Interhospital Lecture

Obstetric Anesthesia: Physiology and Pharmacology



Capt.Preecha Jongstapongpun,MD. FRCAT
Lt.Col.Nuanwan Phuvachoterojanaphokin, MD. FRCAT
Anesthesiologist
Department of Anesthesiology
Phramongkutklao hospital and College of Medicine

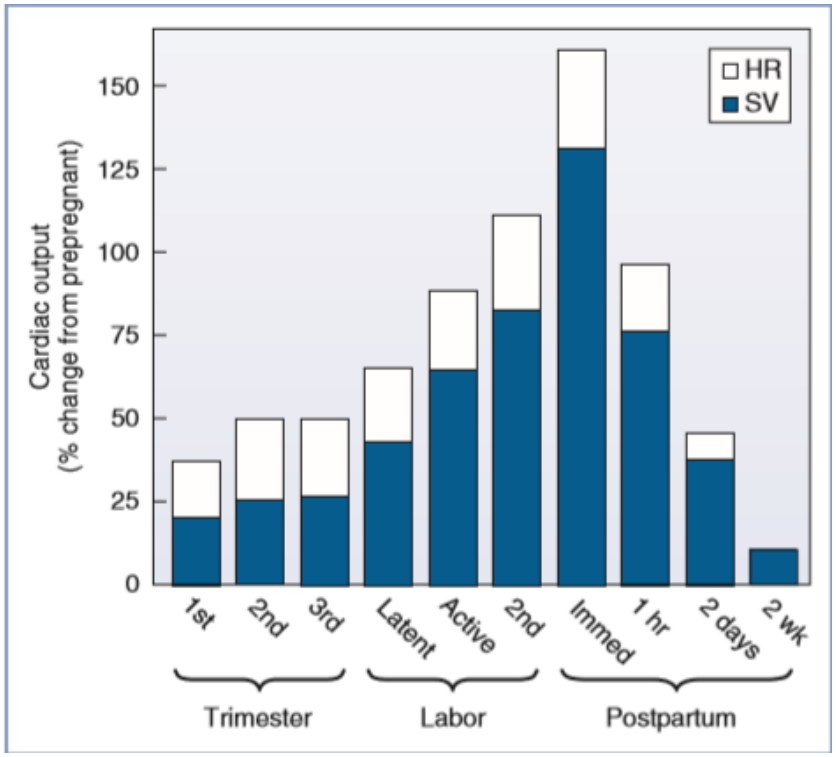
Outlines

- **Physiologic changes of pregnancy**
- **Uteroplacental physiology**
- **Placental transfer of drugs**

Physiologic changes of pregnancy

Cardiovascular changes

Central Hemodynamics



- CO **begins** to increase **by 5 weeks** gestation and is 35% to 40% above baseline
- CO approximately **50% greater than nonpregnant values in second trimester**
- **Immediate postpartum period CO as much as 75% above predelivery measurements**
- CO decreases to just below **prelabor** values at 24 hours postpartum **and returns to prepregnancy levels between 12 and 24 weeks postpartum**

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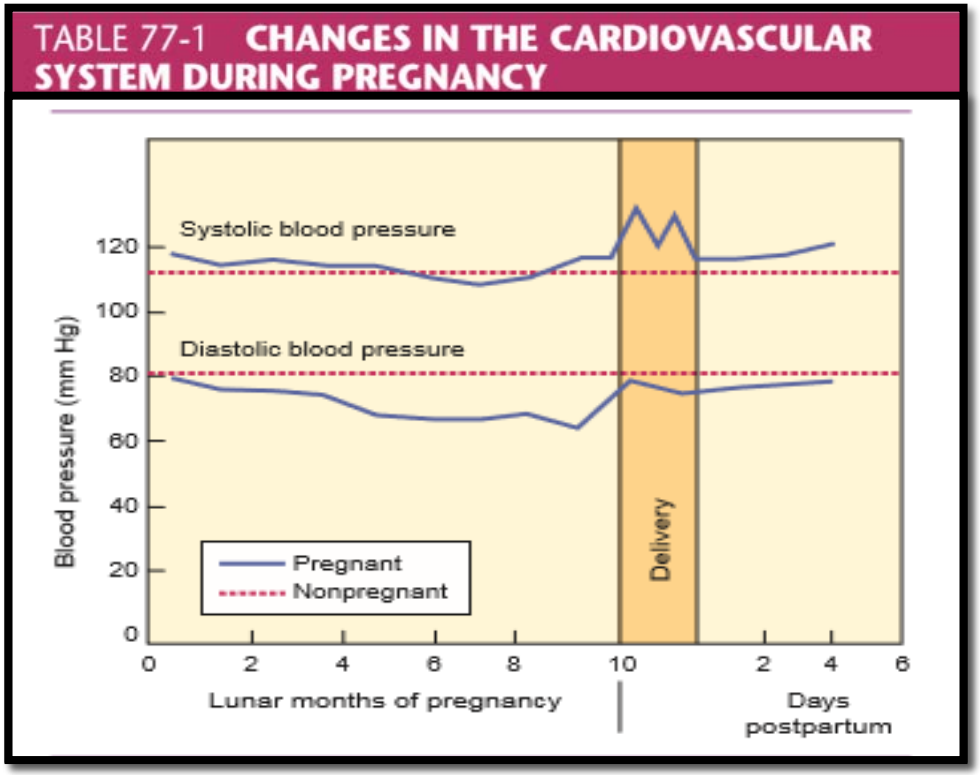
Cardiovascular changes

Central Hemodynamics



- BP decreases slightly because the **decrease in peripheral resistance exceeds the increase in CO**
- DBP decreases more than SBP,with early to mid-gestational decreases of approximately 20%

