Prenatal Development

Stages of Prenatal Growth

- Zygotic (Germinal) Period (conception - 2\textsuperscript{nd} week)
  - Fertilized egg is largely unchanged in size; 2.5mm in size; precarious

- Embryonic Period (3\textsuperscript{rd} week – 2\textsuperscript{nd} month)
  - Differentiation of cells into layers (ectoderm, mesoderm, endoderm) which will form the various body systems; high risk of congenital malformation; 4cm in size at end of 2\textsuperscript{nd} month

Stages of Prenatal Growth

- Early Fetal Period (3\textsuperscript{rd} to 6\textsuperscript{th} month)
  - Fetus continues to grow rapidly; first reflex actions are felt; fetus opens mouth, clenches fist; hands are fully shaped; skeleton forms

- Later Fetal Period (7\textsuperscript{th} to 9\textsuperscript{th} month)
  - Weight triples; adipose tissue forms; resting up for "big event"; brain becomes very active; kicking and frequent changes in position
Critical Periods in Human Development

Prenatal Period

- Negative factors influencing prenatal life are believed to be a result of genetic or environmental causes
- **Teratogen**
  - Environmental agent that causes harm to the embryo or fetus
  - Teratogens are most dangerous between 3 and 8 weeks of gestation

Drugs and Medications

- **Recreational drugs**
  - Alcohol
  - Cocaine
  - Tobacco
  - Marijuana (cannabis)
Alcohol

- CDC estimates that more than 130,000 women in the US consume alcohol during pregnancy at levels known to increase birth defects.
- Prevalence:
  - Use among pregnant women - 12.9%
  - Binge drinking - 2.2%
  - Frequent drinking – 3.3%

Alcohol

- American Academy of Pediatrics
  - There is no safe dose of alcohol for pregnant women
- Growth retardation found with one drink per day

Fetal alcohol syndrome (FAS)
- Cluster of birth defects resulting from prenatal alcohol exposure

Alcohol-related neurodevelopmental disorders (ARND)
- Less severe symptoms

Neonatal abstinence syndrome (NAS)
- Withdrawal symptoms

Alcohol and Birth Abnormalities

<table>
<thead>
<tr>
<th>FAS</th>
<th>ARND</th>
<th>NAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>-Characteristic facial features</td>
<td>-Fine motor dysfunctions, clumsiness</td>
<td>-Withdrawal symptoms from minutes, hours, days after birth</td>
</tr>
<tr>
<td>-Mental retardation</td>
<td>-Delays in motor performance</td>
<td>-Tremulousness</td>
</tr>
<tr>
<td>-Attention deficit hyperactivity disorder</td>
<td>-Speech disorders</td>
<td>-Hyperactivity</td>
</tr>
<tr>
<td>-Retarded physical growth in stature, weight, head circumference</td>
<td>-IQ =67</td>
<td>-Impairability</td>
</tr>
</tbody>
</table>

- Tremulousness
- Hyperactivity
- Impairability

Withdrawal symptoms from minutes, hours, days after birth

- Tremulousness
- Hyperactivity
- Impairability
Cocaine

- Effects of use during pregnancy
  - Users have a 25% higher incidence of preterm birth
  - Fetal brain damage
  - Increased occurrence of miscarriage
  - Extreme fluctuations in heart rate and blood pressure of mother and fetus
  - Constricted blood vessels in uterus
  - When born, baby is at risk for SIDS

- Like alcohol, just a single use can cause severe problems

Tobacco

- 2200 different ingredients in tobacco leaves and smoke
- Carbon monoxide
  - Interferes with hemoglobin’s oxygen carrying capacity
  - Fetal hypoxia
- Nicotine
  - Affects placental blood vessels to induce fetal hypoxia
- 12%-22% of women smoke during pregnancy
Tobacco

- Prenatal complications
  - Premature rupture of membranes
  - Increased chance of spontaneous abortion
  - Higher rates of stillbirth
  - Intrauterine growth retardation

Tobacco

- Postnatal complications
  - Lower average birth weight
    - Small for gestational age
  - Sudden infant death syndrome (SIDS)
  - Long-term retardation of growth
    - Weight, stature, head circumference
  - Respiratory disorders
    - Pneumonia
    - Bronchitis

