WEEK 2 – From conception to birth

Describe the formation and structure of human gametes and the process of fertilization.

Describe the main methods of assisted conception.

Describe the processes of normal human development in utero, including cleavage, compaction, blastula formation, implantation, gastrulation, neurulation and early organogenesis.

Describe the mechanisms that give rise to unusual features or abnormalities of human development, including twinning (incl. conjoined and transfusion syndrome), axis duplications, spina bifida, anencephaly, fetus in fetu, cleft palate, phocomelia and intersex phenotypes.
At the end of the last lecture, the embryo had undergone gastrulation, giving it:

* a 3-Cartesian-axis coordinate system
* a body elongated along the cranio-caudal axis
* the 3 basic layers of the body – ectoderm, endoderm and mesoderm.
Last time, I presented the vertebrate body as a tube within a tube.

This was an oversimplification: there are actually two tubes inside, one open (the gut) and one closed (the central nervous system);

The CNS tube derives from the Ectoderm.
CNS formation begins when the ectoderm along the dorsal surface folds inwards, driven by local cell shape changes along three stripes;
These cells become wedge-shaped with a narrow base. Inward push due to cell proliferation helps bringing edges together.

So tissue folds…
Much later, cells in the neural tube send out processes to each other and to other structures in the body. Bundles of such processes are nerves, and together the processes and the cells make the nervous system (more about this in Year 2).
The sealing up of the edges of the tube, and its separation from the ectoderm, sometimes fails:

This is the exposed inside of the spinal cord: this is not a dissection but 'as it comes'.

Spina bifida (a very serious case)
The sealing up of the edges of the tube, and its separation from the ectoderm, sometimes fails:

Anencephaly (the inside of the brain is open to the back of the head: this stops brain growth so the upper-back head is effectively missing. Incompatible with post-natal life).

Spina bifida (a very serious case)
Neural tube closure can create other (very rare) abnormalities.

Slightly delayed twin is caught inside closing folds of neural tube.

NB: this is not a micrograph of the event happening: I have simply combined two micrographs and drawn some arrows on to indicate what might be the mechanism. This is so rare that we have little more than guesswork.
This creates one form of fetus-in-fetu

A real case:

This very dark and very light mess is the unusual thing (the fact that the ventricles in the whole brain look like a little man upside-down is coincidence – ignore this).

Another photo from a web search (NB: I have not seen the case report for this and cannot therefore be certain that the photo is real and not a clever fake).

Cultural reference: Tom Waits' *Poor Edward*

*Did you hear the news about Edward?*  
*On the back of his head he had another face*  
*Was it a woman's face or a young girl?*  
*They said to remove it would kill him*  
*So poor Edward was doomed ....*

http://www.youtube.com/watch?v=xrbddZuN_8Q&feature=related
Segmentation:

Humans are too, but you have to look on the inside to see it:

Earthworm (whole body)  Human (spinal column)

Cervical vertebrae
Thoracic vertebrae
Lumbar vertebrae
Sacral vertebrae (fused to make the sacrum)
Coccyx
You can see the signs of segmentation on the outside in cases of 'Shingles' (from Lat. *Cingulum* = 'belt' or 'girdle'): re-activation of Varicella Zoster virus that has been dormant in the sensory ganglia that each serve one segment of the body.

(these images are all different people)

Image Credits: NIH Health (Creative Commons)
Segmentation is first seen when the mesoderm each side of the midline divides itself into somites: precursors of vertebrae (in a complicated way), and also of skeletal muscle and skin).
Here's how it works
(not on the exam syllabus – I just want to give you a taste of a real mechanism)

(Head end)

(Tail end)
FGF made here

RA made here

Just-formed somites

FGF made here

Cells here become committed to make a somite

New somites

(Embryo keeps growing)

Cells here become committed to make a somite

FGF

RA

FGF

RA

FGF

RA

New somites

…"tock"…

"tick"

…"tock"…

TIME

Expression of "permission gene" in clock
Once the somites have formed, the body makes more internal differences.

In early embryogenesis, it dragged in information from the 'outside' (free surface) to make what was homogenous acquire differences.

Now that there are some internal differences, the embryo can use them to make more.
The diagrams below look down on this 'cut' through the trunk of an embryo

(upper trunk and head removed)

tail

ectoderm  Neural tube

somite  SHH spreading from notochord

notochord

SHH now made by, and spreading up from, the floorplate
(Don't try to remember the protein names – just get the general point about how signals from a neighbour can pattern a tissue)

This wedge shape depicts the SHH building up (width of wedge) in floorplate and spreading dorsally (length of wedge).
We can prove this experimentally:

NORMAL:

EXTRA:

MISSING:
SHH and Noggin from notochord and floorplate

Wnt (short range)

NT3 (long range)

Wnt & BMP4 → muscle → dermis

→ bone etc

SHH and Noggin from notochord and floorplate

(Again, don't try to learn the protein names – just take away the general picture)
This kind of thing happens again and again: every time one difference is used to make a new cell type, two new borders are generated and two more opportunities to play the same game;

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AAAAAAAGGGG

AAAAADGGGGG

AAADDDDDGG

AABCDDDEFG
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So far, we have been considering cells that stay put.

Some move:
Your face came from the back of your head:
Here's a problem for you:

This image shows conjoined twins. The bodies face each other, but (as you can see) a face looks out at you, at right angles to the bodies. There is an identical face round the back looking the opposite way.

Easy question: when in development must the twinning have occurred, and how?

Hard question: why do the two faces point at right angles to the bodies, and what deep truth about facial organization might this reveal?
Another problem for you:

Easy question: what is this condition called?

Slightly harder question: what does this tell you about the formation of the ventral body all.

Can you relate what you just deduced above to what you already know about the embryo?
Surgeons prepare to operate... unaware of the full scale of the horror they're dealing with. Dr Mehta and his team begin to operate and soon it becomes clear they're not dealing with any tumour. They cut into the mysterious lump and out gushed gallons of [fluid] to reveal a strange, almost human, shape within. Dr Mehta relates "To my surprise and horror I could shake hands with someone inside".

Inside Sanjay's belly is the half-formed body of an infant boy. Dr Suchitra Mehta tells us "The feet and hands were well developed. It had fingers and nails; the nails were quite long".

Source of quotations: UK Channel 5 Extraordinary People
Another photo from a web search (I have not seen the clinical reports and do not know for sure that this is real and not a clever fake).
A much more common problem with ventral body wall closure is spilling out of abdominal contexts (operable).
Another place that needs to be 'sealed up' is the secondary palate: this often fails.
If you are interested in finding out a lot more about how embryos organize themselves, you can do an honours year in Anatomy and Development.