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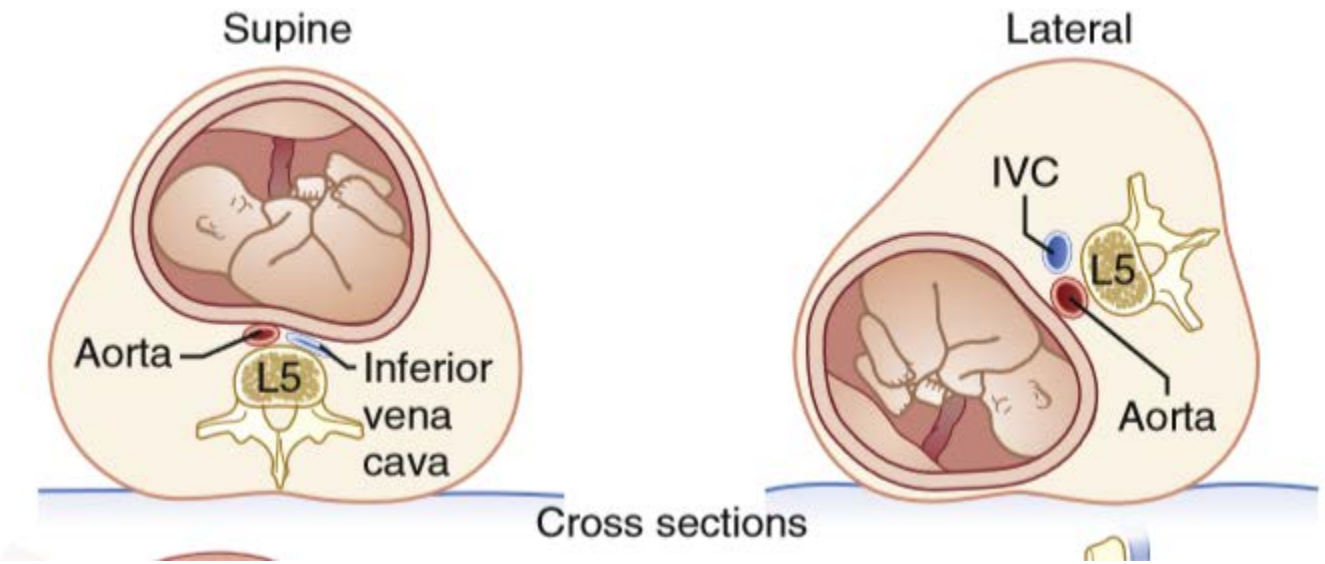
Cardiovascular changes

Supine hypotensive syndrome



- **Onset : 2nd trimester**
- **Maximum effect : 36 to 38 weeks of gestation**

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Cardiovascular changes

Physical Examination and Cardiac Studies

- Causes the heart to increase in size, a result of both greater blood volume and increased stretch and force of contraction
- Elevation of the diaphragm

Changes in the Cardiac Examination in the Pregnant Patient

- Accentuation of first heart sound (S_1) and exaggerated splitting of the mitral and tricuspid components
- Typical systolic ejection murmur
- Possible presence of third heart sound (S_3) and fourth heart sound (S_4); no clinical significance
- Leftward displacement of point of maximal cardiac impulse

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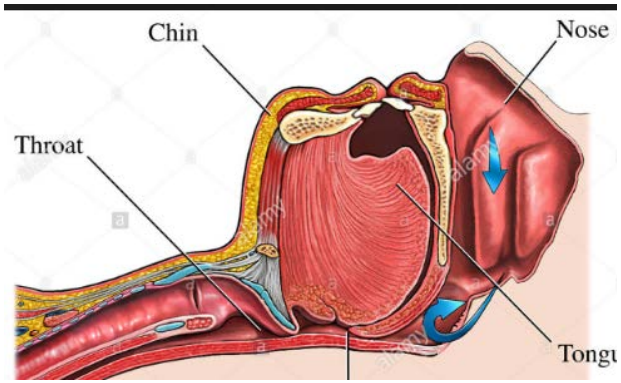
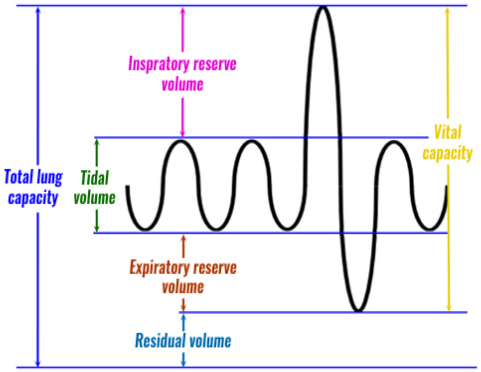
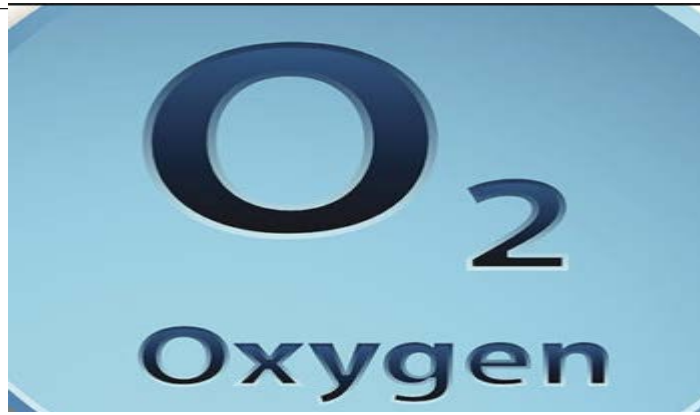
Respiratory changes

- **Pregnancy results in significant alterations**







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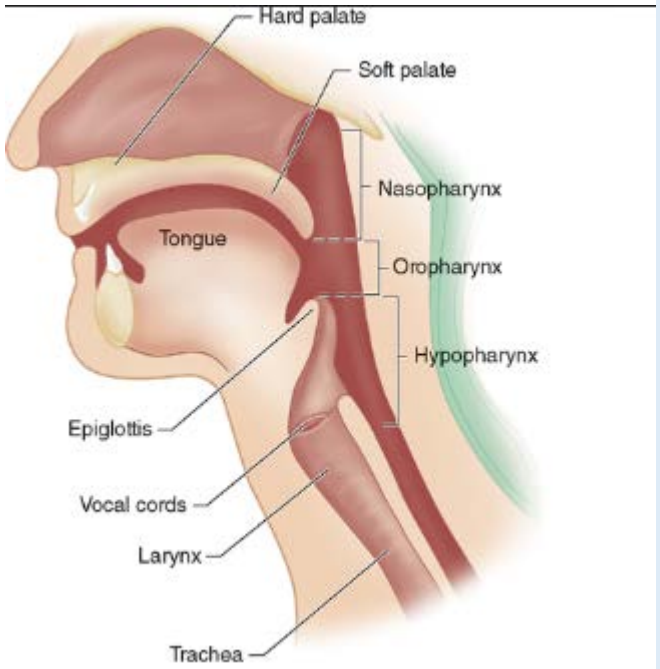
Respiratory changes



- **Capillary engorgement of the larynx and the nasal and oropharyngeal mucosa begins early in the first trimester**
- **During pregnancy can cause severe bleeding, especially on insertion of nasal airways or NG or ETT .**
- **↑ risk difficult ventilation and intubation**
- **Use smaller size ETT cuffed (6.5-7)**
- **Airway edema may be particularly severe in women with preeclampsia**
- **Weight gain , short neck , increase breast tissue → short-handled laryngoscope**

