Physiology of Pregnancy

Normal Pregnancy

- **Pregnancy**

  The course that the embryo and the fetus grow in the maternal body

- **Stages of pregnancy**

1. Early pregnancy: ≤12 weeks
2. Mid pregnancy: ≥13 weeks,≤27 weeks
3. Late pregnancy:≥28 weeks
4. Term pregnancy:≥37 weeks,<42 weeks

Formation of Embryo

- Fertilization

1. Place: oviduct (ampulla)
2. Process

   capacitation → acrosome reaction→ penetrate the zona pellucida→ second meiosis →zygote

Formation of Embryo

- Implantation

1. requirement

1) Disappear of zona pellucida
2) Formation of syncytiotrophoblast
3) Synchronized development of blastocyst and endometrium
4) Adequate progesterone

Formation of Embryo

2. Process

1) morula (day 3) → enter uterine cavity (day 4) → early blastocyst→ late blastocyst (day 6-7) → implantation

2) location→ adherence→ penetration

Development of embryo and fetus

- Definition

1. embryo: ≤ 8 weeks
2. Fetus: ≥ 9 weeks, human shape

Development of embryo and fetus

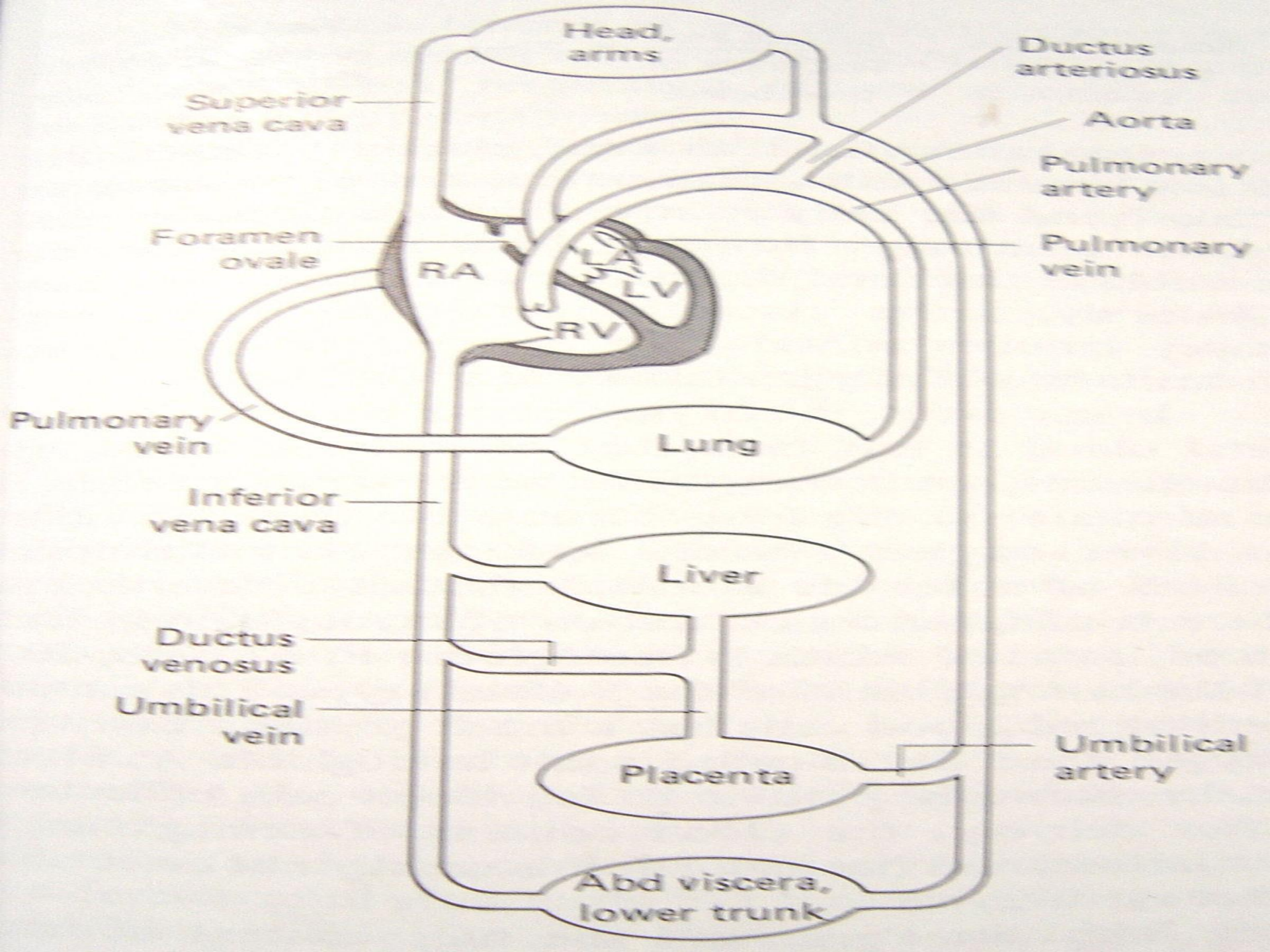
- Physiology of fetus

1. Circulation

1) fetus ←→placenta←→ mater

2) 1 umbilical vein (full of oxygen), 2 umbilical artery (lack of oxygen)

3) Mixed blood (vein and artery)


Head, arms
Superior vena cava
Ductus arteriosus
Aorta
Pulmonary artery
Foramen ovale
RA
LA
LV
RV
Pulmonary vein
Pulmonary vein
Lung
Inferior vena cava
Liver
Ductus venosus
Umbilical vein
Umbilical artery
Placenta
Abd viscera, lower trunk

Development of embryo and fetus

2. Hematology

1) Erythropoiesis

From yolk sac: 3 weeks

From liver: 10 weeks

From bone marrow and spleen: term (90%)

EPO production: 32nd week

Development of embryo and fetus

2) Fetal hemoglobin

Fetal hemoglobin: early pregnancy

Adult hemoglobin: 32nd week

Term: fetal type Hb 25%

3) White cells

Leukocytes: 8 week

Lymphocytes (antibody production): 12 week, thymus and spleen

Development of embryo and fetus

3. Gastrointestinal tract

1) drink amniotic fluid: 4th month

2) no proteolytic activity

3) enzymatic deficiencies in liver:

bilirubin is not easy to be clear.

Development of embryo and fetus

4. Kidney

   Its function begins at 11-14th week

5) Endocrinology

1) Fetal thyroid: the first endocrine gland (6th week), synthesize thyroxine at 12th week

2) Fetal adrenal cortex: widen (20th week), a fetal zone. synthesize steroid hormones (E3, liver placenta mater)

