Pregnancy: A brief overview of physiology & psychology

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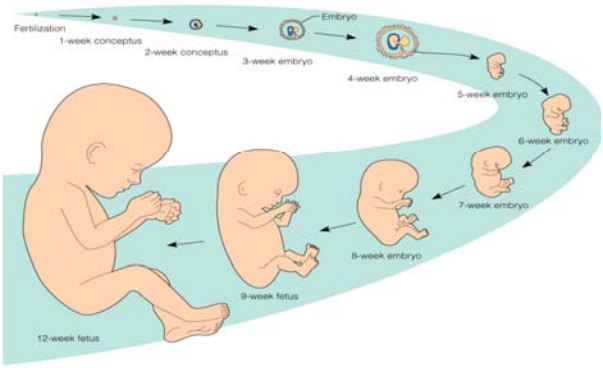
Objectives

- Fetal growth & development
- Placental growth & development
- Maternal physiologic adaptations
  - Cardiovascular- hematologic
  - Pulmonary
  - Renal
  - Gastrointestinal
- Maternal psychological adaptations

Fetal Growth & Development

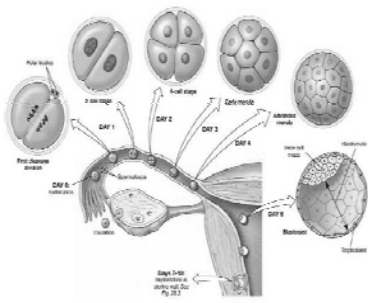


Feto-placental development

- Synchronized cellular communication & interaction
  - Adjacent tissues induce changes in neighboring cells
- DNA sets up basic body plan that establishes plan of early embryo
- Interaction of *genetic & environmental* influences creates final product

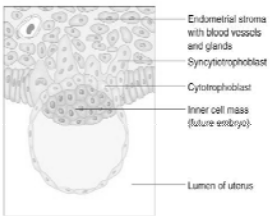
Pre-embryo Development: 0-14 days

- Zygote- 0-2 days
- Morula- 3-4 days
- Blastocyst- 4-14 days
  - Inner cell mass- embryo
- Trophoblast- placenta & chorionic membranes
- Implantation
  - 6-10 days after ovulation
  - 3-5 days prior to beginning of missed menstrual period



Pre-embryo Development

- Formation of primitive yolk sac by 7-8 days post-fertilization
- Primary days 9-10
  - secretions of the oviduct and uterine endometrial glands
- Secondary until 10 weeks
  - capillary plexus surround early spaces in syncitiotrophoblast fill with filtrate of maternal serum provides nutrition
  - becomes primitive gut

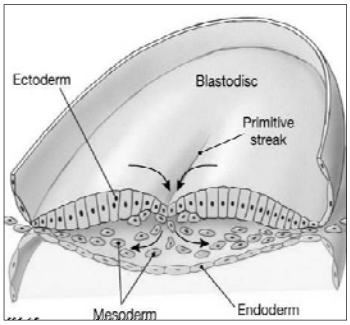


Embryonic Stage: Day 15 through Week 8

- Cellular processes leading to structural changes
  - Development of internal & external structures
  - Organogenesis
- Driven by
  - Genetic code
  - Intrauterine environment
  - Influence of teratogens

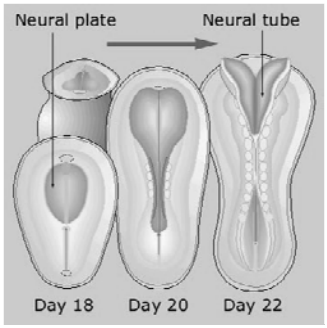
Embryo Development: Week 3 (15-21 days)

- Development of trilaminar embryo
  - Ectoderm
  - Mesoderm
  - Endoderm



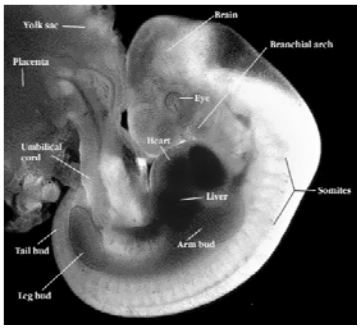
Embryo Development: Week 4 (22-28 days)

- CNS development
  - Neural tube fuses (21-28 days)
    - Anencephaly: 26 days
    - Spina bifida: 28 days
  - Proceeds cranially and caudally
  - Cranial area enlarges, develops cephalic & cervical flexure



Embryo Development: Week 4 (22-28 days)

- Primitive heart begins beating (22 days)
- Arm (26 days) and leg (28 days) buds
- 2-5 mm long
- Formation of primitive gut
- Lung primordia appear



Embryo Development: Week 6 (36-42 days)

- Cardiovascular
  - Heart almost complete
  - Circulation well established
  - Liver producing blood cells
  - Congenital heart defects
- Short webbed fingers, toe rays visible
  - Syndactyly

Embryo Development: Weeks 7 & 8 (43-56 days)

- Limbs distinct
- Fingers longer, toes differentiated
- Gross spontaneous movements begin
- Body covered with thin skin
- 7 cc of amniotic fluid
- GI and GU systems have separated
- Kidneys achieved basic structure

Fetal Stage: Week 9 through Birth

- Growth in size
- Structural & biochemical maturation
- Factors affecting development
  - Genetic code
  - Intrauterine environment
  - Teratogens
  - Maternal environment

Fetal Development: Weeks 17-20

- By 20 weeks weighs about 300 g, 25 cm long
- CNS myelinization begins
- Lung development
  - Bronchial development complete
  - Terminal air sacs begin to develop
- Rapid growth
  - 20 gm by end week 16
  - Length of embryo doubles in this month
- Increased muscle & bone development
  - Increased movement
- Brown fat deposition begins

18 weeks

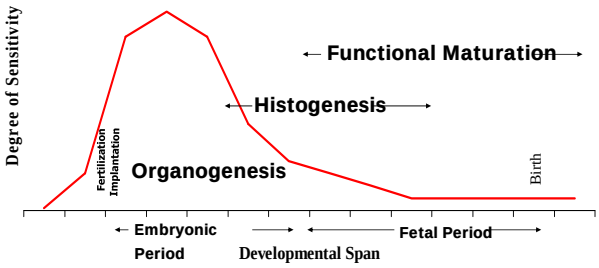
Fetal Development: Weeks 21-29

- Weight begins to increase more rapidly
  - @ 24-25 wks 650-750 gm, 30 cm long
- Skin translucent, no subcutaneous fat
- Fingerprint and foot print ridges form
- Basic structure of eye complete, but functionally immature, lids fused
- Organization of CNS begins
- By 24-25 weeks the lungs are able to support extrauterine life

Fetal Development: 30 Weeks-Term

- Fat and muscle tissue laid down, skin thickness increases
- Bones fully formed, ossification not complete
- Testes descend into scrotum
- Nephrons develop until 36 weeks
- Lung maturation finalizes after 34-35 weeks
- CNS organization prominent
  - Myelinization progresses
  - Sleep-wake cycles established

