Prevalence and Management of Chronic Hepatitis C Virus Infection in Women

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KEYWORDS
- Viral hepatitis
- Women
- Pregnancy
- Antiviral therapy

KEY POINTS
- Women should be tested for hepatitis C virus if they have risk factors for exposure, including birth year between 1945 and 1965.
- Routine hepatitis C virus testing is not recommended in pregnancy, except for women with risk factors for exposure.
- Hepatitis C virus infection does not clearly confer adverse risk during pregnancy, except in patients with cirrhosis.
- Premenopausal women must be carefully counseled about the risks of pregnancy and breast feeding during hepatitis C virus treatment.
- Highly effective hepatitis C virus antiviral therapies are rapidly emerging. All women with hepatitis C virus should be assessed for treatment candidacy.
EPIDEMIOLOGY AND MANAGEMENT OF HEPATITIS C VIRUS IN WOMEN

Hepatitis C virus (HCV) is the most common blood-borne pathogen in the United States, chronically infecting an estimated 1% of the population, including roughly 970,000 women.\textsuperscript{1} HCV is the nation’s leading cause of cirrhosis, liver failure, hepatocellular carcinoma, and liver transplantation. HCV typically remains asymptomatic for 2 to 4 decades until cirrhosis, hepatocellular carcinoma, or liver failure occurs. Therefore, despite a decline in the number of new HCV infections in the United States since 1990, the burden of HCV-related complications is projected to continue increasing over the next 20 years.\textsuperscript{2}

Women account for approximately 35.8% of cases of chronic HCV.\textsuperscript{1} The course of HCV and its complications varies between women and men. In addition, women with HCV face unique risks related to antiviral treatment during pregnancy and breast feeding and the potential for vertical transmission to their offspring. The following review describes the epidemiology, disease progression, and treatment of HCV in women.

TRANSMISSION OF HEPATITIS C VIRUS IN WOMEN

HCV is spread by blood contact. The main modes of transmission include intravenous or intranasal drug use, blood product transfusion before 1990, and percutaneous exposures such as needle stick injuries. Table 1 describes the US prevalence of HCV infection in selected risk groups for men and women.

Unlike hepatitis B virus or human immunodeficiency virus (HIV), sexual transmission of HCV between serodiscordant heterosexual partners is rare, with an incidence of 0.07% per year (or 1 in every 190,000 sexual contacts).\textsuperscript{3} Therefore, from an HCV perspective, most women in long-term monogamous heterosexual relationships can safely maintain their current practices. Women who are concerned about HCV transmission or who have other risk factors that increase their chances of acquiring HCV (eg, HIV, multiple partners, injection drug use) should be counseled about safe sex practices with barrier methods. The rate of HCV transmission between female sexual partners is unknown, but is likely to be exceptionally low.

Table 1
US prevalence of HCV infection in selected groups

<table>
<thead>
<tr>
<th>Population</th>
<th>HCV Infection Prevalence (%)</th>
<th>Range (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1945–1965 birth cohort</td>
<td>3.25</td>
<td>2.80–3.76\textsuperscript{b}</td>
</tr>
<tr>
<td>History of injection drug use</td>
<td>79</td>
<td>72–86</td>
</tr>
<tr>
<td>Unexplained abnormal aminotransferase levels</td>
<td>15</td>
<td>10–18</td>
</tr>
<tr>
<td>Hemophilia with receipt of clotting factors before 1987</td>
<td>87</td>
<td>74–90</td>
</tr>
<tr>
<td>Organ transplant or blood product transfusion before 1990</td>
<td>6</td>
<td>5–9</td>
</tr>
<tr>
<td>Children born to HCV-infected mothers</td>
<td>5</td>
<td>0–25</td>
</tr>
<tr>
<td>Chronic hemodialysis</td>
<td>10</td>
<td>0–64</td>
</tr>
<tr>
<td>Men who have sex with men</td>
<td>4</td>
<td>2–18</td>
</tr>
<tr>
<td>HIV</td>
<td>25</td>
<td>15–30</td>
</tr>
</tbody>
</table>

\textsuperscript{a} Includes both men and women.

\textsuperscript{b} Presented as a 95% confidence interval.

