Adrenaline (plasma, urine)

1 Name and description of analyte

1.1 Name of analyte
Adrenaline

1.2 Alternative names
Epinephrine
(R)-4-(1-hydroxy-2-(methylamino)ethyl)benzene-1,2-diol

1.3 NMLC code
To follow

1.4 Description of analyte
Adrenaline is a catecholamine produced principally by chromaffin cells of the adrenal medulla (the major source of adrenaline in plasma) but also by extramedullary chromaffin cells. It is a sympathetic neurotransmitter. Adrenaline is synthesised from the precursor tyrosine; synthesis is upregulated by increased plasma cortisol concentrations via induction of phenylethanolamine N-methyltransferase, the enzyme that converts noradrenaline to adrenaline. Adrenaline has a short half-life, of the order of several minutes, and is metabolised by methylation and deamination.

1.5 Function of analyte
Adrenaline functions as a hormone, exerting its effects throughout the entire body. It binds both α and β adrenergic receptors and is equipotent at both. Its primary functions are:

- arteriolar vasoconstriction in the kidneys, intestines, skin
- generalised venoconstriction
- arteriolar vasodilatation in skeletal muscle and the heart
- relaxation of smooth muscle surrounding bronchioles, thus facilitating breathing
- raising blood glucose concentrations by promoting glycogenolysis
- promoting lipolysis.

Cumulatively, these effects increase the availability of energy substrates and oxygen in the circulation and preferentially deliver these to the brain, heart and skeletal muscle.

2 Sample requirements and precautions

2.1 Medium in which measured
Adrenaline is typically measured in plasma (lithium heparin) or urine. Serum is not suitable because catecholamines are stored in platelets and may be released in the clotting process and due to the short half-life.

2.2 Precautions re sampling, handling etc.
1. A strict collection protocol is necessary for plasma adrenaline. It is recommended patients are supine, and have an indwelling catheter inserted at least 30 min prior to sample collection for basal samples. Blood should be collected into a chilled lithium-heparin tube.
2. Adrenaline is labile in plasma. Samples should be centrifuged at 4 °C immediately following collection (not >20min after collection). The

resulting plasma should be frozen immediately, using either dry ice or a -40 °C freezer.
3. Urine samples must be taken into containers with acid (pH <3.5). A 24 h collection is preferred for adults and a random collection for children. Three collections are recommended to increase the clinical sensitivity of the test.

3 Summary of clinical uses and limitations of measurements

3.1 Uses
Adrenaline measurements are used exclusively in the diagnosis and management of catecholamine-secreting tumours (see 6.1).

3.2 Limitations
Measurements of plasma adrenaline are, in general, only useful when an individual with a suspected catecholamine-secreting tumour is experiencing an acute attack.

4 Analytical considerations

4.1 Analytical methods
Adrenaline is measured by high performance liquid chromatography (HPLC) with electrochemical detection or HPLC coupled to liquid-chromatography tandem mass spectrometry (LC-MS/MS). Both methods require extraction of catecholamines prior to analysis.

4.2 Reference method: none

4.3 Reference materials: none

4.4 Interfering substances
Grossly haemolysed samples are unsuitable for analysis.

4.5 Sources of error
1. In some assays, a metabolite of labetalol can interfere with HPLC analysis of plasma adrenaline causing falsely elevated results. Paracetamol may interfere with urine analysis of adrenaline.
2. Several drugs used to treat psychiatric patients prevent catecholamine reuptake and may increase urinary excretion of adrenaline.

5 Reference intervals and variance

5.1.1 Reference interval (adults)
Plasma: <4.00 nmol/L
Urine: <144 nmol/24 h (derived in a hypertensive population)

5.1.2 Reference intervals (children)
Plasma: adrenaline is not routinely measured in infants owing to artefacual increases caused by the stress of collection; however, reference ranges are as follows: 2–10 d <2.2 nmol/L; 10 d–3 m <1.1 nmol/L; 3–12 m <2.4 nmol/L; 1–2 y <3.5 nmol/L; 2–3 y <2.4 nmol/L; 3–15 y <2.5 nmol/L.

Urine: 0–24 m <46 nmol/mmol creatinine; 2–4 y <35 nmol/mmol creatinine; 5–9 y <22 nmol/mmol creatinine, 10–19 y <21 nmol/mmol creatinine

5.1.3 Extent of variation

5.1.3.1 Interindividual CV: plasma - no data; urine - 85 %

5.1.3.2 Intraindividual CV: plasma - 48%; urine - 46%

5.1.3.3 Index of individuality: plasma – no data; urine - 0.54

5.1.3.4 CV of method: approximately 10%

5.1.3.5 Critical difference urine - 130% ; plasma – no data

5.1.4 Sources of variation

Stress, exercise, smoking and pain are all known to elevate plasma [adrenaline] and hence urinary excretion. Hypertensive individuals have increased [adrenaline] compared to normotensive individuals.

6 Clinical uses of measurement and interpretation of results

6.1 Uses and interpretation

Adrenaline measurements are used:

- in the diagnosis of catecholamine-secreting tumours e.g. phaeochromocytomas and paragangliomas
- for localisation of phaeochromocytomas when venous catheterisation is performed
- to assess completeness of surgical removal of catecholamine-secreting tumours
- to assess recurrence of a catecholamine-secreting tumour following surgical removal
- to assist in confirmation of catheterization of an adrenal vein.
- (in urine) in the investigation of multiple endocrine neoplasia (MEN2).

7 Causes and investigation of abnormal results

7.1 High values

7.1.1 Causes:

- phaeochromocytomas
- paragangliomas
- neuroblastomas
- acute stress.

7.1.2 Investigation

Adrenaline should only be measured in specific circumstances: unexpectedly high concentrations should not occur. Once a high concentrations or urinary excretion of adrenaline has been demonstrated, further investigation is by imaging and/or venous sampling for localisation of the source.

7.2 Low values

7.2.1 Causes

Pathologically low values do not occur.

7.2.2 Investigation of low values

Not applicable

7.3 Notes

None

8 Performance

8.1 Sensitivity, specificity etc. for individual conditions
Diagnosis of catecholamine secreting tumours (note that the values shown are approximate: exact values will depend on the cut-offs used).
Plasma: sensitivity 90%; specificity 90%.
Urine: sensitivity 95%, specificity 95%.

9 Systematic reviews and guidelines

9.1 Systematic reviews
Peaston RT Weinkove C. Measurement of catecholamines and their metabolites. Ann Clin Biochem 2004;41:17-38.

9.2 Guidelines
None identified

9.3 Recommendations
Pacak KG Eisenhofer G Ahlman H *et al*. International Symposium on Pheochromocytoma: recommendations for clinical practice from the First International Symposium, October 2005. Nat Clin Prac Endocrinol Metab 2007;3:92-102.

10 Links

10.1 Related analytes
Metadrenaline is a metabolite of adrenaline. It can be measured in both plasma and urine and is considered more sensitive than adrenaline in the investigation of catecholamine-secreting tumours.

10.2 Related tests
Adrenaline is usually measured as part of a catecholamine assay set in combination with noradrenaline and dopamine.

Author: Kate Maclagan

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