The Science of Life Before Birth: Lecture Notes

The following lecture notes from the full-length video include endnotes for a deeper dive into the material. There are also links to the 3D models of the organ systems mentioned in the video. Please note that all references to developmental milestones in the video and notes are from fertilization.

Key terms are listed here for reference. More information may be found in the endnotes.

age of viability	fertilization	noradrenalin
alveoli	forebrain	norepinephrine
amnion	germ cells	oocyte
amniotic fluid	germ layers	oogonia
blastocyst	glucose	ossification
blink-startle response	hindbrain	ovulation
cerebral hemispheres	human chorionic gonadotropin (hCG)	physiologic herniation
circadian rhythms	hypoblast	placenta
cochlea	implantation	quickening
conception	inner cell mass	spermatozoon
diaphragm	kidneys	testosterone
DNA	lymphocytes	trimester
early pregnancy factor (EPF)	main stem bronchi	umbilical cord
ectoderm	meconium	uterine or fallopian tubes
embryonic stem cells	mesoderm	uterus or womb
endoderm	midbrain	vernix caseosa
epiblast	mitosis	yolk sac
estrogen	morula	zygote

1. Introduction

a. The dynamic process by which the single-cell human **zygote** (zī´gōt)[1] becomes a 100 trillion (10^{14}) cell adult[2] is perhaps the most remarkable phenomenon in all of nature.
b. Researchers now know that many of the routine functions performed by the adult body become established during pregnancy—often long before birth.[3]
c. The developmental period before birth is increasingly understood as a time of preparation during which the developing human acquires the many structures, and practices the many skills, needed for survival after birth.

2. Terminology

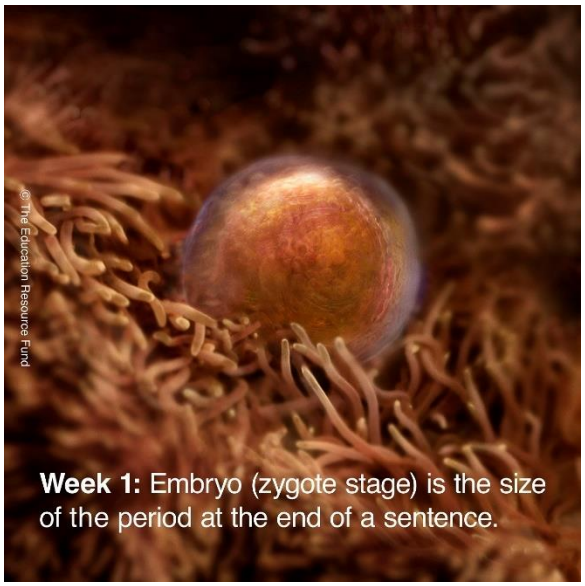
a. Pregnancy in humans normally lasts approximately 38 weeks[4] as measured from the time of **fertilization**,[5] or **conception**,[6] until birth.

b. During the first 8 weeks following fertilization, the developing human is called an **embryo**,[7] which means “growing within.”[8] This time, called the **embryonic period**,[9] is characterized by the formation of most major body systems.[10]
c. From the completion of 8 weeks until the end of pregnancy, “the developing human is called a **fetus**,” which means “unborn offspring.” During this time, called the **fetal period**, the body grows larger and its systems begin to function.[11]
d. All embryonic and fetal ages in this program refer to the time since fertilization.[12]

The Embryonic Period (Fertilization through 8 Weeks)

Embryonic Development: Fertilization through 3 Weeks

3. Fertilization



a. Biologically speaking, "human development begins at fertilization,"[13] when a woman and a man each combine 23 of their own chromosomes through the union of their reproductive cells.
b. A woman's reproductive cell is commonly called an "egg" but the correct term is **oocyte** (ō´ō-sīt).[14]
c. Likewise, a man's reproductive cell is widely known as a "sperm," but the preferred term is **spermatozoon** (sper´mă-tō-zō´on).[15]
d. Following the release of an oocyte from a woman's ovary in a process called **ovulation** (ov´yū-lā´shŭn),[16] the oocyte and spermatozoon join within one of the **uterine tubes**,[17] which are often referred to as **fallopian tubes**.
e. The uterine tubes link a woman's ovaries to her **uterus** or **womb**.
f. The resulting single-celled embryo is called a **zygote**,[18] meaning "yoked or joined together."[19]

4. DNA, Cell Division, and Early Pregnancy Factor (EPF)

a. The zygote's 46 chromosomes[20] represent the unique first edition of a new individual's complete genetic blueprint. This master plan resides in tightly coiled molecules called **DNA**. They contain the instructions for the development of the entire body.
b. DNA molecules resemble a twisted ladder known as a double helix.[21] The rungs of the ladder are made up of paired molecules, or bases, called guanine, cytosine, adenine, and thymine.
c. Guanine pairs only with cytosine, and adenine with thymine.[22] Each human cell contains approximately 3 billion (3×10^9) of these base pairs.[23]
d. The DNA of a *single* cell contains so much information that if it were represented in printed words, simply listing the first letter of each base would require over 1.5 million (1.5×10^6) pages of text.[24]
e. If laid end-to-end, the DNA in a single human cell measures 3⅓ feet or 1 meter.[25]
f. If we could uncoil all of the DNA within an adult's 100 trillion (10^{14}) cells, it would extend over 63 billion (6.3×10^{10}) miles. This distance reaches from the earth to the sun and back 340 times.[26]
g. Approximately 24 to 30 hours after fertilization, the zygote completes its first cell division.[27] Through the process of **mitosis**, one cell splits into two, two into four, and so on.[28]
h. As early as 24 to 48 hours after fertilization begins, pregnancy can be confirmed by detecting a hormone called "**early pregnancy factor**" in the mother's blood.[29]

5. Early Stages (Morula and Blastocyst) and Stem Cells

a. By 3 to 4 days after fertilization, the dividing cells of the embryo assume a spherical shape and the embryo is called a **morula** (mōr´ū-lă).[30]
b. By 4 to 5 days, a cavity forms within this ball of cells and the embryo is then called a **blastocyst**.[31]

c. The cells inside the blastocyst are called the **inner cell mass** and give rise to the head, body, and other structures vital to the developing human.[32]

d. Cells within the inner cell mass are called **embryonic stem cells** because they have the ability to form each of the more than 200 cell types contained in the human body.[33]

6. Implantation and Human Chorionic Gonadotropin (hCG)

a. After traveling down the uterine tube, the early embryo embeds itself into the inner wall of the mother's uterus. This process, called **implantation**, begins at day 6 and ends 10 to 12 days after fertilization.[34]
b. Cells from the growing embryo begin to produce a hormone called **human chorionic gonadotropin** (human kō-rē-on'ik gō'nad-ō-trō'pin), or **hCG**, the substance detected by most pregnancy tests.[35]
c. HCG directs maternal hormones to interrupt the normal menstrual cycle, allowing pregnancy to continue.[36]

7. The Placenta and Umbilical Cord

a. Following implantation, cells on the periphery of the blastocyst give rise to part of a structure called the **placenta** (plă-sen'tă), which serves as an interface between the maternal and embryonic circulatory systems.
b. The placenta delivers maternal oxygen, nutrients, hormones, and medications to the developing human; removes all waste products; and prevents maternal blood from mixing with the blood of the embryo and fetus.[37]
c. The placenta also produces hormones and maintains embryonic and fetal body temperature slightly above that of the mother.[38]
d. The placenta communicates with the developing human through the vessels of the **umbilical** (ŭm-bil'i-kăl) **cord**.[39]
e. The life support capabilities of the placenta rival those of intensive care units found in modern hospitals.

8. Nutrition and Protection

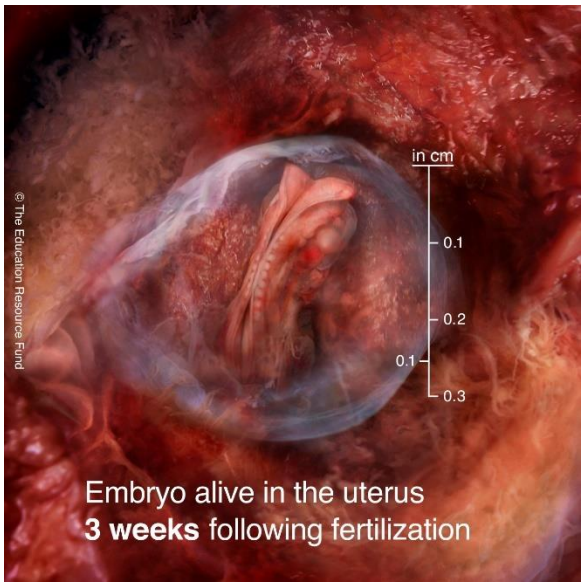
a. By 1 week, cells of the inner cell mass form two layers called the **hypoblast** and **epiblast**.[40]
b. The hypoblast gives rise to the **yolk sac**,[41] which is one of the structures through which the mother supplies nutrients to the early embryo.[42]
c. Cells from the epiblast form a membrane called the **amnion** (am-nē-on),[43] within which the embryo and later the fetus develop until birth.

9. 2 and 3 Weeks: Germ Layers and Organ Formation

a. By approximately 2½ weeks, the epiblast has formed 3 specialized tissues, or **germ layers**, called **ectoderm, endoderm,** and **mesoderm**.[44]
b. The ectoderm gives rise to numerous structures including the brain, spinal cord, nerves, skin, nails, and hair.
c. The endoderm produces the lining of the respiratory system and digestive tract and generates portions of major organs such as the liver and pancreas.
d. The mesoderm forms the heart, kidneys, bones, cartilage, muscles, blood cells, and other structures.[45]

e. By 3 weeks the brain is dividing into 3 primary sections called the **forebrain, midbrain**, and **hindbrain**.[46]
f. Development of the respiratory and digestive systems is also underway.[47]
g. As the first blood cells appear in the yolk sac,[48] blood vessels form throughout the embryo, and the tubular heart emerges.[49]
h. Almost immediately, the rapidly growing heart folds in upon itself as separate chambers begin to develop.[50]
i. The heart begins beating 3 weeks and 1 day following fertilization.[51]
j. The circulatory system is the first body system, or group of related organs, to achieve a functional state.[52]

10. 3 Weeks: The Folding of the Embryo



a. Between 3 and 4 weeks, the body plan emerges as the brain, spinal cord, and heart of the embryo are easily identified alongside the yolk sac.
b. Rapid growth causes folding of the relatively flat embryo.[53] This process incorporates part of the yolk sac into the lining of the digestive system and forms the chest and abdominal cavities of the developing human.[54]

Embryonic Development: 4 and 5 Weeks

11. 4 Weeks: Amniotic Fluid

a. By 4 weeks the clear amnion surrounds the embryo in a fluid-filled sac.[55] This sterile liquid, called **amniotic** (am-nē-ot'ik) **fluid**, provides the embryo with protection from injury.[56]

12. The Heart in Action

a. The embryonic heart typically beats about 113 times per minute.[57]
b. The heart changes color as blood enters and leaves its chambers with each beat.
c. The heart will beat approximately 54 million (5.4×10^7) times before birth and over 3.2 billion (3.2×10^9) times over the course of an 80-year lifespan.[58]

13. Brain Growth

a. Rapid brain growth is evidenced by the changing appearance of the forebrain, midbrain, and hindbrain.