Data from Refs.\textsuperscript{7,28,29}
**Vertical Transmission of Hepatitis C Virus**

Based on systematic review of 77 prospective cohort studies of HCV-infected pregnant women, the overall rate of mother-to-infant transmission is 1.7% for antibody-positive women (indicating past exposure but not necessarily viremia) and 4.3% for women with documented HCV viremia.4 Women with HIV/HCV co-infection have a 19.4% rate of vertical transmission.4 Risk factors for vertical transmission include high HCV viral load, HIV co-infection, prolonged rupture of membranes, and invasive fetal monitoring such as the use of scalp electrodes.5 Meta-analysis suggests that cesarean section does not reduce the risk of vertical transmission in HCV mono-infected women.6 Based on the lack of evidence, professional society guidelines do not currently recommend specific interventions to prevent HCV vertical transmission.

**Hepatitis C Virus Transmission and Breast Feeding**

HCV may be found in human breast milk, but breast feeding does not promote HCV transmission except in cases of cracked, damaged, or bleeding nipples. Breast feeding can safely be recommended for women with HCV, except in HIV/HCV co-infection or instances of cracked, damaged, or bleeding nipples.

**Screening for Hepatitis C Virus in Women**

The 1945 to 1965 (“baby boomer”) birth cohort accounts for 75% of all cases of HCV in the United States, a phenomenon believed to result from high prevalence of HCV risk behaviors and iatrogenic exposure through unscreened blood products.7 Because up to 50% of patients with HCV report no traditional risk factors, the CDC recommends all individuals born between 1945 and 1965 undergo testing for HCV, regardless of sex or risk factor status.7,8 Additionally, testing should be offered to women of any age with risk factors.

**Screening for Hepatitis C Virus in Pregnant Women**

The American College of Obstetrics and Gynecology recommends HCV testing in pregnant women with infection risk factors but does not endorse routine screening for all pregnant women.9 In large studies drawn from the general US population, HCV antibody positivity occurs in 0.24% to 4.3% of pregnant women.5,10,11 In one review including 9 international studies of pregnant women with HCV, most had clear risk factors such as history of intravenous drug use (range, 17%–79%) or blood transfusion (2.5%–19%).12 Furthermore, cost effectiveness analysis does not favor the use of routine HCV screening in pregnancy, even under the assumption that vertical transmission could be prevented.13

Most of HCV in pregnancy represents chronic rather than acute infection. Acute HCV in pregnancy rarely causes adverse maternal or fetal outcomes, although several case reports describe instances of fulminant hepatitis.14 Pregnant women with abnormal liver function and HCV infection risk factors, such as recent intravenous drug use, should be ruled out for acute HCV through quantitative HCV viral load testing even if their antibody test result is negative.

**Natural History of Hepatitis C Virus in Women**

Spontaneous clearance of HCV occurs shortly after infection some exposed persons. Cohort studies of HCV-exposed women find higher rates of spontaneous clearance among women compared with men. In a landmark study of 376 young Irish women who contracted HCV in 1977 to 1978 from contaminated anti-D immune globulin,
Kenny-Walsh\textsuperscript{15} found that 45% had spontaneously cleared the virus after 17 years. In contrast, spontaneous clearance occurs in approximately 20% of the general (predominantly male) HCV-exposed population.

Women with HCV progress to cirrhosis more slowly than men. Kenny-Walsh\textsuperscript{15} reported that half the chronically infected women in their cohort had biopsy evidence of liver fibrosis after 17 years, with 1.9% having definite or probable cirrhosis. A follow-up study of this cohort examined patients who had undergone a repeat liver biopsy at least 5 years later (n = 184).\textsuperscript{16} Compared with the baseline biopsy, fibrosis regressed in 24% of women, progressed in 27%, and remained the same in 49%.\textsuperscript{16} At 24 years postinfection, just 2.1% of the women showed evidence of cirrhosis on liver biopsy.\textsuperscript{16} This study did not address the rate of progression to cirrhosis over longer time intervals, and the cohort was composed of women infected with HCV at a young age and with minimal alcohol intake. However, other studies specifically examining women show low rates of progression to cirrhosis.\textsuperscript{17} Rigorous natural history studies including both men and women consistently find that female sex is protective against liver fibrosis, even after adjusting for age at infection and a tendency toward heavier alcohol consumption in men.\textsuperscript{18}

**Hepatitis C Virus and Pregnancy**

In general, pregnancy does not appear to affect the natural history of maternal chronic HCV.\textsuperscript{19} Most women with chronic HCV experience a temporary decline in transaminase levels during pregnancy, and viral load may fluctuate. No high-quality evidence suggests that pregnancy impacts viral clearance or degree of hepatic fibrosis on a long-term basis.

