

## PedsCases Podcast Scripts

This is a text version of a podcast from PedsCases.com on “**Approach to Neonatal Hypotonia (Floppy baby)**.” These podcasts are designed to give medical students an overview of key topics in pediatrics. The audio versions are accessible on iTunes or at [www.pedcases.com/podcasts](http://www.pedcases.com/podcasts).

### **Approach to Neonatal Hypotonia (Floppy baby)**

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#### **Introduction:**

Hi my name is Dr. Nikytha Antony and I am currently a Pediatrics resident at the University of Calgary. This podcast will review an approach to neonatal hypotonia, or the “floppy baby.” This podcast was done in collaboration with Dr. David Callen, a Pediatric Neurologist at the McMaster Children’s Hospital and Dr. Kim Smyth, a Pediatric Neurologist at the University of Calgary.

After listening to this podcast, the learner should be able to:

- Define neonatal hypotonia
- Recognize the initial presentation of neonatal hypotonia
- Elicit important features on newborn history and physical exam pertinent to causes of hypotonia
- List common causes for neonatal hypotonia
- Order appropriate initial investigations for the common causes of neonatal hypotonia.

#### **Case Presentation**

Let’s start with a clinical case. You are a learner doing a rotation in the Neonatal Intensive Care Unit. Your preceptor tells you that there is a 2-day-old who was found to have hypotonia. They ask you to assess the infant and determine the etiology of the hypotonia. What is your approach to this clinical presentation? What do you need to think about on your differential for neonatal hypotonia?

The hypotonic newborn or “floppy baby” has a vast list of potential etiologies. Hopefully by the end of this podcast, you will have a basic approach to the differential diagnosis for this presentation.

Tone is defined as muscle's intrinsic resistance to passive stretch. Tone is distinct from strength or power, which is a measure of how much force a muscle can generate. Neonatal hypotonia is defined as poor muscle tone in the muscles of the trunk, limbs and face (1). This means that the muscles provide little resistance when someone else is passively moving them. In contrast, a patient with increased tone would have spasticity or rigidity. Hypotonia can be categorized as axial or truncal, predominantly affecting the neck and spinal muscles; appendicular, affecting predominantly the extremities; or global, affecting the entire body. It is identified early in life when the newborn is unable to obtain a normal posture during movements or at rest. (1)

### **Differential Diagnosis**

The differential for neonatal hypotonia is vast. It really helps to split things up the differential into categories. We will discuss the differential using 3 main categories: 1) Systemic illness, 2) neurological disorders and 3) metabolic/genetic conditions.

Systemic illness, sepsis/infection, metabolic crises and electrolyte disturbances such as hypokalemia, hypophosphatemia, hypocalcemia, hypo or hypernatremia can also initially present with hypotonia so it is important to rule out conditions such as meningitis or organ failure. This fact makes it imperative that a child's general health is assessed first in the assessment of hypotonia.

Neurological etiologies can be differentiated into central or peripheral causes of hypotonia. The term "central" refers to problems within the central nervous system, including the brain and spinal cord, whereas "peripheral" refers to problems in a component of the peripheral nervous system, including the anterior horn cell, nerve, neuromuscular junction, and muscle.

Infants with central hypotonia are often "floppy, but strong". They present with a hypotonic posture, but may be able to respond with near appropriate power to applied external stimuli. They may be hyper-reflexic or have normal reflexes and often show other central nervous system abnormalities such as decreased level of consciousness, seizures, apneas and feeding difficulties, and possible abnormalities on head circumference measurements (2).

An example of a central cause for hypotonia would be hypoxic-ischemic encephalopathy or HIE. This condition is caused by the brain not receiving enough oxygen to function for a period of time. Usually there is clear evidence correlating the event and the subsequent neurological sequelae and the degree of hypotonia can vary based on the severity of the injury to the brain. (6) Other causes of central hypotonia include malformations of brain development and vascular events such as intracranial bleeds or strokes.

Infants with peripheral hypotonia are "floppy and weak". They are often found in a "frog leg" type posture with both lower legs wide open on the bed and have a very limited

motor response to applied external stimuli. They may demonstrate normal or hyporeflexia and may have diffusely low muscle bulk and/or multiple congenital contractures. Despite this, they are “centrally bright” with preservation of alertness and consciousness (2).

An example of a cause of peripheral hypotonia is spinal muscular atrophy (SMA). This genetic condition causes the degeneration of the anterior horn cells and thus causes motor deficit with no sensory involvement. The most common type in newborns is SMA type 1 which is also known as Werdnig-Hoffman disease. This condition is characterized by profound symmetric proximal muscle weakness that is greater in the lower limbs along with decreased or absent deep tendon reflexes. Sometimes fasciculations of the muscles, including the tongue can be seen. SMA is typically diagnosed by genetic testing.

