

US CDC Serological Investigations

In response to H7N9 Outbreak

Sept 2013

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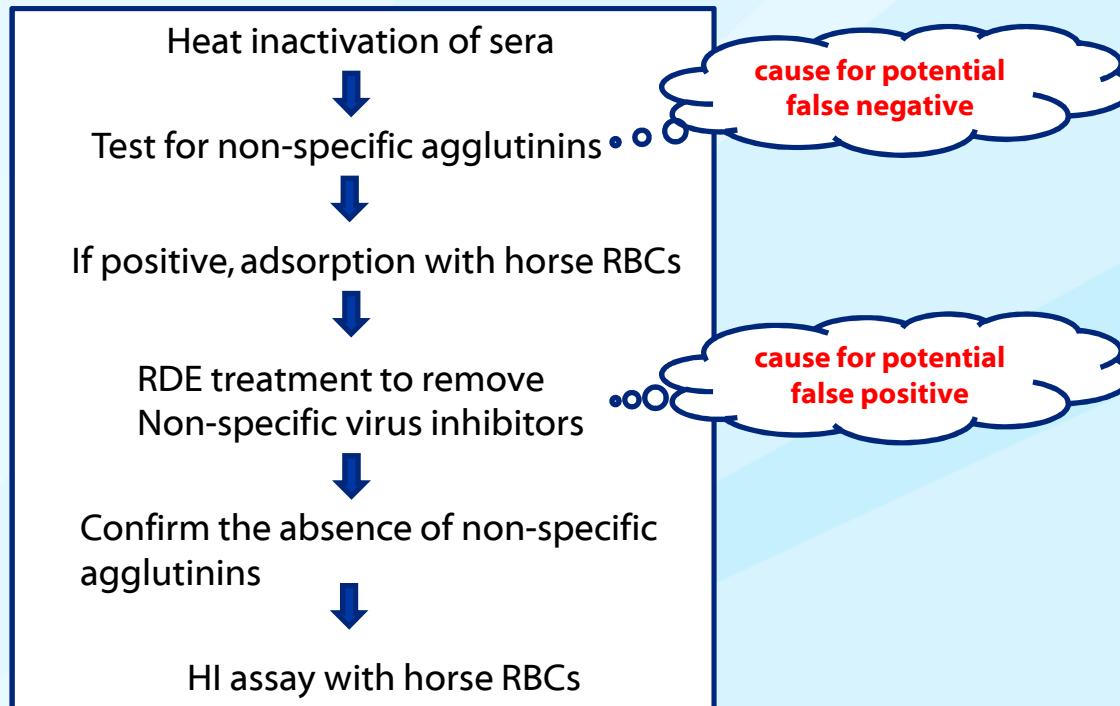
- I. Development of a modified horse RBC HI assay to detect H7N9 sera antibody response with improved sensitivity.**

A Modified HI assay Using Horse RBC for Detection of H7N9 Serum Antibodies

- The receptor specificity of influenza virus HA correlates with their ability to agglutinate RBCs from different animal species:**
Avian viruses: SA α -2, 3
Human viruses: SA α -2, 6
- Horse RBCs express a high proportion of SA α -2, 3 -gal linkages compared with turkey RBCs.**
- With H7 influenza subtype viruses, an improved sensitivity has been observed using horse RBCs for detecting HI antibodies than using turkey RBCs.**

Modified Horse RBC HI Assay

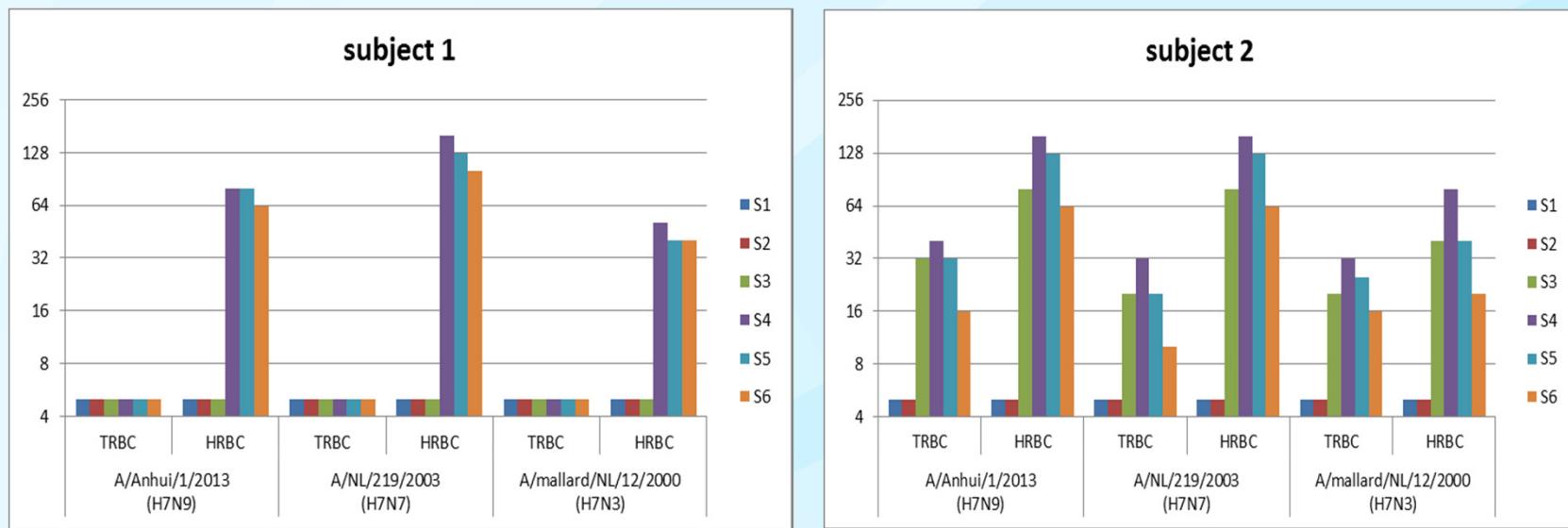
- A modified sample treatment procedure is developed



