See 161

DEVELOPMENT OF EMBRYO (1)

CN: Use light colors throughout. (1) Follow the events from fertilization to implantation. The number of days cited in this and the following two plates are days after (post-) fertilization. Fertilization occurs about 14 days after the last day of menstruation; physicians date fetal age by time since last menstrual period (LMP). Thus, fetal age according to LMP is 14 days earlier than true (post-fertilization) age.

ZONA PELLUCIDA A

FERTILIZATION

(1ST STAGE)

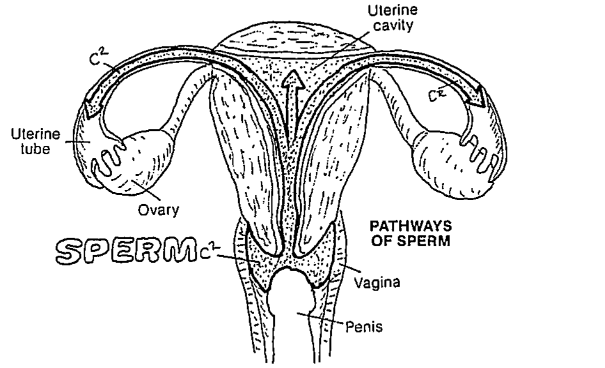
- FEMALE PRONUCLEUS B
- HEAD OF SPERM C
  - MALE PRONUCLEUS C'

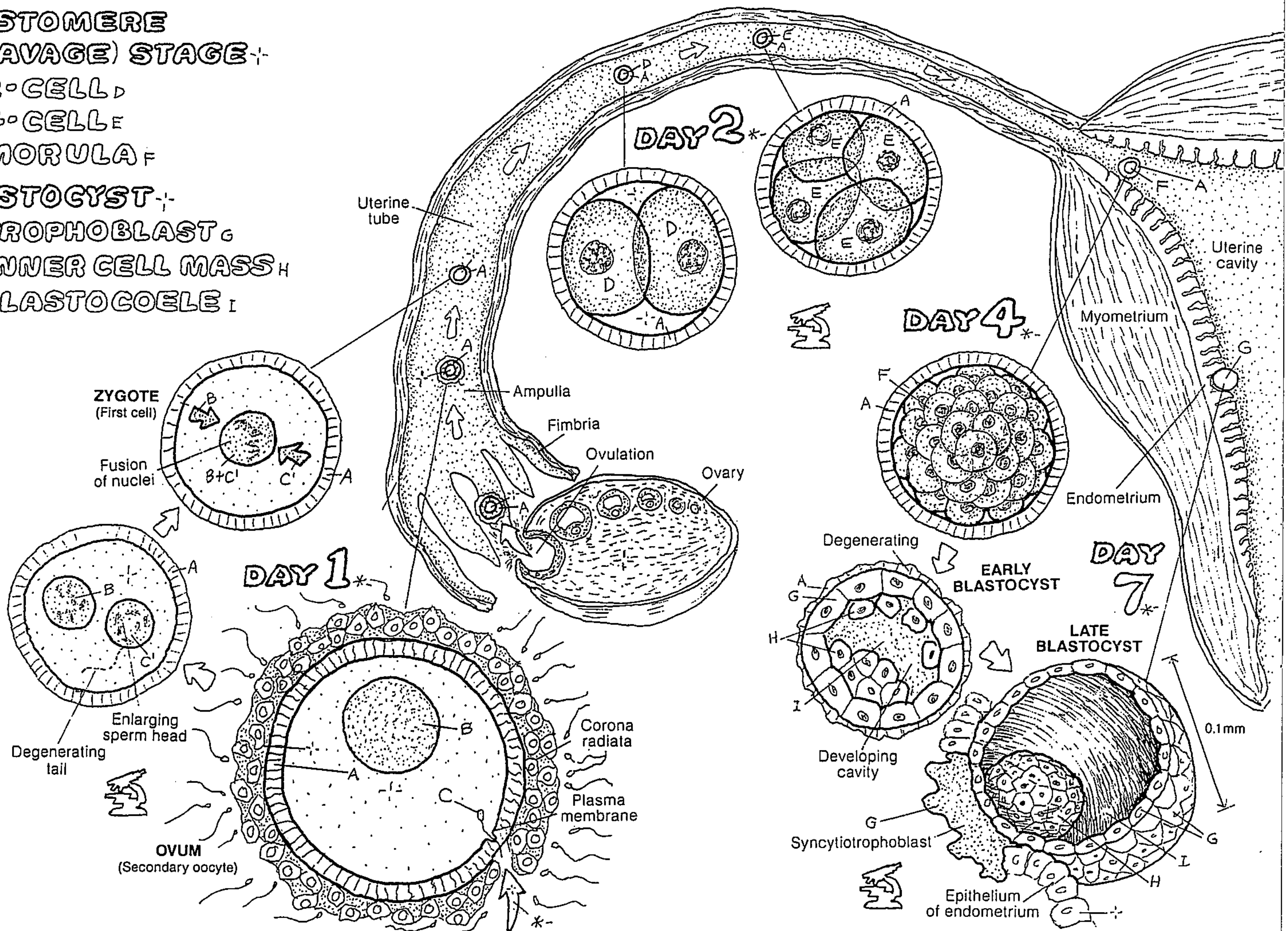
BLASTOMERE (CLEAVAGE) STAGE

- 2-CELL D
- 4-CELL E
- MORULA F

BLASTOCYST

- TROPHOBLAST G
- INNER CELL MASS H
- BLASTOCOELE I





Following ovulation, the ovum enters the uterine tube and proceeds toward the uterus. It reaches the ampulla of the tube in about 30 minutes. If sperm-laden semen has been deposited in the fornices of the vagina in the preceding several minutes to 24 hours, a few hundred of the original 50 million or more sperms will succeed in reaching the ampulla. Over a period of several hours, the sperms become activated, and with the aid of sperm-produced enzymes, one of the sperms will penetrate the corona radiata (retained follicular cells) and *zona pellucida* of the ovum, fuse with the plasma membrane (leaving its cell membrane attached to the ovum's plasma membrane), and enter the ovum. This event is called fertilization. As the tail breaks down and disappears, the *head of the sperm* enlarges and forms the *male pronucleus*. The nucleus of the ovum is the *female pronucleus*. The two pronuclei approach each other, fuse nuclear membranes, and form a single nucleus. The male and female chromosomes join up in the metaphase stage of the first mitotic division of the fertilized ovum. The first cell of the new individual is called a zygote.

