

Pretransplant Psychiatric and Medical Comorbidity of Alcoholic Liver Disease Patients Who Received Liver Transplant

ANDREA DIMARTINI, M.D., MARY AMANDA DEW, PH.D.
LUBNA JAVED, M.D., MARY GRACE FITZGERALD, R.N., M.S.N.
ASHOK JAIN, M.D., NANCY DAY, PH.D.

The authors examined the pretransplant prevalence of comorbid physical and psychological disorders in 112 alcoholic liver disease patients who received liver transplant. Fifty-six percent of the patients had comorbid hepatitis C or hepatitis B virus, 40% had used other substances in addition to alcohol, 25% met the criteria for a lifetime DSM-IV nonalcohol substance use disorder, 36% for a lifetime depressive disorder, and 12% for a lifetime anxiety disorder. The findings suggest the need for pretransplant psychiatric evaluation of alcoholic liver disease patients to identify nonalcohol substance use disorders and other psychiatric disorders that may require treatment.

(Psychosomatics 2004; 45:517–523)

Historically, patients with alcoholic liver disease have been considered less desirable liver transplant candidates than patients with other types of liver disease. In the first decade of liver transplantation, physicians believed these patients' alcohol-associated medical problems would lead to higher perioperative mortality, a higher complication rate, and potentially worse posttransplant outcomes.^{1,2} These patients were also thought to be at high risk for alcohol use relapse and thus unlikely to survive long-term after liver transplantation because of the redevelopment of alcoholic liver disease.³ As a result of these beliefs, a consensus opinion developed in the early 1980s,⁴ which led to only a small proportion of patients with alcoholic cirrhosis being chosen for transplant. Now almost two decades later, studies consistently show that short-term survival rates (1–3 years posttransplant) of patients who received liver transplant because of alcoholic liver disease are comparable to^{5–8} or better than^{9–11} survival rates among patients who receive transplant because of other types of end-stage liver disease. By 1995, alcoholic liver disease accounted for the largest proportion of liver transplants performed in the United States (nearly 27% in 1995).¹⁰

In that same year 32% of patients who received transplant for alcoholic liver disease also had hepatitis C virus listed as a primary liver disease.¹⁰ Now that transfused blood is routinely screened for hepatitis C virus, the majority of newly identified cases of hepatitis C infection are associated with injected drug use.¹² The National Institute on Drug Abuse and the Centers for Disease Control and Prevention have reported that intravenous drug use is responsible for at least 60% of new cases of hepatitis C virus in the United States.^{13,14} It is estimated that 50%–80% of injection drug users are positive for hepatitis C virus, 75%–85% of those who are infected develop chronic hepatitis C infections, and 20%–30% of those cases progress to cirrhosis.¹⁵ Although decreasing as a risk factor for contracting hepatitis B, injected drug use is still one of the most commonly reported risk factors for that infection.¹⁶

Received Dec. 23, 2003; accepted Feb. 10, 2004. From the Departments of Psychiatry and Transplantation Surgery, University of Pittsburgh Medical Center and Starzl Transplant Institute, Pittsburgh. Address reprint requests to Dr. DiMartini, Western Psychiatric Institute and Clinics, 3811 O'Hara St., Pittsburgh, PA 15213; dimartinaf@msx.upmc.edu (e-mail).
Copyright © 2004 The Academy of Psychosomatic Medicine.

