New Opportunities for the Management and Therapy of Hepatitis C in Correctional Settings

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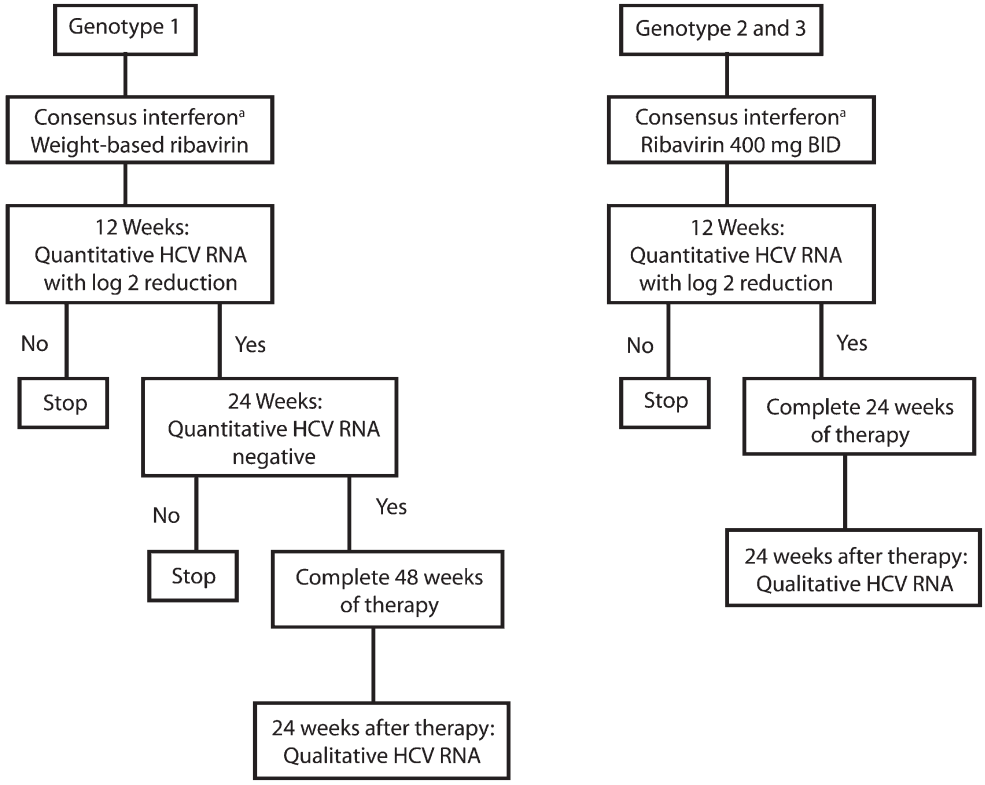
Hepatitis C in prison populations is now a major public health problem, and large numbers of correctional facilities have no comprehensive management program, often because of formidable projected costs and tightening budget constraints. The North Dakota Department of Corrections and Rehabilitation has operated a management and therapy program since 2002 using consensus interferon and ribavirin with 45% cost savings. The program has provided excellent sustained viral responses: 54.2% for genotype 1 hepatitis C, 75% for genotypes 2 and 3, and 63.6% overall. (*Am J Public Health.* 2010;100:13–17. doi: 10.2105/AJPH.2008.147629.)

DETECTION AND MANAGEMENT of hepatitis C in the US prison population is a major public health problem, as evidenced by the estimate that more than one third[1] of the approximately 5 400 000 people in the United States with active hepatitis C enter correctional facilities yearly.[2] In North Dakota (population 642 000), the true incidence and prevalence of hepatitis C is not known; however, 25% of all positive antibody tests for hepatitis C reported yearly by the North Dakota Department of Health originate from the North Dakota Department of Corrections and Rehabilitation (ND DOCR).

In spite of guidelines published by the Federal Bureau of Prisons in 2005,[3] state correctional facilities have only begun to formulate comprehensive management policies,[4,5] a task now complicated by shrinking correctional budgets. Prisons offer an ideal setting for the treatment of hepatitis C[6,7] because maximum compliance, which is necessary for achieving a sustained viral response, can be assured. Limited information is available on the outcome of correctional screening and treatment programs,[4] most of which now use pegylated interferon and weight-based ribavirin. There is limited published data on the use of consensus interferon combined with ribavirin despite its lower cost and theoretical advantages. Studies exist that suggest the usefulness of this product in noncorrectional settings,[8–10] but, to our knowledge, ours is the first report of consensus interferon combined with weight-based ribavirin for the treatment of hepatitis C in a US prison system.

