MOTOR DELAYS: EARLY IDENTIFICATION AND EVALUATION

American Academy for Cerebral Palsy and Developmental Medicine, 2013, BRK 10

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Disclosures

In the past 12 months, I have not had a significant financial interest or other relationship with the manufacturer(s) of the product(s) or provider(s) of the service(s) that will be discussed in my presentation.

This presentation will not include discussion of pharmaceuticals or devices that have not been approved by the FDA.

Objectives

At the end of this presentation, the attendees will be able to
1. Recognize motor delays and specific neurological signs that guide the workup for neuromotor conditions
2. Implement improved motor screening as part of anticipatory guidance and well child care
3. Identify “red flags” – signs or symptoms -- that warrant prompt attention from a specialist

Developmental Surveillance

“Developmental surveillance is a flexible, longitudinal, continuous, and cumulative process to identify children who may have developmental problems” (DSS, 2006)

Components
1. Eliciting and attending to parental concerns
2. Documenting and maintaining the developmental history
3. Making accurate observations about the child
4. Identifying risk and protective factors
5. Maintaining an accurate record of the process and findings

Developmental Screening

In 2006, the AAP published an algorithm for Developmental Surveillance and Screening (DSS) in the Medical Home.


Developmental Screening Instruments

Several Different standardized screening instruments are being used:
Ages and Stages Questionnaire
Parents Evaluation of Developmental Status
Denver II
etc.

These instruments emphasize delays of language and social development.
National Task Force for Early Identification of Childhood Neuromuscular Disorders:

- American Academy of Pediatrics
- American Academy of Neurology
- Association of Academic Physicians
- Childhood Neurology Society
- American Academy of Physical Assistants
- National Association of Pediatric Nurse Practitioners
- National Association of Community Health Centers
- American Physical Therapy Association
- American Academy of Physical Medicine and Rehabilitation

Funded by CDC

Why is early diagnosis important?

- Even incurable disorders, including many neuromuscular disorders, are treatable.
- A delay in diagnosis delays access to information about care options, relevant clinical trials, and support networks for a specific disorder.
- Not having an accurate diagnosis may result in a child missing appropriate therapies or receiving therapies not recommended for a disorder.
- Delays in diagnosis often impede access to services, including Early Intervention and other health care services.
- Early diagnosis facilitates access to genetic counseling to learn about family planning options.
- There can be significant family stress with the delay of an accurate diagnosis. Families often see several clinicians before receiving a referral to a specialist familiar with neuromuscular disorders and may experience unnecessary testing.

Neuromotor Screening Expert Panel

Nancy A. Murphy, MD, Chairperson, Council on Children with Disabilities
Paul H. Lipkin, MD, Council on Children with Disabilities
Gary H. Nottke, MD, Council on Children with Disabilities
Howard M. Sutl, MD, Committee on Genetics
Michelle Maxia, MD, Section on Developmental and Behavioral Pediatrics
Max Wimmerter, MD, Section on Neurology
John F. Sarwark, MD, Section on Orthopedics
Joseph F. Hagan, Jr., MD, Bright Futures Initiatives
Dipesh Navare, MD, MPH, MSILB
Peter Leon Rosenbaum, MD, AACPDM
Georgina Peacock, MD, MPH, Centers for Disease Control and Prevention/National Center on Birth Defects
Penni P. Swanson, MD, MPH, Centers for Disease Control and Prevention/National Center on Birth Defects

Focus Group Results

81% thought motor delays were identified as early as other delays
Participants took parental reports extremely seriously.

"With the infants, you just have to lay your hands on them and figure out tone and strength." 
"Make sure the infant has adequate 'tummy time'; if not, instruct parents to practice." 
"It's a mixed bag... motor delays aren't as common as others, and may be missed from failure to notice them while paying attention for instance to the more common language delays- but parents also tend to be hypervigilant about motor milestones and bring them up (i.e., not walking)"
The Quality Improvement Innovation Network (QuIIN)

An AAP network of over 300 practices, 68 responded

Similar discussion questions
First 2 vignettes the same; 3rd replaced with:
A 3 year old cannot hop on one foot

Responses

Each provider was asked to choose:
• Work-up
• Refer
• Reassure
• Document the concern but not share it with the parents

