TRM6100.01 INFECTIOUS DISEASE MANAGEMENT TECHNICAL REFERENCE MANUAL

U.S. DEPARTMENT OF JUSTICE
FEDERAL BUREAU OF PRISONS

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TRM 6100.01

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TABLE OF CONTENTS

Viral Hepatitis 1

Appendix 1. Algorithm for Interferon-alpha Treatment for Hepatitis B 27
Appendix 2. Algorithm for Interferon-alpha Treatment for Hepatitis C 28
Appendix 3. Contraindications for Interferon-alpha Treatment for Viral Hepatitis 29

HIV Infection 30

Appendix 1. HIV Classification Form 41
Appendix 2. Medical Evaluation and Treatment of HIV Infection by Immunologic Status . . . 43
Appendix 3. Anti-Retroviral Therapy - Nucleoside Analogues 45
Appendix 4. Anti-Retroviral Therapy - Protease Inhibitors 46
Appendix 5. Anti-Retroviral Therapy - Non-nucleoside Analogues 47
Appendix 6. Prophylaxis of Opportunistic Infections . . . 48
Appendix 7. HIV Chronic Care Flowsheet 49
Appendix 8. HIV Post-exposure Prophylaxis 50
Appendix 9. HIV Post-exposure Prophylaxis Fact Sheet . . . 51
Appendix 10. HIV Employee Consent/Declination Form for HIV Post-exposure Prophylaxis 53

Tuberculosis Disease 54

Appendix 1. Tuberculosis Treatment Guidelines 59

Tuberculosis Chemoprophylaxis 61

Appendix 1. Tuberculosis Chemoprophylaxis Record 73
Appendix 2. Monthly Isoniazid Side Effect Interview and Monitoring Form 74

Infectious Disease Treatment Protocol Study Guide 76

FEDERAL BUREAU OF PRISONS
TREATMENT GUIDELINES FOR VIRAL HEPATITIS

PURPOSE. The Federal Bureau of Prisons Treatment Guidelines for Viral Hepatitis provide recommended standards for the medical management of viral hepatitis for federal inmates.

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DEFINITIONS.

Hepatitis A is an acute viral hepatitis caused by a highly infectious RNA picornavirus that is transmitted primarily by the fecal-oral route. Hepatitis A has a mild to fulminant acute clinical presentation that does not progress to a chronic disease state.

HAV is hepatitis A virus

HAV IgM is the antibody developed against hepatitis A during acute infection. HAV IgM is present for 3-6 months after initial infection.

HAV IgG is the protective antibody developed against hepatitis A during convalescence. HAV IgG remains detectable for life and is indicative of remote infection with hepatitis A.

Hepatitis B is an acute or chronic viral hepatitis caused by a DNA virus transmitted perinatally, through blood exposure, and sexual contact. Hepatitis B has a self-limited to fulminant acute clinical presentation with approximately 10% of cases progressing to chronic hepatitis.

HBV is hepatitis B virus

HBsAg is hepatitis B surface antigen, a viral envelope antigen that is detectable during acute or chronic hepatitis B infection and indicative of active, contagious disease.

HBV chronic carrier is a person infected with HBV with a positive serology for HBsAg for 6 months or greater.

HBc is hepatitis B core antigen, an immunogenic protein of the HBV core.

HBeAg is hepatitis B e antigen, a secreted, viral antigen of the hepatitis B viral core that is indicative of active viral replication and increased infectiousness during acute or chronic hepatitis B infection.

Anti-HBs is the antibody to hepatitis B surface antigen that develops during convalescence from hepatitis B. The presence of anti-HBs is indicative of remote infection with hepatitis B and usually indicates protection from recurrent or new infection with HBV.

Anti-HBc IgM is the antibody to hepatitis B core antigen that develops during the acute onset of hepatitis B, becoming undetectable 6-24 months after the onset of illness.

Anti-HBc (total) is the total antibody response to hepatitis B core antigen that develops during the onset of hepatitis B and remains detectable during convalescence. Measurement of anti-HBc is the preferred screen for remote HBV infection.

Anti-HBe is the antibody to hepatitis e antigen that develops as viral replication and active hepatitis B begin to wane. Development of anti-HBe coincides with the loss of HBe antigen.

Hepatitis C is an acute or chronic viral hepatitis caused by a RNA virus that is transmitted primarily by parenteral contact with blood.

HCV is hepatitis C virus.

Anti-HCV is the antibody to HCV core and nonstructural proteins that is detectable from several weeks to months after clinical hepatitis. The presence of anti-HCV is an indicator of HCV infection, not immunity.

Anti-HCV EIA-2 is the second generation enzyme immunoassay used to diagnose HCV infection by measuring antibodies to HCV antigens. The presence of anti-HCV by EIA-2 in a person with risk factors for HCV infection is sufficient to diagnose HCV infection.

Anti-HCV RIBA-2 is the second generation recombinant immunoblot assay that measures antibodies to the HCV antigens used in EIA-2 through immunoblot technology. RIBA-2 measurement of antibodies to HCV is used as a supplementary, "confirmatory," test for persons without risk factors for HCV infection who test positive for HCV antibodies by EIA-2.

HCV RT-PCR assay is the reverse transcriptase polymerase chain reaction assay used to qualitatively measure the presence of HCV RNA.

HDV is hepatitis D (delta) virus, a defective RNA virus that requires HBsAg for structural integrity and replication.

Hepatitis D is an acute or chronic hepatitis caused by HDV that is transmitted primarily through injection drug usage, transfusion, or other parenteral exposures.

Delta coinfection is the simultaneous infection of HBV and HDV usually resulting in a clinical course similar to infection with HBV alone.

Delta superinfection is an acute infection of HDV with preexisting chronic HBV infection (HBsAg+), frequently exacerbating hepatitis B infection.

Anti-HDV IgM is the antibody to HDV that develops during acute delta hepatitis and recurs or persists as a marker for chronic delta hepatitis.

Anti-HDV is the total antibody to HDV that develops following delta coinfection or superinfection. The presence of anti-HDV indicates previous infection with HDV, not necessarily active infection.

Clinician is a physician or mid-level provider.

Compensated cirrhosis is biopsy-proven cirrhosis of the liver without evidence of compromised liver synthetic function or other complications of cirrhosis.

Decompensated cirrhosis is biopsy-proven cirrhosis of the liver with evidence of compromised liver synthetic function or evidence of portal hypertension such as jaundice, variceal bleeding, encephalopathy, and ascites.

Enteric precautions are protective measures used to prevent the spread of infections transmitted by feces. Precautions include wearing gloves for handling infectious material, using gowns when soiling is likely, and discarding contaminated items as infectious waste. Masks are not required for enteric precautions.

PROCEDURES.

a. Hepatitis A

1. Diagnosis. Hepatitis A should be considered as a diagnosis for any inmate presenting with symptoms of acute hepatitis, e.g. jaundice, dark urine, and diarrhea. The mean incubation period of HAV infection until the onset of symptoms is 21 days (range: 15-45 days). Hepatitis A is an acute illness, that can rarely be fulminant and life threatening, but does not evolve to a chronic infection. Acute hepatitis A infection is confirmed by a positive serum HAV IgM that is detectable with the concurrent onset of clinical symptoms and elevation in liver enzymes. Unless evidence of previous hepatitis A infection exists (positive HAV IgG), all inmates presenting with acute hepatitis/diarrhea should be tested for the presence of HAV IgM.

2. Treatment. No specific treatment options exist for hepatitis A infection. Treatment efforts are supportive. Fulminant hepatitis is a rare but serious complication of HAV infection, usually requiring hospitalization.

3. Infection Control Measures. The hepatitis A virus is spread fecal-orally. The virus is stable in the environment for days to several weeks and can be foodborne. Epidemics of hepatitis A can occur in the correctional setting. Inmates diagnosed with hepatitis A infection should be considered contagious three weeks before to 10 days after the onset of jaundice. The spread of infection is greatly augmented by diarrhea. Inmates diagnosed with acute hepatitis A should be managed in accordance with the following:

(a) Isolated in a single cell with separate sink and toilet (e.g. medical unit, Special Housing Unit) until 10 days after the onset of jaundice and until clinically improving without diarrhea.

(b) Immediately removed from any assigned duties as a food handler.

(c) Counseled regarding the importance of strict hand washing practices.

(d) Cared for by staff using enteric precautions

(e) Evaluated by health care staff daily and when medically indicated.

(f) Contact with visitors should be limited and permitted, only if recommended by the attending physician and approved by the Warden

4. Contact Investigation/Post-exposure Management.

(a) Contact investigation should be coordinated with local and state health departments. If the source-case is a food handler, public health officials should be directly involved in the investigation to evaluate the risk and evidence for food borne disease and subsequent indication for widespread prophylaxis.

(b) The following persons are candidates for post-exposure prophylaxis for hepatitis A if exposed to the source-case during the period of contagiousness:

(1) cell mate(s)

(2) sexual contacts

(3) persons routinely sharing toilet facilities

(4) other food handlers if source-case was food handler

(5) very close contacts such as those who have shared eating utensils and cigarettes

(c) Post-exposure prophylaxis is provided by passive immunization with pooled serum immunoglobulin (IG) in accordance with the following guidelines:

(1) Screening for antibodies to HAV is not recommended so that prophylaxis is not delayed.

(2) IG is administered 0.02 mi/kg intramuscularly (single dose).

(3) IG prophylaxis is not effective unless administered within 2 weeks of exposure.

(4) Persons with prior hepatitis A vaccination or previously documented natural immunity do not require passive immunization with IG.

b. Hepatitis B

1. Diagnosis. Hepatitis B should be considered as a diagnosis for any inmate presenting with signs or symptoms of acute or chronic hepatitis.

Acute hepatitis B. The mean incubation period of HBV infection until the onset of symptoms is 70 days (range: 30-180 days). The severity of acute hepatitis B infection can range from subclinical to fulminant disease with 5-10% of patients developing chronic HBV infection. Acute hepatitis B is

associated with arthritis, serum sickness, rash, and myelitis. The diagnosis of acute HBV infection is suggested by the presence of HBsAg and is confirmed by the presence of anti-HBc IgM. (The latter test is a necessary confirmatory test, since persons chronically antigenemic with HBsAg can be acutely infected with other agents causing hepatitis).

Chronic hepatitis B. The diagnosis of chronic HBV infection is confirmed by the presence of HBsAg, the viral marker indicative of ongoing HBV activity and infectiousness. A description of other serologic markers in chronic HBV infection include the following:

(a) Elevation of total anti-HBc is always present.

(b) HBeAg may be present and is indicative of ongoing viral replication and increased contagiousness.

(c) Anti-HBs is usually not detected. The presence of anti-HBs when HBsAg is also measurable does not indicate immunity or recovery from disease.

(d) Anti-HBe develops with the loss of HBe antigen.

2. Disease Course/Monitoring Chronic Infection.

(a) Highly infectious chronic carriers (HBe+/HBsAg+) develop anti-HBe antibodies at an annual rate of 5-10%. (n.b. associated with transient elevation in hepatocellular enzymes). Development of anti-HBe antibodies indicates a nonreplicative stage of infection. In persons in whom HBeAg disappears, the remission is usually sustained and results in an inactive HBsAg carrier state. Resolution of the chronic carrier state (loss of HBsAg) occurs at an annual rate of approximately 1-2%.

(b) Chronic hepatitis B infection may be characterized by intermittent episodes of jaundice and the development of cirrhosis. Flares of hepatitis occur with delta superinfection, immunosuppressive treatments or conditions, and interferon alpha therapy. Hepatocellular carcinoma, highly associated with HBV infection, increases in incidence with the duration of

infection (median onset - 35 years). Other HBV-related conditions include polyarteritis nodosa and membranous glomerulonephritis.

(c) A baseline physician evaluation should be conducted for all HBV chronic carriers (HBsAg+) and include:

(1) Targeted history and physical examination

(2) Serum aminotransferase concentrations (ALT/AST)

(3) Bilirubin, albumin, prothrombin time if liver enzymes are elevated

(4) Renal function assessment

(5) HBeAg

(d) Periodic clinician evaluations and laboratory studies for HBV chronic carriers should be scheduled and ordered on a case by case basis as clinically indicated depending on the severity of the inmate's liver disease. Routine screening tests for hepatocellular cancer are not indicated. Measurement of serum alpha-fetoprotein levels and a liver ultrasound should be considered for inmates with cirrhosis.

3. Treatment

(a) Treatment of acute hepatitis B is supportive. Acute HBV infection may be subclinical, mild, or fulminant.

(b) Treatments for chronic HBV infection are currently evolving. Interferon alpha, the only federally approved therapy, provides effective treatment for a subset of patients yielding sustained response rates in 25% - 40% of patients treated. Evaluation for interferon alpha should be in accordance with Appendix 1 - Algorithm for Hepatitis B Treatment with Interferon-alpha.

(c) Treatment with interferon alpha should be considered in accordance with the following criteria:

(1) Chronic HBV infection (HBsAg+) documented for at least 12 months duration.

(2) Evidence of active viral replication (HBeAg+) for 12 months.

(3) Chronic liver inflammation documented for 12 months, (elevated serum alanine aminotransferase (ALT) levels at least 1.5 - 2.0 times greater than the upper limit of normal determined by averaging 3 ALT levels each measured at least one month apart over 12 months).

(4) Adequate liver synthetic function - e.g. albumin > 3, normal prothrombin time, absence of jaundice.

(5) Absence of decompensated cirrhosis: absence of ascites, jaundice, esophageal varices or other evidence of portal hypertension.

(6) WBC > 3,000/cubic ml.
Platelets > 100,000/cubic ml.

(7) Absence of hyperthyroidism.

(8) Absence of autoimmune disease or solid organ transplantation.

(9) No history of major depression.

(10) No history of other major psychiatric illnesses unless very well controlled by medication.

(11) No evidence of active substance abuse during previous two years (check urine toxicology screen if drug use suspected).

(12) Age < 60 years.

(13) Highly motivated inmate (interferon alpha drug regimen is difficult to tolerate for the patient; duration and side effects of therapy should be fully explained to inmates prior to initiating treatment).

(14) Anticipated incarceration of at least 6 months (inmates who will not predictably complete a course of treatment should receive a baseline evaluation and be referred for medical follow-up and treatment upon release).

(d) Special treatment issues

(1) Renal insufficiency secondary to glomerulonephritis from HBV infection may respond to interferon alpha and is not a contraindication to treatment.

(2) The treatment of persons with hepatitis B and hepatitis C viral co-infections with interferon alpha is relatively contraindicated since safely monitoring the response to treatment and predicting clinical deterioration is difficult.

(3) AIDS or other immunosuppressive illnesses are relative contraindications for interferon alpha therapy, since response rates are poor. Inmates with HIV infection and normal CD4+ T-cell counts should only be considered for interferon treatment in consultation with an infectious disease specialist.

(e) Prior to initiating treatment, inmates who are candidates for interferon should have HBV DNA measured to determine the qualitative presence of detectable HBV levels in the blood. Quantitative HBV DNA measurement by molecular technologies (viral load testing) is considered investigational and not indicated.

(f) Interferon alpha should only be used as a treatment option for hepatitis B with an initial subspecialty consultation and follow-up subspecialty care as clinically indicated.

(g) Inmates with detectable levels of HBV DNA and who are otherwise candidates for interferon alpha treatment should have a screening liver ultrasound for evidence of other liver pathology. If treatment with interferon alpha is considered, the inmate should be referred for

subspecialty evaluation and liver biopsy to confirm the diagnosis of chronic hepatitis, preclude other causes of liver disease, grade the severity of injury, and assess the degree of fibrosis. Interferon treatment should not be initiated without a liver biopsy. Interferon treatment should not be prescribed for persons with decompensated cirrhosis, since treatment often exacerbates disease and severe life threatening side effects have been documented.

(h) Prior to initiating interferon treatment the evaluating physician should carefully review the inmate's medical history for conditions that may be contraindications to treatment or significantly complicate treatment. The benefits and toxicities of treatment should be explained to the inmate and documented in the inmate's medical record by the prescribing physician. The recommended treatment regimen for interferon alpha is 5 million units daily or 10 million units thrice weekly given subcutaneously for 4 months. Predictors of a positive response to interferon therapy for hepatitis B include the following:

(1) Short duration of disease

(2) High aminotransferase levels

(3) Low HBV DNA levels

(4) Liver inflammation on biopsy

(5) Fibrosis on liver biopsy

(6) Absence of renal failure, HIV infection, or other serious co-morbidity.

(i) Inmates should receive at a minimum the following baseline evaluations prior to considering interferon-alpha therapy:

(1) Physician evaluation and clearance

(2) Psychiatrist evaluation and clearance

(3) Serum aminotransferase levels (ALT), albumin, bilirubin, prothrombin time, and creatinine

(4) CBC with differential and platelet count

(5) Thyroid function studies (T4/TSH)

(6) ANA

(7) Serologic assays for HBsAg, HBeAg, and HBV DNA

(8) HCV EIA-2

(9) Screen for delta hepatitis (anti-HDV) if from a high risk country (e.g. Italy, Middle East, Central Africa) (Delta hepatitis is treated differently than hepatitis B alone).

(10) HIV testing

(j) Treatment with interferon alpha almost universally results in significant side effects for the patient. Prior to beginning treatment the prescribing physician should ensure that the inmate has a thorough understanding of the potential side effects of this therapy. An influenza-like reaction usually evolves within 6 to 8 hours of initiating treatment. This acute reaction normally abates with subsequent treatments and can be partially aborted by premedicating with antipyretics. Chronic side effects of fatigue, myalgia, headaches, irritability, rage, confusion, and neuropsychiatric disorders can occur. Severe incapacitating depression can develop in persons without previous histories of depression. Bone marrow suppression of hematocrit, leukocyte count, and platelet count are serious effects of interferon that should be anticipated and monitored closely. Thyroiditis, hyperthyroidism, and hypothyroidism have been reported in 2.5-20 percent of persons treated and may not be reversible upon cessation of drug therapy. Inmates with side effects to alpha interferon should have their dosage reduced or therapy discontinued depending on the

severity of the side effects. Very serious sequelae occur with 2% of persons receiving interferon treatment and can include: cardiac decompensation, renal failure, pneumonitis, severe bone marrow suppression, and suicide.

(k) Inmates should receive at least the following follow-up evaluations during treatment with interferon-alpha:

(1) Clinician evaluations before each injection for the first two weeks of treatment and at least biweekly thereafter (Physician evaluations at least monthly).

(2) Subspecialty evaluations as clinically indicated.