Type 1 α-interferons (IFNs) are mostly made up of proteins containing 166 amino acids with 14 subtypes, all of which have antiproliferative and antiviral activities. Analysis of the subtypes has revealed a high degree of conservation for amino acids in certain positions. Minor amino acid changes result in major changes in binding affinity to cellular receptors; receptor affinity is directly correlated with biologic potency. A synthetic type 1 α-IFN has been manufactured with the most common amino acids at each position for the 14 subtypes, resulting in a protein having the highest binding affinity of all α-IFN molecules. The biopotency of this "consensus interferon,"[11] which is also known as IFN alfacon-1, is 10-fold higher than that of all the natural variants.[12] Its use in the treatment of hepatitis C has been limited by failure of attempts to prolong the half-life in vivo.

The 2 commercial interferons, PegIFNα-2a and PegIFNα-2b, now commonly used for hepatitis C therapy differ by only 1 amino acid. The significant difference is the configuration and weight of the polyethylene glycol polymers attached (by a process called pegylation) to the active interferon, which prolong the half-life. The pegylation process results in a 60% to 90% loss in the biologic activity of IFN, evidenced by comparison of the dosing of the pegylated products (150–180 μg weekly) with the dosing of the nonpegylated products (15 μg 3 times a week).



Note. BID=twice daily; MCG=micrograms.
[a]15 mcg subcutaneously three times a week.

FIGURE 1—Treatment protocol for hepatitis C therapy using consensus interferon and ribavirin: North Dakota Department of Corrections and Rehabilitation, July 2002–November 2008.

TABLE 1—Disposition of Inmates Positive for Hepatitis C Antibody on December 1, 2008: North Dakota Department of Corrections and Rehabilitation

	No. or No. (%)
No. inmates with hepatitis C antibody	146
No. eligible to enter screening	91
Disposition	
Comorbidity precluded treatment	4 (4.4)
Declined treatment	6 (6.6)
Disqualified for noncompliance	8 (8.8)
Negative viral load or biopsy	24 (26.4)
Aged > 60 y	1 (1.1)
Pending completion of screening	15 (16.5)
Eligible for treatment	33 (36.3)

DESCRIPTION OF PROGRAM

The ND DOCR screens all prisoners entering the system for hepatitis C; the prevalence rate among the average census of 1400 prisoners (13%) is consistent with published rates for other prison systems (12%–31%).[4] A pretreatment screening program, which is designed to maximize an inmate's chances of completing therapy, determines eligibility (see the box on the next page). This pretreatment screening program includes education and screening for continuing substance abuse, immunization for hepatitis A and B, and screening for the presence of hepatitis C and HIV.

There is no limit to the number of prisoners undergoing hepatitis C therapy provided they meet the eligibility criteria. The screening criteria pertain only to the primary treatment of hepatitis C. The treatment program is funded by the state legislature under the ND DOCR budget and has received no funding from any other source.

METHODS AND RESULTS

The ND DOCR treatment protocol (Figure 1) follows current National Institutes of Health (NIH) guidelines[14] for primary therapy of hepatitis C, with the exception of replacing weekly pegylated interferon administration with 3-times-weekly consensus interferon administration. The other treatment criteria listed in the box on the next page are to ensure that inmates will complete treatment before their prison terms are completed. Table 1 shows a 1-day snapshot of the treatment final outcome among current inmates who were positive for hepatitis C antibody.

Almost all patients with genotype 1 hepatitis C are biopsied before treatment begins. Very few genotype 2 cases are biopsied. Patients with genotype 3 sometimes are biopsied, depending on whether a higher fibrosis score is suspected during the initial workup. The decision on treatment duration is made primarily on the basis of fibrosis score and the absence of detectable virus after the fourth week of therapy. Genotype 3 patients who begin treatment are assigned to either 24 or 48 weeks of therapy.

In order to optimize response, once therapy begins, no interruption can occur. Decisions to stop treatment are based on

viral load at 12 and 24 weeks.[15] For patients with genotype 1, if virus is detected at 24 weeks, the probability of a sustained viral response is so low that therapy is stopped; if virus is detected at 12 weeks, treatment continues provided viral RNA is either undetectable or has dropped 100-fold (2 logs) from baseline. To maximize the probability of a sustained viral response, dose reductions for hematologic side effects are not allowed. Because depression and psychiatric deterioration can significantly complicate management of therapy,[16] every patient is initially screened with the Center for Epidemiologic Studies Depression Scale index.[17] All inmates with positive screenings and all those with established *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition,* axis I diagnoses are cleared for therapy by a psychiatrist, with monthly follow-up when indicated.