The zygote undergoes division (cleavage stage) to form two *blastomeres*. Over the next two days or so post-fertilization, within the restraints of the zona pellucida, the cells divide to form a *four-cell blastomere* and again to form eight cells, and so on, until a ball of cells (*morula*) is formed. After about five days, the cells within the morula disperse enough to accommodate progressively enlarging fluid-filled cavities. Some cells are pushed aside to form a peripheral rim of cells (*trophoblast*) enclosing a large single cavity (*blastocoele*); some cells form an *inner cell mass* within the blastocoele. This multicellular structure is called a blastocyst. The blastocyst enters the uterus and implants in the endometriurn on about the 7th day post-fertilization.

See 165

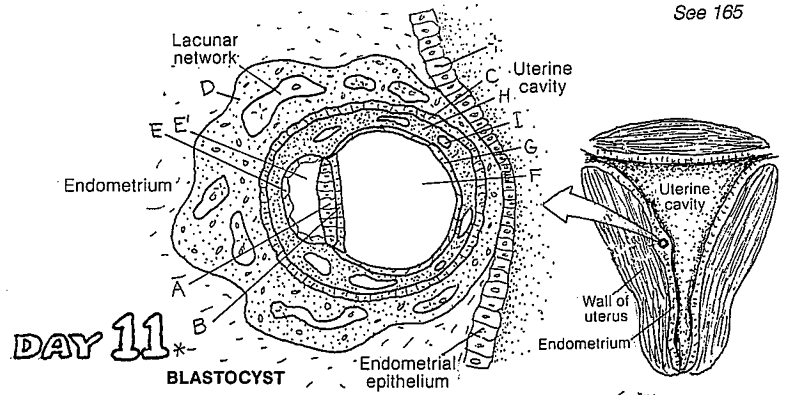
DEVELOPMENT OF EMBRYO (2)

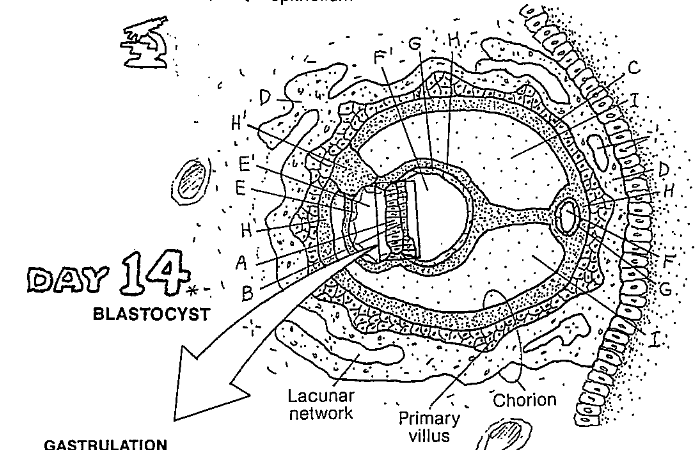
CN: Use the same color as on the previous plate for trophoblast (C) and note that the syncytiotrophoblast (D) is now given a separate color. Use yellow for F. Complete each drawing before proceeding to the next.

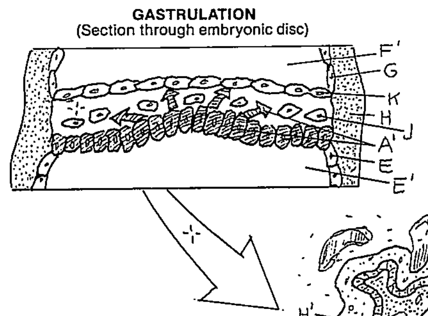
2 LAYER EMBRYONIC DISC ✣
- EPIBLAST A
- HYPOBLAST B

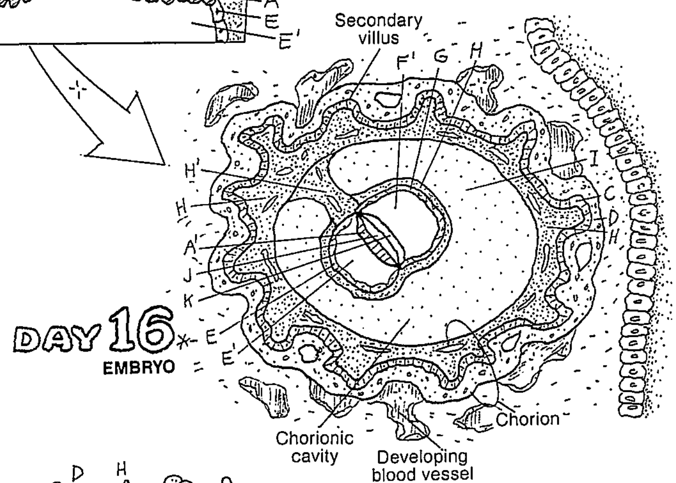
TROPHOBLAST C
- SYNCYTIOTROPHOBLAST D
- AMNION E /AMNIOTIC CAVITY E'
- YOLK SAC: PRIMARY F SECONDARY F'
  - EXOCOELOMIC MEMBRANE G
- EXTRAEMBRYONIC MEMBRANE H
  - CONNECTING STALK H'
- EXTRAEMBRYONIC COELOM I

