Hepatitis A, B, and C Prevention and Treatment: Better, But More Expensive Treatments Available

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Dr. Hawkins practices family medicine at a federally qualified health center in Houston, Texas and works in outpatient Palliative Care. He has been teaching for 29 years. He serves on the AAFP Commission on the Health of the Public and Science and the subcommittee on Clinical Practice Guidelines His topics of specialty include patient-physician relationships and patient-centered communication; physician work-life balance; pulmonary conditions; palliative care; health care reform; and sexually transmitted infections. Dr. Hawkins believes the greatest challenge facing family physicians is communicating the value of family medicine to the public, legislators, and colleagues in other specialties.

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Learning Objectives

1. Follow current AAFP immunization schedules and preventive service recommendations for prevention of hepatitis infection.
2. Identify high-risk patients who should be screened for a hepatitis infection, and considered for hepatitis vaccination.
3. Counsel adult patients, and parents of children and adolescents, using available patient education resources and motivational interviewing about vaccine safety and efficacy.

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Learning Objectives (Continued)

4. Order appropriate laboratory and/or diagnostic tests to confirm diagnosis.
5. Construct an appropriate treatment plan for an adult patient with a confirmed diagnosis, taking into account tailoring of the treatment regimen for the individual, patient-specific barriers to treatment, follow-up monitoring, and making an appropriate referral.

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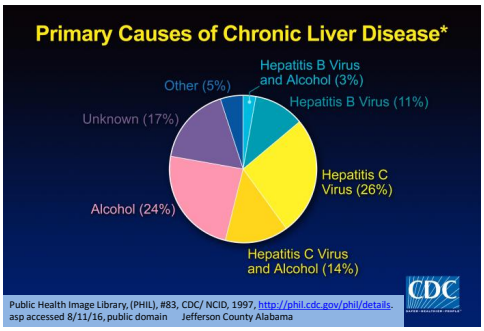
Audience Engagement System

Simplified Objectives: ABC

1. Prevention, Immunize
2. Identify High Risk Patients for screening
3. Counsel adults and children about vaccine
4. Lab Testing: Which and When
5. Develop Treatment Plans



Hepatitis A & B ICD-10

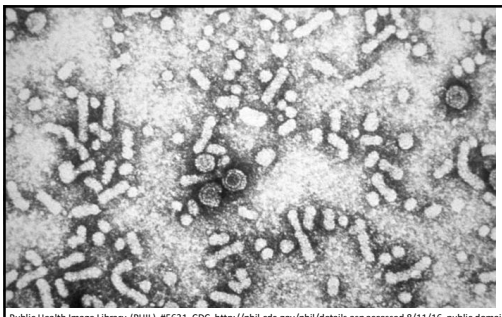
Name	ICD-10
Hepatitis A with hepatic coma	B15.0
Hepatitis A without hepatic coma	B15.9
Hepatitis B acute	B16.-
Hep B with delta-agent with coma	B16.0
Hep B without delta-agent without coma	B16.1
Chronic Hepatitis, unspecified	K73.9

Medical History

- Hep A… (Alphabet begins)
- Hep B vaccination 1981... (Universal Precautions)
- Blood Donor Procedure without screening available (Hep C vector) (Non A, Non B..)
- International Vaccination programs (Hep C vector)
- Hep D, E, ... F "LMNO"

Hepatitis A

- Fecal Oral Transmission
- Vaccination Recommendations



Public Health Image Library, (PHIL), #5631, CDC, http://phil.cdc.gov/phil/details.asp accessed 8/11/16, public domain

Hep B Dane Particles

Virions, 42 nm in diameter
DNA-core 27 nm

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Hepatitis B Prevalence

- 400 million people worldwide
- Subclinical inactive carrier state
- Progressive chronic hepatitis
- Cirrhosis
- Decompensation
- Hepatocellular carcinoma
- Complications may be reduced by viral suppression

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Hepatitis B

- Endemic in SE Asia
- Acquisition at Birth correlates with carrier state, (infective)
- Not necessarily chronic active hepatitis
- Both carry risk for Hepatocellular Carcinoma

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Susceptible or Immune

HBsAg **anti-HBc** **anti-HBs**	Negative Negative Negative	Susceptible
HBsAg **anti-HBc** **anti-HBs**	Negative Positive Positive	Immune due to natural infection
HBsAg **anti-HBc** **anti-HBs**	Negative Negative positive	Immune due to hepatitis B vaccination

