CHAPTER 1

General Embryology

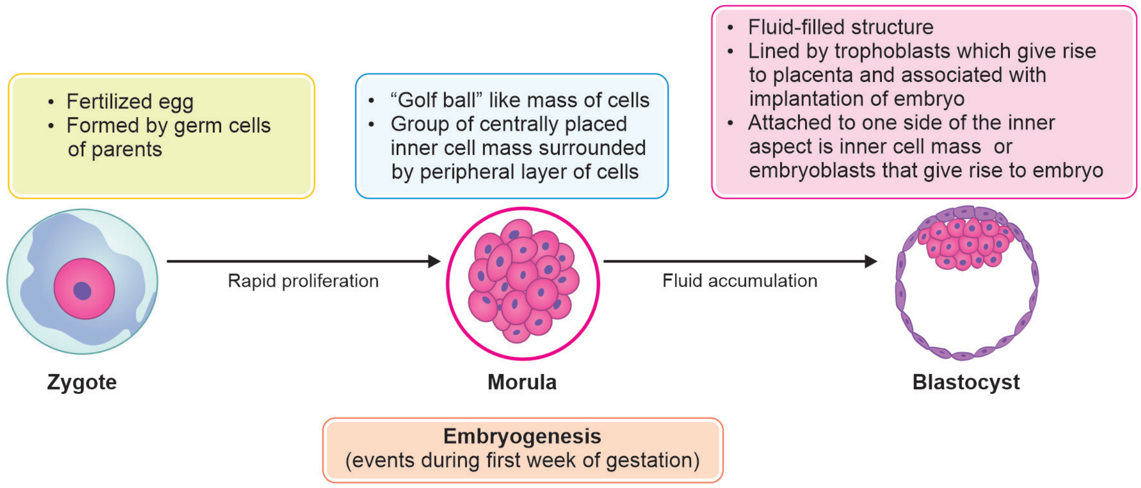
- Formation of blastocyst
- Germ layers
- Neural crest cells
- Pharyngeal arches and pouches

Embryology is the study of growth and differentiation which an organism undergo during its development from a single fertilized cell to a complex independent living being.

Every animal starts life in the form of a simple cell, i.e. the fertilized egg or zygote. Zygote is formed by two cells, namely the germ cells of parents. Fertilization occurs when male and female gamates (spermatozoon and ovum) unite to form zygote.

The intrauterine life of human beings can be divided into embryonic period which lasts for 8 weeks after fertilization which will be followed by fetal period which continues throughout pregnancy that ends in birth approximately after 280 days.

After fertilization, rapid proliferation of cells takes place leading to formation of a cell mass called ***morula***. This morula is a "golf ball" like little mass of cells and consists of a group of centrally placed cells termed inner cell mass, surrounded by a peripheral layer of cells **(Fig. 1.1)**. Once morula enters into the uterine cavity by 7 to 8 days, it turns into a fluid-filled structure due to seepage of fluid, which separates the inner cell mass from peripheral layer of cells. The resultant structure is called ***blastocyst*** **(Fig. 1.2)**.



