

TRANSCRIPTIONS OF NARRATIONS FOR EMBRYONIC FOLDING & COELOM DEVELOPMENT

Embryonic Folding and Coelom Development, slide 2

This is where we ended up at the end of lecture two: median sagittal section of a 21-day embryo. Of course things have been modified to allow you to see neural folds, which would not be seen in a median sagittal section; you can see aortic arches, which wouldn't be seen in a median sagittal section. And some things which are not here, which you would not see which are somites. You wouldn't see them and they haven't been placed here; they are in front of and behind the plane of the computer screen. But you're familiar with this, so I don't have to go into this any further.

Embryonic Folding and Coelom Development, slide 3

Here is the top down view of the embryonic disc, again with ectoderm and its derivatives removed. So we are looking down onto the intraembryonic mesodermal layer. We show the intraembryonic coelom as we finished with last time, opened up into the extraembryonic coelom in that portion caudal to the oropharyngeal membrane. I have not drawn in fluid in the extraembryonic coelom because I have all my labels there, but you know that fluid is there. Now what this slide points out is that different regions of the intraembryonic coelom have different names. The bend in the U-shaped portion of the coelom (way up at the front of the embryonic disc), which overlies the cardiogenic mesoderm, which we can't see because it's behind the plane of the computer screen, that portion of the extraembryonic coelom is going to be the pericardial portion, or the future pericardial portion, and that's why it gets its name, because it's going to be associated with the heart. The left and right channels, at least those parts which have opened up into the extraembryonic coelom, are going to become part of the peritoneal cavity later in development, and so we have these two future peritoneal portions of the intraembryonic coelom, at this stage a left and a right one. And then, the portions of the intraembryonic coelom that connect the future pericardial portion with the future peritoneal portions are called pericardioperitoneal canals. It's obvious why they get their name. They have intact lateral walls; they tend to run mainly on either side of the oropharyngeal membrane, and they will become later in development the pleural cavities associated with the lungs, but their names right now don't suggest that.

Embryonic Folding and Coelom Development, slide 4

This is that attempt at a 3-dimensional drawing of the coelom that you have seen before, with the different parts labeled: the bend in the U being the future pericardial portion of the intraembryonic coelom; the channels to the left and to the right, whose lateral walls have disappeared, those are the future peritoneal portions of the coelom. And then the channels to the left and to the right with intact lateral walls that connect the pericardial with the peritoneal portions, those channels are called pericardioperitoneal canals.

Embryonic Folding and Coelom Development, slide 5

Let's take a section through the future pericardial portion of the coelom. This is something we did last lecture, so you're familiar with it.

Embryonic Folding and Coelom Development, slide 6

This just shows you where that section will be in terms of the top down view that we have also seen before.

Embryonic Folding and Coelom Development, slide 7

And indeed here is the section. It differs from one shown in the previous lecture only in the fact that now the bend at the front of the intraembryonic coelom is labeled as the future pericardial portion.

Embryonic Folding and Coelom Development, slide 8

Let's take a cross-section a little further back - one caudal to the oropharyngeal membrane, but not far caudal to it (like some of the others we've seen). This one will be immediately caudal to it.

Embryonic Folding and Coelom Development, slide 9

This places that section in the top-down view that we are familiar with, except it's clear now that we're going through a portion of the intraembryonic coelom that still has its lateral wall, that is what is the pericardioperitoneal canal portion of the coelom.

Embryonic Folding and Coelom Development, slide 10

Here is that section. In terms of things lying in the median sagittal plane, you should have been able to deduce this. There's the ectoderm of the back, then there's the neural tube, then the notochord ventral to it, then the aorta ventral to the notochord, and then the roof of the yolk sac. These things don't change throughout life really except the yolk sac changes its name to gut. But out to the sides of the notochord we see somites and out to the sides of the aorta we see cardinal veins. Lateral to the somites is the intermediate and lateral plate mesoderm. I'm not interested in intermediate, but in the lateral plate is the intraembryonic coelom. That portion, because of the way we chose our section, still has intact lateral wall and therefore we have the left and the right pericardioperitoneal canals. And then the lateral plate mesoderm merges with the extraembryonic mesoderm that's on the outside of the amniotic sac and yolk sac.

Embryonic Folding and Coelom Development, slide 11

Now let's take a section further back along the length of the embryo.

Embryonic Folding and Coelom Development, slide 12

This lets us know that section will be through the portions of the intraembryonic coelom that are going to become the peritoneal portions of the coelom - the lateral walls are gone - the right and left peritoneal portions of the intraembryonic coelom.

Embryonic Folding and Coelom Development, slide 13

No surprise here - we've just labeled the future peritoneal portions for what they are. How do we know these are future peritoneal portions? It's because the lateral wall is gone, and if your lateral wall is gone, and you are an intraembryonic coelom in communication with the extraembryonic coelom, then you are a future peritoneal portion of the intraembryonic coelom.

Embryonic Folding and Coelom Development, slide 14

This is one of my favorite things to do, and that is to pretend that I am a tiny little person inside the intraembryonic coelom and that I want to get from where I am currently located to a different portion by walking. In the case illustrated here, I am in the left peritoneal channel, and my goal will be to get to the right peritoneal channel. How can I do it? Well one very obvious route is for me to start walking to the left as you are looking at the screen, walking towards the cranial, or front, of the left peritoneal channel, enter the left pericardioperitoneal canal, walk all the way through it until I get to the bend in the coelom, that is the future pericardial portion, walk all the way around that bend and over to the right side, until I enter the right pericardioperitoneal canal, walk backwards in the right pericardioperitoneal canal, and then I can enter and reach my goal, which is the right peritoneal channel. A long trip, but well worth the effort.

