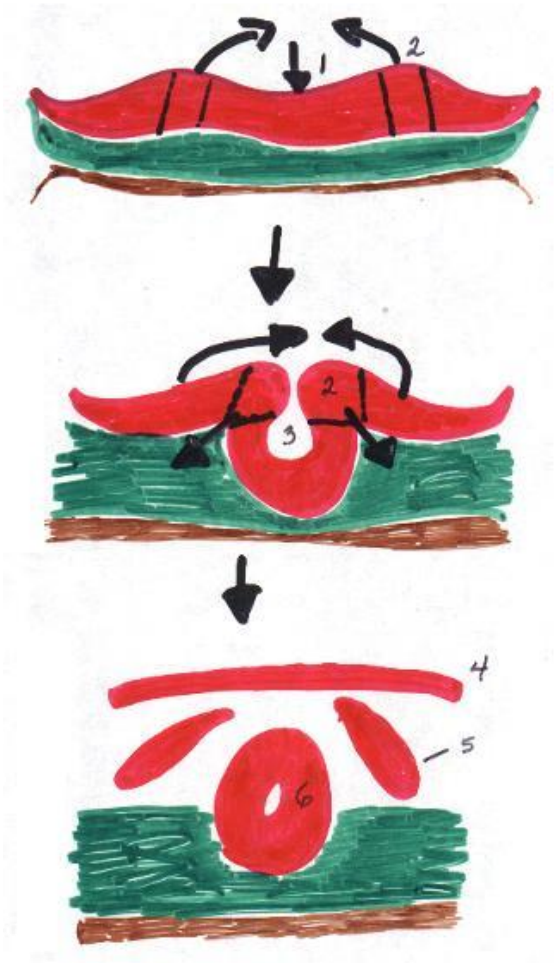


Pre-Embryonic Period



- During the pre-embryonic period, the bilaminar disc differentiates into the trilaminar disc.
- As you can see, left, each layer of the trilaminar disc differentiates into specific tissues of the human body.
- This section is taken at 15-16 days of gestation.

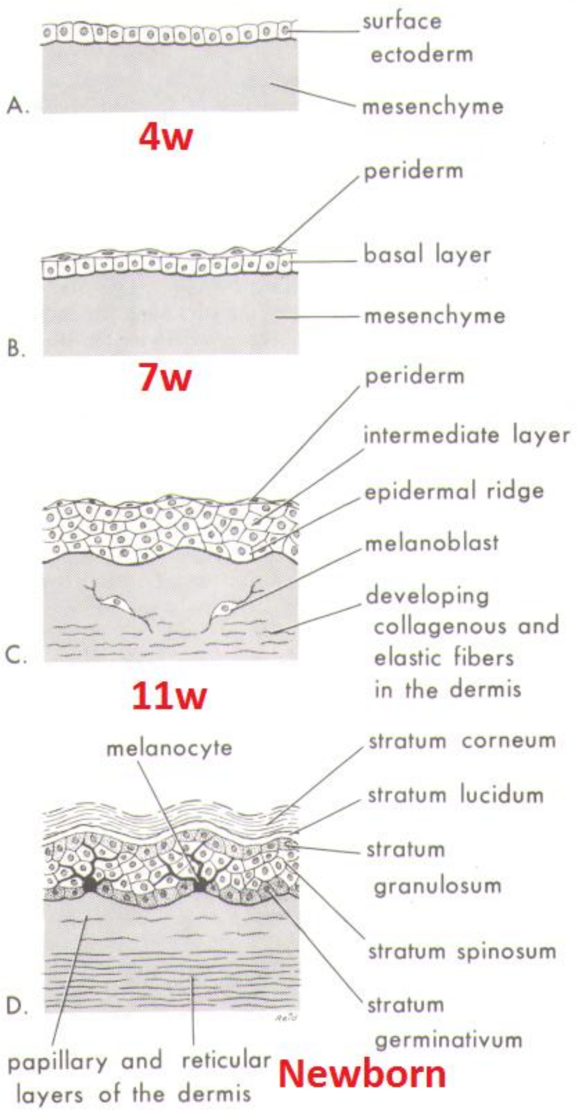
Neurulation is another transition that occurs between roughly days 14 and 28 of gestation

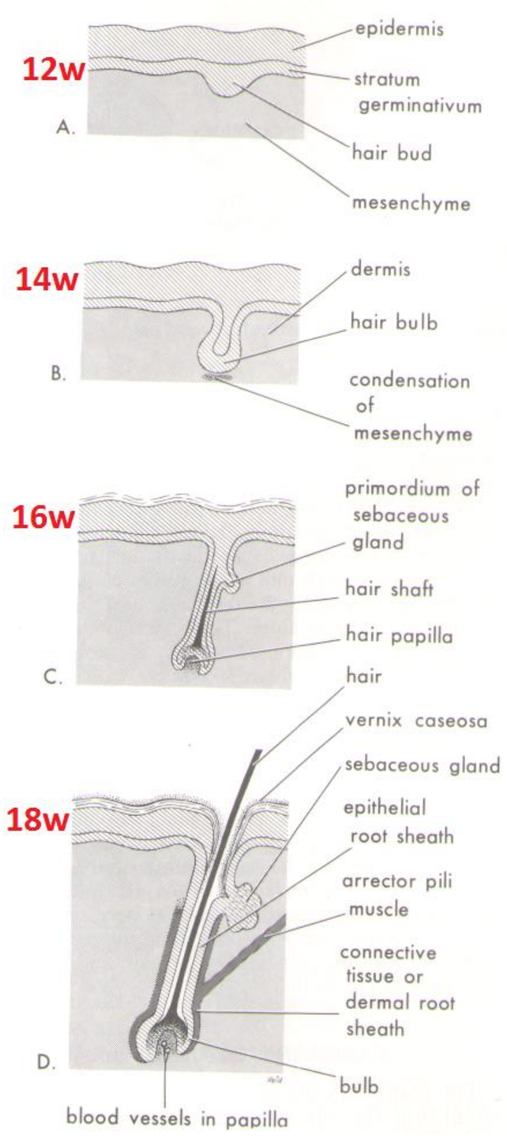


1. Neural plate
2. Neural crest
3. Neural groove
4. Epidermis
5. Developing spinal ganglia
6. Neural tube

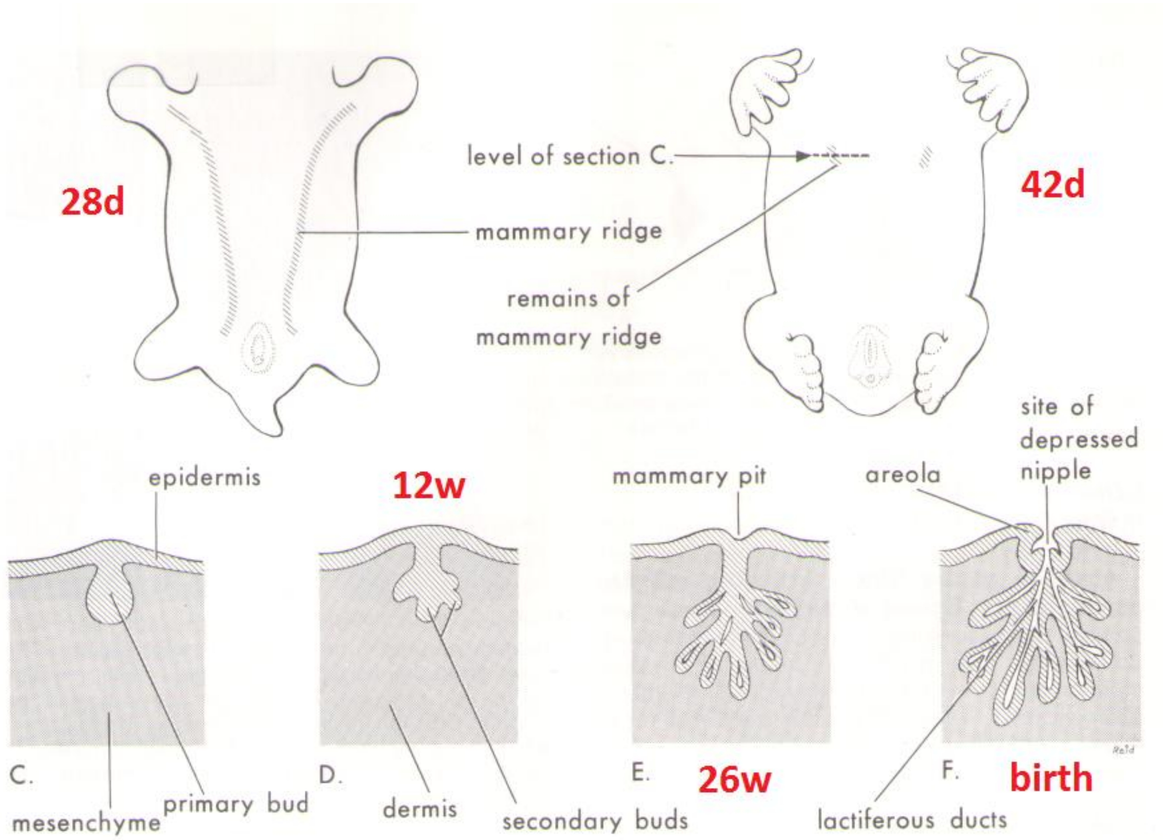
- The middle graphic is at about 18 days of gestation;
- the bottom graphic is at about 28 days of gestation.
- The neural tube goes on to be the central nervous system and houses the brain and spinal cord.
- Note that the neural crests over-grow the neural plate, then push backwards to become the spinal ganglia.

