Common Developmental Disabilities

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Learning Objectives
- Familiarity with the diversity of etiologies for common developmental disorders
- Develop a framework for primary care practitioner to use in initial assessment of children with atypical development
- Understand role of different specialists in helping to evaluate and care for children with common developmental disorders

Developmental-Neurodevelopmental Disorders

Intrinsic
Extrinsic
Multifactorial

Intrinsic Risks and Disorders
- Heritable disorders and errors of morphogenesis and metabolism
- Neuromotor disability
- Disorders of cognition and pervasive developmental disorders
- Higher prevalence conditions and learning disabilities
- Behavioral disorders

Errors of Morphogenesis
- 3% of all live-born infants have a major anomaly
- Additional anomalies are detected during postnatal life – about 6% in 2 year olds, 8% in 5 year olds, other 2% later
- Single minor anomalies are present in about 14% of newborns

Minor Anomalies
Major Anomalies
### Definitions

- **Malformation**
- **Deformation**
- **Disruption**

### Malformation

- Morphologic defect of an organ or region due to an intrinsically abnormal developmental process (e.g. hypoplasia, incomplete closure, incomplete separation)

### Causes of Malformation

- **Multifactorial** 20%
- **Single-gene** 7.5%
- **Chromosomal** 6%
- **Infection** 2-3%
- **Maternal diabetes** 1.5%
- **Maternal medication** 1-2%
- **Unknown** >50%

### Congenital Malformation

- About 20-25% of perinatal deaths are due to lethal malformations
  - Birthweight 500-1500 grams – 10%
  - Birthweight >1500g – 50%

### Deformation

- Abnormal form or position of a body region caused by non-disruptive mechanical forces
  - **Examples:**
    - Clubfoot
    - Congenital hip dislocation
    - Plagiocephaly
Deformation Sequence

- Examples:
  - Intrauterine constraint
  - Robin sequence secondary to mandibular constraint

Disruption

- Morphologic defect of an organ or region resulting from a breakdown of, or interference with an originally normal developmental process

- Example:
  - Amniotic Band Disruption

Porencephalic cyst

Malformations of the neural tube (ex: Spina bifida)
Neural Tube Defects

- Incidence
  - 2nd most prevalent congenital anomaly in U.S. (after congenital cardiac malformations)
  - 1-5/1000 live births
  - Girls affected more than boys
  - Ethnic and geographic factors remain important variables
    - Highest rates: Ireland, UK, Pakistan, India, Egypt
    - In U.S.: rates highest in East and South vs. West

- Etiology
  - Multifactorial
    - Overall recurrence risk in U.S. with one affected offspring 1.5-3% (5.7-12% worldwide)
    - Syndromes (Roberts, trisomy 18)
    - Folate deficiency
    - Folate antagonists (phenobarb, trimethoprim)
    - Disruptions (amniotic bands, warfarin,)
    - Metabolic disorders (folate 'reductase' genes)
  - Genetics
    - High concordance in monozygotic twins
    - 7% of fetuses have aneuploidy (mostly trisomies)

Hydrocephalus

Chari II Malformations
**Common Developmental Disabilities**

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**Chari II Malformations**

- Herniation of medulla, tonsils, vermis
  - 4th ventricle at foramen magnum
  - Towering cerebellum
  - Tectal beaking
  - Myelomeningocele
  - Aqueductal stenosis
  - Hydrocephalus

**Medical Care Priorities**

- Early identification of AC-II symptomatology
- Latex allergy and atopy
- Developmental delay or mental retardation?
- Self-esteem, self confidence, infantilized behaviors
- Bowel and bladder independence
- Focused assessment of acute illness
- Transitional planning
- Adult independence

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**Tethered Cord**

**Prognosis and Development**

- 85% neonatal survival rate
- 72% of survivors are ambulating
- 87% have urinary continence
- T-12+ lesions associated with more severe CNS dysfunction
- 85% attending or have graduated high school and/or college (n=71)
Hurler Syndrome

Tetratogenic Disruptions

Teratogens are exogeneous agents that may cause developmental defects:

**Drugs**
- warfarin; valproic acid; phenytoin;
- vitamin A; thalidomide; cytostatic drugs: cyclophosphamide, lithium carbonate

**Chemicals**
- PCBs, methylmercury, alcohols)

**Infections**
- rubella, cytomegalovirus, herpes, toxoplasma, syphilis

**Ionizing radiation**
- RTG

**Maternal factors**
- diabetes mellitus, hyperthermia, phenylketonuria, hyper-hypo-thyreosis

Fetal alcohol spectrum disorder
(Ethanol embryopathy)
Non-teratogenic Disruption
Severe hypoxia-ischemia

Cerebral Palsy (CP)
- Term “cerebral palsy” often used as a diagnosis
- More precisely, however, it describes a motor manifestation of an underlying condition or event
- May not always present as spasticity
- Parents will benefit from having these distinctions made and clarified

Cerebral Palsy—A Common Special Health Care Need
- 25,000 new diagnoses per year in the U.S.
- Milder forms, especially involving single or distal extremities may elude detection
- Incidence figures reflect varied thresholds for making the diagnosis

