

INTERFERENCES IN BIOCHEMISTRY TESTING

Preamble

The term “assay interference” refers to the situation where a substance in the specimen being tested (the interferent) leads to an inaccurate result. Undetected assay interferences may lead to misleading laboratory results, incorrect clinical decision-making, and subsequent patient harm.

There are many interferents, with some interferents affecting only one test whereas other interferents may affect multiple tests. Three common interferents that may affect multiple tests are **haemolysis**, **icterus** and **lipaemia** (often referred to as H,I and L).

All specimens sent to the core biochemistry laboratory at CHL will be tested for H,I and L interferences by means of a semi-quantitative index. If haemolysis, icterus or lipaemia is detected, this will be noted on the results report, sometimes with a qualifying comment indicating the degree of each interference (e.g. “slightly haemolysed” etc.), and results may be suppressed or reported with a qualifier (e.g. a < or > sign).

The paragraphs below provide some basic background information on each interference and some (but not all) of the assays affected. Results affected by H,I or L interferences should always be interpreted with caution, and recollection should be considered if this is likely to clear the interference.

It is not possible to detect all interferences during the testing process. If you wish to discuss any results that do not fit the clinical picture, or if you require more information on results that have been reported with an interference flag, contact the laboratory on x80376.

Haemolysis

Whilst haemolysis refers to the breakdown of RBCs, in this context it may more accurately be thought of as the release of cellular contents from the RBCs and WBCs into the plasma.

Haemolysis is the most common biochemistry interference with an incidence of 30% or higher in high risk settings (predominantly paediatrics/neonates, and emergency department specimens). Causes of haemolysis include using a small bore needle for collection, prolonged tourniquet time or fist clenching during collection, delayed sample handling and excessive shaking or rough handling of the collection tube. *In vivo* haemolysis is a rare but important cause of haemolysed plasma samples and should be considered, particularly if the haemolysis doesn’t clear with repeat testing using an optimal collection technique.

Most commonly haemolysis causes interference with assays which measure a substance with high intracellular concentration, with falsely elevated results observed (e.g. potassium, LDH, AST). Alternatively, cellular enzymes may break down the measured analyte, leading to falsely low results (e.g. bilirubin, insulin), or may interfere with the assay chemistry in some other unspecified way. A non-exhaustive list of assays prone to haemolysis interference is included in the text box above.

Assays particularly susceptible to haemolysis interference*

(Arrow indicates whether the interference increases or decreases the result)

- Potassium ↑
- AST ↑
- LDH ↑
- Phosphate ↑
- Folate ↑
- Magnesium ↑
- Bilirubin ↓

INTERFERENCES IN BIOCHEMISTRY TESTING

Icterus

Icterus refers to the presence of high concentrations of bilirubin in the specimen. Bilirubin may interfere with assay kinetics leading to interference for some assays (see text box for some examples). Unlike haemolysis and lipaemia, it is unlikely that a recollection will clear an icterus interference. If results are suppressed or potentially inaccurate due to the specimen being icteric and are urgently required for clinical care, please contact the laboratory for further advice and consultation with a chemical pathologist.

Assays particularly susceptible to icterus interference*

(Arrow indicates whether the interference increases or decreases the result)

- GGT ↓
- Lactate ↓
- Lipase ↓
- Cholesterol (total and HDL) ↓

Lipaemia

Lipaemia refers to the presence of large lipoproteins (VLDL and chylomicrons) in the specimen. Lipaemia causes the specimen to become turbid, which interferes with many biochemistry assays that rely on measuring optical absorbance changes within the specimen.

Mild lipaemia may occur in the hours immediately after a meal and may clear if the specimen is repeated in a fasting state. Fasting lipaemia indicates that there are likely to be high levels of circulating VLDL particles or a problem with chylomicron clearance, and should prompt measurement of plasma triglycerides.

Assays particularly susceptible to lipaemia interference*

(Arrow indicates whether the interference increases or decreases the result)

- AST (variable effect)
- ALT (variable effect)
- Iron ↓
- Magnesium ↑
- Lipase ↑

Assays that are likely to be affected by lipaemia are included in the text box.

Other interferences

Many other interferences may also cause inaccurate results. Examples include monoclonal proteins (paraproteins and monoclonal antibody therapy), rheumatoid factor, medications and supplements (e.g. vitamin C, N-acetylcysteine, biotin), heterophile antibodies, macro-analyte complexes and intravenous contrast material. Additionally, some assays require specific pre-analytical handling conditions in order to prevent sample degradation, a subject that is outside the scope of this document.

Concluding remarks

Ultimately, the information obtained from laboratory testing should be interpreted within the full clinical context to help answer a clinical question about a patient. When there is a discrepancy between the clinical picture and the test result, it is important to consider whether there is an undetected interference or pre-analytical condition that is generating an inaccurate result. The biochemistry team are always happy to discuss such cases, and a chemical pathologist is available for consultation if required.

* The text boxes do not contain an exhaustive list of affected assays. If a specimen is flagged as impacted by haemolysis, icterus or lipaemia, all results should be treated with caution.