

Physiological Changes in Pregnancy

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Introductory Comments

- This lecture/presentation is a “work in progress”
- Not possible to cover “all” the changes that occur during pregnancy!
- We will highlight some of the important changes that occur, affecting some of the major organ systems
- Key concept: one needs to know “normal” to be able to diagnose and manage the common problems in pregnancy!
- This may be of personal importance some day!

Physiological Adaptations to Pregnancy

- Numerous normal changes in response to pregnancy
- It is important to have an awareness of what is considered “normal” in pregnancy
- Such awareness allows an obstetrician to diagnose and manage common medical problems such as
 - ✓ Hypertension
 - ✓ Hyperthyroidism
 - ✓ Anemia
 - ✓ Acute appendicitis or acute cholecystitis
 - ✓ Peripartum cardiomyopathy
 - ✓ Mitral stenosis
 - ✓ Asthma
 - ✓ Gestational diabetes or Insulin dependent diabetes

Weight Gain in Pregnancy

- Normal weight gain can be 30-35 lbs in average patient and 50-70 lbs. in twin pregnancy
- Daily requirements of 2000-2500 calories
- Associated with good outcome, ie delivery of normal sized baby
- Excess weight gain associated with variety of complications:
 - GDM, pre-eclampsia, macrosomia
- Total pregnancy expenditure is 75,000kcalories
- Recommendations for appropriate weight gain in pregnancy based on initial weight, BMI

Weight Gain in Pregnancy

	Kg.	Lbs.
Thin (BMI <19.8)	12.5-18	28-40
Average (BMI 19.8-26.0)	11.5-16	25-35
Heavy (BMI 26.1-29.0)	6.0-11.5	15-25
Obese (BMI > 29.0)	6.0	15

Weight Gain in Pregnancy

TABLE 8-1. Analysis of Weight Gain Based on Physiological Events during Pregnancy

Tissues and Fluids	Cumulative Increase in Weight (g) Up To:			
	10 Weeks	20 Weeks	30 Weeks	40 Weeks (Total)
Fetus	5	300	1500	3400
Placenta	20	170	430	650
Amnionic fluid	30	350	750	800
Uterus	140	320	600	970
Breasts	45	180	360	405
Blood	100	600	1300	1450
Extravascular fluid	0	30	80	1480
Maternal stores (fat)	310	2050	3480	3345
Total	650	4000	8500	12,500

Modified from Hytten (1991), with permission.

Breast Changes

- Increased blood flow to breasts
- Increased size
- Increased ductal growth, alveolar enlargement
- Colostrum production
- Lactation dependent on
 - Estrogen
 - Progesterone
 - Prolactin
 - Cortisol
 - Insulin

Musculoskeletal Changes in Pregnancy

- Ligament laxity throughout
- Progressively more bothersome backpain not uncommon
- “Pride of pregnancy”
- Total calcium levels decreased but ionized calcium levels normal
- Increased PTH
- Increased relaxin
- No loss of bone density during pregnancy

Skin Changes

- Vascular spiders
- Palmar erythema
- Striae gravidarum
- Hyperpigmentation effects
 - Linea nigra
 - Mask of pregnancy
- Increased fine hair growth while pregnant
- Pruritus at end of pregnancy with cholestasis

Gastrointestinal Changes

- Key Changes

- Appetite Usually increased, with cravings
- Gastric Reflux Sphincter relaxation
- GI Motility Decreased
- GI Transit Time Slower
- Liver Functionally unchanged
- Gallbladder Dilated

Common GI Changes in Pregnancy

- Nausea and vomiting of pregnancy or “morning sickness”
 - Exact etiology is unknown
 - Supportive therapy usually helpful
 - On rare occasion, TPN and hyperalimentation necessary
- Dietary cravings commonplace
 - Pica
 - Ptyalism
- Increased tendency for gallbladder dysfunction with possible need for surgery, or laparoscopic cholecystectomy

Physiological GI Changes.

- The hormonal effects on the gastrointestinal tract are an issue of debate among anaesthetists. Relaxation of the lower oesophageal sphincter has been described, but there have been differing views about the effect on motility of the gastrointestinal tract and the times at which it is most prominent. Many believe that there is also retardation of gastrointestinal motility and gastric emptying, producing increased gastric volume with decreased pH, beginning as early as 8-10 weeks of gestation.

