WEAKNESS: ACUTE, SUBACUTE, CHRONIC: INTERACTIVE CASE BASED SESSION

Donald L. Gilbert, MD, FAAP FAAN
Professor of Pediatrics and Neurology
Cincinnati Children’s Hospital Medical Center
DISCLOSURES

I have the following financial relationships with the manufacturers of commercial products and/or providers of commercial services:

  Ecopipam Pharmaceuticals, EryDel Pharmaceuticals, and Neurocrine Pharmaceuticals - Research Grant

(Please note: Clinical trial site investigator);

  Elsevier – Royalties for books

I do not intend to discuss an unapproved/investigative use of a commercial products (drugs, devices) related to these relationships.
Learning objectives

1. Develop and implement a standard approach to evaluating weakness in children
2. Recognize that acute and subacute generalized weakness can progress and lead to respiratory failure and death
3. Recognize central versus peripheral causes of low tone/floppiness in infants.
As a result of attending this lecture at the 2017 Practical Pediatrics CME course, I encourage you to make the following change in your practice when you see children with motor problems

1. Apply a systematic approach to taking history and performing physical examinations, in order to efficiently localize problems, and identify appropriate strategies for testing versus referral.
2. Appropriately refer to the Emergency Department any child with acute or subacute progressive weakness.
3. Accurately categorize hypotonic infants as having central versus peripheral nervous system problems.
Can you confidently differentiate Bell’s Palsy from a stroke?

Do you know when a child with droopy eyelids might have myasthenia gravis?

Should every “floppy baby” have a brain MRI?

For this interactive case based format, it’s helpful for learning purposes to be the doctor in the clinic or ER without the answer printed on the child’s forehead (or the slides). So – my advice is not to read the answers, which are at the end of this powerpoint.
APPROACH TO WEAKNESS
I. WHERE IS THE PROBLEM?

- Brain
- Brainstem
- Spinal cord
- Anterior horn cell
- Root
- Nerve
- Junction
- Muscle
Clues to anatomy of weakness

- **Brain**   Cerebrum – unilateral face, face-arm, face-arm-leg, leg
- **Brainstem**   Eyes dis-align, face, palate/tongue; “crossed findings”
- **Spinal cord**  weakness level, sensory level, bowel/bladder
- **Anterior horn cell** A/Hyporeflexia (normal sensory function)
- **Root**   Pain, areflexia/hyporeflexia
- **Nerve**   Areflexia/Hyporeflexia
- **Junction**  Fluctuating strength
- **Muscle**   Proximal distribution, CK elevated
Classic causes of weakness based on anatomical level

- **Brain** Stroke, ADEM, MS, tumor, degenerative diseases
- **Brainstem** Tumor, ADEM, MS
- **Spinal cord** Transverse Myelitis, tumor
- **Anterior horn cell** Polio, Spinal Muscular Atrophy
- **Root** Guillain Barre Syndrome
- **Nerve** Bell’s Palsy, Polio, SMA, Hereditary Sensori-Motor Neuropathy (Charcot-Marie-Tooth)
- **Junction** Myasthenia Gravis
- **Muscle** Muscular Dystrophies, Myopathies, Myositis, Metabolic/mitochondrial conditions
II. WHEN DID IT HAPPEN?

- Acute – peaking in seconds to minutes
- Subacute hours to a few days
- Chronic Static
- Chronic Progressive
Etiologies – “Vitamin CDE”

- Vascular
- Infectious / Post-infectious / Inflammatory
- Traumatic / Toxic
- Autoimmune
- Metabolic / Mitochondrial
- Iatrogenic
- Neoplastic
- Congenital
- Degenerative
- Endocrine
Etiologies – “Vitamin CDE” and typical timing

- Vascular - Acute
- Infectious / Post-infectious / Inflammatory Subacute
- Traumatic Acute Toxic Acute, Subacute, Chronic Progressive
- Autoimmune Subacute
- Metabolic / Mitochondrial Acute or Chronic Progressive, recurring acute
- Iatrogenic Any
- Neoplastic Chronic Progressive
- Congenital Chronic Static
- Degenerative Chronic Progressive
- Endocrine Chronic Progressive
Clinical Pearl:

Patients with acute and subacute onset generalized weakness can die of respiratory failure

*Check Forced Vital Capacity*
Pearl:

*Time* can be the difference between normal function (minimal loss of function) and permanent disability or death.
Approach

I. Localize  Brain, Brainstem......Muscle

II. Timing, types of processes  Acute... chronic, vitaminCDE

III. What else  More history, exam
Case 1: Applying the approach

A 10-year-old boy presents with leg weakness that has progressed over 24 hours

I. Localize

II. Timing, types of processes

III. What else do you want to know by history
Case 1: Approach, more history

A 10-year-old boy presents with leg weakness that has progressed over 24 hours and back pain. There is no history of trauma.

I. Localize

II. Timing, types of processes

III. What else do you want to know by history
Case 1: Approach, more history

A 10-year-old boy presents with leg weakness that has progressed over 24 hours, and back pain. There is no history of trauma. He has become incontinent of urine and stool.

I. Localize

II. Timing, types of processes

III. What should you do now?
Case 1: Approach, exam

- A 10-year-old boy presents with leg weakness that has progressed over 24 hours, and back pain. There is no history of trauma. He has become incontinent of urine and stool. On physical examination, leg reflexes are diminished. Sensory examination shows absent pinprick sensation below T6. Rectal examination demonstrates decreased tone.
Case 1 - Diagnosis
Case 2 Approach

An 8-year-old boy presents to the emergency department following 3 days of progressive difficulty walking. He says that his back hurts.

I. Localize

II. Timing, types of processes

III. What else do you want to know by history?
Case 2

An 8-year-old boy presents to the emergency department following 3 days of progressive difficulty walking. He says that his back hurts. There is no involvement of bowel or bladder function. There are no complaints of numbness. He had the flu one month ago. Review of systems otherwise is normal.

I. Localize

II. Timing, types of processes

III. Now what?
Case 2 - exam

- An 8-year-old boy presents to the emergency department following 3 days of progressive difficulty walking. He says that his back hurts.
- General physical examination shows no abnormalities.
- Mental status alert, makes good eye contact, and responds to questions appropriately.
- Cranial nerve examination results are normal.
- Motor examination strength is diminished in the arms and legs, more proximally, and more in the legs.
- Reflexes are absent.
- Sensory examination findings are normal.
Case 2

• Where is the lesion?

• What is the time course?

• What is the most likely diagnosis?

• What 2 diagnostic tests should be performed?
Case 2 - Diagnosis
Case 3

A 16-year-old girl presents with a 3 month history of intermittent double vision and droopy eyelids. Symptoms fluctuate and tend to worsen with fatigue. She is tiring quickly at home and school and sometimes feels too weak to walk with her peers or get ready for bed. Her father is irritated at her because she never smiles.

I. Localize

II. Timing, types of processes

III. Now what?
Pearl

Acquired ocular malalignment is always bad.
Case 3 Examine the patient carefully

- A 16-year-old girl presents with a 3 month history of intermittent double vision and droopy eyelids and fatigueable weakness.

- **General examination**: Normal except appears tired

- **Mental status**: normal except distressed

- **Cranial nerve exam**: drooping lids, tips head back to see under them

- **Motor exam**: normal grip but fatiguable muscle group testing

- **Reflexes**: normal

- **Sensory examination**: normal
Case 3

A 16-year-old girl presents with a 3 month history of intermittent double vision and droopy eyelids and fatigueable weakness.

I. Localize

II. Time Course
Case 3 - Diagnosis
Cases 4 and 5

Floppy Babies
Case 4 floppy infant

• Full term infant, product of an uncomplicated pregnancy, delivered via C section for breach. Mom smoked throughout the pregnancy.

• Examination shows infant with normal vitals and growth parameters including head circumference, no dysmorphic features, with limbs abducted and very little spontaneous movement. The infant is alert, eyes fix and follow, facial expressions appear normal.
Case 5 floppy infant

• Full term infant, product of a first pregnancy to a mother with no prenatal care.

