

SPONTANEOUS CLEARANCE OF HCV

Alan Franciscus, Editor-in-Chief, HCV Advocate

One of the most frequent questions I receive from people who attend our training workshops is about the rate of spontaneous viral clearance and what factors influence viral clearance. In the literature, there are estimates of spontaneous acute HCV viral clearance that range from 10 to 50%. It has been difficult to come up with a concrete number or percentage due to the limited number of patients who

statistics and sources for viral clearance of HCV, but for the most part educators use a figure that is somewhere between 15 and 25%. To my knowledge most educators use the six month period from time of initial infection to chronic infection as the definition for acute vs. chronic infection. But even this view is being challenged since there is some evidence that the current 6 month period we define for

three years after initial infection.¹

This article will review a study that was published in the *Journal of Viral Hepatitis* in early 2006 that has given us a better picture of the frequency of spontaneous viral clearance and some of the factors that are associated with a better chance of clearance.

J.M. Micallef and colleagues² from Australia conducted a systematic review of published literature using the MEDLINE database from January 1990 to April 2003. The inclusion criteria for their study included longitudinal (observations) assessment of individual cases from the time of acute HCV infection, at least one follow-up assessment within 24 months of initial diagnosis, HCV RNA (viral load) measured and reported for all study subjects, and only individuals who

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HEPSQUADS

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For example, should we be adjusting the pre- and post-test counseling message based on gender since the rate of spontaneous viral clearance is much higher in women than in men?

have been identified as having acute infection and because different criteria were used in the different studies. I have heard different educators quote different

acute is longer than we previously believed. For example, a study by Villano and colleagues found that there was viral clearance in some patients after more than



NEW HEPATITIS B VACCINATION GUIDELINES

Liz Highleyman

People with chronic hepatitis C should be vaccinated against hepatitis A and B, since hepatitis A virus (HAV) and hepatitis B virus (HBV) can cause more severe liver damage, including cirrhosis and hepatocellular carcinoma, in individuals with pre-existing liver disease.

In December 2006, the federal Advisory Committee on Immunization Practices (ACIP) issued new recommendations for increasing hepatitis B vaccine coverage among adults. The revised guidelines were published in the December 8, 2006 issue of *Morbidity and Mortality Weekly Reports Recommendations and Reports* (Vol. 55, No. RR-16).

The updated recommendations were prepared by a panel of 10 hepatology experts with the Centers for Disease Control and Prevention (CDC) National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention.

THE HEPATITIS B VACCINE

HBV is transmitted through exposure to blood or bodily fluids, either through punctures or damage to the skin (e.g., accidental needle sticks or sharing of syringes to inject drugs) or through direct contact with mucous membranes. The virus can be transmitted through sexual activity or from infected mothers to their babies during pregnancy or delivery.

ACIP notes that hepatitis B vaccination is “the most effective measure to prevent hepatitis B virus infection and its consequences, including cirrhosis of the liver, liver cancer, liver failure, and death.” Indeed, since an effective hepatitis B vaccine became available in the early 1980s, the rate of new HBV infections has declined dramatically. Nevertheless, it is estimated that in 2005 there were still 51,000 new HBV infections (down from 232,000 in 1990).

Two single-antigen HBV vaccines are available in the United States: Recombivax HB (made by Merck & Co) and Engerix-B (made by GlaxoSmithKline). Twinrix (also from GlaxoSmithKline) is a combination hepatitis A and B vaccine. The

vaccines use hepatitis B surface antigen (HBsAg), produced by recombinant DNA technology, to stimulate the immune system to produce antibodies against HBV. Three doses are required to ensure optimal protection, with boosters given one and six months after the first injection. Older individuals and people with suppressed immune systems (including HIV positive people) may have a decreased antibody response.

The most common side effects of the vaccine are pain at the injection site and mild fever; anaphylaxis (severe allergic reaction) is rare. HBV vaccines used in the United States do not contain thimerosal, a preservative containing toxic mercury. There has been some concern that the HBV vaccine may be linked to conditions including multiple sclerosis (MS), Guillain-Barré syndrome, and other autoimmune disorders. According to the CDC, “The weight of the available scientific evidence does not support the suggestion that hepatitis B vaccine causes or worsens MS or other demyelinating diseases,” and the American Medical Association maintains that, “the benefits of vaccination far outweigh the known and potential risks.” Nevertheless, studies are underway to further examine any possible connection.

