Gastrulation

1. **GASTRULATION is a complex series of cell movements that:**
   a. rearranges cells, giving them new neighbors. These rearrangements put cells in a new environment, with the potential to receive new signals.
   b. results in the formation of the 3 **GERM LAYERS** (do not confuse with germline) that will form most of the subsequent embryo: ECTODERM, ENDODERM and MESODERM.

2. **While all animals gastrulate, gastrulation can seem very different in different organisms** (mostly due to geometric differences due to yolk content and distribution), but like cleavage the similarities in terms of mechanism and outcome suggest that the same controls operate across species.

3. **Changes in the shape or adhesive properties of single cells in concert can rearrange the entire embryo.**
   a. Cell shape changes, mediated by cytoskeleton lead to indentation of a flat sheet of cells, which can then lead to invagination of a tube or ball of cells.
      • Contraction of the adhesion belt
   b. Other changes in cellular shape drive elongation or shortening of a flat sheet of cells - Can provide motive force for complex rearrangements.
   c. Cells can alter their surface proteins & thus alter relative stickiness to different groups of neighbors or to ECM secreted by those neighbors. Changes in adhesion lead to cell migrations etc.

4. **Changes in cell shape or adhesiveness occur in specific regions of the body.** i.e. individual cells have individual identities or fates very early

5. **Just as with cleavage, if we understand the possible ways cells can move and rearrange, we can mix and match to get gastrulation in different organisms.**
   a. **Individual cells move by:**
      i. MIGRATION - movement of individual cells over other cells or matrix
      ii. INGRESSION - movement of individual cells or small groups from an epithelium into a cavity
   b. **Groups of cells move by:**
      i. INVAGINATION - local inward buckling of an epithelium
      ii. INVOLUTION - inward movement of a cell layer around a point or edge
      iii. EPIBOLY - spread of an outside cell layer to envelop a yolk mass or deeper layer
      iv. DELAMINATION - splitting 1 cell sheet into 2 or more parallel sheets.
      v. CONVERGENT EXTENSION - elongation of a cell layer in one dimension with shortening in another

6. **Gastrulation in the sea urchin embryo, a "simple" example.**
   a. We start with a single-cell thick hollow ball of ~1000 cells, surrounding the central blastocoel cavity.
   b. First actors- **primary mesenchyme cells** (descendents of micromeres).
i. Lose adhesion to immediate neighbors and the hyaline layer & gain affinity for the basal lamina and extracellular matrix on the inside of the sphere, which leads to detachment from the epithelium at vegetal pole (ingression) & crawling along inside of blastocoel like amoebae (migration).

ii. Migrate along the extracellular matrix using filopodia to detect chemical cues.

iii. Home in on special places in the interior, where they apparently have a higher affinity for the surface.

iv. These cells go on to fuse and form the spicules made of calcium carbonate that serve as the larval skeleton (this is a mesoderm cell fate).

c. Apical constriction and changes in the extracellular matrix create a **dome-shaped invagination** at the vegetal pole.
   
i. Invagination = archenteron (primitive gut), opening = blastopore
   
   ii. Cells change shape (ends facing the blastocoel enlarge while apical end contract) driving a dome-shaped invagination.
   
   iii. The extracellular matrix changes: secretion of sulfated proteoglycans (CSPG’s) into inner lamina of hyaline layer critical, sulfated proteoglycans absorb water and cause swelling, which in turn causes inward buckling.

d. Convergent extension **extends dome (archenteron) into long tube** = primitive gut.

e. **Secondary mesenchyme cells** at the leading edge reach out with filopodia, apparently looking for place where they’re programmed to adhere, and draw the gut tube to this position.
   
   • These secondary mesenchyme cells go on to form muscles. (mesoderm)

f. End of the tube fuses with the surface epithelium to form the MOUTH. The original site of invagination forms the ANUS. The tube that makes up the gut =endoderm.

g. Entire gastrulation process takes as little as 9 hours in this type of sea urchin!

2. **Frog gastrulation: Similar to the sea urchin, but more complex.**

   a. Frog eggs differ from sea urchin in many ways. Most obvious at **vegetal pole.** The blastula is not a hollow ball of cells, but is a **solid hemisphere** of yolky cells.

   b. Like sea urchin, frog blastula have a blastocoel. **Functions of the blastocoel.**

   c. **One way to understand gastrulation is to look at a “fate map”** that shows what the progeny of cells present NOW will become LATER. In frogs this shows that all **outside cells** of the blastula will form ectoderm or endoderm, while the mesoderm will form from **inside cells.** Again, compare this situation to a fate map of the sea urchin blastula, where all these three tissue types are generated from outside cells.

   d. **Gastrulation starts by invagination of marginal endoderm cells to form the BLASTOPORE LIP.** This occurs 180° opposite from the point of sperm entry, near the equator of the embryo. The invaginating cells are called BOTTLE CELLS and have a distinctive shape. Just as we saw with the dome-shaped invagination of the archenteron during sea urchin gastrulation, **apical constriction** drives invagination of the blastopore here. The cavity that forms here is also the **ARCHENTERON.**

   e. **Next, the MARGINAL ZONE CELLS (cells at the junction between the animal and vegetal hemispheres) begin involution at 2 levels:**
      
      i. the **outside cells** involute to form the roof of the archenteron, which will form the **endoderm**
      
      ii. the **deep or inside cells involute** to form **mesodermal derivatives.** This movement is dependent on **fibronectin in the extracellular matrix,**
which is secreted by the ectoderm of the blastocoel roof shortly before gastrulation. This was determined by an experiment that involved injecting a synthetic fibronectin peptide competitor into the blastocoel. The mesodermal precursor cells bind the synthetic fibronectin competitor so can’t recognize the normal fibronectin-lined traffic route along the blastocoel roof. The archenteron fails to form and these mesodermal precursors remain at the surface.

f. The dorsal mesoderm undergoes **convergent extension** starting halfway through gastrulation. This pushes the blastopore lip ventrally.

g. The ANIMAL CAP (ectoderm) spreads over the embryo by **epiboly**, converging at the blastopore.

h. **Mesenchyme migration**: mesodermal cells crawling along inner surface of animal pole (ectoderm) presumably via interactions with extracellular matrix.

3. **The three germ layers formed by gastrulation will produce all of the embryonic structures except the germ line.**
   a. The ECTODERM is the most external layer and will produce skin & through later invagination of neural tube---> **central nervous system**. In vertebrates, migrating neural crest cells---> **peripheral nervous system & many other structures**, including some bone, cartilage, and connective tissue in the head.

b. The MESODERM is the middle layer and will produce muscle, connective tissue, bones, blood and blood vessels. In vertebrate also --> **notochord** (progenitor of vertebrae), **bones & cartilage, circulatory and urogenital systems** (kidneys, gonads).

c. The ENDODERM is the inner layer and will produce the gut (entire digestive tube from mouth to anus) and internal organs such as liver, lungs, pancreas. Also --> organs that arise as outpocketings of gut in vertebrates= **lungs, liver, pancreas, salivary glands**.

4. **Human gastrulation**
   a. Major modification in mammalian development results from the need for a connection to mom.

b. Within the blastocyst, only inner cell mass will become the embryo. **Trophoblast cells** cells go on to make the placenta, chorion, amnion.

c. Inner cell mass gastrulates **AFTER** formation of placental connection to mom.

d. **Epiblast** cells move into primitive groove to form the mesoderm and endoderm. **What are the cell movement(s) involved?**