(3) Psychiatry evaluations as clinically indicated during treatment.

(4) ALT weekly for the first two weeks of treatment and monthly thereafter.

(5) Bilirubin, prothrombin time and other liver function studies with new elevations in ALT.

(6) CBC with differential and platelet count weekly for the first month and monthly thereafter.

(7) Thyroid function studies monthly.

(8) Creatinine/electrolytes monthly.

(l) Transient increases in aminotransferase levels are common during therapy and correlate with immune system clearance of HBV and disappearance of HBeAg. Mild to moderate increases in liver enzymes should not be an indication for reducing or discontinuing interferon therapy, unless associated with deteriorating hepatic synthetic function or jaundice.

(m) Loss of HBe antigen after treatment predicts a favorable clinical outcome that may be sustained. Effectiveness of alpha interferon therapy should be assessed 6 months after completion of therapy by measurement of the following parameters:

(1) Absence of HBeAg.
(2) Absence of HBV DNA.
(3) Normalization of ALT.

HBeAg may not return to normal for several months after the completion of interferon treatment. HBsAg may remain positive for years after completion of effective treatment.

(n) Steroids are not indicated for the treatment of chronic hepatitis B infection.

4. Infection Control Measures. Hepatitis B is spread through blood and sexual contact. The following guidelines should be utilized in managing inmates with acute or chronic HBV infection (HBsAg+):

(a) Blood and body fluid precautions should be utilized by staff for management of the inmate.

(b) Inmates should be counseled during clinical evaluations of the importance of preventing blood exposures to others during activities of daily living e.g. sharing toothbrushes, razors.

(c) Inmates should be counseled about the transmission of hepatitis B through sexual contact.

5. Post-exposure Management. Staff and inmates with blood and body fluid exposures to an inmate with contagious hepatitis B should be counseled by a health care provider regarding the transmission, incubation, and natural history of hepatitis B infection. Prompt post-exposure prophylaxis with hepatitis B immunoglobulin and/or hepatitis B vaccine should be provided to inmates and staff when indicated in accordance with CDC guidelines. Staff contacts should be referred for medical evaluation and follow-up.

c. Hepatitis C

1. Diagnosis. Hepatitis C should be considered as a diagnosis for any inmate with a history of injection drug usage, transfusions before 1990, or symptoms and signs of hepatitis.

(a) Acute hepatitis C. The mean incubation period to onset of symptoms with HCV infection is 7 weeks (range 3-20 weeks). Compared to other forms of acute viral hepatitis, acute hepatitis C is often a mild infection with a self-limited course. The infection is subclinical in two-thirds of cases. Fulminant acute hepatitis C is rare. Acute hepatitis C infection is cleared in 15% of infected persons, while 85% of infected persons develop chronic HCV infections of varying severity. The diagnosis of acute viral hepatitis C is based on a positive anti-HCV EIA-2 and clinical or laboratory evidence of acute hepatitis, without evidence of other viral or noninfectious causes of acute hepatitis.

(b) Chronic viral hepatitis C develops in 85% of persons infected with HCV. Although antibodies to HCV are measurable with chronic infection the antibodies do not prevent progression of disease or protect an infected individual from new HCV infections. The diagnosis of chronic HCV infection is confirmed by a positive anti-HCV by EIA-2 in a person at high risk for HCV infection. In asymptomatic inmates at low-risk for HCV infection, a positive EIA-2 should be confirmed by RIBA-2 detection of anti-HCV antibodies.

2. Disease course/Monitoring Chronic Infection

(a) Chronic hepatitis C infection has a waxing and waning natural history with frequent fluctuations in liver function tests and recurrent bouts of hepatitis. Studies of persons with chronic hepatitis C indicate that viral replication and active infection occur in the presence of anti-HCV antibodies with or without evidence of liver function abnormalities. Approximately one-third of persons with chronic HCV infection will have subclinical hepatitis with

persistently normal serum ALT levels. The majority of persons with chronic HCV infection have abnormal serum ALT levels that fluctuate widely over time. Progression to cirrhosis occurs unpredictably, but increases with duration of infection; and although serum ALT levels do not correlate strongly with histologic progression of disease, persons who develop cirrhosis are more likely to have marked elevations in serum ALT levels. An estimated 20% to 30% of persons infected with HCV ultimately develop cirrhosis or clinically significant hepatic disease. Persons with chronic HCV infection are asymptomatic 80% of the time. Fatigue is the most common presenting complaint, but often symptoms do not become apparent until the infected person has developed cirrhosis and the associated complications of liver failure.

(b) HCV infection can be complicated by hepatocellular carcinoma usually in the presence of cirrhosis after longstanding infection of 3 or more decades. Non-hepatic manifestations of HCV infection include essential mixed cryoglobulinemia, membranoproliferative glomerulonephritis, and porphyria cutanea tarda. The presentation of these clinical conditions should prompt evaluation for hepatitis C infection.

(c) A baseline physician evaluation should be conducted for all inmates diagnosed with hepatitis C virus infection and include at least the following:

(1) Targeted history and physical examination.

(2) Serum ALT/AST.

(3) Serum albumin, bilirubin, and prothrombin time if aminotransferases are elevated.

(4) Renal function assessment.

(d) Periodic clinician evaluations and laboratory studies should be scheduled and ordered on a case by case basis depending on the severity of hepatitis C virus

infection and its complications. Screening tests for hepatocellular cancer have not yet proven their efficacy and are not routinely indicated. For inmates with documented cirrhosis or infection of longstanding duration (> 20 years), measurement of serum alpha-fetoprotein levels and liver ultrasound should be considered.

3. Treatment

(a) No widely effective treatments have been developed for hepatitis C. Interferon alpha is FDA-approved for treating hepatitis C but has limited efficacy. Prescription of interferon alpha should be considered in accordance with specific criteria and only with the complete physician and patient understanding of the following:

(1) Reduction in liver enzyme elevations and clearance of HCV after treatment with interferon alpha has been sustained for several years in only 10%-25% of persons treated.

(2) Clearance of HCV may or may not remain sustained for life for those who respond to treatment.

(3) Interferon has serious side effects some of which may be life threatening.

(b) Evaluation for interferon alpha treatment for hepatitis C should be considered in accordance with Appendix 2 - Algorithm for Hepatitis C Treatment with Interferon-alpha.

(c) Interferon alpha therapy should be considered in accordance with the following criteria:

(1) Positive anti-HCV by EIA-2 in serum.

(2) Chronic liver inflammation for at least 12 months (sustained ALT 1.5 to 2 times greater than the upper limit of normal determined by veraging serum ALT levels on three different

occasions measured at least one month apart over 12 months).

(3) Adequate liver synthetic function - e.g. albumin > 3, normal prothrombin time, absence of jaundice.

(4) Absence of compensated or decompensated cirrhosis.

(5) WBC > 3,000 cells/cubic ml.
Platelets > 100,000/cubic ml.

(6) Absence of hyperthyroidism.

(7) Absence of autoimmune disease or history of solid organ transplantation.

(8) No history of major depression.

(9) No history of other major psychiatric illness unless very well controlled.

(10) No evidence of active substance abuse during past 2 years (check urine toxicology screen if drug use suspected).

(11) Age < 60 years.

(12) Highly motivated patient (the lengthy duration and significant side effects of interferon alpha treatment should be explained to the inmate to assess anticipated compliance with therapy).

(13) Anticipated incarceration of at least 12 months (inmates who will not predictably complete a course of treatment should receive a baseline evaluation and be referred for medical follow-up and treatment upon release).

(d) Special treatment issues

(1) HIV infection is a relative contraindication for interferon alpha treatment for hepatitis C since response to therapy is poor and current treatment regimens for this population are investigational. Treatment should only be considered for inmates with normal CD4+ T-cell counts and low viral loads.

(2) Interferon alpha does have efficacy for treatment of chronic hepatitis C infection complicated by mixed essential cryoglobulinemia. Treatment should be considered in consultation with subspecialists.

(3) Treatment with interferon alpha in persons with hepatitis C and chronic active hepatitis B viral coinfections is relatively contraindicated since the response to therapy is unpredictable and difficult to safely monitor.

(e) Prior to initiating treatment, inmates who are candidates for interferon should have qualitative HCV RNA measured by RT-PCR to confirm the presence of infection.

(f) Interferon alpha should be used as a treatment option only with an initial subspecialty consultation and follow-up subspecialty care as clinically indicated.

(g) Inmates with detectable HCV RNA by RT-PCR and who are otherwise candidates for interferon alpha treatment should have a liver/abdominal ultrasound to screen for the presence of other medical conditions that may affect treatment.

(h) Inmate candidates for interferon alpha should be referred for subspecialty evaluation and liver biopsy to confirm the diagnosis of hepatitis, preclude other causes of liver disease, grade the severity of injury, and assess the degree of fibrosis. Interferon therapy should not be initiated without a liver biopsy.

(i) Interferon treatment is relatively contraindicated for persons with compensated cirrhosis, since response to treatment is poor. Interferon treatment is contraindicated for persons with decompensated cirrhosis, since treatment often exacerbates disease resulting in severe life threatening sequelae.

(j) The recommended treatment regimen with interferon alpha-2b is 3 million units subcutaneously three times per week for 12 months. The use of higher doses of interferon-alpha has not proven to provide any additional benefit. Predictors of a positive response to interferon therapy for hepatitis C include the following:

(1) Age < 45.

(2) Short duration of disease.

(3) Low hepatic iron stores.

(4) Absence of cirrhosis or minimal fibrosis.

(k) Inmates should receive the following baseline evaluations prior to considering interferon treatment:

(1) Physician evaluation and clearance.

(2) Psychiatrist evaluation and clearance.

(3) Serum aminotransferase levels (ALT), albumin, bilirubin, prothrombin time, and creatinine.

(4) CBC with differential and platelet count.

(5) Thyroid function studies (T4/TSH).

(6) ANA.

(7) HBsAg.

(8) HIV antibody testing.

(l) Treatment with interferon alpha almost universally results in significant side effects. The treating physician should ensure that the inmate is aware of all potential side effects prior to prescribing therapy. An influenza-like reaction usually evolves within 6 - 8 hours of initial treatment with interferon alpha. This acute reaction normally abates with subsequent treatments and can be partially aborted by premedication with antipyretics. Chronic side effects of fatigue, myalgia, headaches, irritability, rage, confusion, and neuropsychiatric disorders can occur. Severe incapacitating depression can develop in persons without a previous history of depression. Bone marrow suppression of hematocrit, leukocyte count, and platelet count are serious effects of interferon that should be anticipated and monitored closely. Thyroiditis, hyperthyroidism, and hypothyroidism have been reported in 2.5-20% of persons treated with interferon and may not be reversible upon cessation of drug therapy. Inmates with side effects to interferon should have their dosage reduced or therapy discontinued depending on the severity of the side effects. Very serious sequelae of interferon treatment occur in 2% of patients and may include cardiac decompensation, renal failure, pneumonitis, severe bone marrow suppression, and suicide.

(m) Inmates should receive at least the following evaluations during treatment with interferon:

(1) Clinician evaluations before each injection for the first two weeks of treatment and at least biweekly thereafter (physician evaluations at least monthly).

(2) Subspecialty evaluations as clinically indicated.

(3) Psychiatry evaluations when clinically indicated.

(4) ALT weekly for the first four weeks of treatment and monthly thereafter.

(5) Bilirubin, prothrombin time and other liver functions studies with new elevations in ALT.

(6) CBC with differential and platelet count weekly for the first month of treatment and monthly thereafter.

(7) Thyroid function studies monthly.

(8) Creatinine/electrolytes monthly.

(n) An uncommon, but clinically pertinent side effect of interferon alpha treatment of hepatitis C is worsening of hepatitis. New elevations in ALT serum levels during treatment for hepatitis C can progress to liver failure and are an indication for immediate cessation of therapy.

(o) Inmates who have a decline of serum ALT levels to normal or near normal within 8 to 12 weeks of treatment with interferon should be maintained on interferon for a total duration of treatment of 12 months since a sustained remission is probable.

(p) Inmates who do not demonstrate a decline in ALT levels to normal or near normal within 8-12 weeks should be re-evaluated for cessation of interferon treatment, since a sustained remission is unlikely. Prior to discontinuing treatment HCV RNA should be measured by RT-PCR to confirm the continued presence of HCV.

(q) Quantitative virology (HCV viral load) and viral genotype analysis are considered investigational and are not indicated for monitoring treatment. Serial liver biopsies following a prerequisite baseline study are not routinely indicated.

(r) Steroids should not be prescribed for treatment of chronic hepatitis C infection.

4. Infection Control Measures. Hepatitis C is spread primarily through parenteral blood exposure. The following guidelines should be utilized in managing inmates with acute or chronic hepatitis C:

(a) Blood and body fluid precautions should be utilized by staff for management of the inmate.

(b) Health care providers should provide counseling to infected inmates on the prevention of blood exposures to others during activities of daily living such as sharing toothbrushes and razors.

5. Post-exposure Management. Staff and inmates with percutaneous or permucosal blood exposures to hepatitis C should be counseled by a health care provider about the transmission, incubation, and natural history of hepatitis viral infection in accordance with CDC guidelines. No vaccine, passive immunization, or anti-viral treatments are available to abort or treat newly acquired hepatitis C viral infection following an exposure. Contacts should be referred for medical evaluation and follow-up. Anti-HCV antibodies by EIA-2 (confirmed by RIBA-2 if positive) should be measured at 0 and 6 months following an exposure to screen for newly acquired infection.

d. Hepatitis D

1. Diagnosis. Hepatitis D (delta) viral co-infection or superinfection occurs only in the presence of active hepatitis B infection (HBsAg+). Inmates at highest risk for delta hepatitis have a history of injection drug use or have resided in an area of the world with a high prevalence of infection such as Middle East countries, Italy and Central Africa.

(a) Acute delta hepatitis can be diagnosed by the presence of anti-HDV IgM, however, this antibody may be present only transiently.

(b) Chronic delta hepatitis can be diagnosed by the presence of anti-HDV IgM and anti-HDV (total). Anti-HDV IgM is a marker for ongoing viral

activity/hepatitis. The presence of anti-HDV (total) indicates remote infection with hepatitis D virus, but not necessarily active infection.

2. Disease Course/Monitoring Chronic Infection

(a) Acute delta co-infection usually presents as a mild to moderate hepatitis that resolves without development of chronic hepatitis.

(b) Acute delta superinfection often presents as a severe hepatitis that resolves, then recurs as chronic delta hepatitis with a rapid progression to cirrhosis and its associated complications.

(c) Periodic clinician evaluations should be conducted for inmates with chronic hepatitis D infection in accordance with guidelines for monitoring chronic hepatitis B infection. Persistence of chronic delta hepatitis can be assessed by measurement of anti-HDV IgM.

3. Treatment. Treatment of acute delta hepatitis is primarily supportive. Inmates with chronic delta hepatitis should be considered as candidates for interferon alpha therapy using the treatment criteria for managing inmates with chronic hepatitis B infection. The treatment regimen for treating delta hepatitis with interferon alpha, however, differs from the regimens for both hepatitis B and hepatitis C. Treatment should be prescribed and monitored only in consultation with a subspecialist.

4. Infection Control. Hepatitis D is transmitted primarily through parenteral blood exposure. Infection control measures applicable for hepatitis C should be utilized for controlling the spread of hepatitis D.

5. Post-exposure Management. Inmates and staff with blood exposures to hepatitis D should be counseled on the transmission, incubation, and natural history of hepatitis D viral infections. Although no vaccine, passive immunization, or anti-viral treatments are available to specifically abort or treat newly

acquired hepatitis D viral infection, hepatitis D can not newly infect an individual if infection with hepatitis B is prevented with hepatitis B immunoglobulin/hepatitis B vaccine in accordance with CDC guidelines. Contacts who are hepatitis B chronic carriers (HBsAg+) should be counseled on the risk for delta superinfection that can result in severe hepatitis. Inmate contacts should be monitored closely for exacerbations of their liver disease. Staff contacts should be provided prophylaxis for hepatitis B infection when medically indicated and counseled and referred for medical evaluation and follow-up.

ATTACHMENTS.

Appendix 1. Algorithm for Interferon-alpha Treatment for Hepatitis B

Appendix 2. Algorithm for Interferon-alpha Treatment for Hepatitis C

Appendix 3. Contraindications for Interferon-alpha Treatment for Viral Hepatitis

Appendix 1

Algorithm for Treatment of Hepatitis B with Interferon

HBsAg + for 12 months
HBeAg + for 12 months

↓

ALT 1.5-2 x upper limit of normal x 3 over 12 months

↓

Physician clearance
No evidence of decompensated cirrhosis
No contraindications to interferon tx
Anticipated incarceration > 6 months

↓

Psychiatry clearance

↓

HBV DNA +

↓

Screening liver ultrasound

↓

Subspecialty evaluation
Liver biopsy

↓

Interferon tx if medically indicated

Appendix 2

Algorithm for Treatment of Hepatitis C with Interferon

Anti-HCV + by EIA-2 (high risk)
Anti-HCV + by RIBA-2 (low risk)

↓

ALT 1.5-2 x upper limit of normal x 3 over 12 months

↓

Physician clearance
No evidence of decompensated cirrhosis
No contraindications to interferon tx
Anticipated incarceration > 12 months

↓

Psychiatry clearance

↓

HCV RNA + by RT-PCR

↓

Screening liver ultrasound

↓

Subspecialty evaluation
Liver biopsy

↓

Interferon tx if medically indicated

Appendix 3

Interferon Treatment for Viral Hepatitis

Contraindications

1. Normal ALT

2. Decompensated cirrhosis
   albumin < 3, jaundice, ascites, varices

3. WBC < 3,000
   Platelets < 100,000

4. Hyperthyroidism

5. Active autoimmune disease

6. HIV infection with depressed CD4+ T-cell count

7. Solid organ transplantation

8. History of major depression

9. Active drug use

10. Age > 60

Relative contraindications

1. History of psychiatric problems

2. Hepatitis B and C coinfections

3. Diabetes

4. Presence of cirrhosis with hepatitis C infection

FEDERAL BUREAU OF PRISONS TREATMENT GUIDELINES FOR HIV INFECTION

PURPOSE. Federal BOP Treatment Guidelines for HIV Infection define a standard of care for the medical management of HIV infection to ensure that BOP inmates diagnosed with HIV infection are provided effective therapies and monitored appropriately.

REFERENCES.

1993 Revised Classification System for HIV Infection and Expanded Surveillance Case Definition for AIDS Among Adolescents and Adults, *MMWR*, Vol. 41, No. RR-17, December 18, 1992, U.S. Department of Health and Human Services, Centers for Disease Control, Atlanta, Georgia.