Prospective evidence suggests that chronic HCV does not negatively affect pregnancy outcomes, unless there is established cirrhosis. Among Irish women with iatrogenic HCV infection after their first pregnancy (n = 36), no increase in spontaneous abortion, preterm delivery, or obstetric complications in subsequent pregnancies was observed relative to matched controls.\textsuperscript{20} One retrospective population-based study examining birth records from 506 HCV-infected women found an increased rate of low birth weight, small size for gestational age, use of intensive care, or assisted ventilation relative to drug-using and randomly selected HCV-negative women.\textsuperscript{21}

**Comorbid Alcohol Use and Hepatitis C Virus in Women**

Alcohol intake is an important cofactor in the progression of HCV in both sexes, but the effect of alcohol is more pronounced in women than in men. Chen and colleagues\textsuperscript{22} identified 3187 deaths from HCV in a national study of death records from 2000 to 2002. Among women who died of HCV-related causes, the mean age of death declined from 61.0 years with HCV alone to 49.1 years with HCV plus heavy alcohol use. In men, the mean age of death decreased from 55.1 years with HCV alone to 50.0 years with HCV plus heavy alcohol use. The cumulative probability of death before age 65 was much higher in the setting of heavy alcohol with HCV (0.91 for men, 0.88 for women) than in HCV alone (0.68 for men, 0.47 for women). Although women generally seem to have a lower risk of mortality from HCV than men, in the setting of heavy alcohol their mortality rate becomes similar.

**PHARMACOLOGIC MANAGEMENT OF HEPATITIS C VIRUS IN WOMEN**

The goal of HCV antiviral therapy is to achieve sustained virologic response or permanent clearance of the virus as assessed by negative HCV viral load 6 months or more after treatment completion. HCV treatment is a rapidly developing area, with
numerous new drugs entering the marketplace. Choice of regimen now depends primarily on viral genotype, cirrhosis status, and history of prior treatment exposure.

Until the 2013 approval of the polymerase inhibitor, sofosbuvir, and the second-generation protease inhibitor, simeprevir, all HCV antiviral regimens were based on the injectable cytokine interferon. Interferon is typically combined with the nucleotide analogue ribavirin. In 2011, the first protease inhibitors, telaprevir and boceprevir, were approved by the US Food and Drug Administration. These medications increased the effectiveness of interferon and ribavirin but with significantly greater inconvenience, pill burden, side effects, and financial costs. The second generation of direct-acting antiviral medications, including sofosbuvir, simeprevir, and ledipasvir, have significantly improved treatment outcomes and side-effect profiles relative to earlier drugs. Currently approved HCV treatment regimens are the same for both women and men and are outlined in Table 2. Outcomes of treatment are similar between women and men.

Historically, side effects and contraindications to interferon-based therapy (Table 3) constituted a major treatment barrier for men and women alike. Selected side effects of interferon include flulike symptoms, bone marrow suppression including anemia and neutropenia, and depression. Ribavirin causes hemolytic anemia and rash. Contraindications to traditional therapy with interferon and ribavirin include decompensated cirrhosis, severe thrombocytopenia, uncontrolled depression, renal failure, pregnancy or risk for pregnancy, and numerous others. Several interferon contraindications, including autoimmune hepatitis and thyroid dysfunction, are more common in women and should be ruled out before starting interferon.

In the past, low treatment efficacy, burdensome regimens, and treatment duration up to 48 weeks presented significant obstacles to both initiation and completion of therapy. Interferon-based regimens are rapidly becoming obsolete in favor of newer, highly effective, and more tolerable regimens. In the near future, the possibility of virologic cure for the majority of HCV patients may be realized for the first time.

**Determination of Hepatitis C Virus Antiviral Treatment Candidacy**

Antiviral treatment should be considered for all HCV-infected women interested in therapy and able to comply with treatment requirements. HCV-infected women with compensated or mildly decompensated cirrhosis are at high risk for eventual progression to liver failure and should be strongly considered for antiviral therapy. Interferon-free regimens now exist for all genotypes and are the treatments of choice for most patients. As with men, pretreatment counseling to explain the risks, benefits, indications, and expected side effects is essential to successful completion of antiviral therapy.