• Examination shows infant with normal vitals and small growth parameters including head circumference 32 cm. No other dysmorphic features. Limbs abducted and very little spontaneous movement. Child is sleepy, somewhat difficult to arouse.
General Points about Floppy Infants

• The FOCUS is localization at this level initially: Is this Central (usually brain) or Peripheral (nerve, junction, muscle)?
• The main determinant of an effective workup is localization by History and Physical to Central vs. Peripheral
• The main way to reduce unnecessary (diagnostic) costs is localization by History and Physical to Central vs. Peripheral
• Neurology Consultations cost less than many diagnostic tests you are considering right now
Key points of the history

• The BRAIN is more vulnerable than the nerves and muscle to bad environmental factors
• Thus most risk factors are risks for the brain
• Still – the prevalence of exposure to risk factors is HIGH – so lots of kids have risk factors but no weakness or hypotonia. Floppy kids may have central risk factors but still have peripheral disease
• So – the history of risk factors is important, but the EXAM is critical!
### History key points – a short list

<table>
<thead>
<tr>
<th>CENTRAL</th>
<th>BOTH / Either</th>
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<tbody>
<tr>
<td>• Maternal factors – hypertension, illicit drug use, poor weight gain, chronic or acute medical conditions</td>
<td>• Breech position</td>
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<tr>
<td></td>
<td>• Decreased Fetal Movement / congenital joint contractures</td>
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<td></td>
<td>• Polyhydramnios</td>
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</tbody>
</table>
• CASE 4: Full term infant, product of an uncomplicated pregnancy, delivered via C section for breach. Mom smoked throughout the pregnancy. Decreased fetal movement noted.

• Exam shows normal head circumference, normal eye movements, profound symmetric weakness with difficulty swallowing and breathing and loss of reflexes

• Central or peripheral?
• CASE 5: Full term infant, product of a first pregnancy to a mother with no prenatal care. Decreased fetal movement unclear. Vaginal delivery.

• Exam shows small head circumference, limited visual interaction. Tone is low but strength in sucking, breathing, moving limbs appears normal.

• Central or peripheral?
EXAM – what is “Floppy”? Low TONE? Low Strength?

• When the Motor system is **Passive**: you assess tone
  • What the examiner FEELS is **Tone**

• When the Motor system is **Active**: you assess **Strength**
  • Baby spontaneous actions
  • Baby motions elicited by the examiner
Horizontal and Vertical suspension

Peredo DE, Hannibal MC. 
*Ped in Review* 2009

Strength
Evaluation of the active motor system – spontaneous actions

• Vital functions: Sucking/swallowing, breathing (intercostals)
• Head: eye movements, facial movements, lip suction
• Limbs: Normally the preterm baby has more symmetric limb movements; the term baby will have more alternating limb movements
Evaluation of the active motor system – what you elicit

- Grasp
- Moro
- Atonic Neck Reflex
- Placing/Stepping
# Neuro Exam Key Points — Central vs. Peripheral Etiologies

<table>
<thead>
<tr>
<th>Mental Status</th>
<th>Central (brain)</th>
<th>Peripheral (Nerve, jxn, muscle)</th>
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<tbody>
<tr>
<td>Face</td>
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<tr>
<td>Reflexes</td>
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<tr>
<td>Bulk</td>
<td></td>
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<tr>
<td>Strength</td>
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Neuro Exam key points — Central vs. Peripheral Etiologies

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<tbody>
<tr>
<td>Mental Status</td>
<td>Affected</td>
<td>Normal</td>
</tr>
<tr>
<td>Face</td>
<td>Normal</td>
<td>Weak (except SMA)</td>
</tr>
<tr>
<td>Reflexes</td>
<td>Normal or increased</td>
<td>Decreased</td>
</tr>
<tr>
<td>Bulk</td>
<td>OK</td>
<td>Decreased</td>
</tr>
<tr>
<td>Strength</td>
<td>OK</td>
<td>Decreased</td>
</tr>
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Common Diagnoses: Central

• Hypoxic-ischemic injury
• Infections/sepsis
• Genetic/Chromosomal Disorders
  • Brain malformations
  • Inborn errors of metabolism
• Endocrine: thyroic, Ca++, glucose
Common Diagnoses: Peripheral

