

Hepatitis C Evaluation and Treatment Oregon DOC 2003

General Information and Background .

Hepatitis C transmission occurs primarily through exposure to infected blood. This exposure exists in the context of injection drug use, blood transfusion before 1992, solid organ transplantation from infected donors, unsafe medical practices, occupational exposure to infected blood, birth to an infected mother, high-risk sexual practices with an infected person, and intranasal cocaine use. The incidence of new HCV infections appears to have declined significantly in the late 1980's, perhaps related to behavior changes due to concern about transmission of other blood borne diseases. Transmission from blood products and organ transplants was virtually eliminated by the introduction of a more sensitive test for antibody to HCV (HCVab) in mid-1992.¹

In general, studies have shown that 60-85 percent of persons with acute HCV infection will develop chronic infection. HCV replicates preferentially in hepatocytes but is not directly cytopathic, thus often leading to persistent infection. The estimated prevalence of HCV in the United States is at least 1.8% of the whole population, making HCV the most common chronic blood-borne infection nationally. High anti-HCV seroprevalence rates from (15 to 90 percent) have been documented in specific subpopulations, including a rate of about 70 to 80 percent in injection drug users.¹ Oregon has documented a seroprevalence rate of 30 percent of inmates entering the prison system.

Risk of Transmission in Correctional Institutions is Low

Based upon what is known about transmission rates and the natural progression of hepatitis C in the community, the rate of seropositivity found among inmates in the Department of Corrections represents infection that was transmitted before incarceration. Transmission of hepatitis C among inmates while they are incarcerated is estimated to be low because of the documented success the Department has with random drug urinalysis, interdiction of contraband, and the low incidence of acute infections with other blood borne pathogens, and surveillance of all forms of prohibited activity.

Standard precautions is the term used for the procedures which prevent transmission of blood borne communicable diseases caused by exposure to blood or other body fluids. These procedures effectively prevent transmission of hepatitis C. Since the HIV/AIDS epidemic, the workplace in correctional settings has been modified to include new equipment, supplies and

procedures that effectively incorporate additional protections against blood and body fluid exposure, and rapid response to every exposure to blood.

What is the Natural Course of Hepatitis C Infection?

The most important sequelae of chronic HCV infection are progressive liver fibrosis becoming cirrhosis, end-stage liver, and hepatocellular carcinoma. Chronic infection does not always lead to any of these problems. Estimates of the proportion of chronically infected persons who develop cirrhosis 20 years after initial infection vary widely from 2 to 4 percent in studies of children and young women to as high as 20-30 percent in middle-aged transfused subjects. The actual risk is likely intermediate between these two ranges, on the order of 10 to 15 percent. There is little evidence that virologic factors, including viral load or viral genotype significantly affect the risk of progression to fibrosis.¹

When chronic infection leads to progressive fibrosis, the progression to cirrhosis is slow, often taking 10-40 years.²

Some experts suggest that progression to severe end-stage liver disease is inevitable, other experts have concluded that disease progression is not inevitable and actually occurs in a limited number of cases. These opposing views can be accounted for, at least in part, by the quiet nature of the process and the almost snail's pace of progression.³

One study, the NIH Prospective Study of HCV-Infected Donors⁴, followed 280 HCV positive people for 20 years. Liver biopsies were performed on 81 of these people. Only 1.3% had evidence of severe hepatitis and cirrhosis at an average interval of 18 years from exposure.

A study from UCLA published 1993 looked at hepatitis from blood transfusions⁵. They found in their post-transfusion group that at 16 years of known infection, 18-20% had cirrhosis on biopsy.

Two significant natural history studies were recently published reporting the longest follow up yet. The first documents the course in 376 Irish women who had been infected by an injection with a batch of HCV contaminated anti-D immune globulin.⁶ After 17 years of living with HCV all 363 had a liver biopsy, none had received any anti-HCV treatment. After 17 years of infection, no fibrosis was documented in nearly half of the women, and cirrhosis in only 2%.

¹ NIH consensus statement "*Management of Hepatitis C: 2002*"

² Alter HJ & Seeff, LB., *Sem Liv. Dis, 2000*, and lecture at *Management of Hepatitis C in Prisons 2003*.

³ Seeff, LB. *The Natural History of Chronic Hepatitis C virus Infection*, Clinics in Liver Disease, Nov. 1997.

⁴ Alter, HJ. *Hepatitis C virus infection in asymptomatic blood donors*, Hepatolgy Sept. 1997

⁵ Koretz, RL. *Non-A non-B post-transfusion hepatitis*, Hepatology 1993.

⁶ Kenny-Walsh, E. *Clinical Outcomes after hepatitis C infection from contaminated Anti-D immune globulin*, New England Journal of Medicine 1999.

The 45 year study of military recruits by Leonard Seeff⁷, published in 2000, has the longest time span of any study published to date. This study involved 8,568 people who were military recruits in 1948-1954 and had blood drawn. They were divided into two groups, those that had HCV positive blood, and those without. Liver abnormalities, disease, and causes of death as of 1997 were reviewed and compared between individuals with HCV infection and those without infection. The rate of liver disease in the HCV positive group was 11.8% compared to 2.4% in the HCV negative group. But, the study found no significant difference in overall death rate, or average age of death. According to Seeff, long-term natural history data have revealed that only 15% -20% of HCV infected persons will eventually develop progressive to potentially serious end-stage liver disease (namely cirrhosis) and that the remainder will die of causes other than liver disease.⁸

Clearly it appears that the large majority of people with hepatitis C exposure and chronic hepatitis C infection will not progress to development of health problems from liver disease due to chronic infection with hepatitis C.

Most people (80%) with chronic hepatitis C infection do not have progressive liver damage and will not require medical treatment. The natural history course of HCV disease is highly variable, with some patients (perhaps 15-20 percent) progressing to cirrhosis in 10-40 years, and others never progressing to cirrhosis over a life-time.⁹

Medication for Treatment of Hepatitis C Has Improved But Controversy Still Exists

The FDA has approved, Interferon, pegylated interferon, and ribavirin with either interferon or pegylated interferon for use in the treatment of chronic hepatitis C in naïve patients. However medication treatments for HCV disease remain inadequate, because:

- Even with selecting the best patients, only 35 to 50 percent of patients with genotype 1, and 65 to 80 percent of patients with genotype 2 or 3 can achieve a sustained viral clearing from therapy despite completing a full course of treatment¹⁰.
- Medications for treatment of HCV disease have significant side effects,
- Medications must be taken consistently, for 6 to 12 months.
- There are a substantial number of patients who have clinical conditions that are considered contraindications to taking the medications for treatment of hepatitis C infection, Interferon and Ribavirin.
- Treatment is costly of both money and resources.
- Sustained Viral Response seems to last and is often associated with improvement in liver function.

⁷ Seeff, LB. *45 year follow up of hepatitis C virus infection in healthy young adults*, Annual of Internal Medicine, 2000.

⁸ Marco and Schouten, *The Hepatitis Report: a critical review of the research and treatment of Hepatitis C*, XIII International AIDS Conference, July 2000.

⁹ See Natural History Discussion.

¹⁰ Fried, Shiffman, et al, *Peginterferon and Ribavirin*, Pegasys International Study group, NEJM, 2002

In addition, the long-term benefits of the treatment are unknown. Most research equates successful treatment to eradicating the virus from the blood, normalizing blood tests that measure liver function, and improving the microscopic appearance of the liver. Since chronic hepatitis C progresses very slowly and this treatment has become available relatively recently, researchers have had difficulty in assessing the effects of the medications on the progression to cirrhosis and its complications, or in establishing an overall death rate. Definitive data to answer the question of whether the medication prevents these conditions from developing will not be available for many years.

In light of the variable progression of the disease, the variable response rate to treatment, the significant side effects, the length of treatment, the relatively high cost of treatment, and the lack of long term studies, careful selection of appropriate candidates within ODOC for medication is especially important. The goal is to select those patients most in need of treatment, for whom medication is likely to be effective, and for whom the treatment does not present unacceptable risks.

Some patients and their physicians chose to watch and wait. This is often an appropriate approach given that chronic hepatitis C infection progresses to serious liver disease in only a small percent of infected individuals and most complications do not develop for years after initial infection.

Careful Evaluation is Done to Determine When Medication Therapy is Medically Necessary and Will Benefit the Patient

Those individuals who do show evidence of progressive liver damage due to chronic hepatitis C infection, and are likely to benefit from medication treatment, should be given the opportunity to benefit from medical treatment.

Careful medical evaluation of a person with chronic hepatitis C infection is important. The purpose of evaluation is to consider what course of therapy to recommend for each individual. The medical decisions involved in this evaluation can be complex. Treatment recommendations for an individual can involve extensive medical evaluation and complex consideration of many things such as: past progression, current status, risk of future progression, blood tests, liver tests, risk of medication for treatment, medical contraindications to medications, likelihood of benefit from treatment, alcohol counseling, risk behavior counseling, mental health concerns, and other medical problems.