Placenta

- Structure

1. Primary villus
   syncytiotrophoblast cytotrophoblast
2. Secondary villus
3. third class vilus

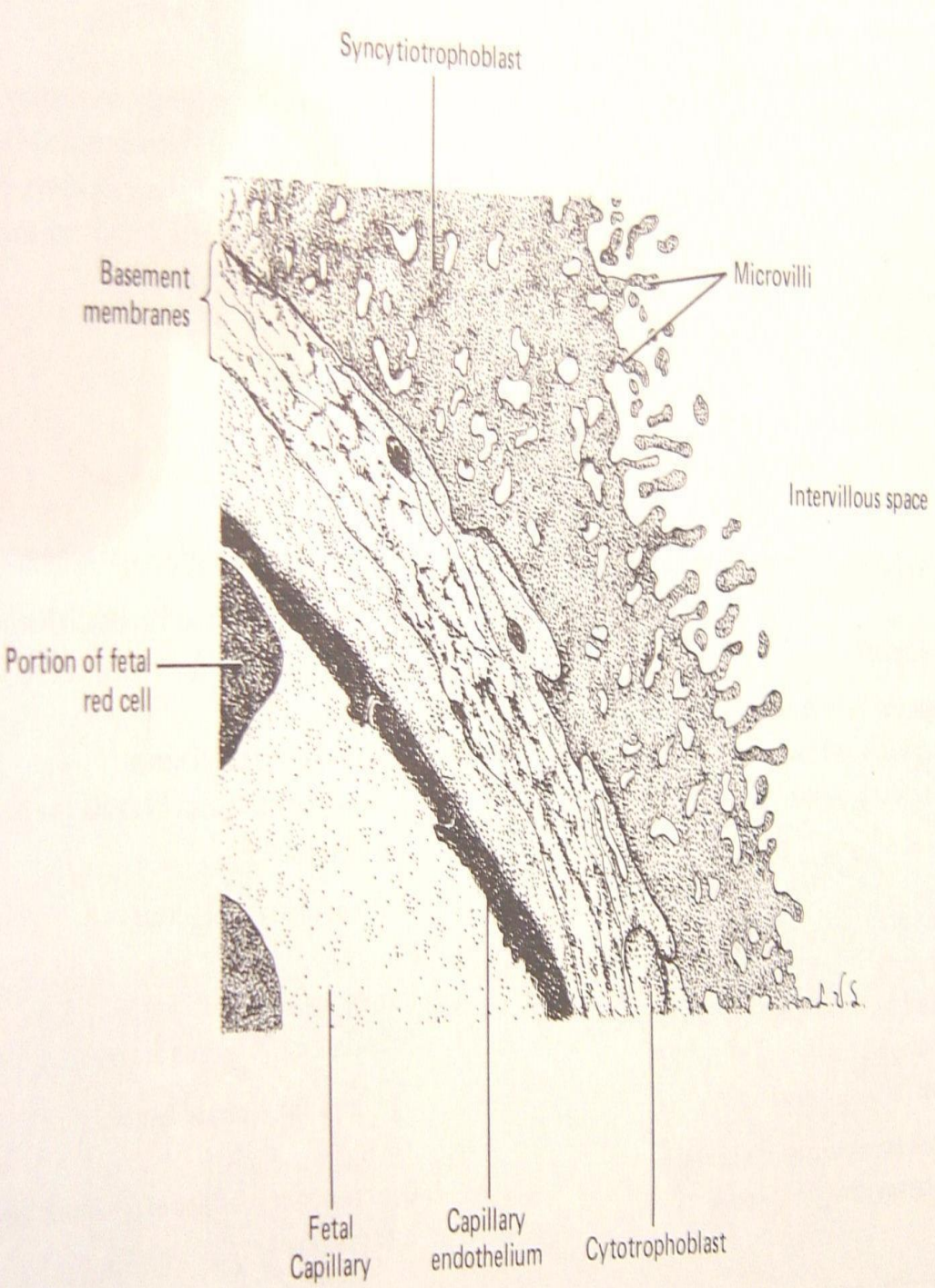
fetal capillary enter the stroma

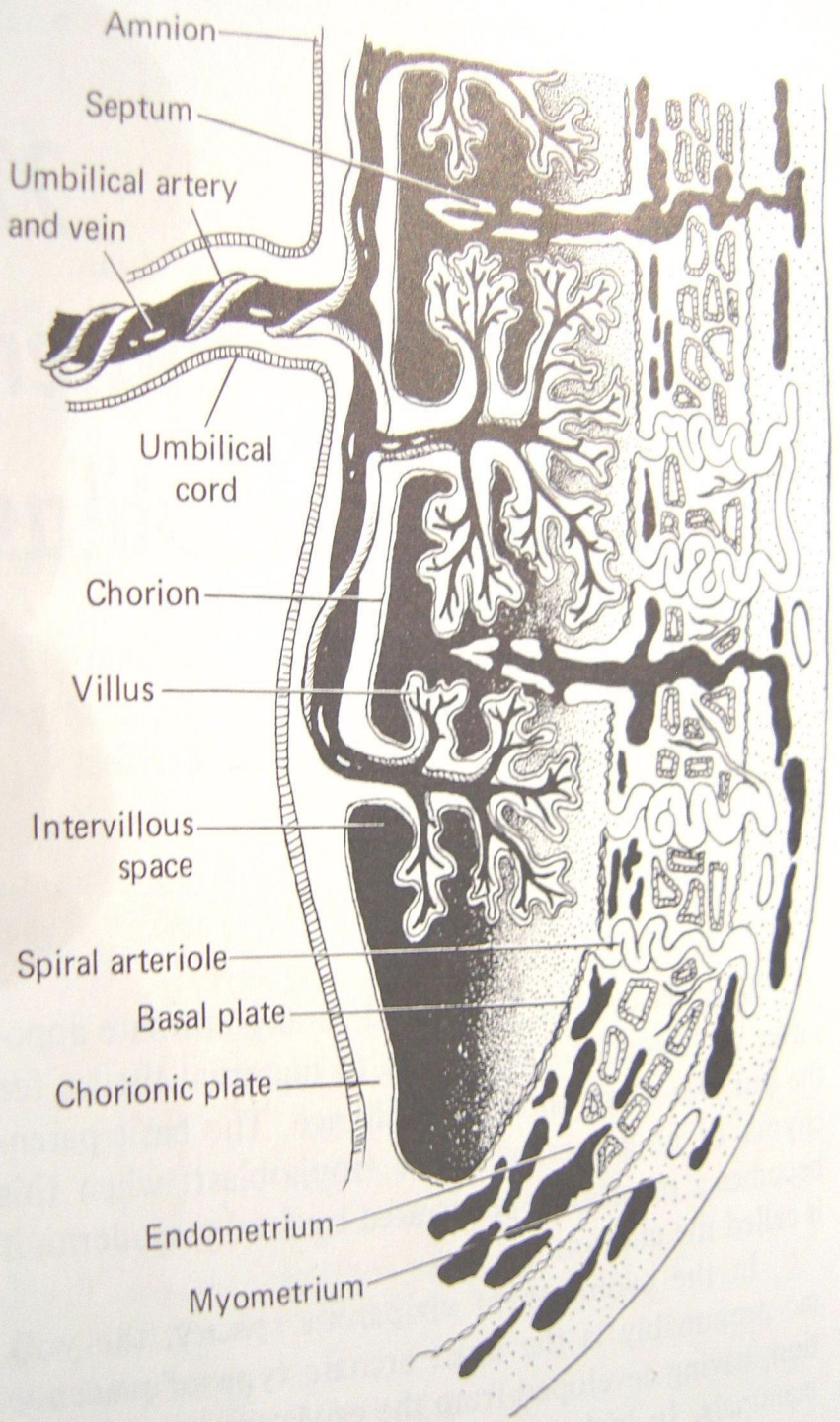
Placenta: Villi

- a. These structures, the functioning units of the placenta, are formed by invading placental tissue (trophoblast) and contain the terminal fetal capillaries of the umbilical arteries.
- b. The villi are surrounded by the intervillous space into which maternal blood from the decidual (uterine) arteries is forced by maternal arterial pressure.
- c. Gases and nutrients pass from the maternal blood in the intervillous space, across the membrane of the trophoblast to the basement membrane of the fetal capillary, and then through the single endothelial cell layer of the fetal capillary to the fetal blood.
- The fetal capillaries drain into the fetal veins that join to form the umbilical vein.
- Maternal blood drains from the intervillous space into the maternal veins.

Placenta: cotyledons

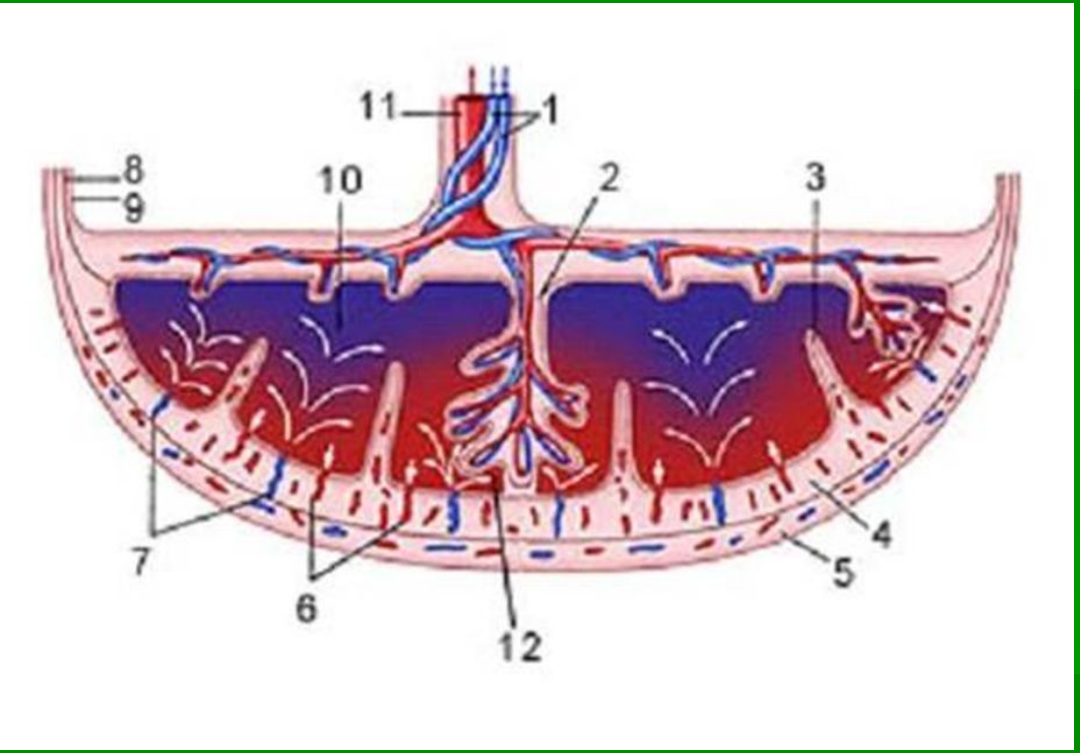
- Placental cotyledons (lobes) are formed from the branching villi supplied by one terminal arterial branch and its partner venous branch of the fetal umbilical vessels.
- On average, about 20 cotyledons make up the fetal side of the placenta.
- The maternal side of the placenta is divided by
- septa into lobes.


