NEONATAL MUSCULAR HYPOTONIA

Differential Diagnosis

- Systemic causes of neonatal hypotonia should be identified rapidly as they are usually transient if treated appropriately. Major differential diagnoses are divided into:

Central Hypotonia	**Peripheral Hypotonia**
Systemic: Sepsis, shock/acidosis, hypoglycaemia, prematurity, drug induced, electrolyte disturbances	Anterior horn cell: Spinal muscular atrophy (SMA) and variants, glycogen storage disease 2
Hypoxia	Peripheral nerve: Hereditary motor and sensory neuropathy (HMSN) and neuropathies
Haemorrhage	Neuromuscular junction: Myasthenia gravis (MG)
Cerebral: Brain abnormalities, malformation syndromes e.g. Down, Prader-Willi, inborn errors of metabolism, hypothyroidism	Muscle: Dystrophies, myopathies, congenital myotonic dystrophy, congenital muscular dystrophy
Brainstem and spinal cord pathology	Connective Tissue: Ehlers Danlos, Marfans
Benign congenital hypotonia – diagnosis of exclusion	

History & Examination

- Reduced fetal movements and polyhydramnios are predictive of a prenatal cause.
- Positive predictive value of a first clinical examination has been shown to be 86% in those with central pathology and 52% in those with peripheral pathology.
- Central hypotonia is five times more common than peripheral.
- Hypoxic +/- haemorrhagic insults could be the cause or consequence of neonatal hypotonia.
- Benign neonatal hypotonia is a diagnosis of exclusion and should only be made when all investigations are normal.
- 71% of encephalopathies had a positive family history and 50% of metabolic disorders were from consanguineous parents in one study.

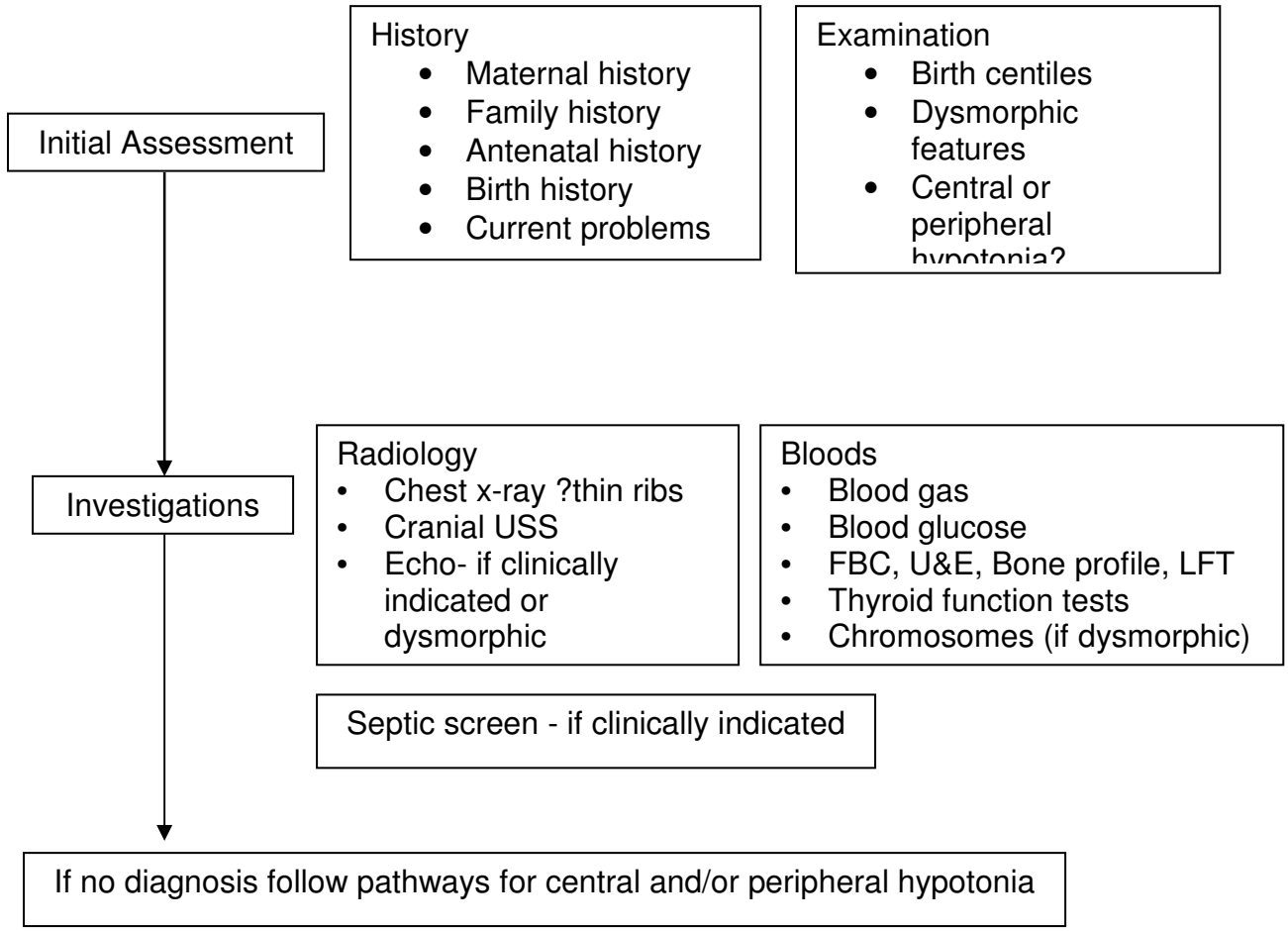
History	Central Hypotonia	Peripheral Hypotonia
Maternal	Medications/ PMHx	Medications / PMHx Maternal myopathy or myasthenia
Family	Consanguinuity	Consanguinuity Neonatal deaths/miscarriages
Antenatal	Abnormal scans Abnormal fetal movements	Polyhydramnios Reduced fetal movements
Birth	Hypoxia / trauma Poor Apgar score / CTG	Hypoxia Poor Apgar score / CTG Breech presentation
Current status	Feeding problems Ventilation and apnoeas Seizures Abnormal posturing Large tongue (storage disorder) Cataracts (peroxisomal)	Feeding problems Ventilation problems Weak low pitched cry Myopathic facies High arched palate (NMD) Tongue fasciculations (AHC) Ptosis/opthalmoplegia (MG)

