University of California
San Francisco

Acute Flaccid Myelitis and Increasing Pediatric Rehabilitation Access

California Society of PM&R

Mai Ngo, MD
Associate Professor, UCSF Orthopedic Surgery Department
Director, Pediatric Rehabilitation Benioff Children's Hospital Oakland

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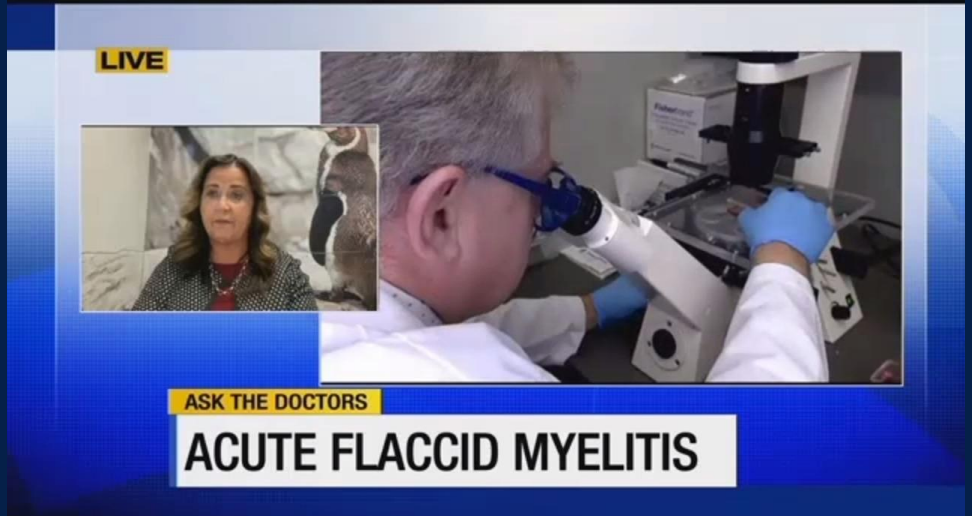
Disclosure

I have no relevant financial relationships with any companies related to the content of this course.



HEALTH

AFM, a Biennial Polio-Like Viral Illness, Is Expected to Hit the U.S. in 2020

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Learning Objectives

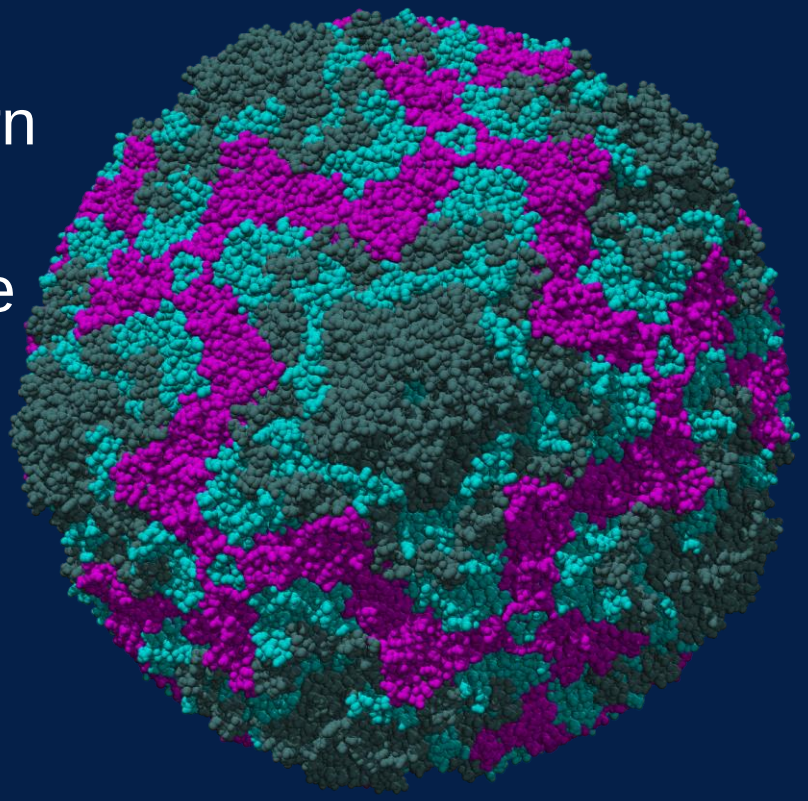
- Provide a clinical overview of AFM
  - Background
  - Etiology
  - Epidemiology
  - Clinical Features
  - Diagnosis
  - Management and Treatment
- Describe the California Children's Services Medical Therapy Program

Case Study

- AH was a 12yo previously healthy female who presented with a viral illness prodrome, sudden onset of chest pain on day of admission that progressed quickly to acute flaccid paralysis and respiratory failure requiring tracheostomy and prolonged mechanical ventilation.
- She had no reflexes below the neck, CNs were normal with the exception of no gag reflex. Sensation to light touch and proprioception were intact, but she had no sensation to pain or temperature below the neck.
- MRI spine showed a hyperintensity from the lower medulla to the mid-thoracic region.
- LP had normal protein, glucose, WBC.
- Diagnosis was suspicious for transverse myelitis versus polio-like myelitis, also known as acute flaccid myelitis.

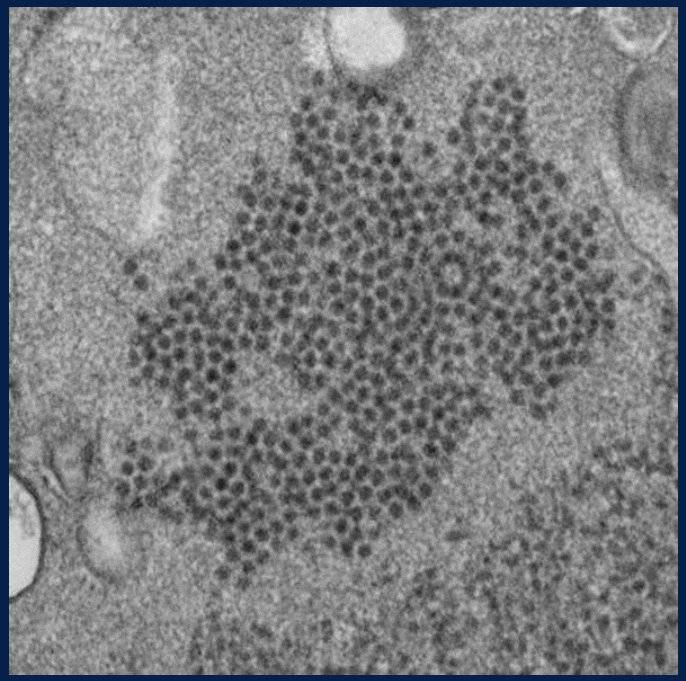
Background

- “Acute flaccid paralysis" (AFP)
- Loss/dysfunction of anterior horn cells in the spinal cord.
- Rapid onset of weakness in one or more limbs, occurred more often in children, and had both infectious and non-infectious causes.
- Poliomyelitis caused by poliovirus was the classic case.