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1997 USPHS/IDSA Guidelines for the Prevention of Opportunistic Infections in Persons Infected with Human Immunodeficiency Virus: A Summary, *MMWR,* Vol. 46, No. RR-12, June 27, 1997, U.S. Department of Health and Human Services, Centers for Disease Control, Atlanta, Georgia.

Recommendations of the U.S. Public Health Service Task Force on the Use of Zidovudine to Reduce Perinatal Transmission of Human Immunodeficiency Virus, *MMWR*, Vol. 43, No. RR-11, August 5, 1994, U.S. Department of Health and Human Services, Centers for Disease Control, Atlanta, Georgia.

Department of Health and Human Services Draft Guidelines on Use of Antiretroviral Agents in HIV-Infected Adults. Report of the NIH Panel to Define Principles of Therapy of HIV Infection, Federal Register, 62 FR 33417, June 19, 1997.

Update: Provisional Public Health Service Recommendations for Chemoprophylaxis after Occupational Exposure to HIV,

MMWR, Vol. 45/No. 22, June 7, 1996, U.S. Department of Health and Human Services, Centers for Disease Control, Atlanta, Georgia.

DEFINITIONS.

Clinician is a physician or mid-level provider.

EIA is Enzyme Immunoassay, a test for detecting antibodies.

PROCEDURE.

a. Diagnosis

1. Inmates who test positive for HIV infection by EIA and confirmed by Western blot analysis should be referred to a physician for baseline evaluation within one month of diagnosis unless more expedient medical evaluation is clinically indicated. Western blots shall be interpreted as positive in accordance with Centers for Disease Control Criteria.

2. An indeterminant test result for HIV-1 infection is associated with the following conditions:

(a) Process of HIV seroconversion

(b) HIV-2 infection (West African, travel to West Africa, or high risk contact with West African)

(c) History of blood or blood product transfusions

(d) Organ transplantation

(e) Pregnancy

(f) Autoimmune disease

(g) Malignancy

(h) Recipients of HIV experimental vaccines

3. Indeterminant results include a positive EIA and usually a single p24 band on Western blot analysis. Inmates with

indeterminant HIV test results should be referred to a physician for further evaluation in accordance with the following guidelines:

(a) Physician interview for HIV infection risk factors, symptoms of HIV infection and AIDS, and causes of indeterminant HIV test results.

(b) Physician evaluation of the inmate for conditions that may result in an indeterminant test result when clinically indicated based on the inmate's history and examination.

(c) Repeat HIV testing in 3 and 6 months.

(d) If HIV test results remains indeterminant at six months with a single p24 band and the inmate has no clinical evidence of HIV infection, consider the inmate uninfected (By three months, most persons in the process of seroconverting their indeterminant result should have a positive Western blot). No additional HIV testing is indicated for screening purposes.

(e) If the inmate remains HIV indeterminant with multiple bands on western blot analysis or has clinical evidence of HIV infection, review case with sub-specialist.

b. Medical Evaluation and Treatment.

1. Baseline evaluation by a physician for inmates diagnosed with HIV infection should include the following as outlined in Appendix 1:

(a) Medical history including assessment of HIV risk factors.

(b) Physical examination including pelvic examination and PAP smear for women.

(c) Referral for dental examination by a dentist for all inmates.

(d) Psychology referral if clinically indicated.

(e) Baseline laboratory studies including:

(1) CBC/platelet count

(2) CD4+ T-lymphocyte cell count and percentage

(3) Viral load assay using FDA-approved method

(4) Serum electrolytes/creatinine/LFTS

(5) RPR/FTA - treatment history review

(6) Toxoplasmosis IgG titer

(7) Hepatitis serologies - anti-HBsAg/anti-HCV by EIA-2 if liver functions are elevated

(8) PPD/symptom review

(9) Chest radiograph

(10) Pneumococcal vaccine for inmates with CD4+ T-cells $\geq$ 200/mm^3 (booster at 5 years x 1)

(11) Influenza vaccine annually prior to influenza season for inmates with CD4+ T-cells $\geq$ 200/mm^3

(f) Comprehensive treatment plan, including subspecialty referrals as clinically indicated.

(g) CDC Classification of HIV infection in accordance with Appendix 1.

2. Periodic medical evaluations for inmates with HIV infection should be conducted by a clinician at least quarterly, including a physician evaluation at least semiannually for inmates receiving anti-retroviral therapy. Immunologic status should be assessed by the measurement of the CD4+ T-cell count and the HIV viral load using an FDA-approved testing method in accordance with current CDC guidelines. Clinician evaluations, CD4+ T-cell count assessments and viral load measurements should

be based on the inmate's immune status as outlined in Appendix 2. CDC classification should be updated with any changes in classification during periodic clinician evaluations. The indications and frequency of other laboratory monitoring will depend on the inmate's antiretroviral treatment regimen and prophylactic regimen for opportunistic infections (Key monitoring parameters are outlined in Appendices 3-6).

3. The HIV viral load should not be measured within one month of an acute illness or immunization due to false elevations. Viral load should be measured periodically in accordance with Appendix 2 and before and one month after changes in anti-retroviral treatment are initiated. Inmates with CD4+ T-cells $\geq$ 350/mm^3 with elevated viral loads who have never received anti-retroviral treatment, should have the elevated viral load confirmed with a second measurement prior to initiating first time anti-retroviral therapy. Inmates with viral loads < 20,000 cps/ml (RNA-PCR) with CD4+ T-cells of 200-499/mm^3, should have the depressed CD4+ cell count confirmed with a second measurement prior to initiating first time anti-retroviral therapy. The same laboratory using the same viral load assay should be utilized to minimize test variability whenever possible. Treatment decisions should not be made on viral load test results when inmates have been noncompliant with a treatment regimen. Viral load can return to pretreatment levels within days of stopping protease inhibitors.

4. Anti-retroviral therapy and prophylaxis for opportunistic infections should be provided to inmates in accordance with U.S. Public Health Service standards and the guidelines outlined in Appendices 2-6. The prescription of anti-retroviral therapy should be based on the inmate's immunologic status, prior treatment history, medication toxicity concerns, anticipated incarceration, and patient motivation and compliance. All decisions to initiate, change, or discontinue anti-retroviral medications should be made by a physician. The effectiveness of anti-retroviral therapy is based on the inmate's CD4+ T-cell count, HIV viral load, and the clinical response to therapy. The goal of treatment is to reduce viral load to less than 500 cps/ml and preferably to undetectable levels. The viral load nadir is correlated with the effectiveness of treatment and is usually not achieved until 2-4 months after initiating treatment or changing treatment. Viral loads should be measured one month after

changing antiretroviral treatment regimens. A 10 fold change (1 log decline) at one month predicts an ultimate nadir of < 500 cps/ml. Treatment failure is suggested by a rapid decline in the CD4+ T-cell count or clinical deterioration and is confirmed by a return of viral load to pretreatment levels (Note: CD4+ T-cell counts are subject to significant variability and can vary up to 30 percent on repeated measures in the absence of a change in the patient's clinical condition. Do not make major treatment decisions based on one CD4+ T-cell measurement). In cases in which the CD4+ T-cell count and plasma HIV RNA levels appear to be inconsistent, prophylaxis for opportunistic infections should be managed according to the CD4+ T-cell count, and anti-retroviral therapy decisions should be based on the viral load. Prophylaxis of opportunistic infections should not be discontinued with improvement in CD4+ T-cells counts, since immune function may still be significantly compromised.

5. The measurement of p24 antigen, neopterin, and $-2 microglobulin levels are less reliable than plasma HIV RNA assays and do not add significant prognostic information for the clinician; and therefore are not routinely indicated.

6. Compliance with each dose of a protease inhibitor is critical to prevent the development of viral resistance. This factor must be strongly considered when determining an anti-retroviral therapeutic regimen. Inmates with suspected noncompliance should be monitored by directly observed therapy when feasible and referred to the Clinical Director for review. Decisions to discontinue protease inhibitors because of persistent non-compliance should be made on a case-by-case basis by the Clinical Director. Dosages of protease inhibitors should not be reduced unless medically indicated because of known drug interactions or reduced drug clearance.

7. Changing antiretroviral therapy should be initiated on a <u>case by case</u> basis. The following criteria should prompt consideration for changing antiretroviral therapy.

(a) Less than a 10-fold (1.0 log) reduction in plasma HIV RNA by 4 weeks following initiation of therapy.

(b) Failure to suppress plasma HIV RNA to undetectable levels within 4-6 months of initiating therapy.

(c) Reproducible 3-fold or greater increase in HIV RNA after effective viral suppression.

(d) Persistently declining CD4+ T-cell counts as measured on at least two separate occasions.

(e) Clinical deterioration

8. An infectious disease consultant or other physician with expertise in treating HIV infection should be consulted when medically indicated to assist in the medical management of inmates with HIV infection, particularly for the following cases:

(a) Inmates who fail first line triple anti-retroviral therapy.

(b) Inmates with active tuberculosis and HIV infection.

(c) Pregnant women with HIV infection.

(d) Inmates with suspected acute HIV infection (treatment may be warranted)

9. All pregnant women should be tested for HIV infection with or without known risk factors for HIV infection. Pregnant women with HIV infection should be counseled on the effectiveness of zidovudine (AZT) in reducing the perinatal transmission of HIV infection. Zidovudine should be prescribed to pregnant women in accordance with current CDC guidelines. Pregnant women who refuse medically indicated zidovudine therapy should be referred for psychologic evaluation and review by the Clinical Director. The effects of other anti-retroviral medications on pregnant women and their fetuses is under investigation. The decision to initiate, continue, or discontinue combination anti-retroviral therapy for pregnant women with HIV infection should be made on a case by case basis by the patient and her physicians after careful consideration of known risks and benefits.

c. Documentation of Medical Treatment.

Documentation of medical care provided to inmates with HIV infection should be maintained in accordance with the following:

1. CDC initial and updated HIV classifications documented on the Federal Bureau of Prisons HIV Classification Form, Appendix 1 and in SMD (Sensitive Medical Data).

2. Baseline and periodic clinician evaluations documented on the Federal Bureaus of Prisons HIV Chronic Care Clinic Flowsheet, Appendix 7.

3. Treatment plans for baseline and periodic clinician evaluations documented in medical record progress notes.

d. HIV Post-exposure Prophylaxis

1. Medical Management. BOP employees and inmate workers who experience occupational-related exposures to HIV infected blood and body fluids should be provided emergent counseling and treatment by a qualified health care professional in accordance with the following:

(a) The injured skin or wound should be emergently cleansed with soap and running water for two minutes. Mild bleeding should be allowed to continue. Antiseptics, bleach, or other cleansing agents should not be used. Aspiration, forced bleeding, and wound incision are not recommended. Mucous membranes should be rinsed with water for two minutes. Exposed eyes should be flushed with water or saline for two minutes.

(b) The evaluating health care professional should interview the injured worker to determine if a potential occupational exposure to HIV has occurred in accordance with CDC guidelines. The worker must have an occupational exposure to a source that is HIV-infected or at high risk for HIV infection. Blood and the following substances are considered potentially infectious for HIV: semen, vaginal secretions, cerebrospinal fluid, pleural fluid, peritoneal fluid, synovial fluid, un-fixed tissue, certain lab specimens, and any substance contaminated by visible blood. Exposure to visibly uncontaminated urine, feces, and saliva does not require HIV post-exposure prophylaxis.

(c) If an exposure or questionable occupational exposure to HIV has occurred, the evaluating health care professional should immediately review the incident with the Clinical Director or other physician designee to determine if HIV post-exposure prophylaxis should be medically recommended or can be reasonably offered in accordance with CDC guidelines as outlined in Appendix 8, HIV Post-exposure Prophylaxis.

(d) If the evaluating physician determines that an occupational exposure to HIV has occurred, the BOP employee should be referred to a community medical provider for ongoing treatment and monitoring once emergency medical care has been rendered. Exposed inmates should be offered or recommended HIV post-exposure prophylaxis if no medical contraindications exist and subsequently treated and monitored by a physician if prophylaxis is requested by the inmate worker.

(e) The provision of emergency medical care to BOP employees may include the prescription of HIV anti-retroviral medications, not to exceed an emergency four day supply, if access to a community medical provider in a timely manner can not be reasonably assured (CDC guidelines recommend that HIV post-exposure prophylaxis be administered promptly, preferably within two hours of exposure). Anti-retroviral medications may only be dispensed and administered to BOP employees with the written or verbal order of the Clinical Director or physician designee.

(f) Emergent doses of anti-retroviral medications should only be offered or recommended to exposed workers in accordance with CDC guidelines. Workers should be informed of the CDC recommendations including but not necessarily limited to the risk, prevention, and drug treatment information included in Appendix 9, HIV Post-exposure Prophylaxis Fact Sheet.

(g) Emergent doses of anti-retroviral medications may have untoward effects, particularly in persons with underlying medical conditions, taking prescribed or over-the-counter medications, and during pregnancy. The provision of emergency doses of HIV anti-retroviral medications to BOP employees with complicating conditions must be considered on a case by case basis after a careful discussion of the known risks and benefits of prophylaxis with the employee and whenever possible the direct involvement of the employee's personal physician.

(h) Employees and inmate workers with occupational exposure to HIV should have HIV antibodies measured at the time of exposure, at 3 months, and at 6 months. A negative HIV antibody 6 months following exposure confirms the absence of HIV transmission. HIV antibody testing should be conducted by community health care providers or by BOP providers in accordance with BOP policy and the institution's bloodborne pathogen exposure control plan.

2. Documentation/Training

(a) The provision of HIV post-exposure prophylaxis to inmate workers should be documented in the inmate's medical record, including the date and description of the exposure, counseling provided, and treatment rendered.

(b) The provision of HIV post-exposure prophylaxis to BOP employees should be documented in the employee's health record, including the date and description of the exposure, counseling provided, emergency treatment rendered, community provider referral, and a signed informed consent or declination for emergent HIV post-exposure prophylaxis (Appendix 10) when appropriate.

(c) Specific administrative, personnel, and medical procedures for implementing the CDC guidelines for HIV post-exposure prophylaxis should be outlined in the institution's exposure control plan for bloodborne

pathogens. The institution's procedures for providing HIV post-exposure prophylaxis to BOP employees should be included in annual training.

ATTACHMENTS.

Appendix 1. Federal Bureau of Prisons HIV Classification Form

Appendix 2. Medical Evaluation and Treatment of HIV Infection by Immunologic Status

Appendix 3. Anti-retroviral Therapy - Nucleoside Analogues

Appendix 4. Anti-retroviral Therapy - Protease Inhibitors

Appendix 5. Anti-retroviral Therapy - Non-nucleoside Analogues

Appendix 6. Prophylaxis of Opportunistic Infections

Appendix 7. Federal Bureau of Prisons HIV Chronic Care Flowsheet

Appendix 8. HIV Post-exposure Prophylaxis

Appendix 9. HIV Post-exposure Prophylaxis Fact Sheet

Appendix 10. HIV Employee Consent/Declination Form for HIV Post-exposure Prophylaxis

Federal Bureau of Prisons HIV Classification Form

Demographics: Name: (Last) _____ (First) _____ (Middle)_____
Reg#: _____ Date of Birth:_____ SSN: _____
Race: W □ B □ Hispn □ Asian □ Nat. Amer □ Country of Birth: _____
Facility: _____ State: _____

Risk Factors: After 1977 and preceding the first positive HIV antibody test or AIDS diagnosis, the patient had the following risk factors (respond to all categories):

1.	Sex with male	Y	N	Unknown
2.	Sex with female	Y	N	Unknown
3.	Injected nonprescription drugs	Y	N	Unknown
4.	Transfused clotting factor for bleeding disorder	Y	N	Unknown
5.	Heterosexual relations with any of the following:			
	Injection drug user	Y	N	Unknown
	Bisexual male	Y	N	Unknown
	Person with hemophilia/coagulation disorder	Y	N	Unknown
	Transfusion recipient with documented HIV infection	Y	N	Unknown
	Transplant recipient with documented HIV infection	Y	N	Unknown
	Person with HIV infection or AIDS/unknown risk	Y	N	Unknown
6.	Transfused blood products (other than clotting factor)	Y	N	Unknown
	product _____ first _____ mo/yr last _____ mo/yr			
7.	Received organ/tissue transplant or artificial insemination	Y	N	Unknown
8.	Health care worker or clinical laboratory worker	Y	N	Unknown
9.	Tattoo (while incarcerated)	Y	N	Unknown

CDC HIV Classification (circle one)

A1	**B1**	**C1**
A2	**B2**	**C2**
A3	**B3**	**C3**

Clinical conditions (Describe clinical status/conditions relevant to A, B, or C classification):

_____
_____
_____

Evaluating clinician: _____ Date:_____

))

1993 Revised Classification System for HIV Infection

CD4+ T-cells/ µliter	CD4+ (%)	A Asymptomatic	B Symptomatic Disease (Not A, B & C)	C AIDS Indicator Conditions
≥500	≥29%	A1	B1	C1
200-499	14-28	A2	B2	C2
< 200	< 14	A3	B3	C3
		* acute (primary) HIV infection *PGL (persistent generalized lymphadenopathy)	Symptomatic conditions that are attributed to HIV infection; or the conditions have a clinical course complicated by HIV. Conditions include but are not limited to the following: * bacillary angiomatosis * oral candidiasis * vulvovaginal candidiasis (persistent - > 1 month or poorly responsive to tx) * cervical dysplasia (moderate-severe/CIS) * ITP * oral hairy leukoplakia * listeriosis * herpes zoster (involving more than 1 dermatome or 2 separate episodes)	* candidiasis: esophageal * coccidiomycosis: extrapulmonary * cryptococcoses: extrapulmonary * cervical cancer, invasive * cryptosporidiosis: chronic (> 1 month) * CMV retinitis, (or CMV in organs other than liver/spleen/nodes) * HIV encephalopathy * herpes simplex: esophagitis, genital/oral ulcers > 1 month * histoplasmosis: extrapulmonary/disseminated * isosporiasis: chronic diarrhea (> 1 month) * Kaposi sarcoma * lymphoma: Burkitt's, immunoblastic, brain primary * MAC or *M. Kansasii*: extrapulmonary/disseminated * *M. tuberculosis*: pulmonary or extrapulmonary * other mycobacterium: extrapulmonary/disseminated * *Pneumocystis carinii* pneumonia (PCP) * pneumonia (recurrent < 12 months) * progressive multifocal leukoencephalopathy (PML) * salmonella septicemia (> 1 occurrence) * toxoplasmosis (CNS) * wasting syndrome secondary to HIV infection

- Category B conditions take precedence over those in Category A; and Category C conditions take precedence over those in Category B.
- For classification purposes, the lowest accurate CD4+ T-lymphocyte count or percentage (not necessarily the most recent) should be utilized.