14. Limb Buds

a. Upper and lower limb development begins with the appearance of the limb buds by 4 weeks.[59]
b. The skin is transparent at this point because it is only one cell thick.
c. As the skin thickens, it will lose this transparency, which means that one may only watch internal organs develop for about another month after this point.[60]

15. 5 Weeks: Cerebral Hemispheres

a. Between 4 and 5 weeks, the brain continues its rapid growth and divides into five distinct sections.[61]
b. The head comprises about one-third of the embryo's total size.[62]
c. The **cerebral** (ser'ĕ-brăl) **hemispheres** appear,[63] gradually becoming the largest parts of the brain.[64]
d. Functions eventually controlled by the cerebral hemispheres include thought, learning, memory, speech, vision, hearing, voluntary movement, and problem-solving.[65]

16. Major Airways

a. Between 4 and 5 weeks, in the respiratory system, the right and left **main stem bronchi** (brong'kī) are present.[66] They will eventually connect the trachea (trā´kē-ă), or windpipe, with the lungs.

17. Liver and Kidneys

a. At five weeks, the massive liver fills the abdomen adjacent to the beating heart.
b. The permanent **kidneys** appear by 5 weeks.[67]

18. Yolk Sac and Germ Cells

a. The yolk sac contains early reproductive cells called **germ cells**. By 5 weeks these germ cells migrate to the reproductive organs adjacent to the kidneys.[68]

19. Hand Plates and Cartilage

a. Also by 5 weeks, the embryo develops hand plates,[69] and cartilage formation begins by 5½ weeks.[70]

Embryonic Development: 6 and 7 Weeks

20. 6 Weeks: Motion and Sensation

a. By 6 weeks the cerebral hemispheres are growing disproportionately faster than other sections of the brain.
b. The embryo begins to make spontaneous and reflexive movements.[71] Such movement is necessary to promote normal neuromuscular development.
c. A touch to the mouth area will cause the embryo to reflexively withdraw its head.[72]

21. The External Ear and Blood Cell Formation

a. The external ear begins to take shape.[73]

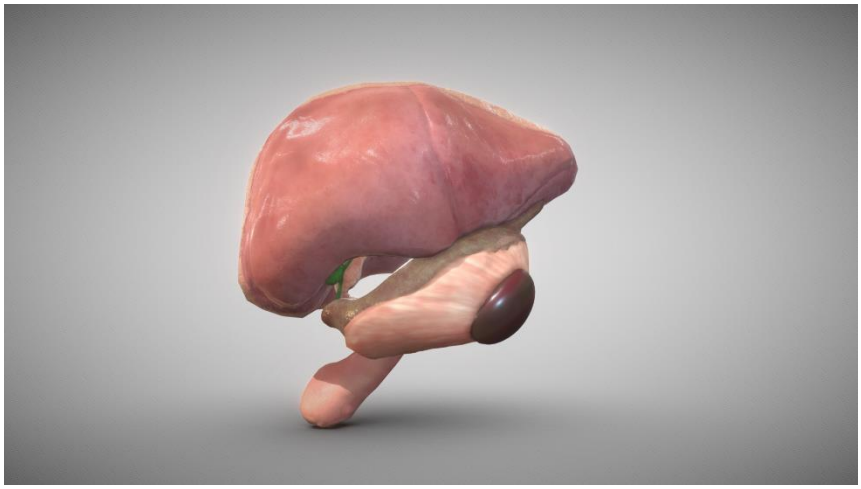
3D model of 8 week embryonic ear

b. By 6 weeks, blood cell formation is underway in the liver where **lymphocytes** are now present.[74] This type of white blood cell is a key part of the developing immune system.

22. The Diaphragm and Intestines

a. The **diaphragm** (dī'ă-fram), the primary muscle used in breathing, is largely formed by 6 weeks.[75]
b. A portion of the intestine now protrudes temporarily into the umbilical cord. This normal process, called **physiologic herniation** (fiz-ē-ō-loj'ik her-nē-ā'shŭn), makes room for other developing organs in the abdomen.[76]

3D model of 8 week embryonic digestive system



[3D model of 8 week embryonic liver, spleen, and pancreas]

23. Hand Plates and Brainwaves

a. At 6 weeks the hand plates develop a subtle flattening.[77]
b. Primitive brainwaves have been recorded as early as 6 weeks and 2 days.[78]

24. Nipple Formation

a. Nipples appear along the sides of the trunk shortly before reaching their final location on the front of the chest.[79]

25. Limb Development

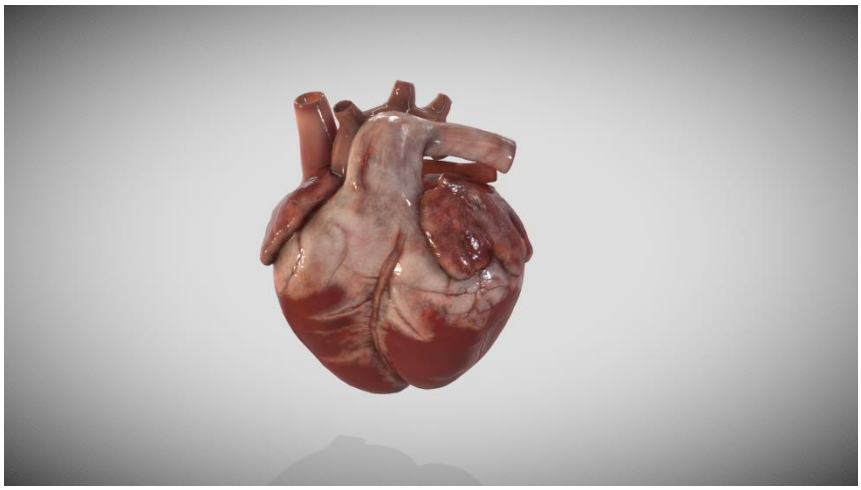
a. By 6½ weeks, the elbows are distinct, the fingers are beginning to separate,[80] and hand movement can be seen.
b. Bone formation, called **ossification** (os'i-fi-kā'shŭn), begins within the clavicle, or collar bone, and the bones of the upper and lower jaw.[81]

26. 7 Weeks: Hiccups and Startle Response

a. Hiccups have been observed by 7 weeks.[82]
b. Leg movements can now be seen, along with a startle response.[83]

27. The Maturing Heart

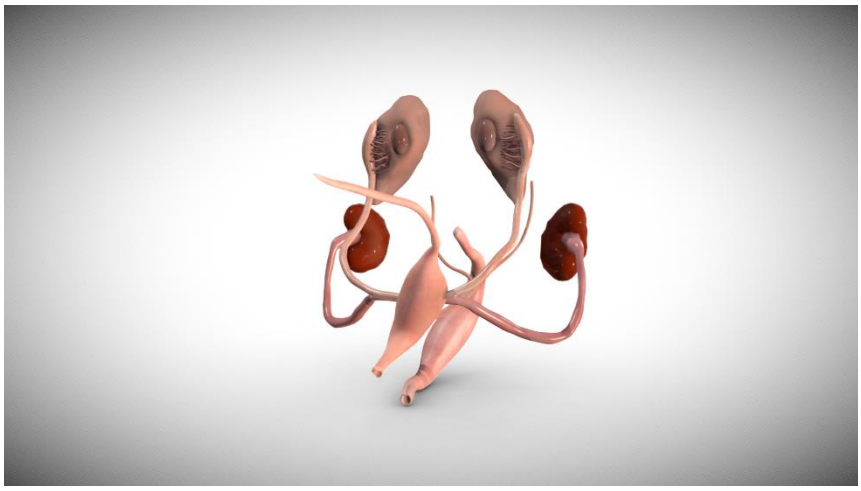
a. By seven weeks, the four-chambered heart is largely complete.[84] On average, the heart now beats 167 times per minute.[85]
b. Electrical activity of the heart recorded at 7½ weeks reveals a wave pattern similar to the adult's.[86]



[3D model of 8 week embryonic heart]

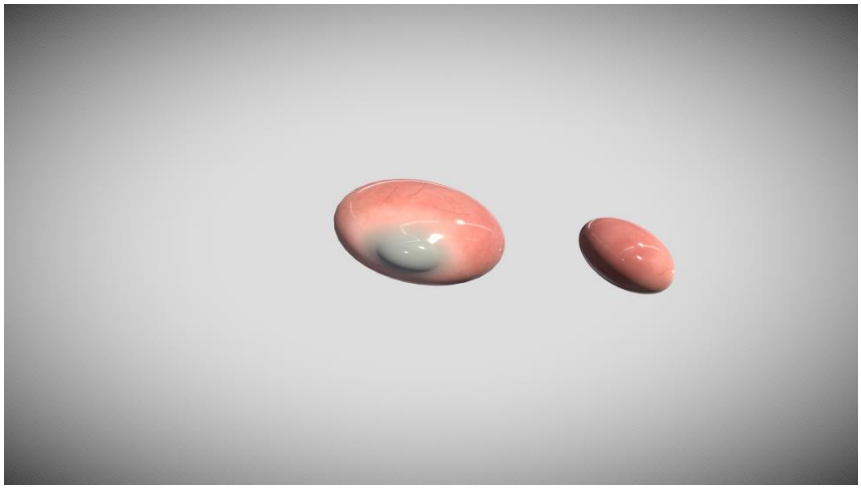
28. Ovaries and Eyes

a. In females, the ovaries are identifiable by 7 weeks.[87]

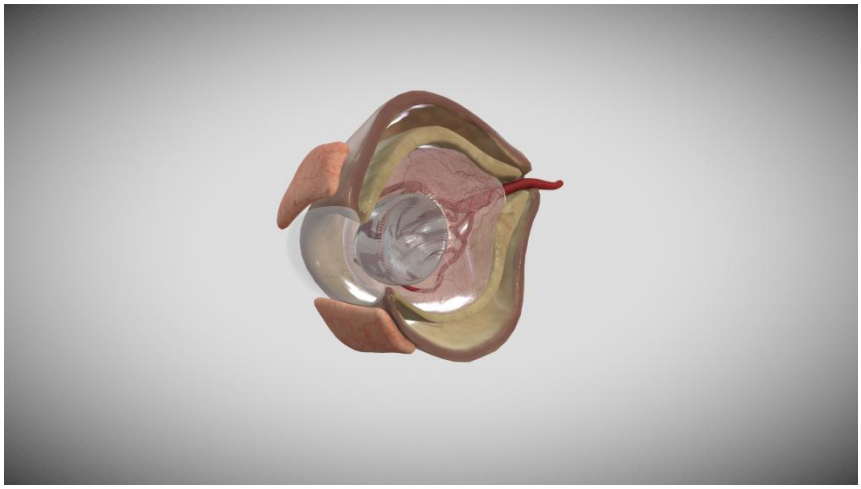


3D model of 8 week embryonic female reproductive system

b. By 7½ weeks, the pigmented retina of the eye is easily seen and the eyelids are beginning a period of rapid growth.[88]



3D model of 8 week embryonic eye (full section)



[3D model of 8 week embryonic eye (cross section)]

29. Fingers and Toes

a. At 7 weeks and 4 days, fingers are separate and toes are joined only at the bases.
b. The hands can now come together, as can the feet.[89]
c. Knee joints are also present.[90]

The 8 Week Embryo

30. 8 Weeks: Brain Development

a. At 8 weeks the brain is highly complex[91] and constitutes almost half of the embryo's total body weight.[92]

3D model of 8 week embryonic brain

b. Growth continues at an extraordinary rate.

