Interference by Dietary Supplements in Lab Assays

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Disclosures

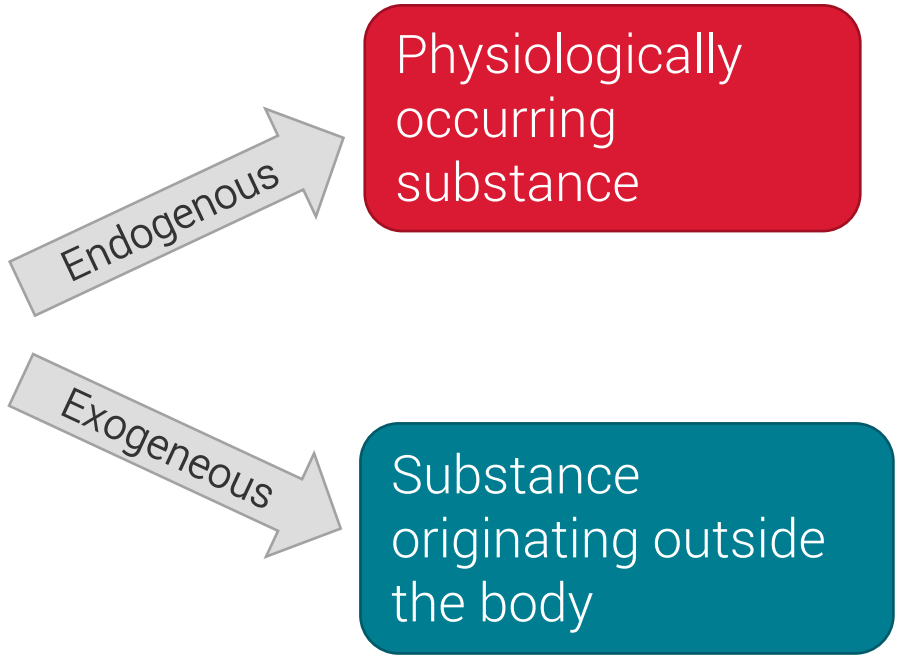
- Nothing to disclose
- Any vendor/brand names shown in the presentation are only for educational purposes

Learning objectives

1. Provide an overview of analytical interferences in laboratory assays.
2. Describe potential interference caused by megadose biotin and vitamin C supplementation.
3. Discuss strategies to detect and mitigate such interferences.

What is analytical interference?

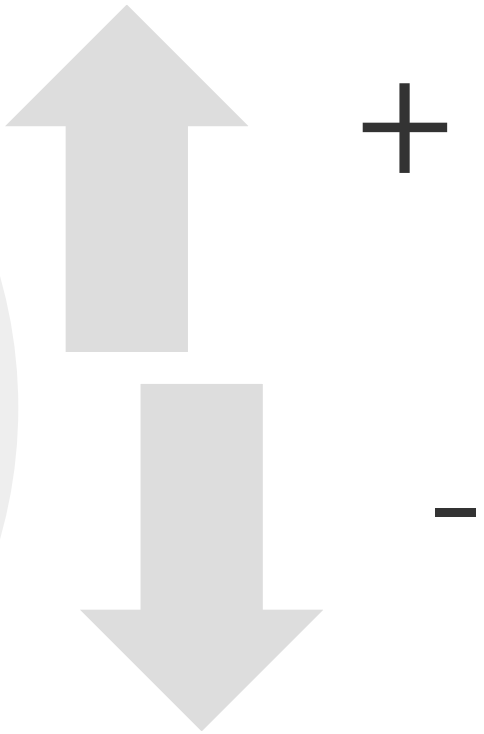
A cause of medically significant difference in the test result due to the effect of another component or property of the sample



CLSI EP07-ED3:2018 Interference Testing in Clinical Chemistry, 3rd Edition

Why interferences are a concern?

The magnitude and direction of error due to an interference can influence **medical decisions**



What are some common interferences?