Medical Evaluation and Treatment for HIV Infection by Immunologic Status

Baseline Evaluation:
(1) history/physical examination including: fundoscopic exam/PAP smear for women (2) dental exam (3) CBC/platelets/CD4+ T-cell count/% (4) viral load (avoid baseline testing during acute illness) (5) electrolytes/creatinine/LFTS (6) RPR/FTA (review tx history) (7) PPD/symptom review (8) toxoplasmosis IgG (9) anti-HBsAg/anti-HCV if LFTs abnormal (10) chest x-ray (11) pneumococcal vaccine - CD4+ T-cells ≥ 200 (booster at 5 yrs x 1)

Periodic Evaluation:
(1) CBC/platelet count, LFTs/creatinine/electrolytes - q 3 months on anti-retroviral tx (2) periodic RPR as clinically indicated (3) Pap smear - q 6 months x 1 then annually (repeat if "inadequate", refer to gynecologist for "atypia") (4) other laboratory tests as indicated (see drug charts).

CD4+ T-cells/mm^3	CD4+ T-cells assessment	Viral load	Clinician exam	Special Evaluations/Treatments
> 350	q 3-6 months	q 6 months off tx q 3-4 months on tx	q 3 months	Observe or initiate anti-retroviral tx depending on viral load Monitor CD4+ T-cell count q 3 months if 350-500 cells/mm^3
200-350	q 3-6 months	q 3-4 months	q 3 months	Initiate anti-retroviral therapy with 3 drugs regardless of viral load
100-199	q 3-6 months	q 3-4 months	q 2 months	Initiate anti-retroviral therapy with 3 drugs regardless of viral load Initiate PCP prophylaxis Baseline fundoscopic exam by eye doctor to screen for CMV
50-99	q 3-6 months	q 3-4 months	monthly	Initiate anti-retroviral therapy with 3 drugs regardless of viral load Initiate toxoplasmosis prophylaxis/Maintain PCP prophylaxis Fundoscopic exam q 6 months by eye doctor to screen for CMV
0-49	q 6 months	q 3-4 months	monthly	Initiate anti-retroviral therapy with 3 drugs regardless of viral load Maintain PCP/toxoplasmosis prophylaxis Initiate MAC prophylaxis Fundoscopic exam q 6 months by eye doctor to screen for CMV

- Viral load should be measured before and 4 weeks after changes in anti-retroviral tx and with evidence of worsening clinical or immune status.
- Effect of change in drug therapy on viral load should be evident in 1 month, but nadir may not be apparent for 2-4 months.
- Viral load should not be measured within one month of an acute illness or immunization (due to false elevations).

Medical Evaluation and Treatment for HIV Infection by Immunologic Status

Immune Status	Treatment Options	Comments
Asymptomatic CD4+ T-cells ≥ 350/mm^3 **AND** - Viral load: <20,000 cps/ml (RT-PCR) <10,000 cps/ml (bDNA)	Observe Initiate treatment on case by case basis for inmates with persistent CD4+ T-cell counts between 350-500/mm^3 and low viral load.	Monitor viral load, CD4+ T-cell count, and clinical presentation for disease progression. Inmates with CD4+ T-cells between 350-500/mm^3 must be monitored closely and should have a low threshold for initiation of triple antiretroviral therapy (see below). Treatment of asymptomatic patients with CD4+ T-cell counts > 500/mm^3 and low viral loads is investigational.
Asymptomatic CD4+ T-cells 200-350/mm^3 **OR** Viral load: > 20,000 cps/ml (RNA-PCR) > 10,000 cps/ml (bDNA) Regardless of CD4+ count	Triple therapy (Confirm depressed CD4+ T-cell count with second test before initiating treatment if viral load is < 20,000 cps/ml) (Confirm elevated viral load with second test before initiating first time treatment if CD4+ T-cell count is ≥ 350/mm^3.)	Triple therapy with 2 nucleoside reverse transcriptase inhibitors (NRTIs) in the combinations listed below plus 1 protease inhibitor (PI) is the preferred regimen. An alternative triple therapy option is 2 (NRTIs) plus nevirapine. Inmate compliance with treatment is critical to prevent the development of resistance, particularly with protease inhibitors. Inmates who fail triple therapy should be switched to an alternative three drug regimen with two new drugs. One drug should not be added to a failing regimen, but a single drug can be switched due to drug intolerance to another drug in the same class with a different side effect profile. Dual therapy (AZT/ddI, AZT/ddC, d4T/3TC, AZT/3TC, d4T/ddI) should be avoided but can be considered for inmates who have CD4+ T-cells ≥ 200/mm^3 and refuse or are noncompliant with triple drug therapy, or have been previously prescribed dual therapy with incarcerations of short duration (e.g. presentenced inmates) and are clinically stable without AIDS. Note: Some experts recommend preserving 3TC for triple therapy options due to the rapid development of cross resistance with other NRTIs. Monotherapy with any drug is a suboptimal regimen and should always be avoided. For asymptomatic inmates who refuse to take a more complicated regimen, the most effective single drug for monotherapy is ddI. D4t and AZT are less effective monotherapy options.
Symptomatic with AIDS or AIDS-related infections; or Asymptomatic with CD4+ T-cell count < 200/mm^3 Viral load = any level	Triple Therapy	

- Monotherapy with 3TC, nevirapine, or any protease inhibitor is contraindicated. Dual therapy with AZT and D4T should be avoided due to antagonism.
- A 3-fold reduction in HIV RNA copies is the minimal response indicating antiviral effect (0.5 log change). Goal of tx is a viral burden < 500 cps/ml (preferably undetectable levels) at 4-6 months after starting a new regimen predicted by a one log (10 fold) decline in viral burden after one month of tx.
- A return of HIV RNA levels to pretreatment levels indicates drug failure: Confirm with repeat viral load test before changing treatment regimen.

Appendix 3

Anti-retroviral Therapy - Nucleoside Reverse Transcriptase Inhibitors

Anti-retroviral Tx	Dosage	Baseline Labs	Monitoring Labs	Toxicities	Comments
Zidovudine (AZT) Retrovir	200 mg TID or 300 mg BID minimum effective dose: 300 mg/day	CBC/diff chem screen	CBC/diff 2,6, and 12 weeks after starting tx. every 3 months if stable	anemia neutropenia myalgia headache insomnia	marrow toxicity with gancyclovir reduce dose for mild-moderate toxicities good CNS penetration
Lamivudine (3TC) Epivir	150 mg BID	none	none	minimal	never prescribe as monotherapy reduce dose for renal disease
Stavudine (d4T) Zerit	> 60kg: 40 mg BID < 60kg: 30 mg BID	CBC/diff amylase	CBC/diff amylase with GI symptoms	neuropathy	reduce dose for neuropathy reduce dose for renal disease based on creatinine clearance
Didanosine (ddI) Videx	> 60kg:200 mg BID < 60kg:125 mg BID take on empty stomach minimum effective dose: 200 mg/day	CBC/diff amylase liver function	CBC/diff amylase/liver function tests with GI symptoms	diarrhea nausea pancreatitis neuropathy hepatitis	do not prescribe with history of pancreatitis or hx of alcohol abuse adjust dose in renal/hepatic disease high Na/Mg load
Zalcitabine (ddC) HIVID	0.75 mg q 8 h	CBC/diff amylase	CBC/diff amylase with GI symptoms	neuropathy stomatitis	reduce dose for renal disease

Anti-retroviral Therapy - Protease Inhibitors

Antiretroviral Tx	Dosage	Baseline Labs	Monitoring Labs	Toxicities	Comments
Nelfinavir Viracept	750 mg q 8 h (250 mg caps) 9 capsules	liver function glucose	liver function glucose at least monthly	diarrhea	take with light snack or with meals
Indinavir Crixivan	800 mg q 8 h (400 mg caps) 6 capsules	liver function renal func. glucose amylase	liver function renal func. glucose at least monthly	kidney stones nausea vomiting pancreatitis	take 1 hr before or 2 hrs after meal/not concurrently with ddI take at least 1.5 liters of water per day dose separately from ddI
Ritonavir Norvir	600 mg q 12 h (100 mg caps) 12 capsules Initiate low dose then escalate to reduce GI effects	liver function glucose amylase	liver function renal function glucose at least monthly	nausea vomiting paresthesias pancreatitis	take with food store in refrigerator many drug interactions: review all meds before prescribing
Saquinavir Invirase	600 mg q 8 h (200 mg caps) 9 capsules	liver function glucose	liver function glucose at least monthly	diarrhea nausea	poor bioavailability/take with high fat meal/second line protease inhibitor in specific combinations

- Never prescribe protease inhibitor (PI) as a single anti-retroviral agent. Compliance with PIs is essential to avoid the rapid development of resistance.
- Dose escalation for ritonavir: 300 mg BID (day 1-2); 400 mg BID (day 3-5); 500 mg BID (day 6-13); then 600 mg BID.
- Consult an infectious disease expert when using protease inhibitors with rifabutin, e.g. active tuberculosis with HIV co-infection.
- Protease inhibitors may have serious interactions with certain drugs metabolized by the liver, e.g. astemizole, cisapride; review drug interactions carefully.
- Follow closely for new onset diabetes and liver failure (particularly with concurrent viral hepatitis).

Anti-retroviral Therapy - Non-nucleoside Reverse Transcriptase Inhibitors

Anti-retroviral Tx	Dosage	Baseline Labs	Monitoring Labs	Toxicities	Comments
Nevirapine Viramune	200 mg daily for 14 days, then if tolerated advance to standard tx. 200 mg BID	electrolytes/creat liver function tests	liver function tests	rash nausea headache hepatitis	incidence of rash reduced by gradual dose escalation whenever drug is stopped; restart at 200 mg daily for 14 day lead in period

- Non-nucleoside analogues should never be prescribed as monotherapy.
- Combination therapy with nevirapine and protease inhibitors is investigational; drug interactions are complex. Consult with infectious disease expert.
- Delavardine (Rescriptor) is an additional FDA-approved non-nucleoside anti-retroviral agent available as a nonformulary medication.

Prophylaxis of HIV-Related Opportunistic Infections

Pathogen	Drug	Dosage	Toxicities	Comments
Pneumocystis carinii	TMP-SMX	1 SS/day **(1st choice)** 1 DS/day 1 DS 3x/week	rash/fever/nausea leukopenia/hepatitis	prevents toxo and bacterial infections monitor CBC q 3 months
Indications: (1) CD4+ ct < 200 cells/mm^3 (2) prior PCP (3) oral candidiasis	Dapsone	100 mg/day	hemolysis/hepatic methemoglobinemia	screen for G-6-PD deficiency
	Pentamidine	300 mg q month aerosolized (administer by Respirgard II nebulizer)	bronchospasm/cough (responds to bronchodilator tx)	obtain screening chest x-ray for TB administer in negative pressure isolation room or in community outpatient facility
Toxoplasmosis gondii	TMP-SMX	1 DS/day **(1st choice)** 1 DS 3x/week	rash/fever/nausea leukopenia/hepatitis	repeat toxo IgG if previously negative when CD4+ T-cells < 100/mm^3
Indication: Toxo IgG+ and CD4+ ct < 100 cells/mm^3	Dapsone **+** Pyrimethamine + Leukovorin	50 mg/day 50 mg/week 25 mg/week	hemolysis/anemia	monitor for anemia/leukopenia with either regimen **-** CBC at least q 3 months
Mycobacterium avium	Azithromycin	1200 mg/week **(1st choice)**	nausea/vomiting	
Indication: CD4+ ct < 50 cells/mm^3	Clarithromycin	500 mg BID	nausea/vomiting	review drug interactions/do not give with terfenadine or astemizole
*R/O disseminated MAC infection with blood culture before giving prophylaxis	Rifabutin	300 mg/day	uveitis, arthralgias hepatitis	uveitis when given with fluconazole creates rifampin resistance review drug interactions

- Routine prophylaxis for fungal infections is not indicated.
- Routine prophylaxis for CMV infection is not indicated: Screen routinely for retinitis.
- Isoniazid for 12 months for inmates with PPD of 5 millimeters or greater or close contact of active case regardless of PPD status.
- Maintain prophylaxis for opportunistic infections once initiated, despite evaluations in CD4+ T-cell counts.

Appendix 7

Demographics Name: (Last) ________________ (First) ________________ REG#: _________Age:___ Gender: M ☐ F ☐ Race: W ☐ B ☐ Asian ☐ Hispan ☐ Nat American ☐ BOP Facility: ___________________

History Date of Initial Dx: __/__/__ Location: ____
AIDS-defining illnesses: ____
Prior Anti-retroviral tx: ____
PPD: _____ mm. PPD Date: __/__/__ Chest x-ray: Normal ☐ Abnormal ☐ Date: __/__/__
RPR/FTA: _____ RPR Date: __/__/__ Tx: ________________________ Tx date(s) ____________
_Pneumovax: Y☐ N☐ Date: __/__/__ Toxo IgG: _______ Drug Allergies: ____________________

Periodic Eval.	Date / /	Date / /	Date / /	Date / /	Date / /	Date / /
CDC Class.						
CD4 count/CD4%						
Viral Load						
WBC/HCT						
Ophthalmology						
Pap/Gyn						
Other						
Anti-Retrov Tx						
Prophylaxis						
AIDS Conditions Hospitalizations						
Follow-up						
Signature						

Appendix 8

HIV Occupational Post-exposure Prophylaxis (PEP)

Exposure	Source	Counsel	Treatment Regimen
Percutaneous	Blood - high risk Blood - increased risk Blood - no increased risk Infectious body fluid Noninfectious fluid	Recommend Recommend Offer Offer Not offer	ZDV + 3TC + IDV ZDV + 3TC +/- (IDV) ZDV + 3TC ZDV + 3TC
Mucosal	Blood Infectious body fluid Noninfectious fluid	Offer Offer Not offer	ZDV + 3TC +/- (IDV) ZDV +/- (3TC)
Skin Increased risk only	Blood Infectious body fluid Noninfectious fluid	Offer Offer Not offer	ZDV + 3TC +/- (IDV) ZDV +/- (3TC)

Exposure - Skin exposure is considered increased risk for exposures with high titer of HIV, prolonged contact, an extensively involved area, or with visibly compromised skin integrity.

Source - High risk blood exposure is exposure to both large volume of blood AND high titer of HIV. Increased risk blood exposure is exposure to large volume of blood OR high titer of HIV. No increased risk is neither exposure to large volume of blood nor blood with a high titer of HIV. Infectious body fluids include: semen; vaginal secretions; cerebrospinal, synovial, pleural, peritoneal, pericardial, and amniotic fluids; or body substances visibly contaminated with blood. Noninfectious fluids include urine, feces and saliva.

Counsel - Recommend means risk of HIV transmission may be significant; PEP should be recommended to the patient. Offer means the risk of HIV transmission is lower, but nonnegligible; PEP should be offered to the patient. Not offer means the risk of HIV transmission is negligible; PEP should not be offered to the patient.

Treatment - Zidovudine (ZDV), 200 mg TID; lamivudine (3TC), 150 mg BID; indinavir (IDV), 800 mg TID. Prophylaxis is given orally for 4 weeks. Some experts recommending substituting nelfinavir or saquinavir if indinavir is poorly tolerated or contraindicated. Treatment regimens remain relatively unstudied with the exception of ZDV. Drug toxicity monitoring should include a CBC and renal and hepatic function tests at baseline and 2 weeks after starting PEP.

Adapted from CDC guidelines: *MMWR*, Vol. 45/No. 22, June 7, 1996.

Appendix 9

HIV Post-Exposure Prophylaxis Fact Sheet

Question #1 - What is my risk of acquiring HIV infection following an exposure?

Answer: The risk of acquiring HIV infection is related to the type and severity of exposure to blood or other potentially infectious body fluids that include: semen, cerebrospinal fluid, pleural fluid, peritoneal fluid, vaginal secretions, pericardial fluid and amniotic fluid. The average risk of acquiring HIV infection following an exposure from a puncture or cut in the skin is 0.3% (3 out of 1,000). The risk increases with the depth of the injury, if visible blood was present on the device causing the injury, if the device was previously in a patient's vein or artery, or if the source of the exposure was a person with AIDS. The risk of acquiring HIV infection after the exposure of mucous membranes of the eyes, nose, or mouth to HIV-infected material is 0.1% (1 out of a thousand). The risk of acquiring HIV infection after the exposure of intact skin to HIV-infected material is < 0.1% (The risk may be increased if the skin is not intact, or there is prolonged exposure with a large amount of blood). Every potential exposure should be discussed with a physician so that the specific risks of the particular exposure can be reviewed and assessed.

Question #2 - If I acquire HIV infection, can I be cured?

Answer: Presently there is no cure for HIV infection. Nearly all persons infected with HIV develop the acquired immunodeficiency syndrome (AIDS). Current treatments for HIV infection prolong life and delay the progression of infection to AIDS, but have not be proven to eradicate HIV. Prevention of HIV infection is critical.

Question #3 - If I have been exposed to HIV, what can I do to prevent infection?

Answer: Studies of health care workers exposed to HIV indicate that medication can reduce the transmission of HIV infection following an occupational exposure by nearly 80%. The Centers for Disease Control (CDC) currently recommends that persons at risk for acquiring HIV infection through occupational exposure to blood or other potentially infectious fluids be recommended or offered 2 or 3 drugs effective against HIV for a one month period. The medications should be initiated within 48 hours of the exposure and preferably within 2 hours. The determination to recommend, offer, or not offer prophylactic treatment should be based on the type of exposure and the HIV status and condition of the source of the exposure.

Question #4 - If I have been exposed to urine, feces, or saliva from a person with HIV infection or AIDS should I take prophylactic medication?

Answer: The CDC does not recommend prophylactic treatment for HIV infection following occupational exposure to urine, feces, or saliva unless these substances are visibly contaminated with blood.

Question #5 - Do the preventive medications have harmful side effects?

