http://www.45worlds.com/cdalbum/cd/5302152

Understanding glucose and the neonate

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Objectives

Synthesize

Synthesize appropriate management plans between the referral and transport setting

Become

Become competent in accurately calculating GIR

Assess and utilize

Assess and utilize GIR in a variety of settings for best practice patient management

Promote

Promote euglycemia and outline relevance to long term neurodevelopmental outcomes

Glucose Infusion Rate (GIR) Calculation mg/kg/min

- NICU infusions usually run continuously over 24h
- Accordingly, can simplify equation:

$$\text{GIR (mg/kg/min)} = \frac{\text{rate (mL/h) x dextrose concentration (g/L)}}{\text{dosing wt (kg) x 60 (minutes/h)}}$$

* g/L equivalent to mg/mL

1: Baby F
To use or not to use glucagon

https://mms.mckesson.com/product/1082180/Fresenius-USA-63323059303

- Baby F is born 35-weeks gestational age with a birth weight of 3.13 kg (92nd percentile).
- Maternal history is significant for Type II Diabetes requiring insulin.
- Baby F is transferred to a tertiary center for Persistent Pulmonary Hypertension (PPHN) management with central umbilical lines placed.
- She is made nil-per-oral and managed on a Total Fluid Intake (TFI) via intravenous (IV) line of 80ml/kg/day for asymptomatic hypoglycemia of 1.6mmol/L.
- Her IV fluid is Dextrose 20%.

Question: Baby F weighs 3.13 kg. Her TFI is 80 mL/kg/d and she is running D20W. What is her calculated GIR given this information?

a)5.9 mg/kg/min

b)4.8 mg/kg/min

c)8.2 mg/kg/min

d)11.1 mg/kg/min

1: Baby F

Answer explained: Whilst her calculated GIR is 11 mg/kg/min which would be very significant for 1st day following birth and warrant consideration of glucagon initiation, r**arely** is maintenance IVF the ONLY thing running.