**Hepatitis C Virus Treatment Considerations in Premenopausal Women**

Premenopausal women face special treatment considerations in relation to the teratogenic potential of HCV antivirals. Ribavirin is contraindicated in pregnancy because it interferes with embryo development and is embryotoxic or embryolethal in animal models. Drug manufacturers recommend avoiding ribavirin during pregnancy and up to 6 months postexposure for both females and their male partners. Ribavirin registries are maintained that track pregnancies occurring after maternal or paternal exposure. Premenopausal women with HCV, and HCV-infected men with premenopausal partners, must be counseled about the teratogenicity of ribavirin before beginning therapy. Two forms of contraception are recommended during ribavirin treatment and up to 6 months thereafter in addition to regular pregnancy testing during therapy.
<table>
<thead>
<tr>
<th>Study</th>
<th>Regimen</th>
<th>Treatment Duration (wk)</th>
<th>Population</th>
<th>Sustained Virologic Response, % (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Women</td>
</tr>
<tr>
<td>Poordad et al</td>
<td>Pegylated interferon/ribavirin/boceprevir</td>
<td>48</td>
<td>Gt 1, treatment naive</td>
<td>67 (145)</td>
</tr>
<tr>
<td>Bacon et al</td>
<td>Pegylated interferon/ribavirin/boceprevir</td>
<td>36</td>
<td>Gt 1, treatment experienced</td>
<td>56 (64)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>65 (49)</td>
</tr>
<tr>
<td>Jacobson et al</td>
<td>Pegylated interferon/ribavirin/telaprevir</td>
<td>48</td>
<td>Gt 1, treatment naive</td>
<td>75 (149)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Men</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>66 (221)</td>
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<tr>
<td></td>
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<td></td>
<td></td>
<td>60 (98)</td>
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<td></td>
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<td></td>
<td></td>
<td>67 (112)</td>
</tr>
<tr>
<td>Jacobson et al</td>
<td>Pegylated interferon/ribavirin/telaprevir</td>
<td>48</td>
<td>Gt 1, treatment experienced</td>
<td>65 (49)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>67 (112)</td>
</tr>
<tr>
<td>Lawitz et al</td>
<td>Pegylated interferon/ribavirin/sofosbuvir</td>
<td>12</td>
<td>Gt 1, 4, treatment naive</td>
<td>94 (118)</td>
</tr>
<tr>
<td></td>
<td>Sofosbuvir/ribavirin</td>
<td>12</td>
<td>Gt 2, treatment naive</td>
<td>79 (85)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>61 (168)</td>
</tr>
<tr>
<td>Zeuzem et al</td>
<td>Sofosbuvir/ribavirin</td>
<td>12</td>
<td>Gt 2</td>
<td>94 (33)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>92 (40)</td>
</tr>
<tr>
<td>Kumada et al</td>
<td>Pegylated interferon/ribavirin/simeprevir</td>
<td>12</td>
<td>Gt 1, treatment naive</td>
<td>94 (16)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Gt 1, prior relapers</td>
<td>100 (13)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Gt 1, prior nonresponders</td>
<td>38 (13)</td>
</tr>
<tr>
<td>Lawitz et al</td>
<td>Sofosbuvir/simeprevir ± ribavirin</td>
<td>12–24</td>
<td>Gt 1</td>
<td>98 (60)</td>
</tr>
<tr>
<td>Jacobson et al</td>
<td>Pegylated interferon/ribavirin/simeprevir</td>
<td>12</td>
<td>Gt 1, treatment naive</td>
<td>80 (116)</td>
</tr>
<tr>
<td>Manns et al</td>
<td>Pegylated interferon/ribavirin/simeprevir</td>
<td>12</td>
<td>Gt 1, treatment naive</td>
<td>85 (117)</td>
</tr>
<tr>
<td>Afdhal et al</td>
<td>Ledipasvir/sofosbuvir</td>
<td>12</td>
<td>Gt 1, treatment naive</td>
<td>100 (86)</td>
</tr>
<tr>
<td>Afdhal et al</td>
<td>Ledipasvir/sofosbuvir</td>
<td>12</td>
<td>Gt 1, treatment experienced</td>
<td>94.3 (35)</td>
</tr>
</tbody>
</table>