Skin/Hair Development – Q&D Version



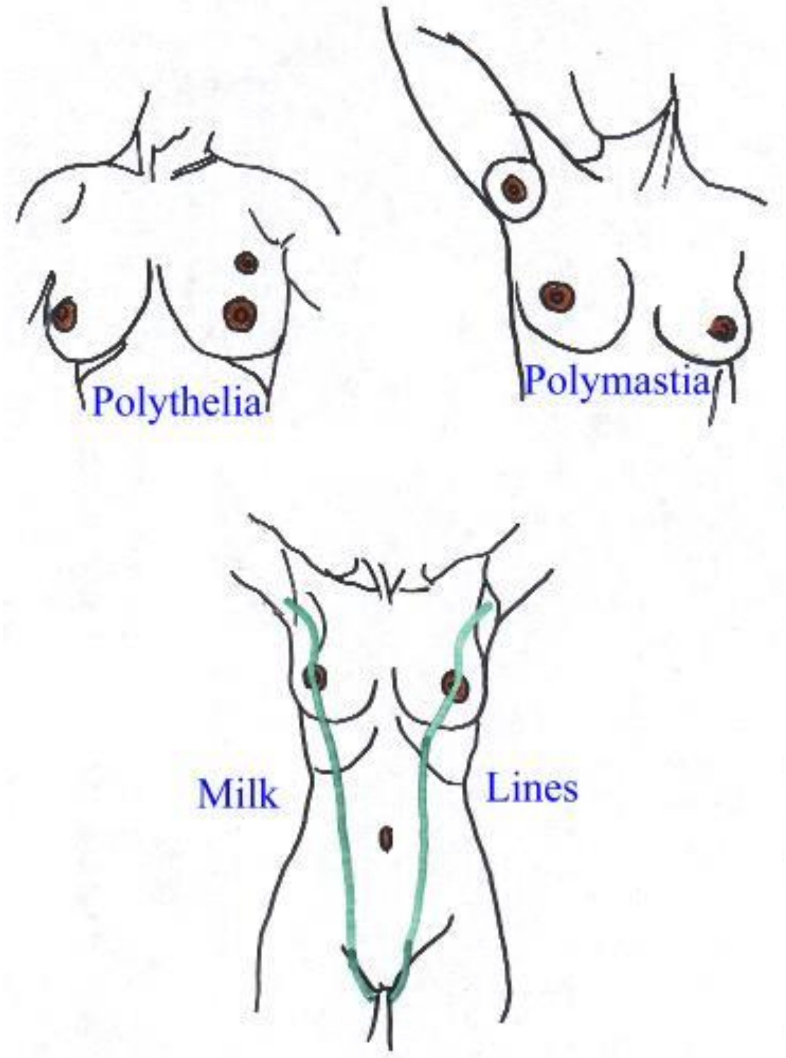


Breasts



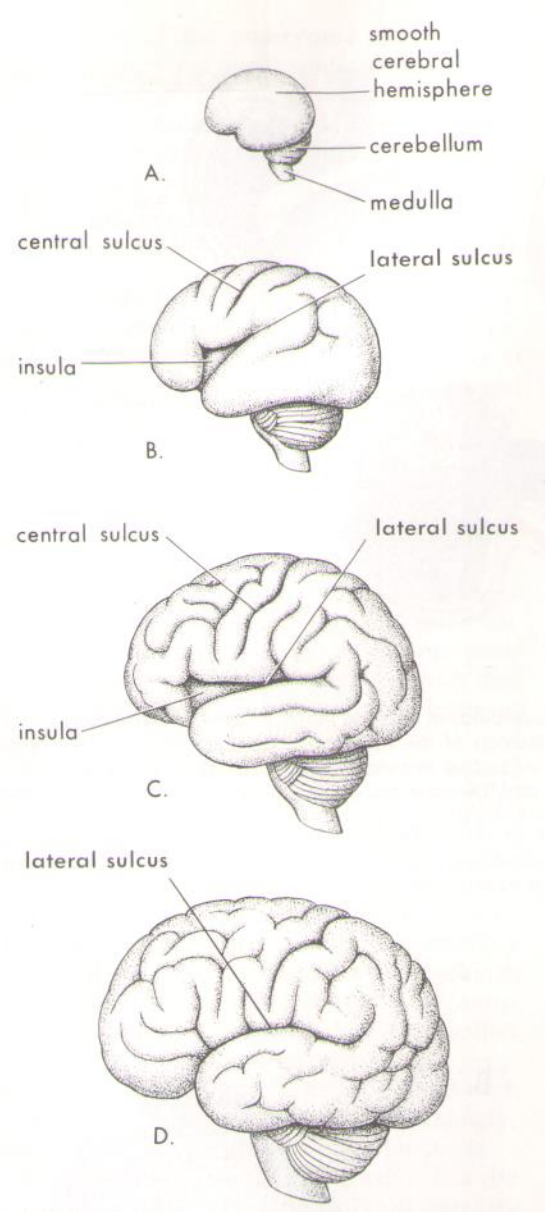
- The milk lines are also called mammary ridges.
- Note that at 28 days of gestation that milk lines are established and that milk line remnants are formed by 42 days of gestation.
- These remnants will form the breast tissue in both sexes.
- In the lower portion of the above graphic, note that breast buds are present by 42 days, secondary buds by 84 days of gestation and, at birth, the nipple is depressed into the aereola and has lactiferous ducts.
- In girl babies, it is not uncommon to observe secretions from their "breasts" after birth.
- This is a normal response to maternal gestational hormones and normal fetal gestational hormones.

