



## GUIDELINE

# Cortisol Estimation and ACTH Stimulation Testing

<b>Scope (Staff):</b>	Nursing and Medical Staff
<b>Scope (Area):</b>	NICU KEMH, NICU PCH, NETS WA

### Child Safe Organisation Statement of Commitment

CAHS commits to being a child safe organisation by applying the National Principles for Child Safe Organisations. This is a commitment to a strong culture supported by robust policies and procedures to reduce the likelihood of harm to children and young people.

This document should be read in conjunction with this [disclaimer](#)

## Aim

To describe the importance of early diagnosis and management of adrenaline insufficiency in the newborn.

## Risk

Untreated adrenal insufficiency can lead to increased risk of mortality and morbidities.

## Relative Adrenal Insufficiency (RAI)

- A temporary condition in critically ill neonates which occurs when the cortisol response is inadequate for the patient's degree of stress and has a reported incidence of 37-86%; often in first 2 weeks of life.

RAI is attributed to: adrenergic receptor insensitivity due to receptor downregulation, pro-inflammatory cytokine-mediated suppression of the function of the pituitary and adrenal glands, inadequate HPA axis response to stress, limited adrenal reserve, gestational age-associated immaturity of the adrenal gland, corticosteroid tissue resistance, and limited adrenal perfusion

- Diagnosing RAI is challenging as there is no consensus on its definition or diagnostic criteria. A random or baseline cortisol level  $<414\text{nmol/L}$  or an ACTH stimulated (short synacthen test – see Neonatal Medication Protocol – [Tetracosactrin](#))  $\Delta$ -cortisol (peak - baseline) of  $<250\text{nmol/L}$  or a peak  $<550\text{nmol/L}$  has been proposed.
- It should be considered in any critically ill neonate with conditions such as severe sepsis, HIE, MAS, PPHN, CDH and severe RDS, particularly in those with vasopressor-resistant hypotension (BP mean  $<$ gestational age despite fluid

bolus and inotropic support; best correlated with functional echo). It is common in 25% term newborns following cardiac surgery (cardiopulmonary bypass) as well.

- Important clinical findings: hypoglycemia, hyponatremia, hyperkalemia (Na/K ratio <20), dehydration, metabolic acidosis, hyperpigmentation and hypotension resistant to vasopressor treatment

**Normal serum cortisol levels**

Preterm infants	Cortisol level nmol/L	Term infants	Cortisol level nmol/L
26-28 weeks	27.6-303.5 (Day 4)	Day 3	47-386
31-35 weeks	69—251 (Day 4)	Day 7	55.2-303.5
		1-11 Months	77.2-634

It has been shown that:

- Hydrocortisone therapy results in haemodynamic stability and reduced use of vasopressors and fluid boluses; with rapid tapering of inotropic support.
- Treatment with hydrocortisone should be weighed up with the potential risks particularly in preterm neonates where there has been shown to be increased rates of GI perforation (in those treated alongside indomethacin therapy; LoEII). Evidence from a recent trial (Premiloc) involving extremely preterm infants indicated that hydrocortisone did not show the detrimental effects on growth and neurodevelopmental outcome seen with dexamethasone treatment.