Tobacco

- Behavioral effects
  - Reduced mental alertness
  - Reduced visual alertness
  - Mother is less likely to breastfeed

Tobacco

- Second hand smoke
  - Leads to same maternal complications
  - Children in homes where there is second hand smoke have more respiratory problems
Cannabis (Marijuana)

- Contains 400 different chemicals
  - THC = active chemical
    - THC can cross placenta and accumulate in the fetus
- Little conclusive research on the effects of marijuana and its effect on the human embryo or fetus
- Cannabis is associated with no known obstetric complications
- Drug does not alter fetal growth

Prescriptive Drugs

- Some Mothers must continue medications during pregnancy
- Does the drug or Mother’s ill health cause complications?
- Some drugs may damage a body part that is growing and developing during the drug use
  - Thalidomide
- Some drugs prescribed for Mother may adversely affect the fetus
  - Thyroid medication

### Nonprescriptive Drugs

- "over-the-counter" drugs (OTC)
  - Many chemicals to treat a wide variety of problems
  - Many contain alcohol
    - Cold medications
- Generally considered “safe”
- OTC medications contain a variety of chemicals and for that reason, caution is warranted during pregnancy
  - Teratogenic effect upon fetus
OTC Medications

<table>
<thead>
<tr>
<th>Considered Safe</th>
<th>Potentially Dangerous</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen (Tylenol)</td>
<td>Aspirin; postterm pregnancy and prolonged labor; bleeding in skull of baby; maternal bleeding during delivery</td>
</tr>
<tr>
<td>Ibuprofen (Advil, Motrin)</td>
<td>Cold medications containing alcohol: FAS and ARND</td>
</tr>
<tr>
<td>Naproxen Sodium (Aleve)</td>
<td>OTC drugs designed to treat a variety of problems</td>
</tr>
</tbody>
</table>

Long term use of any OTC is not recommended

Obstetrical Medications

- There is controversy over the use of obstetrical medications
- These agents are known to enter fetal circulation, exerting their effects on the child, within minutes after administration to the mother
  - Narcotic analgesics
  - Barbiturate sedatives
  - Nonnarcotic analgesics
  - Tranquilizers

Obstetrical Medications

- 7 drugs may be used during a vaginal delivery
- 15 drugs may be used during a Caesarian delivery
  - Oxytocin – aid labor
  - Meperidine – relieve pain
  - Phenergan – relieve anxiety
  - General anesthetic drugs
  - Regional anesthetic drugs

Maternal Diseases

- Viral diseases
  - Rubella and congenital rubella syndrome
  - HIV
- Parasitic diseases
  - Toxoplasmosis
- Hematologic diseases
  - Rh incompatibility
- Endocrine diseases
  - Diabetes mellitus
Rubella & Congenital Rubella Syndrome (CRS)

- German measles
- Damage to fetus is tied to time of maternal infection
- 20%-50% of infected may not notice symptoms
- 2003: 20,000 newborns had CRS

- Associated defects
  - Growth retardation
  - Mental retardation
  - Congenital glaucoma
  - Cataracts
  - Bony lesions
  - Pneumonia
  - Hepatitis
  - Cardiac anomalies
  - Deafness (80%)

HIV

- Human immunodeficiency virus
- Easily passed on to offspring
  - In utero from the mother to the fetus
  - During delivery when the fetus comes in contact with infected blood or infected vaginal secretions
  - Through breast milk
- 7000 HIV babies born each year

HIV

- Zidovudine has decreased number of HIV babies
  - Given
    - During pregnancy
    - During delivery
    - 6 weeks after delivery
- Most children do not survive past two years
  - 90% will die before 4 years of age
Neurological Deterioration in HIV-Infected Children

- Loss of previously acquired milestones
- Failure to attain developmental milestones at the expected age
- Impaired brain growth
- Spasticity or rigidity
- Muscle weakness
- Ataxia – impaired ability to control movement
- Seizures, tremor, athetosis

Toxoplasmosis

- Protozoan parasites
  - Toxoplasma gondii
  - Pregnant women come into contact with this parasite when cleaning a cat’s litter box
  - Infectious oocysts are in soil contaminated by cat’s feces
  - Called “silent infection”
- 85% of newborns will experience convulsions and mental retardation
- 75% of newborns will have motor problems
- 13% - deafness
- 50% - visual problems