Critical periods: Sensitivity to averse effects of environment



Susceptibility dependent upon developmental stage at time of exposure

Stage	Effect
Preconception	Chromosome, mutation, infertility
Preembryo (0-14 days)	"All or nothing", ? syndromes
Early embryo (15-30 days)	Death, NTD, conjoining
Late embryo (31-56 days)	Death, malformation
Early fetus (57-70 days)	Death, malformation, dysfunction
Late fetus (71 days to term)	Dysfunction, altered growth, stillbirth, preterm birth, malignancy

Teratogenesis

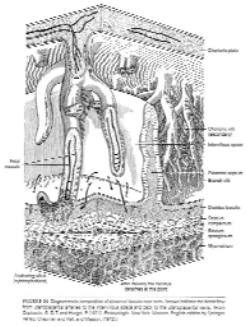
- Hyperglycemia- 1st trimester
  - holoprosencephaly, cardiac defects, sacral agenesis, renal defects, facial clefts
- Folic acid- 24-28 days
  - NTDs- anencephaly- meningomeylocele
- Phenylketonuria (PKU)- entire pregnancy
  - Developmental delay, microcephaly, craniofacial defects
- ETOH- entire pregnancy
  - Developmental delay, altered mid-facies, growth restriction
- Heavy metals- mercury, lead, arsenic- entire pregnancy
  - Developmental delay
- Listeriosis- entire pregnancy
  - SAB, stillbirth, PTB, newborn illness
- Toxoplasmosis- 10-24 weeks
  - CNS defects- developmental delay, microcephaly, blindness

The Placenta

- 10-12 weeks is the period of placentation
- Before implantation
  - blastocyst divides into embryonic cells and placental cells (trophoblast)
- Implantation and placentation requires communication between blastocyst and endometrium
  - hormones, cytokines, growth factors, other regulatory substances
- After implantation- trophoblast proliferates and invades endometrial stroma
  - same molecular mechanisms as tumor growth, but regulated
  - uterine secretions include growth factors that promote placental growth

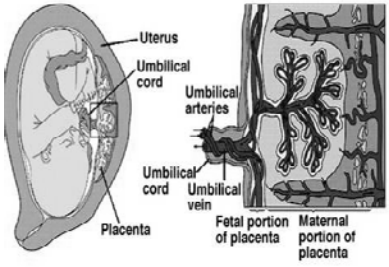
Placental Growth & Development

- Rapid early growth prepares way for fetal growth
- Mature form by about 10 weeks
  - Eventually occupies about 1/3 of inner uterine surface
  - Growth continues by increasing size and branching of villi and fetal capillaries
- Larger than fetus until about 15-16 weeks
- By term, fetus 5-6 times heavier than placenta
- Towards term begins to undergo degenerative changes
  - Variable onset of placental degeneration



Placental Circulation- Fetal

- Deoxygenated blood from fetus via umbilical arteries
- Arteries branch radially onto chorionic plate, then down into villi
- Converge back at cord into umbilical vein
- Exchange occurs across fetal basal & maternal apical membranes- syncitiotrophoblast



Maternal Uteroplacental Circulation

- Abdominal aorta → internal iliac /ovarian arteries → uterine arteries → uteroplacental arteries (altered spiral arteries)
- After 10-12 weeks, blood enter IVS via 100-200 uteroplacental arteries
  - Flows toward chorionic plate, then down around villi
    - Exchange between maternal and fetal circulations
  - Leaves IVS via 50-200 uteroplacental veins
- By term 20-25% of maternal cardiac output supplies uterus and intravillous space (IVS)
- Flow 500-600 ml/min by term, low-pressure circuit
- IVS in mature placenta contains about 150 ml blood
  - Replenished every 3-4 minutes

Remodeling of Spiral Arteries

- Phase I
  - Implantation to around 12 weeks
  - Altered structure of *endometrial* spiral arteries
  - Limited blood enters IVS until 10-12 weeks
- Phase II
  - From 12-14 to 20-24 weeks
  - Final alteration of structure in *myometrial* arteries

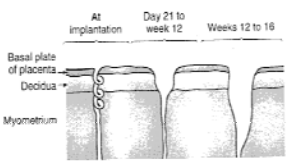
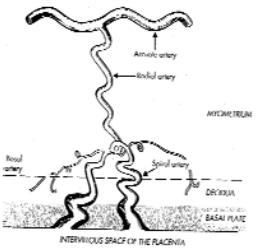


FIGURE 3-16 Diagrammatic representation of the conversion of the spiral arteries in the placental bed into uteroplacental vessels. (From Fox, H. (1997). *Pathology of the placenta* [2nd ed.]. Philadelphia: W.B. Saunders.)

Spiral Arteries: Uteroplacental Circulation

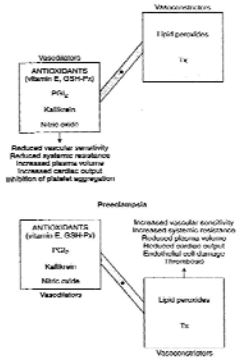
- Adrenergic nerves at base of spiral arteries denervated
- Spiral arteries not responsive to circulatory pressors and autonomic nervous system
- Control is at level of maternal radial arteries



(From Fanaroff & Martin, 1997)

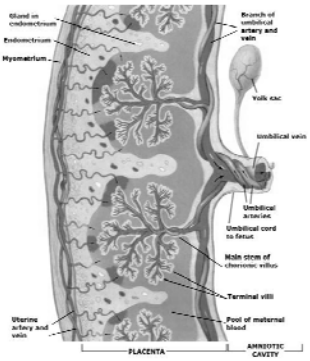
Uteroplacental Circulation

- Mediated primarily by local influences
  - PGI_2 (prostacyclin) is most potent vasodilator produced by placenta
  - Maintains vasodilatation of utero-placental vessels
  - Prevents platelet aggregation
  - Enhances cell disengagement (needed for alterations in elastic and muscular elements)



Normal placental development

- Enhanced capacity of uteroplacental vessels
- Arterial dilation with low resistance circuit
- Increased local control of circulation
- Facilitated maternal-fetal exchange of nutrients, gases, wastes at the intervillous space



Potential consequences of altered uteroplacental development

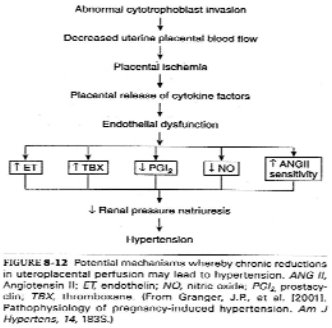


FIGURE 8-12 Potential mechanisms whereby chronic reductions in uteroplacental perfusion may lead to hypertension. *ANG II*, Angiotensin II; *ET*, endothelin; *NO*, nitric oxide; *PGI_2*, prostacyclin; *TBX*, thromboxane. (From Granger, J.P., et al. [2001]. Pathophysiology of pregnancy-induced hypertension. *Am J Hypertens, 14*, 183S.)