Myasthenia gravis is an example of a neuromuscular defect leading to peripheral hypotonia. It is an autoimmune illness. Newborns with myasthenia gravis present with global hypotonia and/or feeding and respiratory difficulties or apneas. In adults myasthenia gravis is typically an acquired autoimmune disorder where the body creates antibodies against the acetylcholine receptors, which inhibits neuromuscular transmission. In neonates the cause can either be transient due to antibodies from a mother with myasthenia gravis passing through to the baby (transient neonatal myasthenia gravis), or genetic due to mutations in genes that produce proteins that function within the neuromuscular junction such as the acetylcholine receptor (congenital myasthenia). Myasthenia gravis is diagnosed through detection of antibodies to the acetylcholine receptor in the blood, repeated nerve stimulation tests, through clinical response to the anticholinesterase inhibitor, neostigmine, or via specific molecular genetic testing (for congenital forms). (5)

Muscle disorders, such as congenital myopathies or muscular dystrophies can also cause neonatal hypotonia.

The third and final category is genetic and metabolic causes. Some genetic syndromes that can present with hypotonia include Prader-Willi syndrome and Down syndrome. Inborn errors of metabolism can also present with newborn hypotonia. It is important to note that combined genetic and metabolic causes make up about 60% of the causes for a floppy baby (2).

Prader-Willi syndrome is a genetic condition that occurs due to the loss of expression of paternal genes on chromosome 15. Typical clinical features in the newborn period include hypotonia and feeding difficulties. Classic physical features include almond shaped eyes, small hands and feet, thin upper lip and hypogonadism. For diagnosis, a DNA based test is required such as a methylation study using polymerase chain reaction (PCR). (4)

May other genetic conditions, such as Down Syndrome, and chromosome deletion and duplication syndromes also present with neonatal hypotonia.

## **History**

Initially on history you will want to assess the timing and the progression of the hypotonia. Was it present at birth, or did it evolve over time? Is it getting better or is it getting worse? Depending on the age of the child you can ask about developmental milestones, and see if the child is attaining appropriate gross motor and fine motor skills.

A thorough prenatal, birth and neonatal history of the newborn is essential in order to determine the cause of hypotonia.

Pertinent components of the prenatal history include: whether there was regular antenatal care including any abnormalities noted on ultrasound as some causes of neonatal hypotonia are associated with polyhydramnios or increased amniotic fluid volume due to impaired swallowing. Ask about abnormal maternal screening for chromosomal abnormalities and history of drug exposures. Ensure you enquire about history of any maternal infections during pregnancy or any complications such as gestational diabetes or hypertension. Ask if the mother has had any neurologic symptoms which could be consistent with myasthenia gravis.

Birth history should include gestational age and mode of delivery, fetal heart rate abnormalities, forceps or vacuum use and any associated complications. Events following birth such as the Apgar score, arterial umbilical arterial cord blood gas, presence of meconium, need for neonatal resuscitation. The timing of onset and progression of the hypotonia should also be determined. Is the problem getting better or worse? Obtain a thorough history of previous pregnancies including gestational age and mode of deliveries, complications, miscarriages and current health status of siblings.

For systemic illness ask about sepsis risk factor such as GBS status, prolonged rupture of membranes and maternal fever. Consider if the newborn has been on any medications or IV fluids which could lead to electrolyte imbalances. Ask if the infant has any other specific symptoms.

For genetic causes, family history is key. A family pedigree of three generations is important to determine if it could have a genetic cause of hypotonia, specifically asking about any neurological conditions. (2)

## **Physical exam**

With all exams, start with a general assessment of the child, including vital signs and level of consciousness. Looking for signs of systemic illness, ensure the child is not unwell as hypotonia can be the first sign of sepsis or a metabolic deterioration.

Assess for any signs of genetic/metabolic conditions by examining the skin for abnormalities, rashes, jaundice or cyanosis. Obtain a height, weight and head circumference in order to plot measurements onto a growth chart. Inspect the head and neck, look for dysmorphic features such as wide set or almond shaped eyes, abnormal or low-set ears, upward slanting palpebral fissures, long face, microcephaly, absent philtrum and thin upper lip. Also look for other features of chromosomal abnormalities such as abnormalities of the genitalia, small hands and feet, single palmar crease, extra digits, and limb contractures. (1)

Finally, the neurological exam is particularly important to look for neurological conditions and to assess and document the degree of hypotonia. Try to ensure that the infant is alert and calm for this exam. On inspection, look for any fasciculations of muscles or seizure type activity. Examine cranial nerves 2 through 12 by assessing pupillary reaction and size, eye movements, facial symmetry and sensation, suck and gag reflexes. Check whether the newborn is able to flex and spontaneously move the upper and lower limbs – this suggests good strength. A profoundly hypotonic infant will be lying in a frog leg position with both lower legs wide open on the bed and will have minimal resistance when limbs are extended and flexed. Check for deep tendon reflexes and other primitive reflexes such as the tonic neck and moro reflex. (1)

