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MSc in Reproductive and Developmental Biology

Growth and differentiation of the female tract: ovary

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Mammalian sex determination

- Genetic sex
  - determined at fertilization by whether sperm is X-bearing or Y-bearing
- Gonadal sex
  - development of testis or ovary from bipotential indifferent gonad
  - determined by genetic information - XX or XY
  - *SRY** on Y chromosome triggers testis development
- Phenotypic sex
  - determined during fetal life and continues through puberty.
  - directed by endocrine products of gonads - act on accessory sex ducts and external genitalia

*Sex determining Region of the Y chromosome

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Two main functions of ovary

- Production of oocytes
- Production of steroid hormones

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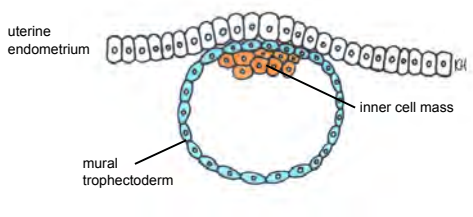
Blastocyst attachment



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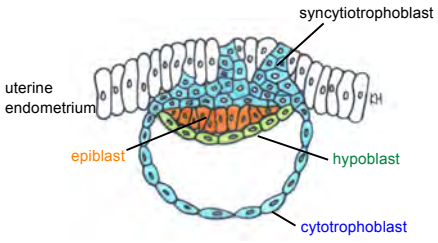
Blastocyst invasion (day 7)



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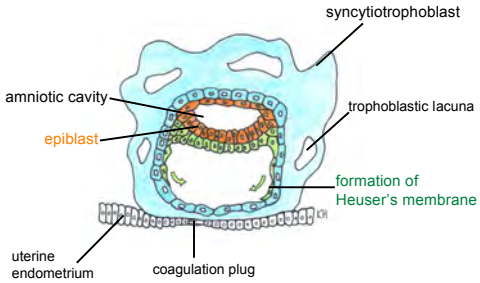
Implanted blastocyst (9d post fertilization)



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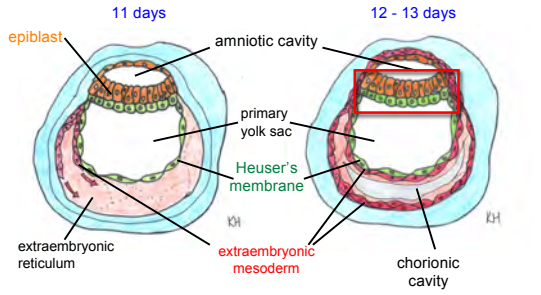
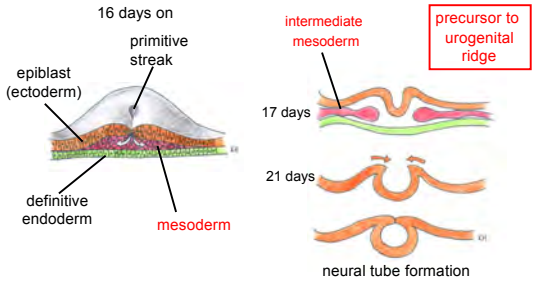
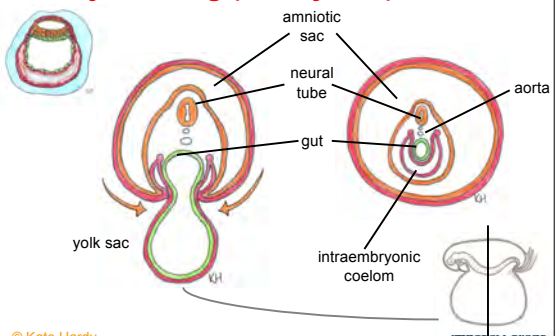
Extraembryonic mesoderm formation



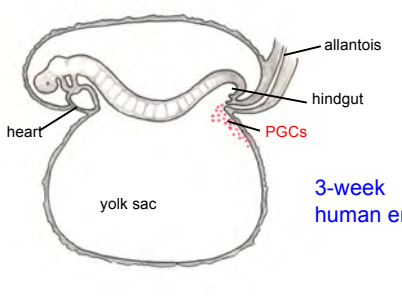
Mesoderm formation



Embryo folding (21 days on)



Origin of primordial germ cells (PGCs)



3-week human embryo

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Gonadal development

- First sign of gonadal development recognizable at 4 weeks
- Genital ridges form either side of central dorsal aorta on posterior wall of embryo (lower thoracic, upper lumbar region)
- 2 bilateral longitudinal prominences - genital ridges
  - mesenchyme
  - overlain by coelomic epithelium