Adapted from CDC MMWR 2005;54(No. RR-16)

Infected

HBsAg **anti-HBc** **IgM anti-HBc** **anti-HBs**	Positive Positive Positive negative	Acutely Infected
HBsAg **anti-HBc** **IgM anti-HBc** **anti-HBs**	Positive Positive Negative negative	Chronically Infected
HBsAg **anti-HBc** **anti-HBs**	Negative Positive negative	-Resolved -False positive -Low level infection -Resolving acute

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Treatment (International Guidelines)

- Pegylated interferon
- Entecavir
- Tenofovir
- Choice controversial
- On-treatment monitoring of Hbsag
- Who to treat, for sustained viral response

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Vaccinate

- Universal Child Vaccination
- Perinatal Vaccination
- Vaccinate Hep C paie
- Consider benefits of vaccination for those undergoing high-risk activities
  - Sexual, employment

Testing for HCC

- Hepatocellular Carcinoma occurs in chronic Hep B & C
- Ultrasound screening
- Surgical and Medical

Case 1 Jason

- 28 yo WM who was incarcerated for 4 yrs, and has both amateur and "licensed" tattoos
- Not reporting MSM and negative for HIV
- Alcohol Dependent prior to incarceration but abstinent since and attends AA
- Chronic Pain syndrome (LBP) taking Hydrocodone 10/ APAP 325 qid (or more?)

ARS question 1

- You should perform the following tests

A. Liver Function Testing
B. RPR
C. HIV
D. Hepatitis Profile
E. All of the Above

ARS question 2

Jason comes back positive for Hepatitis C, you should then;

A. Decide on therapy based on LFT elevation
B. Assume he is not a candidate for Antiviral Therapy based on his income, so don't refer
C. Increase his Hydrocodone/APAP
D. Administer Hep A & B vaccination & offer HIV and Hep C genotype and viral load

Hepatitis C ICD 10

Name	ICD-10
Hepatitis C Acute	B17.1-
Hep C with hepatic coma	B17.11
Hep C without hepatic coma	B17.10
Chronic Hep C	B18.2
Other Chronic Hepatitis	B18.8

CPT Codes

Name	CPT
E & M	992xx.
Time Based: face to face/ >50% counseling/ coordinating care	
Chronic Care Management (20 min monthly)	90739,40,43
Chronic Care Management	90477,90746
Hep C antibody screening (MCR)	G0472

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How Hep C Spread

- Needlestick
- Transfusion
- Ie. While in US and Canada approximately 3% of people are infected with hepatitis C, Egypt has almost 15%
- 1/200 patients with transfusion contracted Hep C

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#2 Identifying High Risk Patients

- Hep A Risk: travel, outbreaks
- Hep B Risk: blood contact, tsf, travel, sex
- Hep C Risk: Blood tsf, injections

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Hep C Infection US

- 3.5 million general population
- 2.7 million in the general non-institutionalized population
- Plus an additional 800,000 incarcerated, institutionalized, or homeless
  - Estimated 29% of incarcerated men are positive
- Half of all infected people are unaware they are infected

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HCV History

- Non A Non B Hepatitis
- Higher incidence of HCV infections in the 1970s and 1980s (peaking at 230,000, compared with 15,000 in 2009)

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Risk Behaviors

- Risk Behaviors
  - Injection-drug use (current or ever, including those who injected once) 60% of all transmissions
  - Intranasal illicit drug use

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Risk Exposures

- Long-term hemodialysis (ever)
- Percutaneous/parenteral exposures in an unregulated setting
  - Healthcare, emergency medical, and public safety workers after needlesticks, sharps, or mucosal exposures to HCV-infected blood
- Children born to HCV-infected women
- Prior recipients of transfusions or organ transplants, including persons who:
  - Were notified that they received blood from a donor who later tested positive for HCV infection
  - Received a transfusion of blood or blood components, or underwent an organ transplant before July 1992
  - Received clotting factor concentrates produced before 1987
- Persons who were ever incarcerated

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Other Considerations

- HIV infection
- Sexually active persons about to start pre-exposure prophylaxis (PreP) for HIV
- Unexplained chronic liver disease and/or chronic hepatitis including elevated alanine aminotransferase levels
- Solid organ donors (deceased and living)

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Less Common Transmission

- mother-to-infant
- contaminated devices shared for noninjection drug use
- sexual transmission also occurs but generally seems to be inefficient except among HIV-infected men who have unprotected sex with men

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#4 Ordering Labs
Birth-Cohort Testing

- One-time HCV testing is recommended for persons born between **1945 and 1965**,* without prior ascertainment of risk. (1b)
- 68% of persons with HCV infection would have been identified through a birth cohort testing strategy, whereas only 27% would have been screened with the risk-based approach.

