Hypoglycemia Guideline Update

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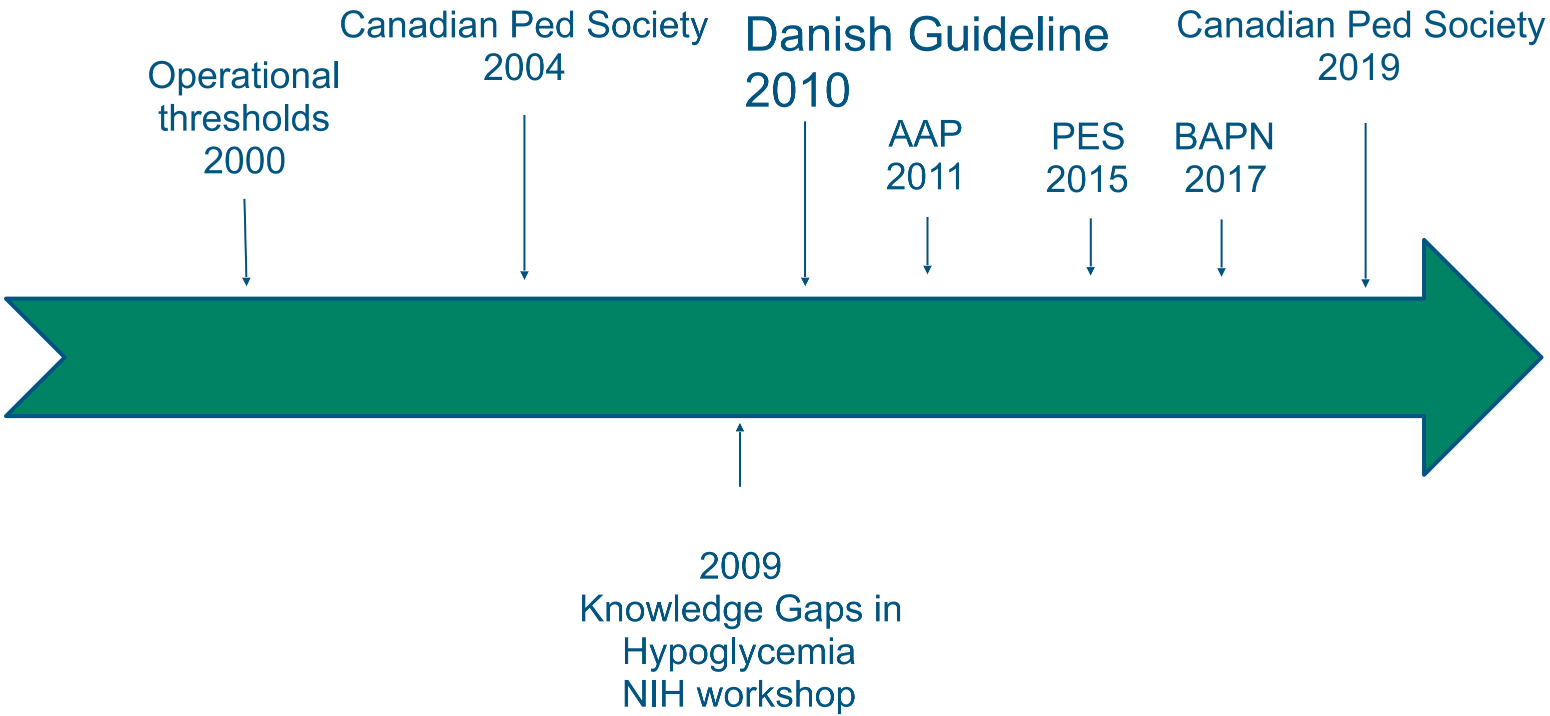
Hypoglycemia Guideline Timeline



What is the goal of these Guidelines?

- CPS 2004:
  - the purpose of the present statement is to provide a consensus guideline that has practical applications for Canadian newborns and their caregivers.
- AAP 2011:
  - offer pragmatic approach to a controversial issue [glucose levels in the first 24 hours of life] for which evidence is lacking but guidance is needed.
- PES 2015:
  - help physicians recognize persistent hypoglycemia disorders, guide their expeditious diagnosis and effective treatment, and prevent brain damage in at-risk babies.

Do the guidelines work?

