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LATE

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HOUSE COMMITTEE ON HEALTH

SB3039, SD1, RELATING ANATOMICAL TRANSPLANTS

Testimony of Loretta J. Fuddy, A.C.S.W., M.P.H.
Director of Health

March 20, 2012
9:00AM, ROOM 329

Department's Position: The Department of Health (DOH) offers comments only. The DOH believes that this measure is unnecessary.

Fiscal Implications: There would be no fiscal impacts to the general fund.

Purpose and Justification: This measure would amend section 327-11, HRS to specify that persons with HIV, AIDS, or ARC shall not be prohibited from receiving anatomical gifts.

The DOH believes that this bill is unnecessary as HIV infected patients are able to obtain organ transplants. The DOH recommends that the decision regarding any transplant needs to be made by health care providers in close consultation with their patients. People are now living longer and relatively healthy lives with HIV/AIDS when viral replication is successfully suppressed with HIV treatment regimes.

The DOH respectfully requests that this bill be held.

Thank you for the opportunity to testify.

(2007). "Transplants. Organ transplantation more readily available to HIV-positive patients." AIDS Policy Law **22**(19): 1, 4.

Bhagani, S., P. Sweny, et al. (2006). "Guidelines for kidney transplantation in patients with HIV disease." HIV Med **7**(3): 133-9.

Blumberg, E. A. and P. Stock (2009). "Solid organ transplantation in the HIV-infected patient." Am J Transplant **9 Suppl 4**: S131-5.

Christie, T., B. Jiwani, et al. (2006). "Ethical and scientific issues surrounding solid organ transplantation in HIV-positive patients: Absence of evidence is not evidence of absence." Can J Infect Dis Med Microbiol **17**(1): 15-8.

End-stage liver disease is emerging as a leading cause of death among HIV-positive patients. Historically, an HIV diagnosis was a contraindication for a liver transplant; however, because of the efficacy of highly active antiretroviral therapy (HAART), HIV-positive patients have one-year, two-year, and three-year post-transplantation survival rates similar to that of HIV-negative patients. Based on this evidence, HIV-positive patients are now considered eligible for transplantation. However, newly emerging guidelines include the stipulation that HIV-positive patients must be on HAART to be placed on a waiting list for transplantation. The purpose of the present paper is to evaluate the scientific and ethical probity of requiring HIV-positive patients to be on HAART as a condition for being on a liver transplant waiting list. It is argued that the emphasis should be placed on the probability of post-transplantation HAART tolerance, and that concerns about pretransplantation HAART tolerance are of secondary importance.

Cooper, C. L., J. DeForest, et al. (2007). "Barriers preventing liver transplantation in Canadians with HIV-infection--perceptions of HIV specialists." Can J Gastroenterol **21**(3): 179-82.

Liver transplantation is a life-saving procedure with demonstrated utility. There are accumulating data indicating that this procedure is helpful in HIV-infected patients as well. Liver transplantation is currently largely unavailable to those living with HIV in Canada. Understanding the obstacles to this procedure is the first step to increasing access. Between August 2005 and November 2005, HIV physicians, one from each Canadian HIV Trials Network site, were asked to complete a quantitative questionnaire on adult liver transplant access and need. Forty-six per cent (16 of 35) of sites responded. A median 20% of the nearly 12,700 HIV patients followed at these sites had concurrent liver disease (20% caused by hepatitis C virus, 5% caused by hepatitis B virus and 5% were alcohol-related). On average, two patients per site were thought to be appropriate candidates for liver transplant evaluation. Eighty per cent of respondents anticipated increased need for liver transplantation over the next five years. Organ supply was universally identified as the chief obstacle to transplantation in patients with HIV. Other key issues included risk of hepatitis C virus reinfection and transplant surgical team willingness. Based on these data,

it is believed that these issues should be the focus of efforts designed to increase access to transplantation in Canadians with end-stage liver disease and concurrent HIV.

