

# **Maternal Physiologic Adaptations to Pregnancy**

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# OBJECTIVES

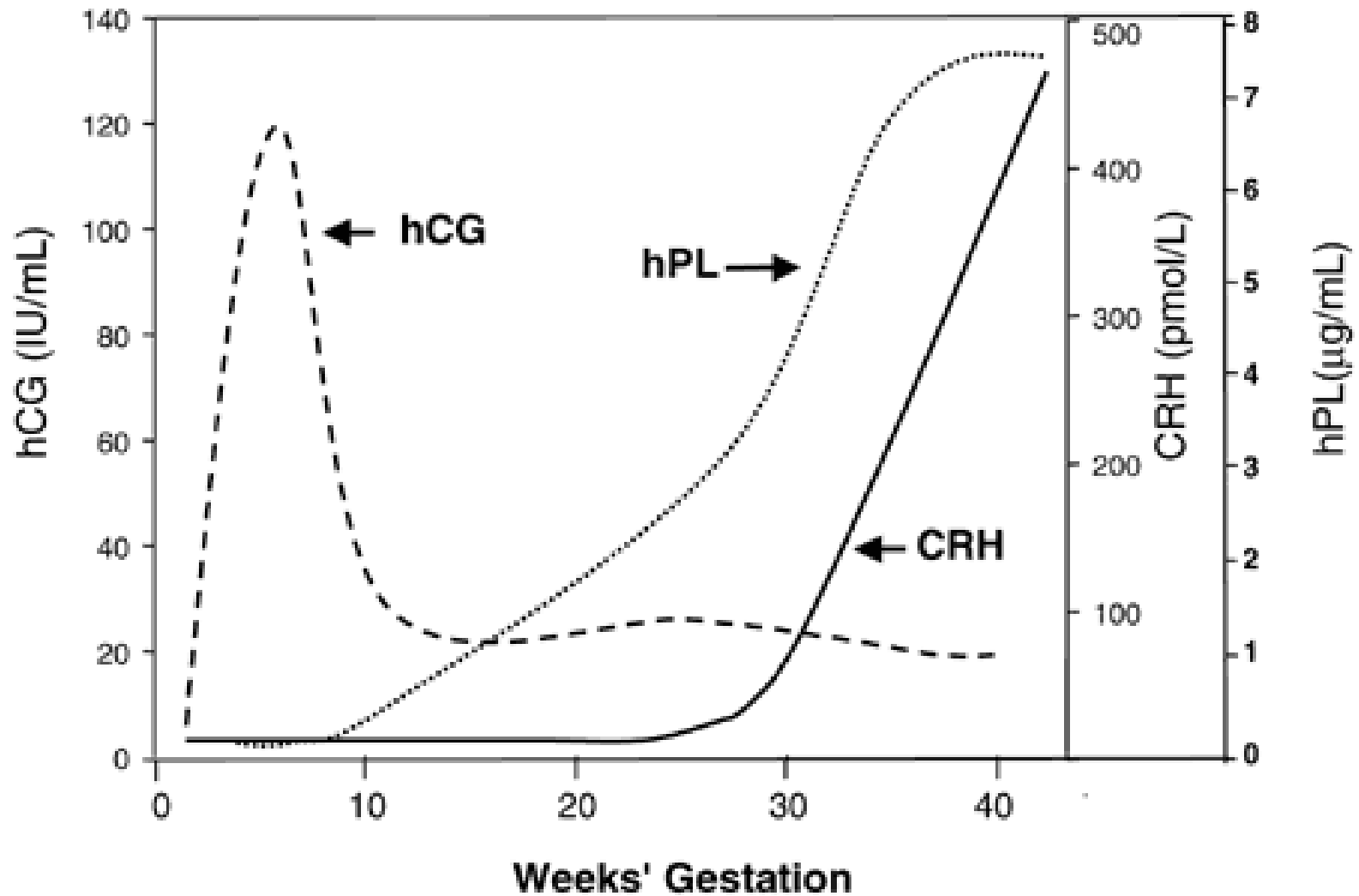
- **To be able to describe the maternal physiological adjustments to pregnancy**
- **To be aware of the importance of the fetus in controlling its destiny**
- **To appreciate that pregnancy can be associated with changes that maybe pathological in non-pregnant women**
- **To respect the state of maternal tolerance and co-existence with the fetus**

# Reasons

- **To retain conception (immunologic tolerance)**
- **To accommodate the growing fetus**
- **To deliver oxygen & growth substrates to fetus**
- **To remove heat & waste products**
- **Expel fetus when separate survival possible**

# Question!

- 22 year old woman had a last menstrual period about 6 weeks ago. She had abdominal pain and ultrasound showed an ovarian cyst. Emergency surgery was done and the cyst was removed. Two days later she loses a pregnancy. What could have caused the pregnancy loss?



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# Human Chorionic Gonadotropin

- **Secreted by trophoblast**
- **Glycoprotein MW 40,000-45,000**
- **Alpha unit similar to LH & TSH**
- **Specific B sub-unit**
- **Pregnancy hormone**
- **8 days after ovulation, peaks at 60-90 days**
- **Maintains corpus luteum for up to 8 weeks**
- **Stimulates placental steroid production**
- **Stimulates fetal adrenal steroid production**
- **Stimulates fetal testes testosterone production**

# Human Placental Lactogen

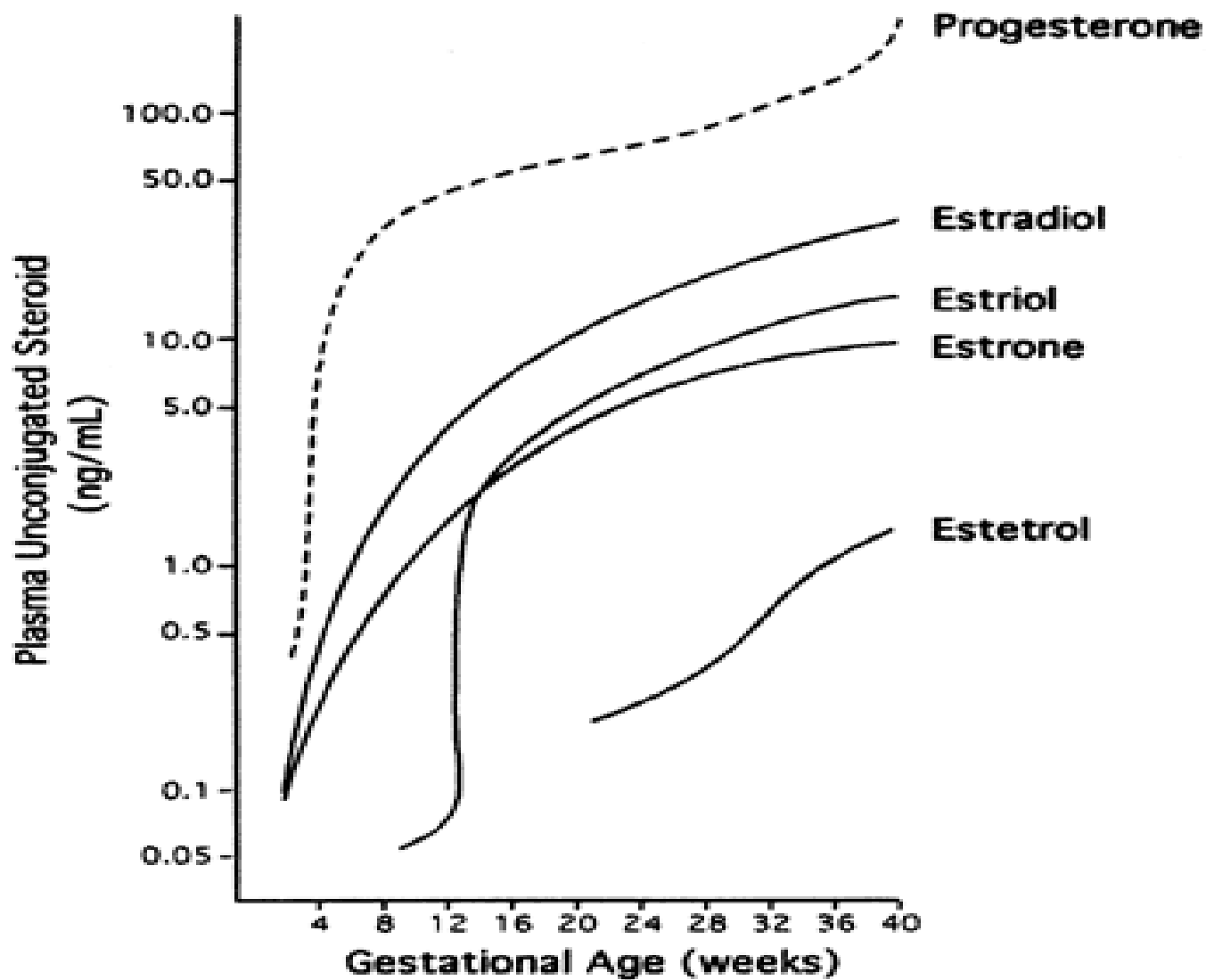
- **Similar to growth hormone**
- **Linked to placental mass**
- **Stimulated by insulin & insulin-like growth factor-1 & inhibited by PGE2 and PGF2**
- **Maternal lipolysis & increase in free fatty acids, providing energy for maternal metabolism.**
- **Anti-insulin or "diabetogenic" action provides glucose & amino acids for transport to fetus.**
- **A potent angiogenic hormone; role in fetal vasculature formation**