Physiological GI Changes

- Recent studies, however, have shed a different light on the subject. Measuring peak plasma concentrations of drugs absorbed exclusively in the duodenum in both non-pregnant and pregnant volunteers, at different times of gestation, it was shown that peak absorption occurred at the same interval in all women with the exception those in labour. This suggests that gastric emptying is delayed only at the time of delivery.

Hepatic Function Laboratory Studies

Albumin	20% decrease
Total Protein	Slight decrease
Alkaline Phosphatase	Markedly elevated
Bilirubin	Unchanged
Triglycerides	Gradual increase at term
Cholesterol	Twice normal value
PT/PTT	Essentially unchanged
Clotting Factors	General increase at term

Hematological Changes in Pregnancy

- Plasma volume increases early in pregnancy with a 50% increase (and higher in higher order multiple pregnancies) and a delayed increase in RBC mass and volume but less than the plasma volume
- Normal pregnancy associated with a “demand” of 1000 milligrams of additional iron
 - 500 mg. to increase maternal RBC volume
 - 300 mg. transported to fetus
 - 200 mg. for normal iron loss
- 60 mg. of elemental iron required daily, provided in 300 mg. of ferrous sulfate
- Serum iron decreased
- Transferrin and TIBC are increased

More Hematological Changes Occurring During Pregnancy

- Pregnancy considered a “hypercoagulable state”
- Fibrinogen increases to 450-600 mg/dl
- Factors VII, VIII, IX and X increase
- Prothrombin, Factor V, and XII are unchanged
- Bleeding time does not change
- Platelet count may increase to 450,000 to 600,000

- WBC count may increase to as high as 20,000 due to an increase in granulocytes

Pulmonary Adaptations

- Anatomical
 - Increased chest diameter, subcostal angle changes, increased diaphragmatic excursion with diaphragm elevated as well
- Physiological
 - Hyperventilation, Increased IC, VC and Minute Volume, Residual volume decreased, Expiratory Reserve Volume decreased Tidal volume increased by 40%, pO_2 increased, pCO_2 decreased, arterial pH unchanged, and serum bicarbonate reduced

Ventilation and Respiratory Gases.

- A progressive increase in minute ventilation starts soon after conception and peaks at 50% above normal levels around the second trimester. This increase is effected by a 40% rise in tidal volume and a 15% rise in respiratory rate (2-3 breaths/minute). Since dead space remains unchanged, alveolar ventilation is about 70% higher at the end of gestation.

Ventilation and Respiratory Gases.

- Arterial and alveolar carbon dioxide tensions are decreased by the increased ventilation. An average PaCO_2 of 32 mmHg (4.3 kPa) and arterial oxygen tension of 105 mmHg (13.7 kPa) persist during most of gestation. The development of alkalosis is forestalled by compensatory decreases in serum bicarbonate. Only carbon dioxide tensions below 28 mmHg (3.73 kPa) will lead to a respiratory alkalosis.

Ventilation and Respiratory Gases

- Oxygen consumption increases gradually in response to the needs of the growing fetus, culminating in a rise of at least 20% at term. During labour, oxygen consumption is further increased (up to and over 60%) as a result of the exaggerated cardiac and respiratory work load.

Cardiac Changes in Pregnancy

- Cardiac output increases around 50% from an increase in HR and SV (3L/min to 6.2L/min)
- There is an additional 40% increase above that level during active labor
- Immediately following delivery, cardiac output may be increased by an additional 10-20%
- Cardiac exam is different during pregnancy
 - Many patients will have an S3 after midpregnancy
 - Diastolic murmurs are usually considered serious
 - Systolic murmurs (“flow murmurs”) common
 - Displacement of heart is to right and upwards
 - EKG shows left axis deviation and low voltage QRS complexes

Key Cardiovascular Changes During Pregnancy

Blood Flow to Other Organs	Increased
Peripheral Vascular Resistance	Decreased
Blood Pressure	Mid pregnancy decrease
Pulmonary Blood Pressure	Unchanged
Heart Size	Increased
Cardiac output	Increased
Stroke volume	Increased
Systolic murmurs	Common
Diastolic murmurs	Potentially pathological
EKG changes	LAD, low voltage

Blood Volume

- **Blood Volume** increases progressively from 6-8 weeks gestation (pregnancy) and reaches a maximum at approximately 32-34 weeks with little change thereafter. Most of the added volume of blood is accounted for by an increased capacity of the uterine, breast, renal, striated muscle and cutaneous vascular systems, with no evidence of circulatory overload in the healthy pregnant woman. The increase in plasma volume (40-50%) is relatively greater than that of red cell mass (20-30%) resulting in hemodilution and a decrease in haemoglobin concentration. Intake of supplemental iron and folic acid is necessary to restore hemoglobin levels to normal (12 g/dl).