Decide when to follow-up

QuIIN Survey Responses

<table>
<thead>
<tr>
<th>Physical Exam Results</th>
<th>% Work-up</th>
<th>% Refer</th>
<th>% Reassure</th>
<th>% Document but not share</th>
</tr>
</thead>
<tbody>
<tr>
<td>Otherwise Normal</td>
<td>58.8</td>
<td>13.2</td>
<td>28.0</td>
<td>7.4</td>
</tr>
<tr>
<td>Physical Exam results note concern</td>
<td>% Work-up</td>
<td>% Refer</td>
<td>% Reassure</td>
<td>% Document but not share</td>
</tr>
<tr>
<td>5 month old</td>
<td>43.7</td>
<td>15.3</td>
<td>14.1</td>
<td>7</td>
</tr>
<tr>
<td>15 month old</td>
<td>20.6</td>
<td>33.4</td>
<td>38.2</td>
<td>7.4</td>
</tr>
<tr>
<td>3 year old</td>
<td>11.0</td>
<td>8.8</td>
<td>66.2</td>
<td>13.2</td>
</tr>
</tbody>
</table>

Conclusions of the Pre-Process

The Pediatricians who participated:
• Described widely varying approaches to motor exams and identification of delays
• Expressed uncertainty regarding their ability to detect, diagnose, and manage these children
• Requested more education, training, and standardization of the evaluation process including an algorithm

Motor Delay: Early Identification and Evaluation
Garey H. Neulitz, Nancy A. Murphy and NEUROMOTOR SCREENING EXPERT

Pediatrics: originally published online May 27, 2013: DOI: 10.1542/ped.2013-0558
Key Components of the Neurological Exam

- History, Developmental Milestones
- Weight, Height, Head Circumference on Appropriate Growth Charts
- Dysmorphic Features
- Signs of Respiratory Distress
- Organomegaly
- Strength Testing by Functional Observation
- Fasciculations, Primitive, and Deep Tendon Reflexes
- Muscle Bulk and Tone

Testing for Tone

**Scarf Sign & Popliteal Angle**

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<tr>
<th>IMPLICATIONS</th>
<th>SCARF SIGN</th>
<th>POPLITEAL ANGLE</th>
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<tr>
<td>Suspect normal tone.</td>
<td>The elbow position is between the bilateral midclavicular line.</td>
<td>5° - 15° for age 1-3 years, 15°-25° for age 4-5 years</td>
</tr>
<tr>
<td>Suspect low tone.</td>
<td>The elbow crosses the midline to the contralateral midclavicular line.</td>
<td>&lt;5° for age 1 year</td>
</tr>
<tr>
<td>Suspect high tone.</td>
<td>The elbow does not cross the midline.</td>
<td>&gt;25° for age 1 year</td>
</tr>
</tbody>
</table>

She went boneless.
Question 1: Recognize the signs and symptoms of Duchenne and other muscular dystrophies

An 18 month old boy is seen for delayed walking. He sat at one year. He does not yet say any words clearly. Which of the following findings is **inconsistent** with Duchenne Muscular Dystrophy?

A. Elevated Creatine Kinase
B. Absent reflexes
C. Speech Delay
D. Abnormal Liver Enzymes
E. A maternal uncle who uses a wheelchair

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**Duchenne/Becker Muscular Dystrophy**

- An X-linked disorder; Dystrophin is coded at Xp21.2
- Duchenne: complete absence of dystrophin; Becker: partial absence
- One third of cases are due to new mutations
- Children are often first identified because of elevated transaminases
- Common signs and symptoms
  - Mildly delayed motor or language milestones (early)
  - Proximal muscle weakness (Gower)
  - Calf pseudohypertrophy
  - Trendelenburg gait
- Treatment
  - Steroids prolong walking
  - Scoliosis repair can preserve pulmonary function
  - Assisted ventilation, Cardiac regimen prolongs survival (18–30s)

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**Know how to plan the evaluation for a child with muscular weakness**

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<th>LMN</th>
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<td>Atrophy</td>
<td>None</td>
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<td>None</td>
<td>Common</td>
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<td>Tone</td>
<td>Spastic</td>
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<td>Babinski</td>
<td>Up</td>
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</tr>
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**Duchenne at 18 months**

http://vimeo.com/25756951

**Duchenne at 5 years**

http://vimeo.com/25843377
Developmental Considerations in D/BMD

- Mean Full Scale IQ 80
- 30% of patients with D/BMD have IQ <70
- Delayed speech acquisition, specific learning disabilities common
- ADHD, OCD, ASD more common than in general population
- Anxiety extremely common as patients age (personal observation)

Testing for a child with Low (or Normal) Tone

- Creatine Kinase (CK):
  - The CK is significantly elevated in Duchenne Muscular Dystrophy, at least 3x normal
  - Cost (Our lab in 2012): around $40
- Thyroid Stimulating Hormone (TSH):
  - Thyroid myopathy may present with either hypothyroidism or hyperthyroidism, and without classical signs of thyroid disease (admittedly uncommon)
  - Cost (Our lab in 2012): around $80
  - Microarray: around $2200

Question 2: Know the signs and symptoms of Spinal Muscular Atrophy (SMA)

A 2 month old infant is seen for well child care and is noted to be floppy. On exam, you note severe hypotonia, absent reflexes, and tongue fasciculations. Which of the following tests should be performed to confirm the diagnosis of Spinal Muscular Atrophy?

