Adrenal insufficiency in neonates can be divided into 2 categories:

**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%.
- It is defined as a random or baseline cortisol level <414nmol/L or an ACTH stimulated (short synacthen test, 1mcg IV) Δ-cortisol (peak - baseline) of <250nmol/L or a peak <550nmol/L.
- 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). It is common in 25% term newborns following cardiac surgery (cardiopulmonary bypass) as well.
- Diagnosis of RAI and treatment with hydrocortisone are controversial and presently there is a lack of good evidence in the literature. However, it is known that:
  - Severe prolonged hypotension is associated with increased mortality and central nervous system morbidity.
  - Inotropic support may lead to decreased organ perfusion causing decreased cerebral perfusion, renal and cardiac failure and fluid boluses are associated with pulmonary oedema and PDA.
- It has been shown that:
  - Hydrocortisone therapy results in haemodynamic stability and reduced use and 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). 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**
- Conditions are primary adrenal such as 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 (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 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 other intropes.

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**Sick/Stressed Neonate**

With sepsis/HIE/MAS/PPHN/CDH/ severe RDS + vasopressor-resistant hypotension* in whom considering diagnosis of relative adrenal insufficiency (RAI)

Perform Random Cortisol Level

Term or near-term (>35/40 gestation)  
Pre-term (<35/40 gestation)

- Give hydrocortisone 1mg/kg IV whilst awaiting result (Expect clinical response within 2-6 hours)
- Consider hydrocortisone therapy 1 mg/kg IV
- D/W consultant (particularly < 28/40 weeks)

- Cortisol level > 414 nmol/L
  - Consider ceasing hydrocortisone, particularly where there has been no clinical response or random level is very high

- Cortisol level < 414 nmol/L
  - Continue hydrocortisone 1mg/kg IV 6-8 hourly until vasopressors ceased (usually 2-5 days)*

- Cortisol level > 414 nmol/L
  - No hydrocortisone therapy

- Cortisol level < 414 nmol/L
  - Continue hydrocortisone 1mg/kg IV 8-12 hrly for as short a time as possible
  - Cease if no clear clinical improvement

Consider performing standard dose (12 microgram/kg), especially if the infant is term or late preterm gestation

- Peak cortisol level > 550 nmol/L
  - Normal result
  - No further action

- Peak cortisol level < 550 nmol/L
  - Abnormal result
  - Discuss with endocrinologist
**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

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**Relatively Well Neonate**

In whom considering primary/secondary adrenal such as:
- Ambiguous Genitalia
- Hypoglycaemia
- Hyponatraemia
- Abnormal Head Scan

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**Hypoglycaemia** (blood sugar < 2.7 mmol/L)

- Take cortisol level whilst hypoglycaemic as part of hypoglycaemic screen

**All others**

- Abnormal cortisol level (< 414 nmol/L)
  - Involve endocrinologist
  - Standard dose (12mcg/kg)
  - ACTH stimulation test

- Normal cortisol level

**Normal result**

- No further action

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**Peak cortisol level > 550**

- Normal result

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**Peak cortisol level < 550**

- Abnormal result
  - Notify endocrinologist
  - Will require further investigation and hydrocortisone replacement therapy
**ACTH Stimulation Testing (Short Synacthen Test)**

The short Synacthen test is a test of adrenal insufficiency which can be used as a screening procedure 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).

The dose of synacthen to use for the testing remains controversial. Our standard practice is to use standard dose of 12 microgram/kg, unless there is a special request by the endocrinologist to use a different dose.

**Standard Dose Test** (for establishing cause of primary/secondary adrenal insufficiency, diagnosis of congenital adrenal hyperplasia and for checking adrenal cortical function post recovery from acute illness and off hydrocortisone therapy).

- 12mcg/kg Tetracosactrin intramuscularly (IMI) or intravenously (IV) if available.

Refer to Neonatal Medication Protocol: **Tetracosactrin.**

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**References**

12. Huysman MW, Hokken-Koelega AC, De Ridder MA, Sauer PJ. Adrenal function in sick very...


## Related WNHS policies, procedures and guidelines

- **Neonatal Medication Protocol**: Tetracosactrin Hydrocortisone

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