Background

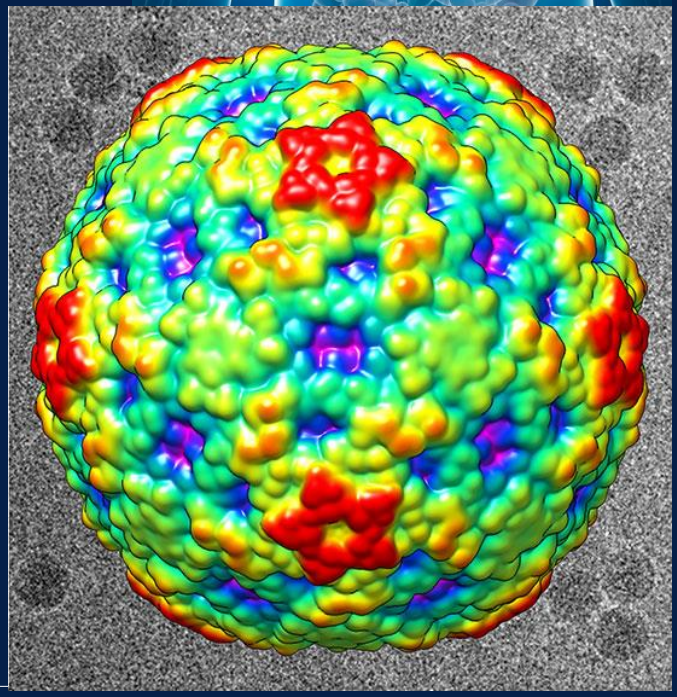
- Polio-like neurologic disease first reported in 2012 in California in a child with evidence of enterovirus D68 in respiratory tract specimens.
- CDPH case definition: acute onset flaccid limb weakness with spinal gray matter lesion on MRI or electrodiagnostic studies consistent with anterior horn cell damage.
- For 2012-2015, 59 cases.



Van Haren, K, et al. JAMA, 2015.

Background

- Colorado with cluster of cases 2014.
- Case definition: acute onset focal limb weakness and/or cranial nerve dysfunction associated with MRI findings of grey matter lesions in the spinal cord and/or brainstem.
- Aug to Oct 2014, 12 cases.
- Utah's Primary Children's Hospital, 11 cases.



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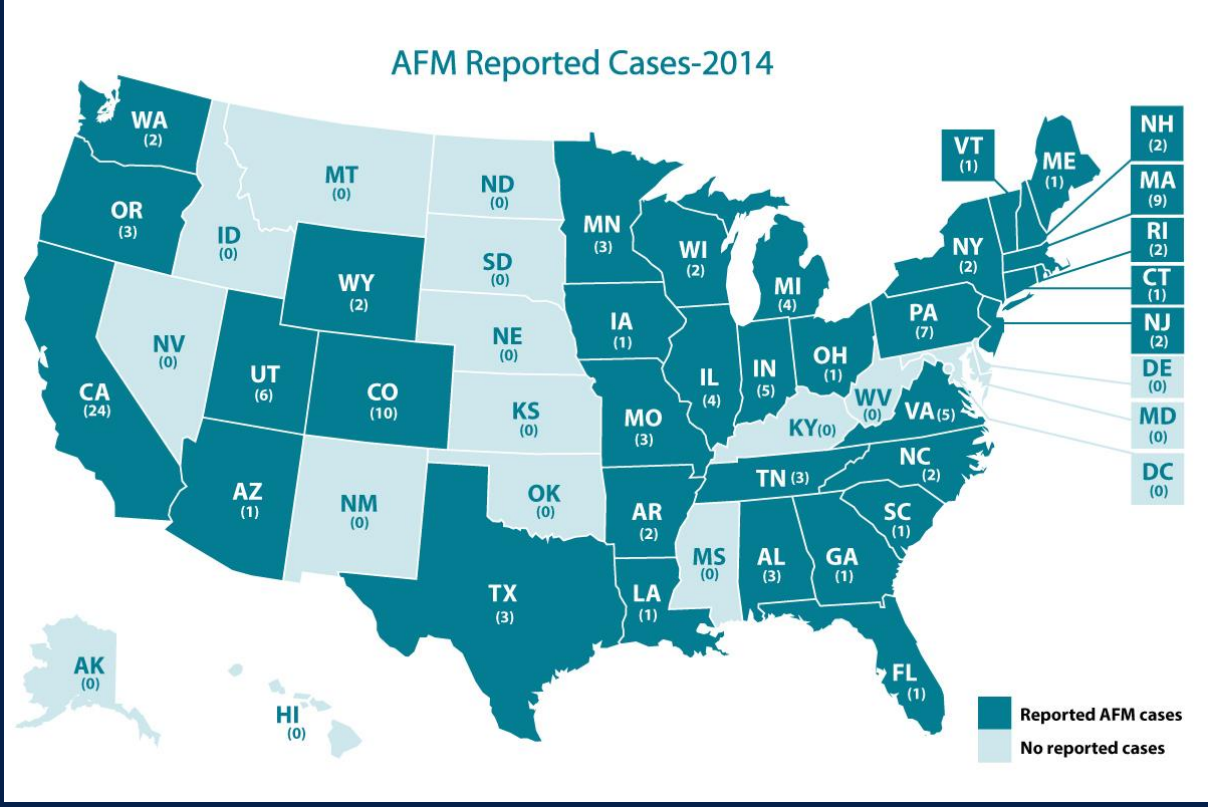
Background

- CDC case definition: <21yo with acute onset flaccid limb weakness AND gray matter lesions in spinal cord and/or brainstem.
- Aug to Dec 2014 from 34 states, 120 cases.



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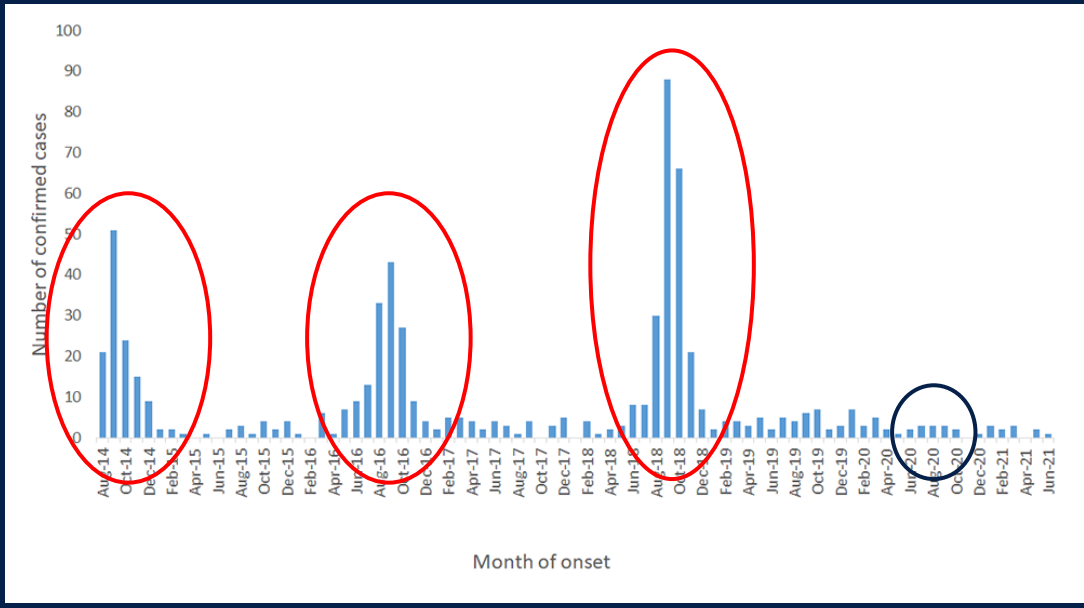
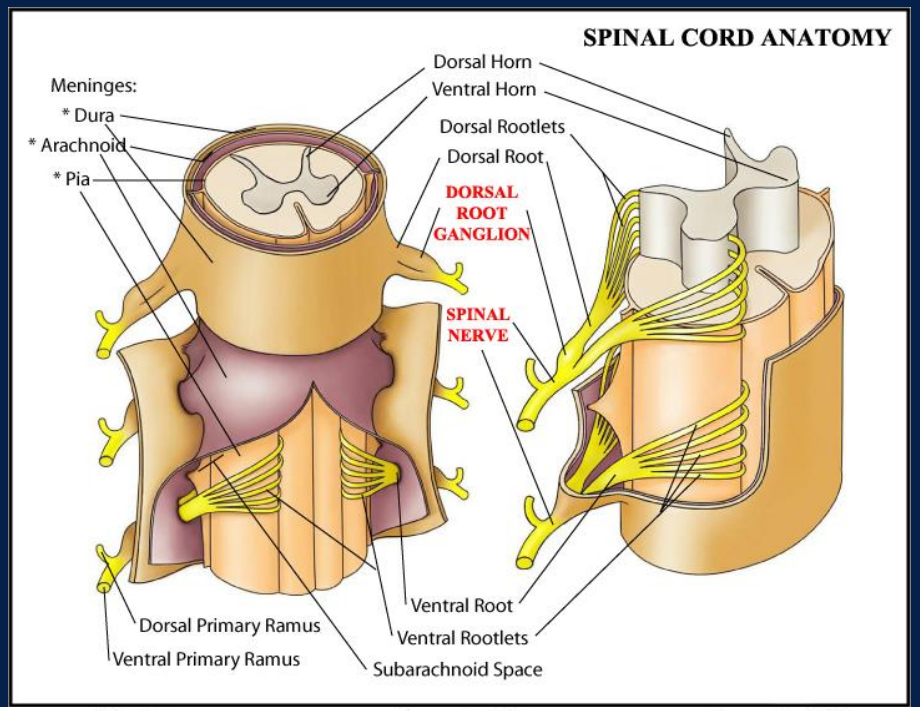
Background

