Chapter 6
Biological Aspects and the Promises of Prevention

Quiz  8 points possible
• 1. List 3 types of Down Syndrome.

• 2. A person diagnosed with Down Syndrome has an increased risk of _______dementia.

• 3. Name the disorder associated with hyperphagia.

• 4. List two sex chromosome anomalies.

• 5. Doctor orders: 150 mg suspension PO.
  • on hand: 25 mg/mL suspension. Dose =_______

Chapter Objectives
• provide an overview of causation
• discuss the basic principles of genetics
• identify and discuss the major biological causes of mental retardation
• discuss various ways that mental retardation can be prevented
• identify and discuss selected ethical issues facing the field
Types of Causes

Terminology

• Biological
  – Physiological
  – Organic
• Environmental
  – Psychological
  – Sociological
  – Psychosocial
  – Cultural-Familial

Statistics

• Approximately 50% of cases of intellectual disability have a known cause
• Biological pathology can be identified in 60% to 75% of cases for IQs falling below 50
• 25% to 40% of all cases of mild retardation may have a specific identifiable cause
• 10-50% of cases of mild retardation are related to genetic etiologies
• State prevalence rates vary between .35% and 2.39%

Terminology

Sources

• conventional wisdom
• names of persons who initially identified or described the condition
• biomedical terms describing the cause or the resultant disabilities.
Basic Information

Genetic Terminology

• Genes
  – basic biological units carrying inherited physical, mental, or personality traits
  – Approximately 30,000 genes are present in each human cell
  – Genes occupy specific positions on chromosomes
  – Pairs of genes carrying the same trait are called homozygous
  – Pairs of genes carrying different traits are called heterozygous

Genetic Terminology

• Chromosomes
  – threadlike or rod like bodies that are composed of genes and contain genetic information and material
  – Each human cell contains 23 pairs of chromosomes; one member of each pair is donated from each parent
**Genetic Terminology**

**Types of Chromosomes**

- **Autosomes**
  - matching pairs
  - constitute 22 of the 23 pairs
- **Sex Chromosomes**
  - The 23rd pair
  - Determine gender
    - Mother always donates an X chromosome
    - Father may donate an X or a Y chromosome
    - XX = female gender; XY = male gender

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**Human Genome Project**

- Federally funded mega-project designed to map all of the human chromosomes

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**Genetic Transmission**
Types of Genetic Transmission

- Autosomal dominant inheritance
- Autosomal recessive inheritance
- Sex-linked inheritance
- Polygenic inheritance

Types of Genetic Transmission

Dominant Inheritance

- Dominant genes mask their partners, and will be expressed.
- Determines a variety of common traits, such as brown eyes and prematurely white hair
- Several rare physical disorders are carried as dominant traits, and these are often structural disorders
  - Marfan's syndrome
  - Dwarfism
  - Neurofibromatosis

Marfan's Syndrome

Autosomal Dominant Genetic disorder affecting collagen/connective tissue
- Long fingers/toes
- Taller than average
- Dislocations of hips & mandible
- Cardiovascular defects

- Michael Phelps – Olympic Swimmer
- Steinberg sign – fold thumb into closed fist
- Walker – Murdoch sign – grip wrist with opposite hand

Positive test – Marfan’s
Dwarfism

What Causes Dwarfism?

- It is a genetic disorder, usually from inheritance.
- A random genetic mutation in either the father's sperm or the mother's egg.
- Most common type, accounting for 70% of all cases of short stature, is called achondroplasia.
- Dwarfism has other causes, including metabolic or hormonal disorders in infancy or childhood.
- There are more than 200 causes of dwarfism.