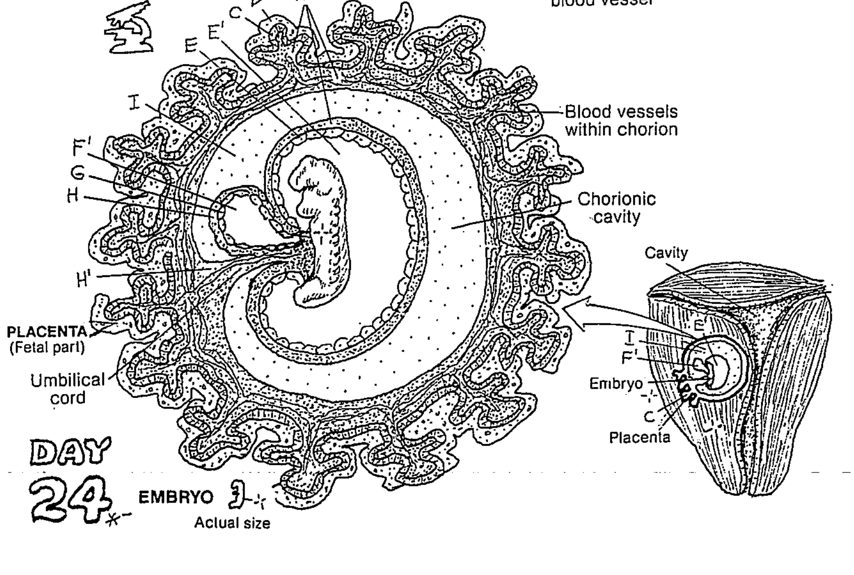
3 LAYER EMBRYONIC DISC ✣
- ECTODERM A'
- MESODERM J
- ENDODERM K











On day 11 post-fertilization, the inner cell mass gives rise to a flat embryonic disc, consisting of a layer of columnar cells (*epiblast*) and an adjacent layer of cuboidal cells (*hypoblast*). The epiblast will develop almost entirely into the embryo. The *amniotic cavity* develops among the *trophoblast* cells adjacent to the epiblast; the roof of the cavity is called the *amnion*. The embryo and subsequent fetus will develop within this cavity. The trophoblast also gives rise to the *primary yolk sac*; the cells lining this sac are continuous with those of the hypoblast. Though it has no yolk, the sac probably has a nutritional function for the embryonic disc. Cells of the trophoblast form an *extraembryonic mesoderm* tissue (*membrane*) that largely fills the cavity once known as the blastocyst.

By day 14, the primary yolk sac diminishes in size, replaced by a *secondary yolk sac*. Cavities within the extra-embryonic membrane form a single cavity (it looks paired, but the connection between yolk sacs does not create two cavities). This cavity (I) surrounds the amnion/amniotic cavity and the yolk sac except where the amnion retains a *connecting stalk* to the trophoblast layer.

By day 16, the epiblast undergoes significant changes. The primary yolk sac is gone. Cells emerge from the epiblast and migrate into the area between the epiblast and hypoblast and into the hypoblast itself. The cells between are embryonic *mesoderm* cells; the cells migrating into the hypoblast layer form embryonic *endoderm*. The remaining epiblast cells become embryonic *ectoderm*. The earlier two-layered embryonic disc has formed into a three-layered embryonic disc. These three layers are called germ layers, and they give rise to the cells and tissues of the body. From ectoderm form the skin and related glands, nervous system, hypophysis, lens of the eye, and inner ear. From mesoderm form bones, muscle and connective tissues, lymphoid organs, blood, the urogenital system, and serous membranes. From endoderm form the epithelial part of the gastrointestinal system and respiratory system as well as the epithelia of the pharynx and thyroid.

By day 24 post-fertilization, the once flat embryonic disc has rounded to form within the amniotic cavity an embryo with a definitive head end and tail end, secured to the chorion (C, D, H) by the connecting stalk. As the lateral folds of embryonic mesoderm encircle the ventral (anterior) part of the embryo to form the anterolateral abdominal walls, the yolk sac is pinched off and formation of the primitive gut begins. By the end of three weeks post-fertilization, the gastrointestinal tract, brain, and heart have begun their development.

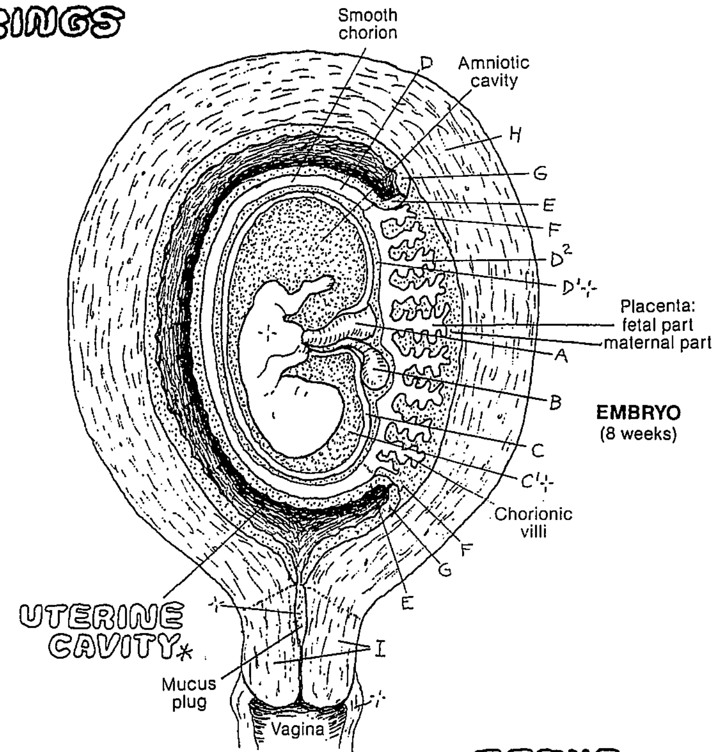
EMBRYO/FETUS COVERINGS

See 166, 170

CN: Use the same colors for structures B and C that were given to them on the preceding plate. Use the color given to "connecting stalk" for the umbilical cord (A), and use the color given to "trophoblast" for chorion (D). (1) Color the embryonic coverings. The uterine cavity is colored gray, though it is actually lined with the decidua capsularis (E). Note that the *amniotic cavity* (C^1), *chorionic cavity* (D^1), and the embryo/fetus are left uncolored. (2) The umbilical cord is composed of different blood vessels but receives one color (A). The band representing the uterine wall (below) is colored with both G and H.