Embryonic Folding and Coelom Development, slide 15

This shows another way of getting from the left peritoneal portion of the coelom to the right peritoneal portion of the coelom. I don't know if it's longer or shorter, but it's a different way. I can walk, as you are looking at it, to the left. That is I can walk out of the intraembryonic coelom into what is shown here in white, but as you know is fluid-filled: the extraembryonic coelom. And I can walk all the way down around the bottom of the yolk sac, come all the way up on the other side of the yolk sac, and enter the right peritoneal portion of the intraembryonic coelom from what, on your perspective, is the right side of this picture.

Embryonic Folding and Coelom Development, slide 16

Now I want to talk about a third way to get from the left peritoneal channel to the right peritoneal channel, one that is a modification of what was described in the previous slide. And in order to present this I have included on my median sagittal section a 3-D representation of the intraembryonic coelom. You see the future pericardial portion

all the way to the left, and that's followed as you progress to the right by the pericardioperitoneal canal, and then by the future peritoneal portion with its lateral wall gone. And I've placed our homunculus at the most caudal part of the coelom, at the most caudal part of the future peritoneal portion. And I want it to walk outside the lateral wall (the broken down lateral wall), but instead of going all the way around the side wall and floor of the yolk sac, as in the previous slide, I wanted to sort of zip backwards and pass beneath the root of the connecting stalk, through that part of the extraembryonic coelom indicated here by an asterisk. And if it does that, it will quickly find itself near the very back end of the right peritoneal channel and it can go through the broken down wall and be where it wanted to be. So it has accomplished its goal of getting from the left peritoneal channel to the right peritoneal channel by what I believe to be the shortest possible route. This identification of the shortest possible path between the left and right peritoneal channels is not of immediate relevance, but it will become very important when we consider the definitive development of the peritoneal cavity.

Embryonic Folding and Coelom Development, slide 17

This is a more typical median sagittal section without the coelom drawn in, but with that very special region of the extraembryonic coelom that I've marked with an asterisk - so marked because we'll have occasion to refer to it later on in the course.

Embryonic Folding and Coelom Development, slide 18

And this is the same median sagittal section, but a product of my laziness, because now I've lost interest in drawing in cell boundaries or in drawing in the aortic arches as they sweep around the oropharyngeal membrane. But otherwise, nothing is different. There is marked that region of extraembryonic coelom at the root of the connecting stalk with an asterisks that will be important in the development of the definitive peritoneal cavity, and also I've labeled the mesoderm that is cranial to the future pericardial portion of the intraembryonic coelom with term septum transversum. This name refers to what will happen to this mesoderm. It will become a transverse septum, as we will see. Right now, it is not a septum, and it is just the name given to the mesoderm cranial to the pericardial part of the coelom.

Embryonic Folding and Coelom Development, slide 19

Now in addition to giving a name to the septum transversum mesoderm, I want to pretend that I could mark the most cranial cell in the mesothelium of the pericardial portion of the coelom with an X, and I will mark the most caudal cell (that is the cell nearest to the oropharyngeal membrane) in the mesothelium of the pericardial portion of the coelom with a Y, because things are going to happen and we're going to want to trace where this X and Y cell end up.

Embryonic Folding and Coelom Development, slide 20

And now I want to pretend I can do a couple of other things. First, I want to pretend that I can encase the side walls and floor of the yolk sac in concrete, so as to stop these portions of the yolk sac from increasing in size. Then I want to pretend I can take a tiny, tiny bicycle pump (it's got to be very tiny because this whole thing is only about 2mm in length), and I want to take the needle of that bicycle pump, and I want to insert it into the yolk sac, and I want to pump up the yolk sac with fluid, remembering that its side walls and floor are encased in concrete and cannot increase in size. The next slide will show what happens.

Embryonic Folding and Coelom Development, slide 21

What has happened is that the roof of the yolk sac has ballooned upward and outward relative to that part which was constrained in size. Now, obviously no one is pumping a constrained yolk sac with fluid from a bicycle pump, but the effect of differential growth between the embryonic disc and the side walls and floor of the yolk sac has led to the same result. Accompanying that, the amniotic cavity and sac are getting larger, and we see that many things have actually rotated from their original position. The oropharyngeal membrane, which used to be a horizontal structure, is now vertically disposed; it's rotated ninety degrees anticlockwise. The cloacal membrane, which used to be a horizontal structure, is now vertically disposed, having rotated ninety degrees clockwise. The pericardial portion of the coelom maintains its same relationship to the oropharyngeal membrane. That relationship used to be that the pericardial portion of the coelom was cranial to the membrane; now it is in fact ventral to it because of the rotation. The cell we had labeled X used to be cranial to the cell we had labeled Y; now it's ventral to the cell

labeled Y, so the pericardial portion of the coelom has undergone the same ninety degree rotation. The septum transversum, which used to be cranial to the pericardial portion of the coelom, is now ventral to it, but is still positioned with respect to cell X as it had been previously. We see that the allantois and connecting stalk are getting tucked in under the back end of the ballooned-out roof of the yolk sac. And that little region of the extraembryonic coelom we had marked with an asterisk is getting tucked in as well, but it still has the same relationship to the allantois and connecting stalk as it always had. And finally, I note that the heart tubes, which ran from anterior to posterior (that is craniocaudally) now run dorsoventrally. They have also shared in the ninety degree rotation that the oropharyngeal membrane and pericardial portion of coelom and septum transversum have all participated in.