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High Risk Testing

- Annual HCV testing is recommended for persons who inject drugs and for HIV-seropositive men who have unprotected sex with men.
- Periodic testing should be offered to other persons with ongoing risk factors for exposure to HCV. (Level IIa-C)

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Test… What Test?

- An anti-HCV test is recommended
  - If positive, current infection should be confirmed by a sensitive HCV RNA test.
  - Rating: Class I, Level A
- If anti-HCV test negative but you suspect liver disease, testing for HCV RNA or follow-up testing for HCV antibody is recommended if exposure to HCV occurred within the past six months
  - testing for **HCV RNA** can also be considered in persons who are immunocompromised.
  - Rating: Class I, Level C
- If reinfection risk after previous spontaneous or treatment-related viral clearance
  - **initial HCV-RNA** testing is recommended because an anti-HCV test is expected to be positive.
  - Rating: Class I, Level C

Test…. What Test (2)

- Quantitative HCV-RNA testing is recommended prior to the initiation of antiviral therapy
  - document the baseline level of viremia (ie, baseline viral load).
  - Rating: Class I, Level A
- Testing for HCV genotype is recommended to guide selection of the most appropriate antiviral regimen.
  - Rating: Class I, Level A
- If found to have positive results for anti-HCV test and negative results for HCV RNA by polymerase chain reaction (PCR)
  - should be informed that they do not have evidence of current (active) HCV infection.
  - Rating: Class I, Level A

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#3 Counsel about Prevention & Vaccination

- "Opt Out"
- For those who refuse: seek to understand why
- Promote Hep B vaccination in adolescents as a sexually related intervention

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#5 Treatment Plan: Barriers & Referral

- Hepatitis A: Supportive
- Hepatitis B: Antiviral
- Hepatitis C: Antiviral

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ISDA 2016 Hep C Goals

- Reduce all-cause mortality and liver-related health adverse consequences, including ESLD and HCC, virologic cure
- Pursue a sustained virologic response, absence of detectable HCV RNA at least 12 weeks
- FDA-approved quantitative or qualitative nucleic acid test (NAT) with a detection level of 25 IU/mL or lower.
- Treatment is recommended for all patients with chronic HCV infection, except those with short life expectancies that cannot be remediated by treating HCV, by transplantation, or by other directed therapy
- Patients with short life expectancies owing to liver disease should be managed in consultation with an expert

http://www.hcvguidelines.org/full-report/initial-treatment-box-summary-recommendations-patients-who-are-initiating-therapy-hcv, accessed August 4, 2016

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Outcome of Current Regimens

- 4 randomized trials of 10 different IFN-based regimens (biopsies separated by a mean of 20 months)
  - 39% to 73% of patients who achieved an SVR had improvement in liver fibrosis and necrosis (Poynard, 2002b),
  - 50% reduction in cirrhosis
  - Portal hypertension, splenomegaly, and other clinical manifestations of advanced liver disease also improved.
  - 70% reduction in the risk of liver cancer (hepatocellular carcinoma [HCC])
  - 90% reduction in need for transplant

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Hep C Manifestations Reduced

- Severe extrahepatic manifestations, including cryoglobulinemic vasculitis, a condition affecting 10% to 15% of HCV-infected patients.
- Non-Hodgkin lymphoma and other lymphoproliferative disorders achieve complete or partial remission in up to 75% of cases following successful therapy for HCV infection
- Improved quality of life

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Waiting to Treat

- Swiss HIV Cohort Study also demonstrated that waiting to treat HCV infection at Metavir fibrosis stages F3 and F4 resulted in 2- and 5-times higher rates of liver-related mortality, respectively, compared with treating at Metavir stage F2.

Zahnd C, Salazar-Vizcaya LP, Dufour JF et al. Impact of deferring HCV treatment on liver-related events in HIV+ patients. Conference on Retroviruses and Opportunistic Infections (CROI) 2015. February 23-26, 2015; Seattle, WA.

