

Prematurity of 23 or less weeks' gestation is a risk for transient late-onset hyperglycemia in neonate

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Take Home Message

“Transient prolonged hyperglycemia in neonates (TPHN)” would be a novel form of hyperglycemia among extremely preterm infants, that requires aggressive therapy, such as insulin.

Transient hyperglycemia of preterm infants

- Transient hyperglycemia is common among very low birth weight infants (LBWI) ¹.
- Occasionally, we experienced atypical transient hyperglycemia that is prolonged and severer than “classical” transient hyperglycemia.

>> A different form of neonatal hyperglycemia?

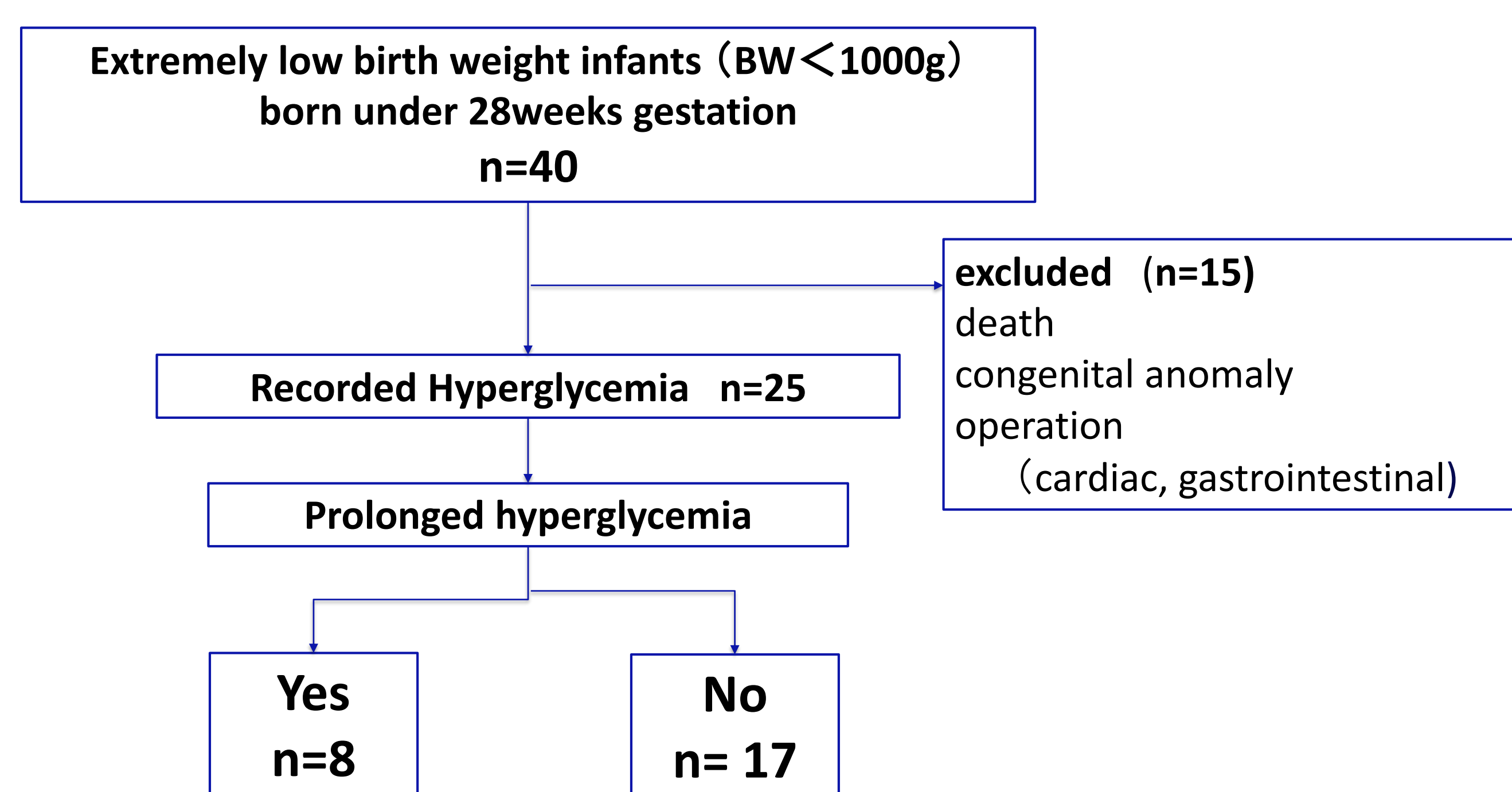
	“Classical” hyperglycemia	Prolonged hyperglycemia
Duration	• Less than 1 week	• More than 1-2 weeks
Risk	• Very low birth weight infants	
BS level	• 200~300mg/dl (11~16 mmol/l)	
Cause²	• Excess of glucose infusion • Drugs (catecholamine, steroid) • Hyperactivation of gluconeogenesis • High insulin resistance • Low insulin secretion	• unknown
Treatment	• Reduction of glucose infusion rate • insulin	• insulin