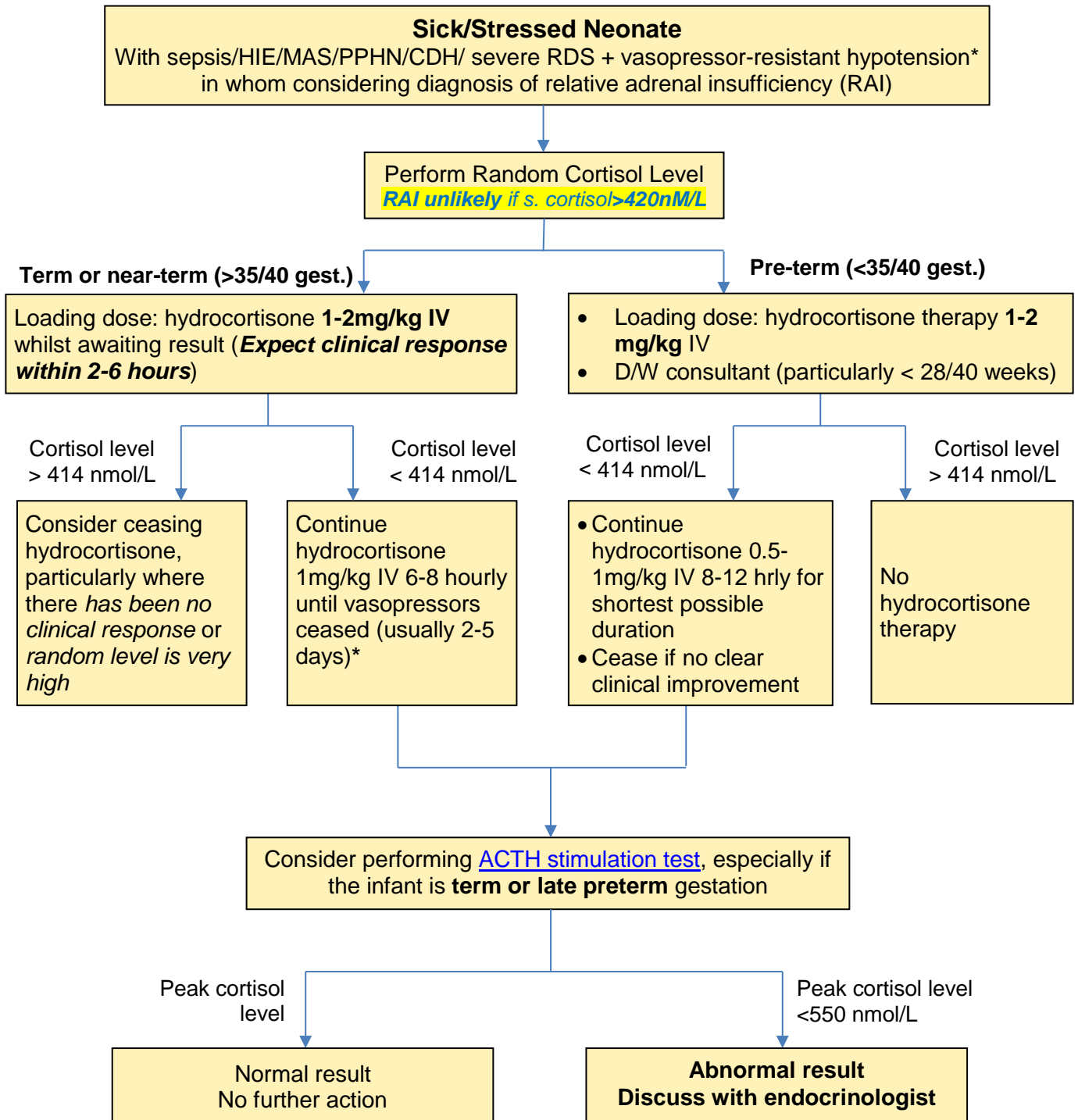
**Primary/Secondary Adrenal Insufficiency**

- Primary or secondary insufficiency: Smith Lemli Opitz syndrome, steroid regulatory protein defects, congenital adrenal hyperplasia or congenital hypoplasia or secondary adrenal/central such as hypopituitarism.
- Suspected in patients with ambiguous genitalia, hyponatraemia, hypoglycaemia, and an abnormal head scan/ MRI (absent pituitary/mal-placed pituitary/septo-optic dysplasia/ midline defects)\*.

**Flowchart for adrenal investigation in the sick/stressed neonate with vasopressor-resistant hypotension in whom a diagnosis of relative adrenal insufficiency (RAI) is being considered:**

\*Vasopressor-resistant hypotension (in 15-30%) defined as mean BP <gestational age despite > 20mL/kg fluid bolus and on >10mcg/kg/min dopamine and/or >10mcg/kg/min dobutamine or multiple intropes.

