HUMAN EMBRYOLOGY

Embryology is the science about embryonic development.

Human embryology studies:

1) Human embryo development;
2) Reasons for congenital abnormalities and deformities in embryo;
3) Influence of environmental factors;
4) Embryogenesis regulatory mechanisms.

Embryogenesis, as a part of ontogenesis, includes the time between fertilization and birth.

The process of embryo development involves different processes, namely cell division, migration, growth, induction and differentiation, which more or less depend on each other.

Human embryogenesis lasts 280 days and it is divided into three periods: initial period (1 week), embryonic period (2^{nd}-8^{th} week), and fetal period (9^{th} week until birth).

Basic human embryogenesis stages are similar to another vertebrates. There are early and late stages of embryogenesis:

Early are next:

1. Fertilization, which results in zygote formation.
2. Cleavage, which results in blastula formation.
3. Gastrulation, which results in formation of the germ layers.
4. Notogenesis, which results in formation axial complex.

Late are next:

5. Histogenesis, which results in tissues formation.
6. Organogenesis, which results in organs and systems of organs formation.

Gametogenesis is a process of sex cell formation. There are spermatogenesis (spermatozoa formation) and oogenesis (ovum formation). In embryo first sex cells called gonoblasts appear early at the end of 3 week of embryogenesis in extraembryonic yolk sac entoderme. After gonoblasts migrate and invade into gonads and then they differentiate into spermatogonia in developing testis and ogonia in developing ovaries.

Spermatogenesis

There are 3 phases of the spermatogenesis: mitotic phase, meiotic phase and spermiogenesis phase.

Spermatogonia are the first cells of the spermatogenesis. They arise from gonoblasts. At puberty, diploid spermatogonia begin to divide actively by mitosis and they continue to do mitosis throughout life.

During meiotic phase type B spermatogonia produces primary spermatocytes. They replicate their DNA shortly after they form and before meiosis begins, so that each primary spermatocyte contains the normal chromosomal number (2*n*) and double the amount of DNA (4*c*).

During meiotic phase, the primary spermatocyte move away from the basement membrane of seminiferous epithelium towards the lumen of seminiferous tubule and enlarge their size up to 4 times (growth period).

Then spermatocytes I enter the meiosis I. The prophase of meiosis I is long and includes 5 stages:

1) Leptotene, when chromosomes shorten and thicken.

2) Zygotene, when chromosomes form homologous (hə'moləgəs) pairs.

3) Pachytene, when chromosomes more shorten and thicken and exchange genetic material in a process called crossing-over.

4) Diplotene, when homologous chromosomes form synapsis with interchange of segments.

5) Diakenesis, when chromosomes to separate.

At meiosis I the primary spermatocyte gives rise to two secondary spermatocytes (II) with haploid chromosome set. Each chromosome is presented by two chromatides. Therefore, meiosis I is called reduction division and chromosome set mark n2c.

At meiosis II each of secondary spermatocytes very rapidly without S period of interfase divides again to form 4 spermatids with haploid chromosome set. But each chromosome is presented by only one chromatid. Therefore, meiosis II is also called equation division and chromosome set mark nc.

Spermiogenesis is the longest phase. It lasts for about 50 days. In this, the spermatids without further divisions transform into spermatozoa.

Ovogenesis

In general it similar spermatogenesis, but it has its particular features:

1) Ovogenesis includes 2 phases - mitotic phase and meiotic phase;

2) Mitotic phase lasts during early embryonic development in the ovary;

3) At the end of embryonic development the number of oogonia is about 7 millions;

4) After birth the division of oogonia is ending and all oogonia transform into primary oocytes;

5) Primary oocytes begin the first meiotic division before birth but do not complete prophase until puberty because they arrest in the diplotene stage of meiosis I prophase. Thus the oocytes I are blocked at a stage of diplotene of first meiotic division.

6) Then the primary oocyte enter the long growth period, which lasts from birth to puberty of girl.

7) After puberty, the period of short growth of primary oocyte happens regularly during each month. This process is accompanied by formation of mature follicle. Thus, the growth period may last 12 to 50 years.

8) Just before ovulation, the primary oocyte completes the first meiotic division with formation 2 unequal cells - haploid secondary oocyte and nonfunctional cell called the polar body.

9) For ovulation, the secondary oocyte without prior S period of interfase begins the second meiotic division progressing only metaphase, then division arrests.

10) Only if fertilization occurs, the second meiotic division will be complete with formation of only one haploid mature ovum and three polar bodies. The polar bodies then are phagocytosed by macrophages.

11) For ovulation the secondary oocyte surrounding by zona pellucida and a follicular cell layer releases into abdominal cavity and then into oviduct where it may be fertilize. Thus, the oogenesis takes place in two organs of female reproductive system – ovary and oviduct.