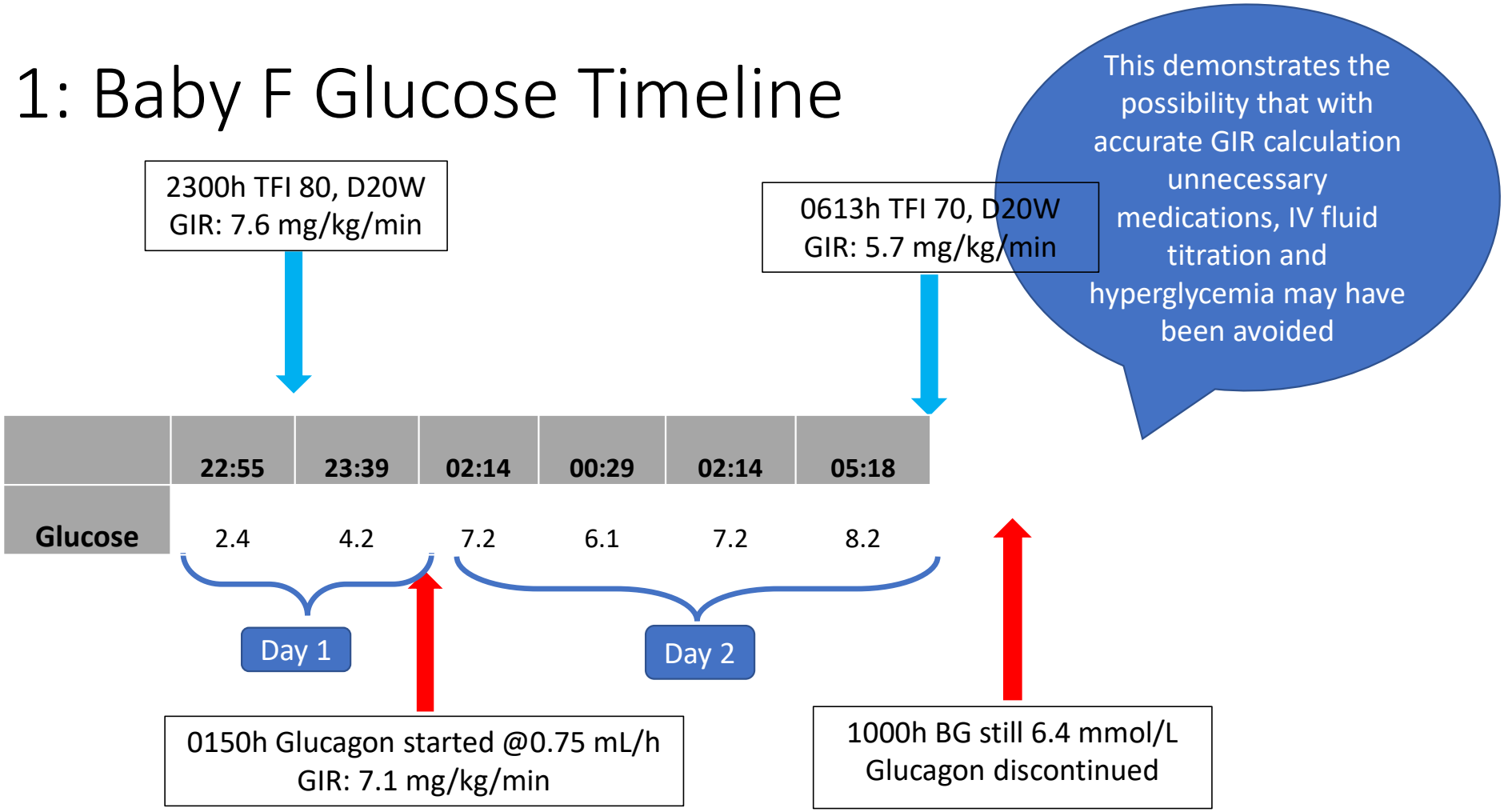
This baby had the following infusions

- **Heparin** (in 0.45%NS) @ **2 mL/h** via Umbilical lines for patency
- **Morphine** (in D5W) @ **1.57 mL/h** for PPHN sedation

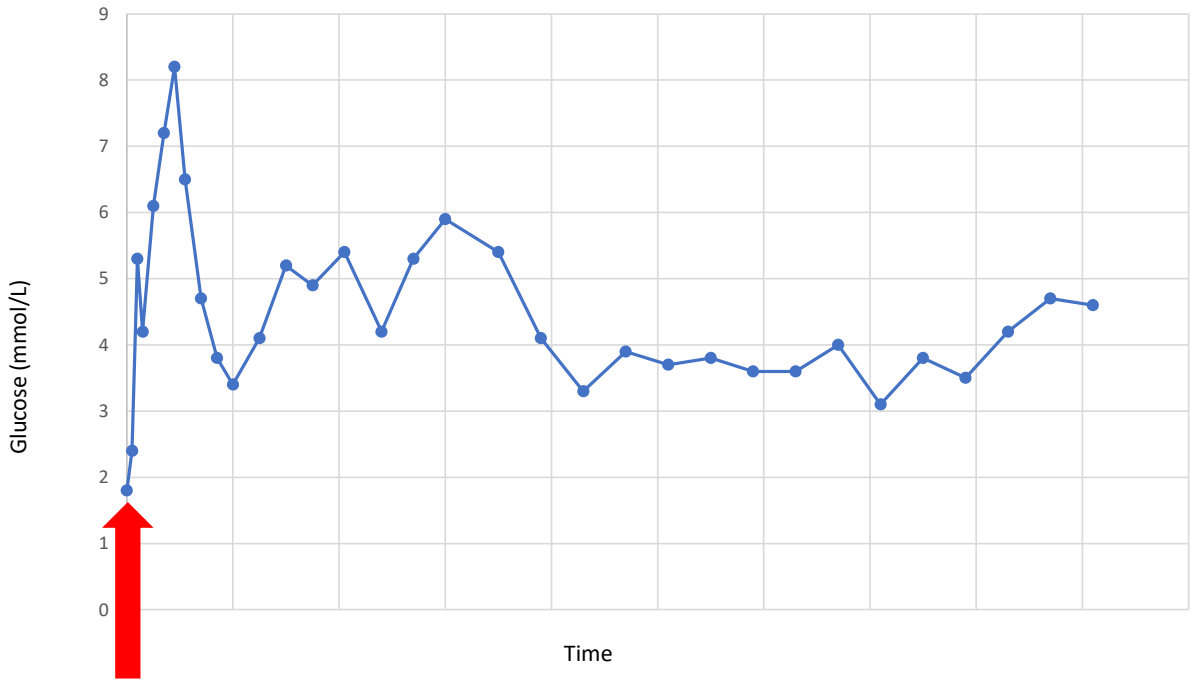
Thus actual **D20W** @ **6.8 mL/h** to make up TFI 80 mL/kg/d

- GIR = 0 (heparin) + 0.4 (morphine) + 7.2 (D20W)
  = 7.6 mg/kg/min

1: Baby F Glucose Timeline



#1: Baby F what happened



- Due to hypoglycemia and fluid management Glucagon was started late evening Day 1, on transport (red arrow on graph)
  - GIR 7.6 mg/kg/min
  - BG 6.1 mmol/L (TFI 80, D20W)
- The baby subsequently developed Hyperglycemic (8.2 mmol/L). Glucagon was discontinued at Day 2, 1000h after re-calculation of GIR
- Blood glucose levels were > 3.1 mmol/L for remainder of admission. Baby transitioned to full oral feeds successfully.