**Abbreviation:** Gt, genotype.

*Results not reported by sex.*

*Data from Refs. 30–42*
The first-generation protease inhibitors, telaprevir and boceprevir, introduced an additional layer of risk for unintended pregnancy because of drug interactions with hormonal contraceptives. Due to cytochrome p450-inducing effects, telaprevir and boceprevir lower the concentration of circulating estrogens, potentially reducing the efficacy of oral contraceptive pills. Women taking telaprevir or boceprevir must be counseled to use 2 nonhormonal forms of birth control to avoid pregnancy. Instead of oral contraceptives, acceptable alternatives include a male condom or female condom with spermicidal jelly (a combination of a male condom and a female condom is not suitable), diaphragm or cervical cap with spermicidal jelly, intrauterine device, or male or female sterilization. Newer HCV antivirals, including sofosbuvir and ledipasvir, have no pharmacokinetic interactions with hormonal oral contraceptives and may be safely co-administered.

**Hepatitis C Virus Treatment Considerations During Pregnancy and Breast Feeding**

Safe HCV treatment options during pregnancy are limited and of limited efficacy (see Table 3). Therefore, treatment for acute HCV in pregnancy is rarely indicated. HCV antiviral medications are not currently approved for use in breast feeding women.

**NONPHARMACOLOGIC MANAGEMENT STRATEGIES FOR HEPATITIS C VIRUS**

Women who opt not to undergo HCV treatment or who have contraindications to treatment should be monitored at least annually for clinical or laboratory signs of cirrhosis. All patients with HCV should be counseled on harm reduction strategies including alcohol abstinence, hepatitis A and B vaccination, and transmission prevention. Treatment candidacy should be reassessed on an ongoing basis to identify patients whose eligibility and interest in treatment may have changed.

**PSYCHOSOCIAL CONSIDERATIONS FOR WOMEN WITH HEPATITIS C VIRUS INFECTION**

HCV is frequently linked to injection drug use in the public and medical consciousness, often creating a climate of stigma for individuals with HCV. Qualitative studies focusing on women with HCV describe intense feelings of social stigma and shame. Virtually all the women in one qualitative study by Grundy and Beeching described fears of transmitting HCV to sexual partners and especially to their children (either vertically or through routine childcare activities), even when the women could verbalize the small absolute risk of such transmission. Grundy and Beeching reported that women frequently avoided disclosing their HCV status to others, and some even perceived medical care for HCV as stigmatizing.

The subjective experience of HCV varies widely, particularly between women who are actively using injection drugs compared with those who quit using or who don’t have traditional HCV risk factors. Qualitative research suggests that many women with a history of injection drug use may regard HCV infection as an expected and inevitable consequence of that behavior. For individuals with HCV diagnosed many years after ceasing injection drug use, it may serve as a negative reminder of a previous identity from which the woman had hoped to separate herself. Women who are actively injecting drugs may not see HCV as immediately relevant in the context of their larger concerns about personal safety, addiction, substance use disorders treatment, and other immediate issues. In contrast, among women without classic HCV risk factors, the diagnosis can be personally devastating and disruptive to their individual identity.