EMBRYO *
- UMBILICAL CORD A
- YOLK SAC B
- AMNION C & CAVITY C¹ *
- CHORION D / CAVITY D¹ * / VILLI D²

UTERUS *
- ENDOMETRIAL DECIDUA *
  - D. CAPSULARIS E
  - D. BASALIS F
  - D. PARIETALIS G
- MYOMETRIUM H
- CERVIX I



EMBRYO
(8 weeks)

FETUS *
- UMBILICAL CORD A
- AMNION C / CAVITY C¹
- CHORION D / VILLI D²

The developing embryo (called a fetus after eight weeks of development) lies within and is supported, nurtured, and protected by membranes and sacs. These coverings have both maternal and fetal origins.

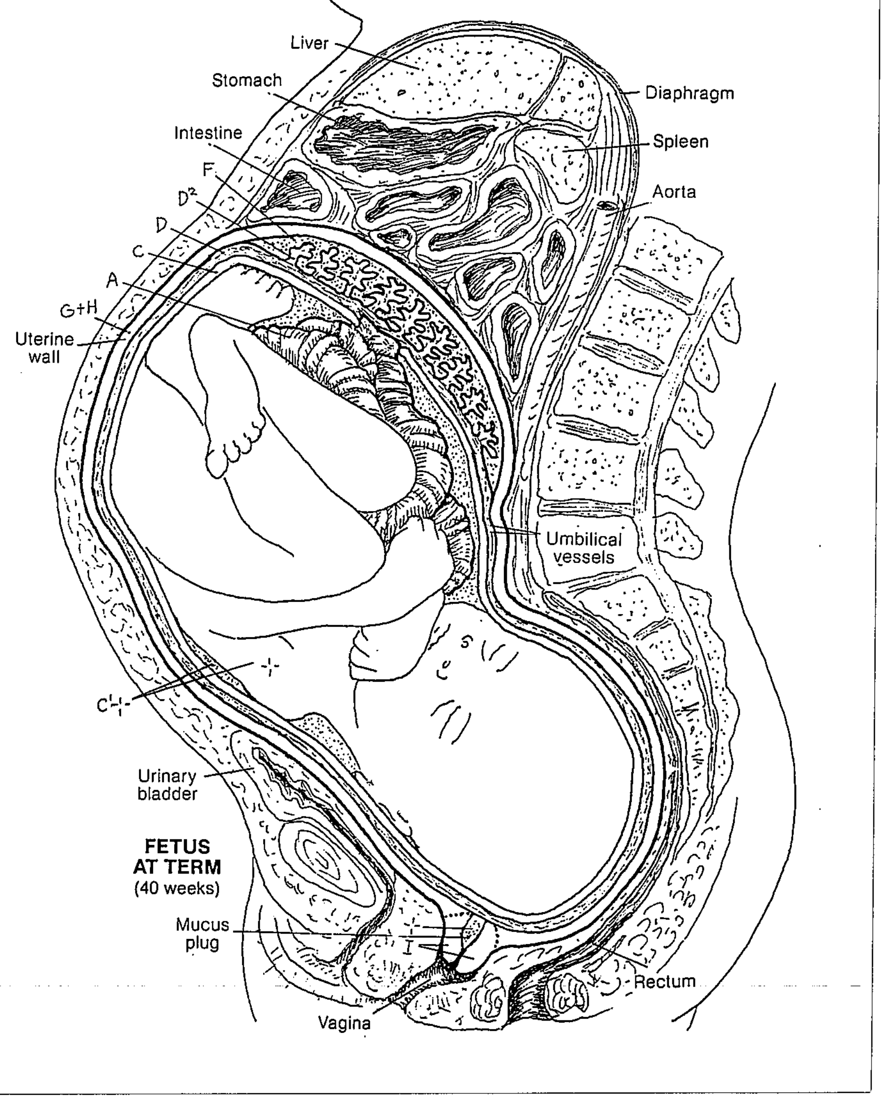
Those of fetal origin include the *amnion* and *chorion/chorionic villi*, the *umbilical cord*, and the *yolk sac*. The chorion forms a sac around the early embryo; the cavity of the sac is the *chorionic cavity* (recall Plate 166). As the embryo grows, the chorionic sac is obliterated and the amnion and chorion fuse (amniochorionic membrane). The chorion exhibits villi circumferentially early on (e.g., 24-day embryo); in time, most of the villi are absorbed except for those in the developing placenta (8-week embryo), creating a smooth chorion around the amnion and a bushy one (the villi and an underlying chorionic plate) in the future placenta. This is the situation of the fetal membranes at term (40 weeks).

The coverings of maternal origin (the *decidua*), are thickened, fairly distinct layers of the uterine mucosa (endometrium) in which the blastocyst implanted. In the 8-week embryo (above), the *decidua basalis* is integrated with the fetal villi to form the placenta. The *decidua capsularis* surrounds the embryo and its membranes. The *decidua parietalis* lines the uterine cavity, superficial to the *myometrium*.

The parietalis is continuous with the capsularis, as shown. This is the situation with the maternal membranes at eight weeks.

When the fetus grows to the point of pushing the decidua capsularis against the parietalis, the uterine cavity is obliterated. The capsularis soon degenerates, leaving only the parietalis (lower illustration). This layer will be retained after birth as the basal endometrium. The decidua basalis and chorionic villi (placenta) will be discharged after birth.

The fetus develops within the fluid-filled amniotic cavity. The plasma-like fluid gives freedom to the embryo to develop its form without mechanical pressure. It also acts as a water cushion, absorbing shock forces. Just prior to birth, the amniochorionic membrane surrounding the fetus bursts, sending a half liter or more fluid into the *vagina* and to the outside (breaking the "bag of waters"). Parturition (childbirth) generally occurs about 280 days (40 weeks) after fertilization.

