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SPRING–SUMMER 2003
PREVENTION AND TREATMENT OF HEPATITIS

Recommended Hepatitis A and B Immunization Schedule for Children and Adolescents, 2003

	Range of Recommended Ages				Catch-Up Vaccination				Preadolescent Assessment			
Vaccine	Birth	1 Month	2 Months	4 Months	6 Months	12 Months	15 Months	18 Months	24 Months	4–6 Years	11–12 Years	13–18 Years
Hepatitis B	**Hep B #1**	Only if mother is HBsAg-negative			**Hep B #2**			**Hep B #3**			**Hepatitis B Series**	
Hepatitis A											**Hepatitis A Series**	

Adapted from American Academy of Pediatrics 2003 Immunization Schedule. Available online at www.cispimmunize.org/pro2002_sch.html

Hepatitis A Vaccines (vaccine formulations are listed in alphabetical order by trade name.)

VACCINE	FDA LABELED INDICATION	DOSING SCHEDULE
Havrix® Inactivated hepatitis A vaccine (GlaxoSmithKline) www.gsk.com	Active immunization of persons ≥2 years of age against disease caused by hepatitis A virus (HAV)	Primary series of 2 injections: Ages 2–18: 0, 6–12 months > Age 18: 0, 6–12 months
Twinrix® Inactivated hepatitis A and recombinant hepatitis B co-formulation (GlaxoSmithKline) www.gsk.com	For vaccination of persons aged >18 years against hepatitis A and B	Primary series of 3 injections at 0, 1, and 6 months
VAQTA® Inactivated hepatitis A vaccine (Merck & Company) www.merck.com	For active pre-exposure prophylaxis against disease caused by the hepatitis A virus in individuals aged >2 years	Primary series of two injections: Ages 2–17: 0, 6–18 months Age >17: 0, 6 months

Notes on Hepatitis A Vaccine:
Protective levels of antibody (anti-HAV) persist for >20 years.
The most frequently reported adverse reactions occurring <3 days after vaccination are soreness at the injection site (53%–66%), headache (14%–16%), and malaise (7%). Reviews of data from multiple sources have not identified any serious adverse events associated with hepatitis A vaccination among either juveniles or adults.
Adverse events suspected to be associated with hepatitis A vaccination should be reported to the Vaccine Adverse Events Reporting System (VAERS). Reporting forms can be obtained by calling 1-800-822-7967.

Hepatitis B Vaccines (vaccine formulations are listed in alphabetical order by trade name.)

VACCINE	FDA LABELED INDICATION	DOSING SCHEDULE
Engerix-B® Recombinant hepatitis B vaccine (GlaxoSmithKline) www.gsk.com	Indicated for immunization against infection caused by all known subtypes of the hepatitis B virus	Primary series of 3 injections at 0, 1, and 6 months
Recombivax® HB Recombinant hepatitis B vaccine (Merck & Company) www.merck.com	For vaccination against infection caused by all known subtypes of the hepatitis B virus	Primary series of 3 injections at 0, 1, and 6 months R 2-dose primary series can be used in patients 11–15 years of age (see www.merck.com)
Twinrix® Inactivated hepatitis B and recombinant hepatitis B co-formulation (GlaxoSmithKline) www.gsk.com	For vaccination of persons aged >18 years against hepatitis A and B	Primary series of 3 injections at 0, 1, and 6 months

Notes on Hepatitis B Vaccine:
Hepatitis B vaccine has >95% final seroprotection rate among adolescents and healthy young adults.
Vaccination of adolescents and adults on a 0-, 2-, and 4-month, and adolescents on a 0-, 12-, and 24-month schedule, achieved final seroprotection rates similar to the 0-, 1-, and 6-month schedule.
Because hepatitis D (caused by the delta virus) does not occur in the absence of hepatitis B infection, it can be expected that hepatitis D will also be prevented by hepatitis B vaccination.
Adverse reactions associated with hepatitis B vaccine include pain at the injection site (3%–29%) and a temperature >37.7°C (1%–6%), but these effects are reported no more frequently among vaccine recipients than among placebo recipients in controlled trials. Anaphylaxis has been reported in 1/400,000 vaccine recipients; however, no deaths have been attributed to vaccinations.
The duration of vaccine-induced antibody and protection from hepatitis B virus (HBV) infection has been evaluated among vaccinated infants, juveniles, and adults. Studies indicate that although loss of detectable hepatitis B surface antibody (anti-HBs) has ranged from 13% to 60% by 9–15 years after vaccination, immune memory provides protection from HBV infection, and protection remains intact for >15 years, the longest period for which follow-up data are available. Because of the long duration of protection afforded by the 3-dose vaccine series, booster doses of vaccine are not needed among vaccinated immunocompetent juveniles or adults.
Adverse events suspected to be associated with hepatitis B vaccination should be reported to the Vaccine Adverse Events Reporting System (VAERS). Reporting forms can be obtained by calling 1-800-822-7967.

