3. Early Embryology.

Embryology, in simple words, is the study of life before birth. A new human being comes into existence at the moment of fertilisation, the meeting of male and female germ cells. The single cell thus formed divides to form a mass which is embedded in the wall of the mother’s uterus, a process called implantation. Further development leads to the formation of a three-layered embryo. The flat three-layer disc then folds in a complex manner and forms a tube. This is followed by the development of the organs and systems of the body. Within a few weeks we can see the almost human form of the embryo. At the end of this stage the organs systems are not necessarily in a fully functional state. The new human is now called a foetus. The foetal stage is characterised by very rapid growth until birth.

Embryology explains how structures in the body come to be what they are and explains their interrelationships. It holds the keys to where development may go wrong, resulting in anatomical defects, malfunction and biochemical abnormalities; all under the umbrella term congenital errors. This is an area of medical speciality, but even to non-medical persons, it can explain many common phenomena that we encounter in this field.

Embryology was, not too long ago, known as developmental anatomy. It has come a long way now, with the tools of molecular biology. In this unit we restrict ourselves to some basic principles and correlate gross anatomy with development.

The events of life before birth take place in the mother’s reproductive system. We therefore begin with an elementary overview of the female reproductive system and the formation of germ cells. In this chapter, the accounts of anatomy of the female reproductive system and the formation of germ cells are limited to what is relevant at this stage. Later in the unit, we shall describe other aspects as well.

Female reproductive system.

We have seen the female reproductive organs in a section of the pelvis in Chapter 1, fig. 10. We now see the parts in a coronal section (Fig 1). The ovary (1) is the egg-producing organ. The uterine tube (also called the oviduct or fallopian tube) carries the egg to the uterus. The end of the tube facing the ovary has a number fronds (anatomical term *fimbriae* in plural, singular : *fimbria*). The fimbriae ‘sweep’ the surface of the ovary and pick up the oocyte. The next part is called infundibulum (2), followed by a dilated portion, the ampulla (3). Next to it is a narrow portion, the isthmus (4). The last part is within the thick wall of the uterus, and is called the intramural part (5).

In the uterus, the great thickness of the wall is largely due to muscle. The lining is formed by epithelium and supporting connective tissue. This lining is the endometrium (metros = uterus). The embryo, when it reaches the uterus, is embedded in the endometrium.

Anatomically, the top of the uterus is the fundus, followed by the body and the narrow cervix (= ‘neck’). The vagina is the birth passage with a muscular wall.

Germ cells (“Gametes”).

The male and female germ cells are quite distinctive. In biological terminology we use the common term ‘gamete’ for both male and female germ cells. The male gamete is a spermatozoon (the short form ‘sperm’ is equally acceptable). It is a small cell, with very little cytoplasm and has a tail which makes it
motile. The female gamete is an ovum. It is one of the largest cells in the body, with a diameter of over 100 µm. It is often called the ‘egg’, which is acceptable, but not quite elegant! Henceforth we avoid the term germ cell and use the term gamete. Both gametes have a haploid number of chromosomes (23 ‘singles’) in the nucleus.

(Truly speaking, we never see a fully mature ‘ovum’ – we ought to call it an oöcyte. This is explained a little later).

**Gamete formation (gametogenesis).**

Gametes have 23 single chromosomes, as opposed to 23 pairs in other cells. The reduction in the number is due to meiotic cell division (meiosis).

In the male, some cells are ‘set aside’ in the testis for this purpose. These are called spermatogonia. After puberty, these cells divide by mitosis, some of the daughter cells undergo meiosis while others stay as spermatogonia to maintain the ‘pool’. This process continues throughout life. Thus, a male can produce sperms indefinitely.

In contrast, the cells set aside in the female form a fixed pool. They begin meiotic division even before the female is born. But this division is not completed – a female is born with a fixed number of such cells, in a state of suspended meiosis. After puberty, approximately every month a few of these cells (oöcytes) mature and proceed with meiosis. Normally only one of these is released for fertilisation by a sperm. This cell completes the second stage of meiosis after the entry of the sperm. Therefore we say that it is an oöcyte that is released for fertilisation.

An oöcyte has a non-cellular covering in addition to the cell membrane. This covering is the zona pellucida (the ‘clear zone’, so called because of its translucent pink appearance under the microscope). Outside the zona pellucida is a layer of ‘supporting cells’. One layer of these supporting cells surrounds the oöcyte even as it is released. This layer appears like a radiating crown in a section and is indeed called the corona radiata.