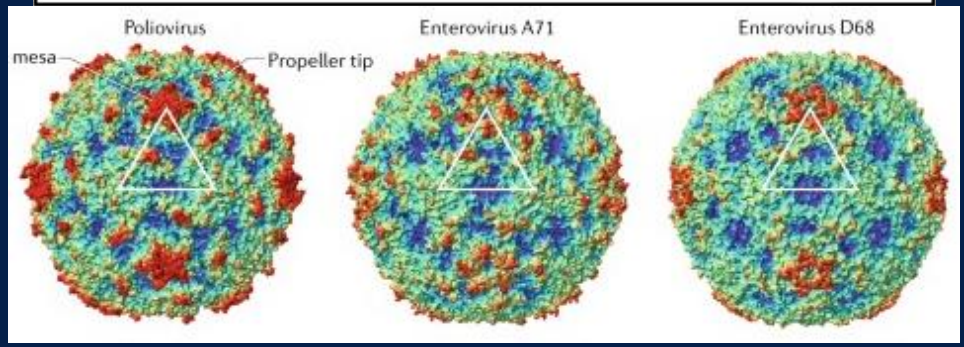
- "Acute Flaccid Myelitis" (AFM) was coined.
- Since Aug 2014, 661 confirmed cases in US.
- Increases of AFM cases late summer/fall of 2014, 2016, and 2018.
- In 2020, 32 cases.
- In 2021, 11 cases in 7 states.



Etiology

- Dysfunction/death of anterior horn cells.
- Damage to LMNs leads to flaccid weakness.
- Enterovirus serotypes: poliovirus, EV-D68, enterovirus A71, flaviviruses, adenoviruses.
- Immune mediated causes: anti-MOG antibody associated disease.





Etiology

- Poliovirus is one of four species within the Picornavirus family.
- Single-stranded RNA viruses include enteroviruses A, B, C, and D. Poliovirus is part of group C.
- Transmitted via the fecal oral route.
- Most commonly affects the lower extremities.

- Enterovirus D68 part of group D within the Picornavirus family.
- Transmitted via the respiratory route.
- Most commonly affects the upper extremities.

Etiology

- The strongest indirect evidence to date is provided by a study of CSF from 42 AFM cases:
  - Testing revealed high levels of anti-enterovirus antibodies in 29 of 42 cases (69%) versus 4 of 58 controls (7%).
  - Enterovirus RNA could not be identified in the majority of case samples (19 of 20).

Schubert RD, et al. Nat Med. 2019.

Etiology

- EV-D68 has been the most commonly identified pathogen in respiratory samples of affected patients.
- AFM cases clustered during periods of peak EV-D68 circulation.
- Animal models have confirmed the ability of EV-D68 to cause flaccid paralysis in mice with symptoms similar to the human condition.

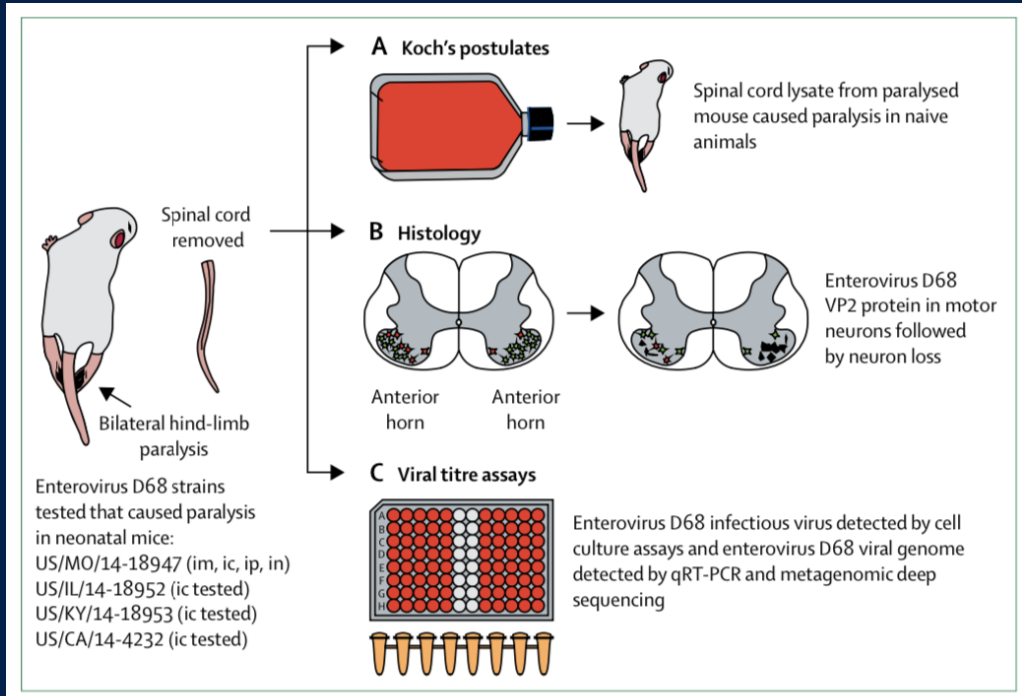


Figure 2: **Experimental mouse model of enterovirus D68 paralytic disease**
Several 2014 strains of enterovirus D68 caused permanent paralysis in neonatal mice by intracerebral (ic) inoculation. One strain tested in further detail, US/MO/14-18947, caused paralysis by multiple routes of inoculation, in inverse order of disease frequency: intramuscular (im, 100%), intracerebral (ic, about 50%), intraperitoneal (ip, about 5%), and intranasal (in, about 3%). During the course of enterovirus D68 infection.