The evaluation that an inmate will undergo as the treating physician works to determine the extent of liver disease and to evaluate the risks and benefits of treatment is rigorous. It is important that the patient enter this process with a clear understanding of the responsibilities the patient is expected to assume. Expectations for the patient include:

- learning about the disease, including its course, prognosis, prevention, transmission
- learning about what the patient can do to care for themselves

- avoiding damaging and/or dangerous behaviors
- complying with the directions of health care providers during the work up and evaluation
- participating in the deliberation to weigh the benefits and risks of each treatment option, including waiting and watching.

Evaluation of Risk Behaviors is also very important. A history of illegal drug use and other needle sharing behavior is common among inmates in the Department of Corrections who are infected with hepatitis C. The department's guidelines include a requirement that, if indicated, inmates complete substance abuse treatment prior to starting treatment with medication for hepatitis C. This requirement exists because chemically dependent inmates who have not been treated for their dependency are much less likely to benefit from treatment. Anyone who is obtains a Sustained Viral Response from treatment for hepatitis C infection can become re-infected. So if someone resumes illegal drug use and/or other needle sharing behaviors they are at risk of becoming infected again. Maximizing treatment effectiveness and benefit thus clearly also depends on reducing risk of re-infection after treatment. Liver damage is more extensive and frequent in patients with Hepatitis C who also have alcohol use problems. It is clear that controlling alcohol use is medically important for all patients with chronic Hepatitis C. Recommendations for substance abuse treatment prior to or as part of Hep C treatment is included in guidelines for treatment which have been developed by other correctional systems, is recommended in the National Institute of Health consensus statement, is recommended by the National Diabetic and Kidney Association, and is recommended in the joint position statement of the National Commission on Correctional Health Care and the Society of Correctional Physicians on Hepatitis C.

Evaluation of Mental Health status is important. Depression and suicidal ideation are serious side effects of the medication used to treat hepatitis C. Consequently, the department's guidelines include an assessment of each inmate's mental health history and current mental health status during the evaluation and again immediately prior to initiating treatment with medication. An offender may be excluded from treatment if his or her mental health may be compromised by these medications.

Time and ability to complete evaluation and treatment is important. Treatment studies clearly indicate that when treatment is initiated for it to be effective it should be continued for a full 24 to 48 weeks depending on the genotype of hepatitis C. There are no studies that show a benefit occurs for patients who have started treatment, stopping after a few months, and then re-starting at some future date. We also realize that when an inmate transitions from prison back to the community there are many issues for him/her to deal with, including housing, food, jobs, reporting, etc. and that there are often barriers or complications to continuing an expensive ongoing medical treatment program that needs clinical monitoring and has significant side effects. Given the generally slow course of disease progression (10-30 years), evaluation and/or treatment of hepatitis C in a patient that could not finish the course of evaluation and treatment during the remaining time of incarceration with ODOC may appropriately be deferred until after release.

ODOC has instituted two separate yet interconnected programs:

- 1) **Public Health Phase** - A community or public health model with widespread awareness education, voluntary testing of individual inmates coupled with counseling about reducing risk behaviors that put them at risk of either getting or giving Hepatitis C.

- 2) **Medical Evaluation Phase** - A program of careful medical evaluation of appropriate individuals to determine their medical status and what treatment is medically necessary, appropriate, and likely to be of significant medical benefit. In the Medical Evaluation program the ODOC Health Services physicians are following medical guidelines for evaluation and treatment of hepatitis C that are similar to nationally recognized guidelines of other major organizations in medicine including correctional health care. All inmates who are Hepatitis C positive are offered this medical evaluation. All these individuals are tracked and have regular ongoing medical appointments. An individual who has a full medical evaluation that indicates they may be appropriate for a liver biopsy and or medication treatment has their case and care evaluated according to the guidelines by a panel of physicians, ensuring equitable treatment of appropriate inmates within ODOC.

Public Health Model of Education and Risk Reduction

Reducing Risk Behavior is the Most Effective Way to Prevent Hepatitis C Infection

The most effective method to control the spread of hepatitis C infection is to prevent transmission. This is because hepatitis C still responds poorly to medical treatment in spite of newer more effective methods of treatment. The people at greatest risk of infection today those who use illegal drugs, sharing needles or engage in other high risk behavior that involves direct blood to blood contact. Since there is not yet a vaccine, preventing transmission requires that people change those behaviors that put them at risk. Information, education and risk reduction counseling have been effective in limiting other blood borne communicable diseases among these same risk groups therefore we anticipate that these same methods should be effective in controlling hepatitis C.

Substance abuse treatment is an important component to controlling the spread of hepatitis C and in limiting the progression of liver disease in those with chronic infection. Treatment of hepatitis C does not prevent re-infection so it is critical that an individual who is to be treated is able to demonstrate an ability to sustain a lifestyle that is free from risk behavior. Chemical dependency treatment is therefore a critical precursor of treatment of hepatitis C for people whose infection resulted from some form of substance abuse. Chemical dependency treatment will also be important for anyone who has chronic hepatitis C infection and a history of alcohol use because continued alcohol use will speed progression to liver damage.

The behaviors that are most likely to put a person at risk of becoming infected with hepatitis C are within that person's control. Working with inmates to change behaviors such as intravenous drug use, treating chemical dependency and reducing other risk behaviors is consistent with the Department's mission to hold offenders accountable and reduce future criminal behavior.

Education and Counseling Are Effective Ways to Reduce Risk Behavior

All inmates receive mandatory education about communicable diseases upon admission to the Department of Corrections. This program was started in 1987 with the funding of the Department's HIV/AIDS prevention program. Since then education of inmates has been expanded to include information on other blood borne diseases and for the last several years has included information on hepatitis C and hepatitis B. The purpose of the education at intake is to inform inmates about diseases that result from high risk but controllable behavior, to inform them of the options for testing and counseling, and to describe how services can be accessed.

Testing and Counseling Inmates for Hepatitis C is Done to Improve the Likelihood of Behavior Change

Inmates may request testing for hepatitis C at any of the department's correctional facilities and at anytime during incarceration. Requests for hepatitis C testing will be forwarded to the Blood Borne Pathogens (BBP) counselor for the facility who will schedule the inmate for pre-test counseling and obtain informed consent before scheduling the inmate for the blood test. Based upon experience, the department estimates that about 25 percent of the inmate population will request a test for hepatitis C at some point during incarceration.

Hepatitis C –Screening and Counseling

Screening for HCV infection by the BBP counselors by measuring anti-HCV antibodies by EIA, should be considered for inmates who request testing and with the following:

- History of ever injecting illicit drugs
- Recipient of blood transfusion or organ transplant before 1992
- Recipient of clotting factor transfusion prior to 1987
- Receiving chronic hemodialysis
- Percutaneous exposures to HCV-positive blood
- History of tattoos or body piercings received while in jail or prison

Important components of pre/post-test counseling are:

- Discussion of the potential risk factors that warrant the test
- Proper informed consent must be obtained
- The counseling relationship must allow for frank discussion since the risk behavior may involve a history of illegal or prohibited activity
- Strategies to change behavior to reduce risk to self and others must be identified, and
- Others whom the person has shared risk behavior with may need to be notified.

Inmates with positive HCV antibodies should be counseled on the specific measures necessary for preventing further transmission of HCV to others during incarceration and upon release, and for limiting the progression of their disease, including the following recommendations:

- Do not shoot drugs
- Do not donate blood, body organs, other tissue or semen
- Do not share personal items that might have your blood on them, such as toothbrushes, dental appliances, nail-grooming equipment or razors
- Cover cuts and skin sores to keep blood from contacting other persons
- Do not share tattooing or body-piercing equipment, as the tools and the hands of the tattoo artist can carry infected blood
- Limit alcohol consumption,
- Speak to a physician prior to taking any new medication, including over-the-counter and herbal remedies, which may be hepatotoxic

The willingness of an inmate to discuss his/her own risk factors in a counseling encounter is also an indicator that the inmate is sincere in his/her intent to change the behaviors that put themselves and others at risk. Testing without creating an expectation of behavior change is a waste of testing and treatment resources. Targeted education and counseling are well established and effective means of producing behavior change among inmates.

After post-test counseling, inmates who are identified as infected with hepatitis C may self refer themselves to the Health Services clinicians. The purpose of this referral is for medical evaluation and to establish a schedule for regular medical follow up.

Inmates with chronic hepatitis C who have had problems with drugs or alcohol are encouraged to attend classes and meetings dealing with substance abuse.

Medical Evaluation Model

Overview of the Medical Evaluation program: ODOC Health Services physicians follow medical guidelines for evaluation and treatment of hepatitis C that are similar to nationally recognized guidelines of other major organizations in medicine, including other correctional health care systems. Inmates who are Hepatitis C positive are offered this medical evaluation, these individuals are tracked and have regular ongoing medical appointments. An individual who has a full medical evaluation that indicates they may be appropriate for a liver biopsy has their case and care evaluated by a panel of physicians, ensuring equitable treatment according to the guidelines.

