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BLOOD UTILIZATION AT MINISTRY SAINT JOSEPH'S HOSPITAL (MSJH)

RIGHT PRODUCT, RIGHT DOSE, RIGHT TIME, RIGHT REASON

Dr. Kathy Puca, Consultant for Marshfield Labs Transfusion Service, Jan Weyhmiller, Manager Transfusion Service, and Kris Melaas Merkel, Director of Process Improvement SJH

As one of the first steps for the Blood Utilization Project, a new order set for ordering blood product transfusions – "*Medical/ Surgical Blood Product Transfusion-Adult Only (00802PPO)*" – was implemented at MSJH on April 30, 2014. The preprinted order set is to be used on 3N thru 8N, MICU, SICU, and 5W (Rehab) for blood transfusion orders (except for those patients meeting the massive transfusion policy). These order sets can be found at the nurse's station. While this order set is being strongly encouraged and is the preferred means to order blood products, providers may use written orders that include these 4 elements: (1) blood product type; (2) number of units to transfuse and when; (3) pre-transfusion lab value (e.g., Hgb, platelet count, INR); (4) indication for transfusion.

What we know about blood transfusions is being challenged. A vast body of literature has shown RBC transfusions to be associated with adverse outcomes including increased rate of infection, increased respiratory complications, longer length of stay, and higher mortality. The best available evidence for transfusion therapy indicates that a more conservative approach to RBC transfusions (Hgb threshold of 7-8 g/dL and giving the minimum amount to resolve the patient's symptoms) not only reduces blood use, but improves patient outcomes and saves lives. In other words, when it comes to blood transfusions, *Less is More*.[1-4]

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Why should standardized transfusion order sets be implemented? Order sets can provide multiple advantages including:

- Support and promote national blood transfusion guidelines and evidence-based practice. (Several studies have shown that transfusion order sets have been fundamental in blood management initiatives.[5-7])
- Assist physicians in the decision making process for the care of their patients, and help guide appropriate transfusion practice.
- Improve patient safety by decreasing transfusion errors.
- Clarify communication to nursing and lab Transfusion Service staff regarding what products, how many units to prepare, and when to administer.
- Educate providers about evidence-based indications for transfusion and the particular type of blood products available at an institution.

In support of the Blood Utilization Project, the Transfusion Service implemented several new processes along with the implementation of the new order set. HUCs will now fax the "*Medical/Surgical Blood Product Transfusion-Adult Only*" order set to the Transfusion Service. Result: no more 'Pink Slips' and a reduced risk of transcription errors.

The faxed order now provides a means for data collection to better understand physician ordering transfusion practices. The Transfusion Service staff is partnering with the MSJH Performance Improvement staff for collection of this data which will be used for learning and process improvement projects in blood management.

For additional information on the new transfusion order set or the Blood Utilization Project contact Dr. Kathy Puca 1-6313 or Jan Weyhmiller 1-6260.

GOALS OF THE MSJH BLOOD UTILIZATION PROJECT

- Promote evidence-based transfusion practice
- Reduce unnecessary transfusions
- Standardize transfusion practice for non-bleeding, adult patients through use of evidence-based order set
- Improve patient outcomes

Transfuse Responsibly

- **Is patient symptomatic?**
- **Consider alternatives**
- **Order single RBC units**
- **Reassess patient after each transfusion**

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NEW TESTING METHODS EXPAND THE REPORTABLE RANGE FOR HEPATITIS C VIRUS QUANTITATIVE ASSAY

Timothy S. Uphoff, PhD, DABMG, Molecular Pathology Laboratory

On April 23, 2014 Marshfield Labs introduced a new Hepatitis C Viral Load (HCVQT) assay which replaces the previous method and expands the dynamic range for detection and quantitation of hepatitis C virus (HCV). The hepatitis C virus quantitative assay is highly sensitive and specific utilizing real time PCR technology to provide a wide linear analytic reporting range. The implementation of this new HCVQT test should be transparent to providers (the test name does not change) with the exception of two enhancements:

- The lower limit of detection and quantitation is now 15 IU/mL. This new lower limit of detection and quantitation enhances the assay's utility at critical treatment decision points for newer direct acting antivirals such as boceprevir, telaprevir, sofosbuvir, and simeprevir. The new reportable range for the assay is 15-100,000,000 IU/mL. Note: the previous reportable range was 43-69,000,000 IU/mL.
- The serum requirement is reduced from 2.5 mL to1.5 mL.