Answer: The toxicities of the drugs used to prevent HIV infection are largely unknown in persons without HIV infection. The drugs do have significant side effects that have been documented primarily in persons with HIV infection (see below). Drug toxicities can be significantly exacerbated due to drug interactions. If you are currently taking prescribed medications for other health reasons you should review potential drug interactions and toxicities with your physician prior to taking preventive anti-viral medications for HIV. Pregnant or potentially pregnant employees experiencing an exposure to HIV infection should emergently contact their obstetrician or other personal physician prior to initiating treatment with anti-retroviral medications. Based on limited data, Zidovudine (AZT) use in the second and third trimesters of pregnancy and early infancy has not been associated with serious adverse effects for the mother or her infant. The safety of Zidovudine (AZT) during the first trimester or any of the other preventive medications for HIV infection during any stage of pregnancy is unknown.

Drug Side Effects

Zidovudine (Retrovir) (AZT) - headache, muscle pains, nausea, sleeping problems, anemia

Lamivudine (Epivir) (3TC) - headache, muscle pains, nausea, sleeping problems

Indinavir (Crixivan) - nausea, vomiting, diarrhea, kidney stones, hepatitis (inflammation of liver), pancreatitis (inflammation of the pancreas); **Nelfinavir** (Viracept) - diarrhea, nausea

Question #6 - How will I know if I have been infected or protected from infection with HIV?

Answer: Your physician should measure your blood for HIV antibodies at the time of exposure, at 12 weeks, and at 6 months. If you do not develop HIV antibodies by 6 months you are not infected with HIV.

Question # 7 - Do I need to take any precautions during the 6 months I am awaiting confirmation that I have not newly acquired HIV infection?

Answer: Yes. As a precaution you should follow these recommendations:

1. Report any unusual symptoms to your physician including fever, swollen glands, or rash.

2. Avoid exposing others to your blood or other potentially infectious body fluids. Use condoms during sexual intercourse. Do not share needles, razors, toothbrushes or other items that may be contaminated with your blood.

3. Use birth control measures to prevent pregnancy.

4. Do not donate blood, sperm, or other potentially infectious body substances.

Appendix 10

Federal Bureau of Prisons
Employee Consent/Declination Form for HIV Post-Exposure Prophylaxis

I, _____ have been counseled on the risks of transmission of HIV infection following an exposure incident while working as a BOP employee. I have also been educated on the benefits and the potential side effects and drug toxicities related to post-exposure prophylaxis with anti-retroviral medications. I understand that post exposure prophylaxis is not a guarantee against HIV infection, but has been reported by the Centers for Disease Control to be effective in reducing HIV transmission following certain exposures.

Consent

I have chosen to take an emergency dose(s) of anti-retroviral prophylactic medication.

_____ _____
Employee Signature Date

_____ _____
Witness (counseling health care provider) Date

Declination

I have chosen not to take an emergency dose(s) of anti-retroviral prophylactic medication.

_____ _____
Employee Signature Date

_____ _____
Witness (counseling health care provider) Date

NOTE: Based on limited data, Zidovudine use in the second and third trimesters of pregnancy and early infancy has not been associated with serious adverse effects for the mother or her infant. The safety of Zidovudine during the first trimester or other anti-retroviral medications during any stage of pregnancy is unknown. Pregnant or potentially pregnant employees experiencing an exposure to HIV infection should emergently contact their obstetrician or other personal physician prior to initiating treatment with anti-retroviral medications.

FEDERAL BUREAU OF PRISONS TREATMENT GUIDELINES FOR TUBERCULOSIS DISEASE

PURPOSE. The Federal BOP Treatment Guidelines for Tuberculosis Disease define a standard of care for the medical management of tuberculosis to ensure that BOP inmates diagnosed with active tuberculosis receive effective therapy, while limiting the development of resistant disease and reducing contagion.

REFERENCES.

Prevention and Control of Tuberculosis in Correctional Facilities, Recommendations of the Advisory Council for the Elimination of Tuberculosis, *MMWR* Vol. 45/No. RR-8, June 7, 1996, U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, Atlanta, Georgia.

Core Curriculum on Tuberculosis, 1994, U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, Atlanta, Georgia.

Guidelines for Preventing Transmission of *Mycobacterium tuberculosis* in Health-Care Facilities, *MMWR*, Vol. 43/ No. RR-13, October 28, 1994, U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, Atlanta, Georgia.

DEFINITIONS.

Acid-fast bacilli (AFB) are bacteria that retain certain dyes after being washed in an acid solution. Most acid-fast bacilli are mycobacteria. When AFB are seen on a stained smear of sputum or other clinical specimen, a diagnosis of tuberculosis should be suspected; however, the diagnosis of tuberculosis is not confirmed until a culture is grown and identified as *M. tuberculosis*.

Culture is the process of growing bacteria in the laboratory so that organisms can be identified.

Directly observed therapy (DOT) is the unit dose administration of medications to a patient by a trained health care provider.

Drug susceptibility tests are the laboratory tests that determine whether the tuberculosis bacteria cultured from a patient are susceptible or resistant to various anti-tuberculosis drugs.

Multi-drug resistant tuberculosis (MDR-TB) is active tuberculosis caused by *M. tuberculosis* organisms that are resistant to more than one anti-tuberculosis drug; in practice, often refers to organisms that are resistant to both isoniazid and rifampin with or without resistance to other drugs.

Mycobacterium tuberculosis is the mycobacterial species that is the primary cause of active tuberculosis disease in the United States.

Smear (AFB smear) is the laboratory technique for visualizing mycobacteria. The specimen is smeared onto a slide and stained, then examined using a microscope. In tuberculosis, a large number of mycobacteria seen on an AFB smear usually indicates infectiousness. However, a positive smear is not diagnostic of tuberculosis, because organisms other than *M. tuberculosis* may be seen on an AFB-smear.

PROCEDURES.

a. All BOP inmates with the clinical or laboratory diagnosis of tuberculosis disease should be considered candidates for four drug anti-tuberculosis initial drug therapy in accordance with the treatment guidelines enumerated in Appendix 1 (Federal Bureau of Prisons Treatment Guidelines for Tuberculosis Disease) adapted from Centers for Disease Control recommendations.

b. Since inmates may have resistance to one or more tuberculosis drugs at baseline, the initial prescription of four-drug therapy is essential for minimizing the development of further drug resistance. Four drug therapy also hastens the conversion of AFB smears from positive to negative; thus reducing infectiousness.

c. Inmates diagnosed with active pulmonary tuberculosis should be maintained in negative pressure AFB isolation in a community hospital or BOP medical referral center until no longer contagious as indicated by the following parameters:

1. Treatment with four drug regimen per treatment guidelines or other equally effective regimen for at least two weeks.

2. Clinical evidence of improvement.

3. If AFB-smear positive, conversion of three (3) morning sputum smears to negative.

4. If drug resistance is suspected, documentation of drug sensitivities and clinical evidence of effective therapy.

d. If AFB smears are negative, but tuberculosis is suspected based on clinical presentation and chest radiograph findings, the inmate should be housed in AFB isolation for two weeks of tuberculosis treatment and released when clinically improving. The inmate should be maintained on tuberculosis treatment until sputum or bronchial washing culture results are available, at which time the need for continued treatment should be assessed.

e. Tuberculosis treatment regimens may require adjustments once drug susceptibility tests become available. Any deviations to the standard regimen are rarely indicated and should always be in accordance with the following caveats:

1. Never treat active tuberculosis with a single drug.

2. Never add a single drug to a failing tuberculosis treatment regimen.

3. Never switch to a two drug regimen of isoniazid and rifampin before drug sensitivities confirm non-resistant tuberculosis.

f. All tuberculosis medications should be prescribed according to the inmate's weight and adjusted appropriately with weight changes.

g. All tuberculosis medications should be administered by directly observed therapy (DOT) to ensure compliance with the prescribed treatment regimen and reduce the emergence of resistant disease.

h. All inmates should be monitored at least monthly by a physician to evaluate clinical response to therapy and monitor side effects to medications. Tuberculosis therapy and side effects to medications should be prescribed and monitored in accordance with the parameters outlined in Appendix 1 and the following guidelines:

1. Inmates who are sputum culture positive for *Mycobacterium tuberculosis* should have three (3) adequate morning sputum cultures obtained monthly until sputum cultures convert to negative. Sputum cultures positive for *Mycobacterium tuberculosis* after two months of drug treatment should be considered suggestive of ineffective therapy. Repeat drug sensitivities should be obtained to evaluate for resistant disease. Inmates who can not voluntarily provide a sputum sample at a BOP facility should be sent to an appropriate community health care facility for sputum induction. A final sputum culture should be obtained at the completion of successful treatment as a reference culture.

2. Liver function studies should be obtained at baseline. If baseline liver enzymes are elevated, inmates should be screened for hepatitis B and C infections. Inmates with elevations in liver enzymes greater than 3-5 times normal are at higher risk for hepatotoxicity from isoniazid and other potentially hepatotoxic tuberculosis medications. Elevations in liver enzymes are not necessarily a contraindication to treatment, but consultation with a tuberculosis expert is recommended. Monthly monitoring of liver enzymes should be considered for the following conditions:

(a) Persons with baseline liver enzymes greater than normal.

(b) Persons 35 years of age or older.

(c) Persons with chronic liver disease from alcohol, viral hepatitis or other etiologies.

(d) Persons with a history of injection drug usage during the past two years.

(e) Persons prescribed other potentially hepatotoxic drugs.

(f) Persons with a history of previous adverse reactions to isoniazid.

(g) African American and Hispanic women.

(h) Pregnant women.

3. Visual acuity and red-green color vision should be assessed at baseline and monthly thereafter for inmates treated with ethambutol. Optometry or ophthalmology evaluations are indicated at three months of treatment and every three months thereafter while inmates are receiving ethambutol.

4. Baseline and monthly creatinine/audiograms are indicated for inmates receiving streptomycin or other aminoglycosides.

5. Chest radiographs should be obtained at baseline, at the completion of therapy, and during treatment when clinically indicated.

6. Clinical improvement following empiric treatment for pulmonary tuberculosis with negative cultures is strongly suggestive of culture-negative pulmonary tuberculosis and can be treated with an abbreviated treatment course in accordance with Appendix 1.

7. Extrapulmonary tuberculosis is generally treated using the same drug regimens as pulmonary tuberculosis. Serial bacteriologic evaluations may be limited by disease location; therefore the response to treatment must be judged on the basis of clinical, and where applicable, radiologic findings.

8. Tuberculosis disease with HIV co-infection is treated with the same treatment regimens as tuberculosis without HIV infection, unless the inmate is being treated with protease inhibitor anti-retroviral therapy. Rifampin is contraindicated in combination with protease inhibitors, so an alternative non-standard tuberculosis treatment regimen must be used in consultation with a tuberculosis expert and CDC guidelines. Although persons with

tuberculosis and HIV infection usually respond well to anti-tuberculosis therapy, drug side effects are more frequent and bacteriologic response may be less sustained in this population, necessitating careful monitoring, and if necessary, an extended treatment course.

9. A physician consultant with tuberculosis treatment expertise and the State health department should be consulted for any of the following tuberculosis cases:

(a) A treated case of tuberculosis that does not result in negative cultures following two months of therapy.

(b) All cases of drug intolerance, pregnancy, or other situations requiring deviation from a standard treatment regimen

(c) All cases of multi-drug resistance

10. Inmates with tuberculosis disease who do not respond to standard drug therapy by two months of treatment may be noncompliant with medications, or may have malabsorption, drug interactions, or other processes resulting in subtherapeutic serum drug levels. Persons with chronic gastrointestinal disease (e.g. Crohns disease, HIV-related diarrhea) are particularly at risk for drug treatment failure. Serum drug levels should be obtained to document the adequacy of medication delivery for inmates with known malabsorption or who fail to respond to tuberculosis treatment. Procedures for obtaining tuberculosis drug levels at a specialty lab should be obtained through the BOP Chief of Infectious Diseases or Chief of Pharmacy Services.

ATTACHMENTS.

Appendix 1. Federal Bureau of Prisons Tuberculosis Treatment Guidelines

Federal Bureau of Prisons Tuberculosis Treatment Guidelines

DIAGNOSTIC CATEGORY	LENGTH OF REGIMEN	INITIAL PHASE INH/RIF/PZA/EMB (or SM) for 8 weeks (daily for 2 weeks, then biweekly for 6 weeks)		CONTINUATION PHASE INH/RIF for 16 weeks (2 options)		MONITORING PARAMETERS
Adults - TB **Culture positive - pulmonary or extrapulmonary**	**6 months minimum** **Longer treatment may be required for TB meningitis or bone/joint TB**	**DAILY DOSE (MAXIMUM DOSE)** Daily dose x 14 doses INH 5 mg/kg (300 mg/day) RIF 10 mg/kg (600 mg/day) PZA 15-30 mg/kg (2g/day) EMB 15-25 mg/kg or SM 15 mg/kg $\leq$ 60 yr. (1.0 g/day) SM 10 mg/kg if $>$ 60 yr. Old (750 mg - 1 g) **Note**: EMB should be started at 15 mg/kg to reduce the risk of ocular toxicity. The use of 25 mg/kg should be reserved for patients requiring retreatment, or treatment of drug resistant TB.	**TWICE WEEKLY DOSE (MAXIMUM DOSE)** Twice weekly x 6 weeks. INH 15 mg/kg (900 mg/dose) RIF 10 mg/kg (600 mg/dose) PZA 50-70 mg/kg (4g/dose) EMB 50 mg/kg/dose or SM 25-30 mg/kg $\leq$ 60 yr. (1.5 g/dose) SM 750 mg - 1 g if $>$ 60 yrs) **Note**: Pyridoxine - 50 mg/day should be given concurrently with INH to prevent INH-associated peripheral neuropathy. Drugs prescribed twice weekly should be administered 2 or 3 days apart.	**DAILY DOSE (MAXIMUM DOSE)** INH 5 mg/kg (300 mg/day) RIF 10 mg/kg (600 mg/day) **Note**: AFTER 8 WEEKS OF 4 DRUG THERAPY NEVER SWITCH TO 2 DRUG THERAPY UNTIL SUSCEPTIBILITY TO INH AND RIF HAS BEEN DEMONSTRATED.	**TWICE WEEKLY DOSE (MAXIMUM DOSE)** INH 15 mg/kg (900 mg/dose) RIF 10 mg/kg (600 mg/dose) Note: Drugs prescribed twice weekly should be administered 2 or 3 days apart.	**Baseline**: Chest x-ray, morning sputums for AFB X 3, CBC, platelet count, creatinine, uric acid, bilirubin, hepatic enzymes, visual acuity/red-green color perception(EMB), and audiogram(SM). Do susceptibility drug testing with first sputum cultures and as needed. **Ongoing**: Monthly evaluation by a physician for symptoms and targeted exam LFTs monthly if elevated at baseline Creatinine/audiogram monthly on SM Visual acuity/red-green color vision monthly, eye doctor evaluation every 3 months while on EMB Certain high-risk groups, may have increased propensity for INH-induced hepatitis and require monthly liver enzymes. Presence of hepatitis does not preclude treatment for TB--patient must be monitored closely. Other labs at discretion of physician. Obtain 3 consecutive daily sputums for smear and culture every month until conversion. Repeat drug susceptibility testing if patient fails to respond clinically or remains culture positive after 2 months. Chest x-ray, sputum smear and culture at end of treatment for future comparisons.
Adults - **Pulmonary with negative smear and culture.** Patient is symptomatic.	**4 months minimum** 6 months if HIV infected.	**INITIAL PHASE** INH/RIF/PZA/EMB (or SM) for 8 weeks		**CONTINUATION PHASE** INH/RIF for 8 weeks		Same as above Chest x-ray at 3 months. Failure of x-ray to respond to treatment within 3 months suggestive of previous (not current) TB or another disease.
		Same as above	Same as above	Doses same as above. Continue EMB and PZA if drug resistance likely.	Doses same as above. Continue EMB and PZA if drug resistance likely.	

INH-isoniazid, RIF-rifampin, PZA-pyrazinamide, EMB-ethambutol, SM-streptomycin. **Adjust dosages as weight. changes. Medicines must be given by directly observed therapy.**

FEDERAL BUREAU OF PRISONS TUBERCULOSIS TREATMENT GUIDELINES - SPECIAL CONSIDERATIONS

DIAGNOSTIC CATEGORY	REGIMEN	MEDICATIONS	MONITORING PARAMETERS
Pregnancy	**9 months minimum.** Treatment should begin as soon as TB is suspected.	Treat with appropriate doses of INH/RIF/EMB. Do not use PZA unless dealing with drug-resistant disease with no alternatives. Inadequate tetratogenicity data for PZA Give Pyridoxine (B6) 50 mg/day concurrently. **SM has documented harmful effects on the fetus and should not be used.** Discontinue EMB once INH/RIF sensitivity results are documented. Consult with an infectious disease expert for appropriate treatment regimen	**Baseline**: Chest x-ray, morning sputums for AFB X 3, CBC, platelet count, serum creatinine, uric acid, liver enzymes, visual acuity, and red-green color vision. **Ongoing:** Monthly symptom review and exam by clinician. Assess visual acuity/ red-green color perception monthly and eye doctor evaluation every 3 months while on EMB. With hepatic disease, renal disease or gout obtain monthly liver function tests, creatinine, or uric acid respectively. Certain high-risk groups for isoniazid-induced hepatitis require monthly liver enzymes. Presence of hepatitis does not preclude treatment for TB. Patient must be monitored closely. Other laboratory studies at the discretion of the physician. Obtain 3 consecutive daily sputums every month until conversion. Do susceptibility drug testing with first cultures and as needed. Repeat drug susceptibilities if patient fails to respond clinically or remains culture positive after 2 months. Chest x-ray, sputum smear and culture at end of treatment and more frequently as indicated. If pregnant woman is HIV positive or has drug resistant TB, consult infectious disease consultant.
HIV Infection	**6 months** of standard regimen unless patient on protease inhibitor which can not be given with RIF. Consult specialist.	(Treatment may need to be prolonged due to adverse drug reactions, poor drug absorption and other complications of HIV infection).	Monitoring same as for adult standard. Consult specialist if patient is taking protease inhibitor. Adverse reactions more common. If there is no culture conversion at the end of 2 months, reevaluate patient and repeat drug susceptibility tests. **Treatment should be prolonged with any evidence of suboptimal response with therapy**.
INH Resistance/ Intolerance	**6 months** of 4-drug standard regimen effective. After INH resistance/intolerance identified, discontinue INH. Tx with RIF/ PZA/EMB for duration of therapy given twice weekly.	Same as adult standard excluding INH from regimen.	Same as adult standard. Monitor cultures and drug sensitivities closely.
INH/Rifampin resistance (MDR-TB)	Continue treatment until bacteriologic sputum conversion **followed by 12-24 months of at least 3 drug treatment.**	Give at least three new drugs to which the organism is susceptible. Consult with tuberculosis expert to ensure effective medical management.	Same as adult and children standards with monthly monitoring of cultures and drug sensitivities until conversion.