Substances produced in pathological conditions

Compounds introduced during patient treatment

Endogenous substances present in large quantities

Contaminants inadvertently introduced during specimen handling

The specimen matrix itself

Substances ingested by the patient

CLSI EP07-ED3:2018 Interference Testing in Clinical Chemistry, 3rd Edition

Types of dietary supplements

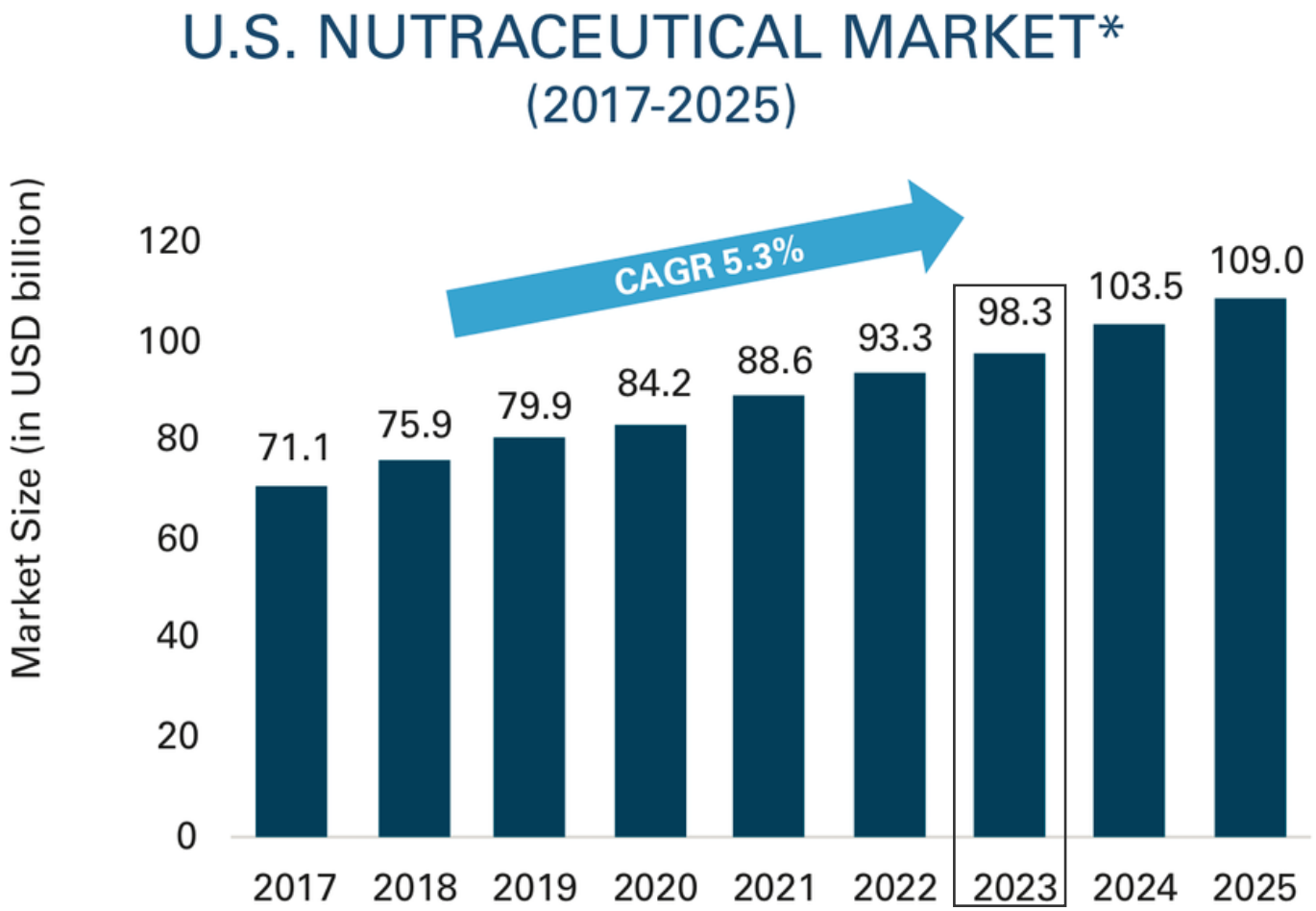
Defined

- Vitamins
- Minerals

Complex

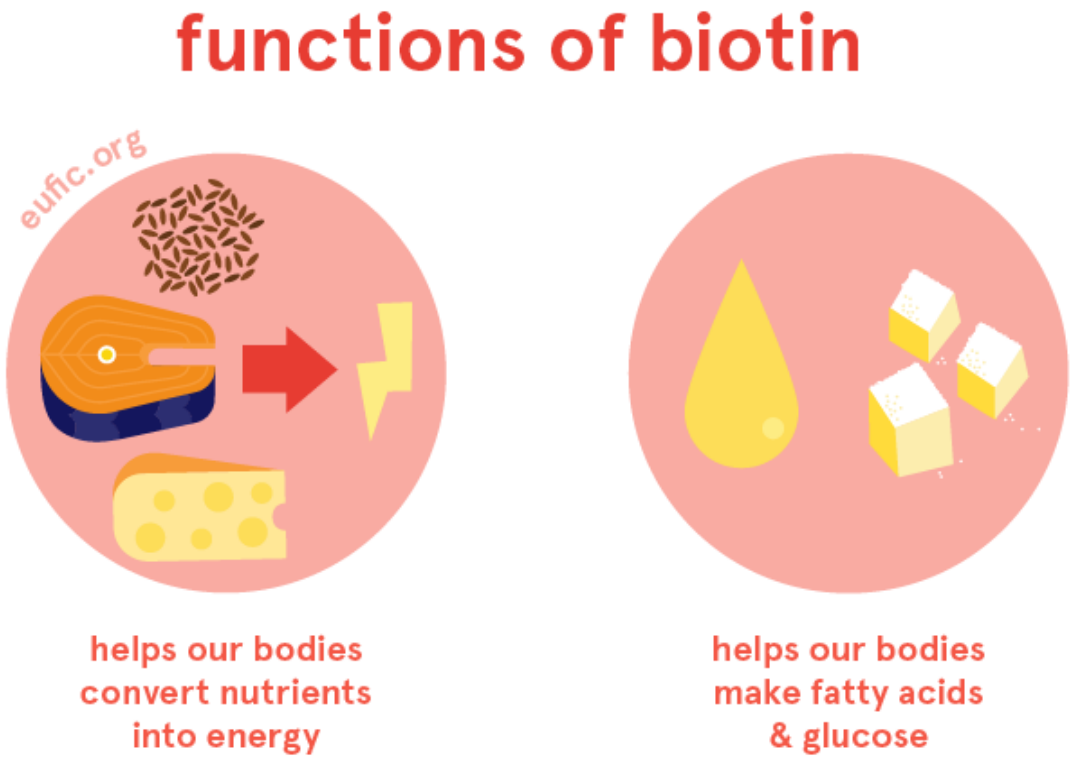
- Energy drinks
- Turmeric
- Blueberry extract
- Ashwagandha

Dietary supplements



https://www.healthcarepackaging.com/markets/neutraceuticals-functional/article/13296428/the-global-market-for-nutraceuticals-set-for-robust-growth

Biotin (vitamin B7)



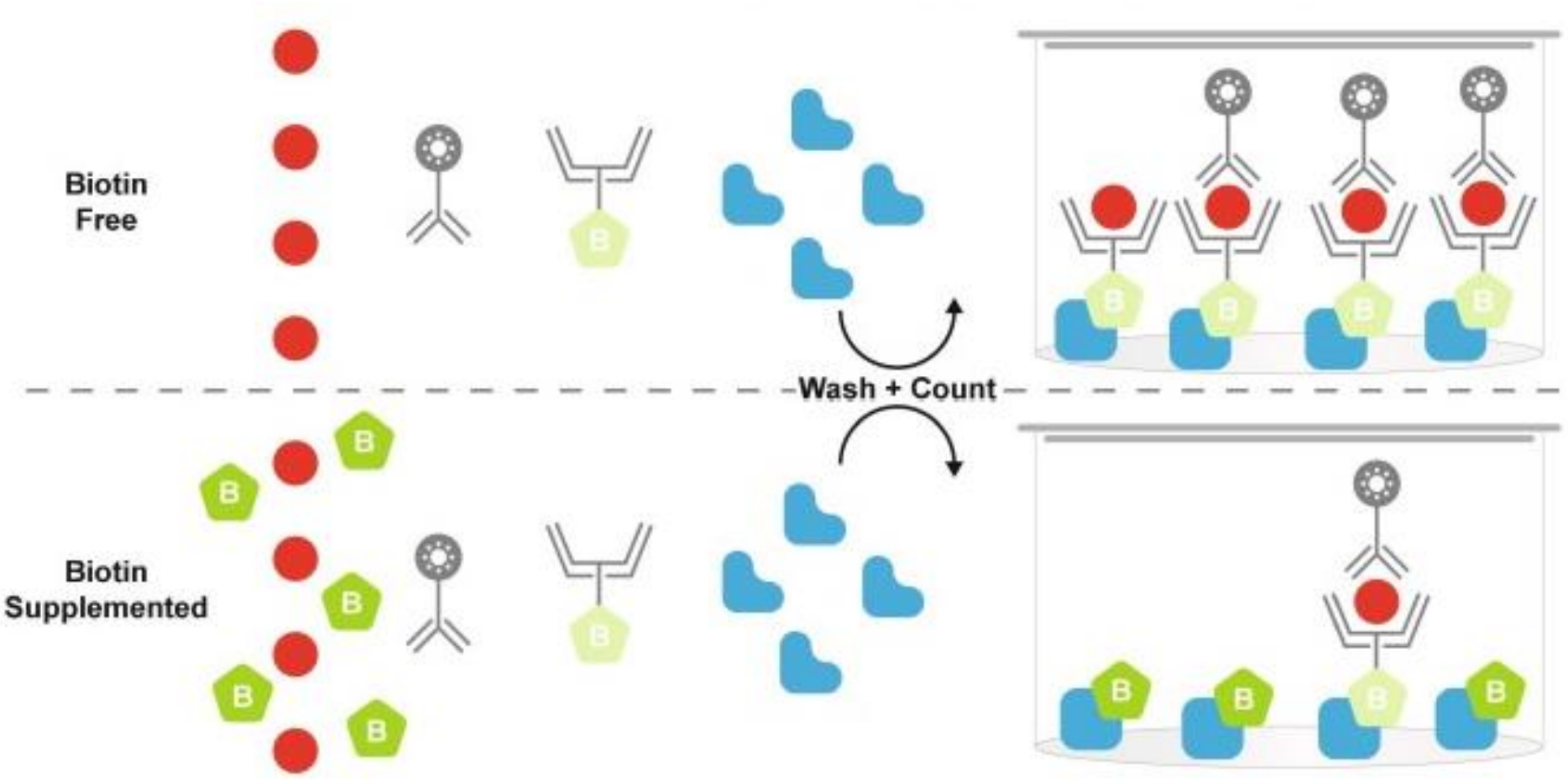
- Daily recommended intake: up to 30 µg
- High-dose (up to 100 mg) biotin supplements available over the counter
- Supplementation for medical necessity:
  - » Biotinidase and carboxylase deficiencies, and peripheral neuropathy
- No evidence for hair and nail health improvement in non-deficient individuals

https://www.eufic.org/en/vitamins-and-minerals

https://ods.od.nih.gov/factsheets/Biotin-Consumer/

How does biotin interfere with lab assays?