Milk Line Abnormalities



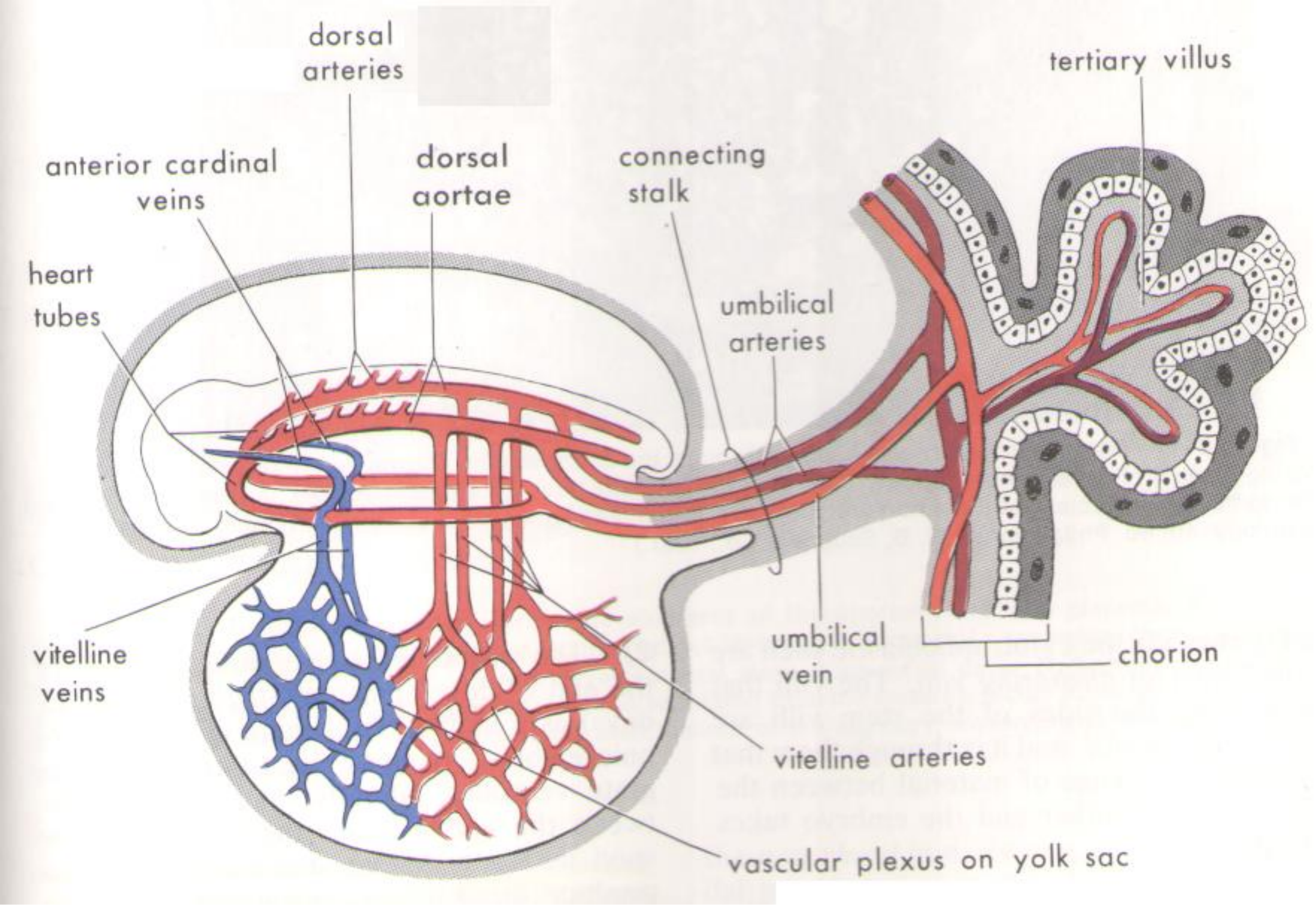
- On occasion, though, extra nipples (polythelia) or extra breasts (polymastia) occur along the milk lines.
- While cosmetically they may present as an embarrassment, I'm unaware of any biological problem that may be related to their presence – they can be removed for aesthetic purposes if so desired.

Brain Development

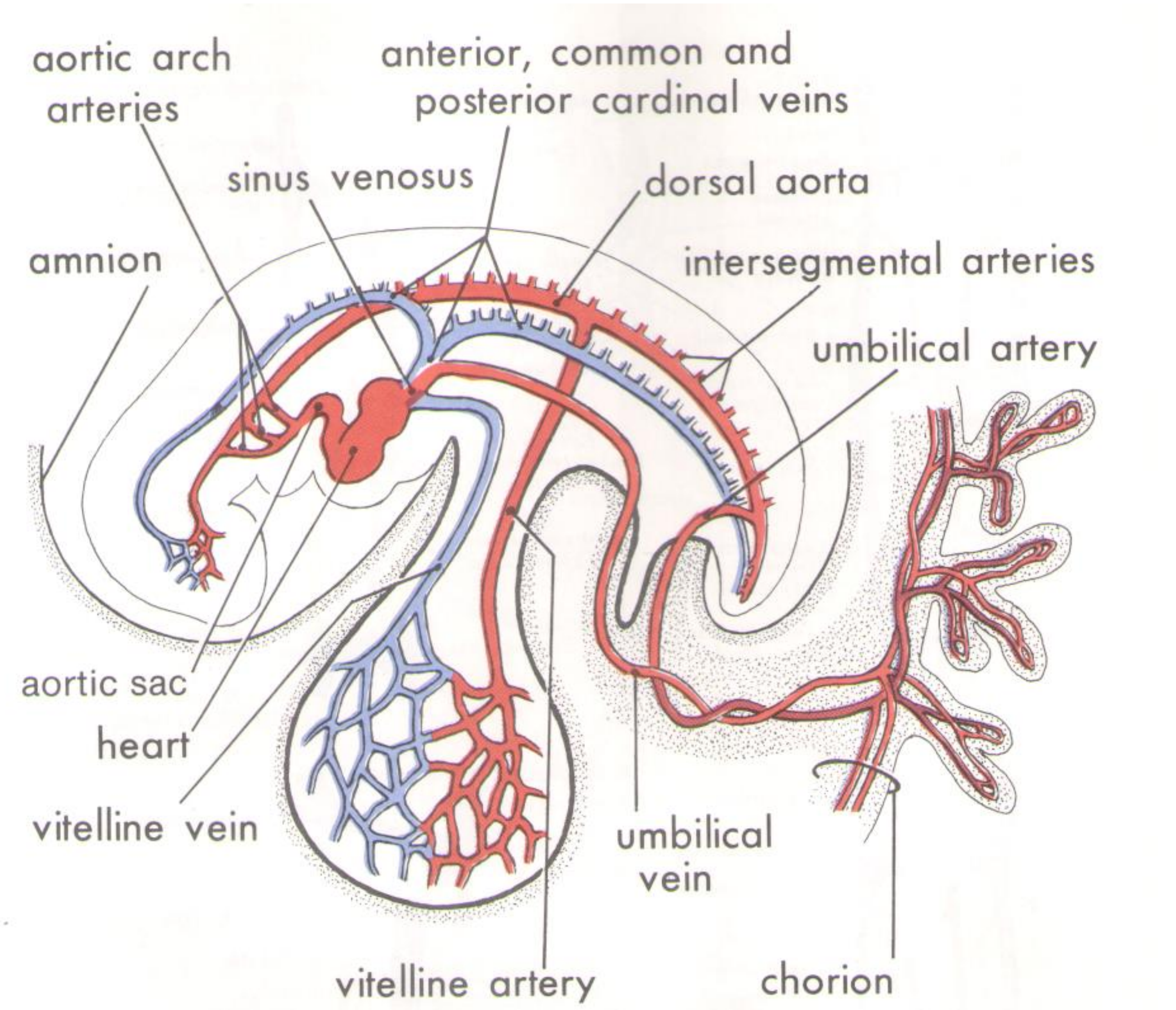


- The graphic at right depicts the brain during various stages of development.
- Note that at 13 weeks (A), the brain has a smooth cerebrum.
- At 26 weeks (B), it has the central sulcus, the lateral sulcus and the insula.
- At 35 weeks (C), the brain is considerably more "wrinkled" and, at birth, the insula is overgrown by the temporal lobe of the cerebrum.
- Newborn (D) has even more “wrinkles”.