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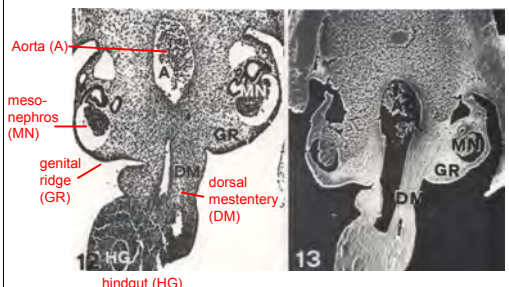
Genital ridges: 4 - 5 weeks



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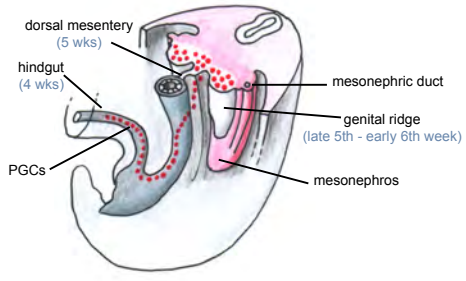
Two origins of ovarian cells

- Somatic cells differentiate from
  - mesonephric mesenchyme
  - overlying coelomic epithelium
- Germ cells (oocyte precursors) first seen in endoderm of dorsal wall of yolk sac, at 3 weeks gestation
  - originate before gonadal differentiation
  - 15 - 20 µm diameter, with large nucleus
  - stain for alkaline phosphatase

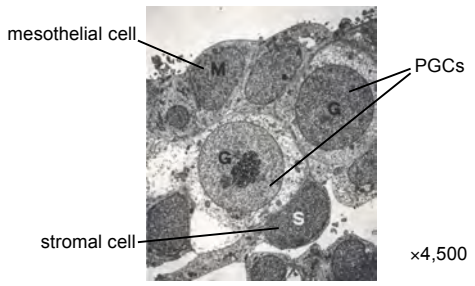
PGCs migrate and proliferate

- PGCs migrate from yolk-sac endoderm
- Found in hindgut at 4 weeks
- Arrive at dorsal mesentery at 5 weeks
- Enter genital ridge at 5 - 6 weeks
- PGCs proliferate while migrating
- Migrate by amoeboid movements
  - demonstrated in vitro by timelapse photography
- May be directed by chemotactic substances from gonadal areas

Primordial germ cell migration



PGCs migrating in dorsal mesentery



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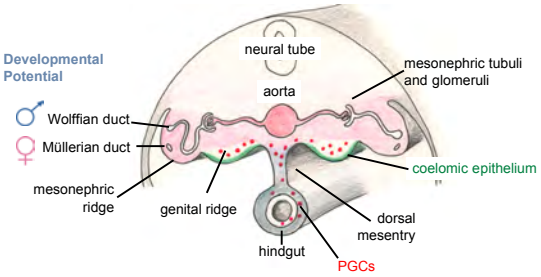
'Indifferent' gonad (4 - 5 weeks)



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Sex differentiation

- Males have testosterone and anti-Müllerian hormone (AMH)

Males, presence of
- testosterone maintains Wolffian duct
- AMH in males leads to degeneration of Müllerian duct

Females, absence of
- ~~testosterone~~ leads to Wolffian duct degeneration
- ~~AMH~~ leads to differentiation of the Müllerian duct into the oviduct, uterus and upper part of vagina.

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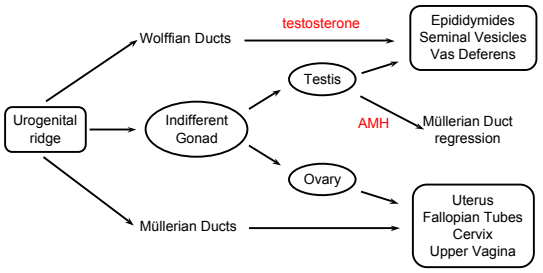
Gonadal differentiation



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PGC colonization of gonads

- After reaching genital ridge, PGCs undergo rapid mitosis
- Somatic tissue also undergoes hyperplasia - gonads increase in size
- PGCs occupy superficial areas of gonad
- Gonads still 'indifferent'

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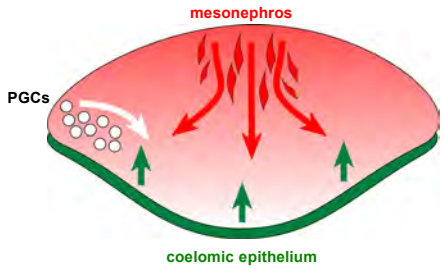
Enlargement (growth) of gonad



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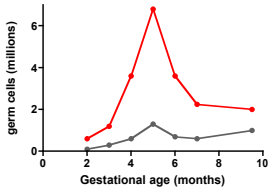
Germ cell proliferation

