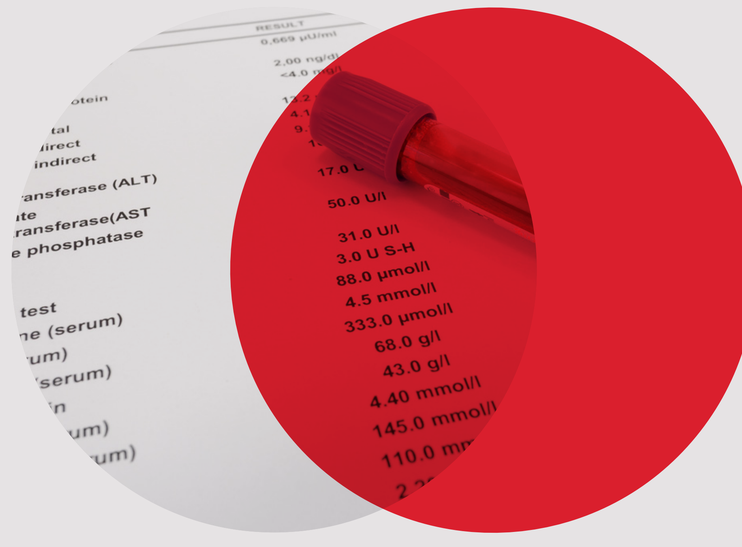
Educational Component of the Royal College of Pathologists of Australasia Quality Assurance Programs (RCPAQAP) Biogenic Amines Program



Gerald Woollard, Kane Fox, Wilson Punyalack, Brett McWhinney, Trisha Andersen, Kirsten Hoad, Sushil Bandodkar, Julia Chang, Talia Novos, Mohammed Saleem

Members of the Australasian Association of Clinical Biochemists RCPAQAP Advisory Committee on Biogenic Amines (ACBA), St Leonards, NSW, 2065, Australia

Introduction

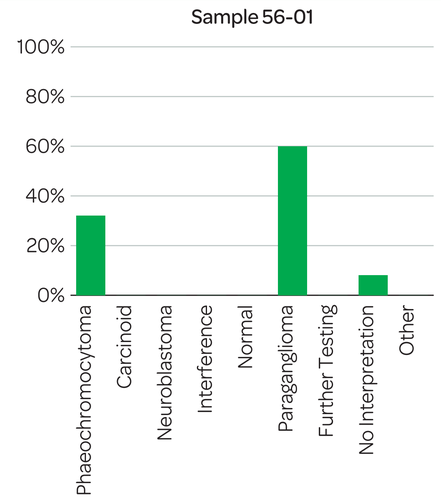
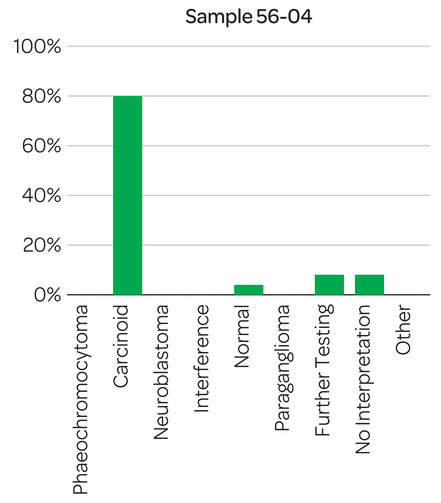
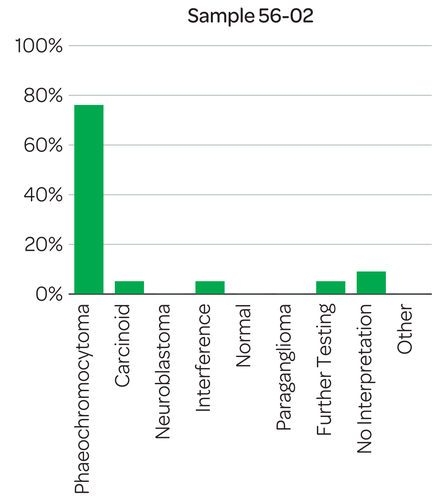
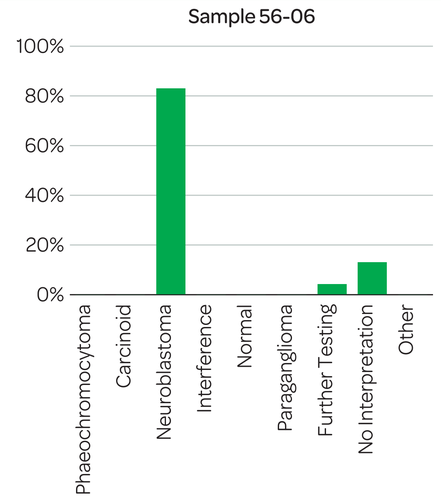
The RCPAQAP co-ordinate an external quality assurance program for laboratories engaged in the measurement of biogenic amines and their metabolites. A linear set of urine samples is provided with known concentrations to assess analytical and methodological performance against predetermined performance limits. This is sufficient to gauge the quantitative aspects of testing but does not portray real-world scenarios seen in practice. To this purpose, ACBA also provides a genuine patient specimen. There is a categorical assessment to allow participants to select a likely diagnosis. But more is needed to help participants appreciate what factors are influential in diagnoses.