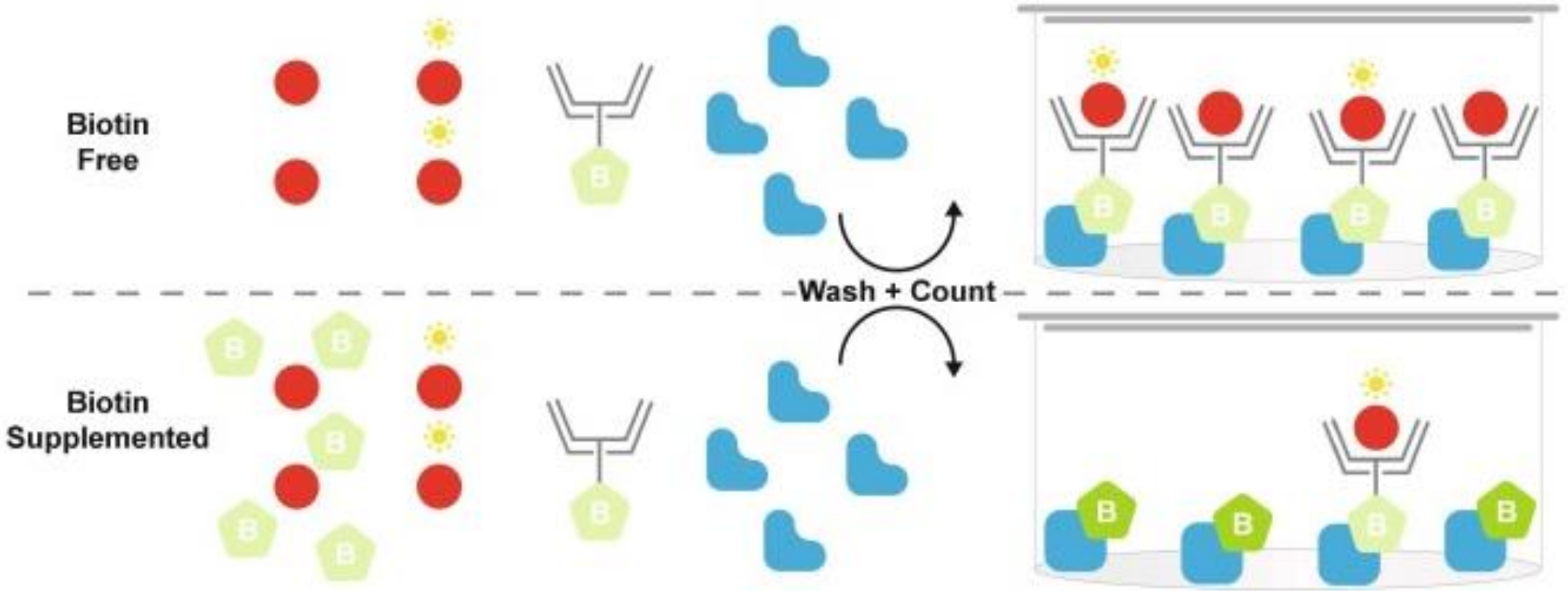
Non-competitive Immunoassay



Bowen et al, Clin. Biochem (2019)

How does biotin interfere with lab assays?

Competitive Immunoassay



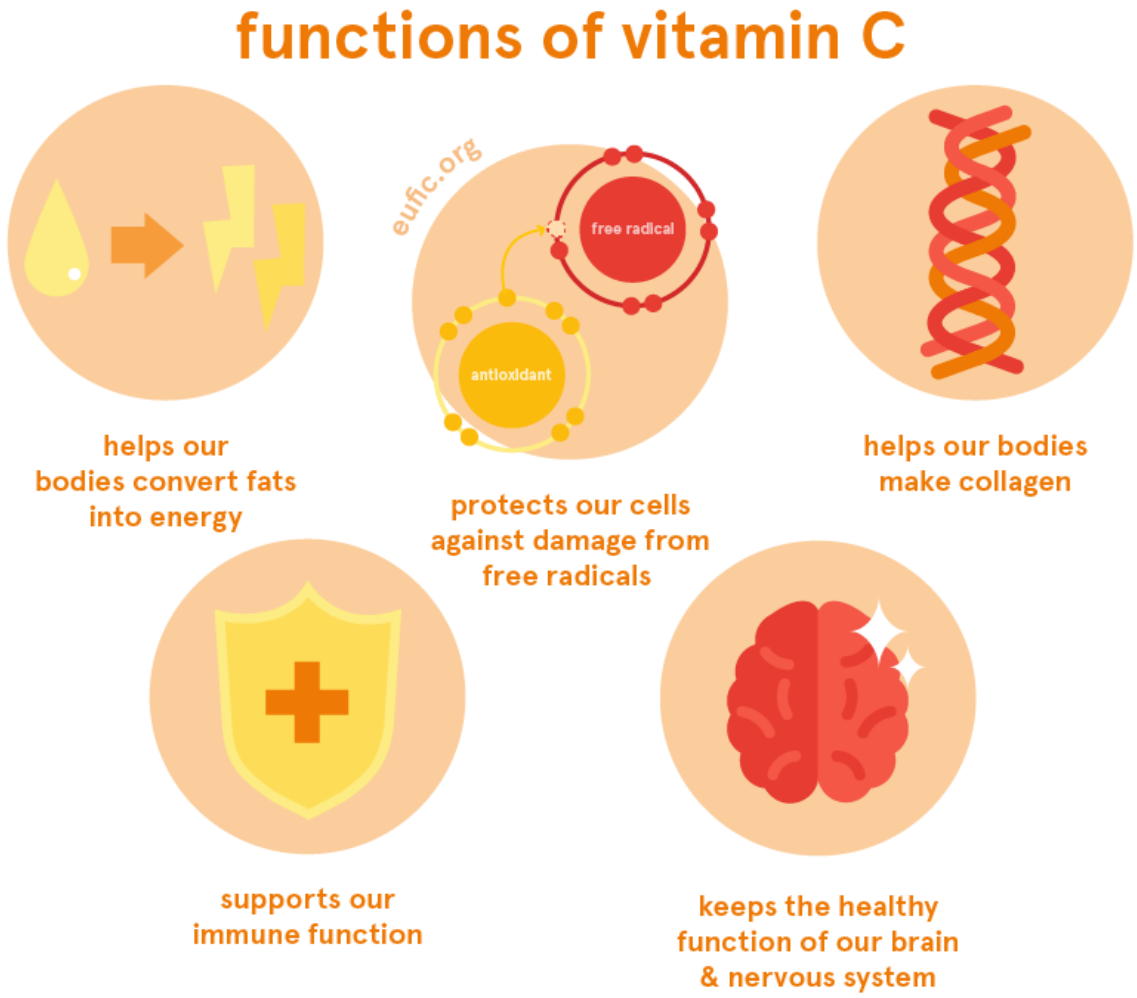
Bowen et al, Clin. Biochem (2019)

Which assays could be affected by biotin overdose?

- Troponin I
- FSH
- Total T4
- Thyroglobulin
- HAV, IgM
- CA 19-9

Li D, Ferguson A, Cervinski MA, Lynch KL, Kyle PB. AACC guidance document on biotin interference in laboratory tests

Ascorbic acid (Vitamin C)



- Daily recommended intake: up to 120 mg
- High-dose (up to 1000 mg) supplements available over the counter
- Supplementation for medical necessity:
  - » Cancer
  - » Sepsis
  - » Burns
- Limited evidence to suggest lower risk of developing cataracts