## Question 2

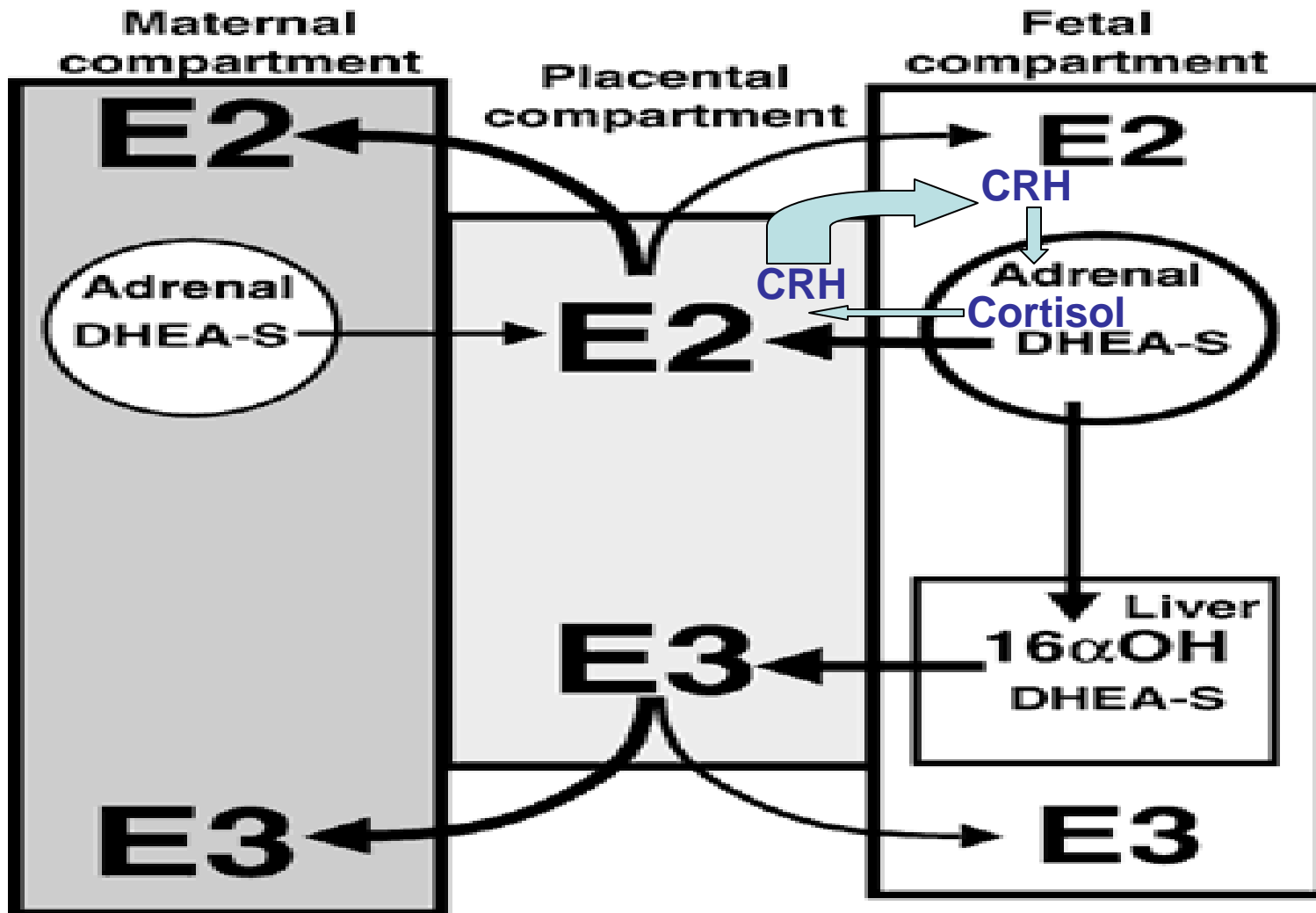
- **You tell your mother about fetal testing. She says when she was pregnant with you she had to collect urine for 24 hours weekly to check your well-being. She had to have an emergency cesarean because the urine test suggested you were in jeopardy inside. What is that about?**

# Progesterone

- **Produced by corpus luteum till 7-8 weeks then by placenta & persist after fetal demise**
- **Level rises till delivery**
- **Maintains uterine quiescence**
- **Establishes immune tolerance for conception**



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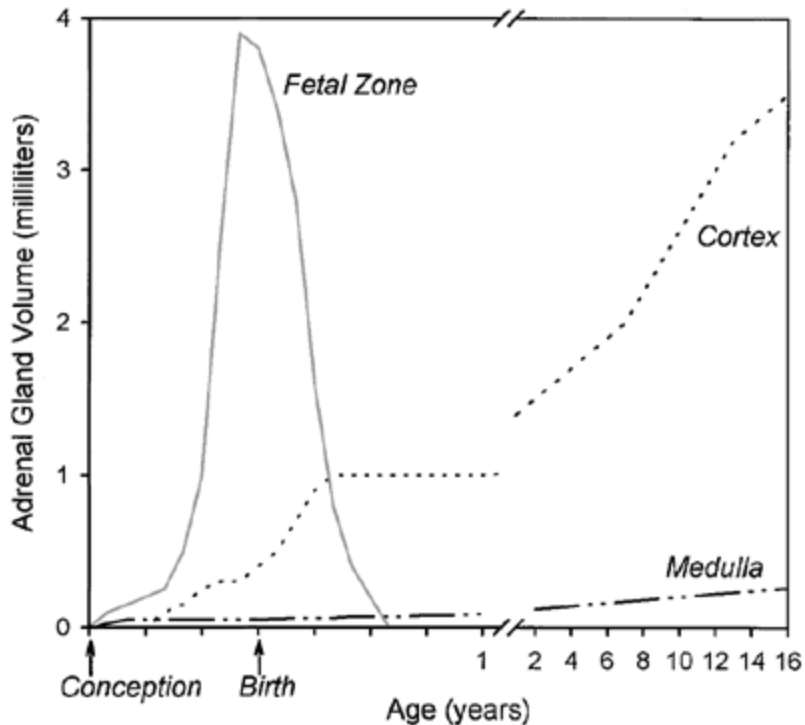
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# Estrogen

