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The 5 Essential Concepts of Developmental Medicine: A New Medical Paradigm for Persons with Developmental Disabilities.

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Introduction

The major functions of the brain include memory and learning, control of motor function, control and routing of sensory input, and emotional regulation/control. These functions require that specific interrelated brain structures work together in a coordinated fashion. When these relationships are improperly developed or disrupted, brain dysfunction will occur.

Regardless of the cause of the brain dysfunction or age of onset, the primary categories of "symptoms" of brain dysfunction in either a child or an adult include 1) cognitive dysfunction, 2) neuromotor dysfunction, 3) seizures, and 4) impulsive destructive behaviors. Any of these four categories of symptoms can be mild, moderate, or severe, and can occur either singly or in various combinations. In addition, the clinical presentations of these four categories varies from person to person. For example cognitive dysfunction may present as mild dyslexia or severe mental retardation, neuromotor dysfunction may present as mild spastic hemiplegia or severe choreoathetosis, seizures may present as brief "Absence" spells or severe generalized tonic-clonic convulsions, and behavior problems may present as mild impulsivity or severe bizarre self-injurious episodes. By convention, we also call these 4 primary symptom complexes the "**complications**" of "neurodevelopmental disorders" (see below).

Brain dysfunction that first becomes apparent in childhood (**Childhood Onset Brain Dysfunction** or C.O.B.D.) can be caused by a large variety of genetic and acquired conditions which are known as **"neurodevelopmental disorders"-see below for classification** *(by convention, we refer to brain conditions-either genetic or acquired-that manifest during the time period between initial embryological brain formation until brain development is complete -approximately age 21 years- as "neurodevelopmental disorders". Neurodevelopmental disorders are conditions (genetic or acquired) which prevent and/or disrupt normal development of brain function and/or structure: they are associated with measurable chemical or structural abnormalities which lead to various clinical symptoms, including cognitive impairment, seizures, neuromotor dysfunction,, and abnormal behaviors. They are often (but not always) associated with substantial functional limitations).*

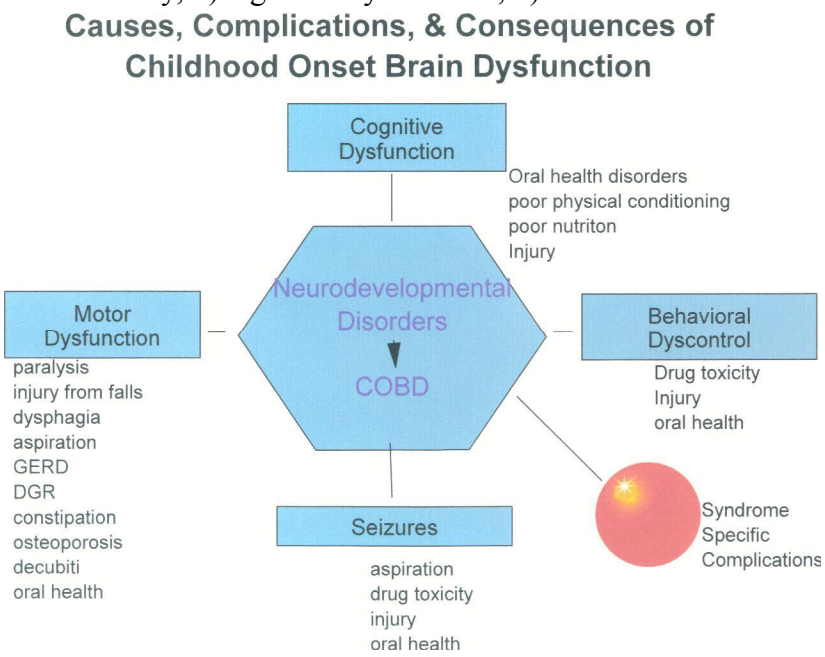
We now know that certain genes that control complex processes are required for normal brain anatomy and function. Brain dysfunction will occur if any one of these genes is

absent or does not function properly in the brain of the developing embryo. Gene abnormalities may occur either because of a spontaneous mutation in the earliest stages of embryological development or as the result of inheritance from the mother or father. In addition to genetic etiologies, brain dysfunction may also result from a multitude of adverse environmental influences during the prenatal, perinatal, or postnatal periods.