Comorbidity in Liver Transplant Patients

These changing patterns in the risk factors for acquisition of viral hepatitis are reflected in the increasing representation of injected drug users in the liver transplantation candidate population. Because of the significant overlap in the liver transplantation population between those with diagnoses of alcoholic liver disease and hepatitis C virus, we believed there would similarly be significant psychiatric comorbidity of both alcohol and substance use disorders in the alcoholic liver disease transplant population.¹⁷ We hypothesized that patients with both alcoholic liver disease and hepatitis C virus or hepatitis B virus would more often have histories of injected drug use. This pattern is especially important to recognize, as nonalcohol substance use may be overlooked in liver transplantation candidates with alcoholic liver disease. We also hypothesized that those with alcoholic liver disease and hepatitis C or hepatitis B virus would have less total lifetime alcohol consumption, compared to those with alcoholic liver disease who did not have hepatitis C or hepatitis B virus, and that the presence of hepatitis C or hepatitis B virus would accelerate the development of end-stage liver disease. In addition, we were interested in gender differences with respect to pretransplant alcohol use and psychiatric histories, given that women can develop alcoholic liver disease with less overall alcohol consumption, compared to men, and can also have an accelerated course of alcoholism that requires specialized psychiatric care.¹⁸ Finally, the pretransplant lifetime histories of psychiatric disorders in alcoholic liver disease transplant recipients have not been reported. Our data demonstrate that in addition to alcohol and other substance use disorders, other axis I psychiatric disorders are common in the alcoholic liver disease liver transplantation population. Thus, our data support the need for thorough psychiatric evaluation and treatment for these patients before they receive liver transplantation. Understanding the specific differences and unique features of this transplant cohort would increase clinical awareness of the complexities of this population, highlight issues for candidate screening, and potentially identify those at higher risk for alcohol and other substance use relapse after transplantation.

METHOD

Subjects and Procedure

As part of an ongoing prospective study, we collected pretransplant demographic and clinical information on 112 patients who received liver transplant for alcoholic liver

disease at the Starzl Transplant Institute. All patients who received liver transplant for alcoholic liver disease at the institute from May 1998 to February 2002 were eligible for the study. After agreeing to participate and signing informed consent, the patients were enrolled in the study. During the period of study recruitment, 145 transplant recipients had either a primary or secondary diagnosis of alcoholic liver disease. Of these, 112 participated (eight refused to participate, 22 died before enrollment, and three were hospitalized or in a nursing home).

The diagnosis of alcoholic liver disease was determined by consensus on the basis of interviews and examinations by a team from the transplant surgery, hepatology, and psychiatry departments. The team members from the psychiatry department included a psychiatric nurse clinical specialist (M.G.F.) and a psychiatrist (A.D.). Most patients with alcoholic liver disease had a history of excessive alcohol use consistent with the development of alcoholic liver disease defined as ≥ 20 grams of ethanol a day for women or ≥ 60 grams of ethanol a day for men,¹⁹ and 90% had consumed this amount for 10 years or longer.

Before transplantation, patients underwent a psychiatric evaluation during which data on the following variables were obtained: alcohol diagnosis, alcohol consumption patterns, length of sobriety, psychiatric history, history of other substance use, other substance use diagnoses, and alcohol rehabilitation experience. This information was documented on structured medical record forms, from which the data for this study were drawn. Studies of transplant cohorts commonly report the medical diagnosis (alcoholic liver disease) rather than the behavioral diagnosis of alcohol abuse or dependence. We similarly chose alcoholic liver disease as the diagnosis of inclusion and performed a structured psychiatric clinical interview to identify the DSM-IV behavioral diagnoses of alcohol or substance abuse or dependence.

Pretransplant Alcohol Variables

The duration of pretransplant sobriety was defined as the time (in months) from the last drink of alcohol to the date of transplantation. Pretransplant amounts of alcohol consumption were calculated as follows. Before abstinence, most patients drank on a daily basis. For nondaily drinkers, the average weekly alcohol usage was converted into average daily standard drinks for purposes of comparison. Standard drinks were defined as 1 ounce of hard liquor, one 12-ounce beer, or 6 ounces of wine. Daily alcohol consumption was calculated as the average number

of daily standard drinks, by patient report, converted into average daily grams of ethanol. The average daily grams of ethanol was calculated by converting ounces of alcoholic beverage to ounces of pure ethanol and then converting the ounces into grams of ethanol. Years of drinking were defined as the number of years a patient drank at the average daily amount. For lifetime ethanol exposure (in kilograms), the average daily amount was multiplied by 365 days and then by the number of years of drinking. For those whose amounts of daily consumption changed over the course of their lifetime, we calculated the average daily amount multiplied by 365 and then by years at this amount and added these totals together for the total lifetime amount.

