

Obstetrics

Marrow Edition 8

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Instructions

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Obstetrics

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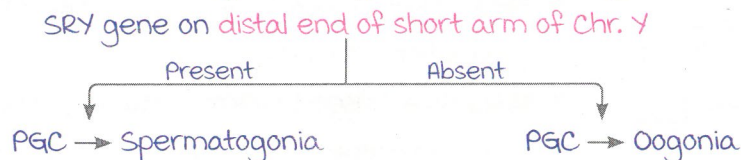
GAMETOGENESIS

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Primordial germ cells :

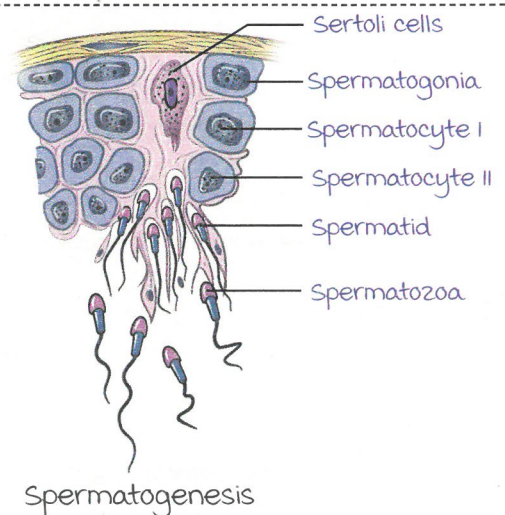
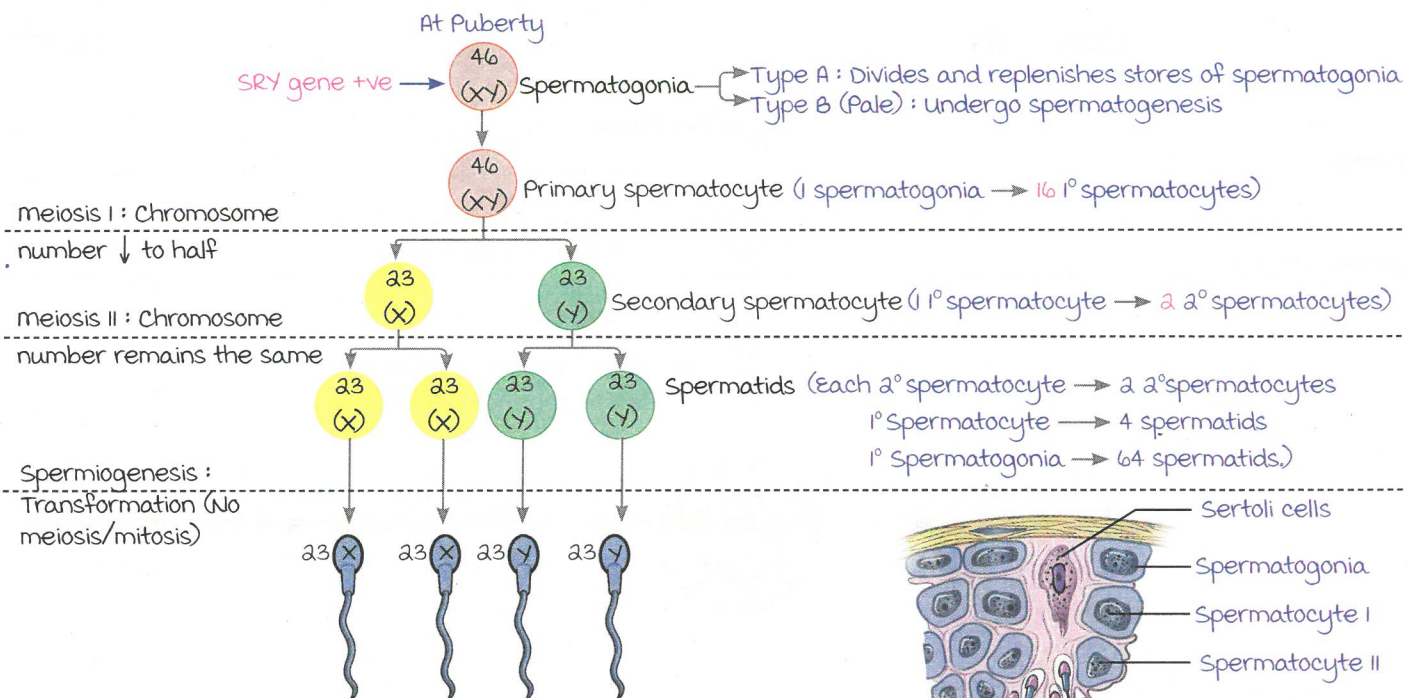
- Gametogenesis begins with the primordial germ cell (PGC).
- Derived from :
 - Epiblast.
 - Ectoderm.
- Bipotent cells : They can form spermatogonia/oogonia.