#1: Baby F – Discussion points

Was glucagon infusion necessary?	Likely not...
Consider: access, TFI, fluid balance, IVF	• Central, 80 mL/kg/d, negative fluid balance, u/o ↑ to 3.9 mL/kg/h while glucagon running • Na most recently 130mmol/L however u/o ↑ and no Na in IVF
Calculate: GIR	• GIR 7.1 mg/kg/min and BG manageable when glucagon was initiated (thus likely did not need to be started)
Be aware: prior to glucagon infusion, consider:	• GIR could be increased - higher TFI or dextrose concentration • IV Dextrose Bolus options. • Start and advance feeds (if appropriate)

Current Evidence Based Guidelines

SICKKIDS NICU NUTRITION GUIDELINES*

Dextrose Targets (mg/kg/min)		
	Preterm	**Term**
Initial Dose*	5-8	
Advance Daily	1-2	1-3
Acceptable Upper Limit	10-16	11-12

https://torontocentreforneonatalhealth.com/wp-content/uploads/2020/10/SickKids-NICU-Nutrition-Guidelines-July-2020.pdf

Normal GIR provision

Target reduction or increase in GIR rather than switching dextrose concentration

- Usual rate of glucose utilization is **4-8** mg/kg/min.

  Common caveats:

  - Lower requirements: term cooled infants; acute sepsis.
  - Higher or lower in extremely preterm infants .

- Action should be driven by <u>actual</u> intake (GIR) rather than assumptions based on dextrose concentration.

Know your numbers...
Always calculate GIR

IMPORTANT: Table assumes no other infusions are running – often NOT the case

SickKids NICU protocol if IVF > D12.5 = central access thus GIR will often be lower than noted below due to co-infusions.

GIR (mg/kg/min) using standard IVF concentrations					
TFI (mL/kg/d)	**5% dextrose**	**10% dextrose**	**12.5% dextrose**	**15% dextrose**	**20% dextrose**
50	1.7	3.5	4.3	5.2	6.9
60	2.1	4.2	5.2	6.3	8.3
80	2.8	5.6	6.9	8.3	11.1
100	3.5	6.9	8.7	10.4	13.9
120	4.2	8.3	10.4	12.5	16.7
140	4.9	9.7	12.2	14.6	19.4
160	5.6	11.1	13.9	16.7	22.2
Q20 mL/kg change	**0.7**	**1.4**	**1.7**	**2.1**	**2.8**

Reacting to serum BG just by switching IVF without calculating can lead to inappropriate GIR provision

2: Baby S – *Consider the impact of Medications*

- Baby S is born 37-week gestational age with a birth weight of 2.95 kg.
- Acute postnatal period was significant for pneumothorax and suspected sepsis.
- Day 3 post birth Baby S has presumed sepsis with hypotension requiring epinephrine infusion prior to transport via Acute Care Transport Services (ACTS) SickKids.
- Blood glucose on admission was 11.6 mmol/L

Question: Baby S weighs 2.95 kg. Her D10W is running for TFI at 8.7 mL/hr. What is her GIR?