Rh Factor

- Blood types in humans
  - A, B, AB, O
- Rh factor – rhesus factor
  - A protein found on the blood cells of most people
  - Positive (+) indicates you have the factor (85%)
  - Negative (-) indicates you do not have the factors (15%)
  - Capable of inducing antigenic effects

Rh Incompatibility

- Rh factor on red blood cells
  - Potential problem when an Rh+ man and Rh- woman conceive an Rh+ child
  - Rh+ blood cells escape fetal circulation
  - Rh+ blood cells in maternal circulation are treated as foreign bodies
  - Antibodies are formed to fight fetal blood cells
Rh Incompatibility

- 1st offspring unaffected
- Subsequent offspring will illicit antibody reaction
- Mother given anti-D IgG immunoglobulin immediately after first delivery

Rh Incompatibility

- Erythroblastosis fetalis
  - Hemolytic disease of the newborn (HDN)
  - Rh+ offspring exposed to maternal antibodies
  - Characteristics
    - Anemia
    - Immature red blood cells
    - Edema
    - Jaundice

Diabetes Mellitus

- The metabolic environment for the fetus constantly changes in utero
  - Normoglycemia to hypoglycemia (low blood sugar) to hyperglycemia (high blood sugar)
- Hyperinsulinemia
  - Maternal hyperglycemia in 3rd trimester leads to increases in fetal glucose
  - Fetal insulin secretion increases
Diabetes Mellitus

• Hyperinsulinemia may result in:
  – Macrosomia
    • Increased insulin production increases glycogen release from liver which results in triglyceride production (birth weight above 90th tile)
    • May be responsible for adult obesity
  – Inhibition of maturation of lung surfactant
  – Muscle weakness/cardiac arrhythmias
  – Permanent neurological damage due to neonatal hypoglycemia

Abnormalities of Infants Born to Diabetic Mothers

<table>
<thead>
<tr>
<th>Condition</th>
<th>Abnormalities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spina bifida</td>
<td>Musculoskeletal deformities</td>
</tr>
<tr>
<td>Hydrocephalus</td>
<td>Asphyxia</td>
</tr>
<tr>
<td>Heart defects</td>
<td>Facial nerve injury</td>
</tr>
<tr>
<td>Skeletal and CNS defects</td>
<td>Brachial plexus injury</td>
</tr>
<tr>
<td>Macrosomia</td>
<td>Cesarean section (cephalopelvic disproportion)</td>
</tr>
</tbody>
</table>

Chromosomal and Genetic Disorders

• Chromosomal Disorders
  – Down syndrome

• Genetic Disorders
  – Phenylketonuria
  – Cystic fibrosis
  – Sickle cell trait
  – Sickle cell disease

Chromosome Disorder

• Down Syndrome
  – Meiotic nondisjunction
  – One sperm or egg cell contains two members of a particular numbered chromosome (#21) while the other member contains none
  – Could result in 47 chromosomes
  – Down Syndrome
    • Trisomy 21
### Symptoms and Signs of Trisomy 21 (Down Syndrome)

<table>
<thead>
<tr>
<th>Symptom</th>
</tr>
</thead>
<tbody>
<tr>
<td>Walking delayed 1 or more years</td>
</tr>
<tr>
<td>Slow speech development</td>
</tr>
<tr>
<td>Slow development of fine motor control</td>
</tr>
<tr>
<td>Toilet training delayed</td>
</tr>
<tr>
<td>Lower than normal birth weight</td>
</tr>
<tr>
<td>Hypotonia</td>
</tr>
<tr>
<td>Short stature</td>
</tr>
<tr>
<td>Delayed puberty</td>
</tr>
<tr>
<td>Prone to respiratory infections</td>
</tr>
<tr>
<td>Heart disease</td>
</tr>
<tr>
<td>Prominent anatomical features</td>
</tr>
</tbody>
</table>

### Down Syndrome

- **Mental retardation**
  - IQ between 20 and 60
  - Mental age of 8 years
- **Walking delayed**
  - Treadmill walking can help the child develop walking pattern
  - Emphasizes neural connections
  - Trains multiple subsystems