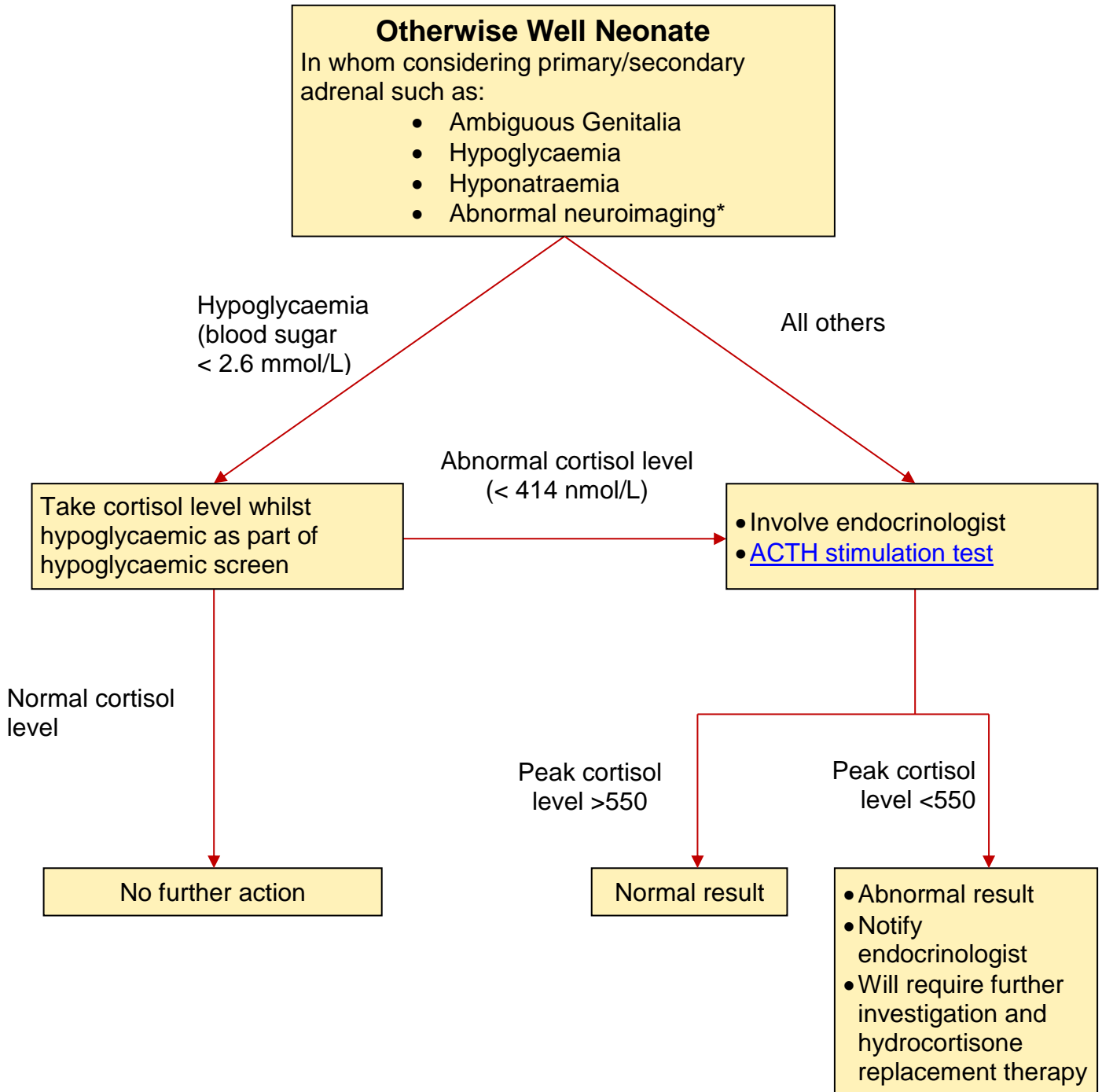
Ensure that the newborn has (1) adequate circulating volume, (2) no mechanical issues with ventilation that impede venous return (high MAP or PEEP), (3) No excessive sedation/ analgesic administration



**Flowchart for Adrenal Investigation in the Relatively Well Neonate in Whom a Diagnosis of Primary or Secondary Adrenal Insufficiency is being considered:**

**\*Note:** If hydrocortisone was not given for > 3 days, it can be discontinued without tapering, otherwise within 24 hours after a positive response to hydrocortisone therapy with improved BP and urine output and tolerance of reduced vasopressor support, it is recommended that hydrocortisone dose be reduced to 0.5 mg/kg/dose 8-12 hrly.