INH-isoniazid, RIF-rifampin, PZA-pyrazinamide, EMB-ethambutol, SM-streptomycin. **Adjust dosages as weight changes. Administer all medicines by directly observed therapy.**

FEDERAL BUREAU OF PRISONS PREVENTIVE TREATMENT GUIDELINES FOR TUBERCULOSIS

PURPOSE. The Federal BOP Preventive Treatment Guidelines for Tuberculosis provide recommended guidelines for tuberculosis chemoprophylaxis to limit active tuberculosis disease among inmates in federal correctional facilities and at the time of release to the community.

REFERENCES.

Prevention and Control of Tuberculosis in Correctional Facilities, Recommendations of the Advisory Council for the Elimination of Tuberculosis, *MMWR*, Vol. 45/No. RR-8, June 7, 1996. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, Atlanta, Georgia.

Core Curriculum on Tuberculosis, 1994. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, Atlanta, Georgia.

Guidelines for Preventing Transmission of *Mycobacterium tuberculosis* in Health-Care Facilities, 1994, *MMWR*, Vol. 43, No. RR-13, October 28, 1994. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, Atlanta, Georgia.

DEFINITIONS.

Anergy is the inability of a person to react to skin-test antigens (even if the person is infected with the organisms tested) because of immunosuppression.

Booster phenomenon is a phenomenon in which some persons (especially older adults) who are skin tested many years after infection with *M. tuberculosis* have a negative reaction to an initial skin test, followed by a positive reaction to a subsequent skin test. The second (i.e.) positive reaction is caused by a boosted immune response. Two-step testing is used to distinguish new infections from boosted reactions.

Clinician is a physician or mid-level provider.

Contact is a person who has shared the same air with a person who has infectious tuberculosis for a sufficient amount of time to allow possible transmission of *M. tuberculosis.*

Directly observed preventive therapy (DOPT) is the unit dose administration of tuberculosis preventive medication to an inmate by a clinician, nurse, pharmacist, or specially trained pharmacy staff member.

Exposure is the condition of being subjected to an infectious agent that could have a harmful effect. A person exposed to *M. tuberculosis* does not necessarily become infected.

Intradermal is within the layers of skin.

Mantoux method is the most reliable method of tuberculin skin testing, involving the intradermal injection of PPD-tuberculin into the forearm with a needle and syringe.

Mycobacterium tuberculosis is the mycobacterial species that is the primary cause of active tuberculosis disease in the United States.

Positive PPD reaction is the induration measured in millimeters that develops after the intradermal injection of PPD-tuberculin suggestive of previous infection with *M. tuberculosis*. The extent of induration indicative of infection depends on the medical history and risk factors of the person being tested in accordance with the following:

5 millimeters - positive for:

- Close contacts of an active case of tuberculosis.
- Persons with HIV infection or other immunocompromised conditions, or persons with HIV risk factors and unknown HIV serostatus.
- Persons with evidence of old tuberculosis infection by chest radiograph.

10 millimeters - positive for correctional staff and inmates.

15 millimeters - positive for persons without any risk factors for tuberculosis.

Preventive therapy or chemoprophylaxis is the treatment of latent inactive tuberculosis infection with an antibiotic to prevent the development of active tuberculosis disease.

Purified protein derivative (PPD) tuberculin skin test is a method used to evaluate the likelihood that a person is infected with *M. tuberculosis*.

Recent convertor is an individual who has a measured tuberculin skin test that has increased within the past 24 months from a baseline of 0-9 millimeters of induration by (1) 10 millimeters or more if < 35 years of age; by (2) 15 millimeters or more if 35 years of age or older; by (3) 5 millimeters or more if immunocompromised regardless of age.

Tuberculosis infection is the condition in which living *M. tuberculosis* organisms enter the body and can elicit a response from the host's immune defenses. Tuberculosis infection may or may not result in tuberculosis disease.

Tuberculosis disease is the condition in which *M. tuberculosis* infection progresses to clinically active, symptomatic disease.

Two-step testing is a procedure used for the baseline testing of persons who will periodically receive tuberculin skin tests to reduce the likelihood of mistaking a boosted reaction for a new infection. If the initial tuberculin skin test result is classified as negative, a second test is repeated 1-3 weeks later. If the reaction to the second test is positive, it represents a boosted reaction indicating old latent tuberculosis infection. If the second test result is also negative, the person is classified as not infected.

PROCEDURES.

a. Screening for Tuberculosis Infection. Inmates are screened for tuberculosis infection using the PPD-tuberculin skin test in accordance with current BOP policy using the following guidelines:

1. The test is administered by the Mantoux method through intradermal injection of 0.1 ml of purified protein derivative (PPD) tuberculin containing 5 tuberculin units (TU) onto the volar surface of the left forearm, using a disposable tuberculin syringe. Only BOP Formulary tuberculin solution should be used.

2. The tuberculin skin test should be read by a trained health care worker 48 to 72 hours after injection. A positive reaction may be measurable up to one week after testing and is considered valid. A negative reaction read after 72 hours is invalid.

3. The tuberculin reaction is quantified by measuring the diameter of the indurated area (palpable swelling) across the forearm, (perpendicular to the long axis by the "pen method") documented in millimeters. Erythema (redness) without induration is not significant. THE TUBERCULIN SKIN TEST RESULTS SHOULD ALWAYS BE DOCUMENTED IN MILLIMETERS; NEVER AS POSITIVE OR NEGATIVE.

4. Multi-puncture tests (Tine) are poorly standardized and should not be administered.

5. A "previous positive" skin test is not a contraindication to repeat testing unless a severe reaction has been documented or described by the inmate (e.g. entire arm swelling, blistering).

6. Pregnancy is not a contraindication to tuberculin skin testing.

7. Bacille Calmette-Guerin (BCG) vaccination is not a contraindication to tuberculin skin testing. There is no reliable method for distinguishing tuberculin reactions caused by BCG from those caused by infection with *M. tuberculosis*. A history of BCG vaccination should not be considered when interpreting skin tests, since BCG vaccination is not always effective in preventing new infections with *M. tuberculosis*.

8. Anergy testing is not routinely indicated as a component of tuberculin skin testing for inmates. Response to anergy panel antigens is not necessarily predictive of an adequate cellular immune response to PPD tuberculin.

9. Inmates screened for tuberculosis infection by tuberculin skin testing should also be interviewed for symptoms of tuberculosis disease: chronic cough, hemoptysis, fever and night sweats, unexplained weight loss. The tuberculin skin test is not a highly sensitive test. On average, 10% to 25% of persons with tuberculosis disease will have a negative tuberculin skin test. ANY INMATE WITH SYMPTOMS OF ACTIVE TUBERCULOSIS SHOULD BE REFERRED TO A PHYSICIAN FOR FURTHER DIAGNOSTIC EVALUATION REGARDLESS OF TUBERCULIN SKIN TEST RESULTS.

b. Baseline Evaluation for Preventive Therapy. Inmates with tuberculin skin tests of 5 millimeters of induration or greater should be referred for evaluation by a physician for possible preventive treatment for tuberculosis. PREVENTIVE THERAPY SHOULD NEVER BE INITIATED UNTIL ACTIVE TUBERCULOSIS DISEASE HAS BEEN ELIMINATED AS A DIAGNOSIS WITH A NEGATIVE CHEST RADIOGRAPH AND A DOCUMENTED NEGATIVE ASSESSMENT FOR SIGNS AND SYMPTOMS OF TUBERCULOSIS. SYMPTOMATIC INMATES SHOULD BE EVALUATED WITH SPUTUM SMEARS AND CULTURES X 3 REGARDLESS OF CHEST RADIOGRAPH FINDINGS PRIOR TO CONSIDERING PREVENTIVE VERSUS ACTIVE TREATMENT OF TUBERCULOSIS.

Baseline evaluation for preventive tuberculosis treatment should include, but not necessarily be limited to the following:

1. Medical history for symptoms of active tuberculosis disease, hepatitis, liver disease, pregnancy, and medication review.

2. Targeted physical examination by a physician.

3. Posterior-anterior chest radiograph (pregnant women should not receive a chest radiograph unless they have symptoms of pulmonary tuberculosis or have medical indications for isoniazid therapy during pregnancy).

4. Liver enzyme screen: aspartate transaminase (AST) if isoniazid chemoprophylaxis is indicated.

5. HIV counseling and testing.

6. Inmates with chest radiograph abnormalities or symptoms of tuberculosis disease should be evaluated for active disease with sputum smears and cultures, prior to initiating preventive therapy.

c. Indications for Preventive Treatment. Indications for initiating tuberculosis preventive therapy are based on the person's tuberculin skin test reaction in millimeters, risk factors for infection and disease, and risk factors for side effects from isoniazid, such as age, gender, race, and baseline liver function. Tuberculosis chemoprophylaxis with isoniazid should be considered when the following indications have been identified, no medical contraindications to treatment exist, and previous adequate treatment can not be documented:

1. Tuberculin skin test is 10 mm or greater for an inmate less than 35 years of age.

2. Recent convertor status: an individual who has a measured tuberculin skin test that has increased within the past 24 months from a baseline of 0-9 millimeters of induration by (1) 10 millimeters or more if < 35 years of age; or by (2) 15 millimeters or more if 35 years of age or older; or by (3) 5 millimeters or more with HIV infection or other immunocompromised condition.

3. Tuberculosis skin test is 5 millimeters or greater regardless of age, with the following concurrent conditions that increase the risk of tuberculosis disease:

(a) Close contact to active tuberculosis case.

(b) HIV infection, risk factors for HIV infection with unknown HIV serostatus, or other immunocompromised condition.

(c) Systemic corticosteroids or other immunosuppressive therapy (equivalent to 15 mg. of prednisone or greater for 3 months or more of treatment).

(d) Fibrotic changes on chest radiograph suggestive of inactive pulmonary tuberculosis.

4. Tuberculosis skin test is 10 millimeters or greater regardless of age with the following concurrent conditions that increase the risk of tuberculosis disease:

(a) Injection drug usage during the past 2 years.

(b) Hematologic or reticuloendothelial neoplasms.

(c) Renal failure (dialysis-dependent).

(d) Diabetes mellitus (insulin dependent).

(e) Gastrectomy and other specific conditions resulting in nutritional deficiencies.

(f) Head and neck malignancies.

(g) Silicosis.

5. Inmates with HIV infection or other immunocompromised conditions who are close contacts of an active case of tuberculosis should be initiated on isoniazid chemoprophylaxis even if their tuberculin skin test measures 0 millimeters with or without evidence of anergy.

6. Inmates should not be considered for preventive therapy if their anticipated incarceration is less than 6 months unless the following high priority indications have been identified:

(a) HIV co-infection or other immunocompromised condition

(b) Close contact of an active case of tuberculosis

(c) Recent convertor status

7. Isoniazid chemoprophylaxis should not be initiated when contraindications to isoniazid exist, including but not limited to the following:

(a) History of severe reaction to isoniazid

(b) Radiologic or clinical evidence of active tuberculosis disease

(c) Symptoms of active hepatitis

(d) Liver enzymes 3-5 times normal (Isoniazid may be indicated despite liver enzyme elevations for certain high risk individuals. Consult with a tuberculosis expert for high risk candidates with liver disease).

d. Preventive Treatment

1. Isoniazid is the standard tuberculosis preventive agent prescribed as 15 mg/kg; (max:900 mg) by mouth, twice weekly and administered by unit dose under direct observation (DOPT**)** at least two days apart. Isoniazid should be prescribed for 52 doses (approximately 6 months) for inmates with known HIV seronegative status; and for 104 doses (approximately 12 months) for inmates with HIV seropositive status, unknown HIV serostatus, or silicosis or fibrotic lung disease regardless of HIV status. At the discretion of the treating physician, isoniazid may also be prescribed as 5 mg/kg; (max:300 mg) by mouth, daily, and administered by DOPT for 182 doses (approximately 6 months) for inmates with known HIV seronegative status; and for 365 doses (approximately 12 months) for inmates with HIV seropositive status, unknown HIV serostatus, or silicosis or fibrotic lung disease regardless of HIV status.

2. Completion of isoniazid chemoprophylaxis should be determined by counting **doses** of isoniazid taken, **not** solely by duration of treatment, since missed doses may occur.

3. For inmates who miss doses of isoniazid or have histories of incomplete isoniazid compliance the following general guidelines can be applied:

(a) For a one-time or cumulative break equivalent to one month of prescribed isoniazid or less, resume isoniazid as initially ordered and extend treatment for the number of missed doses.

(b) For a one-time break exceeding the equivalent of a one month regimen of prescribed isoniazid, reinitiate isoniazid therapy, (i.e. start treatment again).

(c) For cumulative multiple breaks exceeding the equivalent of one month of prescribed isoniazid, extend isoniazid therapy by three months (26 doses, if prescribed biweekly).

(d) For inmates failing to complete isoniazid prophylaxis on two or more occasions, determine on a case by case basis if additional retreatment efforts are clinically prudent based on the inmate's risk factors for tuberculosis disease, previous cumulative doses of administered isoniazid, and anticipated compliance.

4. Pyridoxine should be prescribed concurrently as 50 mg by mouth daily while taking isoniazid.

5. Alternative preventive therapy may be indicated for contacts of resistant tuberculosis cases and should be prescribed in consultation with a tuberculosis expert.

6. Isoniazid chemoprophylaxis is not routinely recommended during pregnancy although no harmful effects on the fetus have been observed. Isoniazid should be prescribed 1-2 months following delivery in most cases. Pregnant women who are close contacts of active tuberculosis cases, are recent convertors, or have concurrent HIV infection or other immunosuppressive conditions should be considered for isoniazid chemoprophylaxis while pregnant. Screening chest radiographs should generally be delayed until after 20 weeks of pregnancy unless the inmate has symptoms of active pulmonary tuberculosis. Chest radiographs should be obtained with appropriate shielding of the fetus.

e. Monitoring

1. All inmates receiving tuberculosis preventive therapy should be evaluated by a clinician in accordance with the following guidelines:

(a) Baseline evaluation by a physician (0 months).

(b) Follow-up evaluations every three months by a clinician for uncomplicated cases.

(c) Monthly follow-up evaluations (0 through 6-12 months) by a clinician for complicated cases included all cases requiring monthly liver enzymes.

2. Liver enzymes for inmates receiving isoniazid should be monitored in accordance with the following:

(a) AST should be obtained prior to initiating isoniazid treatment for all inmates. If the AST is elevated, liver function studies (LFTS) and screens for hepatitis B and C should be obtained.

(b) Isoniazid should generally not be initiated if liver enzymes are greater than 3-5 times normal. Persons with liver enzymes 3-5 times normal with a high risk for tuberculosis (e.g. HIV infection, close contacts) should be considered for isoniazid chemoprophylaxis in consultation with a tuberculosis expert.

(c) Monthly monitoring of liver enzymes (AST) should be considered for persons at high risk for isoniazid-induced hepatitis, including but not necessarily limited to the following persons:

(1) Persons with baseline liver enzymes greater than normal.

(2) Persons 35 years of age or older.

(3) Persons with chronic liver disease from alcohol, viral hepatitis or other etiologies.

(4) Persons with a history of injection drug use during the past two years.

(5) Persons prescribed other potentially hepatotoxic drugs concurrently with isoniazid.

(6) Persons with a history of previous adverse reactions to isoniazid.

(7) African American and Hispanic women.

(8) Pregnant women.

3. All inmates receiving isoniazid should be monitored for symptoms of hepatitis and other drug side effects by a pharmacist, clinician or nurse at least monthly. Inmates reporting potential side effects to isoniazid should be referred to a physician for further evaluation. ISONIAZID SHOULD BE DISCONTINUED IF LIVER ENZYMES INCREASE TO 3 to 5 TIMES NORMAL OR GREATER, WITH SYMPTOMS OF HEPATITIS, OR OTHER SERIOUS DRUG SIDE EFFECTS

4. Chest radiographs, other than baseline, are not indicated during therapy for inmates prescribed isoniazid unless symptoms of tuberculosis develop during treatment.

5. Inmates who are candidates for isoniazid preventive therapy, but decline treatment, or have treatment discontinued because of drug side effects, noncompliance, or other reasons, should be monitored in accordance with the following:

(a) Semiannual chest radiographs and clinician evaluations for symptoms and signs of pulmonary tuberculosis for inmates with HIV infection (or unknown HIV serostatus) or other immunosuppressive conditions.

(b) Semiannual chest radiographs and clinician evaluations for symptoms and signs of pulmonary tuberculosis for two year period, for HIV seronegative inmates who are recent convertors or close contacts of active tuberculosis cases.

(c) Inmates should be counseled during clinician evaluations to reconsider initiation of isoniazid preventive therapy if appropriate.

f. Documentation.

1. Tuberculosis preventive treatment should be documented by the evaluating physician and other designated staff using the Federal Bureau of Prisons Tuberculosis Chemoprophylaxis Record,

(Appendix 1). The form should be maintained in the inmate's medical record and documentation updated:

(a) At the baseline evaluation and initiation of treatment.

(b) Whenever treatment is interrupted or discontinued.

(c) At the completion of chemoprophylaxis.

2. Medication administration of tuberculosis chemoprophylaxis should be documented using the Federal Bureau of Prisons Tuberculosis Preventive Treatment Program Medication Administration Record (BP-634(60)).

3. Side effects to isoniazid treatment should be monitored monthly by a trained health care provider using the Federal Bureau of Prisons Monthly INH Side Effect Interview and Monitoring Form, (Appendix 2). The form requires the inmate's signature upon the initiation of treatment and should be reviewed monthly with inmates at each pyridoxine renewal. (Health care staff should read the form to illiterate inmates). The form should be maintained by pharmacy staff, made available to clinicians for review, and a copy placed in the inmate's medical record at the completion or discontinuation of isoniazid preventive treatment.

4. Inmates who refuse isoniazid chemoprophylaxis should sign a refusal form in their medical record, documenting their declination of treatment.

ATTACHMENTS.