Definition of Cerebral Palsy
- An impairment of movement and posture resulting primarily from either injury to or malformation of the cerebral cortex

Patterns of Cerebral Palsy
- Impairment in movement and posture
  - Increased tone (hypertonia, usually spasticity)
  - Decreased tone (hypotonia, atonia)
  - Altered movements (dyskinesia)
  - Disregulated movement (ataxia)
  - Combination/mixed pattern
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Basic Neural Pathway

- UMN
- LMN
- Muscle

Upper Motor Neurons

- Reside in the motor cortex
- synapse
- UMN
- LMN
- NMJ

Loss of UMN Function

- Without inhibitory action of UMN on LMN, tone becomes abnormal (typically increased/spastic), and uninhibited lower motor neuron function dominates reflex patterns
  - Hyperreflexia
  - Weakness
  - Increase tone

Patterns of Cerebral Palsy

- RESULT:
  Ineffective voluntary movement, and a range of uncontrolled movements and reflexes which interfere with normal skills such as walking, sitting, and swallowing

Epidemiology of CP

- Precise prevalence of CP is uncertain
- Overall incidence in U.S. estimated at 2/1000 live births
- Limited North American data on term infants since mid-1980’s
- Rate of CP is higher for preterm infants and increases with decreasing birth weight and gestational age
- Worldwide incidence is elusive but may be higher than 2/1000

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Epidemiology of CP 2004 data

- CP among 8-year-old children (N = 68,272) living in:
  - North central Alabama
  - Metropolitan Atlanta
  - South central Wisconsin
- Average prevalence of CP in 2004 across the three sites was 3.3 per 1,000

Epidemiology—Term Infants

- All congenital abnormalities
  - 19% of children with CP vs. 4.3% of controls
  - 14% of affected children had CNS abnormality
- CNS malformation/disruption…
- Intrauterine infection
- Multiple births
- Perinatal stroke
- Intracranial hemorrhage
  - 1/3 due to coagulopathy, thalamic hemorrhage predominantly
- Acquired post-natal causes (10-18%)
- Kernicterus

The case for hypoxic-ischemic encephalopathy as an etiology for Cerebral Palsy in children

- HIE accounts for 10-20% of cases of CP
- Intrapartum events that may lead to asphyxia do not correlate strongly with CP
  - Abruption, prolapsed cord, placenta previa, nuchal cord
- Apgar score alone not strongly predictive
  - 7 year risk was 4.7% with 5 min Apgar of 0-3
  - ... but 25x more predictive for scores of 7-10
  - 95% of infants with Apgar scores of 0-3 did not have CP
  - 10min+ Apgar scores may be more predictive

Other Considerations in Children with Cerebral Palsy

- Cognitive disorders (range of cognitive function)
- Developmental delay vs. cognitive disability
- Epilepsy—approx. 43% (range: 35-62%)
- Speech dyspraxia, speech/language disorders
- Strabismus, cortical vision abnormalities
- Gross motor dysfunction
- Fine motor dysfunction
- Self-care and vocational challenges

Genetic—chromosomal
- Cerebral dysgenesis
- Fetal hypoxia-ischemia
- Intra-partum events
- Neonatal events
- Post-neonatal trauma/infection
- Fetal infection

Conception
- Pregnancy
- Labor
- Post-partum
- Cerebral Palsy
Priorities in the Follow-up Care of Children with Cerebral Palsy

- Parent education
- Seating, positioning
- Ambulation
- Education
- Feeding/nutrition
- Social/emotional well-being

Intrinsic Alterations of Gene Function
Clinic Examples

Down Syndrome

Epidemiology of ASD

- All racial and socioeconomic groups
- Prevalence: 1 in 110
- M:F ranges from 3.2:1 to 7.6:1
Prevalence of ASD in WI—2006 Data

- Prevalence 7.6/1000 (1/132)
- About 5.5/1 Male : Female ratio
- Median age of diagnosis in Wisconsin is 53 months

3 Domains Affected

- Social Development
  - Less or no use of non-verbal behaviors
  - Less or no relating to peers
  - Less or no trying to share experiences, play with others
  - Less or no social or emotional reciprocity
- Communication Development
  - Less or no development of speech
  - Less or no trying to join conversation
  - Less or no social imitative or spontaneous make-believe play
  - Repetitive, stereotyped, or idiosyncratic language
- Behavioral Development
  - Very focused, restricted play
  - Repetitive non-functional behaviors
  - Stereotyped, repetitive motor mannerisms
  - Persistent preoccupation with parts of objects

Pervasive Developmental Disorder (PDD)

- Autism Disorder
- Asperger Syndrome
- Rett Syndrome
- PDD-NOS (not otherwise specified)
- Childhood Disintegrative Disorder

Theory of Mind

- The autistic child does not form a mental image of what can go on in other people’s heads and this stems theoretically from a failure in thinking about his or her own mental states