- Anterior horn cell: Spinal Muscular Atrophy
- Nerve: inflammatory, genetic, metabolic neuropathy
- Neuromuscular Junction: Myasthenia gravis, botulism
- Muscle diseases:
  - Dystrophies (Merosin-deficient)
  - Myopathies (central core, nemaline etc)
  - Myotonic Dystrophy (the one you suspect after shaking hands with mom)
When to watch and wait

• Central Cause suspected

• Mild features

• This may be a benign form of central hypotonia, sign of a mild static encephalopathy; recommend increased vigilance about development even if tone normalizes over time
When to evaluate / test – Central (Brain)

• You are worried, child is struggling

• Evaluation Approach
  • Routine labs
  • Brain MRI preferred to US or CT
  • Seizing possibly? Continuous EEG (otherwise don’t order)
  • CSF r/o sepsis, metabolic diseases
  • Metabolic labs Urine OA, Serum AA
  • Consult based on findings
When to refer / consult – Peripheral

• Any suspected peripheral nervous system requires careful evaluation and neurological consultation

• Evaluation approach
  • Labs: CK
  • Chest X ray (big heart?)
  • No brain/spine imaging usually!
  • EMG/Nerve conduction not always needed - consult first
  • Genetic testing - consult first
  • Neuro Consult before discharge
Case 6: Facial Weakness

A 14-year-old boy presents to your office because the side of his face is drooping.

I. Localize

II. Timing, types of processes

III. What else do you want to know?
Case 6: Facial weakness with more history

A 14-year-old boy presents to your office because the side of his face is drooping. His mother states that he complained yesterday of decreased food taste. Today, while at school, he could not use the microscope in science class because he couldn't close his left eye, and his teacher noted that his smile was crooked.

I. Localize

II. Timing, types of processes

III. What else do you want to know?
Case 6: Facial weakness, examination

A 14-year-old boy presents to your office because the side of his face is drooping.

• Physical examination reveals no abnormalities and no vesicles in his ears.
• Mental status is normal.
• Cranial nerves: Pupillary reactions are normal. Vision is normal. Extraocular movements are full and there is no nystagmus or reported double vision. His palate and tongue movements are normal.
• Face: He is unable to close his left eye or raise his left eyebrow, has decreased left-side nasolabial folds, and cannot close his mouth to puff out his cheeks.
• Motor examination normal proximal and distal strength in both arms and normal regular and tandem gait. Reflexes normal.
Diagnosis?
Treatment?
Case 7: Former Premature Infant with spastic, weak legs and feet

- Approach: Where is the problem?

- Time Course:

- What is this called?
Case 7: Former Premature infant with spastic, weak legs and feet

- Periventricular
- Static/non-progressive
- Supportive/ rehabilitative care
Case 8

A mother brings in her 4-year-old boy because she is concerned about his increasing clumsiness. He has been previously healthy and achieved developmental milestones on time. His growth parameters are normal. On physical examination, his mental status is normal, as are results of cranial nerve and sensory examinations and reflexes. However, he cannot rise from the floor without using his hands, and his running looks clumsy.

I. Localize
II. Timecourse
III. Diagnosis?
Case 9

During the health supervision visit of a 10-year-old boy, you note some wasting and weakness of his lower leg muscles, with diminished patellar and ankle reflexes. You examine his parents’ legs and feet and notice that his mother has a bilateral foot drop and deformed feet.

I. Localize
II. Timecourse
III. Diagnosis?
CASES DETAILS BELOW

1. Hemorrhage due to vascular malformation in the spine causing spinal transection syndrome
2. Guillain Barre Syndrome
3. Myasthenia Gravis
4. Infant with Spinal Muscular Atrophy
5. Infant with central hypotonia - Lissencephaly
6. Idiopathic Facial Nerve Palsy – Bell’s Palsy
7. Spastic Diplegia due to Periventricular Leukomalacia
8. Hereditary Sensori-motor Neuropathy (Charcot Marie Tooth)
9. Duchenne’s Muscular Dystrophy
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THANK YOU FOR YOUR ATTENTION
Guillain Barre Syndrome

Acute Inflammatory (Demyelinating) Polyneuropathy
AIDP
Guillain Barre Syndrome

• Subacute onset of ascending weakness (usually starts in hips, not feet), accompanied by pain.
• Due to immune mediated attack on myelin in peripheral nerves
• Hypo/areflexia is key finding
Guillain Barre Syndrome

