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Biotin-Related Interference in Laboratory Testing

Immunoassays are fast, easy, and inexpensive tests used in measurement of analytes ranging from hormones and antibodies to proteins and drugs present in a wide variety of specimens including whole blood, serum/plasma, urine, cerebrospinal fluid, sweat and meconium. Numerous variations of this test including competitive and sandwich immunoassays with either colorimetric, fluorometric, or chemiluminescent signals are available. Despite versatility of the immunoassays, this technology has had some challenges such as interferences, causing results to be falsely high (positive interference) or falsely low (negative interference). The most common and well known interference is due to presence of heterophile antibodies. Autoantibodies in patients diagnosed with autoimmune disorders and therapeutically administered antibodies for disease management have further populated the list of interfering substances.

The most recent addition to the list of interfering substances is biotin, a water soluble vitamin B (B7) and essential co-factor involved in fatty acid synthesis and energy production. Deficiency of biotinidase causes biotin deficiency, a rare inherited metabolic disorder that may present with seizure activity, breathing problems, and later developmental delays. Neonatal screening tests, both in the states of Missouri and Kansas include evaluation of biotinidase enzyme. Secondary causes of biotin deficiency include treatment with certain anticonvulsant drugs, broad-spectrum antibiotics, and total parental treatment without biotin supplement.

The daily requirement of biotin is in the range of 150-300 mcg/d. Intestinal bacteria synthesize significant quantities of biotin and with body's ability to recycle substantial fraction of total biotin, the recommended daily intake (RDI) is low and in the range of 30-70 mcg/d. However, some studies have

shown that high doses of biotin (10,000 times RDI) improve clinical outcomes and quality of life in patients with progressive multiple sclerosis (Sedal F., *et. al.* Neuropharmacology (2015)). Biotin is also a common component of many multivitamin preparations, usually in concentrations approaching 100 times RDI.

Many immunoassays use biotin streptavidin mechanisms in their assay design. Moderate doses of biotin (100 times RDI) have been reported to cause interference resulting in abnormal laboratory tests including thyroid function tests (Sehgal S., *et. al.* ENDO 2016 Poster), ferritin, estradiol and thyroglobulin. A similar study also confirmed falsely low TSH levels resulting from biotin interference. Recently, Endocrine News, a publication of Endocrine Society issued a warning statement regarding biotin interference in test results of patients consuming mega doses of this supplement.

Depending on the immunoassay type, namely competitive or sandwich, the results can be falsely high or falsely low, respectively. At Saint Luke's Laboratories, some commonly requested tests that may be biotin-affected include TSH, iPTH, ferritin, and vitamin B12. Clinicians should consider biotin interference if immunoassay results do not match the clinical presentation. Patients should be requested to withhold biotin intake for 24 to 48 hours before blood draws.

Group B Streptococcus PCR Change

Saint Luke's Molecular Diagnostics has performed PCR testing for Group B streptococcus since December 2005. Effective immediately, this testing has been moved to Microbiology and will be performed on GeneXpert instrumentation, which eliminates the need for batch testing and improves result turnaround time. Sample collection is unchanged and consists of a vaginal/rectal sample submitted on Culturette or Eswab. Susceptibility testing is performed by request on penicillin-allergic patients.

Basics of Urine Culture Interpretation

Urine Culture Result (cfu/mL=colonies per mL urine)	Interpretation
No growth, or <1000 cfu/mL	Urine is sterile, infection is not likely.
Any organism <10,000 cfu/mL	Organism present in low numbers. Usually this indicates contamination or colonization, not infection. Routine identification and susceptibility is not performed. If patient is pregnant, immunocompromised or post-uologic surgery, further work-up may be indicated. Contact Microbiology at 932-2435.
Two organisms with 1,000 to 99,000 cfu/mL	May represent contamination, colonization or infection. Identification reported, routine susceptibility not performed. If clinical circumstances warrant further workup, contact Microbiology at 932-2435.
One organism with 10,000 to 99,000 or one/two organisms >100,000 cfu/mL	May represent infection. Identification and appropriate susceptibility testing routinely performed.
Three or more bacterial species isolated	Contamination during the collection process is likely. Consider repeat specimen collection.
Additional guidelines	
Organisms normally considered to be skin or perineal flora, which do not have susceptibility testing performed	Lactobacillus Corynebacteria, urease-negative Streptococci (non-beta-hemolytic) Coagulase-negative staphylococci
Organisms that may cause infection, but susceptibility testing is not indicated because susceptibility is predictable	Beta-hemolytic streptococci (unless penicillin allergic-indicate on order) Aerococcus Staphylococcus saprophyticus Gardnerella vaginalis
Group B streptococcus	Group B strep in any amount is identified and reported on women of child-bearing age. Per CDC guidelines, if the patient is pregnant, the presence of urinary Group B strep may have the same implications as a positive finding of Group B strep from a vaginal/rectal screen.
Staphylococcus aureus	Staphylococcus aureus is considered significant in any amount and susceptibility testing is performed.
Yeast	Yeast may represent contamination, colonization or infection. The presence of yeast in any amount is reported. Yeast in pure culture is routinely identified to species.

References:

McCarter, et al, *Laboratory Diagnosis of Urinary Tract Infections*, Cumitech 2C, ASM Press.
Urine Culture Procedure, Saint Luke's Microbiology, Reviewed 1/3/16.