https://www.eufic.org/en/vitamins-and-minerals

https://ods.od.nih.gov/factsheets/Biotin-Consumer/

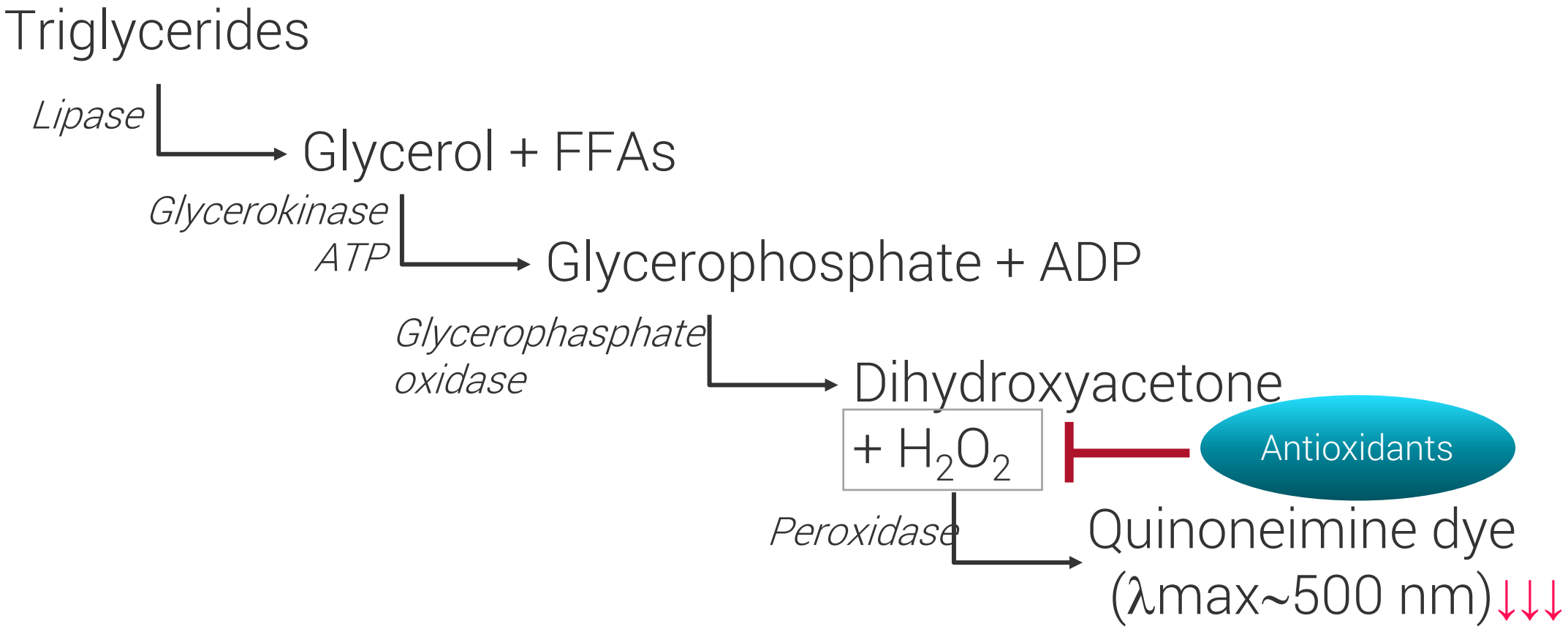
Case study – suspiciously low lipid values in a serum specimen

- A 58-year-old female from a wellness clinic had a lipid panel ordered.
- Other CVD risk assessment tests were also ordered.
- Testing was performed on a Roche Cobas c502 platform.
- Results were flagged and sent for medical director review.

Lipid panel	Results	Desirable
Triglycerides	0	149 mg/dL or less
Total Cholesterol	-8	199 mg/dL or less
HDL-C	30	40 mg/dL or less
LDL-C_{Calc}	n/a	129 mg/dL or less
LDL-C_{Direct}	114	129 mg/dL or less

Pandya et al, Clin Biochem (2021)

Trinder-based assays: triglycerides



The usual suspects

Contents lists available at ScienceDirect

Clinical Biochemistry

journal homepage: www.elsevier.com/locate/clinbiochem

N-acetylcysteine interference of Trinder-based assays

Jonathan R. Genzen [a,b,*], Joshua J. Hunsaker [a], Louis S. Nelson [c], Brett A. Faine [d], Matthew D. Krasowski [c]

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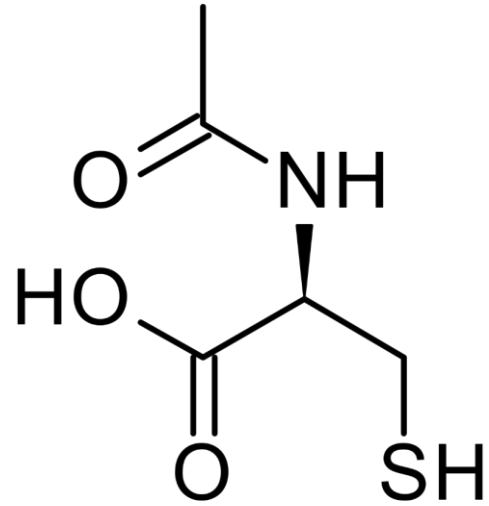
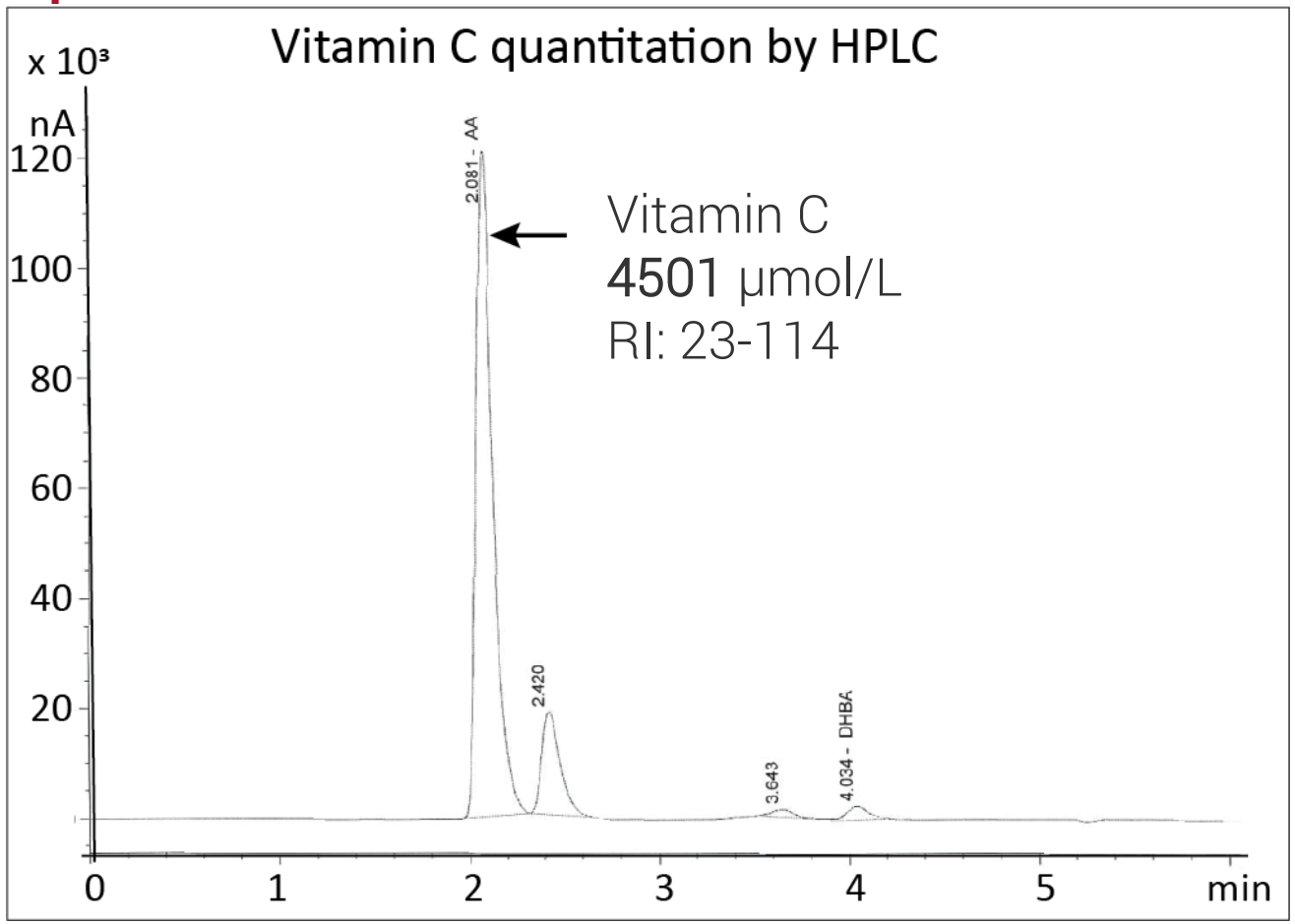