Drugs for the Treatment of Hepatitis B (drugs are listed alphabetically, within each class of agents.)

DRUG NAME	FDA LABELED DOSE	POTENTIAL SIDE EFFECTS/COMMENTS
ORAL AGENTS		
Adefovir dipivoxil **Hepsera™** (Gilead) www.hepsera.com	10 mg tablet orally once daily	Acute exacerbations of hepatitis have been reported in patients who have discontinued anti-hepatitis B therapy, including therapy with Hepsera®. Liver function should be monitored closely in patients who discontinue anti-hepatitis B therapy. If appropriate, resumption of anti-hepatitis B therapy may be warranted. In patients at risk of or having underlying renal dysfunction, chronic administration of Hepsera may result in nephrotoxicity. These patients should be monitored closely for renal function and may require dose adjustment. HIV resistance may emerge in chronic hepatitis B patients with unrecognized or HIV infection treated with anti-hepatitis B therapies that may have activity against HIV. Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogs alone or in combination with other antiretrovirals.
FDA labeled indications: Treatment of chronic hepatitis B in adults with evidence of active viral replication and either evidence of persistent elevations in serum aminotransferases (ALT or AST) or active disease on liver biopsy.		
Lamivudine **Epivir-HBV®** (GlaxoSmithKline) www.gsktrosetx.com/epivir	**Adults:** 100 mg orally once daily **Children:** 2–17 years: 3 mg/kg, to a maximum of 100 mg once daily; 20 mL oral solution once daily	This indication is based on 1-year histologic and serologic responses in adult patients, as well as more limited data from a study in pediatric patients.
FDA labeled indication: Treatment of compensated chronic hepatitis B associated with evidence of viral replication and active liver inflammation in adults and children aged 2 to 17 years.		
INJECTABLE		
Interferon alfa-2b **Intron®-A** (Schering) www.intron.com	**Adults:** 30 to 35 million IU per week, subcutaneously or intramuscularly (either 5 million IU daily or 10 million IU three times a week) for 16 weeks **Pediatrics:** 3 million IU/m² three times a week (TIW) for the first week of therapy followed by dose escalation to a 6 million IU/m² TIW (maximum of 10 million IU TIW) subcutaneously for 16 to 24 weeks	The most frequently reported adverse reactions in clinical trials were "flu-like" symptoms, particularly fever, headache, chills, myalgia, and fatigue. Alpha interferons, including Intron®-A, cause or aggravate fatal or life-threatening neuropsychiatric, autoimmune, ischemic, and infectious disorders. Patients should be monitored closely with periodic clinical and laboratory evaluations. Patients with persistently severe or worsening signs or symptoms of these conditions should be withdrawn from therapy. In many but not all cases these disorders resolve after stopping Intron-A therapy.
FDA labeled indication: Treatment of chronic hepatitis B in patients 1 year of age or older with compensated liver disease. Patients who have been serum HBsAg positive for at least 6 months and have evidence of HBV replication (serum HBeAg positive) with elevated serum ALT are candidates for treatment. Studies in these patients demonstrated that Intron-A therapy can produce virologic remission of this disease (loss of serum HBeAg), and normalization of serum aminotransferases. Intron A therapy resulted in the loss of serum HBsAg in some responding patients.		
Hepatitis B/HIV Co-Infection Currently, there are no treatments approved by the US Food and Drug Administration for the treatment of hepatitis B/HIV co-infection.R recent, small trial showed that treatment with the nucleotide analog tenofovir reduces hepatitis B virus (HBV) levels in patients coinfected with HIV, and appears to be equally effective in patients who have and have not been exposed to lamivudine.This study confirmed an earlier US study finding that adding tenofovir to a patient's current antiretroviral regimens dramatically reduced HBV DNA levels. Nelson M., Portsmouth S., Stebbing J., et al. An open-label study of tenofovir in HIV-1 and Hepatitis B virus co-infected individuals. AIDS (London) 2003; 17:77–F13.		

Drugs for the Treatment of Hepatitis C (drugs are listed in alphabetical order by manufacturer)

