TRANSCRIPTIONS OF NARRATIONS FOR EARLY EMBRYOGENESIS - WEEK 3

Week 3, slide 2
This is where we left off last time, median sagittal section at the end of the second week of development. We see the sphere of cytotrophoblast and within it two smaller spheres, one formed by the amniotic cavity with its roof, side, walls and floor, and one formed by the yolk sac with its roof, side, walls and floor. They are not really spheres because the floor of the amniotic cavity is flattened as is the roof of the yolk sac, the two of these things forming together the embryonic disk. The cranial end of the embryo is to your left. That's where the prochordal plate is. The caudal end of the embryo is to your right, that's where the primitive streak is. And I also want to remind you that the somatic layer of extraembryonic mesoderm is in continuity with the visceral layer of extraembryonic mesoderm only in the region of the connecting stalk. Now you know that the cytotrophoblast is producing syntrophoblast and those things are going to be part of the placenta. And the connecting stalk is now the only path by which something can readily travel from the placenta to the region of the embryonic disk.

Week 3, slide 3
This is just looking down onto the top of the embryonic disc - onto the epiblast layer. We see the zone of proliferation caudally, which is the primitive streak; all the rest is non-proliferating epiblast. And I've indicated by a circular patch that region where columnar hypoblast is tightly adherent to non-proliferating epiblast, i.e., the region of the prochordal plate.

Week 3, slide 4
And now back to the median sagittal section, indicating that the next slide will be a transverse section through the region of the primitive streak.

Week 3, slide 5
We saw this last lecture, there's no real reason to discuss it. Except I want to remind you that surrounding the visceral extraembryonic mesoderm of the amnion and yolk sac is that space called the extraembryonic coelom, I've labeled it here. I have not colored it blue but you should remember that it is indeed filled with fluid, and probably in many slides I will not remember to color it blue, but that doesn't change its contents.

Week 3, slide 6
This is that same section a few hours later, and what we see is that cells from the zone of proliferation, that is the primitive streak, are actually leaving that zone and insinuating themselves between epiblast and the cuboidal hypoblast that forms the roof of the yolk sac. Now, in the region of the prochordal plate, the columnar hypoblast is tightly adherent to epiblast and nothing can insinuate itself between those layers. But elsewhere it's quite easy for these cells that have originated from the primitive streak to push their way in between cuboidal hypoblast and overlying epiblast.

Week 3, slide 7
And now it's even a few hours later, and the migration of cells out of the zone of proliferation is so rapid that it's as if the actual primitive streak has been sucked down and sort of a pit has formed along its dorsal aspect. It's a linear pit it and so it's called the primitive groove. The proliferating zone itself has become narrower as the cells are piling out of it at a very rapid rate. When we go to the top view, you'll see that the zone of proliferation is actually more in the shape of a streak than it was previously.

Week 3, slide 8
But before we do anything else, I want to give a new name to these cells that are derived from the primitive streak and insinuating themselves between non-proliferating epiblast and the hypoblast of the roof of the yolk sac. These cells are called intraembryonic mesoderm cells. I've colored them pink because we always color mesoderm pink in embryology. The extraembryonic mesoderm is also colored pink but the source of the extraembryonic mesoderm is very, very different from the source of the intraembryonic mesoderm. The latter is all derived from the primitive streak.

Week 3, slide 9

This is that same cross-section even a little bit later and we see that the creation of intraembryonic mesoderm has progressed so far that it has now insinuated itself everywhere between epiblast and the hypoblastic roof of the yolk sac. That is, everywhere except the region of the prochordal plate. That region is not in our section, but everywhere else, other than the prochordal plate, intraembryonic mesoderm now has separated epiblast from hypoblast of the yolk sac. Indeed, it has spread so far laterally that it contacts the cells of the extraembryonic mesoderm. I didn't draw in cell boundaries for the extraembryonic mesoderm, but they exist. If you were to look at any particular cell out in this region, you'd be hard pressed to say if it was derived from intraembryonic mesoderm or extraembryonic mesoderm. All along I've been applying the same green color to the proliferating epiblast of the primitive streak, to the non-proliferating epiblast that lies lateral to the primitive streak, and to the amnioblast. But now in the next slide I'm going to start changing colors because these cells have different fates.

Week 3, slide 10

I've kept that green color for that zone of proliferating epiblast that is the primitive streak, and is the source of intraembryonic mesoderm. The non-proliferating epiblast, which lies lateral to the primitive streak, I've changed to a blue color, and I've also given it a new name. I call it now 'ectoderm'. It has a different fate than do the cells of the primitive streak. And the amnioblast, which forms the sidewalls and roof epithelium of the amniotic cavity, are colored blue. They have a fate that in some ways is similar to the ectoderm.