REPORTING

The expanded linear reportable range for Hepatitis C Virus RNA, Quantitative (test code HCVQT) is 15-100,000,000 IU/mL.

- If no HCV was detected, the result is reported as "HCV RNA Not Detected".
- If HCV was detected but the titer was less than 15 IU/mL, the result will be reported as "HCV RNA is detected, less than 15 IU/mL HCV RNA".
- If the result is 15-100,000,000 IU/mL, the numerical result will be reported.
- Results greater than 100,000,000 IU/mL will be reported as "HCV RNA Detected, but was above the analytical limit of 100,000,000 IU/mL".

RECOMMENDED LABORATORY TESTING FOR HEPATITIS C VIRUS (HCV)

Timothy S. Uphoff, PhD, DABMG, Molecular Pathology Laboratory

HCV TESTING BASICS

Four questions can typically be answered by HCV testing.

1. Has the patient been exposed to HCV?
   - Answer with HCV Immune status: Order Hepatitis C Antibody Test (HCVAB)
2. Does the patient have an active HCV infection?
   - Answer with HCV viral titer: Order HCV RNA Quantitative PCR (HCVQT)

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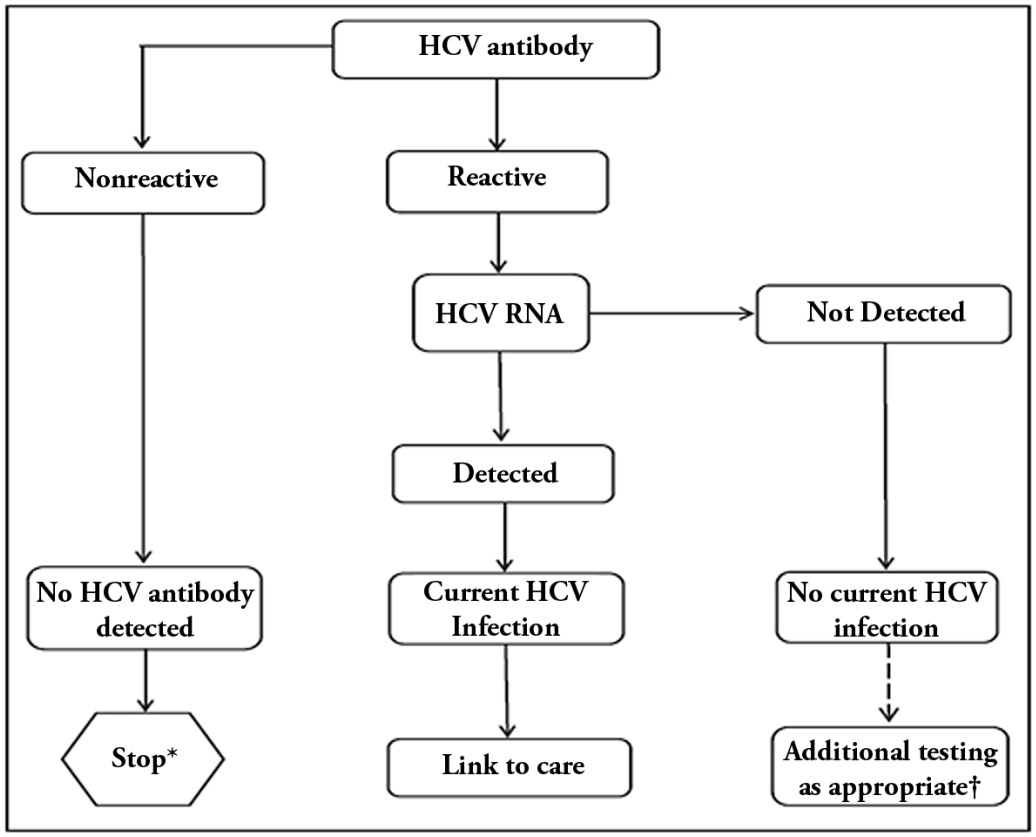
3. What is the recommended therapy for patients with an active infection?
   - Decide based on infecting HCV genotype: Order HCV Genotyping (HCVGEN)
4. Is the current antiviral therapy effective?
   - Answer with HCV viral titer: Order HCV RNA Quantitative PCR (HCVQT)