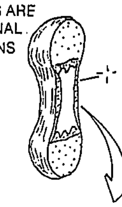


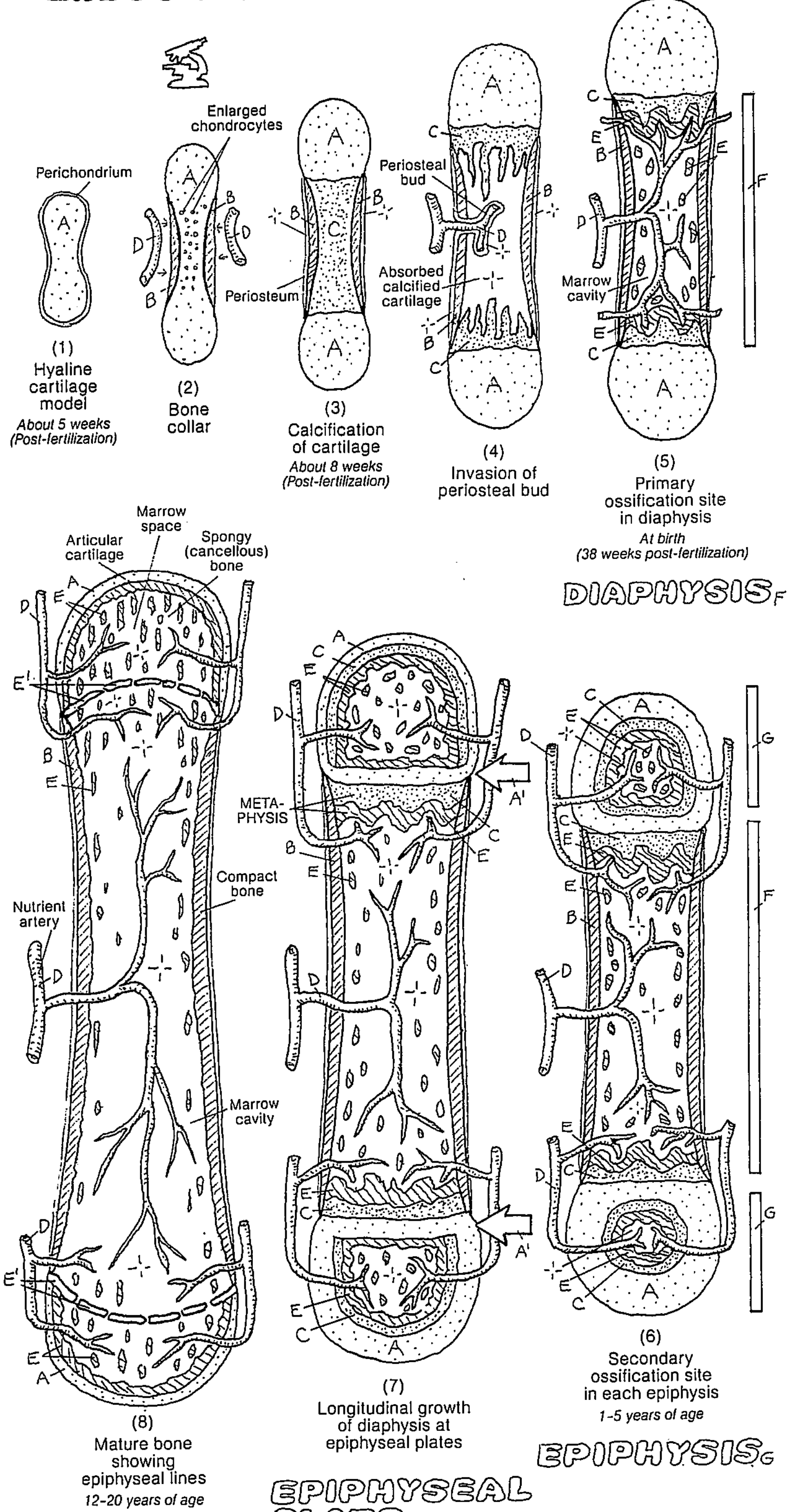
FETUS AT TERM
(40 weeks)

ENDOCHONDRAL OSSIFICATION

CN: Use the same colors as used on the previous plate for hyaline cartilage (A), periosteal bone (B), which was compact bone on Plate 7, and endochondral bone (E), which was spongy bone. Use red for D. Complete each stage before going on to the next. Do not color the periosteum, which appears adjacent to periosteal bone in step 3 and continues to the end. Color the small shapes (E) that appear in the epiphyses and, to a lesser extent, the diaphyses (views 5–8). They represent spongy (cancellous) bone of endochondral origin.

HYALINE CARTILAGE A
PERIOSTEAL BONE B
CALCIFIED CARTILAGE C
BLOOD VESSEL D
ENDOCHONDRAL BONE E





EPIPHYSEAL PLATE A'

EPIPHYSEAL LINE E'

Bone development occurs by intramembranous and/or endochondral ossification. Here we show longitudinal sections of developing long bone, demonstrating both forms of ossification but emphasizing endochondral bone growth.

The endochondral process begins at about 5 weeks of post-fertilization age with formation of cartilage models (bone prototypes) from embryonic connective tissue. Subsequently (over the next 16–25 years), the cartilage is largely replaced by bone. The rate and duration of this process largely determines a person's standing height. Intramembranous bone development begins in embryonic connective tissue (membrane) and does not involve replacement of cartilage. The flat cranial bones, the clavicle, and the bone collar surrounding the shaft of cartilage models develop in this fashion.

Endochondral ossification begins with a *hyaline cartilage* model (1). As the cartilage structure grows, its central part dehydrates. The cartilage cells there begin to degenerate: they enlarge, die, and calcify (2). At the same time, *blood vessels* bring bone-forming cells to the waist of the cartilage model, and a collar of bone is formed around the cartilage shaft (2) within the membranous perichondrium (intramembranous ossification). This vascular, cellular, fibrous membrane around the bone collar is now called periosteum. The new bone collar (*periosteal bone*) becomes a supporting tubular shaft for the cartilage model, with a core of degenerating, calcifying cartilage (3).