Di Benedetto, F., N. De Ruvo, et al. (2006). "Don't deny liver transplantation to HIV patients with hepatocellular carcinoma in the highly active antiretroviral therapy era." J Clin Oncol **24**(14): e26-7.

Eisenbach, C., U. Merle, et al. (2009). "Liver transplantation in HIV-positive patients." Clin Transplant **23 Suppl 21**: 68-74.

Death from end-stage liver disease (ESLD) because of chronic hepatitis B and C has become an increasing problem in human immunodeficiency virus (HIV)-infected patients in the last years. This is mainly because of the dramatic decrease of HIV-related morbidity and mortality since the introduction of highly active antiretroviral therapy (HAART). Although the data on the outcome of liver transplantation in HIV-infected recipients with ESLD is limited, overall results seem comparable to non-HIV-infected recipients. Therefore, liver transplant centres around the world are increasingly accepting HIV-infected individuals as organ recipients. Post-transplantation control of HIV replication is achieved by continuing HAART. As in non-HIV-infected patients, hepatitis B virus recurrence is efficiently prevented by hepatitis B immunoglobulin and antiviral therapy. Re-infection of the allograft with hepatitis C virus, however, remains an important problem, and progress to allograft cirrhosis may even be more rapid than in HIV-negative patients. Interactions in drug metabolism between the HAART components and the immunosuppressive drugs are difficult to predict and require close monitoring of drug levels and dose adjustments. The complexity in this setting makes close cooperation between transplant surgeons, hepatologists, HIV-clinicians and pharmacologists mandatory. As experience on liver transplantation in HIV-infected individuals is still limited, to date results from large prospective trials addressing key issues are needed.

Frassetto, L. A., C. Tan-Tam, et al. (2009). "Renal transplantation in patients with HIV." Nat Rev Nephrol **5**(10): 582-9.

HIV infection has been a major global health problem for almost three decades. With the introduction of highly active antiretroviral therapy in 1996, and the advent of effective prophylaxis and management of opportunistic infections, AIDS mortality has decreased markedly. In developed countries, this once fatal infection is now being treated as a chronic condition. As a result, rates of morbidity and mortality from other medical conditions leading to end-stage liver, kidney and heart disease are steadily increasing in individuals with HIV. Presence of HIV infection used to be viewed as a contraindication to transplantation for multiple reasons: concerns for exacerbation of an already immunocompromised state by administration of additional immunosuppressants; the use of a limited supply of donor organs with unknown long-term outcomes; and, the risk of viral transmission to the surgical and medical staff. This Review examines open questions on kidney transplantation

in patients infected with HIV-1 and clinical strategies that have resulted in good outcomes. It also describes the clinical concerns associated with the treatment of renal transplant recipients with HIV.

Huprikar, S. (2009). "Solid organ transplantation in HIV-infected individuals: an update." Rev Med Virol 19(6): 317-23.

In the era of highly active antiretroviral therapy (HAART), the survival of patients with HIV has improved. Increasing morbidity and mortality are now related to chronic liver and kidney disease. Transplantation in HIV patients has been reported for nearly two decades and outcomes have generally improved in the HAART era. This review summarises the published experiences with liver and kidney transplantation in HIV patients.

Johnston, B. and J. Conly (2008). "Solid organ transplantation and HIV: A changing paradigm." Can J Infect Dis Med Microbiol 19(6): 425-9.

Miro, J. M., F. Aguero, et al. (2007). "Liver transplantation in HIV/hepatitis co-infection." J HIV Ther 12(1): 24-35.