31. Right- and Left-Handedness

a. By 8 weeks, 75 percent of embryos exhibit right-hand dominance. The remainder is equally divided between left-handed dominance and no preference. This is the earliest evidence of right- or left-handed behavior.[93]

32. Rolling Over

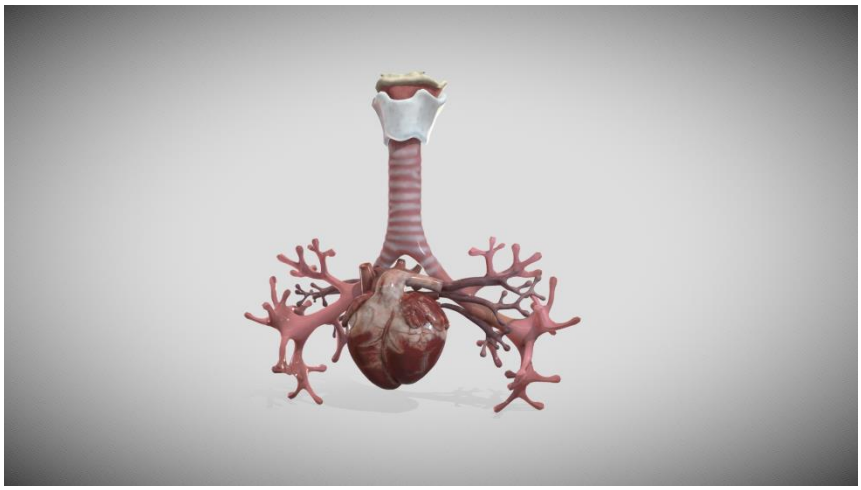
a. Pediatric textbooks describe the ability to "roll over" as appearing 10 to 20 weeks *after birth*.[94] However, this impressive coordination is displayed much earlier in the low-gravity environment of the fluid-filled amniotic sac.[95] Only the lack of strength required to overcome the higher gravitational force outside the uterus prevents newborns from rolling over.[96]
b. The embryo is becoming more physically active during this time.
c. Motions may be slow or rapid, single or repetitive, spontaneous or reflexive.
d. Head rotation, neck extension, and hand-to-face contact occur more often.[97]
e. Touching the embryo elicits squinting, jaw movement, grasping motions, and toe pointing.[98]

33. Eyelid Fusion

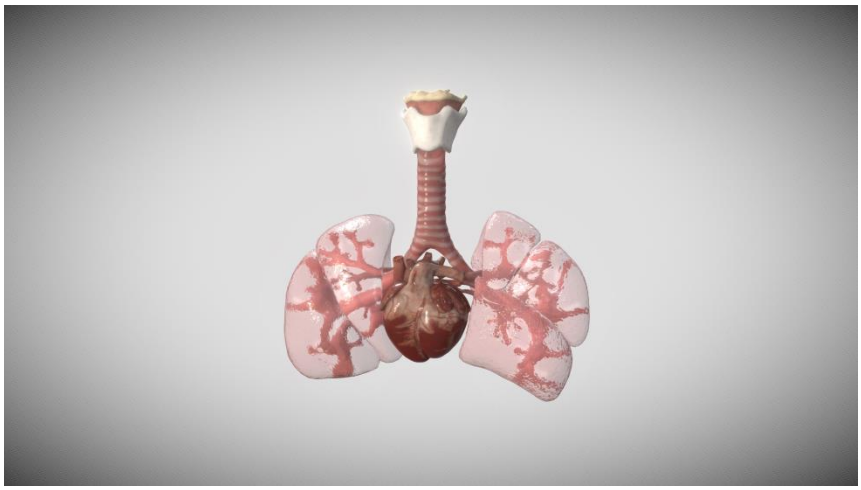
a. Between 7 and 8 weeks, the upper and lower eyelids rapidly grow over the eyes and partially fuse together.[99]

34. "Breathing" Motion and Urination

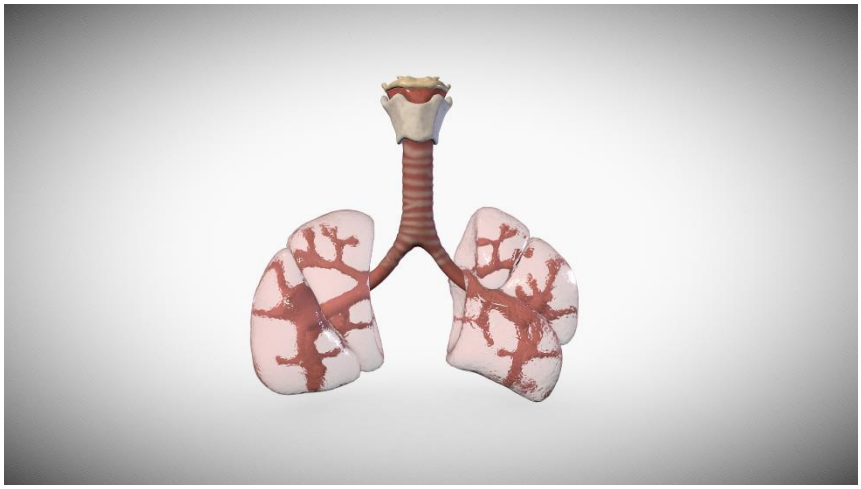
a. Although there is no air in the uterus, the embryo displays intermittent breathing motions by 8 weeks.[100]



3D model of 8 week embryonic heart and bronchial airways

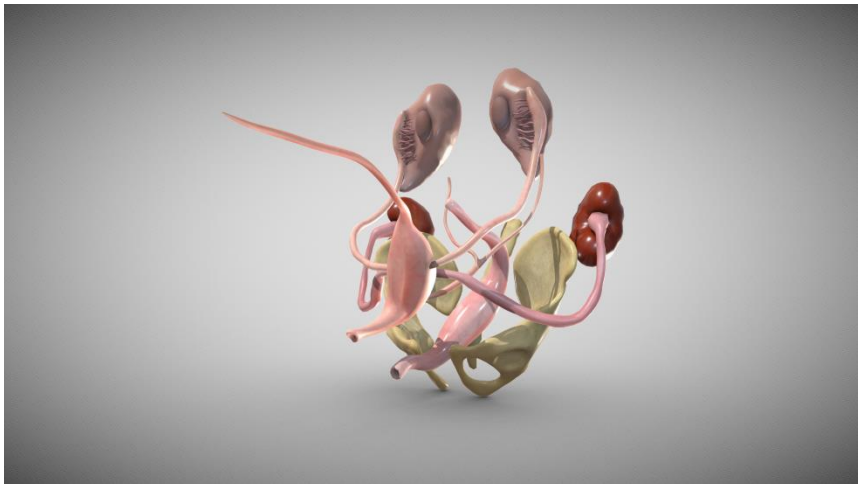


3D model of 8 week embryonic heart and lungs



[3D model of 8 week embryonic pulmonary system]

b. By this time, kidneys produce urine which is released into the amniotic fluid.[101]
c. In male embryos, the developing testes begin to produce and release **testosterone** (tes-tos´tĕ-rōn).[102]



[3D model of 8 week embryonic male reproductive system]

35. The Limbs and Skin

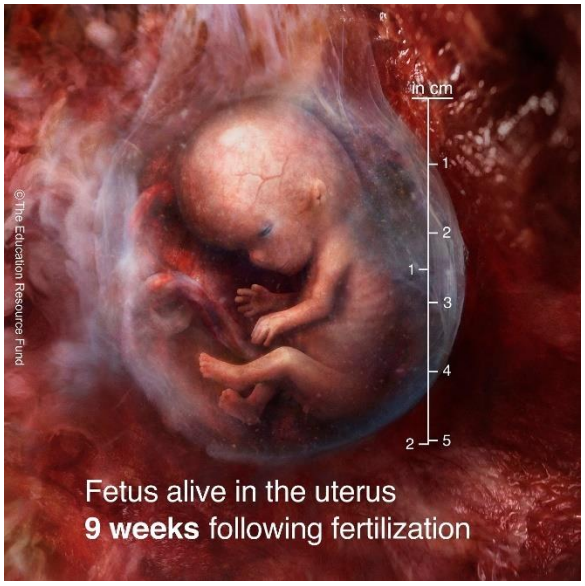
a. The bones, joints, muscles, nerves, and blood vessels of the limbs closely resemble those in adults.[103]
b. By 8 weeks the epidermis, or outer skin, becomes a multi-layered membrane,[104] losing much of its transparency.
c. Eyebrows grow as hair appears around the mouth.[105]

36. Summary of the Embryonic Period

a. Eight weeks marks the end of the embryonic period.
b. During this time, the human embryo has grown from a single cell into the nearly 1 billion (10^9) cells[106] which form over 4,000 (4×10^3) distinct anatomic structures.
c. The embryo now possesses more than 90 percent of the structures found in adults.[107]

The Fetal Period (9 Weeks through Birth)

37. 9 Weeks: Swallows, Sighs, and Stretches



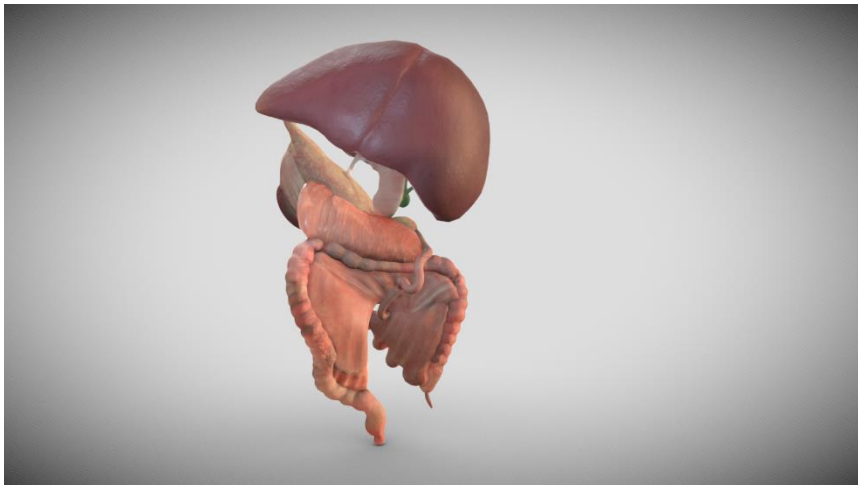
a. The fetal period continues until birth.
b. By 9 weeks, thumb sucking begins[108] and the fetus can swallow amniotic fluid.[109]
c. The fetus can also grasp an object,[110] move the head forward and back, open and close the jaw, move the tongue, sigh,[111] and stretch.[112]
d. Nerve receptors in the face, the palms of the hands, and the soles of the feet can sense light touch.[113]
e. In response to a light touch on the sole of the foot, the fetus will bend the hip and knee and may curl the toes.[114]
f. The eyelids are now completely closed.[115]
g. In the larynx, the appearance of vocal ligaments signals the onset of vocal cord development.[116]
h. In female fetuses, the uterus is identifiable[117] and immature reproductive cells called **oogonia** (ō-ō-gō′nē-ă) are replicating within the ovary.[118]
i. External genitalia begin to distinguish themselves as either male or female.[119]

