TOPIC 1: Introduction to Embryology

Learning Objectives

- Understand that embryogenesis is a complex process
- Be able to define factors and influences which can disrupt normal embryonic / fetal development
- Understand the meaning of a 'critical period' in embryogenesis / fetal development
- Name some factors that can adversely influence this process
- Understand the process of fertilisation in mammals

Why Study Embryology

- Embryology offers an understanding of the development, structure, final form and relationships of tissues and organs
- Developmental defects and associated signs can be more clearly understood through the knowledge of the factors which control developmental processes and the effects that environmental teratogens can have on normal development

Understanding Normal Embryogenesis

- Embryogenesis is a remarkable and complex process driven by evolutionary, genetic, epigenetic and environmental factors
- Involves discrete coordination of complex biological and cellular processes many instances where it can go wrong
- These processes are fundamental to our understanding of disease, regeneration and repair during the post-natal period (juvenile to adult)
- Desirable outcome is a normal foetus, delivered alive but does not always occur
- Errors in the sequential steps normally giving rise to a normal embryo/foetus can result in:
    - Embryonic loss
    - Fetal death
    - Fetal mummification
    - Abortion
    - Stillbirth
    - Birth of nonviable neonates
    - Or birth of viable offspring with defects
    - Understanding the processes which give rise to a normal foetus is critical to understanding how these abnormalities occur

Factors Influencing Embryogenesis

- Embryogenesis is a multifactorial process
- Congenital - a developmental disruption results in a deviation from normal that is present or apparent at birth
- Genetic, environmental (nutritional), physical and infectious agents have all been defined as etiologic, determinants
- Can be multi-factorial

Biological molecules that can affect growth and development in the adult and embryo

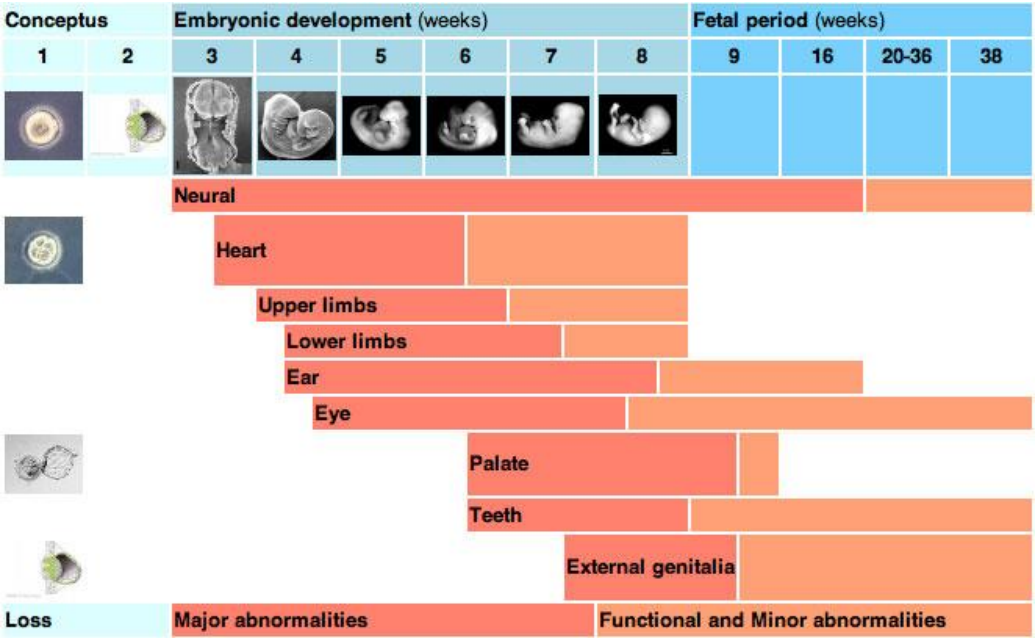
- Carcinogens: agents or factors that initiate or induce neoplasia/carcinogenesis
- Mutagens: agents or factors that produce a change in the genetic code of an organism
- Tetratogens: agents or factors that cause the development of physical defects in the embryo or foetus
- Some chemicals/agents can be one, two or all of the above