DIFFERENCES BETWEEN SPERMATOGENESIS AND OVOGENESIS

SPERMATOGENESIS	OVOGENESIS
1. Spermatogenesis starts from puberty and lasts throughout life	1. Ovogenesis starts during embryonic development and finishes in menopause
2. Spermatogenesis includes 3 phases: mitotic, meiotic and spermiogenesis phase	2. Ovogenesis includes 2 phases: mitotic and meiotic
3. Spermatogenesis includes the short growth period	3. Ovogenesis includes the long and then short growth periods
4. Meiotic phase of spermatogenesis is characterized by equal spermatocytes divisions	4. Meiotic phase of ovogenesis is characterized by unequal oocyte divisions
5. At spermatogenesis the primary spermatocyte gives rise to 4 sperms (two with X sex chromosome and two with Y sex chromosome)	5. At ovogenesis the primary oocyte gives rise only to 1 ovum with X sex chromosome
6. Spermatogenesis is a constant process	6. Ovogenesis is a cyclical process
7. In whole the spermatogenesis leads to formation of sperms millions	7. In whole the oogenesis leads to formation of 1 ovum
8. Spermatogenesis takes place in testis	8. Ovogenesis begins in ovary and finishes in oviduct

Spermatozoon (sperm)

The mature human sperm is a highly specialized cell. It consists of a head, a neck and a tail. The tail is subdivided into three segments: a middle piece, chief piece and end piece.

The length of sperm is about 60 micrometers. There is a big dense nucleus in region of head. The genetic material is haploid and contains 22 autosomes and 1 sex chromosome (X or Y). The cytoplasm is reduced.

In head the anterior pole of nucleus is capped by the acrosomal cap. Acrosome is a derivative of Golgi complex and it has similar structure as lysosome.

Acrosomes of sperms contain hydrolytic enzymes. These enzymes are necessary to dissociate cells of the corona radiate and to digest the zona pellucida, covering ovulated egg.

The neck sperm contains a proximal and a distal centrioles. The part of distal centriole gives rise to the axoneme of the flagellum. The another part of distal centriole migrates to the end of the middle piece and encircles the longitudinal axoneme as a ring called annulus.

The axoneme passes through middle piece and other parts of the tail. It consists of

two central microtubules and nine outer doublet microtubules.

In middle piece, the axoneme is surrounded by mitochondrial sheath.

Movement of the sperm flagellum is a result of the interaction among microtubules, ATP of mitochondria and an ATPase protein of axoneme arms called dynein. Due to the tail movements the spermatozoa are able to move with the speed 1,5 mm per minute.

Ovum

Ovum (egg, oocyte II) is a large round haploid cell about 120-150 micrometers in diameter. It is surrounded by noncellular cover called zona pellucida and by a layer of follicular cells called corona radiate.

The genetic material is haploid and contains 22 autosomes and 1 sex chromosome (X). The ovum has all general organelles but only one centriole. The ovum gets another centriole from the sperm during fertilization.

There are pigment and yolk or lecithin inclusions in cytoplasm of the ovum. But the human ovum contains the small amount of yolk inclusions distributing throughout the cytoplasm of the cell. Thus, the human ovum belong to the secondary isolecithal, oligolecithal type of ovums.

Complex of ovicell membrane and cytoplasm layer just under it is called cortical layer. This layer contains granules with several enzymes, which can change properties ('propətis) of zona pellucida after fertilization .The ovicells have very well developed cytoskeleton also.

Features of germ cells

1. Haploid set of chromosomes;
2. Disability to divide;
3. Unusual nucleocytoplasmic ratio;
4. Low level of metabolism;
5. Higher degree of specialization.

The nucleo-cytoplasmic ratio is a ratio of the nucleus size of a cell to the size of it’s cytoplasm.

Fertilization

The development of organism begins from one cell, called zygote**.** The zygote appears as a result of the mature gametes fusion. This process is called fertilization.

The fertilization happens in the ampullar part of uterine tube, where the secondary oocyte enters from the ovary. The fertilization consists of two phases - distant phase and contact phase.

In time of distant phase sperms and ovum produce physiological active substances, which are necessary for distant interaction, for stimulation of the sperms moving and gametes meeting. The sperms get the ability to fertilize the ovum only after they have been in the female genital tract. This final step in their maturation is called capacitatio.

The second phase of fertilization is contact phase when the sperm and the ovum fuse. To perform fertilization process it is necessary to have at least 200 millions of spermatozoa.

After distant phase, only a few hundreds of the sperms reach the ovum and attached by their heads to the corona radiate, to release their acrosomal enzymes (acrosome reaction). These releasing enzymes of sperms make a local lysis in the follicular cells layer and zona pellucida, after that the only one sperm's head with nucleus and proximal centriole penetrates the ovum membrane and sinks into the cytoplasm of egg.