Specifically, when assessing tone, there are three tests that should be done when possible (i.e. if baby is well enough, not intubated) (7):

- 1) Horizontal suspension – support the baby with one hand on the chest. Normally, the baby should make an attempt to hold its head up and keep the spine straight. If the baby has low tone, you will notice an inverted U shape as the baby rests against your hand since the baby will make no attempt to straighten out the spine or keep its head up.
- 2) Vertical suspension – Support the baby with two hands under the armpits and lift up vertically. Normally, the baby will have its arms flexed so that it does not fall out of the examiner's hand but a baby with hypotonia will slip through the examiner's hands.
- 3) Traction Response – Hold both of the newborn's arms with each hand and lift up from the supine position. Normally, the baby older than 3 months will attempt to lift up its head as well as it is lifted by the arms but a floppy baby will have significant head lag.

### **Investigations**

So given that the differential diagnosis for a newborn with hypotonia is vast, the potential diagnostic workup can be extensive and hence should be guided by your history and physical examination.

For systemic illness, initial investigations should be conducted to rule out life-threatening and reversible causes, which include a full septic workup, electrolytes including magnesium and calcium, liver function tests, ammonia and lactate.

For infants with neurological causes of hypotonia, such as risk factors for HIE or signs of central causes of hypotonia, such as lethargy, upper motor neuron signs, or seizures, an MRI of the brain +/- EEG should be completed. In infants with peripheral hypotonia, a creatinine kinase, electromyography/nerve conduction study, and potentially a muscle biopsy could be considered.

For genetic/metabolic causes, additional specialized testing may be needed, including genetic screen through karyotype and microarray analysis depending on the dysmorphic features and congenital anomalies displayed. Specific genetic testing for disorders such as Prader Willi Syndrome or SMA should also be considered based on the clinical presentation. It is important to get additional specialists involved early, particularly pediatric neurologists.

### **Case conclusion**

History obtained from the patient's chart revealed an unremarkable prenatal history except for mild polyhydramnios early in the pregnancy. An elective C-section was done at 38 weeks of gestation and the newborn neurological exam was documented as abnormal due to severe hypotonia that required mechanical ventilation for 24 hours as the baby was unable to breathe on his own. The cord gas was normal, as were initial glucose, CBC, electrolyte, and liver/renal function tests. A full septic work-up has been completed showing no overt signs of infection thus far, with cultures still pending. The patient is covered on broad spectrum antibiotics.

On exam, the baby demonstrates dysmorphic features that included almond shaped eyes that were wide-set and thin upper lip. On neurological testing, the patient is mildly lethargic, but does rouse and cry weakly with vigorous stimulation. Cranial nerves were grossly intact. Motor exam showed poor tone on horizontal suspension, slip through on vertical suspension, and severe head lag on traction response with minimal spontaneous movements of the upper and lower limbs. Deep tendon reflexes were decreased but present (graded 1). Primitive reflexes were grossly normal except for a decreased suck reflex. Sensory exam is normal.

**WHAT IS YOUR DIFFERENTIAL DIAGNOSES?** Based on your history and exam findings, you conclude that this presentation is most consistent with global hypotonia. Systemic infection/illness has either been ruled out or is being treated. The top of your differential diagnoses includes an underlying genetic disorder (based on dysmorphic features) versus a central cause (given mild lethargy), although there is a lack of corroborating history (e.g. HIE history) and other clinical findings (seizures, focal



neurologic signs) typically associated with central etiologies. The presence of deep tendon reflexes and lethargy make peripheral causes of hypotonia less likely.

**WHAT INVESTIGATIONS WOULD YOU ORDER?** You decide to order an MRI brain, chromosomal array, Prader Willi gene test, and a CK level to assess both genetic and central causes of neonatal hypotonia. The MRI and CK levels come back normal. One week later your preceptor pages you to tell you he just received word that the Prader Willi test was positive. You meet with the family to counsel them on the diagnosis and provide anticipatory guidance on the diagnosis of Prader Willi syndrome.

### **Summary:**

Before we finish, let's leave with a few key take-home points.

- 1) Neonatal hypotonia is defined as poor muscle tone in the trunk, upper and lower limbs and face.
- 2) A complete prenatal, birth and postnatal history is essential along with a thorough physical examination placing special attention on the neurological examination and special tests for hypotonia.
- 3) The differential diagnosis includes 3 main categories: 1) systemic illness like infection or electrolyte abnormalities, 2) neurologic disease such as central hypotonia stemming from cortical or brainstem deficits or peripheral causes stemming from anterior horn cell or neuromuscular junction or muscles, and 3) genetic, chromosomal and metabolic abnormalities.

Thanks for listening!

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