Finally, you might notice that I've labeled something new here - the caudal eminence, at the back end of the embryo. Sometime during the 4th week of development, the primitive streak stops sending out mesoderm laterally, and stops sending cells into the notochord, and instead settles down to become this thing called the caudal eminence, or tail bud. The cells that overlie the caudal eminence just become ectoderm, but the rest of the cells - those I've indicated here in green - are still pluripotential, which means they can become anything they want. Indeed, they give rise to the most caudal of the somites (that is, numbers 32 and higher); they give rise to the caudal end of the notochord, and they're even responsible for forming the part of the neural tube that will become the third through fifth sacral and coccygeal segments. This most caudal part of the neural tube forms as a cylindrical structure that joins the back end of the major part of the neural tube which, as you know, comes from the neural folds. It's also believed that the caudal eminence gives rise to the most caudal part of the hindgut. All this stuff related to the caudal eminence is detail that I won't mention further.

Embryonic Folding and Coelom Development, slide 22

Here's a 3D picture of the coelom after this change has occurred. It's as if someone grabbed the pericardial portion of the coelom and just pulled it downward. We now see that the X cell is ventral to the Y cell, and the pericardial portion of the coelom is ventral to the oropharyngeal membrane. The pericardioperitoneal canals now run essentially a dorsoventral course. All the different regions of the intraembryonic coelom have the same relationships to one another that they did before this occurred, so hence they have the same labels.

Embryonic Folding and Coelom Development, slide 23

And here again is a median sagittal section of the embryo after the roof of the yolk sac has ballooned upward. I've taken the liberty of showing somites here even though they are in front of the plane of the computer screen (or behind it as the case may be), just because, when I take my cross-section through this, I'll want to draw the somites in, and so I remind you that they haven't disappeared off the face of the earth.

Embryonic Folding and Coelom Development, slide 24

And this cross-section shows you that the ballooning upward of the roof of the yolk sac is occurring in a transverse plane as well as in a longitudinal plane, as we saw previously. This is a section through the future peritoneal portions of the coelom. It's further back in the embryo. That's why we see the intraembryonic coelomic cavity in open communication with the extraembryonic coelomic cavity.

Embryonic Folding and Coelom Development, slide 25

And this is the way things are, let's say in the middle of the fourth week of development, and reminding you that we want to continue placing concrete around the side-walls and floor of the yolk sac because we're going to want to pump this up even more as the next slide will show.

Embryonic Folding and Coelom Development, slide 26

Now we have allowed the roof of the yolk sac to balloon out to its completion, and it forms a hollow endodermal tube capped at both ends, which we can identify as the gut. By the way, this process is called embryonic folding; it occurs by differential growth of dorsal structures relative to ventral structures - the more dorsal you are, the more you grow. And it is the mechanism by which the roof of the yolk sac becomes incorporated into the embryo to form the gut. It is also the mechanism by which we are transformed from a disc shaped organism into a sausage shaped organism, after all we are very much shaped like sausages. We see that the oropharyngeal membrane has undergone an additional 90 degrees of anti-clockwise rotation. It is horizontal again, but what used to be the front

end of the membrane is now the back end and what used to be the back end is now the front end. We see the pericardial portion of the coelom continues its rotation. It has undergone an additional 90 degrees of anti-clockwise rotation. Cell X, which used to be cranial to cell Y, is now caudal to cell Y. But nonetheless, cell Y is still the cell nearest the oropharyngeal membrane. The septum transversum, which is still nearest cell X, has been incorporated into the embryo and now is a genuine transverse septum made up of mesoderm. The heart tube, which started out ventral to the pericardial portion of the coelom, as a result of this 180 degree rotation now lies dorsal to the pericardial portion of the coelom. The cloacal membrane itself has undergone an additional 90 degree rotation, but this time clockwise. The allantois has now been folded into the body of our sausage-shaped embryo, as has part of the connecting stalk, but the allantois still runs into the connecting stalk. And that portion of the extraembryonic coelom that we had marked with an asterisk has also been incorporated into the body of the embryo, and we'll talk more about this later. Even though it is the roof of the yolk sac that makes up the gut, the term yolk sac is now restricted and reserved for that portion of the original yolk sac which did not get folded into the embryo. And finally in this picture, because it is meant to be the end of the 4th week, which is called the period of embryonic folding, I have also indicated that the neural tube is also completely separated off from the overlying ectoderm. As you may recall, earlier I had said that the neural tube closure begins at the very end of week 3, and most of it takes place during week 4, so that by the end of the fourth week, we have a completely individuated neural tube.

Embryonic Folding and Coelom Development, slide 27

As it was said previously, the gut is an endodermal tube closed at its front end, and closed off at the back end, connected in its middle to the remnant of the yolk sac - what we still call the yolk sac. In fact, that zone of connection of the gut to the yolk sac is given the name midgut. The portion of the gut that lies cranial to the connection to the yolk sac is called foregut, and it is separated from the amniotic cavity by the oropharyngeal membrane. The portion of the gut that lies caudal to the connection to the yolk sac is called the hindgut. It is separated from the amniotic cavity by the cloacal membrane. The allantoic diverticulum connects to the hindgut. It's another endodermal tube. The connection between the midgut and the yolk sac is called the vitelline duct. The allantoic diverticulum runs into the mesoderm which we have called connecting stalk. I haven't drawn here the umbilical arteries, which are branching off from the back end of the aorta, and they will travel along the either side of the allantoic diverticulum, and into the mesoderm of the connecting stalk and out to the placenta that way. You will note that the walls of the amniotic cavity - the amnion itself - have ballooned out considerably. Now we have a structure that surrounds the vitelline duct, which has an outer layer of amnioblast cells, and then they are lined by mesoderm, and then there is extraembryonic coelom and the vitelline duct and yolk sac, all contained within this structure. This is the umbilical cord, which will become narrower and better defined as time goes on. I don't want to dwell on it now, but I think it's worth mentioning that eventually the oropharyngeal membrane will rupture, establishing a communication between the amniotic cavity and the foregut. Eventually the cloacal membrane will rupture, establishing a communication between the lumen of the hindgut and the amniotic cavity.