Week 3, slide 11

Now I want to mention a detail that I wouldn’t hold you responsible for, but I mention it because it’s true and you may read about it. Some of the epiblast cells do not enter and form intraembryonic mesoderm. Instead, they move into the roof of the yolk sac, where they insinuate themselves, and push hypoblast cells out of the way.

Week 3, slide 12

These primitive-streak-derived cells that are moving into the roof of the yolk sac, and pushing hypoblast out of the way, are called endoderm cells. They get a different name because they have a very different origin. Eventually, the entire roof of the yolk sac will be comprised of endoderm cells. All of the hypoblast will have been pushed out to the sides.

Week 3, slide 13

This is a familiar shot of Dr. Larson looking down onto the top surface of the embryonic disc, but now I've made it clear that the non-proliferating epiblast cells which we now call ectoderm will have a different fate from the primitive streak. I've colored the ectoderm blue and it is contiguous with the amnioblast cells which are sweeping up to form the sidewalls of the amniotic cavity.

Week 3, slide 14

This very attractive slide indicates what Dr. Larson or you would see if you look down onto the top of the embryonic disk. We are still early in the third week of development, very early. Number one you see that the primitive streak is in fact confined to a more or less midline structure in the caudal half of the embryo. We see the mechanically produced primitive groove down the middle of the primitive streak. We see that up at the cranial end of the primitive streak (this zone of proliferating epiblast), there is like a knob of proliferation, which is called the primitive node or Hensen's node. And it has its own mechanically produced depression, which is called a primitive pit. All of the rest of the top layer of the embryonic disk is non-proliferating epiblast, which is now called ectoderm. So the mass of what we are looking at is ectoderm. And I have indicated also that up in the cranial region the embryo, if we could see through the ectoderm, we would see the columnar endoderm of the prochordal plate. It is now the endoderm because it's been replaced by the primitive streak cells. At this stage, when these columnar hypoblast cells have been replaced and are columnar endoderm cells, most of the people change the name prochordal plate to something called the oropharyngeal membrane. And we'll trace its history throughout the rest of development. Also I want to point out that caudal to the primitive streak, at the caudal most point of the embryonic disc, there is a zone where ectoderm is also adherent to underlying endoderm and this is called the cloacal membrane. Again we'll trace what happens to it later on.

Week 3, slide 15

This is the same top view with one modification. Now I've allowed all the ectoderm to be translucent, so that we can see that below it, intraembryonic mesoderm is sweeping out from the primitive streak, sweeping laterally and forward to interpose itself between ectoderm and endoderm everywhere. That is everywhere except the zones of the oropharyngeal membrane and cloacal membrane, where ectoderm and endoderm are adherent and intraembryonic mesoderm cannot squeeze in between them. I also want to draw your attention to the fact that intraembryonic mesoderm sweeps around the sides of the oropharyngeal membrane and actually gets into the space in front of it. Finally, if you look at Hensen's node, you'll see this little purplish stuff, which is extending forward from it towards the back edge of the oropharyngeal membrane. This is a very short column of intraembryonic mesoderm that has a fate different from all of the rest of the intraembryonic mesoderm and soon we will give it its own name.

Week 3, slide 16

Now I've slid the ectoderm layer a bit off to the side. I've also made it opaque, so we cannot see the other layers which are below it. But, because I've slid the ectoderm layer off to the side, we can see those layers. We can see the middle layer, which is the intraembryonic mesoderm layer. And then, if I slide that a bit, we can see the endoderm layer down below that. And this points out that early in the 3rd week of development the embryonic disc becomes a 3-layered structure.

Week 3, slide 17

Now I have removed the top layer of the embryonic disk. I've taken away the ectoderm and the proliferating epiblast that is the primitive streak, so we can look down onto the middle layer, which is the intraembryonic mesoderm. And we see all of these mesodermal cells interposed between the top layer and the endodermal bottom layer. I've indicated the endoderm, the columnar endoderm of the oropharyngeal membrane, as a little darker yellow to give you an impression that it's thicker endoderm than elsewhere. And I've also shown that there is no intraembryonic mesoderm interposed between endoderm and ectoderm in the vicinity of the cloacal membrane. And now let's take a look at this little chunk of mesoderm that had extended forward from Hensen's node, and we can see that it is really comprised of two bits. First Hensen's node gives off a little pulse of mesoderm and then there's a rest period, and then it starts to give off some more. And that pulse, that first pulse, is called prechordal mesoderm. The second bit is part of what will ultimately become a much longer structure - the notochord. Prechordal mesoderm was only discovered about 10 years ago. In the early days, the structure immediately in front of the notochord was the prochordal plate (that's how it got its name). When this early pulse of intraembryonic mesoderm from Hensen's node was discovered people knew it lay in front of the notochord so they had to give it a name appropriate to its location, so it was called prechordal mesoderm but it is not to be confused with the prochordal plate. Prechordal mesoderm is not so important to us; it gives rise to some muscles associated with the eyeballs, and it will be discussed a bit more when we do embryology of the head and neck. The fate of the notochord is far more important to us at this stage in the course, and we will be talking a lot about it.

