


Exclusion of Progressive Brain Disorders of Childhood for a Cerebral Palsy Monitoring System: A Public Health Perspective

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Overview

- ❑ How is cerebral palsy defined? How are progressive disorders defined?
- ❑ How does CDC monitor the prevalence of cerebral palsy?
- ❑ Can we create a standardized definition and list of progressive conditions for cerebral palsy monitoring?
 - Study Goals
 - Methods
 - Results
 - Challenges
 - Future Implications

Definition of Cerebral Palsy

- ❑ Group of permanent disorders
- ❑ Affects development of motor and posture
- ❑ Due to *non-progressive* disturbances
- ❑ Occurs in the developing brain

Rosenbaum L, Paneth N, Leviton A, Goldstein M, Bax, M. The definition and classification of cerebral palsy. *Dev Med Child Neurol*. 2007;49(Suppl 109):8-14.



1959 - *THE LITTLE CLUB* MEMORANDUM ON TERMINOLOGY AND CLASSIFICATION OF "CEREBRAL PALSY" (Cerebral Palsy Bulletin No. 11, 1959)
 MacKeith and Polani- "a persisting but not unchanging disorder of movement and posture, appearing in the early years of life and due to a **non-progressive** disorder of the brain..."

1964 - Bax- "For practical purposes, it is usual to exclude from cerebral palsy those disorders of posture and movement which are (1) of short duration, (2) due to **progressive** disease..."

1992 - *DMCN* (Developmental Medicine & Child Neurology)
 Mutch et al.- "...an umbrella term covering a group of **non-progressive**, but often changing, motor impairment syndromes secondary to lesions or anomalies of the brain arising in the early stages of development."

2007 - Report released as a result of the 2004 International Workshop on Definition and Classification of Cerebral Palsy by Rosenbaum et al.- "...a group of disorders of the development of movement and posture, causing activity limitation, that are attributed to **non-progressive** disturbances..."

Other Points to Consider Related to Progressive Brain Disorders

- Progressive disorders of motor function defined as loss of skills previously acquired in the first 5 years of life (Cans, 2007)
- Motor dysfunction which results from recognized progressive brain disorders is not considered CP (Rosenbaum et al., 2006)
- Non-progressive is used to denote that pathophysiological mechanisms leading to CP are assumed to arise from a single, *inciting event* or discrete *series of events* which are no longer active at time of diagnosis (Rosenbaum et al., 2006)
- By definition, the cerebral lesion neither resolves nor progresses (Stanley, Blair, Alberman, 2000)

CP Surveillance at CDC: The Autism and Developmental Disabilities Monitoring (ADDM) Network

- Ongoing, population-based surveillance of autism and other developmental disabilities, including CP
- Multisource, records-based surveillance methodology
- ADDM CP Network– four sites in the ADDM Network that monitor CP
 - Alabama, Georgia, Missouri, Wisconsin

Trained abstractors review and abstract selected records at multiple data sources in the community that educate, diagnose, treat, and provide services to children with developmental disabilities.



Trained clinicians review abstracted information from all data sources for a given child. These trained clinicians then determine if the child meets the case status for CP

ADDM CP Network's Official Surveillance Case Definition

- Cerebral palsy (CP) is defined as a group of permanent disorders of the development of movement and posture that are attributed to **non-progressive** disturbances that occurred in the developing brain.*
 - The motor disorders of cerebral palsy are often accompanied by disturbances of sensation, perception, mental ability, communication, and behavior.*
 - CP is also often accompanied by co-occurring epilepsy; and by secondary musculoskeletal problems.*
 - The impairment of motor function may result in paresis, involuntary movement, or incoordination.
 - CP does not include motor disorders that are transient, that result from **progressive disease of the brain**, or that are due to spinal cord abnormalities/injuries.
 - CP acquired after birth (post-neonatal CP) are included as cases.

*Modification of the definition by Rosenbaum L, Paneth N, Leviton A, Goldstein M, Bac, M. The definition and classification of cerebral palsy. *Dev Med Child Neurol*. 2007;49(Suppl 109):8-14.

Study Goals

- Create a standardized definition and list of progressive conditions for public health surveillance purposes that most would agree are not CP
- Update the list of excludable conditions used by the ADDM Network's non-physician field staff who review and abstract health and education records in community settings at our ADDM CP Network sites

Methods

- ❑ Develop selection criteria for progressive brain disorders of childhood to apply to our literature review
- ❑ Identify broad classes of disorders likely to include individual conditions that are progressive
- ❑ Review information about the relative frequency and natural history of candidate disorders
- ❑ Create list of progressive brain disorders of childhood

Results

- ❑ 19 criteria were developed to apply to our literature review of candidate conditions
- ❑ 98 disorders met selection criteria and were identified as progressive brain disorders of childhood

Public Health Surveillance Criteria for Progressive Brain Disorders of Childhood

A. For CP surveillance purposes, progressive disorders of childhood are those conditions causing progressive loss of motor skills (as opposed to those solely affecting memory and related dementia).

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B. The loss of motor skills must result from a recognized progressive brain disorder (as opposed to those solely of spinal, peripheral nerve or muscular origin).

Public Health Surveillance Criteria for Progressive Brain Disorders of Childhood (continued)

2 A. For a condition to be considered a progressive disorder of childhood, the natural history of the condition should describe regression or a progressive or (neuro)degenerative course with onset during childhood. For CP surveillance purposes, "during childhood" is defined as <=8 years old.

B. If at least two references do not mention that the condition is progressive, then the condition is not progressive (e.g., 18q- syndrome).

