

Human embryonic development: days 14 to 28



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“ Describe human embryonic development from day 14 to day 28, including any possible abnormalities and their potential causes.” 1500 words

From day 14 to day 28 the embryo transitions from a small collection of undifferentiated cells into an organism with a definite body plan, differentiated tissues and primitive organs.

Day 14 follows shortly after the blastocyst has implanted into the uterine wall. The blastocyst is essentially a ball of cells dividing by mitosis, following a sequence of instructions from the combined DNA of the parents. At this stage, shortly before day 14, within the blastocyst, the embryoblasts (or inner cell mass) have differentiated into a bilaminar disk, a layer of two cells types called the epiblast (with the amnion cavity above) and the hypoblast (with the yolk sack below).

Whilst the blastocyst becomes an embryo, various surrounding structures support this process.

Development of the placenta: The blastocyst has now implanted within the uterus and trophoblasts (the outer layer of the blastocyst) have differentiated into cytotrophoblasts and syncytiotrophoblast with the latter permeating and embedding further into the uterus. Around day 14 the cytotrophoblasts start forming the chorionic villi, finger like projections that

grow in size and then up and out from the chorion (the membrane surrounding the embryo) then branch like trees (*embryology. ch* , 2019). Whilst the villi continue to form, cytotrophoblast cells grow toward the decidua basalis (endometrium adapted for pregnancy), outward from the chorion and form a cytotrophoblastic shell around the embryo so that now the embryo looks like a ball within a ball and the chorionic villi are tree like structures connecting the balls. The space surrounding the villi (now called anchoring villi) is now the intervilli fluid filled space – this is the site of exchange for nutrient, oxygen and waste exchange between the mother and the growing life form. This is also the start of the connection of the heart to the umbilical cord (Tortora and Derrickson, 2017).

Development of the yolk sac and amnion which supply nutrients and support the growth of the embryo: The cavity of the blastocyst is lined with new cells (exocoelomic membrane) to create the yolk sac (Tortora and Derrickson, 2017). At the time the embryo starts to morph, bend and fold from around day 15 to 17 the amniotic sac will grow to encase the embryo. This process pinches the fluid filled yolk sac cavity so that some of the yolk sac becomes enclosed in the amnion, this forms the gut. The rest of the yolk sac remains outside but attached to the enclosed embryo. The yolk sac supports the growth of the embryo only for the second and third week of development and will disappear around day 28.

Gastrulation

With help from the supporting structures described above, the process of gastrulation starts from around day 14. This transforms the bilaminar disk

into the trilaminar disk. This event is significant as the trilaminar disk is the three germ layers from which all of the structures, organs and tissues of the body are derived (see Appendix 1). The first clue of gastrulation is the appearance of the primitive streak on the surface of the ectoderm (formerly the epiblast) (Tortora and Derrickson, 2017). The primitive streak is a shallow groove that progresses to a downward folding-in of the cells from the ectoderm toward the endoderm. The cells enter and populate between the ecto and endoderm and form what is called the mesoderm.

As cells proliferate, the mesoderm spreads within the middle layer from the caudal end to the cranial end of the embryo, the notochord is also arising from the primitive pit of the primitive streak within the mesoderm as it spreads. The notochord is important for the structure of the growing form as well as coordinating development with the use of signals (Stemple, 2005). Signalling instructs the cells of their tasks, this is facilitated by signalling proteins, examples of tasks could vary from migration, proliferation to differentiation. For this to occur the cells that accept these orders possess the appropriate receptors and are called 'target cells' (Webster and de Wreede, 2016). Once the trilaminar disk has formed the gastrulation process has concluded. It is also around day 14 that the prochordal plate (cranial end) and cloacal membrane (caudal end) appears, the sites of the future mouth and anus.

The following processes involve the morphing and bending of the structures of the embryo whilst the differentiated cells continue to proliferate at a fast rate. Around day 17 the mesoderm differentiates and forms cylindrical masses adjacent and parallel to the notochord, these paraxial mesoderm

then divide to form a series of segments called somites, these are populations of cells that give rise to body structures (DeRuiter, 2010). The somites form in pairs on either side of the notochord at a rate of around 3 sets a day until there are from 42 to 44 pairs (Webster and de Wreede, 2016).

Around day 18, the heart tube, the first organ to develop in the embryo, forms in order to create the primitive heart. This is evidenced by the blood islands (lacunae) dispersed throughout the embryo, these are the formation of blood vessels. The heart tube forms from lacunae at the cranial end of the embryo. The U shaped tube with the loop at the cranial end forms so that there are two tubes running in parallel. As the embryo folds, the tubes come together, fuse and create the primitive heart. The heart starts to beat from around day 21 to 22. This vitelline blood supply from the yolk sack ensures oxygen and nutrients can support further growth whilst the rest of the blood vessels and cardiovascular system form. Recent research from the University of Oxford has shown that the heart may start beating as early as day 16 (The British Heart Foundation, 2016).

After receiving signals from the notochord, a section of the ectoderm thickens and forms the neural plate, thus commencing neuralation and the formation of the neural tube, at around day 19. The neural groove develops as the sides continue to thrust upwards and together to join and form a tube. The neural tube, which has formed above the notochord is completed around day 21 to 23.

The neural tube which spans the axis of the embryo from the caudal end to the cranial end will remain but expand into all the structures of the central nervous system (Hill, 2019). At the dorsal point of the neural tube are the neural crest cells (from the ectoderm), these migrate throughout the embryo differentiating into many different and specific features and forms of the body including the "...skin, teeth, head, face, heart, adrenal glands, gastrointestinal tract" (Hill, 2019). This commences from day 22. By day 24 the forebrain appears.

By day 25 the embryo is "...tube like, curved and has a distinct tail end visible." The yolk sac is being absorbed and sustenance is provided from the mother through the placenta (Tortora and Derrickson, 2017). This time period is eventful with many processes occurring in symphony to proliferate and arrange all the body systems for the future life. The neck (pharyngeal arches) start to form as well as the sensory system (placodes). Lacunae are joining to form blood vessels and the vascular network. All the while what has already been laid before, develops further and grows. The following systems have also begun development from day 21 to 22: Body cavities, eyes, ears and urinary, muscular, endocrine and skeletal systems.

See ' Appendix 2' for outcomes of embryonic structures.

At the point of 28 days after fertilisation most of the vital organs and systems have been mapped out. This is a significant period of growth and should anything transgress, it could have a considerable and even fatal effect to the unborn baby.

Potential abnormalities include (See Appendix 3 for more abnormalities):

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Teratogens: Agents or factors that have a damaging effect on the embryo.

Teratogens include alcohol, tobacco and caffeine, medications such as temazepam, radiation, infections, and viruses. Deficiency in certain nutrients, such as folic acid, can cause irrevocable harm to the baby (Webster and de Wreede, 2016).

Sacrococcygeal teratomas: A rare tumour that can occur at the tail bone, thought to be caused by leftover cells from the primitive streak. Most are external and can be removed.

Rectal portosystemic venous anastomoses: Interference with the blood flow from the portal vein to the vena cava this will force the blood to find another route, this can result in haemorrhoids.

Germ cell tumours: Cancerous or non-cancerous tumours that can develop from reproductive cells in the reproductive organs. A teratoma is also a type of germ cell tumour (Cancer Research UK, 2019).

Neural tube defects: Spina bifida (Latin: split spine) Failure of the vertebra of the spine to form completely; Exencephaly is when the brain is outside the skull; anencephaly, a forebrain that has not fully developed and is fatal.

Cleft lip and palate: insufficient amount of neural crest cells.

Albinism: Might be related to a defect in neural crest cell migration but also possibly a defect in the melanin production mechanism.

Waardenburg syndrome: Pigmentation abnormality thought to involve the neural crest cells. This syndrome is also associated with hearing loss, and facial abnormalities.

DiGeorge syndrome: Faulty migration of neural crest cells to the pharyngeal arches can lead to abnormalities in development of thyroid glands, facial structure, heart, aorta and pulmonary trunk. Can cause immune system issues.

Congenital diaphragmatic hernia: failure of the diaphragm to form completely can lead to abdominal content to hernia into lung area, impeding development.

Gastroschisis: Herniation on the bowel so that it develops outside of the body and may be caused by the outer body layer not forming properly.

Congenital scoliosis: Caused by segmentation error with the somites, a hemivertebra may cause this condition.

(Webster and de Wreede, 2016; *embryology. ch* , 2019)

With an understanding and chartering of these developmental processes we can widen and deepen our understanding of healthy growth and development in relation to the environment we are gestated, born and grow in.

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Appendix

Appendix 1: A brief outline to the fate of the three germ layers

Germ

layer

The form the cells will eventually take

Ectoderm The nervous system, skin, hair and the epithelium of various cavities and

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Skeleton, muscle and connective tissues. Kidney, ureters, adrenal cortex e

Endoder The epithelial linings to many of the organs, tubes and glands including re

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tracts. Sperm and oocytes.

(Tortora and Derrickson, 2017)(Webster and de Wreede, 2016)

Appendix 2: What embryonic structure eventually become

Structure	approx. time appearance	End result
Notochord	Day 14	Nucleus pulposus of the spine
Prochordal plate	Day 17	Mouth opening
Cloacal membrane	Day 17	Anal canal opening
Somites	Day 18 - 20	Dermatomes, skeletal muscle, tendons, cartilage, bone
Neural tube	Day 19 - 21	Brain and spinal cord (CNS)

Heart tube	Day 18	Heart
Gut (hind, mid and fore)	Day 18	GI tract
Neural Crest Cells	Day 22	PNS, SNS, parts of the skin, teeth, head, face, head, adrenal glands, gastrointestinal tract

(Tortora and Derrickson, 2017)(Webster and de Wreede, 2016)

Appendix 3: Summary and timings of abnormalities and causes

Abnormality	time period	potential cause
Deformations / damage	Gastrulation	Teratogens
Rectal portosystemic venous anastomoses	Germ layers around day 15	Interference with the blood flow from the portal vena cava
Sacrococcygeal teratomas	Germ layers around day 15	Cells from the primitive streak are left behind in the sacrococcygeal region
Germ cell tumours	Germ layers around day 15	


Teratoma	Germ layers around day 15	
Neural tube defect	Days 18 to 28	Defects at cranial or caudal end (folate deficiency)
Exencephaly	Days 18 to 28	Neural tube fails to close
Anencephaly (fatal)	Days 18 to 28	Neural tube fails to close
Cleft lip and cleft palate	From day 22	deficiency of neural crest cells to form mesenchyme developing face
Albinism	From day 22	likely a defect in the melanin production mechanism
Waardenburg syndrome	From day 22	gene mutations of one of at least four genes
DiGeorge syndrome	From day 22	Abnormality of migration of neural crest cells into pharyngeal arches can lead to improper development of parathyroid gland, thymus, facial skeleton, heart and pulmonary trunk.
Congenital diaphragmatic hernia	From day 21 to week 8	failure of the diaphragm to form completely
Gastroschisis	From day 17 to week 8	Anterior abdominal wall defect
Congenital scoliosis	Days 18 to 35	Error in segmentation


Prune belly embryonic absence of entire abdominal wall musculature
syndrome development


(Webster and de Wreede, 2016; *embryology. ch* , 2019)

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