- CPS guideline audit 2009
  - 1:8 Canadian babies were screened
  - 1:30 babies were treated
  - 5% of babies who should be screened were not
  - Mean number of tests 5-6
  - Average age of screening was 3h not 2 as per guideline
- Audit of Danish Guideline
  - There was a reduction in hypoglycemia following implementation of the hypoglycemia reduction strategy

Review of changes in practice re PES recommendations

- Skovrlj, Marks and Rodd: .Pediatric Child Health 2019 Jul;24(4):263-269.
  - Compared 2011-2015 with post PES publication 2016
  - Results
    - Increase in number of consults to Ped Endo service
      - Average 6/y pre versus 33/yr post
    - All patients had HI except 2 with metabolic disease
  - Conclusion: Since introduction of the recommendations more patients were identified with real disease requiring treatment

The good

- A Quality-Improvement Initiative to Reduce NICU Transfers for Neonates at Risk for Hypoglycemia (PEDIATRICS Volume 141, number 3, March 2018)
  - Infants at risk of hypoglycemia were subjected to a QI project
  - Skin to Skin contact, early feeding and glucose test by 90 mins
  - Results:
    - NICU transfer rate dropped from 17% to 3%
    - Unnecessary transfers (babies who did not need IV dextrose) dropped from 5% to 0.3%
    - No change in the number of symptomatic hypoglycemia babies

Canadian Paediatric Surveillance Program

- Hypoglycemia in unmonitored full-term newborns—a surveillance study. (*Paediatrics & Child Health*, 2018, Vol. 23, No. 8)
- Evaluated the number of healthy term babies not at risk of hypoglycemia who developed hypoglycemia over 2 years
  - 93 case = 1:8378 births
  - 78% had perinatal stress
  - 98% had symptoms
    - 35% jitteriness, 28% poor feeding, 25% hypothermia
    - 15% hypotonia
    - 15% lethargy
    - 12% seizures
    - 12% apnoea

Canadian study continued

- 20% had major clinical signs of seizure, apnoea and cyanosis
  - Glucose was 0.8mmol/L (14mg/dL) compared to rest 1.6mmol/L (29mg/dl)
  - Hypoglycemia detected later (>6 hr of life) compared to rest
- MRI performed on 14% of the babies and 78% of the MRIs were abnormal
- 21% babies at time of discharge were determined to be neurologically abnormal
- 52% had evaluation for cause and 37% had a cause found
  - HI 14/93 = 15%

The Bad

- Lower versus Traditional Treatment Threshold for Neonatal Hypoglycemia
  (van Kempen 2020 NEJM)
  - Compared neurological outcome in 689 babies using two thresholds for treating hypoglycemia in at risk babies >35w gestation (<36mg/dL [2mmol/L] and <47mg/dl[2.6mmol/L])
  - Found cognitive and motor skills were similar in both groups
  - Conclusion: In asymptomatic newborns there is no difference in outcome if you treat babies when the glucose is < 36mg/dL or < 47mg/dL
  - *Implication: Babies with glucose levels in first 48 hours of life do not need to be treated unless glucose is <36 mg/dl*
- What was not made clear was that they excluded 585 babies because they had received IV glucose (373) before the start of the trial or they had inborn errors of metabolism or HI (87)

The Ugly

- Glucose Profiles in Healthy Term Infants in the First 5 Days: The Glucose in Well Babies (GLOW) Study
  - Plasma glucose and CGM data over 5 days in a group of 67 healthy term breast fed babies
  - Showed glucose profile was very similar to previous studies and that babies normalize their glucose levels by 4 days of age to equal adult levels
  - Confirmed the PES expert working group publication on normal glucose levels in babies transitioning from intra uterine life to the outside world

Table IV. Numbers of infants with episodes of glucose concentrations below recommended thresholds for treatment

Postnatal ages (h)	0-4	4-24	24-48	48-72	72-120
American Academy of Pediatrics*					
Plasma	0/64 (0)	2/67 (3)	1/67 (1)	1/67 (1)	0/67 (0)
Interstitial	0/60 (0)	6/55 (11)	3/57 (5)	1/56 (2)	0/47 (0)
British Association of Perinatal Medicine†					
Plasma	3/64 (5)	3/67 (4)	2/67 (3)	2/67 (3)	0/67 (0)
Interstitial	4/60 (7)	9/55 (16)	5/57 (9)	1/56 (2)	0/47 (0)
World Health Organisation‡					
Plasma	12/64 (18)	16/67 (24)	9/67 (13)	7/67 (10)	1/67 (1)
Interstitial	23/60 (38)	35/55 (63)	19/57 (33)	17/56 (30)	4/47 (9)
Pediatric Endocrine Society§					
Plasma	16/64 (25)	27/67 (40)	15/67 (22)	31/67 (46)	4/67 (6)
Interstitial	30/60 (50)	40/55 (73)	33/57 (58)	41/56 (73)	26/47 (55)