A. MRI of the brain
B. EMG/NCV
C. Muscle Biopsy
D. Genetic testing for SMN1 gene
E. Genetic testing for SMN2 gene

Spinal Muscular Atrophy

Autosomal recessive defect in the Survivor Motor Neuron gene (SMN1); SMN2 may act as a modifier in some patients.
1/6000 births; range of severity.
Type 1: Cannot sit independently
Type 2: Can sit, but not walk
Type 3: Can walk (at least for a time)
Treatment is Supportive: Respiratory, Nutrition, Palliative
Cognitive Profile: Thought to be above average
Again, anxiety common.

Spinal Muscular Atrophy

http://vimeo.com/47749876
Question 3: Know the causes of congenital hypotonia

You are seeing a 6 month old for global developmental delay. You note hypotonia. Which of the following genetic syndromes does NOT present with hypotonia?

A. Prader-Willi Syndrome
B. Angelman Syndrome
C. Fragile X syndrome
D. Noonan syndrome
E. Freeman-Sheldon Syndrome

Common genetic disorders for which neuromotor delays may be a presenting

<table>
<thead>
<tr>
<th>Condition</th>
<th>Inheritance</th>
<th>Clinical testing</th>
<th>Clinical features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spinal muscular atrophy</td>
<td>Autosomal recessive</td>
<td>Gene sequencing for SMN1 gene</td>
<td>Clinical heterogeneity; usually presents in infancy or early childhood with proximal muscle weakness; respiratory failure seen in &gt;50% of cases</td>
</tr>
<tr>
<td>Friedreich's ataxia</td>
<td>Autosomal recessive</td>
<td>Gene sequencing for FRDA gene</td>
<td>Ataxia, areflexia, sensory neuropathy, scoliosis, heart disease</td>
</tr>
<tr>
<td>Mitochondrial myopathies</td>
<td>Sporadic</td>
<td>Gene sequencing of mitochondrial DNA</td>
<td>Neuromuscular problems, often with respiratory insufficiency</td>
</tr>
<tr>
<td>Motor neuron disease</td>
<td>Sporadic</td>
<td>Gene sequencing for SOD1 gene</td>
<td>Usually presents in adulthood with progressive muscle weakness and atrophy</td>
</tr>
<tr>
<td>Peripheral neuropathies</td>
<td>Sporadic</td>
<td>Nerve conduction studies</td>
<td>Neuromuscular symptoms, often with sensory and motor deficits</td>
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</thead>
<tbody>
<tr>
<td>Duchenne muscular dystrophy</td>
<td>X-linked recessive</td>
<td>Gene sequencing for DMD gene</td>
<td>Infantile hypotonia and very delayed motor milestones; usually present with global delays; dysmorphic features in early infancy</td>
</tr>
<tr>
<td>X-linked muscular dystrophy</td>
<td>X-linked</td>
<td>Gene sequencing for X-linked dystrophin gene</td>
<td>Milder forms identified at later ages</td>
</tr>
<tr>
<td>Spinal muscular atrophy</td>
<td>Autosomal recessive</td>
<td>Gene sequencing for SMN1 gene</td>
<td>Clinical heterogeneity; usually presents in early infancy with severe hypotonia and may be static at birth</td>
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<td>Neuromuscular symptoms, often with sensory and motor deficits</td>
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<tr>
<td>Neonatal encephalopathies</td>
<td>Sporadic</td>
<td>Brain imaging, metabolic panel</td>
<td>Severe hypotonia, often with seizures and developmental delay</td>
</tr>
</tbody>
</table>

Spinal Muscular Atrophy

http://vimeo.com/47717183
**Freeman-Sheldon Syndrome**

Elevated CK to greater than 3X normal value (male and females) 

Facial dysmorphism, organomegaly, signs of heart failure, and early joint contractures