Clinical implications

- Recurrent pregnancy loss
- IUGR
- Pre-eclampsia

Placental Functions

- Metabolic
- Maintains immunological distance between mother and fetus
- Special endocrine organ: "transient hypothalamo-pituitary-gonadal axis"
- Responsible for exchange of nutrients, gases & metabolic waste products between maternal and fetal circulation

Placental Function: Metabolic

- High metabolic rate
  - Glucose & O_2 consumption similar to brain
- Contributes to quality & quantity of fetal nutrient supply particularly in early pregnancy through active synthesis of glycogen, fatty acids, cholesterol
  - Glycogen synthesis: from maternal glucose & stored
  - Cholesterol synthesis: placental cholesterol is precursor for placental progesterone and estrogens
  - Protein production: rises to 7.5 g per day at term
- Synthesis of hormones
  - Steroids, polypeptides and enzymes that influence embryo/fetal growth and development
  - Hormone precursors

Placental Function: Immunologic

- Maternal tolerance of fetus
- Protection of fetus from pathogens
  - Limits passage of some bacteria
  - Allows passage of maternal immunoglobulin antibodies (IgG)

Placental Endocrinology

- Placenta hormones essential
  - Maintaining pregnancy
  - Inducing maternal physiologic changes
  - Embryo/fetal growth and development
- Primary hormones synthesized by placenta
  - Polypeptides: human chorionic gonadotropin (hCG), human placental lactogen (hPL), Insulin-like growth factors (IGF)
  - Steroids: estrogens, progesterone
  - Many others!

Placental Endocrinology

TABLE 3-3 Examples of Growth Factors, Neuropeptides, and Proteins Identified in Placental Tissues

Protein and Peptide Hormone	Neurohormone or Neurpeptiodes	Growth Factors	Binding Proteins	Cytokines
Human chorionic gonadotrophin	Gonadotrophin-releasing hormone	Activin	Corticotrophin-releasing-hormone-binding protein (CRH-BP)	Interleukin-I (IL-1)
Human placental lactogen	Thyroid-releasing hormone	Follistatin	Insulin-like growth factor-binding protein-1 (IGFBP-1)	IL-2
Growth hormone variant	Growth hormone-releasing hormone	Inhibin	IGFBP-2	IL-6
Adrenocorticotrophic hormone	Somatostatin	Transforming growth factor (β and α)	IGFBP-3	IL-8
	Corticotrophin-releasing hormone	Epidermal growth factor	IGFBP-4	Interferon-α
	Oxytocin	Insulin-like growth factor 1 (IGF-1)	IGFBP-5	Interferon-β
	NeuropeptideY	IGF-2	IGFBP-6	Interferon-γ
	β-Endorphin met-enkephalin dynorphia	Fibroblastic growth factor		Tumor necrosis factor-α
		Platelet-derived growth factor		

From Liu, J.H. & Rebar, R.W. (1999). Endocrinology of pregnancy. In R.K. Creasy & R. Resnik (Eds.). *Maternal-fetal medicine* (4th ed.). Philadelphia: W.B. Saunders.

Human Chorionic Gonadotropin

- Glycoprotein produced by primarily by syncitiotrophoblast
- Production begins around implantation
- Detected in maternal serum and blood by 7-8 days after ovulation
  - Pregnancy tests most reliable by 3 weeks after conception/ 5 weeks after LMP
- Peaks at 60-90 days post conception
- Decreases to plateau at low levels
- Disappears by 2 weeks post delivery

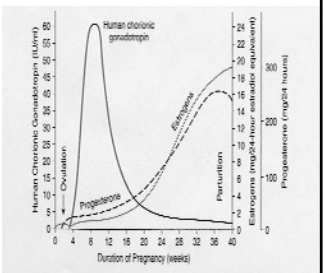


FIGURE 3-16 Patterns of excretion of human chorionic gonadotropin, progesterone, and estrogen during pregnancy. (From Guyton, A.C. [1981]. *Human physiology and mechanisms of disease* [4th ed.]. Philadelphia: W.B. Saunders.)

Human Chorionic Gonadotropin

- Functions
  - Maintain corpus luteum in early pregnancy (major function)
  - Stimulate development of fetal adrenal gland, gonads
  - Stimulation of maternal thyroid gland
  - Suppress maternal T-lymphocyte responses to 'foreign' tissue of fetus
  - May promote uterine vascular vasodilation and myometrial smooth muscle relaxation

Human Placental Lactogen

- Polypeptide similar to growth hormone
  - Also called human somatomammotropin
- Produced by syncitiotrophoblast beginning 5 to 10 days after implantation
  - Increases into to 3rd trimester
  - Secretion influenced by maternal glucose
    - Decreased maternal serum glucose = increased hPL
    - Increased hPL = increased maternal lipolysis
- Functions
  - Regulates glucose availability for fetus
  - Alters maternal protein, CHO, and fat metabolism
  - Promotes fetal growth
  - Insulin antagonist

Steroid Formation in the Placenta

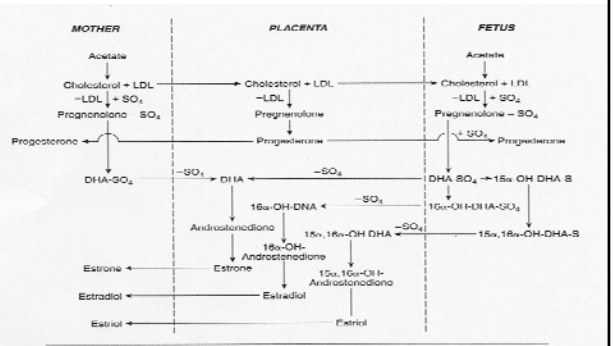


FIGURE 3-19 Steroidogenic pathways in the maternal placental fetal unit. *DHA SO4*, Dihydro epiandrosterone sulfate; *LDL*, low-density lipoprotein; *OH*, hydroxy. (From Siler-Khodr, T. M. [1998]. Endocrine and paracrine functions of the human placenta. In R.A. Polin & W.W. Fox (Eds.), *Fetal and neonatal physiology* (2nd ed.). Philadelphia: W.B. Saunders.)

Progesterone & Estrogens

- Early pregnancy
  - Progesterone from corpus luteum
  - Estrogens from ovary
- Placenta main source p 7 weeks
- Dependent on maternal-fetal interaction
  - Requires precursors from both mother and fetus

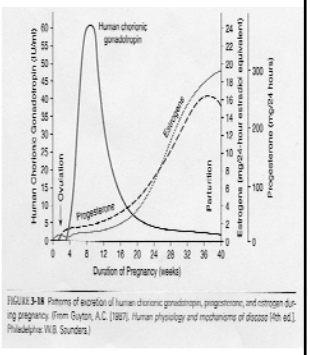


FIGURE 3-18 Patterns of excretion of human chorionic gonadotropin, progesterone, and estrogen during pregnancy. (From Guyton, A.C. [1997]. *Human physiology and mechanisms of disease* [6th ed.]. Philadelphia: W.B. Saunders.)