The middle piece and the tail of sperm don't penetrate into the ovum. Another sperms cannot penetrate the ovum, as a result, of several mechanisms of polyspermia blocking. They are:

1. The cortical reaction in the ovicell that leads to liberation of cortical granules enzymes into the perivitelline space with formation of perivitelline barrier on the surface of zona pellucida.

2. The enzymes of cortical granules degrade ZP2 and ZP3 receptors of sperms heads and block their more acrosome reaction.

3. After fertilization the charge of ovicell cytoplasm is changed to negative. Most negative charged spermatozoa begin to repulse from negative charged ovicell.

The condition of the fertilized ovum, when it has two pronuclei (nucleus of a sperm and nucleus of an ovum) is called syncaryon. When the male and female pronuclei fuse the new diploid cell called zygote appears. In human the process of fertilization last 24 hours. Therefore, zygote appears at the end of the embryogenesis first day.

Cleavage

Cleavage is the quickly mitotic divisions of the zygote, resulting to formation of multicellular unilayer embryo called blastula. For cleavage the cells are called blastomeres. They have capacity to more rapid mitotic division because G_1 period or period of cell growth of the interphase absent for cleavage and after every division the size of blastomeres become more small. A zona pellucida prevents the growth of blastomeres also. Therefore, there is not the total growth of embryo for stage of cleavage. It is changes the unusual nucleocytoplasmic ratio of cells to the standart relationship between the volume of nucleus and cytoplasmic material characteristically for somatic cell of our organism.

The type of cleavage depends on the amount of yolk and it distribution into ovum cytoplasm. The human ovum contains the small amount of yolk granules which uniform distributed into ovum cytoplasm. That's why the human cleavage is:

1) complete, because all zygote cytoplasmic material undergoes to division;

2) unequal, because the cells blastomeres have different size;

3) asynchronic, because small light blastomeres divide more rapid then large dark cells.

The human cleavage has been accompanied by embryo passing down the uterine tube towards the uterus. This process lasts about from 3 to 4 days.

The stage of cleavage when embryo looks like a mulberry and consists of 12 to 16 cells is called morula.

About 5 or 5 and half day of embryogenesis the morula enter the uterus cavity, where it transforms into human blastula called blastocyst. Blastocyst consists of more number of blastomeres and contains a cavity called blastocoele. In blastocyst the zona pellucida disappears rapidly.

Blastocyst consist of:

1) a wall presenting by single layer of small light blastomeres called trophoblast, which further differentiates into extraembryonic organs - chorion and then placenta, providing the nutrition of embryo;

2) a nodular aggregation of large dark blastomeres at one pole of blastocyst called embryoblast, which further produces an embryo body and all other extraembryonic organs.

Gastrulation

The gastrulation is a third stage of embryo development. It is the process that is accompanied by mitotic division, growth, migration and differentiation of cells leading to development of three germinal layers called ectoderm, endoderm and mesoderm and a complex of axial organs.

The gastrulation has two phases:

1) Early gastrulation lasts from 7 to 13 days of the embryogenesis. Principal mechanism is delamination;

2) Late gastrulation lasts from 14 to 20 days of embryogenesis. Principal mechanism is migration.

On day 7 of the embryogenesis the embryoblast splits into two layers: primary ectoderm called epiblast and primary entoderm called hypoblast. The proliferation of epiblast cells and their movement leads to the formation of upper sac called amniotic sac. The proliferation of hypoblast cells and their movement leads to the formation of lower sac called primitive yolk sac.

The cells of epiblast producing a floor of the amniotic sac with the cells of hypoblast producing a roof of the primitive yolk sac together form an embryonic disc.

Then the cells of extraembryonic mesoderm appears by the way of their migration from the embryonic disk. They surround both sacs producing their outer walls. Thereafter, the upper bilayer bubble will be called amnion and the lower bilayer bubble will be called yolk sac.

The embryo is suspended to the trophoblast by the connecting stalk, which is formed by the extraembryonic mesoderm. Also the extraembryonic mesoderm lays

everywhere under trophoblast. Thereafter the last is called chorion. Thus, the main events of early gastrulation are;

1) Formation of bilayer embryo consisting of epibiast and hypoblast.

2) Formation of 3 extraembryonic organs – amnion, yolk sac, chorion.

The second phase of gastrulation begins on 14 or 15 day of embryo development. It is performed by cells migration and partial invagination of cells. The cells of epiblast are intensivly reproduced by mitosis and migrate to medial axis of the epiblast producing the primitive streak that extends caudally. There is a small node called primitive knot in front of the primitive streak. Thus the primitive streak and primitive knot are two cellular accumulations in the axis of epiblast. After the two cellular invaginations produce in primitive streak and primitive knot: in primitive knot the cellular invagination is called the primitive pit and in primitive streak the cellular invagination is called the primitive groove. Further the both these cellular invaginations transform into two openings for more migration of epiblast cells.