VACCINE RECOMMENDATIONS

Today, the HBV vaccine is included in the standard series of immunizations for all infants, and is recommended for all adolescents who were not vaccinated as children. In addition, routine HBV screening is recommended for all pregnant women, and babies born to women with positive HBsAg tests or unknown serostatus should receive post-exposure prophylaxis using the HBV vaccine plus hepatitis B immunoglobulin (HBIG).

Hepatitis B vaccination is also recommended for “at-risk” adults, but this important public health measure has not been as widely implemented as hoped. Many at-risk individuals remain unprotect-

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ed, either because they have not been vaccinated at all or because they have not completed the full series of three shots. In fact, an estimated 95% of new HBV infections in 2005 occurred among unvaccinated adults.

ACIP recommends that the following individuals should be vaccinated against HBV due to behavioral risk factors:

- Heterosexuals with multiple sex partners;
- Men who have sex with men;
- Injection drug users (IDUs);
- Household contacts and sex partners of individuals with known chronic HBV infection.

In addition, the committee recommends universal HBV vaccination for all unvaccinated adults in settings in which a high proportion of individuals are at risk for HBV infection, including:

- Sexually transmitted disease and HIV testing and treatment facilities;
- Drug abuse treatment and prevention settings;
- Healthcare settings targeting services to IDUs, including needle-exchange sites;
- Healthcare settings targeting services to men who have sex with men;
- Prisons and other correctional facilities.

Further, ACIP recommends that in other primary care and specialty medical settings in which adults at risk for HBV infection may receive care, healthcare providers should:

- Provide information to all adults regarding the health benefits of hepatitis B vaccination, including risk factors for HBV infection and persons for whom vaccination is recommended;
- Help all adults assess their need for vaccination by obtaining a history that emphasizes risks for sexual transmission and percutaneous or mucosal exposure to blood;
- Vaccinate all adults who report risks for HBV infection;
- Vaccinate all adults who request protection from HBV infection, without requiring them to acknowledge a specific risk factor;

- Offer vaccination in a way that is accessible, convenient, and flexible for patients;
- Develop tracking and reminder systems to ensure completion of the full vaccine series;
- Use available reimbursement mechanisms to remove financial barriers to hepatitis B vaccination.

The HBV vaccine is also recommended for persons at risk of occupational exposure – such as medical and public safety personnel – and such employees typically require vaccination, as well as universal precautions (e.g., use of gloves) to prevent the spread of blood-borne infections. Individuals who administer tattoos and body piercings could also benefit from HBV vaccination.

However, the CDC estimates that about 80% of newly acquired HBV infections today are due to high-risk sexual activity (39% heterosexual; 24% among men who have sex with men) or drug injection practices (16%). Other known exposure routes – such as occupational exposure or exposure while undergoing medical procedures – together account for only 5% of new cases, while 16% of newly infected individuals have no known risk factors.

A combination of more widespread public education about the benefits and safety of the HBV vaccine and more active encouragement of vaccination by healthcare providers is needed to move toward the ultimate goal of eliminating all new hepatitis B infections. If current ongoing research comes to fruition, there may also be an effective hepatitis C vaccine in the coming years.

References

CDC. A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States: Recommendations of the Advisory Committee on Immunization Practices. Part 2: Immunization of Adults. *MMWR* Vol. 55, No. RR-16. December 8, 2006. <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5516a1.htm>.

CDC. A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States: Recommendations of the Advisory Committee on Immunization Practices. Part 1: Immunization of infants, children, and adolescents. *MMWR* Vol. 54, No. RR-16. December 23, 2005.



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were *untreated* during the follow-up period.

In all, 31 studies (a total of 675 patients) of acute hepatitis C were included in the analysis. The mean age of the study population was 22 (range 4-67 yo) and the follow-up period ranged from 6 to 157 months. The time period for viral clearance differed in the studies – 7 studies used 6 months of follow up, 6 studies used 12 months and the remaining 18 studies used longer periods of time ranging from 18 to 48 months after baseline assessment. The study populations were composed of 19 series of **acute clinical** HCV, nine of **post-transfusion** HCV, and three of **sero-incident** cases (sero-incident refers to those who seroconverted – i.e., developed antibodies – under observation).

