Introduction to Developmental Biology
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Lecture No-02
Life Cycles and Evolution of Developmental Patterns

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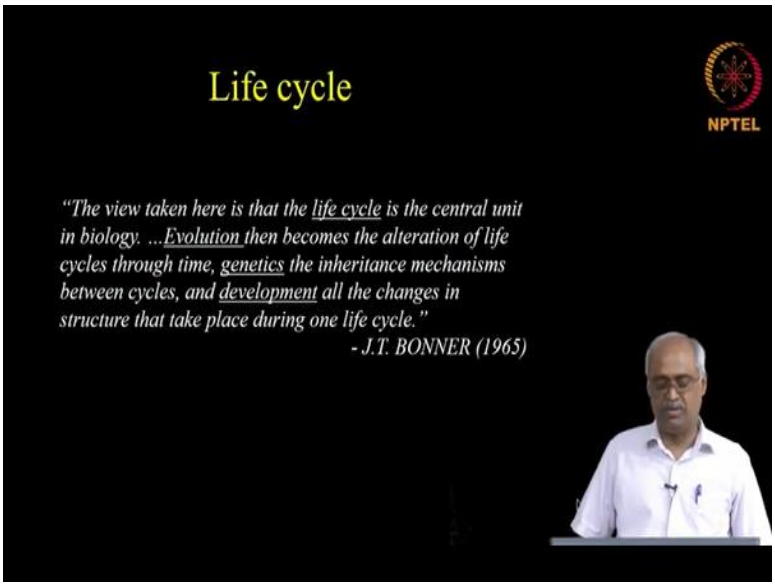

So today we will get into some details of that for a better grasp of it and then we will move into other concepts.

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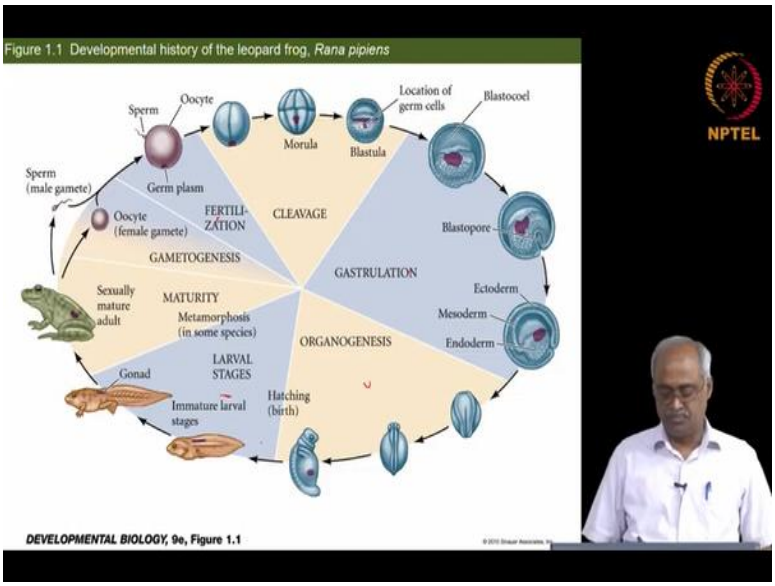

So you are already familiar with this diagram. So, fertilization, cleavage, gastrulation, organogenesis, maturity, and gametogenesis. So, this is what we saw and, in some organisms, you have significant metamorphosis from the newly hatched organism to the adult.

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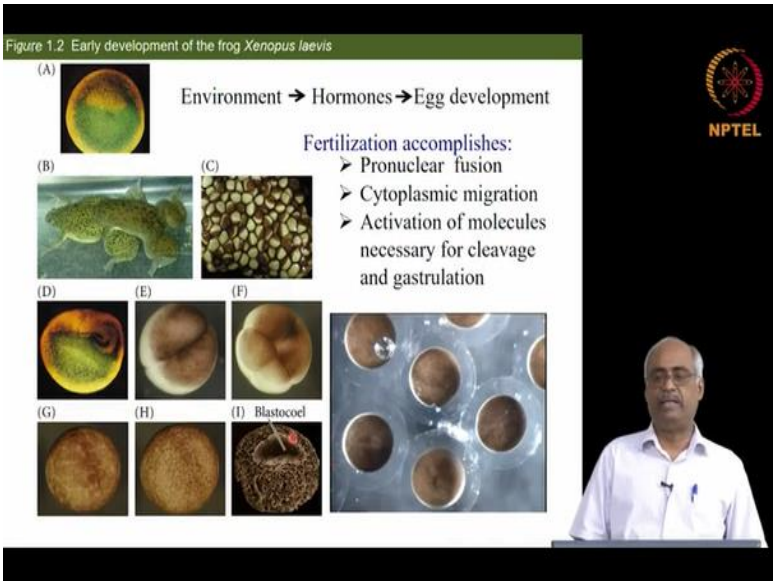

So let us look at some details of the life cycle of one organism that has significant metamorphosis also, that gives you an idea of what we are talking about when we talk about the life cycle. So the first image if you look at it, that is an egg, newly fertilized. So there I want to highlight one important point particularly in the current times this is important.

So what makes the oocyte to develop first in the female? believe it or not, in most organisms it is the environment; light, duration, temperature matters. For example; in frogs both of them matter, the long day, short day matters because tadpole during the larval stage needs to feed and for that it needs the spring season. So it has to happen at the right time, so the changes in the photoperiod, as well as the temperature, stimulate its pituitary to secrete hormones that are going to induce the ovary to a signal. Now as the egg develops and it triggers the hormone from the ovary, the ovary is an endocrine gland and that stimulates the liver to produce all the food materials like the yolk to fill in the developing oocytes. So that is how oocytes mature, so the environment plays a key role in development starting with fertilization itself. The same happens not that dramatically but with sperm production as well in this species, in some species, it is continuous sperm, sperm production is from reaching adulthood till the end of life most organisms produce sperm but in some organisms that are seasonal too. Like in frogs it is seasonal and I am not sure how many of external fertilization.

What is it? What did they do? so external fertilization is, for example in humans the fertilization and the embryonic development happens inside the mother's body and that is what you are probably familiar with and you may not even know that this whole thing can happen externally.

So here when in the correct season the male frog grasps this female that stimulates the egg discharge as well as the sperm release; both are coordinated, so therefore in that microenvironment, the probability of the sperm and oocyte fusing is very high otherwise suppose if the female releases egg somewhere and with no males around and what will happen to those eggs? Other animals will eat right away.