Dominant Inheritance Neurofibromatosis

- Also known as von Recklinghausen's disease
- Associated with a site on chromosome 17
- Affects about 1 in 3,000 newborns
- Symptoms:
  - Light brown patches (called café-au-lait) on the skin
  - Multiple, soft, fibrous swellings or tumors (neurofibromas)
  - Severe physical deformities
- Tumors may be surgically removed, but reappear

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Neurofibromatosis: An Overview

- It is the most common neurological disorder caused by a genetic disorder.
- A mutation in the NF1 gene located on chromosome 17 which is caused by different genes or defects.
- NF is the most common affecting 1 in 3,000 people.
- About 1 in 1,000 people develop it.
- Neurofibromatosis is not inherited.
- It is caused by the NF1 gene located on chromosome 17.
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Dominant Inheritance
Neurofibromatosis

• Great functional variation among cases
• Tumor placement determines mental development
  – Mental retardation may occur if tumors are located on the brain
  – 30%–60% have learning disabilities
• The psychological consequences of deformity are paramount

Types of Genetic Transmission
Recessive Inheritance

• Recessive genes cannot control their partners, and will not be expressed when paired with a dominant gene
• Become influential only when matched with another recessive gene (homozygous)
• Determines a variety of common traits such as blue eyes
• Responsible for health disorders such as sickle cell anemia and galactosemia
• Since the gene may not be expressed in parents, genetic screening is needed for prediction

Recessive Inheritance
Disorders Related to Intellectual Disability

• Tay Sach’s Disease
  – disproportionately prevalent among Ashkenazic Jews
  – typically manifested late in the child’s 1st year
  – severe retardation, convulsions, blindness, paralysis, and death by the age of 4
  – no cure
Recessive Inheritance

PKU
- the most common of the genetic disorders
- the most publicized success story in the literature
- may be associated with aggressiveness, hyperactivity, and retardation
- incidence of 1 in every 12,000 to 15,000 births.
- virtually eliminated as a causative factor in severe retardation
- the treatment regimen for PKU is related to restrictions in intake of phenylalanine, common in high-protein foods

Recessive Inheritance

The PKU Diet
- Unappealing and hard to follow
- Often discontinued during school years, but research shows this practice may lead to deterioration
- The longer the diet is followed, the better the outcome
- Pregnant women with PKU must follow the diet or risk retardation, heart disease, and microcephaly in their children

Types of Genetic Transmission

Sex-Linked Inheritance
- Also called X-linked inheritance
- Occurs through recessive traits carried on the X chromosome
- Females are affected only if both parents pass along the recessive gene
- Males are affected if the mother passes along the recessive gene, because there is not another X chromosome
Sex-Linked Inheritance

Statistics

• More than 70 disabilities
• 200 genes on X-chromosome linked to intellectual disability
• 50 genes have been mapped

Sex-Linked Inheritance

• Associated physical conditions
  – Color blindness
  – Duchennes Muscular Dystrophy
  – Hemophilia
• Associated physical/intellectual disabilities
  – Lesch-Nyhan Disease
  – Fragile X syndrome

Lesch-Nyhan Disease

• Second most common metabolic disorder
• Associated with extreme impulse to self-injure and, to a lesser degree, injure others
• Biting is the most prominent form, but other forms of self-injury are common
• Some form of restraint is usually necessary for physical and psychological safety
Lesch Nyhan Syndrome

Fragile X Syndrome

- Most common hereditary cause of intellectual disability
- Second most common clinical type (after Down syndrome)
- Absence or severe deficiency of a specific protein (FMRP) that is deemed to be essential for the functioning of the brain
- Level of protein available affects clinical outcomes

Fragile X Syndrome

Inheritance Pattern

- One in 260 women are carriers.
- The most common form of transmission is from mother to son, which can be:
  - pre-mutated (carrier) to mutated (affected)
  - mutated (affected) to mutated (affected)
  - pre-mutated (carrier) to pre-mutated (carrier)
- A father can be pre-mutated (unaffected and a carrier) and pass the fragile X gene on to his daughter.
- There is no male-to-male transmission.
- Fragile X occurs in about 1 in 1,500 males and about 1 in 1,000 females in the general population
Fragile X Syndrome
Physical Characteristics

• prominent jaws
• macro-orchidism (large testes)
• long and thin faces
• long and soft ears and hands
• prominent foreheads
• enlarged heads