DRUG NAME	FDA LABELED DOSE	POTENTIAL SIDE EFFECTS/COMMENTS
Peginterferon alfa-2a **Pegasys®** (Roche) www.pegasys.com	180 µg subcutaneously per week	The most commonly reported adverse reactions in clinical trials were psychiatric reactions, including depression, irritability, anxiety, and flu-like symptoms such as fatigue, fever, myalgia, headache, and rigors. Pegasys® may cause or aggravate fatal or life-threatening neuropsychiatric, autoimmune, ischemic, and infectious disorders. Patients should be monitored closely with periodic clinical and laboratory evaluations. Therapy should be withdrawn in patients with persistently severe or worsening signs or symptoms of these conditions. In many, but not all cases, these disorders resolve after stopping Pegasys therapy. Pegasys should be used with caution in patients with creatinine clearance <50 mL/min.
FDA labeled indication: Pegasys is indicated alone or in combination with Copegus™ (ribavirin) for the treatment of adults with chronic hepatitis C virus infection who have compensated liver disease and have not been treated previously with interferon alpha.		
Ribavirin **Copegus™** (Roche) www.pegasys.com	**Genotypes 1, 4:** **<75 kg:** 1,000 mg orally per day, divided dose **≥75 kg:** 1,200 mg orally per day, divided dose **Duration:** 48 weeks **Genotypes 2, 3:** 2 x 200 mg capsules orally, twice daily **Duration:** 24 weeks	Ribavirin should not be given to pregnant women or women contemplating pregnancy. May cause birth defects and/or death of the fetus. Extreme care must be taken to avoid pregnancy in female patients and in female partners of male patients. Ribavirin can cause hemolytic anemia. The anemia associated with ribavirin therapy may result in a worsening of cardiac disease. Ribavirin is genotoxic and mutagenic and should be considered a potential carcinogen according to the FDA label. Ribavirin should not be used in patients with creatinine clearance <50 mL/min.
FDA labeled indications: In combination with Pegasys (peginterferon alfa-2a) for the treatment of adults with chronic hepatitis C virus infection who have compensated liver disease and have not been previously treated with interferon alpha. Patients in whom efficacy was demonstrated included patients with compensated liver disease and histological evidence of cirrhosis (Child-Pugh class B).		
Peginterferon alfa-2b **Peg-Intron®** (Schering) www.peginteron.com	1.5 µg/kg subcutaneously per week	Treatment with alpha interferons, including Peg-Intron®, is associated with neuropsychiatric, cardiac, pulmonary, GI, and systemic (flu-like) adverse effects. Because these adverse reactions may be more severe in the elderly, caution should be exercised in the use of Peg-Intron in this population. Alpha interferons, including Peg-Intron, cause or aggravate fatal or life-threatening neuropsychiatric, autoimmune, ischemic, and infectious disorders. Patients should be monitored closely with periodic clinical and laboratory evaluations. Patients with persistently severe or worsening signs or symptoms of these conditions should be withdrawn from therapy. In many but not all cases, these disorders resolve after stopping Peg-Intron therapy.
FDA labeled indication: For use alone or in combination with Rebetol (ribavirin) capsules for the treatment of chronic hepatitis C in patients not previously treated with interferon alpha who have compensated liver disease and are at least 18 years of age.		
Ribavirin **Rebetol®** (Schering) www.rebetol.com	2 x 200 mg capsules orally, twice daily	Must not be used by women, or male partners of women, who are or may become pregnant during therapy and during the 6 months after stopping therapy. Rebetol® and combination Rebetol/Peg-Intron therapy should not be initiated until a report of a negative pregnancy test has been obtained immediately prior to initiation of therapy. Women of childbearing potential and men must use effective contraception (at least two reliable forms) during treatment and during the 6-month post-treatment follow-up period. Significant teratogenic and/or embryocidal effects have been demonstrated for ribavirin in all animal species in which adequate studies have been conducted. These effects occurred at doses as low as one twentieth of the recommended human dose of Rebetol. If pregnancy occurs in a patient or partner of a patient during treatment or during the 6 months after treatment stops, physicians are encouraged to report such cases by calling 1-800-727-7864. Ribavirin can cause hemolytic anemia. Anemia associated with Rebetol therapy may exacerbate cardiac disease, leading to fatal and nonfatal myocardial infarctions. Patients with a history of significant or unstable cardiac disease should not be treated with Rebetol. It is advised that complete blood counts (CBC) be obtained at baseline and at weeks 2 and 4 of therapy or more frequently if clinically indicated.
FDA labeled indication: In combination with Peg-Intron (peginterferon alfa-2b, recombinant) injection for the treatment of chronic hepatitis C in patients with compensated liver disease who have not been previously treated with interferon alpha and are at least 18 years of age. The safety and efficacy of Rebetol copulses with interferons other than Intron-A or Peg-Intron products have not been established.		

Hepatitis C/HIV Co-Infection
Currently, there are no treatments approved by the US Food and Drug Administration for the treatment of hepatitis C/HIV co-infection. Trials of pegylated interferon and ribavirin for treatment of HCV/HIV co-infection are ongoing. Pending the results of these trials and FDA approvals, the emerging standard of care for HCV/HIV co-infection is based on a clinical trial of combination pegylated interferon and ribavirin in HCV monoinfected patients.
Potter M et al. Peginterferon alfa-2b plus ribavirin for chronic hepatitis C virus infection. N Engl J Med. 2002; 347:975–982.

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