The prognosis of HIV infection has dramatically improved in recent years with the introduction of combined antiretroviral therapy. Currently, liver disease is one of the most important causes of morbidity and mortality, even more so given the high rate of hepatitis C virus co-infection in countries where drug abuse has been an important HIV risk factor. Survival of HIV-co-infected patients with end-stage liver disease (ESLD) is poor and shorter than that of the non-HIV-infected population. One-year survival of HIV-infected patients with ESLD is only around 50-55%. HIV infection is no longer a contraindication to transplantation, which is becoming a standard therapy in most developed countries. The HIV criteria used to select HIV-infected patients for liver transplantation are quite similar in Europe and North America. Current criteria state that having had an opportunistic infection (e.g. tuberculosis, candidiasis, PCP) is not a strict exclusion criterion. However, patients must have a CD4 count above 100 cells/mm3 and a plasma HIV-1 RNA viral load that is suppressible with antiretroviral treatment. More than 200 orthotopic liver transplants (OLT) in HIV-infected patients have been published in recent years and the mid-term (3-year) survival was similar to that of HIV-negative patients. The main problems in the post-transplantation period are the pharmacokinetic and pharmacodynamic interactions between antiretroviral and immunosuppressive agents and the recurrence of HCV infection, which is the principal cause of post-transplantation mortality. There are controversial results regarding mid-term survival of HIV-HCV co-infected patients compared with HCV mono-infected patients. However, one study showed a trend of poorer 5-year survival of HIV-HCV co-infected patients. There is little experience with the treatment of recurrent HCV infection. Preliminary studies showed rates of sustained virological response ranging between 15% and 20% in HIV-HCV co-infected recipients. Liver transplantation in HIV-HBV co-infected patients had a good prognosis because HBV recurrence can be successfully prevented using

immunoglobulins and anti-HBV drugs. Finally, this field is evolving continuously and the indications for liver transplantation or the management of HCV co-infection may change in the future as more evidence becomes available.

Norris, S. and D. Houlihan (2008). "Liver transplantation in HIV-positive patients." Expert Rev Gastroenterol Hepatol **2**(1): 39-46.

This article reviews the worldwide evolution of liver transplantation as a therapeutic intervention in HIV-infected patients. Since the introduction of highly active antiretroviral therapy (HAART), liver disease secondary to viral hepatitis has become a leading cause of morbidity and mortality among HIV-positive individuals. The authors contrast survival data from pilot studies in the pre-HAART era to those data emerging from more recent trials. Particular emphasis is placed on current selection criteria for HIV-positive transplant candidates. Additional consideration is given to the effect of prolonged transplant waiting time on survival outcome. The complexity of the post-transplant medication regime, including drug interactions, optimal immunosuppression and most appropriate HAART regimes, are discussed in detail. Postoperative challenges including optimal management of hepatitis B virus and recurrent hepatitis C virus post-transplant are reviewed separately. The ethical and practical arguments relating to the use of a scarce and valuable resource in this population are debated. The authors conclude with several recommendations to assist pretransplant assessment and postoperative management of such complex patients and speculate on the direction and evolution of this field in the coming years.

O'Grady, J., C. Taylor, et al. (2005). "Guidelines for liver transplantation in patients with HIV infection (2005)." HIV Med **6 Suppl 2**: 149-53.

Ragni, M. V., S. H. Belle, et al. (2006). "Liver transplantation in HIV-seropositive individuals." Ann Intern Med **144**(3): 223; author reply 223-4.

Rockstroh, J. K. (2009). "Hot topics in HIV and hepatitis coinfection: noninvasive diagnosis of liver disease, liver transplantation, and new drugs for treatment of hepatitis coinfection." HIV Clin Trials **10**(2): 110-5.

Although liver biopsy still remains the globally accepted gold standard for assessing liver disease, the more recent introduction of noninvasive markers in form of blood tests as well as transient elastography have led to the development of new algorithms for assessing liver disease in HIV and hepatitis coinfected individuals. Other hot topics in coinfection include need and outcome for liver organ transplantation in the increasing number of HIV-infected patients with end-stage liver disease as well as development of new agents and strategies for treatment of hepatitis B or C coinfection.

Roefs, A., M. van der Ende, et al. (2009). "Long-term survival after kidney transplantation in an HIV-positive patient." Clin Transplant **23**(2): 278-81.