Differentiation : Determined by the SRY gene (Sex related gene on chromosome Y).



Spermatogenesis

00:03:46



- Site : Seminiferous tubules in testis.
- Spermiation : Process of release of sperm into the lumen of seminiferous tubules.
- Spermatogenesis begins at puberty.
- Time taken for spermatogenesis : 70-74 days (~ 72 days).
- Time taken for spermiogenesis : 10-14 days.

----- Active space -----

Compartments of seminiferous tubules :

- i. Basal compartment : Spermatogonia + 1° Spermatocyte (Early stages of development).
- ii. Adluminal compartment : 2° Spermatocyte + Spermatid + Sperms.

Spermiogenesis :

Transformation of spermatid to sperm.

Structural analogues :

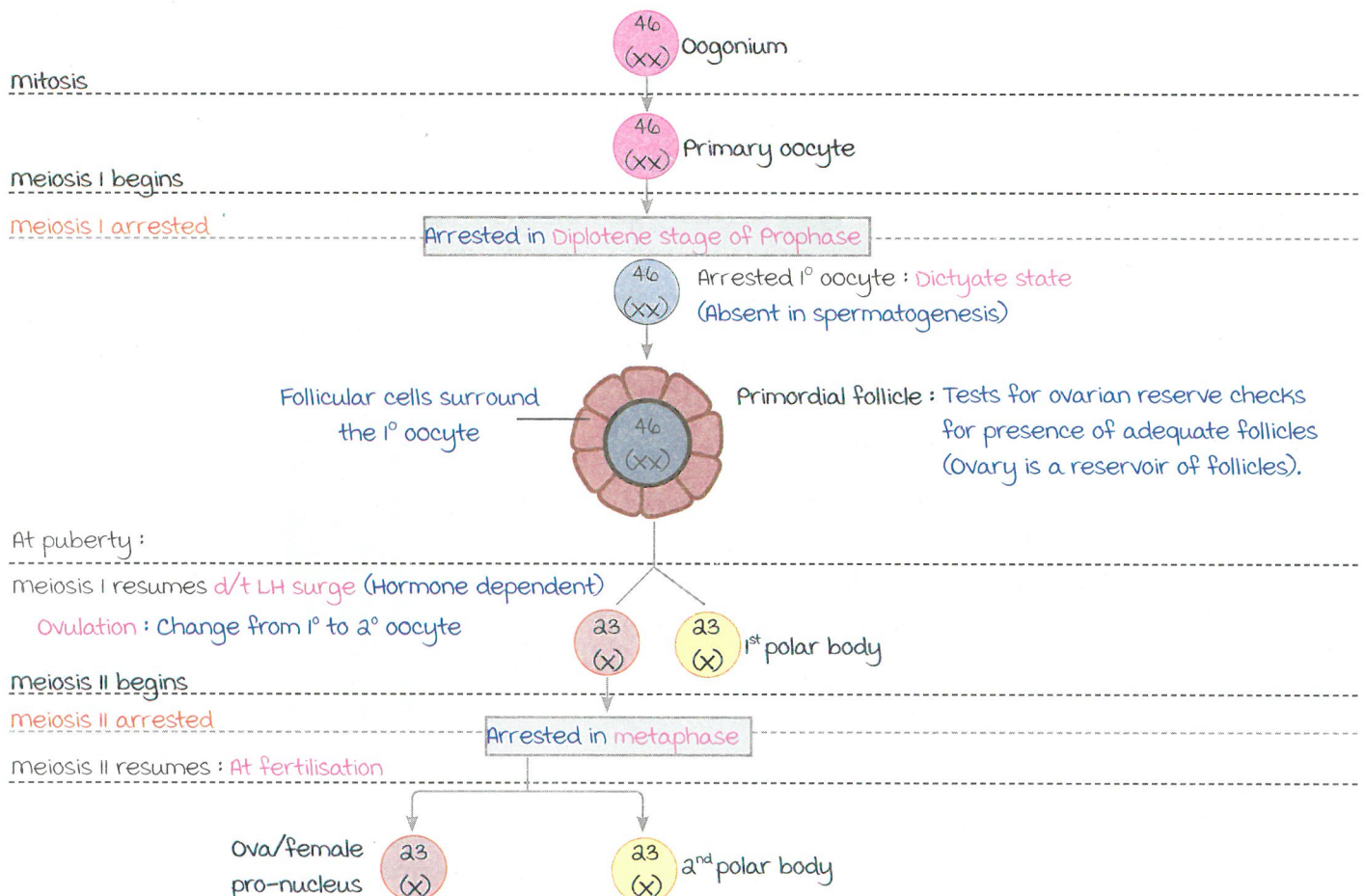
Spermatid	Sperm
Nucleus	Head
mitochondria	middle piece (Powerhouse of the sperm)
Golgi Apparatus	Acrosomal Cap
Centriole	Axial filament/Tail