Chronic hepatitis C (natural history): An estimated 60%-85% of persons infected with HCV develop chronic hepatitis of varying severity, while 15%-40% of newly infected persons are able to spontaneously clear the virus by unknown mechanisms. In chronically infected persons, viral replication within hepatocytes and – viremia occur despite the presence of anti-HCV antibodies. HCV RNA blood levels are often extremely elevated ranging from 10^5 to 10^7 international units (IU)/mL, but levels range widely among different patients and doesn't correlate with disease severity, acuity, or progression.

Chronic HCV infection has a waxing and waning course with frequent fluctuations in ALT levels associated with unpredictable degrees of inflammation and fibrosis despite the presence of anti-HCV antibodies. Approximately one-third of persons with chronic HCV infection will have subclinical hepatitis with persistently normal serum ALT levels.

An estimated 15% to 20% of persons infected with HCV ultimately develop cirrhosis or clinically significant hepatic disease over a 20-30 year period. Individuals with high levels of alcohol use, or HIV co-infection, or HBV co-infection, tend to have more advanced disease at biopsy and these are complicating problems that need to be considered in evaluation and treatment decisions. . The degree of viremia (“viral load”) and the HCV genotype, however, do not affect disease progression. The degree of ALT elevation also does not correlate strongly with the risk of disease progression, however persons with persistently normal or near normal ALT levels usually have mild disease on biopsy whereas persons who develop cirrhosis are more likely to have marked elevations in serum ALT levels.

Symptoms and Signs: Persons with chronic HCV infection are asymptomatic 80% of the time. Fatigue is the most common presenting complaint, but significant symptoms may not develop until the onset of cirrhosis and the associated complications of liver failure. HCV infection can be complicated by hepatocellular carcinoma in approximately 1% to 5% of persons with chronic hepatitis, almost exclusively in the presence of cirrhosis after longstanding infection of 3 or more decades. Non- hepatic manifestations of HCV infection include cryoglobulinemia,

glomerulonephritis, lymphoma, rheumatoid symptoms, and porphyria cutanea tarda. The diagnosis of these associated symptoms/findings should prompt evaluation for HCV infection.

Chronic hepatitis C (diagnosis): A positive enzyme linked immunoassay (EIA) for HCV antibodies is sufficient to initially diagnose HCV infection in inmates with definitive risk factors for HCV infection **and** elevations in serum alanine aminotransferase levels (ALT) for greater than six months. A signal to cutoff ratio of the EIA > 3.8 is also sufficient to diagnose HCV infection. (Confirmation by RIBA, Western Blot, or HCV RNA is not necessary for this group of individuals). (Proof of actual viral particles by HCV RNA, however, should be obtained for confirmation of ongoing infection before initiating antiviral therapy)

Inmates with a positive EIA for HCV antibodies, but with normal ALT levels, should have repeat ALT every 6-12 months for 2 years, then per practitioner discretion.

Patient counseling: Inmates diagnosed with HCV infection should be counseled on the specific measures necessary for preventing further transmission of HCV to others during incarceration and upon release, and for limiting the progression of their disease, including the following recommendations:

- Do not shoot drugs
- Do not donate blood, body organs, other tissue or semen
- Do not share personal items that might have your blood on them, such as toothbrushes, dental appliances, nail-grooming equipment or razors
- Cover cuts and skin sores to keep blood from contacting other persons
- Do not share tattooing or body-piercing equipment, as the tools and the hands of the tattoo artist can carry infected blood
- Limit alcohol consumption,
- speak to a physician prior to taking any new medication, including over-the-counter and herbal remedies, which may be hepatotoxic

HEPATITIS C –SCREENING

Screening for HCV infection by measuring anti-HCV antibodies by EIA, should be considered for inmates with the following:

- Elevated ALT levels of unknown etiology
- Signs and symptoms of hepatitis or when otherwise medically indicated
- History of ever injecting illicit drugs
- Recipient of blood transfusion or organ transplant before 1992
- Recipient of clotting factor transfusion prior to 1987
- Receiving chronic hemodialysis (screen ALT levels monthly and anti-HCV antibodies semiannually if negative)
- Percutaneous exposures to HCV-positive blood
- History of tattoos or body piercing received while in jail or prison

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HEPATITIS C –EVALUATION and TREATMENT

Acute hepatitis C: Inmates diagnosed with acute hepatitis C should be considered for antiviral therapy in consultation with a physician specialist. Limited data indicate that antiviral therapy is beneficial when started early in the course of HCV infection, however, the timing and the optimal treatment regimen in this setting are uncertain; therefore treatment decisions should be made on a case by case basis.

Chronic hepatitis C:

Baseline evaluation: A baseline clinical evaluation should be conducted for patients with HCV infection and include at least the following:

Targeted history and physical examination

- Serum liver transaminases (ALT and AST), bilirubin, alkaline phosphatase, albumin, and prothrombin time
- CBC with differential and platelet count
- Renal function assessment (serum creatinine/BUN) -HBsAg
- HIV serology if risk factors for HIV infection are identified
- Consider immunization for Hep A and Hep B, if appropriate.
 - Hepatitis A vaccination should be considered for inmates with risk factors for HAV infection or evidence of chronic liver disease (prescreening for immunity to HAV by testing for HAV IgG should be considered prior to vaccination particularly in foreign born inmates where hepatitis A is endemic and among inmates 50 years of age or older. ODOC base rate appears to be about 10%)
 - Hepatitis B vaccination should be considered for inmates with HCV infection if the inmate is considered at risk for future infection or if liver disease is present. (prescreening for immunity by testing for anti-HBc in high risk inmates or anti-HBs in younger inmates with high rates of vaccination, should be considered prior to vaccination. ODOC base rate appears to be about 10%).

Periodic evaluations : Evaluations for inmates with chronic HCV infection should be conducted at least:

- every 6-12 months for inmates with normal ALT levels,
- every 6 months for minimally elevated ALT levels with no other evidence of liver disease.
- If baseline ALT is normal or minimally elevated along with other markers of liver disease and synthetic function, then these parameters should be reassessed in 3-4 months, and if normal, repeated every 6-12 months thereafter.)
- Inmates with ALT levels twice normal, or other evidence of significant liver disease, should be monitored in chronic care clinics every 3-4 months or more frequently as indicated.

- HepatoCellular Cancer (HCC) Screening: Measurement of serum alpha-fetoprotein levels and a liver ultrasound though often done in the community have no demonstrated benefit in the absence of cirrhosis and thus are not routinely indicated.¹¹¹² Indeed the value of early detection of HCC is uncertain because there are not available data to demonstrate the clinical impact of the screening on the management of HCC or associated mortality.¹³ It appears that HCC does not occur in the absence of cirrhosis, and after the development of cirrhosis it is estimated that HCC occurs in only 1% of cirrhotic patients with Hepatitis C.

Considerations about Treatment for chronic hepatitis C:

Physicians should consider the following facts and discuss them with patients while evaluating and before recommending antiviral therapy for individuals with chronic hepatitis C.

- Most people with HCV have their normal life span, do not develop complications of chronic liver disease and end up dying of other causes.
- Only 10%-15% of persons with HCV infection develop significant complications of liver disease, usually 20-30 years after initial infection. At most an estimated 3% to 4% of HCV-infected persons may die of complications of their infection.¹⁴
- No laboratory parameters definitively predict which persons infected with HCV will develop cirrhosis or respond to medical therapy. Persons with a history of alcohol abuse and HIV co-infection are at greater risk of developing cirrhosis.
- Antiviral therapy for hepatitis C is increasingly effective in clearing viremia and establishing sustained viral response (SVR). Currently in 2003 at best it appears to be about 35-45% SVR for those with genotype 1 who complete treatment course, and 60-75% SVR for those with genotype 2 or 3 who complete treatment.
- Factors that predict a favorable response to antiviral therapy include: genotypes other than type 1, low baseline HCV RNA levels, less fibrosis or inflammation on liver biopsy, and lower body weight.
- The treatment course is not benign.
- Treatment is not protective against re-infection.

Treatment indications for chronic hepatitis C:

¹¹ Alpha-fetoprotein (AFP) and ultrasound every 6 months were used in a single study of patients with cirrhosis secondary to HCV. Identification of HCC was not significantly increased in the screened population.

¹² “Test Characteristics of AFP for detecting HCC in patients with Hepatitis C”, Annals of Int. Med. July 2003, V139

¹³ NIH consensus statement 2002.

¹⁴ See natural history discussion.

Antiviral drug therapy should be considered for inmates with chronic hepatitis C and the following parameters:

1) Elevations ALT levels greater than normal with other laboratory or clinical evidence of liver disease, OR ALT levels > 2 times normal over at least a 6 month period, OR ALT levels greater than normal but less than 2 times normal for 3 years.

NOTE: The appropriate evaluation and treatment of patients with hepatitis C and normal ALT levels, or mildly elevated ALT levels, is debatable and should therefore be considered on a case-by-case basis. Approximately 30% of patients with chronic hepatitis C have normal ALT levels; and another 40% of persons have ALT levels less than twice normal. Most of these patients have mild liver disease. A small subset of these patients have significant fibrosis or cirrhosis despite normal or mildly elevated ALT levels, however, in these patients some other marker of liver disease is usually present such as elevations in AST, bilirubin, or alkaline phosphatase, abnormal prothrombin time, or decreases in albumin or platelets. The more persistently normal over time the ALT level and other enzymes remain the more likely any disease process is mild, and the less clear treatment produces any benefit. Evaluation of patients with ALT levels elevated but less than twice normal level may proceed more deliberately.