Embryonic Folding and Coelom Development, slide 28

Here is that three dimensional representation of the walls of the intraembryonic coelom, with the future pericardial portion in its definitive position (that is, it's undergone a complete 180degree rotation), and cell X is now caudal to cell Y, and we see that the pericardioperitoneal canals at first run dorsally, and then make a turn caudally, before they eventually join the future peritoneal portions of the intraembryonic coelom (that is those portions whose lateral walls have disintegrated).

Embryonic Folding and Coelom Development, slide 29

Now I want to take a cross-section through our folded embryo. It will be posterior, or caudal, to the oropharyngeal membrane; it will be through the pericardial portion of the coelom, and as you'll see, through the pericardioperitoneal canals. I've also drawn on this something that I didn't mention before, which is in fact that the aortic arches, which initially swept on either side of the oropharyngeal membrane, are now caudal to it; they don't need to sweep around the sides of the oropharyngeal membrane. Now in fact each one sweeps around the side of the foregut - the left one on the left side of the foregut, the right one on the right side of the foregut, and join dorsal to the foregut to form the aorta, which then passes ventral to the notochord all the way towards the caudal end of the embryo, where it splits into umbilical arteries.

Embryonic Folding and Coelom Development, slide 30

Here is that cross-section, and because our embryo has taken on the shape of a sausage, the cross-section through it looks like a cross-section through a sausage but with lots of internal structure. Obviously, up near the top we have the neural tube with neural crest clumps dorsolateral to it on either side. Ventral to the neural tube here, as always, is the notochord. On either side of the neural tube and notochord are the somites, and ventral to the notochord here, as always, is the aorta bracketed by cardinal veins. And ventral to the aorta is, in this case, the foregut, which lies dorsal to the heart tube. The heart tube itself appears to have pushed down into the intraembryonic coelom - the region of the future pericardial cavity - without entering it. And that future pericardial portion of the coelom is connected up to the pericardioperitoneal canals.

Embryonic Folding and Coelom Development, slide 31

The somites and notochord are going to have a very different fate than the rest of the mesoderm. We'll discuss that in the gross anatomy lectures. But, because of this different fate I've now changed the color of the lateral plate mesoderm to make it a lighter pink, which probably wasn't important but I did it anyway.

Embryonic Folding and Coelom Development, slide 32

And now let's take a cross-section through our folded embryo a bit caudal to the one we just looked at. Rather than going through the pericardial portion of the coelom, we'll be caudal to it, and in fact we'll be going through that bit of mesoderm which we have given the name "septum transversum".

Embryonic Folding and Coelom Development, slide 33

Here is that cross-section. We obviously don't see the heart because we are caudal to it. We do see the mesoderm which lies ventral to the foregut and caudal to the heart and pericardial part of the coelom, which mesoderm is called septum transversum. The pericardioperitoneal canals had at first swept dorsally from the pericardial portion of the coelom, then they turned and ran caudally on either side of the foregut to reach the future peritoneal portion of the coelom. Well, we're catching them in this section as they are running caudally toward the future peritoneal portion of the coelom.

Embryonic Folding and Coelom Development, slide 34

And now all I've done is color the septum transversum a little darker pink yet, because we will want to trace its separate history from the rest of the mesoderm of this region.

Embryonic Folding and Coelom Development, slide 35

Let's take a section even further caudally, that is, one through the hindgut. This section also goes through the allantois, which has been incorporated into the ventral body wall. And it's going to go through that little portion of the extraembryonic coelom which we had marked with an asterisk, and which has been folded into the embryo, and as a result of this, is now really part of the intraembryonic coelom. The folding has taken this portion of the extraembryonic coelom and made it part of the intraembryonic coelom.

Embryonic Folding and Coelom Development, slide 36

Here is that cross-section. As in all those I've shown, we are standing at the head of the embryo looking towards its tail. The area marked by an asterisk is that bit of extraembryonic coelom that had been at the root of the connecting stalk but is now incorporated into the embryo. I also show the left peritoneal channel and the right peritoneal channel. These channels had lateral walls to begin with, but those walls were lost and they are indicated here by dotted green lines. They were means of egress from intraembryonic coelom to extraembryonic coelom. But now if you're standing in the left peritoneal channel, you can get to the right peritoneal channel without ever leaving the embryo, because you can walk through that region marked with an asterisk that used to be extraembryonic coelom but has been incorporated into the embryo. In other words we have gone from the situation where you have two peritoneal channels, left and right, to one in which you have one single peritoneal cavity, the two channels being connected by that portion of the extraembryonic coelom which has been brought into the embryo and incorporated into the intraembryonic coelom.

Embryonic Folding and Coelom Development, slide 37

This slide just emphasizes what I said a few moments ago. The embryo now has one big future peritoneal cavity, as opposed to the two separate channels it had prior to embryonic folding.

Embryonic Folding and Coelom Development, slide 38

Back to a median sagittal section with the septum transversum now colored a darker pink. This does not imply any change in the nature of the mesoderm of the septum transversum. It's still the same stuff it always was; it derived from the primitive streak, cells that had migrated all the way around to the front of the embryonic disc and took up a position cranial to the future pericardial portion of the coelom, but now has been folded into the embryo and has a position ventral to the foregut and caudal to the future pericardial portion of the coelom.