Sperms :

- Size of sperm : 50-60µm.
- Tail of the sperm has a 9+2 arrangement.
(Formed by centriole)
- Fertilisable span of sperm : 48-72 hours.
- maturity attained in : Proximal epididymis.
- motility attained in : Distal epididymis.
- Time taken to reach fertilisation site after ejaculation : 30 mins.
- Total time taken to form mature sperms (Spermatogenesis + maturation) : 90 days.
- Time taken for epididymal maturation : 12-14 days.

Oogenesis

00:15:04



Salient points :

----- Active space -----

- Oogenesis begins in intrauterine (IU) life.
- Size of ovum : 120µm.
- Fertilisable life span of ova : 12-24 hrs.
- Size of follicle just before ovulation : 18-20mm.
- Follicle formation begins at : 14 weeks.
- Follicle formation is complete by : 22-24 weeks.
- Each oogonia gives rise to : 1 ova/female pronucleus.

No. of follicles in ovary based on age :

Age	No. of follicles
5m of IU life	6 - 7 million (max)
At birth	1 - 2 million
At puberty	4 - 5 lakh
Every month	1000 follicles undergo atresia
At menopause	No follicles in ovary

Note :

- Germ cells : Pluripotent (Ability to form all 3 germ layers).
- Zygote (After 8 cell stage) : Totipotent (Ability to form embryonic + extraembryonic tissue).
- Germ cells $\xrightarrow{\text{migrate}}$
 - Yolk sac → Genital ridge → Gonads formed.
 - Failure of migration (Aberrant location) → Form teratomas.

FERTILIZATION AND IMPLANTATION

----- Active space -----

Events Prior to Fertilization

00:01:30

Capacitation :

Process by which sperms become capable of fertilizing the ova.

Site : Female reproductive tract.

Time taken : 6 - 8 hours.

Begins at : Cervix.

In vitro capacitation : 2 hours.

main site : Fallopian tube (FT).

Sequence of events :

Step 1 : Capacitation - Sperms become hypermotile (In FT).

Step 2 : Sperms bind to zona pellucida.

Step 3 :

Acrosomal reaction : Release enzyme → Digest zona pellucida.
(Hyaluronidase)

Step 4 : Head of single sperm (male pronucleus) fuses with oolema.