Examination	Central Hypotonia	Peripheral Hypotonia
Assess gestational age, dysmorphic features & birth centiles		
Anti gravity movements when supine	Normal Partially reduced	Absent Severely reduced Partially reduced
Peripheral Tone (ventral suspension / pull from supine)	Normal or increased	Globally reduced
Tendon reflexes	Normal or brisk	Normal/Reduced/Absent
Seizures	Present	Absent
Visual alertness	Reduced	Normal

Investigations

1. Exclude common transient causes - see flow chart 1.
2. If history and examination indicate central hypotonia - see flow chart 2.
3. If history and examination indicate peripheral hypotonia - see flow chart 3.
4. It may be necessary to follow flow charts 2 & 3 if problems are mixed, i.e. peripheral and central insult.

All Floppy Babies (Chart 1)



Central Hypotonia (Chart 2)

Karyotype & Genetics

Tertiary genetics referral
Evelina Children's Hospital, St Thomas'
Dr Shehla Mohammed
shehla.mohammed@gstt.nhs.nhs.uk
Phone: 0207 188 1364

Neuroimaging
- MRI brain with DWI
- MRI spine ?cervical cord injury
- Acute concern- USS / CT
- EEG

Tertiary neurology referral:
Paediatric Neurosciences,
King's College Hospital
Dr Tammy Hedderly
tammyhedderly@hotmail.com
Phone: 020 3299 3323

Metabolic Tests

- Plasma amino acids
- Urine organic acids
- Ammonia & lactate

Discuss with tertiary centre and then proceed with the following as advised.