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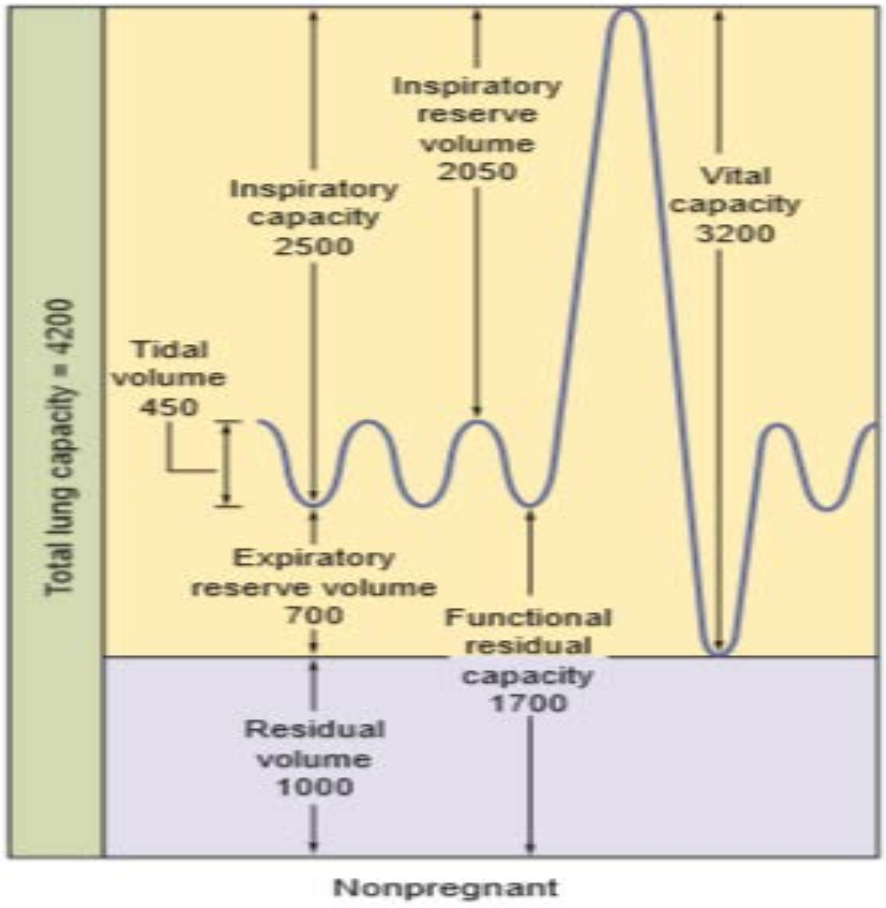
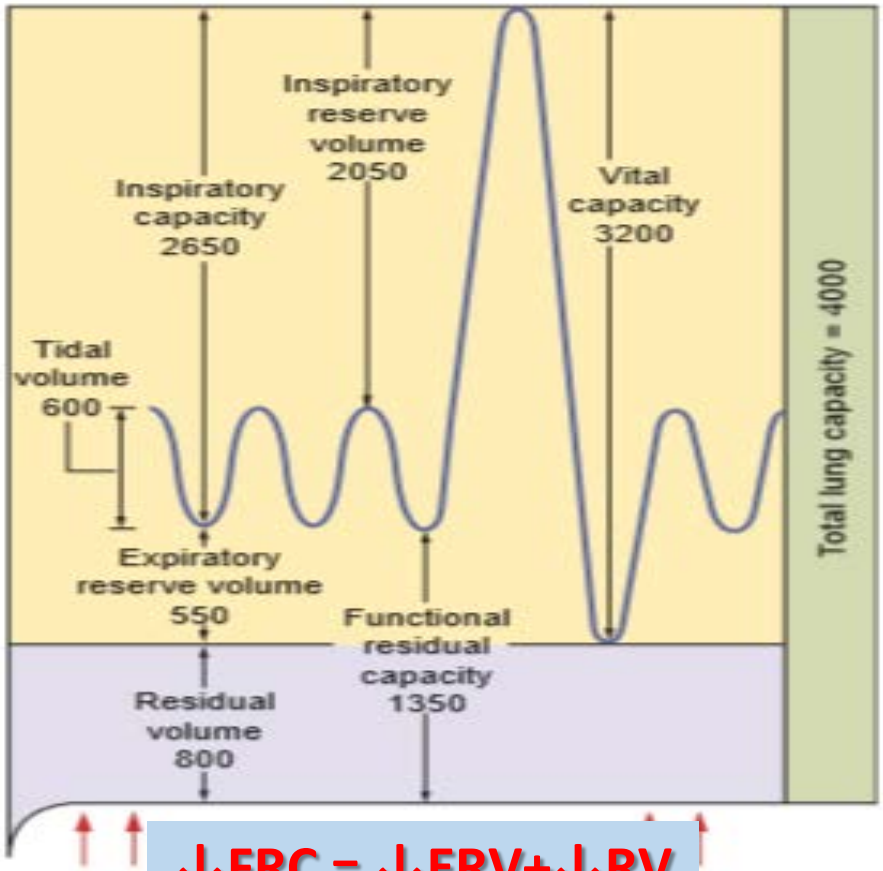
Respiratory changes