Progesterone

- Produced by corpus luteum until 8 weeks p fertilization
- Then synthesized primarily by placenta using maternal cholesterol, low-density lipoproteins
  - 90% secreted into maternal circulation
- Inhibits smooth muscle contractility
  - Myometrium
  - GI tract
  - Renal
  - Vascular system
- Altered metabolism
  - Fat storage
- Altered in sodium balance
- Stimulates respiratory center to alter CO_2 sensitivity
- Inhibits action of prolactin on breast
  - Decreases sensitivity of oxytocin

Estrogens

- All 3 forms increase in pregnancy
  - Estrone and estradiol increase about 10 fold
  - Estriol increases about 100 fold
- Uterine hyperplasia, hypertrophy, increased blood supply
- Breast development
- Alterations in connective tissue
  - Altered joint mobility
  - Cervical ripening
- Alterations in blood composition (plasma proteins, fibrinogen, serum binding proteins)
  - Skin changes
  - Sodium and water retention
  - Altered HCL and pepsin in gut

The Known and Unknown of Leptin in Pregnancy (Hauguel-de-Mouzon, Am J Obstet Gynecology, 2006)

- "Placental Growth Hormone"
- Maternal plasma leptin levels rise in pregnancy
- Leptin is produced by placenta
- Overproduction of placental leptin is seen with diabetes and htn in pregnancy
- Umbilical leptin levels are biomarker of fetal adiposity
- "Leptin may be sensitive to maternal energy status and coordinate metabolic response accordingly." (King, Ann Rev Nutr, 2006)

Placental Function: Transfer

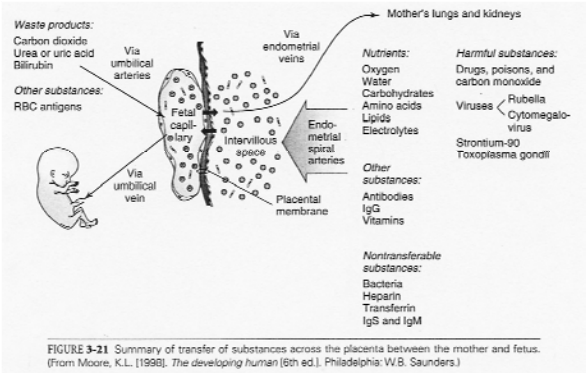
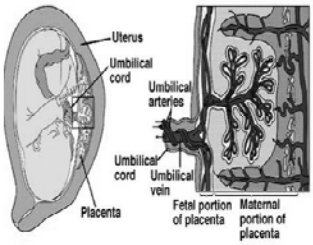


FIGURE 3-21 Summary of transfer of substances across the placenta between the mother and fetus. (From Moore, K.L. [1998]. *The developing human* [6th ed.]. Philadelphia: W.B. Saunders.)

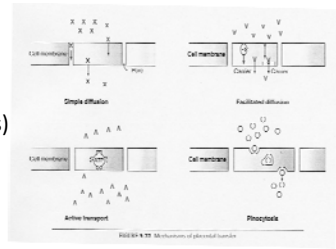
Placental "barrier"

- Maternal and fetal blood do not mix
- Fetal blood flows through capillary networks within highly branched terminal chorionic villi
- Maternal blood flows through intervillous space
  - Uterine arteriols bring blood in
  - Uterine venules drain blood



Placental Transfer Mechanisms

- Simple diffusion
- Facilitated diffusion
- Active transport
- Pinocytosis (endocytosis/exocytosis)
- Bulk flow and solvent drag
- Accidental capillary breaks
- Independent movement



Placental Transfer of Nutrients

TABLE 3-4 Mechanisms by Which Selected Substances are Transported Across the Placenta

Mechanism	Substance
Simple (passive) diffusion	Water, electrolytes, oxygen, carbon dioxide, urea, simple amines, creatinine, fatty acids, steroids, fat-soluble vitamins, narcotics, antibiotics, barbiturates, and anesthetics
Facilitated diffusion	Glucose, oxygen
Active transport	Amino acids, water-soluble vitamins, calcium, iron, iodine
Pinocytosis and endocytosis	Globulins, phospholipids, lipoproteins, antibodies, viruses
Bulk flow/solid drag	Water, electrolytes
Accidental capillary breaks	Intact blood cells
Independent movement	Maternal leukocytes, organisms such as *Treponema pallidum*

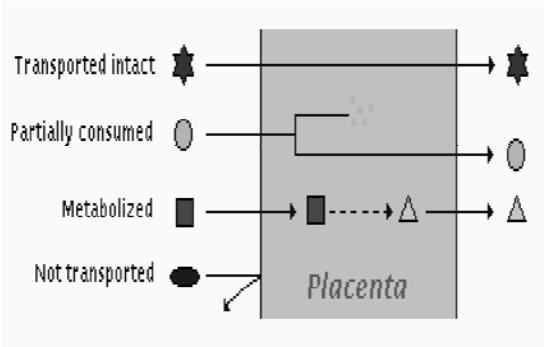
Placental Transfer of Nutrients

TABLE 3-5 Relative Concentrations of Nutrients and Other Substances in Maternal Versus Fetal Circulation

Higher in Fetus	Similar in Fetus and Mother	Higher in Mother
Amino acids	Sodium	Total proteins
Total phosphorus	Chloride	Globulins
Lactate	Urea	Fibrinogen
Serum iron	Magnesium	Total lipids
Calcium		Phospholipids
Riboflavin		Fatty acids
Ascorbic acid		Glucose
		Cholesterol
		Vitamin A
		Vitamin E

Compiled from Longo, L. (1981). Nutrient transfer in the placenta. In *Placental transport*. Mead Johnson Symposium on Perinatal and Developmental Medicine (No. 18). Evansville, IN: Mead Johnson.

Placental Transfer of Nutrients



Factors Affecting Placental Transfer

- Placental size
  - Surface area
- Diffusion distance
  - Distance *decreases* as pregnancy progresses, fetal needs increase
  - Inflammation
    - Infection, Cytokines, Vascular interruption
    - DM, obesity
- Maternal-placental blood flow
  - Maternal vascular health
  - Normal placental architecture

Factors Affecting Placental Transfer

- Concentration or electrochemical gradient of substance
  - Increased lipid solubility
  - Molecular characteristics
    - Size (smaller <600mc), Ionization (non-ionized)
  - Blood saturation with gases, nutrients
- Maternal-placental metabolism of the substance
- Presence of nutrient transporters
  - Altered by maternal nutrition & disease states
    - DM, HTN, ETOH abuse

Determinants of fetal growth

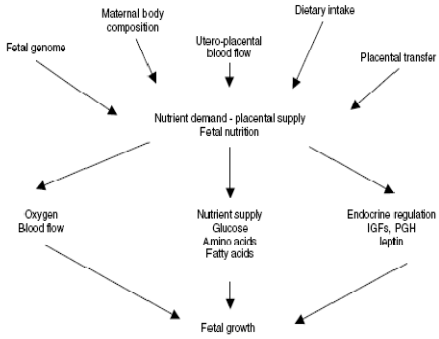


Figure 1. Main determinants of fetal nutrition and growth.