Aim of this study

Identifying risks and clinical features of prolonged hyperglycemia

Method

- Study population: Extremely preterm infants (<28weeks) admitted to a single Neonatal Intensive Care Unit in Japan
- Duration From Apr. 2015 To Mar. 2018
- Method: Retrospective analysis based on medical records



- Prolonged hyperglycemia: prolonged more than 1-2 wks + persistent after withdraw of parenteral nutrition
- Hyperglycemia: More than 180 mg/dL (10mmol/L) of preprandial glucose levels was sequentially demonstrated twice or more

Clinical features of Prolonged Hyperglycemia

Duration: > 6 weeks
Treatment: required aggressive insulin infusion therapy

	“Classical” hyperglycemia		Prolonged hyperglycemia		P value
	Median	(25-75 %tile)	Median	(25-75 %tile)	
Total days with hyperglycemia	3.0	(2-4)	47.5	(21.7-63.0)	<0.001
Maximum duration (days)	2	(2-3)	44	(17-56)	<0.001
Age at remission (corrected GA)	27w1d	(25w6d-27w6d)	30w1d	(29w3d-33w0d)	<0.001
Insulin therapy	4 (23%)		7 (87%)		0.007

Fischer's exact test, Mann-Whitney U-test

Exacerbated after the transition from parenteral to enteral nutrition

At the peak of hyperglycemia	“Classical” hyperglycemia		Prolonged hyperglycemia		P value
	Median	(25-75 %tile)	Median	(25-75 %tile)	
Age (day)	5.0	(4-7)	15.5	(9.7-17.5)	<0.001
Blood sugar level (mg/dl)	272	(241-304)	461	(415-499)	0.007
Glucose infusion rate (mg/kg/min)	5.7	(4.3-6.6)	0.7	(0-2.3)	0.008
Enteral feeding (ml/kg/day)	25.0	(7-38)	114.5	(93.2-127.5)	0.010

Mann-Whitney U-test

Risks of Prolonged Hyperglycemia

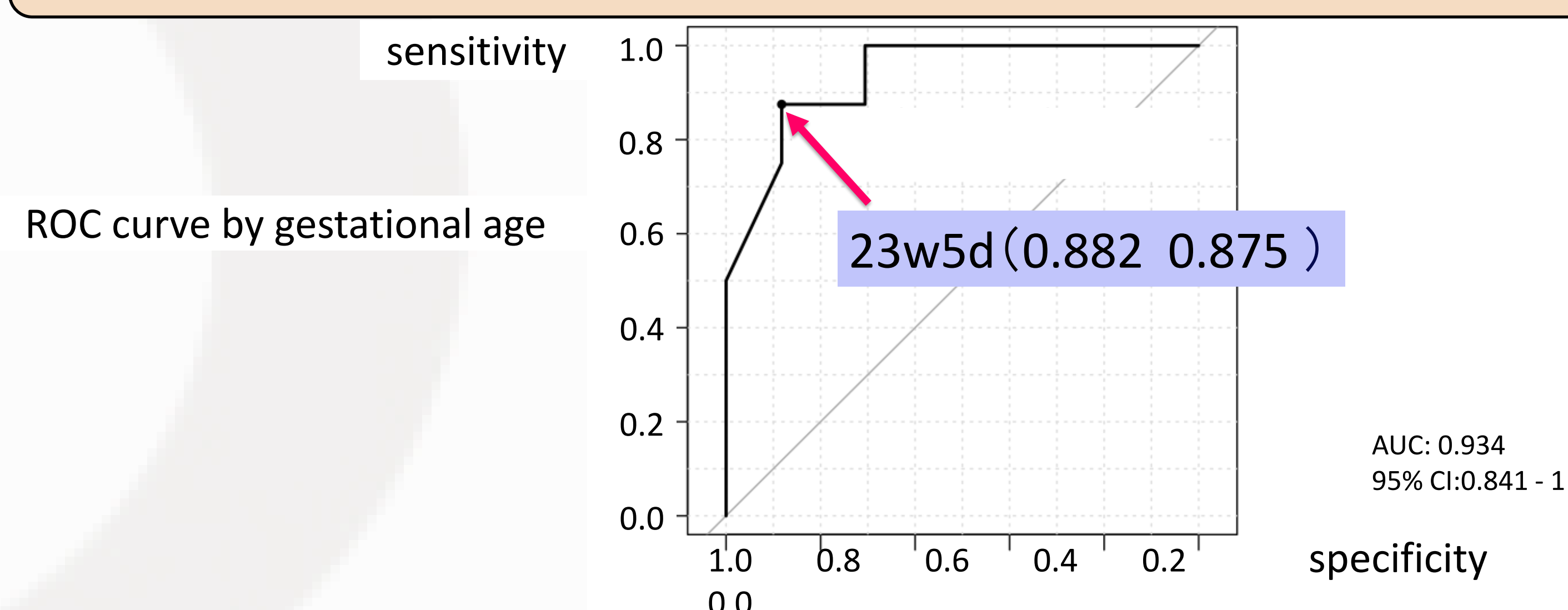
Risks: Extreme preterm (GA ≤ 23W), and lower birth weight