Statistical Analysis

Continuous variables are presented as means and standard deviations, and categorical variables are presented as proportions. The variables of length of sobriety, average drinks per day, and average amount of ethanol were positively skewed (asymmetrically shifted toward positive values) and were log transformed to normalize the distributions before comparisons were made. To normalize the distribution for the number of years of drinking, one outlier was removed. Comparisons between group means were tested by t tests for independent samples. Cross-tabulations were used to test associations between categorical data.

A p value equal to or less than 0.05 was considered statistically significant. All analyses were performed by using SPSS for Windows software (version 9.0) (SPSS Inc., Chicago).

RESULTS

Demographic and Psychiatric History Variables

The patients were predominantly Caucasian men (see Table 1). The mean age was 50 years (SD = 8). Seventy-three percent (N = 82) had been living at the same location for more than 2 years, indicating a high level of residential stability. Only 16% (N = 18) lived alone. This cohort was demographically similar to subject groups described in previous studies of patients with alcoholic liver disease who received liver transplant^{7,10,11,20} and similar to a separate cohort from a previous study at our center.²¹

Only 34% (N = 38) had a diagnosis of alcoholic liver disease only. Fifty-six percent (N = 63) had comorbid hepatitis C or hepatitis B infection; 44% had hepatitis C virus (N = 49), 4% had hepatitis B virus (N = 5), and 8% (N = 9)

had both. Other comorbid liver diseases included hemochromatosis in 4% (N = 5), autoimmune liver disease in 4% (N = 5), α 1-antitrypsin deficiency in 6% (N = 7), hepatocellular carcinoma in 2% (N = 2), hepatitis D virus in 1% (N = 1), and polycystic disease in 1% (N = 1).

The alcoholic beverage of choice was beer in 80% (N = 90) and wine in 13% (N = 15) of subjects. Sixty-three percent (N = 71) drank hard liquor, but mostly in combination with beer. Sixty-two percent (N = 69) had a family history of alcoholism in a first-degree biologic relative. Forty-eight percent (N = 54) had attended a rehabilitation program, which could include inpatient or outpatient rehabilitation or regular attendance (two or more meetings per week) at Alcoholics Anonymous meetings. We did not count alcohol detoxification as rehabilitation unless it was followed by a structured rehabilitation program.

Seventy-one percent (N = 80) of the patients met the DSM-IV criteria for alcohol dependence, 25% (N = 28) met the criteria for alcohol abuse, and 4% (N = 4) did not meet the criteria for either diagnosis. Lifetime (before transplantation) diagnoses of psychiatric disorders included depressive disorders (major depression, depression due to a general medical condition, and adjustment disorder with depressed mood) in 36% percent (N = 40) of patients and anxiety disorders (generalized anxiety disorder, panic disorder, and adjustment disorder with anxious mood) in 12% (N = 13) of patients. Of those who had affective disorders, only 34% (N = 18) had received psychotropic medications for their disorders. Forty percent (N = 45) of patients had used substances other than alcohol, and 25% (N = 28) had a diagnosis of a substance use disorder (14% [N = 16] had a diagnosis of substance abuse and 11% [N = 12] had substance dependence). In addition, 26% (N = 29) had used intravenous drugs.

The Venn diagram (Figure 1) illustrates one of our

TABLE 1. Sociodemographic Characteristics of 112 Patients With Alcoholic Liver Disease Who Received Liver Transplant

Characteristic	%
Male	90
Age <50 years	57
Caucasian	95
Married	56
Less than high school education	56
Last occupation nonprofessional	74
Living at current residence >2 years ^a	73
Living alone	16

^aAn indication of residential stability.

Comorbidity in Liver Transplant Patients

primary goals, which was to identify the overlap of alcoholic liver disease, comorbid viral infections, and other substance use exposure. Although the group with comorbid viral infections included patients who had not used other nonalcohol substances, the majority (67%, N=42) had used other substances. Of the patients who had ever used nonalcohol substances regardless of route, 93% (N=42) had a comorbid virus, compared to 31% (N=21) of those who had never used nonalcohol substances. Only three patients who had used nonalcohol substances did not also have hepatitis C or hepatitis B virus. Of those who had a virus, 46% (N=29) also had a history of intravenous drug use, and 100% of the patients who had used intravenous drugs were infected with hepatitis C or hepatitis B virus.