So there will not be any eggs left, so these happen simultaneously. So the female releases the egg and the male releases the sperm and they get fertilized. So now let us look at what is fertilization? So you already know the fusion of sperm and egg is what we call as fertilization. So it achieves the following three points: one pronuclear fusion, both the nuclei fuse and create the diploid first nucleus of the next generation. Then cytoplasmic migration, the internal rearrangement of the cytoplasmic components for example in this it is colored stained to distinguish, in frog one part is called the animal hemisphere where cell division is more rapid and migration is also more and the opposite side of that is the vegetal pole where you have mostly the yoke stored, and there the cell division is not rapid and which is going to be animal pole and which is going to be vegetal hemisphere? we will get into details later when we are going to talk about embryonic polarity. So, for now, do not worry about it but these can be easily distinguished and in the frog, you have pigments if you see this figure c where I am pointing out the brown thing is the animal hemisphere.

You have a clear pigment that marks, and this is one of the reasons why people select certain embryos for study because natural pigments help you to follow what happens and if you see figure d you will see that if you compare with a, a and d you see the cytoplasmic rearrangement and this also leads to activation of molecules. So what are the molecules that are activated and how that is choreographed? that itself is an entire branch of study within developmental biology.

So we will not get into the details but the main point is there are molecular changes that happen triggered by fertilization and these changes are necessary for the cleavage and gastrulation. So the first cleavage you see in e okay, the first division starts here, again in the last class I mentioned cleavage as opposed to cell division, so this is a cell division but

without any change in volume so the existing cytoplasm gets partitioned into smaller compartments.

So you have nuclear division but there is no increase in cell volume, so it goes on (E), (F), (G), (H), (H) is a late-stage blastula, and then during this process, a cavity forms too, so this is a dissection of that embryo revealing a cavity formed inside called blastocoel and that helps in migrations that happen at a later stage during gastrulation.

So, if I play this video so if you watch this is just showing you as a time-lapse the same thing if it plays okay, this is not playing.

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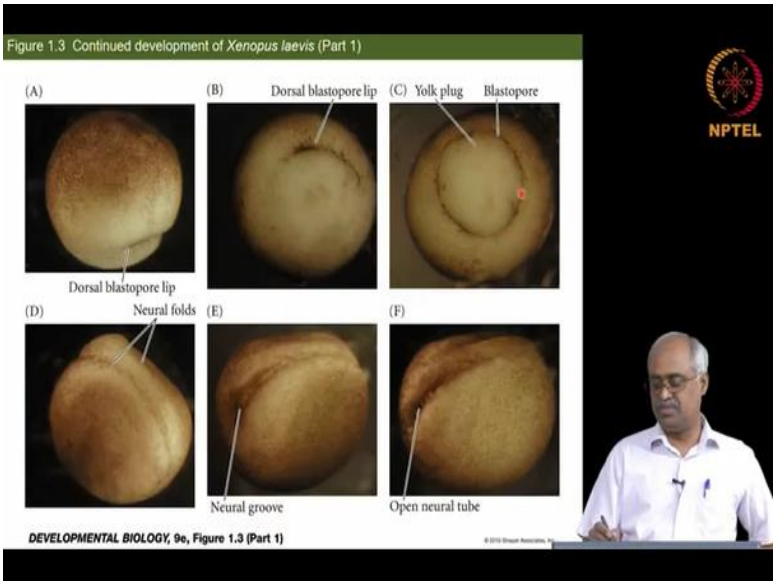

But, let us see the next video. So say this video is going to show you the same thing that is there in d2i. So the next is gastrulation; so let us look at that, in this the starting point is so the start is the formation of a depression called the blastopore. So, it is an invagination of the cytoplasm and the membrane starts to go in and this continues and forms a circle like structure and where the cells actively move inward into the embryo and those cells that move inward they are the ones that are going to form the mesoderm and the cells that are going to stay outside at the end of gastrulation are going to be the ectoderm and this yolk filled cells that are going to be internal to the cells that are moving in are going to be the endoderm. So that is what is going to happen so next movie when we can play you can see this process happening and once this ends then you have another depression that forms which is going to be called the neural fold.

You can see that two mountainous ridges like structures forming and depression in the center and that is going to move and then these two mountains like ridge are called the neural crest and the middle the depression this is the neural groove, so this is going to be the animal at the end. So the one end is going to be the head another one is going to be the tail and this entire thing is going to be your spinal cord this is not your vertebral column, this is the neuronal structures, so the brain and the spinal cord and then these neural crests come and fuse, then this neural fold eventually goes and fuse.

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So that is what happens and that is visible in the next.

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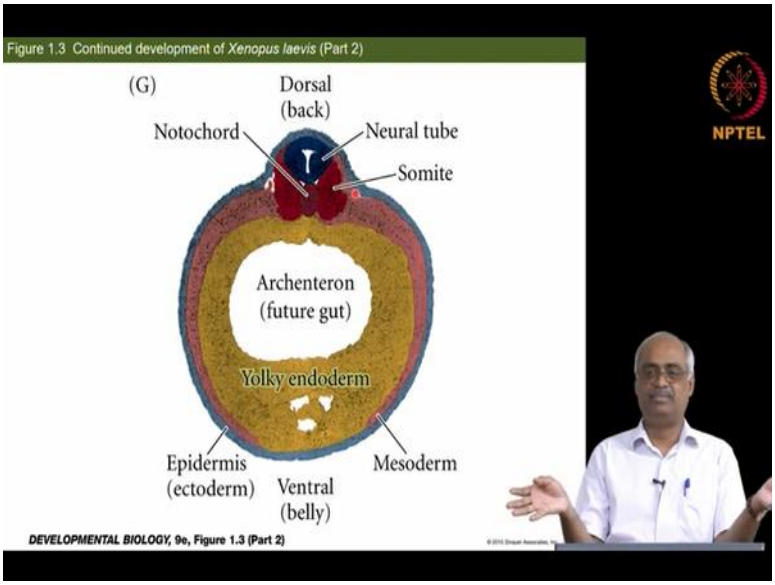

then we will come back to play the movie, so this is a cross-section and it is stained where you are seeing that the two ridges, have fused and formed this neural tube. So one end of the neural tube is what is the brain, and the cells that moved in those are the important things you need to see in this. So you have this light pink color one this is the mesoderm and this blue outside is the ectoderm and then you have the endoderm. So this is the mesoderm the one that moved in and a set of mesodermic cells form these structures called somites and some of these mesoderm cells form a tube-like structure called notochord this is a transient structure required for embryonic development but later it is not found in our body. So this is required to instruct these cells to stay as neural cells not to become pigment-producing ectoderm.