Step 5 :

a. and meiotic division complete → Female pronucleus + 2nd polar body.

b. Cortical reaction : Cortical granules (Cytoplasm of 2° oocyte)

Release

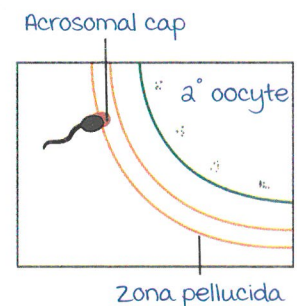
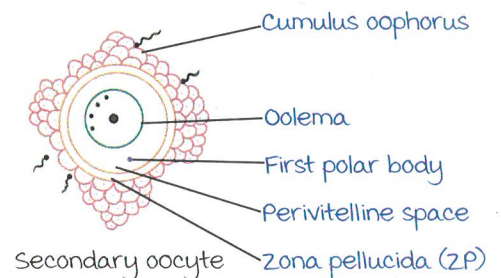
Ca^{2+} + other substances

Step 6 : Substances released by cortical granules

Zona reactions : Hardening of zona pellucida (Doesn't allow entry of any other sperm)

Note :

- Polyspermy is prevented by : Cortical reaction, Zona reaction.
- Time taken by sperms to reach the site of fertilization : 30 mins.
- male sperm attain mobility in epididymus (Distal part).
- Sperm attain hypermotility in female reproductive tract.
- Zona pellucida :
 - Acellular membrane.
 - made of glycoprotein.
 - Receptors for sperm head : ZP_3 receptor.
 - Function : To prevent polyspermy.



Process of Fertilization

00:14:00

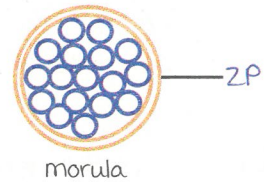
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male pronucleus (23) + Female pronucleus (23) $\rightarrow$ Zygote (46 : Diploid)

- Occurs in : Ampulla of fallopian tube.
- Day of fertilization = Day of ovulation = Day 14 (In a 28 day cycle) :
 - Fertilisable span of 2^o oocyte : 24 hours.
 - In IVF : Day of ovulation = Day of oocyte retrieval = Day of fertilization.

• Zygote formation $\xrightarrow[\text{hours}]{\text{After 30}}$ 2 Cell zygote $\rightarrow$ 4 Cell zygote $\rightarrow$ 8 Cell zygote $\rightarrow$ 16 Cell zygote

- 16 cell morula enters the uterine cavity.



Note :

- Ectopic pregnancy :
 - $\downarrow$ peristalsis of FT.
 - Cilia absent.
 - Blockage in tube
 } morula implanted in FT
(w/t adhesion formation).
- High chances of ectopic pregnancy :
 - Immotile cilia syndrome (Kartagener syndrome).
 - Adhesion inside tube (E.g. PID, salpingitis).
 - Failure of contraceptive (with progesterone containing pills).
(Smooth muscle relaxant action $\rightarrow$ $\downarrow$ peristalsis).

morula :

- moves towards uterine cavity.
- morula is pushed towards uterine cavity due to :
 - Peristalsis in tube.
 - movement of cilia (FT lined by ciliated columnar epithelium).

Till 3 days after fertilization : Stays in FT (Nutrition by secretory cells).

4th day after fertilization : Enters uterine cavity (16 celled).

(Day 18 of cycle)

5th day after fertilization :

- Zona hatching : ZP is lost.
- Fluids enter morula $\rightarrow$ Converted to blastocyst.

Implantation

00:25:50

Salient features :

- Attachment of blastocyst to endometrium.
- On day 6 after fertilization (Day 20 of cycle).

Implantation window : Time period (Day 20 - Day 24) when endometrium/uterus is most receptive for blastocyst.

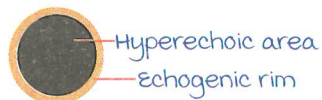
Type of implantation : Interstitial implantation deep inside endometrium.

Placental/Hartmann sign : Few experience bleeding at the time of implantation.

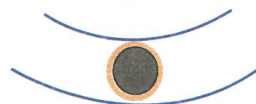
Applied aspect : USG in pregnancy :

1st structure seen :

Gestational Sac (G. sac)



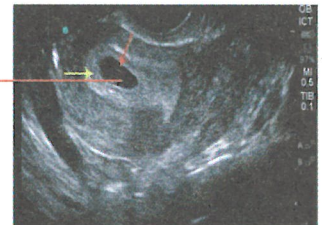
First sign seen :



Intradecidual sign :

Presence of G. Sac deep inside endometrium.