2) Sufficient time remains of the inmate's sentence to allow for full work-up, evaluation, and full course of treatment. (Currently this typically will mean the inmate will need at least 18 months remaining on sentence to begin work up, or at least a year for treatment after potential biopsy date.)

3) Absence of decompensated cirrhosis: no evidence of endstage liver disease, such as ascites, jaundice, esophageal varices, or significantly poor liver synthetic function (e.g., prothrombin time international normalized ratio (INR) > 1.5), albumin < 3.0 g/dL, total bilirubin > 4 mg/dL.)

Compensated cirrhosis is not an absolute contraindication (e.g., mildly abnormal liver synthetic function with evidence and history of no edema, no esophageal varices, no ascites, or no encephalopathy.)

4) Absence of absolute contraindications, and minimal relative contraindications to interferon and ribavirin therapy as listed in, Contraindications to Interferon or Ribavirin Therapy.

5) No Mental Health contraindications.

6) Risk factors for re-infection and/or disease transmission have been addressed.

7) No evidence of active substance abuse. (check urine toxicology screen if drug use suspected; check for disciplinary actions related to drug or alcohol use).

8) ETOH use has been addressed. ETOH use is a significant co-morbid problem in patients with chronic hepatitis C. If ETOH use has been a problem in the past, ETOH classes should have been attended, Many patients may not be able to clear their hepatitis C infection (due to multiple reasons), but all patients with chronic hepatitis C will benefit from controlled ETOH consumption.

9) Detectable HCV RNA levels. Either a positive Qualitative test or positive Quantitative test (viral load) is acceptable. Qualitative tests are more sensitive (down to 50 IU/mL.) and slightly cheaper, however a Quantitative viral load is important for treatment length if the patient has genotype 1.

10) Liver Biopsy results compatible with treatment recommendations; evidence of peri-portal or bridging fibrosis and at least moderate inflammation and necrosis consistent with hepatitis C. HCV causes-the following changes in the liver: necrosis and inflammation around portal areas, sometimes referred to as "piecemeal necrosis" or "interface hepatitis," necrosis of hepatocytes and focal inflammation in the liver parenchyma, inflammation of cells in the portal areas, and fibrosis. Fibrosis evolves through the following stages: in the early stages fibrosis is confined to the portal tracts, then in the intermediate stages has greater involvement of the portal tracts with bridging between portal areas or to central areas, and finally to the late stages of frank cirrhosis.

Grade number	Grade of inflammation	Stage Number	Stage of Fibrosis
0	None-Minimal	1	None
1	Portal inflammation	2	Peri-portal Fibrosis
2	Mild interface Hepatitis	3	Bridging Fibrosis
3	Moderate interface Hepatitis		
4	Severe interface hepatitis plus bridging necrosis	4	Cirrhosis

The Stage of Fibrosis is much more important than the Grade of inflammation.

Current term	Old term	Grade/Stage	Knodell Score	Recommendations
Mild liver disease	Chronic persistent	Stage 1	3-6	Monitor – may not be progressive disease
Moderate liver disease	Chronic Active	Stage 2 & Grade 3 or 4	7-8	Depending on other characteristics monitoring or interferon or INF/ribavirin may be recommended
Severe Liver Disease	Severe Chronic Active	Stage 3 & Grade 2,3,4	9-11	Recommend interferon or INF/ribavirin
Advanced - Cirrhosis Compensated		Stage 4 & Any Grade	12+	INF/RBV may improve, offer in conjunction with GI specialist.
Decompensated cirrhosis		Stage 4 & Any Grade	12+	INF/RBV unlikely to improve care, and is not recommended

INF/RBV is not indicated individuals with Stage I fibrosis.

INF/RBV is controversial in individuals with Stage 2 fibrosis, and should be weighed within the context of the individual medical case and to heavily stress maximizing likelihood of success. (For example a patient who is Grade 4 and Stage 2 after only 5 years of infection with very elevated ALTs, no medical contraindications and highly motivated who has 15 years with ODOC, may be considered differently than a patient who is Grade 1 and Stage 2 after 30 years of infection, low ALT levels, who has some relative contraindications, does not seem motivated and is leaving ODOC in 19 months.) Given the evidence of slow progression from one stage to another (some say an average of 10 years between stages) some physicians have suggested re-biopsy in 5 - 10 years as an alternative.

INF/RBV is most indicated for consideration for individuals with Stage 3 fibrosis with any degree of inflammation, who meet the other criteria.

INF/RBV may be indicated for individuals with Stage 4 fibrosis with compensated cirrhosis, but must be approached cautiously in consultation with GI Specialist.

INF/RBV is not indicated individuals with Stage 4 fibrosis with clinical signs of decompensated cirrhosis.

11) Inmates entering custody on antiviral therapy for hepatitis C should ordinarily be maintained on treatment unless there is a clinical reason for discontinuing the medications.

Special tests

HCV RNA assays:

Candidates for antiviral therapy should have HCV viremia confirmed. Either a positive Qualitative test or positive Quantitative test (viral load) is acceptable. Qualitative tests are more sensitive (down to 50 IU/mL) and slightly cheaper, however a Quantitative viral load is important for treatment length if the patient has genotype 1 and if a person has a positive Quantitative HCV there is no need for Qualitative HCV to prove viremia.

Quantitative HCV RNA levels should be selectively ordered for the following:

- In patients with HCV genotype 1; prior to treatment and 12 weeks after starting treatment as an early indicator of effectiveness of antiviral therapy.
- Quantitative HCV level may be useful to help assess the likelihood of treatment success in patients where the need or benefit of antiviral therapy is questionable. (HCV RNA levels are considered "high" when greater than 2 million copies/ml. High levels of HCV RNA do not correlate with the degree of hepatitis or fibrosis, but are inversely correlated with the likelihood of responding to antiviral therapy.)

Liver biopsy: candidates for HCV antiviral therapy ordinarily require a liver biopsy to assess the degree of fibrosis and inflammation and to establish the need for treatment. In situations where a liver biopsy is contraindicated, or where compensated cirrhosis is suspected or previously confirmed, empiric antiviral therapy may be considered without a liver biopsy. Liver Biopsy results compatible with treatment recommendations: evidence of peri-portal or bridging fibrosis and at least moderate inflammation and necrosis consistent with hepatitis C. HCV causes-the following changes in the liver: necrosis and inflammation around portal areas, sometimes referred to as "piecemeal necrosis" or "interface hepatitis," necrosis of hepatocytes and focal inflammation in the liver parenchyma, inflammation of cells in the portal areas, and fibrosis. Fibrosis evolves through the following stages: in the early stages fibrosis is confined to the portal tracts, then in the intermediate stages has greater involvement of the portal tracts with bridging between portal areas or to central areas, and finally to the late stages of frank cirrhosis.

HCV genotype testing: The HCV genotype should be determined prior to prescribing antiviral therapy for hepatitis C since it helps determine both the response to antiviral therapy and the duration of therapy.

Co-morbid Screening studies: Prior to initiating antiviral therapy for chronic hepatitis C, inmates should be evaluated by a physician and screened for complicating co-morbid conditions or other causes of liver disease, including the following examinations: CBC with differential and platelet count, TSH, renal function, and serum chemistries, HIV antibody, HBsAg, pregnancy test for female inmates, psychiatrist or psychologist evaluation to screen for mental illness, anti-nuclear antibodies (ANA), serum ferritin, and other patient-specific diagnostic tests as indicated.

Treatment options for chronic hepatitis C:

Combination treatment with pegylated interferon and ribavirin is the most effective drug regimen for treating hepatitis C. A 24-week course of pegylated interferon and ribavirin is recommended for patients with genotypes 2 or 3; whereas a 48-week course of treatment is recommended for patients with genotype 1. The optimal duration of antiviral therapy is unknown for persons with genotypes 4, 5, 6, or non-typeable HCV. Current recommendation is that these patients should be treated with the more aggressive 48-week course of treatment recommended for genotype 1 patients.

Note: Persons with genotypes 2 or 3 have a 76% to 82% response rate to pegylated interferon/ribavirin compared to persons with genotype 1, who have a 42% to 46% response rate.

Pegylated interferon: Pegylated interferon is currently available in two formulations: Alpha 2b (PEG-intron^R Schering Corporation) and Alpha 2a (Pegasys^R Roche Pharmaceuticals). Peg-Intron is weight dosed and prescribed as a 1.5 mcg/kg subcutaneous injection, administered once weekly. Pegasys is prescribed as flat 180 mcg per week

Nonpegylated interferon: Nonpegylated interferon is prescribed as 3 million units, by subcutaneous injection, three times a week.

Ribavirin: Ribavirin is completely ineffective as monotherapy and should never be prescribed without interferon. Ribavirin prescribed in combination with pegylated interferon for persons with genotypes 2 or 3 is prescribed as 400 mgs taken orally in the morning and 400 mgs taken orally in the evening¹⁵.