- **DHEA-S produced by fetal adrenal glands, is converted to (16 OHDHEA-S) in the fetal liver.**
- **DHEA-S is converted in the placenta to 17 - estradiol (E2)**
- **16 OHDHEA-S, is converted in placenta to estriol (E3).**
- **Near term, half of E2 is from fetal adrenal & half from maternal DHEA-S.**
- **90 % of E3 in the placenta arises from fetal 16 OHDHEA-S & 10 % from all other sources.**



# Fetal adrenal gland

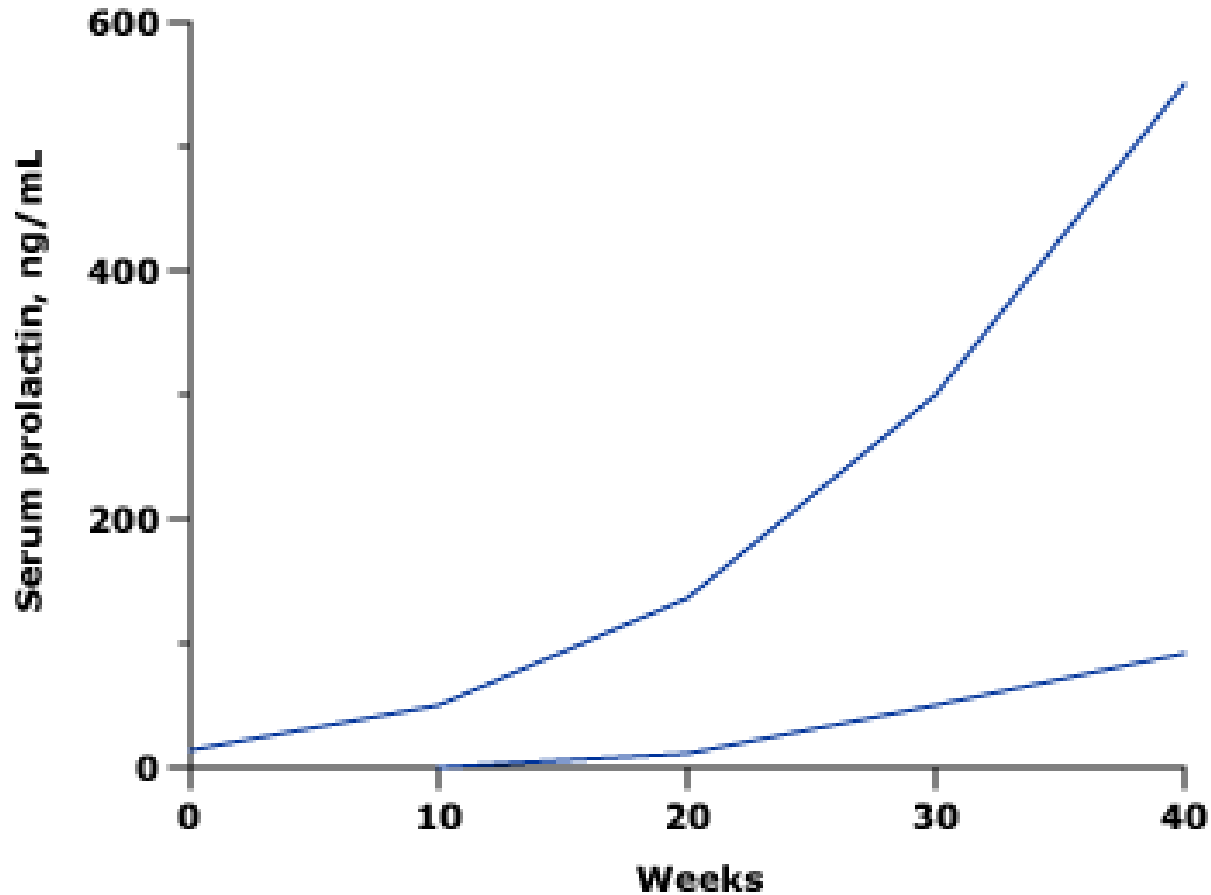


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Outer cortex	→	Cortisol
Fetal zone	→	DHEAS
Medulla	→	Catecholamine

**Cortisol induces fetal lung maturity**  
**Involved in labor initiation**

## Serum Prolactin levels in pregnancy



Stimulated  
by estrogen

Postpartum  
milk  
production

Fluid &  
electrolyte  
shifts  
across fetal  
membranes

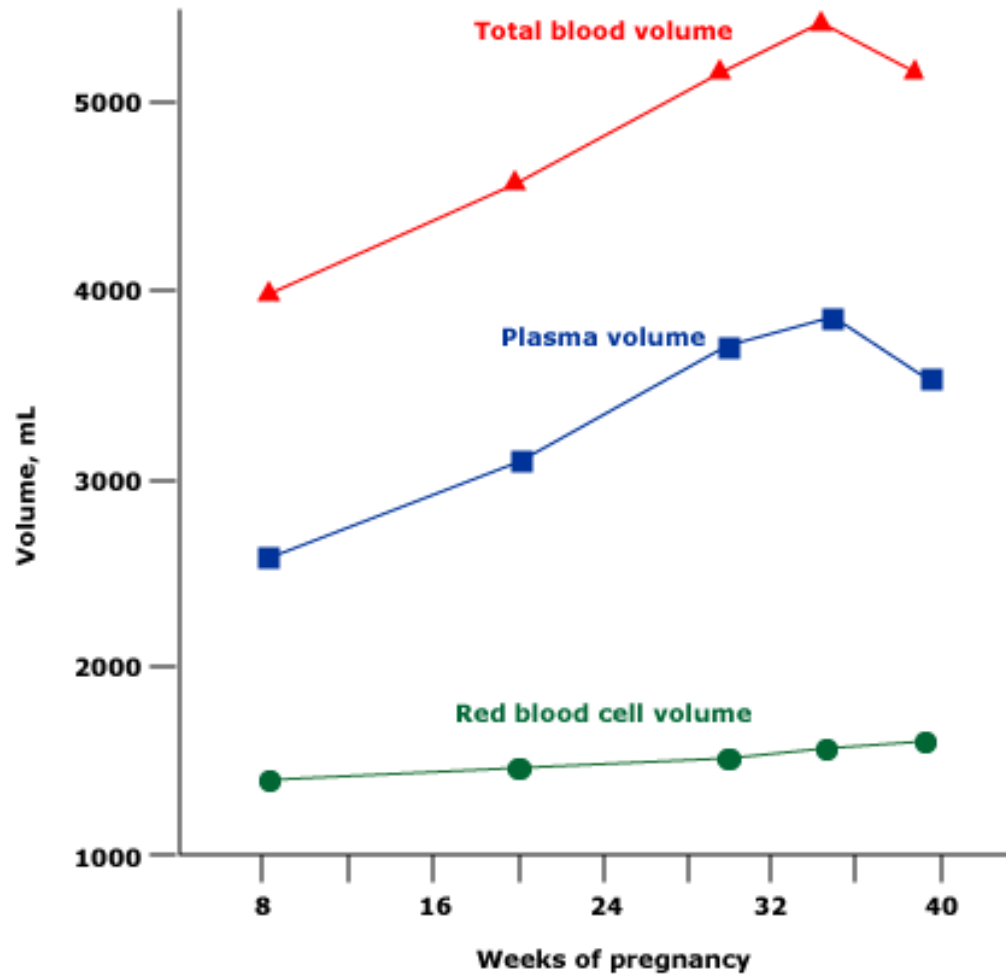
## Question 3

- 28 year old female had in vitro fertilization and is 32 weeks pregnant with twins. She presents with shortness of breath, dyspnea on mild exertion with heat intolerance, pulse is 102, blood pressure is 90/60 which is lower than her regular BP of 120/80. There is displacement of the apical pulsation and a systolic murmur is present. She has 4+ bilateral lower limb edema. What is the most likely diagnosis?