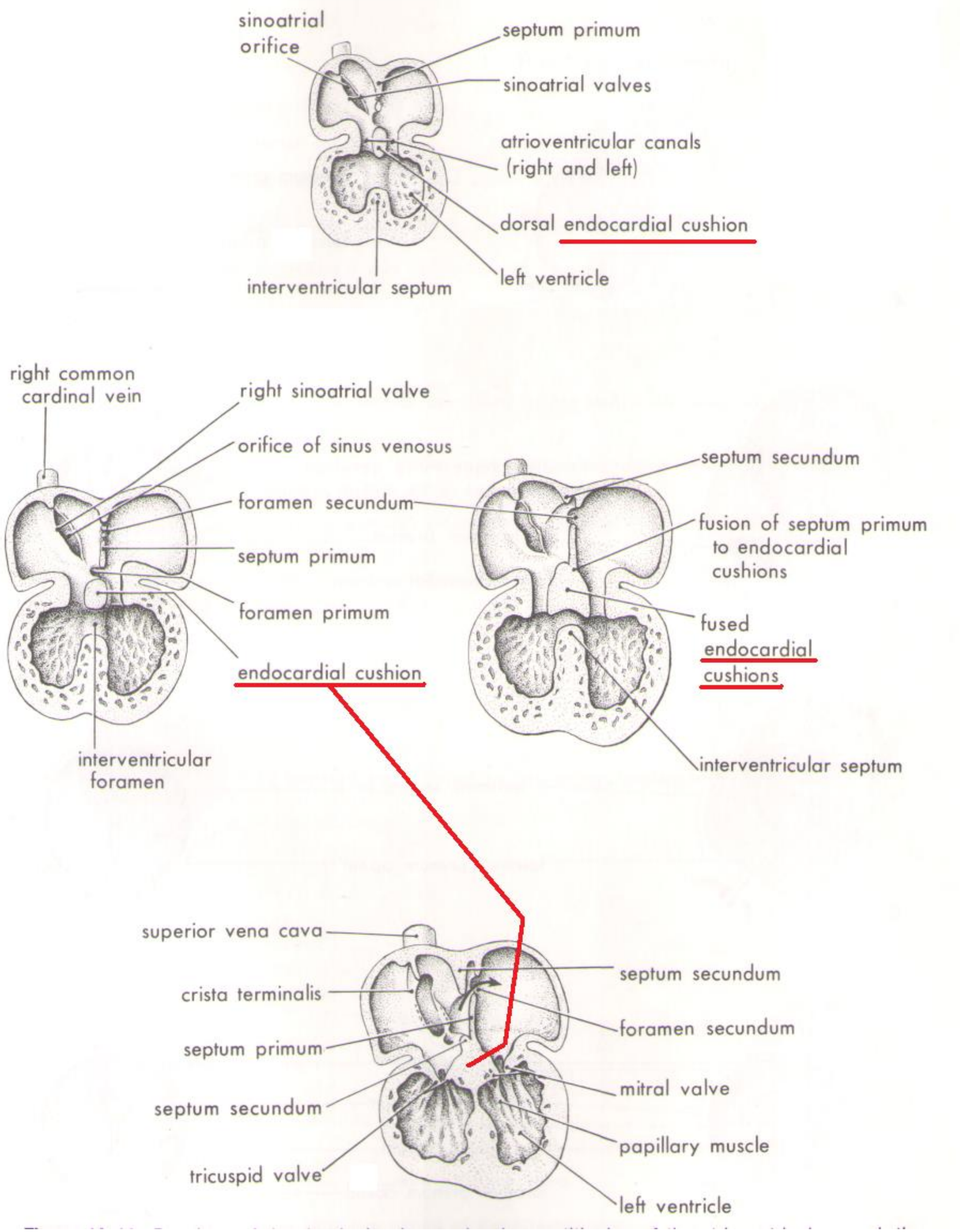
The graphic, below, illustrates the primitive cardiovascular system at 20 days of gestation:



Left Side Vessels only, ca 26 Days Gestation



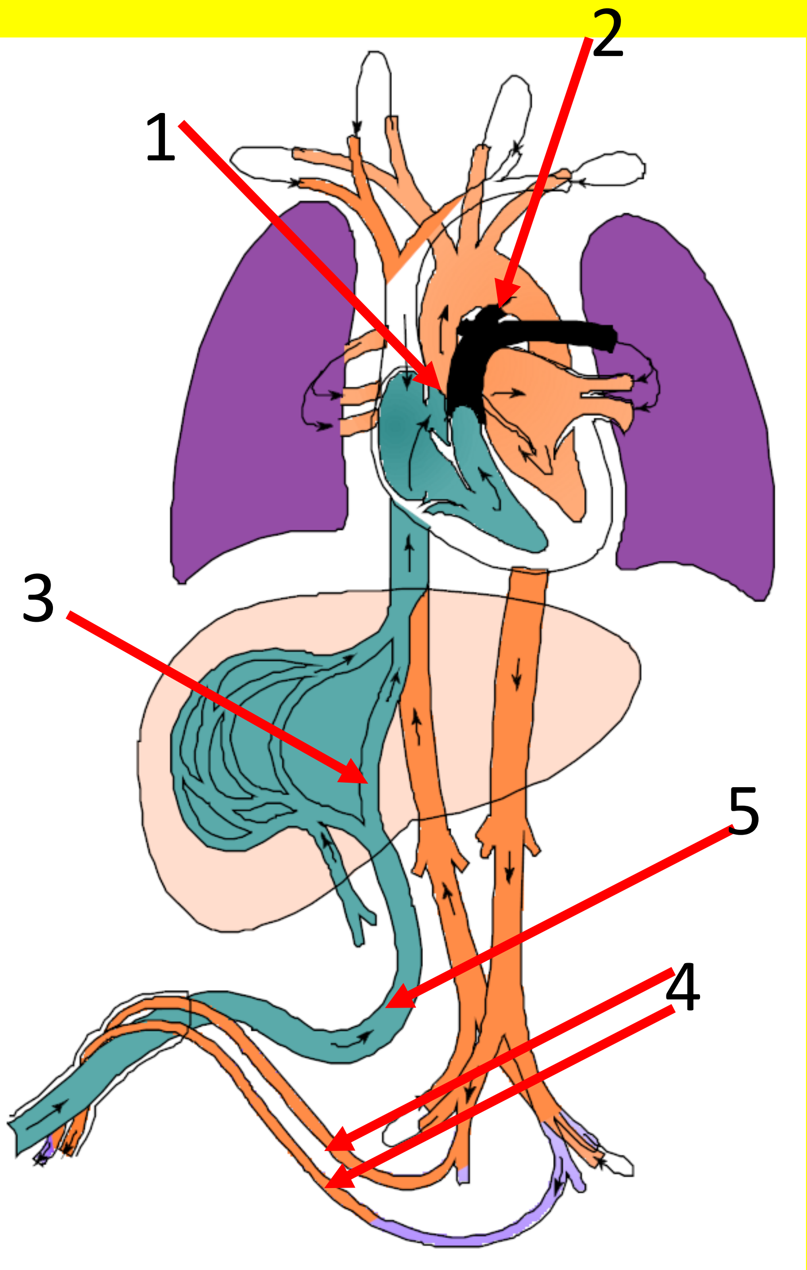
The Heart at 28, 32, 35 and 56 Days of Gestation:



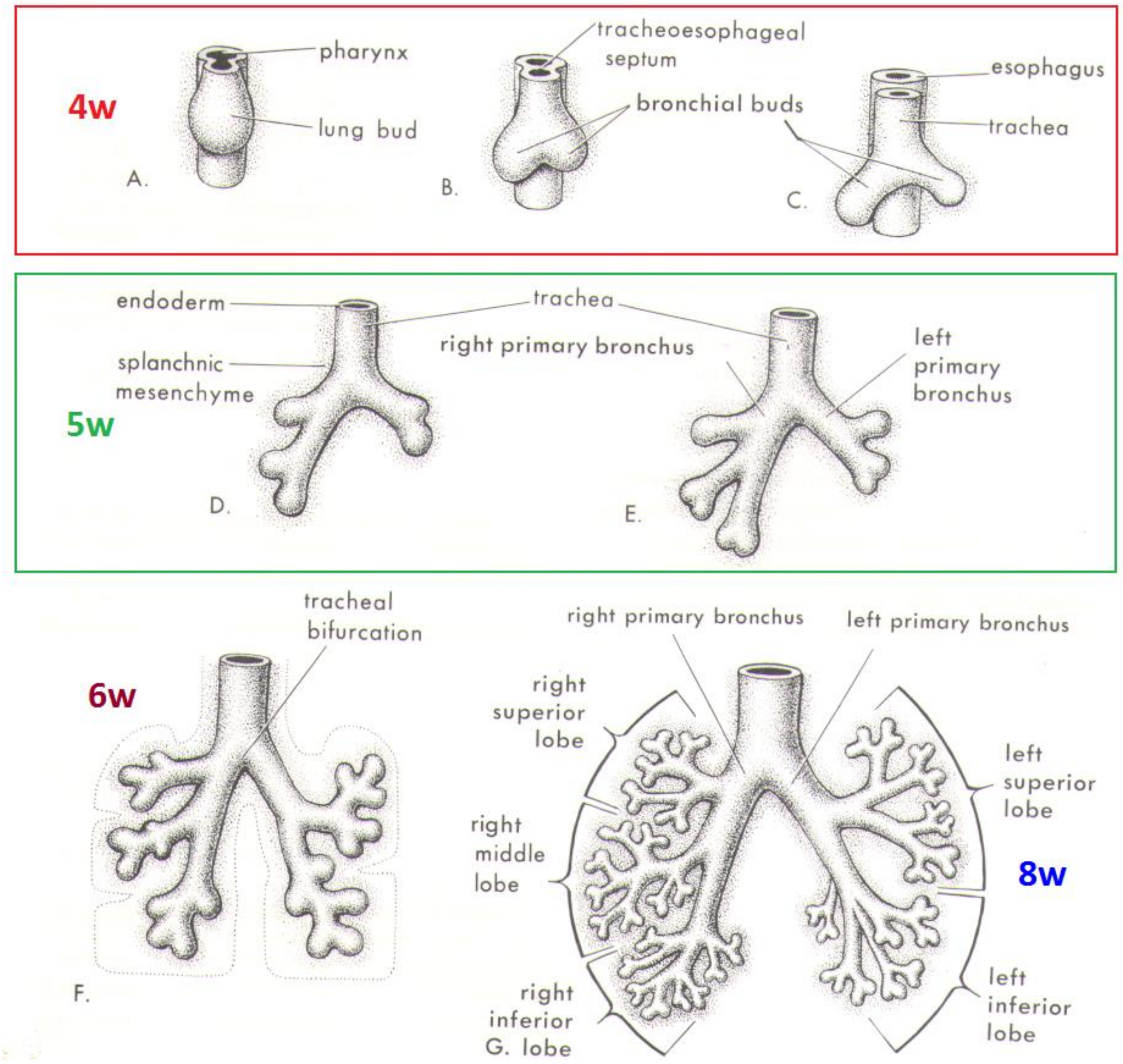
- On occasion, children with Trisomy 21 will be born with endocardial cushion defects -- a "hole" in their heart between chambers.
- This can be surgically repaired.
- The point, though, is that the heart is formed by 56 days of gestation (8 weeks) -- WOW!

Fetal Circulation: Over-view

- Foramen ovale (1)
  - Between atria – bypasses lungs
- Ductus arteriosus (2)
  - From pulmonary trunk to aorta; bypasses lungs
- Ductus venosus (3)
  - Umbilical vein shunts blood to IVC, bypassing liver
- Umbilical Arteries (4)
  - Two each
  - Transports **deoxygenated blood/wastes** back to placenta for disposal
- Umbilical vein (5)
  - One each
  - Transports **oxygenated blood/nutrients** to baby

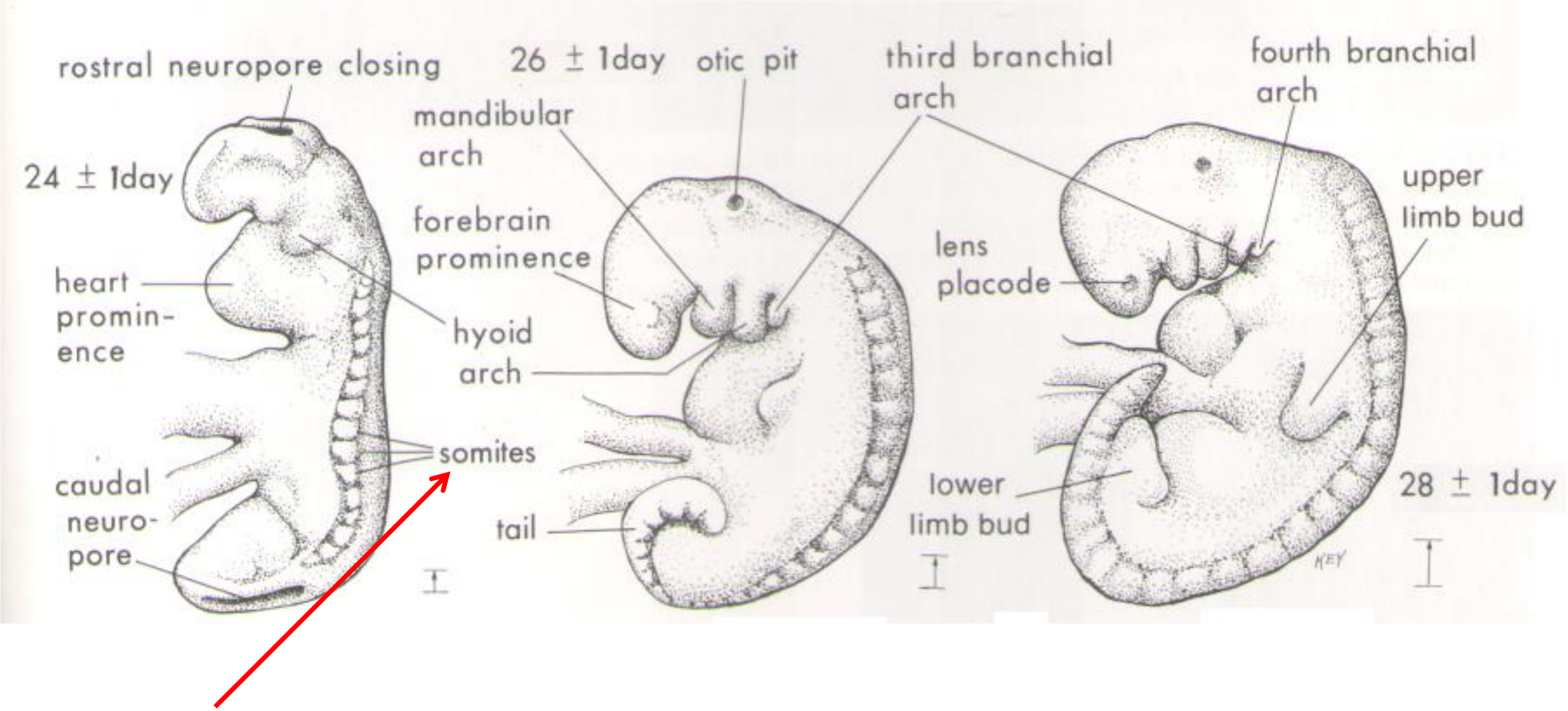


Superficial Respiratory System: Lungs, *et al*



12.5-16.7% of the adult alveoli are present in newborn infants.

The period between 4 and 8 weeks of gestation is a period of rapid differentiation. The graphic, below, illustrates a 28 day old embryo:



- Somites differentiate into myotomes, dermatomes and sclerotomes (which form skeletal muscle, connective tissues and vertebra, respectively).