So this is the one that inhibits that and so that is required transiently to ensure that these do not become pigment-producing cells and these somites are the ones that are going to produce the spinal cord, vertebrae, and muscles at the back, not pigmentation, the pigment-producing cells come from the ectoderm. So, if notochord does not tell the ectoderm not make pigment-producing cells they will all by default get into that, so you will not have the brain. So notochord tells them and then it stops. So this is the end of the gastrulation

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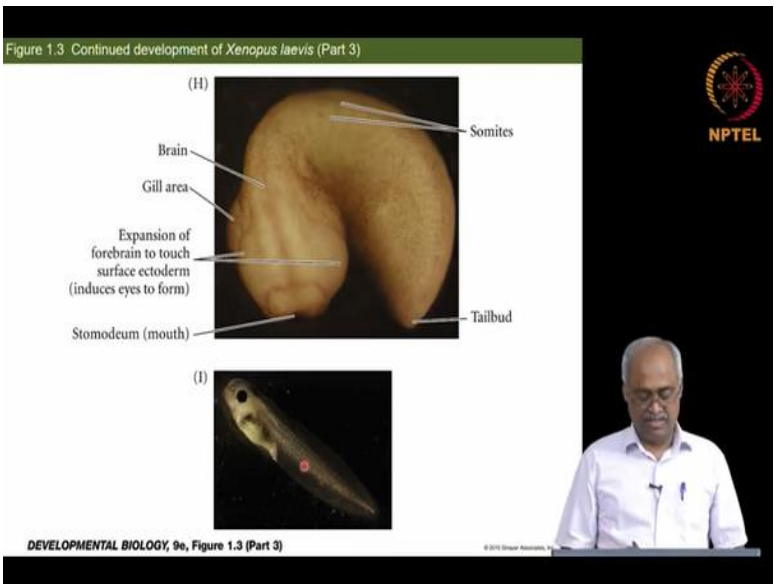

So at the end of which this is the structure you get after gastrulation. So, we are giving up a lot of details because that is what we are going to learn in the rest of the course, so this is just a summary. So at the end of that, you have this is in one end of the neural tube, so that is the head and these four brain projections are the ones that are going to induce eye formation.

So that is why all your sensing ports are all on the head very close to the brain and so this is the tailbud and the limbs will develop much later so and then you get the swimming tadpole. So this is the end of embryogenesis, so if we go back to our thing. So we have come up to this, so now we need to see this is, this is a very, very remarkable change that is going to happen in this organism. So that is in the next one.

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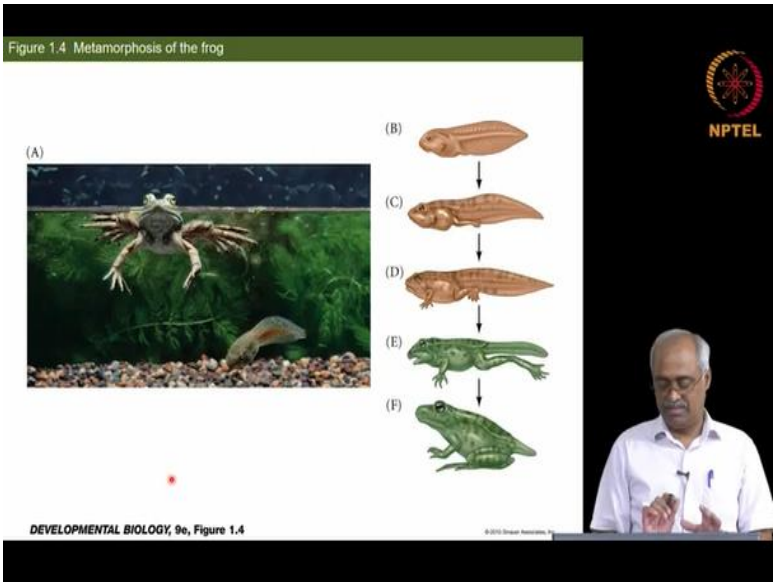

Metamorphosis, so essentially the tadpole which is an herbivore, it eats all these plants that grows in the pond or the river bed or whatever in a water body that it is in. So it has a big fin-like tail and that is going to slowly regress into the frog; it has a gill-like structure for respiration inside the water and that is going to shrink and then the lung is going to expand.and then this has a big digestive system which is characteristic of any herbivore and that is going to become smaller and become like the one of the carnivorous frogs and similarly, the teeth meant for grinding grass they are going to be replaced with for carnivorous thing particular development is the tongue that it can push out and catch a fly, so all these things are going to change. The cartilaginous skeleton is going to become a proper bone of the frog. So all these changes happen from here to here, so that is the metamorphosis, so this is characteristic of a large number of species, and since it is not this obvious in many organisms that we encounter every day including human we do not worry too much about it but it is a remarkable change that happens.

It is just that this process has been either exaggerated in some organisms like frogs and butterfly and silkworm etc and kind of reduced in some other organisms like humans, the changes are not that remarkable but the basic process remains and it is conserved.

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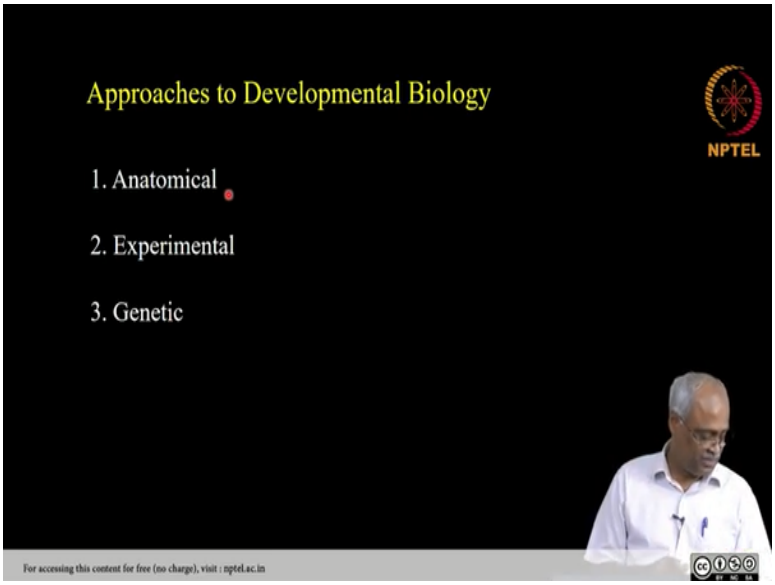

So that is some in-depth into an organism's life cycle. Now, we come back to learning developmental biology; remember the three approaches that we talked about- anatomical, experimental, and genetic. She asked a question after leaving the class and that is an important question: are in the genetic experiments, the experimental approach and why should it be a third one.