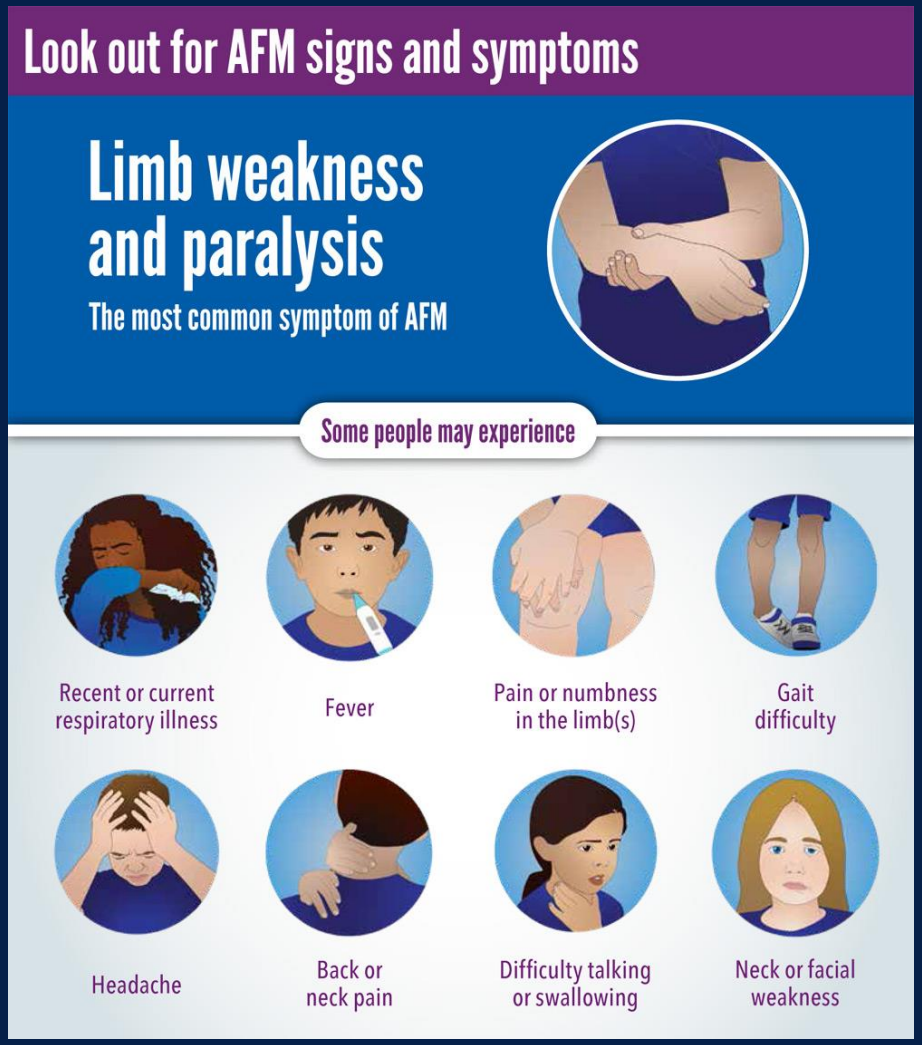
Messacar, K, et al. Lancet Infect Dis, 2018.

Epidemiology

- Incidence of <1 case per one million population in the United States.
- Cases have been recognized in 48 American states.
- Global regions including Europe, Canada, Asia, South America, and Australia.
- Reported cases of acute flaccid paralysis from South Africa suggests that AFM may also be occurring on the African continent.
- AFM affects children in approximately 90% of cases, and affected children are typically under 12 years of age, with some as young as 5 months old.
- Some of the reported adult cases have occurred in immunocompromised individuals.
- Several case series have noted a slight male preponderance of cases.

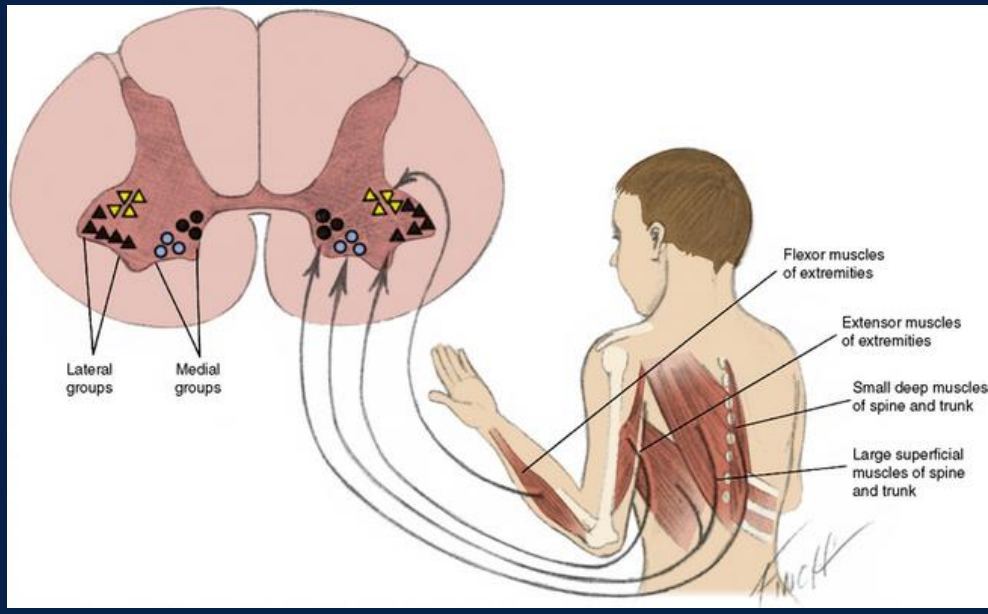
Clinical Features

- Prodrome of upper respiratory symptoms or fever preceding onset of weakness.
- Evolution of flaccid weakness can occur over hours to days.
- Some have cranial nerve dysfunction, bowel or bladder dysfunction, and/or sensory alterations.



Clinical Features

- In a report of 193 confirmed AFM cases from 2015 through 2017:
  - Fever, cough, rhinorrhea, vomiting/diarrhea >80%
  - Preceded neurologic symptoms by a median of 5 days.
  - Weakness involved 1-2 limbs 55%, 3-4 limbs 45%, and >=1 one upper limb 80%.
  - Quadriparesis was present in 36%.
  - Cranial nerve dysfunction 33%.
  - Altered mental status 28%.
  - Ventilator support 33%.



Ayers T, et al. Pediatrics. 2019.