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Child Turcotte Pugh (CTP) Classification

	Class A	Class B	Class C
Total points	5-6	7-9	10-15
Factor	1 point	2 points	3 points
Total bili	<34	34-50	>50
Abumin (g/l)	>35	28-35	<28
PT/INR	<1.7	1.7-2.3	>2.3
Ascites	None	Mild	Mod-Severe
Encephalopathy	None	I-II (or surpressed)	III-IV (refractory)

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Noninvasive Methods to Assess Liver

- Liver-directed physical exam (usually N)
- routine blood tests (eg, ALT, AST, albumin, Bili, INR & CBC
- Serum fibrosis marker panels
- Liver imaging (eg, ultrasound, computed tomography scan)
- Transient elastography
- APRI, (AST-to-platelet ratio index),
- FIB-4
- Assessment of liver surface nodularity and spleen size for occult portal hypertension

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Antiviral Drugs for Hep C

- **SMV** simeprevir; used for the treatment of those with genotype 1 of hepatitis C virus (HCV) who have compensated liver disease, including cirrhosis
- **SOF** sofosbuvir; a nucleoside analogue used in combination with other drugs for the treatment of HCV infection
- **TVR** telaprevir; an antiviral agent to treat hepatitis C

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Special Populations

- Coinfection with HIV
- Decompensated Cirrhosis
- Reinfection after Liver Transplant
- Renal Failure

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Combinations: Guidelines Hep C: ISDA (July 2016 ver b)

- Genotype 1a without cirrosis (evidence 1A)
  - **Daily oral elbasvir (50 mg)/grazoprevir (100 mg) 12 weeks (no baseline NS5A RAVs) ***
  - **Daily oral ledipasvir (90 mg)/sofosbuvir (400 mg) 12 weeks***
  - **Daily oral paritaprevir (150 mg)/ritonavir (100 mg)/ombitasvir (25 mg) plus twice-daily dosed dasabuvir (250 mg) with weight-based ribavirin 12 weeks**
  - **Daily oral simeprevir (150 mg) plus sofosbuvir (400 mg) for 12 weeks**
  - **Daily oral sofosbuvir (400 mg)/velpatasvir (100 mg) for 12 weeks***
  - **Daily oral daclatasvir (60 mg*) plus sofosbuvir (400 mg) for 12 weeks**
- Genotype 1a with cirrosis uncompensated (compensated see *)
- Genotypes 1b, 2,3,4, 5-6
  - **ledipasvir (90 mg)/sofosbuvir (400 mg) (HARVONI)**
  - **ledipasvir (90 mg)/sofosbuvir (400 mg) (EPCLUSA) regardless of genotype or cirrosis status**

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Newer Combinations

- Solovadi: Sofosbuvir
- Harvoni: Ledipasvir/Sofosbuvir
- Epclusa: sofosbuvir/velpatasvir
  - – Effective against all genotypes

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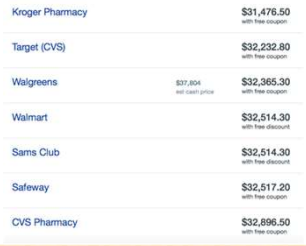
Harvoni Good Rx Price Per Month



Kroger Pharmacy		$31,476.50 with free coupon
Target (CVS)		$32,232.80 with free coupon
Walgreens	$37,804 out cash price	$32,365.30 with free coupon
Walmart		$32,514.30 with free discount
Sams Club		$32,514.30 with free discount
Safeway		$32,517.20 with free coupon
CVS Pharmacy		$32,896.50 with free coupon

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Drug Caution with Combination Pills

- Bradycardia with Amiodarone
- CYP2B6, CYP2C8 or CYP3A4: Rifampin, St. John's wort, and carbamazepine
- headache and fatigue; and when used with RBV in decompensated cirrhotics were fatigue, anemia, nausea, headache, insomnia, and diarrhea

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High Cost in US

- $94,500 price tag for standard 12-week treatment, Harvoni is one of the most expensive medicines in the world. However, many patients seek out a generic version of Harvoni from India which only costs around $900 – a fraction of a cost of the original.