# Maternal total blood volume and cardiac output mechanisms

- **Erythrocyte volume increases due to erythropoietic effect of placental HPL, progesterone, & prolactin.**
- **Maternal blood volume increases due to uteroplacental circulation functioning as a low-resistance circuit.**
- **This increases cardiac output and nutrient delivery for further growth of the products of gestation.**
- **Thus a feedback mechanism with fetal growth/increasing steroidogenesis by the developing fetal adrenal gland result in the maternal cardiovascular adaptations to pregnancy that optimize further fetal development.**
- **In certain complications of pregnancy the less-than-normal maternal blood volume increase may result from failure of these mechanisms, while in turn contributing to the further genesis of these disorders.**

## Total blood volume, plasma volume and red cell volume in normal pregnancy

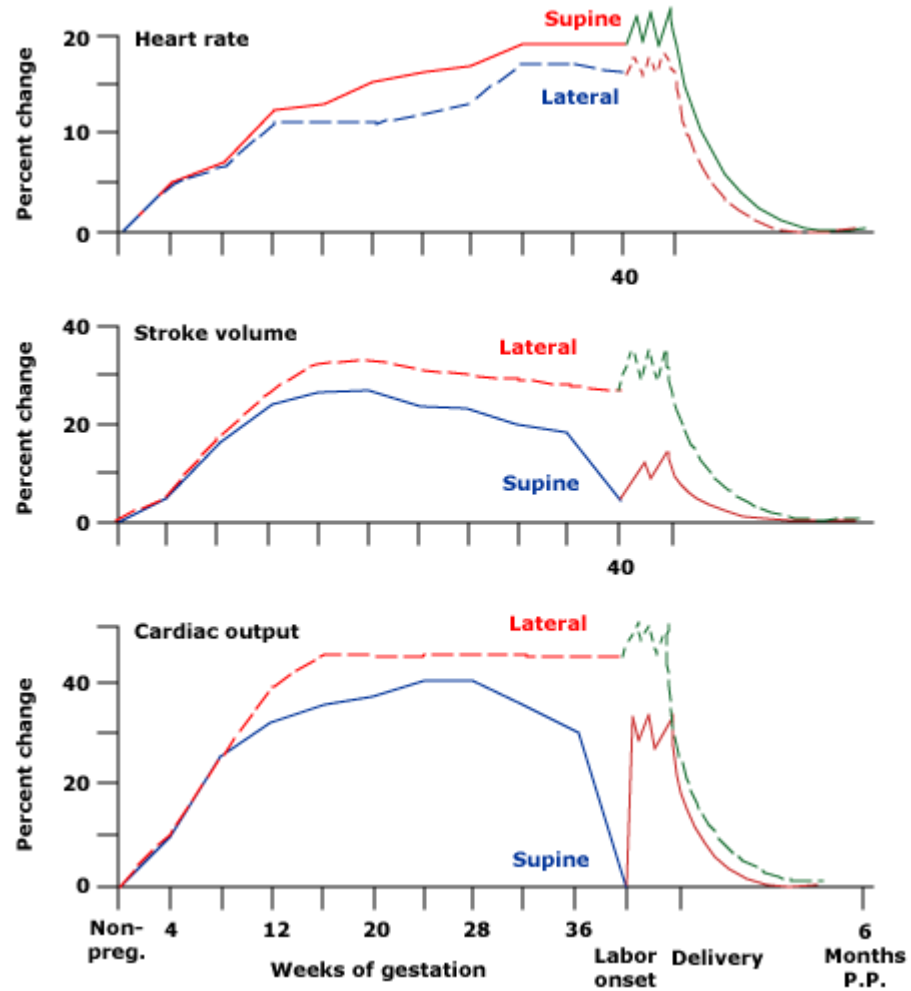


TBV=40%

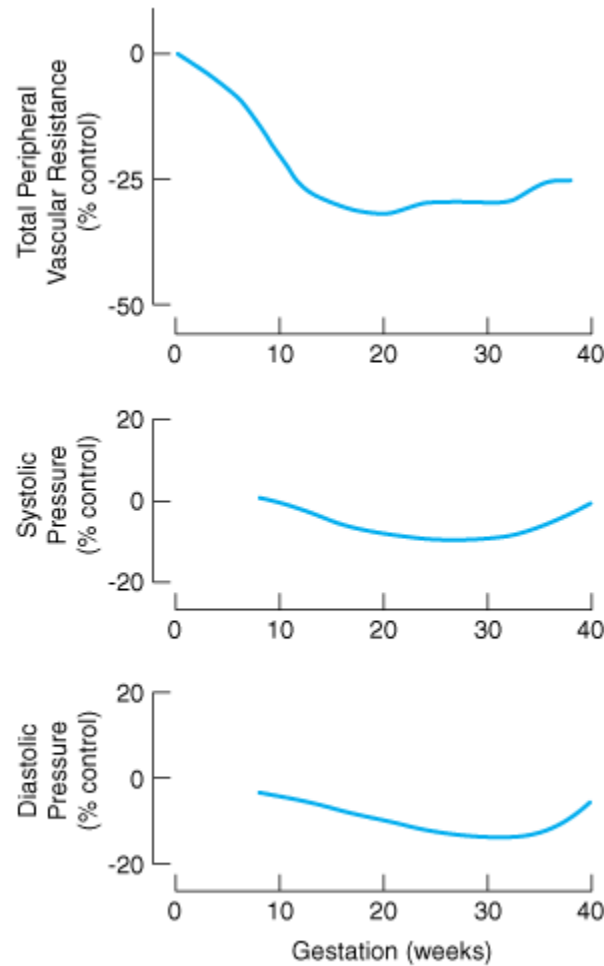
PV= 50%, 70% in twins

RBV =20-35%

## Systemic hemodynamics during normal pregnancy



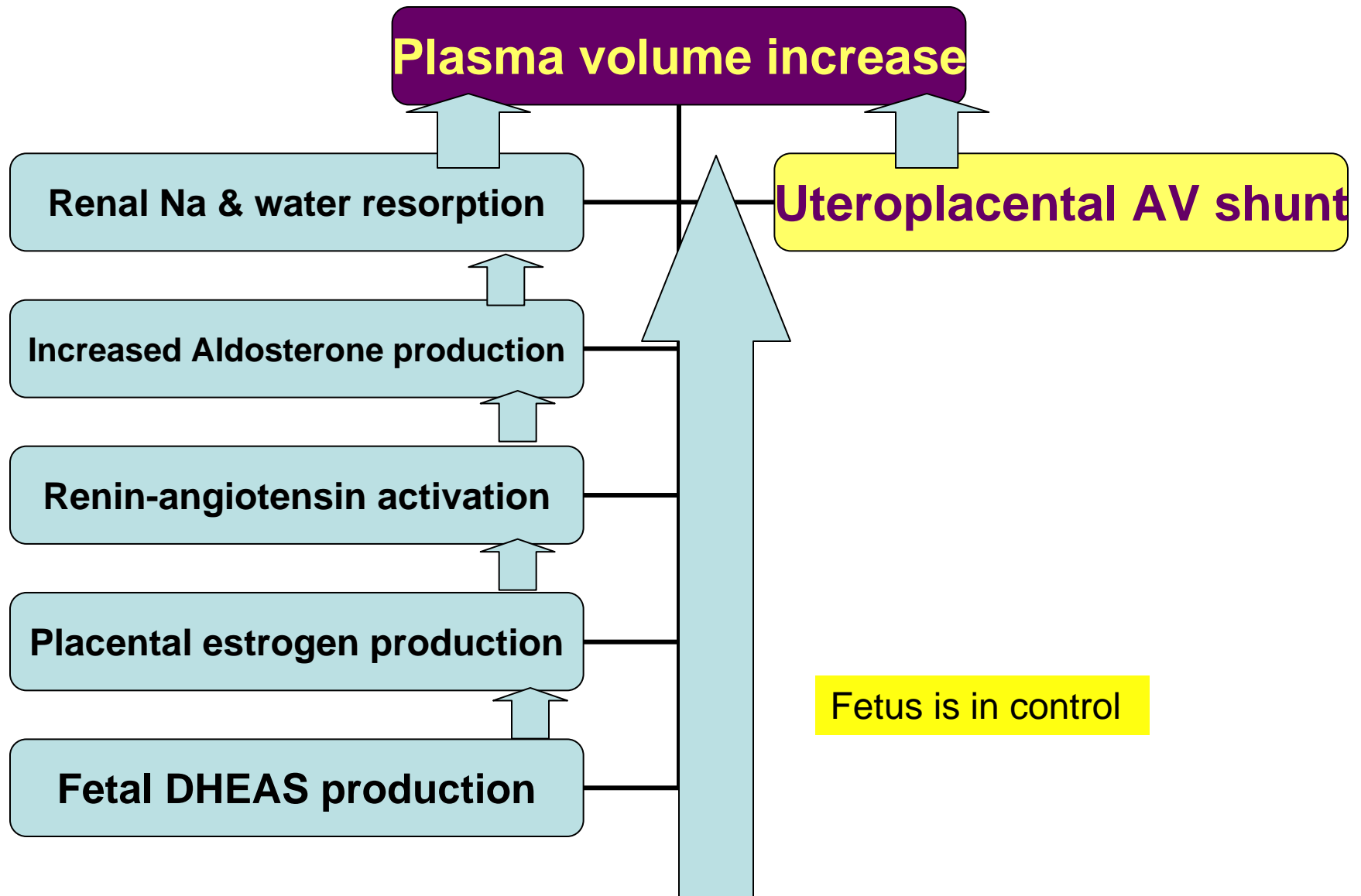
# Peripheral vascular & arterial pressures in pregnancy.



