Chapter 5: Future Research

Question 1b (Relation of Initial Liver Biopsy Findings to Outcomes of Treatment)

Future treatment studies need to be designed to appropriately answer the question of whether initial liver biopsy findings are associated with a virologic or histologic response to therapy. These studies should use standard techniques for obtaining adequate liver biopsy samples and standardized reporting of liver biopsy results. The studies also should report the details of both univariate and multivariate analyses of the relation of initial biopsy findings to outcomes, including adjusted and unadjusted parameter estimates of the relationship. Such studies would help to provide better estimates of the independent value of liver biopsy in predicting outcomes of treatment options.

Question 1e (Tests for Predicting Fibrosis on Liver Biopsy)

Future studies need to be designed to address this question more directly. Such studies should give attention to the methodologic limitations we encountered in trying to extract meaningful information from the studies performed to date. In particular, the studies should provide enough details about the liver biopsy methods to convince readers of the adequacy of the reference standard. Future studies also should give more attention to the potential value of a panel of tests for predicting fibrosis on liver biopsy.

Questions 2a/c (Treatment of Chronic Hepatitis C)

Future studies need to be designed to further address the questions of the optimal doses and duration of therapies. In addition, randomized controlled trials should include traditionally understudied populations with high rates of hepatitis C, such as blacks, injection drug users, alcoholics, and persons with renal disease or HIV. In particular, randomized controlled trials of treatments for chronic hepatitis C should include subgroup analysis by sex and race/ethinicity, as some studies have suggested different response rates between women and men and between different racial/ethnic groups. Such studies should give attention to the methodologic limitations we encountered in trying to extract information from the studies performed to date.

Question 2d (Long-term Outcomes of Chronic Hepatitis C)

Future studies will need to assess the long-term outcomes of current treatment options, particularly studies with standard interferon plus ribavirin, as well as new studies with peginterferon. Although some data have suggested that longer treatment is better for improving virologic outcomes, little is known about the long-term outcomes of different treatment

durations. Finally, while natural history studies may no longer be practical in the current treatment era, following certain subgroups at high risk for complications— such as patients co-infected with HIV or hepatitis B, injection drug users, and alcoholics— will be useful in making clinical recommendations regarding follow-up for these patients.

Questions 3a and 3b (Screening for HCC)

Future studies should include randomized controlled trials of screening for HCC in patients with chronic hepatitis C. While it may be difficult to conduct large randomized controlled trials in all patients with hepatitis C, including patients at highest risk for HCC in screening trials will make it more likely for future research to determine definitively the benefits of screening. Future studies should consider the use of a combination of screening tests and should consider examining the relative cost-effectiveness of alternative strategies.

Overall Areas of Future Research

Most studies reviewed provided limited information on the type and degree of involvement of the funding source. Consistent with new reporting guidelines accepted by many major journals, this information should become part of the standard data report in future trials.[170]

To improve the quality of publications on these study questions, standardized methods should be developed and disseminated to investigators. Journals should encourage standardized approaches to presenting data on these questions. For published articles, full copies of protocols should be made available, perhaps on the Web. Detailed descriptions of methods are important because the pressure to shorten manuscripts often is met by reducing the description of study methods.