When prescribed in combination with standard interferon for any patient, or with Pegylated intereron for patients with genotype 1, ribavirin dosing is weight-adjusted: for persons weighing 75 kg or less it is taken 400 mgs orally in the morning and 600 mgs orally in the evening; for persons weighing more than 75 kg it is taken 600 mgs in the morning and 600 mgs in the evening.

¹⁵ Note that the dosage of Ribavirin is slightly different when using Pegylated interferons than for when using standard interferon.

Other treatment options include; 1) combination therapy with non-pegylated interferon/ribavirin, or 2) interferon preparations alone. Interferon monotherapy should be considered only when ribavirin is contraindicated.

Sustained Response Rates

	Interferon	PegInf	Inf +RBV	PegInf +RBV
Genotype 1	6-10%	~ 14%	~ 33%	~ 42%
Genotype 2 or 3	~ 29%	~ 40%	~ 75%	~ 82%

Data on SVR from multiple sources including: Fried et al.; Manns et al; Lindsey et al; McHutchinson et al.; product inserts

Interferon/ribavirin side effects and adverse reactions:

Interferon: The side effect profile for standard interferon preparations and both Pegylated interferons are similar.

The treating physician should ensure that the inmate is aware of all potential side effects prior to prescribing therapy. An influenza-like reaction often occurs within 6-8 hours of initial treatment with interferon. 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 with interferon treatments. Severe incapacitating depression can occur, even in persons without previous histories of depression. Bone marrow suppression with reduced 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 often result in irreversible thyroid dysfunction, even with 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. Serious sequelae occur in approximately 2% of persons receiving interferon treatment and can include: renal failure, pneumonitis, severe bone marrow suppression, and suicide.

Ribavirin: Ribavirin causes a dose-related red cell hemolysis to variable degrees in nearly all persons who are treated. A decrease in the hemoglobin of 2 to 3 gm/dL and a decrease in hematocrit of 5% to 10% should be anticipated. Therefore, persons with a preexisting hemolysis or severe anemia (hemoglobin < 11 g or hematocrit < 33%) or underlying cardiovascular or cerebrovascular disease should not receive ribavirin. Anemia ordinarily develops between 1 and 4 weeks of therapy. Symptoms of sudden hemolysis such as dyspnea, fatigue, headache, and palpitations may develop. If anemia occurs ribavirin should be reduced in dosage or discontinued.

Ribavirin also causes histamine-like side effects such as nasal stuffiness and itching in an estimated 10% to 20% of treated persons. More severe effects can include an asthma-like syndrome or bronchitis.

NOTE: Ribavirin may cause fetal abnormalities. Female inmates of childbearing potential must have a pregnancy test prior to initiating therapy. Both women AND men must be counseled to use adequate birth control during treatment and 6 months after treatment is completed.

Treatment Dosage Options for Chronic Hepatitis C

Medication	Dosage	Baseline tests	Monitoring	Toxicities	Comments
Interferon Alpha	3 million units SC 3x/wk	History and physical Liver enzymes Liver function CBC, diff, plts Creatinine/BUN Thyroid function Hep B status HIV status HCV genotype HCV RNA Mental health evaluation Risk behavior hx evaluation	Weekly x 4 then monthly: CBC, diff, plts Chem panel, (ALT, Cr, BUN, Alb. Etc.) Depression Pregnancy test monthly as indicated. MH evaluation as indicated.	Fever Fatigue Myalgia Psychiatric (rage, confusion, depression) Bone marrow suppression Thyroid dysfunction Renal failure	See “contraindications” Not for use in decompensated cirrhosis.
Ribavirin with Standard interferon	< 75 kg= 1000mg qd (400mg q am + 600 mg q pm) >75 kg= 1200mg qd (600 mg BID)	CBC, diff, plts Pregnancy tests	Quant. HCV RNA at 12 wks if genotype 1. Qualitative HCV at 24 wks. Drug screening as indicated.	Hemolysis (5%-10% decrease in HCT is expected)	Ribavirin dosage varies by weight.
Pegylated interferon –	Peg-Intron ^R (1.5mcg/kg/wk SC) <40 kg= 50 mcg 40-50kg=64mcg 51-60kg=80mcg 61-75kg=96mcg 76-85kg=120mcg >85kg=150mcg Pegasys ^R 180 mcg/wk SC			Same as interferon	
Ribavirin with Peg-Inf	Genotype 2 or 3 400 mg PO BID Genotype 1 – same as with standard Interferon <75kg=1000mg qd >75kg=1200mg qd			See ribavirin	Ribavirin dosage differs for genotype when used with Pegylated interferon

Duration of Treatment:

For genotype 1 (1a or 1b), administer antiviral therapy for 12 weeks and check quantitative HCV RNA assay. A minimum 2 log decrease in viral load after 12 weeks of treatment predicts a sustained viral response (SVR) and warrants continued treatment for another 36 weeks (total 48 weeks course of treatment). Antiviral therapy should be discontinued if HCV RNA levels do not adequately decline after 12 weeks of treatment.

For genotypes 2 and 3, administer antiviral therapy for 24 weeks in all patients unless complications develop. At the end of treatment, check a qualitative HCV RNA assay to determine treatment response.

ALT levels should be obtained every 2 months for 6 months following the completion of antiviral therapy.

Monitoring inmates during treatment for chronic hepatitis C:

Inmates should receive clinical evaluations while receiving antiviral therapy for hepatitis C that are generally consistent with the following:

Clinician evaluations weekly for one month, then monthly thereafter, to assess drug side effects and potential complications (Note: Inmates with compensated cirrhosis are at greater risk of complications and require more frequent monitoring, as do patients who develop significant side effects or complications while on therapy).

Psychiatry or psychology evaluations as clinically indicated during interferon treatments.

ALT at weeks 1, 2, and 4, and at 8-12 week intervals thereafter.

NOTE: An unusual but serious complication of interferon or interferon and ribavirin combination therapy is the paradoxical worsening of hepatitis. This is more likely to occur if the inmate is co- infected with hepatitis B and C. If ALT levels increase significantly, antiviral therapy should be discontinued and ALT levels should be monitored closely and further treatment provided in consultation with a specialist.

CBC with differential and platelet count at weeks 1, 2, and 4 and at 4-8 week intervals thereafter.

Bilirubin, prothrombin time and other liver function studies with any new elevations in ALT or symptoms or signs of liver disease

Thyroid function studies every 3 to 6 months during interferon therapy

Fundoscopy evaluation for inmates starting INF, and a repeated exam with any complaints of vision problems during treatment. (Optometrist is acceptable.)

Monitoring

	Baseline	Wk1	Wk2	Wk3	Wk4	Wk8	Wk12	Wk16	Wk20	Wk24	Q4wk
CBC and Platlets	X	X	X	X	X	X	X	X	X	X	X
Chem Panel	X	X	X	X	X	X	X	X	X	X	X

(ALT, Alb, Bili)											
Pregnancy test	X				X	X	X	X	X	X	X
TSH	X						X				
Quantitative HCV-RNA (viral load) If genotype 1							X				
Qualitative HCV – RNA If genotype 2-3										X	

Retreatment of chronic hepatitis C:

Retreatment of relapsers and non-responders is not routinely done by ODOC and should only be considered on a special case-by-case basis preferably in a research study group only.

Treatment of chronic hepatitis C with co-morbid conditions:

Active substance abuse: Inmates with histories of substance abuse and hepatitis C should be referred for drug education, nonresidential drug treatment, and residential drug treatment, as appropriate and in accordance with ODOC policy as a component of their treatment plan. The timing of antiviral therapy and participation in drug treatment programs should be coordinated on a case-by-case basis.

HBV and HCV co-infections: Anti viral therapy for inmates with HBV and HCV co-infections should be initiated in consultation with a specialist, and with great caution, due to the uncertainty of the risks and benefits of different recommended treatments.

HIV and HCV co-infections: HIV infection may cause chronic hepatitis C to progress more rapidly to cirrhosis. As HIV treatments have become more effective, chronic hepatitis C is an increasingly serious health problem for co-infected persons. Treatment indications and strategies for persons with HCV and HIV co-infections are evolving and unproven; therefore treatment decisions should be patient-specific in consultation with a specialist in HIV treatment while considering the following:

- Treatment for HIV and HCV infections should not be initiated simultaneously. .
- For treatment naive patients, consider treating HIV infection first if the patient is a candidate for HIV therapy (AIDS or CD4+ T-cell count < 350 cells/mm³); otherwise consider treatment for HCV infection in the absence of absolute contraindications and the presence of liver disease.
- For patients on antiretroviral therapy; consider therapy for hepatitis C with documented liver disease, if the HIV viral load is undetectable and the CD4+ T-cell count is > 350 cells/mm³.