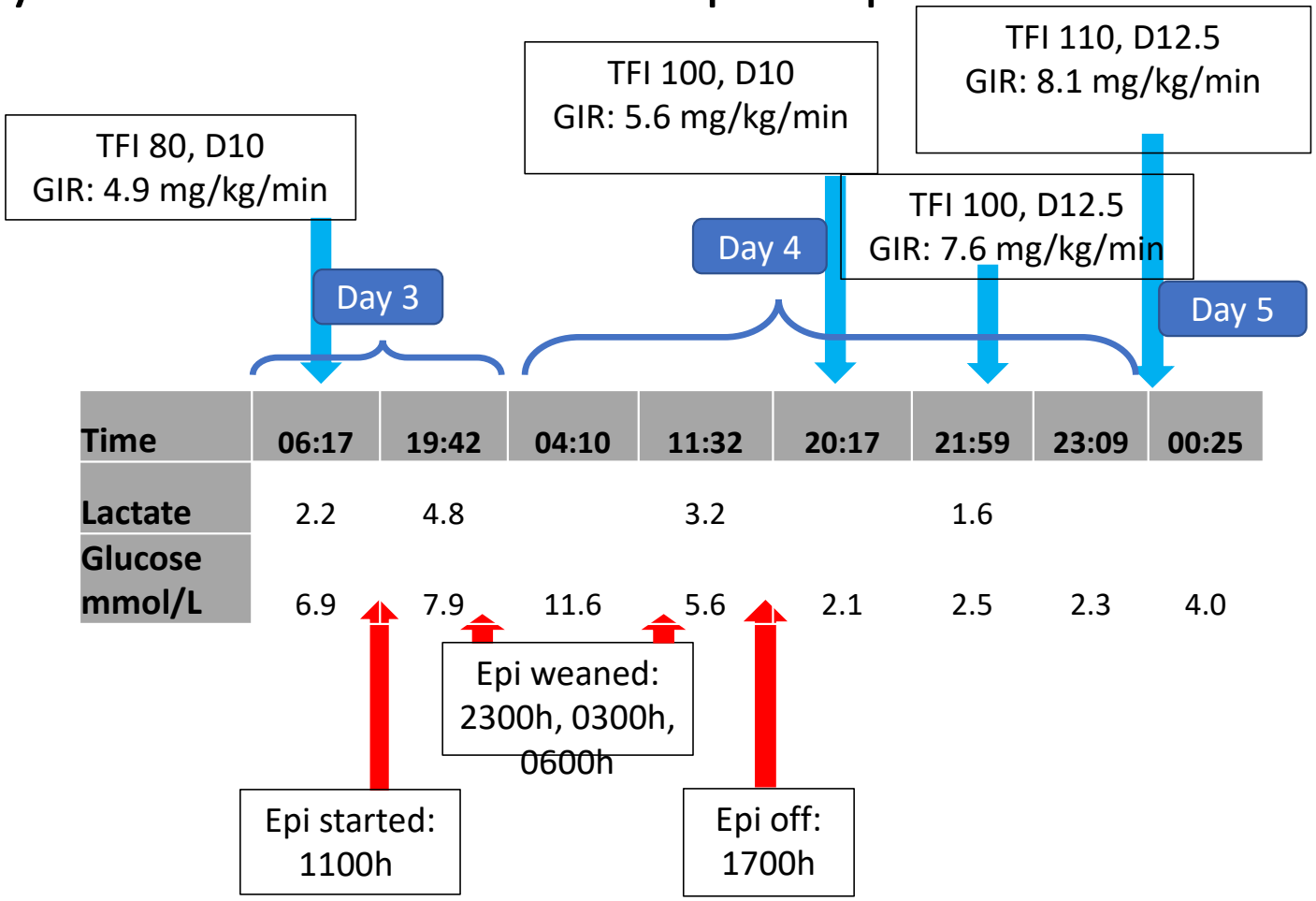
a)4.9 mg/kg/min

b)6.7 mg/kg/min

c)8.8 mg/kg/min

d)11.1 mg/kg/min

2 Baby S – Glucose and Epinephrine timeline



Time	06:17	19:42	04:10	11:32	20:17	21:59	23:09	00:25
Lactate	2.2	4.8		3.2		1.6		
Glucose mmol/L	6.9	7.9	11.6	5.6	2.1	2.5	2.3	4.0

2 Baby S – Discussion points

Could hypoglycemia have been avoided?	Yes
Consider: BG trend, expected changes	• BG dropped 11.6 to 5.6 mmol/L over 6h with epinephrine weans • Anticipate BG rise with epinephrine and drop as weaned off
Calculate: GIR	KNOW THE GIR
Be aware: BG trends, GIR, and medications that impact glycemia	• BG values alone may not indicate the whole picture • Where possible: act prophylactically in predictable glycemia control issues

Medications/Conditions Affecting Glycemia

	Causes of HYPOglycemia	Causes of HYPERglycemia
Medications	• PGEs • Propranolol	• Epinephrine • Hydrocortisone • Dexamethasone
Conditions	• Prematurity • Fetal Growth Restriction/IUGR • LGA • Maternal DM/GDM • Maternal labetalol use • Transient hyperinsulinism • Perinatal asphyxia/stress • Family hx IEM • BWS, CAH, hypopituitarism	• Sepsis • Extreme prematurity • Surgery/stress
Iatrogenic	• Inadequate substrate provision • Rapid discontinuation of IV dextrose	• Excessive substrate provision

3: Baby O in hospital *Don't forget glucose when correcting electrolytes*

Baby O is post-op day 2 for ileostomy creation. He has gained 500g secondary to post-op edema and requirement of a significant amount of blood products. The TFI has been strictly set at 100 mL/kg/d to prevent further fluid accumulation and wound dehiscence. A concentrated PN solution with D24 runs to maintain blood glucose level. BID Lasix has been prescribed to help promote diuresis. However, the patient's potassium level is dropping because of the Lasix and he requires a potassium correction overnight.