But the patient is from a wellness clinic not ED

https://en.wikipedia.org/wiki/Acetylcysteine

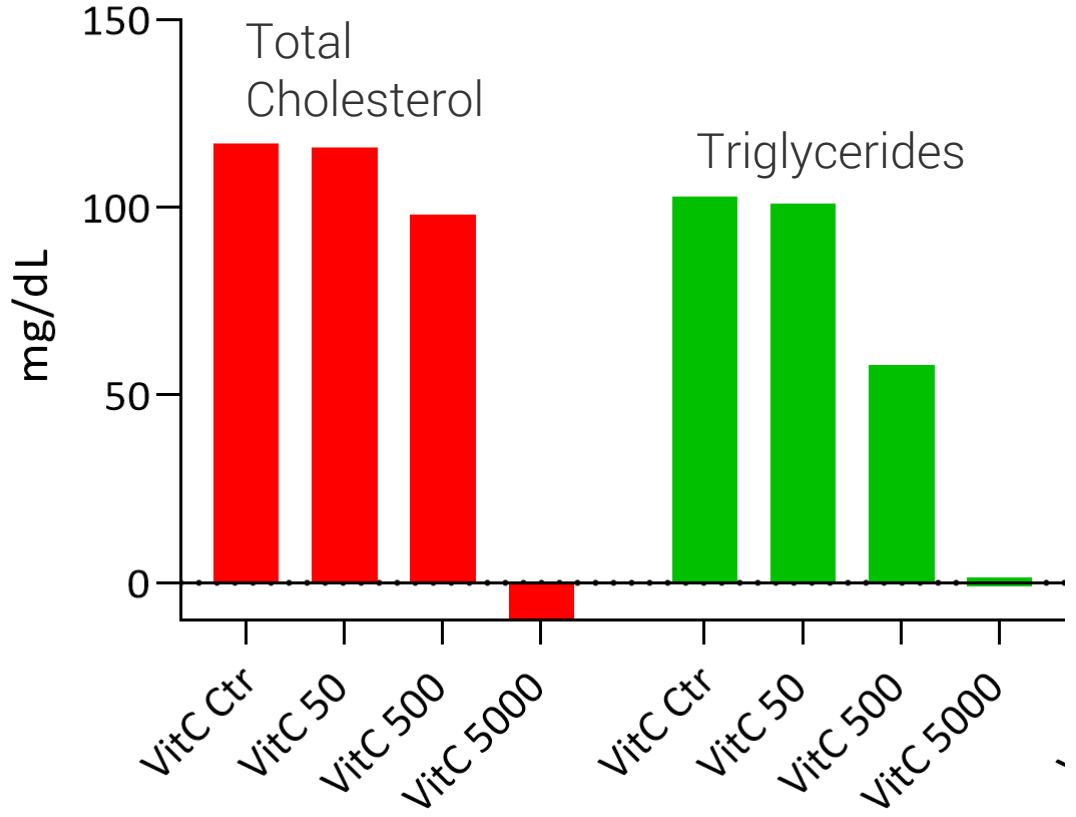
Detection of vitamin C in the patient's specimen



4 of these 1000 mg tablets

Pandya et al, Clin Biochem (2021)

Dose-dependent effect of vitamin C on lipid assays

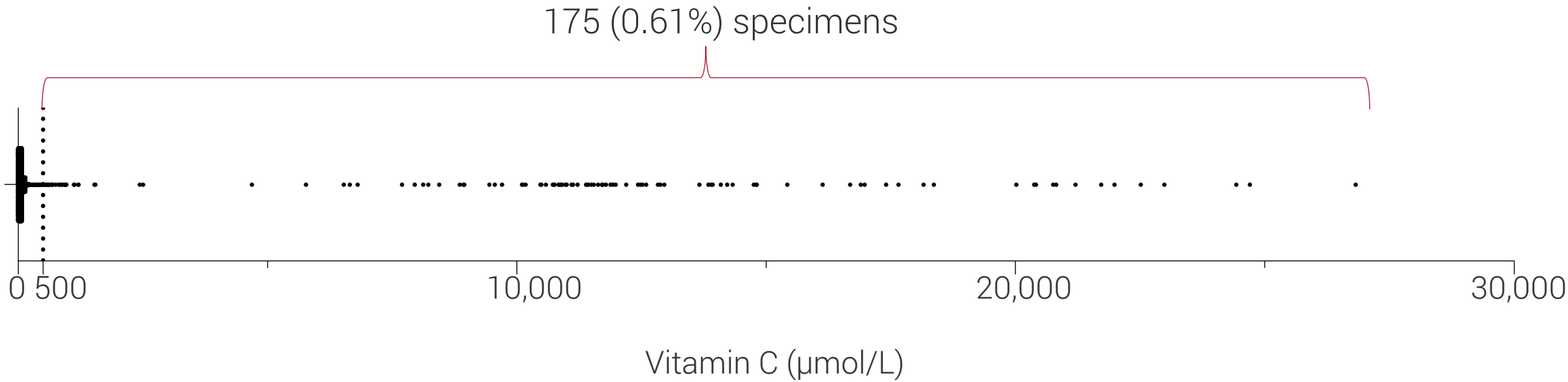


Vitamin C-spiked serum

Why are these results concerning?

While a drastic change may be obvious, changes that bring analyte values **from abnormal to normal** may go unnoticed

Is this an isolated case?



n= 28611

Courtesy: ABC Lab, ARUP

Which assays might be affected by vitamin C overdose?

- Lipid panel
- Uric acid
- Enzymatic creatinine
- Potentiometric assays for electrolytes
- Urine dipstick tests
- Point of care glucometers

Interference in point of care glucometers

Unintended Consequence of High-Dose Vitamin C Therapy for an Oncology Patient: Evaluation of Ascorbic Acid Interference With Three Hospital-Use Glucose Meters

Brooke M Katzman [1], Brandon R Kelley [1], Gayle R Deobald [1], Nikki K Myhre [1], Sean A Agger [2], Brad S Karon [1]

Unlicensed Published by De Gruyter November 19, 2020

Significant interference on specific point-of-care glucose measurements due to high dose of intravenous vitamin C therapy in critically ill patients

Daan ten Berge, Wim Muller, Albertus Beishuizen, Alexander Daniel Cornet, Robbert Slingerland and Johannes Krabbe

From the journal Clinical Chemistry and Laboratory Medicine (CCLM)
https://doi.org/10.1515/cclm-2020-1445

Delayed Diagnosis of Severe Hypoglycemia in a Septic Patient With Chronic Renal Failure

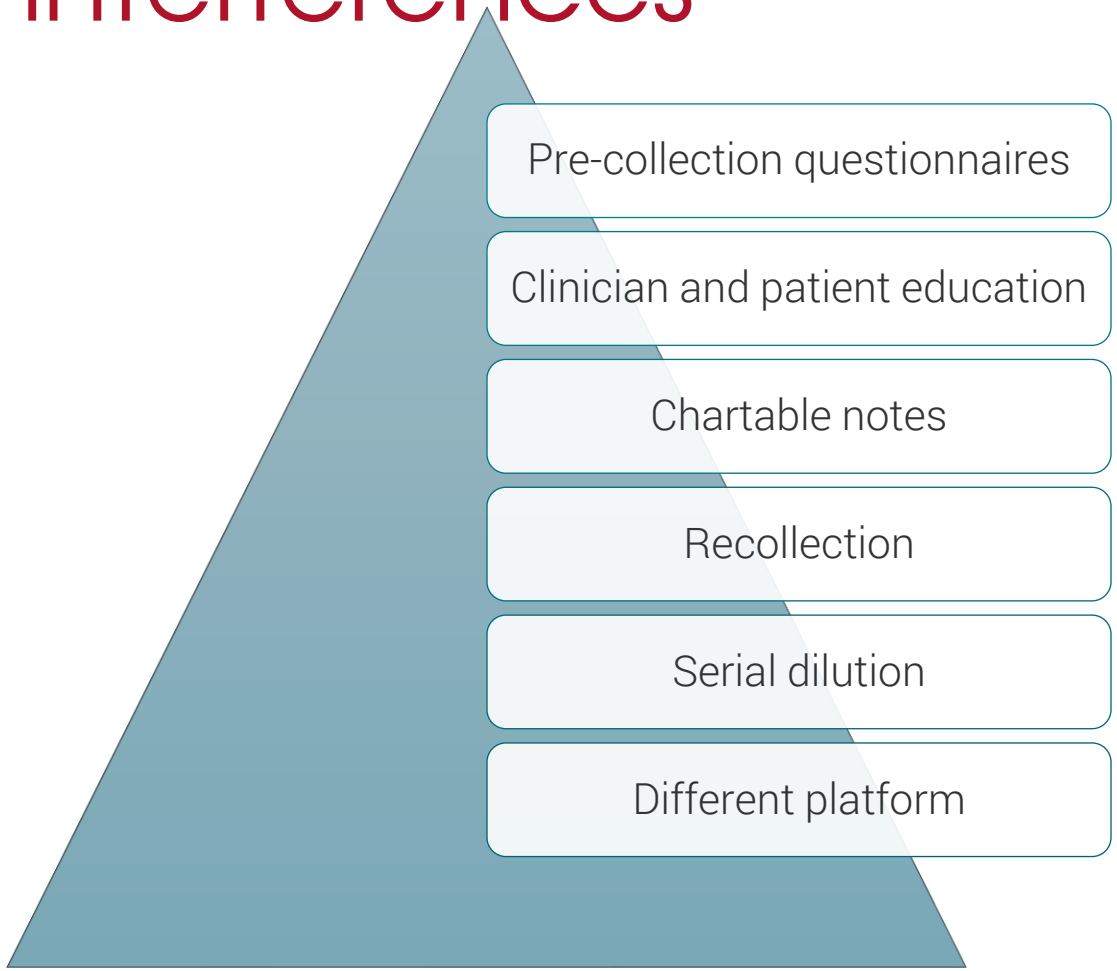
Daan Ten Berge [1], Fokko Manning [2], Vera Silderhuis [2], Saskia Deijns [3], Marie-Jose Pouwels [3], Hans Krabbe [1, 4], Albertus Beishuizen [2]