Blood Volume

- The increased blood volume serves two purposes. First, it facilitates maternal and fetal exchanges of respiratory gases, nutrients and metabolites. Second, it reduces the impact of maternal blood loss at delivery. Typical losses of 300-500 ml for vaginal births and 750-1000 ml for Caesarean sections are thus compensated with the so-called "autotransfusion" of blood from the contracting uterus

Blood Constituents.

- As mentioned above, red cell mass is increased 20-30%. Leukocyte counts are variable during gestation, but usually remain within the upper limits of normal. Marked elevations, however, develop during and after parturition (delivery). Fibrinogen, as well as total body and plasma levels of factors VII, X and XII increase markedly. The number of platelets also rises, yet not above the upper limits of normal. Combined with a decrease in fibrinolytic activity, these changes tend to prevent excessive bleeding at delivery. Thus, pregnancy is a relatively hypercoagulable state, but during pregnancy neither clotting or bleeding times are abnormal

Cardiac Output

- **Cardiac Output** increases to a similar degree as the blood volume. During the first trimester cardiac output is 30-40% higher than in the non-pregnant state. Steady rises are shown on Doppler echocardiography, from an average of 6.7 litres/minute at 8-11 weeks to about 8.7 litres/minute flow at 36-39 weeks; they are due, primarily, to an increase in stroke volume (35%) and, to a lesser extent, to a more rapid heart rate (15%). There is a steady reduction in systemic vascular resistance (SVR) which contributes towards the hyperdynamic circulation observed in pregnancy.
- During labor, further increases are seen with pain in response to increased catecholamine secretion; this increase can be blunted with the institution of labour analgesia. Also during labour, there is an increase in intravascular volume by 300-500 ml of blood from the contracting uterus to the venous system. Following delivery this autotransfusion compensates for the blood losses and tends to further increase cardiac output by 50% of pre-delivery values. At this point, stroke volume is increased while heart rate is slowed.

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Cardiac Size/Position/ECG.

- There are both size and position changes which can lead to changes in ECG appearance. The heart is enlarged by both chamber dilation and hypertrophy. Dilation across the tricuspid valve can initiate mild regurgitant flow causing a normal grade I or II systolic murmur. Upward displacement of the diaphragm by the enlarging uterus causes the heart to shift to the left and anteriorly, so that the apex beat is moved outward and upward. These changes lead to common ECG findings of left axis deviation, sagging ST segments and frequently inversion or flattening of the T-wave in lead III.

Blood Pressure

- . Systemic arterial pressure is never increased during normal gestation. In fact, by midpregnancy, a slight decrease in diastolic pressure can be recognized. Pulmonary arterial pressure also maintains a constant level. However, vascular tone is more dependent upon sympathetic control than in the nonpregnant state, so that hypotension develops more readily and more markedly consequent to sympathetic blockade following spinal or extradural anaesthesia. Central venous and brachial venous pressures remain unchanged during pregnancy, but femoral venous pressure is progressively increased due to mechanical factors.

Renal Changes in Pregnancy

- Minimal renal enlargement, bilaterally
- Both renal pelvises and ureters are dilated (“hydronephrosis of pregnancy”)
- Greater urinary stasis, ureteral compression, leading to urinary stasis and possible urinary tract infections, pyelonephritis
- Loss of urinary control
- Bladder capacity diminished
- RPF increases to 75% of non-pregnant value

More Renal Changes in Pregnancy

- GFR increases 50% over non-pregnant state
- Creatinine clearance increases to 150-200 ml/min
- Plasma osmolality decreases
- Urine output is unchanged
- There is an increased sensitivity to renin and angiotensin
- Renal glycosuria common
- Proteinuria up to 300 mg/24 hours normal

Endocrine Changes with Pregnancy

- Carbohydrate Metabolism
 - Overall effect is that pregnancy is diabetogenic
 - First half: tendency to hypoglycemia
 - Second half: tendency to hyperglycemia
 - Progressive insulin resistance as pregnancy progresses
 - Progesterone
 - Estrogen
 - HPL
 - “Typical” FBS less than in non-pregnant state
 - Blunting response to meals, eating as pregnancy progresses
 - Hypertrophy of beta cells as well

Metabolism

- All metabolic functions are increased during pregnancy to provide for the demands of fetus, placenta and uterus as well as for the gravida's increased basal metabolic rate and oxygen consumption. Protein metabolism is enhanced to supply substrate for maternal and fetal growth. Fat metabolism increases as evidenced by elevation in all lipid fractions in the blood.

