Introduction

In medicine foundations you were given a broad overview of human development. Now in BGDA we will be working through the human development process in more detail, focussing on key events.

- Begin by reviewing the recent Foundations Lecture and Practical.
- This BGDA lecture covers conceptus development from fertilization to implantation to trilaminar embryo formation.
- The lecture will also introduce early fetal membranes and placentation.

Currently being updated for 2014 (this notice removed when completed).

**Lecture Archive:** 2013 Lecture | 2012 | 2010 | 2008

**Human Reproductive Cycle**

- Meiosis in gonad produces haploid gametes (egg and sperm)
Gametogenesis

Male
The testes have two functions.

1. produce the male gametes or **spermatozoa**
2. produce male sexual hormone, **testosterone** (internal and external genitalia, sex characteristics)

- Historic testis drawing
- Child Seminiferous tubule
- Adult Seminiferous tubule showing spermatozoa developmental stages
- Seminiferous tubule cross-section and supporting cells

Human spermatozoa take about **48 days** from entering meiosis until morphologically mature spermatozoa.

- **Spermatogonia** - are the first cells of spermatogenesis
- **Primary spermatocytes** - large, enter the prophase of the first meiotic division
- **Secondary spermatocytes** - small, complete the second meiotic division
- **Spermatid** - immature spermatozoa
- **Spermatozoa** - differentiated gamete

**Spermatozoa development:** primordial germ cell - spermatogonia - primary spermatocyte - secondary spermatocytes - spermatid - spermatozoa

**Sertoli cells** (support cells) **Interstitial cells** or Leydig cells (produce hormone)

**Female**

The ovaries have two functions.

1. produce the female gametes or **oocytes**
2. produce female hormones, **estrogen** and **progesterone** (secondary sex characteristics, menstrual cycle)

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- three stages of follicle development
In an adult human female the development of a primordial follicle containing an oocyte to a preovulatory follicle takes in excess of **120 days**.

**Human ovary follicle development**

**Ovarian Follicle Stages:** primordial follicle - primary follicle - secondary follicle - tertiary follicle - preovulatory follicle

**Follicle cells** (support cells) **Theca cells** (produce hormone)

**Links:** Spermatozoa Development | Oocyte Development | MBoC - Figure 20-18. Influence of Sry on gonad development | Endocrinology - Comparative anatomy of male and female reproductive tracts

**Fertilization**

- **Oogenesis** - 1 gamete produced/meiosis + 3 polar bodies, meiosis is slow, 1 egg produced and released at ovulation
- **Spermatogenesis** - 4 gametes produced/meiosis, meiosis is fast, 200-600 million sperm released at ejaculation
Fertilization Site

- Fertilization usually occurs in first 1/3 of uterine tube (oviduct, Fallopian tube)
- Fertilization can also occur outside uterine tube associated with Assisted Reproductive Technologies (IVF, GIFT, ZIFT...) and ectopic pregnancy
- The majority of fertilized eggs do not go on to form an embryo

Fertilization - Spermatozoa

- **Capacitation** - alteration of the spermatozoa metabolism and surface proteins
- **Sperm Binding** - zona pellucida protein ZP3 acts as receptor for sperm
- **Acrosome Reaction** - exocytosis of acrosome contents (Calcium mediated) MBoC - Figure 20-31.
  - The acrosome reaction that occurs when a mammalian sperm fertilizes an egg
    - enzymes to digest the zona pellucida
    - exposes sperm surface proteins to bind ZP2
- **Membrane Fusion** - between sperm and egg, allows sperm nuclei passage into egg cytoplasm

Fertilization - Oocyte

- **Membrane Depolarization** - caused by sperm membrane fusion, primary block to polyspermy
- **Cortical Reaction** - IP3 pathway elevates intracellular Calcium, exocytosis of cortical granules MBoC - Figure 20-32. How the cortical reaction in a mouse egg is thought to prevent additional sperm from entering the egg
  - enzyme alters ZP3 so it will no longer bind sperm plasma membrane
- **Meiosis 2** - completion of 2nd meiotic division
  - forms second polar body (a third polar body may be formed by meiotic division of the first polar body)

Week 1 and 2
Week 2 Implantation
Normal Implantation

- Uterine body
  - posterior, anterior, superior, lateral (most common posterior)
  - inferior implantation - placenta overlies internal os of uterus **Placenta Previa**

Abnormal Implantation

- Ectopic Sites
  - external surface of uterus, ovary, bowel, gastrointestinal tract, mesentery, peritoneal wall
  - If not spontaneous then, embryo has to be removed surgically
- Uterine - tubal pregnancy (most common ectopic)

Early Placenta

- interaction between implanting conceptus and uterine wall (endometrium)
- The uterine lining following implantation (Decidua)
  - forms 3 distinct regions, at approx 3 weeks
  - **Decidua Basalis** - implantation site
  - **Decidua Capsularis** - enclosing the conceptus
  - **Decidua Parietalis** - remainder of uterus
- uterine cavity is lost by 12 weeks

Week 3 Gastrulation

Gastrulation, (Greek = belly) means the formation of gut, but has been used in a more looser sense to describe the formation of the trilaminar embryo. The **epiblast layer**, consisting of totipotential cells, derives all 3 embryo layers: **endoderm, mesoderm** and **ectoderm**. The **primitive streak** is the visible feature which represents the site of cell migration to form the additional layers. Historically, gastrulation was one of the earliest observable morphological event occurring in the frog embryo.