Prostacyclin  
Nitric oxide  
Aldosterone  
ANP



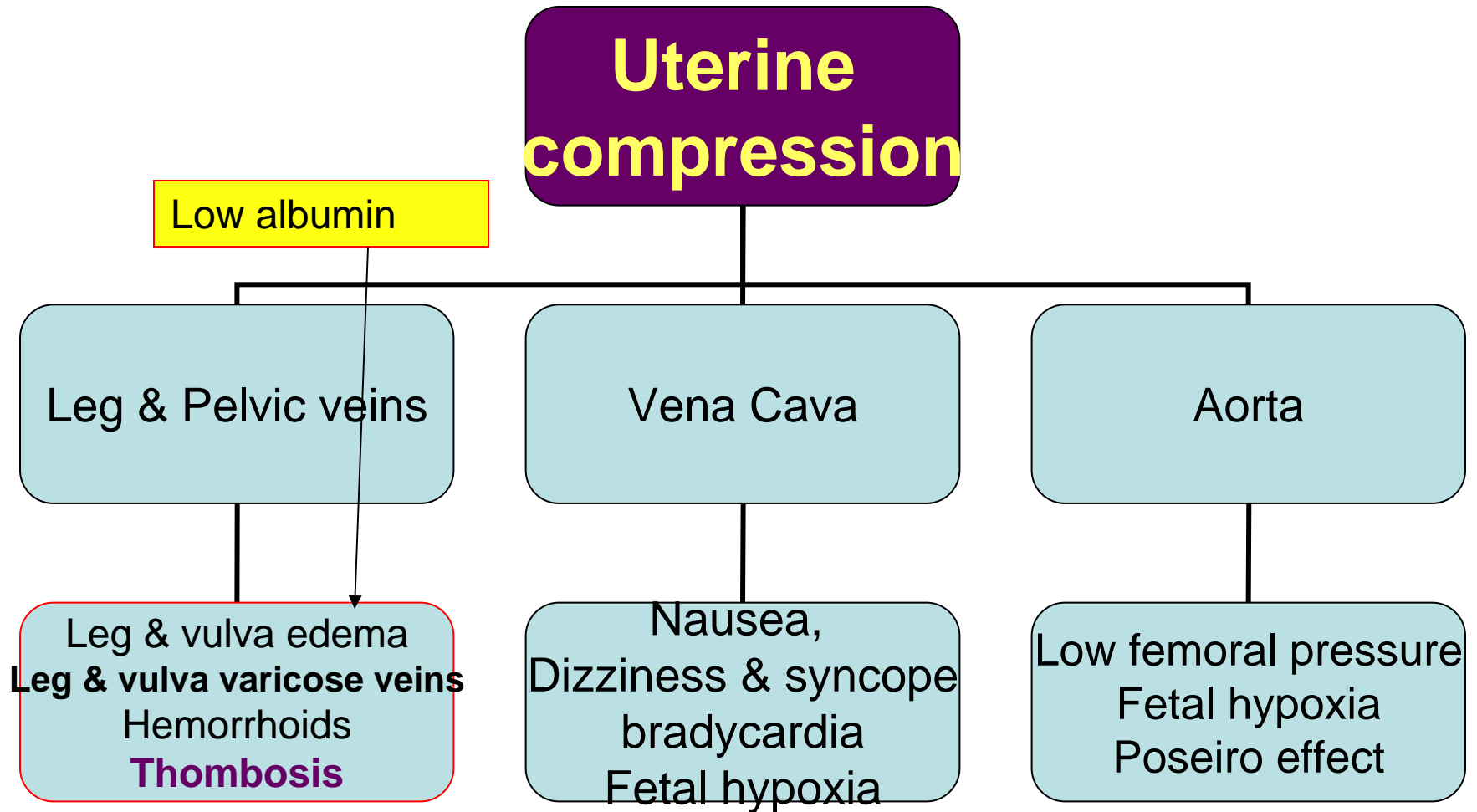
# Maternal total blood volume mechanisms



# Cardiac changes

- Cardiac output increases in early pregnancy, initially as a result of an increased heart rate, soon followed by an increased stroke volume.
- Cardiac output continues to increase until midpregnancy, and remains stable afterward, with a possible small decline in the last weeks of pregnancy.
- Blood pressure decreases in early pregnancy, reaching a minimum in midpregnancy, then returning to baseline levels at term.
- Peripheral vascular resistance is reduced throughout pregnancy.
- Myocardial contractility seems to be increased during all trimesters of pregnancy, thus gradually provoking the development of a mild ventricular hypertrophy.
- The increase in preload, which develops in concert with the increment in blood volume, leads to an increase in left atrial diameter, which also begins during early pregnancy.
- During labor, both cardiac output and blood pressure increase. After delivery, cardiac output initially increases, but begins to decrease within the first hour to reach baseline levels 2 weeks postpartum.
- Most cardiovascular parameters show their greatest changes within 2 weeks postpartum. Five months postnatally, only a mild residual ventricular hypertrophy persists.

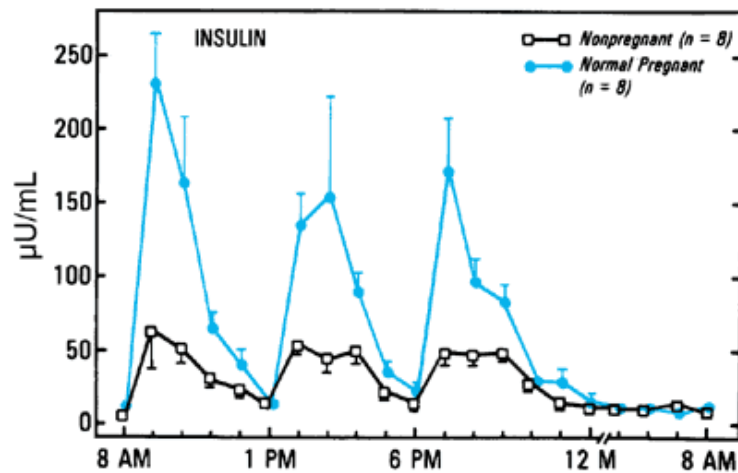
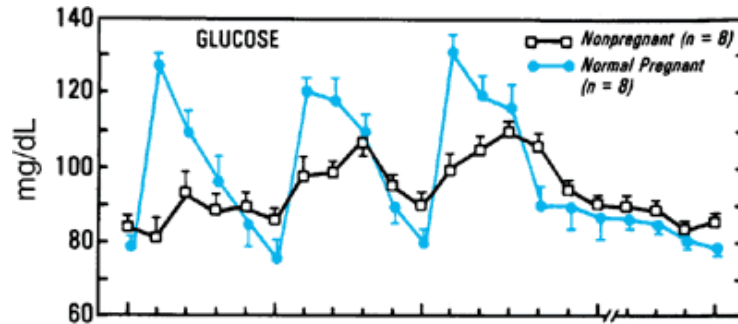
# Mechanical Circulatory Effects