Embryonic Folding and Coelom Development, slide 39

Here I've just drawn the septum transversum in its position as it relates to the pericardial portion of the coelom and the pericardioperitoneal canals. Reminder, that it is a transverse sheet of tissue that runs from in front of the plane of the computer screen to behind the plane of the computer screen.

Embryonic Folding and Coelom Development, slide 40

Here I've drawn the foregut in position. The two pericardioperitoneal canals sweep dorsally from the future pericardial portion of the coelom, take up a position on either side of the foregut, and then turn and run caudally. Once they get past the septum transversum they lose their lateral walls, and then by definition are no longer pericardioperitoneal canals but in fact are part of the future peritoneal cavity.

Embryonic Folding and Coelom Development, slide 41

Now we know that the aorta is always dorsal to the gut and so I've drawn the aorta in position here. The heart indents the dorsal wall of the pericardial portion of the coelom, it does not enter the coelom, it simply pushes down the dorsal wall. Coming out of the heart are the two aortic arches, one sweeping to the left of the foregut, one sweeping to the right of the foregut, before they join one another to form the aorta.

Embryonic Folding and Coelom Development, slide 42

Now you see I've drawn in the cardinal veins, which run on either side of the aorta, and I've labeled them by the name 'posterior cardinal veins' because there are a set of veins (which are coming from the head region, which is cranial to the aorta), which are called 'anterior cardinal veins' (and in the next slide we will see what demarcates them precisely), and I've also pointed out that umbilical and vitelline veins are passing through the septum transversum in order to reach the back end or the venous end of the heart.

Embryonic Folding and Coelom Development, slide 43

And here I show what truly demarcates posterior cardinal veins from anterior cardinal veins, and that is, the two of them join (this occurs on each side) to form a single common cardinal vein, which sweeps down around the lateral sides of the pericardioperitoneal canals, and joins with the umbilical and vitelline veins to enter the venous end of the heart.

Embryonic Folding and Coelom Development, slide 44

Now let's take a transverse section through the embryo, as indicated here by the dashed line in this blow-up of the coelom and related structures. Among the things it's going to pass through are the two pericardioperitoneal canals. It will pass through the aorta, which will have posterior cardinal veins on either side of it. It will pass through the foregut. It will pass through the left and the right common cardinal veins, as they are on the lateral sides of the pericardioperitoneal canals. And then it will eventually reach the pericardial portion of the coelom indented dorsally by the heart.

Embryonic Folding and Coelom Development, slide 45

Here is that section; this really looks very familiar to one we looked at earlier. Two differences: one is I've labeled the cardinal veins as being posterior cardinal veins now that we know that they are in fact behind the junction with

the anterior cardinals. And number two, I've drawn in the common cardinal veins. These are really the only differences between what we have seen previously.

Embryonic Folding and Coelom Development, slide 46

Here is the same picture without all the words to obscure structures, because what I want to talk about now is better seen in an unlabeled version. The heart is going to, if you will, sink ventrally, pushing the dorsal wall of the pericardial portion of the coelom ahead of it and encroaching on the pericardial portion of the coelom. Now, look at the next three slides. The third one is labeled, and we can skip to that in terms of narration, to discuss what the result of this ventral sinking of the heart is.

Embryonic Folding and Coelom Development, slides 47-48

No narration.

Embryonic Folding and Coelom Development, slide 49

As a result of this sinking of the heart, a thin sheet of mesoderm has been stretched out between the foregut and the heart - mesoderm lined on its outer surfaces by mesothelium. And we can now start to give names to some of these mesodermal mesothelial layers. The mesoderm that is in actual contact with the outer surface of the heart and its mesothelial coating, is called visceral pericardium, or epicardium. This mesoderm is going to turn into connective tissue surrounding the heart with a mesothelial layer on its outer surface. The thin sheet of mesoderm which runs from the back surface of the heart towards the foregut will also turn into connective tissue with a mesothelial outer layer. And that thin sheet is called the mesocardium.

Embryonic Folding and Coelom Development, slide 50

Now as all these things are going on, other things are going on as well. And among these other things is the development of a ventrally directed diverticulum from the midline of the floor of the foregut just caudal to the oropharyngeal membrane. This endodermal diverticulum is called the laryngotracheal diverticulum, and its name tells you a lot about what it will become.

Embryonic Folding and Coelom Development, slide 51

Soon after the laryngotracheal diverticulum arises from the floor of the foregut, it turns caudally, and extends dorsal to the heart tube, pushing mesoderm out of the way.

Embryonic Folding and Coelom Development, slide 52

Let's take a cross-section of the embryo with the laryngotracheal diverticulum in place. This cross-section will be caudal to the origin of the laryngotracheal diverticulum, but somewhat before its end.

Embryonic Folding and Coelom Development, slide 53

This looks just like a cross-section we saw previously, but now we have caught the laryngotracheal diverticulum in section, lying dorsal to the heart and ventral to the foregut.

Embryonic Folding and Coelom Development, slide 54

What's going to happen next is that the mesoderm in the vicinity of the common cardinal veins (this is occurring on each side) is going to start to grow in the direction of the mesoderm that's in the vicinity of the laryngotracheal diverticulum, and this little mesothelial-covered sheet of mesoderm gets the name pleuropericardial membrane, so there's a left and a right pleuropericardial membrane. And if you go through the next few slides until you get to the one that's labeled, you will see the process of growth of the pleuropericardial membranes towards the mesoderm in the vicinity of the laryngotracheal diverticulum. I have colored them a deeper shade of pink, but they are no different than any other mesoderm.