Factors affecting normal embryonic and foetal development

- Teratogens: agents or factors that cause the development of physical defects in the embryo or foetus
    - Teratogenic effects on the embryo/foetus: windows of susceptibility
- Early embryogenesis: teratogens primarily cause effects on DNA – mutations at a genomic or chromosomal level
- Mid embryogenesis/early foetal: effects on cell proliferation, differentiation or cell death
- Late foetal: most tissues relatively protected, only highly proliferating tissues still susceptible

Critical periods of sensitivity to external/internal factors affecting development

- Factors include: teratogens, environment, genetic, mechanical
- Systems that take the longest to develop, or are most complex, generally exhibit most severe effect



Common congenital defects of domesticated animals

Name	Presentation	Teratogen
Amelia	Absence of a limb or limbs	*Nicotiana tabacum*
Arthrogryposis	Persistent flexure or contracture of a joint or joints	*Sorghum* spp, *Lupinus* spp
Brachygnathia	Abnormally short lower jaw	*Nicotiana tabacum*, locoweed toxicity
Cerebellar hypoplasia	Loss or reduction of neurons of the cerebellum	Bovine diarrhoea virus (cattle), panleukopenia virus (cats)
Cheiloschisis	Abnormal division of the lip (harelip)	Vitamin A deficiency

Cyclopia	Fusion of the facial midline and formation of a single eye and orbit	*Veratum californicum* (day 14 of gestation only)
Hemimelia	Absence of all or part of the distal half of a limb	Thalidomide
Hydranencephaly	Virtual absence of cerebellar hemispheres and replacement by cerebrospinal fluid	Bovine diarrhoea virus (BDV, Pestivirus)
Microcephaly	Abnormally small cranium	Maternal phenylketonuria (high levels of phenylalanine)
Microopthalmia	Abnormally small eye	Vitamin A deficiency
Palatoschisis	Fissure of the palate (cleft palate)	Vitamin A excess, *Lupinus* spp.
Polydactyly	Supernumerary digits	
Prognathia	Marked projection of the lower jaw	Bluetongue virus
Scoliosis	Lateral deviation of the spinal axis	*Conicum maculatum* (hemlock), Akabane virus

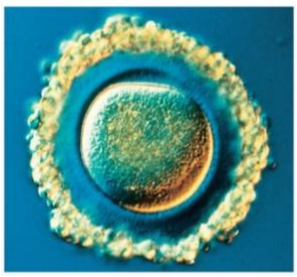
Physical causes of embryonic/foetal abnormalities

- Physical effects during gestation can also cause embryonic or fetal abnormalities
- Congenital joint contracture can be cause by in-utero crowding
- Spinal deformities and limb abnormalities can present in foals following a transverse or caudal presentation
- Aggressive palpation for pregnancy diagnosis can result in limb deformities or disruption of the delicate vascular supply to the intestinal tract (atresia coli)

So where does this start?