Syncytiotrophoblast
Basement membranes
Microvilli
Intervillous space
Portion of fetal red cell
Fetal Capillary
Capillary endothelium
Cytotrophoblast

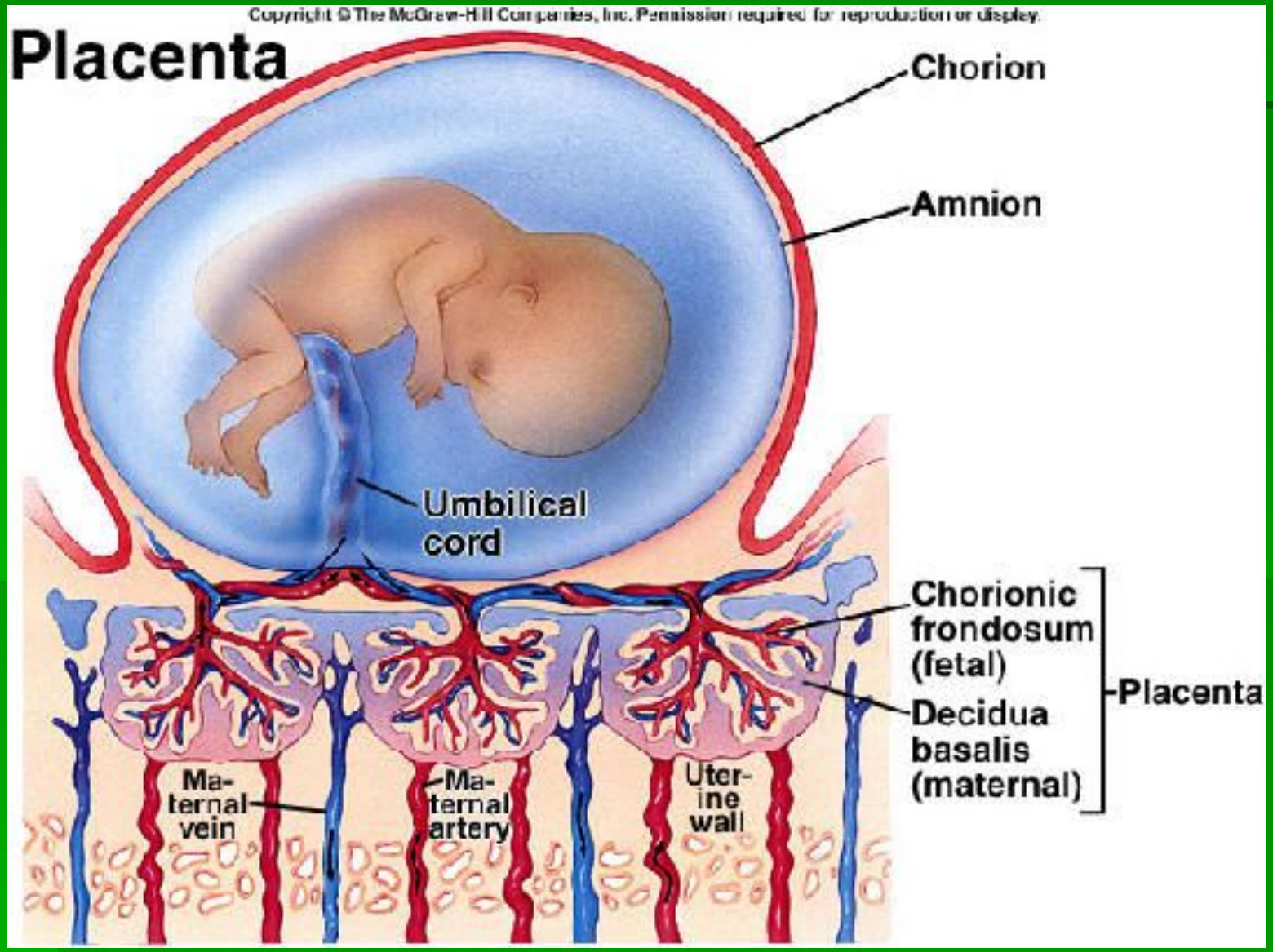

Amnion
Septum
Umbilical artery and vein
Umbilical cord
Chorion
Villus
Intervillous space
Spiral arteriole
Basal plate
Chorionic plate
Endometrium
Myometrium

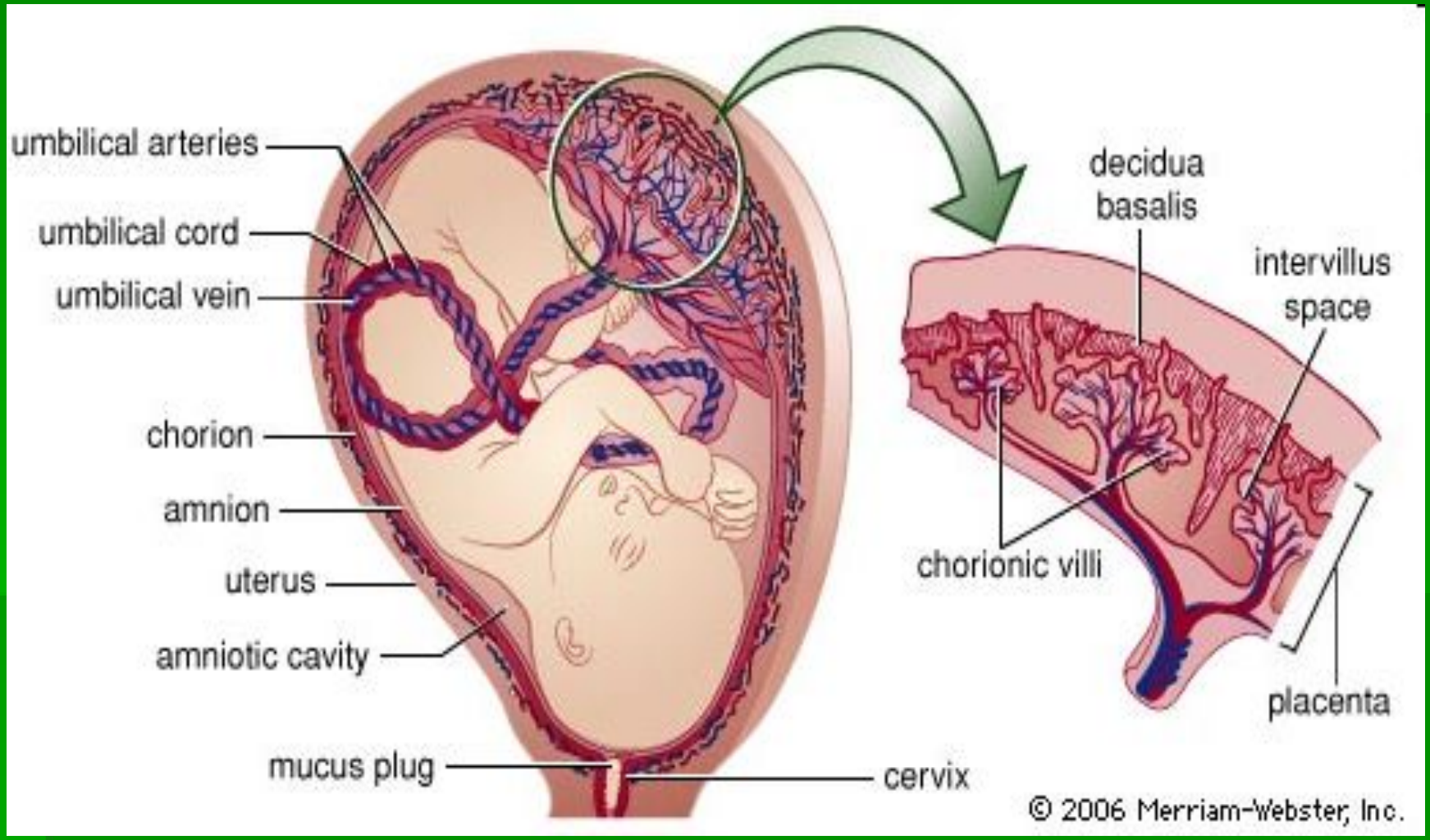
Placenta: structure

1 – umbilical arteries,
2 – stem villus,
3 – decidual septa,
4 – decidual layer,
5 –myometrium,
6 – veins,
7 – spiral arteries,
8 – chorion,
9 – amnion,
10 – intervillous space,
11 – umbilical vein,
12 – cotyledon.