Week 3, slide 18

Now I have re-assembled the embryonic disc, just to indicate that we want to take a median sagittal section through it, and we’ll take a look at the cut edge.

Week 3, slide 19

We see many of the things we are familiar with in a median sagittal section, among them the oropharyngeal membrane. But now I have indicated the cloacal membrane, that area of adherent ectoderm and endoderm caudal to the primitive streak. And I have indicated that at the front end of the primitive streak, the proliferation (that nob of proliferating epiblast) is called the primitive node, and that it has a pit within it - the primitive pit, and behind that is the rest of the primitive streak. The intraembryonic mesoderm that we see and is so labeled is coming out of the floor of the primitive streak. And coming out of the primitive [node] - or Hensen's node - region, first we see that pulse called prechordal mesoderm, and then the longer column of intraembryonic mesodermal cells is called the notochord. In the upper left hand corner I have simply indicated to you that this is still pretty early in the third week of development.

Week 3, slide 20

During the next few days there are going to be many changes in the embryonic disk. But I want to consider separately something that is going on simultaneously, and that is rotation of this entire apparatus within the large sphere of cytotrophoblast. Now in the previous median sagittal section we saw that the connecting stalk ran from the roof of the amnion up to the cytotrophoblastic shell. But for reasons I don't understand, there is a rotation of the amniotic sac and embryonic disk and yolk sac, as a unit, within the sphere of cytotrophoblast so that the attachment site of the connecting stalk goes further and further caudally towards the back end, or tail end, of the embryonic disk, that is, towards the cloacal membrane. In this slide I have just shown a slight shift in attachment of the connecting stalk towards the caudal end of the embryonic disk.

Week 3, slide 21

Now I show the rotation of the embryonic disc and its two sacs, having progressed a bit further so the that connecting stalk which originally ran to the roof of the amniotic sac now goes to the back wall of the amniotic sac and actually has made a little bit of contact with the cloacal membrane region.

Week 3, slide 22

And here the rotation has proceeded yet further, and the connecting stalks runs indeed to the tail end of the embryonic disc right in the vicinity of the cloacal membrane and overlaps onto the back walls of the amniotic sac and the yolk sac. I'm not mean enough to draw all subsequent pictures like this and make you tilt your head so you can see what's going on, so when you look at the next slide, you'll see I've taken this entire structure - cytotrophoblastic sphere, connecting stalk, and embryonic disc with its sacs - and simply rotated it virtually 90 degrees clockwise.

Week 3, slide 23

As I said, I've rotated the entire picture so that the embryonic disc is now horizontal again, in a familiar view that we can develop in future slides.

Week 3, slide 24

And now that the connecting stalk has changed its attachment to the back of the embryonic disk, it induces a finger-like out pocketing of the endoderm of the yolk sac just caudal to, right adjacent to, the cloacal membrane. This out pocketing, this diverticulum, is called the allantoic diverticulum. In birds it grows very big; it plays an important role in respiration while the chick embryo is growing within its egg. It has no such important role in mammals. It does induce the mesoderm of the connecting stalk to develop some blood vessels I'll talk about later, and also it has a minor role in the urinary system formation, which Dr. Jungers will talk about.

Week 3, slide 25

Just a little reminder that we are still very early in the 3rd week of development. At this stage, the embryonic disk is essentially a circular 3-layered structure. When we look down on it, we saw it was a circle, but what's going to happen in the next few days is tremendous growth in the length of the embryonic disk. That growth is going to be concentrated between the back edge of the oropharyngeal membrane and the front edge of Hensen's node. As growth occurs in this region, and as these 2 structures get further and further apart, the notochord pays out like a rope and gets increasingly longer.

Week 3, slide 26

This is a top view of the embryonic disc indicating where the growth will occur between the back edge of the oropharyngeal membrane and the front edge of Hensen's node. And of course, as this growth occurs, you have to create new ectoderm to fill in the newly created space, and new intraembryonic mesoderm, new endoderm, and the notochord (as I said) gets increasingly long.

Week 3, slide 27

This is a median sagittal section after some of that growth has occurred, showing that it's concentrated in the area between oropharyngeal membrane and Hensen's node, and that in a median sagittal section, we can see that the notochord has become longer. We cannot see things on the embryo's left and right sides, but obviously they have had to grow in length as well.

