



“We shall never forget”
9/11/01



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Hepatitis C Antibody Reporting: An Update

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Tests to detect antibody to Hepatitis C virus were first licensed by the FDA in 1990. Since that time, new versions of these and other FDA-approved anti-HCV tests have been used widely for clinical diagnosis and screening of asymptomatic persons, such as in blood product screening. Enzyme immunoassay antibody screening requires that the specimen be initially screened in singlet, and any initially reactive specimens are retested in duplicate. A specimen that is reactive in 2 of 3 tests, or 3 of 3 tests is considered to be Repeatedly Reactive (positive). Although it is recommended that all positive specimens be routinely reflex tested with a more specific assay (RIBA or HCV RNA), the majority of clinical laboratories report a positive result based on a positive screening test only. The Montana Public Health Laboratory (MTPHL) has been performing EIA screening for Hepatitis C antibodies since 1996. At that time, a supplemental RIBA assay was not offered, as was the practice of transfusion services, since screening was done primarily on high risk individuals with a high prevalence of HCV infection, thus providing an acceptable Positive Predictive Value. In addition, RIBA or HCV

RNA confirmatory testing was expensive, and difficult to justify with limited public health funding. During the years 1997 through 2002, the EIA positive rate at the MTPHL ranged from 16% to 23%, with some populations having a positive rate in excess of 30%. However, more screening was being performed for populations with a low (<10%) prevalence of HCV infection (health care workers, or asymptomatic persons for whom no clinical information was available). Based on communications with Hepatitis experts at the Centers for Disease Control, in 1999 MTPHL began monitoring the Signal to CutOff ratios (S/CO) of EIA positive results. The S/CO ratio is determined by dividing the absorbance of the patient specimen by the absorbance of the cut-off. A ratio of 1.0 has a specimen absorbance equal to the absorbance of the calculated cutoff for the EIA run. See Table 1 on next page.

In 2002, I was invited to be part of a CDC Working Group convened to help establish guidelines for testing and reporting Hepatitis C antibody results. In early 2003, CDC published *Guidelines for Laboratory Testing and Result Reporting of Antibody to Hepatitis C Virus*, (MMWR Recommendation and Reports, Vol. 52, No. RR-3, February 7, 2003).

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Hepatitis C Antibody **cont'd**.....

Table 1. Percentage of specimens with low reactive results

Year	Total # Tested	Total # Repeat Reactive	# S/CO < 3.8	% of Total	% of RR
1999 (6 mo)	1146	238	11	1.0 %	4.6 %
2000	2188	413	18	0.8 %	4.4 %
2001	2638	619	24	0.9 %	3.9 %
2002	3059	514	20	0.7 %	3.9 %

Specimens with S/CO values greater than 3.8 are most likely to confirm as true antibody regardless of prevalence; those less than 3.8 are less likely to be a true positive, and require supplemental or confirmatory testing. In data presented, the proportion that tested RIBA-positive was 5.8% for samples with S/CO ratio 1.0 - 2.9; and ~ 95% for those with S/CO ratio \geq 3.8. See Figure 1 for a brief summary of the guidelines.

Figure 1. Guideline Summary

- Screening-test-negative (non-reactive) specimens require no further testing, and are reported as anti-HCV negative
- Screening-test-positive specimens require reflex serologic or nucleic acid supplemental testing, using the following two approaches:

1. All screening-test-positive specimens are reflexed, OR
2. Screening-test-positive specimens are reflexed based on Signal to CutOff ratios, (enzyme immunoassay [EIA] S/CO <3.8, or chemiluminescence immunoassay [CIA] S/CO < 8). For screening-test-positive samples that require reflex testing, the anti-HCV result should not be reported until the results from the additional tests are available.

If using approach #2, screening-test-positive samples with high S/CO ratios can be reported as anti-HCV positive without supplemental testing. A comment should accompany the report stating that supplemental serologic testing was not performed, and that samples with high S/CO ratios usually (\geq 95%) confirm positive. The ordering physician should be informed that more specific testing can be requested, if indicated.

When determining which reflex supplemental test to order, consider the following:

- RIBA can be performed on the same sample collected for the screening test, but only provides information about the antibody status of the patient, not the HCV infection status.
- HCV RNA requires that the serum be collected and processed within specific parameters, so this usually requires a second specimen collection. If the HCV RNA result is positive, the presence of active HCV infection can be reported as well as a positive anti-HCV result. However, a HCV RNA negative result still requires reflex RIBA testing to verify the anti-HCV status.