- Can cause death from respiratory insufficiency, aspiration, dysautonomia
- **ADMIT to Hospital and monitor Forced Vital Capacity or Negative Inspiratory Force**
- Treat Pain
- IVIG
- Consult Neurology
Guillain Barre Syndrome diagnostic results

- CSF classic: “albumino-cytologic dissociation” high protein, normal cells
  - May not be present the first week
- Nerve conduction studies
  - Prolonged distal/F wave latencies
  - Reduced conduction velocity
  - Conduction block
Myasthenia Gravis

Usually acquired, can be congenital
A disease at the neuromuscular junction
Myasthenia Gravis

• Auto-antibodies generated by disease which bind to the post-synaptic acetyl-choline receptor and prevent acetyl-choline signal from travelling from the nerve to the muscle
• This causes fluctuating weakness which gets worse with repeated or sustained action – hence it is fatiguable
• The diagnosis is confirmed by testing for elevated AChR Antibodies
• Repetitive Stimulation Nerve Conduction Testing of muscle shows decrement
Myasthenia Gravis Diagnosis

• At the bedside in the Intensive Care Unit, administration of edrophonium IV, also known as the “Tensilon Test”, transiently improves strength. This acetylcholinesterase inhibitor increases the acetylcholine available at the synapse, improving strength

• Treatment then is oral pyridostigmine plus immune suppression/modulation, usually with prednisone

• Many patients should undergo thymectomy, whether or not they have thymoma, as this has been shown to improve recovery in a randomized controlled trial

• MG patients who appear stable can die from a myasthenic crisis
Spinal Muscular Atrophy

• This is a degenerative diseases of anterior horn cells and motor nuclei in the lower brainstem

• It is usually caused by deletions or mutations in coding regions for the SMN1 gene. The various types of SMA are determined by mutation severity and compensation (or lack) by SMN2

• SMA 1 is infantile and can cause early respiratory insufficiency and death

• Nusinersen (Spinraza) was recently approved by the FDA for treatment
Central hypotonia with microcephaly

Congenital CMV

Lissencephaly
Periventricular Leukomalacia

Case courtesy of Dr Bita Abbasi, Radiopaedia.org, rID: 22712
https://radiopaedia.org/articles/periventricular-leukomalacia

PVL with IVH
Treatment of Idiopathic Facial Nerve (Bell’s) Palsy?

• Prednisone 2 mg/kg/day for 5 days and then taper

• Valacyclovir recommended by some, for severe cases

• Acyclovir if otic vesicles
Differential diagnosis: Childhood Stroke – clinical features

- Cerebrovascular disorders: arterial ischemic stroke, venous infarctions, intracranial hemorrhage
- Stroke involving face only would be lower face – eye closure, eyebrow rasing would be preserved
- Suspected stroke is an emergency. Refer to ER and call neurology
Pediatric Stroke – Key features

• Acute onset focal neurological deficit
• Unexplained altered consciousness, especially with headache
• Seizures in a near-term newborn
• Seizures in an infant recovering from cardiac surgery
Childhood muscle diseases

• Primary muscle diseases present with nonspecific findings including hypotonia, weakness, developmental delay. Muscle cramps may occur.
• Myopathies, dystrophies, myositis
• Serum CK is most commonly obtained blood test
Serum CK for muscle disease

• >10,000 or even > 100,000 myolysis/myoglobinuria
• >1,000 Duchenne’s Muscular Dystrophy, other myopathies
• Chronic myopathy can occur without elevated CK
• In children presenting with fatigue, proximal weakness, and discoloration of eyelids and cheeks, CK should be obtained
Hereditary Sensorimotor Neuropathies

• There are many!

• Key features – gradually progressive wasting of muscles, weakness, and numbness in legs more than arms

• Many are genetic, with autosomal dominant inheritance

• Old Eponym is Charcot Marie Tooth
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REFERENCES – THESE WERE ALL ACTUAL CASES

• A great all purpose text book of child neurology that is not incredibly detailed and has a nice emphasis on the diagnostic process is: