

Hepatitis C

UPDATE

Canadian Hemophilia Society
We're all related  by blood.

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INTRODUCTION

BY MICHAEL MCCARTHY, *Guest Editor, Chair CHS, Hepatitis C Task Force*

I am pleased to have the opportunity to introduce the Supplement to *Hemophilia Today – Hepatitis C Update*. This issue really represents how far we have come in addressing the needs of those in our community who are infected with hepatitis C. After years of advocating to governments about the seriousness of this virus, we are now seeing an effort to help those infected and affected.

The issue contains a variety of articles by medical experts relating to the care and treatment of persons infected with hepatitis C. We have tried to present as much information as possible to our readers to help them make informed decisions. It is encouraging to read how the medical issues relating to hepatitis C are being openly debated with the individuals' interest at the forefront.

Topics addressed in this issue include transmission, testing, treatment options, the pros and cons of liver biopsies, and liver transplantation. After years of having only one treatment option (monotherapy interferon) it is now encouraging to read about new treatments. The development of combination drug therapies promises to provide sufferers with renewed hope that hepatitis C can be controlled and eventually eradicated.

This supplement also addresses issues specific to hepatitis C and hemophilia and other inherited bleeding disorders. Hepatitis C is now the number one cause of death for persons with hemophilia. Treatment issues regarding hepatitis C and hemophilia pose a challenge to our treating physicians. Co-infection with HIV plays prominently in determining treatment options. The issue of the co-infected not being eligible for liver transplantation presents our greatest challenge.

Living with hepatitis C takes its toll not only on those who are infected but also on families at home. It causes stress in the workplace and limits the quality of life at play. Reading the personal testimonies of Canadians that are suffering from the effects of hepatitis C is a poignant reminder of the human face that is behind the disease. The determination of these brave people to lead normal lives, in spite of living with a serious life-threatening illness, is a testament to their courage.

Health Canada has signaled that it is recognizing hepatitis C as a major health concern by establishing the Hepatitis C Division and by providing 50 million dollars over 5 years to implement community based programming, research and public health initiatives. Funding from Health Canada will enable the key national stakeholders to organize a national forum to discuss and debate current hepatitis C issues. The CHS is taking the lead role in the planning of a National Hepatitis C Conference. The conference, planned for spring 2001, will provide a forum for researchers, clinicians, healthcare providers and persons infected with hepatitis C to have access to cutting edge information and state of the art practices for the treatment and management of hepatitis C.

Finally in this special edition an update of the 1986-1990 Hepatitis C Compensation Program is reviewed. This issue continues to be a contentious one in our community.

Efforts are ongoing to provide financial assistance to the victims as soon as possible but the road to justice has been full of bumps. The CHS will continue to advocate for all victims of tainted blood regardless of date of infection. The CHS believes that eventually all governments will follow Justice Krever's recommendation and acknowledge the need for full accountability and provide financial assistance to all.

As you read through this special issue you will see that our efforts on behalf of those suffering from the effects of hepatitis C have produced results. It is our hope that tomorrow will provide an eventual cure for this dreaded disease.

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**The Canadian Hemophilia Society exists
to improve the quality of life for all
persons with hemophilia and other
inherited bleeding disorders.**

The purpose of this *Hepatitis C Update*
is to inform persons living with
hepatitis C about current news
and relevant issues.

Opinions expressed are those of writers
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THE MANY FACES OF HCV

BARRY ISAAC Ph.D. *Editor, Hemophilia Today*

When our Editorial Board met through a teleconference call earlier this year to discuss the contents of this special issue of *Hemophilia Today*, we decided that an article featuring those suffering in various ways with HCV would be both interesting and informative. I embarked on a telephonic odyssey across Canada, speaking with the four individuals who agreed to tell us their



stories: Neil Van Dusen in Halifax, Karttik Shah in Toronto, Catherine Hordos in Calgary and a family in Victoria. (As one of the boys in this family is quite sensitive about his condition, we have agreed not to use their real names.) Each suffers from HCV with the exception of the West Coast family, whose two sons, both hemophiliacs, have different stories: the youngest has HCV, while the eldest, who also has an inhibitor to factor VIII, even with all of his infusions, tests negative to hepatitis C. Karttik Shah also has the added burden of being HIV positive, so his life may be further complicated because of the co-infections. We had intended to include an interview with Rob Friesen in Winnipeg - in fact, the interview took place, but for some reason it was not recorded by the telephone company as had been arranged. So we apologize to Mr. Friesen and thank him for generously giving us his time. My memory is not good enough to reconstruct the details of our conversation.

Describing himself as always being a "sick kid," suffering with all kinds of viruses, Karttik Shah was originally diagnosed with HIV when he was eight years old and with HCV in 1991. He has been hospitalized twice during the past year or so: once for a condition called "HIV Related Joint Issue". This problem looks very much like a "normal" hemorrhage or attack of arthritis; the joint swells, becomes tender and extremely painful, sometimes to the point where even morphine offers little relief. Mr Shah describes the pain as throbbing and different than that which one feels from a bleed. One of these episodes required more than a week in hospital. Steroids were administered, but the episode lasted more than a month. He was also hospitalized a year ago this month in Intensive Care with an anaphylactic reaction to one of his AIDS medications. Mr Shah says this was a close call: he was in the hospital when he took the drug, luckily; for within about nine minutes he lapsed into unconsciousness, where he remained for twelve hours. It is not at all clear if his co-



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infection with HCV had any impact on these two episodes.

However, Mr Shah has grade three fibrosis of the liver, esophageal varicities and portal hypertension. And his retelling of the experience of a biopsy is frightful. When his ALT levels reached over 900, the physicians decided that a biopsy had to be done. But Mr Shah's biopsy had to be attempted twice because of the extensive cirrhosis, which makes the liver tissue tough and fibrous. He describes the actual biopsy as being like "a kicking in the gut, repeatedly," reducing him to tears. The pain was extreme enough that he had to have Demerol.

He now takes medication for the portal hypertension as he is at risk for bleeding from the extended blood vessels in his esophagus. But he describes his general health as being quite good. He is so sensitive to reactions from the protease inhibitors he tried to take to counter AIDS (they have caused some bleeding in his joints and other areas) that he has had to quit taking them. And even though he says that most of his problems have been caused by AIDS (shingles and other opportunistic infections), he admits that he has occasional pain in his abdomen and his liver is swollen. He has been told that the pain in his liver is from the organ capsule expanding as the liver swells from the cirrhosis. He has also been informed that others with HCV have experienced the same kind of discomfort.

Mr Shah says he has had no negative feedback from his friends, who treat him simply as one of the guys. Neither AIDS nor HCV have caused any problems for him in his normal relationships. While he has reduced his workload because of his health (he was a full time student in medicine at McMaster University), he has been able to continue his studies, while experiencing less stress, as a part time student in social work at Ryerson Institute in Toronto. As well, he continues to work in financial investments, which is the primary source of his income.

While he looks forward to the compensation package for HCV sufferers, Mr Shah says that his life will not change very much when it finally arrives. As his needs are quite few, the actual monies will have little impact on his life. He says that he has trouble making long-term plans simply because of his compromised health. He lives pretty much on a day to day basis, a story that is familiar to many of us, but at the same time he has a good outlook on life in general and looks forward to each new experience with a kind of wonder. This philosophy is shared with Catherine Hordos.

First diagnosed in the 1980s with non-A, non-B hepatitis, Ms Hordos, who has mild hemophilia B, tested positive for HCV in 1990. She has had very few problems, only suffering from one spell of fatigue in the middle 1990s. Since then she has had her liver enzymes tested every two or three months, but they have remained reasonably low. Her specialist wants to put her on interferon, but she is unwilling to undergo a biopsy until

her enzyme levels are significantly higher. Her attitude is delightful. When her liver specialist recently attempted to convince her that the new forms of interferon had fewer side effects, her response was, "You haven't made a sale yet." She believes that if she keeps treating her liver with respect, totally abstaining from alcohol and taking such forms of natural treatment as milk thistle, the hepatitis C might not raise its horrid head.

Ms Hordos's one concern is that she, like so many others, will not receive compensation for acquiring HCV through blood products because she was not infused with blood during the proscribed period of time: 1986 to 1990. She misses the compensation period by four months because her mild hemophilia did not require her to have blood or blood products very often. She is angry both for herself and for others who are extremely sick with HCV but who fall outside the compensation period like herself. She feels "almost abandoned and violated" by the Federal and Provincial governments, which, in her opinion, ought to be providing help.

But for the time being she is content to continue her life without worrying herself unduly about the disease. While she worries a bit about the future, wondering if she will finally become ill, she laughingly admits, "I might be in denial." But her attitude towards life is a testament to the power of a good humour and a smile. When Ms Hordos feels she really needs treatment for HCV, she will have it; until then, don't cast shadows on her disposition. And the youngest son in the West Coast family, "Tom," feels roughly the same way.

The two sons, "Tom", aged 16, and "Ben," aged 19, are both factor VIII hemophiliacs, and the eldest has inhibitors. Both boys test positive to the HCV antibody, but only the youngest is positive for the PCR test. Ben is in all probability free of the virus, for he did not test positive until the third generation test was used. This indicates that, while he has been infected with HCV at some point, he has probably cleared the virus. But Tom has HCV, and his attitude seems to be if he doesn't think too much about his infection perhaps it will never harm him. He only found out he tests positive just before Christmas. He has told his friends about his hemophilia, but he is having some problems coming to terms with his HCV status. In fact, it may be the case that he has not yet figured out that his brother is HCV free, his mother says. Or it may simply be that he is not talking about HCV with his mother.

So far, Tom has had few problems with his liver, only experiencing one large spike in his liver function tests in 1990, but there have been no other manifestations of disease since then. That is good news, of course, for Tom and his mom. However, his mother says that what Tom wants is a test that will tell him whether or not he will get sick, not like the PCR test that simply shows a patient is carrying live, replicating virus but with no indication of whether or not this will progress to actual cirrhosis or

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worse. Like many of us, Tom finds not knowing the extent of his disease is actually worse than knowing he is really sick: the uncertainty is the worst state of all. As a result neither Tom nor his mom have asked for, nor received, his PCR log figures, the numbers that indicates one's virus load. Tom's mom feels that the fact he has not become ill yet is a good sign, for she believes that those who get sick from HCV soon after their exposure to the virus are the ones who might fare the worst. Tom has been told that the fact he was exposed to HCV at a young age is in his favour: his immune system was stronger. He has been informed that the older the patient at the point of infection, the worse the outcome might be.

As part of the educational approach, Tom and Ben's mom has told the boys that, in fact, they are not sick; they have a communicable illness that they must be careful about around their friends. And the issue of safer sex has been a topic as well. Their mother believes that openness and honesty are the keys to handling the disease, and that is the way she wants the boys to handle their private relationships, when they become sexually active. For once someone tests positive for HCV, they must assume they are contagious. This means that Ben, whose PCR test indicates he has no live, replicating virus, must also practice safer sex to ensure his partner does not contract HCV.

But at their relatively young age, the boys have more or less shrugged, saying, "Oh, I'm HCV positive. OK." In fact, Tom has managed to work his positive status into a kind of positive in his life, at least so far as the HCV Compensation package is concerned. His mom says he has realized that having a positive PCR test for HCV means that he will get more money, and right now that means something positive to him. As his mother says, this kind of compartmentalization is a good thing right now, as both boys find it easier to deal with their problems this way. Ben, suffering as he has with a severe inhibitor, has learned "not to borrow trouble", his mom says, and so too has Tom. "If [Tom] had to get a virus, I'm glad it was that one", his mother says, indicating that HIV has taken so many young hemophiliacs in B.C. that Ben is the only young man with hemophilia in his age group alive in the province: "If [Tom] had to pick up something, well... , let it be hepatitis." But she has one real worry: from some things that he has let slip, she fears, "Tom's biggest challenge, if he's not ill, will be how to handle it with a partner." Being honest and open with one's sexual partner, particularly during the earlier stages of sexual experience, can be the most harrowing thing of all. So far as the hepatitis C is concerned, Tom's mother believes that by the time he becomes ill, if he ever does, there will be drugs and treatment available to make the disease no more difficult to treat than herpes, for example. Whether or not she is correct, their mother's optimistic outlook will go some distance in making sure the boys maintain their own positive view for the foreseeable future.

Neil van Dusen in Halifax has much less reason to be optimistic. He was diagnosed with HCV after his brother passed away from AIDS and liver failure in 1993. His brother never told his family that he had AIDS and it was a tremendous blow for Mr. van Dusen to learn of his tragic circumstance in such a way. It shook him up enough that he asked to be tested for AIDS, HCV, anything, just to determine if he too was ill with any of the blood borne viruses. The results were a classic "good news, bad news" story; he was free of AIDS, but he had contracted HCV. And his account since then is not good nighttime reading.

He began to suffer the usual symptoms of HCV, and they were severe. The fatigue is so severe that watching television nearly always puts him to sleep; so severe that he has been unable to work for the past four years; so severe that his social life has diminished to the point that he has lost most of his friends; so severe that he and his family have had to move to Halifax from Cape Breton so he could be close to appropriate medical care when the new liver that he needs becomes available. His liver is now cirrhotic enough that it can no longer function as a filter of all the body's toxins the way it should; a liver transplant is the only answer.

The move to Halifax has been particularly difficult for Mr. van Dusen and his family. Both he and his wife, Kim, had to quit their jobs, and the bills just keep piling up. While she has found some work, it is not enough and financial problems are beginning to plague them. Lack of funds and friends mean that they seldom go out to a movie or a restaurant: he would probably fall asleep in any case. The hepatitis has been hard on everyone in his family, and the frustrations are beginning to mount, particularly those caused by their financial situation.

Mr. van Dusen reports that he has "never been so frustrated with politicians," as he is now. "To me it would be great to have (financial) relief for the family," he says. While the disease itself is hard to deal with, it is doubly hard when facing a future without a job, a salary, or any kind of reasonable income. His health problems are compounded by this, and they are mounting as well. He has been suffering from spontaneous bruising in a thigh and nosebleeds, something he never had before. And his recovery from the bleeds takes much longer. But he hopes that the HCV Compensation plan will bring some relief for those problems that money can help, not simply for himself, but for his other brothers as well. Out of four brothers with hemophilia in his family, all have HCV and one is dead. Mr. van Dusen's anger still boils up over that: as he says, "money won't bring him back."

Of the four stories, Mr. van Dusen's is the hardest to listen to and to write about. But one thing stands out in all their comments, whether frustrated or optimistic: a sense of good humour. That seems to be characteristic of families with hemophilia.

CURRENT RISK OF HEPATITIS C WITH THE CANADIAN BLOOD SUPPLY

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Hepatitis C is an inflammatory process of the liver caused by hepatitis C virus (HCV). The virus is present in the blood of infected individuals and can be transmitted through blood transfusion. In addition, HCV can be transmitted through other means which expose an individual to contaminated blood or body fluids, such as sharing drug injecting equipment (the major risk) and less significantly unprotected sex with multiple sexual partners.

Following infection by HCV, individuals develop antibodies against the virus (anti-HCV). However, the antibody does not appear to confer immunity or protection to the individual and merely serves as a marker for HCV infection although some infected individuals do recover from their infection.

Before HCV was discovered in 1989, some transfusion recipients developed post-transfusion hepatitis even though the donated blood was screened for hepatitis B virus and other known bloodborne pathogens. In the last decade, tremendous progress has been made in improving the donor screening questionnaire and donor deferral, in the study of HCV itself, in the development of assays for the detection of HCV infection and in the implementation of screening assays for donated blood. As a result, the current risk of HCV infection associated with blood supply has been successfully reduced to a minimum.

In Canada, Canadian Blood Services (CBS) and HemaQuebec (HQ) are currently responsible for the safe supply of blood to Canadians whereas Health Canada is responsible for the regulation of blood and blood products as well as surveillance activities for bloodborne pathogens. Increased efforts have been made on several fronts to improve the safety of the blood supply.

First, donor selection has been further tightened and a new questionnaire has been designed to reduce the number of donors who might have been exposed to HCV. Anyone who has had hepatitis, has used illicit drugs, or has had a history of risky sexual contact is excluded from donating blood. Blood donated by individuals who have not indicated in the questionnaire of the above major risk factors but has indicated that his or her blood should not be used is discarded confidentially. Consequently, blood collected at the present time carries a much lower risk of being contaminated with bloodborne pathogens including HCV, HBV and others even before the blood is screened for these pathogens. According to data from CBS, the anti-HCV positive rate among donors was at 0.02% from January 1 to September 30, 1999, compared to 0.16% in 1990.

Following the collection of blood from donors, sensitive and specific assays are used to screen out any blood units collected that may have been contaminated with HCV. Currently, both CBS and HQ use the third generation of enzyme immunoassay (EIA) for initial detection of anti-HCV followed by supplementary testing with the third generation of recombinant immunoblotting assay (RIBA). It is estimated by the Laboratory Centre for Disease Control (LCDC) that with such a stringent screening scheme the current risk of HCV in the Canadian blood supply should be lower than 1 in 100,000, that is, among 100,000 blood donations, less than one unit of blood may be contaminated by HCV. Recently, a more sensitive nucleic acid testing method has been introduced as an investigative project for HCV testing of pooled blood, which should further reduce the risk of HCV transmission in the Canadian blood supply.

To facilitate the detection of post-transfusion hepatitis infections, a surveillance system for blood recipients is being piloted in four provinces by LCDC. Once established, the system will follow up blood transfusion recipients in those provinces for evidence of infection with HCV, HBV and other blood borne pathogens, and thus will be able to detect a breakdown in the safety procedures used in the blood supply and to assess the risk of new or emerging bloodborne infections.

With the reduction of risk associated with blood supply, other transmission routes become relatively more important in the spreading of HCV in this country. In addition to sharing drug injecting equipment, which may account for as much as two-thirds of current hepatitis C infections in Canada, the risk of transmission through inapparent parenteral exposure and sexual activities is being actively investigated. According to data from the enhanced surveillance in Calgary, Edmonton, Winnipeg and Ottawa-Carleton, approximately 7% of acute hepatitis C cases could be attributed to tattooing or body piercing and 4% to sexual contact with HCV infected individuals. To prevent transmission of hepatitis C through the former routes, LCDC has issued a guideline *Infection Prevention and Control Practices for Personal Services: Tattooing, Ear/Body Piercing, and Electrolysis (1999)*. For sexual transmission, the report LCDC prepared from the Second Canadian Consensus Conference on Hepatitis C (*Hepatitis C - Prevention and Control: A Public Health Consensus, 1999*) recommends that people with multiple sexual partners should practise safer sex, e.g. by using barrier methods, and longstanding sexual partners need to be informed that although the risk is low it is not absent, and barrier methods are available.

A THERAPEUTIC TRIAL OF INTERFERON ALPHA-2B PLUS RIBAVIRIN IN SUBJECTS WITH CONGENITAL COAGULATION ABNORMALITIES INFECTED WITH HEPATITIS C WITH OR WITHOUT HIV CO-INFECTION

BY JENNY HEATHCOTE, MD

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Drs. Jenny Heathcote (liver specialist at Toronto Western Hospital), Jerome Teitel (blood specialist in charge of the hemophilia program at St. Michael's Hospital in Toronto) and Ignatius (Bill) Fong (infectious diseases in charge of the HIV clinic at St. Michael's Hospital) were successful in securing funding to conduct the above study from monies donated by both the Medical Research Council of Canada and Schering Canada in June of 1998. Because this treatment with combination therapy otherwise called Rebetron has not been licensed for use in persons who are co-infected with HIV, the protocol had to be reviewed by the Health Protection Branch in Ottawa. Unfortunately this took an inordinate length of time, almost one year. Many other issues also had to be settled which further delayed the start of this study, but in the late summer of 1999 enrollment was started. There are currently 7 centres in Canada who have agreed to recruit suitable subjects to this study. The central site is in Toronto, other sites are in Hamilton, London, Edmonton, Calgary, Vancouver and Halifax. Both the liver specialists and the hemophilia specialists at these sites are closely involved with this study. Persons suitable for this study include all those who have hepatitis C with abnormal liver enzymes with or without co-infection with HIV. There are a number of exclusion criteria simply because in certain people it is not safe to use Rebetron: for example those who have in addition chronic renal failure. There are also certain requirements with regards to the CD4 count in patients who are infected with HIV, ie: $CD4 > 200$. Those patients who are currently taking AZT will need to be changed over to another anti-retroviral drug prior to starting Rebetron as it is contraindicated to give these two drugs together.

Prior to entering the study certain conditions are necessary. First, it has to be demonstrated that the blood aminotransferase (ALT) levels are elevated. If the ALT levels remain elevated then the patient is required to undergo a liver biopsy. In most centres the liver biopsy will be done via the transjugular route with appropriate factor support being given within one hour prior to the biopsy and again the following day. At some centres physicians prefer to do a regular percutaneous liver biopsy again with appropriate factor coverage. To date 30 biopsies have been performed, there have been only four minor complications, none required either a blood transfusion or stay overnight in hospital, i.e.: all procedures are done as an out-patient. The tissue obtained on liver biopsy indicates the degree of severity of both inflammation and scar tissue. Biopsy is the only way that one can tell whether a patient has cirrhosis. If cirrhosis is found on biopsy other investigations are required to make sure that complications of their liver disease have not occurred and to prevent them occurring in the future.

Once a patient has fulfilled all the criteria for entering the study they will be randomized to one of two treatment groups. One treatment group will receive standard Rebetron therapy, that is 3 million units of Interferon alpha-2b given by subcutaneous injection every other day and daily oral Ribavirin, either 1000 or 1200 mg per day depending on body weight. The other group will be randomized to daily

treatment with Interferon alfa 2b for the first 8 weeks (induction therapy) as well as daily oral Ribavirin. Thereafter the treatment will become as for standard therapy. The reason why the two different treatment regimens are being compared is to see if those who receive the daily Interferon treatment for the first 8 weeks have a better response rate than those who are receiving standard treatment. Neither the patient, nurse or physician can dictate which treatment group is chosen, it has to be by random allocation – standard practice in all clinical trials of therapy. Regardless of which treatment group a patient finds themselves in, the treatment will be no less than would be received outside this therapeutic trial. Depending on the genotype (there are six genotypes of hepatitis C) treatment will be for 24 weeks or for 48 weeks.

So far 16 patients have been recruited to this study. No patient has had to withdraw because of adverse side effects. Data published suggests that those patients who have been treated with Interferon in the past but who responded and then relapsed have a very good chance (49%) of responding to retreatment with Rebetron. These patients are therefore suitable for this trial as well as those who have never received any treatment in the past. In those who have never received treatment before the overall response rate to treatment with standard Rebetron therapy is between 29 and 43%.

During treatment blood tests will be taken at frequent intervals to test the liver biochemistry and the levels of virus present. If detectable HCV RNA remains present after 12 weeks of therapy then the treatment will be abandoned. If the virus test is negative at 12 weeks then the treatment will be continued. In those who complete therapy, once treatment has been stopped the patient will be followed up for a full six months after treatment cessation as the virus test at 6 months after stopping treatment is crucial. Those patients in whom HCV RNA is undetectable 24 weeks after stopping treatment have a 95% chance of remaining free of the virus for up to 10 years, i.e.: a cure. Studies to date of antiviral therapy in patients with hepatitis C co-infected with HIV suggest that the response rate is somewhat lower but treatment is still worthwhile and the relapse rate after successful treatment is no higher than in persons without HIV infection. As the treatment for HIV has so markedly improved over the last few years the importance of treating the hepatitis C is particularly important.

At a recent meeting held in Banff of all the Canadian physicians who treat subjects with hemophilia and other congenital coagulation disorders, a morning discussion was devoted to the issue of hepatitis C. Once the results of all previously published studies were discussed it became clear to everyone present that it would be foolish to ignore the potential benefits of this MRC/Industry study, as the therapy of hepatitis C has improved so dramatically over the last three years. It is appreciated, however, that there are still many patients who do not respond to the current therapies available. Such patients will nevertheless continue to be followed and we are confident that there will be other new therapies available down the road.

LIVER BIOPSIES IN PEOPLE WITH HEMOPHILIA

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The issue of whether or not liver biopsies should be performed in people with hemophilia and chronic hepatitis C has engendered a great deal of controversy in members of the hemophilia community and among their treating physicians. I believe that the decision regarding biopsy must be made individually for each person with a bleeding disorder, and that furthermore it must be broken down into two distinct questions. The first is whether or not liver biopsy will be of substantial assistance in managing chronic hepatitis. The second question is how much riskier the liver biopsy is likely to be in that individual because of his or her hemophilia or other bleeding disorder. Arriving at a decision is complicated because it requires that three different parties contribute their knowledge and views, a situation which can make it difficult to achieve consensus. The question regarding the usefulness of a biopsy can be best answered by a hepatologist, whereas the question regarding specific risk must be answered by a hematologist. Of course the third key player in the mix is the patient himself, who will have certain attitudes and preferences which must be respected, and who in any event is the final judge about whether or not a biopsy will be performed.

Our hepatologist colleagues tell us that liver biopsy is the only way to accurately assess the extent of liver damage in chronic hepatitis C. They also tell us that information gained from liver biopsy is of great value in counseling individuals about their risk of complications of chronic hepatitis, and in making decisions about the value of treatment. As a non-specialist I must accept the opinions of the experts, which are based on knowledge and experience which are beyond my own area of expertise. As a hematologist and hemophilia specialist I will therefore concentrate on the question of safety of liver biopsy in the patient with a bleeding disorder.

First, it should be noted that like any invasive procedure, liver biopsy carries inherent risks, including a risk of bleeding (which may be intensified in cases in which the liver disease itself results in impaired blood clotting). However, the magnitude of this risk is small. In a 1993 editorial which reviewed nine studies performed over the previous 20 years, the authors found that significant bleeding complications occurred in 0.65% of over 2000 liver biopsies¹. Of note, all the biopsies in these studies had been performed by the percutaneous route, in which a needle is inserted blindly through the skin to obtain the liver sample. Currently, the preferred method for liver biopsy in patients with a bleeding tendency is the transvenous approach, in which a catheter is inserted through a vein and directed into the liver under X-ray guidance. A cutting needle is inserted through the catheter to obtain the sample. This guided approach is safer than the percutaneous route and in skilled hands it yields excellent biopsy samples.

To accurately assess the additional risk of liver biopsy in the person with hemophilia we must consider our ability to treat the bleeding disorder, and the actual experience with liver biopsies in this setting, as reported in the medical literature. In the absence of an inhibitor antibody, safe and effective replacement therapy can temporarily reverse congenital deficiency of factor VIII or IX. In this sense hemophilia is temporarily abolished by treatment. Thus, for hemophiliacs who respond well to factor VIII and IX concentrates (the large majority of affected individuals), liver biopsy should have precisely the same risks as it does in the person without a congenital bleeding disorder. Does the evidence support this assumption?

An early report published by Dr. Lou Aledort and colleagues in 1985 suggested that liver biopsy was in fact quite risky in people with hemophilia². They reported a 12.5% incidence of bleeding into the abdominal cavity, and anecdotally referred to two resultant deaths. However, this study was based on a survey questionnaire, and subsequent prospective studies do not support their findings. The group from Sheffield in the UK reported on over 100 liver biopsies done through their hemophilia program over a 20 year period³. Only one significant bleed occurred, and it was not fatal. Other British groups from Cambridge and from Edinburgh have reported on 35 and 50 biopsies respectively, with no bleeding complications whatsoever^{4,5}. In all the above reports liver biopsy was performed by the percutaneous route, described above. There is much less published information on the use of the safer transvenous approach in the hemophilia population. Dr. Craig Kessler and colleagues reported a very small group of six hemophiliacs in whom this approach was used without complications⁶. In our own hemophilia program in Toronto, we have now performed 30 transvenous liver biopsies done as outpatient procedures in patients with hemophilia or von Willebrand's disease. We observed two very minor bleeding complications, only one of which required administration of an extra dose of factor concentrate (due to slight oozing at the puncture site). We hope to present our experience at the 2000 WFH Congress in Montréal.

Based on the above considerations, I believe that in most cases the presence or absence of hemophilia should not be considered as a factor in the decision whether or not to perform a liver biopsy. To do so would be to subject the hemophiliac to unfair discrimination on the basis of his bleeding disorder. There are indeed some hemophiliacs in whom the bleeding risk may be unacceptably high, and in whom this should be included in the decision making process regarding biopsy. These include people with inhibitor antibodies, and those who don't have access to a hemophilia treatment centre through which a prophylactic

ABOUT BIOPSIES: EXTRACT FROM AN EXPERT OPINION

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factor replacement regimen can be designed and supervised. However, in the large majority of cases logic and fairness would suggest that precisely the same criteria should apply to those with and those without hemophilia.

In summary, I am eager to closely follow the ongoing debate among knowledgeable experts about whether or not liver biopsies need to be done to manage any patient with chronic hepatitis C, and to apply new knowledge as it emerges to people with hemophilia. But I reject the argument that all hemophiliacs should be considered to be at higher risk as a group, and that the potentially valuable information which can be gained from the safe procedure of liver biopsy should be systematically withheld from them.

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"Hepatic biopsy is a very important tool for assessing the severity of hepatic disease. In fact, it is the only tool currently available allowing early diagnosis of cirrhosis..."

The natural history of hepatitis C in hemophiliacs does not seem to differ from that described for other patients without hemophilia. In this group too, the presence of the AIDS virus accelerates progression of hepatitis C. A study recently published in England (Darby SC et al. Lancet 350;1425-1431, 1997) dealt with 4865 male hemophiliacs treated between 1965 and 1985 and followed until 1993. The findings showed that mortality from hepatoma (tumor of the liver) is 5.6 times higher among hemophiliacs than in the general population... The risk of dying from the consequences of cirrhosis or liver cancer is thus clearly demonstrated in these patients and is a growing problem. Only effective treatment can or will be able to control this problem.

Given the risk of hemorrhage associated with any invasive procedure, a liver biopsy may only be performed on a hemophiliac patient after coagulation has been corrected by administering an appropriate quantity of clotting factors, and if the jugular vein approach is used (transjugular biopsy). Although considered safe, this method is not totally risk-free, the main danger being perforation of the liver or intra-hepatic hematoma.

LIVER BIOPSY: PATIENT PERSPECTIVES

My name is Jeff and I am 43 years old. I am one of three hemophiliacs (one of two surviving) in a family of four boys and 1 girl. I have mild (9%) factor VIII (type A) hemophilia and tested positive to HCV in 1993.

In 1994 I participated in a study to decide the effectiveness of Interferon-A for treating hepatitis C. Unfortunately, I was amongst the majority for whom the treatment had no lasting effect. In the fall of 1999 my family doctor referred to me a researcher who was treating hepatitis C with the Interferon/Ribivarin combination therapy. When I visited that physician I discovered that he was locally responsible for the combination therapy study for persons with bleeding disorders. I am convinced that he told me a liver biopsy was a prerequisite to being considered for the study. He assured me that while every procedure has its risks, a transvenous biopsy would be relatively painless, and carried little of the risk associated with the usual technique. All of this was corroborated by another individual who had had a transjugular biopsy with little or no side effects.

On the morning of the biopsy I received a 3400 unit dose of Kogenate factor VIII immediately prior to the procedure. It was only after I was wheeled into the angio room that I was informed that my biopsy was going to be transfemoral and not transjugular. I found the procedure to be painful and unpleasant. I spent the next six hours in the angio recovery room waiting for the incision to stop bleeding. After spending all that time flat on my back, it was determined that I required more factor 8. I received more factor again the next morning. For days afterward I continued to have substantial pain in my groin and made at least two visits to emergency to receive factor. I still have occasional twinges of pain in my groin some months after the procedure.

I have been asked by others if I thought they should consent to a biopsy. My opinion is that although the medical community continue to suggest that a biopsy is the only way to have a conclusive diagnosis of the condition of the liver, I believe that a biopsy is an unnecessarily risky procedure for hemophiliacs. Given the fact that the disease has every possibility of, at the very least, reducing a person's quality of life, if not worse, I think that a diagnosis of chronic hepatitis C is sufficient reason to proceed with any treatment that might stop the virus or at least reduce the impact of the symptoms and improve the chances for an individual to live a reasonably healthy, normal life.

What were the results of my biopsy? Inconclusive. Even though twelve tiny chunks of my liver were extracted, only one was investigated by the pathologist. His determination was that there was evidence of portal fibrosis, but the sample was not good enough to determine the extent of the fibrosis or whether or not cirrhosis was present. I understand that despite these findings, I am still a candidate for the study. I have to say that I was angry and distressed that the only conclusive evidence was inconclusive and that we knew little more than we did before the biopsy. Its time to review the need for this invasive and costly procedure.

My name is Charles and I am 45. I am the third of four children (three boys and a girl). One of my brothers died a few years ago. I am a severe hemophiliac with factor IX deficiency. I infuse myself every day.

In the early 1990s, I was told I was infected with the hepatitis C virus. This came as a shock to me. My parents were also devastated. In the last few years, I have suffered from jaundice, stomach pains, fatigue and frequent indigestion, and I think all these problems are owing to the hepatitis.

One day, my gastroenterologist asked me if I would agree to a biopsy. He said my enzyme levels were too high and he was afraid I had cirrhosis. He explained that the biopsy would provide information about the health of my liver. It would involve removing a tiny piece of the liver through a vein in my neck. This is called a transjugular biopsy.

The procedure was prepared with the help of my hematologist at the hemophilia treatment centre. Before the biopsy, I infused myself with a lot of clotting factor to prevent bleeding. I was awake throughout but I felt no pain, except for a minute or two at the end. After the procedure, I was again infused with clotting factor. My doctor decided to keep me in the hospital under observation, especially as he needed to do other tests concerning my health. I had stomach pain for a few days.

Based on the biopsy results, it was decided to give me interferon treatment. I feel the biopsy went well and did not give me any problems afterwards. In general, I was satisfied with the procedure.

HEPATITIS C MEDICAL UPDATE

BY MARC DESCHÊNES, MD

Hepatologist, Division of Gastroenterology/Hepatology, Royal Victoria Hospital, Montreal, QC

The following article is to inform you on the recent developments in the field of hepatitis C as we now enter our second decade of research on this virus. It will touch upon issues related to the epidemiology of hepatitis C, its natural history, diagnosis, treatment and prevention.

The hepatitis C virus was only discovered back in 1989. Soon after its discovery it became apparent that it was the most common of what we used to refer to back then as non-A, non-B hepatitis. The virus is a ribonucleic acid (RNA) virus, which belongs to the family of flaviviridae viruses. The structure of the virus is now well identified, although the functions of its certain regions still remains to be determined. We now realise that there is a great deal of genetic variability to the virus which makes the design of a vaccine difficult. It is best to think of hepatitis C as a family of viruses which can be broken down into at least six different strains or genotypes; these are referred to as genotypes 1-6. The most common genotype in Canada is genotype 1, however genotypes 2 and 3 are not uncommon. Genotype 3 is more prevalent amongst multitransfused hemophiliacs than the general population.

It is estimated that the prevalence of hepatitis C in the world is 3%. In Canada the prevalence is thought to be less than 1%. The greatest prevalence is found in the population age 30-49 years old. Nowadays, most new cases are reported in people ages 20-39 years who are using intravenous drugs. Hepatitis C is responsible for the majority of post-transfusional hepatitis contracted before 1992. And hepatitis C is the principal cause of chronic liver disease in Canada. Decompensated liver disease associated with hepatitis C constitutes the number one indication for liver transplantation in this country.

TRANSMISSION OF HEPATITIS C

The transmission of hepatitis C is essentially through contaminated blood. Whereas, the risk of acquiring hepatitis C through a blood transfusion was in the range of about 5% in the 1980's, with screening of blood donors this risk has now been reduced to less than 1 in 100,000. As well, procedures for inactivation for coagulation factors are now more effective and the risk of transmission using these factors since 1987 is therefore very low; in fact the risk is mostly theoretical. Synthetic or recombinant products which have been in use for factor VIII and factor IX have no risk of transmission of hepatitis C.

The most important means of transmission of hepatitis C nowadays is the use of intravenous drugs. It has been reported that about 60% of people will develop hepatitis C

within one year of use of intravenous drugs. After five years about 90% of users will be infected. The use of intranasal cocaine inhalation is also possibly associated in the transmission of hepatitis C. It seems that the risk here would be associated with the induction of nose bleeds which is quite frequent when cocaine is taken in that fashion.

Historically about 10% of people receiving hemodialysis for renal failure have been found to be infected with hepatitis C. Somehow these people were exposed to contaminated blood during the dialysis process. In recent years most hemodialysis units have segregated themselves and people with hepatitis C from those free of, reducing the risk for newer patients beginning dialysis.

The risk of transmission of hepatitis C when exposed to tattooing, body piercing, electrolysis and acupuncture depends on whether sterile needles are used. Nowadays most facilities offering these services are in observance of universal measures for infection control.

About 1-4% of spouses of people infected with hepatitis C are also infected. Thus it appears that the sexual transmission of hepatitis C is possible but most authorities agree that this risk is quite low in the absence of other risk factors.

The risk of transmitting hepatitis C to a new born baby at birth from a mother infected with hepatitis C is about 5%; however, that risk is increased to a range of 10-15% if the mother is also co-infected with the human immunodeficiency virus (HIV) virus. Thus far, there is no evidence to support one mode of delivery versus another: i.e.-caesarean vs vaginal delivery. Although theoretically possible, transmission of hepatitis C through breastfeeding has never been documented.

As in the use of blood product, the risk of transmission of hepatitis C through transplantation of infected organs has for most practical purposes, been eliminated through the systematic screening of organ donors for hepatitis C.

Although theoretically possible, the risk of acquiring hepatitis C through the close contacts that occur with the daily activities of a household is in practice quite rare.

In the majority of people infected with hepatitis C we are able to identify one of the risk factors; however, a number of people, particularly immigrants to Canada, seem to not have any of these risk factors. It is thought that these people were infected through poorly sterilised syringes or needles when they received health care or vaccinations in their native countries.

HEPATITIS C MEDICAL UPDATE

NATURAL HISTORY OF HEPATITIS C

Most people who contract hepatitis C actually do not get sick enough to consult with a physician at the time. Although people may experience a flu like illness, only about 1 in 5 will consult with their physician. Unfortunately, it appears that the majority of people who are exposed to hepatitis C go on to develop a chronic infection. In the past, we used to quote that 85% of patients went on to develop a chronic infection, but this number has been a subject of debate recently since it has been highlighted that people that get infected at a younger age may have a greater tendency to get rid of the hepatitis C virus after their original infection. As many as 50% of children infected with hepatitis C may actually be able to eliminate the virus. In patients with chronic hepatitis C about 10% per decade will go on to develop significant scarring of the liver or cirrhosis. Therefore, people infected with hepatitis C warrant long term follow-up to determine the evolution of their hepatitis. Once people have cirrhosis about 5% per year will start to show signs of liver failure and 1-4% per year will develop liver cancer or hepatoma. Generally speaking, in people infected with hepatitis C, hepatoma does not occur without cirrhosis.

The following factors seem to influence the progression of hepatitis C and tend to favour the development of cirrhosis: alcohol consumption, an age greater than 40 years old at the time of infection, being a man, as well as the presence of co-infections with HIV or other hepatitis viruses. As well, the duration of infection seems to be a determinant; the longer the duration of infection the greater the risk of developing cirrhosis. As well, people with chronic hepatitis C seem to be at greater risk of developing a severe acute hepatitis if they contract hepatitis A.

There are some manifestations of hepatitis C that lie outside of the liver. These include vasculitis or inflammation of blood vessels, kidney problems termed glomerulonephritis, skin and mucus membrane problems such as porphyria cutanea tarda, lichen planus, Sjögren's syndrome, arthritis, thyroid disease, diabetes and lymphoma.

THE DIAGNOSIS OF HEPATITIS C

Generally speaking, the diagnosis of hepatitis C is made on the basis of a blood test. In a person with the previously mentioned risk factors for contracting hepatitis C who has elevated liver enzyme levels, the presence of the antibody against hepatitis C in the serum is enough to warrant a diagnosis of hepatitis C.

However, under special circumstances, the physician may request a more specific molecular test for hepatitis C or PCR

(polymerase chain reaction) to actually identify the virus itself. Such circumstances include when the diagnosis is unclear or during treatment for hepatitis C. It is also possible to look for the specific genotype of hepatitis C causing the infection. This is generally done prior to initiating treatment for hepatitis C, since the recommended duration of the treatment and the response to the treatment differs for various genotypes of the virus.

At the present time a liver biopsy remains the procedure of choice to evaluate the severity of the liver disease and to give an idea of its future behaviour.

The monitoring of people infected with hepatitis C involves following the liver enzymes and other molecules synthesized or eliminated by the liver to monitor liver function. Most physicians will monitor those at least twice a year. In people with cirrhosis an abdominal ultrasound and a serum alpha-fetoprotein (which is a marker for liver cancer) are usually monitored once or twice a year in screening for liver cancer.

PREVENTATIVE MEASURES AND TREATMENT

Prevention:

It is recommended that people infected with hepatitis C abstain from donating blood.

Education programs targeted at intravenous drug users are necessary in order to decrease the incidence of hepatitis C in our society.

Generally speaking for people in a monogamous relationship we do not recommend that specific means be taken in order to prevent sexual transmission hepatitis C given the very low risk. However, if a "zero" risk is aimed for, indeed the use of barrier methods is advised.

There are studies under way in Canada to define the behaviour of hepatitis C in the context of pregnancy. Currently, however, there is little ground for routinely screening all pregnant women for hepatitis C, since there are no known measures to decrease the transmission to the baby. When it is known that the mother has hepatitis C, breastfeeding should not be discouraged.

Unfortunately, after an exposure to hepatitis C we currently do not have any vaccine that can be given to prevent its transmission. However, we recommend that people who are infected with hepatitis C be vaccinated for hepatitis A and B in order to prevent added liver injury. The most significant intervention that can be brought about in someone infected with hepatitis C is to avoid alcohol consumption. Clearly alcohol consumption adds to the liver injury caused by hepatitis C.

HEPATITIS C MEDICAL UPDATE

Treatment:

Currently the recommended treatment for chronic hepatitis C infection is combination therapy with interferon injected three times a week and with ribavirin taken orally. It is clearly superior to the therapy given in the past which consisted of interferon alone. It is recommended that people with genotype 2 and 3 infections be treated with this regimen for 24 weeks. Those infected with genotype 1 who have low viral levels in the blood should also be treated for 24 weeks. People infected with genotype 1 who have high viral levels should be treated for 48 weeks. But if they do not lose the virus in the blood by 24 weeks of treatment they will likely not respond to further treatment and it should be stopped. It appears that the most significant predictor of the long-term outlook for these people is, whether they achieve a "sustained response", that is normal enzymes and no virus in the blood six months after the end of treatment. Over the long term more than 95% of these people will not show any signs of recurrence of hepatitis activity. Presumably the virus is eradicated with an arrest in the progression of the disease. With the combination therapy of interferon and ribavirin we have such an outcome in roughly 40% of cases. The sustained response rate is 29% for genotype 1 and 65% for genotype 2 and 3 infections. Besides the amount of virus in the blood and the genotype of the hepatitis C virus, the age of the person, male gender, and amount of scarring appear to be the factors that adversely affect the response to combination therapy. However, the factors that could be predictive of a positive outcome with this form of therapy still need to be better defined. For the time being, we recommend this treatment for people who are less than 60 years of age with abnormal liver enzymes and who have at least a moderate amount of inflammation on the liver biopsy, acceptable levels on the complete blood cell count, no important previous psychiatric history, no immunity related disease and no coronary artery disease. The response to treatment is the same for hemophiliacs as for other people and depends on the characteristics listed previously.

There are a number of side effects associated with the treatment with interferon and ribavirin. Interferon causes a flu-like illness especially in the first couple of weeks of treatment. In the long term, however, symptoms such as fatigue, difficulty concentrating, irritability, insomnia, and loss of appetite may persist throughout the treatment. Treatment with interferon may lower the blood counts, the white blood cell count necessary to fight infection and platelets necessary for preventing bleeding. As a modulator of immune function it may promote immunity against oneself and about 10% of people on the treatment will develop a thyroid problem which is usually reversible after the treatment is stopped. It is also advised that the treatment

not be prescribed to people with important psychiatric disorders since they may worsen, particularly those with depression or psychosis. One of the major issues with the use of ribavirin is that it can induce anemia. There is also a concern that ribavirin, which can remain in tissues for a number of months after treatment, may cause malformation to a newborn. It is therefore recommended not to get pregnant while on therapy and for at least six months after the end of the treatment. This recommendation applies to both men and women who are treated. Overall, it is imperative that people being treated with interferon/ribavirin be monitored particularly closely during treatment.

The use of interferon is now reserved for people who are felt not to be able to tolerate the combination with Ribavirin. Interferon alone is given by subcutaneous injection three times a week for 12 months. If liver enzymes do not normalize and people do not lose the hepatitis C virus in their blood by 12 weeks of treatment, the treatment is stopped. These people will not respond to further treatment. This regimen unfortunately, is associated with a sustained response rate in the range of only 10-20% overall.

It is expected that there will be newer medications available in the near future. A polyethyleneglycol-interferon (PEG-interferon) is expected to be available soon. The advantage of this molecule appears to be a prolonged duration of action. It is administered only once a week and a response rate which seems to approach that of combination therapy with interferon/ribavirin. It is currently being tested alone as well as in combination with ribavirin. Other molecules, such as more specific inhibitors of the hepatitis C virus like the helicase, polymerase and protease, are also entering into tests soon. Combination therapies will likely be more successful than the monotherapies, of the past so although the preliminary results of treatment with Interferon were not very encouraging, already our results appear to be better and there is ground for optimism about the future.

CO-INFECTION WITH HIV

HIV has an impact on the behavior of hepatitis C; it causes an increase in the amount of virus in the blood. With the progression of immunosuppression associated with the HIV disease, there seems to be a faster progression to cirrhosis and liver failure. In the past the results of treatment of hepatitis C with interferon used alone were not very favorable. However, it is now the impression of most specialists in the area that the whole natural history of hepatitis C in the context of HIV disease will now have to be revisited. More effective therapy for both HIV and hepatitis C will no doubt affect on their progress. This is presently being studied. Given that presently there is no established therapy

HEPATITIS C MEDICAL UPDATE

for hepatitis C in this setting, people wishing to be treated ideally should do so in the context of well controlled studies.

LIVER TRANSPLANTATION FOR HEPATITIS C RELATED LIVER DISEASE

Hepatitis C related liver disease is now the most common indication for liver transplantation in Canada. It accounts for over 30% of all liver transplantations. Liver transplantations are offered to people infected with hepatitis C who have cirrhosis and are starting to show signs of liver failure, as well as people with small liver cancers. Over the short to midterm the results of transplantation for hepatitis C are quite good. The five-year survival for liver transplantation for hepatitis C related liver disease is the same as that of other indications, in the 70% range.

However, unfortunately liver transplantation does not rid somebody of the hepatitis C virus. Hepatitis C seems to live in other tissues than the liver and after the liver is removed and replaced by a new one we can still detect hepatitis C in the serum of people who have received a liver transplantation. Unfortunately, the majority of people who have a liver transplant for hepatitis C related liver disease, again will develop a hepatitis related to hepatitis C in the months after transplantation. The degree of severity of the hepatitis, however, varies from one person another. Generally speaking, however, the progression of the damage to the liver graft after a transplantation seems to be faster than in people who are not transplanted. In fact about 10% of people transplanted for hepatitis C related liver disease will require a retransplantation because of serious damage to their graft within five years of the initial liver transplantation. Therefore, this is cause of great concern for a number of these people who are now a few years out of their liver transplantation. Also about five percent of people receiving a liver transplant for hepatitis C related liver disease will have a severe recurrence of hepatitis C disease within a few months after liver transplantation and will behave in a subfulminant manner progressing to liver failure within a few months. Therefore, although the overall statistics for transplantation for hepatitis C related liver disease are good, there is certainly cause for concern over the long term for these people. Relatively speaking, there is already a shortage of organs for liver transplantation in the country. If a great number of people will be awaiting a repeat transplantation for hepatitis C, it is expected that the shortage of organs will likely become more acute. Already 10% of people awaiting a liver transplantation in Canada will die before they get the opportunity to be offered a graft. Therefore, if nothing changes this could be the cause of the crisis in this country. Moreover, the results of the re-transplantation are poor.

There have been a number of recent developments in research in the field of hepatitis C in liver transplantation. Whereas treatment with interferon or ribavirin when used alone did not prove to be very effective, the treatment with the combination after liver transplantation is giving us better results. As well, it appears that early treatment after transplantation greatly decrease the rate of re-infection with hepatitis C. A number of studies to that effect are now underway in Canada, the United States and Europe. The results of these studies should be available in the foreseeable future. And thus, there is a lot of work still needed in this area; nevertheless we can be optimistic about the future of liver transplantation in this area.

Given the recent changes in the natural history of HIV disease with the use of more effective antiviral therapy, the issue of liver transplantation in co-infected people with liver disease will have to be revisited. A few centers in the U.S. have already performed transplantations in this situation. However, it is still too early to draw conclusions. Of concern is the effect of immunosuppression to prevent graft rejection on the natural history of HIV disease.