1. Department of Clinical Chemistry and Laboratory Medicine, Medisch Spectrum Twente, Enschede, NLD 2. Intensive Care Center, Medisch Spectrum Twente, Enschede, NLD 3. Department of Internal Medicine, Medisch Spectrum Twente, Enschede, NLD 4. Department of Clinical Chemistry and Laboratory Medicine, Medlon BV, Enschede, NLD

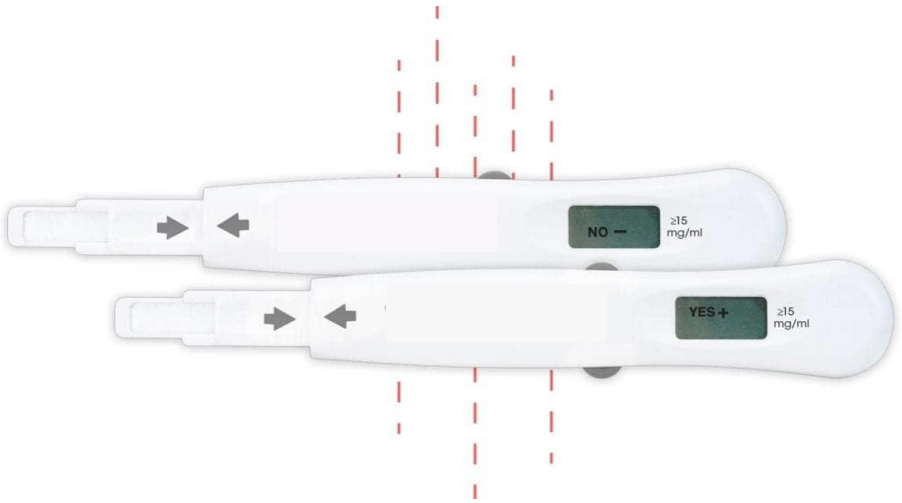
What are the signs of assay interference?

- Delta flags without obvious clinical or technical explanation
- Non-physiological results (e.g., negative values)
- Non-linear dilutions
- Clinician inquiries