Respiratory insufficiency with generalized weakness

Loss of motor milestones

**RED FLAGS**

<table>
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<th>Red Flags</th>
<th>Implications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevated CK to greater than 3X</td>
<td>Muscle destruction such as in Duchenne Muscle Dystrophy, Becker Muscle</td>
</tr>
<tr>
<td>normal value (male and females)</td>
<td>Dystrophy, other disorders of muscle</td>
</tr>
<tr>
<td>Congenital heart defects</td>
<td>Congenital heart defects</td>
</tr>
<tr>
<td>Facial dysmorphism, organomegaly</td>
<td>Trisomy 21 (Down syndrome), Trisomy 18, and others</td>
</tr>
<tr>
<td>Respiratory insufficiency with</td>
<td>Trisomy 21 (Down syndrome), Trisomy 18, and others</td>
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**Question 4:**

An 18 month old male is seen because he is not yet walking. He was full-term, with a benign prenatal history, and the delivery was uneventful. He can pull to stand since the age of 6 months. Your exam is notable for spasticity and hypertreflexia in the legs. Which test is most likely to lead to the diagnosis?

A. Creatine Kinase (CK)
B. EMG/NCV
C. MRI of the Brain
D. MRI of the Spinal Cord
E. Microarray

**Question 4: Features of Cerebral Palsy**

An 18 month old male is seen because he is not yet walking. He was full-term, with a benign prenatal history, and the delivery was uneventful. He can pull to stand since the age of 6 months. Your exam is notable for spasticity and hypertreflexia in the legs. Which test is most likely to lead to the diagnosis?

A. Creatine Kinase (CK)
B. EMG/NCV
C. MRI of the Brain
D. MRI of the Spinal Cord
E. Microarray
Cerebral Palsy

- CP describes a group of permanent disorders of the development of movement and posture that cause activity limitations that are attributed to nonprogressive disturbances that occurred in the developing fetal or infant brain. The motor disorders of CP are often accompanied by disturbances of sensation, perception, cognition, communication, and behavior and by epilepsy and secondary musculoskeletal problems.
  
- With a prevalence of 3.6 per 1000, more than 100,000 children in the United States are affected.

Bonuses Questions

Who stated “Static encephalopathy, in the vast majority of children, cannot be attributed to birth asphyxia, and that difficult birth in itself is merely a symptom of deeper effects that influenced the development of the fetus”?

A. William Little
B. Sigmund Freud
C. Abraham Jacobi
D. William Osler
E. Walter Reed

Diagnostic Testing in Cerebral Palsy

- 70-90% of children with CP have an MRI finding that suggests diagnosis or treatment (but usually not pathognomonic)
- 2004 Practice Parameter from the American Academy of Neurology:
  - Level A: Neuroimaging is recommended, with MRI preferred to CT
  - Level B: In children with hemiplegic CP, diagnostic testing for coagulation disorders should be considered
  - Level B: Metabolic and genetic studies should not be routinely obtained in the evaluation of the child with CP
  - Level C. If the clinical history or findings on neuroimaging do not determine a specific structural abnormality or if there are additional and atypical features in the history or clinical examination, metabolic and genetic testing should be considered. Detection of a brain malformation in a child with CP warrants consideration of an underlying genetic or metabolic etiology.

MRIs in Spastic Quadriplegia

- Full Term, Birth Anoxia
- Exam: Spastic Quadriplegia, Profound Intellectual Disability
- MRI: Diffuse white matter injury with volume loss
Question 5
You are seeing a 2 month old full-term infant who had a difficult birth. Which of the following findings would NOT be consistent with a later diagnosis of Cerebral Palsy?

A. Asymmetric kicking movements  
B. Asymmetric fisting  
C. Scissoring of the legs  
D. Ability to Roll  
E. Good Head Control

Question 5
You are seeing a 2 month old full-term infant who had a difficult birth. Which of the following findings would NOT be consistent with a later diagnosis of Cerebral Palsy?

A. Asymmetric kicking movements  
B. Asymmetric fisting  
C. Scissoring of the legs  
D. Ability to Roll  
E. Good Head Control

MRI in Spastic Diplegia

32 weeker with history of Intraventricular Hemorrhage  
Spastic Diplegia. MRI: Periventricular Leukomalacia  
PVL described as: wavy contour of the lateral margins of the lateral ventricles

MRIs in Spastic Hemiplegia

Full-Term, Spastic Hemiplegia  
MRI: Gliosis in area of prior MCA infarct  
Full-Term, Spastic Hemiplegia  
MRI: Schizencephaly

Question 6: A Group of Disorders
Which of the following disorders of the brain is NOT a common cause of spastic Cerebral Palsy?