38. 10 Weeks: Rolls Eyes and Yawns, Fingernails & Fingerprints

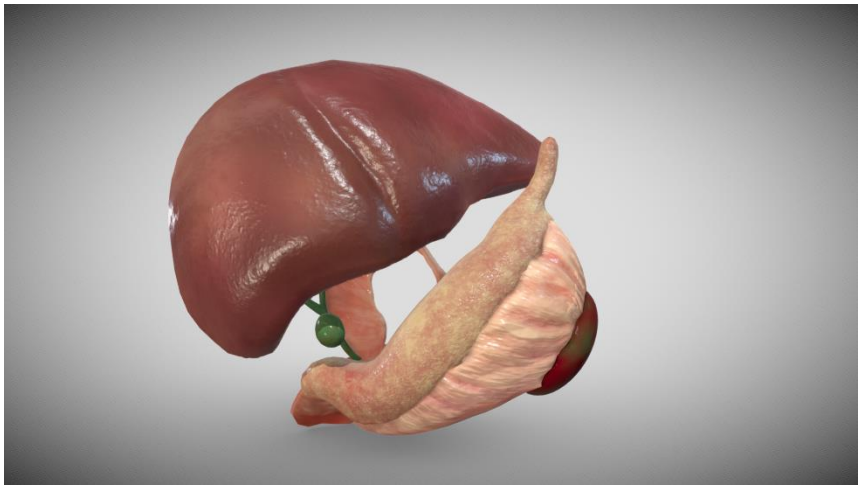
a. A burst of growth between 9 and 10 weeks increases body weight by over 75 percent.[120]
b. By 10 weeks, stimulation of the upper eyelid causes a downward rolling of the eye.[121]
c. The fetus yawns and often opens and closes the mouth.[122]
d. Most fetuses suck the right thumb.[123]
e. Sections of intestine within the umbilical cord are returning to the abdominal cavity.[124]
f. Ossification is underway in most bones.[125]
g. Fingernails and toenails begin to develop.[126]
h. Unique fingerprints appear 10 weeks after fertilization. These patterns can be used for identification throughout life.[127]

39. 11 Weeks: Absorbs Glucose and Water

a. By 11 weeks the nose and lips are completely formed.[128] As with every other body part, their appearance will change at each stage of the human life cycle.
b. The intestine starts to absorb **glucose** and water swallowed by the fetus.[129]

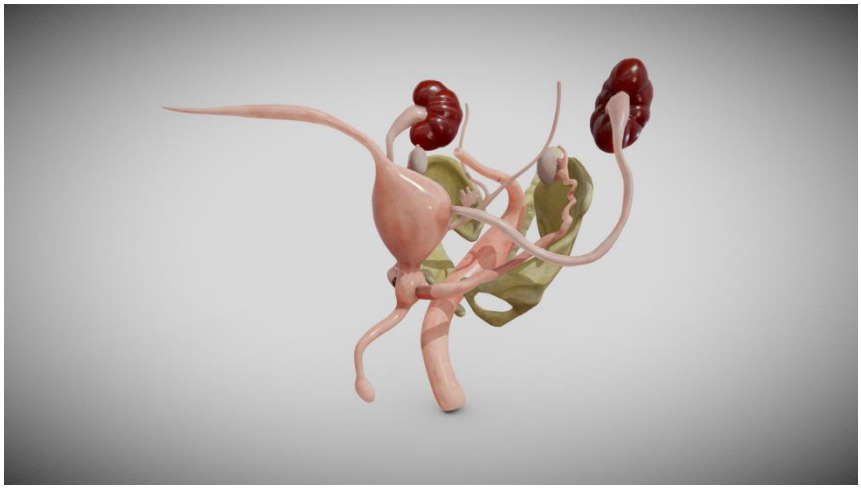


3D model of 16 week fetal digestive system

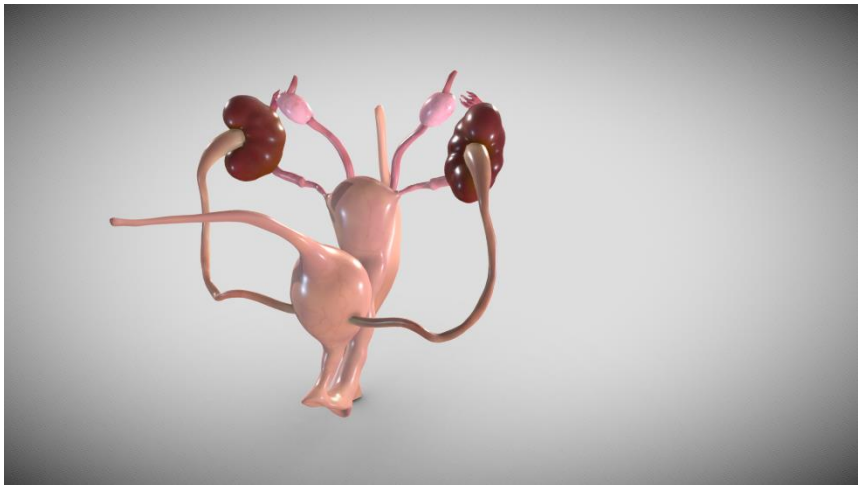


3D model of 16 week fetal liver, spleen, and pancreas

c. Though sex is determined at fertilization, external genitalia can now be distinguished as male or female.[130]



3D model of 16 week fetal male reproductive system



3D model of 16 week fetal female reproductive system

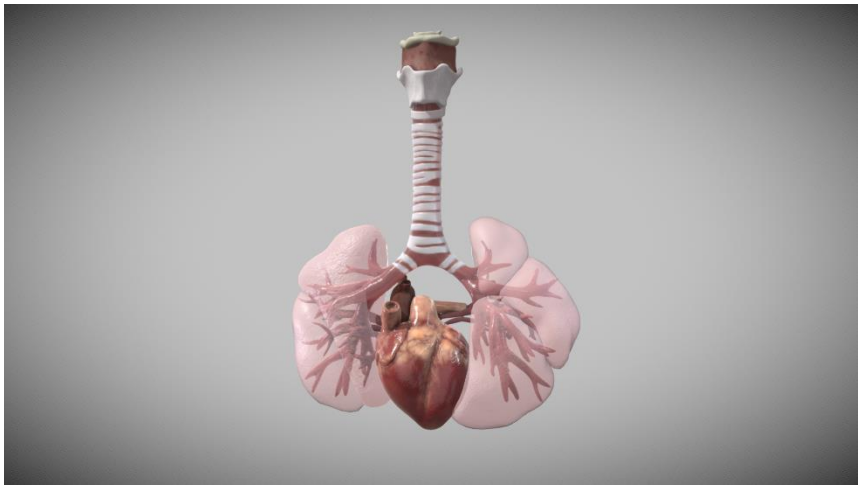
40. 3 Months (12 through 15 Weeks): Taste Buds, Jaw Motion, Rooting Reflex, Quickening

a. Between 11 and 12 weeks, fetal weight increases nearly 60 percent.[131]
b. Twelve weeks marks the end of the first third, or **trimester**, of pregnancy.
c. Distinct taste buds now cover the inside of the mouth. By birth, taste buds will remain only on the tongue and roof of the mouth.[132]
d. Bowel movements begin as early as 12 weeks and continue for about 6 weeks.[133]
e. The material first expelled from the fetal and newborn colon is called **meconium** (mĭ-kō'nē-ŭm).[134] It is composed of digestive enzymes, proteins, and dead cells shed by the digestive tract.[135]
f. By 12 weeks, upper limb length has nearly reached its final proportion to body size. The lower limbs take longer to attain their ultimate proportions.[136]
g. With the exception of the back and the top of the head, the body of the entire fetus now responds to light touch.[137]
h. Sex-dependent developmental differences appear for the first time. For instance, female fetuses exhibit jaw movement more frequently than males.[138]
i. In contrast to the withdrawal response seen earlier, stimulation near the mouth now evokes a turning *toward* the stimulus and an opening of the mouth.[139] This response is called the "rooting reflex" and it persists after birth, helping the newborn find his or her mother's nipple during breastfeeding.[140]
j. The face continues to mature as fat deposits begin to fill out the cheeks[141] and tooth development begins.[142]
k. By 15 weeks, blood-forming stem cells arrive and multiply in the bone marrow. Most blood cell formation will occur here.[143]
l. Although movement begins in the 6-week embryo, a pregnant woman first senses fetal movement between 14 and 18 weeks.[144] Traditionally, this event has been called **quickening**.[145]

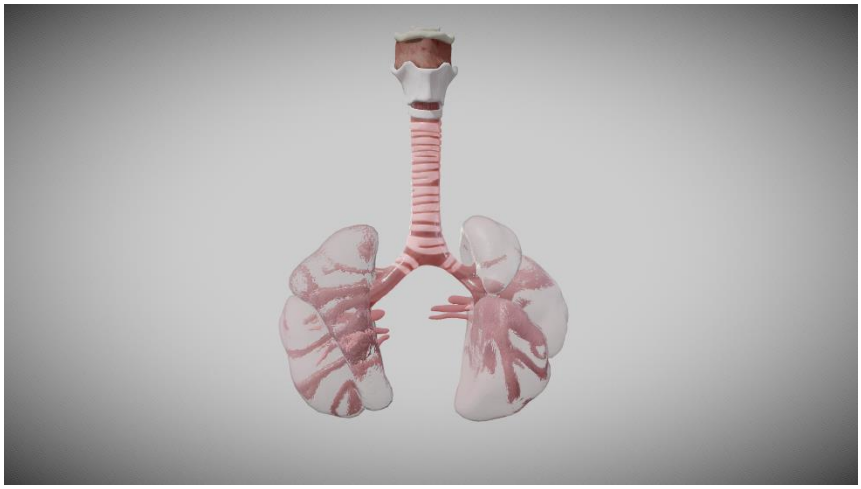
41. 4 Months (16 through 19 Weeks): Stress Response, Vernix Caseosa, Circadian Rhythms

a. By 16 weeks, procedures involving the insertion of a needle into the abdomen of the fetus trigger a **hormonal stress response** releasing **noradrenalin**, or **norepinephrine** (nor-ep'i-nef'rin), into the bloodstream.[146]
b. In the respiratory system, the bronchial tree is now nearly complete.[147]