Approaches for preventing and mitigating interferences

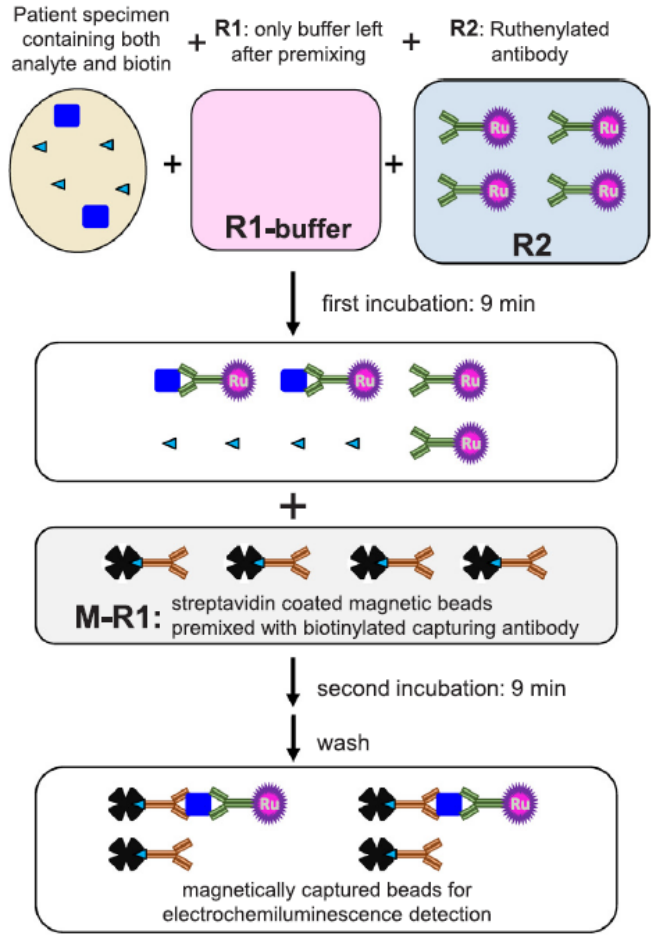


Detecting and mitigating biotin interference



Biotin detection

Biotin pre-capture

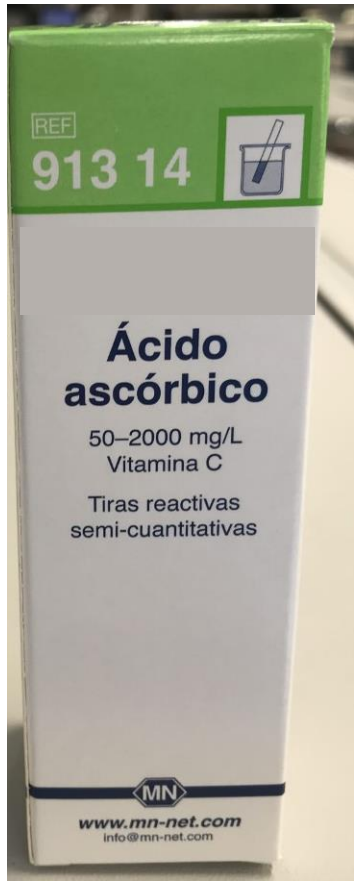


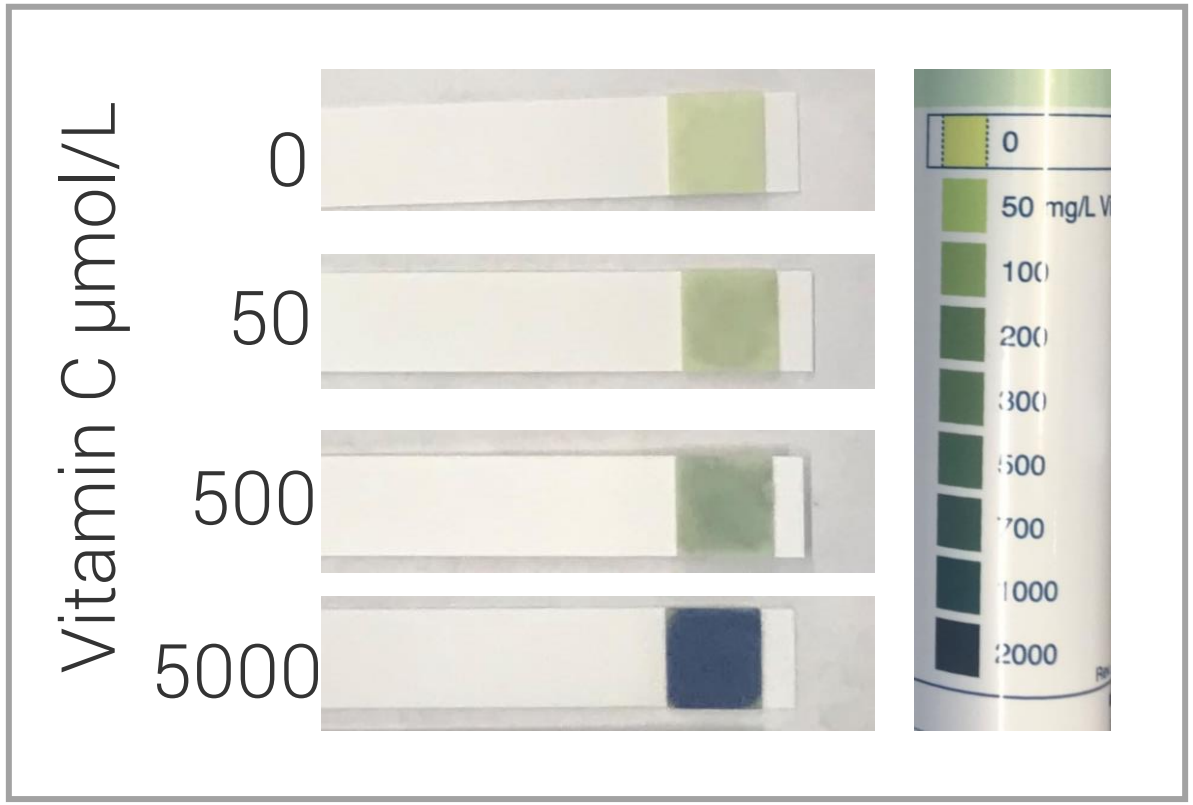
Pre-conjugation strategies

https://www.veravas.com/sample-interference

Yang and Wiencek, Clin Chim Acta (2020)

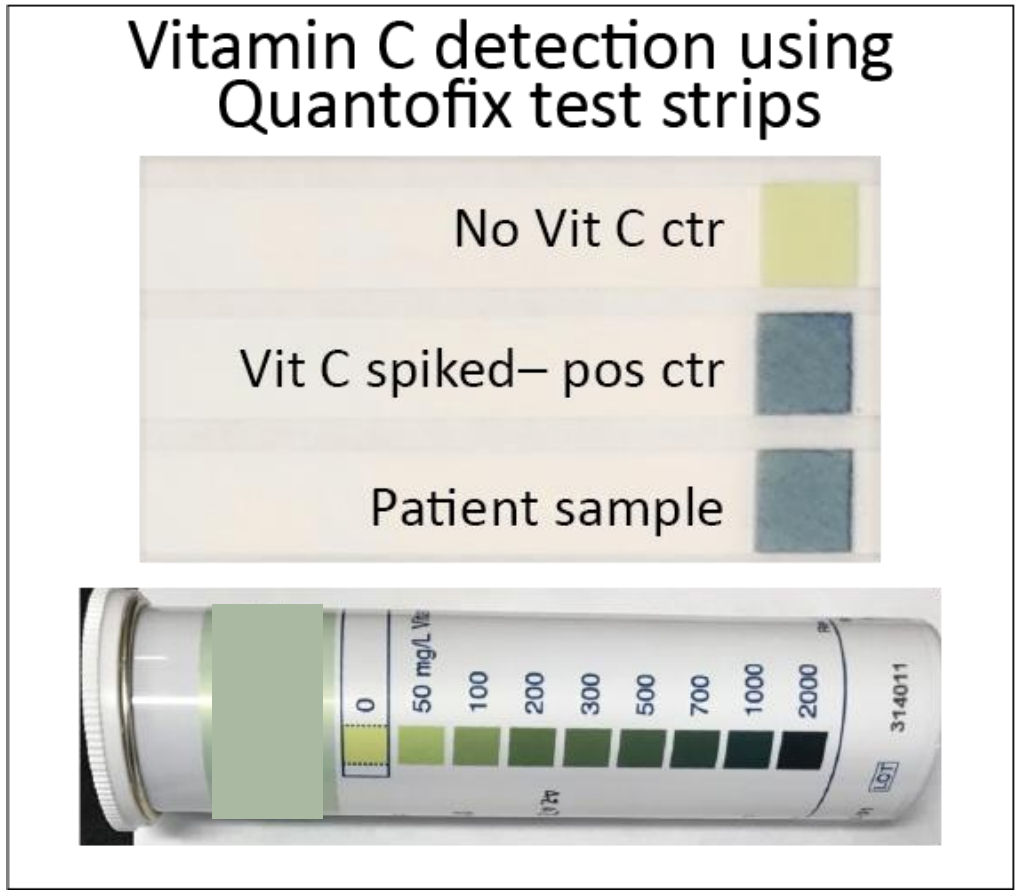
Vitamin C detection using test strips





Vitamin C-spiked serum

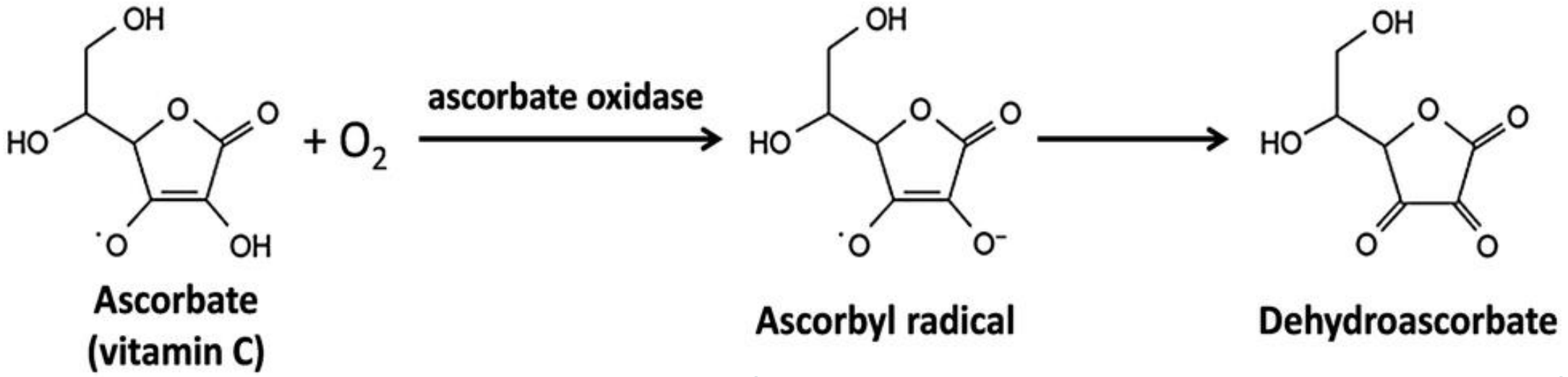
Could patient specimens be tested by this method?