The authors found that the rate of spontaneous viral clearance was 0.26 or 26% (weighted mean). Additional analysis found that viral clearance was much more common in women than men (40% vs. 19% (weighted mean)). The rate of viral clearance was not associated with HCV genotype or age at the time of infection. But it was found that the study population of **acute clinical** hepatitis C patients had a higher proportion of viral clearance (31%) than both **post-transfusion** (18%) and **sero-incident** studies (18%). This finding is consistent with other studies which have found that people with a robust immune response (and symptoms) have a better chance of spontaneous viral clearance. In other words, people who sought medical care because of their symptoms (**acute clinical**) were more likely to spontaneously clear HCV because of their symptoms (robust immune response). The people in the **post-transfusion** and **sero-incident** studies were less likely to spontaneously clear the virus because they didn't have symptoms (weak immune response) that would have prompted a visit to a clinic or doctor.

It was noted that for many of the studies, the mean follow-up period was less than 12 months, detection of HCV RNA (viral load), and elevated ALT levels. The authors pointed out that the general time period for viral clearance usually occurs during the first 12 weeks of infection so there is a possibility that some acute HCV cases were excluded from the studies because the viral load was negative at initial assessment. This led the

authors to conclude that “Given the limitations inherent in studies of acute hepatitis C, particularly the exclusion of initially HCV RNA-negative subjects, the true extent of viral clearance may be even higher.”

The implications for counseling messages for people who test positive to HCV antibody and are not given a confirmatory viral load test are many. For example, should we be adjusting the pre- and post-test counseling message based on gender since the rate of spontaneous viral clearance is much higher in women than in men? Should we be telling clients that even though most people will spontaneously clear HCV by 12 weeks, that there is a possibility of viral clearance occurring 6, 12, 18 months or even longer after initial infection?

The authors of this study recommend that more studies (with consistent criteria) be performed especially in injection drug users who comprise the population that is at highest risk for acquiring HCV. Hopefully, these studies will be conducted in the near future and give us a better understanding of spontaneous viral clearance and the implications for people who test positive so that we can give a clear and concise counselling message.

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Got an Event?

Have your events listed on the HCV Web site. Send the following to cdmazoff@hcvadvocate.org

Event: _____

When: _____

What: _____

Where: _____

Contact information: _____

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References:

¹Villano, S.A. Persistence of viremia and the importance of long-term follow-up after acute hepatitis C infection. *Hepatology*. 1999 Mar;29(3):908-14.

²Micallef, J.M. et al, Spontaneous viral clearance following acute hepatitis C infection: a systematic review of longitudinal studies. *J Viral Hepat*. 2006 Jan;13(1):34-41



Action alert!

Urge your Members of Congress to fund hepatitis C prevention in their appropriations request letters.

The first thing you can do this year to fight for HCV funding is to contact your elected representatives and ask them to include funds for hepatitis C prevention programs in their programmatic appropriations request letter. Please take a few minutes to make these important phone calls!

To find out more please go to:
<http://www.hcvadvocate.org/community/advocacy.asp>

Attention Trainers!

The Hepatitis C Support Project has launched a new program to help trainers with their educational efforts. Included are tools to help you educate others. Listed below are various files to download and use for your training needs.

1. **One Day 2006** is the entire slide presentation that we are currently using for our trainings. Included in the slides are notes – just click on the note function. *Format:* MS PowerPoint
2. **Overview of HCV in English** is a template for general information about hepatitis C in English. Included in the slides are notes – just click on the note function. *Format:* MS PowerPoint
3. **Overview of HCV in Spanish** is a template for the above file in Spanish. *Format:* MS PowerPoint
4. **HCV Myths** is a presentation about various myths about hepatitis C. Included in the slides are notes – just click on the note function. *Format:* MS PowerPoint
5. **Game:** Hecardy contains a sample game board, questions/answers. *Format:* MS Word.
6. **Crossword Puzzle:** Puzzle #1 and answers *Format:* Adobe pdf.

To access these files just cut and paste the following into your browser:

<ftp://trainer:1234Qwer@www.hcvadvocate.org>

Note: For those people who have had problems downloading materials on our FTP site we have switched servers and you should be able to download and use all the tools available on our ftp site.

YOUR BROWSER MUST BE ENABLED FOR FTP.

To enable ftp in Internet Explorer

1. In internet explorer, click on tools, internet options, advanced
2. Then click on Enable folder view for ftp
3. Scroll down
4. Click on Use passive ftp

Please keep checking back – we will be posting additional files to help educate people about hepatitis C. If you have any suggestions for information that will help you, please email alanfranciscus@hcvadvocate.org