Embryonic Folding and Coelom Development, slide 55-58

No narration.

Embryonic Folding and Coelom Development, slide 59

The previous slide showed the pleuropericardial membranes joining the mesoderm in the vicinity of the laryngotracheal diverticulum. In this slide it shows them as well, but I have removed the darker color just to again indicate they're just the same as any other kind of mesoderm of this region. The important thing that has occurred is that there has now been complete separation of the pericardioperitoneal canals from the pericardial cavity. That is why in previous slides and when I thought about it I always refer to a future pericardial cavity because that's all it was when it was in contact with pericardioperitoneal canal. Now it has been completely isolated from those other coelomic channels, and is a definitive pericardial cavity. And we know that the connective tissue with the mesothelial lining in actual contact with the surface of the heart is called visceral pericardium or epicardium. The mesothelial-backed connective tissue which forms the outer boundary of the pericardial cavity that is not in physical contact with the heart is now given the name parietal pericardium. And the parietal pericardium is connected to the visceral pericardium by this thin sheet of connective tissue with mesothelium on it on its outer surfaces, which is called the mesocardium. What are the contents of the pericardial cavity? It is simply the fluid that was in the coelom. The heart is not in the pericardial cavity. The heart has pushed into the back wall of the pericardium, but it has not entered the cavity. The cavity is filled with fluid that was the original fluid content of the coelom.

Embryonic Folding and Coelom Development, slide 60

The mesocardium actually has a fairly brief life, because it soon starts to disintegrate, or dissolve.

Embryonic Folding and Coelom Development, slide 61

And this shows it gone, and we still have the layer of connective tissue surrounded by a mesothelium that's in physical contact with the heart as the visceral pericardium. We have the mesothelial-backed connective tissue which is the outer wall of the pericardial cavity as the parietal pericardium, and the pericardial cavity is by definition the space between the visceral pericardium and the parietal pericardium. And I remind you again, this only has in it fluid. That's the way it is now and that's the way it is, will be, until the day you die unless you have a disease which introduces something other than fluid into the pericardial cavity. Now, the space encompassed by the parietal pericardium is often called the pericardial sac. So even though we could never say legitimately that the heart is in the pericardial cavity, because that is the space between visceral and parietal pericardium, it would be legitimate to say that the heart is in the pericardial sac. In fact, the pericardial sac contains within it the fluid of the pericardial cavity, plus the heart with its own epicardial layer. It's probably difficult for you to imagine what this looks like in three-dimensions. The next slide is an attempt to show this.

Embryonic Folding and Coelom Development, slide 62

The pericardial sac is like a stretched out inner tube filled with fluid. And here we see the parietal pericardium, and we also see that at either end (anteriorly and posteriorly), the parietal pericardium turns the corner and merges with the visceral pericardium, which is on the surface of the heart and hidden from view here.

Embryonic Folding and Coelom Development, slide 63

This shows the complete separation of one portion of the coelom from another, or other portions of the coelom, by the development of the pleuropericardial membranes. We see what happens is that, actually, the definitive pericardial sac is our old future pericardial portion of the coelom plus a bit of each pericardioperitoneal canal. And then caudal to the region of the common cardinal veins (that was the region where the pleuropericardial membranes formed), caudal to that we have the rest of the pericardioperitoneal canal and its junction with the future peritoneal portions of the coelom.

Embryonic Folding and Coelom Development, slide 64

And here is our old friend: a median sagittal section, but with one change. You will notice I have colored the anterior region of the septum transversum grey, and that is not because it is a different kind of tissue. It is simply because it is going to have a fate different from the more extensive posterior, deeper pink, portion of the septum transversum. Just to indicate that these parts of the septum transversum are going to have different fates, I've given them different colors.

Embryonic Folding and Coelom Development, slide 65

And now let's take a cross-section through the embryo in the region of the anterior part of the septum transversum.

Embryonic Folding and Coelom Development, slide 66

And this looks exactly the same as a section through the septum transversum we saw before, with one exception. Instead of it being a dark pink, now I have colored it gray because we are specifically through the anterior part of the septum transversum, and we know that the anterior part has a special fate.

Embryonic Folding and Coelom Development, slide 67

That special fate is linked to the fact that the mesoderm dorsal to the pericardioperitoneal canals is going to start to grow down towards this anterior region of the septum transversum. This little sheet of mesoderm - one on the left, one on the right - covered by mesothelium, each one is called a pleuroperitoneal membrane. And the next few slides are simply going to show the progress in growth of these pleuroperitoneal membranes towards the anterior region of the septum transversum.

Embryonic Folding and Coelom Development, slides 68-70

No narration.

Embryonic Folding and Coelom Development, slide 71

And as the pleuroperitoneal membranes get bigger, the mesothelium on their outer surfaces contacts the rest of the mesothelium of the pericardioperitoneal canals, and these two mesothelial layers will merge with one another, and then the cells of the mesothelium will dissolve or disintegrate. And at that point you have complete separation of the portion of the intraembryonic coelom that is cranial to the pleuroperitoneal membranes and anterior part of the septum, from the portion of the intraembryonic coelom that is caudal to the pleuroperitoneal membranes and this anterior portion of the septum transversum. The next few slides illustrate this process.

Embryonic Folding and Coelom Development, slides 72-74

No narration.

Embryonic Folding and Coelom Development, slide 75

And now you see that I've colored the mesoderm of the pleuroperitoneal membranes grey, because in fact, they have the same fate as that anterior portion of the septum transversum.