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Hepatitis C Antibody cont'd.....

Based on the increase in low reactive specimens in 2003 (see Table 1), along with the recently published guidelines, the MTPHL began educating clinicians that specimens with S/CO ratios less than 3.8 need additional testing (HCV RNA or RIBA) prior to advising the patient of their HCV antibody status. Since February 2003, the following seventeen specimens have been identified as needing additional testing (See Table 2). To complete the screening, the negative HCV RNA specimens should be tested by RIBA to determine whether the individual was ever infected with HCV (confirm the presence of antibody).

Without the RIBA or RNA results, all 17 of these patients would have been informed that they were HCV positive, and counseled as such.

Of the 14 specimens with additional test results, only one (1) was confirmed as positive for Hepatitis C antibody.

The data in Table 2 support the need for supplemental or confirmatory testing. By using a S/CO ratio, the number of specimens that require supplemental or confirmatory testing is minimized, yet a result that has a high probability of reflecting the person's true antibody status is reported.

The Montana Public Health Laboratory has instituted these guidelines because it provides the most cost-effective approach to accurate and correctly interpreted HCV antibody test results.

The complete MMWR report is available on the CDC website at www.cdc.gov/hepatitis, and continuing education credit can be obtained.

Table 2. Low Reactive Serum samples with Confirmatory Results

Sample	S/CO	RIBA	HCV RNA	Sample	S/CO	RIBA	HCV RNA
1	1.03	TNP [†]	TNP [†]	10	1.93		Neg
2	1.18	IND*	Neg	11	2.08	IND*	TNP [†]
3	1.27	IND*	TNP [†]	12	2.41		Neg
4	1.43	Neg		13	2.50		Neg
5	1.47	TNP [†]	TNP [†]	14	2.50		Neg
6	1.56	Neg	Neg	15	2.52	Pos	
7	1.58		Neg	16	2.69		Neg
8	1.76		Neg	17	3.1	TNP [†]	TNP [†]
9	1.78	Neg					

[†] = No Additional Testing Performed, * = Indeterminate results





West Nile Virus: 2003



The West Nile virus appears to be firmly established in the United States, and researchers expect its continued spread and entrenchment in wildlife populations. Since 1999, WNV has been detected in humans, horses, birds, or mosquitoes in 46 states and the District of Columbia. Only Hawaii, Alaska, Oregon, and Utah have yet to report detection of WNV in human, equine, bird, or mosquito populations.

According to the U.S. Centers for Disease Control and Prevention, 4156 people in the the U.S. tested positive for the West Nile Virus in 2002, and 284 people died of the virus. Many more people were likely to have been infected with the virus, but experienced mild or no symptoms, and were never tested.

As of 18 August 2003, the CDC has confirmed 536 human cases of West Nile Virus for the year, resulting in 11 deaths.

Statistically, a person's risk of contracting West Nile is low. In most areas where the virus is established, only 1% of the area's mosquitoes carry the virus. Less than 1% of people bitten by these infected mosquitoes develop serious complications from the virus; the remainder exhibit flu-like symptoms, or no symptoms at all. Those at highest risk are the elderly and people with weakened immune systems; it is important, however, for *all* people to protect themselves from mosquito bites to minimize the risk of infection.

FDA Clears First Test for West Nile Virus

The Food and Drug Administration (FDA) today cleared the first test for use as an aid in the clinical laboratory diagnosis of West Nile virus infection. The West Nile Virus IgM Capture ELISA is intended for use in patients with clinical symptoms consistent with viral encephalitis/meningitis.

“Emerging infectious diseases such as West Nile virus present a challenge to the public health community,” said Tommy G. Thompson, Secretary of Health and Human Services. “When industry and government collaborate closely to meet a public health need, the resulting new technology will strengthen our joint efforts to confront diseases earlier and should lower rates of infection.”

The new test works by detecting the levels of a particular type of antibody, IgM, to the disease in a patient's serum. IgM antibodies can be detected within the first few days of the onset of illness and can assist in the diagnosis of these patients.