So the answer to it is partly historical and partly certain experiments are not involving genetic manipulations. For example, you open up the embryo and change the plane of cell division or you introduce some dye and watch the movement of a cell as the embryo develops. So those kinds of experiments are changing the conditions like for example; you take the egg of a reptile-like a crocodile and keep it at different temperatures. And see what happens to sex determination. So or you cut off a certain part of the embryo and see what part does not form or what part still forms? in which organism this happens? and in which organism it does not happen?. Like for example; if I take a human embryo at a very early stage if I cut half of the embryo still it is going to form a proper normal wild type human. But if you take *C. elegans* embryo and if you do that it is not going to form that.

So that we will learn when we are going to learn about determination, fate specification etc. So those kinds of experiments were the ones initially done, people did not appreciate the power of genetics to learn biology very early on. You will be surprised to know much of the genetic approaches to learning development started in the mid-80s and was really at its peak during the early 90s.

So, in a sense it is historical, so there are a whole lot of experimentations that were done before introducing genetic approaches and that is why for convenience, we consider them as two separate approaches here experimental and genetic. So, in a practical definition experimental approach means the approaches that did not involve genetic experiments. so, the next what we are going to do is we are going to focus on anatomical because there are a lot of important historical points that help us to shape our thinking of developmental biology.

So, you might think why should I go and worry about all the historical things but that gives you a framework to think about the basic concept of developmental biology.

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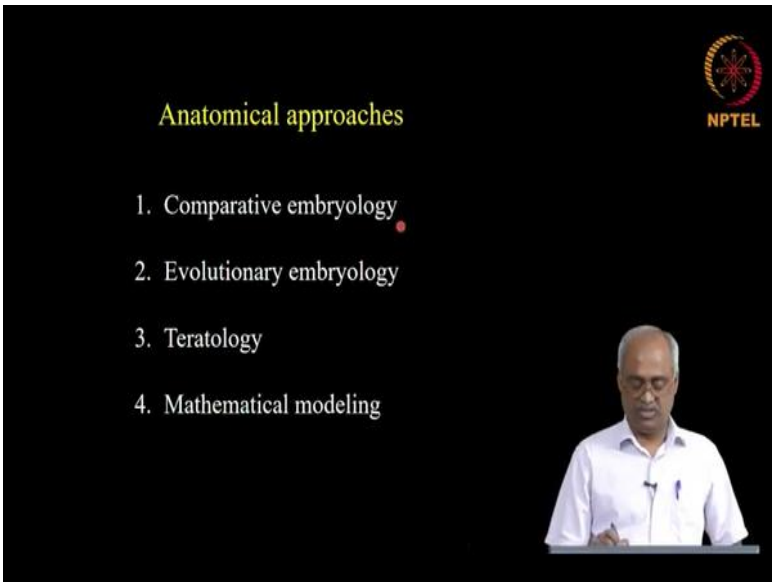

So, therefore, we will look at some of them all right so let us look at anatomical approaches first; so, the very first one that we are going to look at is the comparative embryology. So, you are going to find how useful it has been historically in connecting evolution and development.

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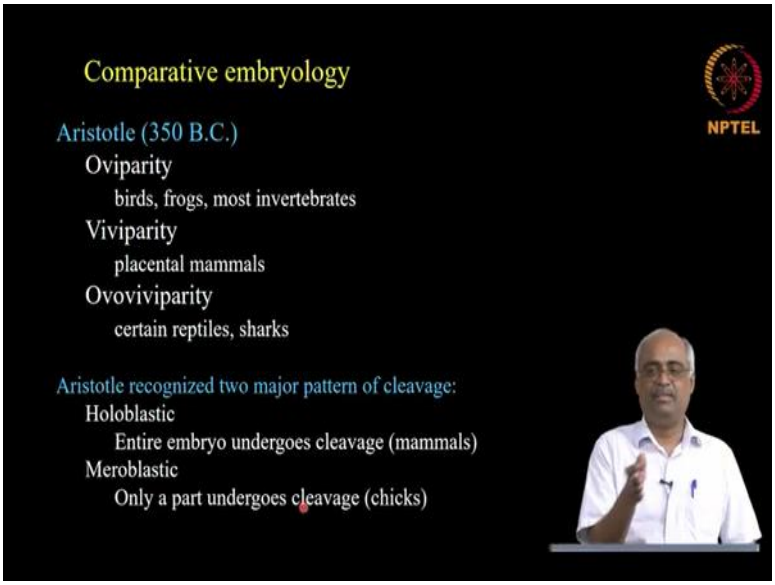

So often this is called evo-devo, some scientists work on this interface between these two disciplines and there they call it the evo-devo problem. So, they are evo-devo biologists, so the very first embryologist is Aristotle, he was the first one to observe and note the variations in the way in the initial stage. Like for example; he identified there are certain organisms like frogs, birds, and many invertebrates, they all lay eggs and from the egg, the new individual organism comes out.

And then he noticed the placental mammals, the entire embryo develops inside the mother's body, so he called that Viviparity, coming from the body and oviparity coming from the ovum and then he also noticed some of them that have both Ovoviviparity. So the whole egg develops inside and then it is laid and hatches. So certain reptiles and sharks do this.

So, he classified this and then he also noticed that there are some embryos where the entire egg undergoes cleavage. So, we saw in the frog the entire thing undergoes cleavage except that the animal hemisphere cell division is more rapid and more divisions than the vegetal pole but the whole thing cleaves but in some of them only a part of the embryo undergoes cleavage.