Week 3, slide 28

Here is a top view of the embryonic disc after some of that growth has occurred. It's no longer a circular structure any more. It's becoming an oval structure. Again you can see how the notochord is increasing in length. Intraembryonic mesoderm from the primitive streak is filling in the newly created space.

Week 3, slide 29

Here is a picture with ectoderm and primitive streak removed, looking down onto the top of the middle, or mesodermal, layer of the disc. You should have been able to deduce what this is going to look like but, more or less, I've colored in solid pink intraembryonic mesoderm that was created a few hours before, and in little dots of pink intraembryonic mesoderm that's being created as we are looking at this.

Week 3, slide 30

Now let's take a cross-section through the embryo in this newly created region between the oropharyngeal membrane and Henson's node. You should be able to deduce what this cross- section will look like in the midline. It's going to go through the roof of the amniotic sac and then through the amniotic cavity. It will go through the ectoderm that is the dorsal layer of the embryonic disc and then through the notochord and through the endoderm in the midline of the roof of the yolk sac, then through the fluid and the floor of the yolk sac.

Week 3, slide 31

Here is that cross-section. In the middle, in the midline, are all the things that I had mentioned, most notably the notochord. But now we can see things out to the left and to the right of the midline. In particular we see the sheets, left and right, of intraembryonic mesoderm that are derived from the rear portion of the primitive streak, the notochord having been derived from Henson's node at the very front end of the primitive streak. But we see that the intraembryonic mesoderm merges imperceptibly with extraembryonic mesoderm, and we also see something that hasn't been mentioned before. And those are some mesodermal cells that have not organized themselves into compact layers, or compact structures, like the sheets of intraembryonic mesoderm or the notochord,. Instead, these are free-floating mesodermal cells in the fluid between the various layers of the embryonic disc. Such free-floating mesodermal cells are referred to as mesenchyme, or mesenchymal cells. You will hear this term later in the course, and also will come across it in your readings, should you do any.

Week 3, slide 32

This is the same cross-section as was shown on the previous slide. But now I want to focus on these two sheets of intraembryonic mesoderm that lie one to the left and one to the right of the notochord. Regions of these sheets get specific names. The part of the sheet that is closest to the notochord is called the paraxial mesoderm. I have only labeled these things on the right side, but they exist equally on the left. The more extensive portion of the sheet of intraembryonic mesoderm that actually merges with extraembryonic mesoderm is referred to as the lateral plate. And the mesoderm at the junction of the paraxial and lateral plate regions is referred to as intermediate mesoderm. Intermediate mesoderm is going to play a role in urogenital development. I'm not going have much occasion to refer to it.

Week 3, slide 33

Again this is the same cross-section, but now I want to focus on what is simultaneously happening with the ectoderm that overlies the notochord. The notochord induces, or causes, that ectoderm to be thrown up into folds. These are longitudinal ridges or folds that we are seeing in cross-section here: one is to the left of the midline, one is to the right of the midline. Each one runs the length of the embryonic disc, dorsal to the notochord. Their names are neural folds - that's a clue as to what they will become. The midline groove between the neural folds is called the neural groove. It is directly dorsal to the notochord.

Week 3, slide 34

And now all I've done is color the ectoderm that runs from the crest of one neural fold down through the groove and back up to the crest of the other neural fold a different color. I've colored it green (actually I think it's a shade darker than epiblast). This is not epiblast in any way, shape or form. This special part of the ectoderm is called the neural plate. It plays a very important role in development of the brain and spinal cord, and I want to remind you that this is a cross-section and so just as the neural folds ran lengthwise along the embryonic disc, so does the neural plate.

Week 3, slide 35

Here we are back to the median sagittal section. You ask where are the neural folds, and the obvious answer is that they are not in the plane of this section. One is to the left of the midline (that would be in front of the computer screen); the other is to the right of the midline (that would be behind the plane of the computer screen). What you do see is in fact the floor of the neural groove, which I have colored in green, because we know the neural plate has a fate different than the rest of the ectoderm. Also I've indicated on this slide that the growth in the length of the embryonic disk that had occurred between the back edge of the oropharyngeal membrane and Hensen's node is going to continue.

Week 3, slide 36

This is a median sagittal section a little later in the third week. It shows that the embryonic disc has grown longer, and that means that so has the notochord, and the neural folds with the neural groove in between them, and everything else between the oropharyngeal membrane and Hensen’s node. And I’ve also made the allantoic diverticulum a bit more projecting.

Week 3, slide 37

This is a top view of our elongated embryonic disc. It now is more oval shaped than circular, and it shows the long notochord, and the fact that newly created intraembryonic mesoderm fills in the space between endoderm and ectoderm as this structure elongates.