Gestational sac



Intradecidual sign

Stages of implantation :

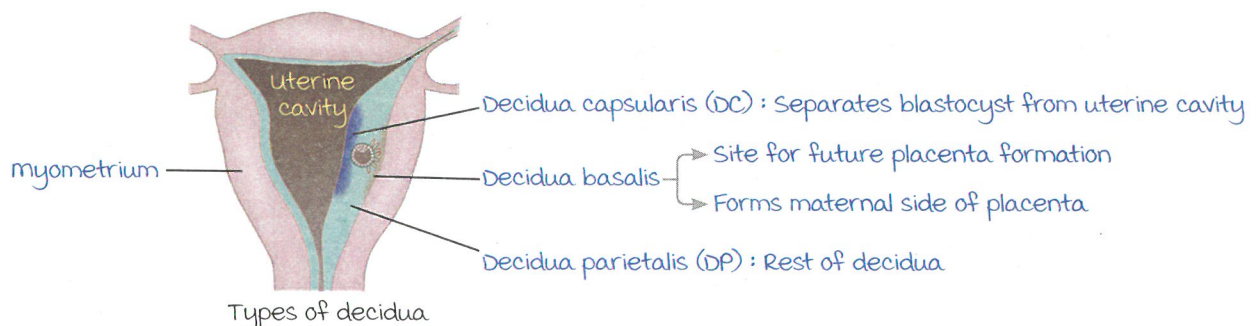
Stage	Factor responsible
1. Stage of Apposition	Selectin
2. Stage of Adhesion	Integrin (most important)
3. Stage of Penetration	matrix metalloproteinases enzymes

Implantation is eccentric :

- Piskacek sign : Growth of uterus in early pregnancy is asymmetrical.
- True gestational sac (Of intrauterine pregnancy) : Always eccentric.

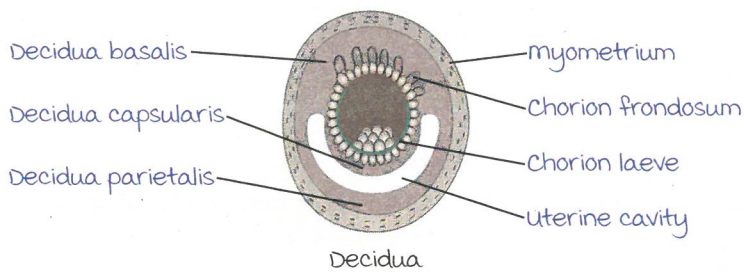
DECIDUALISATION

After implantation, endometrium is called decidua.

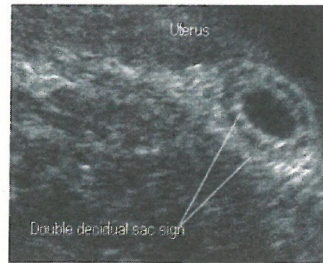


Types of decidua

As blastocyst grows :



On USG :



----- Active space -----

Double decidual sac sign

Obliteration of uterine cavity :

As blastocyst grows → DC comes closer to DP → DC fuses with DP

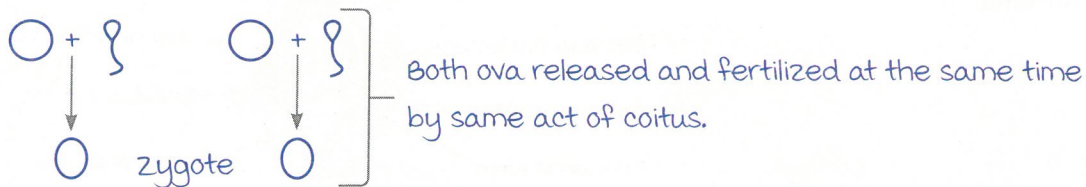
(14-16 weeks of pregnancy)

↓ Leads to

Obliteration of uterine cavity

(14-16 weeks of pregnancy)

Dizygotic Twin Pregnancy :



Superfetation :

- Not seen in humans.
- 2 ova released in 2 different cycles & fertilized by 2 different acts of coitus.
- In humans : Superfetation possible till 14-16 weeks of pregnancy (Only theoretical).

