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Heterophilic interference in specimens yielding false-reactive results on the Abbott 4th generation ARCHITECT HIV Ag/Ab Combo assay

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ABSTRACT

Background: False-reactivity in HIV-negative specimens has been detected in HIV fourth-generation antigen/antibody or 'combo' assays which are able to detect both anti-HIV-1/HIV-2 antibodies and HIV-1 antigen.
Objectives: We sought to characterize these specimens and determine the effect of heterophilic interference.
Study design: Specimens previously testing as false-reactive on the Abbott ARCHITECT HIV Ag/Ab combo assay and re-tested on a different (Siemens ADVIA Centaur HIV Ag/Ab) assay. A subset of these specimens were also pre-treated with heterophilic blocking agents and re-tested on the Abbott assay.
Results: Here we report that 95% (252/264) of clinical specimens that were repeatedly reactive on the Abbott ARCHITECT HIV Ag/Ab combo assay (S/Co range, 0.94–678) were negative when re-tested on a different fourth generation HIV combo assay (Siemens ADVIA Centaur HIV Ag/Ab). All 264 samples were subsequently confirmed to be HIV negative. On a small subset (57) of specimens with available volume, pre-treatment with two different reagents (HBT; Heterophilic Blocking Tube, NABT; Non-Specific Blocking Tube) designed to block heterophilic antibody interference either eliminated (HBT) or reduced (NABT) the false reactivity when re-tested on the ARCHITECT HIV Ag/Ab combo assay.
Conclusions: Our results suggest that the Abbott ARCHITECT HIV Ag/Ab combo assay can be prone to heterophilic antibody interference.

1. Background

The recent publication of the CLSI-M53 HIV testing guidelines by the Clinical Laboratory Standards Institute (CLSI) and recommendations by the Centers for Disease Control and Prevention (CDC) represents the most significant change to HIV testing algorithms since the mid-1980's (Fig. 1) [1,2].

Both sets of guidelines propose screening by a laboratory-based fourth generation test capable of detecting antibodies to HIV-1 and HIV-2 and p24 antigen to HIV-1. Fourth generation assays are able to detect the presence of HIV infection 4–7 days earlier than previous 3rd generation (antibody-only) assays resulting in improved detection of specimens in the pre-seroconversion (acute infection) phase [3–5]. Several fourth generation HIV assays are approved for use in Canada and the United States including; Abbott ARCHITECT HIV Ag/Ab Combo assay (Canada/USA), Siemens ADVIA Centaur HIV Ag/Ab Combo assay (Canada/USA) and Bio-Rad GS HIV Combo Ag/Ab assay (USA). One fifth generation assay, the Bio-Rad BioPlex 2200 HIV Ag-Ab Combo assay (USA), is able to determine reactivity separately for HIV Ab and HIV antigen.

The detection of either HIV antibodies, HIV antigen or both in fourth generation assays is technically complex requiring two different test principles. Concerns regarding the specificity and low positive predictive value especially in low-risk, low-prevalence populations