↓FRC = ↓ERV+↓RV

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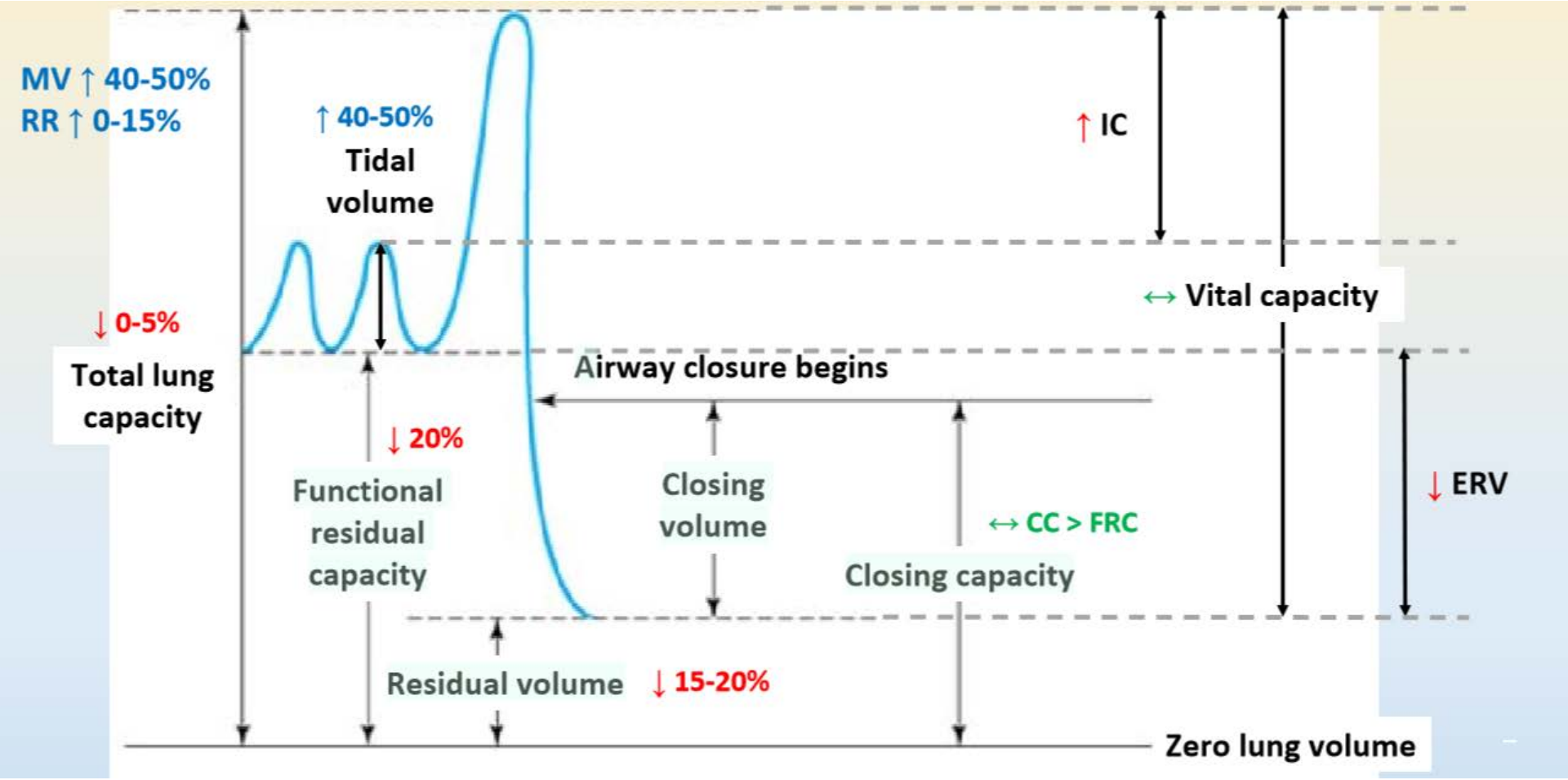
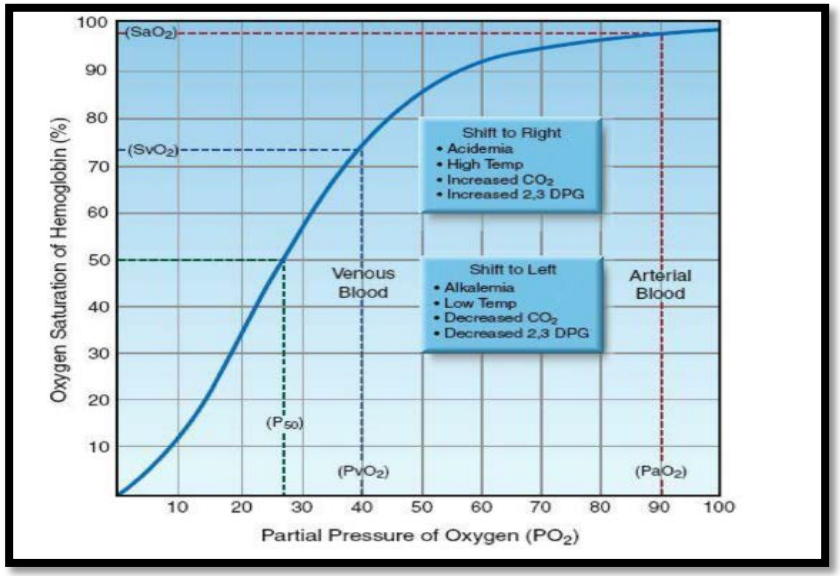
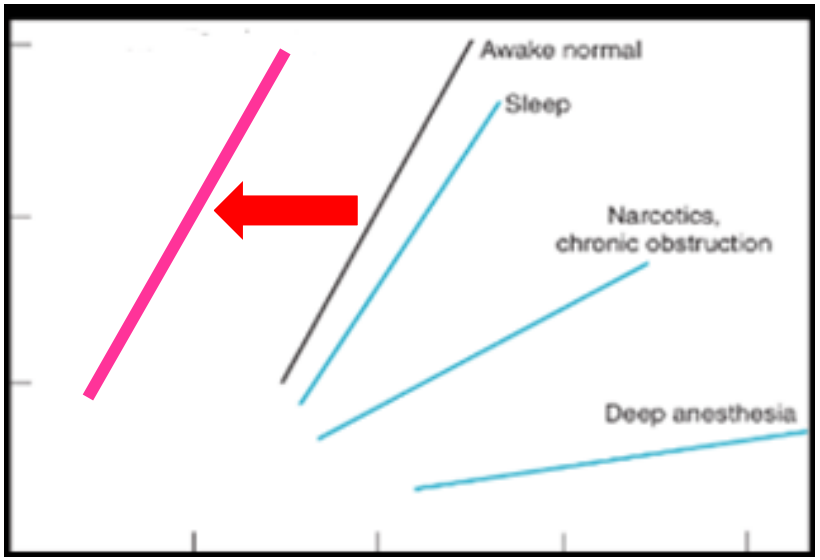
Respiratory changes



Respiratory changes





- Increase minute ventilation
- Increases CO_2 production
- Increase basal oxygen consumption 20%
- Reduction in the $PaCO_2$ to 28 to 32 mmHg and an increase in the PaO_2 to 106 mmHg
- Rightward shift of O_2-Hb dissociation curve(P_{50} 27 to 30 mmHg)
- Arterial pH remain constant

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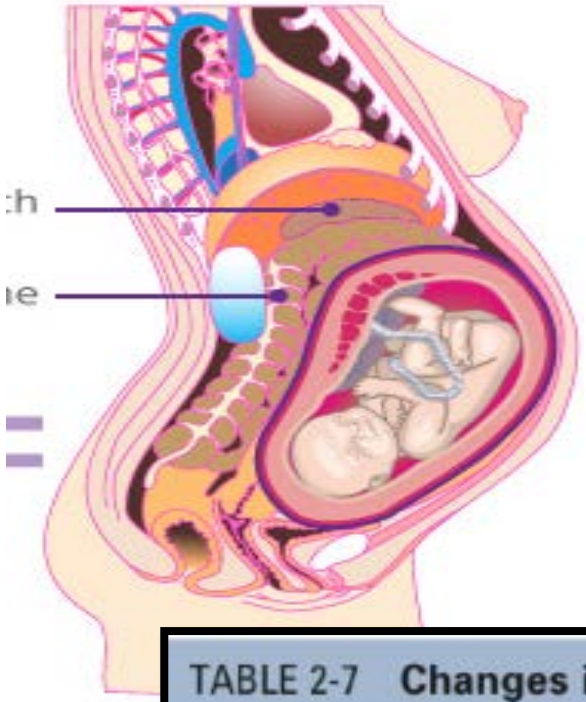
Gastrointerstinal changes



- ↓lower esophageal high-pressure zone (LEHPZ), which normally prevents the reflux of gastric contents.
- Progestin and stomach displaced
- The prevalence of GERD is approximately 10% in the first trimester, 40% in the second trimester, and 55% in the third trimester.