At times the precise etiology of Childhood Onset Brain Dysfunction cannot be determined. In these cases of COBD of unknown etiology (i.e. the precise neurodevelopmental disorder is not known), it is important to continue to search for the exact cause for the reasons discussed below.

Some children with these early genetic and/or acquired brain deficits will be stillborn. Others will die in childhood. However, depending on the nature and severity of the neurodevelopmental disorder that is responsible for the Childhood Onset Brain Dysfunction, many will survive into adulthood and more and more appear to be experiencing a normal life span.

Those children who survive early problems and who eventually become adults will likely demonstrate one or more of the four "primary"medical **complications** of the neurodevelopmental disorder: namely, 1)cognitive dysfunction, 2)neuromotor dysfunction, 3)seizures, and/or 4) abnormal impulsive behavior.



Depending on which of these four primary complications is present and its severity (some have all four), the adult who suffers from a neurodevelopmental disorder may also demonstrate a number of "secondary" conditions-or health "**consequences"**- that result from those "primary" complications.

For example, as shown in the figure above, because neuromotor dysfunction (a primary complication) can cause immobility, the adult with a neurodevelopmental disorder may develop inactivity osteoporosis (a secondary condition-or health consequence of neuromotor dysfunction).

In addition to the "complications and consequences" of neurodevelopmental disorders as discussed above, any adult individual with a neurodevelopmental disorder, depending on the precise etiology of the neurodevelopmental disorder, may also demonstrate,

"syndrome-specific" conditions. For example, if the specific etiology of the neurodevelopmental disorder is Down Syndrome, in addition to the symptoms of brain dysfunction, the person with Down Syndrome may also experience "congenital heart disease", because congenital heart disease is a complication often associated with Down Syndrome.

It is therefore important to distinguish the primary (complications) and secondary (consequences) symptoms of brain dysfunction (which are the same whether onset of the brain dysfunction is in childhood or during adulthood) from the syndrome-specific conditions which may be multisystem and etiologically unrelated to brain dysfunction.

"Developmental Disability": The term developmental disability is a term that is confusing to most physicians. The term has legal, social, and medical aspects. If a person meets the criteria for having a developmental disability, he or she becomes eligible for certain government services through the State Medicaid program. Benefits vary from State to State. In general the "diagnosis" of "developmental disability" requires that the onset of the condition occurs before age 18 years, is chronic, will require lifelong services, and is associated with substantial functional limitations in most areas of daily living. To determine the diagnosis of developmental disability a psychologist performs 2 different tests. The first is a test of intellectual or cognitive function (eg the Stanford-Binet IQ test) and the second is a test of functional limitiation (eg the Vineland test). While neurodevelopmental disorders are the underlying cause of "developmental disabities", determination of the precise neurodevelopmental disorder is not usually a part of the determination of "developmental disability". Sub-categories of developmental disability include mental retardation, epilepsy, cerebral palsy, and autism. These are all conditions that result from neurodevelopmental disorders, although the precise etiology of the neurodevelopmental disorder has usually not been determined (although we feel it should be).

In order to avoid confusion and to understand the "medical" approach to the individual who is determined by the government to meet the criteria for "developmental disability", it is important that the physician have a clear understanding of the 5 Essential Concepts of Developmental Medicine, as explained below. Each concept should stimulate the practitioner to ask a critical question (the 5 Critical Questions, which correspond to the 5 Essential Concepts). We believe that the 5 Essential Concepts offer a conceptual framework that provides the physician with an orderly approach to the evaluation and management of those health conditions that frequently occur in their patients with developmental disabilities.

The 5 Essential Concepts of Developmental Medicine: *The 5 Critical Questions.*

1. Childhood Onset Brain Dysfunction (COBD)

Symptoms of brain dysfunction that first occur before the age of 22 years (the age when brain development is complete). The most common symptoms of brain

dysfunction are cognitive dysfunction, motor dysfunction, behavior dysfunction, and seizures.