That is what happens in our embryogenesis and generates this inner cell mass and the bulk of the embryo is not part of that, only a small portion is the inner cell mass from which our whole body is derived and then some of them you have the entire embryo undergoing cleavage and some like chicks, only part of it undergoes cleavage. So holoblastic and meroblastic, so that is the classification he could observe.

So these are very early observations and classification, so no experimentation here but this helps to know these differences helps to generate the questions like why is it doing this and why not that and why the other one does that and not this and those questions form. Initial observation, a systematic observation and classification often is the starting point of asking addressable questions.

So that is important in addressing anything in science, so now you see the timeline 350 BC, then the field sleeps for a long time; a dormant stage. It is going on in the brains of people but then no breakthrough.

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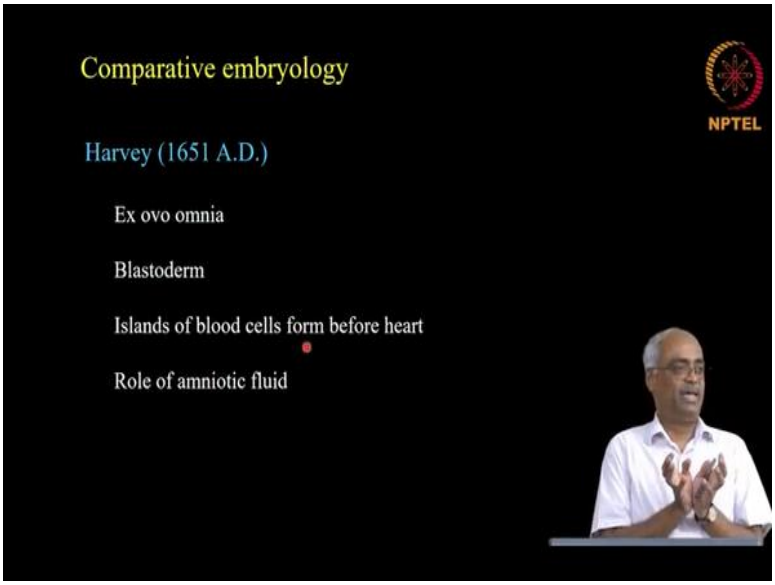

And, then 1300 years later Harvey observed that all life come from the ovum or the egg. So, Ex ovo omnia, meaning omnia is everything, ex means coming out from the ovo, everything comes from the ovo and then he was the first one to identify this blastoderm stage in some organisms, and then he also identified the formation of blood cells in the embryogenesis.and he noticed that happening before the heart and then he also found what is the purpose of the function of amniotic fluid, that is the fluid-filled sack that cushions the embryo in most organisms including humans and he was the first one to describe the function of the fluid. So there is some progress.

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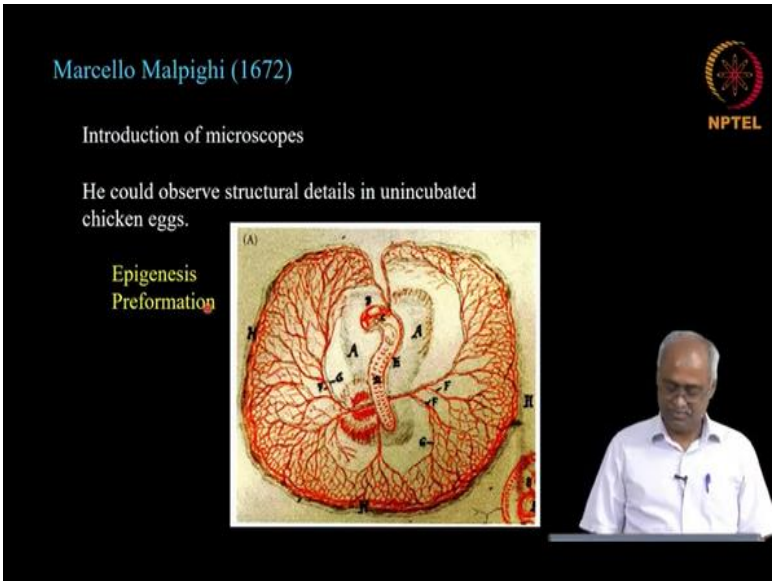

And, then microscopes were invented and that made some rapid progress as well as a controversy that lasted for a long time and now when we look at them you will find it very hilarious. So we will get into that in a couple of slides, so when the microscopes were introduced like Marcello Malpighi he could see details he could open the egg, egg meaning the chick egg, break open the eggshell, and then you can observe it. This is big enough that you can do without a microscope and once he got the microscope, he could make detailed observations and draw. So he did not have a CCD camera and all the sophisticated microscopes and recording devices that we have now. So on those days this was there even when I did BSc like when we do dissections and observe in the microscope we have to draw that. So whatever we see in the microscope exactly you have to picture that on your practical record notebook, so that we did it for practice but in the 17th century that was the only way they could record any microscopic observations there is no way to record it on a film or on a digital device. So, this is one such early drawing of what Malpighi and his contemporaries observed using microscopes of the chick embryo.

So when they could see a lot of details, here structural details means we mean the biological structures we do not mean molecular structures here, remember that he could see a lot of structural details in unincubated chicken eggs meaning, embryogenesis is not it taking place but then he could see the details but he saw too much more than what is there, so that led to a hypothesis called preformation.

And what this preformationist proposed was, this the entire body like the human body if you take our entire structures including external morphology and internal structures, everything is

preformed in a miniature form and that is already there and now you need to unfold it and allow it to grow, so that is the preformation. So now how does the next generation happen in that preformed structures gonad inside the gamete, the further smaller structure exists.

And they did not have cell theory to deal with the size of cell etc. So therefore they could think as Scott Gilbert remarks on, they thought that nature works as small as it wishes. There was no cell theory to deal with and they thought it can be infinitely small and also they did not think that we have the potential to exist forever on earth, if we do not mess up the environment and kept things going.

We may be able to live forever meaning the species survival; I do not mean individual survival. Homo-sapiens can exist forever, so why I am bringing that point is if you are going to live forever like a whole lot of infinite number of generations. So can you have that many preformed structures one within the other like that, so they did not need to worry about it. So they thought life starts at genesis ends at the resurrection.

So perfectly fitted with the religious thought that existed in Europe and therefore biologists were not shaking the church. So they were all okay, happy going fine right? But then truth as always comes out.