C. If the typical age of onset for a progressive disorder is after age 8, then the condition is not considered a progressive disorder of childhood (e.g., CADASIL – onset in mid-life; earliest age in 20s).

D. If fewer than 5 cases of a progressive disorder are reported in the literature, then the condition is not considered a progressive disorder of childhood for surveillance purposes. Rationale: a sufficient number of cases needs to be reported in the literature to obtain a general description of the natural history of the disorder.

Public Health Surveillance Criteria for Progressive Brain Disorders of Childhood (continued)

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- A. If there are typical and atypical forms of a condition described in the literature, decide whether the condition is progressive based on what is true for the typical form of the disorder (e.g., regression is seen in typical cases with Rett syndrome, but might not be a feature for atypical forms).
- B. If progression is a rare feature of a condition, do not consider the condition progressive (e.g., craniometaphyseal dysplasia). Rationale: when the association is almost unheard of, do not exclude all potential children with CP who might coincidentally have the genetic condition.
- C. Conditions where progression during childhood is a possible but not universal feature (and progression is not a rare feature) will not be considered categorically progressive. Decisions about CP case status for individual children with these conditions should be made on a case by case basis through the review of the child's medical history, motor findings and clinical course rather than the diagnosis per se.
- D. Progressive disorders that typically result in stillbirth or early mortality (before age 2) will not be included. Rationale: to be included in the monitoring program, the minimum age for CP diagnosis is age 2 years. In the unlikely event that a child with one of these disorders survives until age 8 and comes into the surveillance program, the decision about CP case status will be made on a case-by-case basis through the review of the child's medical history, motor findings and clinical course.

Public Health Surveillance Criteria for Progressive Brain Disorders of Childhood (continued)

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- A. For surveillance purposes, therapies to halt the progression of a condition will not be taken into account.
- B. Conditions that involve an accumulation of static cerebral lesions (e.g., cerebrovascular complications of sickle cell disease) and predispose the child to repeated cerebral insults should not be considered progressive ("deterioration resulting from repeated insults is not the usual meaning of progressive").
- C. Conditions where seizures are a feature (e.g., tuberous sclerosis): do not take deterioration resulting directly from repeated seizures ("insults") into account when deciding if the condition is progressive, as opposed to when the progressive effects of the underlying disorder cannot be separated from the associated seizures themselves, as in epileptic encephalopathies (e.g., Dravet syndrome).

*Badawi N, Watson L, Petterson B et al. What constitutes cerebral palsy? *Dev Med Child Neurol* 1998; 40: 520-527.

Public Health Surveillance Criteria for Progressive Brain Disorders of Childhood (continued)

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- A. If the infantile/childhood form is progressive, then the condition is categorically progressive (e.g., Krabbe disease, Alexander disease, CACH).
- B. Any condition with "adult onset" or "late onset" in the name is not considered a progressive disorder of childhood (e.g., autosomal dominant late-onset leukoencephalopathy).
- C. If the condition is progressive during childhood and stabilizes during adulthood, then consider the condition progressive (e.g., Sjogren-Larsson syndrome).
- D. If there are infantile and adult forms of a progressive condition, assume the child has the infantile form if the child shows neurologic signs during childhood.

Public Health Surveillance Criteria for Progressive Brain Disorders of Childhood (continued)

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- A. Conditions described as acute are not considered progressive for surveillance purposes (e.g., acute disseminated encephalomyelitis/ADEM).
- B. Conditions without clinical symptoms are not considered progressive for surveillance purposes (e.g., extensive cerebral white matter abnormality without clinical symptoms).

Examples of Progressive Brain Disorders of Childhood for Public Health Surveillance

MIM#	Disorder	Other Terms
300100	Adrenoleukodystrophy, X-linked (X-ALD)	Adrenoleukodystrophy (ALD)
204200	Ceroid lipofuscinosis, neuronal, 3 (CLN3)	Neuronal ceroid lipofuscinosis, juvenile (JNCL) Batten disease Spielmeier-Vogt disease
256000	Leigh syndrome (LS)	
603896	Leukoencephalopathy with vanishing white matter (VWM)	Childhood Ataxia with Central Nervous System Hypomyelination/Vanishing White Matter (CACH/VWM)
272800	Tay-Sachs disease (TSD)	GM2-gangliosidosis, type 1

Challenges

- ❑ **Few articles with focus on this question as it relates to CP**
 - A need for information but little to build upon
- ❑ **Difficult to categorize conditions where clinical presentation varies**
 - Without exact laboratory confirmation of type, no guidance for whether conditions that fall within that group should be excluded

Challenges

- ❑ **Concept of a condition being “slowly progressive” is debated**
 - ❑ No consensus as to whether such a condition is considered progressive or not
- ❑ **No agreement on:**
 - ❑ How long to wait to exclude the possibility of progression
 - ❑ Minimum age at which motor impairment may be assumed to be permanent and non-progressive

Future Implications

- ❑ **List of progressive brain disorders of childhood can be useful in public health surveillance and research**
 - Can also be useful in **clinical settings**--when discussing prognosis with parents, it is important to distinguish conditions that may be progressive from those that have static course
 - ❑ **Open to critiques and expansion of this work**
 - List does not represent a comprehensive catalog of progressive genetic conditions
 - A condition's absence does not have clinical implications for a favorable prognosis
 - Criteria can be applied in future as more children with very rare disorders are followed and new candidate disorders are identified
- We invite others to expand upon our list and extend the work we have started!**

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Thank you!

**For questions and comments,
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The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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