Neonatal Hypotonia Guideline

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Hypotonia: reduced tension or resistance to range of motion

Localization can be central (brain), peripheral (spinal cord, nerve, NM Junction) or both. Central more common: about 60 to 80 per cent vs 15 to 30 per cent peripheral
Definitive diagnosis possible in 65 to 85 per cent

Suggestive of Central Cause

- Strength preserved: movements and movement against gravity present
- Deep tendon reflexes present or increased
- Dysmorphic features
- Seizures or encephalopathy
- Abnormal vision, hearing or involvement of other organs

Clues in History

Prenatal

- Maternal age
- Fetal movements, loss of fetal movement suggesting hypoxia, rhythmic movements suggesting seizures
- History of infections, teratogens, ETOH during pregnancy
- Prenatal ultrasound abnormalities: arthrogryposis multiplex, more common in peripheral neuromuscular disorders
- Breech presentation more common in hypotonia or neuromuscular disorders
- Positive family history, features of myotonic dystrophy in mother

Exam Findings

General Exam

- Dysmorphic features
  - Downs: flattened occiput, flat nasal bridge, upslanting palpebral fissures, and short neck.
  - Prader-Willi: almond shaped eyes, frontal narrowing, small hands
- Skin abnormalities: neurofibromatosis, Tuberous sclerosis, other neurocutaneous disorders
- Abnormal eye exam: optic atrophy suggesting septo-optic dysplasia, cerebral dysgenesis, nystagmus
- Hepatosplenomegaly: TORCH infection, glycogen storage, other inborn metabolism errors
- Extremities: abnormal digits suggestive of genetic syndrome
- Abnormalities in other organ systems suggesting genetic syndrome

Neurological Exam

- Mircocephally: TORCH infections, cerebral dysgenesis, prenatal insult
- Macrocephaly: hydrocephalus
- Facial weakness: decreased facial movement, open down turned mouth
- Other cranial nerve dysfunctions: hearing loss, VI, VII involvement suggest central or genetic cause

Motor System

- Frog leg posture (hips abducted, legs externally rotated
- Arms extended
- Muscle atrophy--- decreased muscle bulk more common in peripheral disorder

- Decreased spontaneous movement
- Distribution of movements: anterior horn cell (SMA) may have only distal movements
- Ventral Suspension: Normal term infant will hold head 45 degrees or less below horizontal, back straight, some flexion at elbows and knees
- Traction of hands from supine: full term infant will show some flexion of head but prominent head lag in hypotonia
- Decreased strength: decreased movements, decreased ability to move or sustain posture against gravity.
- Reflexes usually diminished or absent in neuromuscular disorders and increased or normal in central disorder.

Specific Lower motor neuron disorders (peripheral hypotonia)

Myopathy

- Congenital myopathy: Central Core, nemaline rod
- Myotonic dystrophy
- Congenital Muscular dystrophy: Fukuyama causing severe hypotonia, abormal muscle and lissencephally

Neuromuscular function disorder

- Transient neonatal myasthenia gravis: mother affected
- Waxing and waning weakness, with prominent ptosis
- NCV may show incremental response
- Responds to Tensilon
- RARE
- Congenital Myasthenic Syndromes
    - Present in infancy with feeding difficulty, poor suck, choking spells, arthrogryposis
    - Repeated apneic and respiratory crises

Anterior Horn Cell

- SMA I presenting at birth
- Severe weakness, respiratory distress,
- Face usually not involved
- Characteristic EMG findings, SMA gene test

Spinal Cord

- Hypotonia and loss of function below level of lesion
- Traumatic injury
- Congenital abnormality

Neuropathy

- Absent reflexes

Stocking/ glove pattern or motor and sensory involvement

- Abnormal EMG NCV

Central Hypotonia

Acute Systemic causes:

- Sepsis
- Electrolyte disturbance
- Endocrine abnormality : thyroid function abnormality
- Hypoxia

Abnormal development or brain injury

- Cerebral dysgenesis: Lissencephally, holoprosencephaly
- Joubert Syndrome: cerebellar vermis hypoplasia, hyperpnea, apnea, abnormal eye movements
- Ponto cerebellar hypoplasia
- "Cerebral Palsy"

Genetic and Metabolic Disorders

- Prader Willi Syndrome 15q 11-13
- Fragile X syndrome
- Down Syndrome

Metabolic Disorders

Associated with obtundation and seizures

- Mitochondria Disorder
- Amino Acid Disorders
- Organic Acid Disorders
- Urea cycle defects

Metabolic Disorders

Associated with Multisytem abnormalities (Cataracts, cardiomegaly, retinopathy, arthrogryposis)

- Pompe's disease
- Peroxisomal disorders (Zellwegger)
- Congenital gylcosylation disorders
- Smith Lemli Opitz