- Persons with HIV infection may be at greater risk of developing hepatotoxicity during interferon/ribavirin therapy. ALT levels should be monitored every 1-2 months while on therapy.
- Ribavirin and didanosine (ddI) should ordinarily not be co-administered due to the increased risk of pancreatitis and lactic acidosis.
- The risk of psychiatric complications or hematologic problems with interferon and ribavirin therapy is greater in persons with HIV co-infection.
- In patients with compensated cirrhosis, the concerns for initiating interferon/ribavirin therapy are higher due to the greater risk of liver failure, and this should be done only in consultation with GI specialist.

GENERAL MEASURES FOR PATIENTS WITH CIRRHOSIS

The following preventive measures should be considered for inmates with viral hepatitis that is complicated by decompensated cirrhosis:

- Vaccination against: influenza (annually), pneumococcal pneumonia, and hepatitis A and B (if susceptible)
- Patient education on selecting a low-salt, low fat, "heart healthy" diet
- Patient education regarding complete abstinence of alcohol consumption during incarceration and after release
- Avoidance of iron supplements and hepatotoxic medications, such as nonsteroidal inflammatory drugs
- Endoscopy to screen for esophageal varices if platelets <90,000
- Nonselective beta-blocker therapy for inmates with large esophageal varices on endoscopy (The dose of beta-blocker should be titrated weekly to reduce the resting heart rate by 25%, but not less than 55 beats/minute or reducing the systolic blood pressure to lower than 90 mm Hg.) Long-acting nitrates can be added to nonselective beta-blockers in patients who do not respond to beta-blockers alone.
- Primary prophylaxis for spontaneous bacterial peritonitis (SBP) with an antibiotic, such as ciprofloxacin, should generally be limited to short treatment periods in high-risk patients such as those with upper gastrointestinal hemorrhage.
- Avoid aspirin if history of GI Bleed or esophageal varices.

OREGON DEPARTMENT OF CORRECTIONS

**SUBJECT: MEDICAL GUIDELINES FOR HEPATITIS C
EVALUATION AND TREATMENT - 2003**

**FROM: Steve Shelton, MD.
Medical Director, Health Services**

DATE: July 24, 2003

Discussion: Only 5% to 20% of patients with viral hepatitis C develop any liver complication. The usefulness of specific Hepatitis C treatment to try to eradicate hepatitis C virus is questionable in the vast majority of individuals. Only a limited number of patients with viral hepatitis respond to medication treatment. Medication treatment takes 6-12 months and has significant side-effects. Appropriate medical screening of candidates should occur before initiating this therapy. Any candidate for therapy should understand before treatment, that testing is required and liver biopsy may be required. Treatment and liver biopsy are not without risk, and these risks must be weighed against the probable course of untreated Hepatitis C. We must fully discuss with patients the side effects of interferon and ribavirin, the length of treatment and the need for monitoring. If there are reasonable doubts about a patient's ability to comply with the work- up, treatment, and reduction of risk behaviors we should be cautious about beginning evaluation.

Deciding on treatment of patients with Hepatitis C can be a complicated task due to many factors. These guidelines have been developed (1) to help discern patient eligibility for treatment and 2) establish some criteria for the use of alpha interferon and ribavirin in the treatment of chronic Hepatitis C within ODOC. These are guidelines only, each individual's care should be decided on a case-by-case basis using professional knowledge and judgement within the physician-patient relationship. We welcome any comments on these guidelines.

PATIENT ELIGIBILITY CRITERIA:

Patients already on interferon, or interferon and ribavirin at the time of initiating these guidelines or at the time of entry into custody will be maintained on the drug if tolerated. Other inmates with hepatitis can be evaluated for medication treatment, the decision will be made on an individual, case by case, basis.

Hepatitis C Requests evaluation, Testing, and Treatment Guidelines

1. Patient requests Hepatitis C testing or treatment. Refer to CTS/HIV counselor (Blood Bourne Pathogen counselor) who will initiate pre-test counseling, and evaluate risk factors. After counseling and discussing risk factors this counselor will have an HIV test, and/or Hepatitis Viral marker panel (at least HC ab, HBc ab, HBs ag, HA IGg ab if on panel) drawn as indicated, and do post-test counseling about the test results. (Note that patients having Hep C testing should have HIV test results due to similar risk factors, and importance of HIV status to the work-up and treatment of Hepatitis C). All positive test results will be brought to the attention of Health Services for interpretation and action as warranted.
2. Hepatitis C test Positive, and patient requests medical evaluation: Health Services will schedule a practitioner appointment, order a Chemistry Panel and CBC, and will enter the patient into Inmate Health Plan, Special Needs - Hep C .
3. Evaluate HCV test results, chemistry panel, CBC, and patient for signs/symptoms of liver disease and other major medical illnesses.
 - a) Negative HCV antibody test & Normal liver enzymes-- no work-up or follow up needed.
 - b) Negative HCV antibody test & Elevated liver enzymes-- work up abnormal findings.
 - c) Positive HCV antibody test & Normal liver enzymes -- Enroll patient in “Hepatitis C Special Needs” for tracking purposes, repeat chemistry panels every 6 to 12 months as indicated. If persistently normal liver enzymes and no other evidence of liver disease then counsel the patient that there is no evidence that a patient with consistently normal enzymes is improved by interferon treatment.
 - d) Positive HCV antibody test & Elevation of ALT -- Enroll patient in “Hepatitis C Special Needs”. If enzymes have not been elevated for more than 6 months, repeat chemistry panel in 3 and 6 months and evaluate. If ALT > Normal over a 6 month period , and patient continues to want evaluation for interferon/ribavirin treatment, re-counsel about the natural course of chronic Hep C infection and the risks and “benefits” of treatment options. IF Patient continues to request treatment continue work-up as per guidelines.
 - e) Normal enzymes but other clinical evidence of liver disease, initiate evaluation according to guidelines.

1) **Evaluate if patient have enough time left within ODOC to complete evaluation and full course of treatment? (18 months in most cases.)**

2) **Medical Contraindications**

Absolute contraindications

Clinical signs of decompensated cirrhosis

- ◆ Jaundice or elevated Bilirubin
- ◆ Ascites
- ◆ Decreased Platelets < 60,000
- ◆ Increased Protime; INR > 1.5
- ◆ Decreased albumin < 3.5
- ◆ Absolute Neutrophils < 1,000
- ◆ Active or History of Hepatic encephalopathy
- ◆ Previous variceal hemorrhage

Active Auto-immune disorder – e.g. psoriasis, arthritis, etc.

Active Hyperthyroid disorder

Cancer

Chronic Hepatitis B infection - Concurrent

Solid organ Transplant recipient

Additional Medical Contraindications for using **Ribavirin**

Pregnancy or likely pregnancy (HIGHLY TERATOGENIC)

Major Medical Conditions worsened by anemia; e.g., angina, hypoperfusion states, CHF, etc. (expect a 2gm/dl drop in hemoglobin in the 1st month.)

Hemoglobinopathies

Relative Contraindications:

Hx of Major Depression or suicide attempt

Major Medical illness poorly controlled

Platelets < 100,000

Protime INR > 1.2

Absolute Neutrophils < 2,500

Evidence of drug or alcohol abuse issues in the past 6 months

Time left to serve less than 18 months (full treatment program may take 18 months)

Life expectancy less than 10 years

Evidence of prior medical non-compliance

Age > 60 or <18

HIV disease – discuss options with HIV specialist

Chronic active Hepatitis B infection

2) **Mental Health Contraindications**

Current Major Depression

Significant suicide attempt within past 5 years (some sources extend this to “the remote past”

Major Mental Illness poorly controlled.

Recent poorly controlled aggressive behavior should be closely reviewed.

Uncorrected risk factors as Contraindications

Drug or Alcohol use/abuse or a new tattoo within the prior 6 months is a contraindication to medication treatment for Hep C.

If there is any medical or criminal history of substance abuse, the inmate must be presently active in drug/alcohol recovery (including AA or NA), if available, and must have been active for a least three months preceding the evaluation

{Baseline work up would thus include: History, physical and chart review, to evaluate hepatic status and to evaluate for any other major medical problems like diabetes, ASCVD, COPD, autoimmune disorder, HIV, etc. If not already done, baseline labs to include: CBC, Multi-chemistry panel, TSH with reflex, Anti-nuclear antibody, Chest x-ray for baseline, pregnancy test for women, review of material relevant to mental health and corrected/uncorrected risk factors. (See work sheet.)}

4. If there are no contraindications to treatment and you consider a liver biopsy and or treatment with interferon and ribavirin, a physician must give counseling about the risks and difficulty of liver biopsy as well as interferon treatment, or combination therapy. If for medical or other reasons patient is not eligible for treatment, the patient will not be sent for liver biopsy.
5. Have patient review “Hepatitis C Treatment Contract”. Inmate may be subject to random alcohol and drug testing and inmate will maintain participation in a drug and/or alcohol rehabilitation program if there is any medical or criminal history of substance abuse. Possession or use of alcohol or non-prescribed drugs or fresh tattoos or equipment will result in removal from Interferon/Ribavirin therapy.
6. Have patient review informed consent about liver biopsy. Refer case to physician review committee (TLC) for consideration of biopsy.
7. Refer Biopsy findings (done within one year before start of medication) and case information to physician review committee.