UO weighs 1.65 kg. He has a D24 in his PN.
A high K+ has been ordered to run at 0.8 mL/hr (in D5*0.45%NS) and included in TFI. To maintain TFI, PN is decreased by 0.8 mL/hr.
What is the net change in GIR?

a)-0.3 mg/kg/min

b)-1.5 mg/kg/min

c)-2.1 mg/kg/min

d)-0.8 mg/kg/min

#3: Baby O

TFI 100 mL/kg/day

- Infusions: Heparin (PAL, PICC), Morphine, SMOF Lipid
- Concentrated PN @4.3 mL/h
  - Dex 240 g/L = 10.4 mg/kg/min
  - K 50 mmol/L = 3.1 mmol/kg/d

K correction started

	19:45	23:41	01:50	02:59	03:01	06:10
Lactate	2.1					2.3
Sodium	141					146
Potassium	2.8	3.9	3.6			2.9
Chloride	112					113
Glucose	4.4		2.2	1.8	2.9	3.7
Creatinine						27
Urea						3.4
Albumin						22

3: Baby O - Discussion

Was hypoglycemia preventable?	• Perhaps, **Preterm infants have poor nutrient reserves and immature counter-regulatory hormone systems thus increased risk of hypoglycemia.**
Consider: dextrose composition of PN and/or IVFs	• Check the orders • Ideally check bedside pumps for accurate rates & composition
Calculate: GIR and change in GIR	• GIR expected to have been acceptable at reduced rate
Be aware: Patient's historical tolerance to GIR changes	• GIR change >1 mg/kg/min can be clinically significant • Pt historically required high GIRs to maintain glucose control

Fluid restriction often requires use of high dextrose concentration

- Check what dextrose concentration is running before reducing rate
- Post op – watchout for the rebound hyperglycaemia!
  - Initial hyperglycemia then usually need to ↑ GIR once post-op stress hormones ↓
  - Compounded by needs pre-op to maintain serum glucose

4: Baby G *Consider rate relative for weight when changing IVF*

- Baby G is born 26-weeks gestation, now day 3 post birth and on a TFI 200 mL/kg/day. Her dosing weight is 600 grams.
- She is currently with adrenal insufficiency requiring hydrocortisone (0.5 mg/kg/dose q12h) and has a peripheral arterial line (PAL) with heparin 1ml/hr for haemodynamic monitoring.
- Her PAL is removed at 1800h and Dextrose 10%/Saline 0.2% is hung overnight.

Question: Baby G (0.6 kg) has a PAL in situ running at 1 mL/hr. This heparin makes up:

a)10 mL/kg/d

b)40 mL/kg/d

c)20 mL/kg/d

d)5 mL/kg/d

Question: Baby G's PAL is running 1 mL/hr Heparin (in 0.45%NS); the PAL is removed and 1 mL/hr D10W*0.2%NS is run for TFI. Baby's dosing weight is 0.6 kg.
What is the effect on GIR?