Blood vessels from the fibrous periosteum penetrate the bone collar, enter the cartilage model (periosteal bud), and proliferate, conducting periosteal osteoblasts into the cartilage model (4). Starting at about 8 weeks post-fertilization, these bone-forming cells line up along peninsulas of *calcified cartilage* at the extremes of the shaft (*diaphysis*) and secrete new bone (5). The calcified cartilage degenerates and is absorbed into the blood; endochondral bone has now replaced the cartilage. The two sites of this activity are called primary centers of ossification (5). The direction of growth at these sites is toward the ends of the developing bone. The calcified cartilage and some endochondral bone of the diaphysis are subsequently absorbed, forming the medullary or marrow cavity (5). This cavity of the developing tubular bone shaft becomes filled with gelatinous red marrow in the fetus. Productive primary (diaphyseal) centers of ossification are well established at birth.

Beginning in the first few years after birth, secondary centers of ossification begin at the ends or *epiphyses* as blood vessels penetrate the cartilage there (6). The healthy cartilage between the epiphyseal and diaphyseal centers of ossification becomes the *epiphyseal plate* (7). It is the growth of this cartilage that is responsible for bone lengthening; it is the gradual replacement of this cartilage by bone cells in the metaphysis (7) that thins this plate and ultimately permits fusion of the epiphyseal and diaphyseal ossification centers (8), ending longitudinal bone growth (at 12–20 years of age). Dense areas of bone at the fusion site may remain into maturity (*epiphyseal line*). Epiphyseal bone is less structured (irregular beams) than that of the diaphysis (organized columns or osteons), and in maturity it is called spongy or cancellous bone (recall Plate 7).

Intramembranous ossification of the diaphyseal shaft (bone collar to compact bone) is responsible for the widening of developing long bone. The ossification process is regulated by growth hormone (from the pituitary gland) and the sex hormones.

DEVELOPMENT OF CENTRAL NERVOUS SYSTEM

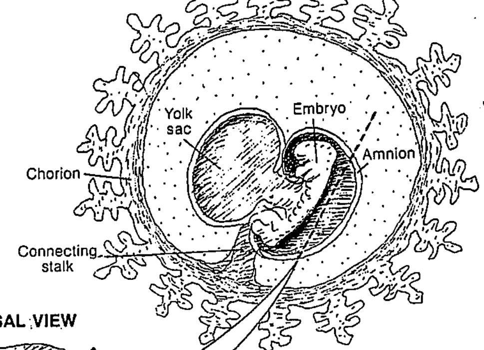
CN: Use light colors for A and C. (1) Begin with the two dorsal views of the 20-day-old embryo. Color as well the large arrows pointing to the surface locations. Simultaneously color the diagrammatic cross section to its right. Follow the same procedure for the later views of the growing embryo. (2) Color the stages of brain development in the head end of the neural tube.