## Weight Gain during Pregnancy

<b>Fetus</b>	<b>3,400</b>
<b>Placenta</b>	<b>650</b>
<b>Amniotic fluid</b>	<b>800</b>
<b>Uterus</b>	<b>970</b>
<b>Breasts</b>	<b>405</b>
<b>Blood</b>	<b>1,450</b>
<b>Extravascular fluid</b>	<b>1,480</b>
<b>Maternal stores (fat)</b>	<b>3,345</b>
<b>Total</b>	<b>12,500 grams</b>

## Metabolic changes



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**Increased lipolysis with free fatty acids**  
**Tendency to ketones (accelerated starvation)**  
**FFA for mum, glucose & amino acids for fetus**

### EARLY PREGNANCY:

↑ Fasting insulin

Fasting glucose ↓

↑ Glycogen synthesis & storage

Gluconeogenesis ↓

### 2nd HALF PREGNANCY:

↑ Insulin resistance

↑ post-meal glucose

### ANTI-INSULIN EFFECT:

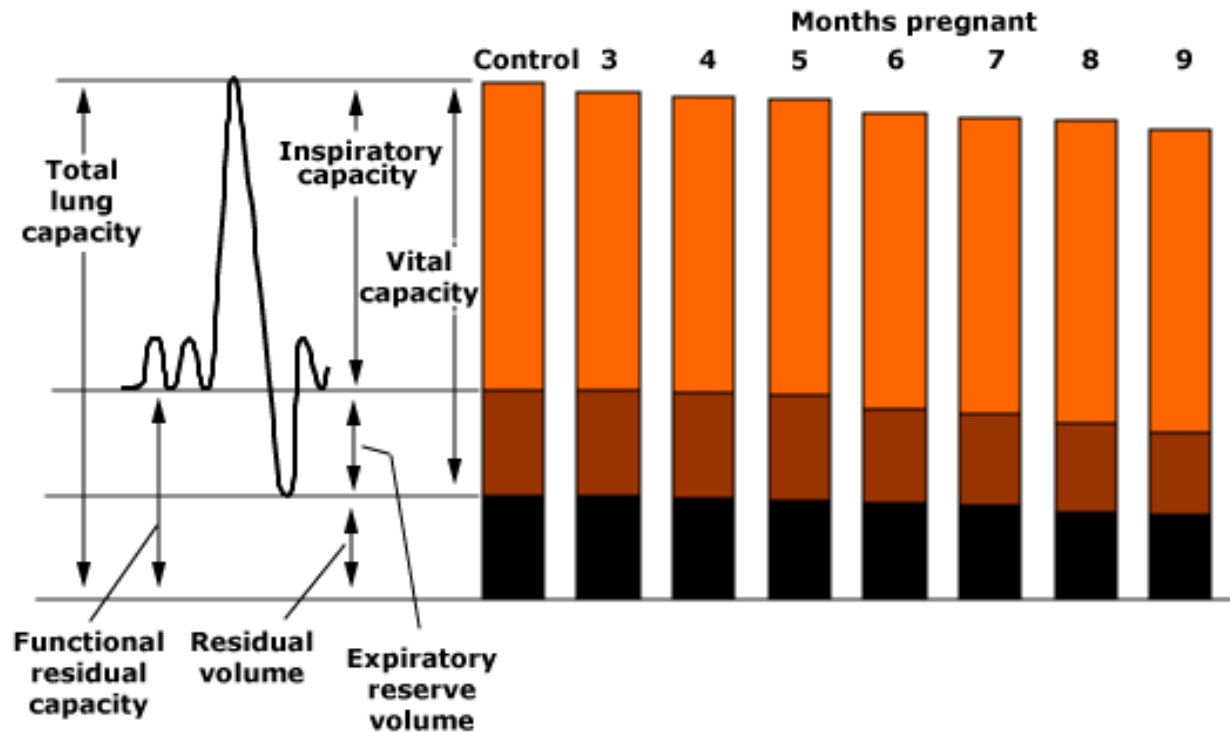
HPL

Cortisol

Cytokines

Progesterone; Estrogens

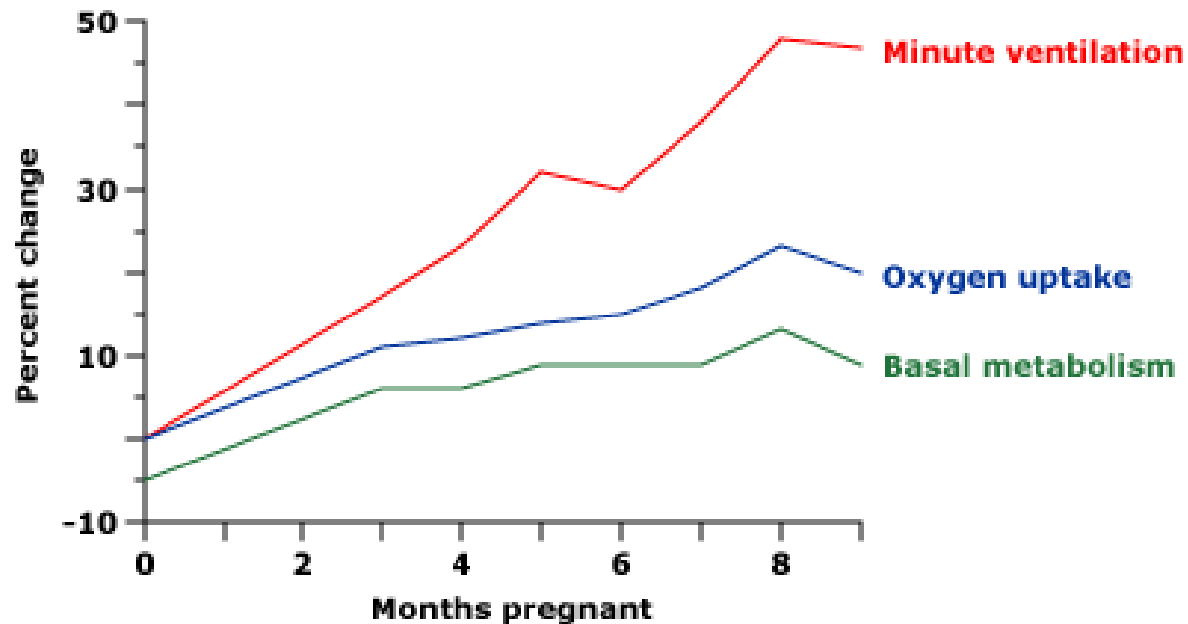
## Changes in pulmonary function tests during pregnancy