### Genetic Disorders

- **Phenylketonuria (PKU)**
  - Caused by a disturbance in amino acid metabolism by a gene that suppresses activity of the liver enzyme phenylalanine hydroxylase
  - This enzyme converts L-phenylalanine to tyrosine
  - If L-phenylalanine not converted, the CNS is affected

### PKU

![PKU Diagram]

- **Dietary Protein**
- **L-Phenylalanine**
- **Tyrosine**
- **Phenylalanine hydroxylase**
Genetic Disorders

- **Cystic Fibrosis (CF)**
  - Causes a thick, sticky mucus to be secreted in the lungs
  - Person with CF has repeated respiratory infections
  - Scar tissue develops on the lungs
  - There is no cure
    - Due to new drugs, children living longer

- **Sickle Cell Trait (SCT)**
  - Individual inherits normal gene for hemoglobin (Hb-A) and one abnormal gene (Hb-S)
  - Asymptomatic
  - Live normal lives
  - Can pass the SCT gene to offspring
  - No problems with physical activity

- **Sickle Cell Disease (SCD)**
  - Child inherits two abnormal Hb genes (SS or Hb-S and Hb-S)
  - Red blood cells are sickle-shaped and can get caught in small blood vessels blocking blood flow
  - Red blood cells are also easily destroyed or may concentrate in high levels in the spleen
SCT and SCD

- Who may be at risk? ….. People from
  - Parts of Africa (the region south of the Sahara Desert)
  - Spanish-speaking areas like South America, Cuba, and Central America
  - Saudi Arabia
  - India
  - Mediterranean countries, such as Turkey, Greece, and Italy
  - US
    - 1 in 600 African Americans
    - 1 in 1000 to 1400 Hispanic Americans

Genetic Disorders

- Fragile-X Syndrome
  - Due to gene mutation
  - Causes autism
  - Delay in early motor skills
    - Crawling, sitting, walking
    - Poor balance, flat feet, hyperextensibility of joints
    - Difficulty playing games with other children
  - Treatment
    - Physical therapy
    - Adapted physical education

Prenatal Diagnostic Procedures

- One at high risk for giving birth
  - Will be over 35 years at time of delivery
  - Has already given birth (or whose partner has) to child with genetic disease or birth defect
  - Has a family history of genetic disease or birth defects
  - Has a medical history of genetic traits

Prenatal Diagnostic Procedures

- Common procedures
  - Ultrasound
  - Amniocentesis
  - Chorionic villus sampling
  - Alpha-fetoprotein test
  - Triple marker screening blood test
<table>
<thead>
<tr>
<th><strong>Ultrasound</strong></th>
<th><strong>Amniocentesis</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Sonogram</td>
<td>• Needle inserted through abdominal wall</td>
</tr>
<tr>
<td>• Can be used to measure head size of baby</td>
<td>• Sample of fluid from amniotic sac removed</td>
</tr>
<tr>
<td>• Helps to determine exact length of gestation</td>
<td>• Fetal cells can be tested to determine abnormalities</td>
</tr>
<tr>
<td>• Used to examine placement and structure of placenta</td>
<td>• Ultrasound is used to guide needle placement</td>
</tr>
<tr>
<td>• Can detect baby’s gender; multiple pregnancies</td>
<td>• Employed when mother is at high risk for giving birth to child with abnormalities</td>
</tr>
</tbody>
</table>

**Chorionic Villus Sampling (CVS)**
- Can detect abnormalities earlier than amniocentesis
  - Between 10-12 weeks of gestation
- Instead of amniotic fluid, a sample of the villi of the chorion are collected and tested
- Carries a greater risk than amniocentesis

**Chorionic Villus Sampling (CVS)**
- A plastic catheter is inserted through the cervix and guided by ultrasound

**Method 1: Chorionic Villus Sampling**
Chorionic Villus Sampling (CVS)
A biopsy needle is inserted through the abdominal wall and guided by ultrasound

Method 2: Chorionic Villus Sampling

Alpha-fetoprotein (AFP) Test
- Blood test performed at 15-20 weeks into pregnancy
- Measures the amount of AFP to detect neural-tube defects (high levels) or Down Syndrome (low levels)
- Because of the number of false positives, it is used mainly as a screening test