Week 3, slide 38

Nothing special here in this top-down view. I've just removed ectoderm and primitive streak to show you what the intraembryonic mesoderm would look like at this later stage, around the middle of the third week I'm guessing.

Week 3, slide 39

Well, growth will continue. Human beings are a lot longer than we are circular. At least most of us are; I don’t know about Jungers.

Week 3, slide 40

A median sagittal section later in the third week, showing that the embryonic disc has now gotten very long.

Week 3, slide 41

A top view of our very long embryonic disk. You'll notice that the primitive streak takes up a very small part of the entire length of the embryo now. Actually, its length is pretty much what it was when it got started, but everything else has grown in front of it.

Week 3, slide 42

Ho hum, a top down view with ectoderm and primitive streak removed, showing you the intraembryonic mesoderm of this very long embryonic disc.

Week 3, slide 43

As the embryo grows in length, it means that some of the intraembryonic mesoderm was created five minutes ago, and some of it was created five or ten hours ago. And the older, more mature, intraembryonic mesoderm is going to undergo some changes that will eventually affect all of the intraembryonic mesoderm.

Week 3, slide 44

This is a cross-section of the embryo taken before the changes I am about to describe in the intraembryonic mesoderm, but we've seen it before. It could have been taken anywhere between the caudal edge of the oropharyngeal membrane and Hensen's node. The next slide shows the first change in the intraembryonic mesoderm as it matures.

Week 3, slide 45

And the first change that does occur is separation of the paraxial mesoderm from the lateral plate and the intermediate mesoderm (this occurs on both sides), and what is created are two columns (one left and one right) of paraxial mesoderm that run the whole length of the embryonic disc from the oropharyngeal membrane to Henson's node, and they bracket the notochord. Each column of paraxial mesoderm is triangular in cross-section as shown here.

Week 3, slide 46

Here is a top view of the embryonic disc with translucent ectoderm, so we can see the underlying intraembryonic mesoderm, and it shows that the paraxial mesoderm has separated of from the lateral plate and intermediate mesoderm on both sides of the embryo.

Week 3, slide 47

Same view as the previous slide, but now the ectoderm has been removed. It illustrates the same things as the previous slide, but here it's a little bit easier to note that the lateral plate mesoderm is continuous with the intraembryonic mesoderm that lies in front of the oropharyngeal membrane.

Week 3, slide 48

Same thing, but later on, as this structure has grown in length, and the paraxial columns are very much longer than they were before.

Week 3, slide 49

And now, as we approach the end of the 3rd week of development, we see that the paraxial mesoderm on both sides has divided itself up into chunks in craniocaudal sequence. That is, a series of transverse clefts have formed within the paraxial mesoderm, and from that blocks have been separated from one another. Each block of paraxial mesoderm is referred to as a somite. Many somites form on the left. Many somites form on the right. This is the basis of the segmentation of the human body. Humans, like all vertebrates, are essentially segmented organisms. This will become apparent to you when you study adult anatomy. The very basis for this segmentation is established by the division of paraxial mesoderm into somites.

Week 3, slide 50

Let’s take a cross-section of our embryonic disc through a pair of these somites.

Week 3, slide 51

It looks the same as the earlier cross-section we saw, because somites are separated from one another in a craniocaudal direction, and so we can't tell that there's a separation between a somite behind the screen of the computer and a different somite in front of the screen of the computer. So the cross-section looks the same, so we can label that thing which we had previously labeled paraxial mesoderm as a somite, because we know it's a chunk of paraxial mesoderm.

Week 3, slide 52

And simultaneous with the formation of somites, something is going on in the lateral plate. The lateral plate, as you know, is formed of a compact arrangement of intraembryonic mesodermal cells. And just as we saw in formation of the blastocoele, that little microdroplets of fluid can accumulate between the cells of the morula, and just as we saw in creation of the amniotic cavity that microdroplets of fluid can accumulate between the embryoblast cells, we see here also in the lateral plate mesoderm, that microdroplets of fluid accumulate between the mesodermal cells.

Week 3, slide 53
And this is a top view of our elongated embryonic disc. Obviously the ectoderm has been removed, and it just shows the mesodermal layer, highlighting the fact that microdroplets of fluid have accumulated between the cells of the left lateral plate and between the cells of the right lateral plate.

Week 3, slide 54
This shows that the same process of fluid accumulating between cells of the lateral plate extends forward into the region of intraembryonic mesoderm in front of the oropharyngeal membrane.

