Inconclusive hepatitis C virus antibody results in African sera

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Colleagues—In Africa, the prevalence of hepatitis C virus antibody (anti-HCV) is low compared to the frequency of serologic markers of hepatitis B, but high levels of false-positive anti-HCV ELISA results have been reported [1-3]. To investigate the causes of false-positive results, sera from 688 outpatients living on the eastern coast of Kenya were evaluated.

Sera and epidemiologic data were originally obtained in 1987 for a survey of hepatitis B and arboviral infections [4, 5]. Sera had been stored for 4 years at -70°C before testing for anti-HCV by ELISA using a second-generation test kit (Abbott). The mean ELISA optical density ratio (ODR = mean test optical density/cutoff optical density) was calculated as previously described [6]. All sera repeatedly reactive by ELISA were further tested with a second-generation immunoblot assay (RIBA HCV Test System; Chiron, Emeryville, CA). Samples containing sufficient volume were further tested with a dot immunobinding assay (Abbott MATRIX HCV), which detects antibody to recombinant proteins derived from putative core, NS3, and NS4 regions of the HCV genome and is interpreted as positive for anti-HCV when there is reactivity to two distinct HCV proteins. Only sera positive by both ELISA and either the immunoblot or dot immunobinding assays were considered to be positive for anti-HCV and to represent active infection. In addition, 42 sam-
samples were randomly selected and tested for Plasmodium falci-parum antibody using an indirect immunofluorescent assay (IFA).

The mean age of the population was 21 years (range, 1-79); 80% were female. Sixty-two subjects (9.0%) had a history of acute hepatitis, and 55 (8.0%) had received a blood transfusion. Sera from 179 subjects (26.0%; ODR = 1.3) were repeatedly reactive by ELISA for anti-HCV; however, only 6 sera (0.7%; ODR = 1.8) were positive and 18 (2.6%; ODR = 1.9) indeterminate by RIBA-2. By dot immunobinding assay, 5 serum samples were positive (ODR = 2.2) and 33 inconclusive (ODR = 1.6) among 129 samples that could be tested. Of 4 RIBA-2-negative samples with sufficient volume for further testing, 1 was positive and 3 negative by Abbott MATRIX HCV; of 13 RIBA-2-indeterminate samples further tested, 2 were positive, 2 negative, and 9 inconclusive by Abbott MATRIX HCV.

Hepatitis B surface antigen was found in 43 subjects (6.3%) and antibody to hepatitis B surface antigen or antibody to hepatitis B core antigen in 359 (52.2%). By IFA, 21 subjects (3.1%) had antibody to dengue-2, 14 (2.0%) to chikungunya, 24 (3.5%) to Sindbis, 15 (2.2%) to West Nile, 16 (2.3%) to Rift Valley fever, 18 (2.6%) to duggbe, 8 (1.2%) to Ganjam, and 0 to Crimean-Congo hemorrhagic fever viruses. All 42 tested sera had antibody to P. falciparum, and 40% had a titer of < 1:1000.

None of the subjects positive for anti-HCV by immunoblot or dot immunobinding assay had ever had an acute episode of jaundice or had received a blood transfusion. Subjects positive by RIBA-2 (mean age, 33 years) or Abbott MATRIX HCV (mean age, 41 years) tended to be older than other subjects (mean age, 21 years), but there was no age trend for subjects with false-positive ELISA or inconclusive RIBA-2 and Abbott MATRIX HCV results. False positive ELISA results and inconclusive immunoblot or dot immunobinding results were not associated with the subjects' sex, history of blood transfusion or acute hepatitis, antigen and antibody markers of hepatitis B infection, arboviral antibodies, or malaria antibody.

These data suggest that hepatitis C infection is very infrequent in eastern Kenya; however, false-positive ELISA results and inconclusive confirmatory assay results are common but unrelated to flavivirus infection (dengue, West Nile) [7] and antibody to P. falciparum. False positivity and inconclusive reactions could be related to prolonged storage of samples, cross-reacting antibody to unknown antigens, or infection by HCV variants [8-10].

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