Embryonic and Placental Development

- http://www.youtube.com/watch?v=UgT5rUQ9EmQ
- http://www.youtube.com/watch?v=jo3NjApFSQE

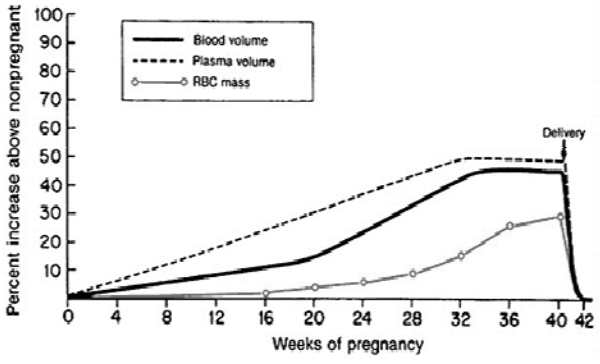
Maternal Adaptations to Pregnancy: Cardiovascular

- Increased demands on maternal CV system
- Increased circulating maternal blood mass
- Hemodynamic changes directly related to
  - Development of uteroplacental circulation (arteriovenous shunt of maternal vascular compartment)
  - Alterations in SVR- mediated by estrogen, progesterone, prostaglandins
- Mechanical forces due to anatomic alterations

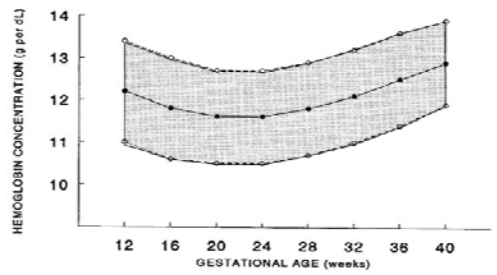
Hemodynamic changes: Increased TBV & PV

- Increased total blood volume
  - 30 to 45% (normal
  - Begins as early as 6 weeks, increases rapidly to midpregnancy, then increases slowly in last half
- Due to increase in both plasma and RBC volume
  - Peaks by 28 to 34 weeks, may plateau or decrease slightly to term
- Increased plasma volume
  - 40-60% increase (1250-1600 ml)
  - Begins at 6-8 weeks, increases rapidly in 2nd trimester, followed by slower, progressive increase, peaking around 32 weeks
  - Correlates with number of fetuses and fetal weight
- RBC increase lags behind plasma increase in PV
  - 25-33% (250-450 ml)
  - 'Physiologic anemia of pregnancy' result of hemodilution

TBV & PV changes



Mean hemoglobin concentrations (5th and 95th percentiles) for healthy pregnant women taking iron supplements



Basis for changes in TBV and PV

- Progesterone inhibits the action of aldosterone on the renal tubular cells, thus contributing to sodium retention and an increase in total body water
- NO mediated vasodilatation induces RAA and stimulates Na and H_2O retention
- Mechanical factors
  - increasing uteroplacental circuit capacity, low-resistance
  - increased distensibility of maternal vascular system

Increased cardiac output

- ↑ CO driven by increased maternal O_2 consumption maternal heart and respiratory muscle demands
  - concomitant ↓ in SVR and redistribution of blood flow
- ½ of total increase occurs by 8 weeks, the increases slowly to the 3rd trimester
  - 3rd tri CO may ↓ due to fall in systemic vascular resistance (SVR)
- CO peaks at 30-50% above non-pregnant at 28-32 weeks
  - possibly 20-26 wks
- Result of changes in both stoke volume (early pregnancy) and HR (late pregnancy)
  - ↑ SV secondary to increased ventricular muscle mass and increased end diastolic volume
- No associated increase in BP because of the marked decrease in SVR

Increased HR & SV

- ↑ Heart rate by 10-20% (10-20 beats per minute)
- Begins as early as 5 weeks, gradually increases during pregnancy
- Peaks by 32 weeks
  - Plateaus to term
- Stroke volume increases 25-30%
  - Peaking at 16 to 24 weeks then declining to term
- Leads to elevated myocardial oxygen requirement

Decreased systemic vascular resistance

- 20% decrease - may be the stimulus for HR, SV, CO changes
- Begins as early as 5 weeks, reaching lowest point at 16-34 weeks, gradually increases (slightly) toward term
- Result of vascular smooth muscle relaxation
  - Softening of cartilage and hypertrophy of vascular smooth muscle
  - Remodeling of the maternal spiral arteries
  - Addition of the low resistance UP circulation
  - Progesterone and vasoactive prostaglandins
  - Endothelial derived relaxant factors such as NO

Decreased systemic vascular resistance

- Allows changes in CO without increase in arterial pressure
- Slight decrease in mean blood pressure
  - Diastolic falls toward mid pregnancy (by ~ 10 to 15 mm with nadir at 24-32 weeks, then increases to term)
  - Systolic pressure decreases less, also reaching a nadir by mid pregnancy
  - Values significantly influenced by maternal position

Altered regional blood flow

- Uterus receives 10-20% of cardiac output by term
  - 10-fold increase → average of 500-600 L/min flow by term
  - Decreased uterine vascular resistance due to remodeling of spiral arteries
- ↑ cardia output above needs of UP unit diverted to other organ systems, acts as reservoir
  - Renal blood flow ↑ 50-80% by end of 1st trimester
  - ↑ Mammary blood flow
  - ↑ Skin, mucosa perfusion
  - ↑ Pulmonary vascular bed

Clinical Implications

- Nutrient concentration declines due to increased plasma volume, but total amount of vitamins and minerals in circulation actually increases
- During most pregnancies increased cardiovascular demands are met without compromising the mother
  - Superimposed upon existing disease state with compromised hemodynamics ↑ risk to mother
  - If maternal hemodynamics do not change
- Compromised uteroplacental circulation ↑ risk of fetal compromise
- Effects of abnormal placentation on maternal & fetal well-being reflected in pregnancy-related vascular disease

Maternal Adaptations: Respiratory

- Changes in maternal respiratory function
  - 30% ↑ production of CO_2 due to O_2 consumption
  - fetus & placenta; ↑ maternal cardiac, ventilatory, renal func; ↑ maternal tissues; ↑ CHO & lipid metabolism
- 50% ↑ volume air and gas exchange
  - Increase availability of O_2 and removal of CO_2
- Related to mechanical & biochemical factors
  - Increased thoracic dimensions, elevated diaphragm → gradual overall increase in lung volume
  - Progesterone- respiratory stimulant, smooth muscle effects
    - Decreased airway resistance
- Increased tidal volumes & sl ↑ in rate→ ↑ minute ventilation

Ventilatory Function in Pregnant Women

Factor	*10 Weeks*	*24 Weeks*	*36 Weeks*
Respiratory rate	15-16	16	16-17
Tidal volume (mL)	600-650	650	700
Minute ventilation (L)	—	—	10.5
Vital capacity (L)	3.8	3.9	4.1
Inspiratory capacity (L)	2.6	2.7	2.9
Expiratory reserve volume (L)	1.2	1.2	1.2
Residual volume (L)	1.2	1.1	1.0

Clinical Implications

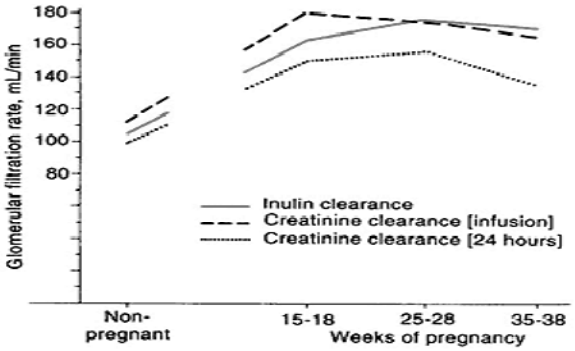
- Increased maternal CO_2 sensitivity
  - Progesterone related increase in maternal minute ventilation
  - Begins early in pregnancy, 60% of total ↑by 20 wks
- Results in state of mild *compensated* maternal respiratory alkalosis
  - Slight ↓ in maternal alveolar and plasma CO_2 & ↑ maternal O_2
  - Facilitates transfer of CO_2 from fetus to mother by increasing maternal arterial CO_2 pressure gradient