Evaluation

Central Hypotonia Initial lab evaluation

- CMP, liver function tests, thyroid, CBC, Toxic screen
- CK to rule out possible muscle disorder

Dysmorphic major abnormalities

- High resolution Karyotype
- Chromosome microarray analysis
- Testing for Prader Willi, Very long Chain Fatty Acids
- Amino Acids, Organic Acids

Peripheral Hypotonia

- SMN1 gene test
- Consider EMG NCV
- Consider muscle biopsy
- Test for myasthenia if maternal history suggestive

References

See Algorithms in the following articles:

Lisi EC, Cohn, RD Genetic evaluation of the pediatric patient with hypotonia. Dev Med Child Neurol 2011; 53(7) 586-99

Prasad AN, Prasad C Genetic evaluation of the floppy infant. Semin Fetal Neonatal Med 2011;16(2): 99-108

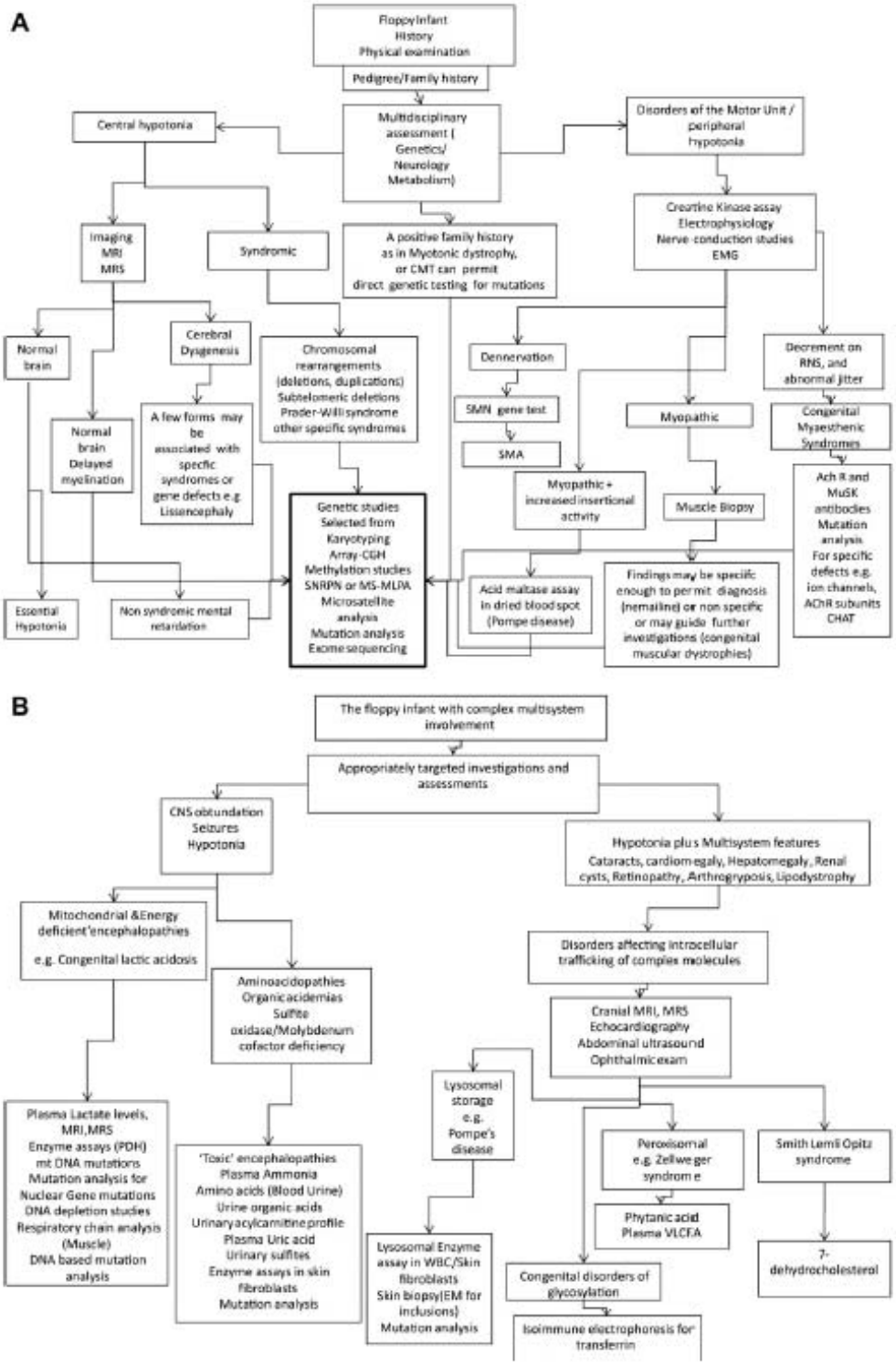

Figure 3. (A) Suggested schema for the laboratory evaluation of an infant with central or peripheral hypotonia with the different paths ending in a careful selection of genetic tests to establish