A REGIONAL AUDIT OF INVESTIGATION OF HYPERTENSION

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Background

Hypertension is a prevalent condition with significant morbidity and mortality, and while most cases are classified as primary (essential) hypertension, a subset arises from identifiable secondary causes. Timely recognition and investigation of secondary hypertension are crucial, as targeted treatment can significantly improve patient outcomes and reduce long-term cardiovascular risk.

This clinical audit aimed to evaluate the current practices in the investigation of secondary hypertension, assessing adherence to national and local guidelines. By identifying gaps in diagnostic workup and referral pathways, we sought to highlight areas for improvement in laboratory practice and ensure that patients with potentially reversible causes of hypertension receive appropriate and timely care.

Method

A questionnaire was prepared with reference to current guidelines and circulated to the Thames Audit Group committee for comment. Once finalised, the survey was circulated to laboratories within the region, and the 14 responses were collated using Microsoft Excel. The results of the audit were presented at the meeting of the Thames Audit Group held on 12th November 2024.

Cushing's Syndrome

- Of the 14 participating laboratories, the majority used Roche or Abbott immunoassays for measurement of cortisol (Figure 1)
- Reference ranges for 9am cortisol were not quoted by all laboratories. There was variation in reference intervals, even between laboratories using the same method and manufacturer derived reference intervals (Figure 2)
- Overnight dexamethasone suppression test (ONDST) cut offs also varied between laboratories (Figure 3). 3 laboratories offer dexamethasone analysis either as standard for all ONDST or on request.
- 7 laboratories offer salivary cortisol service. 6 report salivary cortisone, 1 did not.

Figure 1: Cortisol Methods

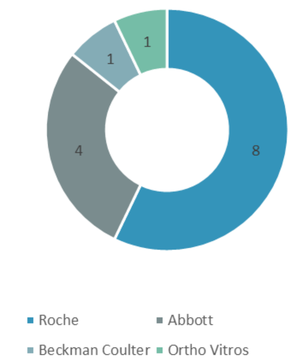


Figure 2: Reference Intervals

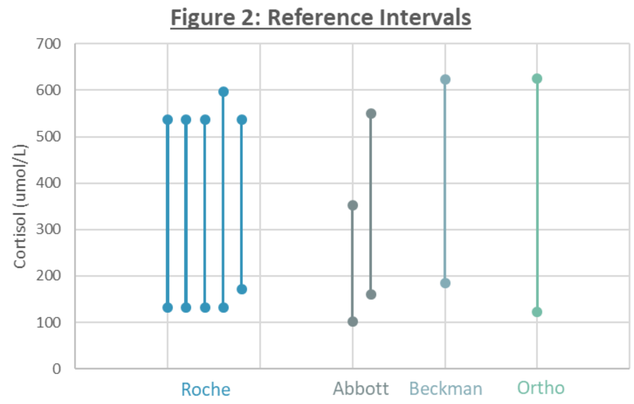
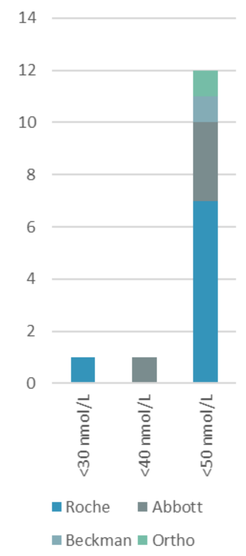


Figure 3: Diagnostic Cutoff for ONDST



Phaeochromocytoma / Paraganglioma

- The tests offered by participants for investigation of adult patients with suspected phaeochromocytoma / paraganglioma (PPGL) included 24hr and random urine metanephrines, 24hr urine catecholamines, 24hr HVA/HMMA, and plasma metanephrines (Figure 4).
  No laboratories recommended random urine or plasma catecholamines.
- 3-methoxytyramine was included in metanephrine profiles by the majority of participants in both urine (85% of participants) and plasma (83% of participants)
- 5 (36%) participants recommended taking samples for plasma metanephrines in a supine position, 4 recommended a seated position and 4 recommended either seated or supine. However, 2 of these participants quoted only a single reference interval (Figure 5)

Primary Hyperaldosteronism

- All laboratories offered a renin/aldosterone service either referred or measured in house for the investigation of suspected primary hyperaldosteronism (PHA)(Figure 6).
- 5 (36%) laboratories always report the aldosterone/renin ratio (ARR), 1 (7%) laboratory reports the ARR if requested, and 1 (7%) laboratory never reports the ARR.
- Patient preparation instructions varied between laboratories; 6 (43%) participants recommended a random sample, and 5 (36%) recommended a morning sample. 1 (7%) participant recommended supine sampling, and 8 (57%) recommended seated sampling.
- Confirmatory tests recommended included repeat ARR, repeat ARR either supine or seated, saline infusion test and captopril challenge test. No laboratories recommended the furosemide test or the fludrocortisone suppression test.
- The withdrawal of antihypertensive medications before ARR sampling was recommended by most laboratories with some variation in drug classes and the length of time they should be withdrawn (Figure 7)

Figure 4: Tests offered for Investigation of Suspected Phaeo/PPGL in Adult Patients