Scheme of placental circulation.




umbilical arteries
umbilical cord
umbilical vein
chorion
amnion
uterus
amniotic cavity
mucus plug
cervix
decidua basalis
intervillus space
chorionic villi
placenta
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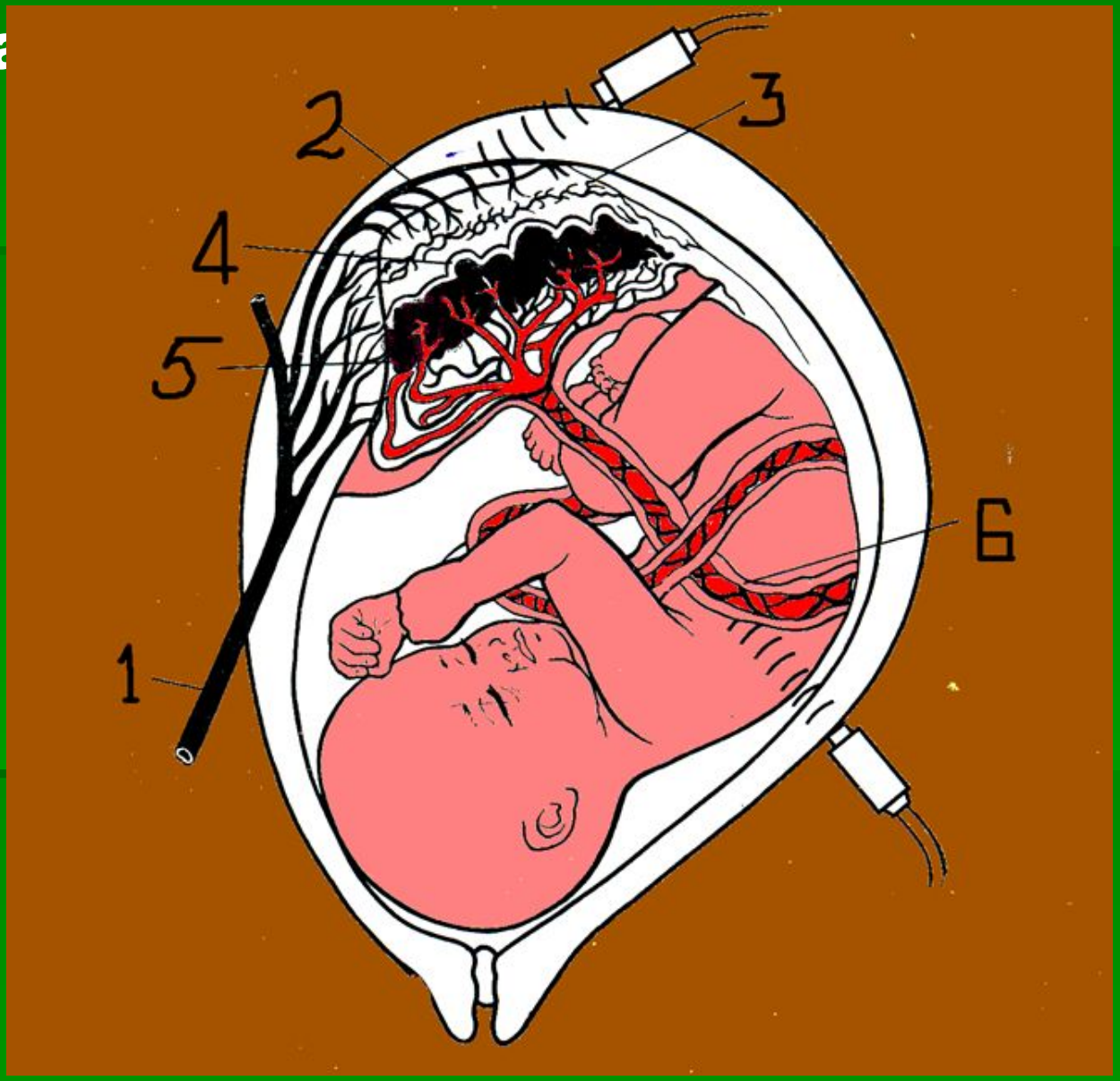
Feto-placenta circulation

1- uterine artery
2- arcade arteries
3- spiral arteries
4- intervillous space
5- placental vessels
6- vessels of the umbilical cord



Placenta

- Function

1) Exchange of nutritive factors and waste
2) Exchange of O_2 and CO_2
3) Secretion of proteins and steroid hormones
4) Immunology
5) metabolism
6) Defensive - Limited. IgG, virus, drug

Placenta: functions

- The placenta transfers nutrition and oxygen from the mother to the fetus, removes metabolic waste products from the fetus to be eliminated by the mother, and synthesizes proteins and hormones that support fetal development and important maternal physiologic changes.

1. Mother-to-fetus transfer of nutrients

- a. The essential substances for growth and development move from the mother to the fetus in four ways:
- (1) Active transport: amino acids, calcium
- (2) Facilitated transport: glucose
- (3) Endocytosis: cholesterol, insulin, iron, immunoglobulin G (IgG)
- (4) Sodium pumps and chloride channels: ions
- b. Solute size and lipid solubility are also important factors that influence transport.

2. Gas exchange

- This process involves supplying oxygen to the fetus and removing carbon dioxide from the fetus.

3. Secretion of proteins and steroid hormones

- a. Progesterone is produced by the placenta from maternal cholesterol, is secreted into the maternal circulation, and is important for maintaining pregnancy.
- b. Estrogen is converted from circulating fetal androgens (dehydroepiandrosterone sulfate [DHEAS] produced in the fetal adrenal glands. Estrogen plays an important role in maternal physiologic changes in pregnancy, labor, and lactation.
- c. Numerous proteins, peptides, and growth factors are produced in the placenta. They are important for placental growth, fetal growth and development, and the maternal physiologic changes necessary to ensure adequate nutrition to the fetus.

4. Immunology.

- Invading placental cells express a unique antigen, HLA-G, which is not recognized as a "foreign" antigen by the mother.
- Other unique antigens and local immune suppression contribute to the prevention of rejection of the fetal-placental unit.
- 5. Metabolism. Glucose is the primary substrate for placental aerobic metabolism.