Grade number	Grade of inflammation	Stage Number	Stage of Fibrosis
0	None-Minimal	1	None
1	Portal inflammation	2	Peri-portal Fibrosis
2	Mild interface Hepatitis	3	Bridging Fibrosis
3	Moderate interface Hepatitis	4	Cirrhosis
4	Severe interface hepatitis plus bridging necrosis		

Current term	Old term	Grade/Stage	Knodell Score	Recommendations
Mild liver disease	Chronic persistent	Stage 1	3-6	Monitor – may not be progressive disease
Moderate liver disease	Chronic Active	Stage 2 & Grade 3 or 4	7-8	Depending on other characteristics monitoring or interferon or INF/ribavirin may be recommended
Severe Liver Disease	Severe Chronic Active	Stage 3 & Grade 2,3,4	9-11	Recommend interferon or INF/ribavirin
Advanced - Cirrhosis Compensated		Stage 4 & Any Grade	12+	INF/RBV may improve, offer in conjunction with GI specialist.
Decompensated cirrhosis		Stage 4 & Any Grade	12+	INF/RBV unlikely to improve care, and is not recommended

INF/RBV is not indicated individuals with Stage I fibrosis.

INF/RBV is controversial in individuals with Stage 2 fibrosis, and should be weighed within the context of the individual medical case. (For example a patient who is Grade 4 and Stage 2 after only 5 years of infection with very elevated ALTs, no medical contraindications and highly motivated who has 15 years with ODOC, may be considered differently than a patient who is Grade 1 and Stage 2 after 30 years of infection, low ALT levels, who has some relative contraindications, does not seem motivated and is leaving ODOC in 19 months.) Given the evidence of slow progression from one stage to another (some say an average of 10 years between stages) some physicians have suggested re-biopsy in 5 years as an alternative, and it is certainly reasonable when considering an individual with stage 2 fibrosis to maximize the likelihood of success.

INF/RBV is most clearly indicated for consideration for individuals with Stage 3 fibrosis with any degree of inflammation, who meet the other criteria.

8. If using interferon alone then Quantitative HCV- RNA needs to be checked prior to initiation of therapy. (Used to evaluate responders).

If using combination therapy of INF and Ribavirin, then HCV Genotyping should be done to assist with decision about length of course of therapy, and quantitative HCV should be done if Genotype 1.

9. Response rates

Sustained Response Rates

	Interferon	PegInf	Inf +RBV	PegInf +RBV
Genotype 1	6-10%	14%	33%	42%
Genotype 2 or 3	29%	40%	75%	76-88%

Data on SVR from multiple sources including: Fried et al.; Manns et al; Lindsey et al; McHutchinson et al.; product inserts

Treatment Dosage Options for Chronic Hepatitis C

Medication	Dosage	Baseline tests	Monitoring	Toxicities	Comments
Interferon Alpha	3 million units SC 3x/wk	History and physical Liver enzymes Liver function CBC, diff, plts Creatinine/BUN Thyroid function Hep B status HIV status HCV genotype HCV RNA Mental health evaluation Risk behavior hx evaluation	Weekly x 4 then monthly: CBC, diff, plts Chem panel, (ALT, Cr, BUN, Alb. Etc.) Depression Pregnancy test monthly as indicated. MH evaluation as indicated.	Fever Fatigue Myalgia Psychiatric (rage, confusion, depression) Bone marrow suppression Thyroid dysfunction Renal failure	See “contraindications” Not for use in decompensated cirrhosis.
Ribavirin with interferon	< 75 kg= 1000mg qd (400mg q am + 600 mg q pm) >75 kg= 1200mg qd (600 mg BID)	CBC, diff, plts Pregnancy tests	Quant. HCV RNA at 12 wks if genotype 1. Qualitative HCV at 24 wks.	Hemolysis (5%-10% decrease in HCT is expected)	Ribavirin dosage varies by weight.
Pegylated interferon –	Peg-Intron ^R (1.5mcg/kg/wk SC) <40 kg= 50 mcg 40-50kg=64mcg 51-60kg=80mcg 61-75kg=96mcg 76-85kg=120mcg >85kg=150mcg Pegasys ^R 180 mcg/wk SC			Same as interferon	
Ribavirin with Peg-Inf	Genotype 2 or 3 400 mg PO BID Genotype 1 – same as with standard Interferon <75kg=1000mg qd >75kg=1200mg qd			See ribavirin	Ribavirin dosage differs for genotype when used with Pegylated interferon

Duration of Treatment:

For genotype 1 (1a or 1b), administer antiviral therapy for 12 weeks and check quantitative HCV RNA assay. A minimum 2 log decrease in viral load after 12 weeks of treatment predicts a sustained viral response (SVR) and warrants continued treatment for another 36 weeks (total 48 weeks course of treatment). Antiviral therapy should be discontinued if HCV RNA levels do not adequately decline after 12 weeks of treatment.

For genotypes 2 and 3, administer antiviral therapy for 24 weeks in all patients unless complications develop. At the end of treatment, check a qualitative HCV RNA assay to determine treatment response.

Follow-up qualitative HCV RNA assays should be obtained 24 weeks after the completion of therapy. Effective antiviral therapy results in a sustained viral response (SVR), defined as the absence of detectable HCV RNA in the serum measured by a qualitative HCV RNA assay with a lower limit of detection of 50 IU/ml or less at 24 weeks after the end of treatment.

During Therapy Monitoring:

Monitoring

	Baseline	Wk1	Wk2	Wk3	Wk4	Wk8	Wk12	Wk16	Wk20	Wk24	Q4wk
CBC and Platelets	X	X	X	X	X	X	X	X	X	X	X
Chem Panel (ALT, Alb, Bili)	X	X	X	X	X	X	X	X	X	X	X
Pregnancy test	X				X	X	X	X	X	X	X
TSH	X						X				
Quantitative HCV-RNA (viral load) If genotype 1	X						X				
Qualitative HCV – RNA If genotype 2-3										X	

Hepatitis C Evaluation Worksheet

Initial Screening Information				Date
Blood Borne Pathogen Counseling completed?	<input type="checkbox"/> Yes	<input type="checkbox"/> No		
HIV testing done?	<input type="checkbox"/> Yes	<input type="checkbox"/> No		
HCV antibody positive?	<input type="checkbox"/> Yes	<input type="checkbox"/> No		
Time left to serve greater than 18 months?	<input type="checkbox"/> Yes	<input type="checkbox"/> No		

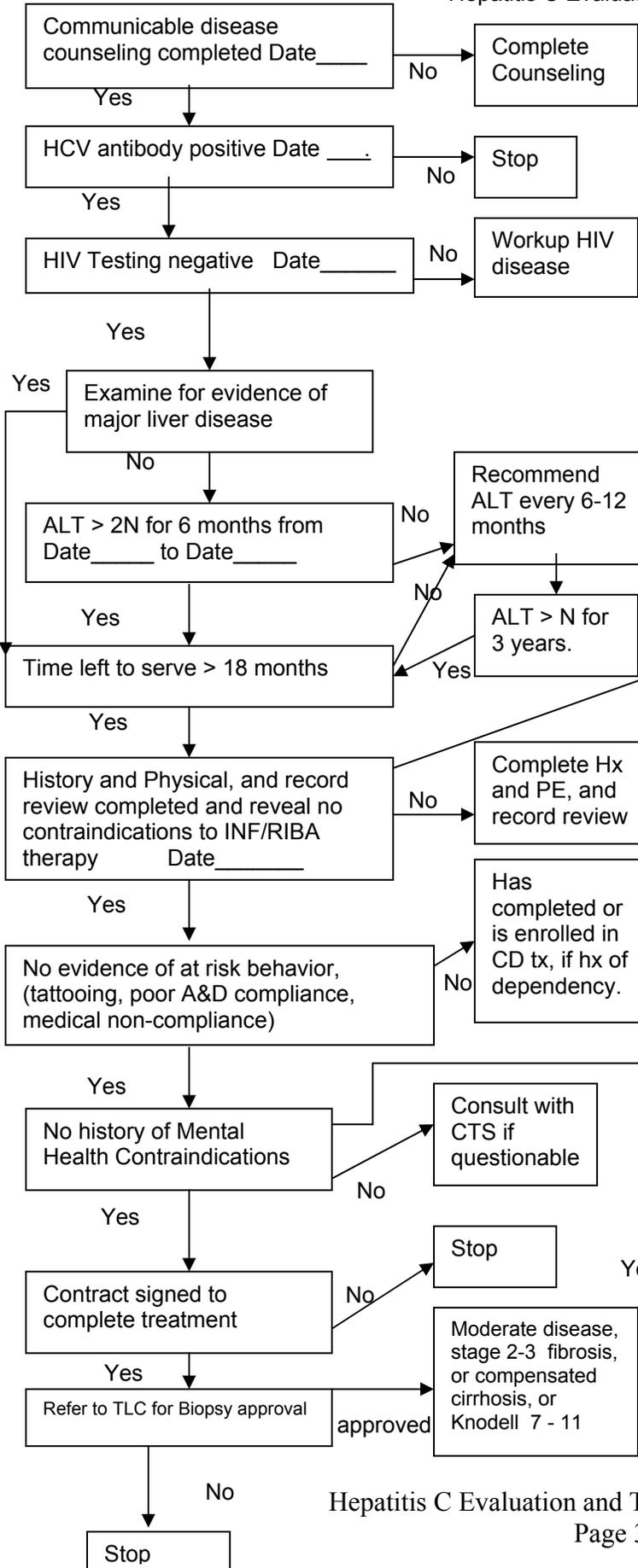
Medical Evaluation, as indicated					Date
History and Physical for indications of disease status		<input type="checkbox"/> Yes	<input type="checkbox"/> No		
Evidence of decompensated liver disease or clinical evidence of cirrhosis, e.g., ascites, hx of hepatic encephalopathy, hx of esophageal varices, etc.		<input type="checkbox"/> Yes	<input type="checkbox"/> No		
HIV/AIDS?		<input type="checkbox"/> Yes	<input type="checkbox"/> No		
Major Medical Illness poorly controlled, e.g. diabetes, ASCVD, angina, COPD, thyroid, HIV, MH, cancer, autoimmune disorder, etc.		<input type="checkbox"/> Yes	<input type="checkbox"/> No		
LABS -	Abnormal values	<input type="checkbox"/> Yes	<input type="checkbox"/> No		
ALT levels / Dates	Bilirubin Elevated >1.5?	<input type="checkbox"/> Yes	<input type="checkbox"/> No		
	Albumin <3.5?	<input type="checkbox"/> Yes	<input type="checkbox"/> No		
	Protime INR > 1.5?	<input type="checkbox"/> Yes	<input type="checkbox"/> No		
	HCT/Hgb Abn?	<input type="checkbox"/> Yes	<input type="checkbox"/> No		
	WBC < 2500?	<input type="checkbox"/> Yes	<input type="checkbox"/> No		
	Platelets < 100,000?	<input type="checkbox"/> Yes	<input type="checkbox"/> No		
	TSH Abn?	<input type="checkbox"/> Yes	<input type="checkbox"/> No		
	Hep BsAg Positive?	<input type="checkbox"/> Yes	<input type="checkbox"/> No		
	HIV ab Positive?	<input type="checkbox"/> Yes	<input type="checkbox"/> No		