Does this patient demonstrate any signs or symptoms of brain dysfunction?

2. Neurodevelopmental Disorder

The specific medical disorder or disease that causes the childhood onset brain problems (eg Down syndrome, Angelman Syndrome, Fragile X, Perinatal hypoxic/ischemic brain injuy, Congenital rubella syndrome).

If brain dysfunction is present, what is the specific neurodevelopmental disorder responsible?

3. Complications (of neurodevelopmental disorders)

Refers to cognitive dysfunction, motor dysfunction, behavior dysfunction, and seizures: the symptoms of neurodevelopmental disorders, or the clinical manifestations of COBD.

What complications of the neurodevelopmental disorder does this patient demonstrate?

4. Consequences (of the "complications")

Refers to the medical conditions that result from the 4 complications (eg osteoporosis is a consequence of severe motor dysfunction, oral health disorders result from cognitive dysfunction).

What are the health consequences that have resulted from those complications

5. Syndrome-specific complications

Refers to health conditions that are associated with a given specific neuro-developmental disorder. For example, thyroid dysfunction with Down syndrome, renal angiomyolipomata with Tuberous Sclerosis, or obesity with Prader Willi syndrome.

Does my patient demonstrate any syndrome-specific health complications?

A Brief Classification of "Neuro-developmental disorders"

1. "Genetic" Disorders (abnormal gene/genes)

A. Metabolic: Missing enzyme leads to build-up of toxic metabolite {secondary brain damage)and/or deficiency of essential end product needed for neuronal function {primary brain damage).

"Primary" metabolic causes
l. Lipids: Sulfatide-lipidosis {Metachromatic Leukodystrophy)
2. Mucopolysaccharides: (,Sanfilippo Syndrome)
"Secondary" metabolic causes
l. Amino Acids: Phenylalanine accumulation (Phenylketonuria),
Homocysteine accumulation (Homocystinuria)
2. Purines/pyrimidines: Uric acid accumulation(Lesch-Nyhan Syndrome)

B. Structural Malformations: Cellular derangement or malfunction of brain tissue, usually with structural abnormalities of the brain and often other body parts. No known enzyme deficiency or chromosomal abnormality.

1. Neurodysplasia
a. Tuberous Sclerosis
b. Neurofibromatosis

2. Neuro-dysgenesis: neurulation, prosencephalic segmentation, neuronal proliferation, neuronal migration, organization, myelination
a. Lissencephaly (some types)
b. Schizencephaly (some types)
c. Septo-Optic Dysplasia (some types)

3. Unknown
a. Sturge Weber Syndrome ?
b. Rett Syndrome-MEC-P2 mutation

C. Chromosomal Abnormalities:
1. Triplet Repeat Disorders
a. Fragile X Syndrome (C-X)
b. Myotonic Dystrophy(C-19)

2. Aneuploidies
a. Down Syndrome
b.Trisomy 8 Mosaic Syndrome
c. Trisomy 13
d. Trisomy 18

3. Microdeletions
a.William's Syndrome (C-7)
b. Prader-Willi Syndrome (paternal C-15)
c. Angelman's Syndrome (maternal C-15)
d. Smith-Magenis Syndrome (C-I7)
e. Rubenstein-Taybi Syndrome (C-16)
f. Velo-cardio-facial Syndrome (C-22)

4. Rearrangements
a. Ring 22 Syndrome

2. "Acquired" Disorders
A. Prenatal Disorder
l. Infections (TORCH, Rubella)
2. Toxins (alcohol, maternal PKC)
3. Traumatic (ischemia-hypoxia)
4. Structural Malformations
a. Arnold-Chiari Malformation
b. Dandy-Walker Cyst

c. Agenesis of Corpus Callosum
d. Septo-Optic Dysplasia (some types)
e. Lissencephaly (some types)

B. Perinatal Disorder
l. Traumatic(hypoxia-ischemia)
2. Toxins (Kernicterus)
3. Prematurity/Low Birth Weight

C. Post-Natal Disorder
1. Infection {measles)
2. Traumatic
3. Metabolic (hypothyroid)
4. Neoplasm
5. Toxins(lead)