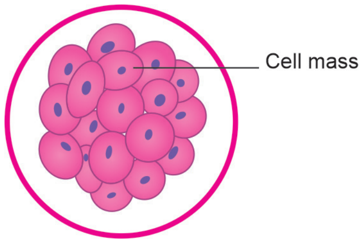


Fig. 1.1: Morula

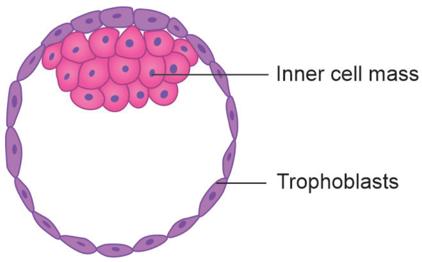
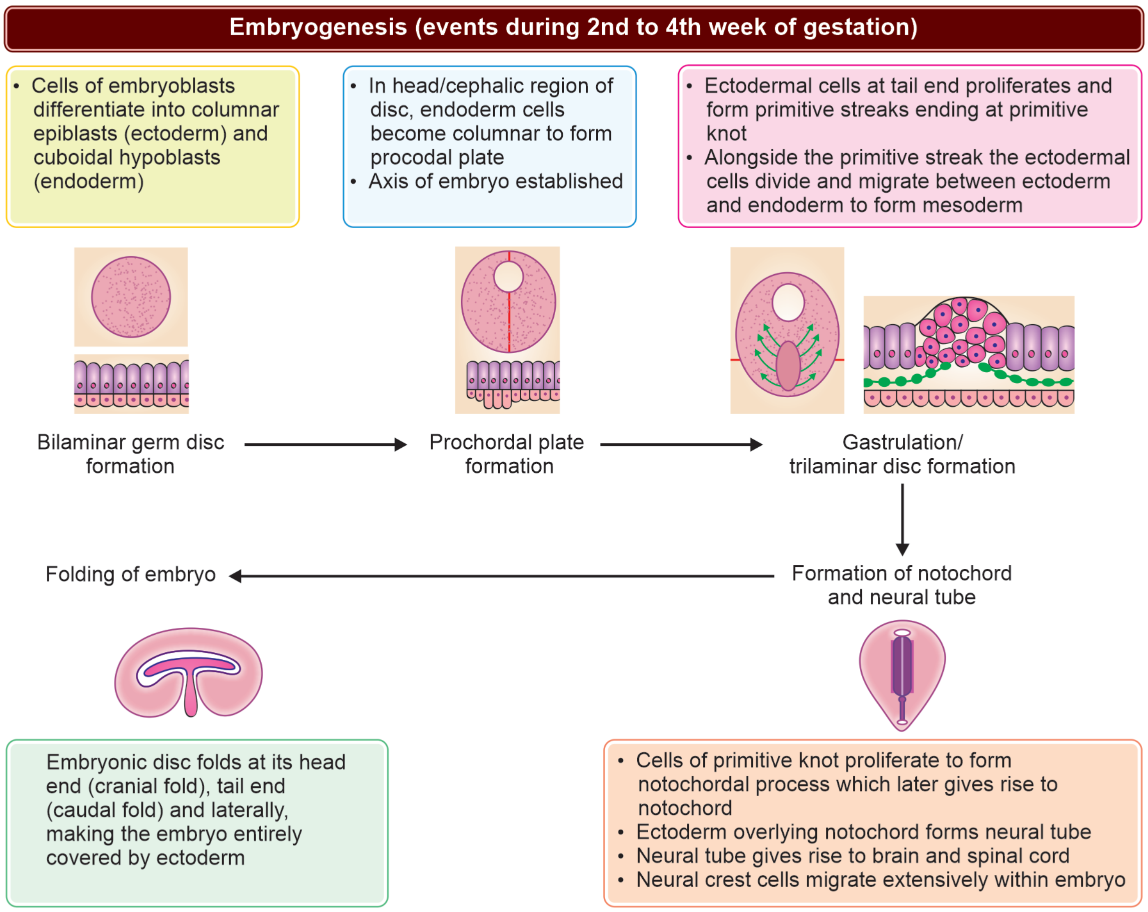


Fig. 1.2: Blastocyst

At this stage, the blastocyst has two different types of cells. The inner cell mass that occupies the center portion and an outer layer that surrounds this cell mass. The outer layer of cells lining the blastocyst is called trophoblasts. The trophoblasts are derived from the outer layer of morula, which later gives rise to placenta and is also involved in implantation of the embryo. Within the blastocyst, the inner cell mass can be seen attached to one side of the inner aspect. This inner cell mass or embryoblasts form the embryonic stem cells that give rise to embryo.

As the blastocyst develops further, some cells of the inner cell mass differentiate into flattened cells and line the free surface while the other cells change into columnar cells. The flattened cells constitute the endoderm while the columnar cells form the ectoderm. Thus, by



8th day of gestation the embryo appears like a 'bilaminar circular disc'.

As the development proceeds, in a localized area close to the future cephalic end of the disc, flattened cells of endoderm changes into columnar cells. This circular area where the changes take place is called 'prochordal plate'. The region where the prochordal plate is formed is the head end and opposing end is tail end of the embryo. Prochordal plate provides the disc an antero-posterior axis and a bilateral symmetry.