- Germ cells proliferate while migrating, and after colonizing ovary
- 5 week embryo: 700 - 1,300 primordial germ cells
- 8 week embryo: 600,000



Baker 1963

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Formation of oogonia from PGCs

- Germ cell differentiation starts in cortical regions of ovary during 9th week
- Oogonia form from PGCs, with similar structure:
  - large round nucleus with 1 - 3 nucleoli

	PGCs	Oogonia	Oocytes
Migration	✓	×	×
Proliferation	✓	✓	×

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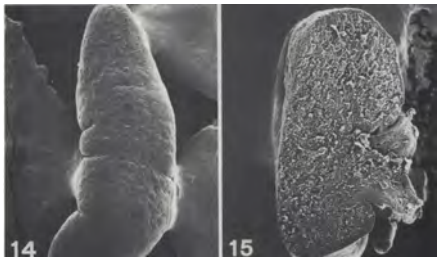
Fetal ovaries: 9 - 10 weeks



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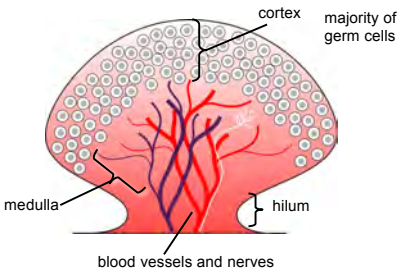
Gonadal differentiation



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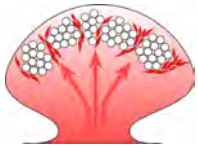
Germ cell nests

- Oogonia and oocytes form 'nests' in cortex of developing ovary (3rd to 4th month)
- Oocytes in nests connected by cytoplasmic bridges
- Bridges thought to coordinate and synchronize germ cell differentiation, entry into meiosis etc
- Nests surrounded by layer of flattened pre-granulosa cells.
- Thought that nests derived from single PGC



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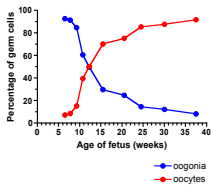
Oogonia → oocytes

- After numerous mitotic divisions,
- oogonia differentiate into oocytes from 10 weeks onwards
- Most oogonia have become oocytes by 25 weeks
- Oogonia are capable of mitosis, oocytes are not



Kurilo, 1981

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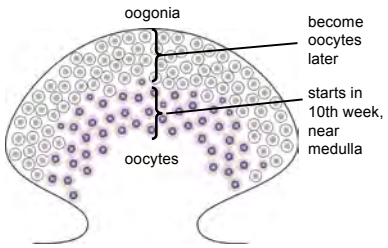
Oogonia → oocytes



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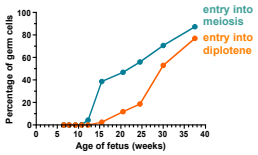
Entry into meiosis and then arrest

- Oocytes enter meiosis during the 12th - 13th week
- oocytes pass through
  - leptotene (DNA synthesis)
  - zygotene (pairing)
  - pachytene (SC formation)*
- and arrest in diplotene for between ~10 and 50 years



* see lecture on "oocyte maturation and meiosis"

Kurilo, 1981

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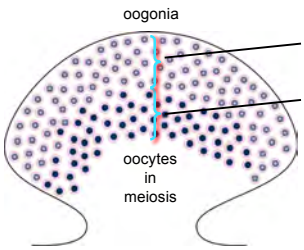
Inner oocytes enter meiosis first



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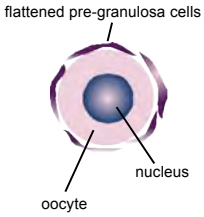
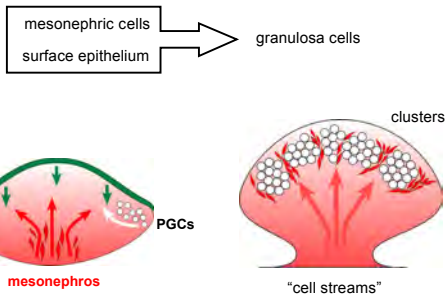
Oocytes in diplotene form follicles

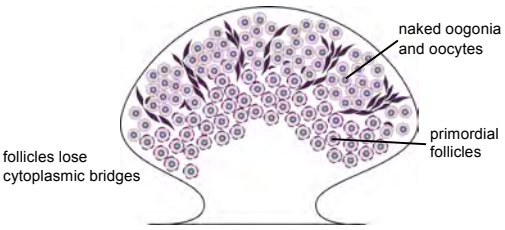
- Oocyte reaches diplotene,
- becomes enveloped in pre-granulosa cells and forms a primordial follicle
- Follicle formation begins during the 15th - 16th week and continues early postnatally
- some oocytes do not form follicles and die