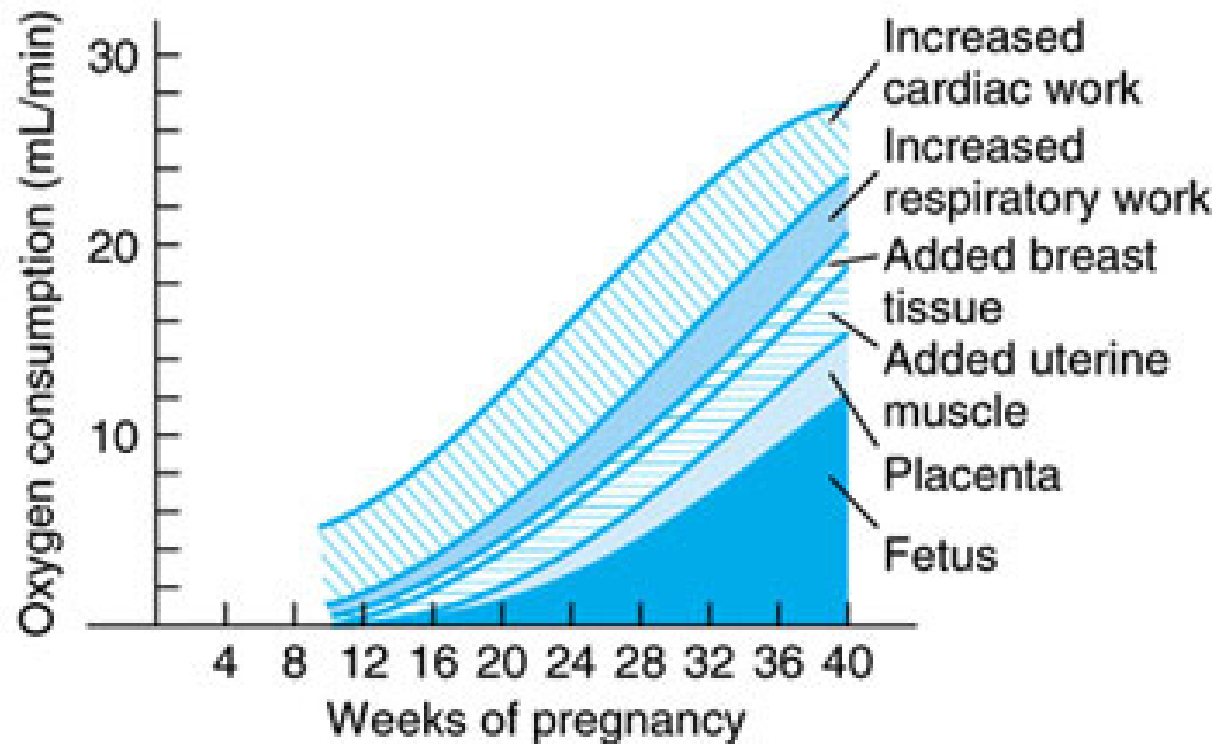
### Mechanical effect of enlarging uterus

Functional residual capacity decreases approximately 20 percent during the latter half of pregnancy, due to a decrease in both expiratory reserve volume and residual volume.

## Changes in ventilation during pregnancy



Time course of percent increases in minute ventilation, oxygen uptake, and basal metabolism during pregnancy. Redrawn from Prowse, CM, Gaensler, EA, *Anesthesiology* 1965; 26:381.



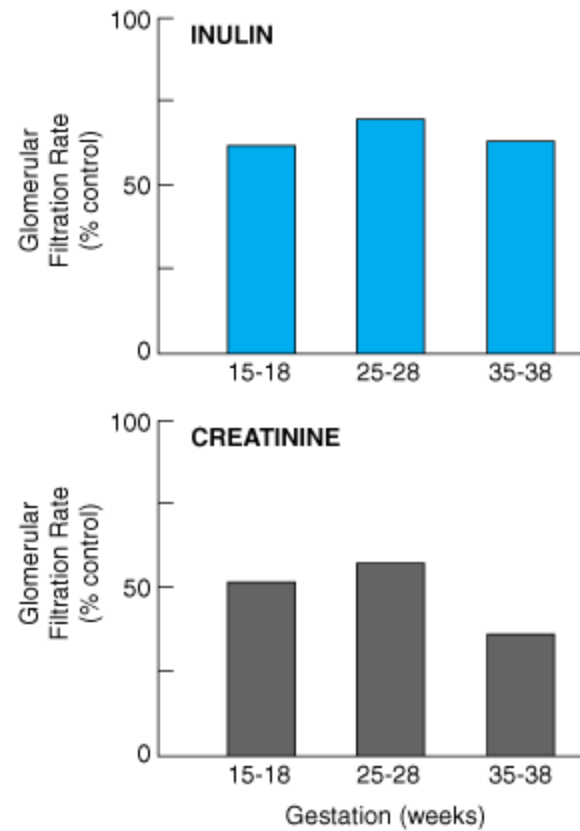
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Components of increased oxygen consumption during pregnancy.  
(Reproduced, with permission, from Hytten FE, Leitch I: *The Physiology of Human Pregnancy*. Blackwell, 1964)

# Respiratory Changes

- Mechanical effect of enlarging uterus
- Increased oxygen consumption
- Stimulant effect of Progesterone
- Increased minute volume thru tidal volume
- Hyperventilation results in a reduced maternal PCO<sub>2</sub> (respiratory alkalosis) facilitates transport of CO<sub>2</sub> from fetus to mum but *impair* release of oxygen from maternal blood to the fetus (Bohr effect).
- Increase in blood pH, stimulates increase in 2,3-diphosphoglycerate in maternal rbc. This counteracts the Bohr effect by shifting the oxygen dissociation curve back to the right, facilitating oxygen release to the fetus
- Dyspnea in 60-70%

Increases in glomerular filtration over gestation as reflected by changes in inulin and endogenous creatinine clearances.



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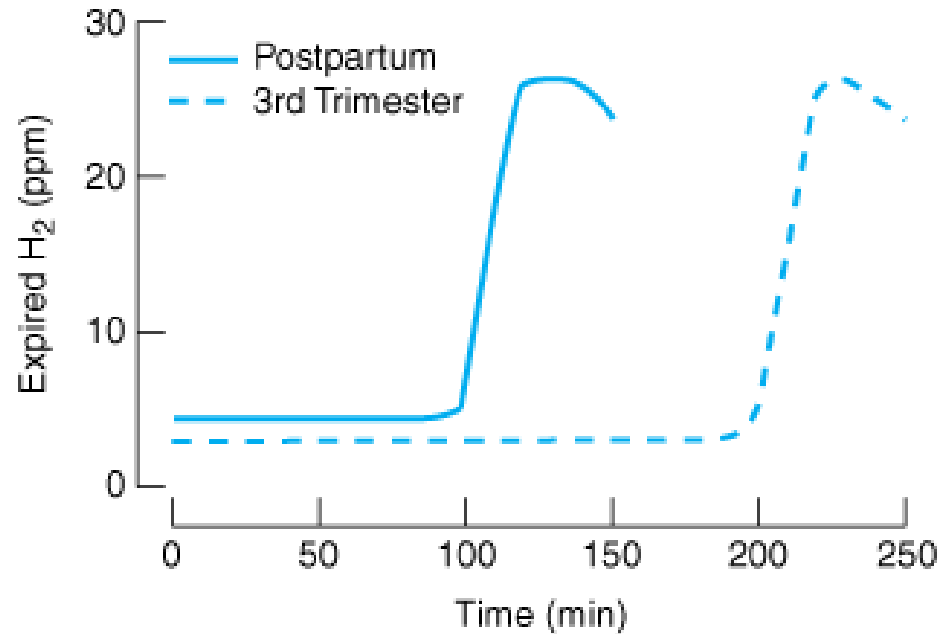
## Renal Changes in Normal Pregnancy

Increased renal size	Renal length 1 cm greater on Xray	Postpartum decreases in size mistaken for parenchymal loss
Dilatation of pelves, calyces, and ureters	Resembles hydronephrosis on ultrasound or IVP (more marked on right)	mistaken for obstructive uropathy; retained urine leads to collection errors; upper UTI more virulent; "distention syndrome" elective pyelography at least 12 weeks postpartum
Increased renal hemodynamic	Glomerular filtration rate and renal plasma flow up 50%	Serum creatinine and BUN decrease protein, AA, & glucose excretion increase
Changes in acid-base metabolism	Renal bicarbonate threshold decreases; progesterone stimulates respiratory center	Serum bicarbonate and Pco <sub>2</sub> are 4–5 mEq/L and 10 mm Hg lower, a Pco <sub>2</sub> of 40 mm Hg represents CO <sub>2</sub> retention
Renal water handling	Osmoregulation altered: osmotic thresholds for AVP release and thirst decrease; hormonal disposal rates increase	Serum osmolality decreases 10 mOsm/L (serum Na 5 mEq/L); increased metabolism of AVP cause transient diabetes insipidus

# GASTROINTESTINAL TRACT

- 22 year old gives history of nausea & vomiting for 2 months which just got better. She now has severe heartburn and constipation. She is found to have gallstones and her liver enzymes are elevated. Ultrasound reveals a 26 week pregnancy. Are all these changes caused by pregnancy?