**Understand the relationship of the oöcyte with the zona pellucida and the corona radiata from fig. 2.**

During each stage of meiosis two cells are produced. However, one of these receives almost all cytoplasm, is large and capable of being fertilised. The other small cell remains within the zona pellucida and is called the polar body. There can be two or three polar bodies – we shall ignore them!

**Note :** This discussion is limited to understanding the oöcyte, its haploid nature and the zona pellucida. These concepts are relevant to the understanding of the events of early embryology. A few more details will be studied later during the unit.

You may also wish to revise the description of the basic process of meiosis from chapter 2.

**Fertilisation – the beginning.**

Sperms are deposited deep into the vagina just below the opening of the uterus. Though sperms are motile, their speed is far from adequate to carry them to the oöcyte in time. Remember that the oöcyte has a ‘long’ journey along the length of the tube! Other factors operate in transporting sperms to the oöcyte, probably movements in the smooth muscle wall of the uterus.
The nucleus and the scanty cytoplasm of the sperm is all in the ‘head’ of the sperm. At the very tip is a tiny structure called acrosome. (*akron* = highest point, *soma* = body, here taken to mean a structure or a feature). The acrosome (shown as a tiny green line in fig. 2) has enzymes which allow it to penetrate the zona pellucida. In the female reproductive tract, the acrosome undergoes changes which allow the acrosomal enzymes to be exposed. This is called capacitation. Fertilisation takes place most commonly in the dilated part of the uterine tube, the ampulla. When a sperm comes in contact with the zona pellucida, the acrosomal enzymes act on it and facilitate entry of the sperm. The cell membranes of the sperm and the oocyte fuse and the sperm enters the oocyte. The zona pellucida undergoes *molecular* changes which prevent the entry of any other sperm. (Think of what happens to the brick wall after Harry Potter enters Diagon Alley in the first movie!)

The fertilised oocyte immediately completes meiosis II and the second polar body is released. The fertilised cell (also called the zygote) has two haploid nuclei. These are called the male and female pronuclei. The pronuclei enlarge as the DNA within them is replicated. The nuclear envelopes disappear and the mixed lot of 23 pairs of replicated chromosomes are lined up for separation. Depending upon the sex chromosome present in the *sperm*, the sex of the individual is determined at fertilisation. The oocyte can only have an X chromosome, the *sperm* can have either X or Y.

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**Fig. 3.**
A. Acrosome and zona pellucida.  
B. “No entry” for other sperms. Note polar bodies.  
C. Male and female pronuclei.

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**The embryo becomes multicellular.**

The zygote now undergoes the first few divisions. These divisions, called *cleavage*, are preceded by DNA replication, but the cytoplasm does not increase. Remember: the oocyte has an enormous amount of cytoplasm! Thus, gradually the amount of cytoplasm in the zygote is distributed among the cells. The ‘nucleo-cytoplasmic ratio’ comes down to ‘normal’.

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**Fig. 4.** Cleavage. Note the change in cell size. Also note that the zona pellucida is intact.
The cells of the embryonic mass are initially a loose clump. They gradually get compacted, and after a while show two distinct regions, an inner cell mass and an outer cell mass. The inner cell mass eventually develops into the embryo proper. The outer mass is called trophoblast (“nutrition forming”). It is somewhat like a shall around the inner cell mass. Part of it gives rise to the placenta which is the link between the embryo/foetus and the mother – it the structure responsible for nutrition of the embryo and the foetus. Well, the placenta does more than that: it supplies the developing human with oxygen, gets rid of its waste and even more.

All this while the embryo is being propelled through the uterine tube towards the uterus. The cell mass resembles a mulberry and is called morula. The zona pellucida is still intact when it enters the uterus. This is important, because it prevents the attachment (implantation) of the embryo to the wall of the tube.

**Blastocyst and implantation.**

Fluid seeps in through the zona pellucida and a cavity appears in the embryo. This stage is called the blastocyst (Fig. 5). Soon, the zona pellucida disappears. The trophoblast has an invasive property. When it comes in contact with the endometrium, it burrows into the endometrium by loosening the epithelium and destroying the connective tissue. Gradually the embryo sinks deeper into the endometrium until finally it is covered by the uterine epithelium, completing this process called implantation. Implantation begins at the end of the first week and is complete in the second week (Figs. 6 and 7).
Our aim now is to understand how this almost microscopic embryo is transformed into a plate of three layers, and later into the recognisable human form. It is a series of complex steps, but the following description is simplified to suit our purpose in this unit.

Changes in the inner cell mass.
The inner cell mass shows two layers – a layer of tall cells (epiblast) and one of smaller cells, the hypoblast. A cavity appears in the epiblast: this is the amniotic cavity. The amniotic cavity enlarges. The cells lining this cavity, facing the trophoblast are called amnioblasts, whereas the cells in contact with the hypoblast are the cells of the epiblast proper. The hypoblast faces the original cavity of the blastocyst.