Mental Health Considerations					Date
Evidence or history of suicide ideation and/or suicide attempt?		<input type="checkbox"/> Yes	<input type="checkbox"/> No		
History of severe psychiatric disorder?		<input type="checkbox"/> Yes	<input type="checkbox"/> No		
Major mental illness poorly controlled?		<input type="checkbox"/> Yes	<input type="checkbox"/> No		
Recent aggressive behavior problems?					

Ancillary Concerns			Date
Evidence of concerns with risk behaviors?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	
Evidence of non-compliance with treatment or evaluations?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	
Patient refused to sign contract?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	
Other?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	

Other information			Date
Liver biopsy approved?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	
Liver biopsy results?			
Genotype			
HCV RNA results			
Type 1 Quantitative – Pre			
Type 2,3 Qualitative			

Oregon Department of Corrections
Health Services Division
Hepatitis C Evaluation Worksheet



History and Physical	Yes	No	Date
*1 Evidence of decompensated liver disease or clinical cirrhosis	___	___	___
*2 Evidence of hemoglobinopathies	___	___	___
History of solid organ transplant	___	___	___
Autoimmune disorder	___	___	___
Chronic Hepatitis B	___	___	___
Hyperthyroid disease	___	___	___
Cancer (type _____)	___	___	___
Major medical illness poorly Controlled (type _____)	___	___	___
*3 Laboratory tests completed	___	___	___

Mental Health evaluation	Yes	No	Date
Hx of suicide ideation and/or suicide attempt	___	___	___
*4 Hx of severe psychiatric disorder	___	___	___
Major mental illness poorly controlled	___	___	___

Refer to TLC for treatment approval	approved	Treatment initiated date
-------------------------------------	----------	--------------------------

Name _____
SID Number _____
DOB _____

*1 Evidence of decompensated liver disease: ascites, history of hepatic encephalopathy, or history of esophageal varices, etc.

*2 Evidence of hemoglobinopathies: thalassemia, hemolytic anemia, CBC abnormalities.

*3	Laboratory	Test	Yes	No	Date
		Bilirubin elevated?	___	___	_____
		Albumin < 3.5?	___	___	_____
		T4, TSH abn.?	___	___	_____
		Pro Time:INR >1.2?	___	___	_____
		Hep Bs Ag Pos?	___	___	_____
		ANA Pos?	___	___	_____
		HIV ab Pos?	___	___	_____
		WBC < 3000?	___	___	_____
		HCT / Hgb Abn?	___	___	_____
		Platelets < 100,000?	___	___	_____
		Pregnancy Test?	___	___	_____
		CXR	___	___	_____
		EKG if over 45	___	___	_____

*4 History of psychiatric disorder: major psychoses, major depression, or major mental illness treatment.

PATIENT CONTRACT CONCERNING HEPATITIS C MEDICATION

1. I understand that treatment with therapy (interferon / pegylated interferon / ribavirin) may cause flu-like symptoms (fever, chills, headache, aching muscles and or joints, rapid pulse, nausea, vomiting, general feeling of being "rundown"). It may also cause fatigue, hair loss, bone marrow suppression, apathy, irritability, depression, suicidal ideation, and changes in my thinking processes. Tolerance to these side effects may develop within a few weeks, or may persist. For some patients the side effects may necessitate stopping treatment.
2. I understand some of the side effects can be lessened by taking motrin as needed for symptom management, drinking at least 64 ounces of water/day, pacing my activities and my rest, and maintaining a healthy diet. I understand I am expected to follow these suggestions as necessary to help with any side effects.
3. I understand that one of the medications in this therapy, interferon, is by injections (shots). Standard interferon injections will be given three times a week. Pegylated interferon injections will be given once a week. I agree to be consistent in coming in for these injections.
4. I agree to periodic health evaluations including blood tests to monitor my overall health, side effects of the medicine, and to monitor treatment.
5. I understand that treatment will be required for at least a 24-week period. I understand that depending on the type of virus I have, the length of treatment and the terms of this contract may extend to 48 weeks; for a possible total of 72 weeks of medication, lab work, and provider checkups.
6. I understand this therapy can cause severe birth defects. I understand that it is extremely important and absolutely required that I do not become pregnant, or father a baby!!! If female, I agree to have a pregnancy test prior to starting treatment, and to have monthly pregnancy tests. (Only women who have had a hysterectomy are exempt from this requirement). If male, I will ensure that birth control measures are used. I understand that if I or my partner become pregnant, this therapy for Hepatitis C will be discontinued, I will be counseled about pregnancy termination, and I will assume all liability for any complications and/or birth defects.
7. I will abstain from any medication not prescribed for me or approved in writing for me to purchase from the canteen during the evaluation or the course of this treatment. I understand failure to do so can result in discontinuing this treatment.

8. I agree that I will not drink any beverage or medicine containing alcohol during my evaluation or course of this treatment. If I fail to follow this requirement, I will not be considered a candidate for this therapy, and therapy may be discontinued or not started until I have completed chemical dependency treatment.
9. I understand I may be requested to participate in chemical dependency treatment prior to starting this treatment.
10. I will abstain from all illegal substances, including but not limited to, IV drug use and inhaled drugs, during the evaluation or course of this treatment. If I fail to follow this requirement, I will not be considered a candidate for this therapy and therapy may be discontinued or not started until I have completed chemical dependency treatment.
11. I will submit to random urine drug tests prior to and during treatment, if my provider requests it. If I refuse, I will not be considered a candidate for this treatment.
12. I understand if my drug screen checks are positive during the course of this treatment, treatment may be discontinued until I have completed chemical dependency treatment.
14. I will not participate in tattooing during the course of this treatment. I understand if I do, treatment may be discontinued.
15. I understand if I do not come in for my medication as prescribed to treat my Hepatitis C, therapy may be discontinued.
16. I understand that the medications to treat Hepatitis C may make me feel angry and irritable, but that controlling my behavior is my responsibility and taking this medication will not excuse any misconduct.
17. Finally, I understand that this therapy may not cure my disease and that even without treatment I could maintain good health.

Patient Signature _____

Date _____

Witness _____
(Health Services provider who conducted informed consent)

HEALTH SERVICE REQUEST FOR INFORMATION

INMATE _____

SID# _____

DATE _____

	Yes	No
Ongoing compliance with recommended institutional programming		
Current participation in alcohol and/or drug treatment programming If not within time frames, when will he be eligible? Did the inmate refuse treatment?		
Current participation in AA group		
Previous participation in alcohol and/or drug treatment programming. If so date of completion.		
Certificates for completion of alcohol and/or drug treatment programming. If so what program(s)		
Current incarceration related to alcohol and/or drugs		
Repeat incarcerations related to alcohol and/or drug use		

ADDITIONAL COMMENTS:

COUNSELOR _____

DATE _____

Return to Health Services.

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