Changes in decidualization :

Hormone responsible : Progesterone

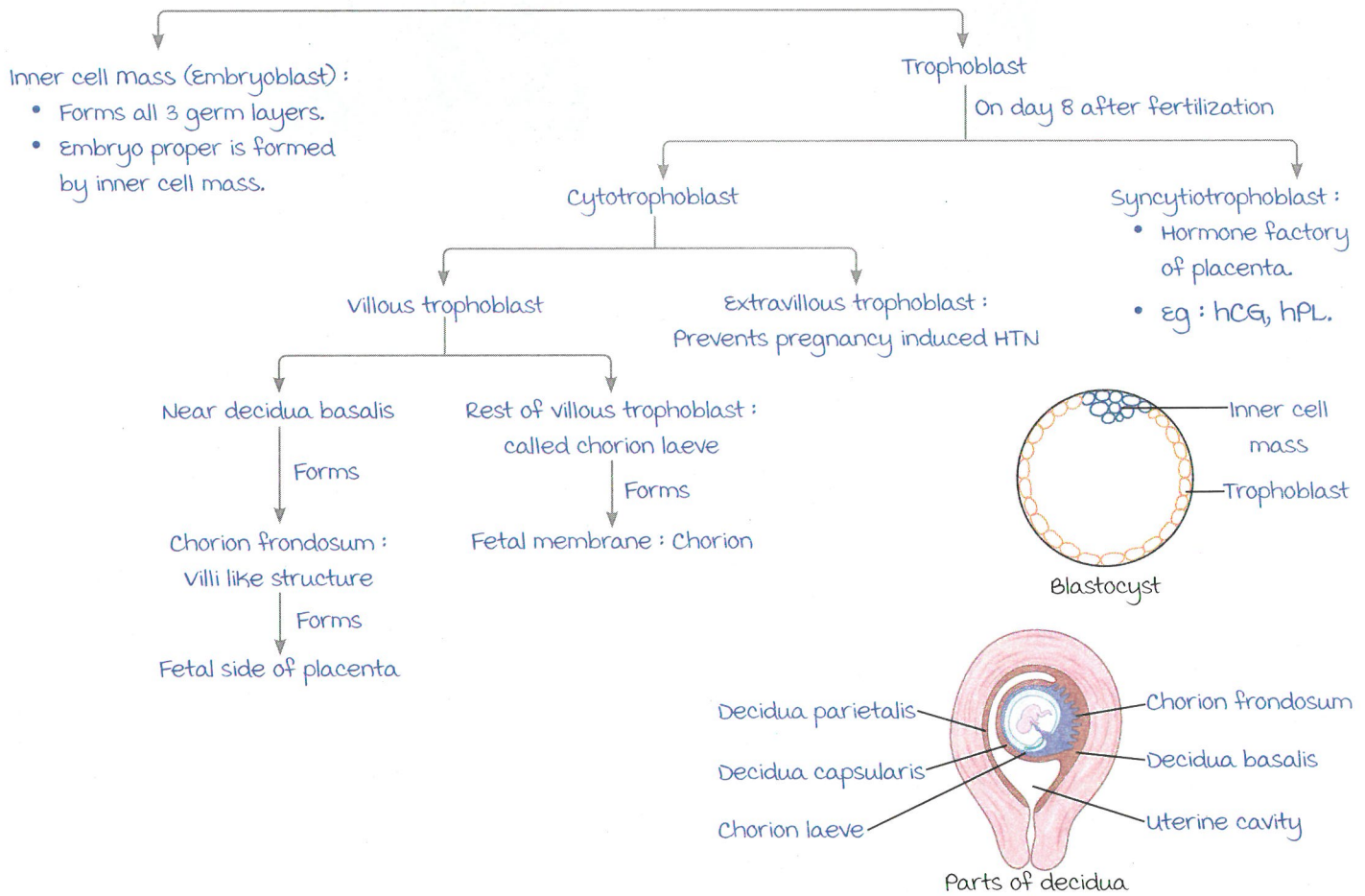
1. Secretory changes in endometrium.

a. ↑ thickness of endometrium (10-12mm) d/t **stromal edema** (most important histological finding).