At the end of the second week the embryo is a bilaminar disc (bi = two, lamina = plate or layer). At the circumference the layers are continuous with the walls of one cavity each. Think of this arrangement as two soap bubbles touching each other. The junction between the bubbles is flat! (See fig. 9 on the next page).

The bilaminar stage of the embryo may be seen as a ‘burden on memory’ by some students. The most important concept is that the epiblast will give rise to all the three basic layers of the embryo shortly. The hypoblast will disappear and the ‘original blastocyst cavity will become smaller and eventually disappear. You may wish to omit the detail as long as you know about the epiblast, explained in the next stage.
Amniotic cavity and its wall
“The upper bubble”!

Bilaminar disc

“Extension” of the hypoblast lining the blastocyst cavity.

Fig. 9. 3-D representation of the bilaminar embryo. On the right, the amniotic cavity is “cut open”. A ‘view from the top’, will show the epiblast! In fact, such a view is used in fig. 10.

We shall now take a quick look at the trophoblast and return to the embryonic disc.

Changes in the trophoblast. (See fig. 8 on the previous page). The trophoblast is like a shell around the two ‘bubbles’.

The trophoblastic tissue, as it develops further, differentiates into two layers. The outer part appears like a mass of cytoplasm with multiple nuclei. This is because the cells fuse and lose their cell membranes. For this reason, this layer is called the syncytiotrophoblast. (Syncytium = “cells together”). The inner zone shows clear cell boundaries – it is called the cytotrophoblast. Further development of the trophoblast, in conjunction with the amnion and a part of the endometrial tissue forms the placenta.

In this unit we do not study structural details of the placenta. However, some key points are important:

- Trophoblastic tissue, which forms the bulk of the placenta, belongs to the embryo/foetus.
- Maternal blood comes in contact with the trophoblast.
- The trophoblast, some embryonic connective tissue and walls of foetal blood vessels form the barrier between maternal and foetal blood – the two bloodstreams do not mix.

These points will be referred to in the development of the heart and foetal circulation.

The primitive streak.

The primitive streak, a temporary structure, plays a vital role in establishing the ‘form’ of the embryo. The streak is seen as a faint ridge of the epiblast side of the embryo. At one end the streak has a knot-like swelling, the primitive node. In the adjoining picture, a pale spot is seen beyond the node. We shall discuss this spot a little later. At this stage: notice that the streak is in the midline. This establishes the axis of the embryo. The part of the embryo beyond the node will be the head end of the embryo. The other end, near the narrow tip of the streak is the tail end of the embryo.
**Formation of the germ layers. (Fig. 11)**

Cells of the epiblast tend to ‘heap up’ at the primitive streak. From the streak, they sink deeper inside. The ‘first wave’ of these cells **displace the hypoblast** and forms the endoderm (also spelt entoderm). **More cells** proliferate and pour **between the epiblast and the endoderm**, forming the mesoderm. The **remaining cells of the epiblast form the ectoderm**. By the middle of the third week the embryo is thus trilaminar.

The head end of the embryo begins to differentiate first. The sequence of development is often described a cephalocaudal. (From head to tail. *kephale* = head, *cauda* = tail). Even as the head end begins to differentiate, movement of mesoderm in the caudal part of the embryo continues well into the 4th week.

**Thus, in the final reckoning, the three layers are all formed by the epiblast, through the medium of the primitive streak.**

**At this stage**, you need not worry about the names oropharyngeal membrane and cloacal membrane. They will be mentioned again later in the unit.

The trilaminar embryo has two cavities around it. The cavity on the side of the ectoderm is the amniotic cavity, as mentioned earlier. The cavity on the other side undergoes modifications (details not essential). It now faces the endoderm and is named the yolk sac.

**When the three layers are established, the primitive streak has served its purpose and disappears.** If a trace of the primitive streak persists, it can cause considerable trouble! Remember that its cells are capable of giving rise to all three layers. Persistent bits of the streak are seen at the tail end of the embryo and form tumours with all kinds of tissues. Babies may be born with huge tumours arising from such remnants. Such tumours are seen at the lower end of the back.

**Notochord.**

While these changes are taking place, cells from the **tip of the primitive streak** grow and form a strip in the midline, in the plane of the endoderm. This midline strip detaches itself and forms a solid column, the **notochord**. The notochord is illustrated in figures later in this chapter.