Fetal membranes

- Structure

  chorion and amnion
- Amnion

  A double-layered translucent membrane

  Become distended with fluid

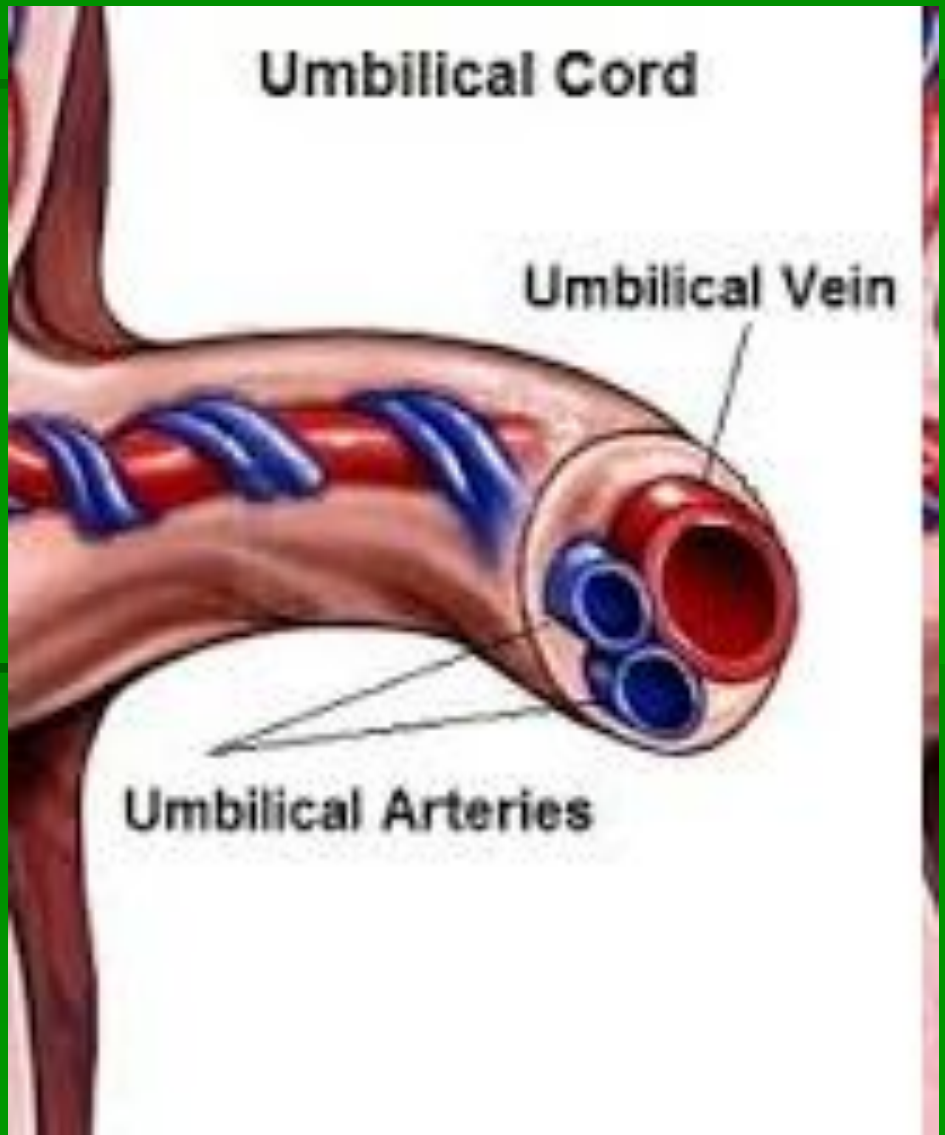
Umbilical cord

Umbilical cord

- A. Umbilical arteries. Two umbilical arteries originate from the fetal aorta. They supply fetal blood to all portions of the placenta for gas and solute exchange. A single umbilical artery is associated with low birth weight and chromosomal anomalies in about 10 to 15% of infants.
- B. Umbilical vein. One umbilical vein returns nutrient-rich, oxygen-rich blood to the fetus.
- Wharton jelly

Umbilical cord

- In most cases, the cord is about 20 inches long and almost 1 inch in diameter. It usually appears loosely coiled. Inside the cord are two arteries and one vein. The vein supplies the baby with oxygenated, nutrient-rich blood, and the arteries carry de-oxygenated, nutrient-depleted blood back to the placenta. On occasion, the umbilical cord will only have two vessels; one artery and one vein.



Here is a normal three vessel umbilical cord. Note that there are two arteries toward the right and a single vein at the left. Most of the parenchyma of the cord consists of a loose mesenchyme with intercellular ground substance (Wharton's jelly).

Amniotic fluid

Amniotic fluid

- Amniotic fluid (AF) - the habitat of the fetus, performs several functions simultaneously : the creation of spaces for free movement of the growing fetus , protection from mechanical injury , maintaining temperature balance , preventing compression of the umbilical cord at birth , the implementation of the transport function and participation in metabolism .
- AF is yellowish in early pregnancy, then lighter and transparent, and - cloudy , opalescent at the end of pregnancy ; pH - 6,98-7,23, specific gravity- 1007-1080 g / l , the protein content - 0.18-0.2 % glucose - 22 mg% urea - 23 mg%. AF may contain embryonic hair (lanugo), cells of the epidermis , sebaceous gland cells (vernix caseosa).

Amniotic fluid

- AF volume depends on the term of pregnancy. Increase in volume is uneven. The peak of AF volume fixed at 33.8 weeks and is 931 ml. AF volume in the range 22-39 weeks does not change significantly (630 ml and 817 ml, respectively) and averaged 777 ml .

Amniotic Fliud

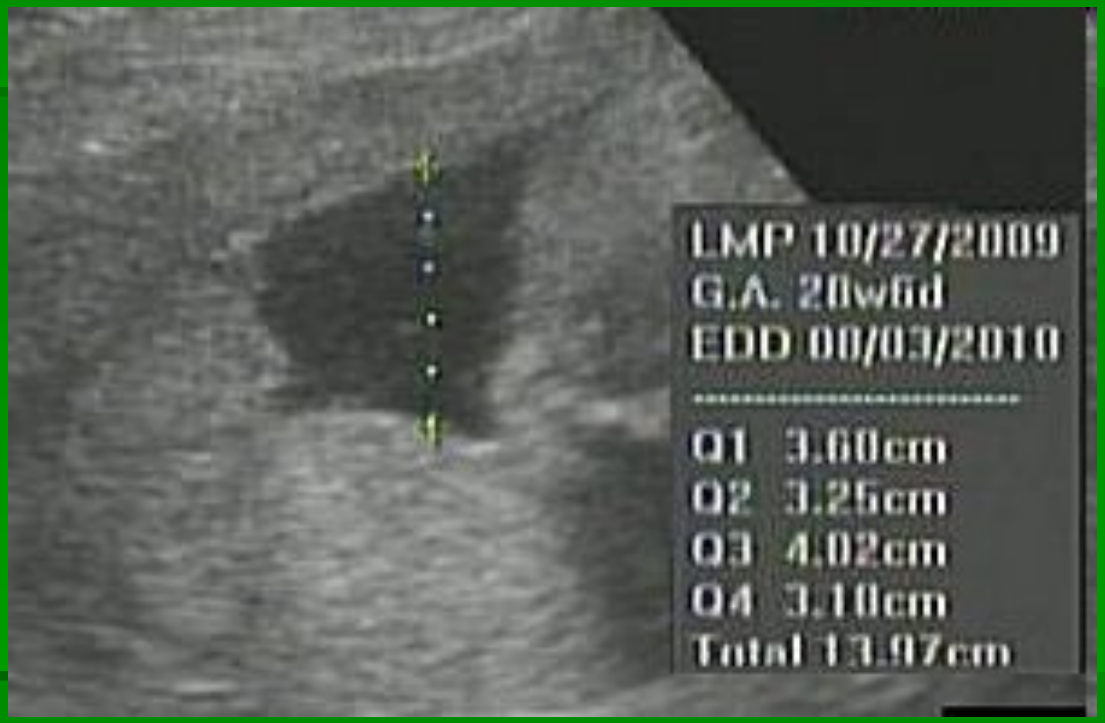
- Towards the end pregnancy (term of labor) the volume of amniotic fluid comes up to 1-1.5 liters, and every three hours it is completely updated, with one-third recycled by fetus.

Amniotic Fluid Index (AFI)

- An ultrasound procedure used to asses the amount of amniotic fluid. The amniotic fluid index is measured by dividing the uterus into four imaginary quadrants . The linea nigra is used to divide the uterus into right and left halves.The umbilicus serves as the dividing point for the upper and lower halves.

Amniotic fluid index

- The transducer is kept parallel to the patient's longitudinal axis and perpendicular to the floor. The deepest, unobstructed, vertical pocket of fluid is measured in each quadrant in centimeters.



AFI at different terms of pregnancy

(Amniotic Fluid Index Percentile Values)

Weeks	2.5th	5th	median	95th	97th
16	7.3	7.9	**12.1**	18.5	20.1
17	7.7	8.3	**12.7**	19.4	21.1
18	8	8.7	**13.3**	20.2	22
19	8.3	9	**13.7**	20.7	22.5
20	8.6	9.3	**14.1**	21.2	23
21	8.8	9.5	**14.3**	21.4	23.3
22	8.9	9.7	**14.5**	21.6	23.5
23	9	9.8	**14.6**	21.8	23.7
24	9	9.8	**14.7**	21.9	23.8
25	8.9	9.7	**14.7**	22.1	24
26	8.9	9.7	**14.7**	22.3	24.2
27	8.5	9.5	**14.6**	22.6	24.5
28	8.6	9.4	**14.6**	22.8	24.9
29	8.4	9.2	**14.5**	23.1	25.4
30	8.2	9	**14.5**	23.4	25.8
31	7.9	8.8	**14.4**	23.8	26.3
32	7.7	8.6	**14.4**	24.2	26.9
33	7.4	8.3	**14.3**	24.5	27.4
34	7.2	8.1	**14.2**	24.8	27.8
35	7	7.9	**14**	24.9	27.9
36	6.8	7.7	**13.8**	24.9	27.9
37	6.6	7.5	**13.5**	24.4	27.5
38	6.5	7.3	**13.2**	23.9	26.9
39	6.4	7.2	**12.7**	22.6	25.5
40	6.3	7.1	**12.3**	21.4	24
41	6.3	7	**11.6**	19.4	21.6
42	6.3	6.9	**11**	17.5	19.2