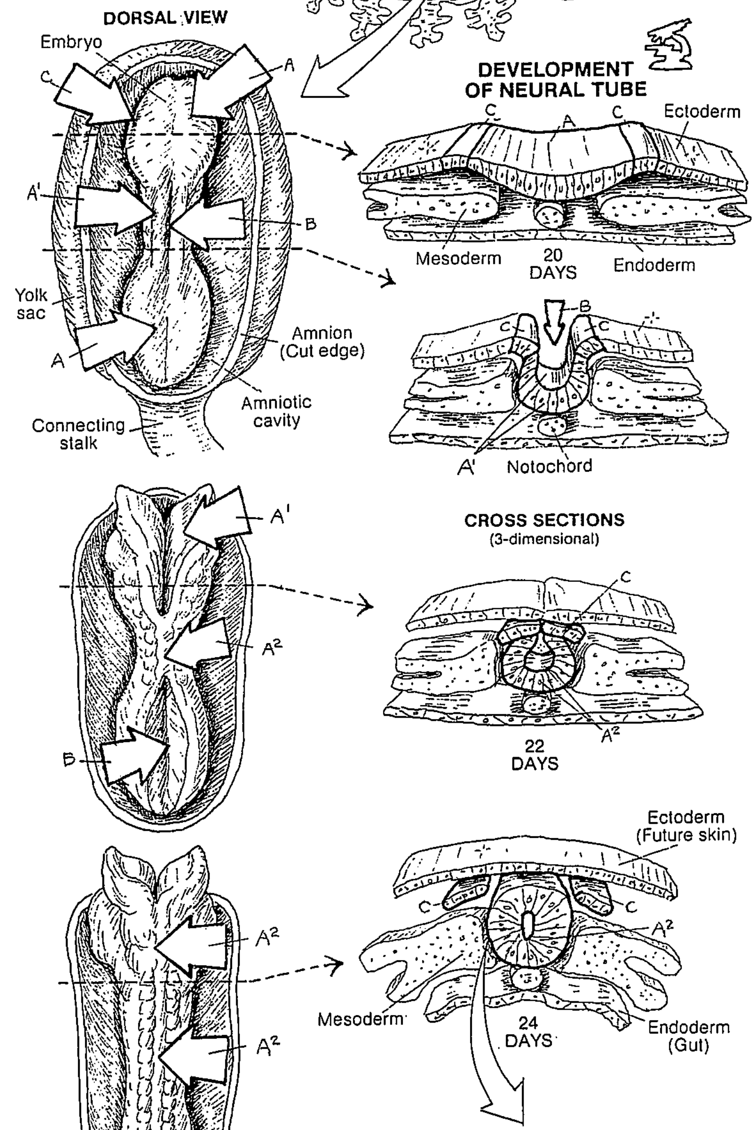
NEURAL PLATE A
FOLD A^1
TUBE A^2
NEURAL GROOVE B
NEURAL CREST C

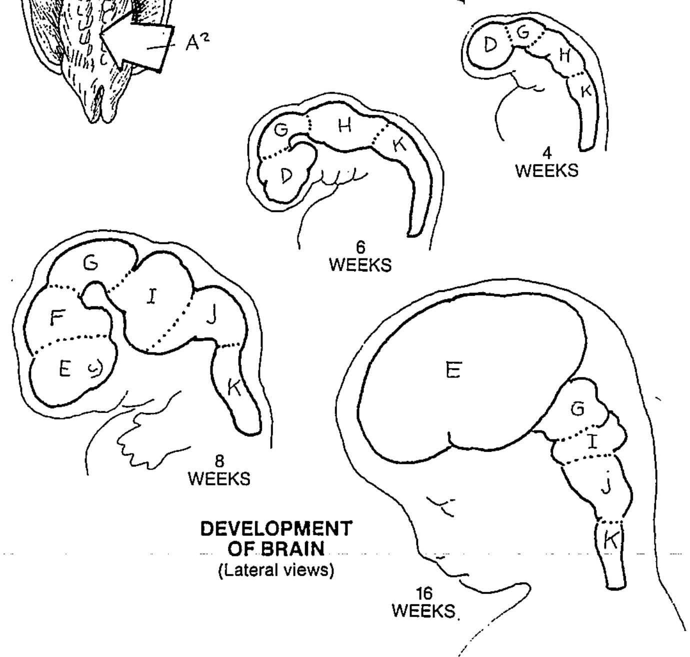
The nervous system develops from the dorsal surface of the ectodermal germ layer (future skin) of the embryo. In the 20- to 21-day embryo, a longitudinal groove (*neural groove*) begins to form on this thickened layer (*neural plate*). In the central part of the plate, the groove deepens, forming *neural folds* on either side. Deepening of the neural groove proceeds toward the head and tail ends of the embryo. By 22 days, the dorsal part of the folds fuse in the central part of the groove, forming a *neural tube*. During this process, the neural tube separates from the ectoderm. By 24 days, formation of the neural tube has progressed to the extreme ends of the embryo. Much of the neural tube will form the spinal cord; the head end of the tube will form the brain. The *neural crest* cells, formed from the neural folds, will develop into certain nerve cells of the peripheral nervous system and Schwann cells. The surrounding mesoderm will form the cranium and the vertebral column and related muscles. The notochord (a primitive supporting rod for the embryo) will be absorbed by the developing vertebral column, and remnants of it will remain as the core of the intervertebral discs (nucleus pulposus). The endoderm will contribute to the development of the digestive tract.

FOREBRAIN D
TELENCEPHALON E
DIENCEPHALON F
MIDBRAIN G
(MESENCEPHALON) G
HINDBRAIN H
METENCEPHALON I
MYELENCEPHALON J
SPINAL CORD K

By the end of three weeks of embryonic development, three regions of the developing brain are apparent: *forebrain, midbrain,* and *hindbrain.* With further growth, the forebrain expands to form the massive *telencephalon* (endbrain; future cerebral hemispheres) and the more central *diencephalon* ("between" brain; future top of the brain stem). The midbrain retains its largely tubular shape as the *mesencephalon* (midbrain; future upper brain stem). The hindbrain differentiates into the upper *metencephalon* ("change" brain; future middle brain stem) with a large dorsal outpocketing (future cerebellum), and the lower *myelencephalon* (spinal brain; lowest part of the future brain stem). The brain stem narrows to become the *spinal cord* at the level of the foramen magnum of the skull.







FETAL CIRCULATION

PLACENTA A
- OXYGEN-RICH BLOOD B
- UMBILICAL VEIN B'

DUCTUS VENOSUS C
- OXYGEN-POOR BLOOD D
- MIXED BLOOD E

FORAMEN OVALE F

DUCTUS ARTERIOSUS G

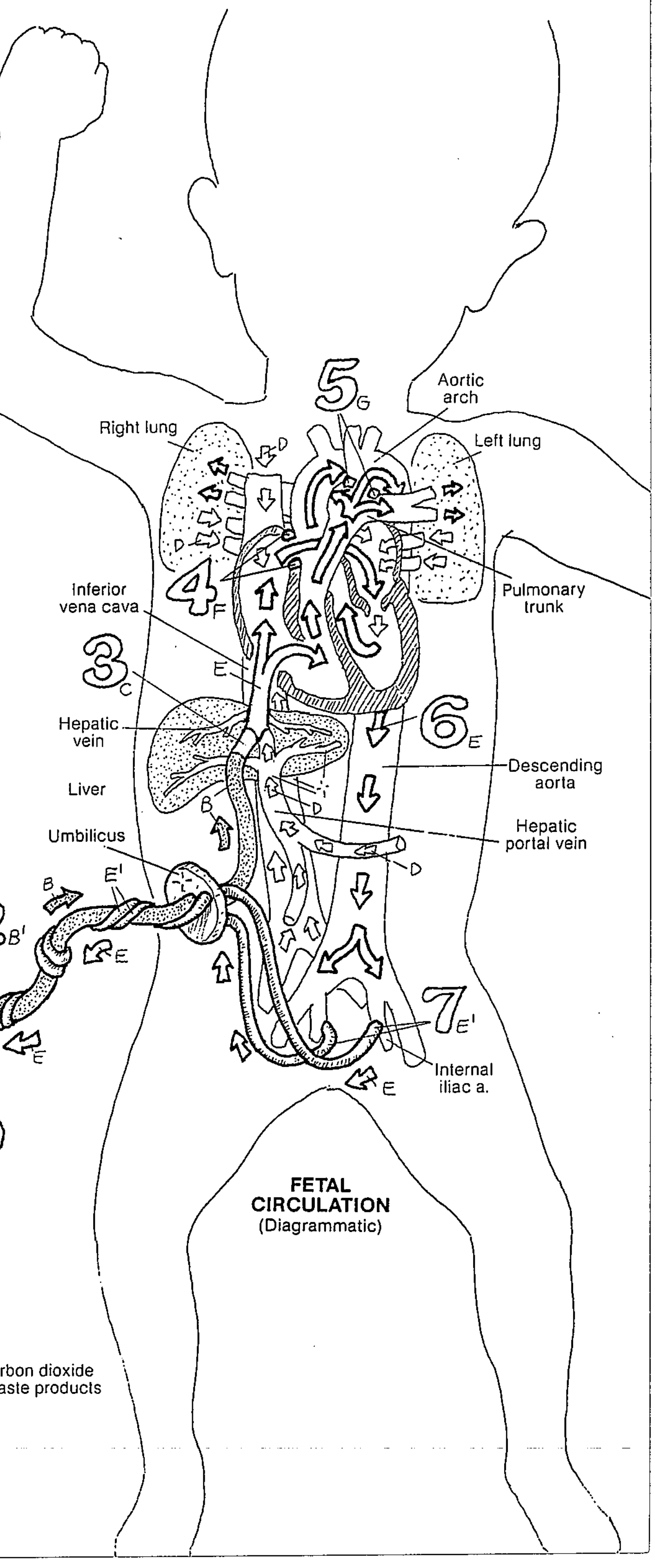
UMBILICAL ARTERY E'