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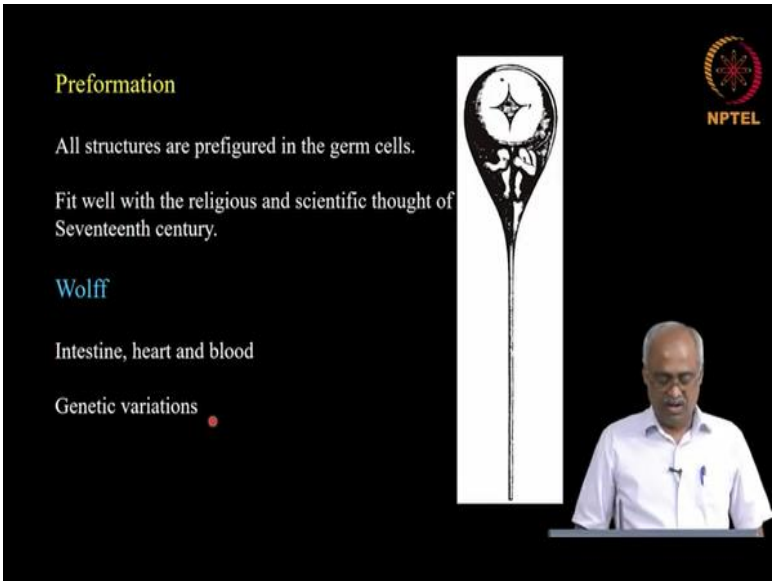

Another hilarious thing I want to bring out is, there are two gametes which gamete has this preformed structure the sperm of course right? So, because the religious domination plus

male domination of the society that shaped the scientific thinking. So they thought that the structure is preformed inside the sperm head, and the egg provides nourishment.

So therefore in the fertile ground the organism, the preformed structure is unfolded and it grows. So this is what they thought all structures are prefigured in germ cells it should be called in the sperm and this fits well with the religion and science of the 17th century. But then other inquisitive minds want to look at the actual evidence and then they want to reconcile with the existing model.

And if the model does not accept or is not explaining some of the observations then you refine the model, so that starts happening. So can you think of any such early observations that would have contradicted this but can you focus on this what would have challenged this what everyday observation would have challenged this idea, even features like if you have your grandfather's style of hair and not your mother's or father's, so how is that possible?

That is one and second, the plant breeding people when they generated hybrid and the hybrid looked different from either of the parents. So, these things challenged the idea of preformation, and then when people started realistically observing more without imagining. In the microscope, they saw structure shaping like some tubes shaping from flat structures, so all that made them think that preformation may not be true.

So, this pretty much happened in Germany because Germany is where that is a place where early embryology took root. So, Wolf, he found the formation of intestine, heart, and blood, these things were happening from structures that were not resembling them. There are no blood cell-like structures from which blood cells came, the pigmentation for example.

And similarly, the heart is a tubular structure that came from the folding of flat tissues that were there and same to do with the intestine or any tube, tube structures came from flat structures and then genetic variation this is where I said, hybrid plants that did not resemble either of the parents. So, all of this made people think that preformation may not be true. So, there was a raging argument and debate as you can imagine between the two groups.

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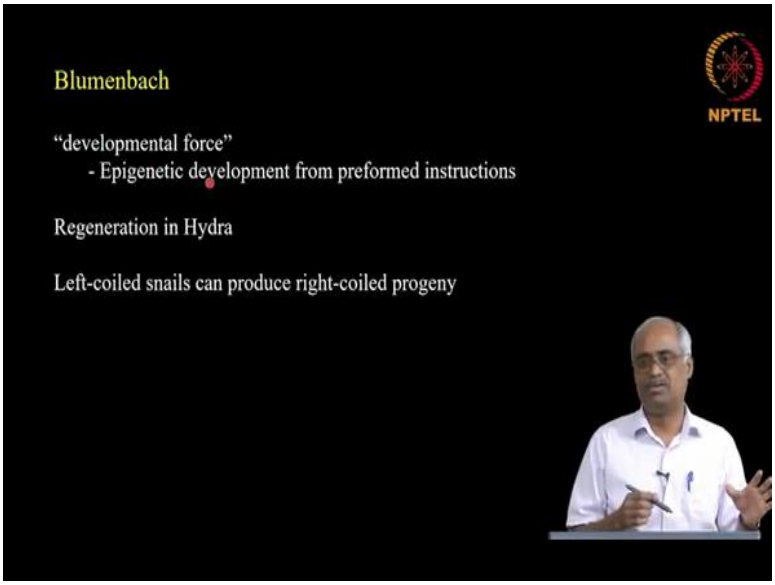

And then Blumenbach attempted reconciliation and that is he came up with the idea of developmental force, so he said developmental force is a preformed instruction that is there in the embryo not anywhere else and that directs what is going to develop and he said it is not merely a hypothesis he can demonstrate it and he could take hydra and cut part of it and see that the cut structure develops not any random structure, but exactly the missing structure developed, so that means the left out cells in the rest of the hydra they could rearrange and they knew what structure to form, they had the instruction otherwise they cannot make it and that is what makes and then he also accommodated variations that happened in this, this developmental force is not having one set of instruction and that instruction is subject to change.

For example; left coiled snails could produce right coiled progeny or vice versa, so this is now very close to our modern view, we have genetic instructions that lead to the development of an organism. So this is how in the end you come to putting epigenesis into the dominant place and preformation is laid to rest. So after that, there is nothing about preformation.

But you see unless otherwise, you go through this history you will not understand these things how the thought shaped because our thought is a continuation of that.