The notochord is another vital link in the chain of events. In vertebrates, it exists as a continuous column only during embryonic life. Parts of it persist as normal structures in the vertebral column (discussed with the vertebral column). In some animals it forms a stiff support for the body in the midline.

Embryologically the notochord is of great importance. After the primitive streak disappears, it is the definitive ‘axis’ of the body. Moreover, it ‘directs’ a strip of ectoderm to develop into the nervous system. This process, where one structure influences the development of another, is called embryonic induction.
The spread of the mesoderm. (Fig. 12)
Mesodermal cells spread out laterally and towards the head end in a definite pattern. They follow arc-like courses between the epiblast (later ectoderm) and the endoderm. When the spread is complete the mesoderm is seen mainly as three columns along the length of the embryo.

Cells from the head end of the streak keep close to the midline, spreading in ‘narrow’ arcs. In the final picture, this column of mesoderm is close to the midline or the axis. This column is the paraxial (“para + axial”) mesoderm.

Cells from the middle part of the streak occupy a position just lateral to the paraxial mesoderm. They form a column called the intermediate mesoderm.

Cells from the tail end (caudal part) of the streak spread out in broad arcs and finally form a plate close to the lateral boundaries of the embryo. This part of the mesoderm is called the lateral plate mesoderm.

Cells migrating through the extreme tail end of the streak move outside the boundaries of the embryonic disc and form a part of the mesoderm outside the embryo proper. This is called extra-embryonic mesoderm. We shall mention this as additional notes later in this course reader – it is not core material for this unit.

Some cells from the region near the head end are special – they reside at the cranial tip of the lateral plate and indeed form a horseshoe-like band at the head end of the embryo. These cells form the mesodermal precursor of the heart (cardiogenic area). We shall deal with this with the development of the heart.

The spread of the mesoderm to the head end, however, leaves a small area where ectoderm and endoderm are in contact. This is called the oropharyngeal membrane. At the tail end there is a similar small area where ectoderm and endoderm are in contact with no mesoderm in between. This is called the cloacal membrane. We shall discuss these with the study of the development of the digestive system.

The primitive streak is formed by the ‘heaping up’ of cells which migrate to form mesoderm. With the enormous development of the head region, the streak appears to become shorter. When all mesoderm is formed, there is no more ‘heaping up’ of cells and the streak disappears.
Divisions of the mesoderm.
In fig. 12 B, the three divisions are shown as if they are completely separate from each other with gaps in between. This is for the sake of clarity in the picture! However, the fates of these divisions are quite specific.

The column of **paraxial mesoderm** begins to form segmental masses called **somites**. In a real embryo, these can be seen as blocks stacked up parallel to the midline. A semi-diagrammatic picture (fig. 13) shows two columns of somites below the oropharyngeal membrane (the pale spot).

The division of paraxial mesoderm into somites begins at the head end. As more and more somites appear towards the tail end, the cephalic somites begin to specialise into the structures they form. Thus, the sequence is again cephalocaudal (‘head to tail’). These segments (“slices” or “blocks”) are the basis of the structure of the body wall. **We shall refer to these frequently during further study in the unit.**

Each somite soon shows two distinct parts. One part, the sclerotome contributes to the vertebral column (From the Greek words, *skleros* = hard, *tomon* = cutting, a cut). The other part is the dermomyotome (*derma* = skin, *mys* = muscle). The dermomyotome further differentiates into a dermatome and a myotome.

*(Beware : in the anatomical context, the dermatome gives rise to the connective tissue or *dermis* of the skin, not the entire thickness of the skin.)*

The **lateral plate mesoderm** splits into two parts by the formation of a cavity. One layer of mesoderm is closely related to the ectoderm and the other close to the endoderm. The cavity between the two layers is called the coelomic cavity.

The **intermediate mesoderm** is mainly involved in the formation of the urinary and reproductive systems.

Fig. 12 B gave us a surface view of the divisions of the mesoderm, as if the ectoderm is transparent. Another way of studying it is to see a transverse section of the embryo. Since a transverse section also shows other events occurring in the embryo, it is shown on the next page along with a description of neural tube formation.

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The segmental structure as illustrated by the somites is a part of the very basic plan of the body wall. Parts of the somites also form the vertebral column which surrounds the axis of the body. For this reason, we study the vertebral column early in the unit. We then focus on the lateral plate mesoderm, because it is involved in the formation of the body wall and the coelomic cavities. We visit the intermediate mesoderm in the context of the abdomen and the pelvis, when we study the urinary and reproductive systems.

These events mark the end of the third week of development.