Refer to Neonatal Medication Protocol - [Hydrocortisone](#)



## ACTH Stimulation Testing (Short Synacthen Test/ SST)

The short Synacthen test is a test of adrenal insufficiency which can be used for screening in the non-critically ill patient. The test is based on the measurement of serum cortisol before and after an injection of synthetic ACTH (also known as Tetracosactrin). Advice of paediatric endocrinologist is to be sought before undertaking SST in the neonatal period.

**Consider for any infant** exposed to:

- ≥7 days of hydrocortisone for profound hypotension unresponsive to conventional BP management or suspected adrenal crisis
- >10 days of dexamethasone for chronic lung disease (eg: multiple DART courses)
- >10 cumulative days of steroid treatment (hydrocortisone or dexamethasone) for any indication

Testing performed at least 4-6 days after the last dose of steroids. Test to be performed in the morning as response to co-syntropin is subnormal in morning and afternoon in infants with adrenal insufficiency.

### Result interpretation

There is ongoing debate about the dose of Synacthen ([Tetracosactrin](#)) to use for the testing remains controversial. Our standard practice is to use 15 microgram/kg, unless there is a special request by the endocrinologist to use a different dose. If there is a suboptimal cortisol response, seek review by the endocrinologist.

- Refer to Neonatal Medication Protocol: [Tetracosactrin](#)

### Related CAHS internal policies, procedures and guidelines

Neonatal Medication Protocols

- [Tetracosactrin](#)
- [Hydrocortisone](#)


### References

1. Kumbhat N, Noori S. Corticosteroids for Neonatal Hypotension. Clin Perinatol. 2020 Sep;47(3):549-562.
2. <https://thoracickey.com/the-neonate-with-relative-adrenal-insufficiency-and-vasopressor-resistance/>
3. Baud O, Trousson C, Biran V, Leroy E, Mohamed D, Alberti C; PREMILOC Trial Group. Association Between Early Low-Dose Hydrocortisone Therapy in Extremely Preterm Neonates and Neurodevelopmental Outcomes at 2 Years of Age. JAMA. 2017 Apr 4; 317(13):1329-1337.
4. Buonocore F, McGlacken-Byrne SM, Del Valle I, Achermann JC. Current Insights Into Adrenal Insufficiency in the Newborn and Young Infant. Front Pediatr. 2020 Dec

14;8:619041.

5. Yi S, Turkmen M, Tuncer O et al. Neonatal adrenal insufficiency: Turkish Neonatal and Pediatric Endocrinology and Diabetes Societies consensus report. Turk Pediatri Ars. 2018; 53(Suppl 1): S239–S243.
6. Crawford JH, Hull MS, Borasino S, Steenwyk BL, Hock KM, Wall K, Alten JA. Adrenal insufficiency in neonates after cardiac surgery with cardiopulmonary bypass. Paediatr Anaesth. 2017 Jan; 27(1):77-84.
7. Johnson PJ. Hydrocortisone for Treatment of Hypotension in the Newborn. Neonatal Netw. 2015; 34(1):46-51.
8. Finken MJ, van der Voorn B, Heijboer AC, de Waard M, van Goudoever JB, Rotteveel J. Glucocorticoid Programming in Very Preterm Birth. Horm Res Paediatr. 2016;85(4):221-31
9. Robert SM, Borasino S, Dabal RJ, Cleveland DC, Hock KM, Alten JA. Postoperative Hydrocortisone Infusion Reduces the Prevalence of Low Cardiac Output Syndrome After Neonatal Cardiopulmonary Bypass. Pediatr Crit Care Med. 2015 Sep; 16(7):629-36.
10. Fernandez E, Schrader R, Watterberg K. Prevalence of low cortisol values in term and near-term infants with vasopressor-resistant hypotension. Journal of perinatology : official journal of the California Perinatal Association. Feb 2005;25(2):114-118.
11. Ng PC. Effect of stress on the hypothalamic-pituitary-adrenal axis in the fetus and newborn. The Journal of pediatrics. Feb 2011;158(2 Suppl):e41-43.

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