Amniotic Fluid Index Percentile Values (mm)

Wks	2.5th	5th	50th	95th	97th
16	73	79	121	185	201
17	77	83	127	194	211
18	80	87	133	202	220
19	83	90	137	207	225
20	86	93	141	212	230
21	88	95	143	214	233
22	89	97	145	216	235
23	90	98	146	218	237
24	90	98	147	219	238
25	89	97	147	221	240
26	89	97	147	223	242
27	85	95	156	226	245
28	86	94	146	228	249
29	84	92	145	231	254
30	82	90	145	234	258
31	79	88	144	238	263
32	77	86	144	242	269
33	74	83	143	245	274
34	72	81	142	248	278
35	70	79	140	249	279
36	68	77	138	249	279
37	66	75	135	244	275
38	65	73	132	239	269
39	64	72	127	226	255
40	63	71	123	214	240
41	63	70	116	194	216
42	63	69	110	175	192

US - amniotic fluid

Amniotic Fliud

- Function

1. Protect fetal
   move freely, warm
2. Protect mater
   prevent infection

Amniotic fliud

- Source

1. exudation of fetal membranes (early pregnancy)
2. Fetal urine
3. Fetal lung
4. Exudation of amnion and fetal skin

Amniotic fliud

- Absord

1. Fetal membrane
2. Umbilical cord
3. Fetal skin
4. Fetal drinking

- Feature

1000-1500ml at 36^{th}-38^{th} week (peak),
transparent → slightly turbid

Critical periods of development:

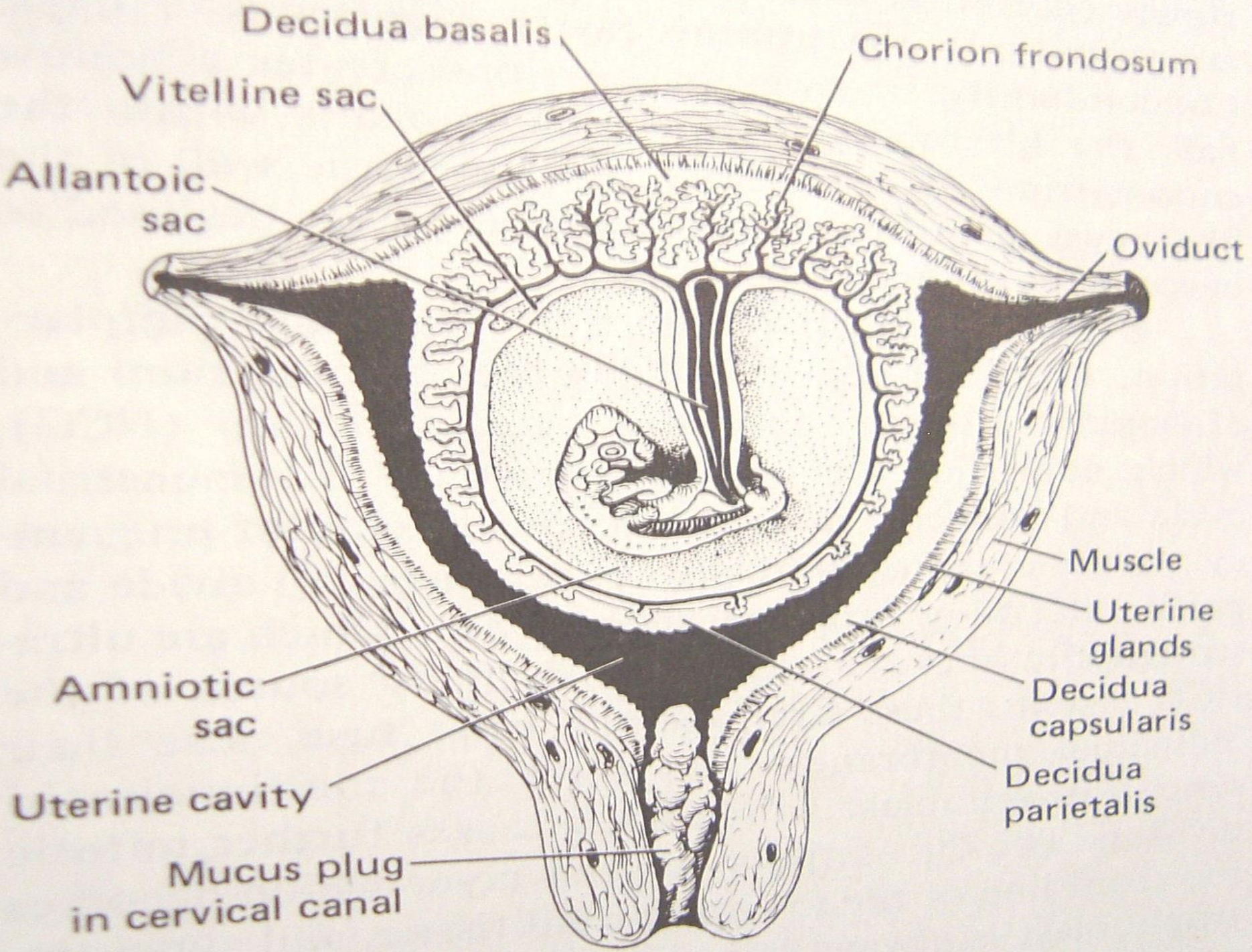
- 1 - progenez - a meiosis (step maturation of gametes) and fertilization process.
- 2 - in the prenatal ontogenesis to critical periods include implantation (6-8 days), placentation and development of axial organ rudiments (3-8 week) during embryogenesis {};
- 3 - Fetal: the period of intensive development of the brain (15-20-th week), during the formation of the main functional systems of the body (20-24 week)
- 4 - the birth process.

Physiologic changes in pregnant woman

- Genital organs

1. Uterus

1) capacity: 5ml-5000ml.weight: 50g-1000g
2) Hypertrophy of muscle cells
3) Endometrium→decidua: basal decidua, capsular decidua, true decidua
4) Contraction: Braxton Hicks
5) Isthmus uteri: 1cm→ 7-10cm


Decidua basalis
Chorion frondosum
Vitelline sac
Allantoic sac
Oviduct
Muscle
Uterine glands
Amniotic sac
Decidua capsularis
Decidua parietalis
Uterine cavity
Mucus plug in cervical canal

Physiologic changes in pregnant woman

6) Cervix: colored
7) Ovary: placenta replaces ovary (10^{th} week)
8) Vagina: dilated and soft, pH ↓ (anti-bacteri bacteria)
9) Ligaments: relaxed

Physiologic changes in pregnant woman

- Cardiovascular system

1. Heart:
   move upward, hypertrophy of cardiac muscle
2. Cardiac Output
   increase by 30%, reach to peak at 32^{nd} –34^{th} week
3. Blood pressure
   early or mid pregnancy Bp ↓ . late pregnancy Bp↑ .Supine hypotensive syndrome

Physiologic changes in pregnant woman

- Hematology

1. Blood volume

1) Increase by 30%-45% at 32nd –34th (peak)

2) Relatively diluted

2. Composition

1) Red cells

Hb:130→110g/L, HCT:38%→ 31%.

2) White cells: slightly increase

3) Coagulating power of blood: ↑

4) Albumin: ↓, 35 g/L

Physiologic changes in pregnant woman

- The Respiratory system

1. R rate: slightly ↑
2. vital capacity: no change
3. Tidal volume: ↑ 40%
4. Functional residual capacity: ↓
5. O_2 consumption: ↑ 20%

Physiologic changes in pregnant woman

- The urinary system

1. Kidney

1) Renal plasma flow (RFP): ↑ 35%

2) Glomerular filtration rate (GFR): ↑ 50%

2. Ureter

Dilated (P ↑)

3. Bladder

Frequent micturation

Physiologic changes in pregnant woman

- Gastrointestinal system

1) Gastric emptying time is prolonged→ nausea.
2) The motility of large bowel is diminished → constipation
3) Liver function: unchanged

Physiologic changes in pregnant woman

- Endocrine

1. Pituitary (hypertrophy)

1) LH/FSH: ↓
2) PRL: ↑
3) TSH and ACTH: ↑

2. Thyroid

1) enlarged (TSH and HCG ↑)
2) thyroxine ↑ and TBG ↑ → free T_3 T_4 unchanged

Diagnosis of pregnancy

- *Questionable signs of pregnancy*
- *Probable signs*
- *True signs*
- *Laboratory tests : β-HCG, ptrogesterone*
- *Additional methods : US*

Questionable signs of pregnancy

- Change of appetite.
- Changes of smell (aversion to perfume, tobacco, any other smells).
- Changes of the nervous system: quick fatigability, sleepiness, irritability, quick change of mood (instability of mood).