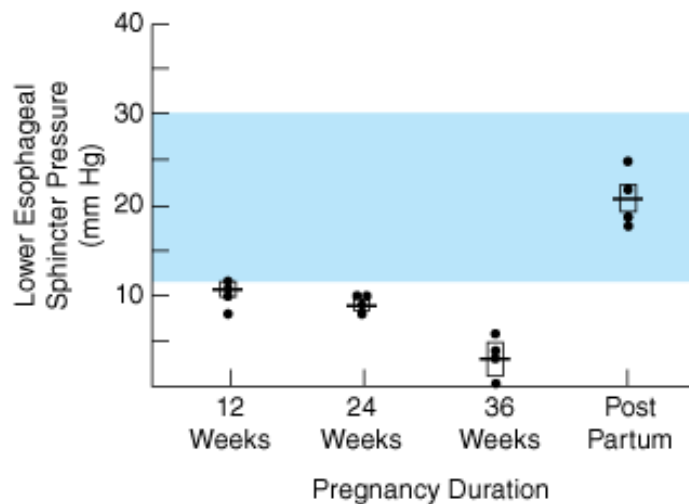
Small-bowel transit times measured by the lactulose hydrogen breath method in a single woman in the third trimester and postpartum.



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Progesterone effect

Uterine displacement



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Morning sickness

Stomach and intestines are displaced,

Appendix is displaced upwards

Delayed gastric emptying  
increase regurgitation risk

Esophageal pressures are lower  
and intragastric pressures higher

Esophageal peristalsis is lower

Gums hyperemic and softened

Impaired gallbladder contraction

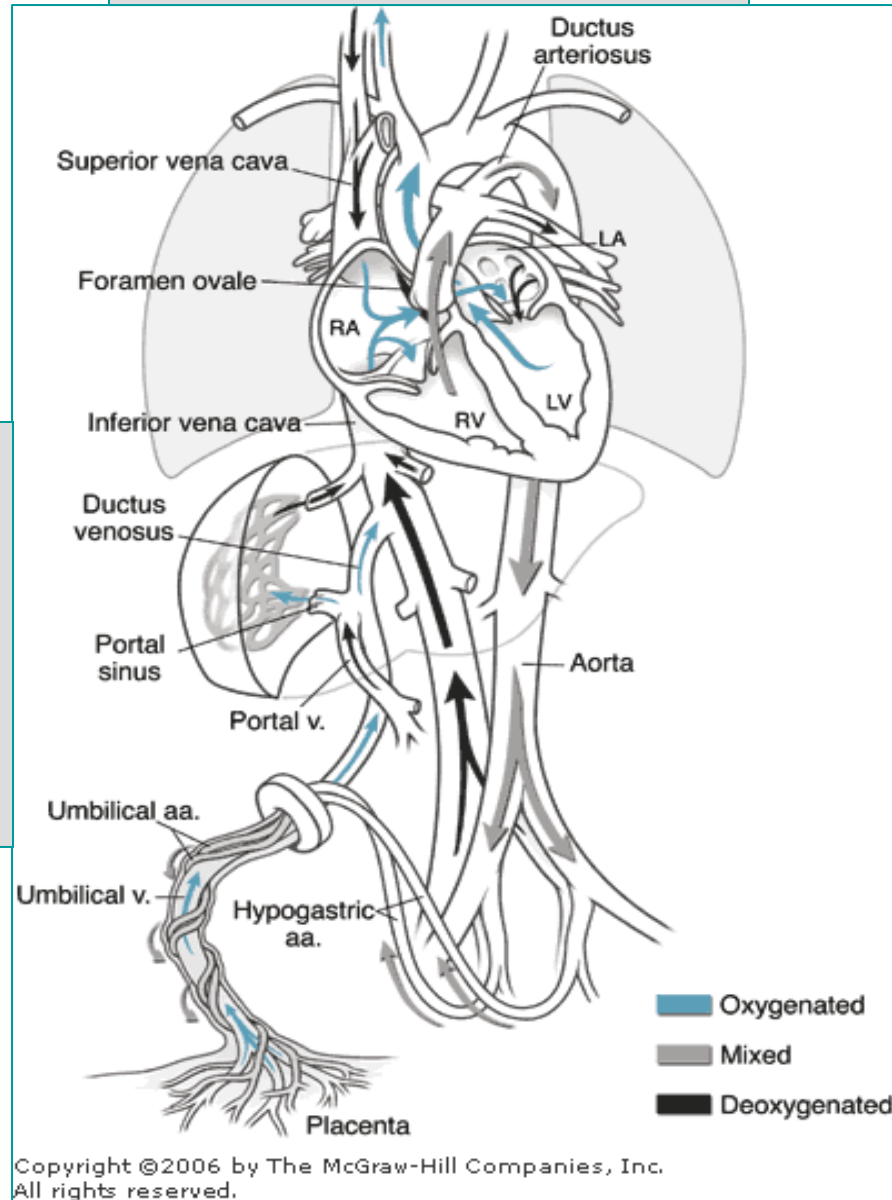
Intrahepatic cholestasis

Lower esophageal sphincter pressures for 3 periods of pregnancy and the postpartum state. The shaded area represents the normal range in nonpregnant women. The horizontal bars show the mean  $\pm$  SE for measurements in 4 women. The rectangles show the mean  $\pm$  SE for each gestational age.

(Modified from Van Theil DH, Gravalier JS, Joshi SN et al: Heartburn in pregnancy. *Gastroenterology* 1977;72:666)

## Fetal Parallel circuit system

Ductus venosus shunts oxygenated blood thru Foramen ovale to left ventricle to ascending aorta



Right ventricle pumps mixed blood thru ductus arteriosus to descending aorta

# Non-specific Immunity

## Innate Immunity

Natural killer cells

Lysis of viruses

Macrophages

Phagocytosis of  
bacteria

Serum  
Complement

Bacterial lysis

# ADAPTIVE IMMUNITY

Macrophage: Antigen processing & presenting

T cell recognition

**IL-4; IL-5**

B cell proliferation &  
antibody production

Humoral antibody

**IL-2**

T cell clonal  
proliferation

Cell mediated immunity

# Survival of fetal allograft

- **Privileged immunologic site (decreased/altered afferent lymphatic)**
- **Suppressor T cells**
- **Separation of maternal & fetal circulation (tight intracellular junctions & fibrinous layer)**
- **No class II HLA antigen at maternal-fetal interphase which are necessary for immune response**
- **Limited T response to trophoblast**
- **HPL, HCG, estrogen, progesterone, pregnancy specific  $\alpha_2$  globulins, 1-glycoproteins cause local nonspecific immune suppression.**
- **Placenta as immuno-absorbent**

# SUMMARY

- **Placenta/fetus produce HCG, HPL, Estrogen, Progesterone, CRF & other hormones which support the pregnancy & modify mother**
- **Maternal immune tolerance to the pregnancy**
- **Increase in cardiac output, blood volume, minute ventilation and GFR allow delivery of energy to fetus and clearance of heat and waste**
- **Changes in metabolism allows preferential delivery of AA & glucose to fetus with utilization of fatty acids by mum**
- **Changes cause symptoms that may be confused with pathology**
- **Changes predispose to medical complications**