diagnosis (box with bold highlighting). (B) Suggested schema for the laboratory evaluation of an infant where the clinical features suggest hypotonia with multisystem manifestations with a focus on selection of appropriate biochemical tests. MRI, magnetic resonance imaging; MRS, magnetic resonance spectroscopy; CMT, Charcot–Marie–Tooth; EMG, electromyography; SMN, Survival Motor Neuron; RNS, repetitive nerve stimulation; SMA, spinal muscular atrophy; CGH, comparative genomic hybridization; SNRPN, small nuclear ribonucleoprotein polypeptide N; MS-MLPA, methylation-specific multiplex ligation-dependent probe amplification; AChR, acetylcholine receptor; CHAT, choline acetyltransferase; CNS, central nervous system; PDH, pyruvate dehydrogenase; VLCFA, very long chain fatty acids; WBC, white blood cells; EM, electron microscopy.

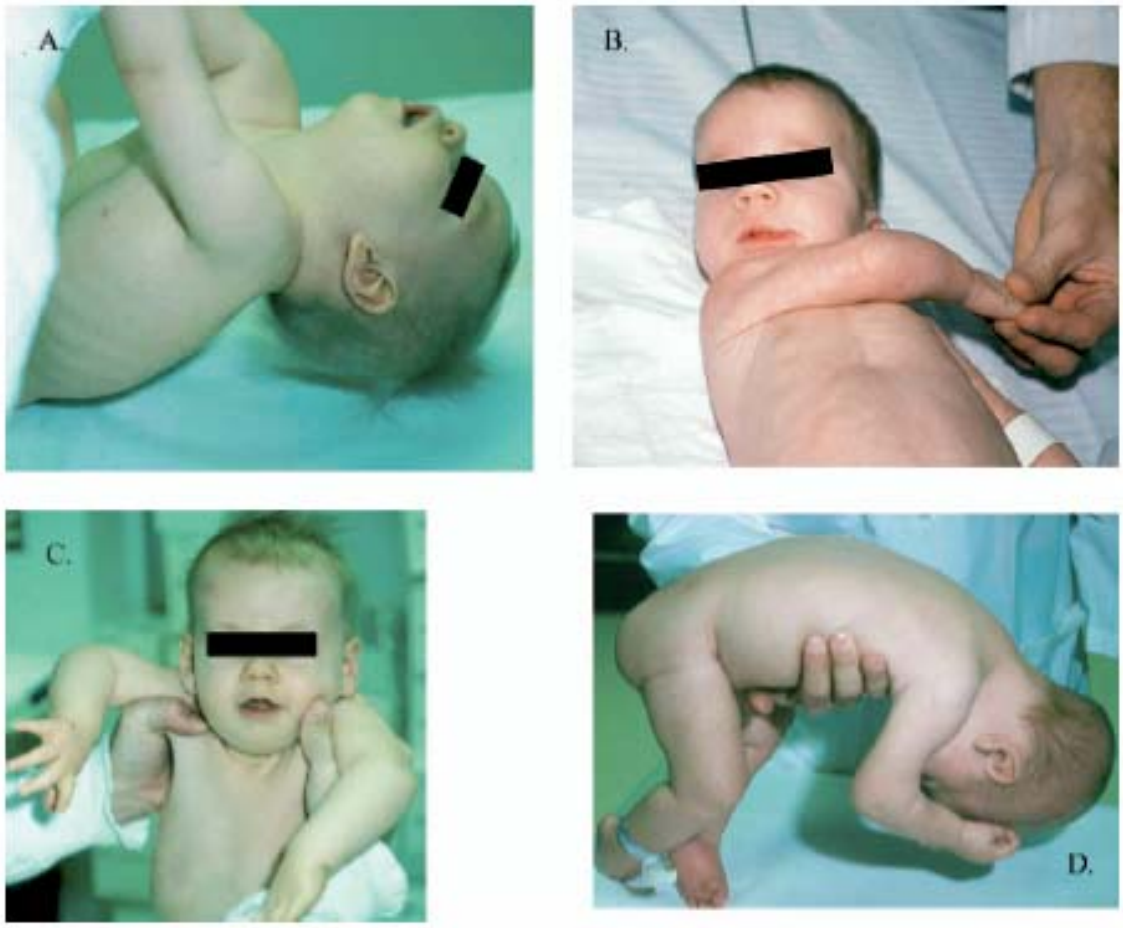

Figure 1 Measurers of hypotonia: (A) pull to sit, (B) scarf sign, (C) shoulder suspension, and (D) ventral suspension.