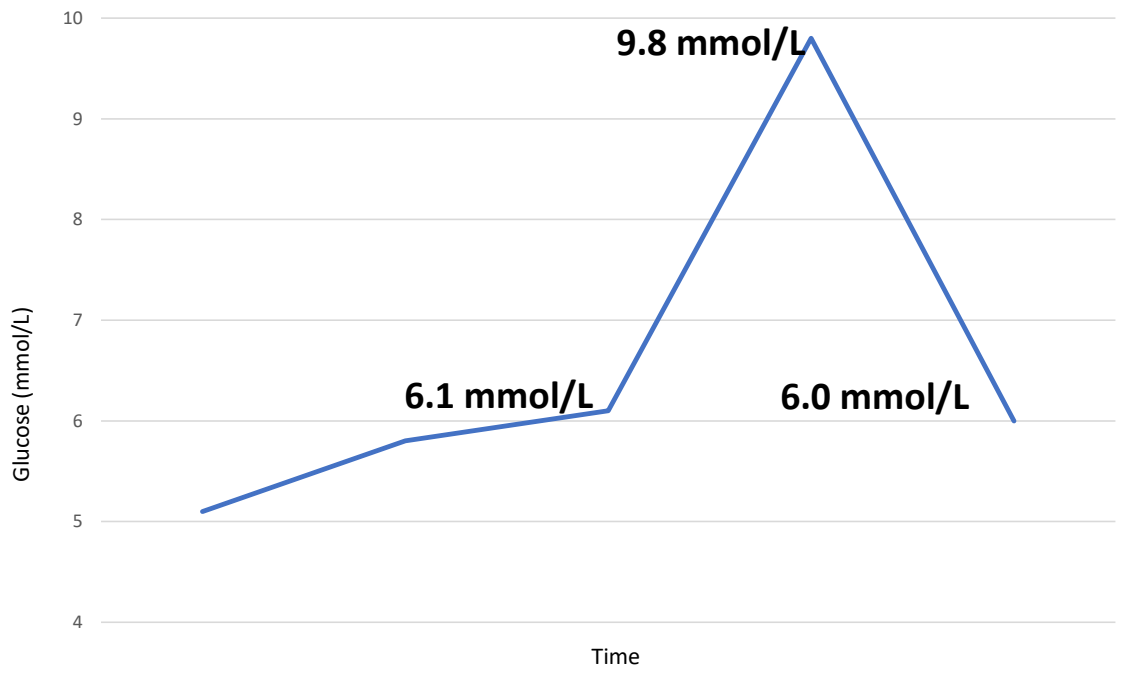
a)+0.8 mg/kg/min

b)+1.1 mg/kg/min

c)-0.5 mg/kg/min

d)+2.8 mg/kg/min

#4: Baby G - outcome



- With the increased GIR baby G had iatrogenic rapid hyperglycemia with serum glucose values normalizing once a New parenteral nutrition fluid bag was ordered and commenced early.
- Interim management was, increased rate of heparin running through her PICC line

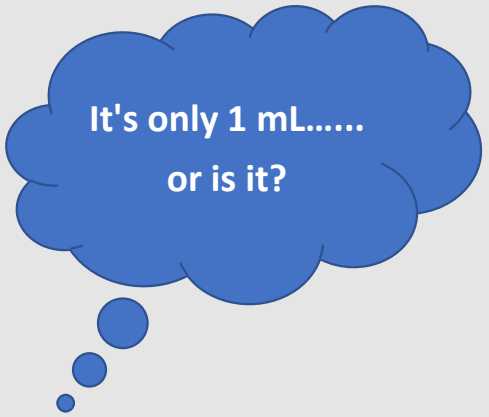
4: Baby G – discussion points

Was hyperglycemia preventable**?**	• Perhaps…
Consider: rate compared to weight	• 1 mL/h = 40 mL/kg/d • Significant!
Calculate: GIR & Δ GIR	• 1 mL/h with D10W = 2.8 mg/kg/min • 27% increase in GIR – now total 13.2 mg/kg/min
Review: patient's historical tolerance to GIR changes	• **GIR** > 1 mg/kg/min can be clinically significant • Historically had BG trending high, climbing with GIR increases, HC

(Dosing) Weight Matters

Wt (kg)	TFI (ml/kg/d)	D10W at 1 ml/hr Change in GIR (mg/kg/min)
0.5	48	3.3
0.75	32	2.2
1	24	1.7
1.25	19	1.3
1.5	16	1.1
2.5	10	0.7
3	8	0.6

Check impact of the change in IV fluids relative to pt's wt



Prematurity & Glycemic Control

HYPOglycemia	HYPERglycemia
Immaturity of counter-regulatory hormone systems	Inability to suppress hepatic glucose production
Poor nutrient stores (low glycogen stores)	Insulin resistance
Iatrogenic	Glucose intolerance
	Iatrogenic

- ↑ risk of abnormal blood sugars – especially if extremely premature +/- IUGR
- Clinical and scientific literature and extensive common experience document many adverse outcomes associated with neonatal hyperglycemia, including increased mortality, worse retinopathy of prematurity, brain white matter injury, reduced neuronal density and synapse formation, adverse neurologic outcomes, and reduced long-term growth

The long-term effects of neonatal hypoglycemia have been studied extensively. Most notably, there is a known relationship between neonatal hypoglycemia and long-term neurodevelopmental outcomes. See the following references for more information. These articles represent only a small proportion of the published literature examining neonatal hypoglycemia.

Research

JAMA Pediatrics | Original Investigation

Association of Neonatal Glycemia With Neurodevelopmental Outcomes at 4.5 Years

Christopher J. D. McKinlay, PhD; Jane M. Alsweiler, PhD; Nicola S. Anstice, PhD; Nataliia Burakevych, PhD; Arijit Chakraborty, PhD; J. Geoffrey Chase, PhD; Gregory D. Gamble, MSc; Deborah L. Harris, PhD; Robert J. Jacobs, PhD; Yannan Jiang, PhD; Nabin Paudel, PhD; Ryan J. San Diego, MSc; Benjamin Thompson, DPhil; Trecia A. Wouldes, PhD; Jane E. Harding, DPhil; for the Children With Hypoglycemia and Their Later Development (CHYLD) Study Team

Neonatology

Systematic Review and Meta-Analysis

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Neonatal Glycaemia and Neurodevelopmental Outcomes: A Systematic Review and Meta-Analysis

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Reviews

Neurologic Aspects of Neonatal Hypoglycemia

Arie L. Alkalay MD[1], Harvey B. Sarnat MD[2*], Laura Flores-Sarnat MD[2*] and Charles F. Simmons MD[1]

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ORIGINAL ARTICLES

Relationship between Measures of Neonatal Glycemia, Neonatal Illness, and 2-Year Outcomes in Very Preterm Infants

Anna Catherine Tottman, MBBS[1], Jane Marie Alsweiler, PhD[2,3], Frank Harry Bloomfield, PhD[1,3], Maggie Pan[2], and Jane Elizabeth Harding, DPhil[1]