AN ADVOCACY UPDATE

by Michael McCarthy, Chair of the CHS Hepatitis C Task Force

PRE-86 / POST -90 COMPENSATION

The CHS continues to advocate to governments to live up to Justice Krever's number one recommendation and compensate all tainted blood victims. As of today, Ontario and Quebec are the only provincial governments to show leadership and compassion for people excluded from the 1986-1990 compensation settlement. Premier Harris's government has committed two hundred million dollars to help treat Ontario victims equally. He has provided \$10,000 to these victims without any delays or need for lawyers. Moreover, the Ontario Ministry of Health has found the numbers of eligible applicants to be a tenth of what the federal government was projecting. Only 1,950 victims could be found in Ontario: a far cry from earlier estimates of 20,000. Mr. Harris is now committed to distributing the remainder of this money and we applaud his efforts. In Quebec, the government set aside eighty million dollars for an estimated 8,000 victims who were to receive \$10,000 each. To date, the Quebec government has received only 120 applications from pre-86 victims.

The CHS continues to work to encourage the other provinces and the Federal Government to do the right thing and provide compensation for all.

CANADIAN RED CROSS BANKRUPTCY PROTECTION UPDATE

One of the major repercussions of the governments' decision to exclude pre 86 and post 90 tainted blood victims has been the potential bankruptcy of the Red Cross. Left to the courts for redress, victims have had no other option other than to litigate for financial restitution. The Red Cross is offering sixty million dollars to these forgotten victims. The current potential liability of the Red Cross is over nine billion dollars. The Red Cross has received another extension by the courts to delay a vote by their creditors. They are seeking time to convince the federal and provincial governments to provide additional monies to help forgotten victims. As things stand, the Red Cross offer is worth \$3000 dollars per victim. Unless there is movement from the federal and provincial governments, it is difficult to see how the issues of forgotten victims will be addressed by these proceedings.

PRISON BLOOD ISSUE

This issue continues to be of concern to members of our community as the scope of potential negligence against those who imported, approved, and manufactured blood products that were distributed to our hemophilia community comes to light. The Federal Government has acknowledged that this risky plasma contributed to the infection of

Canadian hemophiliacs with HIV and HCV, but hold the USA health authorities responsible for allowing it into our country. Furthermore, the government claims that since hemophiliacs are included in the 1986-1990 compensation settlement, there is no need to further compensate those who were exposed to prison blood. In fact, over 130 hemophiliacs are not eligible for compensation because they were exposed to this high risk plasma prior to 1986. We will continue our efforts to have the Federal Government recognize its responsibility for this group of Canadians.

RCMP INVESTIGATION

The RCMP continues to investigate potential criminal activity into the contamination of the blood supply. Recently the RCMP had to hire lawyers to prevent the federal government from accessing the active investigation files. We fully support the RCMP in their efforts to investigate wrongdoing without political interference of any kind.

On behalf of the CHS Hepatitis C Task Force, I would like to thank you, the hemophilia community, for your continued support in the fight for justice. We will not give up until our goal of help to all victims is achieved.

Canadian Hemophilia Society
We're all related by blood.



1986-1990 COMPENSATION UPDATE

BY THE COUNSEL OF THE HEMOPHILIA CLASS ACTION

As of December 22, 1999 the Courts in Ontario, British Columbia and Quebec have approved the settlement of the Hemophiliac Class Actions, among others, for persons infected with the Hepatitis C virus (“HCV”) through blood or blood products received in Canada in the period January 1, 1986 to July 1, 1990.

During the approval process, the Courts imposed the following three modifications:

- persons with thalassemia major infected with HCV who received a blood transfusion in Canada in the period January 1, 1986 to July 1, 1990 will qualify and receive benefits under the Hemophiliac HCV Plan as if they were hemophiliacs except that, unlike hemophiliacs, persons with thalassemia major will be required to prove their medical condition at certain levels by biopsy;
- the federal, provincial and territorial governments (the “FPT Governments”) will be liable to pay any judgments or settlement which may be obtained by persons who would have been eligible to receive benefits under the settlement but choose to opt out or are deemed to have opted out of the settlement and who proceed to successfully litigate individual actions against the FPT Governments; and
- in the event that the Courts determine, from time to time, that there is a surplus in the Trust Fund, they may decide if the surplus should be utilized for the benefit of the class members, or paid to the FPT governments or retained in the Trust Fund.

In order to establish the infrastructure necessary to administer the Plans created by the settlement, the Courts have appointed:

- (a) Royal Trust Company as Trustee of the Trust;
- (b) TD Asset Management Inc. as Investment Manager;
- (c) Towers Perrin as Investment Consultant;
- (d) Deloitte & Touche as Auditor;
- (e) Bonnie Tough, Harvey Strosberg, J.J. Camp and Pierre Lavigne as Joint Committee members to oversee the operation of the Plans;
- (f) Representatives in Quebec, Ontario and British Columbia to act as Fund Counsel; and
- (g) Representatives across Canada to act as Arbitrators/Referees.

On December 30, 1999, the federal government began funding the Trust.

The Courts have begun to devise a notice program. The purpose is to advise class members who may qualify that if they do not wish to participate in the settlement they must “opt out” by June 30, 2000. Given recent events regarding the appointment of an Administrator for the settlement, it is likely that there will be an extension of this date. It is important for a person who is contemplating opting out of the settlement to pursue his or her individual claim to know that the FPT Governments do not admit any wrongdoing or liability on their part. Significantly, the FPT Governments have said they will vigorously defend any individual action because the settlement is a compromise of disputed claims.

Of course, if a person opts out, he or she will have no further entitlement to claim under the class action settlement because he or she cannot re-elect to opt in.

In March, 2000 the courts appointed Crawford Expertises as Administrator of the settlement. Prior to the court decision, Peterson Worldwide was acting as “Interim” Administrator. Class counsel has assured CHS that they will be working diligently with Crawford to minimize any delays in the initiation of the application process. Application forms will automatically be sent to individuals who have contacted the 1986-1990 Hepatitis C Claim Centre or who have registered with class counsel. You may contact the 1986-1990 Hepatitis C Claims Centre and obtain a copy of the legal settlement agreement by calling toll-free 1-888-726-2656, e-mailing info@hepc8690.com, or visiting the web site at www.hepc8690.com.

THE HEPATITIS C JANUARY 1, 1986-JULY 1, 1990 CLASS ACTIONS SETTLEMENT - WHAT YOU NEED TO KNOW

Q: Who qualifies for the class actions settlement?

- A:** You would qualify as a class member if:
- You were infected with HCV for the first time through a blood transfusion received in Canada in the period January 1, 1986 to July 1, 1990;
 - You are a hemophiliac who contracted HCV and received blood or blood products in Canada in the period January 1, 1986 to July 1, 1990;
 - You were infected with HCV by a spouse, partner or parent who qualifies; or
 - You are a family member of someone who qualifies.

Q: What are the benefits of the settlement?

- A:** A key feature of the settlement is that HCV-infected individuals will be able to return for additional compensation if their disease progresses. Those who are the sickest will receive the most money. This recognition of the evolving nature of HCV is a unique feature of the settlement.

This disease-based compensation schedule is particularly important for children. They will be eligible for compensation, including income loss, if their medical condition worsens in the coming years.

Q: What do I have to do to join the class actions?

- A:** Nothing. If you qualify as a class member, you will be entitled to the benefits of the settlement. You should contact the 1986-1990 Hepatitis C Claims Centre or Class Counsel (see For More Information below) to ensure that you are on a mailing list so that you will automatically receive a claims application form when they are ready.

Q: What types of compensation are available to me?

- A:** If you qualify as a HCV-infected class member, you will be entitled to a fixed payment as compensation for pain and suffering based upon your medical condition. You will also receive reimbursement for uninsured HCV treatment and medication costs and out-of-pocket expenses such as travel, hotels or meals attributable to seeking medical advice regarding HCV. In addition, based on the stage of your medical condition, you may be eligible to receive \$1,000 per month of completed compensable HCV Drug Therapy (i.e. interferon or ribavirin), compensation for loss of income, loss of services in the home and/or the costs of care such as home nursing services.

Q: I have no symptoms. What happens if I develop symptoms later?

- A:** The settlement assures you, at a minimum, an initial fixed payment now (see Chart regarding compensation levels). If your disease progresses, your case can be reassessed. For example, you may be entitled to Level 2 compensation this year, but 10 years from now, you may be entitled to Level 5 compensation. The settlement accommodates the reality that HCV is a progressive disease and that some people will benefit from making additional claims over time.

Q: What if I am a hemophiliac and I am also infected with HIV?

- A:** If you are a hemophiliac, co-infected with HIV and HCV, you are entitled to the payments described in the compensation levels if you meet the medical requirements. Alternatively, you can elect a one-time compensation payment of \$50,000 in lieu of all other payments to you or your family members.

Q: Will I need to have medical tests or treatment to qualify for compensation?

