Evaluation of the floppy infant

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Abstract
This review outlines a clinical approach to the evaluation of the floppy infant. Attention is drawn to the varied manner in which the condition can present, and emphasis is placed upon a detailed assessment of characteristic clinical findings. A distinction is drawn between central and peripheral causes for hypotonia. Guidance is given regarding the importance of evaluating the child for signs of weakness, which is an important marker of neuromuscular pathology. Reference is made to situations where peripheral pathology may mimic central disorders. A diagnostic algorithm is outlined for the investigation of neuromuscular disorders, and reference is made to the discrepancy in findings that often exists between electromyography and muscle biopsy findings. Attention is drawn to available therapeutic options, as well as the importance of addressing ethical issues, which become of particular importance once a diagnosis is reached.

Keywords hypotonia; neuromuscular; neuropathy

Introduction and definition
The word ‘floppy’ can be used to mean:

- decrease in muscle tone (hypotonia);
- decrease in muscle power (weakness);
- ligamentous laxity and increased range of joint mobility.

Strictly speaking, the term ‘floppy’ should be used to describe hypotonia. The interconnection between tone, muscle strength and joint mobility can be appreciated through a consideration of the definition of tone – the resistance to passive movement around a joint. Phasic tone is assessed by the response of the muscle to a rapid stretch, illustrated classically by a tendon reflex, whilst postural tone is measured by the response of the muscle to a sustained low-intensity stretch, as illustrated by the body’s ability to maintain posture against the force of gravity.

Clinical appearance
Some features are common to all floppy infants regardless of the aetiology and location of the abnormality. A child is generally said to be floppy if he/she assumes a frog-like posture, is unable to maintain normal posture against gravity, exhibits diminished resistance to passive movements and has an excessive range of joint mobility. Table 1 lists some of the clinical signs with which a floppy infant may present; these features may or may not coexist in the same infant.

Common modes of presentation
The clinical consequences of hypotonia and/or weakness may be evident even in antenatal life. Specific questions in the history should address whether fetal movements were normal, as well as whether there was evidence of polyhydramnios. In the neonatal period, the manner of presentation depends on the severity of the condition. This ranges from the consequences of fetal immobilization, such as hip dislocation, arthrogryposis, talipes and flexion deformity of all limbs, to respiratory and feeding difficulties (slow feeding, recurrent choking or aspiration episodes). Later in infancy, hypotonia may be more obvious once delayed achievement of motor milestones becomes evident, with or without accompanying delay in other areas of development.

Clinical confirmation of hypotonia
Once the suspicion of hypotonia has been raised, the evaluation of the floppy infant should proceed by searching for those clinical signs that corroborate the diagnosis (Figures 1 and 2).

Diagnostic approach
The initial approach to a floppy infant is to determine whether the problem is of central or peripheral origin. This is of crucial importance when forming a plan for diagnostic investigations. As a general rule, an attempt is made to gauge whether there

Clinical signs in a floppy infant

- Observation of a ‘frog-leg’ posture. This generally implies reduced spontaneous movement, with the legs fully abducted and arms lying beside the body either extended or flexed
- Significant head lag on traction or pull-to-sit manoeuvre and excessively rounded back when sitting (>33 weeks)
- Rag-doll posture on ventral suspension
- Vertical suspension test – feeling of ‘slipping through the hands’ when the infant is held under the arms
- Various associated examination findings such as flat occiput or congenital dislocation of the hips, arthrogryposis

Table 1
is a significant element of weakness. Paralytic hypotonia with significant weakness suggests a peripheral neuromuscular problem, whereas non-paralytic hypotonia without significant weakness points to a central cause which may be neurological, genetic, syndromic or metabolic.

A central cause is suggested by clinical features as described in Table 2. The presence of these findings does not, however, exclude a peripheral aetiology of weakness. In some cases features suggesting both central and peripheral aetiologies may be seen.

### Clinical features suggestive of hypotonia of central origin

- Social and cognitive impairment in addition to motor delay
- Dysmorphic features implying a syndrome or other organ malformations sometimes implying a syndrome
- Fisting of hands
- Normal or brisk tendon reflexes
- Features of pseudobulbar palsy, brisk jaw jerk, crossed adductor response or scissoring on vertical suspension
- Features that may suggest an underlying spinal dysraphism
- History suggestive of hypoxic-ischaemic encephalopathy, birth trauma or symptomatic hypoglycaemia
- Seizures