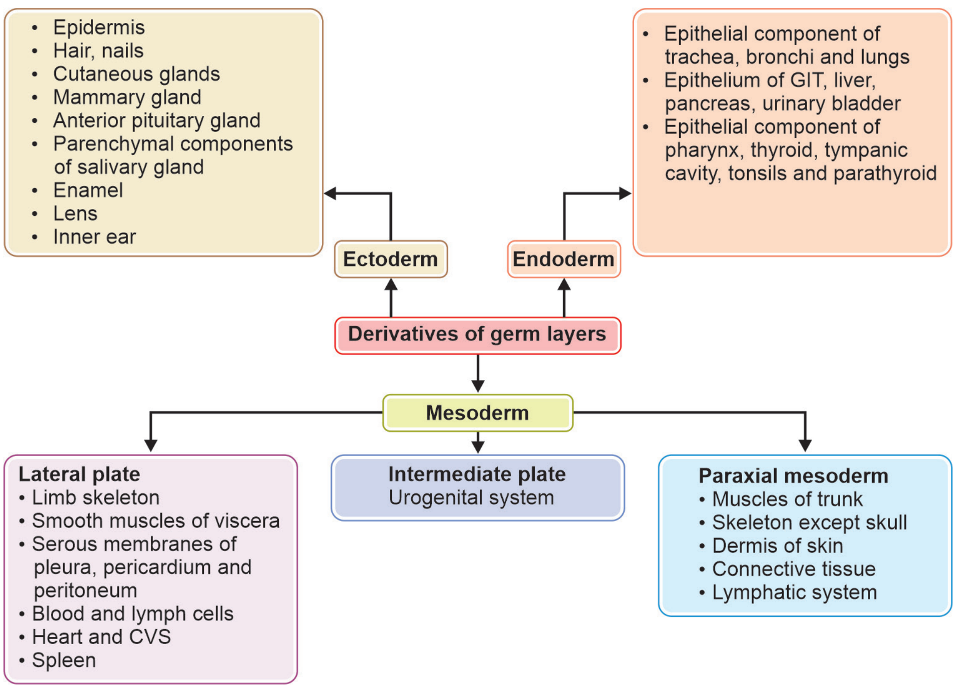
After the formation of the prochordal plate, the cells of ectoderm proliferate near the tail end, forming another structure called the primitive streak. These proliferating cells initially form a thickening and later spread sideways between ectoderm and endoderm forming a third layer called mesoderm. This mesodermal layer spreads and separates the ectoderm and endoderm throughout the disc except for the circular region of prochordal plate. So by the 16th day, the embryonic disc has three layers: Ectoderm, endoderm and mesoderm. These three primary germ layers give rise to different tissues and organs of our body.

Germ Layer Derivatives

As the development progresses, the circular disc-shaped embryo becomes elongated and pear shaped. The region of prochordal plate where ectoderm and endoderm remain in contact forms the *'buccopharyngeal membrane'*.

The cranial end of the primitive streak thickens to form primitive node. The cells proliferate from primitive node and extend between the ectoderm and endoderm, along the central axis uptill the prochordal plate. This forms notochordal process or head process. Ectoderm over the notochord differentiates to form neural plate which develops an invagination and forms the neural tube. This neural tube extends from primitive node to prochordal plate. The cranial part of neural tube forms the brain and caudal part forms the spinal cord.

The enlarging embryonic disc develops folds at its head end (cranial fold), tail end (caudal fold) and laterally, making the embryo entirely covered by ectoderm. The head fold is critical to the formation of primitive oral cavity or stomatodeum. The stomatodeum is separated



from developing gut by buccopharyngeal membrane.

Neural Crest Cells

Neural crest cells are a group of pleuripotent cells that develop from ectoderm along the lateral margins of neural plate. These cells migrate extensively in the developing embryo between ectoderm and endoderm and intra-mesodermally and differentiate into different types of cells that form various tissues of the body.

The neural crest cells move around the sides of the developing head beneath the surface of ectoderm as sheets of cells. They migrate and form the entire connective tissue of upper facial region; while in the lower facial region they migrate into already existing mesenchyme. Therefore, the connective tissue beneath the developing ectoderm in this region is called ectomesenchyme.

