Biotin: Potential for interference in Roche Immunoassay tests

NHS Lothian transitioned its automated laboratory equipment to Roche diagnostics on Monday 25th October, 2021. High levels of circulating biotin have the potential to interfere with Roche immunoassays due to their component biotin-streptavidin binding mechanism. **Biotin levels associated with normal dietary intake and multivitamin use are insufficient to cause assay interference**. However, very high doses may be prescribed as a therapy for multiple sclerosis (300 mg/day [(1)]) as well as biotinidase deficiency (5-10 mg/day) and holocarboxylase synthetase deficiency (30-40 mg/day) [(2)]. Doses > 5 mg/day are also present in increasingly popular over-the-counter supplements for hair and nail strength. Numerous reports of erroneous lab results have been linked to supra-physiological biotin intake [(3)].

For the majority of our immunoassay analytes, Roche recommends that samples should not be collected until at least 8 hours post-dose in patients receiving > 5 mg biotin per day, with interference thresholds ranging from 21 to 100 ng/mL (see Table 1). However, endogenous biotin interference is not thought to be a significant concern for hs Troponin T, NTproBNP, total T3, testosterone, PSA and thyroglobulin (no interference detected up to at least 1200 ng/mL biotin). The lack of susceptibility to biotin interference in troponin and total T3 assays may reduce the risk of two particular concerns: inappropriate MI rule-out due to false negative troponin results and misdiagnosis of hyperthyroidism. The latter is present in the majority of biotin interference case reports to date.

Immunoassays that may be falsely **elevated** with biotin interference		Immunoassays that may be falsely **decreased** with biotin interference	
Vitamin B12	(50 ng/mL)	ACTH	(70 ng/mL)
Cortisol	(70 ng/mL)	AFP	(180 ng/mL)
DHEAS	(70 ng/mL)	AMH	(30 ng/mL)
Digoxin	(100 ng/mL)	hCG	(70 ng/mL)
Folate	(21 ng/mL)	CA125	(70 ng/mL)
Free T3	(70 ng/mL)	CEA	(70 ng/mL)
Free T4	(100 ng/mL)	C-peptide	(60 ng/mL)
Oestradiol	(36 ng/mL)	Ferritin	(50 ng/mL)
Progesterone	(30 ng/mL)	FSH	(60 ng/mL)
Thyroglobulin Antibody (TgAb; 60 ng/mL)		GH	(30 ng/mL)
TSH Receptor Antibody (TRAb; 600 ng/mL)		Insulin	(60 ng/mL)
Vitamin D	(30 ng/mL)	LH	(50 ng/mL)
		Prolactin	(40 ng/mL)
		PTH	(50 ng/mL)
		SHBG	(70 ng/mL)
		TSH	(25 ng/mL)

Table 1. Potential for biotin interference in Roche immunoassays (interference threshold indicated in brackets).

A recent summary of case reports of interference found MS and metabolic disease therapy to be the most common reasons for high-dose biotin intake [(3)]. The risk for MS patients should be mitigated going forward due to recent recommendations advising against biotin therapy owing to the risk of adverse events [(4)]. Biotin-treated IEMs are therefore the group most likely to be impacted, particularly as biotin washout in advance of testing is likely to be unsafe.

In the wider population, a UK study detected biotin levels associated with interference in 0/524 patient samples [5]. While a larger US study found 7.4 % and 0.5 % prevalence of biotin levels >10 ng/mL and >30 ng/mL respectively in an ED cohort, only a single patient had a test ordered for which their biotin level exceeded the manufacturer's threshold [6]. Available evidence would therefore indicate interference due to non-prescribed biotin to be relatively rare.

Study (Ref)	Country	Study size	n (%) > 10 ng/mL	n (%) > 30 ng/mL
(5)	UK	524	0 (0%)	0 (0%)
(6)	USA	1442	107 (7.5%)	7 (0.5%)
(7)	Australia	490	4 (0.8%)	2 (0.4%)
(8)	Netherlands	1000	2 (0.2%)	2 (0.2%)

Locally, if there is any concern over result reliability, please discuss this with the endocrine biochemist (0131 242 6880) who can arrange for consistency checking using an alternative assay.

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