A. Perinatal infection  
B. Birth Asphyxia  
C. Postnatal Intracranial Hemorrhage associated with prematurity  
D. Kernicterus  
E. Congenital Brain Malformations

Question 6: A Group of Disorders
Which of the following disorders of the brain is NOT a common cause of spastic Cerebral Palsy?

A. Perinatal infection  
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C. Postnatal Intracranial Hemorrhage associated with prematurity  
D. Kernicterus  
E. Congenital Brain Malformations
**Genetic Syndromes may look like**

**Dyskinetic CP**

On the MRI: Globus Pallidus- think neurogenetic; Putamen- think hypoxia

Consider:
- Angelman syndrome (ataxic, microcephaly, fascination with water)
- Rett syndrome (repetitive hand movements, cold hands and feet)
- Lesch-Nyhan (choreoathetoid, self-mutilation)
- Kernicterus (Dystonia, hearing impairment, paralysis of upwards gaze)
- HIE, Kernicterus, DRD (diurnal, worse in the evening), Segawa, PDH deficiency, Pelizaeus-Merzbacher, Glutaric Aciduria, MMA academia, NCL, Mitochondrial, disorders of glycosylation, AT, SCA, Huntington's, PKAN

(from Levey, Hoon, Fatemi, lecture at AACPDM 2011)

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**Genetic MRI Findings**

**Joubert Syndrome:**

- The “Molar Tooth” Sign

**Pantothenate Kinase-Associated Neurodengeneration:**

- The “Eye of the Tiger” Sign

(http://ultimate-radiology.blogspot.com/2012/03/pantothenate-kinase-associated.html)

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**Dyskinetic Cerebral Palsy**

http://www.youtube.com/watch?v=GEB6mEVTReC&feature=player_embedded

6:00-7:00

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**MRI in Dyskinetic CP**

Full-term, postnatal meningitis

Mixed Spastic and Athetoid CP

MRI: liquefactive lesions of white matter and basal ganglia

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**Spasticity**

Spasticity is the velocity-dependent resistance to movement, caused by hyperexcitable stretch reflex. (The Clasp Knife)

Usually accompanied by hyperreflexia or clonus.

Often, there is persistence of the neonatal reflexes

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**Spasticity**

Spasticity is caused by the abnormal processing of afferent activity that generates excessive force to the motor units.
What is Dyskinetic Cerebral Palsy?

- Dystonia: Rigidity that is not dependent on velocity (like a lead pipe)
- Athetosis: Involuntary writhing movements
- Ataxia: Failure of Coordination

Usually elements of all three are present:
- Common with basal ganglia involvement from severe asphyxia in the past, kernicterus.

Diagnosis and Treatment

- Children with motor delays should be simultaneously referred to:
  - Medical Specialists (Neurology, Dev. Peds, PM&R) for Diagnostic testing and medical treatment
  - Therapy and Early Identification Services for motor treatment

Know how to plan the evaluation for a child with muscular weakness

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<td>Down</td>
<td>Down</td>
</tr>
<tr>
<td>Test</td>
<td>MRI</td>
<td>EMG/NCV (or SMN testing)</td>
<td>CK</td>
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</tbody>
</table>

What about Hypotonic Cerebral Palsy?

Children with Cerebral Palsy are often hypotonic in the first year of life. (Trunk > Extremities)

Workup should include MRI and CK…Genetics…EMG, muscle biopsy if necessary.

If hypotonia persists…rethink the diagnosis.
- Does the perinatal history fit?
- Does the exam fit?
- Does the MRI fit?

Changes You May Want to Make in Your Practice

- Implement screening for all developmental delays, including motor delays.
- Use a validated screening instrument and carefully assess the child’s tone.
- Begin the initial workup for neuromotor delay in your practice
  - CK and TSH when the child has low or normal tone
  - MRI of the brain when the child has increased tone
- Refer simultaneously for diagnosis and treatment
- Look for “red flags” to determine which children with neuromotor delay need expedited referral to specialists

Persistence of Neonatal Reflexes is common in Cerebral Palsy

From Up to Date
THANK YOU!

garey.noritz@nationwidechildrens.org

Our work was supported by PEHDIC:
Program to Enhance the Health and Development of Infants and Children, a cooperative agreement between the American Academy of Pediatrics and the Centers for Disease Control and Prevention's National Center on Birth Defects and Developmental Disabilities

References

For more information on this topic, see the following publications:


