Disclosures

• Investor in Medolac Laboratories

• I will not discuss any off-label use and/or investigational use in my presentation
Objectives

• Review postnatal glucose homeostasis from fetal to neonatal transition
• Demonstrate the different strategies used to define normoglycemia and hypoglycemia in the neonate
• Evaluate the controversies in screening, diagnoses and management of low glucose levels

Neonatal Hypoglycemia

- Relatively common and important disorder
- Most often temporary
  - Infants of Diabetic Mothers
  - Prematurity
  - Small-for-gestational-age infants
- Long term concern - seizures and permanent brain injury
- Recognize genetic and non-genetic persistent hypoglycemia disorders
QUESTIONS
- Definition of Neonatal Hypoglycemia (NH)
- Who is at risk?
- When should at risk be screened?
- How should screening be performed?
- Level of blood glucose requiring intervention?
- What interventions should be done when neonatal hypoglycemia is suspected?
- How frequently should asymptomatic be screened?
- How do we educate caregivers and standardize guideline

WHAT IS A NORMAL BLOOD GLUCOSE?

NICHD EXPERTS CONSENSUS
No rational basis to identify any specific value or even range of plasma glucose concentrations at any one time that is sufficient to define “hypoglycemia” as a pathologic entity (NICHD 2008)

NEONATAL HYPOGLYCEMIA

Hay et al. J Ped 2009
GLUCOSE CONSUMPTION AND ENERGY STORAGE BALANCE in the FETUS

**High Insulin: Glucagon Ratio**

- **Insulin Dominance**
- **Glucose Consumption**
- **Energy Storage**
- **Suppressed lipolysis**
- **Glycogenolysis**
- **Glycogen Synthesis**
- **Glycogen Synthase**
- **Phosphorylase**
- **Cortisol**

Glucose Homeostasis in Newborn

**Catabolic Cascade**

- **Glucose**
- **Term infants have enough hepatic glycogen (by 4-6 hours of life)**
- **Glucose 1st 24-48 hrs**
- **Blood glucose**
- **Adaptation to enteral feeds**
- **Cortisol**
- **HGH**
- **Gluconeogenesis**
- **Free AA's**
- **Glycogenolysis**
- **Glycogenesis**
- **Glucagon**
- **Insulin**
- **FFA's**
- **Catecholamines**
- **Immediate**

Abrupt interruption umbilical glucose delivery

**Trigger**

Volume enteral feeds
Mean plasma glucose for suppression of insulin secretion is 55-65 first 48 hours of life vs 65-85 in older infants. Defines "normal" level for the first 48 hours of life in their statement.

The decreased glucose concentrations are associated with:
- Decreased lactate
- Decreased β hydroxybutyrate and acetoacetate (hypoketonemic)
- Decreased glycerol
- Large glycemic response to glucagon or epinephrine

Which is identical to hyperinsulinemia.

Basal glucose utilization 4 to 6 mg/Kg/min (2x wt specific rates in adult)

Birth – 70% maternal level
- first few hours
  - as low as 30 mg/dl (1.7mmol/L)
- then attains

Metabolic transition to independent glucose production and establishes postnatal glucose homeostasis.

Until exogenous supply of substrate provided, hepatic glucose output serves as most significant source of glucose to meet demands.
Hepatic Glucose Production

To maintain normal levels of hepatic glucose production

1) Adequate stores of glycogen
2) Adequate gluconeogenic precursors (e.g., FA’s, glycerol, AA’s, lactate)
3) Appropriate concentrations of hepatic enzymes required for gluconeogenesis/glycogenolysis
4) Normally functioning endocrine system

Absence of any leads to disruption of glucose homeostasis, most commonly resulting in Neonatal Hypoglycemia

Approaches to Define “Hypoglycemia”

- Based on measured range of glucose values (Epidemiological Definition)
  - Cross sectional data
  - Longitudinal data
- Based on clinical manifestations (Clinical)
- Based on acute changes in metabolic and endocrinologic responses (Physiologic Definition)
  Sentinel in Peds Endocrine Statement: They focus on MEAN VALUES of glucose being most representative for normal newborns.
- Based on neurologic and neurodevelopmental outcome. Level at or below which can cause injury (Functional Definition) Sentinel in AAP Statement

Starting Point: Definition of Normoglycemia

**Statistical Approach**

Majority are above ~2.5 mmol/L (45mg/dL)
30mg/dl ~5th percentile BF/AGA/Term

Does not define the glucose concentration below which irreversible neurological injury invariably or even probably occurs or the associated conditions that might augment or ameliorate the primary effects of glucose deficiency.

Statistical norm Does Not Define Biologic Norm

hay, rozance. Biol Neonate 2006
Normal Glucose levels in the Newborn (Mean and 5th %) Population Meta-Analyses (Increase over the first few days) AAP Guideline First 24 hours only

<table>
<thead>
<tr>
<th>Time</th>
<th>1-2 hours</th>
<th>3-23 hours</th>
<th>24-47 hours</th>
<th>48-72 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>56</td>
<td>63</td>
<td>66</td>
<td>67</td>
</tr>
<tr>
<td>Estimate of 5th percentile</td>
<td>27</td>
<td>40</td>
<td>41</td>
<td>48</td>
</tr>
</tbody>
</table>


Plasma Glucose Concentrations (mmol/l) in Term, Appropriate Size for Gestation, Breast-fed Infants at Four Different Ages

<table>
<thead>
<tr>
<th>Age (hr)</th>
<th>Mean (hr)</th>
<th>Median (hr)</th>
<th>Range (hr)</th>
<th>Interquartile Range (41-60)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>3.00 (1.05)</td>
<td>2.8</td>
<td>1.4-8.3</td>
<td>2.3 – 3.3</td>
</tr>
<tr>
<td>6</td>
<td>2.95 (0.75)</td>
<td>2.8</td>
<td>1.6-5.4</td>
<td>2.4 – 3.3</td>
</tr>
<tr>
<td>24</td>
<td>2.89 (0.79)</td>
<td>2.9</td>
<td>1.3-7.6</td>
<td>2.6 – 3.3</td>
</tr>
<tr>
<td>72</td>
<td>3.00 (0.79)</td>
<td>2.8</td>
<td>1.4-7.1</td>
<td>2.6 – 3.3</td>
</tr>
</tbody>
</table>

Mmol/l | mg/dl | Repeated analysis of variance, p=0.9
1.4 | 25   |
3.0 | 54   | Wight et al: Breastfeeding Medicine 2006
8.0 | 144  |

Breastfeeding average intake of colostrum ± 7 mls/food in the first 24 hours (Houston et al Early Human Development 1983 (15-20mls/k/d)

Suckling ketogenesis

12 – 14% of normal AGA breastfed newborns have a blood glucose level of <47mg/dl in the first 3 days of life
Peds Endocrine Society (2014)

- Recommendations for evaluation and management are for plasma glucose concentrations below the normal threshold for neurogenic responses to hypoglycemia (55-65) as in the older child or adult.
- Feeds should maintain glucose > 50 first 48 hours
- >70 for those requiring IV fluids first 48 hours
- Feeds should maintain glucose > 70 after 48 hours.

- NO MENTION AS TO THE IMPORTANCE OF BEING ASYMPTOMATIC in decision making nor any consideration of neurodevelopmental outcome data.

CLINICAL APPROACH

Classical Report

- Glucose concentration is safe if clinical symptoms associated with hypoglycemia are not observed, or if these symptoms disappeared at that specific concentration.
- Symptoms at 1.4 mmol/L (25mg/dl) resolved at >2.2 mmol/L (40mg/dl) by increasing the blood glucose concentration.

Cornblath, J of Peds 1959

40 “classic standard”

Clinical Approach Is Flawed

Many concerns with this approach:
1) Observation of extremely low blood glucose concentrations in asymptomatic infants.
2) Nonspecificity of symptoms, especially when also associated with other neonatal diseases. Symptoms just as likely among normoglycemic
3) Studies did not evaluate availability of other energy substrates to neonate that may compensate for lower glucose concentration that might protect the brain (ketogenesis with human milk feeding spares glucose for brain consumption).
SYMPTOMS of HYPOGLYCEMIA
- Neuroglycopenic: confusion, coma, seizures, caused by brain dysfunction because of deficient glucose supply (Don't know level for newborns).

DON'T KNOW LEVEL NEWBORNS BECOME NEUROGLYCOPENIC

CEREBRAL ENERGY DEFICIENCY and SIGNIFICANT HYPOGLYCEMIA
- Since the avoidance of and treatment of cerebral energy deficiency is the principle concern, greatest attention should be paid to neurologic signs (eg):
  - variation in tone
  - change in level of consciousness
  - seizures
The English and Canadian Guidelines prioritize neurodevelopmental studies.

Long Term Effects of Neonatal Hypoglycemia on Brain Growth and Psychomotor Development in SGA PT Infants

Duvanel et al J of Ped 1999

n=85 PT SGA* ~32 weeks, <1200g
<47mg/dl vs Controls

RESULTS – Hypoglycemic infants at 3.5 and 5 years
- Lower HC
- Lower developmental scores
- Increased severity of sequelae with increased duration of hypoglycemia, even when asymptomatic

*majority were symmetric SGA

Adverse neurodevelopmental outcome of moderate neonatal hypoglycaemia.

The last 4 lines of abstract states:
FIND THE THRESHOLD THAT RELIABLY PREDICTS ADVERSE OUTCOMES™

These data suggest that, contrary to general belief, moderate hypoglycaemia may have serious neurodevelopmental consequences, and reappraisal of current management is urgently required.
EVOLUTION of the DEFINITION of NH as 47


NEURODEVELOPMENTAL APPROACH

• BW <1850 g
• N= 661 infants, 6808 samples,
• Mean (SD) BW 1337 (315) g
• Mean (SD) gestation 30.5 (2.7) wks
• Large Nutrition Study (5 centers)

Sampling
- Daily for all requiring intensive care until clinically stable (2nd to 3rd week)
- Weekly till discharge or weighed 2000g (9th week)
- Developmental Testing

NEURODEVELOPMENTAL APPROACH


• Maximum slope and significance were seen for PDI and MDI when a cut off of 45mg/dl was used
• 2/3 had <47mg/dl ranging from 3 to 30 days

• Reduced development scores were associated independently with number of days on which level was < 47mg/dl.

<table>
<thead>
<tr>
<th>Days of NH</th>
<th>Adjusted RR</th>
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<tbody>
<tr>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>1 - 2</td>
<td>1.1 : 1</td>
</tr>
<tr>
<td>3 - 4</td>
<td>2.2 : 1</td>
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<tr>
<td>≥ 5</td>
<td>3.5 : 1</td>
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Not sustained at 7-8 years of age!!!!!!!!!!!!!!!!!!!! Later Editorial, data not optimal

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Quadrigenta Septum Phobia profoundly influenced neonatal care

The Northern Neonatal Nursing Initiative "Hypoglycemia" Study (1990-91)

**Aim and Design:**
- To compare the neurodevelopmental outcome of preterm (<32 weeks) who had frequent low blood glucose levels (< 47mg/dl) in the first ten days of life vs that of matched controls.
- Prospective, Observational
- Daily glucose as well as other samples recorded the first 10 days
- Index 3 days <47, controls all > 47 (47/566)

TIN W Early Human Devt 2005

**MEAN GRIFFITHS DEVELOPMENTAL QUOTIENTS OF 47 MATCHED PAIRS (2 Years)**

Tin W. Early Human Develop 2005
The Northern Neonatal Nursing Initiative
“Hypoglycemia” Study  15 year Follow Up

Methods: Assessments at 15 year

- Psychometric assessment (WISC-III)
- Behaviour Problems (Aschenbach)
- Daily Living and Adaptive Skills (Vineland)
- Education attainments
- Health Status

- Outcome information on ALL but two children
- Full Assessment on 38 pairs (82%)

Win Tin et al Pediatrics 2012

The NNNI “Hypoglycemia” Study

Summary of Assessments at 15-16 years

<table>
<thead>
<tr>
<th>Measure</th>
<th>Mean ± SD</th>
<th>Mean paired difference</th>
<th>95% confidence interval</th>
<th>Number of pairs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full Scale IQ (Weschler III)</td>
<td>80.7±19.8</td>
<td>81.2±15.16</td>
<td>-0.6 (0.3 to +0.2)</td>
<td>38</td>
</tr>
<tr>
<td>Reading (Weschler WORD score)</td>
<td>91.1±18.3</td>
<td>90.2±15.18</td>
<td>+0.9 (-0.7 to +9.2)</td>
<td>36</td>
</tr>
<tr>
<td>Behaviour (Total Aschenbach score)</td>
<td>51.0±10.2</td>
<td>54.4±13.8</td>
<td>-3.4 (-9.3 to +2.5)</td>
<td>37</td>
</tr>
<tr>
<td>Adaptation to Daily Living (Vineland)</td>
<td>24.4±19.1</td>
<td>68.5±16.7</td>
<td>+5.5 (-2.8 to +14.9)</td>
<td>37</td>
</tr>
<tr>
<td>Cerebral palsy</td>
<td>6±4</td>
<td></td>
<td></td>
<td>47</td>
</tr>
</tbody>
</table>

Win Tin et al Pediatrics 2012

Incidence Hypoglycemia in At Risk Infants

- N= 514 At Risk (NH < 47, Severe NH <36) > 35weeks ...Glucose Oxidase.
  - 260 (51%) glucose ≤ 47 mg/dl of which 81% (208) occurred in the first 24 hours, 48% in ≤6 H (100)
  - 97 (19%) glucose ≤ 36 mg/dl
  - 31 (6%) required IV glucose to treat hypoglycemia
  - 98 (19%) had > 1 episode.
  - Using 47mg/dl as screen means 50% of at risk have “HYPOGLYCEMIA” with 9.9% breast fed.

SYMPTOMS
- 79% were asymptomatic, 15% poor feeding and 16% jittery

The Significance of these “hypoglycemic episodes” remains undetermined.
Endocrine Opinion AAP Guidelines: Do they work based on Harris study

- 6% (15) had their first hypoglycemia > 24H and would have been missed with 24 hour screening.
- 37% babies had 3 “normal” glucose before 1st hypoglycemia and would have been missed.
- 20 babies had glucose <47 mg/dl for > 48 hrs
- 31 babies needed IV glucose but we do not know the outcome
  - What should we do with them?
  - Did they develop persistent hypoglycemic syndromes

ENDOCRINE INTERPRETATION OF AAP GUIDELINES Based on Harris study

- SENSITIVITY of 3 Glucose > 50 = 63%
- SPECIFICITY of 3 Glucose > 50mg/dl = 100%

(Sensitivity no. of people who have disease who tested positive.
Specificity no. of people who do not have disease who tested negative)

Neonatal Hypoglycemia Harris Editorial-"Answers but More Questions"

The higher the threshold(> 47mg), and the more often the screens (48 h), the more often asymptomatic patients with low glucose will be identified.

Rozance and Hay J or Ped 2012
Editorial to Harris et al 2012

- What the clinician does with the information depends on how they view any particular glucose concentration in an asymptomatic newborn.

QUESTIONS
- Is there immediate harm?
- Is it a harbinger for severe or persistent NH which may cause harm?
- Or is it the normal low transition of establishing glucose homeostasis??
- STUDY DOES NOT ANSWER THESE QUESTIONS

Why the Initial Low Glucose Concentration?

1) Promote Gluconeogenesis
2) Stimulate appetite for feed-fast cycles
3) Carry over from Fetal environment that facilitates glucose transport from mother to fetus
- All mammals have these lower transitional glucose values the first days of life

Editorial by Rozance and Hay

- Little consensus on the significance of transient and asymptomatic hypoglycemia
- Most data indicate that adverse outcomes do not occur with such conditions
- Transient, asymptomatic hypoglycemia may herald metabolic disorders that can cause serious injury.
- Therefore such infants do not go home without solid evidence they can maintain normal glucose through normal feed fast cycles.
- As with normal infants, transient asymptomatic low glucose, there is no evidence demonstrating improved outcome following identification and tx of low glucose in IDM, LPT, small and large infants
Little consensus on the significance of transient and asymptomatic hypoglycemia

Most data indicate that adverse outcomes do not occur with such conditions

Transient, asymptomatic hypoglycemia may herald metabolic disorders that can cause serious injury.

Therefore such infants do not go home without solid evidence they can maintain normal glucose through normal feed fast cycles.

As with normal infants, there is no evidence that treating transient, asymptomatic low glucose improves outcome in IDM, LPT, or small and large infants.

Many doubt whether low levels of glucose are ever damaging when there are no associated clinical sign.....

(9 studies, articles 1990-2008)

Systematic review 18 eligible studies concluded none provided a valid estimate of hypoglycemia and neurodevelopment. (Boluyt, Ped 2006)

Concentrations of glucose that have not been shown to be associated with any deviations in metabolic, physiologic or neurologic dysfunction.

Significant hypoglycemia is not and can never be defined by a single number that can be applied universally to every individual patient.

Rather it is characterized by value(s) that are unique to each individual and varies with both their state of physiologic maturity and the influence of pathology.
NEURONAL FUEL ECONOMY

AVAILABLE ALTERNATIVE FUELS

• KETONE BODIES
• LACTATE
• AA’s
• ADAPTABILITY OF LOCAL MICROCIRCULATION

CONCURRENT NEONATAL CONDITIONS

• HYPOXIA
• SEPSIS

Given complexity of defining adequacy of neuronal fuel adequacy – concept of rigid threshold for blood glucose is challenged

Clinical exam is more important than glucose level

PERINATAL STRESS HYPERINSULINISM (PSHI)

• Associated with Perinatal Stress
  Birth Asphyxia
  Intrauterine Growth Restriction, SGA
  C/S

Median age (d) at initial hypoglycemia 1, range (0 to 168)
Persistent hypoglycemia beyond 48 hours of age and can last for several weeks to months.
Responsive to treatment with Diazoxide in contrast to severe neonatal onset hyperinsulinism associated with K ATP mutations.

Maintenance of Plasma Glucose Concentration is Highly Protected

• Suppression of insulin
• Glucagon stimulation
• Increase Cortisol and HGH
LABS for GLUCOSE < 50mg/dl

Serum bicarbonate

Major Metabolic Fuels (glucose, beta-hydroxybutyrate, FFA, Lactate)

Hormones (Insulin, HGH, Cortisol)

Peds Endocrine Society Concerns About Persistent Hypoglycemia (2014)

- Because normal neonates may commonly have low blood glucose concentration in the first 48 hours of life, it makes it difficult to identify those who have a persistent hypoglycemia disorder.
- Published guidelines for neonates focus on the first day of life but do not address diagnosis and management of prolonged or persistent hypoglycemia.
- Transitional Neonatal Hypoglycemia resembles a known genetic form of congenital hyperinsulinism which causes a lowering of plasma glucose threshold for suppression of pancreatic insulin secretion (glucokinase mutations).
- Brain glucose utilization is limited at 55-65 mg/dl and neuroendocrine responses are activated similar to the adult.

Hypoglycemia “Red Flags”

- Most neonatal hypoglycemia is due to aberrant metabolic adaptation after birth. Strategies to enhance the normal adaptive processes should help prevent such episodes.

Further investigations and specific interventions should be considered

1. hypoglycemia persists
2. is of unusual severity
3. OR occurs in the absence of identified risk factors.
**Neonates in Whom to Exclude Persistent Hypoglycemia Prior to Discharge**

- Neonates with severe hypoglycemia (e.g., an episode of symptomatic hypoglycemia or requiring iv dextrose to treat hypoglycemia)

- Neonates unable to consistently maintain pre-prandial plasma glucose concentrations > 50 mg/dL by day 3

- Family history of a genetic form of hypoglycemia

- Congenital syndromes (e.g., Beckwith-Wiedemann), abnormal physical features (e.g., midline facial malformations, microphallus)

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**Patterns of Cerebral Injury and Neurodevelopmental Outcomes After Symptomatic Neonatal Hypoglycemia (NH)**

Burns et al, Peds July 2008

- Symptomatic NH first week (acute neurol dysfunction)
- Median glucose ≤ 20mg/dl [defined NH ≤ 47mg/dl, severe NH ≤ 30mg/dl]
- Early MRI (<6 weeks)
- No evidence of HIE
- Neurodevelopment outcomes at 18 months

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**NEURO-DEVELOPMENT**

23/35 (65%) had impairments at 18 months related to severity of white matter injury and involvement of post limb of internal capsule

(86% glucose ≤ 30MG) (20/35 presented day 1 with NEONATAL HYPOGLYCEMIA)

Early MRI findings were more instructive than the severity or duration of hypoglycemia for predicting neurodevelopmental outcomes
Symmetric patchy hyperintensities (arrows) in the occipital white matter in the brain of an infant with transient neonatal hypoglycemia on coronal T1-weighted image. L refers to the left side of the brain.

- Differs vs HIE
  - Superficial cortical vs deeper cortical
  - Occipital greater than frontal

- No imaging evidence that mild hypoglycemia of short duration causes brain injury nor that asymptomatic of any duration causes brain injury

Studies relate to:
- Severe Prolonged Hypoglycemia
- Encephalopathy

NIH Expert Conference
- There are no evidence based guidelines that can be used for treating all newborn infants with low glucose concentrations
  - The actual threshold glucose concentrations at which treatment decisions are made have remained arbitrary
  - At present there is insufficient data to produce definitive guidelines

Hay et al. J Ped 2009

Plasma glucose @ which clinicians may consider appropriate may differ from plasma judged to be @ increased clinical risk

Flexible “margin of safety”

Operational Threshold

Plasma Glucose & Risk Factors

Analogous to “Continuous variables”
Providing Guidance Where Evidence Is Lacking

FOUR OBSERVATIONS USED IN DEVELOPING ALGORITHM FOR USA

1. Almost all infants with proven symptomatic NH during the first hours of life have plasma glucose <20 to 25mg/dl
2. Persistent or recurrent NH syndromes present with equally low plasma glucose concentrations

FOUR OBSERVATIONS USED IN DEVELOPING ALGORITHM (cont)

3. Little or no evidence exists that asymptomatic NH at any concentration in the first days of life results in any adverse sequelae in growth or neurologic development
4. This allows a large margin of safety over concentrations associated with the development of clinical signs

Cornblath & Ichord Sem Perinatology 2000
Screening and management of Postnatal Glucose Homeostasis in Late Preterm and Term SGA, IDA/LGA Infants

LPT: Infants 34 – 36 6/7 weeks and SGA (screen 0-24 hrs); IDM and LGA > 34 weeks (screen 0 -12 hrs)

Symptomatic and <40mg/dl ——— IV Glucose

**ASYMPTOMATIC**

<table>
<thead>
<tr>
<th>Birth to 4 hours of age</th>
<th>4 – 24 hours of Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>100% FEED within 1 hour</td>
<td>100% FEED within 1 hour</td>
</tr>
<tr>
<td>Screen glucose 30 minutes after 1st feed</td>
<td>Screen Glucose prior to each feed</td>
</tr>
<tr>
<td>Initial Screen &lt;25mg/dl</td>
<td>Screen &lt;35mg/dl</td>
</tr>
<tr>
<td>Feeding and check in 1 hour</td>
<td>Feeding and check in 1 hour</td>
</tr>
<tr>
<td>&lt;25mg/dl</td>
<td>&lt;35mg/dl</td>
</tr>
<tr>
<td>IV Glucose*</td>
<td>IV Glucose*</td>
</tr>
<tr>
<td>25 – 40mg/dl</td>
<td>35 – 45mg/dl</td>
</tr>
<tr>
<td>Refeed IV Glucose* as needed</td>
<td>Refeed IV Glucose* as needed</td>
</tr>
</tbody>
</table>

Target Glucose screen 24mg/dl prior to routine feeds

*Glucose dose = 200mg/kg (dextrose 10% at 2ml/kg) and/or IV infusion at 5 – 8mg/kg/min (80 – 100ml/kg/d)
Achieve plasma glucose 40 – 50mg/dl

Symptoms of Hypoglycemia include: Irritability, tremors, diaphoresis, exaggerated startle reflex, high-pitched cry, seizures, lethargy, floppiness, cyanosis, apnea, poor feeding.

**Endocrine “Fast” to Diagnose Pathologic NH**

- The 6 hour flex to 9 hour fast for those > 50 mg/dl but < 65 mg/dl will ensure all patients will be diagnosed and only 25% unaffected babies will need 9 hr fast

**Neonates Endocrinologists Suggest are At increased risk of Hypoglycemia Who require Glucose Monitoring**

1. Neonates with symptomatic hypoglycemia
2. Neonates who had perinatal stress
   - Birth asphyxia/ischemia; C-section for fetal distress
   - Maternal pre-eclampsia/eclampsia or hypertension
   - Intra-uterine growth restriction (small-for-gestational-age birth-weight)
   - Meconium aspiration syndrome, erythroblastosis fetalis, polycythemia, hyperthermia
3. Congenital syndromes (such as Beckwith-Wiedemann), abnormal physical features (such as midline facial malformation, microphallus)
4. Family history of a genetic form of hypoglycemia
5. Large-for-gestational-age birth-weight
6. Premature or post-mature delivery
7. Infant of diabetic mother
Postnatal-Glucose Homeostasis

App “The Sugar Wheel”

Changes you may want to make in your practice

- Only screen at risk asymptomatic babies and of course any neonate with symptoms that could be related to abnormal postnatal glucose homeostasis.
- Always screen 30 minutes after the first feed which should always take place within the first hour of life.
- Determine institutional preferences for operational thresholds to practice within for asymptomatic infants.

THE END