Fragile X

Fragile X Syndrome
Socio-emotional Characteristics

• Mental Retardation is common
  — Moderate-Severe is most common
• Common Behavioral Manifestations:
  — Gaze Avoidance
  — Attention Problems
  — Repetitive Speech (Including Echolalia and Palilalia)
  — Repetitive Behaviors
Fragile X Syndrome

Relationship with Autism

• A definite sub-group appears to have behaviors commonly associated with autism (with some individuals meeting the diagnostic criteria for autism).
• Fragile X mutations may increase the risk of a child developing autistic-like tendencies.
• It is unclear what the precise relationship is between autism and fragile X.
• Fragile X mutations may increase the susceptibility for autism in conjunction with other genes associated with autism susceptibility.

Fragile X Syndrome

Females

• frequently classified as carriers
• may not be identified because of low expressivity
• an estimated one-third may also be partially affected
• a pattern of varied strengths and weaknesses is particularly apparent in girls who have fragile X.
• although intellectual disability is rare, such girls often have learning disabilities.

Beirne-Smith et al. Mental Retardation, Seventh Edition
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Polygenic Inheritance

• Refers to the interaction of many genes to produce a clinical outcome
• Precise evaluation is difficult in single cases
• Predictions based on statistical data from large population
• Suspected to be an agent of cause in intellectual disability of unknown etiology, or psychosocial retardation

Chromosomal Differences

• Identified through karyotyping
• Approximately 10% of pregnancies begin with some chromosomal imbalance, but most of these abort spontaneously during the first 3 months of pregnancy
• Chromosomal errors can be identified in approximately 1 in 200 live births.
• Abnormal chromosome arrangement is innate, or present at conception but is not the product of hereditary exchange
Chromosomal Abnormalities

• **Nondisjunction**
  - chromosomes fail to split at conception, causing the formation of a group of three chromosomes (a trisomy) in lieu of the normal pair

• **Translocation**
  - a fragment of chromosomal material is located across from or exchanged with another chromosomal pair

Chromosomal Abnormalities

• **Mosaicism**
  - an uneven pattern of dissimilar cells (such as some cells with 46 and some with 47 chromosomes)

• **Deletion**
  - Part of a chromosome is missing

• **Disomy**
  - 2 copies of the chromosome from one parent are present instead of a copy from each

Down Syndrome

• Prevalence is 1 in 700-1000 births

• 5-7% of people with mental retardation have Down syndrome

• May be caused by types of chromosomal abnormality
  - 92% have Trisomy 21, a nondisjunction form
  - found more often in children born to older mothers (1 in 30 births to women over age 45)
Down Syndrome
Trisomy 21

- Possible causes
  - deterioration of the ovum associated with the cumulative effects of chronic stress burden
  - Prenatal exposure to medication, drugs, radiation, chemicals, or hepatitis viruses
  - absence of a mechanism in the mother to abort the fetus spontaneously

Down Syndrome
Translocation and Mosaicism

- Translocation
  - Extra material from Chromosome 21 translocates to Chromosome 13 or 15
  - 3-5% of cases of DS

- Mosaicism
  - Some, but not all, cells have an extra chromosome 21
  - Number of cells with the extra chromosome dictates degree of symptoms
  - Most rare form of DS

Down Syndrome
Associated Physical Traits

- Short stature
- Flat, broad face with small ears and nose
- Short, broad hands with incurring fingers
- Upward slanting of the eyes with folds of skins (epicanthic folds) at the inside corner of the eye
- Small mouth and short roof, which may cause the tongue to protrude and contribute to articulation problems
- Single crease across the palm
- Reduced muscle tone (hypotonia) and hyperflexibility of joints
- Incomplete or delayed sexual development
Down Syndrome
Relationship with Alzheimer’s Disease

- Two genes implicated in AD are located on Chromosome 21
- People with DS have increased risk for developing AD
- Life expectancy for individuals with DS is increasing
- Chances of developing AD increase with age

Prader-Willi Syndrome

- Majority of cases are caused by a deletion of the paternal 15 chromosome
  - Significant subset has a maternal disomy of chromosome 15