To establish if the patient has ever been exposed to HCV the first step is to determine their immune status against HCV. If a patient demonstrates an antibody response to HCV, the next step is to determine if they have an active infection. Since HCV culture is not routinely performed in clinical laboratories, active infections are identified by performing a quantitative viral RNA test to establish the viral titer. If an active infection is found, there are now a number of factors that will determine whether or not to treat the infection and what is the best therapeutic option. Some genotypes of HCV respond much more favorably to current therapies than others. HCV is highly variable genetically and there are six different HCV genotypes. Treatment options and duration vary depending on the infecting HCV genotype. Of the four most common genotypes in the U.S., genotype 1 accounts for about 77% of cases, genotype 2 for 14%, genotype 3 for 7%, and genotype 4 for 1%. HCV does not replicate clonally but as a quasispecies; even within an infected host there can be up to 2% nucleotide sequence variation among RNA genomes. Once treatment has been initiated, periodic testing for viral RNA levels is used to determine the effectiveness and duration of therapy.

Figure 1. CDC Recommended Testing Sequence for Identifying Current HCV Infection



* For persons who might have been exposed to HCV within the past 6 months, testing for HCV RNA or follow-up testing for HCV antibody should be performed. For persons who are immunocompromised, testing for HCV RNA should be performed.
† To differentiate past, resolved HCV infection from biologic false positivity for HCV antibody, testing with another HCV antibody assay can be considered. Repeat HCV RNA testing if the person tested is suspected to have had HCV exposure within the past 6 months or has clinical evidence of HCV disease, or if there is concern regarding the handling or storage of the test specimen.
(Adapted from CDC, 2013. MMWR. 2013;62(18):362-365.)

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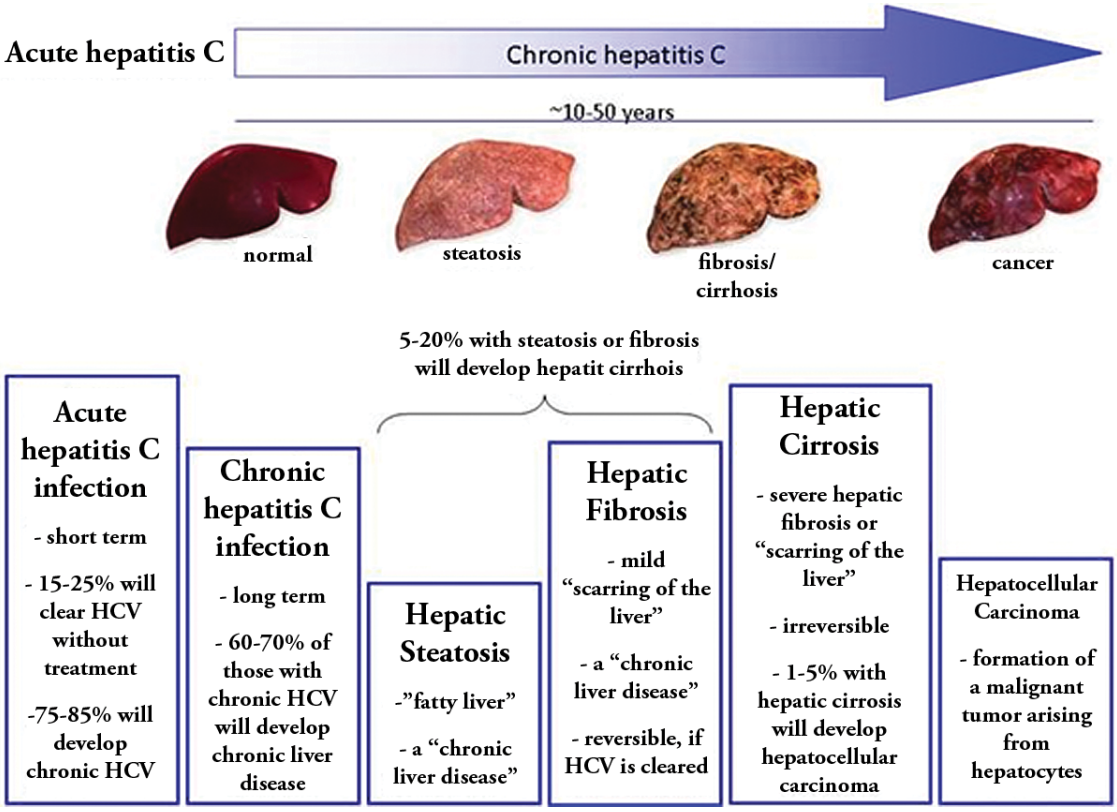
BACKGROUND