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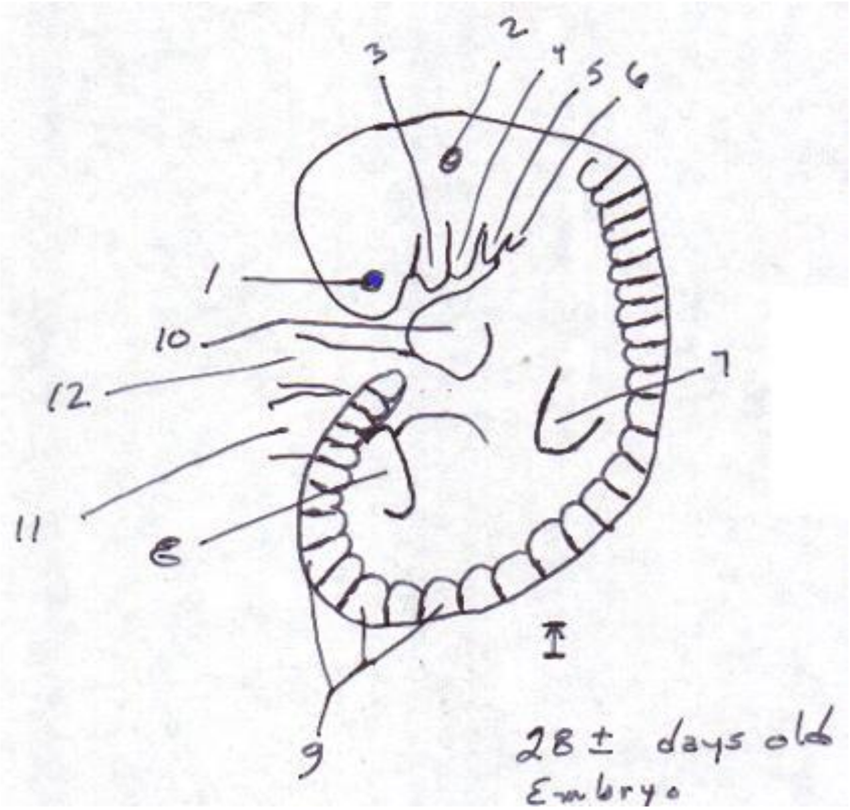
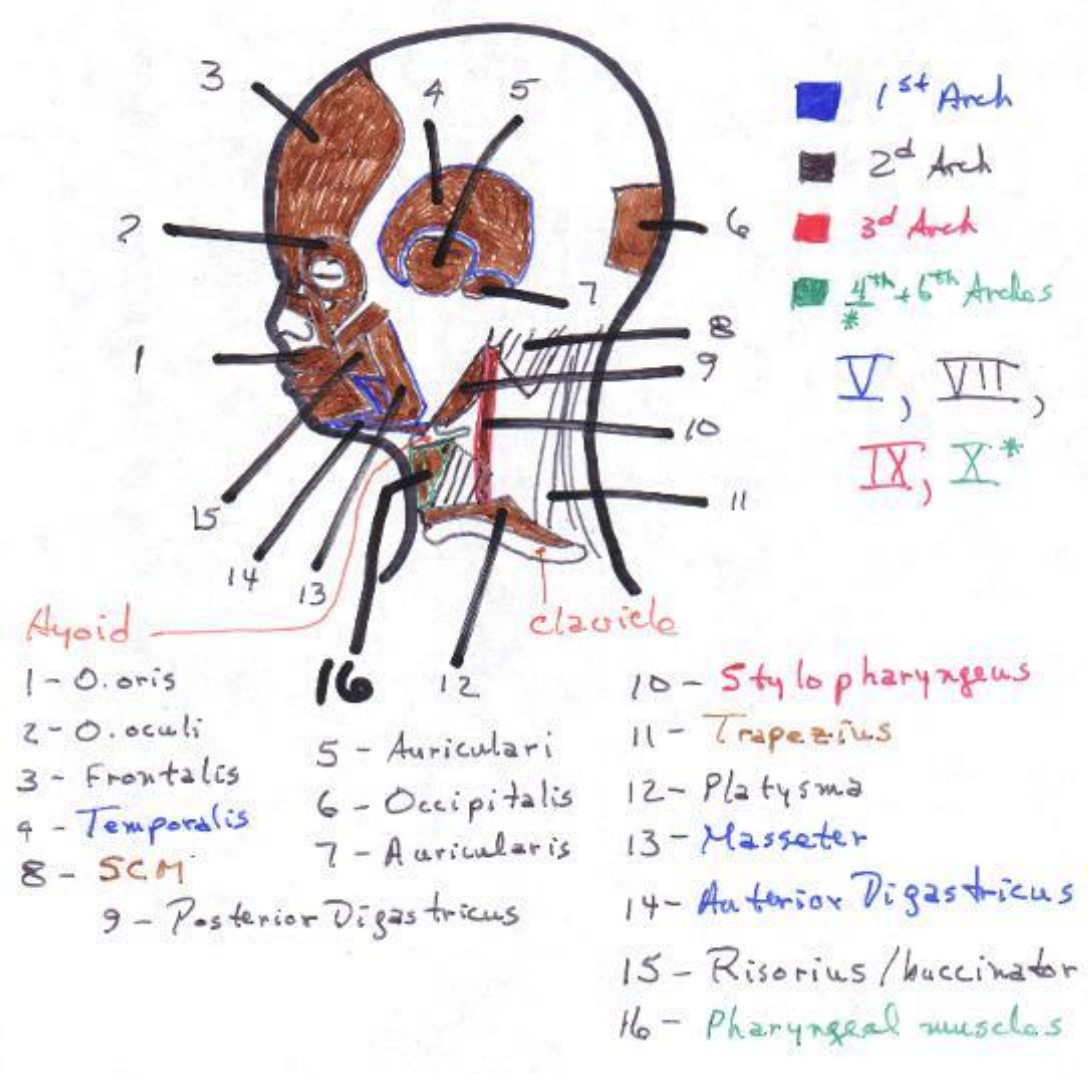
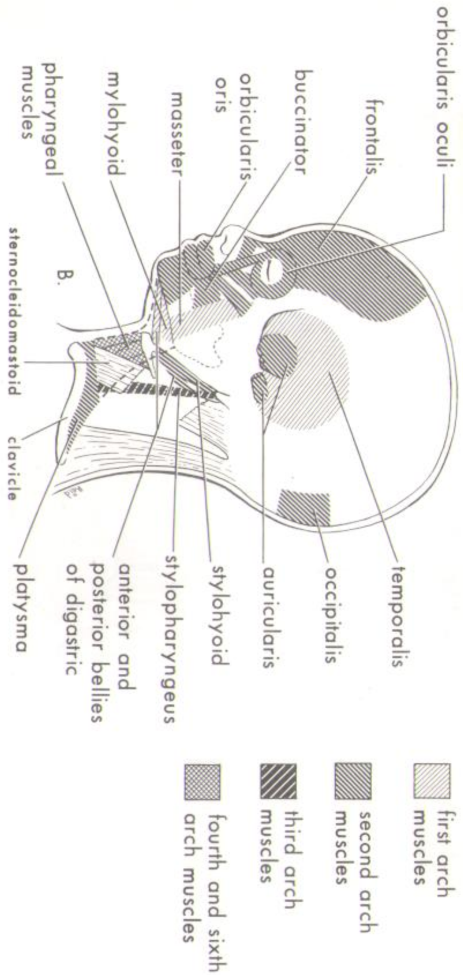


1. Lens placode
2. Otic pit
3. First branchial arch
4. Second branchial arch
5. Third branchial arch
6. Fourth branchial arch
7. Upper limb bud
8. Lower limb bud
9. Somites
10. Heart prominence
11. Connecting stalk
12. Yolk sac