#### Table 2

Indicators of peripheral hypotonia

- Delay in motor milestones with relative normality of social and cognitive development
- Family history of neuromuscular disorders/maternal myotonia
- Reduced or absent spontaneous antigravity movements, reduced or absent deep tendon jerks and increased range of joint mobility
- Frog-leg posture or ‘jug-handle’ posture of arms in association with marked paucity of spontaneous movement
- Myopathic facies (open mouth with tented upper lip, poor lip seal when sucking, lack of facial expression, ptosis and restricted ocular movements)
- Muscle fasciculation (rarely seen but of diagnostic importance when recognized)
- Other corroborative evidence including muscle atrophy, muscle hypertrophy and absent or depressed deep tendon reflexes

#### Table 3
SympoSium: neurology

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Investigations where central hypotonia is suspected
The range of investigations that may yield diagnostic clues in the clinical setting of non-paralytic/central hypotonia are listed in Table 7. The diagnosis of central hypotonia attributable to hypoxic-ischaemic encephalopathy is based upon an appropriate clinical history along with concordant imaging studies of the brain. Metabolic disorders are rare and despite extensive investigations the diagnostic yield may be quite low.

Investigations where peripheral hypotonia is suspected
Investigations likely to yield diagnostic clues in cases where paralytic/neuromuscular hypotonia is suspected are listed in Table 8. Myotonic dystrophy is usually suspected on the basis of known family history or recognition of the disorder in an affected mother, and can be confirmed by testing for the expanded CTG trinucleotide repeat sequence on chromosome 19q13.2–q13.3. In the absence of a diagnosis of myotonic dystrophy, we support the early use of electromyography (EMG)/nerve conduction studies (NCS) when a peripheral cause is likely.2 Areflexia, decreased limb movements and denervation on EMG should prompt investigation for anterior horn cell disorders (spinal

Conditions where central and peripheral hypotonia may coexist
- Familial dysautonomia
- Hypoxic–ischaemic encephalopathy
- Infantile neuroaxonal degeneration
- Lipid storage diseases
- Lysosomal disorders
- Mitochondrial disorders
- Perinatal asphyxia secondary to motor unit disease

Table 4

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Conditions associated with central (non-paralytic) hypotonia

Acute encephalopathies
- Birth trauma
- Hypoxic-ischaemic encephalopathy
- Hypoglycaemia

Chronic encephalopathies
- Cerebral malformations
- Inborn errors of metabolism (mucopolysaccharidoses, aminocacidurias, organic acidurias, lipidoses, glycogen storage diseases, Menkes syndrome)
- Chromosomal disorders (Prader-Willi syndrome, trisomy 21)
- Genetic disorders (familial dysautonomia, Lowe syndrome)
- Peroxisomal disorders (neonatal adrenoleukodystrophy, Zellweger syndrome)
- Endocrine (hypothyroidism)
- Metabolic (rickets, renal tubular acidosis)

Connective tissue disorders
- Ehlers-Danlos syndrome
- Osteogenesis imperfecta
- Congenital ligamentous laxity
- Benign congenital hypotonia

Table 5

Causes of paralytic/neuromuscular hypotonia

Spinal muscular atrophy
Paralytic poliomyelitis
Neuropathies
- Hereditary motor-sensory neuropathy
- Congenital hypomyelinating neuropathy
- Acute demyelinating polyneuropathy

Neuromuscular junction problems
- Botulism
- Transient neonatal myasthenia
- Autoimmune myasthenia
- Congenital myasthenic syndromes

Muscular disorders
- Congenital myopathies (neural rod myopathy, myotubular myopathies, central core disease, minicore disease, etc)
- Congenital muscular dystrophies (CMD) (Walker-Warburg, Fukuyama, muscle-eye-brain disease, merosin-positive CMD, etc)
- Congenital myasthenic syndromes
- Congenital myotonic dystrophy
- Metabolic myopathies (acid maltase deficiency, phosphorylase deficiency, mitochondrial myopathy
- Endocrine myopathies (hypothyroidism)

Table 6

Investigations in cases where a central cause for hypotonia is suspected
- Serum electrolytes, including calcium and phosphate, serum alkaline phosphatase, venous blood gas, thyroid function tests
- Plasma copper/ceruloplasmin assay (as screening test for Menkes syndrome)
- Chromosomal analysis (trisomy), testing for Prader-Willi syndrome (15q11–13)
- Plasma amino acids and urine organic acids
- Urine mucopolysaccharide screen (GAG)
- Molecular/biochemical diagnosis of pro-collagen disorders
- Very long chain fatty acids
- Medical genetics opinion
- Ophthalmology opinion
- Brain imaging (CT/MRI)

Table 7
muscular atrophy), and can be confirmed by testing for the homozygous deletion of exon 7 in the telomeric survival motor neurone gene. Failure to identify electrophysiological abnormalities should prompt testing for Prader-Willi syndrome. Arthrogryposis, feeding difficulties, recurrent apnoeic/choking episodes, ophthalmoplegia, ptosis and fatigability should prompt investigations for congenital myasthenic syndromes. Finally, muscle biopsy is recommended in neonates with weakness, even if needle EMG is normal (Figure 3). Care should, however, be taken in patient selection for muscle biopsy because of an increased risk of anaesthetic complications (postoperative respiratory failure and reactions to anaesthetic agents, particularly malignant hyperthermia and rhabdomyolysis).