“The rapid review and approval of this blood test, which uses antibody levels to identify persons who were recently exposed to West Nile virus, reflects FDA's commitment to making safe and effective medical products available promptly,” said FDA Commissioner Mark B. McClellan, M.D., Ph.D. “This test provides a useful tool to combat the important public health problem of West Nile virus infection, just in time for the start of the West Nile season.”

The PanBio West Nile IgM assay was evaluated using over 1000 patient sera, which were tested at four different clinical sites. The test correctly identified antibody in up to 90 to 99% of West Nile virus disease cases. Because detection of antibody is not always specific in patients with acute viral infections, this test is considered presumptive and should be confirmed by more specific testing. Although the PanBio test is a valuable aid in the diagnosis of West Nile virus encephalitis, due to similarities with other viruses in the same family, there is a need to confirm positive results by an additional test or by using the current CDC diagnostic guidelines for diagnosis of this disease.

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FDA Clears West Nile Virus Test cont'd...

West Nile virus is a mosquito-borne virus which first appeared in the United States in 1999. While the virus often presents as a mild infection that clears without further treatment, some patients develop severe infection resulting in neurological disease and even death. The disease is most prevalent during the peak mosquito season which is expected to begin in July and end in October. Over the past several years, the geographic range of the virus as well as the number of new infections has expanded and now covers most of the continental United States.

Since last September, FDA has also worked very closely with industry to prepare for this upcoming West Nile virus season and has encouraged industry to develop blood donor screening tests. In mid June 2003, blood testing centers began testing the blood supply for West Nile virus, using experimental test kits that FDA has evaluated and permitted to be used. FDA also developed guidance to industry recommending procedures to assess donor suitability and to retrieve and quarantine potentially contaminated blood products. The investigational screening procedure has now successfully identified the first human West Nile virus infection in an asymptomatic blood donor. The West Nile Virus IgM Capture ELISA is manufactured by PanBio Limited in Windsor, Australia.

September 11 2001 Remembrance





Abstract Alley



The abstracts below were taken from *Microbiology Journals* where full text can be accessed through the links provided. If you wish to access the Full Text of the article, the URL is provided below.

Automated Laboratory Reporting of Infectious Diseases in a Climate of Bioterrorism

M'ikanatha NM, Southwell B, Lautenbach E. Automated laboratory reporting of infectious diseases in a climate of bioterrorism. *Emerg Infect Dis* [serial online] 2003 Sept [*date cited*]. Available from: URL: <http://www.cdc.gov/ncidod/EID/vol9no9/02-0486.htm>

While newly available electronic transmission methods can increase timeliness and completeness of infectious disease reports, limitations of this technology may unintentionally compromise detection of, and response to, bioterrorism and other outbreaks. We reviewed implementation experiences for five electronic laboratory systems and identified problems with data transmission, sensitivity, specificity, and user interpretation. The results suggest a need for backup transmission methods, validation, standards, preserving human judgment in the process, and provider and end-user involvement. As illustrated, challenges encountered in deployment of existing electronic laboratory reporting systems could guide further refinement and advances in infectious disease surveillance.

Consumer Attitudes and Use of Antibiotics

Vanden Eng J, Marcus R, Hadler JL, Imhoff B, Vugia DJ, Cieslak P, et al. Consumer attitudes and inappropriate use of antibiotics. *Emerg Infect Dis* [serial online] 2003 Sept [*date cited*]. Available from: URL: <http://www.cdc.gov/ncidod/EID/vol9no9/02-0591.htm>

Recent antibiotic use is a risk factor for infection or colonization with resistant bacterial pathogens. Demand for antibiotics can be affected by consumers' knowledge, attitudes, and practices. In 1998-1999, the Foodborne Diseases Active Surveillance Network (FoodNet) conducted a population-based, random-digit dialing telephone survey, including questions regarding respondents' knowledge, attitudes, and practices of antibiotic use. Twelve percent had recently taken antibiotics; 27% believed that taking antibiotics when they had a cold made them better more quickly, 32% believed that taking antibiotics when they had a cold prevented more serious illness, and 48% expected a prescription for antibiotics when they were ill enough from a cold to seek medical attention. These misguided beliefs and expectations were associated with a lack of awareness of the dangers of antibiotic use; 58% of patients were not aware of the possible health dangers. National educational efforts are needed to address these issues if patient demand for antibiotics is to be reduced.