Week 3, slide 55
And now back to our cross-section, which illustrates that, just as in the case of the formation of the blastocoele, and just as in the case of the formation of the amniotic cavity, the little microdroplets of fluid coalesce and form a big droplet of fluid. We now have two fluid-filled channels which run throughout the length of the lateral plate mesoderm on either side of the embryo. These fluid-filled channels are said to constitute an intraembryonic coelom.

Week 3, slide 56
And now we can see in this top down view that there is indeed only one intraembryonic coelom, because our left channel and our right channel join one another up in front of the oropharyngeal membrane. So there is created by this process of microdroplets coalescence a single U-shaped intraembryonic coelom with left and right channels that communicate anteriorly.

Week 3, slide 57
Those mesodermal cells that actually contact the fluid of the intraembryonic coelom take on a special morphology. They take on the morphology of epithelial cells. An epithelium is a specialized cellular layer where each cell has a special connection to one another, and it enables them to form some kind of barrier that controls metabolite and fluid transport across this sheet of cells, this epithelial sheet. In general, epithelial cells are derived from endoderm or ectoderm. But, where mesodermal cells contact the fluid of the intraembryonic coelom, they take on the structure of an epithelium. They are not epithelial cells, because they are derived from mesoderm, so we call them mesothelial cells, and the layer that they form that's in actual contact with the fluid is called a mesothelium. And I want to highlight the existence of this layer of specialized cells, so I will draw the mesothelium of the intraembryonic coelom in orange in this and in future slides.

Week 3, slide 58
The only new thing shown in this top view with ectoderm removed is that layer of cells called the mesothelium, that is, those intraembryonic mesodermal cells that actually contact that fluid of the intraembryonic coelom.

Week 3, slide 59
Now I want to take a median sagittal section of the embryonic disc after intraembryonic coelom formation.

Week 3, slide 60
Back to a median sagittal section, not unlike what we saw several slides ago. Here I've indicated neural folds labeled in italics, mainly because you really wouldn't see the neural folds in median sagittal section. That section would be through the floor of the neural groove, but I wanted to remind you that they're here (one in front and one behind the plane of the computer screen), so I drew them in anyway. The most important change in this median sagittal section is now you see, up in front of the oropharyngeal membrane, the bend in the U-shaped intraembryonic coelom, and indicated in orange, the mesothelial layer which contacts the fluid of that coelom. So this is something I've added now - that we have an intraembryonic coelom. And I also want to point out a very special mesoderm which is ventral to the bend of this U-shaped intraembryonic coelom. This is called cardiogenic mesoderm. It's derived from the primitive streak. It's migrated all the way around the sides, and then up in front of the oropharyngeal membrane, and has a position here ventral to the bend in the coelom. And as its name suggests, it is destined to give rise to the heart. Where are the left and right channels of this intraembryonic coelom? Well, the left channel is in front of the plane of the computer screen, and the right channel is behind the plane of the

computer screen. And it would be nice if we could see this whole coelom in a sort of 3-dimensional view, and that's what I am going to attempt to do in the next slide.

Week 3, slide 61
Okay, here is my attempt to show you this U-shaped intraembryonic coelom in sort of a three dimensional view, with its left channel, which would in reality be in front of the computer screen, and its right channel behind the computer screen, and the bend out anterior to, or in front of, the oropharyngeal membrane. This is the orange mesothelial lining of this coelom, which is filled with fluid, nothing more than fluid.

Week 3, slide 62
Now back to a median sagittal section so I can show you what this cardiogenic mesoderm is going to do. It's going to organize itself into two longitudinal tubes in front of the oropharyngeal membrane and ventral to the bend in the coelom. These tubes lie side by side, one to the left of the median sagittal plane and one to the right of the median sagittal plane. Therefore in a pure median sagittal section, we couldn't see them, but I've taken some liberties in this drawing so that we can. These tubes are called heart tubes, and it's obvious from their names what they will become.

Week 3, slide 63
Let's take a cross-section through these heart tubes. You can predict what you'll see starting at the dashed black line and working down. You'll go through the roof of the amniotic cavity, then through the fluid of the amniotic cavity, then through some ectoderm that lies dorsal to the bend in the coelom, then the actual bend in the coelom itself, then the heart tubes, then the roof of the yolk sac and below that the rest of the yolk sac. The next slide shows this cross-section.

Week 3, slide 64
Here it is (what I said you could have predicted), and you want to focus in on the fact that we are through the bend in the front of the U-shaped intraembryonic coelom, and we have these two heart tubes - one slightly to left of the midline, one slightly to the right of the median sagittal plane.

Week 3, slide 65
What I want to show here is that these two heart tubes, both of them, are going to grow caudally Now, they're not going to grow through the middle of the oropharyngeal membrane. When they reach this zone of the oropharyngeal membrane, which is a region of tightly fused columnar endoderm with overlying ectoderm, they are going to have to separate from one another and deviate around the sides of the oropharyngeal membrane, with one going to the left side and the other to the right side.