Only a decade ago, human immunodeficiency virus (HIV)-seropositivity was considered an absolute contraindication for organ transplantation. With the currently available experience, it is no longer justified to deny HIV-positive patients access to transplantation. To the best of our knowledge, we here present the longest surviving HIV-positive patient after renal transplantation. The follow-up period after renal transplantation in this HIV-positive female is now 13 yr and she is in good general condition with excellent renal function. Throughout her post-transplant follow-up, we encountered a number of problems that are illustrative of the HIV-positive patient.

Samri, A., A. M. Roque-Afonso, et al. (2009). "Preservation of immune function and anti-hepatitis C virus (HCV) immune responses after liver transplantation in HIV-HCV coinfected patients (ANRS-HC08 "THEVIC" trial)." J Hepatol **51**(6): 1000-9.

BACKGROUND/AIMS: Liver transplantation (LT) in immune-suppressed human immunodeficiency virus (HIV) and hepatitis C virus (HCV) coinfected patients is feasible but raises questions regarding the severity of HCV recurrence on the liver graft and preservation of immune function. We investigated whether LT is deleterious to the immune system. METHODS: Fourteen HIV-HCV coinfected patients (HIV viral load [VL] <50 copies/ml; median CD4 count of 276/mm(3) pretransplantation) were grafted for HCV-cirrhosis and followed over 2 years. Nine patients received anti-HCV therapy post-transplantation. HCV and HIV VLs and degree of acute and chronic hepatitis were monitored. Peripheral blood T-cell phenotypes and interferon-gamma (IFN-gamma) immune responses against opportunistic pathogens, HCV, and HIV-1 p24 were evaluated. RESULTS: Median HCV VLs, CD4 counts, T-cell subsets, and IFN-gamma-producing T-cell frequencies against opportunistic pathogens and HIV-1 p24 did not change over time. HCV-specific T cells were observed ex vivo in two patients pretransplantation and in two others post-transplantation. HCV-specific in vitro amplification enabled the detection of HCV-specific IFN-gamma-producing responses in three further patients post-transplantation. Anti-HCV responses were observed independently of anti-HCV therapy and were undetectable in patients with severe hepatitis or liver fibrosis. CONCLUSIONS: These results demonstrate that LT in HIV-HCV coinfected patients is not deleterious to the immune system and does not alter immune responses directed against HCV, HIV, or opportunistic pathogens.

Samuel, D., R. Weber, et al. (2008). "Are HIV-infected patients candidates for liver transplantation?" J Hepatol 48(5): 697-707.

Tan-Tam, C. C., L. A. Frassetto, et al. (2009). "Liver and kidney transplantation in HIV-infected patients." AIDS Rev 11(4): 190-204.

HIV infection has evolved into a chronic condition as a result of improvements in therapeutic options. Chronic exposure with HIV and associated co-pathogens as well as toxicities from prolonged therapy with antiviral medications has resulted in increased morbidity and mortality rates from end-stage liver and kidney disease in the HIV-infected population. Since the definitive treatment for

end-stage organ failure is transplantation, demand has increased among HIV-infected patients. Although the transplant community has been slow to recognize HIV as a chronic condition, many transplant centers have eliminated HIV infection as a contraindication to transplantation as a result of better patient management and demand. This review examines the current clinical strategies and issues surrounding liver and kidney transplantation in HIV-infected patients.

Testillano, M., J. R. Fernandez, et al. (2009). "Survival and hepatitis C virus recurrence after liver transplantation in HIV- and hepatitis C virus-coinfected patients: experience in a single center." Transplant Proc 41(3): 1041-3.