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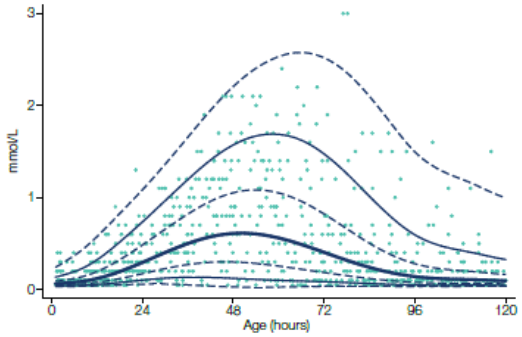
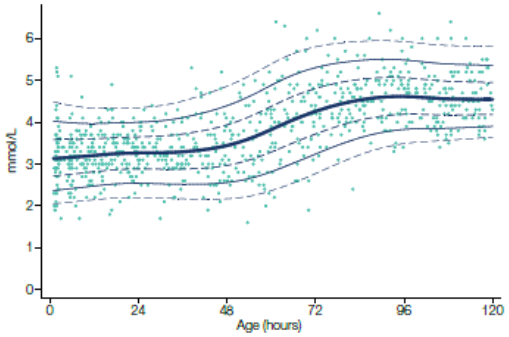
Alternative cerebral fuels in healthy babies: The Glucose in Well Babies (GLOW) Study

Deborah Harris [1,2], Phil Weston [1], Jane Harding [2]
[1]Waikato Hospital, Hamilton, New Zealand. [2]Liggins Institute, University of Auckland, Auckland, New Zealand

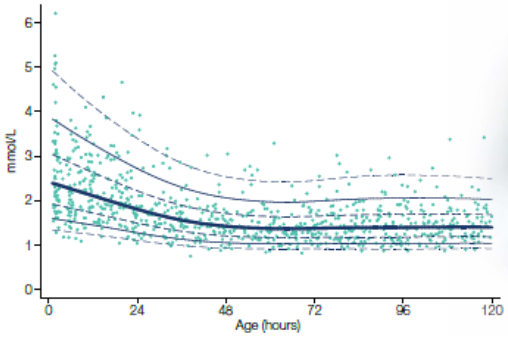
Beta-hydroxybutyrate concentrations by age



Blood glucose concentrations by age



Lactate concentrations by age



Background

The normal blood concentrations of metabolic fuels in healthy babies are not well described.

Aim

The GLOW study sought to identify patterns of blood glucose, lactate, and beta-hydroxybutyrate in healthy babies over the first five post-natal days.

Methods

- Appropriately grown, healthy singleton term babies
- Heel prick blood samples, 4 on day 1, 2 in each of days 2-5, results masked
- Analysis using Cole-Green for normative curves, and mixed model regression.

Results

67 babies provided 816 samples.

Table: Relationships between alternative fuels and pre-specified risk factors

	Lactate	Beta-hydroxybutyrate
Maternal weight gain in pregnancy	0.16 higher (0.01, 0.31)	NS
Maternal BMI (pre-pregnancy)	NS	NS
Gestational age ≥ 40	0.16 higher (0.02, 0.30)	NS
Sex = male	0.15 higher (0.01, 0.29)	NS
Weight loss > median	NS	0.13 higher (0.07, 0.19)
Glucose < median	0.15 higher (0.06, 0.25)	0.07 higher (0.04, 0.11) and see plot on duration of low glucose

Conclusion

Normative values for metabolic fuels in normal babies over the first five days are available.

Lactate concentrations are:

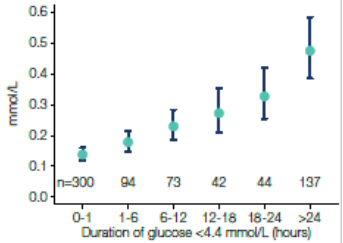
- Greater than 5 mmol/L on day 1 is not normal
- Greater than 2.5 on days 2 to 5 is not normal

Beta-hydroxybutyrate concentrations:

- A surge is common on day 3, up to 2.5 mmol/L
- Are responsive to duration of low glucose concentration

Beta-hydroxybutyrate concentrations by duration of glucose concentration < 4.4mmol/L

(adjusted means with 95% Confidence intervals)



(Adjusted for glucose concentration at the time, and day of age)

Conclusions

- There are different guidelines with different goals
- The PES Guideline was designed to help physicians diagnose babies with HI and other serious forms of hypoglycemia
- There has been an attempt to try undermine the message
- There have been some good papers looking at the effectiveness of the PES guidelines in diagnosing the cause of the hypoglycemia
- There have also been good papers looking at the effect of the guidelines on the frequency of blood glucose testing and length of stay in hospitals.
- Overall the impact of the guidelines has been beneficial to advancing the science and understanding of hypoglycemia in the newborn period.

Peaks The Dragon

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Peaks the dragon says

I wear a mask to keep **others** safe

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