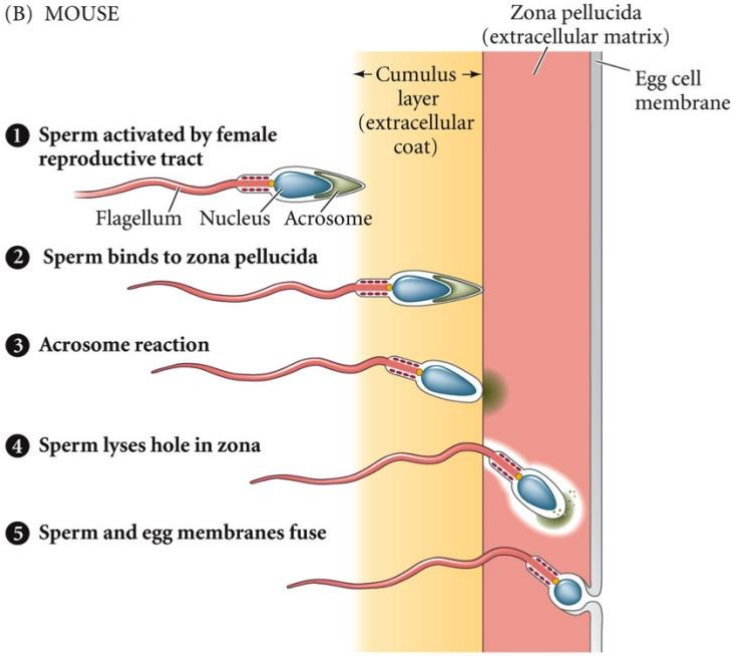
Fertilisation

- Fertilisation: the process whereby a spermatozoon and an ovum fuse to form a single-celled zygote
- When it leaves the ovary, the egg is surrounded by accessory follicle cells
    - These cells, now call the corona radiata, form a barrier between the sperm and the egg
    - A second barrier, the jelly-like zona pellucida ('clear area'), lies between the corona radiata and the egg
- In the uterine tube, hundreds of sperm reach the egg and encircle the corona radiata



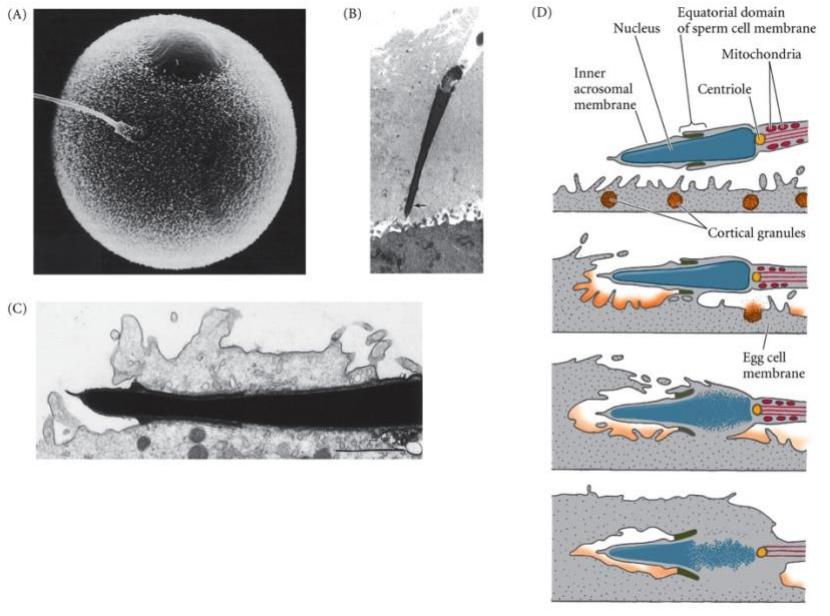
- In order to fuse it's genetic material with the egg, the sperm must transit through the thick outer coating of the egg (the zona pellucida)
- To achieve this each sperm releases enzymes from its acrosome
    - These enzymes weaken both the corona radiata and the zona pellucida, allowing the sperm to wiggle through to the egg
    - If there aren't enough sperm, not enough enzyme is released, and none of the sperm will reach the egg
    - When the first sperm finally contacts the egg's surface, the plasma membrane of egg and sperm fuse, and the sperm's head is drawn into the egg cytoplasm

Events leading to cell membrane fusion of egg and sperm during fertilization



DEVELOPMENTAL BIOLOGY, 9e, Figure 4.8 (Part 2)

Entry of sperm into a golden hamster egg



DEVELOPMENTAL BIOLOGY, 9e, Figure 4.34

- Scanning EM micrographs – fertilisation occurs near the equator of the egg in A

Fertilisation

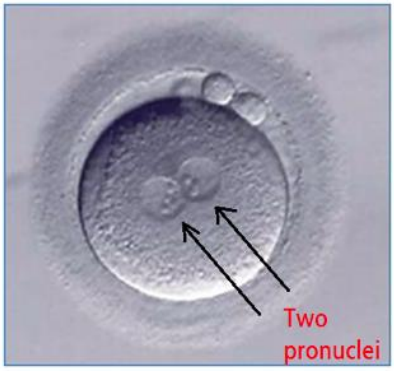
- As the sperm enters, it triggers two critical changes
    - First, vesicles near the surface of the egg release chemicals into the zona pellucida that reinforce it and prevent additional sperm from entering
    - Secondly the egg has been held in a dormant state until fertilisation (that is: no cell division or replication of genetic material has occurred since the germ cell was laid down in the embryo)
    - In order for embryogenesis to proceed the fertilised ovum must be 'activated'
    - This occurs after fusion of the sperm head to the cell membrane of the ova (egg)
- Results in a series of calcium 'waves' which finally results in:
    - reactivation of the genetic material of the ova;
    - a resumption of proliferation;
    - release of inhibition of the maternal genome;
    - exocytosis of the male and female pronuclei