- Higher levels of non-specific agglutinins can be detected in sera samples using horse RBCs causing false negative results. The serum must be adsorbed with horse RBC before testing in the HI assay.
- However, during adsorption with horse RBCs, non-specific virus inhibitors may be introduced into serum, which will cause a false positive result in HI assay with horse RBC. These non-specific inhibitors can be eliminated by RDE treatment.

Modified Horse RBC HI Assay has better sensitivity to detect H7Ab

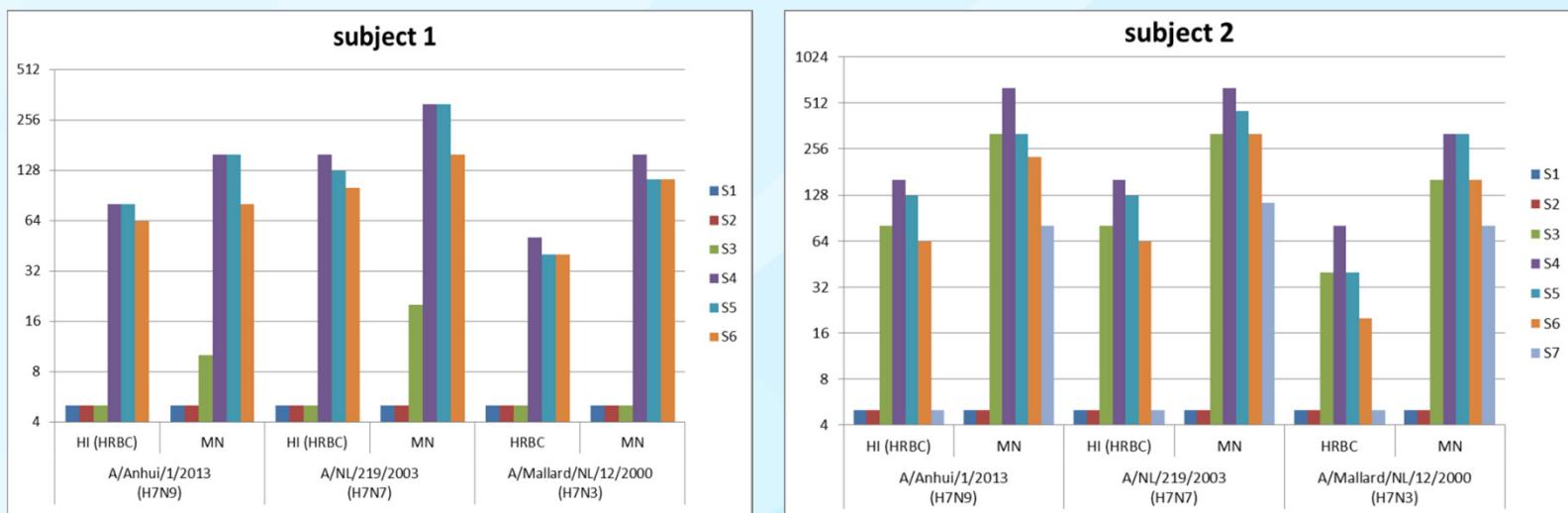
- HI assay using horse RBCs provides better sensitivity to detect serological responses against several H7 viruses, including wild type H7N9 virus. Ab titers detected by modified horse RBC HI assay are 2-8 folds higher than titers detected using turkey RBCs.



Comparison of horse and turkey RBCs in HI assay using human sera from a H7 vaccine study (Two doses of A/NL/219/2003 live attenuated vaccine prime and One dose of A/Mallard/NL/12/2000 inactivated vaccine boost). Sera were kindly provided by K. Subbarao and J. Treanor.

Modified Horse RBC HI Assay to Detect H7N9 Ab

- HI assay using horse RBC yielded generally comparable titers as the microneutralization assay.



Comparison of antibody titers achieved by horse RBC HI assay vs microneutralization (MN) assay using human sera from a H7 vaccine study with A/NL/219/2003 live attenuated vaccine prime and A/Mallard/NL/12/2000 inactivated vaccine boost.

Protocol Shared with Other Labs

- H7N9 Modified horse RBC HI protocol was shared with WHO, China CDC, and CONSIE on July 3rd, 2013.
- Protocol was also shared with Public Health Agency of Canada (PHAC) for confirmation of a H7N9 suspected case.
- The protocol is currently posted on the CONSIE website:
<http://consie.tghn.org/articles/consie-and-avian-influenza-h7n9/>

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Other studies conducted:

- II. To assess the level of pre-existing cross-reactive antibodies to H7N9 in the current US population.**

- III. Evaluation if existing vaccinations (e.g. seasonal vaccines) provide any cross reactive antibodies to H7N9 infection.**

Thank you