	Classical hyperglycemia		Prolonged hyperglycemia		P value
	Median	(25-75 %tile)	Median	(25-75 %tile)	
Gestational weeks	26w1d	(24w0d-27w0d)	23w3d	(23w2d-23w4d)	<0.001
Birth weight (g)	765	(615-837)	595.5	(546-619)	<0.001
SGA	35%		0%		0.064

Fischer's exact test, Mann-Whitney U-test

Not significant: maternal antenatal steroid administration, intravenous glucose/ amio acid/ fat infusion rate, catecholamine / steroid / caffeine administration,

Cut off value to predict prolonged hyperglycemia: 23w5d

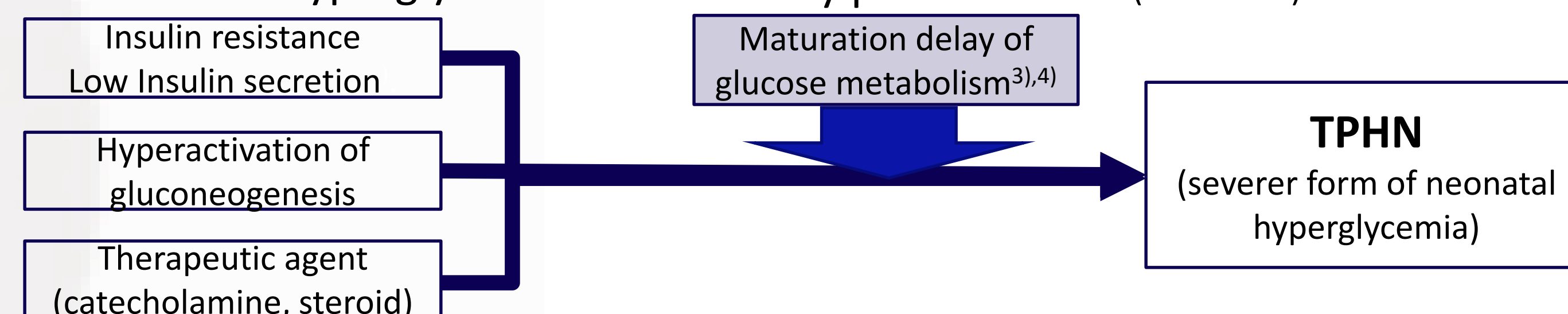


Discussion

- Based on our observation, we propose a novel type of transient neonatal hyperglycemia, “Transient prolonged hyperglycemia in neonates (TPHN)”
- It is characterized by
 - Persistent more than 6 weeks
 - Prolonged after the transition from parenteral to enteral nutrition
 - Requires aggressive treatment, such as insulin infusion.
- Risk factor: **Extremely Preterm (23w5d or less)**

A possible hypothesis for TPHN pathophysiology

Risks for “classical hyperglycemia” Extremely preterm birth (= < 23w5d)



- Possible reasons why few studies reported TPHN to date
 - Limited number of viable neonates who were born 23w or less of gestation
- As improving viability of extreme preterm infants (= < 23w), the number of neonates with TPHN will increase.
 - More detailed multicenter-studies are required

Reference

- Hays et al. Pediatrics 2006; 118(5): 1811-1818
- Meetez et al. Biol Neonate 1998; 74: 214-21
- Mola-Schenzle et al. Arch Dis Child Fetal Neonatal Ed 2015; 100: F126-F131
- Beardshall et al. J of Paediatrics 2010; 157(5): 715-719