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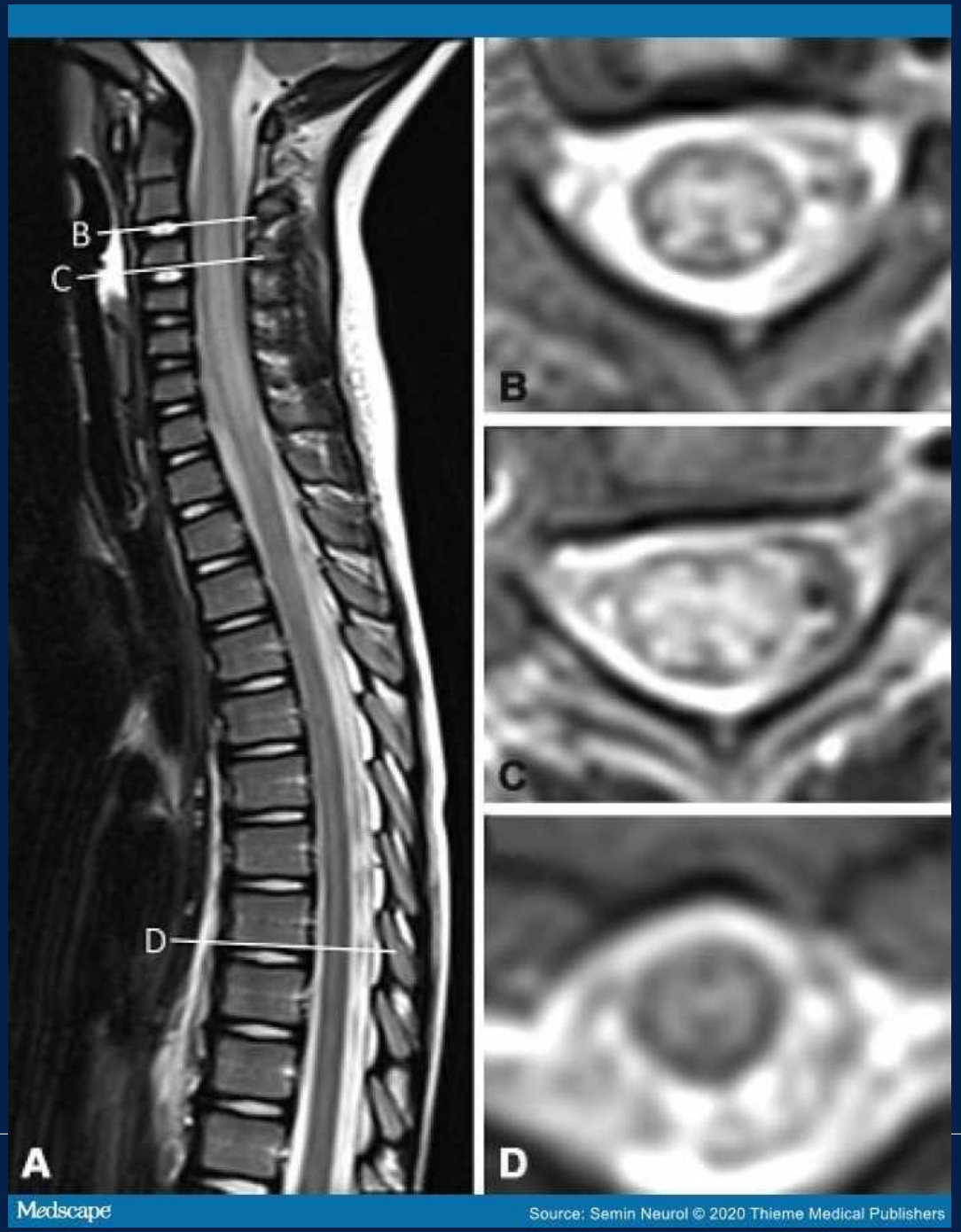
Diagnosis

- MRI brain and cervical and thoracic spine w/wo contrast
- CSF analysis
- Nasopharyngeal swabs for viral testing
- Fecal samples for viral testing
- Serum testing (eg, enterovirus PCR, aquaporin-4 antibodies, anti-MOG antibodies, and arbovirus panel including West Nile virus antibodies).
- Collect specimens as early as possible in the course of the illness.
- In addition to local diagnostic laboratory testing, clinicians In the US should send all specimens to their state or local health department

Diagnosis



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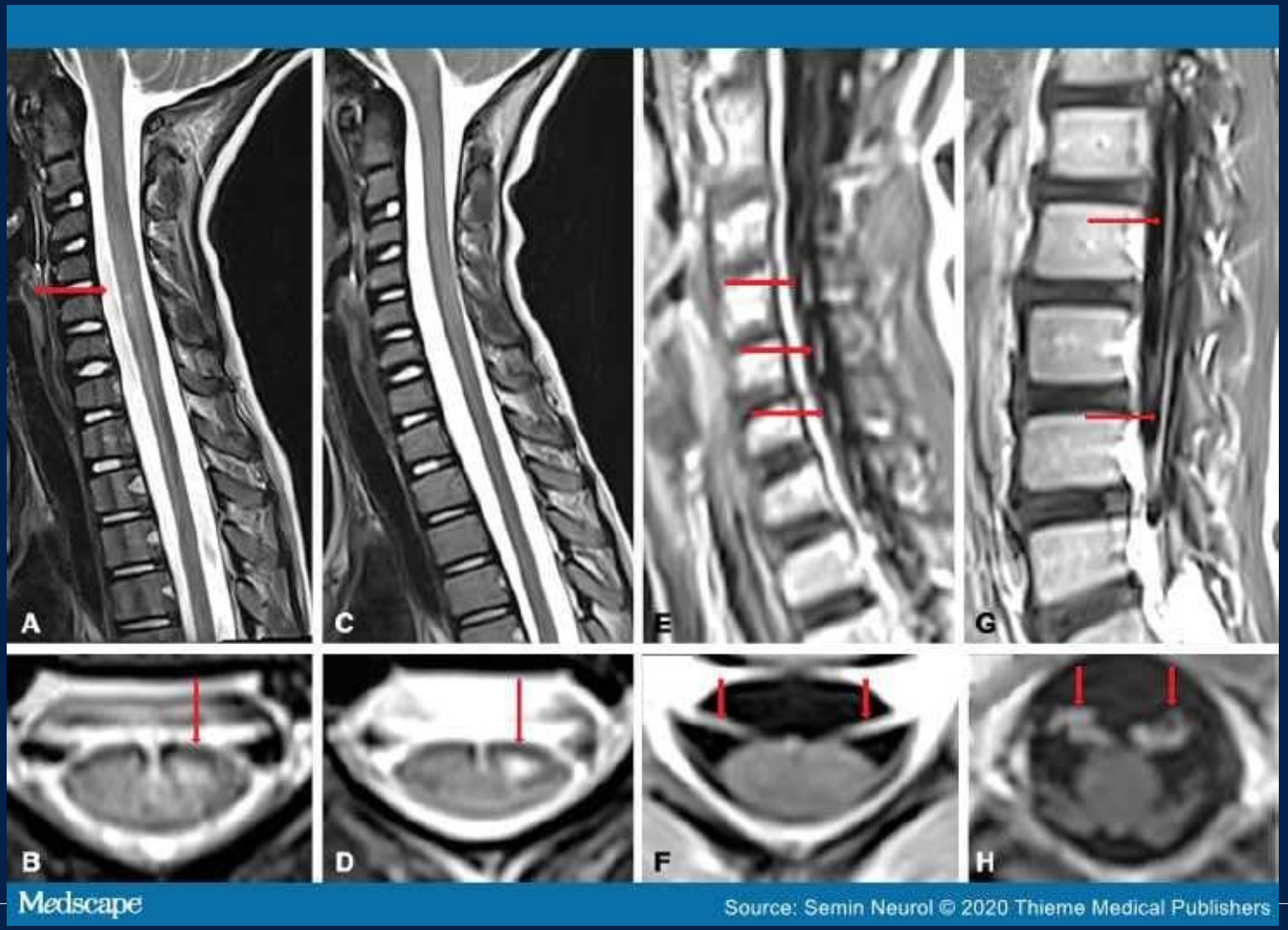
Diagnosis



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Diagnosis

- Electrodiagnostic studies can be useful in confirming a diagnosis of AFM.
  - Diminished or absent CMAPs.
  - Diminished or absent F-waves.
  - Reduced recruitment of voluntary motor potentials followed by development of fibrillations or positive sharp waves.
  - Sensory abnormalities should be absent or minimal.
- In many cases of AFM, EMG/NCS may not be necessary to confirm a diagnosis but can be useful in the subacute/convalescent phase for assessing the extent of muscle group involvement in individual limbs or planning surgical interventions such as nerve or tendon transposition.