INTRODUCTION: Posttransplant hepatitis C virus (HCV) recurrence has been shown to negatively impact graft and patient survivals. It has been suggested that HCV recurrence among HIV- and HCV-coinfected transplant recipients is even more aggressive. OBJECTIVE: To compare the histological severity and survival of posttransplant HCV recurrence between HIV- and HCV-coinfected and HCV-monoinfected patients. PATIENTS AND METHODS: Among 72 adult patients who underwent primary liver transplantation at our institution for HCV-related cirrhosis between October 2001 and April 2007. We excluded one coinfected patient who died on postoperative day 5 leaving 12 HIV- and HCV-coinfected patients for comparison with 59 monoinfected patients. When listed, all coinfected patients fulfilled the criteria of the Spanish Consensus Document for transplantation in HIV patients. Immunosuppression did not differ between the two groups: all were treated with tacrolimus + steroids (slow tapering). Aggressive HCV recurrence was defined as cholestatic hepatitis and or a fibrosis grade > or =2 during the first posttransplant year. RESULTS: Coinfected patients were younger than monoinfected patients: 45 +/- 6 years vs 55 +/- 9 years (P = .0008). There were no differences in Child score, Model for End-stage Liver Disease score, donor age, graft steatosis, ischemia time, HCV pretransplant viral load or genotype between the groups. Significant rejection episodes were also equally distributed (25% vs 14%; P = .38). Seven coinfected patients and 29 monoinfected patients developed aggressive HCV recurrences (58% vs 49%; P = .75). Median follow-up was 924 days. Global survival at 3 years was 80%. Survivals at 1, 2, and 3 years were 83%, 75%, 62% in the coinfected vs 98%, 89%, 84% in the monoinfected patients, respectively (log-rank test = 0.09). CONCLUSIONS: The severity of histological recurrence was similar among HIV- and HCV-coinfected and monoinfected HCV liver recipients in the first posttransplant year. Mortality attributed to recurrent HCV was similar in the groups. There were no short-term (3-year) differences in survival between the two groups of patients.

Vennarecci, G., G. M. Ettorre, et al. (2007). "Liver transplantation in HIV-positive patients." Transplant Proc 39(6): 1936-8.

AIMS: The aim of this study was to evaluate the feasibility of liver transplantation (OLT) in human immunodeficiency virus (HIV), hepatitis C virus (HCV) coinfected patients in Italy. METHODS: Between September 2002 and April 2006, 12 HIV(+) coinfected patients (11 men, mean age 42 years) underwent

OLT at our Institute. Eleven (91%) patients were HCV-positive and one was hepatitis B virus-positive. Pre-OLT plasma HIV 1-RNA level was undetectable and CD4(+) T-cell count >200 cells/microL for 3 months in all patients. Six patients had to stop highly active antiretroviral therapy (HAART) before OLT because of liver disease severity (n = 2) and for hepato cellular carcinoma (n = 4). RESULTS: The actuarial 1-, 2-, and 3-year survival rates were 83.3%, 58.3%, and 58.3%, respectively, which were significantly lower than those observed among HIV-negative patients transplanted in our center. Six patients are alive with a mean follow-up of 26 months (range: 5 to 46 months). We recorded a low rate of opportunistic infections and rejection. All alive patients have low levels of HIV RNA, and the CD4(+) T-cell counts increased after OLT. Nine patients developed early recurrence of hepatitis C requiring combination therapy with peg-interferon plus ribavirin. Significant improvement in the quality of life was observed in 7/11 patients. CONCLUSIONS: OLT in HIV-positive patients was feasible with good results in the short and medium term. Early severe HCV recurrence may be observed. Key challenges for the management of HIV(+) patients after transplantation included treatment of severe HCV recurrence and attention to the pharmacological interactions of HAART with immunosuppressive drugs.

Walmsley, S. (2006). "Organ transplantation in HIV-infected individuals: The time has come - should there be criteria?" Can J Infect Dis Med Microbiol **17**(1): 8-10.

Wright, C. E. and V. D. Bowers (2002). "Organ transplantation in HIV-infected patients." N Engl J Med **347**(22): 1801-3; author reply 1801-3.

Zink, S., H. Smolen, et al. (2005). "NATCO, the organization for transplant professionals public policy statement. HIV-to-HIV transplantation." Prog Transplant **15**(1): 86-90.