Questionable signs

- Morning sickness.
- Pigmentation of the skin (nipple and areolae, *linea alba*, forehead and cheeks).
- Increase of fatty tissue, enlargement of abdomen.
- Frequency of micturition- due to: 1) pressure of the bulky uterus on the fundus of the bladder because of excessive anteverted position of the uterus; 2) congestion of the bladder mucous membrane, 3) stretching of the bladder base due to backward displacement of the cervix.
- Breast discomfort.

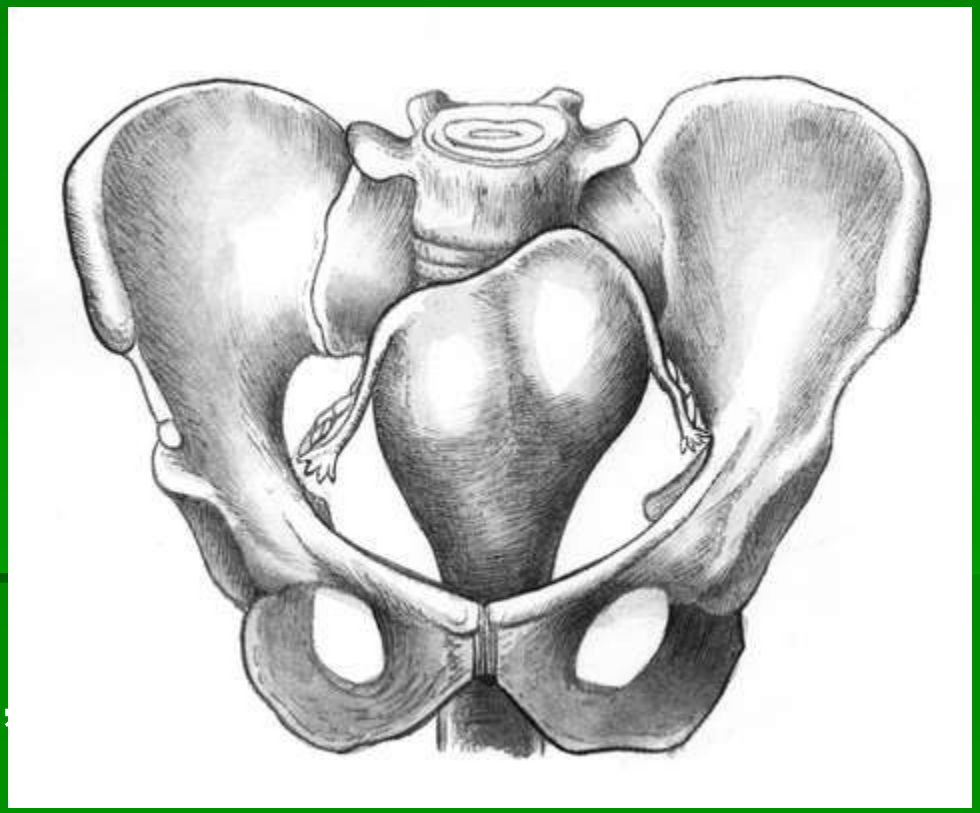
Probable signs

- Cessation of menses (or amenorrhea).
- Breast changes - enlargement of breasts with vascular engorgement evidenced by the delicate veins visible under the skin. The nipple and areola become more pigmented and prominent. Thick yellowish secret (foremilk) usually appears.
- Discolouration of the vestibule and anterior vaginal wall - cyanotic due to local vascular congestion.
- Changes of size, shape and consistence of the uterus.

Pregnancy' sign in VE:

- **Piskacek's sign.**

It is an asymmetrical enlargement of the uterus due to the lateral implantation of fertilized ovum. In such cases one half of the uterus is larger than another. As pregnancy advances, symmetry is restored.

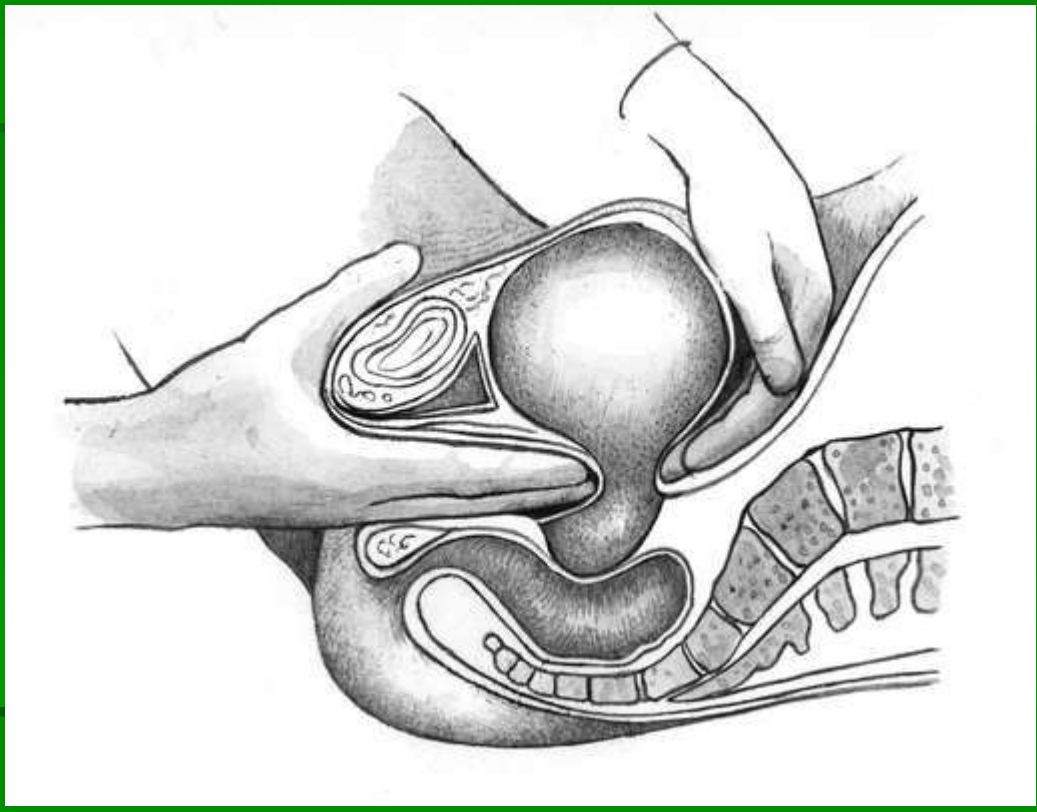


Pregnancy' sign in VE:

Hegar's sign.

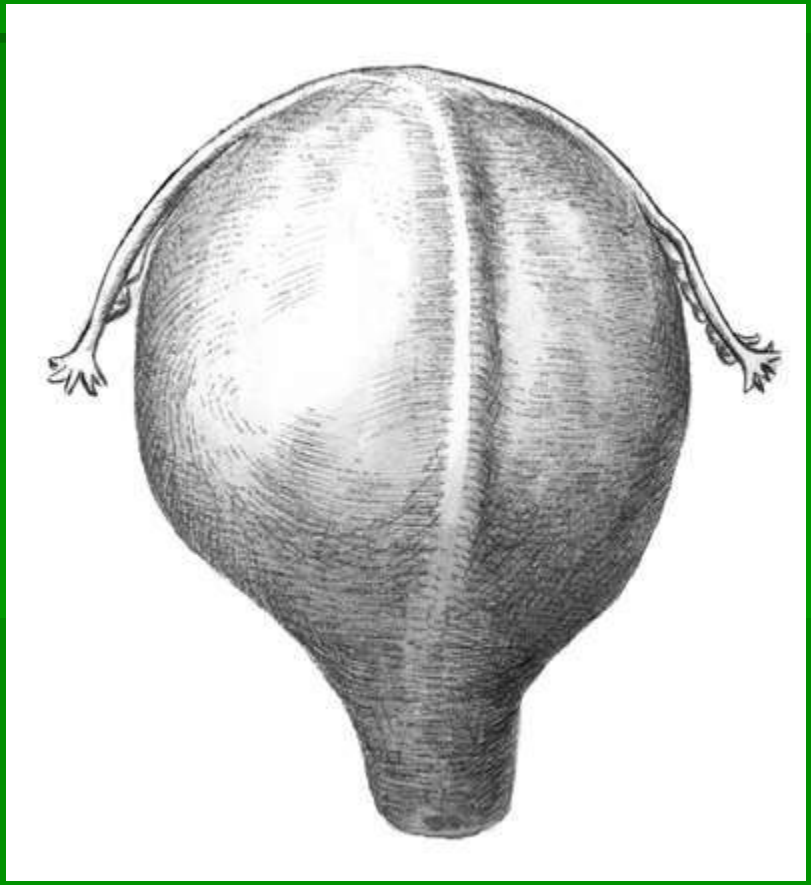
It is present in two-thirds of cases. It can be manifested at term of 6-10 weeks, or a little earlier in multiparae. This sign is based on the fact that:

1) the upper part of the body of the uterus is enlarged by the growing ovum;
2) the lower part of the body is empty and extremely soft, and
3) the cervix is comparatively dense. Because of variation in consistency, on bimanual examination the abdominal and vaginal fingers seem to appose below the body of the uterus.