Differential Diagnosis

- Synovitis
- Neuritis
- Limb injury
- Guillain–Barre syndrome
- Transverse myelitis
- Stroke, including spinal stroke
- Tumor
- Acute cord compression
- Conversion disorder

Infectious
Poliomyelitis
Vaccine-associated paralytic polio
Vaccine-derived poliomyelitis
Nonpolio enteroviruses
West Nile virus
Diphtheria
Myelopathic
Postinfectious transverse myelitis
Anti-MOG associated myelitis
Anti-AQP4 associated myelitis
Arterial or venous spinal cord infarction
Compression from spinal abscess, hemorrhage, or tumor
Neuropathic
Guillain-Barré syndrome
Acquired motor axonal neuropathy
Acquired motor sensory axonal neuropathy
Mononeuritis multiplex
Multifocal motor neuropathy
Acute intermittent porphyria
Toxic neuropathies
Disorders of neuromuscular transmission
Myasthenia gravis
Lambert-Eaton myasthenic syndrome
Botulism
Tick paralysis
Myopathic
Inflammatory myopathy
Rhabdomyolysis
Carnitine deficiency
Periodic paralysis

Case Study

- AH was treated with pulse steroids on HD#1 x 5d with taper and repeated on HD#10 when repeat MRI demonstrated increased edema and 'evolution' of the cord.
- On HD#2 she had bradycardia that proceeded to a period of asystole and required CPR x 4 minutes. She required pressors for about a week but was hemodynamically stable for the rest of her hospitalization.
- IVIG and plasmapharesis were started on HD#4 and given a total of five times.
- Despite aggressive treatment, she had no change in her underlying neurologic exam besides the loss of propioception over the initial week and the gain in ability to stick out her tongue and shrug her shoulders. Due to persistent ventilation needs, a trach and G-tube were placed.

Management and Treatment

- No specific therapies for AFM and/or EV-D68.
- Supportive care, agents that may limit damage to the spinal cord, and early/intensive rehabilitation.
- Hospital admission is recommended to monitor for rapid deterioration of weakness and respiratory failure.
- Approximately 20 to 35 percent of patients have respiratory failure requiring ventilatory support.

Management and Treatment

- Treatments commonly used for AFM in the acute phase include:
  - IVIG
  - Corticosteroids
  - Plasmapheresis
- There is not enough human evidence to indicate a preference or avoidance for their use at this time.
  - Treatment decisions should be made in conjunction with neurology and disease experts.
  - Potential benefits of using corticosteroids for spinal cord edema or white matter involvement must be balanced by potential harm due to immunosuppression in the setting of a possible viral infection.
  - There is no indication for the use of fluoxetine, antiviral, and/or other immunosuppressive agents for AFM.

Management and Treatment

- Early and regular rehabilitation therapies are essential to maximal recovery.
- Techniques used include activity-based therapy, electrical stimulation, and functional electrical stimulation.

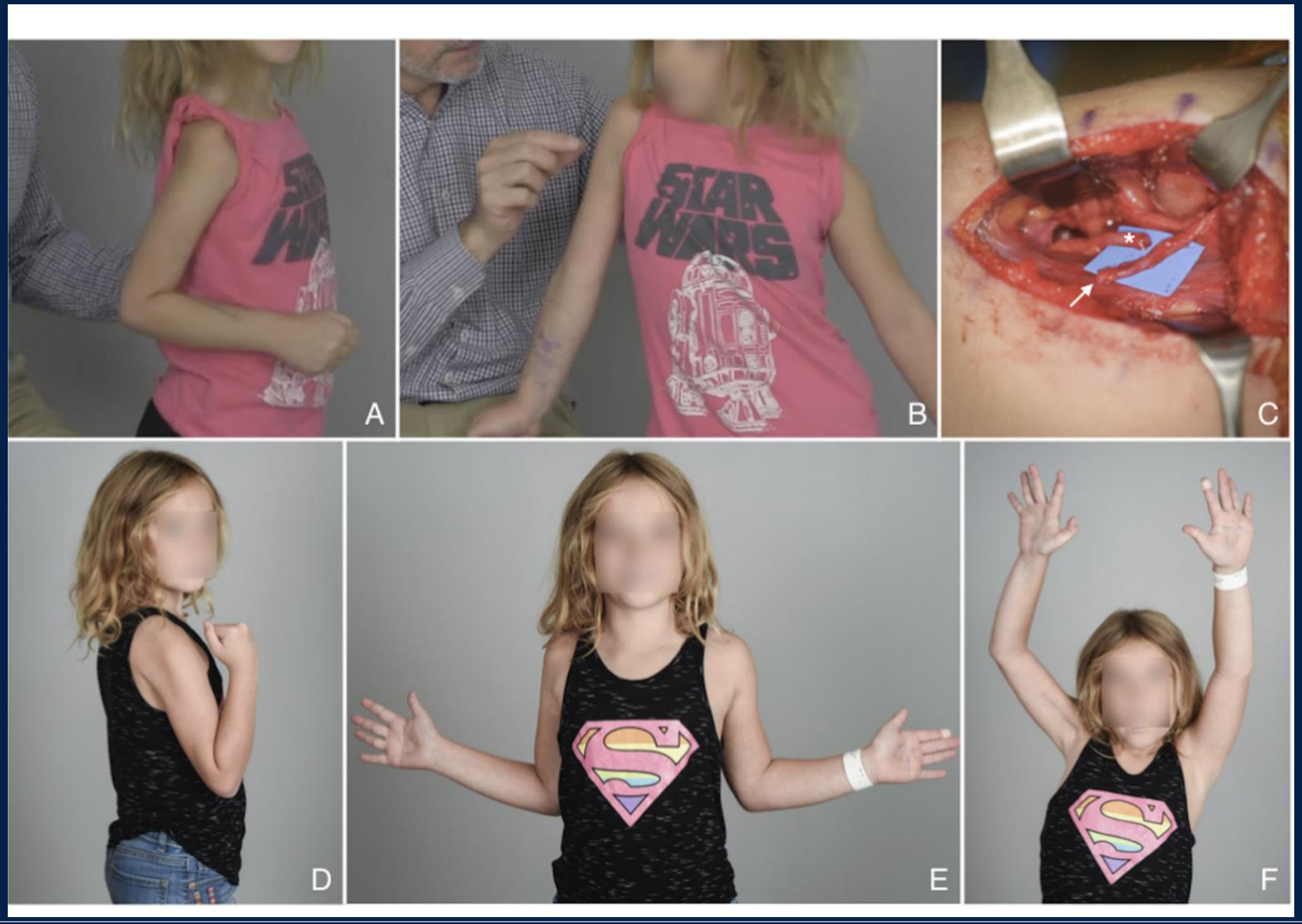
Management and Treatment

- Nerve transfer procedures: identification of "donor" nerves in proximity to a denervated muscle, followed by the surgical transfer of the healthy nerve to a recipient target.