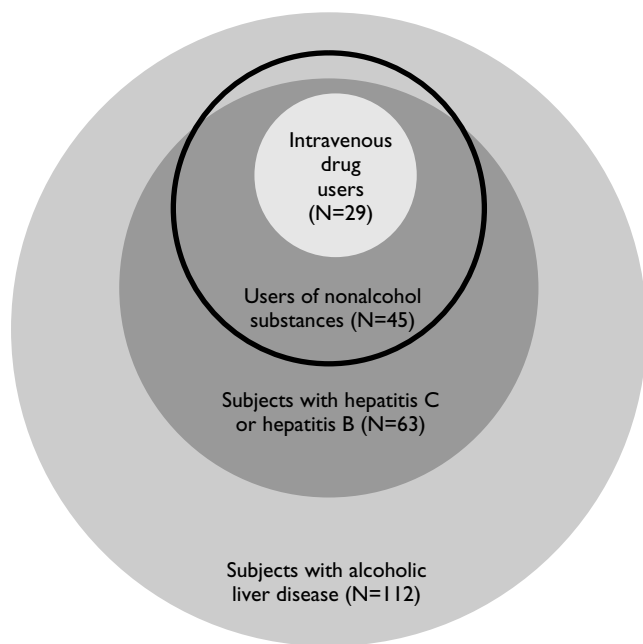
Group Comparisons

Patients with a Comorbid Viral Infection Patients with both alcoholic liver disease and hepatitis C or hepatitis B virus were significantly younger than patients without a viral component to their liver disease (mean=47 years [SD=6], compared to mean=53 years [SD=8] for all others; $F=7.3$, $df=1, 110$, $p<0.0001$). As Table 2 shows, patients with a comorbid virus had significantly fewer years of heavy drinking before liver transplantation (19

years, compared with 22 years for all others) and had a longer duration of sobriety but did not have lower average daily alcohol consumption or less total lifetime ethanol exposure. Those with a virus were significantly more likely to have a history of nonalcohol substance use. They were also more likely to have a psychiatric diagnosis of alcohol dependence or to have attended an alcohol rehabilitation program, although these differences did not reach significance (see Table 2). Those with hepatitis C or hepatitis B virus were no more likely than those without a virus to have a depressive or anxiety disorder.

Patients with Nonalcoholic Substance Use Since we were specifically interested in the contribution of other substance use to pretransplant alcohol use histories, we then looked at the differences between patients with and without other substance use. As Table 2 shows, those with nonalcohol substance use histories were significantly more likely to have a diagnosis of alcohol dependence. Although patients with nonalcohol substance use had had fewer years of heavy drinking before transplantation, compared to others, their total lifetime consumption was not different, most likely because their daily alcohol consumption was heavier. In addition, patients with other substance use were much more likely to have participated in an alcohol and/or drug rehabilitation program.

FIGURE 1. Pretransplant Substance Use in 112 Patients With Alcoholic Liver Disease Who Received Liver Transplant



Gender Differences Although the age distribution of men and women was similar and the average daily and average weekly alcohol consumption before transplantation was not different between men and women, men drank heavily for significantly more years and had significantly greater lifetime alcohol consumption than women (see Table 2). Women were no more likely than men to have a family history of an alcohol disorder, to have spent less time sober, or to meet the criteria for alcohol dependence. However, women were less likely to have used nonalcoholic substances, compared to men. In fact, no woman had used intravenous drugs (see Table 2). Perhaps because of their lesser exposure to nonalcohol substances, women were also less likely than men to have a comorbid hepatitis C or hepatitis B infection and were more likely, although not significantly more likely, to have alcoholic liver disease only.