Methods

ACBA members retain and send de-identified patient urines from their facilities to Australian Scientific Enterprise (ASE). These are processed and distributed as part of the program. The participants are provided only with the clinical history supplied by the original requestor. This mimics what is usually experienced in real practice and is seldom comprehensive. Phaeochromocytoma and paraganglioma (PPGLs) are rare and complex. Participants indicate the likely clinical scenario from a list of outcomes based on returned results.

Results

ACBA provides clinical comments based on extensive collective experience in their laboratories. Biogenic amines are frequently the first test to be requested when PPGL is suspected. The primary intention is not to formulate a diagnosis (which is not actually known for privacy reasons) but to train participants how to recognise possibilities and probabilities via the biomarker patterns, patient demographic, possible genetic predispositions, confounders and interferences to mirror situations they are likely to encounter in their own facilities.

	Case 1	Case 2	Case 3	Case 4
Patient Information				
Demographic	Female, 27	Male, 42	Male, 54	Male, <16
24Hr Urine Vol (L)	3.57	3.56	4.02	0.94
Creatinine (mmol/L)	3.38	2.73	3.21	2.86
Clinical Notes	36w Pregnant – Hypertension – Previous Paraganglioma resection in 2010	? Neuroendocrine Tumour	Admitted w/ hypertensive crisis – On alpha + beta blockers – ?Invasion into IVC – Right adrenal & liver lesions noted	? Neuroblastoma
Urine Panel *(umol/day)*				
Adrenaline	0.04	0.02	0.60	0.03
Noradrenaline	**11.53**	0.18	0.71	0.37
Dopamine	2.1	0.5	1.17	**21.43**
5HIAA	10	**1161**	12	4
HMMA	**100**	28	42	**105**
HVA	24	32	23	**733**
Serotonin	0.12	**10.3**	0.46	0.1
T-Met	0.5	0.46	**9.45**	0.4
T-Normet	**45**	1.21	**4.4**	**7.12**
T-3MT	**2.88**	0.98	1.05	**13.12**
Participants' Diagnoses				
ACBA Comment	This patient has a PPGL recurrence after a previous resection. The tumour has a noradrenergic phenotype with normal adrenaline & metanephrine. The raised 3-methoxytyramine is suggestive of malignancy from a syndromic tumour. Genetic testing must be done with the greatest likelihood of an SDHB, SDHD or VHL mutation.	These results confirm the presence of a serotonin secreting neuroendocrine tumour probably situated in GI tract. The very high levels predispose to an increased risk of carcinoid heart disease.	This patient presented with classical phaeochromocytoma symptoms with evidence of an adrenal mass. The raised normetanephrine and extreme metanephrine are confirmatory of a phaeochromocytoma. Of particular note is the normal noradrenaline in the face of its raised metabolites. This is reflective of its inferior diagnostic usefulness. Adrenaline is more aligned to metanephrine in this case.	Not much is known about this patient, but his results clearly demonstrate a neuroblastoma. Dopamine and its major metabolites HVA and 3-methoxytyramine are all raised. Raised normetanephrine with normal noradrenaline is also a common feature of neuroblastoma. Adrenaline and metanephrine are invariably unaffected.

Conclusion

Requests for the measurement of biogenic amines and their metabolites serve the diagnostic purpose to assess the presence or absence of PPGL. These compounds are not uniquely tumour products and levels can be raised for pathological physiological or pharmacological reasons. RCPAQAP linear set provides quantitative surety.

The demonstration of raised levels is insufficient for labs to provide a complete diagnostic service. Hence RCPAQAP provides real patient samples with interpretive comments as a conduit for participants to gain further insight into how to assess biogenic amine levels. In naturalistic settings the interpretation can be affected by sampling errors, meagre clinical details, co-morbidity, genetic predisposition, drug therapy and so on.

RCPAQAP offers participants instructive commentary from the experienced ACBA group. This will assist participants to extend their service by recognizing confounders, gauging likelihoods and prognostic indicators. These go beyond the issue of numeric data against reference limits alone.

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