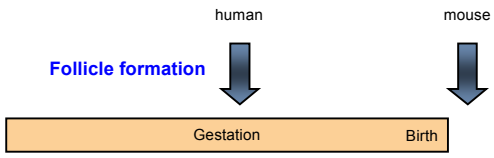
Origin of granulosa cells unclear



First follicles form near medulla



Comparison between mouse and human



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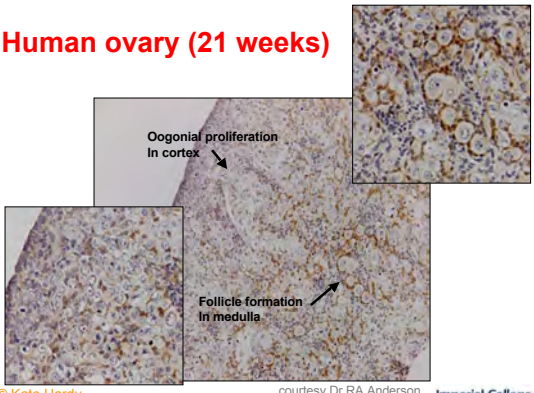
Human ovary (21 weeks)



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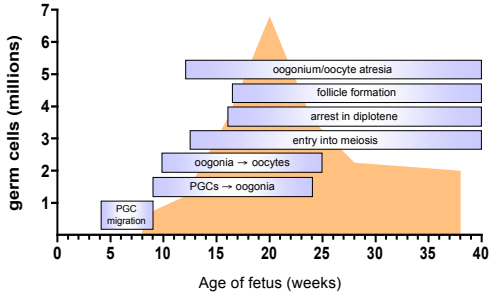
Asynchrony of developmental stages of female germ cells during gestation



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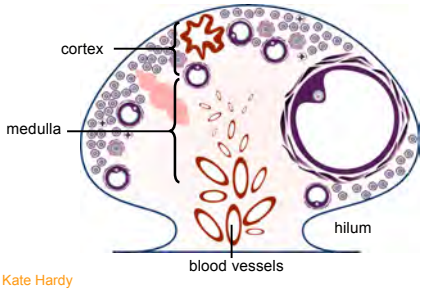
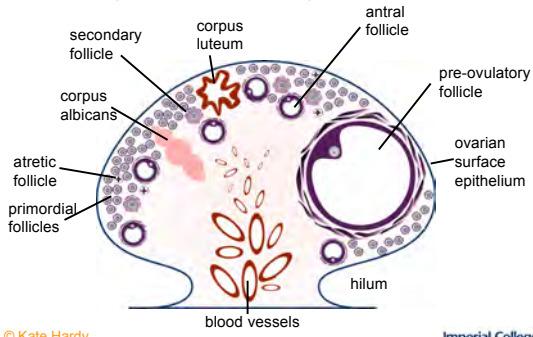
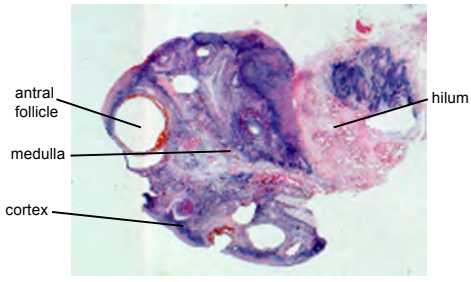
Anatomy of adult ovary

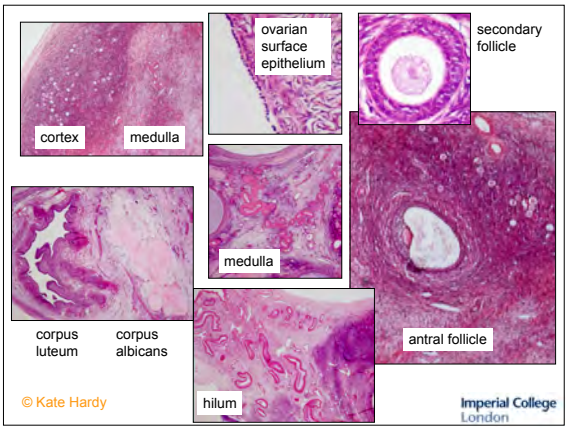


Anatomy of adult ovary

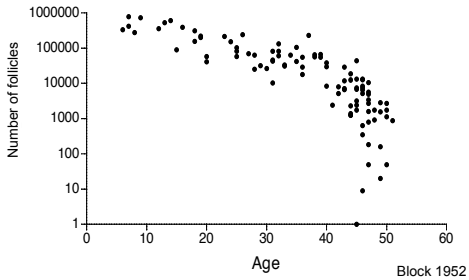


Section of ovary





Declining number of oocytes



Block 1952
Richardson 1987
Gougeon 1994

Ovarian volume increases with age, then decreases