TABLE 2-7 Changes in Gastrointestinal Physiology during Pregnancy*

Parameter	Trimester		
	FIRST	SECOND	THIRD
Barrier pressure†	Decreased	Decreased	Decreased
Gastric emptying	No change	No change	No change
Gastric acid secretion	No change	No change	No change

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Gastrointerstinal changes

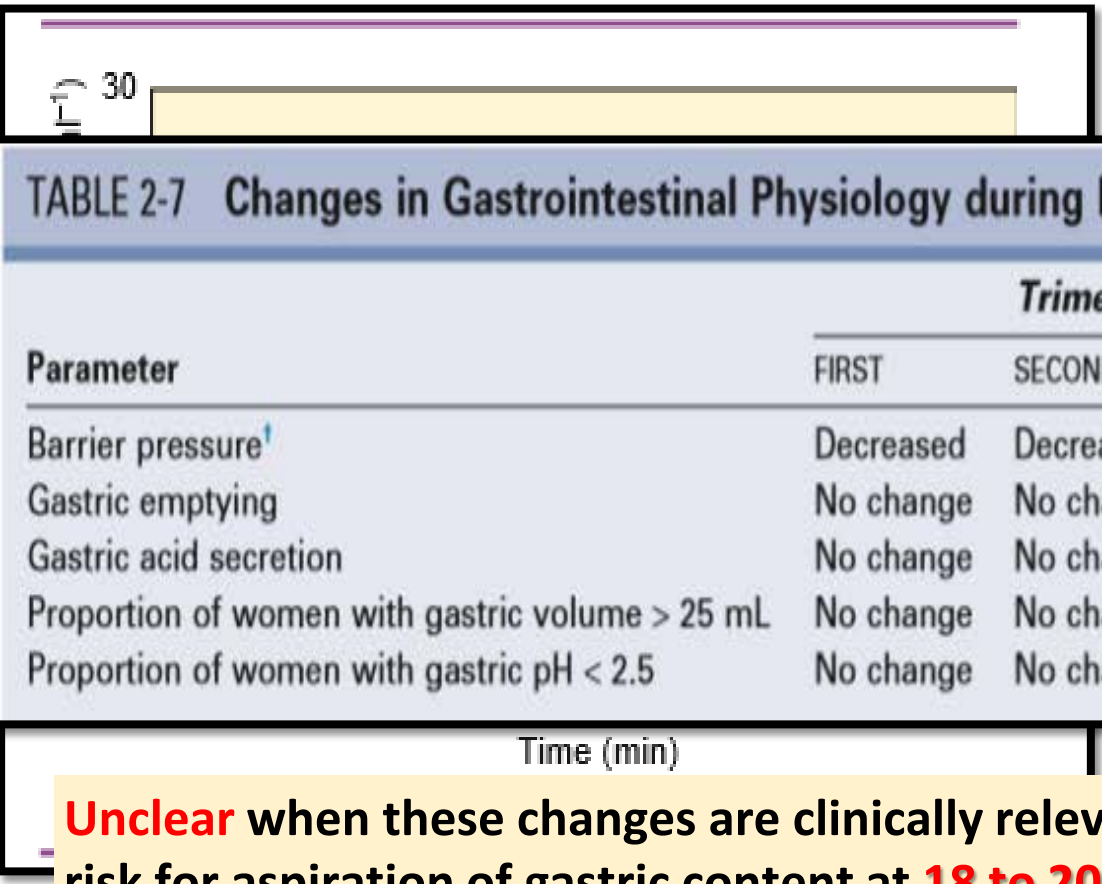

TABLE 2-7 Changes in Gastrointestinal Physiology during Pregnancy*

Parameter	Trimester			Labor	Postpartum (18 h)
	FIRST	SECOND	THIRD		
Barrier pressure†	Decreased	Decreased	Decreased	Decreased	?
Gastric emptying	No change	No change	No change	Delayed	No change
Gastric acid secretion	No change	No change	No change	?	?
Proportion of women with gastric volume > 25 mL	No change	No change	No change	Increased	No change
Proportion of women with gastric pH < 2.5	No change	No change	No change	No change	No change

Unclear when these changes are clinically relevant some consider all women at risk for aspiration of gastric content at 18 to 20 weeks but certainly any woman with symptoms of acid reflux , should be considered at risk.

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Hematologic changes

Cardiovascular Parameter	Value at Term Compared With Nonpregnant Value
Intravascular fluid volume	Increased 35%-45%
Plasma volume	Increased 45%-55%
Erythrocyte volume	Increased 20%-30%
Cardiac output	Increased 40%-50%
Stroke volume	Increased 25%-30%
Heart rate	Increased 15%-25%
Systemic vascular resistance	Decreased 20%
Pulmonary vascular resistance	Decreased 35%
Central venous pressure	No change
Pulmonary capillary wedge pressure	No change
Femoral venous pressure	Increased 15%
Coagulation System	
Increased factors	I, VII, VIII, IX, X, XII, and von Willebrand factor
Decreased factors	XI, XIII, antithrombin III, and tPA
Platelets	Decreased 0%-10%

- Mineralocorticoid activity → sodium and water retention
- ↑Plasma volume > ↑RBC volume
- Dilutional anemia (Hct 35%) plateau at GA 32-34weeks
- Hypercoagulable state
- 20% decreased PT, PTT
- ↔ factor II, V
- Serum cholinesterase activity declines to a level of 20% below normal but not clinical significant
- Leukocytosis, Neutrophilia

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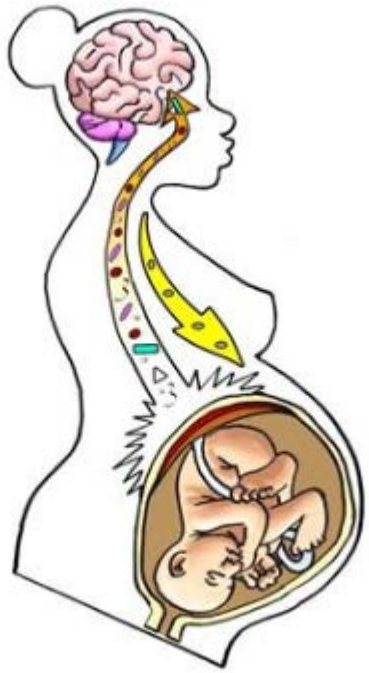
Neurologic changes



- **MAC for inhalation agents is decreased 30 % by 8 to 12 weeks of gestation and may be related to an increase in progesterone levels.**
- **Maximal cephalad block level after neuraxial administration of LA is higher in the 2nd to 3rd trimester**
- **Epidural venous engorgement, decreases intrathecal volume, increased sensitivity LA**