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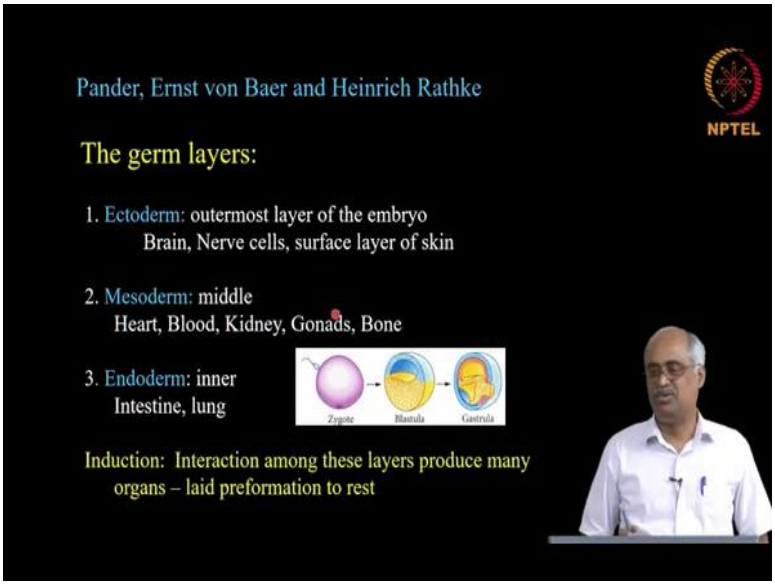

And that is why it is good to revisit these things, so then microscopes became more and more sophisticated and more and more people got interested in observing embryo and there was a lot of activity and the German university system allowed all of this to happen readily and of the many, these three Pander, Von Baer about whom we will learn a lot and Heinrich Rathke.

So these people made a lot of observations and made some really useful summary of that and one of the main points that they observed is the formation of three layers. So for the first time, they recognized the three layers; ectoderm the outermost and then the mesoderm, the one that went into the blastopore expansion, so during that cell migration the cells that go in which finally give rise to the internal organs; heart, blood, and kidney and so on and endoderm, the innermost cells that form the intestine and lung, in the luminal part of it, the internal of the tubes, the external is mesoderm again. So that is again to highlight the point that some of the organs have multiple cell layers contributing to them and during this process they also recognized that by experimental manipulation of the three layers they were able to show the existence of induction, meaning one set of cells, for example, mesoderm could be induced by ectoderm or vice versa. So you saw notochord inducing the ectoderm in the neural tube formation, so that process is called induction, which we will learn in great detail several lectures later induction, competence, and so on.

But these guys were the first ones to recognize this and the induction also in the context of the epigenesist preformation argument was the final nail on the coffin, so to say when you have one layer inducing another layer to form and where is the preformation right. So after that, there is no talk of preformation.

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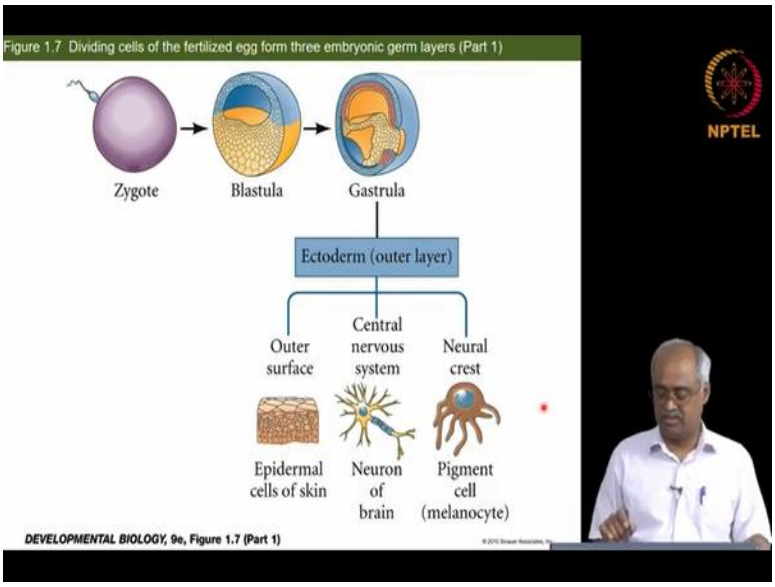

So this is details of what kind of cells come from which layers, so in the entire lecture series we will have these colors maintained this blue color will be the ectoderm, that pink would be the mesoderm, and then yellow would be or orange would be the endoderm. So the ectoderm, the outer layer gives rise to the surface cells of the skin, not the entire skin remember that.

So oftentimes people make that mistake and the inside portion of your skin called the dermis is from mesoderm and neurons and then the neural crest from which you get this pigment forming cells. So the entire set of your skin cells are not melanocytes, so melanocytes are few which are just below the surface they produce the pigments and they are there in other parts of the body to in the internal organs too it is not only in the surface.

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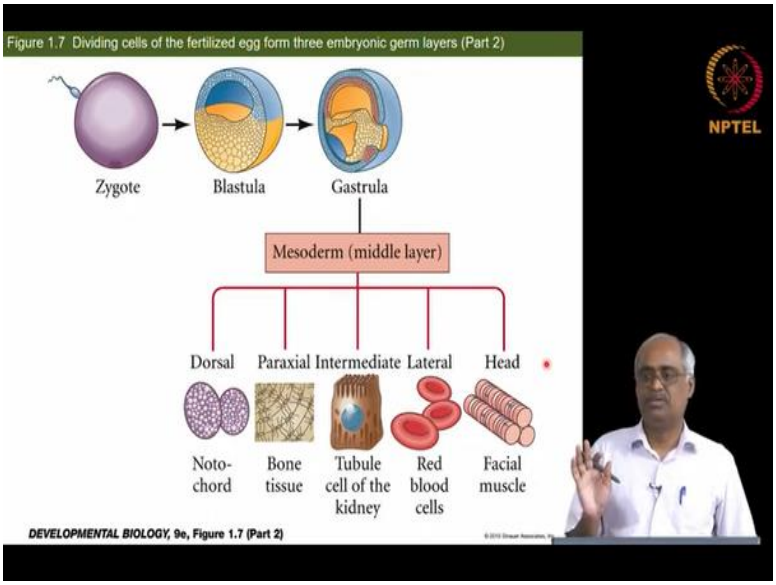

Then mesoderm gives rise to notochord we already saw that then bone tissue, then tubules of the kidney, unlike the tubules of the lungs or intestine, tubules of the kidney come from the mesoderm the other two that I mentioned are from the endoderm, red blood cells, muscles etc. So the very precise details you need not remember but you should know what is ectoderm, mesoderm, and endoderm and loosely what structures come from them.

Then every one of them you need not know like you need not know all of the cell types that come from mesoderm but at least you should be able to say mesoderm means internal organs are formed from that and some outstanding examples like intestine the outer side is mesoderm and inside is made from endoderm and brain and the skin surface is ectoderm. So at least that much you should know.

