Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the editor

Evaluation of interference effects from hemolysis, icterus and lipemia on the Roche Elecsys® Anti-SARS-CoV-2 assay

Dear Editor,

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes coronavirus disease 2019 (COVID-19), emerged from Wuhan, China in December 2019. As of May 24, 2020, 5.2 million cases have been reported across 216 countries [1]. Immunoglobulins G and M (IgG, IgM) antibodies are commonly produced after viral infections. It has been reported that 100% and 94% of SARS-CoV-2 patients developed detectable IgG and IgM antibodies peaking 17–19 days and 20–22 days after symptoms onset, respectively. The median day of seroconversion was 13 days post symptom onset for both IgG and IgM [2].

Serology tests interrogate adaptive immune response to the virus, indicating recent or prior infection. The Roche Diagnostics' Elecsys Anti-SARS-CoV-2 assay is an automated immunoassay intended for qualitative detection of antibodies to SARS-CoV-2 with a specificity of 99.8% and 100% sensitivity for patients 14 days post-PCR confirmation [3]. It has received Emergency Use Authorization from the U.S. FDA on May 3, 2020. It is a double-antigen sandwich electrochemiluminescence immunoassay which uses a recombinant protein representing the nucleocapsid antigen (1 of the 4 structural proteins of the virus) for the determination of total antibodies against SARS-CoV-2, without distinguishing between IgG, IgM, and IgA. A result is given as a cutoff index

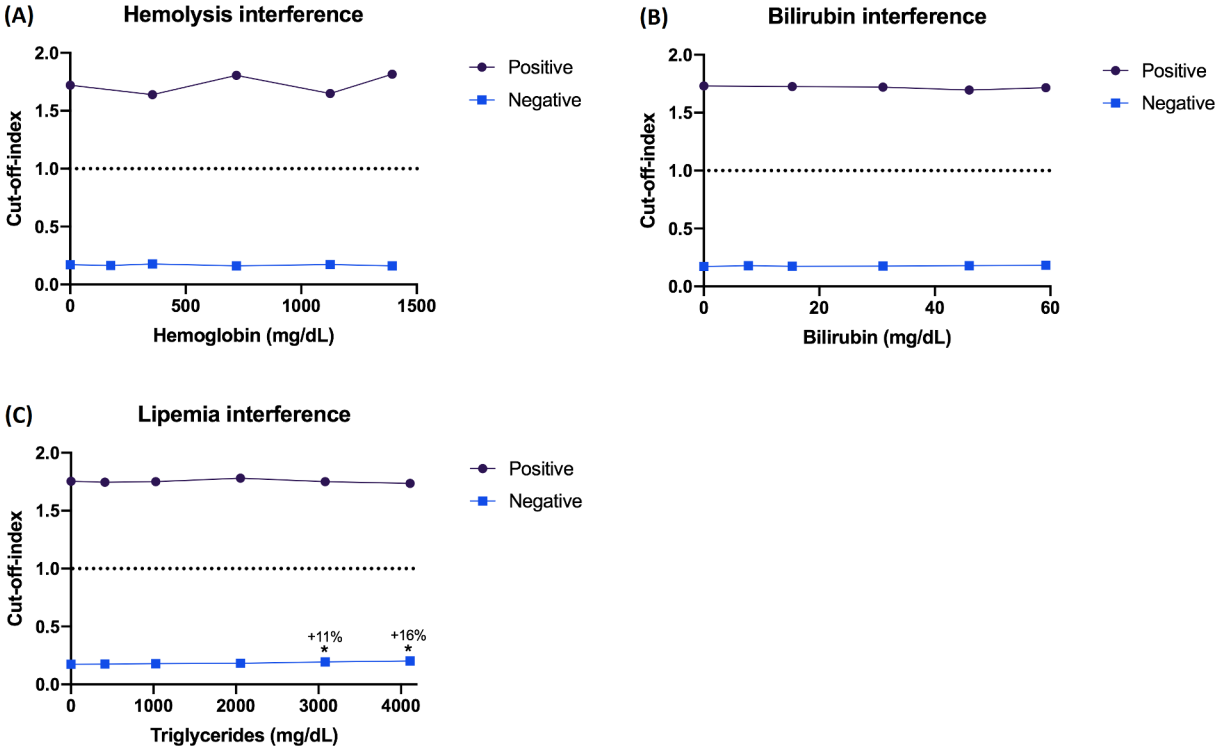

Fig. 1. Interferographs showing interference effects for (A) hemolysis (B) bilirubin and (C) lipemia on anti-SARS-CoV-2 positive and negative samples. (*) Recovery exceeded ± 10% of the baseline value measured in sample without interferents.

Abbreviations: SARS-CoV-2, Severe Acute Respiratory Syndrome Coronavirus 2; COVID-19, coronavirus disease 2019; Ig, immunoglobulin; COI, cutoff index

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(COI), and is then interpreted either as reactive/positive (COI ≥ 1.0) or non-reactive/negative (COI < 1.0).

The method sheet states "*This assay has no biotin interference in serum concentrations up to 1200 ng/mL*." and "*Potential endogenous interferences* e.g. *hemolysis, bilirubin, rheumatoid factors and pharmaceutical compounds other than biotin have not been tested and an interference cannot be excluded*." [3]. Although electrochemiluminescence immunoassays are, in general, less susceptible to hemolysis, bilirubin and lipemia interferences compared to spectrophotometric assays, interferences are still observed, especially for hemolysis, e.g., with the (high sensitivity) cardiac troponin T assay as the most representative example [4]. While we must be aware of biotin interference, we should not overlook the potential effects of these three common interferences on immunoassays. Therefore, we performed interference studies for hemolysis, bilirubin and lipemia on the Roche Cobas® e602 analyzer. Interference studies were performed by spiking different concentrations of interferents (hemolysate prepared using heparinized O-negative blood lysed by freeze-thawing in type 1 water, conjugated bilirubin purchased from Sigma Aldrich, and 20% Intralipid® purchased from Baxter International) into plasma pools. Interferents were mixed with saline at volume ratios of 10:0, 7.5:2.5, 5:5, 2.5:7.5, 1.25:8.75 and 0:10, and these interferent-saline mixtures were spiked into the plasma pools, making up 10% of the total volume of each specimen to be analyzed. Samples were then measured in duplicate. We used two plasma pools, one with a COI of 0.18 (negative) and one with a COI of 1.8 (positive). Hemoglobin, bilirubin and triglycerides concentrations were measured as well as the hemolysis (H) icterus (I) and lipemia (L)-indices, which are commonly measured on Roche analyzers to assess specimen acceptability. [H-index (100 ~ hemoglobin 100 mg/dl), I-index (100 ~ 70 mg/dl conjugated bilirubin) and L-index (100 ~ 210 mg/dl triglycerides) have arbitrary units.] No significant interference was defined as values within 10% deviation of the baseline COI measured in the control samples.

Our results showed that the assay was not significantly interfered by hemoglobin (≤1350 mg/dl, H-index 1350), bilirubin (≤59 mg/dl, I-index 79) and triglycerides (≤2100 mg/dl, L-index 950) (Fig. 1). Mild interference was observed in negative samples with triglycerides 3100 mg/dl (L-index 1400) or above; however, the COI remained below 1.0, and thus the qualitative interpretation was unaffected. In conclusion, we found that this assay is essentially resistant to interferences from hemolysis, icterus, and lipemia, and qualitatively different results due to these common interferences are unlikely.

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