

All Wales Clinical Biochemistry Audit Group

Standards for the Laboratory Investigation of Suspected Pheochromocytoma in Adults

INTRODUCTION

Pheochromocytoma is a rare hormone-secreting tumour usually arising in the adrenal glands which typically causes severe labile hypertension and can have serious consequences. It is therefore desirable to have a simple but sensitive screening strategy. A recent survey of investigations for pheochromocytoma undertaken by Welsh laboratories, presented at an audit meeting in November 2003, showed wide variations in practice. The following core standards are recommended in the light of the survey findings, discussion at this meeting and subsequent consultation.

STANDARDS

1. Availability of Written Protocols

- a) Guidance on urine collection should be available to patients, with instructions on how to collect 24 hour urine samples, a warning about acid splash hazard and advice in the event of a spill.
- b) Guidance for clinicians should be agreed locally by consultation and should include:
 - Advice on sample type.
 - Advice on information required on request forms.
 - Advice on sample transport to the laboratory.
 - Information on which tests will be performed.
 - Indication of "usual" turnaround times.
 - Contact name(s) and number(s) for further advice.

2. Choice of Test

- a) Quantitative assays of either urine metadrenalines (metadrenaline AND normetadrenaline) OR urine catecholamines (adrenaline AND noradrenaline) should be the first choice for initial investigation, as they have the best sensitivity and specificity^{1,2} of currently available tests.
- b) Urine 4-hydroxy 3-methylmandelic acid (HMMA) should not be used alone.
- c) All laboratories should have access to quantitative assays of dopamine, homovanillic acid (HVA) and HMMA for the investigation of neuroblastoma and ganglioneuroma.

3. Acid Preservative

- a) Hydrochloric acid is recommended, but the volume and strength of acid is not important so long as a pH below 3.0 is achieved.
- b) Sample pH should be confirmed on receipt in the laboratory. Samples with a pH exceeding 3.0 are unsuitable for catecholamine assay, but may still be suitable for metadrenaline assay if the pH is adjusted to below 3.0 on receipt.

4. Number of Samples Required

- a) For screening hypertensive patients, a single 24 hour or overnight collection should suffice.
- b) If there is a strong clinical suspicion of pheochromocytoma, 2-3 consecutive collections are recommended.
- c) If the patient has episodic symptoms, consider collection during the period after an "attack"

5. Reference Ranges

- a) Although reference ranges may be difficult to determine locally, where kit manufacturers' or literature ranges are used, their origins should be traceable.
- b) Users of the same commercial reagents should quote similar reference ranges.
- c) Regular audits of investigations for pheochromocytoma are recommended to evaluate case detection rates and confirm the appropriateness of the reference ranges in use.

6. Service Provision

- a) The appropriateness of providing an analytical service locally should be assessed in the context of clinical need, available laboratory expertise and number of requests received.
- b) If assay is delayed, acidified samples may be stored at 4°C for up to 1 week or at -20°C for up to 2 months. However, it is recommended that the turnaround time should not exceed 2 weeks.

- c) Laboratories that provide "in house" assays should participate in an accredited external quality assessment scheme (EQAS).

ACKNOWLEDGEMENTS

Mr. G. Davies.

REFERENCES

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3. Peaston RT, Weinkove C. Measurement of catecholamines and their metabolites. (Review) Ann Clin Biochem 2004; **41**: 17-38.
4. Pillai DN, Earl JW, Duncan MW, *et al.* Biogenic Amines: Significance, Measurement and Clinical Applications. Clin Biochem Revs 1991; **12**: 14-21.
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APPENDIX Calendar of audit process for standards for investigation of phaeochromocytoma

- Nov. 2003 Findings of a survey of 13 Welsh biochemistry laboratories on the tests used for investigating phaeochromocytoma, undertaken by Mr G Davies (Wrexham), presented at an All Wales Clinical Biochemistry Audit Group meeting in Cardiff.
- April 2004 Initial draft standards presented by Mr G Davies at an audit meeting held in Llanelli.
- April 2005 Written draft standards prepared and sent for consultation to clinical biochemists and endocrinologists in Wales, to seek their views.
- Nov. 2005 Final draft presented at an audit meeting held in Llandudno.