Prader-Willi Syndrome
Characteristics

- Small stature
- Borderline to Moderate Mental Retardation
- Insatiable Appetite (Hallmark Feature)
- Obsessive-Compulsive Behaviors, especially with regard to food
- Infantile failure to thrive / hypotonia
- Onset of appetite increase around age 2
- Life-threatening obesity if appropriate interventions are not undertaken
- Significant externalizing behaviors (tantrums/ aggression/ passive aggression, etc.)
Williams Syndrome

- Incidence is approximately one in 20,000 births
- Caused by a microdeletion of chromosome #7
- Genes missing impact elastin, or connective tissue

Williams Syndrome

Physical Characteristics

- Petite stature
- “Pixie-like” appearance
- Identified medical concerns including cardiac, digestive, and feeding difficulties

Williams Syndrome

Learning & Educational Characteristics

- Wide range of IQ, but most have Mild Mental Retardation to Borderline Intellectual Functioning
- Developmental delays in speech/language, motor and academic skills
- An ability to learn to read over time and with strength in phonics-based spelling
- Limited visuo-spatial development and poor visual-motor skills (e.g., handwriting problems)
- Limited mathematical and numerical knowledge
- Musical abilities common
**Williams Syndrome**  
Socioemotional Characteristics  
- Overly friendly in their interactions  
- Highly anxious  
- Well-developed vocabulary but difficulty with reciprocal conversation

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**Sex Chromosomal Differences**  
**Klinefelter syndrome**  
- Males receive extra X chromosome(s)  
- Sterility and underdevelopment of the male sex organs and the acquisition of female secondary sex characteristics  
- Psychosocial problems include language problems, difficulties in social relationships, and mood disturbance  
- Intellectual deficits increase with number of X chromosomes  
- Incidence: 1 in 500 to 1,000 births  
- Surgery and testosterone treatment can help

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**Sex Chromosomal Differences**  
**Turner syndrome**  
- Results from the absence of one of the X chromosomes (XO) in females  
- Incidence is 1 in 2,500 female births  
- Usually results in learning disability – not mental retardation  
- Common problems are in spatial relations, mathematics, memory, attention, and social competence  
- Physical development includes lack of secondary sex characteristics, sterility, and short stature
Cranial Malformations

Types

- Anencephaly
  - the absence of major portions of the brain
- Microcephaly
  - a small, conical skull and a curved spine that typically leads to a stooping posture
- Hydrocephaly
  - interference in the flow of cerebrospinal fluid within the skull that may result in an enlarged cranium

Microcephaly

- May be transmitted genetically as an autosomal recessive trait
- Most often the result of prenatal toxin exposure
- Often associated with severe intellectual disabilities and an energetic, outgoing personality
Hydrocephalus

• Literally, “water on the brain”
• The degree of pressure inside the skull modulates outcomes
• May result from polygenic inheritance or prenatal exposure to toxins
• **Shunts** are valves or tubes surgically inserted under the child’s skin to pump the fluid away from the brain and maintain proper flow

Other Congenital Factors

Maternal Disorders

• **Rubella**
• **Syphilis**
• **Blood-Group Incompatibility**
  – Affects the second and subsequent children
Substance Exposure
Fetal Alcohol Syndrome
• 1 - 3 cases per 1,000 births
• A leading cause of intellectual disability
• Risk rates are particularly high during the first trimester
• Research cannot pinpoint how much exposure is safe
• Symptoms include central nervous system dysfunction, craniofacial malformations and inhibited growth development
• Behavioral effects include attention deficit, distractibility; impulsivity; restlessness; inept social interactions; self-control problems; and memory, problem-solving, and organizational difficulties.