- Transferrin isoforms (reduced in carbohydrate deficient glycoprotein disease)
- Urate
- Urine purine studies (rare but treatable)
- VLCFA (peroxisomal disease)

Tertiary metabolic referral
Evelina Children's Hospital, St Thomas'
Dr Mike Champion
michael.champion@gstt.nhs.uk
Phone: 020 7188 0848

Peripheral Hypotonia (Chart 3)

Blood
- Genetics: SMA, MD, PWS. SMARD if diaphragmatic failure
- DNA to store
- Creatine Kinase (may be high for first few days of life then normalises)
- Maternal Ach receptor Abs (even if no maternal history of myasthenia)

Tertiary neuromuscular referral:
Evelina Children's Hospital St Thomas'
Dr Elizabeth Wraige
(Elizabeth.Wraige@gstt.nhs.uk)
Dr Heinz Jungbluth
(Heinz.Jungbluth@gstt.nhs.uk)
Phone: 020 7188 3998

Discuss with tertiary centre

Where is the pathology?

Muscle?
- Muscle biopsy & respiratory chain complexes
- Skin biopsy for fibroblast culture
- Echo & ECG ?myopathy
- +/- muscle MRI

Neuromuscular Junction?
- Trial of neostigmine / pyridostigmine
- Tensilon test (rarely useful)
- Genetics for congenital myopathy
- Serology sample for Abs to epsilon subunit of fetal Ach receptor
- Consider muscle biopsy
- EMG / Nerve conduction studies & include single fibre and repeat nerve stimulation

Anterior Horn Cell?
- SMA: SMN 1 positive. If SMN 1 is negative do SMARD 1
- Diaphragm involvement: ?SMARD 1
- Spinal MRI ?cervical cord injury
- Muscle biopsy including respiratory chain enzymes
- Metabolic screen ?mitochondrial
- Consider viral infection in early pregnancy eg polio

Peripheral Nerve?
- Consider nerve biopsy
- Consider Chronic Inflammatory Demyelinating Neuropathy (spinal MRI, CSF protein)
- Genetic tests for Congenital

Hypotonia Investigations Results Sheet

Investigation	Details	Date Sent	Results
ROUTINE			
U&E, LFT, Bone, Glu, CRP, FBC	1xEDTA 1xLiHep 1XFlOx		
Septic Screen	Blood Culture		
	CSF MC&S		
	Urine/other		
TORCH Screen			
C-USS			
Echo			
GENETICS (Lab sends to Guy's)			
Karyotype SMN1 SMARD 1 Prader-Willi MD	Chrms-LiH DNA-EDTA DNA to store- EDTA		
METABOLIC (Lab sends to Guy's some samples)			
Blood			
Creatine Kinase	1xLiH		
Ammonia	1xEDTA on ice		
Lactate	Blood gas		
Amino acids	1 clotted tube		
Thyroid function (Free T4, TSH, TBG)	1xLiH		
Acylcarnitines	1xLiH		
VLCFAs	1xEDTA		
Transferrin Isoforms	1 clotted tube		
Gal1Put	1xLiH		
Urine			
Reducing subs	Plain urine		
Organic acids	Plain urine		
Orotic acid	Plain urine		
CSF			
Lactate	1xFlOx		
Aminoacids/Glycine	d/w biochemist		
NEUROMUSCULAR			
MRI / CT head			
EEG	Fax form to Hurstwood Park		
Skull X-ray	RSCH		
EMG	Refer to neurologist		
Nerve Conduction	Refer to neurologist		
Muscle biopsy	Refer to neurologist		
Tensilon test	100 mcg IM order from pharmacy		

Referral Contacts & Result Chasing

Department	Tel/Fax
Guy's Genetics Lab (Karyotype, SMN 1, SMARD 1)	T: 0207 188 2582 F: 0207 188 7273
Guy's Molecular Lab Aminoacids, CSF glycine, fatty acids, GAGs, oligosaccarides	T: 0207 188 1226 (advice) T: 0207 188 8008 (results) F: 0207 9285698
St George's Molecular Genetics Lab (PWS, MD)	T: 0208 7255904 F: 0208 7252138
Queens Sq Neurometabolic Unit (mitochondrial enzymes)	T: 0207 8298768