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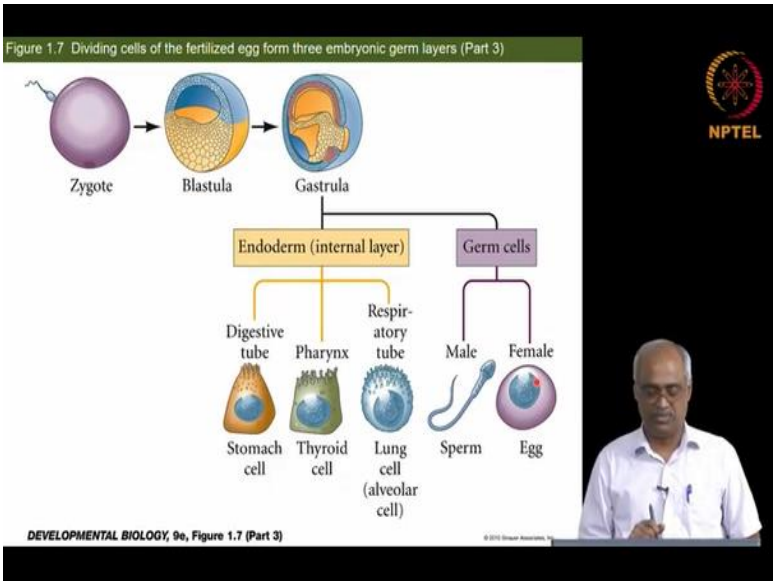

So this is the endoderm you have the digestive tube, the intestinal mucosal layer the inside the cells that have the microvilli they come from endoderm, similarly the glandular cells in the thyroid and then alveolar cells in the lungs come from this and our special cells do not come from any of the three they come even before that and they are the germ cells that are going to make the egg and sperm.

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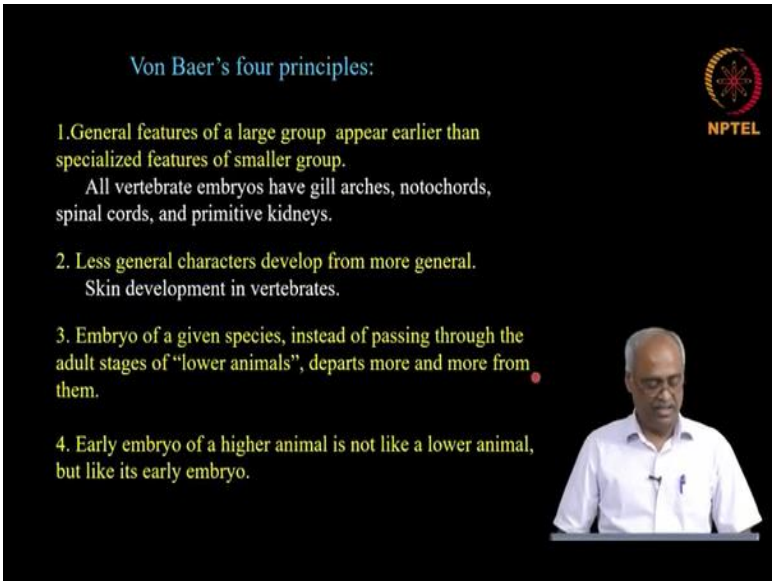

I will quickly probably tell a little bit about this but then we will do it in detail in the next class. So Von Baer what he did is, so I kind of briefly summarized their work but it is a really large body of work. So they did a lot of comparative analysis of early embryos of many, many organisms and by observing the embryos at different stages Von Baer proposed four

major principles. And that are the guiding principles till today and that influenced the Darwin in his understanding of how developmental variations help in evolutionary adaptation and the main thing that came out of that is when you want to look for evolutionary connectedness like if you want to find which organism is evolutionarily more closely related to which other organisms the right thing, right stage of the life cycle to compare is the embryonic stages and not the adult stages and that idea comes from Von Baer's principles.

So, let us at least look at the first two principles today which are quite easy, so what Von Baer proposed is that the general features of a large group appear earlier than the specialized features of a smaller group. So meaning, if we take all mammals so that is a larger group as opposed to taking only primates, primates means some of these monkey species and the human you would consider as primates but mammal means you will go all the way up to including all cattle as well. It will relate us not just with the monkey jumping on the corridor but also the deer downstairs, so if you take such a larger group and if you go to the early embryo you will find they are resembling each other. So very early during embryogenesis, the general features of the larger group are there, and as the embryo develops you tend to lose that and you get specialized features.

So general features of the larger group appear earlier in the embryogenesis, so the primary idea is this if you think, in the mammal evolutionary phylogenic tree if humans are the latest, so a human embryo while developing it does not go through making deer and then the cow and then on a blackbuck and then a primitive monkey and then an ape and chimpanzee and then human, it does not go through that.

So, these specializations happen from a common starting material, so that is the crux of all the four points. So that is why he says general features of a larger group appear earlier than the specialized feature of a smaller group like the primate features do not appear earlier in our embryo so what appears early applies to the entire mammal group so you will see when I am going to show a picture.

That not just the mammals even the fish embryo and our embryo resemble when you go sufficiently early enough and a derivative of that is what is the second point, less general characters develop from more general ones like from the very early feature which we are going to call as general feature encompassing a very large group of organisms from them only specialized features come.

Like for example, the structure from which your hand forms, is your hand like with the digits split and with the two joints, etc, this is a specialized structure and it starts from the limb bud which is present in all the vertebrates and this is a specialized structure and this comes from the limb bud which is a general structure this is the same case if you look at the other organisms.

For example, here I have taken the skin development in vertebrates as an example, so initially, all of them have a similar skin in the very early, skin-like cells but then in birds, it forms the claws and the scaly legs and so on in, if you take crocodile it is the skin has a certain different kind of scales, fish has some other kind of scales and birds develop feathers as well and then so. These are specialized features of the skin and these specialized features come from a more general skin-like structure that is present in an early stage. So, as a result a more evolved organism so here we are using lower animals for convenience actually but it is not an organism that is existing now, it is in no way inferior or lower to any other more evolved organisms. So primarily what we mean is simpler anatomy and like you did not go through as an embryo the simpler anatomy that the other mammals have and then reach the human anatomy. So both the simpler one and complex one start from a general feature and from that you are more and more specialized. So, therefore early embryo of a higher animal is not like a lower animal but it is like the early embryo of that lower animal.

So, this is the main point of the Von Baer principle, so tomorrow we will look at tomorrow meaning the next class we will look at how this influenced Darwin's thinking, so I will stop here.