EMG studies are used as a supportive diagnostic tool in deciding whether there is true weakness due to neuromuscular disease, or hypotonia from causes in other systems or other parts of the nervous system, and whether the process is due to a myopathic, neuropathic or a denervating process. In general, EMG can be performed at any age, although some caution is required in the interpretation of results within the first 6–8 weeks of life, particularly if the baby was premature. Whilst severe myopathy or neuropathy is not usually difficult to diagnose on EMG, studies on cases of mild weakness are usually inconclusive. In general, EMG and biopsy studies more often concur in denervation than myopathy. Classic EMG/NCS findings in myopathic and neurogenic disorders are outlined in Table 9. Recent advances in the diagnosis of congenital myasthenic syndromes allow for DNA testing in some of the common syndromes where there is strong clinical suspicion, particularly in young children where accurate neurophysiology evidence is sometimes difficult to obtain.

### Therapeutic approach

Various aspects of function may be affected in a floppy infant. In most cases, supportive therapies are indicated. Few conditions have specific treatments. These include hypothyroidism (thyroxine), some types of congenital myasthenic syndromes (pyridostigmine or neostigmine) and rickets (vitamin D). Some metabolic disorders may respond to specific dietary modifications or enzyme replacement therapies. The mainstays of treatment are outlined in Table 10.

### Prognosis and prevention

Rapid as well as accurate diagnosis of individual cases is vital in order to provide precise prognostic information. Ethical considerations, such as the appropriateness of cardiopulmonary

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**Table 8**

Investigations of peripheral hypotonia

- Creatinine kinase
- Lactate
- EMG/NCS/repetitive nerve stimulation test
- Muscle biopsy (histology, immunohistochemistry, electron microscopy, respiratory chain enzyme analysis)
- Genetic testing (SMN gene deletion present in 95% of cases of spinal muscular atrophy type 1, myotonic dystrophy, congenital myasthenic syndromes)
- Nerve biopsy (rarely)
- Tensilon test

**Table 9**

Useful EMG features in peripheral hypotonia

- EMG/NCS studies may distinguish between neurogenic, myopathic and myasthenic aetiologies for hypotonia
- Neurogenic – large amplitude action potentials, reduced interference pattern, increased internal instability
- Myopathic – small amplitude action potentials with increased interference pattern
- Myotonic – increased insertional activity
- Myasthenic – abnormal repetitive and single fibre studies

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**Figure 3**

Left, muscle biopsy (histochemistry) and right, electron microscopy in nemaline rod myopathy (congenital myopathy).
resuscitation in the event of cardiac arrest or acute respiratory failure, need to be addressed sensitively. Informed discussion around these issues requires detailed knowledge, where available, of specific conditions and, in particular, their presentation, clinical features, course and outcomes. Prenatal diagnosis using amniocentesis or chorionic villus sampling is often feasible if a definitive diagnosis has been reached in the index case.

Principles of management

- Physiotherapy - stretches aimed at prevention of contractures
- Occupational therapy - appliances, improvement of posture and function, facilitating activities of daily living
- Prevention and correction of scoliosis
- Evaluation and treatment of associated cardiac dysfunction
- Respiratory support - assessment of requirement for invasive or non-invasive ventilation and/or tracheostomy
- Feeding - nasogastric feeding, caloric supplementation, gastrostomy
- Management of gastro-oesophageal reflux - medical or fundoplication
- Orthopaedic intervention in setting of established or evolving joint contractures
- Encouragement of overall development and stimulation of learning
- Prevention (influenza and pneumococcal vaccination) and prompt treatment of respiratory infections

| Table 10 |

Recent developments

- Recent advances in genetics have uncovered new conditions causing hypotonia and weakness such as congenital myasthenic syndromes and spinal muscular atrophy variants
- Advances in immunohistochemistry, electron microscopy and genetics have led to a more specific diagnosis of myopathies
- Some of these advances have allowed for specific therapeutic interventions, e.g. use of acetylcholinesterase inhibitors in some congenital myasthenic syndromes

REFERENCES


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