Prison inmates undergoing therapy are treated exactly as private patients, except that instead of once-weekly injections of pegylated interferon, consensus interferon (15 mcg) is administered subcutaneously 3 times a week. For genotype 1 hepatitis C, ribavirin dosage is based on body weight, with a maximum dose of 1400 mg per 24 hours, administered orally in 2 doses. The dose for genotype 2 or 3 is usually a standard 400 mg administered orally twice daily.

From July 2002 through November 2008, data for 50 patients were collected (Figure 2). Patient characteristics are listed in Table 2, along with characteristics of all ND DOCR inmates for comparison purposes. The liver biopsy rate was 56%; rates of metavir fibrosis were 37% for stage 1, 27% for stage 2, 36% for stage 3, and 0% for stage 4. On December 1, 2008, six inmates were in treatment, 2 inmates were discharged early or transferred, and 3 were withdrawn from treatment. The remaining 39 inmates who completed treatment were as follows: of 19 with genotype 1, 13 had a sustained viral response; of 20 with genotype 2 or 3, 15 had a sustained viral response. Response rates calculated by intention-to-treat analysis (but not including the 6 inmates then in treatment) were 54.2% for genotype 1 and 75% for genotypes 2 and 3, with an overall sustained viral response of 63.6%. These rates compare favorably with those of clinical trials[18–20] using pegylated interferon, which reported sustained viral responses of 40% to 50% for genotype 1 and 70% to 80% for genotypes 2 and 3, with an overall sustained viral response of 40% to 55%. Table 3 shows comorbid medical conditions preceding or arising during the treatment period as well as initiation or adjustment of medications to treat these conditions. Antidepressant adjustment was required for 30% of inmates, and thyroid replacement was necessary for 14%.

DISCUSSION

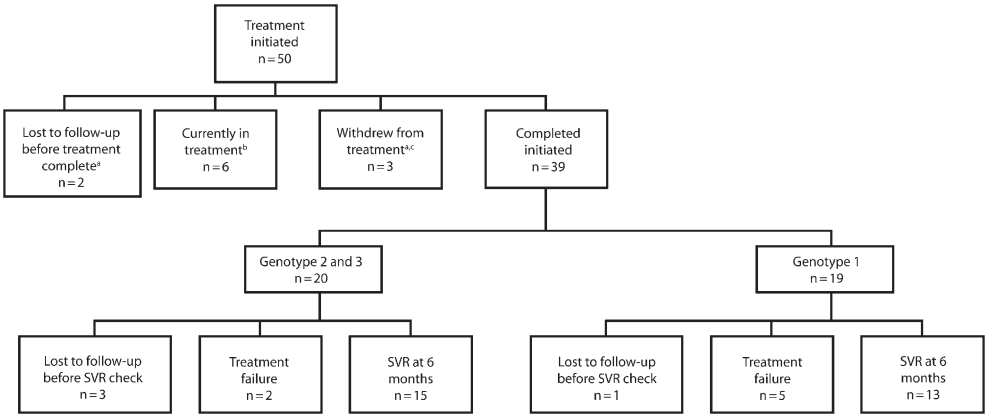
Reported response rates in previous papers have included those who withdrew prior to completion of treatment as well as those who were lost to follow-up. This practice assumes that all those lost to follow-up did not achieve

CRITERIA FOR DETERMINING ELIGIBILITY FOR HEPATITIS C THERAPY USING CONSENSUS INTERFERON AND RIBAVIRIN: NORTH DAKOTA DEPARTMENT OF CORRECTIONS AND REHABILITATION, JULY 2002–NOVEMBER 2008

Pre-treatment Screening Criteria

1. Age 18-60 years.
2. Confirmation of hepatitis C RNA with genotype.
3. Immunization and serology confirming immunity to hepatitis A and B.
4. Hemoglobin A1c < 9%.
5. Adequately treated heart disease.
6. Adequately treated thyroid disease.
7. Absence of renal disease.
8. Absence of decompensated cirrhosis with ascites.
9. Hemoglobin > 10 grams.
10. Absence of autoimmune disease.
11. Absence of life-threatening nonhepatic disease.
12. Satisfactory clinic compliance with screening appointments.
13. If HIV postive, a CD4 (Helper T-cell) count > 200.
14. Two negative alcohol and drug tests 6 months apart.
15. Prison stay certain for at least 14 months for genotype 2,3 once treatment begins.
16. Prison stay certain for at least 20 months for genotype 1 once treatment begins.
17. Female inmates: recent negative pregnancy test and documentation of counseling in avoiding pregnancy until 6 months after treatment is complete.
18. Compliant with drug and alcohol treatments recommendations.
19. Absence of severe axis I diagnosis or psychiatric clearance for therapy.
20. No body piercing or tattoos for 6 months.