Maternal Adaptations: Renal

- Fluid & electrolyte homeostasis during pregnancy
- Structural alterations
  - Dilation & loss of tone- renal pelvis, ureters, bladder
  - Primarily progesterone driven
  - Pressure from enlarging uterus
- Functional alterations in hemodynamics
  - Significant cardiovascular alterations
  - ↓ vascular resistance→ ↑ renal blood flow
  - Altered glomerular filtration & tubule reabsorption of certain substances

Renal function changes

- Increased renal blood flow
  - Increases 50-80% by end of 1st trimester
  - Decreases gradually to term
- Glomerular filtration rate (GFR)
  - Increases 40-50% 110-180 (avg 120-150) ml/min
  - Begins at 5 weeks, peaks at 9-16 weeks, elevated to 36 weeks
  - May decrease 15-20% from 36 weeks to term



Mean glomerular filtration rate in healthy women over a short period with infused inulin (*solid line*), simultaneously as creatinine clearance during the inulin infusion (*broken line*), and over 24 hours as endogenous creatinine clearance (*dotted line*).

Renal function changes

- GF altered by ↑renal blood flow & ↓ colloid osmotic pressure (hemodilution)
- Altered tubular reabsorption
  - Increased solute reabsorbed, to balance increase filtered solute
  - However tubular reabsorption may be exceeded
- Net loss (excretion) of some solutes
  - Glucose, protein, amino acids
  - Urea, uric acid, bicarbonate
  - Water soluble vitamins, calcium, H+ ions, phosphorus
- Net retention of K^+ , sodium & water
  - selective increased reabsorption

Clinical Implications

- Proteinuria
  - Protein excretion rises from <150 mg/24 hrs to up to 250 to 300 mg/24 hrs
- Glycosuria
  - Urinary glucose values may be 10 to 100 fold greater at normal plasma levels
  - From normal 20 mg/24 hrs to 100 mg/24 hrs
  - About 70% excrete >100 mg/24 hrs; 50% excrete >150
- Renal acid-base balance altered to compensate for mild respiratory alkalosis
  - Increased excretion of sodium bicarbonate, retention of H^+
  - Serum bicarbonate levels fall to 18-22 mEQ/L

Clinical Implications

- Accumulation of water and sodium
  - Tubular reabsorption of sodium
  - 99% of filtered Na^{++} reabsorbed → Net retention of an additional 2-6 mEQ/day
  - Pregnant woman remains in sodium balance
  - Na^{++} retention proportional to water retention
  - Maintains Na^{++} & H_2O, electrolyte balance similarly to nonpregnant woman
- Increased nutrient needs
  - Increased intake and gi absorption of calcium
  - Increased intake of B vitamins, C, folate, niacin

Maternal Adaptations: GI

- Alterations include:
  - increased intestinal absorption, reduced excretion
- Alterations are driven by:
  - hormonal changes, fetal demands, maternal nutrient supply
- There may be more than one adjustment for each nutrient.
- Maternal behavioral changes augment physiologic adjustments
- When adjustment limits are exceeded, fetal growth and development are impaired
- The first half of pregnancy is a time of preparation for the demands of rapid fetal growth in the second half
- Alterations in maternal physiology facilitate transfer of nutrients to the fetus

Maternal Adaptations to Pregnancy: GI

- Anatomic changes
  - Effects of growing uterus
- Hormonal changes
  - Progesterone
    - relaxation of gastrointestinal smooth muscle
  - Estrogen
    - increased tissue vascularity, hypertrophy
    - influence carbohydrate, lipid, and bone metabolism
  - Appetite driven by insulin, glucagon, progesterone, estrogen, leptin
- Functional changes

TABLE 12-1 Alterations in the Gastrointestinal System During Pregnancy

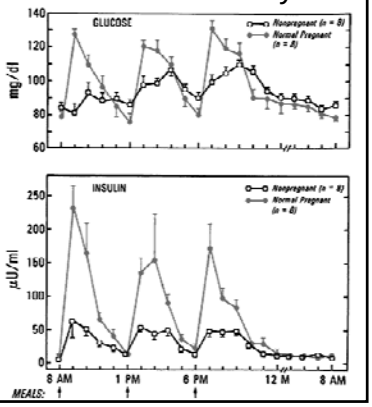
Organ	Alteration	Significance
Mouth and pharynx	Gingivitis	Friable gum tissue with bleeding and discomfort with chewing Increased periodontal disease
	Epulis formation	Bleeding and interference with chewing
	Increased saliva production	Annoyance
Esophagus	Decreased lower esophageal sphincter pressure and tone	Increased risk of heartburn
	Widening of hiatus with decreased tone	Increased risk of hiatal hernia
Stomach	Decreased tone and motility with delayed gastric emptying time	Increased risk of gastroesophageal reflux and vomiting Increased risk of vomiting and aspiration with use of sedatives or anesthetics
	Incompetence of pyloric sphincter	Reflux of alkaline biliary material into stomach
	Decreased gastric acidity and histamine output	Improvement of peptic ulcer symptoms
Small and large intestines	Decreased intestinal tone and motility with increased transit time	Facilitated absorption of nutrients such as iron and calcium Increased water absorption in large intestine with tendency toward constipation Increased flatulence
	Increased height of duodenal villi	Increased absorption of calcium, amino acids, other substances
	Altered enzymatic transport across villi; increased activity of brush border enzymes	Increased absorption of specific vitamins and other nutrients; increased sodium and water absorption
	Displacement of cecum and appendix by uterus	Complicates diagnosis of appendicitis
Gallbladder	Decreased tone and motility	Alteration in measures of gallbladder function Increased risk of gallstones
Liver	Altered position	May mask mild to moderate hepatomegaly
	Altered production of liver enzymes, plasma proteins, bilirubin, and serum lipids	Some liver function tests less useful in evaluating liver disorders Early signs of liver dysfunction may be missed Altered early recognition of liver dysfunction
	Presence of spider angiomata and palmar erythema	Discomfort because of itching

Meeting nutrient needs during pregnancy

- Energy costs of pregnancy
  - Kcal intake does not parallel changes in BMR or fetal growth
  - Energy needs of term fetus met by CHO 80% (glucose), amino acids 20% (alternate energy source, substrate for lipid formation)
- Increased maternal BMR
  - Altered to spare energy for fetal growth
- Tissue anabolism
  - Maternal tissues, uteroplacental tissues, fetal growth
- 2nd tri 300-340 kcal/day → 3rd tri 450 cal/day
  - Total average 80,000 kcal up to 120,000 kcal
  - Altered by increasing intake, decreasing activity, limiting maternal fat storage

Late gestation is characterized by

- Anti-insulinogenic , lipolytic effects of hp lactogen, prolactin, cortisol, glucagon
- Glucose intolerance, insulin resistance, decreased hepatic glycogen, mobilization of adipose tissue