3D model of 16 week fetal heart and bronchial airways

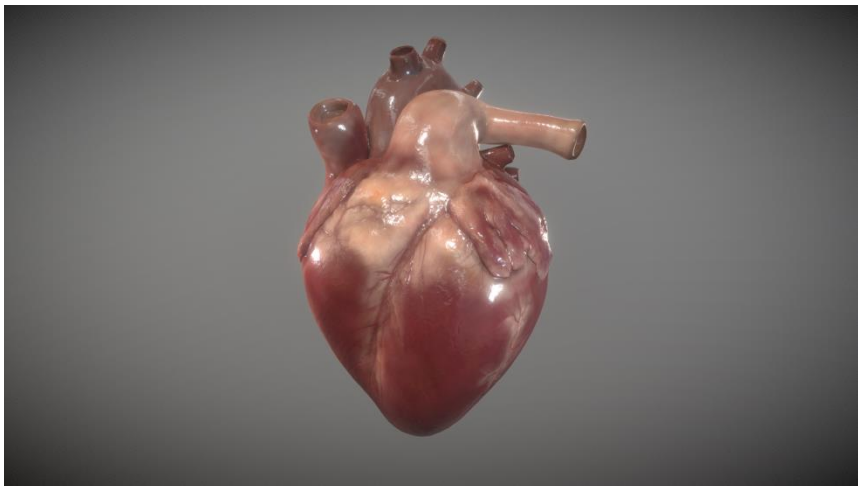


3D model of 16 week fetal heart and lungs



[3D model of 16 week fetal pulmonary system]

c. A protective white substance, called **vernix caseosa** (ver'niks caseo'sa), now covers the fetus. Vernix protects the skin from the irritating effects of amniotic fluid.[148]
d. From 19 weeks fetal movement, breathing activity, and heart rate begin to follow daily cycles called **circadian** (ser-kā'dē-ăn) **rhythms**.[149]



[3D model of 16 week fetal heart]

42. 5 Months (20 through 23 Weeks): Responds to Sound; Hair and Skin; Age of Viability

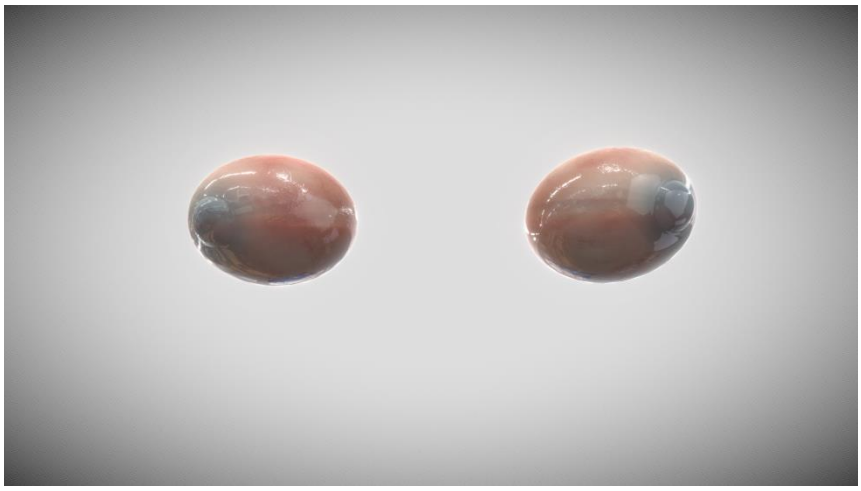
a. By 20 weeks the **cochlea**, which is the organ of hearing, has reached adult size[150] within the fully developed inner ear. From now on, the fetus will respond to a growing range of sounds.[151]

3D model of 16 week fetal ear

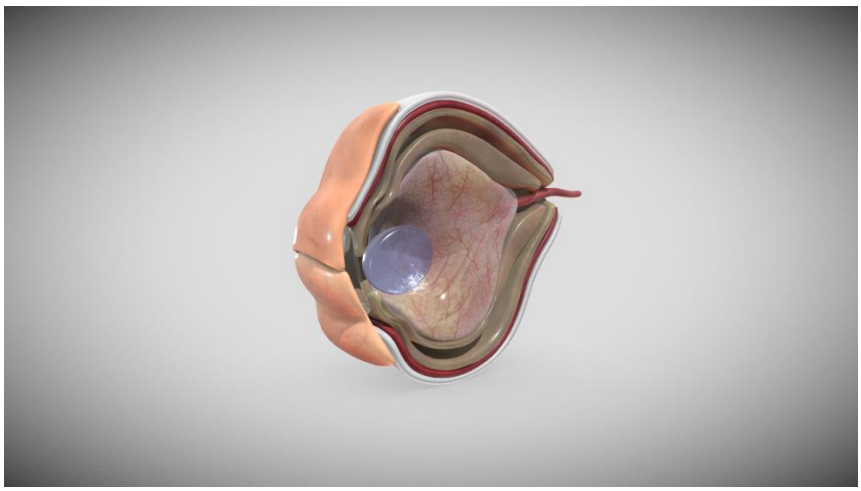
b. Hair begins to grow on the scalp.
c. All skin layers and structures are present, including hair follicles and glands.[152]
d. By 21 to 22 weeks after fertilization, the lungs gain some ability to breathe air.[153] This is considered the **age of viability** because survival outside the womb becomes possible for some fetuses.[154]

43. 6 Months (24 through 27 Weeks): Blink-Startle; Pupils Respond to Light; Smell and Taste

a. By 24 weeks the eyelids reopen[155]
b. and the fetus exhibits a **blink-startle response**.[156] This reaction to sudden, loud noises typically develops earlier in the female fetus.[157]



3D model of 16 week fetal eye (full section)



3D model of 16 week fetal eye (cross section)

c. Several investigators report exposure to loud noise may adversely affect fetal health. Immediate consequences include prolonged increased heart rate, excessive fetal swallowing, and abrupt behavioral changes.[158] Possible long-term consequences include hearing loss.[159]
d. The fetal respiratory rate can rise as high as 44 inhalation-exhalation cycles per minute.[160]

e. During the third trimester of pregnancy, rapid brain growth consumes more than 50 percent of the energy used by the fetus. Brain weight increases between 400 and 500 percent.[161]

3D model of 16 week fetal brain

f. By 26 weeks the eyes produce tears.[162]
g. The pupils respond to light as early as 27 weeks.[163] This response regulates the amount of light reaching the retina[164] throughout life.
h. All components required for a functioning sense of smell are operational. Studies of premature babies reveal the ability to detect odors as early as 26 weeks after fertilization.[165]
i. Placing a sweet substance in the amniotic fluid increases the rate of fetal swallowing. In contrast, decreased fetal swallowing follows the introduction of a bitter substance. Altered facial expressions often follow.[166]
j. Through a series of step-like leg motions similar to walking, the fetus performs somersaults.[167]
k. The fetus appears less wrinkled as additional fat deposits form beneath the skin.[168] Fat plays a vital role in maintaining body temperature and storing energy after birth.

44. 7 Months (28 through 31 Weeks): Sound Discrimination, Behavioral States

a. By 28 weeks the fetus can distinguish between high- and low-pitched sounds.[169]
b. By 30 weeks, breathing movements are more common and occur 30 to 40 percent of the time in an average fetus.[170]
c. During the last 4 months of pregnancy, the fetus displays periods of coordinated activity punctuated by periods of rest. These behavioral states reflect the ever-increasing complexity of the central nervous system.[171]

45. 8 Months (32 through 35 Weeks): Alveoli Formation, Firm Grasp, Taste Preferences

a. By approximately 32 weeks, true **alveoli** (al-vē'ō-lī), or air "pocket" cells, begin developing in the lungs. They will continue to form until 8 years *after* birth.[172]
b. At 35 weeks the fetus has a firm hand grasp.[173]

c. Fetal exposure to various substances appears to affect flavor preferences after birth. For instance, fetuses whose mothers consumed anise, a substance which gives licorice its taste, showed a preference for anise after birth. Newborns without fetal exposure disliked anise.[174]

46. 9 Months through Birth (36 Weeks through Birth)

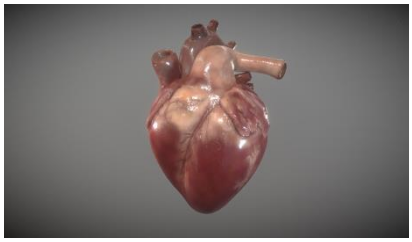
a. The fetus initiates labor[175] by releasing large amounts of a hormone called **estrogen** (es´trō-jen)[176] and thus begins the transition from fetus to newborn.
b. Labor is marked by powerful contractions of the uterus, resulting in childbirth.[177]

47. Conclusion

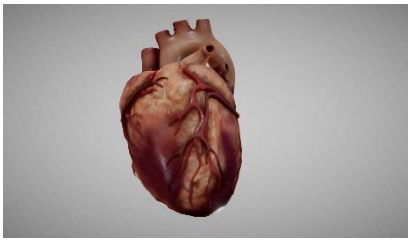
a. From fertilization to birth and beyond, human development is dynamic, continuous, and complex. New discoveries about this fascinating process increasingly show the vital impact of fetal development on lifelong health.
b. As our understanding of early human development advances, so too will our ability to enhance health—both before and after birth.

Links to 3D models of organ systems at 8 weeks, 16 weeks, and adult for comparison:

8 week embryonic heart



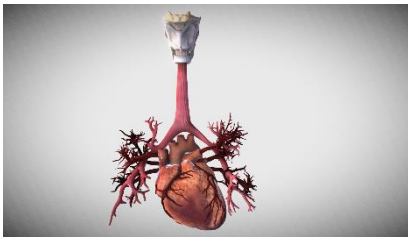
16 week fetal heart



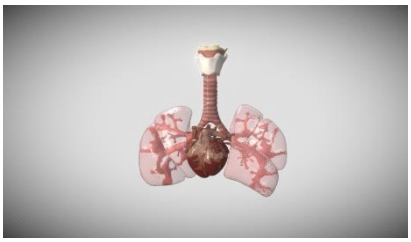
adult heart

8 week embryonic heart and bronchial airways

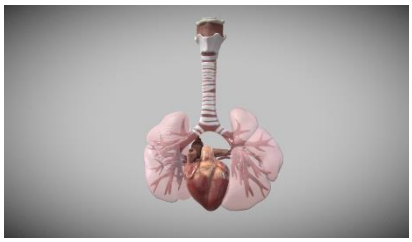
16 week fetal heart and bronchial airways