- In non-pregnant female during secretory phase (6mm).

Blastocyst

0:58:10

FATE OF BLASTOCYST**Fetal Membranes**

01:06:10

Chorion:

- Formed by chorion laeve (Cytotrophoblast).
- Outermost fetal membrane.
- Formed earlier than amnion (Day 8 after fertilization).

Amnion:

- Formed by ectoderm.
- Innermost fetal membrane.
- Day 10 after fertilization.
- Avascular.
- No nerves or lymphatics.
- Gives tensile strength.

Yolk Sac:

- First site for fetal hematopoiesis.
- Source of α fetoprotein.

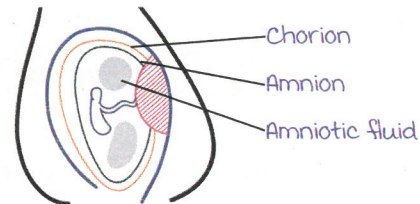
Allantois :

Diverticulum which connects hindgut to connecting stalk.

----- Active space -----

Note :

- membrane rupture $\rightarrow$ membrane releases $\text{PGE}_a \rightarrow$ Accelerates labour during labour
- Layers penetrated during amniocentesis (Outside to inside) : 16-18 weeks.
 1. Skin.
 2. Abdominal wall muscles.
 3. uterine serosa.
 4. myometrium.
 5. Endometrium (DC + DP : Decidua Vera).
 6. Chorion.
 7. Amnion.

**Preimplantation Genetic Testing**

01:13:35

Done only in assisted reproductive techniques.

Indications :

If one or both parents are carriers of any genetic disorder : Advise IVF

Genetic testing before implantation

Only healthy zygotes will be transferred into uterus

Disease tested :

- monogenic disorders :
 - Sickle cell anemia.
 - Cystic fibrosis.
 - Thalassemia.
 - muscular dystrophy.
- Aneuploidy.
- Structural rearrangement of chromosomes.
 - Eg. Balanced translocation.
- HLA typing.

Specimen :

- Polar body :
 - Drawback : Only maternal inherited disorders can be tested.
- Blastomeres (Cells of inner cell mass) : may harm the fetus.
- Trophectoderm : Best material.

----- Active space -----

TERATOGENIC EXPOSURE OF FETUS

Fetal Growth Period & Radiation Exposure in Pregnancy

00:00:50

Fetal growth period :

Calculated from : Day of fertilization.

Growth Period	Definition	Applied aspect
1. Period of fertilised ova	upto 2 wks after day of fertilization.	Teratogenic exposure : All or none law (fetus either escapes injury/aborts).
2. Embryonic period	3-8 wks after fertilization (5 th -10 th week of pregnancy).	most teratogenic period.
3. Fetal period	≥ 9 wks after fertilization.	

Radiation exposure in pregnancy :

maximum permissible exposure : 5 Rad (0.05 Gy).

Complications :

a. > 5 Rads exposure :

- ↑ Risk of congenital anomalies.
- IUGR
- Intellectual disability.

b. ≥ 10 Rads exposure (≥ 0.1 Gy) :

- Fetal loss/abortion.

Absolute C/I in pregnancy :

- Gadolinium enhanced MRI.
- Radioactive iodine.
- Radio opaque/paramagnetic contrast agents.

Avoided in pregnancy —→ X-Ray
—→ CT Scan

Accidental X-Ray in pregnancy :

- Continue the pregnancy.
- upto 2 X-rays : <0.5 Rads.