Energy intake & weight gain

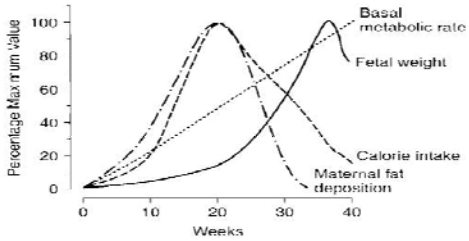
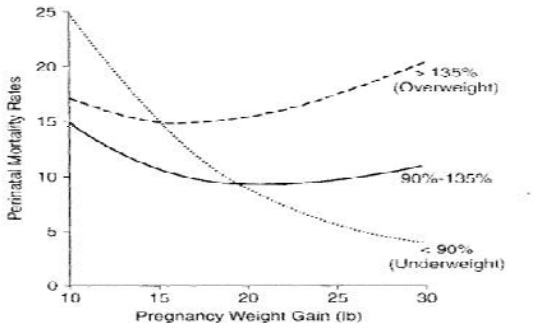
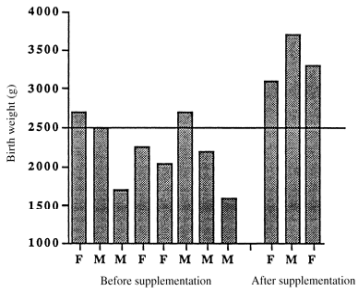


FIGURE 12-2 Changes in maternal caloric intake, maternal fat deposition, fetal weight, and basal metabolic rate during pregnancy. (Values are expressed as a percentage of marginal change.) (From Bosso, P. [1987]. Regulation of food intake during pregnancy and lactation. *Ann N Y Acad Sci, 499*, 191.)

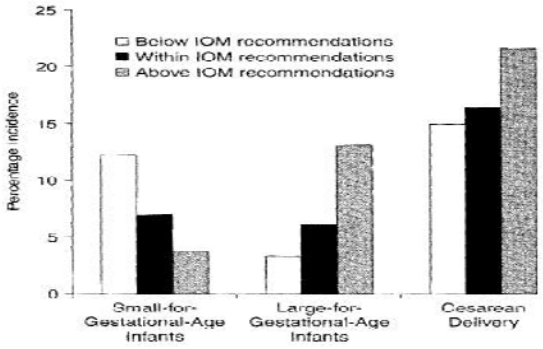
Infant birth weight & maternal weight gain





Birth weight of 11 children born to a poor woman in Montreal; 8 children were born before receiving nutritional counseling and food supplements from the Montreal Diet Dispensary and 3 children were born afterward

Wight gain & perinatal m&m



Meeting nutrient needs during pregnancy

- Protein requirements
  - 60 gm or sl more
  - provide adequate nitrogen for tissue synthesis
  - All essential amino acids and essential fatty acids (linoleic)

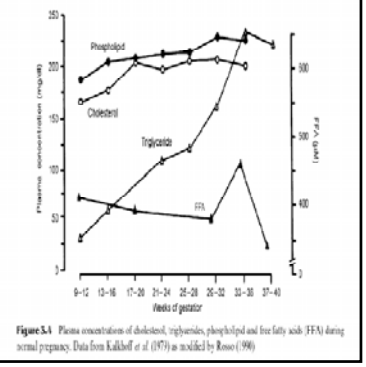


Figure 3-1 Plasma concentrations of cholesterol, triglycerides, phospholipid and free fatty acids (FFA) during normal pregnancy. Data from Kalkhoff *et al.* (1973) as modified by Rosso (1990)

Nitrogen Balance (g/day)

Source	Early pregnant	Late pregnant	Non-pregnant
Intake	12.03	12.19	11.88
Fecal	0.82	0.92	0.64
Urinary	10.52	9.02	10.56
Integumental	0.14	0.18	0.21
Retention	0.56	2.10	0.46

Lipid requirements

	Non pregnant	Early Pregnancy	Late Pregnancy
Total triglycerides	60	75 to 100	210
Total cholesterol	170	175 to 200	250
VLDL cholesterol	10	10	25
LDL cholesterol	105	100 to 125	150
HDL cholesterol	55	55 to 75	65

Vitamins & Minerals

- Dietary references ↑ by 20-100% of water soluable
  - Vit C, thiamin, niacin, Vit B_6 & B_{12}
- Lipid soluable vitamins cross placenta more easily
- Trace minerals usually sufficient
- IOM recommendations balanced diet *do not* require routine vitamin & mineral supplementation

TABLE 12–4 Basis for Increased Nutrient Needs in Pregnancy

Nutrient	Reason for Increased Need in Pregnancy
Protein	Rapid fetal tissue growth Placental growth and development Maternal tissue growth (e.g., uterus, breasts) Increased blood volume (increased hemoglobin, plasma proteins) Maternal storage reserves (for labor, delivery, and lactation)
Calories	Increased basal metabolic rate (BMR), energy needs, and protein sparing
Calcium	Fetal skeleton and tooth bud formation Increased maternal calcium metabolism
Phosphorus	Fetal skeleton and tooth bud formation Increased maternal phosphorus metabolism
Iron	Increased maternal circulating blood volume and increased hemoglobin Fetal liver iron storage; iron cost of pregnancy
Iodine	Increased BMR and thyroxine production
Magnesium	Coenzyme in energy and protein metabolism; enzyme activator Tissue growth; cell metabolism; muscle action
Vitamin A	Essential for cell development and thus for tissue growth Fetal tooth bud formation (development of enamel forming cells in gum tissue) Bone growth
Vitamin D	Absorption of calcium and phosphorus Mineralization of fetal bone tissue and tooth buds
Vitamin E	Tissue growth Cell wall integrity and red blood cell integrity
Vitamin C	Tissue formation and integrity Increased iron absorption Integrity of connective and vascular tissues
Folic acid	Increased metabolic demands of pregnancy and increased heme production Production of cell nucleus materials
Niacin	Coenzyme in energy and protein metabolism
Riboflavin	Coenzyme in energy and protein metabolism
Thiamin	Coenzyme in energy metabolism
Vitamin B_6	Coenzyme in protein metabolism Increased fetal growth requirement
Vitamin B_{12}	Coenzyme in protein metabolism, especially proteins in nucleic acid Formation of red blood cells

Adapted from Worthington-Roberts, B.S. & Williams, S.R. (1996). *Nutrition in pregnancy and lactation*. New York: McGraw-Hill.

Adjustments in Nutrient Metabolism

- Goals
  - support changes in anatomy and physiology of mother
  - support fetal growth and development
  - maintain maternal homeostasis
  - prepare for lactation
- Adjustments are complex and evolve throughout pregnancy

Psychosocial Adaptations

- Understanding maternal role attainment behavior
- Process which occurs over time and is a prerequisite for development of parenting identity & behavior
- Pregnancy
- Birth
- Postnatal attachment to newborn

Variables affecting attachment

- Psycho-social
  - Culture, education, SES, social support
  - Life experiences
    - Personal experience of being parented
    - Previous pregnancies or parenting
- Physical health
  - Maternal, pregnancy, fetal, newborn
- Mental health, personality characteristics
  - Maternal
  - Newborn

Health implications of parent-infant attachment

- Medical focus on the physical well-being of mother and fetus
  - *partially* successful in meeting health outcome goals
- Countries incorporate social, as well as medical, models of care have demonstrated *greater success* in reaching health outcomes