Although the subjective disease experience of women with HCV may vary, it has the potential to impact intimate and family relationships and influence their health care
<table>
<thead>
<tr>
<th>Drug</th>
<th>Common Side Effects</th>
<th>Pregnancy Category</th>
<th>Breast Feeding Safety</th>
<th>Additional Concerns for Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pegylated interferon-alfa</td>
<td>Flu-like symptoms, fatigue, marrow suppression, depression, insomnia, irritability,</td>
<td>C</td>
<td>Unknown</td>
<td>Potential abortifacient; may disrupt normal menstrual cycle or cause amenorrhea</td>
</tr>
<tr>
<td></td>
<td>retinopathy, weight loss, nausea, diarrhea</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ribavirin</td>
<td>Hemolytic anemia, rash</td>
<td>X; call pregnancy</td>
<td>Unknown</td>
<td>May cause birth defects and fetal death; not to be initiated until negative pregnancy test and 2 forms of birth control; concern for female partners of male patients undergoing HCV treatment; continue birth control for 6 mo after completion of treatment</td>
</tr>
<tr>
<td></td>
<td>registry if exposed while pregnant</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Telaprevir</td>
<td>Anemia, rash, pruritis, hemorrhoids, diarrhea, dysgeusia, fatigue, vomiting,</td>
<td>B</td>
<td>Unknown; Manufacturer</td>
<td>May interfere with hormonal contraceptives</td>
</tr>
<tr>
<td></td>
<td>anorectal pain</td>
<td></td>
<td>recommends discontinuing treatment or taking into account the importance of therapy</td>
<td></td>
</tr>
<tr>
<td>Boceprevir</td>
<td>Anemia, hypersensitivity reactions, dysgeusia, dry mouth, vomiting, diarrhea,</td>
<td>B</td>
<td>Unknown; Manufacturer</td>
<td>May interfere with hormonal contraceptives; may affect estrogen in hormone replacement therapy</td>
</tr>
<tr>
<td></td>
<td>nausea, neutropenia, thrombocytopenia</td>
<td></td>
<td>recommends discontinuing treatment or considering the importance of therapy</td>
<td></td>
</tr>
<tr>
<td>Drug</td>
<td>Side Effects</td>
<td>Category</td>
<td>Cautions</td>
<td>No Data regarding use with hormonal contraceptives</td>
</tr>
<tr>
<td>---------------------</td>
<td>------------------------------------------------------------------------------</td>
<td>----------</td>
<td>---------------------------------------------------------------------------------------------</td>
<td>--------------------------------------------------</td>
</tr>
<tr>
<td>Sofosbuvir</td>
<td>Nausea, pancytopenia, depression</td>
<td>B</td>
<td>Unknown; Manufacturer recommends discontinuing treatment or considering the importance of therapy</td>
<td>No data regarding use with hormonal contraceptives</td>
</tr>
<tr>
<td>Simeprevir</td>
<td>Photosensitivity, rash, nausea, pruritis</td>
<td>C</td>
<td>Unknown; Manufacturer recommends discontinuing treatment or considering the importance of therapy</td>
<td>No data regarding use with hormonal contraceptives</td>
</tr>
<tr>
<td>Ledipasvir/sofosbuvir</td>
<td>Fatigue, headache, nausea, diarrhea, insomnia</td>
<td>B</td>
<td>Unknown; Manufacturer recommends weighing benefits of breastfeeding vs potential adverse effects on breastfed child</td>
<td>No clinically significant drug interactions with oral contraceptives</td>
</tr>
</tbody>
</table>

*Category A: adequate and well-controlled (AWC) studies in pregnant women failed to show risk to the fetus in the first trimester of pregnancy (and there is no evidence of a risk in later trimesters). Category B: animal reproduction studies failed to show a risk to the fetus, and there are no AWC studies in pregnant women or animals that show an adverse effect; but AWC studies in pregnant women fail to demonstrate risk to the fetus during the first trimester of pregnancy (and there is no evidence of risk in later trimesters). Category C: animal reproduction studies show adverse effect on the fetus, there are no AWC studies in humans, and the benefits from the use of the drug in pregnant women may be acceptable despite its potential risks; or animal studies have not been conducted and there are no AWC studies in humans. Category D: positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience in humans, but potential benefits from use of the drug in pregnant women may be acceptable despite potential risks. Category X: studies in animals or humans show fetal abnormalities, or there is positive evidence of fetal risk based on reports from investigational or marketing experience, or both, and the risk of the use of the drug in a pregnant woman clearly outweighs any possible benefit.*

Data from Refs. 43–49

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**Chronic Hepatitis C Virus Infection in Women**
interactions. Providers caring for women with HCV should consider proactively reassuring them that the virus is generally not transmissible to household members, including children, and that sexual transmission between monogamous partners is extremely rare.

**FUTURE CONSIDERATIONS**

HCV continues to be an important cause of liver-related morbidity and mortality as the high-prevalence “baby boomer” cohort transitions through the clinical phases of chronic infection and cirrhosis. New HCV antiviral regimens based on direct-acting antiviral agents without interferon have greatly expanded the pool of patients eligible for treatment and have dramatically improved treatment outcomes. Premenopausal women with HCV should be counseled regarding the risk of vertical transmission and risks surrounding HCV treatment during pregnancy and breast feeding. As newer treatments promise even greater efficacy, the challenge for health care providers is to identify women in need of HCV testing and to understand the rapidly developing array of HCV treatments.

**REFERENCES**