

Dear User,

Potential for interference in immunoassays

Summary: *Biotin supplements can interfere significantly with immunoassay tests used in the clinical biochemistry laboratory and produce artefactually low or high results. If you have an unexpected result, please ask your patient if they are taking biotin.*

Immunoassays tests are biochemical tests commonly employed in the clinical biochemistry laboratory to measure the concentration of analytes. The basic mechanism of an immunoassay test is dependent on antibody and antigen interaction from which a signal is generated to indicate the concentration of the analyte of interest. Manufacturers of laboratory tests commonly use the Biotin-Streptavidin binding couple as an analyte extraction step in an immunoassay test's design.

Biotin containing supplements may interfere with the Biotin-Streptavidin binding couple and so in patients taking biotin supplements – (depending on assay design), biotin interference may cause artefactually high results (competitive assay), or artefactually low results (sandwich design).

If you have a test result that does not fit the clinical picture, you may wish to exclude possible biotin interference as a cause by asking the patient/parent/carer about any over the counter supplements or checking for a biotin prescription. Patients may not know they are taking Biotin due to sometimes obscure product labelling. N.B. products marketed for hair, skin and nails often contain Biotin.

In patients with normal diets and low dose multivitamin preparations, biotin should not be present at concentrations high enough to cause interference.

5 to 10mg biotin supplements per tablet are available over the counter in many health stores and online. High-dose biotin (100mg) is sometimes used to treat metabolic diseases (isolated carboxylase defects and defects of biotin metabolism).

Mega doses (up to 300mg/day) of biotin have also been used in clinical trials in the treatment of Multiple Sclerosis.

Table1: Suggested time between biotin supplementation and venepuncture

	Dose per day (µg)	Equivalent dose per day (mg)	Advised period between last biotin dose and venepuncture
Low dose	100-150	0.1 – 0.15	>8hrs
High Dose	5000-10000	5 - 10	>48hrs
Mega dose	100000	100	>72hrs

N.B. Biotin is renally excreted – it is therefore likely that in renal dysfunction, plasma biotin concentrations are higher than expected, and interference with immunoassay performance may occur at lower doses of biotin supplementation.

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Table 2: Effect of Biotin on Roche Immunoassays

Analyte	Will the interference increase or decrease the analyte level?	Estimated oral intake that may cause interference (mg per day)
Alpha-Fetoprotein	Decrease ↓	100
CA-125	Decrease ↓	100
CA19-9	Increase ↑	100
Carcinoembryonic antigen	Decrease ↓	100
Cortisol	Increase ↑	100
C-Peptide	Decrease ↓	100
Cyclosporin	Increase ↑	5-10
Oestradiol	Increase ↑	100
Ferritin	Decrease ↓	100
Folate	Increase ↑	5-10
Follicle Stimulating Hormone	Decrease ↓	100
Free T3	Increase ↑	100
Free T4	Increase ↑	100
Human Chorionic Gonadotropin	Decrease ↓	100
Growth Hormone	Decrease ↓	5-10
Luteinising Hormone	Decrease ↓	100
Progesterone	Increase ↑	5-10
Prolactin	Decrease ↓	100
Parathyroid hormone	Decrease ↓	100
Sex-Hormone Binding Globulin	Decrease ↓	100
Tacrolimus	Increase ↑	5-10
Testosterone	Increase ↑	5-10
Thyroid Peroxidase	Increase ↑	1.0-1.5
Vitamin B12	Increase ↑	100
Vitamin D	Increase ↑	5-10

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Manufacturers have been working to address biotin assay interference and have released new generations of assays to reduce biotin interference. The assays listed in table 3 state previously affected assays that are now Biotin resistant with the date the change came into effect.

Table 3: Assays previously affected by biotin interference

Assay	Possible interference prior to this date: (Biotin interference no longer an issue after this date)	Would the interference increase or decrease the analyte level?	Estimated oral intake that may cause interference (mg per day)
NT- proBNP	19.06.2020	Decrease ↓	5-10
Prostate Specific Antigen	03.06.2020	Decrease ↓	100
Troponin-T	13.05.2019	Decrease ↓	5-10

**Finally, erroneous results can occur unexpectedly with any specimen and there is no practical means of identifying specimens likely to cause problems in immunoassays.
Please contact the clinical biochemistry laboratory if there is any doubt about a result and/or potential interference.**

Sources

Sturgeon C.M. and Viljoen A. (2011). *Analytical error and interference in immunoassay: minimizing risk*. Annals of Clinical Biochemistry, Volume 48, p418-432.

Grimsey P., Frey N., Bendig G., Zitzler J., Lorenz O., Kasapic D. and Zaugg C.E. (2017). *Population pharmacokinetics of exogenous biotin and the relationship between biotin serum levels and in vitro immunoassay interference*. International Journal of Pharmacokinetics, Volume 2 (4), p247-256.

Trambas C., Lu Z., Yen T. and Sikaris K. (2017). *Characterization of the scope and magnitude of biotin interference in susceptible Roche Elecsys competitive and sandwich immunoassays*. Annals of Clinical Biochemistry, Volume 55(2), p205-215.

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