ASD Causal Genetic Variations

- 15q11-q13 region (also called the Prader-Willi/Angelman syndrome, or PW/AS region)
- Down syndrome, Smith-Magenis syndrome
- 22q13 deletion syndrome (SHANK3/PROSAP2)
- Rett syndrome MeCP2 gene
- Fragile X syndrome FMR1 gene
- Tuberous sclerosis TSC genes
- Smith-Lemli-Opitz syndrome DHCR7 gene
- Neureilgin genes (NLGN3 and NLGN4), ATR-X, and neurotrypsin
ASD Susceptibility Loci

- More than 90 association studies have been published
- Chromosomes X, 2, 3, 6, 7, 10, 11, 12, 13, 16, 17, 19

Rett Syndrome

- A progressive developmental disorder occurring in girls
- Multiphasic pattern of disability sharing features with autism
- Progressive debilitating

Rett Syndrome—Necessary Criteria

- Normal prenatal and perinatal development, normal psychomotor development through first 5 months (5-18 mo)
- Normal head circumference; deceleration of head growth 5-48 mo.
- Loss of purposeful hand skills between 5-30 mo.
- Development of stereotypic hand movement (wringing, squeezing, clapping, tapping, mouthing, washing, rubbing)
- Development of severely impaired expressive and receptive language
- Evolution of severe psychomotor retardation
- Appearance of gait ataxia, truncal apraxia/ataxia between 1-4 years, social withdrawal
- Diagnosis tentative until age 2-5 years

Aserperger Syndrome

Rett Syndrome

Rett syndrome MeCP2 gene

Pervasive Developmental Disorder-Not Otherwise Specified (PDD-NOS)

- DSM-IV-TR includes PDD-NOS in the category of “autism”
- DSM-V may introduce changes
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Angelman Syndrome
15q11-g13 region

Prader-Willi Syndrome
15q11-g13 region

William’s Syndrome
Fragile X Syndrome
FMR1 gene

Smith-Lemli-Opitz Syndrome
DHCR7 gene

Tuberous Sclerosis
TSC genes

Cornelia deLange Syndrome
Gene linked to chromosome 3q26.3
Diagnosis of Autism Spectrum Disorders

- No established medical "tests" in use to make the diagnosis of autism
  - Electroencephalogram (EEG)
  - Microarray
  - S-Amino acids, urine organic acids
  - High resolution chromosome analysis
  - Fragile-X testing (PCR)

Intrinsic Alterations of Cortical Elaboration

Learning Disabilities

- Specific problems in the acquisition and processing of information, old and new
  - Difficulties with attention
    - ADD/ADHD
    - Anxiety
  - Difficulties with language processing
    - Auditory processing disorders
    - Praxia (dyspraxia, apraxia)
    - Hearing loss and deafness
  - Difficulties with memory
    - Visual memory difficulties
    - Auditory memory difficulties
  - Difficulties with visual processing
    - Problems with vision
    - Problems in visual cortex
    - Motor problems impacting eye-hand coordination
  - Difficulties with visual/spatial organization
    - Dyslexia
    - Dysgraphia
  - Sensory processing difficulties

Dyslexia

- One out of 25 school-age children have dyslexia
4% to 12% of school-aged children. About 3 times more boys than girls are diagnosed with ADHD.

ADD/ADHD Measures

- ADHD-specific checklists
  - Connors Rating Scale
  - Swan, Nolan, Pelham-IV (SNAP)
  - Vanderbilt ADHD Teacher and Parent Rating Scales
  - ADHD Symptom Rating Scales

- Broad view of behavior tools
  - Behavior Assessment System for Children, 2nd ed. (BASC-2)
  - Achenbach Scales

- Research measures
  - Connors Continuous Performance Test
  - Test of Visual Attention (TOVA)
  - Gordon Diagnostic System
Cognitive Disability
(Replaces the term “Mental Retardation”)

Definition of Intellectual Disability
Significant limitations both in intellectual functioning and in adaptive behavior, which covers many everyday social and practical skills. Originates before the age of 18.

Intellectual Disability
• Intellectual functioning—(aka) intelligence
• Adaptive behavior (three skill types)
  o Conceptual skills—language and literacy; money, time, and number concepts; and self-direction
  o Social skills—interpersonal skills, social responsibility, self-esteem, gullibility, naiveté (i.e., wariness), social problem solving, and the ability to follow rules/obey laws and to avoid being victimized
  o Practical skills—activities of daily living (personal care), occupational skills, healthcare, travel/transportation, schedules/routines, safety, use of money, use of the telephone

Intellectual Disability
• Other factors
  o Community environment typical of the individual’s peers and culture
  o Linguistic diversity and cultural differences in the way people communicate, move, and behave
  o Co-existent strengths

Intellectual Disability
Impairment in Intellectual Function
• Can be screened and suspected in infancy and childhood
• Definitively diagnosed after 5 years
• Diagnosis of made via formal cognitive testing and adaptive abilities assessment
• Often missed cause of anxiety, depression, school avoidance; other behavioral problems
• Irrefutably qualifies the child for an Individualized Education Program (IEP)
Other Extrinsic Influences

- Bullying
- Conditions of low self-esteem
- Emotional trauma, abuse, neglect
- Others impacting mental health

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