- **primitive node** - region in the middle of the early embryonic disc epiblast from which the
primitive streak extends caudally (tail)
  - nodal cilia establish the embryo left/right axis
  - axial process extends from the nodal epiblast
- **primitive streak** - region of cell migration from the epiblast layer forming sequentially the two germ cell layers (endoderm and mesoderm)

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**Notochord**

The **notochord** is a structure which has an early **mechanical role** in embryonic disc folding and a major **signaling role** in patterning surrounding embryonic tissue development. This signaling role patterns many different tissues (**neural plate, neural tube, somites, endodermal organs**). It has its own sequence of development from a primitive axial process and is a developmental feature not present in the adult anatomy.
- **axial process** an initial epiblast hollow epithelial tube which extends in the midline from the primitive pit, cranially in the embryonic disc (toward the oral membrane).
  - neuroenteric canal is a transient communication between the amnionic cavity and the yolk sac cavity formed by the axial process.
- **notochordal plate** forms from the axial process merging with the endoderm layer.
- **notochord** forms from the notochordal plate which then separates back into the mesoderm layer as a solid column of cells lying in the midline of the embryonic disc and running rostro-caudally (head to tail).
  - An alternate name for the notochord is "axial mesoderm".

**Somitogenesis**

Mesoderm means the "middle layer" and it is from this layer that nearly all the bodies connective tissues are derived. In early mesoderm development a number of transient structures will form and then be lost as tissue structure is patterned and organised. Humans are vertebrates, with a "backbone", and the first mesoderm structure we will see form after the notochord will be **somites**.

**Coelom**, meaning "cavity", and major fluid-filled cavities can be seen to form both within the embryo (intraembryonic coelom) and outside the embryo (extraembryonic coelom). The **intraembryonic coelom** is the single primitive cavity that lies within the mesoderm layer that will eventually form the 3 major anatomical body cavities (pericardial, pleural, peritoneal).

- neural tube and neural crest
Somite initially forms 2 main components

- ventromedial- sclerotome forms vertebral body and intervertebral disc
- dorsolateral - dermomyotome forms dermis and skeletal muscle

- sclerotome and dermomyotome
- dermatome and myotome
- epaxial and hypaxial muscles

Week 4 Neuralation

Ectoderm - 2 parts

- midline neural plate (columnar cells)
- lateral surface ectoderm (cuboidal cells)
- sensory placodes
- epidermis of skin, hair, glands, anterior pituitary, teeth enamel

**Neural Plate**

- extends from buccopharyngeal membrane to primitive node
- forms above notochord and paraxial mesoderm
- neuroectodermal cells
  - broad brain plate
  - narrower spinal cord
- 3 components form: floor plate, neural plate, neural crest

**Links:** Neural System - Abnormalities | Folic Acid and Neural Tube Defects

**Cardiogenesis**
The Human Heart from day 10 to 25 (scanning electron micrograph)

- forms initially in splanchnic mesoderm of prechordal plate region - **cardiogenic region**
  - growth and folding of the embryo moves heart ventrally and downward into anatomical position
- week 3 begins as paired heart tubes that fuse to form single heart tube
- begins to beat in Humans- day 22-23

**Blood Islands**

- 2 populations of cells
  - peripheral- form **endothelial cells** that form the lining of all blood vessels
  - core- form blood cells (**haemocytoblasts**)
- all vessels (arteries and veins) appear initially the same

**Blood Formation**

- blood formation from stem cells occurs initially in the **extraembryonic mesoderm of the yolk sac**
- then later (week 5) throughout embryonic mesenchyme
- blood stem cells then migrate into the liver
  - then spleen, bone marrow, lymph nodes

**Red Blood Cells**

The only cells in the blood are nearly entirely fetal red blood cells (RBC).

These red blood cells differ from adult red blood cells in:

- often remaining nucleated
- contain **fetal haemoglobin** - has different oxygen and carbon dioxide binding characteristics

**Links:** Basic Cardiac Embryology

**Early Placentation**
The trophoblast layer has now differentiated into two morphologically distinct cellular layers.

- **Syncytiotrophoblasts** - form a multinucleated cytoplasmic mass by cytotrophoblast cell fusion and both invade the **decidua** and secrete **hCG**
- **Cytotrophoblasts** - form a cellular layer around the **blastocyst**, proliferates and extends behind syncytiotrophoblasts

Early Utero-Placental exchange - transfer of nutrition from maternal lacunae filled with secretions from **uterine glands** and maternal blood from blood vessels. The development of trophoblast villi extending into the uterine decidua.

There are three stages of villi development:

1. **Primary Villi** - cytotrophoblast
2. **Secondary Villi** - cytotrophoblast + extraembryonic mesoderm
3. **Tertiary Villi** - cytotrophoblast + extraembryonic mesoderm + blood vessels

   - Primary chorionic villi
   - Tertiary chorionic villi
   - Placenta anchoring villi

There are two main types of early villi:

- Anchoring villi - attached to **decidua**
- Floating villi - not attached to **decidua**, floating in maternal **lacunae**.

**BGDA: Lecture 1** | **Lecture 2** | **Practical 3** | **Practical 6** | **Practical 12** | **Practical 14** | **Histology Support**
- Female | **Tutorial 2011**

**Glossary Links**

A | B | C | D | E | F | G | H | I | J | K | L | M | N | O | P | Q | R | S | T | U | V | W | X | Y | Z |
Numbers | Symbols