- A:** You will be required to provide results of a blood test (HCV antibody and/or a PCR test). The settlement allows for a range of diagnostic methods to meet the criteria at the disease-based compensation levels. Your medical records may be reviewed.

No one should undergo any medical procedure unless it is recommended by a physician. It is understood that hemophiliacs may have unique reasons for avoiding biopsies and their entitlement to compensation may be determined based on other health factors.

Q: Someone in my family would have qualified as a class member but is now deceased. Is compensation available?

- A:** If your family member died from HCV before January 1, 1999, the estate is entitled to \$50,000 and uninsured funeral expenses up to \$5,000, and family members would be entitled to additional compensation. Alternatively, the estate can receive uninsured funeral expenses up to \$5,000 and the family members and the estate can jointly elect to receive \$120,000 in compensation in full settlement of all claims.
- If your family member died after January 1, 1999, the estate is entitled to the compensation your family

member could have claimed on the disease-based compensation schedule for the period up to the death and uninsured funeral expenses up to \$5,000. The family members may be entitled to additional compensation if HCV caused the death.

- If your family member was a hemophiliac and co-infected with HIV and HCV, the estate and family members may elect to receive a one-time payment of \$72,000 without further proof that HCV was a cause of death.

Q: What compensation is available for family members?

A: If HCV caused the death of your HCV-infected family member, his or her spouse, partner, child, grandchild, parent, grandparent and/or sibling will be entitled to a lump-sum payment and in some circumstances, loss of support.

Q: Would the money I receive be taxable? Are the payments protected against inflation?

A: If you live in Canada no tax is payable on any money received by a class member. If you live outside Canada, some provisions of the tax acts may apply. Compensation payments will, generally, be indexed annually in accordance with the Canada Pension Plan Act.

Q: Would the money I receive affect any government benefits I currently receive?

A: The settlement contains special protection for those who are receiving income or certain benefits from the Federal and Provincial governments. Certain income loss payments may affect entitlement to some government benefits.

Q: How will the fund be managed?

A: The settlement has several safeguards for the effective and prudent management of the fund:

- The fund will be in two parts. The Federal government will advance approximately \$850 million. The Provincial and Territorial governments will either advance their share of the settlement funds or promise to pay them as required plus interest on any money which is not advanced.
- The money advanced will be held in trust by an arms length trustee appointed by the courts who will invest the fund within investment guidelines approved by the court.
- The interest and the investment income will be tax free and added to the fund.

- The fund assets will be audited annually by court appointed independent professional auditors.
- At least every three years the court will assess the viability of the fund and evaluate if it is being managed properly.
- The courts have the power to vary the compensation paid from the fund if necessary.

Q: What will the fund cover?

A: The vast majority of the assets of the fund will be used to pay the claims of the transfusion class members and their families and the hemophiliac class members and their families. A small portion of the fund will pay the administration costs of the settlement, class counsel fees as approved by the court and the HIV secondarily-infected program previously announced by the governments.

Q: Who will assess and process the claims?

A: The court has appointed an independent company with expertise in complex claims administration. The Administrator, Crawford Expertises, will assist claimants, process applications and expedite payment.

Q: What if I don't agree with the decision the Administrator made about my claim?

A: You will have the right to appeal the Administrator's decision to either a court appointed arbitrator or a court-appointed referee. In some circumstances you will have a further right of appeal to the courts in British Columbia, Quebec or Ontario.

FOR MORE INFORMATION

Q: How can I get more detailed information about the settlement?

A: You may obtain a complete copy of the class actions settlement agreement and a brochure that explains the settlement by calling the 1986-1990 Hepatitis C Claims Centre toll-free at (888) 726-2656, or by sending an e-mail request to info@hepc8690.com or by visiting the web site at: www.hepc8690.com.

**PROPOSED
DISEASE-BASED
COMPENSATION
SCHEDULE FOR
HCV INFECTED
CLASS MEMBERS**

NOTE:
Fixed payments are cumulative

LEVEL	MEDICAL CONDITIONS CAUSED BY HCV	MAXIMUM CUMULATIVE FIXED PAYMENTS AS COMPENSATION FOR DAMAGES	FIXED PAYMENTS AS COMPENSATION FOR DAMAGES
6	You are considered a Level 6 claimant if: 1. you receive a liver transplant; 2. you develop a) decompensation of the liver; b) hepatocellular cancer; c) B-cell lymphoma; d) symptomatic mixed cryoglobulinemia; e) glomerulonephritis requiring dialysis; or f) renal failure.	\$225,000*	You will receive \$100,000
5	You are considered a Level 5 claimant if you develop: a) cirrhosis (i.e. fibrous bands in the liver extending or bridging from portal area to portal area with the development of nodules and regeneration); b) unresponsive porphyria cutanea tarda which is causing significant disfigurement and disability; c) Unresponsive thrombocytopenia (low platelets) which is associated with purpura or other spontaneous bleeding, or which results in excessive bleeding following trauma or a platelet count below 30×10^9 ; or d) glomerulonephritis not requiring dialysis	\$125,000*	You will receive \$65,000
4	You are considered a Level 4 claimant if: you develop bridging fibrous (i.e. fibrous tissue in the portal areas of the liver with fibrous bands bridging to other portal areas or to central veins but without nodular formation or nodular regeneration.	\$60,000*	There is no further fixed payment at this level
3	You are considered a Level 3 claimant if: 1. you develop non-bridging fibrosis (i.e. fibrous tissue in the portal areas of the liver with fibrous bands extending out from the portal area but without any bridging to other portal tracts or to central veins); or 2. you receive compensable HCV Drug Therapy (i.e. interferon or ribarivin); or 3. you have met or meet a protocol for compensable HCV Drug Therapy even though you have not taken the therapy.	If you elect OPTION 1 \$60,000	OPTION 2 If you waive the \$30,000 payment, you may claim loss of income or compensation for loss of services in the home OPTION 1 You receive \$30,000
2	You are considered a Level 2 claimant if: you test positive on a polymerase chain reaction (PCR) test demonstrating that HCV is present in your blood.	\$30,000	You will receive \$15,000 immediately plus a further \$5,000 if and when the Court says that the Fund is sufficient
1	You are considered a Level 1 claimant if: your blood test demonstrates that the HCV antibody is present in your blood.	\$10,000	You will receive \$10,000

* assuming the \$30,000 Fixed Payment was not waived at Level 3

COMPENSATION					LEVEL
LOSS OF INCOME OR COMPENSATION FOR LOSS OF HOME SERVICES (CLAIM ONE OR THE OTHER)	ADDITIONAL PAYMENT IF YOU TAKE HCV DRUG THERAPY	REIMBURSEMENT FOR UNINSURED TREATMENT AND MEDICATION COSTS	REIMBURSEMENT FOR OUT-OF-POCKET EXPENSES	REIMBURSEMENT FOR CARE COSTS	
Yes	\$1,000 per month of completed therapy	Yes	Yes	up to \$50,000 per year	6
Yes	\$1,000 per month of completed therapy	Yes	Yes	No	5
Yes	\$1,000 per month of completed therapy	Yes	Yes	No	4
Yes	\$1,000 per month of completed therapy	Yes	Yes	No	3
No					
No	Not applicable	Yes	Yes	No	2
No	Not applicable	Yes	Yes	No	1

HEPATITIS C INFORMATION WEB SITE LINKS

Compiled by Michael McCarthy, Chair, CHS Hepatitis C Task Force

HCV INFORMATION SITES

www.aegis.com.
www.epidemic.org
www.egroups.com/group/hepcan/
www.hivandhepatitis.com/
www.medscape.com/Home/Topics/AIDS/AIDS.html medscape

INFORMATION ON HEMOPHILIA/HCV/HIV

Canadian Hemophilia Society
www.hemophilia.ca

Hemophilia Ontario
www.hemophilia.on.ca

Association of Hemophilia Clinic Directors
of Canada
ahcdc.medical.org

Canadian Blood Services
www.bloodservices.ca

World Federation of Hemophilia
www.wfh.org

Hemophilia Federation of America
www.hemophiliafed.org

The Hemophilia home page
www.web-depot.com/hemophilia

National Hemophilia Foundation (US)
www.infonhf.org

Committee of Ten Thousand
www.cott.org

Hepatitis C Class Action Settlement
Agreements
www.hepc8690.com

Hepatitis C Society
web.idirect.com/~hepc/table_of_contents/index.html

BLOOD SCANDAL LINKS

www.seark.net/~budge/page29.htm
www.bloodtrail.com