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Anesthetic implication

- **Positioning**

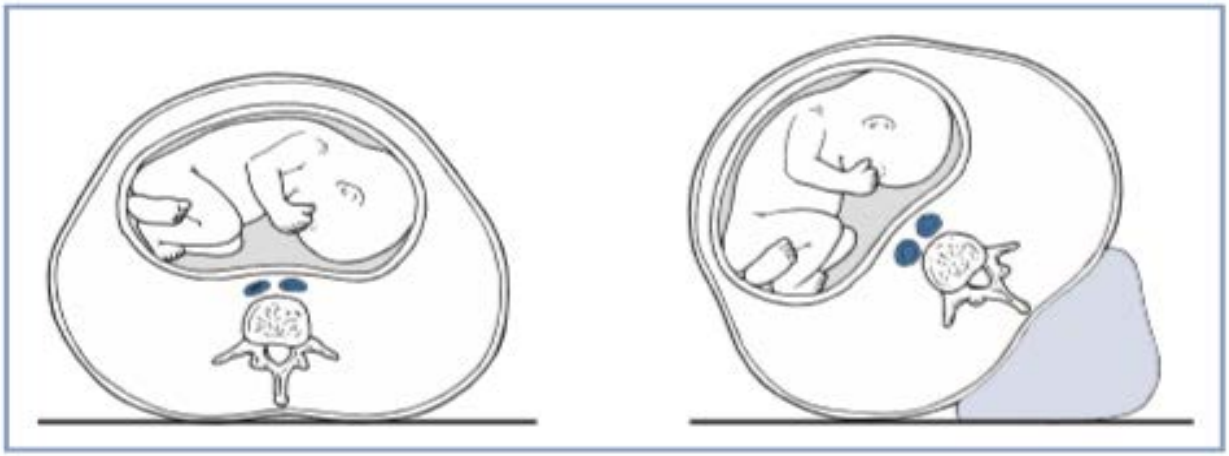

FIGURE 2-12 ■ **Compression of the aorta and inferior vena cava in the supine (*left*) and lateral tilt (*right*) positions.** (Redrawn from Camann WR, Ostheimer GW. Physiologic adaptations during pregnancy. Int Anesthesiol Clin 1990; 28:2-10.)

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Anesthetic implication

- **Positioning**

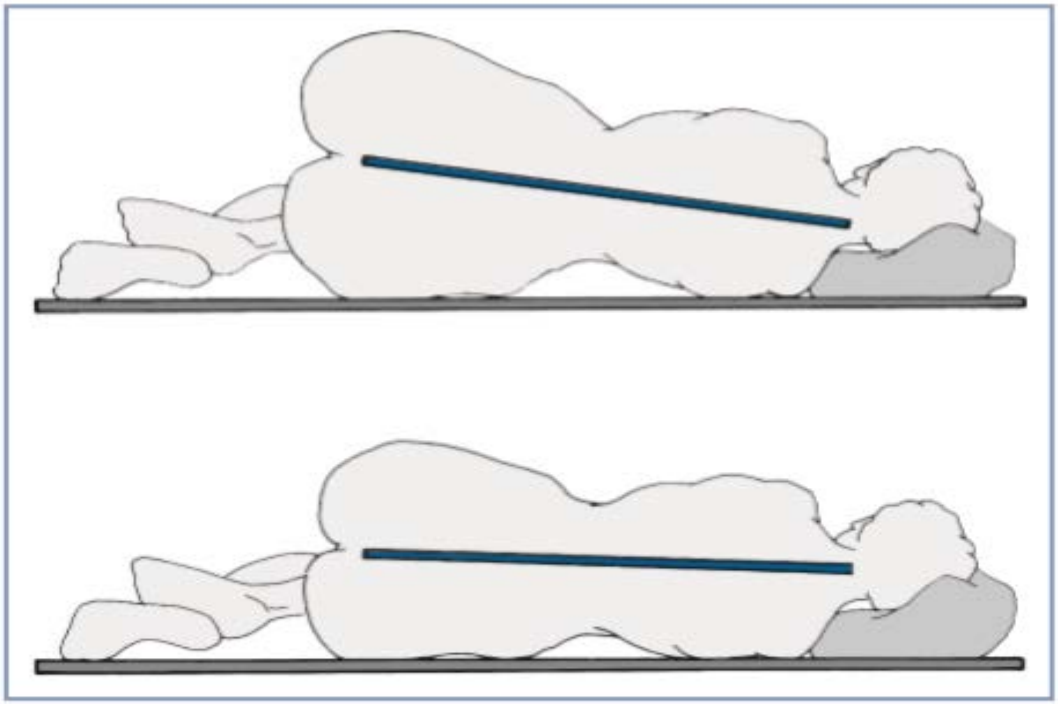

FIGURE 2-14 ■ Pelvic widening and resultant head-down tilt in the lateral position during pregnancy. *Upper panel,* pregnant; *lower panel,* nonpregnant. (Modified from Camann WR, Ostheimer GW. Physiological adaptations during pregnancy. Int Anesthesiol Clin 1990; 28:2-10.)

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Anesthetic implication

- **General Anesthesia : airway management, oxygenation, and ventilation**

BOX 2-3 Considerations for General Anesthesia during Pregnancy

DRUGS

- Propofol
  - Induction dose decreased
  - Elimination half-life unaltered
- Thiopental
  - Induction dose decreased
  - Elimination half-life prolonged
- Volatile anesthetic agents
  - Minimum alveolar concentration (MAC) decreased, but unclear whether hypnotic dose requirement differs from that in nonpregnant women
  - Speed of induction increased
- Succinylcholine
  - Duration of blockade unaltered
- Rocuronium
  - Increased sensitivity
- Chronotropic agents and vasopressors
  - Decreased sensitivity

TRACHEAL INTUBATION

- Increased rate of decline of Pa_{O_2} during apnea
- Smaller endotracheal tube required (6.5 or 7.0 mm)
- Increased risk of failed intubation with traditional laryngoscopy
- Increased risk of bleeding with nasal instrumentation

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Anesthetic implication

- **Neuraxial Analgesia and Anesthesia**

BOX 2-4 Neuraxial Anesthesia:

ANESTHETIC IMPLICATIONS OF MATERNAL PHYSIOLOGIC CHANGES

TECHNICAL CONSIDERATIONS

- Lumbar lordosis increased
- Apex of thoracic kyphosis at higher level
- Head-down tilt when in lateral position