Health implications of parent-infant attachment

- Ameliorating effects of psychosocial intervention during pregnancy and early postpartum
  - Improved parent-infant attachment
    - Improved child care, decreased child neglect/abuse
  - Improved maternal physical well-being
    - improved pregnancy & neonatal outcomes
  - Improved parenting
    - Decreased risk of child abuse, maltreatment in this generation & next
    - Improved parental well-being (generational effect)

Disrupted attachment

- Energy required to cope with stressors detracts from opportunity, ability to do developmental work required
- Risk factors vary
  - intensity, length of exposure, potential consequences
- And, have varying modifiability
  - Parental control of risk, motivation & resources
  - Healthcare provider's ability to offer effective prevention/intervention

Benedick: pregnancy as a transition

- Normal transitional period
  - pregnancy to parenthood a developmental phase for mother (both parents)
- Opportunity to work through past issues
  - reorganize ideas about herself as a woman, how she was mothered, how she will mother
  - Transform idea of baby to be
- Two central goals of this work
  - Acceptance, embodiment of role of mother
  - Awareness of and bonding with fetus

Bibring: Pregnancy as crisis

- Developmental phenomenon- point of no return
  - Passage from one phase of life to another
  - Old ways no longer relevant
- Induce acute disequilibria
  - Opportunity for the individual to move to higher level of self-awareness and behavioral maturation
  - Mastery of new knowledge & skills
- Far-reaching effects on mother-child relationship

Rubin: Attainment of maternal role

- Mother's *experience* of pregnancy, childbirth and early postpartum that leads to the development of her maternal role identity
- Progressive transition from a 'woman without' to a 'woman with'
- Maternal 'role-taking' seen as inseparable, irreversible incorporation into her whole personality
- Grief with loss of incompatible roles, diffusion of her identity,

Maternal role attainment: Developmental tasks of pregnancy

- *Ensuring safe passage for self and baby*
- Care and knowledge seeking behaviors
- Manifested as characteristic worrying
  - 1st Focus on her own well-being
  - 2nd Shifts focus to fetus/baby
  - 3rd Finally, surviving labor and birth
- Goal: personal survival and safe birth of healthy baby

Developmental tasks of pregnancy

- *Seeking acceptance of and support for self and baby*
- Re-defining relationships with spouse/partner, family, friends
  - Re-examine relationship with family of origin, friends
  - Development of new social support networks
  - Healthcare provider/system included
- Goal: to ensure a place in the world for herself, as a woman with a child, and her baby

Developmental tasks of pregnancy

- *"Binding-in" to unborn child*
  - Attachment to fetus → infant
- Begins in childhood
  - Intensifies in pregnancy with fantasizing about unborn infant, assigning attributes to fetus
  - Well-developed relationship with 'baby' by 3rd tri
  - At birth, mother lets go of being pregnant and adjusts to being a mother, lets go of fantasy baby and begins to integrate real baby
- Considered by Rubin to be corner stone of maternal identity development

Developmental tasks of pregnancy

- *Giving of oneself*
- Willingness and ability to make personal sacrifices for well-being of fetus/infant
  - Supported by social systems and memory of her own childhood
- Goal is to insure baby's future well-being

Role attainment: theoretical strategies

- *Mimicry*- seeking information, mimicking observations
- *Role-play*- seeking role models, seeking information
- Fantasy- fantasizing about herself as a mother, imagining the idealized fetus/unborn baby
- *Introjection-projection-rejection (de-differentiation)* introjects observed behaviors, projects how those behaviors would be for her, and rejects behaviors that don't 'fit'- process of sorting, processing & selecting
- *Identity*- end-point to maternal role-taking, incorporation of image of herself as a mother, starts with ideal, stabilizes as she 'gets to know' her baby

Rubin: Maternal role attainment

- Maternal identity - inseparable incorporation in to the whole personality
- Constructs an internal concept of herself as a mother during pregnancy as preparation for motherhood
- Chooses the behaviors which give her a sense of becoming a 'good mother', of being successful and in control
- When reality does not reflect what she imagined/prepared for → cognitive dissonance

Mercer: Becoming a mother

- Progressive process in which a mother achieves competence in her role, integrates mothering behaviors into her established role set, and becomes comfortable with this new identity
- Stages progress through postpartum period
- Progress in becoming a mother marked by *self-appraisal/maternal perception*
  - Competence as parent, satisfaction with parenting, relationship with infant, stressors

Stages of becoming a mother

- Anticipatory stage
  - Pregnancy
  - Psychosocial preparation for role of mother
  - Commitment, attachment to the unborn baby, and preparation for delivery and motherhood
- Formal stage
  - Birth- the first 2 to 6 weeks following birth
  - acquaintance/attachment to the infant, identifies her infant's uniqueness
  - Begins care-taking tasks by copying experts' behaviors, following advice
  - physical restoration

Stages of becoming a mother

- Informal stage
  - 2 weeks to 4 months postpartum
  - Moving toward a new normal
  - Progresses from rigidly following directions of others to using her judgment about the best care for her infant
- Personal (maternal)identity stage
  - Postpartum- by around 4 months
  - Achievement of a maternal identity through redefining self to incorporate motherhood
  - Characterized by sense of harmony, confidence, satisfaction in the maternal role, attachment to infant, congruence of self and motherhood as others accept her performance

Mercer: Becoming a mother

- Majority achieved maternal identity by 4 months
- 4% had not achieved it at one year
- Self-reported and observed maternal behaviors and feelings of attachment and competence vary over time
  - Peak at 4 months
  - Appear and feel significantly less competent around 8-12 months

Becoming a mother (BAM)

- Variables affect successful achievement of becoming a mother
- Maternal variables
  - age, SES, perception of the birth experience, her parenting in early infancy, social stress/support, personality traits (temperament, empathy, rigidity), self-concept, child-rearing attitudes, perception of the infant, role strain, health status, perception of her mothering competence
- Infant variables
  - temperament, appearance, responsiveness, health status

BAM: Dynamic Transformation

- Transformation and growth of self
  - Intensive commitment
  - Active involvement
- Begins before or during pregnancy
- Expansion of maternal identity after birth of baby
  - With growth of child, new challenges, subsequent pregnancies, aging
- Congruent with psychosocial developmental and transition theories

Psychology: 'Prenatal attachment'

- Relates attachment theory to pregnancy drawn form Bowlby's theories about attachment
- Maternal emotional affiliation with fetus
  - Women form concrete inner representational models of their unborn child, related to a woman's own attachment history
  - Feelings of attachment begin early in pregnancy, increase rapidly beginning at approximately 16 weeks, peak levels reported in the second trimester

Psychology of successful prenatal attachment

- Predictive of postnatal maternal behavior and attitudes, postnatal maternal attachment to the infant, and mother–infant interaction and attachment patterns after the child is born
- Correlate with pregnancy-related health practices, such as receiving prenatal care and adhering to prenatal care regimens and reducing alcohol consumption during pregnancy

Putting it all together

- Understanding the physiologic processes and adaptational changes occurring in pregnancy is critical to understanding the role maternal nutrition plays in outcomes
- Understanding the particular psychosocial developmental changes that occur during pregnancy helps our understanding of motivational factors involved in behavior changes

Reference

- Blackburn, Susan T. *Maternal, Fetal & Neonatal Physiology- A Clinical Perspective.* 2007, 3rd edition. Saunders-Elsevier, St. Louis, MO. (ISBN: 978-1-4160-2944-1)