Metabolism

- Carbohydrate metabolism, however, demonstrates the most dramatic changes. Metabolically speaking, pregnant women live in a state of "accelerated starvation." First, nutritional demands of the growing fetus are met by the intake of glucose and, second, secretion of insulin in response to glucose is augmented. As early as 15 weeks of gestation, maternal blood glucose levels after an overnight fast are considerably lower than in the nongravid state.

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Hypoglycaemia.

- Optimal blood glucose levels in pregnant women range between 4.4 to 5.5 mmol/l. In healthy non-pregnant individuals, signs of hypoglycaemia usually begin when the blood glucose level declines to approximately 2.2 mmol/l (40mg/dl); in pregnant women, however, hypoglycaemia is defined as a concentration below 3.3 mmol/l (60mg/dl).

Hypoglycaemia.

- Hypoglycaemia initiates the release of glucagon, cortisol and, importantly, catecholamines. In the anaesthetised state, however, these compensatory mechanisms, particularly the release of epinephrine (adrenaline), are blocked. Autonomic derangements in the form of hypotension and tachycardia tend to ensue during high regional blockade or deep general anaesthesia, which may mask the symptoms and signs of hypoglycaemia

Endocrine Changes in Pregnancy

- Thyroid Function in Pregnancy
 - The normal pregnant woman remains euthyroid while pregnant despite/ with hormonal changes which occur
 - Estrogen production increases
 - Increased TBG
 - Increased total thyroxine, and T3
 - Free T4 and T3 remain unchanged
 - BMR increases 15-20% above normal
 - There is lowered T3 uptake during pregnancy
 - TSH does not cross the placenta

Endocrine Changes in Pregnancy

- GnRH concentration increases during pregnancy, but the physiological significance of this change has not been determined
- corticotropin-releasing hormone (CRH) is expressed by placental and chorionic trophoblasts, amnion, and decidual cells . Its concentration in maternal circulation is high and rises exponentially throughout pregnancy

Endocrinology Changes in Pregnancy

Endocrine Changes in Pregnancy

- The placenta produces a hormone (similar to thyroid-stimulating hormone) that stimulates the thyroid, causing hyperplasia, increased vascularity, and moderate enlargement. Estrogen stimulates hepatocytes, causing increased thyroid-binding globulin levels; thus, although total thyroxine levels may increase, levels of free thyroid hormones remain normal.

Endocrine Changes in Pregnancy

- The placenta produces corticotropin-releasing hormone (CRH), which stimulates maternal ACTH production. Increased ACTH levels increase levels of adrenal hormones, especially aldosterone and cortisol, and thus contribute to edema. Increased production of corticosteroids and increased placental production of progesterone lead to insulin resistance and an increased need for insulin, as does the stress of pregnancy and possibly the increased level of human placental lactogen

Endocrine Changes in Pregnancy

- The placenta produces melanocyte-stimulating hormone (MSH), which increases skin pigmentation late in pregnancy. The placenta also produces the β subunit of human chorionic gonadotropin (β -hCG), a trophic hormone that, like follicle-stimulating and luteinizing hormones, maintains the corpus luteum and thereby prevents ovulation.

Endocrine Changes in Pregnancy

- Effects of thyroid hormone tend to increase and may resemble hyperthyroidism, with tachycardia, palpitations, excessive perspiration, and emotional instability. However, true hyperthyroidism occurs in only 0.08% of pregnancies

Endocrine Changes in Pregnancy

- **The pituitary gland enlarges by about 135% during pregnancy. The maternal plasma prolactin level increases by 10-fold. Increased prolactin is related to an increase in thyrotropin-releasing hormone production, stimulated by estrogen. The primary function of increased prolactin is to ensure lactation. The level returns to normal postpartum, even in women who breastfeed.**