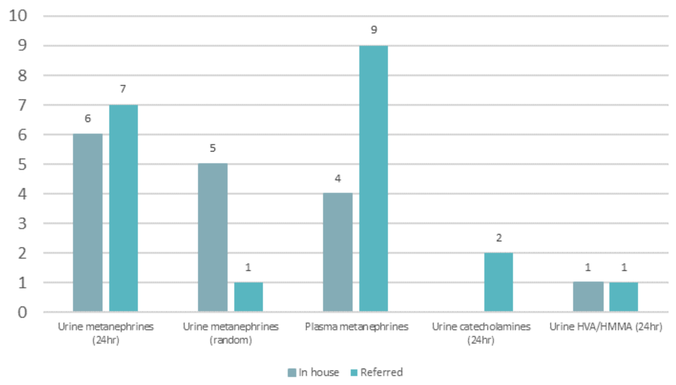


Figure 5: Seated vs Supine Sample Collection for Plasma Metanephrines

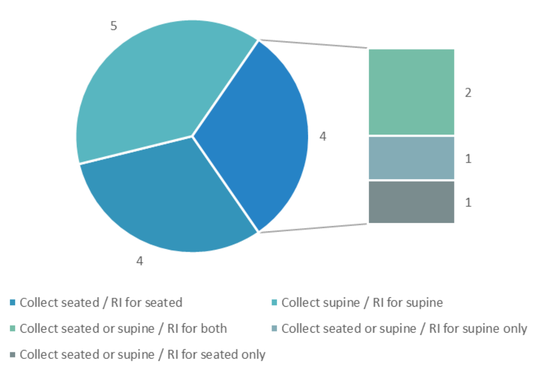


Figure 6: Measurement of Aldosterone & Renin

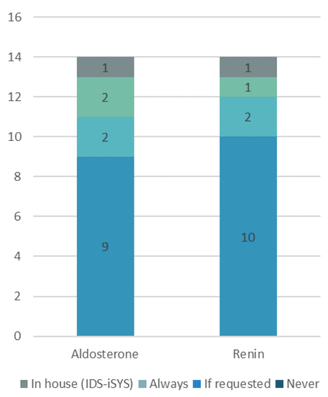
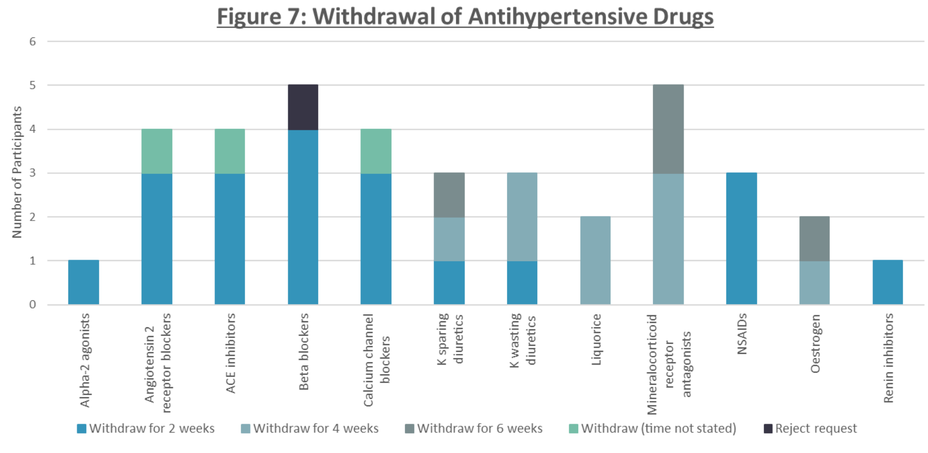


Figure 7: Withdrawal of Antihypertensive Drugs



Recommendations, Standards

Standards were agreed at the meeting of the Thames Audit Group held on 12th November 2024. They are published in full on the website of the Association for Laboratory Medicine and are available from the authors on request. Some of the key standards are presented in the table below.

Investigation of Cushings	Investigation of Phaeochromocytoma and Paraganglioma	Investigation of Primary Hyperaldosteronism
• Laboratories should give advice regarding the choice of investigations for patient groups where the results of investigations may be misleading. • Where salivary cortisol is offered, cortisone should also be reported, particularly if an adrenal tumour is suspected.	• Urine and/or plasma metanephrines should be the recommended first line test in adult patients. • 3-methoxytyramine should be included in urine and plasma metanephrine profiles. • Reference ranges for plasma metanephrines should be specific for seated and/or supine sampling, whichever is offered by the laboratory.	• Aldosterone, renin and ARR should be reported for all patients being investigated for possible PHA. • Ideally samples for renin & aldosterone should be taken in the morning after the patient has been out of bed for at least 2 hours, after being seated for 5-15 minutes.

References: Consensus on Diagnosis and Management of Cushing's Disease: A Guideline Update, M Fleseriu et al, Lancet Diabetes Endocrinol 2021 9(12): 847 – 875. Phaeochromocytoma and Paraganglioma: An Endocrine Society Clinical Practice Guideline, JWM Lenders et al, J Clin Endocrinol Metab 2014 99: 1915 – 1942. A UK National Audit of the Laboratory Investigation of Phaeochromocytoma and Paraganglioma, C Boot et al, Ann Clin Biochem 2022 59(1): 65 – 75. Plasma Methoxytyramine: Clinical Utility with Metanephrines for Diagnosis of Phaeochomocytoma and Paraganglioma, D Rao et al, Eur J Endocrinol 2017 177(2): 103 – 113. The Management of Primary Aldosteronism: Case Detection, Diagnosis and Treatment: An Endocrine Society Clinical Practice Guideline, JW Funder et al, J Clin Endocrinol Metab 2016 101:1889 – 1916