TREATMENT OF HYPOTENSION

- Decreased sensitivity to vasopressors*

LOCAL ANESTHETIC DOSE REQUIREMENTS†

- Subarachnoid dose reduced 25%
- Epidural dose unaltered or slightly reduced

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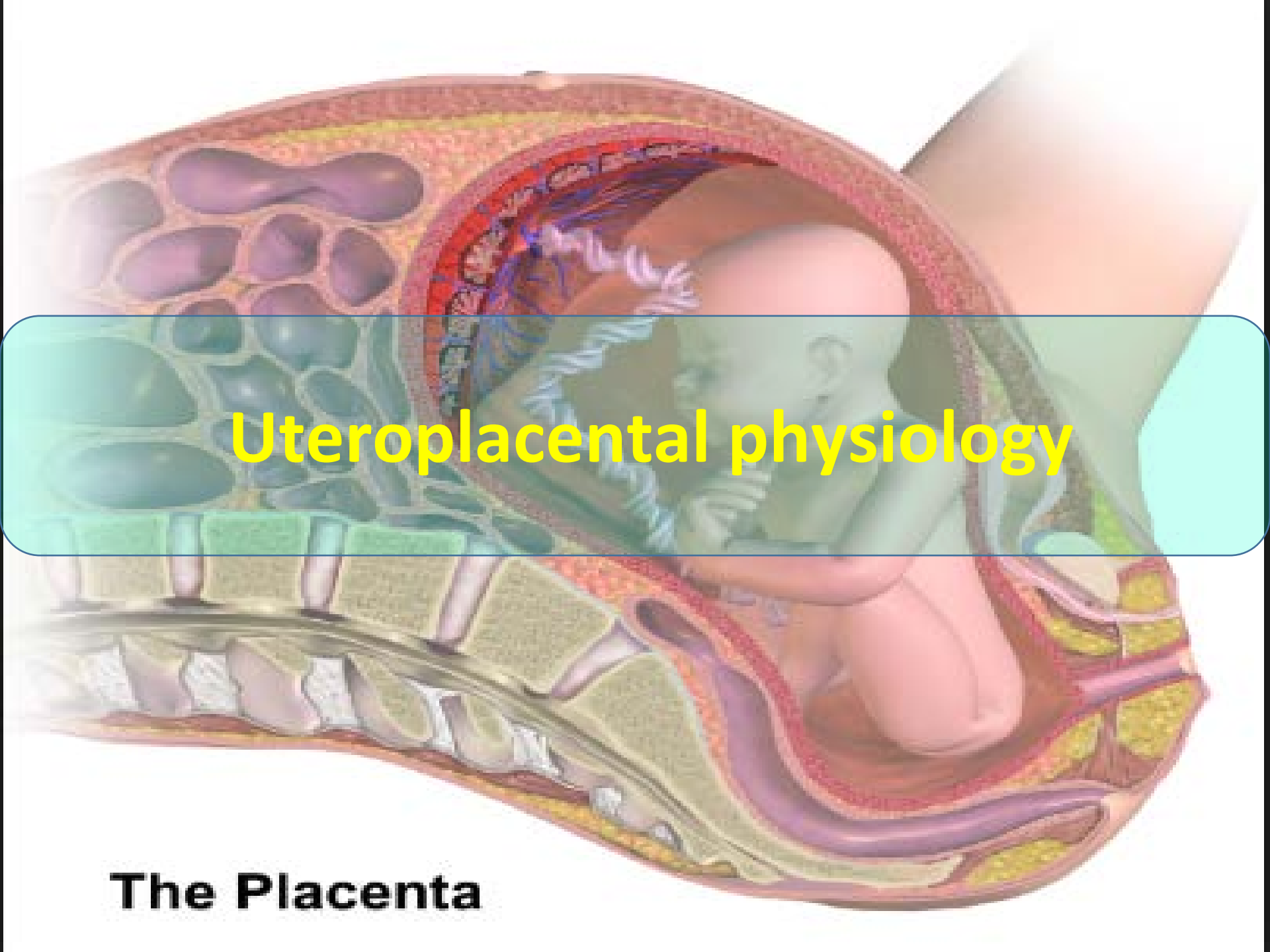
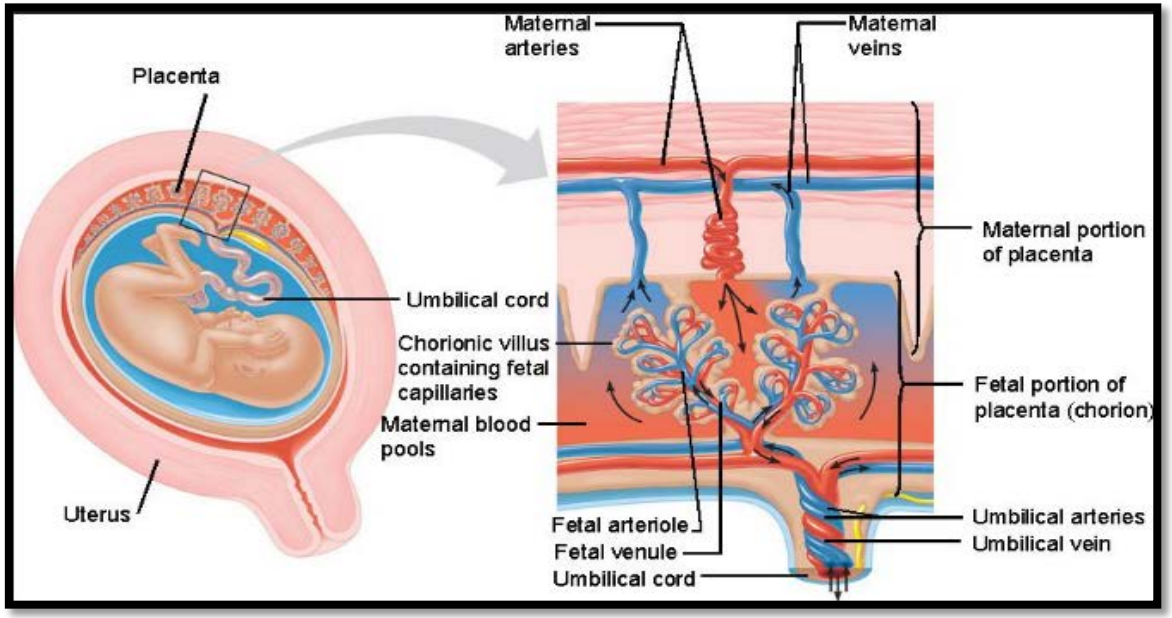
Uteroplacental physiology



Uterine blood flow



- UBF increases progressively during pregnancy (100ml/min-700ml/min)(~10%CO)
- 80% of the uterine blood flow perfuses the intervillous space perfuses the myometrium
- During pregnancy has minimal autoregulation, and the vasculature remains essentially fully dilated

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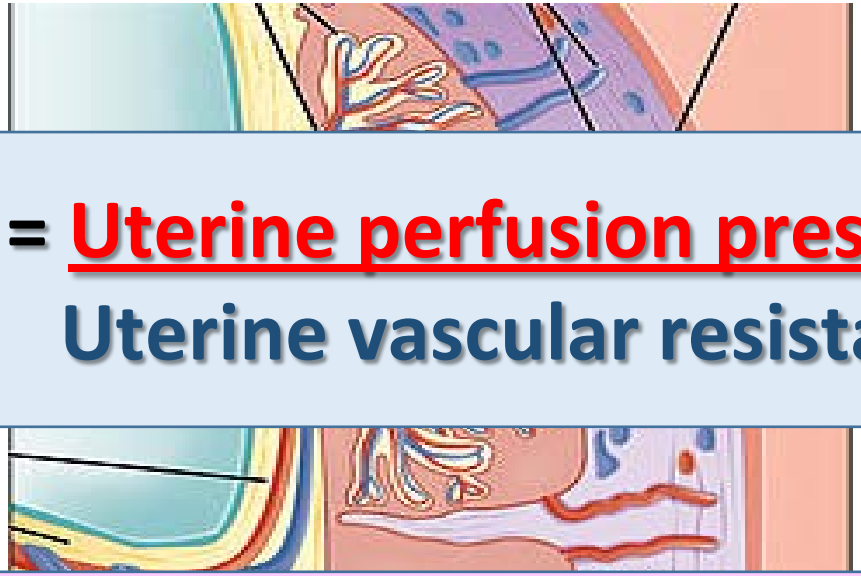
Uterine blood flow



$$UBF = \frac{\text{Uterine perfusion pressure}}{\text{Uterine vascular resistance}}$$

$$UBF = \frac{\text{Uterine arterial pressure - Uterine venous pressure}}{\text{Uterine vascular resistance}}$$