Seventy percent of women and 61% of men had any pretransplant psychiatric diagnosis (including affective disorders and nonalcoholic substance use disorders). Women were more likely to have had a depressive disorder, compared with men (70% versus 32%; $p=0.02$, chi-square

TABLE 2. Pretransplant Substance Use Characteristics of 112 Patients With Alcoholic Liver Disease Who Received Liver Transplant, by Comorbid Liver Disease Status, Substance Use History, and Gender

Patient Group	Daily Drinks ^{a,b}		Years of Drinking		Lifetime Ethanol Exposure (kg) ^{a,c}		Sobriety (months) ^a		Attended Rehabilitation Program		Alcohol Dependence Diagnosis		Nonalcohol Substance Use		Intravenous Drug Use		
	Mean	SD (df=110)	Mean	SD (df=110)	Mean	SD (df=110)	Mean	SD (df=110)	%	χ^2 (df=1)	%	χ^2 (df=1)	%	χ^2 (df=1)	%	χ^2 (df=1)	
Comorbid liver disease status																	
No hepatitis C or B (N = 49)	9	2	22	9	675	2	20	3	49	67	6	0					
Hepatitis C or B (N = 63)	10	2	19	8	685	2	31	3	62	79	67	46					
Substance use history																	
Alcohol only (N = 67)	9	2	22	9	630	2	22	3	35	62							
Other substances with alcohol (N = 45)	12	2	18	7	761	2	29	3	66	90							
Gender																	
Men (N = 101)	10	2	21	9	721	2	26	3	49	75	43	30					
Women (N = 11)	8	2	14	6	383	2	18	2	40	67	10	0					

^aData for daily drinks, lifetime ethanol exposure, and length of sobriety were log transformed to normalize the distribution before analysis. For these items geometric means and standard deviations are presented.

^bCalculated in standard drinks; one standard drink is equal to 1 ounce of hard liquor, one 12-ounce beer, or 6 ounces of wine.

^cMean daily amount multiplied by 365 days and then by years of drinking.

* $p < 0.05$

** $p < 0.01$

*** $p < 0.004$

Comorbidity in Liver Transplant Patients

test). Similar proportions of men and women had a diagnosis of an anxiety or other psychiatric disorder, and women were no more likely than men to have been treated for such disorders. Men and women were equally likely to have attended a rehabilitation program.

DISCUSSION

We have seen a dramatic rise in the numbers of alcoholic liver disease patients who are coinfecting with hepatotropic viruses, from 32% in the early 1990s²¹ to more than 50% in this cohort. Because of improvements in the screening of transfused blood, transplant patients are now more likely to have contracted hepatotropic viruses from substance use, especially injected substance use. This pattern is reflected in our study's cohort of alcoholic liver disease patients, in which a significantly higher risk of hepatitis C or hepatitis B infection was found in those with prior nonalcohol substance use exposure, regardless of route. Nearly 50% of patients with hepatitis C or hepatitis B infection had used injected drugs. Similarly, in another study, 60% of patients with alcoholic liver disease who were wait-listed for liver transplant were infected with hepatitis C virus, and 21% of those patients had a history of injected drug use.²²

In the current study, the patients with comorbid viruses tended to be younger, perhaps because the combined effect of alcohol and hepatotropic viruses accelerated the time course to end-stage liver disease. Among the patients with comorbid hepatitis C or hepatitis B infection, 67% had exposure to substances other than alcohol. This group was more likely to be male, to have a diagnosis of alcohol dependence, to have a history of heavy alcohol consumption for a shorter length of time, and to have attended alcohol and/or drug rehabilitation. Although we did not identify specific alcohol typologies, this group may represent the type II alcoholic defined by Cloninger²³ (male, early age of onset, more severe course, associated antisocial behavior). Their combined use of alcohol and other substances may have led them to rehabilitation more readily, compared to those with alcohol use only, and this intervention may have contributed to their longer period of sobriety. Although we hypothesized that patients with polysubstance use histories would have consumed less alcohol than those with alcoholic liver disease only, the lifetime consumption was similar between these two groups.