Week 3, slide 66
Here's what things will look like after these two heart tubes have extended caudally in the embryo. Each one will sweep on one side of the oropharyngeal membrane and then the two of them will meet together in a position just ventral to the notochord. They will run side by side ventral to the notochord heading caudally. They will then, near the very tail end of the embryo, encounter the allantoic diverticulum. One will sweep to its left side and one will sweep to its right side. Together, they will enter the connecting stalk. I've indicated the one closest to you in red and the one furthest from you (the right one) in salmon color. As you know, the connecting stalk leads out to the placenta, which is forming from trophoblast. These extensions of the heart tube, as they lie ventral to the notochord, are called aortae. That's the same word that you see here but with an "e" on the end. One of them is called an aorta. I've labeled the left one, and there is one behind the plane of the computer screen which would be the right aorta. As they are sweeping along the side of the oropharyngeal membranes they are called aortic arches. Again, I've labeled the left aortic arch but the right one is behind the plane of the computer screen. And then these tubes, when they sweep into the connecting stalk, are referred to as umbilical arteries (left and right). We now have a system whereby any fluid, or blood if you will, that could get into these heart tubes could be sent backwards through the aortic arches and then through the aortae into the umbilical arteries and out to the placenta.

Week 3, slide 67
Let’s take a cross-section through the midregion of the embryo and the aortae.

Week 3, slide 68
Here it is - you’ve seen something very much like this before. The only new stuff are these two aortae, ventral to the notochord, and dorsal to the roof of the yolk sac.

Week 3, slide 69
Let’s take a cross-section through our embryo, cranial to the oropharyngeal membrane, two days after the heart tubes form, which means very close to the end of the third week of development.

Week 3, slide 70
The two heart tubes have merged with one another, and you have a single heart tube.

Week 3, slide 71
And now a little later, let’s take a cross-section through the middle of the embryo.

Week 3, slide 72
This shows that the two aortae have fused, and so now you have a single aorta, ventral to the notochord and dorsal to the yolk sac.

Week 3, slide 73
This more or less median sagittal section shows what you may have already deduced. There are two regions where these vascular structures do not fuse. The aortic arches sweep around either side of the oropharyngeal membrane, therefore, these arches are not close together and do not fuse with one another. But once they are caudal to the oropharyngeal membrane, they do join to form the single aorta, which runs ventral to the notochord all the way down the length of the embryonic disc until it gets to the region of the allantois, and there the aorta divides again into its two umbilical arteries, which travel out the connecting stalk to reach the placenta.

Week 3, slide 74
Now as all these arteries are forming, veins are forming as well. We don't put a lot of emphasis on veins in the embryology section of the course. But they do exist and we should mention a few of them. Among the veins that form are veins that drain the yolk sac. These are called vitelline veins. I've shown the one on the left, but there's one on the right as well, behind the computer screen. Each vitelline vein runs forward towards the cranial end of the embryo and empties its blood into the heart tube. Now, I haven't drawn all the tiny little arteries that come off of the aorta and feed the yolk sac, nor have I drawn the capillary system and the veins that form from it that drain into the vitelline vein, but you have to understand that these things exist.

Week 3, slide 75
Another set of veins that forms comes from the placenta. These veins run in the connecting stalk, sweep around the sides of the roof of the yolk sac, and then also enter the front of the heart tube. These are called umbilical veins. There's one on the left, that's the one I've shown, but again, there's one on the right behind the plane of the computer screen.

Week 3, slide 76
And the final major set of veins that I want to talk about are the veins that actually drain the embryonic disc itself. These are called cardinal veins and they lie on either side of the aorta as we'll see momentarily. They too enter the cranial end of the heart. In fact on each side these three big veins: the cardinal vein, umbilical vein, and vitelline vein, join one another just before they enter the heart tube.

Week 3, slide 77
Now let’s take a cross-section through the midbody of our embryo, right at the end of the third week of development, after all of these arteries and veins that I have mentioned have formed.

Week 3, slide 78
It shows you the two cardinal veins on either side of the aorta. I've also drawn in umbilical veins and vitelline veins, but I didn't bother labeling them. The most interesting thing about the cardiovascular system at the end of the third week is that it is functioning, the circulatory path is complete. The heart tube is pumping, it's sending blood backwards into the aorta and from the aorta blood is being distributed to the embryonic disk, to the yolk sac, and equally importantly it is being sent to the umbilical arteries and then to the placenta where it receives its oxygen and foodstuff, and is returned via umbilical veins back into the circulatory system of the embryo. So, don't forget that by the end of the third week you have a functioning circulatory system.