Substance Exposure
Illicit Drugs
• Estimated 500,000-750,000 exposed children born each year
• A wide array of behavioral effects have been hypothesized, including social, learning, language and attention deficits
• Research conclusions are ambivalent because drug abuse usually occurs simultaneously with other events (such as smoking, alcoholism, and environmental deprivation) that affect developmental outcomes

Prematurity and Perinatal Concerns
Prematurity

- Survival rates for premature infants have increased significantly
- Developmental Risks
  - Low IQ
  - Cerebral palsy
  - Attention deficits
  - Neurological and medical complications

Birth Complications

- Anoxia/Hypoxia
- Trauma
- Forceps effects
- Anesthetic effects

Postnatal Concerns
Common Postnatal Concerns

• Head Injuries
• Child Abuse
  – can result from and aggravate primary disabilities
• Lead Poisoning
• Nutritional Deficiency

Child Abuse

• Children with disabilities
  – are less able to defend themselves
  – have greater difficulty determining appropriate and inappropriate contact
  – are less likely to report the abuse
  – are more dependent on those who abuse them
  – are seen as less credible when they report abuse

Child Abuse
Shaken Baby Syndrome

• Can lead to brain hemorrhage, hypertension, cerebral palsy, mental retardation, coma, or even death
• Signs:
  – Vomiting
  – Seizures
  – blood pooling in the eyes
  – apnea (spells of interrupted breathing)
  – Irritability
  – sleeping difficulties
  – drowsiness
Lead Poisoning

• permanently and progressively damaging to the central nervous system
• may lead to encephalitis
• developmental outcomes may include seizures, cerebral palsy, and retardation

Nutritional Deficiencies

• Can occur pre- or post-natally
• Malnutrition during gestation or the first 6 months of life can lead to as much as a 40% deficit in brain cells
• The effects of early malnutrition have long been viewed as irreversible

Prevention
Graham & Scott’s Model of Prevention

- primary
  - risk conditions can be eliminated so that a condition never comes into existence
- secondary
  - reduce or eliminate the effects of an existing risk factor
- tertiary
  - assists a child who has a disability

Preconception

- Genetic counseling
- Immunization for maternal rubella
- Adequate maternal nutrition
- Family planning

During Gestation
Prenatal Care

- Adequate nutrition
- Fetal monitoring
- Protection from disease
- Avoidance of teratogenic substances
During Gestation
Genetic Analysis

- Recommended when the mother is 35 or older,
  when the risk of the disorder is greater than the risk
  of the procedure, and/or when couples are known to
  be at risk
  - Triple screen
  - Amniocentesis
  - Chorionic villi sampling (CVI)
  - Fetoscopy
  - Fetal biopsy
  - Ultrasound

At Delivery

- Apgar test of vital signs
- Computerized monitoring
- Screening for specific genetic disorders

Early Childhood

- Proper nutrition
- Maintaining a safe environment
- Psychosocial considerations
Ethical Issues

Genetic Screening
- Value of a person with a disability
- Prenatal information leads to actions
- New Eugenics?

Medical Care
- Denial of maximal care
- DNR orders
- Financial Considerations
- Informed Consent
Summary

Introduction
• The causes of mental retardation are many and varied.
• Professionals in the field of mental retardation need to have a general awareness of causes.
• Terminology used to describe various etiologies comes from three sources: conventional wisdom, names of specific people, and biomedical vocabulary.

Genetic and Chromosomal Considerations
• Genetics is the study of heredity with a focus on genes and chromosomes.
• Mental retardation can result from problems with genetic material on either autosomes or sex chromosomes.
• Genetic transmission can occur through autosomal dominant or recessive means or through X-linked patterns.
• Karyotypes are charts of chromosomes.
• The most recognizable condition associated with chromosomal anomalies is Down syndrome.
Other Etiological Considerations

- Cranial malformations involve conditions such as hydrocephaly.
- Many different toxic substances can significantly affect prenatal and postnatal development.
- Prematurity and other perinatal factors are related to developmental delays.
- Events such as head injuries and child abuse can also contribute to mental retardation.

Prevention & Ethics

- Prevention requires an intensive program that begins before conception and continues throughout the developmental period.
- Every specifiable cause can be matched with one or more preventive measure.
- Advances in medical technology have created ethical problems that society must face.