Women are more susceptible than men to the toxic effects of alcohol on hepatocytes and develop cirrhosis at a more rapid rate and with a lower total alcohol consumption.¹⁸ This phenomenon may be due to smaller body size, lower volume of distribution, and lower activity levels of alcohol dehydrogenase, which lead to higher peak blood alcohol levels in women than in men after the same dose of alcohol per kilogram of weight.^{24,25} Thus, our findings that women with alcoholic liver disease had fewer years of heavy drinking and consumed less ethanol over their lifetime than did men are expected. However, alcoholic women have been described as having an accelerated course of symptom severity.²⁶ Women can become heavier drinkers at later ages, are often solitary drinkers, often have polysubstance abuse, and may need psychiatric treatment.¹⁸ Although the women in our study were more likely to have a history of depression, compared with men, they had less complicated addiction histories, were less likely to have polysubstance use disorders, and were less likely to be infected with hepatitis C or hepatitis B virus. In addition, women and men had spent similar amounts of time sober.

The high prevalence of pretransplant psychiatric disorders in this cohort attests to the need for pretransplant psychiatric evaluation to diagnose both addictive and other psychiatric disorders that may require treatment. Careful screening for all types of substance use prevents the inadvertent assumption that patients with alcoholic liver disease would not have an additional substance use disorder. Detection of a comorbid hepatotropic virus should lead the clinician to inquire about other substance use, as should be done with all patients regardless of their primary liver disease. Although high rates of depression are reported in patients with hepatitis C virus,²⁷ in the current study, the patients with comorbid viral infections were no more likely to have experienced depression than those without a comorbid infection. Few patients with pretransplant affective disorders had received treatment, perhaps because of clinicians' reluctance to use psychotropic medications in patients with advanced liver disease. However, psychotropic medications can often be used safely, if the severity of the liver disease is taken into consideration and the patient's overall care is coordinated with the transplant team.²⁸

This work was supported by grant AA00257 from the National Institute on Alcohol Abuse and Alcoholism.