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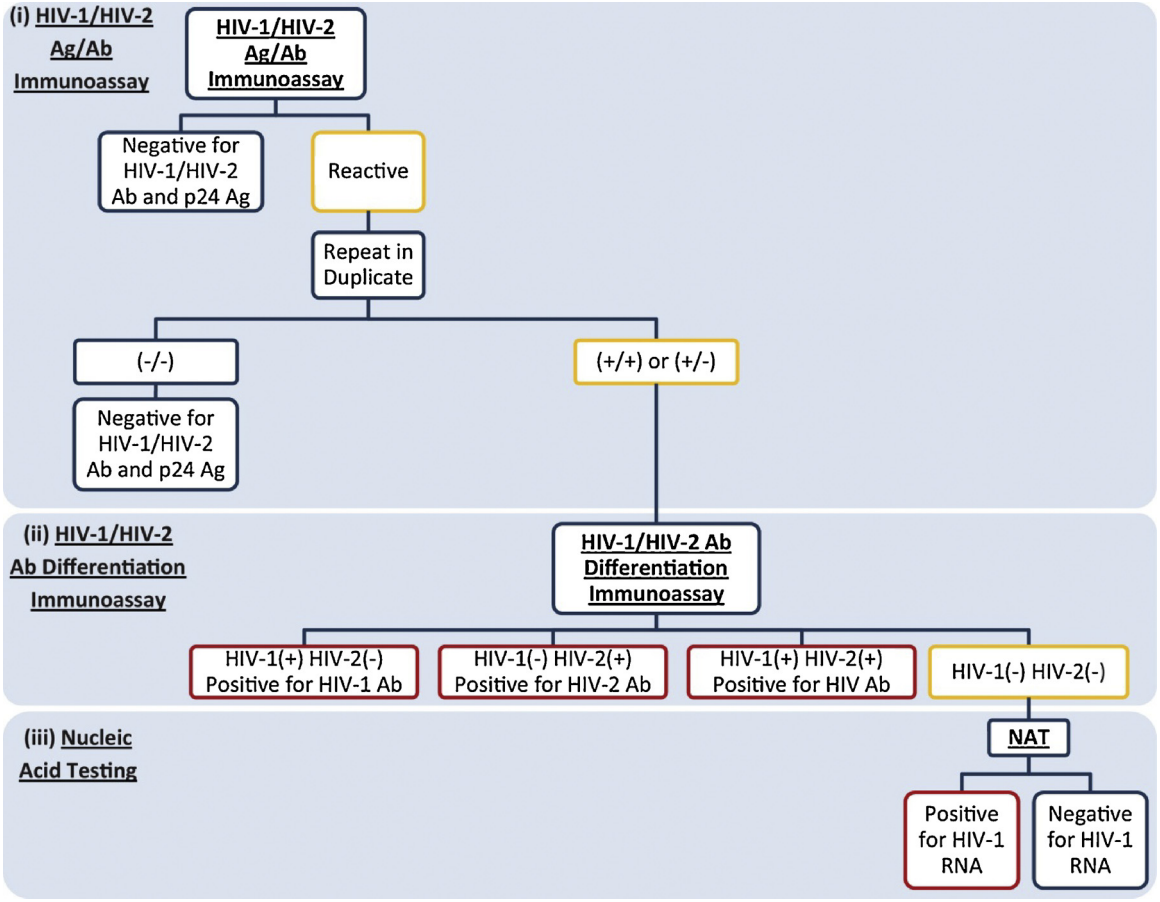

Fig. 1. Clinical and Laboratory Standards Institute (CLSI) M53-A algorithm I, 2012.

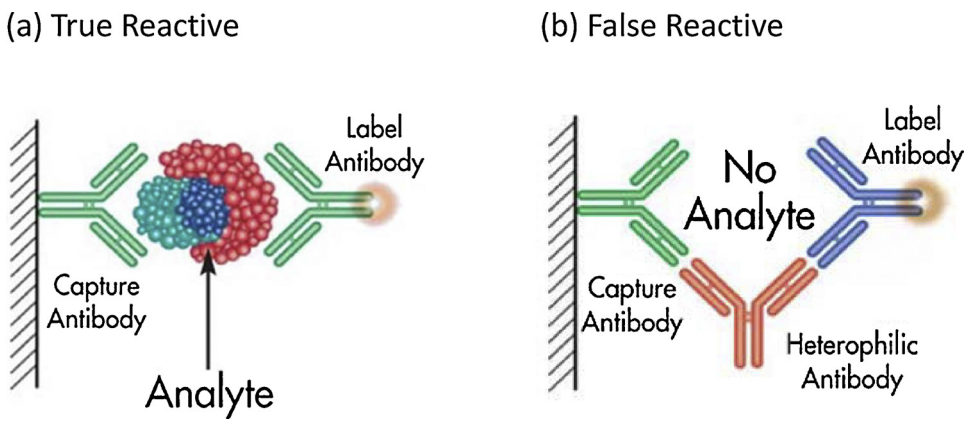

Fig. 2. Mechanism of heterophilic antibody interference, (a) True reactive; (b) False reactive. Figure used with kind permission from Scantibodies Laboratory, Inc. CA.

have been raised [6]. Nonspecific factors leading to false-reactive test results can range from general sub-optimal conditions related to ionic strength and pH, salt concentration, hemolysis, lipemia and hyperbilirubinemia while some specific factors including the presence of cross reacting antibodies to other infectious agents, autoantibodies and heterophilic antibodies (HAbs) are also of concern [5]. HABs are human antibodies that can bind to components of the immunoassay where they form a bridge between the capture and detection antibodies resulting in elevated Signal-to-Cutoff (S/Co) ratios often leading to a false-reactive result (S/Co > 1.0) in the absence of a true analyte (Fig. 2). As heterophilic interference is unpredictable, clinicians and even laboratorians may be unfamiliar with this phenomenon leading to repeat testing and delayed reporting or referral to a reference laboratory.

2. Objectives

In this study, we provide examples from HIV-negative specimens which tested markedly different on two different Health Canada and FDA-approved HIV 4th generation assays (Abbott ARCHITECT HIV Ag/Ab Combo and Siemens ADVIA Centaur Ag/Ab Combo). We also demonstrate the impact of pre-treating these specimens with two different blocking reagents in reducing or eliminating the impact of heterophilic antibody interference upon retesting on the ARCHITECT HIV Ag/Ab Combo assay.