Fate of the germ layers.
The ectoderm gives rise to the epidermis – the epithelium of the skin. Note that the skin comprises epidermis and dermis, the latter is a connective tissue layer which develops from the dermatome part of the somites. Ectoderm also gives rise to hair and nails. Besides these, a specialised area of the ectoderm close to the midline forms the nervous system (Discussed in the next section).

The endoderm gives rise to the epithelial lining of the digestive tube, plus specialisations of this lining.
Almost everything else in the body comes from the mesoderm. This includes almost all muscle tissue and all connective tissue including cartilage and bone, blood cells and cells of the defence system. The mesoderm also gives rise to parts of the urinary and reproductive systems and a part of the adrenal gland.

- It is interesting to consider the broad functional implications of the fate of the germ layers.
- The ectoderm is the interface between the body and the surroundings.
- The endoderm mainly forms the lining of the digestive tube and lungs – it is thus concerned with food and air intake.
- The mesoderm forms everything else: structural support (connective tissue), movement mechanisms (muscle), maintenance department (heart, blood vessels, kidneys), defence department and even the reproductive apparatus for propagation of the species.

**Formation of the neural tube (Neurulation).** (Fig. 14)

A band of **ectoderm** across the midline becomes thickened to form a plate called the neural plate. Since it forms nervous tissue and it is a part of ectoderm, it is called neuroectoderm. As we have mentioned above, the notochord ‘induces’ the formation and subsequent modification of the plate.

The plate becomes grooved along the midline. Its junction with the rest of the ectoderm is like a lip on either side. Soon, the groove closes to form a tube if the edges are zipped together. The fusion begins in the middle of the embryo and proceeds towards both ends. The tube ‘sinks’ in the surrounding mesoderm, losing its contact with the ectoderm on the surface. The ‘surface ectoderm’ becomes continuous across the midline when the tube closes.

**The lips of the groove separate out as a long column on either side of the tube.** These form the neural crest, which also sinks deeper along with the tube.

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The neural tube forms the brain and the spinal cord. The main derivatives of the crest are the **ganglia of peripheral nervous system and sensory nerve fibres.** This explained further with the introduction to the nervous system. Besides these the neural crest gives rise to a number of **non-neural structures.** These will be referred to as we come across them.
Folding of the embryo.
The flat trilaminar embryo undergoes complex changes in form, with the head and tail ends and the sides folding up making it a three-dimensional tubular structure. Actually, it folds more like an envelope with four flaps – one flap at the head and tail ends each, and two flaps on the sides. At this stage we just recognise the fact that this happens. The mechanism and its implications will be studied later in appropriate context.

Summary

The foregoing discussion is an overview of the embryology content of ANHB 1101. To the uninitiated this may appear complex. Some of this will be explained as background or introductory material during some of the lectures in this unit. However, there are some fundamental concepts which are important as starting points. There are other concepts which form the basis, and guide our study, of both embryology and anatomy in this unit. It is worth reiterating them here.

Do not try to memorise this list! Understand the explanations from the discussion so far.

Concepts and facts fundamental to embryology:

- Haploid gametes unite: beginning of a new human being.
- Each gamete has a unique mixture of genetic material from two parents. Effectively, the offspring is a unique mixture of genetic material from four grandparents. (This aspect is explained with meiosis). If we extend this argument backwards into the past, it is obvious that the process of sexual reproduction is capable of creating an immense variety of genetic combinations. This indeed, is an area where anatomy, cell biology, genetics and evolutionary science meet!
- Fertilisation most commonly takes place in the ampulla of the uterine tube.
- Zona pellucida prevents the entry of more than one sperm. It also prevents implantation as long as it is intact.
- The early embryonic cell mass specialises into two groups – inner cell mass → embryo proper, outer cell mass (trophoblast) → significant contribution to the interface between mother and foetus.
- Trophoblastic tissue is invasive. This property is responsible for implantation.
- The epiblast layer of the bilaminar embryo gives rise to the three basic layers of the embryonic body: ectoderm, mesoderm and endoderm. (You can afford to forget the fate of the hypoblast, as long as you do not confuse it with the endoderm!)

Concepts and facts that will be relevant to our study of human structure in this unit:

- The primitive streak, a thickening of the epiblast, is the site where epiblast cells migrate to form the three layers of the trilaminar embryo.
- The notochord, which arises from the tip of the streak, defines the axis and symmetry of the embryo. It also induces the formation of the neural tube.
- The neural tube is an ectodermal structure.
- The mesodermal layer has three subdivisions – paraxial, intermediate and lateral plate.
- Paraxial mesoderm forms ‘blocks’ or slices stretching from the head end to the tail end of the embryo. These blocks, called somites, establish the structural pattern of the body wall.
- Lateral plate mesoderm splits to form a cavity.

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