ORGANOGENESIS

The next stage in development – make tissues and organs.

Since the nervous system is very complex, in most animals and especially vertebrates development of the nervous system is one of the earliest organ systems to take shape.
One instruction to cells, based on where they are born, is to migrate and divide. This causes gross feature development like the neural crest.

**FORMATION OF NEURAL TUBE**

1. Notochord forms from mesoderm cells soon after gastrulation is complete.
2. Cells in and near notochord induce the formation of the neural tube (and other structures along dorsal side of embryo).
3. Formation of neural tube is complete. Cells of notochord are fated to die.

The neural crest is itself an organizer region for the further development of the nervous system.
Neural tube of a chick embryo
Transplantation experiments can show when cells become committed to a particular phenotype, in this case muscle.

These cells are not yet committed, so a cell that would turn into skin based on its original location, is still controllable.

When transplanted its fate switches to become muscle.
Later in development, muscle cells “know” they are muscle cells and cannot be told otherwise via transplantation.
Local gradients of factors specify the fate of cells

Signals from neural tube

Signals from dorsal ectoderm

Signals from mesoderm at side of embryo

Signals from notochord
Cells committed to be muscle cells start making muscle-specific proteins, including soluble trophic factors that are attractants for the outgrowth of axons from embryonic motor neurons.
Every muscle cell in a muscle must receive one and only one axon branch from a neuron.

One neuron may connect to more than one muscle cell.

No muscle cell can be left without an axon connection

No neuron can be left without at least one muscle cell that it controls.

How does the developing nervous system fabricate such a precise arrangement?
Many more neurons are made during development than are needed.

Only neurons that make functional connections to muscle cells receive a trophic factor to abort a self-destruct (apoptosis) program built into the neuron.

When a neuron runs out of time, it will scuttle itself.
Some milestones and the sequence of organ development in humans:

Some organ system develop completely in the prenatal period.

Examples – ears, heart, skeleton

However, this does not mean that there is not continued growth after birth!

Different “prenatal” organs complete development at different times.

The heart is fully formed and functional by week 8, ears not until 16 weeks, yet both start within one week of each other.
Some milestones and the sequence of organ development in humans, cont'd:

Organ systems late to complete:

- central nervous system
- immune system
- lungs
- reproductive system

...and some of these complete postnatal:

CNS – not completely functional until age 20.

immunocompetence poor for 1st year after birth; continues to improve until age 18.

more than 80% of lung alveoli are formed after birth, not complete until age 10.
Toxins and disease are more critical early in development.

In the early stage of organogenesis (4 to 16 weeks), toxins are typically lethal – organs too messed up. Effects lessen as development progresses.

Example:

Rubella infection at 10th week → heart defects and deafness

Rubella infection at 17th week → deafness but no heart defects
Discussion point: The FDA has been criticized for slow adoption/ approval of new drugs...

1950's – thalidomide tested for use as an anti-nausea drug for pregnant women.

1. Animal studies at therapeutic doses – no adverse effects.

2. Multi-generational studies in animals – no adverse effects.

3. Multi-generational studies in animals at much larger than therapeutic doses -
   no adverse effects.

4. Therapeutic doses in human trials – no toxicity observed.

Thalidomide interferes with angiogenesis – the formation of new blood vessels.

Of course this means limb growth cannot progress.

But now thalidomide is being tested as an anti-cancer therapy (growing tumors release tissue angiogenesis factor to promote vascularization).
Common bad practices during pregnancy

- alcohol → fetal alcohol syndrome
- cocaine → brain defects
- smoking → reduced birth weight, incr probability of SIDS
- exposure to solvents & pesticides...

Organophosphate insecticides are “teratogens” in animal studies.

Humans: Birth defects higher in agricultural areas with heavy pesticide use.

Discussion point: What might be inconclusive about the agricultural studies?
messing around with development…

Brain sections from newborn rats injected with saline versus ethanol

Brain injected with saline

Brain injected with ethanol

Black specks indicate degeneration of neurons

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Weights of brain tissue from newborn rats injected with saline versus ethanol

- **Saline**
  - Whole brain
  - Forebrain, midbrain
  - Cerebellum

- **Ethanol**
  - Whole brain
  - Forebrain, midbrain
  - Cerebellum

**Weight (g)**
- 1.25
- 1.00
- 0.75
- 0.50
- 0.25
- 0.00
And then there is lead ingestion by kids.

Is lead toxic?

Not so much for adults, but a problem for kids when the nervous system not fully constructed.

What does it do?

Lead ions swap for calcium ions, but in neurons (in particular) the lead ions not work the same way.

Sub-functional neurons engage their apoptosis mechanism.

So you get kids with too few neurons == “developmentally challenged”.
Back to development mechanisms:

The developing embryo needs nutrients, and builds up waste. How is this handled?

**Simpler aquatic organisms** - minimal yolk, make a self-feeding embryo as quickly as possible.

**More complex organisms** - take longer to assemble. This means more yolk. Must build a vascular supply to transport nutrient from yolk to embryo, and transport waste to…?
The fanciest eggs have a series of “extra-embryonic” membranes. These are the eggs of “amniotes”: mammals, birds & reptiles.
Functions of the membranes

Shell: Like Goretex – permeable to respiratory gases only (& water vapor), so no dehydration.

Amnion: Surrounds the embryo itself. Filled with amniotic fluid. Cushions embryo.
Functions of the membranes

**Chorion**: lines inner surface of egg, vascularized for gas transport.

**Allantois**: 1. Nitrogen waste storage. The adult urinary bladder grows from the base of the allantois. 2. Gas transport.

**Yolk sac**: contains yolk, vascularized for transport of nutrients.
Mammals inherit the amniote egg from reptiles:

**Monotremes** – lay eggs

**Marsupials** – no egg, but the embryo does not implant

**Placental mammals** (94% of class Mammalia) – placenta derived from extra-embryonic membranes
Chorionic villi (old chorion membrane) bury into the uterine endometrium to form the placenta.

Gas exchange still a primary function.
Villi increase exchange surface area: in humans at 7 weeks the placenta is 7 inches in diameter, but with a surface area of 140 square feet!
The yolk sac – no longer has yolk. It now is a source of blood stem cells (they later migrate into the embryo).

The allantois (was waste storage, bladder) becomes the umbilical cord.
Enhancing the transport efficiency of the placenta

Countercurrent blood flow in the placenta

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We will see this again, more detail, in upcoming lectures.
After development is finished, young are hatched.

Internal brooding in many groups of animals:
  mouths (some fishes)
  pouches (marsupials, sea horses)
  modified part of oviduct (mammals, some reptiles)

If eggs are laid: **oviparous**

If internal brooding:
  -- **ovoviviparity** = complete dependence on yolk nutrients.
  -- **viviparity** = complete dependence on placenta for nutrients.

Note: ovoviviparity in many invertebrates, in some sharks, lizards, snakes.
(a) Some *Sceloporus* lizards lay eggs; other members of the same genus bear live young. Theory that selection favors a mutation that leads to longer egg retention in the body…

…if in a cold temperature environment.

(b) Phylogeny of *Sceloporus* from central Mexico

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Placental development can accommodate more than one embryo

Dizygotic (fraternal) twins: Genetic relatedness is the same as any sibling.

Monozygotic (identical) twins: Share genome