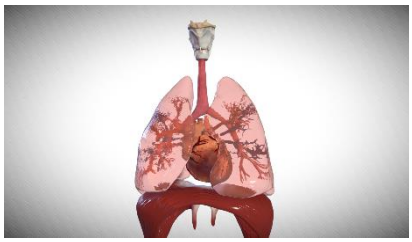
adult heart and bronchial airways



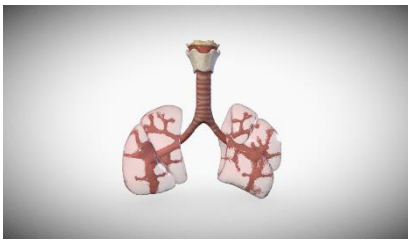
8 week embryonic heart and lungs



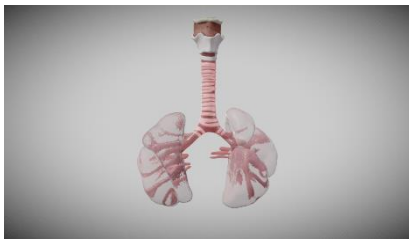
16 week fetal heart and lungs



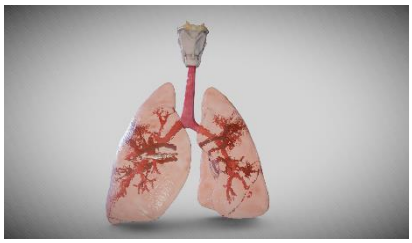
adult heart and lungs



8 week embryonic pulmonary system



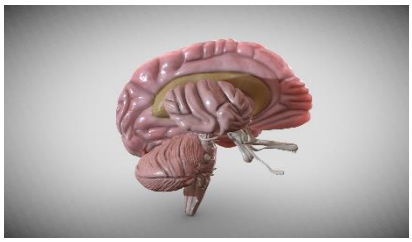
16 week fetal pulmonary system



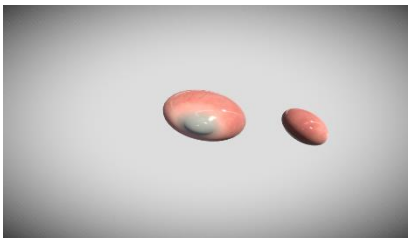
adult pulmonary system

8 week embryonic brain

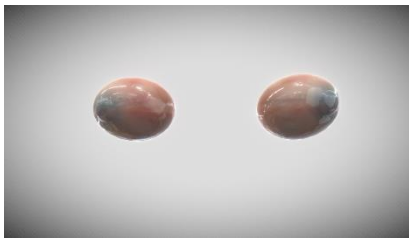
16 week fetal brain



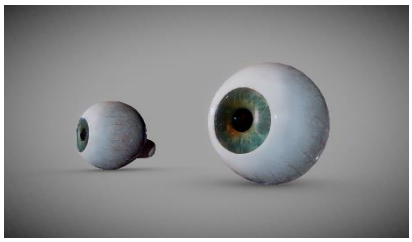
adult brain



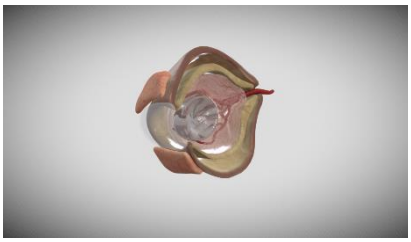
8 week embryonic eye (full section)



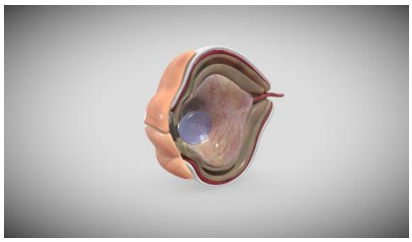
16 week fetal eye (full section)



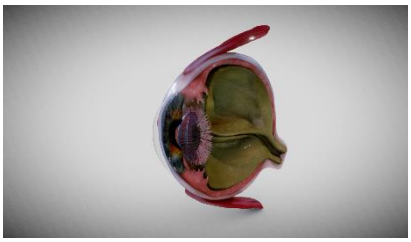
adult eye (full section)



8 week embryonic
eye (cross section)



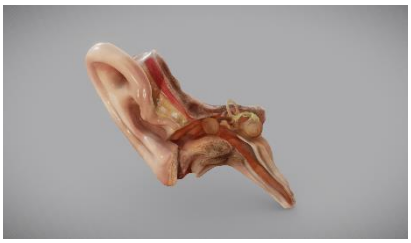
16 week fetal
eye (cross section)



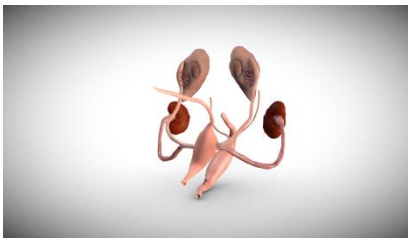
adult
eye (cross section)

8 week embryonic ear

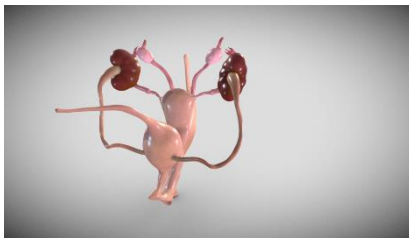
16 week fetal ear



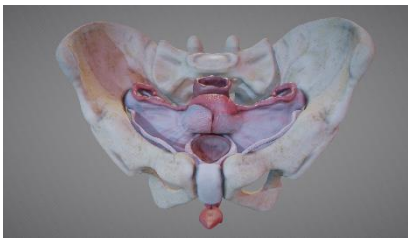
adult ear



8 week embryonic
female reproductive system



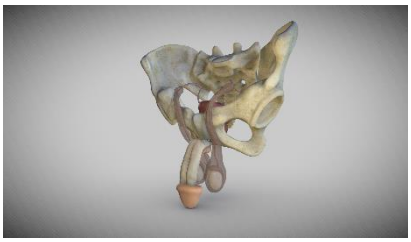
16 week fetal
female reproductive system



adult
female reproductive system

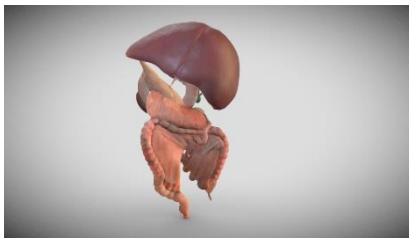
8 week embryonic
male reproductive system

16 week fetal
male reproductive system

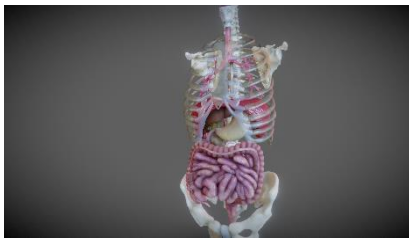


adult
male reproductive system

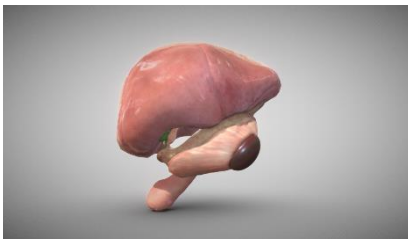
8 week embryonic
digestive system



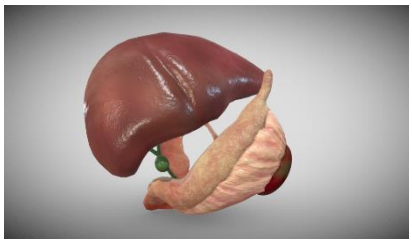
16 week fetal
digestive system



adult
digestive system



8 week embryonic
liver, spleen, and pancreas



16 week fetal
liver, spleen, and pancreas

adult
liver, spleen, and pancreas

Endnotes:

[1] Gasser, 1975, 1.
[2] Guyton and Hall, 2000, 2; Lodish *et al.*, 2000, 12.
[3] Vindla and James, 1995, 598.
[4] Cunningham *et al.*, 2001, 226; O'Rahilly and Müller, 2001, 92.
[5] O'Rahilly and Müller, 1987, 9.
[6] Spraycar, 1995, 377 & 637.
[7] O'Rahilly and Müller, 2001, 87.
[8] Quote from Ayto, 1990, 199.
[9] Human development during the 8-week embryonic period has been divided into a series of 23 stages called Carnegie Stages. These stages are well described in O'Rahilly and Müller, 1987. Because human growth is unique and dependent on multiple factors, different embryos may reach a certain developmental milestone or a certain size at slightly different ages. This internationally accepted staging system provides a way to describe development independent of age and size. Each of the 23 Carnegie Stages has specific structural features. As we describe various milestones of development, the Carnegie Stage at which they occur will be noted by a designation such as: [Carnegie Stage 2].
[10] Moore and Persaud, 2003, 3.
[11] Quotes from Moore and Persaud, 2003, 3: “After the embryonic period (eight weeks), the developing human is called a fetus.” Also see O'Rahilly and Müller, 2001, 87.
[12] This convention, termed “postfertilization age” by O'Rahilly, has been long preferred by embryologists [see Mall, 1918, 400; O'Rahilly and Müller, 1999b, 39; O'Rahilly and Müller, 2001, 88 & 91]. Obstetricians and radiologists typically assign age based on the time elapsed since the first day of the last menstrual period prior to fertilization. This is correctly termed “postmenstrual age” and

begins 2 weeks *before* fertilization occurs. To summarize: postmenstrual age = postfertilization age + 2 weeks. Therefore, postmenstrual age equals approximately 2 weeks at the time of fertilization. The commonly used term “gestational age” has been used with both age conventions and is best either avoided or carefully defined with each use.
[13] Quote from Moore and Persaud, 2003, 16. From O'Rahilly and Müller, 1987, 9: “Fertilization is the procession of events that begins when a spermatozoon makes contact with an oocyte or its investments and ends with the intermingling of maternal and paternal chromosomes at metaphase of the first mitotic division of the zygote.” See Carlson, 2004, 3; O'Rahilly and Müller, 2001, 8. [Carnegie Stage 1]
[14] O'Rahilly and Müller, 2001, 25: “The term ‘egg’ should be discarded from human embryology.” From O'Rahilly and Müller, 1987, 9: “The term ‘egg’ is best reserved for a nutritive object frequently seen on the breakfast table.”
[15] O'Rahilly and Müller, 2001, 23-24.
[16] O'Rahilly and Müller, 2001, 30.
[17] Dorland and Bartelmez, 1922, 372; Gasser, 1975, 1; Mall, 1918, 421; O'Rahilly and Müller, 2001, 31.
[18] Gasser, 1975, 1; O'Rahilly and Müller, 2001, 33.
[19] Quote from Saunders, 1970, 1; Spraycar, 1995, 1976.
[20] Guyton and Hall, 2000, 34.
[21] Guyton and Hall, 2000, 24; Watson and Crick, 1953, 737.
[22] Guyton and Hall, 2000, 24; Lodish *et al.*, 2000, 103; Watson and Crick, 1953, 737.
[23] Lodish *et al.*, 2000, 456.
[24] See https://www.ehd.org/resources_bpd_documentation_english.php#AppADNApages.
[25] See https://www.ehd.org/resources_bpd_documentation_english.php#AppADNAlength; Alberts *et al.*, 1998, 189.
[26] See https://www.ehd.org/resources_bpd_documentation_english.php#AppADNAlength.
[27] Hertig, 1968, 26; Hertig and Rock, 1973, 130; (cited by O'Rahilly and Müller, 1987, 12); Shettles, 1958, 400.
[28] Guyton and Hall, 2000, 34.
[29] Moore and Persaud, 2003, 33 & 60; Morton *et al.*, 1992, 72; Nahhas and Barnea, 1990, 105.
[30] Gasser, 1975, 1; O'Rahilly and Müller, 2001, 37; Spraycar, 1995, 1130: “Morula” is derived from the Latin word *morus* meaning “mulberry.” [Carnegie Stage 2]
[31] O'Rahilly and Müller, 2001, 39. [Carnegie Stage 3]
[32] Gasser, 1975, 1; O'Rahilly and Müller, 2001, 39; Sadler, 2005, 6.
[33] Alberts *et al.*, 1998, 32.
[34] O'Rahilly and Müller, 2001, 40. Implantation begins with attachment of the blastocyst at about 6 days after fertilization. [Attachment of the blastocyst to the inner wall of the uterus is a transient event and is the hallmark of Carnegie Stage 4.] See also Adams, 1960, 13-14; Cunningham *et al.*, 2001, 20; Hamilton, 1949, 285-286; Hertig, 1968, 41; Hertig and Rock, 1944, 182; Hertig and Rock, 1945, 81 & 83; Hertig and Rock, 1949, 183; Hertig *et al.*, 1956, 444. [Carnegie Stage 5]
[35] Chartier *et al.*, 1979, 134; Cunningham *et al.*, 2001, 27; O'Rahilly and Müller, 2001, 43.
[36] Cunningham *et al.*, 2001, 20 & 26-27; O'Rahilly and Müller, 2001, 31.
[37] Hertig, 1968, 16; Cunningham *et al.*, 2001, 86 & 136. For a detailed description of the placenta see Hamilton and Boyd, 1960. For a detailed description of the placenta vasculature see Harris and Ramsey, 1966. This separation of maternal and fetal blood is almost but not quite perfect as a small number of fetal cells may be found in the maternal circulation and vice-versa. See Cunningham *et al.*, 2001, 96 & 136.
[38] Liley, 1972, 101; O'Rahilly and Müller, 2001, 78-79.
[39] For a detailed description of umbilical cord formation see Florian, 1930.
[40] O'Rahilly and Müller, 2001, 39.
[41] Moore and Persaud, 2003, 50; O'Rahilly and Müller, 2001, 82. [Carnegie Stages 5 & 6] In humans, the term “yolk sac” has fallen out of favor among some embryologists (including O'Rahilly and Müller) because it is not a nutrient reservoir and does not contain yolk. The technically preferred