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Causes of decreased Uterine Blood Flow

UBF = Uterine arterial pressure-Uterine venous pressure
Uterine vascular resistance

↓Uterine arterial pressure

- Aortocaval compression
- Hemorrhage/hypovolemia
- Hypotension during sympathetic blockade

↑Uterine venous pressure

- Vena caval compression
- Uterine contractions
- Drug-induced uterine tachysystole (oxytocin, local anesthetics)

↑Uterine vascular resistance

- Stress
- Vasopressors (phenylephrine > ephedrine)
- Local anesthetics (in high concentrations)
- Extreme hypocapnia ($PaCO_2$ < 20 mm Hg)

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Placental Drug Transfer

Placental drug transfer

- Drugs cross biologic membranes by **simple diffusion**

$$Q/t = KA(C_m - C_f)/D$$

- Q/t is the rate of diffusion
- K is the diffusion constant
- A is the surface area
- C_m is the concentration of free drug in maternal blood
- C_f is the concentration of free drug in fetal blood
- D is the thickness of the diffusion barrier

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Placental drug transfer

$$Q/t = KA(C_m - C_f)/D$$

K : diffusion constant depend on physicochemical of drugs

- **Molecular size(<500Da or >500-1000 Da)**
- **Lipid solubility**
- **Degree of ionization**

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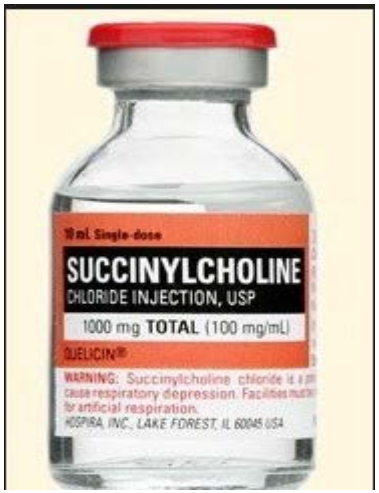
Placental drug transfer

➢ **High molecular weight and poor lipid solubility of nondepolarizing neuromuscular blocking drugs result in limited ability of these drugs to cross the placenta**



➢ **Succinylcholine has a low molecular weight but is highly ionized and therefore does not readily cross the placenta**

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Placental drug transfer

- **Henderson—Hasselbalch equation**

Log (cationic form/uncharged form) = pKa-pH

- ➢ **In acidotic fetus, local anesthetics may be relatively more ionized than in maternal blood, and "ion trapping" may occur, leading to fetal drug accumulation**
- ➢ **Bradycardia, ventricular arrhythmias, severe cardiac depression**

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Placental drug transfer

TABLE 4-1 Factors Affecting Placental Transfer of Drug (Maternal to Fetal)

	Increased Transfer	Decreased Transfer
	drug in maternal plasma	

- General consideration, drugs that readily cross the blood-brain barrier also readily cross the placenta (induction,inhalation,opioid,BZP,anticholinergic agents)

Drugs That Do Not Readily Cross the Placenta

Anticholinergic agent
- Glycopyrrolate

Anticoagulants
- Heparin

Muscle relaxants
- Depolarizing: succinylcholine
- Nondepolarizing agents

Vasopressor
- Phenylephrine

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Placental drug transfer

$$Q/t = KA(C_m - C_f)/D$$

- **Maternal blood concentration of a drug is typically the primary determinant of how much drug will ultimately reach the fetus**
- **Dose**
- **Mode and site of administration**

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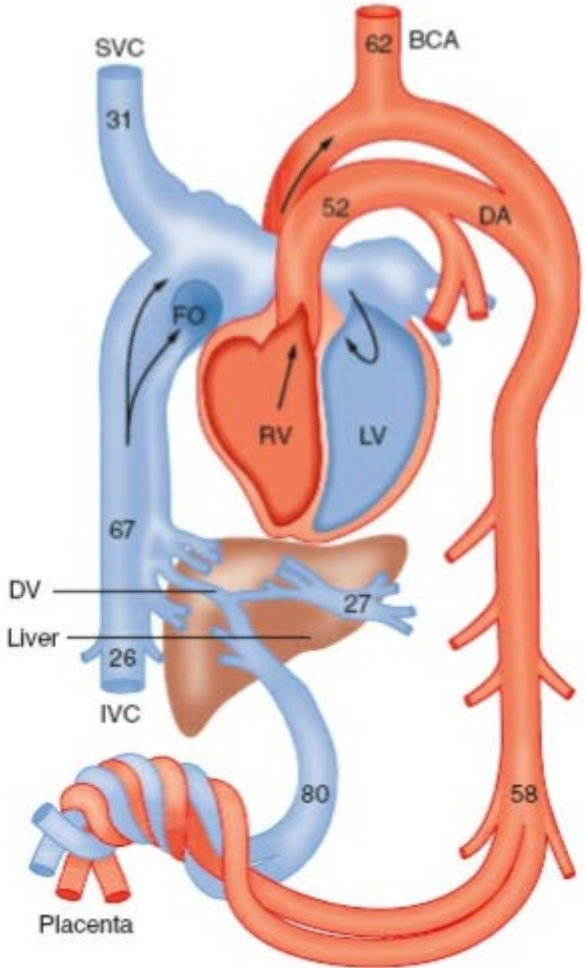
Placental drug transfer



Delay the depressant effects and onset of anesthetic drugs in fetus

I. **Liver is the first fetal organ perfused by the umbilical venous blood, which carries drug to the fetus.**

II. **Dilution of umbilical vein blood by venous blood from GI , head and extremities**

- **During asphyxia and acidosis ???**
- **Induction-to- delivery interval ???**
- **Uterine incision to delivery interval ???**

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Take home messages

- **Physiologic changes** of pregnancy begin in the **1st trimester** and continue to the postpartum period
- **Paturients in labor** are considered **"full stomach"** and risk for pulmonary aspiration
- **Maintain uteroplacental perfusion pressure**
- Drugs cross biologic membranes by **simple diffusion**
- Drugs that readily **cross the blood-brain barrier** also **readily cross the placenta**
- **Delay the depressant effects** and onset of anesthetic drugs in fetus

Thank you for your attention