GUIDELINE FOR THE MANAGEMENT OF HIV AND HEPATITIS C INFECTION IN PEOPLE WITH HAEMOPHILIA

Australian Haemophilia Centre Directors’ Organisation

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Disclaimer
This document is a general guide to appropriate practice, to be followed subject to the clinician’s expert judgement and the patient’s preference in each individual case. The guidelines are designed to provide information to assist decision-making and are based on consensus opinion at the time of compilation. The guidelines were reviewed in 2008.

These guidelines will be reviewed again in 2011.

Users of these guidelines are encouraged to contact the Australian Haemophilia Centre Directors’ Organisation if they have comments to make. These comments will inform the revision process.

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1. Introduction

The Guideline for the Management of HIV and Hep C Infection in People with Haemophilia has been developed by the Australian Haemophilia Centre Directors’ Organisation (AHCDO). Consultation has occurred with a range of stakeholders including the Australian Liver Association of the Gastroenterological Society of Australia, the Australasian Society for HIV Medicine, the Australian Hepatitis Council and the Royal Australasian College of Physicians.

The Australian National Council on AIDS, Hepatitis C and Related Diseases (ANCAHRD) has published a comprehensive guideline, A Model of Care for the Management of Hepatitis C Infection in Adults [1] which, ‘by providing best practice information to medical practitioners, seeks to provide a framework in which people with hepatitis C are clearly informed about treatment and management options available to them’. The Model of Care aims to ‘enable both clients and clinicians to make informed decisions regarding management options’. The National Health Act Section 100 criteria for access to pegylated interferon combination therapy are updated regularly and should be referred to determine up to date treatment options.

The Australasian Society for HIV Medicine (ASHM) has published a clinical guideline for the management of HIV [2] which comprehensively deals with basic HIV virology, immunology and tools to monitor HIV disease; antiretroviral therapy and clinical presentations. In addition, the ASHM has also published an extensive guide for the clinical management of HIV and hepatitis co-infection [3] which is designed to meet the needs of clinicians and addresses HIV/hepatitis C coinfection and hepatotoxicity associated with antiretroviral therapy.

These three clinical guidelines [1, 2, 3] offer expert guidance to appropriate practice for the management of HIV and hepatitis C infection and AHCDO endorses the recommendations contained within these documents. Although it is not the intention of these AHCDO guidelines to duplicate material already published, it is pertinent that for those patients with HIV and/or hepatitis C
infection who also have haemophilia or a related bleeding disorder there are additional issues to be considered. Hence, the aim of this guideline is to address the clinical management of issues relating to HIV and/or hepatitis C infection specifically in people with haemophilia or a related bleeding disorder (PWH).

Data from the Australian Bleeding Disorder Registry (ABDR) suggests that over 50% of people with haemophilia A are infected with hepatitis C and over 45% of people with haemophilia B are infected with hepatitis C. Data indicates that all the PWH and HIV are also coinfected with hepatitis C.

The primary audience for these AHCDO guidelines is intended to be clinicians treating people with haemophilia who are also infected with HIV and/or Hepatitis C. Physicians, nurses, medical students, allied health professionals and individuals with a specific interest in these conditions may also find these guidelines of use.

2. Methods

The guidelines were drafted by a small Working Party of Haemophilia Centre Directors appointed by the AHCDO Executive Committee. Members of the Working Party made a declaration of interest to the Chairman AHCDO. A draft copy of the guideline was widely circulated for consultation.

3. Management

3.1. General

It is recommended that PWH be managed within a comprehensive Haemophilia Treatment Centre (HTC). These HTCs have been established in all states and territories. The associated management of HIV and hepatitis C should be in collaboration with specialised HIV medicine/infectious disease units, specialised

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1 The ABDR does not include data from New South Wales
liver/gastroenterology units, liver transplant physicians and surgeons and/or general practitioners with appropriate experience. Access to specialised clinics should be available irrespective of whether the place of residence of the PWH is in a metropolitan, regional or rural setting.

Care should be taken by staff or individuals performing IV injections for factor replacement for PWH to avoid needle stick injuries.

### 3.2. Hepatitis C

Many of the PWH receiving pooled plasma concentrates prior to the late 1980s were infected with hepatitis C. In many cases the duration of infection is greater than 20 years and PWH are at significant risk of developing cirrhosis and hepatoma.