Embryonic Folding and Coelom Development, slide 76

This shows these pleuroperitoneal membranes pushing down into the dorsal wall of the pericardioperitoneal canals in this three dimensional view, I couldn't have done this very readily with the pleuropericardial membranes. But go ahead slide by slide the next few slides and you'll see the pleuroperitoneal membranes growing down, meeting the anterior surface of the septum transversum, and then in the last one I've colored them grey as well.

Embryonic Folding and Coelom Development, slides 77-80

No narration.

Embryonic Folding and Coelom Development, slide 81

And now we can start to give names to some of the things that have been created. When the development of the pleuroperitoneal membranes is complete, and they fuse to the anterior (or cranial) region of the septum transversum, we have separated off, cranial to these membranes, definitive pleural sacs. They were previously separated from the definitive pericardial sac, now they have been separated from all of the portion of the coelom caudal to the pleuroperitoneal membranes. The portion of the coelom caudal to the pleuroperitoneal membranes is the definitive peritoneal sac. Now you see I've put the "s" in parentheses because there are still two separate ones in the region dorsal to the pink part of the septum transversum. But caudal to the septum transversum the lateral walls of the peritoneal sacs have dissolved, and that region of the extraembryonic coelom marked with an asterisk has been incorporated into the embryo, and therefore caudal to the septum transversum we have a single peritoneal sac. And you also see that I have now labeled this gray mesodermal tissue, which was the anterior part of the septum

transversum joined to the pleuroperitoneal membranes, by the fate of this tissue. It will become the central tendon of the abdominal diaphragm. The rest of the septum transversum (indicated here by dark pink) has a different fate, which we will discuss when we talk about the embryology of the gut.

Embryonic Folding and Coelom Development, slide 82

And now we take a cross-section through our definitive pleural sacs, left and right, and it also goes through the definitive pericardial sac, with the heart within it.

Embryonic Folding and Coelom Development, slide 83

Here's that cross-section, and now I've labeled the cavity of the pleural sacs as the pleural cavity. It, like every coelomic cavity, is filled with fluid and nothing other than fluid. I haven't shown the common cardinal veins on this section. They've gone on to do other things, so forget about them for the moment and maybe forever.

Embryonic Folding and Coelom Development, slide 84

And here we are a little later in time, showing that the tip of the laryngotracheal diverticulum bifurcates, sends one branch out to the left, and one branch out to the right. These are hollow endodermal tubes extending from the tip of the laryngotracheal diverticulum. Each of these is called a lung bud. The name tells you what they will become.

Embryonic Folding and Coelom Development, slide 85

Each lung bud grows laterally until it contacts the wall that surrounds the pleural cavity. This wall is a connective tissue with a mesothelial lining, and that connective tissue with its mesothelial lining is called pleura, just like the connective tissue with its mesothelial lining of the pericardial cavity was called pericardium. These two lung buds grow laterally, they contact the pleura, which surrounds the pleural cavity.

Embryonic Folding and Coelom Development, slide 86

And they push a little bit of this pleura out in front of them as they start to encroach upon the pleural cavity without entering it. Again, the pleural cavity is filled with fluid and nothing is going to enter it in a normal person. But now we can give different names to the pleura: that portion of the pleura (that is, connective tissue with a mesothelial lining or surface), that portion of the pleura which is in physical contact with the lung bud is called the visceral pleura, and the analogy to the heart visceral pericardium is clear. All of the rest of the pleura that is not in physical contact with the lung is called parietal pleura. And the pleural cavity, by definition, is the space between visceral pleura and parietal pleura.

Embryonic Folding and Coelom Development, slide 87

Here the lung buds are shown as growing bigger, pushing visceral pleura out in front of them, encroaching upon, but never entering, the pleural cavity.

Embryonic Folding and Coelom Development, slide 88

The lung buds are bigger yet, and now we see the pleural cavities really getting squeezed to a pretty small space, and this is not good, because there is not a lot of room for the lung buds to grow any further, and the lungs have got to become very big. So the next slide will show how you make space for ever bigger lungs.

Embryonic Folding and Coelom Development, slide 89

And that additional space is made by growth of the parietal pleura ventrally, insinuating itself between the parietal pericardium and the ventrolateral body wall.

Embryonic Folding and Coelom Development, slide 90

In here we show the continued growth of the parietal pleura into the ventrolateral body wall, and we show the pericardial cavity getting reduced to a very narrow space between visceral pericardium and parietal pericardium. And we show the increasingly large lungs taking advantage of the new room made for them by the growth of the parietal pleura, that is growth of the pleural sac, which is the space encompassed by the parietal pleura.

Embryonic Folding and Coelom Development, slide 91

This shows the full development of the pleural sacs as they would be seen in this kind of cross-section. The right pleural sac has grown so extensively that it comes very close to the anterior midline, and the left pleural sac has grown a little less, because the heart develops primarily on the left side and so it interferes with the growth of the left pleural sac to a certain degree. The pleural spaces, as you see, have been squeezed to a very thin area, so they are really occupied by a film of fluid between visceral and parietal pleura, and also the pericardial space has been squeezed to a very thin region occupied by a film of fluid between visceral and parietal pericardium. I remind you that the pleural sacs are the spaces enclosed by parietal pleura, and the pericardial sac is the space enclosed by parietal pericardium. The sacs not only contain the fluid of the cavities, but the structures within them - a pleural sac containing the lung with its visceral pleural covering, and the pericardial sac containing the heart with its visceral pericardial covering.