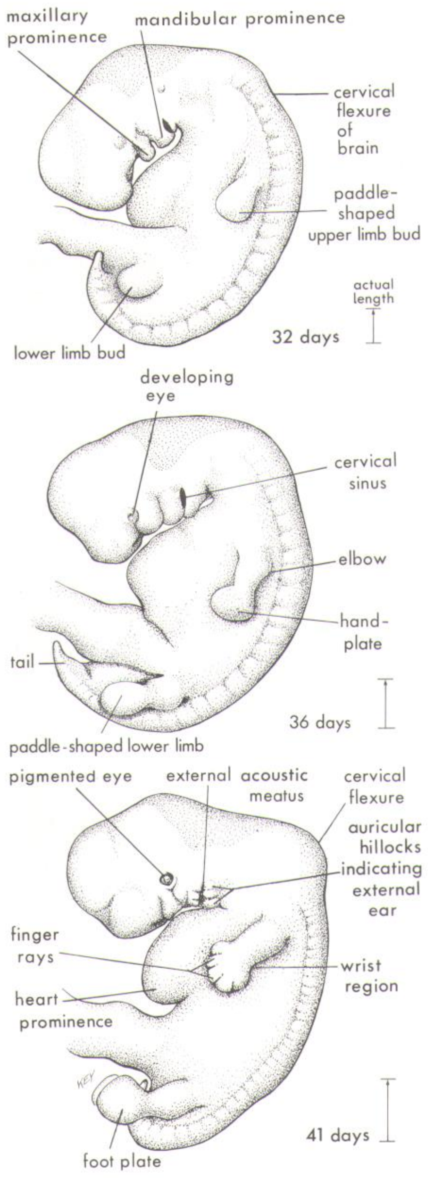
- Somites differentiate into myotomes, dermatomes and sclerotomes (which form skeletal muscle, connective tissues and vertebra, respectively).

The branchial arches are unique structures in that they give rise to numerous nerves and muscles about the head, neck and face:

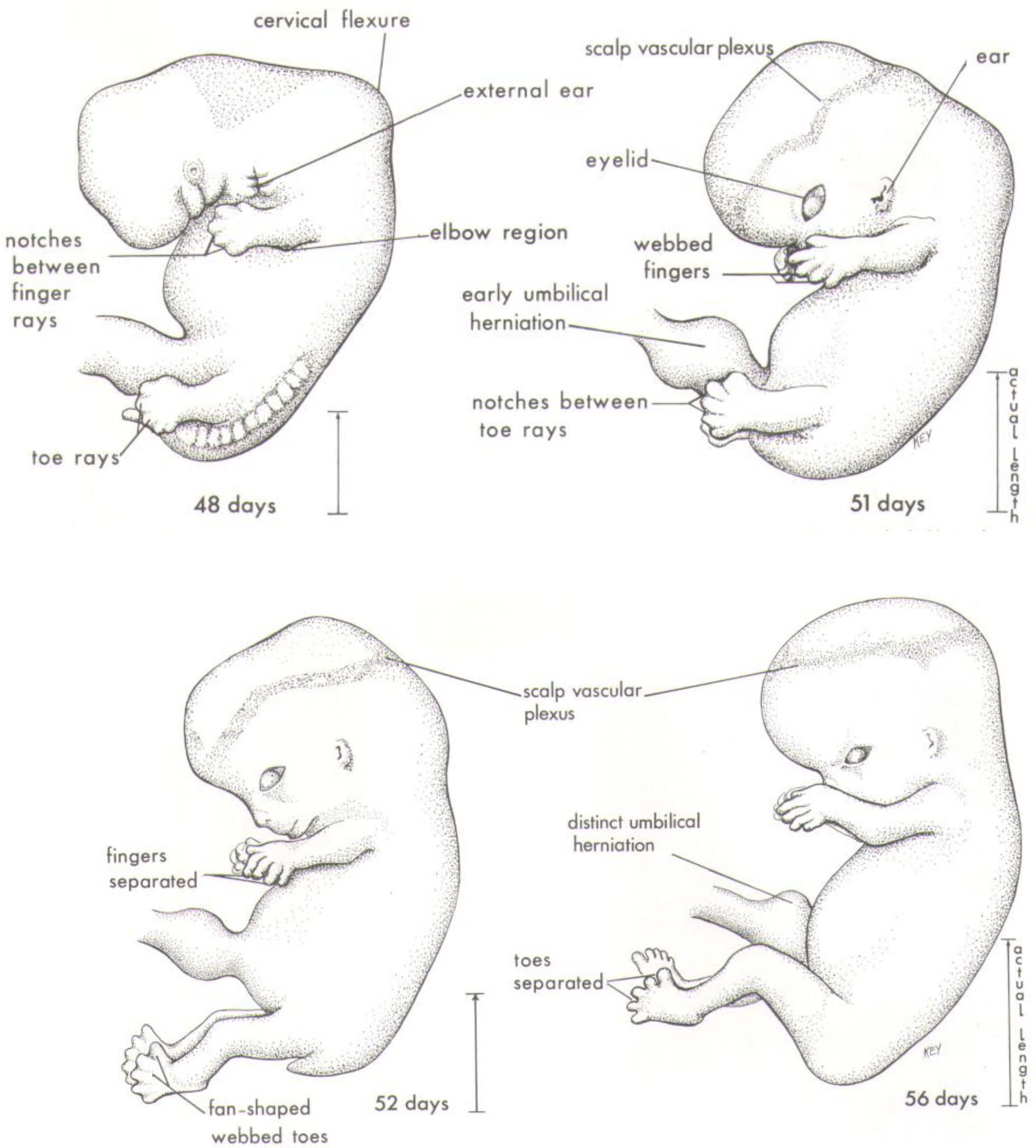




Further Growth and Development

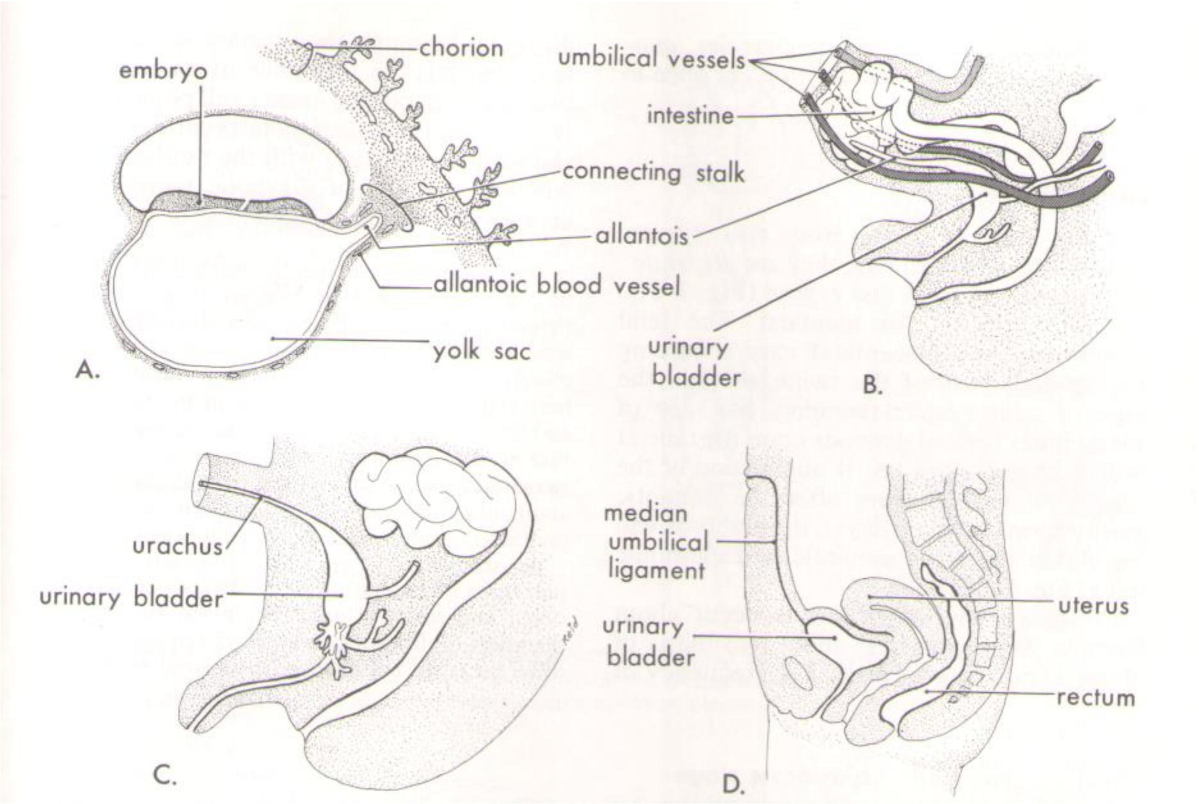


- THE point of significance to get out of these last sets of illustrations is that we grow from the top down.
- This is BEST illustrated by following the sequence of hand and foot development.
- That is also how we heal: best at our head and worst/slowest at our feet.