#### 3.2.1. Assessment of liver disease

A liver biopsy is the optimal assessment of liver function. Aledort [4] reported in 1985 a significant risk of morbidity and mortality from liver biopsy in PWH. However, more recent studies [5, 6, 7] have demonstrated that liver biopsy can be performed safely in PWH if appropriate hospitalisation and factor replacement are undertaken.

McMahon et al [5] reported 21 percutaneous liver biopsies undertaken in PWH with no bleeding with either intermittent or continuous factor infusion for up to 5 days. DiMichele et al [6] reported transjugular liver biopsy as safe and diagnostic in 13 adult patients. PWH had factor replacement for up to 5 days and remained hospitalized for 48 hours. Stieltjes [7] reported a large series of transjugular liver biopsies in 69 of 151 PWH and hepatitis C. Mild adverse events were recorded in 8% with haematoma at the puncture site and abdominal pain without evidence of intra-abdominal haemorrhage. Saab et al [8] reported eleven patients undergoing outpatient transjugular liver biopsy who were monitored initially for 4 hours and received factor replacement for 3 days. No complications were noted.

Liver biopsy should only be performed by an experienced operator, with factor replacement monitored at a HTC, and only if the result will clarify the diagnosis or
have an effect on therapeutic options. Transjugular biopsy can be performed if experienced staff are available.

Prior to biopsy, (in addition to routine coagulation assessment and treatment) factor levels should be raised to 0.7-1.0 U/ml by bolus infusion of Factor VIII or IX for PWH A and B respectively and then maintained by either intermittent bolus infusions or continuous infusion for 3 days. Reduced factor replacement to maintain levels of 0.3 U/ml should be considered for the next 2 days. PWH undergoing liver biopsy may be hospitalised for 48 hours. Post biopsy ultrasound can be considered.

### 3.2.2. Liver transplantation

Liver transplant may be considered for Hepatitis C or its complications. As both Factor VIII and IX are produced in the liver, liver transplantation cures haemophilia. Haemophilia should not be an exclusion for consideration for liver transplantation. HIV coinfection is not a contraindication to liver transplant.

### 3.3. HIV

#### 3.3.1. Increased bleeding in PWH

In 1999 Wilde et al [9] reported increased bleeding tendency in PWH on protease inhibitor (PI) therapy. There was an increased frequency of bleeds and atypical bleeds into small joints, soft tissues and muscles. Increased bleeding in the genitourinary tract has also been reported [9]. Ritonavir was the most common PI implicated and bleeding episodes decreased after changing the PI. Racoosin [10] summarized reported adverse events to the FDA, noting an increase in bleeding episodes in haemophiliacs compared to non-haemophiliacs on PIs. Rechallenge with other PIs was associated with bleeding. Serious haemorrhages can occur, including intracranial haemorrhage, and may necessitate cessation of PI therapy [11]. Amprenavir [12] and Lopinavir-Ritonavir [13] have been reported to be associated with atypical bleeding. All PWH on PIs should be closely observed for atypical bleeds.
3.3.2. Septic arthritis

Septic arthritis may occur in arthritic joints and joint replacements in PWH with HIV [14]. Septic arthritis, which may be afebrile, should be considered in any joint bleed which is unresponsive to factor replacement and may require increased amounts of pain relief.

3.3.3. Reproductive choices

HIV infection may now be considered a chronic illness and many PWH of reproductive age may desire to have children. Previous options for HIV discordant couples with haemophilia were the use of frozen quarantined HIV negative donor sperm, adoption or not to have children. With improvements in HIV treatment, assisted reproductive techniques including IVF and intracytoplasmic sperm injection (ICSI) or sperm washing can now be considered [15]. Collection of sperm when viral loads are unrecordable following HAART should be considered to further reduce risks. Specific counselling and collaboration with IVF clinics is recommended.

3.3.4. Thrombocytopenia

Thrombocytopenia can be due to a variety of causes. The risk of bleeding in a PWH will vary due to the cause. Prophylactic factor replacement infusions can be considered on an individual basis and clinical grounds.

3.4. HIV/HCV Coinfection

PWH are more likely to be infected with HCV- genotype 1. The duration of infection is usually greater than 20 years. HIV has been shown to accelerate the course of HCV chronic liver disease and HCV appears to worsen the prognosis of HIV [16]. Wilde et al [16] suggest that pegylated interferon/Ribavirin combination therapy should be considered in patients with stable HIV on or off HAART with CD4 counts \(>0.2 \times 10^9/L\), but each case should be assessed individually. As with hepatitis C mono-infection, liver biopsy should only be considered if the result will affect diagnosis or therapeutic options and only after adequate factor replacement.
REFERENCES