Recipient Nerve	Donor Nerve	Procedures, n	Evaluated Function	Poor (AMS = 0–4)	Good (AMS = 5)	Excellent (AMS = 6–7)
SSN	All	10	Shoulder external rotation	30%[a]	20%	50%
	SAN	7		42%	14%[b]	42%
	ICN	3		—	33%	66%
Axillary	All	10	Shoulder abduction	70%[a]	10%	20%
	ICN	5		80%	20%	—
	Radial	2		—	—	100%
	Ulnar	1		100%	—	—
	Long thoracic	2		100%[b]	—	—
MSC	All	8	Elbow flexion	13%	—	87%
	Ulnar	5		20%[b]	—	80%
	Median	3		—	—	100%
Triceps branch	All	6	Elbow extension	33%	—	67%
	Ulnar	4		25%	—	75%
	ICN	1		—	—	100%
	Long thoracic	1		100%	—	—
PIN	All	1	Finger extension	—	—	100%
	Supinator	1		—	—	100%

Pino, P, et al. Ann Neurol, 2019.

Management and Treatment



Pino, P, et al. Ann Neurol, 2019.

Outcomes

- Persistent neurologic deficits in the majority of children affected by AFM.
- More than half of all children have persistent motor deficits and significant muscle atrophy in the affected limbs a year or more after disease onset.
- In one series of 21 patients who were diagnosed with AFM in Texas during 2016, recovery of the ability to perform ADLs with only mild deficits or complete independence was achieved by 16 patients (71%), including complete recovery by 5 patients (24%).
- Deficits related to white matter corticospinal tract damage appear to recover faster and more completely than LMN deficits.

Outcomes

- Long-term complications may resemble poliomyelitis survivors:
  - Leg length discrepancies
  - Joint dislocation or subluxation
  - Scoliosis
  - Deformities of weight-bearing joints and later degenerative arthritic changes
  - Persistent pain
- Various medical complications may also be associated with chronic neurological disability:
  - Pressure ulcers
  - Injuries from falls
  - Urinary tract infections
  - Renal disease secondary to neurogenic bladder
  - Respiratory infections and tracheitis

Case Study

- AH was treated with pulse steroids x 2.
- Repeat MRI showed increased edema and evolution of the cord. She had bradycardia that proceeded to a period of asystole and required CPR x 4 minutes. She required pressors for a week but was stable for the rest of her hospitalization.
- IVIG and plasmapharesis were started on HD4, received 5 treatments.
- Despite aggressive treatment, she had no change in her underlying neurologic exam besides the loss of propioception over the initial week and the gain in ability to stick out her tongue and shrug her shoulders.
- She was discharged to home on trach/vent and GT feeds after 3 months.

California Children's Services Medical Therapy Program

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Outline

- Brief History
- MTP facts
- Referrals
- County demographics
- Medical direction
- MTP functions

Brief History

- California Children's Services (CCS) Program, established in 1927.
- To provide services to children with conditions (such as infantile paralysis) that have since been eliminated through preventive measures.
- The CCS Program responsibility has shifted as more conditions that are chronic and less preventable in nature have been made eligible for the program.

Brief History

- Medical Therapy Program (MTP), established in 1945
- For children with orthopedic impairments associated with cerebral palsy (CP)
- Services moved from public hospitals to public school sites
- Budget Act, 1961, expanded MTP eligibility to include children with various other neuromuscular and msk conditions
- Robert Crown Act, 1968, established county responsibility for administering the MTP

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MTP Facts

- Serves clients/patients with medically eligible conditions, from birth to age 21.
- Provides the following services in an outpatient setting at no cost to families:
  - Physical Therapy
  - Occupational Therapy
  - Medical Therapy Conference (MTC)

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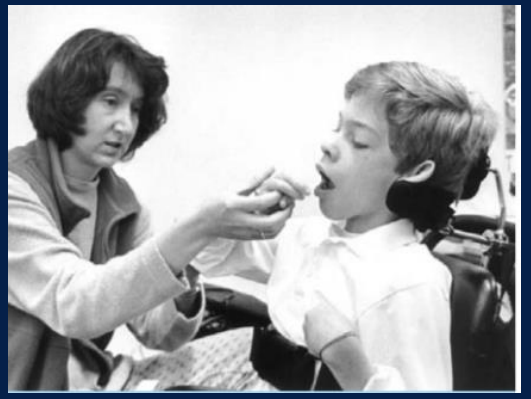
MTP Facts

- Families do not need to meet any financial eligibility criteria for MTP services.
- Client/patient just needs to be medically eligible.
- Services are provided in a Medical Therapy Unit (MTU) which is an outpatient therapy clinic located in a public school setting.
- The cost of the MTP is split 50/50 between the county.

MTP Facts

- Education agencies are required by statute and regulation to provide the space and equipment necessary (the MTU) for the therapists to provide MTP services.
- There are currently 130 MTUs in the state of California.
- There are approximately 600 FTE PTs/OTs working in the MTUs.
- CCS Program therapists are experts in providing services to children with chronic disabilities and determining appropriate rehab equipment usage.