CN: Use red for B (oxygenated blood, represented by a dotted arrow) and B^1 (umbilical vein). Use blue for D (deoxygenated blood, represented by a light-lined arrow). Use purple for E (mixed deoxygenated and oxygenated blood, represented by a dark-lined arrow) and E^1 (umbilical artery). Use bright colors for C, F, and G. (1) Color the placenta and the large number 1, as well as the enlarged rectangular portion of the placenta magnified to show capillary exchange between fetal and maternal vessels. (2) Color the large numbers while coloring related structures and blood flow arrows. (3) Color the placenta and components of the umbilical cord in the uterus at lower left.

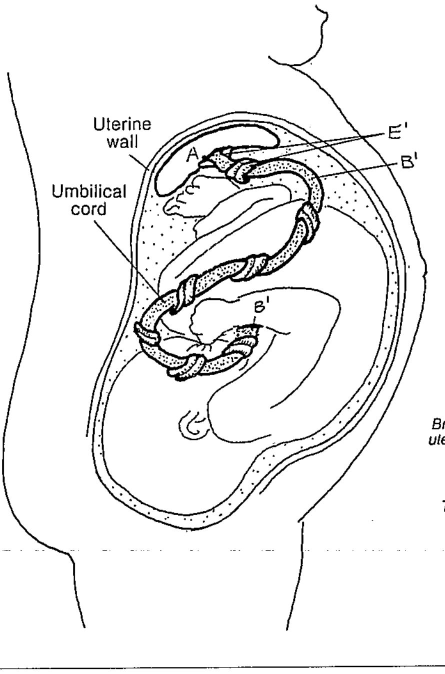
The fetus in the uterus does not breathe air; its lungs are deflated. This plate reveals how the fetus gets oxygen-rich blood to its system (in the absence of breathing air) and gets oxygen-poor blood out of the body.

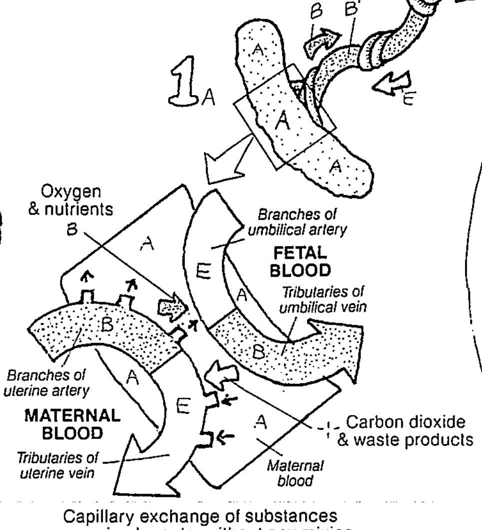
The placenta (numeral 1) is an organ in the uterus of a pregnant woman that provides gaseous and nutritional support for the fetus. The placenta communicates with the fetus by an umbilical cord (2). The vessel taking oxygen-rich blood from the placenta to the fetus is the *umbilical vein* (2) which runs to the underside of the liver (3) to join the portal vein. Here the oxygen-rich blood of the former is mixed with the oxygen-poor blood of the latter. A vein existing only in the fetus (*ductus venosus*) diverts the blood directly to the hepatic vein, bypassing the liver sinusoids. The mixed blood then enters the inferior vena cava to the right heart. The blood is directed to the left (systemic) side of the heart by two means: an opening in the interatrial wall (*foramen ovale*; 4) and a short vessel between the pulmonary trunk and the descending part of the aortic arch (*ductus arteriosus*; 5). Only a fraction of mixed blood gets pumped to the non- functioning (but living) lungs. The mixed blood leaves the heart via the aorta (6) to reach the body tissues. The oxygen-carrying capacity of fetal hemoglobin is particularly great in comparison with that of the adult; the fetal tissues get sufficient oxygenation from mixed blood to permit remarkably rapid growth.

Paired umbilical arteries, arising from the internal iliacs, return the oxygen-poor blood from the fetus to the umbilical cord and placenta. After birth, because of altered hemodynamic patterns associated with breathing, the circulation in the fetal umbilical vessels and ducts of the newborn diminishes significantly and the vessels soon thrombose. The umbilical vein atrophies to become the ligamentum teres in the falciform ligament (Pl. 106); the umbilical arteries become the medial umbilical ligaments (Pl. 75); the ductus venosus becomes the ligamentum venosum; revised circulation to the lungs induces closure of the foramen ovale; flow through the ductus arteriosus trickles down and the vessel closes and becomes a ligamentous strand (ligamentum arteriosum; Pl. 66).



FETAL CIRCULATION
(Diagrammatic)





Capillary exchange of substances occurs in placenta, without any mixing of maternal and fetal blood.