Summary

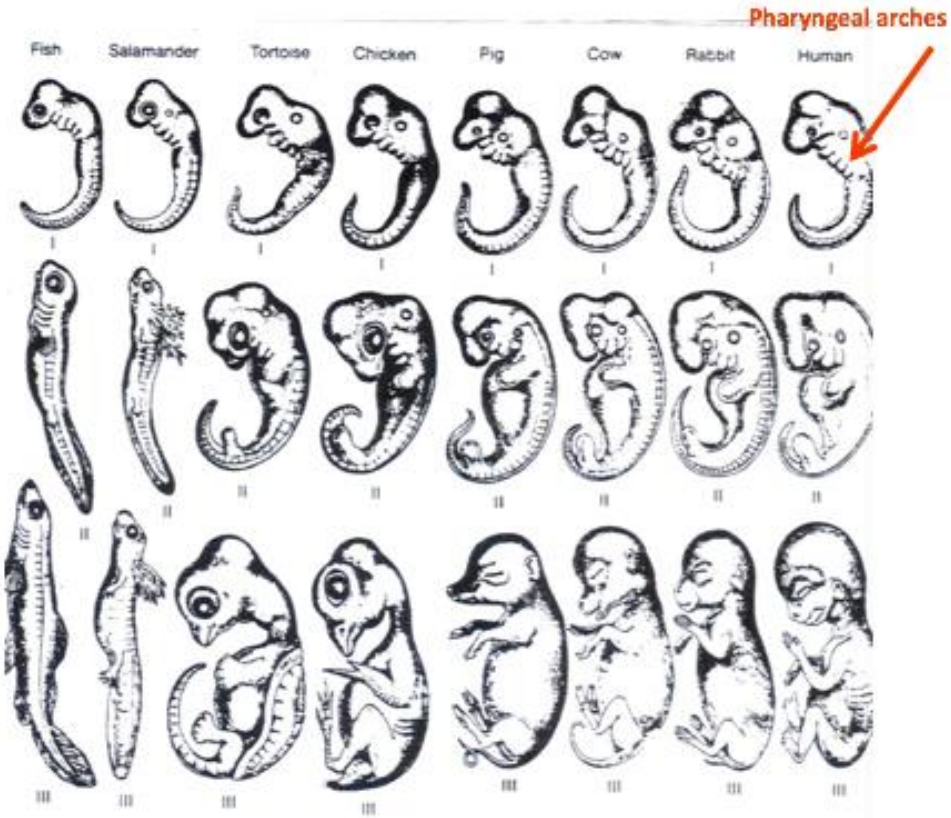
- Fertilisation occurs by a process of chemo-attraction between sperm and ova, an interaction that proceeds in a 5 step process:
    1. Sperm is attracted to the egg by secretion of soluble molecules from the egg itself
    2. Exocytosis occurs from the sperm acrosomal vesicle to release degrading enzymes
    3. The sperm binds to the extracellular matrix surrounding the egg (zone pellucida in mammals)
    4. The sperm passages through the extracellular matrix
    5. Cell membranes of the eggs and sperm fuse – fertilisation and a zygote is produced.

Regardless of species, all embryos start from the same place, the fertilised zygote

- The pronuclei represent the genetic material of the fertilized zygote, one of maternal and one of paternal origin



- Structural similarities exist between all species during early embryogenesis
- Evolution, environment and genetics drive species specific differences in development during gestation and beyond
- Note: the number of pharyngeal arches of all these embryos is the same



Haeckel's ABC of evolution and development." *Biological Reviews*. Cambridge *Philosophical Society*. 2002 Nov; 77(4):495-528
From an original drawing in Mayr's 'What Evolution Is'. 2001.