Source. North Dakota Department of Corrections and Rehabilitation.[13]



Note. SVR=sustained virologic response; EVR=early virologic response.
[a]All genotype 1.
[b]Four genotype 1, one genotype 3 and one genotype 4.
[c]One inmate quit voluntarily, one inmate discontinued due to illegal drug use, and one inmate failed EVR.

FIGURE 2—Outcomes of hepatitis C therapy using consensus interferon and ribavirin: North Dakota Department of Corrections and Rehabilitation, July 2002–November 2008.

a sustained viral response. Given the relatively small sample size we report, this results in a negative bias for a sustained viral response, because most inmates lost to follow-up did complete therapy.

Early experience at the ND DOCR in treating hepatitis C with pegylated interferons was associated with prohibitive expense. This is not a unique problem.[21–23] The use of consensus interferon and pretreatment screening have reduced the costs of effective therapy. Consensus interferon is 40% to 50% cheaper than pegylated interferons.[24] The average cost for medication is $10 900 for genotype 1 and $5300 for genotype 2 or 3. Use of consensus interferon has avoided many of the hematologic and psychiatric side effects associated with standard therapy.

The success of this approach is likely multifactorial, but tight control maintained over medication adminstration is a major contributor. This therapy is essentially directly observed therapy. Prescreening is also a factor, because it intentionally selects for patients with a higher likelihood of successful completion. Racial distribution in the ND DOCR population is dissimilar to that of other states, so caution is advised when our results are generalized to other prison populations.

TABLE 2—Demographic Characteristics of Inmates: North Dakota Department of Corrections and Rehabilitation, July 2002–November 2008

Characteristic	Inmates Treated for Hepatitis C	All Inmates
No. inmates	50	1467
Mean age, y	40	31
Male, %	98	89
Race/ethnicity, %		
White	76	66
Native American	10	22
Hispanic	10	5
African American	4	6
Asian	0	0.2
Weight, kg, mean ±SD	94.4 ±15.7	NA
Viral load, log/mL	6.22 ±0.71	NA
Genotype 1, %	56	NA
Had biopsy, %	56	NA

Note. NA=not available.

TABLE 3—Comorbid Medical Conditions Preceding or Arising During Treatment with Consensus Interferon and Ribavirin for Hepatitis C: North Dakota Department of Corrections and Rehabilitation, July 2002–November 2008

Comorbid Condition	No. (%)
Psychiatric	
Axis I disorder diagnosed before initiation of therapy	24 (48)
Taking antidepressants at initiation of therapy	22 (44)
Taking antipsychotics at initiation of therapy	6 (12)
Antidepressant adjustment during therapy	15 (30)
Antipsychotic adjustment during therapy	1 (2)
Endocrine: thyroid replacement started during therapy	7 (14)
Hematologic	
Erythropoietin started during therapy	1 (2)
GCSF started during therapy	0

Note. GCSF=granulocyte colony-stimulating factor.

However, the previously cited studies by Sjogren et al.[9,10] included a more typical racial mix without loss of efficacy.

Pegylated interferons are used in other prison programs, for 2 reasons: (1) consultants formulating treatment programs are not aware of the advantages of consensus interferon, and (2) consensus interferon would not be the agent of choice outside the prison setting because pegylated interferons are more convenient for patients and, because they are recommended by the NIH as standard treatment and the administered drug levels are more constant than with consensus interferon, they are preferred by physicians.

Consensus interferon is less expensive than pegylated interferons and also saves money by limiting the need for growth factors. Use of consensus interferon could save millions of dollars for large correctional systems. A formal comparison trial with much larger numbers is needed to verify our results. ■

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Contributors

C. K. Martin initiated the hepatitis C program at the department of corrections, directed the hepatitis C treatment of every patient in this study, and led the writing of the article. J. E. Hostetter provided program direction for the hepatitis C treatment program, assisted with all stages of the study, led the analysis of the data, and assisted in the writing of the article. J. J. Hagan provided primary care to the patients in the study, assisted in all stages of the study, abstracted the data for the study, and assisted in the writing of the article.

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Human Participant Protection

This project was reviewed by the University of North Dakota institutional review board and approved as exempt.

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