HCV is a Hepacivirus in the Flaviviridae family. Its positively stranded RNA genome is about 9,600 nucleotides in length and encodes a single large open-reading frame from which 11 proteins are derived. It is estimated that 1.6% of Americans have been infected with HCV and between 3 and 4 million of these are chronically infected. Worldwide, HCV affects an estimated 130 million to 150 million people and results in 350,000 to 500,000 deaths per year. Acute infections are often asymptomatic and chronic HCV infections may eventually lead to liver cirrhosis or carcinoma. Progressive liver damage from chronic HCV infection is a leading indication for liver transplants in the U.S.

Figure 2. Progression of Hepatitis C Infection to Hepatocellular Carcinoma



From: http://islaslab.wikispaces.com/Hepatitis+B+and+Liver+Cancer

Patients at highest risk for HCV include: IV drug users or those with a history of a needle stick injury with HCV infected blood, recipients of clotting factors made before 1987, hemodialysis patients, recipients of blood and/or solid organs before 1992, patients with undiagnosed liver problems, health care workers after possible exposure, and infants age 12-18 months born to HCV infected mothers (approximately 4 of every 100 infants born to HCV-infected mothers become infected with the virus). HCV testing is indicated for all of these high and intermediate risk patients. In August of 2012, the Centers for Disease Control (CDC) issued a recommendation that all persons born in the U.S. between 1945 and 1965 be screened for HCV infection.

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NEW TREATMENT OPTIONS AND MANAGEMENT GUIDELINES

Historically, treatment of HCV infected individuals has been very difficult. The introduction of direct-acting agents against HCV in 2011 (boceprevir and telaprevir being first, later sofosbuvir and simeprevir) has rapidly changed the treatment of HCV and has improved the outlook for patients; however, the timely diagnosis of infection remains essential. The rapid evolution of HCV therapeutics has prompted the release of newly updated practice guidelines at a very frequent pace. In May of 2013, the CDC released Testing for HCV Infection: An Update of Guidance for Clinicians and Laboratorians (MMWR May 10, 2013 / 62(18);362-365 available at http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6218a5.htm). The American Association for the Study of Liver Diseases (AASLD), the Infectious Diseases Society of America (IDSA), and the International Antiviral Society-USA released their latest joint treatment recommendations for hepatitis C virus (HCV) infection in March of 2014 which are now available at www.hcvguidelines.org. The World Health Organization (WHO) issued their first guidance on the treatment of HCV in April 2014 and it is available at: http://apps.who.int/iris/bitstream/10665/111747/1/9789241548755_eng.pdf?ua=1.

Response-guided therapy (RGT) is part of all treatment guidelines for the new direct-acting agents. RGT involves the use of HCV viral load monitoring during treatment to guide treatment duration decisions and has become an important part of patient management protocols. Clinicians typically base treatment duration decisions on the viral genotype as well as the rate of change in RNA levels—i.e., shorter treatment if declining rapidly and achieving non-measurable levels at defined time points, or longer if declining slowly, with possible cessation of treatment if declining little or not at all. Despite the complexities that RGT can add to patient management, it represents a personalized approach that can help optimize treatment safety and outcomes while minimizing the duration of periods when patients suffer drug side effects.

HCV treatment decisions are further based on a number of other parameters including the patient's health, likelihood of compliance, and liver function test results. Current treatment recommendations using the results of all patient information are beyond the scope of this document. We recommend the following references for further testing and treatment guidelines:

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