Triple Marker Screening
- Test for detecting Down syndrome in pregnant women younger than 35 yr
- Determine triple marker in blood
  - Human chorionic gonadotropin
  - Conjugated estriol
  - Alpha-fetoprotein
- Safe, with a 40%-60% accuracy rate

Maternal Nutrition
- Sedentary women need to increase caloric intake by 300 kcal/day
- Active women must make additional adjustments based upon caloric expenditure
- Weight gain is based upon pregravid weight (weight prior to conception)
**Maternal Nutrition**

- In women who have a *pregravid weight* appropriate for height, the weight gain will equal 25-30 lb
- Overweight women will want to gain less (BMI > 25)
- Underweight women will want to gain more (BMI < 19.8)

---

**Recommended Weight Gain**

<table>
<thead>
<tr>
<th>Pregravid</th>
<th>BMI</th>
<th>Weight Gain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ideal</td>
<td>19.8</td>
<td>25-35 lb</td>
</tr>
<tr>
<td>Overweight</td>
<td>&gt;26</td>
<td>15-25 lb</td>
</tr>
<tr>
<td>Underweight</td>
<td>&lt;19.8</td>
<td>28-40 lb</td>
</tr>
</tbody>
</table>

---

**Maternal Nutrition**

- Lack of protein in mother can lead to impaired prenatal brain growth
- The developing fetal brain should achieve 25% of its mature weight prior to birth
- Perinatal mortality common in underweight mothers

---

**Maternal Nutrition**

- *Grandmother effect*
  - The second – as well as the first-generation – show the effects of poor nutrition
  - Even if a woman attains adequate nutrition throughout life, she has an increased chance of giving birth to an abnormal offspring if her mother was undernourished
Birth Weight

- Low birth weight is not always associated with premature birth
- Premature and small full-term infants have very different problems
- Gestational age and weight are no longer used to describe an infant as premature

Three major diagnostic groupings of birth weight

- **SGA**
  - Growth retardation from inadequate nutrition in utero
  - Poor brain development
    - Mental retardation
  - May have motor problems later

- **AGA**
  - >1500 g
  - Preterm AGA at less risk than SGA
  - There is some developmental delay before 1 yr
  - Catch up by 2 yr

- **LGA**
  - > 90th percentile in weight for given gestational age
  - Due to large size, birth injuries are common
    - Fracture of clavicle
    - Brachial plexus injury
    - Respiratory distress syndrome
  - Diabetic mothers are often macrosomic and have LGA infants
Exercise During Pregnancy

Women who exercised before pregnancy and continue to do so during pregnancy tend to weigh less, gain less weight, and deliver smaller babies.

All women, regardless of initial level of physical activity, decrease their activity as pregnancy progresses.

Exercise During Pregnancy

No information is available to assess whether active women have better pregnancy outcomes.

Physically active women appear to tolerate labor pain better.

Exercise During Pregnancy

Maternal responses
- Blood volume increases by 35% to 45%
- Cardiac output increased at rest
- Blood shunted to muscles during exercise
  - Does this maternal response decrease fetal oxygen supply?
- Body temperature rises
  - Could be dangerous to the fetus
  - Important to stay hydrated during exercise

Exercise During Pregnancy

Fetal responses
- Heart rate increases 10-30 beats per minute when mother exercises
- Heart can stay elevated during recovery depending upon the intensity of maternal exercise
- Very little research conducted to determine fetal responses to maternal exercise
Exercise During Pregnancy

Absolute contraindications to exercise
- Hemodynamically significant heart disease
- Restrictive lung disease
- Incompetent cervix/cerclage
- Multiple gestation at risk for premature labor
- Persistent second- or third-trimester bleeding
- Placenta previa after 26 weeks of gestation
- Premature labor during the current pregnancy
- Ruptured membranes
- Preeclampsia/pregnancy-induced hypertension

Relative contraindications to exercise
- Severe anemia
- Unevaluated maternal cardiac arrhythmia
- Chronic bronchitis
- Poorly controlled Type I diabetes
- Extreme morbid obesity
- Extreme underweight (BMI < 12)
- History of extremely sedentary lifestyle
- Intrauterine growth restriction in current pregnancy
- Poorly controlled hypertension
- Orthopedic limitations
- Poorly controlled seizure disorder
- Poorly controlled hyperthyroidism
- Heavy smoker