Embryonic Folding and Coelom Development, slide 92

We really aren't going to talk much about lung development in this course, but there is one fact you should know because it has clinical import. The lungs become functional as respiratory organs sometime during the seventh month of fetal life when that is measured from first day of the last normal menstrual period - that is the way physicians normally measure it. That means that sometime during the period between the 24th week and 28th week of last normal menstrual period life, your lungs start to be able to do what they're intended to do. Most children by the 28th week, if they are born that prematurely, will have functional lungs. Most children, if born at the 24th week, will have nonfunctional lungs, but like all things in biology there is some variation in this regard. If you're born too early in this period of time you are going to probably require some special medical intervention in order to survive. That intervention often takes the form of administering artificial surfactants, which is really one of the limiting factors in lung function in children born too early in this period of time.

Embryonic Folding and Coelom Development, slide 93

Alright, back to a cross-section slightly modified from the previous one, because now I've shown what's been going on with the somites. You've either had this lecture in gross anatomy or are about to have it soon. Somites contribute to the formation of vertebrae, so I've shown a vertebra here. They also give rise to these things called dermomyotomes, which are going to form the skeletal muscles of the body wall, and I've shown those in sort of dark pink. And then within the body wall, we actually have the body cavity which contains the pleural sacs with the lungs, the pericardial sac with the heart, and the laryngotracheal diverticulum, the foregut, the aorta and the cardinal veins. Those are the structures contained within the body cavity of the chest or of the thorax.

Embryonic Folding and Coelom Development, slide 94

Here is a picture with a lot of those structures removed. And, in fact, everything between the right pleural sac with its lung and the left pleural sac with its lung is gone; it's been replaced by this white area. By definition, the space between the right and left pleural sacs is called the mediastinum, and its contents are, as you must have deduced, the pericardial sac with the heart in it, the trachea, the foregut representation in the chest (which is the esophagus), the aorta, and the veins on either side of the aorta. Also, I might add, that the parietal pleura that faces this area called the mediastinum is also called the mediastinal pleura. So there is the mediastinal pleura of the right pleural sac and the mediastinal pleura of the left pleural sac, which I have so labeled.

Embryonic Folding and Coelom Development, slide 95

Here's a picture in which the contents of the mediastinum are highlighted. Obviously, the main content of the mediastinum is the pericardial sac with its contained pericardial cavity, which has only fluid in it, and the heart itself. Just dorsal to that, one of the contents of the mediastinum is the trachea and the first parts of the two bronchi which branch off from it. Dorsal to that, a content is the foregut representation in the chest, which is, I said before, the esophagus, and then the aorta and some veins on either side of it. In dissection, you will see that there is also a considerable amount of fat in the mediastinum. There are some important nerves, some lymphatic structures, but I have not bothered to illustrate those here.

Embryonic Folding and Coelom Development, slide 96

This is a pretty highly schematized drawing of the embryo as if we could see it from the front. You can see the two pleural sacs, right and left, and how they have expanded towards the midline ventrally and partially obscure our

view of the pericardial sac. You see the septum transversum with the cranial surface, which is going to be the central tendon of the diaphragm, in gray, and all the rest of the septum transversum that we will talk about later. Now, this expansion of the pleural sacs into the ventral body wall to accommodate or allow for growth of lung - even that is insufficient to provide all the space that is necessary. And so as indicated by the arrows here, the pleural sacs are going to additionally expand into the lateral body wall.

Embryonic Folding and Coelom Development, slide 97

And this shows the expansion of the pleural sacs into the lateral body wall, separating off some mesoderm from the lateral body wall to actually join what is the central tendon of the diaphragm. Now that light pinkish mesoderm that is attached to the edges of the central tendon of the diaphragm will be invaded by muscle cells, and the next slide illustrates that.

Embryonic Folding and Coelom Development, slide 98

This just shows these lateral regions of the diaphragm in some sort of color appropriate for muscle. The actual muscle cells that invade this part of the diaphragm come from the 3rd cervical through 5th cervical dermomyotomes. And you will learn later that the innervation of the muscle of the diaphragm is via the phrenic nerve, which is derived from the 3rd through 5th cervical spinal nerves. The central tendon of the diaphragm, indicated here in grey, as we know, is derived primarily from the cranial surface of the septum transversum, but also to a certain extent from the pleuroperitoneal membranes.

Embryonic Folding and Coelom Development, slide 99

I don't have to read this to you. This just summarizes the important events that occurred during the 4th week of development: the most important being that the embryo changes its shape quite dramatically, from a flat, although multilayered, disc to something which is shaped like a hotdog. And in fact after you read this, go to the next slide because there will be a picture of what the 28-day embryo really looks like.

Embryonic Folding and Coelom Development, slide 100

Well, the 28-day embryo doesn't look all that much like a hot dog. It looks like a hot dog, I guess, that has been bent and has some very unusual characteristics. I've labeled a few things here. 'm' is the mouth region of the embryo; it's actually called the stomodeum, but we'll talk about it later. The letter 'n' refers to the neck region. You can see that there are some things going on here I haven't previously spoken about. These things are called branchial arches; we have an entire lecture devoted to them. They have begun to develop in the fourth week, but let's forget about them for the moment. 'h' refers to the heart; it's that big bulge ventrally in the trunk region. 'ul' is the very beginnings of the upper limb. 'll' is even a more rudimentary beginning of the lower limb. The embryo has a tail at this stage of development. And you can see very clearly positioned dorsally in the tail, and then even extending dorsal to the lower limb and along the back of the embryo, these little squares, which are in fact the somites that we are seeing through the translucent ectoderm of the embryo.