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Cost

- – the US ($94,500)
- – Canada ($80,000)
- – the UK (£39,000)
- – Germany (48,000€)
- – Egypt ($1200)
- – India ($900)

http://esofosbuvir.com/harvoni-cost-in-usa-canada-europe-egypt-india/ accessed August 5, 2016

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Other Counseling for HCV patients

- Abstinence from alcohol, including treatment programs and interventions (IIa, B)
- Evaluation for other conditions that may accelerate liver fibrosis, including HBV and HIV (IIb, B)
- Cirrhosis?: liver biopsy, imaging, and/or noninvasive markers to determine treatment choice & HCC risk (I, A)
- Vaccination against hepatitis A and hepatitis B (IIa, C)
- Vaccination against pneumococcal infection is recommended to all patients with cirrhosis (IIa C)
- Education how to avoid HCV transmission to others (IC)

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Even More Counseling for HCV Patients

- Weight Reduction for Overweight or Obese (as "fatty liver" steatohepatitis, can accellerate cirrhosis)
  - Including structured programs, medical or surgical
- Statins are safe and effective in HCV patients
- Avoid hepatotoxic drugs (eg, excessive acetaminophen [ie, >2 g/d] or certain herbal supplements)
- Avoid nephrotoxic drugs (NSAID)
- Ongoing imaging surveillance for liver cancer and gastroesophageal varices.

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Specialty Referral

- Refer to a practitioner with expertise in assessment of liver disease severity and HCV treatment
- Subspecialty care and consultation are required for persons with HCV infection who have advanced fibrosis or cirrhosis (stage F3 or above on Metavir scale)
- Possible referral for consideration of liver transplantation
- Only 13% to 18% of HCV-infected persons had received treatment by 2013

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Historical Barriers to Care

- Contraindications to treatment (ie Affective illness in IFN regimens)
- Asymptomatic nature of disease
  - competing priorities
  - low treatment efficacy
  - long treatment duration
  - adverse effects
- Provider Inertia, lack of specialty access
- Resistance to treating persons currently using illicit drugs or alcohol

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Current Barriers to Care & Opportunities

- $$$
- Co-localized care
- Integrated care in high-risk areas/ clinics
  - correctional facilities
  - programs providing needle exchange, substance abuse treatment, and methadone maintenance
- Project ECHO (NM and rural areas)
- DOTS, Case Managers, Navigators

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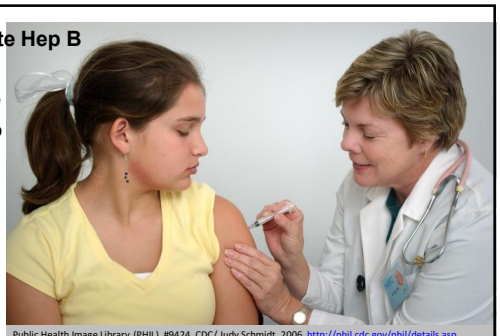
- **Vaccinate Hep B**
- **Teens**
- **Neonate**
- **1,3,6 mo**



Public Health Image Library, (PHIL), #9424, CDC/ Judy Schmidt, 2006, http://phil.cdc.gov/phil/details.asp accessed 8/11/16, public domain

Practice Recommendations - 1

- Be aware of A,B,C vectors and symptoms
- Educate for primary Prevention
- Test for Hep C in target Populations
- Test for Hep B in target Populations
- Test for HCC in patients with Hep B and C
- Immunize Hep C patients with A & B vaccines

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References

- ISDA guidelines www.hcvguidelines.org
- Nguyet-Cam V et al. Caring for Pregnant Women and Newborns with Hepatitis B or C. AFP 2010;82(10):1225-1229

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Questions

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Contact Information

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Billing & Coding

When services performed in conjunction with:

Office Visit 992xx *

*Time-based selection documentation criteria:

- Face-to-face time

Additional tests to confirm or monitor:

99490	**Chronic Care Management-20 minutes monthly**
90739, 90740, 90743, 90477, 90746, 90747	Hep B vaccines (under MCR)

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Billing & Coding (Continued)

Additional tests to confirm or monitor (continued):

G0010	Hep B vaccine administration (under MCR)
90471	Non-Medicare vaccine administration
86704	Hep B antibody core (HBcAb); total
86705	Hep B antibody core (HBcAb); IgM antibody
86708	Hep A antibody (HAAb)
86709	Hep A antibody (HAAb)l IgM antibody
G0472	Hep C antibody screening (MCR)
90632, 90633, 90634, 90636	Hep A vaccines

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