Structures that Develop from the Neural Crest Cells

In the head and neck region neural crest cells differentiate to form most of the connective tissue components including bone, cartilage, dermis and tissues that form tooth except enamel and also contributes to formation of muscles and arteries of this region.

Neural crest cells migrate to the trunk region giving rise to neural, endocrine and pigment producing cells. In the trunk sensory ganglions, Schwann cells and neurons are also derived from neural crest cells.

Neural crest cells have a significant role in craniofacial development and formation of teeth. A developmental disorder called Treacher Collins syndrome which manifests with various craniofacial developmental defects is caused due to defective migration of neural crest cells. Defective migration of neural crest cells can also cause defective dentition.

As the neural tube forms, the mesoderm adjacent to the neural tube and notochord thickens on each side of midline to form paraxial mesoderm. This breaks into segmented blocks called somites, the first being occipital somites.

A series of events takes place in the head region. The neural tube undergoes massive expansion to form forebrain, midbrain and hindbrain. The hindbrain exhibits segmentations forming a series of eight bulges known as rhombomeres, which play important role in development of the head. The midbrain and rhombomeres 1 and 2 contribute to the face and first branchial arch.

Each somite has three components: (a) the sclerotome giving rise to two adjacent vertebrae and their discs, (b) myotome giving rise to muscles of the body wall, limbs and tongue, (c) the dermatome giving rise to the dermis/connective tissue of the skin overlying the somite. The lymphatic endothelium of multiple organs including skin, liver and cardiopulmonary system is developed from paraxial mesoderm.

Further laterally the mesoderm thickens and form lateral plate mesoderm, giving rise to: (a) connective tissue associated with muscle and viscera, (b) the serous membranes of the pleura, pericardium and peritoneum, (c) the blood and lymphatic cells, (d) heart and cardiovascular, (e) spleen.

The intermediate mesoderm exists as a longitudinal strip between paraxial mesoderm and lateral plate mesoderm. This intermediate mesoderm gives rise to urogenital system.

Branchial Arches and Pouches

The developing oral cavity, stomatodeum is situated between the developing brain and pericardium. In the early stages, neck is not present. Later, series of mesodermal thickenings develop in the wall of the cranial part of foregut resulting in the formation of neck between stomodeum and pericardium. These cylindrical thickenings are called ***branchial arches or pharyngeal arches*** **(Fig. 1.3)**. Pharyngeal arches are six in number and extend from lateral wall of pharynx, towards the medial direction, to approach its counterpart extending from other side. The inner aspect of each arch is covered by endoderm and outer aspect by ectoderm. The central core is made up

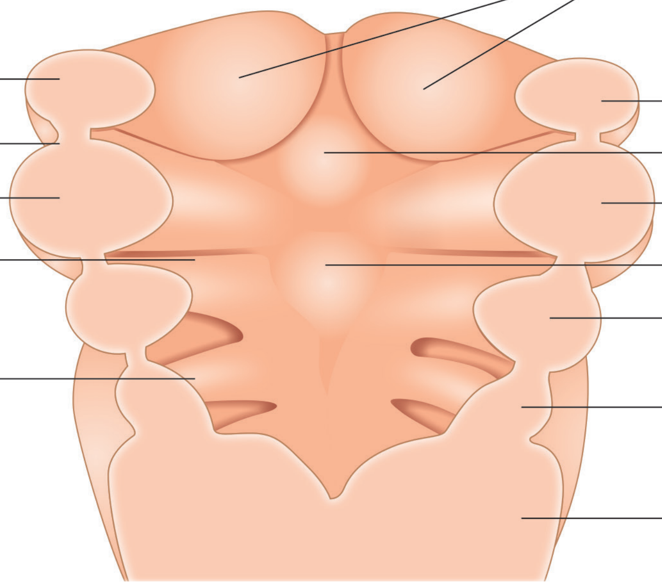


Fig. 1.3: Pharyngeal arches and pouches

of mesenchyme, which is surrounded by ectomesenchyme, which is of neural crest origin. The endoderm extends outwards between the branchial arches in the form of pouches called ***pharyngeal pouches***. The pharyngeal pouches meet the ectodermal clefts which are formed by invagination of ectoderm lining the outer surface of the pharyngeal arches.