Week 3, slide 79
We've talked about a lot of things that happen in the third week: segmentation of the embryo via the mechanism of somite development, formation of an intraembryonic coelom, establishment of a functioning circulatory system, and now I want to consider what's happening with the neural folds.

Week 3, slide 80
You will recall that the neural folds are longitudinal ectodermal ridges on either side of the midline, induced to form by the notochord, and that from the crest of one neural fold to the crest of the other neural fold is a specialized zone of ectoderm called the neural plate. Now, what's going to happen very soon after these folds develop is that they will rise higher. The left one will move upward and to the right, and the right one will move upward and to the left. These motions are shown in the next slide.

Week 3, slide 81
The crests of the two folds approach one another in the median sagittal plane.

Week 3, slide 82
The crests of the two folds will touch one another, and this is actually where things are at the end of the third week, but in the next couple of slides I'm going to carry you into the fourth week of development just to finish up what's going to happen with the neural folds.

Week 3, slide 83
A separate lecture will be devoted to discussing the changes that will happen during the fourth week of development, and there are lots of them. One of the important things going on in the fourth week involves the neural folds, and it's just more convenient for me to talk about it now rather than make you wait until the next lecture. The two neural folds, right and left, are going to merge with one another and separate off a hollow tube - the neural tube - that runs the length of the embryo. And in addition, cells from the crests of the neural folds do not join the neural tube, but instead form long cellular columns, again running the length of the embryo, dorsolateral to the neural tube. These are called neural crest columns; there's one on the left and one on the right. But they don't last as columns very long because, just as the paraxial mesoderm segmented itself into somites, these columns of neural crest cells break into clumps such that there is one clump of neural crest cells for each somite. We have a whole series of somites on the left and a whole series of somites on the right. And you have equally, a whole series of neural crest clumps on the left and a series of neural crest clumps on the right - one clump for every somite. And finally, let's consider what happened dorsal to the neural tube and neural crest. The ectoderm that was not part of the neural plate has reconstituted a dorsal surface to the embryo. This ectoderm in fact will differentiate ultimately into the epidermis of the skin of your back.

Week 3, slide 84
The fusion of the neural folds, and sealing off of a the neural tube, is referred to as neural tube closure, and this slide gives you (in text) some more accurate information about it. It's important to know that this is a phenomenon of the fourth week of development, and that insults to the embryo during the fourth week are most likely to cause serious problems with spinal cord or brain formation.

Week 3, slide 85
And there is one more thing that actually does happen in the third week that I want to talk about in this lecture, and that concerns the coelom.

Week 3, slide 86
A little self-test here: what do you think this area is that has all these questions marks placed in it?

Week 3, slide 87
Anyone who knew that was the extraembryonic coelom deserves a pat on the back, because I've ignored it throughout almost all of this lecture. And now I have colored it blue, because I want to remind you that it has fluid in it, just like the intraembryonic coelom does, and the amniotic cavity, and the yolk sac, and in fact, even between the layers of the embryo.

Week 3, slide 88
The final change in the coelom that occurs at the end of the 3rd week is that the lateral wall of the intraembryonic coelom, that is that mesoderm between intraembryonic coelom and extraembryonic coelom, starts to break down, or fluid starts to accumulate in that region. And if you go to the next slide, you'll see the outcome.

Week 3, slide 89
An open communication is formed between the intraembryonic coelom and the extraembryonic coelom. Fluid in one now becomes freely exchangeable with fluid in the other, flow right from one into the other, and this occurs on both sides in these left and right channels of the intraembryonic coelom.

Week 3, slide 90
This is our familiar top view of the embryonic disk with the ectoderm removed. What it points out is that the lateral wall of the intraembryonic coelom does not break down along its entire length, but in fact, this breaking down is confined to the region caudal to the oropharyngeal membrane. So I've shown on both sides, left and right side, that the lateral wall of the intraembryonic coelom caudal to the oropharyngeal membrane has broken down, and now there is an open communication between the intraembryonic coelom and the extraembryonic coelom in these regions.

Week 3, slide 91
This is that attempt at a 3D view of the intraembryonic coelom, and it shows that caudal to the oropharyngeal membrane the lateral wall of the left coelomic channel has broken down and take my word for it, caudal to the oropharyngeal membrane the lateral wall of the right coelomic channel has also broken down but you can't see it because its behind the plane of the computer screen. Take note that the lateral wall has not broken down in the vicinity of the oropharyngeal membrane or in the vicinity of the bend of the U-shaped coelom.

Week 3, slide 92
If you've actually proceeded through this entire lecture, you know that lots have things have gone on during the third week. This slide simply summarizes for you the status of the embryo at the end of this period of time.