Pregnancy' sign in VE:

Early as 4-8 weeks Henter's sign is appear: expressed anteflexion of uterus due to softening of isthmus, and at the same time the crest on the anterior wall of the uterus are palpable.



Pregnancy' sign in VE:

- Haus-Gubarev's sign - the cervix of the uterus becomes very mobile, due to softening of the isthmus of the uterus.
- Snegiryov's sign – Increased irritability of the uterus body presented with appearance of hypertonicity of the uterus under palpating fingers during bimanual examination.

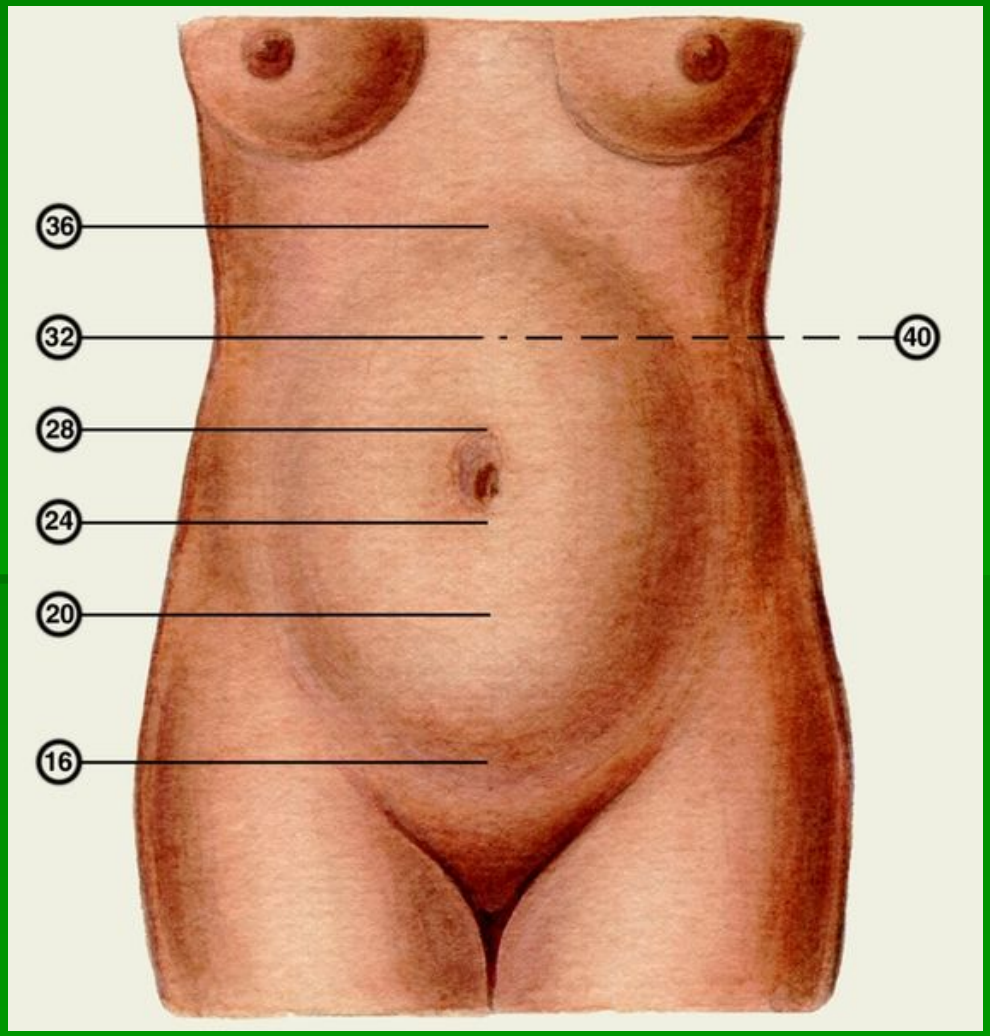
Uterus sizes

- Week 6: Plum or golf ball size (hen's egg)
- Week 8: Tennis ball size
- Week 10: Large orange size
- Week 12: Grapefruit size (palpable at suprapubic area)
- Week 14: Cantaloupe size
- Week 16 : between the symphysis pubis and the navel

Uterus sizes

- Week 20: at the 2 cross fingers (4 cm) below the navel
- Week 24: uterus reaches the navel
- Week 28: 2-3 cross fingers higher the navel
- Week 32: midway between the umbilicus and xiphoid process of sternum
- Week 36- 38: uterus reaches the xiphoid and costal arches
- Week 40 : fundus of the uterus drops to the middle of the distance between the navel and the xiphoid process. At the end of pregnancy belly button sticks out.

Uterus sizes at different terms of pregnancy



Uterus size at different term of gestation

Term of pregnancy (weeks)	Symphysis-Fundal height (cm)
16	6-7
20	12-13
24	20-24
28	24-28
32	28-30
36	32-34
40	28-32

True (authentic) signs of pregnancy

- Palpation of the fetal parts.
- Evidently audible fetal heart sounds.
- Active movements of the fetus felt by examiner.
- Cardiography of the fetus.
- The US examination of the fetus, which evidently shows fetal parts, or fertilized ovum in the uterus.

Laboratory diagnosis - HCG

- Immunological test of pregnancy - increased Beta-human chorionic gonadotropin level in blood serum and in urine. Detection in maternal serum and urine is evident only after implantation and vascular communication has been established with the decidua by the syncytiotrophoblast 8-10 days after conception.

hCG levels in weeks from the last normal menstrual period:

- 3 weeks LMP 5 – 50 mIU/ml
- 4 weeks LMP 5 – 426 mIU/ml
- 5 weeks LMP 18 – 7,340 mIU/ml
- 6 weeks LMP 1,080 – 56,500 mIU/ml
- 7-8 weeks LMP 7, 650 – 229,000 mIU/ml
- 9-12 weeks LMP 25,700 – 288,000 mIU/ml
- 13-16 weeks LMP 13,300 – 254,000 mIU/ml
- 17-24 weeks LMP 4,060 – 165,400 mIU/ml
- 25-40 weeks LMP 3,640 – 117,000 mIU/ml
- Women who are not pregnant <5.0 mIU/ml
- Women after menopause 9.5 mIU/ml

Laboratory diagnosis - Progesterone

- Viable intrauterine pregnancy can be diagnosed if the serum progesterone levels are greater than 25 ng/mL (>79.5 nmol/L).
- Conversely, finding serum progesterone levels of less than 5 ng/mL (< 15.9 nmol/L) can aid in the diagnosis of a nonviable pregnancy.

Pregnancy diagnosis: Sonography

- Transvaginal ultrasonography (TVUS), and transabdominal ultrasonography (TAUS) are used to determine:
- the fertiliezed ovum in the uterinbe cavity,
- the size of the uterus (term of gestation),
- cardiac motion can sometimes be identified in a 2- to 3-mm embryo but is almost always present when the embryo grows to 5 mm or longer. At 5-6 weeks' gestation, the fetal heart rate ranges from 100-115 beats per minute. At 9 week of gestation the heart rate ranges from 140 bpm.

Laboratory diagnosis - Progesterone

- Viable intrauterine pregnancy can be diagnosed if the serum progesterone levels are greater than 25 ng/mL (>79.5 nmol/L).
- Conversely, finding serum progesterone levels of less than 5 ng/mL (< 15.9 nmol/L) can aid in the diagnosis of a nonviable pregnancy.

US exam

- The yolk sac can be recognized by 4-5 weeks' gestation and is seen until approximately 10 weeks' gestation. The yolk sac is a small sphere with a hypoechoic center and is located within the GS

END