Adverse neurodevelopmental outcome of moderate neonatal hypoglycaemia

A Lucas, R Morley, T J Cole

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Neonatal Glycemia and Neurodevelopmental Outcomes at 2 Years

Christopher J.D. McKinlay, Ph.D., Jane M. Alsweiler, Ph.D., Judith M. Ansell, Ph.D., Nicola S. Anstice, Ph.D., J. Geoffrey Chase, Ph.D., Gregory D. Gamble, M.Sc., Deborah L. Harris, Ph.D., Robert J. Jacobs, Ph.D., Yannan Jiang, Ph.D., Nabin Paudel, B.Optom., Matthew Signal, Ph.D., Benjamin Thompson, D.Phil., Trecia A. Wouldes, Ph.D., Tzu-Ying Yu, Ph.D., and Jane E. Harding, D.Phil., for the CHYLD Study Group*

#5: Baby R
Practice calculating GIR & implementing an appropriate plan

- Baby R is born at term gestation with small for gestation age birth weight of 2.83kg and antenatal suspicion of Ompahlocele, clinically confirmed after birth.
- He undergoes uncomplicated repair and is now with return of bowel function a few days post-operative and able to trial oral feeds.
- He has a history of hypoglycemia and is currently on a TFI of 160ml/kg/day = 18.9 mL/h
  - PN (D14) @13.9 mL/h
  - EBM @8mL Q3h (incr 1 mL q6h)

Question: what is the carbohydrate content of EBM

A) 105 g/L

B) 90 g/L

C) 72 g/L

D) 65 g/L

#5: Baby R

NICU Yellow card

Nutrient Content per Litre

Nutrient	Expressed Breast Milk (EBM)				Standard Formulas					Therapeutic Formulas	
	Mature EBM (Donor EBM)	Fortified EBM: EBM +Similac LHMF (Liquid Human Milk Fortifier)		Fortified EBM: EBM + EnfaCare	Enfamil A+ Premature (Preterm Formula)		Enfamil A+ EnfaCare (Post-Discharge Formula)	Enfamil A+ (Term Formula)		Good Start (Whey)	PURAMINO A+ (Free AA)/ Nutramigen A+ (Hydrolyzed Casein)
Concentration kcal/ml	0.68	0.74 (1pk HMF: 50ml EBM)	0.8 (1pk HMF: 25ml EBM)	0.8	0.68	0.8	0.74	0.68	0.8	0.67	0.68
Energy kcal/L	680	745	800	809	680	810	740	680	810	670	680
Protein g/L	12 (9)	20.0	26.7	15.8	20	24	21	14	17	15	18.9
Fat g/L	39	39.3	39.5	46	34	41	39	36	43	34	36
Carbohydrate g/L	72	79.1	85.0	85	74	89	77	76	88	75	72/70
Sodium mmol/L	7.8	11.1	13.8	9.9	17.1	20	11.3	7.9	9.5	7.8	13.8

- What is the current PN GIR?

(13.9 mL/h x 140 g/L)

(60 min/h x 2.83 kg)

= 11.5 mg/kg/min

- What is the current enteral GIR?

Note: EBM has 72g/L CHO

(8/3 mL/h x 72 g/L)

(60 min/h x 2.83 kg)

= 1.1mg/kg/min

https://torontocentreforneonatalhealth.com/wp-content/uploads/2020/10/SickKids-NICU-Nutrition-Guidelines-July-2020.pdf

#5: Baby R

Gen Surg gives go ahead to ↑ feeds 3mL Q3h...

- How much will the GIR decrease by with each feed increase?

Note: 3 mL Q3h = 1 mL/h

$$\frac{(1\ \text{mL/h} \times (72\text{-}140)\ \text{g/L})}{(60\ \text{min/h} \times 2.83\ \text{kg})} = -0.4\ \text{mg/kg/min}$$

- Net GIR change in 24h:

-0.4 mg/kg/min x 8 feeds/d

= -3.2 mg/kg/min

There are many options this baby could have, keep the wider “big picture” goals in mind when forming a plan.

Consider feed increases <u>below</u> protocol with hx hypoglycemia

- Especially if significant discrepancy between IV and feed CHO content
- If BG stable, can reassess to advance more quickly

If hypoglycemia persists:

1) Slow feed increases
2) Increase TFI
   and decrease dextrose concentration to bridge discrepancy between IV and feed CHO content
3) Change to q2h feeds
4) Increase feed duration
5) Fortification (eg. PolyCal)

Macronutrient Modules

PolyCal: Carbohydrate (CHO) – corn maltodextrin

- Used for hypoglycemia management
- 0.96 g CHO and 3.84 kcal per gram powder
- Approximate CHO content when added to EBM:

Concentration (kcal/ml)	0.74	0.8	0.85	0.9
CHO (g/L)	87.5	103.5	117.5	131.3

Be aware: fluids are titrated at the feed following increase

6: Baby P *Selecting appropriate fluids on admission*

Baby P is born 28-weeks gestation with a birth weight of 1.28 kg (88%ile Fenton)

- ACTS use D10W en-route from an out-born center to tertiary neonatal center
- She is admitted @ ~2200h (~7.5hrs of life) to the tertiary neonatal center.

Question: What fluids would you order on admission?

- D10
- Electrolyte Free PN
- **SMOF (*s*oybean oil, *m*edium-chain triglycerides, *o*live oil, *f*ish oil) lipids + Electrolyte Free PN**

Evidence Based Recommendations

Recommendations for first day of life (ESPGHAN, 2018):

- ***Start amino acid provision (min 1.5 g/kg/d)***
- ***Start lipid emulsion***
- ***Provide minimum 45-55 kcal/kg/d***

NICU Nutrition Guidelines

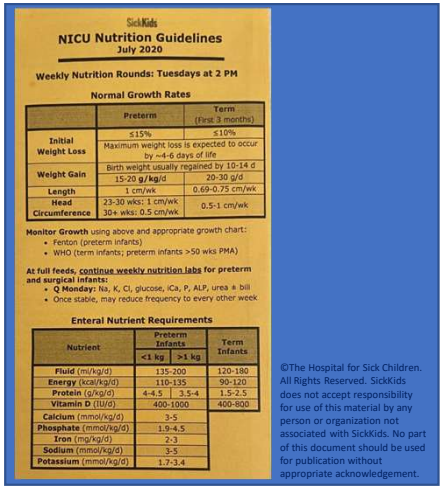
BW <1.5kg	BW >1.5kg
Start Electrolyte Free PN + SMOF at 1 g/kg/d *within first 24h of life*	Start 25/100 +/- SMOF 25= Amino Acids 25g/L 100 = Dextrose 100gm/L

Both available 24h/d and safe for PIV at many Level 2 and higher neonatal centers.

TFI 80 mL/kg/d = 4.3 mL/h hep @ 0.5 mL/h via UVC	D10W @ 3.8 mL/h	Sickkids Electrolyte Free PN @ 3.8 mL/h	SickKids Electrolyte Free PN @ 3.5 mL/h + SMOF @ 0.3 mL/h
Glucose Content (g/L)	100	100	100
GIR (mg/kg/min)	**4.9**	**4.9**	**4.6**
Protein Content (g/L)	-	25	25
Protein (g/kg/d)	-	**1.8**	**1.6**
Calcium Content (mmol/L)	-	12	12
Calcium (mmol/kg/d)	-	**0.86**	**0.79**
Fat (g/kg/d)	-	-	**1.1**
Energy (kcal/kg/d)	**24**	**31**	**40**

There are not many contraindications within first 24hrs

- Glycemic control/access issues requiring >D10
- Closer to the end of first 24h, already diuresing, requiring some electrolytes



SickKids

NICU Nutrition Guidelines
July 2020

Weekly Nutrition Rounds: Tuesdays at 2 PM

Normal Growth Rates

	Preterm	Term (First 3 months)
Initial Weight Loss	≤15%	≤10%
	Maximum weight loss is expected to occur by ~4-6 days of life	
Weight Gain	Birth weight usually regained by 10-14 d	
	15-20 g/kg/d	20-30 g/d
Length	1 cm/wk	0.69-0.75 cm/wk
Head Circumference	23-30 wks: 1 cm/wk 30+ wks: 0.5 cm/wk	0.5-1 cm/wk

Monitor Growth using above and appropriate growth chart:
- Fenton (preterm infants)
- WHO (term infants; preterm infants >50 wks PMA)

At full feeds, continue weekly nutrition labs for preterm and surgical infants:
- **Q Monday:** Na, K, Cl, glucose, iCa, P, ALP, urea + bili
- Once stable, may reduce frequency to every other week

Enteral Nutrient Requirements

Nutrient	Preterm Infants		Term Infants
	<1 kg	>1 kg	
Fluid (ml/kg/d)	135-200		120-180
Energy (kcal/kg/d)	110-135		90-120
Protein (g/kg/d)	4-4.5	3.5-4	1.5-2.5
Vitamin D (IU/d)	400-1000		400-800
Calcium (mmol/kg/d)	3-5		
Phosphate (mmol/kg/d)	1.9-4.5		
Iron (mg/kg/d)	2-3		
Sodium (mmol/kg/d)	3-5		
Potassium (mmol/kg/d)	1.7-3.4		

Know the WEIGHT, RATE and SUBSTRATE

CALCULATE before you TITRATE/MEDICATE*

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