Patient specimen

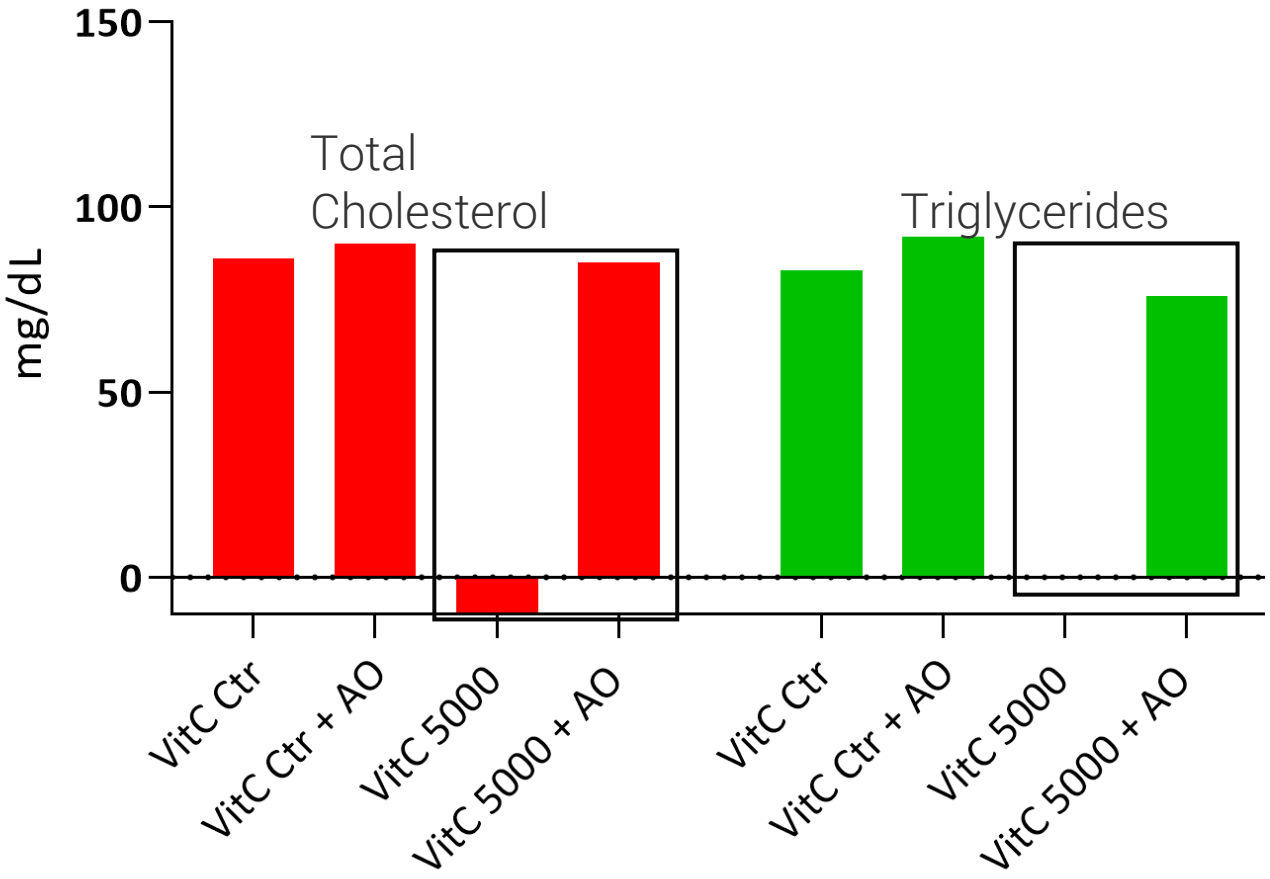
Pandya et al, Clin Biochem (2021)

Enzyme pre-treatment to neutralize vitamin C



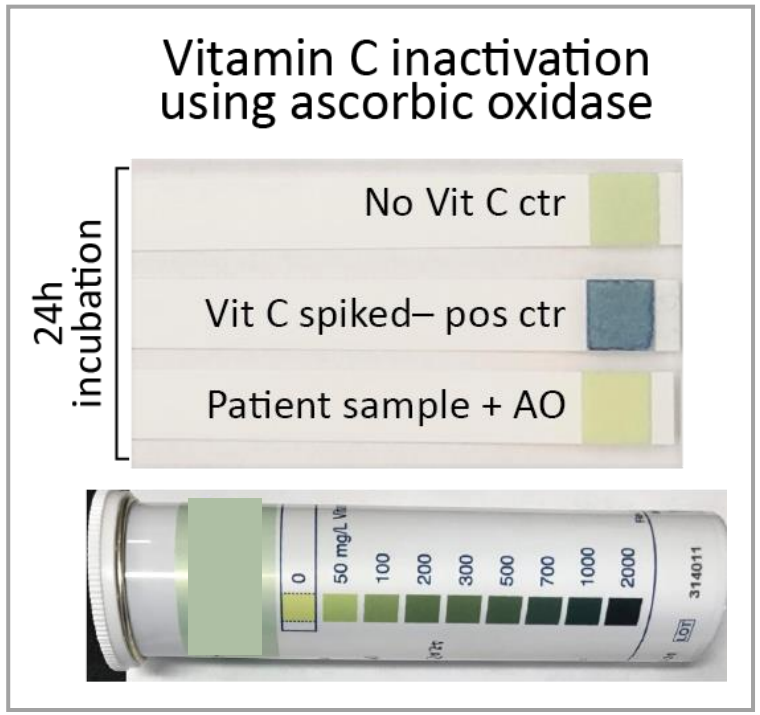
Chen et al, J. Mat. Chem. (2016)

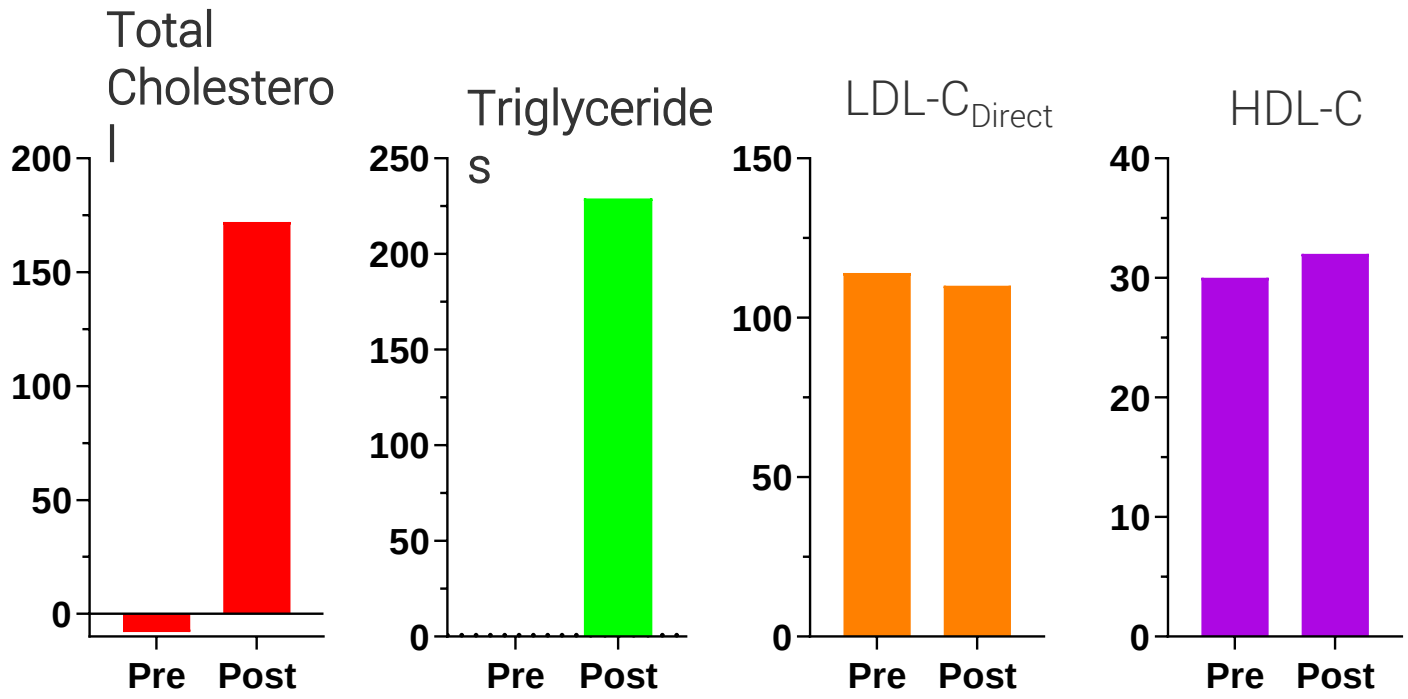
Effect of ascorbate oxidase treatment



Vitamin C and/or AO-spiked serum

Detecting and eliminating vitamin C interference in a patient sample





Patient specimen treated with AO

Pandya et al, Clin Biochem (2021)

Key takeaways

- Interferences in laboratory assays can affect medical decision making.
- Certain dietary supplements may affect lab assays.
- High-dose biotin can affect immunoassays dependent on streptavidin-biotin interaction.
- Vitamin C due to its strong reducing potential may impact a variety of chemistry and POC assays.
- Laboratorians need to be aware of hallmark signs of assay interference.
- Clinician-laboratorian communication may reduce patient impact due to assay interference.
- Not all interferences are possible to detect.
- Patients may need to be asked “Are you taking any health supplements?”

ARUP is a nonprofit enterprise of the University of Utah and its Department of Pathology.