The mesoderm of each arch gives rise to a skeletal element (which can be either a cartilage or bone), muscle and an arterial arch. Each pharyngeal arch has a nerve which supplies the structures that develop from that arch.

There are six pharyngeal arches. 1st arch is named mandibular arch, which plays a very important role in craniofacial development **(Table 1.1)**.

2nd arch is hyoid arch and the 5th arch disappears soon after formation. The remaining 3, 4, 6 arches do not have specific names.

Table 1.1: Derivatives of the branchial arches, pharyngeal pouches and cranial somites

Branchial arch	Branchial pouch	Arch arteries	Muscles	Nerves	Skeleton
1st: Mandibular Contributes to facial prominences and anterior tongue mucosa	(D) Tubotympanic recess, which forms auditory tube and middle ear cavity (V) Obliterated by tongue	Contributes to external carotid and maxillary arteries	Muscles of mastication (temporal masseter, and pterygoids), mylohyoid, ant. digastric, tensor veli palatini, tensor tympani (originates from somitomere 4)	Vth nerve; Trigeminal nerve, three divisions: Sensory, mandibular, motor	Facial bones, incus, malleus, anterior ligament of melleus, sphenomandibular ligament and core of mandible from Meckel's cartilage
2nd: Hyoid Contributes to anterior tongue mucosa	(D) Mostly filled in by own proliferation to form palatine tonsillar fossa (V) Obliterated by tongue	Stapedial artery (in part), possibly small contribution of facial artery	Muscles of facial expression, posterior digastric, stylohyoid, stapedius (originates from somitomere 6)	VIIth nerve: Facial nerve, motor to facial muscles, sensory to ant. 2/3rds of the tongue	Stapes styloid process, stylohyoid ligament, lesser horn and upper part of hyoid body (Reichert's cartilage)
3rd Contributes to posterior tongue mucosa	(D) Inferior parathyroid III (V) Thymus	Proximal 1/3rd of internal carotid, possibly small contribution to common carotid	Stylopharyngeus, upper pharyngeal muscles (originates from somitomere 7)	IXth nerve: Glossopharyngeal nerve (pharyngeal plexus), motor to pharynx	Greater horn and lower part of hyoid body
4th	(D) Superior parathyroid IV (V) Lateral thyroid Vestigial thymus	Arch of aorta (left), proximal part of right subclavian (right)	Pharyngeal constrictors, cricothyroid and laryngeal muscles Palatoglossus Palatopharyngeus Levator veli palatini	Sensory to post 1/3rd of tongue	Thyroid and laryngeal cartilages
5th	Ultimobranchial body or calcitonin C cells	Rarely seen	Same as 4th branchial arch	Xth nerve: Vagus nerve, superior laryngeal nerve (pharyngeal nerve plexus)	Lower part of thyroid cartilage and laryngeal cartilages
6th	None	Proximal part of both pulmonary arteries and most of ductus arteriosus (left)	Laryngeal muscles except cricothyroid striated muscles of esophagus (originates from occipital somites 1 and 2)	Xth nerve: Vagus nerve, inferior laryngeal nerve	Cricoid cartilage (probably) and arytenoid cartilages

(*Contd...*)

Table 1.1: Derivatives of the branchial arches, pharyngeal pouches and cranial somites *(Contd...)*

Branchial arch	Branchial pouch	Arch arteries	Muscles	Nerves	Skeleton
Derivatives of the branchial arches, pharyngeal pouches and cranial somites					
Post-branchial region, somites, somitomeres, 4 occipital somites			Trapezius, sternomastoid Myotonic Muscle, intrinsic tongue muscles, styloglossus, hyoglossus tongue, genioglossus muscles extrinsic ocular muscles	XIth: Spinal accessory XIIth nerve: Hypoglossal nerve, IIIrd: Oculomotor, IVth: Trochlear, VIth: Abducens	Tracheal cartilages? sclerotomes basioccipital bone, nasal capsule? Nasal septum?
Upper cervical somites			Geniohyoid, infrahyoid muscles	Spinal nerves C1, 2	Cervical vertebrae