Imaging studies with no effect on fetus :

1. USG.
2. MRI.
3. Dental X-Ray.
4. CT scan (Not involving pelvis/abdomen).

Teratogenic Drugs

00:08:48

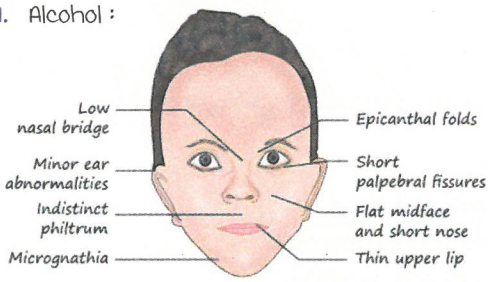
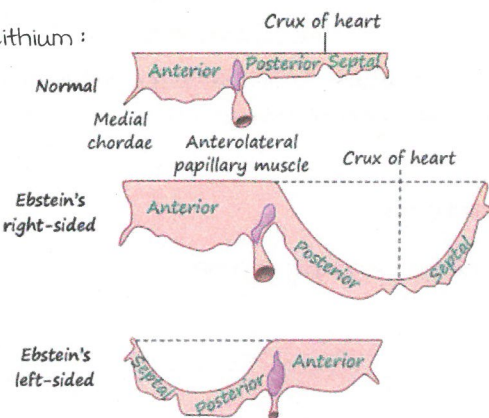
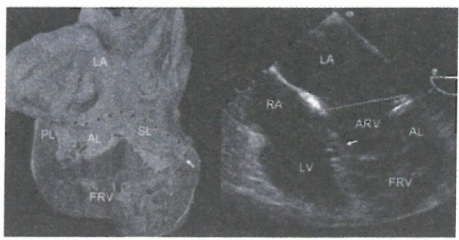
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CATEGORY X DRUGS

Teratogenic drugs absolutely C/I in pregnancy.

1. Androgens/Testosterone.
2. DES (Synthetic estrogen).
3. Warfarin.
4. ACE Inhibitors.
5. Tetracyclines : Discoloration of bone & teeth.
6. Thalidomide.
7. Lithium.
8. Valproate : CNS defects, NTDs, congenital heart disease, cleft lip/palate.

TERATOGENIC DRUGS & MALFORMATIONS

Drug	Teratogenicity
1. Alcohol :  Fetal alcohol syndrome	Fetal alcohol syndrome (FAS) : Mnemonic : Goa's famous beer bar. • Growth restriction. • Abnormal facial features : Smooth philtrum, thin vermilion border, small epicanthal folds. • Abnormal brain development, microcephaly. • Abnormal behavioral development : Cognitive impairment.
2. Phenytoin	Fetal hydantoin syndrome : a. midfacial hypoplasia. b. upturned nose. c. Distal digital hypoplasia ± cardiac defects.
3. ACE inhibitors/ARBs	Oligohydramnios in the 2nd trimester.
4. Lithium :  Ebstein anomaly	• Ebstein anomaly : - Apical displacement of tricuspid valve → Tricuspid regurgitation. - Right atrial enlargement. • Neonate : Floppy baby syndrome, diabetes insipidus & hypoglycemia.  Echocardiography : Tricuspid regurgitation

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Drug	Teratogenicity
5. Isotretinoin	microtia/anotia, CNS defects, cleftlip/palate.
6. Thalidomide	- Phocomelia (Proximal limb amputation). - Stillbirth.  Phocomelia
7. Warfarin :  Depressed nasal bridge  Stippled epiphysis	DiSala syndrome - Chondrodysplasia : Defective cartilage formation. - Stippled epiphysis. - Nasal hypoplasia. - CNS : Corpus callosum agenesis, microcephaly. - Cataract.
8. methotrexate	Craniosynostosis : Clover leaf skull.
9. Tamoxifen (SERM) Note : minimum time gap b/w stoppage of tamoxifen and pregnancy : 3 months	- Similar to DES : - Vaginal adenosis - Craniofacial defects. - Ambiguous genitalia. - Mother : Endometrial cancer.
10. misoprostol	- moebius syndrome : 6th & 7th nerve palsy. - Limb reduction defects. - Applied aspect : - C/I in T1 and T2. - T3 : can be used for cervical ripening.
11. Indomethacin	>32 weeks : Premature closure of ductus arteriosus. <32 weeks : Tocolytic of choice.

Note :

Distal digital hypoplasia/amputation —→ Phenytoin
 —→ Amniotic band syndrome