term is umbilical vesicle. This structure plays a vital role in the transfer of nutrients from mother to embryo before placental circulation becomes fully functional.
[42] Campbell *et al.*, 1993, 756; Kurjak *et al.*, 1994, 437; O'Rahilly and Müller, 2001, 82.
[43] O'Rahilly and Müller, 1987, 29; O'Rahilly and Müller, 2001, 43. [Carnegie Stages 4-5]
[44] O'Rahilly and Müller, 2001, 14 & 135. [Carnegie Stage 7] It should be noted there are many examples of organs derived from multiple germ layers. For instance, the liver is largely derived from endoderm but contains blood vessels and blood cells derived from mesoderm and nerves of ectodermal origin.
[45] Moore and Persaud, 2003, 80 & 83; Sadler, 2005, 9.
[46] Bartelmez, 1923, 236; Müller and O'Rahilly, 1983, 419-420 & 429; O'Rahilly and Gardner, 1979, 123 & 129; O'Rahilly and Müller, 1984, 422; O'Rahilly and Müller, 1987, 90; O'Rahilly and Müller, 1999a, 47 & 52. [Carnegie Stage 9]
[47] DiFiore and Wilson, 1994, 221; Fowler *et al.*, 1988, 793; Grand *et al.*, 1976, 793-794 & 796 & 798; O'Rahilly, 1978, 125; O'Rahilly and Boyden, 1973, 238-239; O'Rahilly and Müller, 1984, 421; O'Rahilly and Tucker, 1973, 6 & 8 & 23; Streeter, 1942, 232 & 235.
[48] Carlson, 2004, 117.
[49] Gilmour, 1941, 28; O'Rahilly and Müller, 1987, 86. [Carnegie Stage 9]
[50] Campbell, 2004, 14; Carlson, 2004, 116 & 446; Navaratnam, 1991, 147-148; O'Rahilly and Müller, 1987, 99. [Carnegie Stage 10]
[51] Campbell, 2004, 14; Carlson, 2004, 430; de Vries and Saunders, 1962, 96; Gardner and O'Rahilly, 1976, 583; Gilbert-Barness and Debich-Spicer, 1997, 650; Gittenger-de Groot *et al.*, 2000, 17; van Heeswijk *et al.*, 1990, 151; Kurjak and Chervenak, 1994, 439; Navaratnam, 1991, 147-148; O'Rahilly and Müller, 1987, 99; Wisser and Dirschedl, 1994, 108. [Carnegie Stage 10, possibly late Stage 9]
[52] Moore and Persaud, 2003, 70: “The cardiovascular system is the first organ system to reach a functional state.”
[53] Moore and Persaud, 2003, 78.
[54] Gasser, 1975, 26; Moore and Persaud, 2003, 78.
[55] Gasser, 1975, 30; O'Rahilly and Müller, 2001, 80.
[56] O'Rahilly and Müller, 2001, 81.
[57] van Heeswijk *et al.*, 1990, 153.
[58] See https://www.ehd.org/resources_bpd_documentation_english.php#AppAHeart.
[59] Gasser, 1975, 49 & 59; O'Rahilly and Gardner, 1975, 11; O'Rahilly and Müller, 1985, 148 & 151; O'Rahilly and Müller, 1987, 143; Streeter, 1945, 30; Uhthoff, 1990, 7 & 141. [upper and lower limb buds: Carnegie Stages 12 & 13]
[60] Moore and Persaud, 2003, 486; O'Rahilly, 1957, 459; O'Rahilly and Müller, 2001, 165. For information about the first-trimester direct-imaging technique used in this program (called embryoscopy) see Cullen *et al.*, 1990.
[61] O'Rahilly and Müller, 1999a, 134; Sadler, 2005, 106. [Carnegie Stage 15]
[62] Laffont, 1982, 5.
[63] Bartelmez and Dekaban, 1962, 25; Campbell, 2004, 17; O'Rahilly and Gardner, 1979, 130; O'Rahilly *et al.*, 1984, 249; O'Rahilly and Müller, 1999a, 115; van Dongen and Goudie, 1980, 193. [Carnegie Stage 14]
[64] Moore, 1980, 938.
[65] Guyton and Hall, 2000, 663-677.
[66] Moore and Persaud, 2003, 245; O'Rahilly and Boyden, 1973, 239; O'Rahilly and Müller, 2001, 291; Sparrow *et al.*, 1999, 550.
[67] Angtuaco *et al.*, 1999, 13; Lipschutz, 1998, 384; Moore and Persaud, 2003, 288; O'Rahilly and Müller, 1987, 167 & 182; O'Rahilly and Müller, 2001, 301; Sadler, 2005, 72. [Carnegie Stage 14]
[68] O'Rahilly and Müller, 2001, 23; Waters and Trainer, 1996, 16; Witschi, 1948, 70, 77 & 79.
[69] O'Rahilly and Müller, 1987, 175; Streeter, 1948, 139. [Carnegie Stage 15]
[70] O'Rahilly and Gardner, 1975, 4. [Carnegie Stages 16 & 17]
[71] Birnholz *et al.*, 1978, 539; de Vries *et al.*, 1982, 301 & 304: “The first movements were observed

at 7.5 weeks postmenstrual age." [or 5½ weeks postfertilization age]; Humphrey, 1964, 99: earliest reflex 5½ weeks; Humphrey, 1970, 12; Humphrey and Hooker, 1959, 76; Humphrey and Hooker, 1961, 147; Kurjak and Chervenak, 1994, 48; Visser *et al.*, 1992, 175-176: "Endogenously generated fetal movements can first be observed after 7 weeks postmenstrual age (i.e. 5 weeks after conception)"; O'Rahilly and Müller, 1999a, 336: 5½ weeks postfertilization; Sorokin and Dierker, 1982, 723 & 726; Natsuyama, 1991, 13: spontaneous movement observed by "Carnegie stage 15" (about 33 days postfertilization); Hogg, 1941, 373: reflex activity begins at 6½ weeks [adjusted to postfertilization age].
[72] Goodlin, 1979, D-128.
[73] Karmody and Annino, 1995, 251; O'Rahilly and Müller, 2001, 480; Streeter, 1948, 190.
[74] Kurjak and Chervenak, 1994, 19.
[75] de Vries *et al.*, 1982, 320.
[76] Gilbert-Barness and Debich-Spicer, 1997, 774; Grand *et al.*, 1976, 798; O'Rahilly and Müller, 1987, 213; Sadler, 2005, 66; Spencer, 1960, 9; Timor-Tritsch *et al.*, 1990, 287.
[77] O'Rahilly and Müller, 1987, 202-203.
[78] Borkowski and Bernstine, 1955, 363 (cited by Bernstine, 1961, 63 & 66; O'Rahilly and Müller, 1999a, 195; van Dongen and Goudie, 1980, 193); Hamlin, 1964, 113. For a summary of *in utero* fetal encephalography (measuring brainwaves) in the near-term fetus using abdominal and vaginal electrodes see Bernstine *et al.*, 1955.
[79] O'Rahilly and Müller, 1985, 155: "The nipple appears at stages 17 and 18." [41-44 days postfertilization]; Wells, 1954, 126.
[80] O'Rahilly and Müller, 2001, 221; Streeter, 1948, 187.
[81] Carlson, 2004, 189; O'Rahilly and Gardner, 1972, 293; O'Rahilly and Gardner, 1975, 19; O'Rahilly and Müller, 2001, 385; Sperber, 1989, 122 & 147. [Carnegie Stage 19]
[82] de Vries *et al.*, 1982, 305 & 311; Visser *et al.*, 1992, 176.
[83] de Vries *et al.*, 1988, 96; Visser *et al.*, 1992, 176.
[84] Cooper and O'Rahilly, 1971, 292; James, 1970, 214; Jordaan, 1979, 214; Streeter, 1948, 192; Vernall, 1962, 23: "The four chambers of the heart and the associated major vessels are externally apparent in a close approximation to their adult positions." [Carnegie Stage 18]
[85] van Heeswijk *et al.*, 1990, 153.
[86] Straus *et al.*, 1961, 446 (cited by Gardner and O'Rahilly, 1976, 571): "… an electrocardiogram with the classical P, QRS, and T configuration has been obtained from a 23mm human embryo (Straus, Walker, and Cohen, 1961)."
[87] O'Rahilly and Müller, 2001, 320. [Carnegie Stage 20]
[88] Andersen *et al.*, 1965, 646; O'Rahilly, 1966, 35; O'Rahilly and Müller, 1987, 259; Pearson, 1980, 39; Streeter, 1951, 193. [Carnegie Stage 22] Pigment within the retina is present from about 37 days postfertilization per O'Rahilly, 1966, 25. [Carnegie Stage 16]
[89] Streeter, 1951, 191; reiterated by O'Rahilly and Müller, 1987, 257.
[90] O'Rahilly and Gardner, 1975, 11; O'Rahilly and Müller, 1987, 262.
[91] O'Rahilly and Müller, 1999a, 288: "The brain at [Carnegie] Stage 23 is far more advanced morphologically than is generally appreciated, to such an extent that functional considerations are imperative."
[92] Jordaan, 1979, 149.
[93] Hepper *et al.*, 1998, 531; McCartney and Hepper, 1999, 86.
[94] Bates, 1987, 534.
[95] de Vries *et al.*, 1982, 320; Goodlin and Lowe, 1974, 348; Humphrey, 1970, 8.
[96] Liley, 1972, 101.
[97] de Vries *et al.*, 1982, 311.
[98] Humphrey, 1964, 102; Humphrey, 1970, 19.
[99] Process described by Andersen *et al.*, 1965, 648-649; O'Rahilly, 1966, 36-37; O'Rahilly and Müller, 1987, 261. [Carnegie Stage 23]
[100] Connors *et al.*, 1989, 932; de Vries *et al.*, 1982, 311; McCray, 1993, 579; Visser *et al.*,1992, 177.
[101] O'Rahilly and Müller, 2001, 304; Windle, 1940, 118. (Windle reports urine formation begins at