Appendix 1. Federal Bureau of Prisons Tuberculosis Chemoprophylaxis Record

Appendix 2. Federal Bureau of Prisons Monthly Isoniazid Side Effect Interview and Monitoring Form

Appendix 1

Federal Bureau of Prisons Tuberculosis Chemoprophylaxis Record

Demographics

Name: (Last) _____ (First) _____ Reg #: _____

DOB: ___/___/___ Age: ____ Sex: ___ Race: W □ B □ Asian □ Hispanic □ Native American □

Medical History

PPD: Current test: Date ___/___/___ ____mm; Previous test: Date ___/___/___ ____ mm Unknown □

HIV status: Positive □ Negative □ Not tested □ Date tested: ___/___/___ BCG: Y □ N □

Chest x-ray: Negative □ Abn □ Fibrotic Lesion (old TB) □ Other _____

Previous INH: Y □ N □ DOPT: Y □ N □ Adverse rx: Y □ N □ _____

Indication(s) for Preventive Rx

Close contact □ Recent convertor □ Age < 35 □ Clinical condition □ _____

Screening History and Exam

Jaundice/hepatitis hx Y □ N □ Dark urine Y □ N □ Wt loss Y □ N □ Cough/TB symptoms Y □ N □

Liver disease Y □ N □ Pregnancy Y □ N □ Other symptoms/conditions: _____

_____

Examination: T _____ P _____ R _____ BP _____ Weight: ____ lbs _____ kgs

_____

Treatment History

INITIATION
Start date: ___/___/____ Drug tx: _____ mgms. Freq _____ Duration _____ doses
Prescribing clinician: Name _____ Facility: _____

DISCONTINUATION
Preventive treatment interrupted or discontinued prior to prescribed duration - list indication(s):
Active case □ Deceased □ Released □ Inmate decision □ Adverse rx □ Medical advice □
Noncompliance □ Other □: _____
_____

Doses taken: _____ Discontinuation date: ____/____/_____
Evaluating clinician: Name _____ Facility: _____

COMPLETION
Doses taken : _____

Preventive treatment completion date: ___/___/___ Facility: _____
Comments: _____
_____
_____
_____
_____
_____
_____

Appendix 2

MONTHLY INH SIDE EFFECT INTERVIEW AND MONITORING FORM

INH is an antibiotic that is the first line treatment for latent tuberculosis infection. As with all medications, there are side effects that can occur from its use. INH may affect your body's stores of vitamin B6. For this reason it is absolutely mandatory that you take the vitamin B6 prescribed daily. Failure to do this could contribute to many of the side effects listed below.

I have read and understand this form and agree to accurately record any potential side effects I may experience monthly when I am interviewed as below:

X_____ _____ _____
Signature Printed Name/Register Number Date

Record either a "Y" for yes or a "N" for no at each symptom or sign monthly:

Month:	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
numb hands/feet												
headache												
seizure												
vision decrease												
memory loss												
loss of appetite												
nausea/vomiting												
yellow skin or eyes												
fatigue/wt. loss												
abdominal pain												
brown urine												
Initial monthly:												
Inmate												
MD/PA/RN/RPH												

Termination of Medication date:_____

Physician/PA/NP Comments: ("Y" response requires brief note here and immediate referral to clinician for evaluation and documentation of treatment plan in medical record)

))

ENTRAVISTA Y FORMA PARA REGULAR MENSUALMENTE LOS EFECTOS DE INH

INH es un antibiotica que trata la forma latente de la Tuberculosis. Como con todos los medicamentos, pueden ocurrir efectos seundarios con su uso. INH puede afectar la reserva de la vitamina B6 en su cuerpo. Por este motivo es absolutamente mandatorio que tome la vitamina B6 recetada diariamente. No tomar la vitamina B6 puede contribuir a los varios efectos secundarios identificados abajo.

Yo he leido y entendido esta forma y estoy de acuerdo en documentar mensualmente si tengo algunos de estos sintomas cuando me entrevisten.

_____ _____ _____

Firma Nombre Escrito y Numero de Registro Fecha

Indique con una "Y" para SI o con una "N" para No al lado cada sintoma.

MES:	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
adormecimiento de pies/manos												
dolor de cabeza												
ataque epileptico / convulsiones												
perdida de vision												
perdida de memoria												
falta de apetito												
nauseas/vomitos												
piel u ojos amarillos												
dolor abdominal												
orina color cafe												
Firme con sus iniciales cada mes:												
RECLUSO												
MD/PA/RN/RPH												

Termination of medication date: _____

Physician/PA/NP comments: ("Y" response requires brief note here and immediate referral to clinician for evaluation and documentation of treatment plan in medical record)

))

1. An inmate presents to your clinic with new onset jaundice with elevated transaminases and normal alkaline phosphatase. You suspect acute viral hepatitis. How should you confirm the diagnosis?

   A. Measure Hep A IgG, HBsAg, and anti-HCV
   B. Measure Hep A IgM, anti-HBc IgM, and anti-HCV
   C. Measure Hep A IgM, anti-HBs, and anti-HCV
   D. Measure Hep A IgM, anti-HBe, and anti-HCV
   E. Measure Hep A IgG, HBsAg, and anti-HCV

2. An inmate is diagnosed with acute hepatitis A. Which of the following statements is false?

   A. The estimated period of contagiousness for the inmate is three weeks prior to the onset of jaundice until 10 days after the onset of jaundice.
   B. The inmate is more contagious if he has diarrhea.
   C. If the inmate is a food worker widespread inoculation with immunoglobulin may be indicated.
   D. Immunoglobulin prophylaxis of contacts can be given up to four weeks after exposure.
   E. If the inmate's cellmate has a history of hepatitis A (HAV IgG+), immunoglobulin prophylaxis is not indicated.

3. An inmate is diagnosed with chronic hepatitis B by confirming hepatitis B surface antigen positivity (HBsAg+). Which of the following statements is false?

   A. Because the inmate is HBsAg+ he is considered a chronic carrier and is contagious.
   B. The inmate could spontaneously develop antibodies to the HBV surface antigen and no longer be HBsAg+.
   C. If the inmate is HBe antigen positive, he is less contagious.
   D. The risk for liver cancer will increase with the duration of infection.
   E. Liver transaminases may be completely normal.

4. Which of the following is not an indication for treatment of hepatitis B with interferon alpha?

   A. ALT is elevated 2X normal for 12 months
   B. Anti-HBe+
   C. HBsAg+
   D. HBV DNA +
   E. Fibrosis on liver biopsy

5. An inmate with chronic hepatitis B is started on interferon alpha treatment. Which of the

following statements is false?

A. If ALT increases during treatment, interferon should be stopped.
B. Flu symptoms usually abate with repeated interferon treatments.
C. Treatment should be considered successful if HBe antigen is lost 6 months following treatment.
D. HBsAg may remain positive for several years even with successful treatment
E. Interferon treatment will result in normalization of ALT in approximately 30% of persons treated.

6. Which of the following is false regarding the diagnosis of HCV infection?

A. The recommended test for confirming hepatitis C infection for an inmate with a history of injection drug use is EIA-2.
B. Even in persons with the presence of anti-HCV, recurrent infections with HCV can occur.
C. Measuring anti-HCV by RIBA-2 is recommended only for low risk persons with a positive EIA-2.
D. Qualitative PCR for HCV is recommended for all persons with positive antibodies to HCV.
E. With acute HCV infection, anti-HCV can be measured with the onset of symptoms in the majority of persons.

7. Which of the following statements is false regarding evaluation of inmates with hepatitis C for treatment with interferon alpha?

A. Persons with a normal ALT should not be considered for treatment.
B. Persons with fibrosis have a poor response to treatment.
C. Persons with AIDS have a poor response to treatment.
D. Persons with cryoglobulinemia and renal disease should not be considered for treatment.
E. Persons with liver failure should not be considered for treatment.

8. Which of the following is always indicated when treating inmates with hepatitis C with interferon alpha?

A. Serial liver biopsies
B. Qualitative measurement of HCV
C. HCV genotype analysis
D. Quantitative HCV viral load
E. Anti-HCV by RIBA

9. Which of the following is false regarding the treatment of inmates with hepatitis C with interferon alpha?

   A. The treatment regimen of choice is 3 million units of interferon alpha three times per week for 12 months.
   B. Response to treatment can be reliably predicted based on the normalization of ALT within 2-3 months of initiating treatment.
   C. Rise in ALT during treatment is an indication to stop therapy since progression of liver disease may occur.
   D. Approximately 20% of inmates will have a sustained response to treatment.
   E. Steroids are sometimes a helpful adjunct to treatment.

10. Which statement is false regarding prevention of hepatitis B and C infections?

   A. All staff and inmates should be screened for antibodies to hepatitis B prior to immunization.

   B. HBIG (hepatitis B immunoglobulin) is indicated for susceptible persons parenterally exposed to hepatitis B.
   C. There is no prophylaxis for hepatitis C exposures.
   D. Persons immunized with hepatitis B vaccine may require additional immunoprophylaxis if exposed to hepatitis B.
   E. Persons exposed to hepatitis C should be monitored for the development of antibodies to HCV.

11. Which of the following statements is false concerning tuberculin skin testing?

   A. Testing should be performed using the Mantoux method of intradermal injection.
   B. Tests should be read in millimeters of induration, not erythema.
   C. A reading of 15 millimeters 7 days after administering a PPD is valid.
   D. A reading of 0 millimeters 4 days after administering a PPD is valid.
   E. Pregnant women can safely receive a tuberculin skin test.

12. Which of the following is false concerning assessment of PPD positivity?

   A. A 5 millimeter PPD is considered positive for inmates with HIV infection.
   B. A 10 millimeter PPD is considered positive for all inmates, even those without underlying risks for tuberculosis.
   C. A 5 millimeter PPD is considered positive for inmates and staff who are close contacts of an active case of tuberculosis.
   D. A 5 millimeter PPD is considered positive for inmates with radiographic evidence suggestive of old tuberculosis infection.
   E. Millimeter thresholds for PPD positivity are different in persons with BCG vaccination.

13. Which of the following inmates is not a candidate for isoniazid preventive treatment?

    A. 60 year old inmate who boosts his PPD from 0 millimeters to 15 millimeters after two step testing at intake
    B. 55 year old HIV-infected inmate with 7 millimeter PPD at intake
    C. 30 year old inmate with 10 millimeter PPD at intake
    D. 26 year old inmate whose skin test increases from 3 millimeters to 14 millimeters during annual testing
    E. 67 year old inmate whose skin test increases from 2 millimeters to 20 millimeters during annual testing

14. Which of the following inmates is not a candidate for isoniazid preventive treatment?

    A. A 20 year old inmate with a new PPD of 6 millimeters whose cell mate has been diagnosed with active tuberculosis
    B. A 40 year old inmate on renal dialysis with a PPD of 11 millimeters at intake.
    C. A 64 year old inmate with a PPD of 7 millimeters who develops lymphoma and requires high dose steroid treatment
    D. A 23 year old inmate whose PPD increases from 0 millimeters to 4 millimeters during annual testing
    E. A 70 year old inmate with PPD of 13 millimeters at intake with head and neck cancer

15. Which of the following persons are not at increased risk for isoniazid hepatotoxicity?

    A. Hispanic men
    B. Persons with history of alcoholism
    C. African-American women
    D. Pregnant women
    E. Older persons

16. Which of the following statements is false concerning isoniazid hepatotoxicity?

    A. All inmates should have baseline AST measured prior to receiving INH
    B. Hepatotoxicity most frequently occurs within 4-8 weeks of initiating INH
    C. An inmate with transaminase levels 2X normal should not be given INH
    D. All inmates at high risk for hepatotoxicity should have monthly AST measurements
    E. Hepatitis from INH usually resolves when INH is discontinued at the onset of symptoms

17. You are asked to evaluate an inmate with AIDS who has roomed with a cellmate with active, smear-positive pulmonary tuberculosis for one month. How would you manage the inmate with HIV infection after ruling out active tuberculosis by symptom review and chest radiograph?

    A. Give INH regardless of PPD test results
    B. Give INH if PPD is 5 millimeters or greater
    C. Give INH if PPD is 5 millimeters or greater or less than 5 millimeters with anergy
    D. Give INH if PPD is 10 millimeters or greater
    E. Give INH if PPD is 2 millimeters or greater

18. Which of the following statements is false concerning treatment of active tuberculosis?

    A. Active tuberculosis should never be treated by a single drug.
    B. Multi-drug resistant TB may require 24 months of treatment with TB drugs.
    C. A single drug should never be added to a failing tuberculosis drug regimen.
    D. Pulmonary and extra-pulmonary tuberculosis are usually treated with the same drug regimens.
    E. Initiation of drug therapy with three drugs is the standard BOP treatment regimen.

19. An inmate with active tuberculosis should be housed in AFB isolation until which of the following criteria have been met:

    A. The inmate is clinically improving from symptoms of tuberculosis.
    B. The inmate has been treated with four drug therapy for at least two weeks.
    C. The inmate has three consecutive negative AFB smears from sputum.
    D. Drug sensitivities are available if multi-drug resistance is suspected.
    E. All of the above

20. Which of the following statements is false regarding treatment of active tuberculosis?

    A. If treatment is effective sputum cultures should convert to negative within two months of treatment.
    B. If HIV co-infection is present rifampin and protease inhibitors should not be prescribed concurrently.
    C. If color vision becomes impaired toxicity from pyrazinamide should be suspected.
    D. Pregnant women with tuberculosis should be treated, but pyrazinamide and streptomycin should be avoided.
    E. Isoniazid, rifampin, pyrazinamide, and ethambutol doses should all be administered daily or biweekly not in split daily dosages.

21. Which of the following statements is false regarding the staging of HIV infection?

    A. A person with asymptomatic infection but CD4+ T-cells of 120/mm^3 should be staged as A3.
    B. A person previously staged as C3 with CD4+ T-cells of 100/mm^3 that increases to 300 when placed on protease inhibitors should be reclassified as C2.
    C. An asymptomatic person with CD4+ T-cells of 250/mm^3 with a CD4+ T-cell percentage of 10% should be classified as A3.
    D. A person with oral candidiasis and CD4+ T-cells of 340/mm^3 should be classified as B2.
    E. A person with PCP pneumonia and CD4+ T-cells of 220/mm^3 should be classified as C2.

22. Which of the following statements is false regarding viral load testing?

    A. Viral load should not be measured within one month of immunizations or acute illnesses.
    B. The nadir (lowest level) of the viral load may not be reached for 2-4 months after changing anti-retroviral therapy.
    C. Viral load can return to pretreatment levels within several days of stopping anti-retroviral therapy.
    D. A tenfold (1 log) change in viral load one month after initiating an anti-retroviral regimen predicts undetectable viral levels at 4-6 months.
    E. If CD4+ T-cell counts are stable and the inmate is asymptomatic viral load testing is not indicated.

23. Which of the following is not indicated during baseline evaluation of an inmate with HIV infection:

    A. Chest radiograph
    B. Viral load testing
    C. Anergy panel
    D. Pneumovax if CD4+ T-cell count is greater than 200/mm^3 repeated X 1 at 5 years
    E. Influenza vaccination before flu season and repeated annually if CD4+ T-cell count is greater than 200/mm^3

24. Which of the following statements is false regarding nucleoside reverse transcriptase inhibitors (NRTIs)?

    A. AZT and d4T are antagonistic and should not be used in combination
    B. ddI is the most potent NRTI when used as monotherapy
    C. Only AZT has excellent CNS penetration
    D. ddI must be taken on a full stomach
    E. Macrocytosis can often be attributed to AZT

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25. Which of the following statements is false regarding treatment with protease inhibitors?

    A. A major side effect of indinavir is nephrolithiasis.
    B. Ritonavir has the fewest drug interactions of the protease inhibitors.
    C. Viral resistance develops rapidly with patient noncompliance.
    D. Saquinavir is poorly absorbed.
    E. Use of protease inhibitors with cisapride can be life threatening.

26. You are asked to evaluate an asymptomatic inmate with a CD4+ T-cell count of 700/mm^3 and a viral load of 1,000 copies/ml on no treatment. You recommend:

    A. Observe and monitor
    B. Initiate treatment with one drug
    C. Initiate treatment with two drugs
    D. Initiate treatment with three drugs

27. You are asked to evaluate an asymptomatic inmate with a viral load of 500,000 copies/ml and a CD4+ T-cell count of 700/mm^3. You recommend:

    A. Observe and monitor
    B. Initiate treatment with one drug
    C. Initiate treatment with two drugs
    D. Initiate treatment with three drugs

28. Which of the following general principles regarding anti-retroviral treatment for HIV infection is false?

    A. When changing a failing anti-retroviral treatment regimen add two new drugs
    B. Effectiveness of anti-retroviral therapy should be based on viral load
    C. Viral load should be measured before and approximately one month after each change in anti-retroviral therapy.
    D. Prophylaxis for opportunistic infections should be based on the CD4+ T-cell count
    E. If the CD4+ T-cell count increases with anti-retroviral therapy prophylaxis for opportunistic infections can be discontinued.

29. Which of the following statements is false regarding the initiation of prophylaxis for opportunistic infections?

    A. PCP prophylaxis should routinely be initiated when the CD4+ T-cell count is <200/mm^3.
    B. Toxoplasmosis prophylaxis should routinely be initiated when the CD4+ T-cell count is < 100 cells/mm^3 if the inmate has a positive toxoplasmosis IgG.
    C. MAC prophylaxis should routinely be initiated when the CD4+ T-cell count is <50/mm^3.
    D. Fungal prophylaxis should routinely be initiated when the CD4+ T-cell count is <50/mm^3.
    E. CMV prophylaxis with oral gancyclovir is not routinely indicated.

30. Which of the following statements is false regarding the management of opportunistic infections for BOP inmates with HIV infection?

A. The prophylactic agent of choice for MAC infection is azithromycin 1200 mg given once weekly by directly observed therapy.
B. Before initiating MAC prophylaxis blood cultures should be obtained to screen for disseminated MAC infection.
C. The prophylactic agent of choice for PCP is trimethoprim-sulfamethoxazole.
D. TMP-SMZ provides effective prophylaxis for both PCP and toxoplasmosis.
E. Aerosolized pentamidine is effective for preventing toxoplasmosis as well as PCP pneumonia.

Infectious Disease Treatment Protocol Study Guide

Question #1 - Answer is **B**

Acute hepatitis A is confirmed by a positive HAV IgM titer that is present during the onset of clinical symptoms. Acute hepatitis B is confirmed by a positive IgM antibody to HBV core antigen (anti-HBc IgM) that develops concurrently with symptoms. Acute hepatitis C is diagnosed by eliminating other causes of viral hepatitis and documenting the presence of anti-HCV antibodies that are present in 60% of patients at the onset of symptoms. An assay for anti-HCV IgM antibody is not commercially available.