More migration of epiblast cells leads to appearance of the notochordal process or notochord, prechordal plate and mesoderm.

A cord of cells migrating from primitive knot sinks inside and grows forward in the axis of the embryonic disc between the epiblast and the hypoblast producing the notochordal process.

Some cells of primary knot migrate to entodermal layer and form the prechordal plate.

Then the cells of primitive streak migrate through groove into space between epiblast and hypoblast producing third layer of embryo called embryonic mesoderm.

Differentiation of ectoderm

Primary ectoderm includes skin ectoderm, neuroectoderm and prechordal plate.

After formation of mesoderm, the mitotic division and migration of neuroectodermal cells of the central region of primary ectoderm lying in front of the primitive knot leads to production of the neural plate. Thereafter the primary ectoderm or epiblast is called skin (secondary) ectoderm.

At the end of gastrulation, the neural plate begins to undergo the process called neurulation. For this process the neural plate invaginates to produce the neural groove and then the neural tube by ectoderm infolding.

The neurulation process is accompanied by the neural crest formation also. The neural crest is diffuse lying neuroectodermal cells between ectoderm and neural tube.

Nervous tube is a source for formation of a brain, spinal cord, pituitary gland, motor spinal nerves, cranial nerves, retina. The derivates of the neural crest are: spinal, cranial and autonomic ganglions, and adrenal medulla, tooth dentin.

Some ectoderm cell travel to primary entoderm, invade into it and situate among them. This is prechordal plate. Epithelium of esophages, respiratory epithelium, stroma of the thymus arise from it.

After the primary ectoderm become secondary entoderm or skin ectoderm. It is a source for formation of striated eithelia: skin epidermis and its derivates (hairs, nails, glands), oral cavity epithelium, anus epithelium, vagina epithelium, anus epithelium, teeth enamel, adenohypophysis, cornea, lens, olfactory epithelium and so on.

Differentiation of mesoderm

Differentiation of presomite mesoderm presenting by diffuse irregular mesodermal cells aggregation begins at the end of gastrulation. Presomite mesoderm differentiates into dorsal and ventral mesoderm. Growing dorsal mesoderm becomes segmented and forms 43-44 paired round somites lying along the notochorda.

Each somite consists of three parts: external - dermatom, intermediate - myotom, internal - sclerotom. Derma of the skin arises from dermatom. Myotom gives rise for striated skeletal muscular tissue. Sclerotom is source of bone and cartilage tissues.

Between ventral and dorsal mesoderm there is intermediate mesoderm - nephrotom. It is subject to segmentation in anterior end of the body and it is not segmented in caudal end. It gives rise to epithelium of kidney and reproductive organs.

Ventral mesoderm (splanchnotom) is not subject to segmentation. It is subdivided into two layers; visceral and parietal. They enclose secondary cavity of a body -

coelom. The layers of splanchnotom give rise to mesothelium, striated cardiac tissue, adrenal gland cortex.

Except the dense mesoderm there is a rather loose its portion, which lies everywhere between germ layers and axial organs and it's called an embryonic mesenchyme or embryonic connective tissue. The mesenchymal cells are produced from all embryonic germ layers but most part of them arises from mesoderm. Small mesenchymal cells with their processes form a meshwork and participate in the nutrition of all embryonic structures. Embryonic mesenchyme gives rise to the fibrous connective tissues, smooth muscle tissue, blood, lymph, hematopoietic organs, blood and lymph vessels.

The very important process of embryo separation from extraembryonic organs starts on day 20 of embryo development. The embryo body is lifted above extraembrionic organs with help of two lateral body's folds. So the embryo body acquires the tubular shape. It leads to division of entoderm into two parts – intestinal tube (primitive gut) which is embryonic part of entoderm and an yolk sac entoderm belong to the extraembryonic entoderm. Primitive gut is linked with yolk sac by the yolk stack.

In embryo except lateral body folds, a head fold in cranial part and a tail fold in caudal part produce.

Primitive gut forming by embryonic entoderm is a source for formation of gastric epithelium, intestinal epithelium, liver, gall bladder and pancreas.

Notogenesis

Notogenesis is formation of complex of the axial embryonic organs. The notogenesis includes three main processes: neurulation, differentiation of germinal layers and formation of body's folds. Axial complex includes following structures:

I. Skin ectoderm.

2. Nervous tube and neural crest.

3. Somites.

4. Nephrotom.

5. Splanchnotom.

6. Notochord.
7. Intestine tube.
8. Mesenchyme.