Developing Urinary System

- A. The urinary system needs some embryological explanations, as well.
- At about 3 weeks of gestation, a structure called the allantois is developing from the yolk sac and aiming towards the chorion:

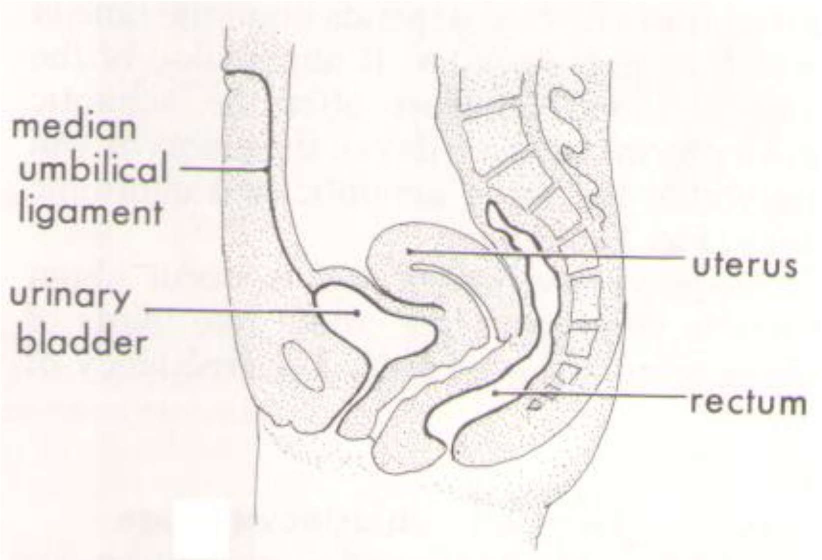


B. By 9 weeks of age, though, you can see that the allantois is a part of the urinary bladder.

C. At 3 months of gestation, the allantois has differentiated into the urachus (yerr AE cuss) for urine removal from the fetus to the mother for excretion.

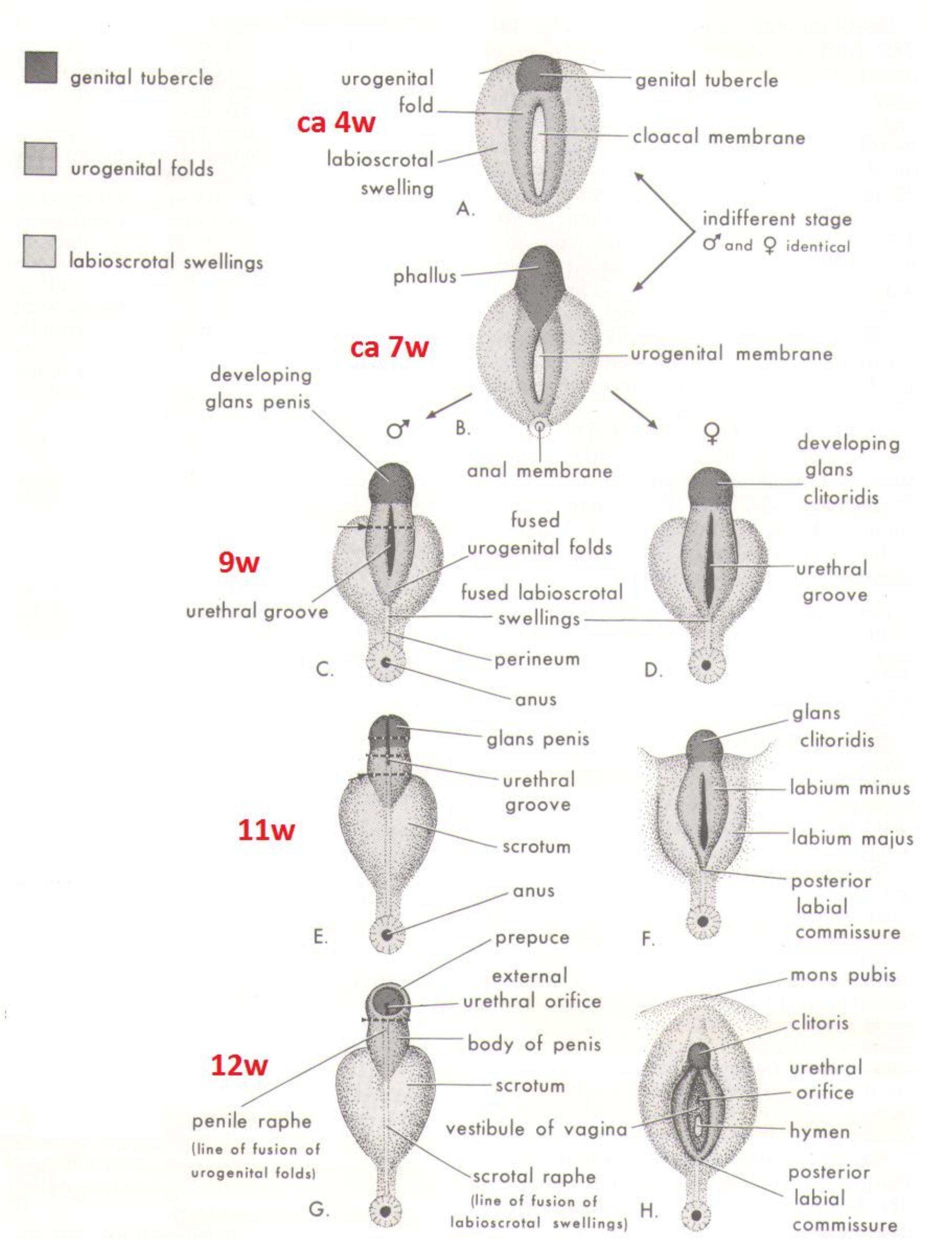
D. The significance of the urachus is shown above in the adult view.

The significance of the urachus is shown below in the adult view:



- The median umbilical ligament is necessary to "hold" the bladder in proper position. If this ligament is stretched -- as happens in pregnancy(ies) -- then the bladder falls, leading to incontinence. The repair of this is called a cystocele repair. More or less it amounts to tightening the ligament up so that the bladder is no longer "fallen".
- Probably one of the easiest problems to correct surgically is the "fallen bladder" after having children -- some as few as 1 to some who have as many as 8 or 10 children before they have incontinence.

External Genitalia Development



- Note that at 4 weeks of gestation, both genders have identical external genitalia.
- By 7 weeks of gestation, i.e., near the end of the embryological period, genders can not be differentiated, either.

In the embryo, the embryonic cloaca divides into a posterior region that becomes part of the anus, and an anterior region that has different fates depending on the gender of the individual: **in females**, it develops into the vestibule that receives the urethra and vagina, while **in males** it forms the entirety of the penile urethra.

- Note that it's not until 12 weeks of gestation that the external differences between male and female fetuses become obvious.
- All hashing, BTW, is coded to match embryological tissue of origin between the genders, e.g., glans clitoris and glans penis are derived from the same tissue; the scrotum and the labia majora are from the same tissue, embryologically; the penile shaft is identical to the labia minora.
- Did you note that embryos are pretty much female until the effects of testosterone take over to drive the differentiation of the male genitals? Good!