Question #2 - Answer is **D**

Expedient diagnosis of acute hepatitis A is critical in the correctional setting since large scale outbreaks of infection can occur, particularly if the index case is a food handler. Infected individuals are contagious from three weeks prior to the onset of jaundice until 10 days after the onset of jaundice. Diarrhea markedly increases contagion. Cell mates, sexual contacts and other very close contacts of an infectious case should be administered immunoglobulin in accordance with CDC guidelines. If the index case was a food handler widespread prophylaxis in the correctional setting may be indicated. Immunoglobulin prophylaxis must be administered within 2 weeks of exposure to be effective.

Question #3 - Answer is **C**

By definition chronic HBV carriers are HBsAg + and are considered contagious. Contagiousness is markedly increased with the presence of HBe antigen. Loss of HBe antigen occurs at an annual rate of 5-10%, indicates reduced contagiousness and predicts clinical improvement from chronic hepatitis. Loss of HBsAg occurs at an annual rate of 1-2% and usually indicates resolution of hepatitis and the development of immunity. Chronic HBV carriers (HBsAg +) can have normal liver transaminases. The risk of cancer increases with the duration of infection.

Question #4 - Answer is **B**

Persons infected with HBV are candidates for interferon alpha treatment only if they are HBsAg + , HBe antigen + , HBV DNA + with elevated liver transaminases over a 12 month period. Chronic HBV carriers that are HBe antigen negative with antibodies to HBe (anti-HBe +) either have resolving hepatitis or an atypical form of hepatitis that will not respond to interferon treatment. Chronic HBV carriers that have normal liver transaminases have immunotolerance to HBV with minimal liver inflammation and respond poorly to interferon. The presence of HBV DNA should be confirmed prior to treatment, to ensure the presence of ongoing active infection since spontaneous clearance of HBV infection occurs. Fibrosis on liver biopsy correlates with a positive response to interferon treatment for HBV infection, but not for HCV infection.

Question # 5 - Answer is **A**

Interferon treatment results in a sustained clinical response in approximately 30%-35% of persons treated. The effectiveness of treatment is confirmed by the loss of HBe antigen six months following the completion of therapy. Responders to treatment may remain HBsAg + for many years. Influenza symptoms are commonly associated with interferon alpha treatment. Symptoms can be disabling, are partially aborted with anti-pyretics, and usually abate with repeated treatments. The serum ALT often increases during interferon treatment as an immune response is induced and HBV is cleared. Interferon should not be discontinued as ALT increases unless the hepatitis is severe or associated with signs of liver dysfunction.

Question #6 - Answer is **D**

Among high risk inmates, hepatitis C infection can be adequately diagnosed by measuring anti-HCV by EIA-2. Measuring anti-HCV by RIBA or qualitative measurement of HCV by PCR is not necessary to confirm infection. Inmates without known risk factors for HCV infection should have their diagnosis confirmed by measuring anti-HCV by RIBA. Acute HCV infection is difficult to diagnose but in 60% of cases anti-HCV by EIA will be measurable at the onset of symptoms and is associated with rising ALT. Many different quasi-species of HCV can be identified since the viral envelope changes frequently similar to HIV. Reinfection with different species of HCV can occur and exacerbate underlying disease (e.g. ongoing drug use). Anti-HCV does not convey immunity.

Question #7 - Answer is **D**

Persons with chronic hepatitis C and normal liver transaminases are not candidates for interferon alpha treatment and may actually decompensate if treatment is prescribed. In contrast to hepatitis B infection, the presence of fibrosis on liver biopsy with hepatitis C infection is a poor prognostic indicator for response to interferon therapy. The prescription of interferon for persons with liver failure and hepatitis C infection is absolutely contraindicated. The prescription of interferon for persons with AIDS is relatively contraindicated since response rates are extremely poor and toxicities potentially life threatening. Persons with renal disease and cryoglobulinemia, a relatively common complication of hepatitis C infection, may respond to interferon therapy and should be considered for treatment if they are otherwise appropriate candidates.

Question #8 - Answer is **B**

The qualitative presence of HCV RNA should be confirmed prior to beginning treatment with interferon since infection may spontaneously clear and treatment has potentially significant toxicities for the patient. A baseline liver biopsy is indicated prior to treatment, but serial biopsies are not routinely necessary for monitoring disease. Quantitative HCV viral load testing is not FDA-approved and is considered investigational. Although certain HCV genotypes (1a and 1b) are associated with poorer response rates, genotype analysis is considered investigational and should not be the basis for prescribing or not prescribing therapy. Measurement of anti-HCV by RIBA is indicated to confirm HCV infection in a low risk individual, not to monitor treatment.

Question #9 - Answer is **E**

The recommended treatment for hepatitis C is interferon alpha, 3 million units subcutaneously, three times per week for 12 months. Treatment should be initiated only with great caution since response rates are low and drug toxicities significant. Approximately 20% of treated individuals have a sustained response. Response rates to interferon therapy for HCV infection can be accurately assessed at 2-3 months after the initiation of treatment. Treated patients who fail to normalize their ALT at 2-3 months will not respond to further treatment and should have interferon discontinued, once confirming the ongoing qualitative presence of HCV by PCR. In contrast to treatment of HBV infection, a rise in ALT following treatment of HCV infection with interferon is an ominous sign and is an indication to discontinue therapy. Steroids are contraindicated for the treatment of hepatitis B or C viral infections.

Question #10 - Answer is **A**

Persons with percutaneous exposures to hepatitis C virus should be monitored for symptoms of hepatitis and screened for the development of HCV antibodies. The mean incubation of HCV infection is 50 days. Approximately 60% of infected persons will have measurable anti-HCV at the onset of symptoms. There is no effective immunoprophylaxis for HCV exposures. Routine screening for previous hepatitis B infection is not indicated for staff or inmates prior to initiating the hepatitis B vaccine series. Inmates with high risk histories for HBV infection can be considered for screening on a case by case basis. Unimmunized persons exposed to HBV infection should be administered hepatitis B immunoglobulin (HBIG) with initiation of the hepatitis B vaccine series. Both interventions can be administered simultaneously intramuscularly at two separate sites (deltoid for adults). Previously immunized persons exposed to HBV infection should have their HBV antibody status confirmed. Although the risk of developing active hepatitis when previously vaccinated is exceedingly low, exposed previously vaccinated persons with subtherapeutic antibody levels (< than 10 milli-international units) should receive HBIG and in some cases a booster of the HBV vaccine.

Question #11 - Answer is **D**

All tuberculin skin testing should be performed using the Mantoux method by injecting 0.1 ml of intermediate strength PPD solution intradermally into the volar surface of the forearm. Tests are measured in millimeters of induration and should be read 48-72 hours after administering the test. A positive test can be read up to one week after administering the test. A negative test read after 72 hours of administering the test is considered invalid. Pregnant women can receive tuberculin skin testing without complications.

Question #12 - Answer is **E**

A 5 millimeter PPD is considered positive for immunocompromised persons, close contacts of active TB cases, and for persons with inactive old TB by chest radiograph. A 10 millimeter PPD is considered a positive reaction for correctional staff and inmates. Persons previously vaccinated with BCG should have their TB skin tests interpreted the same as unvaccinated individuals.

Question #13 and #14- Answers are **A and D**

The indications for isoniazid (INH) prophylaxis are based on the likelihood of TB infection, the risk for developing TB disease, and the risk of INH induced hepatotoxicity. For healthy inmates at intake without concurrent illnesses, INH should be offered to inmates under age 35 with a PPD of 10 millimeters or more. Healthy inmates at intake without concurrent illnesses who are 35 years of age or older with a boosted or unboosted PPD of 10 millimeters or greater should not be prescribed INH since the risk of hepatotoxicity outweighs the risk of TB disease from old latent TB infection. A positive booster PPD test (a positive PPD test repeated two weeks after a negative PPD test at intake) indicates old latent TB infection.

Persons with HIV infection, close contact to an active TB case, or evidence of inactive old TB by chest radiograph, who have a PPD of 5 millimeters or greater should be considered for INH prophylaxis regardless of age. (Persons with abnormal chest radiographs should not be prescribed INH until active tuberculosis has been eliminated as a diagnosis based on symptom review, clinical evaluation, and sputum analysis). Persons with insulin dependent diabetes, dialysis-dependent renal failure, gastrectomy, silicosis, head and neck cancer, hematologic malignancies, or injection drug usage within the past two years with a PPD of 10 millimeters or greater should be considered for INH preventive therapy regardless of age.

Healthy persons evaluated for TB infection during annual tuberculin skin test screening should be considered for INH prophylaxis with an increase in their PPD skin test within the past 24 months of 10 millimeters if < 35 years of age and of 15 millimeters if 35 years of age or older. Note: Any person with an increase in their PPD reading to greater than 5 millimeters during annual screening should be evaluated on a case by case basis by a physician, since a lower threshold for INH prophylaxis may be warranted if the person has concurrent illnesses such as HIV infection or evidence of close contact with an active tuberculosis case.

Question #15 - Answer is **A**

The risk of isoniazid hepatotoxicity increases with age, evidence of underlying liver disease, pregnancy, and among African-American and Hispanic women. INH hepatotoxicity is not increased among Hispanic men independent of other factors.

Question #16 - Answer is **C**

INH hepatotoxicity can occur anytime during treatment, but most commonly occurs within 4-8 weeks of initiating therapy. All inmates should have baseline AST levels drawn before initiating treatment. Persons at high risk for hepatotoxicity or elevated baseline AST levels should have monthly AST levels measured during INH treatment. All inmates should have a monthly symptom review for side effects to INH. Inmates with AST levels 3-5 times normal should generally not be started on INH, unless the risk for TB is very high and a physician consultant has reviewed the case.

Question #17 - Answer is **A**

Persons with HIV infection who are contacts of an active tuberculosis case are at high risk for developing active tuberculosis (approximately 10% per year once infected). HIV-infected contacts should be evaluated on a case by case basis to determine if INH prophylaxis is indicated. In this case, the risk of TB infection was extraordinarily high and the inmate contact was markedly immunocompromised, making PPD testing unreliable. Anergy testing is poorly standardized and of uncertain predictive value. Even a positive anergy panel would not necessarily indicate adequate cellular immunity to respond to PPD antigen. PPD testing should be conducted on HIV-infected contacts since many AIDS patients do have measurable reactions. In this high risk case, INH prophylaxis should be initiated even with a PPD result of zero millimeters.

Question #18 - Answer is **E**

Active non-resistant tuberculosis should always be treated in accordance with BOP protocols adapted from CDC guidelines unless medical contraindications to the recommended regimen are identified. Initial treatment with four drugs for two months for cases of suspected or confirmed active TB is recommended to reduce the emergence of resistant disease and to hasten the conversion of AFB smears from positive to negative, thus rapidly reducing contagion. Active TB should never be treated with a single agent. At least two new drugs should always be added to a failing TB regimen. Pulmonary and extra-pulmonary TB are generally treated the same, although TB meningitis, lymphadenitis, osteomyelitis, and arthritis may require more prolonged treatment. Multi-drug resistant TB should be treated in consultation with a TB expert often for 24 months.

Question #19 - Answer is **E**

Persons with non-resistant pulmonary tuberculosis rapidly become non-contagious within two weeks of therapy when placed on a four drug TB regimen as recommended by the CDC. Inmates should remain in AFB isolation until they are clinically improving, on two weeks of four drug treatment, and have three consecutive negative AFB smears of the sputum. Persons who remain smear positive or clinically unimproved should remain in isolation since multi-drug resistance is more likely. If multi-drug resistance is suspected based on history or clinical course, the inmate should remain in isolation until culture sensitivities confirm non-resistant TB. Confirmed multi-drug resistant cases of TB should be managed in isolation on a case by case basis, usually until three consecutive negative cultures are obtained, and the inmate is clinically improving.

Question #20 - Answer is **C**

Active tuberculosis should always be monitored by monthly sputum smears and cultures. Susceptible TB should respond to appropriate treatment within two months of initiating therapy, confirmed by negative sputum cultures. Persons with persistently positive sputum cultures should be referred to a TB expert. Rifampin is contraindicated in combination with protease inhibitors, since drug interactions will result in subtherapeutic protease inhibitor levels. TB cases with HIV co-infection should be managed in consultation with an infectious disease expert if protease inhibitors are included in the HIV treatment regimen. Pregnant women should not be prescribed streptomycin or pyrazinamide. The standard four drug TB regimen should be prescribed as daily or biweekly doses in accordance with BOP guidelines. Doses should not be split to reduce side effects, since drug effectiveness may be compromised. Impaired color vision is a symptom suggestive of optic neuritis, a dose-related toxicity of ethambutol. Monthly screening for visual acuity and red-green color blindness should be implemented for all inmates prescribed ethambutol.

Question #21 - Answer is **B**

The 1993 CDC classification system for the staging of HIV infection is based on CD4+ T-cell count or percentage (Categories 1, 2, and 3) and clinical symptoms (Categories A, B, and C). For classification purposes, the lowest accurate CD4+ T-cell count or percentage should be utilized. For classification purposes, Category B conditions take precedence over those in Category A; and Category C AIDS conditions take precedence over those in Category B.

Question #22 - Answer is **E**

Viral load testing is indicated for all persons with HIV infection since even asymptomatic persons with normal CD4+ T-cell counts may be at high risk for disease progression. Viral load can return to pretreatment levels within days of stopping anti-retroviral medications and is markedly affected by concurrent illnesses and recent immunizations. Viral load should be measured before and one month after any changes in anti-retroviral therapy. A tenfold (1 log) change in viral load one month following initiation of an anti-retroviral treatment regimen predicts a viral load decline at 4-6 months to < 500 copies or undetectable levels.

Question #23 - Answer is **C**

All inmates diagnosed with HIV infection should have a baseline CD4+ T-cell count, viral load testing, chest radiograph and other studies as enumerated by protocol. Pneumovax is indicated for HIV-infected inmates with CD4+ T-cell counts greater than 200 cells/mm^3. A one time booster immunization with Pneumovax is indicated after 5 years for HIV-infected persons. Influenza immunization is indicated annually for HIV-infected inmates with CD4+ T-cell counts $> 200/mm^3$. Immunization with Pneumovax and flu vaccine for inmates with low CD4+ T-cells has not been strongly recommended because of concerns of transiently increasing HIV viral load and reduced benefit from vaccination. Anergy testing is poorly standardized with an unknown predictive value and is not routinely indicated for inmates with HIV infection.

Question # 24 - Answer is **D**

Monotherapy anti-retroviral therapy is suboptimal and should be avoided whenever possible. The single most effective monotherapy NRTI is ddI. d4T and AZT are less effective monotherapy options. Protease inhibitors, nevirapine, and 3TC are absolutely contraindicated as monotherapy anti-retroviral treatments. Dual anti-retroviral therapy with 2 NRTIS (e.g. AZT/3TC, AZT/ddI, AZT/ddC, d4T/ddI) has proven more efficacious than monotherapy and forms the basis for many triple therapy options. The combination of AZT/d4T, however, is antagonistic and should not be prescribed. Some experts recommend preserving 3TC for triple therapy options due to the rapid development of cross resistance with other NRTIs.

Of the nucleoside reverse transcriptase inhibitors (NRTI) only AZT has good CNS penetration. A common side effect of AZT is macrocytosis that may or may not be associated with a severe anemia. Common causes of macrocytic anemia (e.g. B12 and folate deficiency) should always be investigated. Both ddI and the protease inhibitor, indinavir must be given on an empty stomach and never at the same time.

Question #25 - Answer is **B**

The protease inhibitors are a new class of anti-retroviral drugs for treatment of HIV infection that are extremely potent inhibitors of HIV. Four protease inhibitors are currently FDA-approved and on the BOP formulary: saquinavir, ritonavir, indinavir, and nelfinavir. Saquinavir has poor bioavailability and must be administered with food, preferably food with a high fat content. Ritonavir must be refrigerated and has significant drug interactions that may affect drug potency and toxicity. Indinavir must be taken on an empty stomach with at least 1.5 liters of water per day to reduce the incidence of nephrolithiasis, a common drug side effect. Nelfinavir can be administered with a light snack. All protease inhibitors must be taken religiously, since noncompliance results in the rapid development of viral resistance. Protease inhibitors should never be prescribed with terfenadine, astemizole, or cisapride, since life threatening cardiotoxicity can occur.

Questions #26 and #27 - Answers are **A and D**

All anti-retroviral treatment must be considered on a case by case basis depending on the patient's CD4+ T-cell count, viral load, previous treatment history, drug tolerance, and patient motivation. Triple therapy with two NRTIs and a protease inhibitor is the preferred treatment option for most patients when drug therapy is recommended. Asymptomatic inmates with CD4+ T-cells < 350-500/mm^3, should be treated regardless of viral load. Asymptomatic inmates with CD4+ T-cells > 350-500/mm^3, should be treated only when viral load is elevated.

Question #28 - Answer is **E**

Anti-retroviral therapy should be managed based on changes in the patient's viral load. Viral load should be measured periodically and before and after any changes in anti-retroviral therapy. When changing treatment regimens for patients taking triple anti-retroviral therapy, two drugs should be switched whenever possible. Prophylaxis of opportunistic infections is based on the patient's immune status as assessed by the CD4+ T-cell count. If CD4+ T-cell counts increase after beginning a new anti-retroviral regimen, prophylaxis for opportunistic infections should not be discontinued, since the patient's immune status may still be compromised.

Question #29 - Answer is **D**

Prophylaxis for opportunistic infections related to HIV infection is critical for reducing patient morbidity and mortality. Prophylaxis for PCP, toxoplasmosis (IgG+), and *Mycobacterium avium* complex (MAC) are routinely indicated based on CD4+ T-cell count. Oral gancyclovir is not routinely recommended for prevention of CMV systemic disease, due to concerns about the drug's effectiveness, toxicity, and cost. Prevention of fungal disease with fluconazole or other agent should be prescribed on a case by case basis. Routine prophylaxis with fluconazole has not decreased overall mortality and can result in significant drug resistance.

Question #30 - Answer is **E**

The prophylactic agent of choice for PCP is trimethoprim-sulfamethoxazole due to its superior effectiveness and its concurrent prevention of toxoplasmosis and many bacterial infections. The drug of choice for prevention of MAC infection among inmates is azithromycin since the drug can be given weekly with limited toxicity and concurrently prevents many atypical bacterial infections. Screening for disseminated MAC by surveillance blood cultures prior to prophylaxis is recommended since disseminated disease requires a more complicated treatment regimen. Aerosolized pentamidine provides effective local prophylaxis for PCP in the lungs, not systemic prophylaxis for other opportunistic infections.