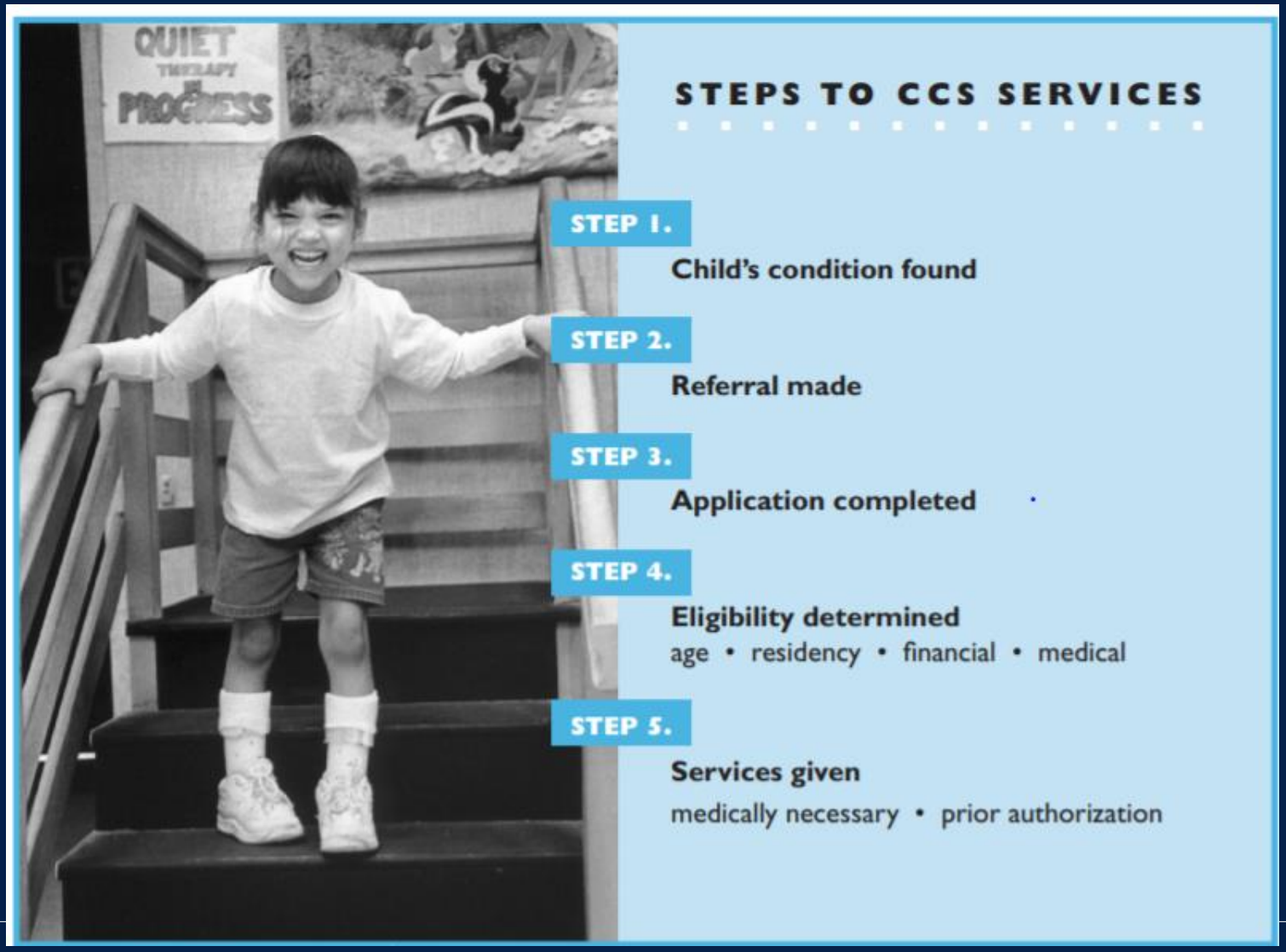
MTP Facts



- MTP has its own medical eligibility criteria separate from the general CCS Program.
- Children with cerebral palsy (CP) make up the majority of MTP eligible clients.

- Other MTP eligible conditions include:
  - Spina Bifida
  - Muscular Dystrophy
  - Rheumatoid Arthritis
  - Spinal Cord Injuries
  - Arthrogryposis
  - Osteogenesis Imperfecta
  - Head Injuries

Referrals


QUIET
PROGRESS
STEPS TO CCS SERVICES
STEP 1.
Child's condition found
STEP 2.
Referral made
STEP 3.
Application completed
STEP 4.
Eligibility determined
age • residency • financial • medical
STEP 5.
Services given
medically necessary • prior authorization

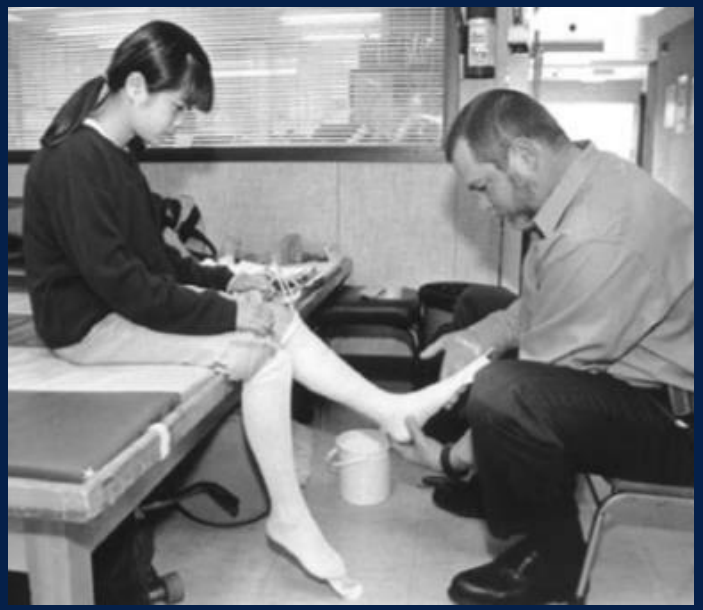
County Demographics

- Every county, no matter how small, has an MTP and is responsible for providing MTP services.
- Not every county has an MTU.
- That is based on the size of the MTP eligible caseload.
- Independent Counties – larger population counties. Their programs perform virtually all functions of the MTP.
- Dependent Counties – smaller population counties. Their programs perform limited MTP functions with the State completing the balance of activities.

Medical Direction

- Physician oversight for the MTP eligible condition is provided by various means:
  - Medical Therapy Conference (MTC)
  - Private physicians who are paneled and approved by the CCS Program
  - Special Care Centers (SCC) that have specialty teams for a particular condition
- MTP services require a prescription/therapy plan from one of these sources.

Medical Direction



- The MTC is a multidisciplinary team conference that is directed by physician(s).
- Core team members are the parents/caregivers, the client/patient, the physician(s) and the PT and/or OT.
- The MTC physicians serve a role much like the medical director of a facility.
- The MTC is the “special care center” for children with CP.
- MTC physicians are most often pediatric physiatrists, orthopedists or pediatricians.

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MTP Functions

- Evaluation
- Treatment
  - Weekly
  - Periodic
  - Consultation
- Comprehensive rehab case management
- Family centered care

MTP Functions

- Services for O&P must be provided by paneled providers at CCS Program approved facilities.
- DME-R is equipment designed for mobility and ADLs.
  - Wheelchairs, adaptive strollers, braces, bath/shower chairs, adaptive carseats, etc.
- DME-Medical is equipment designed to treat medical conditions.
  - Ventilators, apnea monitors, hospital beds, etc.

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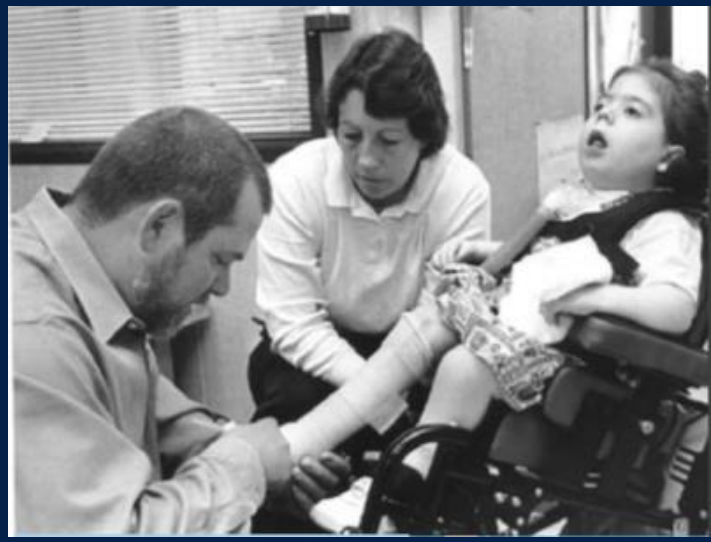
MTP Functions

- DME-R for children has to be durable to withstand everyday hard usage, lightweight, and adaptable.
- The item/service requested must address the MTP eligible condition.
- A prescription, current medical report with appropriate justification are required.
- Medical necessity in rehab addresses either a mobility or ADL need.



MTP Functions

- Home evaluations possible.
- DME-R requested predominantly for school use is not a benefit.
- DME-R should, when at all possible, have growth built into it. Children grow!
- Replace AFOs as often as you would shoe sizes, prostheses as often as clothing size.
- Functional gains achieved during therapy can also result in clients/patients being able to utilize higher level DME.

Conclusion

- Consider the MTU the rehab medical home.

References
upon request

mai.ngo@ucsf.edu

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