nine weeks.)
[102] Moore and Persaud, 2003, 307; Waters and Trainer, 1996, 16-17.
[103] O'Rahilly and Gardner, 1975, 15: “By the end of the embryonic proper (Stage 23, 8 postovulatory weeks), all of the major skeletal, articular, muscular, neural, and vascular elements of the limbs are present in a form and arrangement closely resembling those of the adult.” See O'Rahilly, 1957, for a summary of joint types and a description of limb joint development during the embryonic period. See Gray *et al.*, 1957, for a detailed examination of the bones and joints of the hand throughout the embryonic and fetal periods.
[104] Hogg, 1941, 407; Pringle, 1988, 178.
[105] Hogg, 1941, 387; O'Rahilly and Müller, 2001, 169.
[106] Pringle, 1988, 176.
[107] O'Rahilly and Müller, 2001, 87: “It has been estimated that more than 90% of the more than 4500 named structures of the adult body become apparent during the embryonic period (O'Rahilly).”
[108] Liley, 1972, 103.
[109] Campbell, 2004, 24; de Vries *et al.*, 1982, 311; Petrikovsky *et al.*, 1995, 605.
[110] Robinson and Tizard, 1966, 52; Valman and Pearson, 1980, 234.
[111] de Vries *et al.*, 1982, 305-307.
[112] de Vries *et al.*, 1982, 311.
[113] Humphrey, 1964, 96; Humphrey, 1970, 16-17 (cited by Reinis and Goldman, 1980, 232); Humphrey and Hooker, 1959, 77-78.
[114] Robinson and Tizard, 1966, 52; quote from Valman and Pearson, 1980, 234.
[115] Andersen *et al.*, 1965, 648-649; O'Rahilly and Müller, 2001, 465; Pearson, 1980, 39-41.
[116] O'Rahilly and Müller, 1984, 425. See also Campbell, 2004, 29.
[117] O'Rahilly, 1977a, 128; O'Rahilly, 1977b, 53; O'Rahilly and Müller, 2001, 327.
[118] O'Rahilly and Müller, 2001, 25 & 322.
[119] Campbell, 2004, 28 & 35; O'Rahilly and Müller, 2001, 336.
[120] Brenner *et al.*, 1976, 561.
[121] Goodlin, 1979, D-128; Humphrey, 1964, 102.
[122] de Vries *et al.*, 1982, 309.
[123] Hepper *et al.*, 1991, 1109.
[124] Grand *et al.*, 1976, 798; Pringle, 1988, 178; Sadler, 2005, 66; Spencer, 1960, 9. [Pringle reports the bowel returns into the abdomen during the ninth or tenth week.]
[125] Cunningham *et al.*, 2001, 133.
[126] O'Rahilly and Müller, 2001, 170-171.
[127] Babler, 1991, 95; Penrose and Ohara, 1973, 201. For an overview of ridge formation in the skin of the hands see Cummins, 1929.
[128] Timor-Tritsch *et al.*, 1990, 291.
[129] Koldovský *et al.*, 1965, 186.
[130] O'Rahilly and Müller, 2001, 336; Wilson, 1926, 29.
[131] Brenner *et al.*, 1976, 561.
[132] Lecanuet and Schaal, 1996, 3; Miller, 1982, 169; Mistretta and Bradley, 1975, 80.
[133] Abramovich and Gray, 1982, 296; Ramón y Cajal and Martinez, 2003, 154-155, report visualizing defecation (bowel movements) with ultrasound *in utero* in all 240 fetuses studied between 15 and 41 weeks [postmenstrual age].
[134] O'Rahilly and Müller, 2001, 257. For a description of meconium by Aristotle see Grand *et al.*, 1976, 791.
[135] Grand *et al.*, 1976, 806.
[136] Moore and Persaud, 2003, 105.
[137] Lecanuet and Schaal, 1996, 2; Reinis and Goldman, 1980, 232.
[138] Hepper *et al.*, 1997, 1820.
[139] Mancia, 1981, 351.
[140] Bates, 1979, 419.
[141] Poissonnet *et al.*, 1983, 7; Poissonnet *et al.*, 1984, 3: In a study of 488 fetuses, Poissonnet's

group found that adipose tissue (fat) appears in the face from 14 weeks postfertilization. By 15 weeks, fat appears in the abdominal wall, back, kidneys, and shoulders. By 16 weeks, fat is also present throughout the upper and lower limbs.
[142] Pringle, 1988, 178. [Thirteenth week postfertilization]
[143] Pringle, 1988, 179.
[144] Sorokin and Dierker, 1982, 720; Leader, 1995, 595: “Some pregnant women reported fetal flutters as early as 12 weeks (quickening).” Women also tend to accurately recognize fetal movement at earlier fetal ages during second and subsequent pregnancies as compared to first pregnancies.
[145] Spraycar, 1995, 1479; Timor-Tritsch *et al.*, 1976, 70.
[146] Giannakoulopoulos *et al.*, 1999, 494 & 498-499; Glover and Fisk, 1999, 883; Smith *et al.*, 2000, 161. Cortisol levels also rise after invasive procedures following 21 weeks postfertilization - see Giannakoulopoulos *et al.*, 1994, 80.
[147] DiFiore and Wilson, 1994, 221-222; Pringle, 1988, 178. [There is some disagreement among experts regarding when the bronchial tree is complete. Some say completion occurs as early as 16 weeks postfertilization while others say it occurs after birth.]
[148] Campbell, 2004, 48; Moore and Persaud, 2003, 107; O'Rahilly and Müller, 2001, 168.
[149] de Vries *et al.*, 1987, 333; Goodlin and Lowe, 1974, 349; Okai *et al.*, 1992, 391 & 396; Romanini and Rizzo, 1995, 121. For a description of the circadian system see Rosenwasser, 2001, 127. From Vitaterna *et al.*, 2001, 92: Glossary: “Circadian: A term derived from the Latin phrase ‘circa diem,’ meaning ‘about a day’; refers to biological variations or rhythms with a cycle of approximately 24 hours.”
[150] Lecanuet and Schaal, 1996, 5-6; Querleu *et al.*, 1989, 410.
[151] Glover and Fisk, 1999, 882; Hepper and Shahidullah, 1994, F81; Querleu *et al.*, 1989, 410; Sorokin and Dierker, 1982, 725 & 730; Valman and Pearson, 1980, 233-234.
[152] Pringle, 1988, 180.
[153] Hansen and Corbet, 1998, 542.
[154] O'Rahilly and Müller, 2001, 92, report the age of viability as 20 weeks postfertilization; Draper *et al.*, 1999, 1094, report a survival rate of 2% at 20 weeks postfertilization, 6% at 21 weeks, and 16% at 22 weeks. Moore and Persaud, 2003, 103, report viability at 22 weeks; Wood *et al.*, 2000, 379, report survival rates of 11% at 21 weeks, 26% at 22 weeks, and 44% at 23 weeks (postfertilization weeks) based on premature birth data from the United Kingdom during 1995. Cooper *et al.*, 1998, 976 (Figure 2), report infants with a birth weight over 500 grams experienced survival rates (all approximate) of 28% at 21 weeks postfertilization, 50% at 22 weeks, 67% at 23 weeks, and 77% at 24 weeks. Draper *et al.*, 2003, updated their previously published survival tables for premature infants and now report an overall survival rate of 7% at 20 weeks, 15% at 21 weeks, 29% at 22 weeks, 47% at 23 weeks, and 65% at 24 weeks. [All ages corrected to reflect postfertilization age.] These survival tables are available online at http://bmj.bmjjournals.com/cgi/content/full/319/7217/1093/DC1. Their methodology is described in their earlier paper (Draper *et al.*, 1999, 1093-1094). Note: These published survival tables reflect postmenstrual ages. Hoekstra *et al.*, 2004, e3, report a survival rate of 66% at 23 weeks and 81% at 24 weeks “gestational age” [not specifically defined] for premature births from 1996 to 2000 at their center in Minneapolis, Minnesota.
[155] Open eyes are visualized by 4D ultrasound following 22 weeks postfertilization per Campbell, 2002, 3; De Lia, 2002, personal communication; O'Rahilly and Müller, 2001, 465. For a detailed ultrastructural study of the union between the upper and lower eyelids see Andersen *et al.*, 1967, 293.
[156] Birnholz and Benacerraf, 1983, 517 (cited by Drife, 1985, 778). See also Campbell, 2002, 3: Professor Stuart Campbell correctly points out that the eyes of the fetus are closed most of the time and a true blink requires the eyes to be open. Perhaps the “blink-startle” response would be more accurately termed “squint-startle.”
[157] Lecanuet and Schaal, 1996, 9.
[158] Visser *et al.*, 1989, 285.

[159] Gerhardt, 1990, 299; Petrikovsky *et al.*, 1993, 548-549; Pierson, 1996, 21 & 26.
[160] Natale *et al.*, 1988, 317.
[161] Growth of the human brain, 1975, 6; Mancuso and Palla, 1996, 290.
[162] Isenberg *et al.*, 1998, 773-774.
[163] Robinson and Tizard, 1966, 52.
[164] Noback *et al.*, 1996, 263.
[165] Lecanuet and Schaal, 1996, 3.
[166] Lecanuet and Schaal, 1996, 3; Liley, 1972, 102; Moore and Persaud, 2003, 219; Reinis and Goldman, 1980, 227.
[167] Liley, 1972, 100.
[168] England, 1983, 29.
[169] Glover and Fisk, 1999, 882; Hepper and Shahidullah, 1994, F81.
[170] Connors *et al.*, 1989, 932; de Vries *et al.*, 1985, 117; Patrick *et al.*, 1980, 26 & 28; Visser *et al.*, 1992, 178.
[171] DiPietro *et al.*, 2002, 2: “One of the hallmarks of development before birth is the coalescence of patterns of fetal and behavioral and cardiac function into behavioral states, which is widely viewed as reflective of the developing integration of the central nervous system.”
[172] Lauria *et al.*, 1995, 467.
[173] Moore and Persaud, 2003, 108.
[174] Schaal *et al.*, 2000, 729.
[175] Liley, 1972, 100.
[176] Moore and Persaud, 2003, 131.
[177] Cunningham *et al.*, 2001, 252.

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