References

1. Van Thiel DH, Schade RR, Gavaler JS, Shaw BW, Iwatsuki S, Starzl T: Medical aspects of liver transplantation. *Hepatology* 1984; 4(suppl 1):S79–S83
2. Schenker S, Perkins HS, Sorrell MF: Should patients with end-stage alcoholic liver disease have a new liver? (editorial) *Hepatology* 1990; 11:314–319
3. Atterbury CE: The alcoholic in the lifeboat: should drinkers be candidates for liver transplantation? *J Clin Gastroenterol* 1986; 8:1–4
4. Bernstein MJ: Consensus conference: liver transplantation. *JAMA* 1983; 250:2961–2964
5. DiMartini AF, Jain A, Irish W, Fitzgerald MG, Fung JJ: Liver transplantation in alcoholic and non-alcoholic cirrhosis: survival according to UNOS status, medical variables, and sobriety. *Transplantation* 1998; 66:298–302
6. McCurry KR, Baliga P, Merion RM, Ham JM, Lucey MR, Beresford TP, Turcotte JG, Campbell DA Jr: Resource utilization and outcome of liver transplantation for alcoholic cirrhosis. *Arch Surg* 1992; 127:772–777
7. Lucey MR, Merion RM, Henley KS, Campbell DA Jr, Turcotte JG, Nostrant TT, Blow FC, Beresford T: Selection for and outcome of liver transplantation in alcoholic liver disease. *Gastroenterology* 1992; 102:1736–1741
8. Bird LA, O'Grady G, Harvey JG, Felicity AH, Calne RY, Williams R: Liver transplantation in patients with alcoholic cirrhosis: selection criteria and rates of survival and relapse. *Br Med J* 1990; 301:15–17
9. Poynard T, Naveau S, Doffoel M, Boudjema K, Vanlemmens C, Manton G, Messner M, Launois B, Samuel D, Cherqui D, Pageaux G, Bernard PH, Calmus Y, Zarski JP, Miquet JP, Chaput JC: Evaluation of efficacy of liver transplantation in alcoholic cirrhosis using matched and simulated controls: 5-year survival. Multi-centre group. *J Hepatol* 1999; 30:1130–1137
10. Belle SH, Beringer KC, Deter KM: Liver transplantation for alcoholic liver disease in the United States: 1988 to 1995. *Liver Transpl Surg* 1997; 3:212–219
11. Gish RG, Lee AH, Keefe EB, Rome H, Concepcion W, Esquivel C: Liver transplantation for patients with alcoholism and end-stage liver disease. *Am J Gastroenterol* 1993; 88:1337–1342
12. Conry-Cantilena C, VanRaden M, Gibble J, Melpolder J, Viladomiu L, Cheung L, DiBisceglie A, Hoofnagle J, Shih JW, et al: Routes of infection, viremia, and liver disease in blood donors found to have hepatitis C virus infection. *New Engl J Med* 1996; 334:1691–1696
13. Alter MJ, Margolis HS, Bell BP, Bice SD, Buffington J, Chamberland M, Coleman PJ, Cummings BA, Dentinger CM, Garfein RS, Hodgson W, Braatz Ivie K, Kelly MG, Khabbaz R, Lyerla R, Mahoney LD, Mast EE, Moyer LA, Sabin KM, Shapiro CN, Venczel LV, Wasley A, Williams IA: Recommendations for Prevention and Control of Hepatitis C Virus (HCV) Infection and HCV-Related Chronic Disease. Atlanta, Centers for Disease Control and Prevention, Oct 16, 1998
14. National Institute on Drug Abuse: Facts About Drug Abuse and Hepatitis C. Rockville, Md, NIDA, 2001
15. Management of Hepatitis C. NIH Consensus Statement Online 1997; 15(3):1–41
16. Goldstein ST, Alter MJ, Williams IT, Moyer LA, Judson FN, Mottram K, Fleenor M, Ryder PL, Margolis HS: Incidence and risk factors for acute hepatitis B in the United States, 1982–1998: implications for vaccination programs. *J Infect Dis* 2002; 185:713–719
17. DiMartini A, Weinrieb R, Fireman M: Liver transplantation in patients with alcohol and other substance use disorders. *Psychiatr Clin North Am* 2002; 25:195–209
18. Blume SB: Women and alcohol: a review. *JAMA* 1986; 256:1467–1470
19. Diehl AM: Alcoholic liver disease. *Liver Transpl Surg* 1997; 3:206–211
20. Beresford TP, Turcotte JG, Merion R, Burtch G, Blow FC, Campbell D, Brower KJ, Coffman K, Lucey M: A rational approach to liver transplantation for the alcoholic patient. *Psychosomatics* 1990; 31:241–254
21. DiMartini A: Evaluation and listing of alcoholic cirrhotics for liver transplantation, in *Proceedings of the Liver Transplantation for Alcoholic Liver Disease Conference*. Bethesda, Md, National Institute on Alcohol Abuse and Alcoholism, 1996
22. Weinrieb RM, Van Horn DH, McLellan AT, Volpicelli JR, Calarco JS, Lucey MR: Drinking behavior and motivation for treatment among alcohol-dependent liver transplant candidates. *J Addict Dis* 2001; 20:105–119
23. Cloninger CR: Neurogenetic adaptive mechanisms in alcoholism. *Science* 1987; 236:410–416
24. Marshall AW, Kingstone D, Boss M, Morgan MY: Ethanol elimination in males and females: relationship to menstrual cycle and body composition. *Hepatology* 1983; 3:701–706
25. Arthur MJP, Lee A, Wright R: Sex differences in the metabolism of ethanol and acetaldehyde in normal subjects. *Clin Sci* 1984; 67:397–401
26. Piazza NJ, Vrbka JL, Yeager RD: Telescoping of alcoholism in women alcoholics. *Int J Addict* 1989; 24:19–28
27. Zdilar D, Franco-Bronson K, Buchler N, Locala J, Younossi Z: Hepatitis C, interferon alfa, and depression. *Hepatology* 2000; 31:1207–1211
28. Trzepacz PT, DiMartini AF, Gupta B: Psychopharmacologic issues in transplantation, in *The Transplantation Patient: Biological, Psychosocial and Ethical Issues in Organ Transplantation*. Edited by Trzepacz PT, DiMartini AF. Cambridge, UK, Cambridge University Press, 2000, pp 187–199