KEY POINTS

• Many Australians with haemophilia, von Willebrand disease and other bleeding disorders acquired hepatitis C virus (HCV) through blood products for their treatment before 1993, usually through plasma-derived clotting factor concentrates

• Males and females with mild bleeding disorders may have had few treatments in their lifetime and not be aware of their HCV risk or status

• All individuals with bleeding disorders who received blood products before 1993, including plasma-derived clotting factor treatments, should be tested for exposure to HCV and, if positive, for current HCV infection

• People with inherited bleeding disorders may also be at risk of HCV infection for reasons independent of their bleeding disorder and should be tested if they have risk factors.

• In adults with bleeding disorders, HCV infection is likely to be of at least 25 years duration, a risk factor for cirrhosis, and further assessment with a referral to a hepatitis or liver specialist is appropriate

• Clinical management of the person with a bleeding disorder and HCV should be the same as in the general population of people with HCV, with some further considerations:
  - If the person has advanced liver disease, it is important to liaise with the patient’s Haemophilia Treatment Centre for information on their individual bleeding problems and to manage any potential bleeding complications encountered with HCV treatment or management
  - Attention may need to be given to access/travel to clinic appointments and referrals for testing if there are mobility or financial problems.
BACKGROUND

New direct-acting antiviral (DAA) therapies for chronic hepatitis C virus (HCV) infection that are highly effective, well tolerated and simple to administer are now available for all Australians with HCV. The World Health Organisation has a goal of eliminating HCV by 2030. With their high cure rates and ease of administration these new therapies mean that Australia is well placed to achieve this.

The new DAAs encompass a range of treatments suitable for the variety of HCV genotypes and levels of liver disease. This includes a simple 12 week treatment regimen of one tablet per day that is suitable for all genotypes and is now listed on the PBS. To ensure wide access across the community, the PBS listing was updated on 1 June 2017 so that all medical practitioners, including general practitioners (GPs), and authorised nurse practitioners, can prescribe these medicines if they are experienced in the treatment of HCV, or in consultation with a specialist experienced in the treatment of HCV. National consensus guidelines on the management of HCV have been developed to support the Australian treatment campaign.

Although most people with bleeding disorders and HCV have now been treated and cured of their HCV, there remains a number of people who have not yet pursued treatment, either because they are not aware of their HCV status or because they experience barriers to treatment. General practitioners may encounter these individuals in their practice, particularly if these people have a mild bleeding disorder and are not aware of their risk for HCV or live at some distance from their Haemophilia Treatment Centre and would like to undertake HCV treatment locally.

Australians with bleeding disorders: a special population

A large proportion of Australians with bleeding disorders were exposed to blood-borne viruses before 1993 through blood products for their treatment, usually human plasma-derived clotting factor concentrates.

This included:

- HIV in the mid-1980s
- HCV (previously known as non-A non-B hepatitis), which was most likely prevalent in the community from the 1970s but diagnosis was only confirmed when testing began in the early 1990s.

A study in one Australian Haemophilia Centre suggests that:

- up to 50% of people exposed to clotting factor during this time may be HCV positive
- while > 80% of those with severe haemophilia may be HCV positive due to increased product exposure.

For most individuals HCV diagnosis took place in the context of the HIV epidemic, which resulted in high mortality in the haemophilia population.

- Diagnosis was often made when checking stored blood samples and confirmatory testing in the early 1990s
- If the person has not had a hepatitis C review recently, their understanding of HCV, their status and treatment options may arise from this early period and may need to be updated.
A substantial number of males and females with mild bleeding disorders, such as haemophilia and von Willebrand disease (VWD), have had very few treatments with clotting factor concentrates in their lifetime and may not realise they were at risk of HCV infection. They may never have had HCV testing and may not be aware of their HCV status.

These epidemics have had a profound physical and psychological impact on the community.

Effects on individuals are variable and can include:

- Increased complexity of co-morbidities, which intensifies as people age, leading to mobility problems and overload with health conditions and services
- For some, unresolved anger at the route of infection and mistrust of the medical system
- Concerns about privacy due to past experiences of stigma and discrimination.

**SOME CONSIDERATIONS WHEN SEEING A PATIENT WITH A BLEEDING DISORDER**

The diagnosis, counselling, initiation of treatment and monitoring of HCV and treatment of HCV-associated complications in infected people with bleeding disorders should be the same as in the general population with HCV, with some additional considerations.

### Who to consider for HCV testing

- People with an inherited bleeding disorder who were treated with a plasma-derived clotting factor replacement therapy or whole blood product in Australia prior to 1993
- People with an inherited bleeding disorder who had blood product treatments in their country of origin prior to migrating to or visiting Australia after 1993
- People with an inherited bleeding disorder who have ever injected illicit drugs or steroids, have tattoos or body piercing, have ever been in a custodial setting or have other risk factors for acquiring HCV.

HCV infection is likely to have been of long duration and evaluation for the presence of cirrhosis would be appropriate.

If they have had HCV testing or treatment in the past, their test documentation and treatment history should be reviewed and confirmed with them.

* For the full list of risk factors, see Table 1, “Populations to consider for a hepatitis C virus screening test” in the Australian recommendations for the management of hepatitis C virus infection: a consensus statement.
Who should be tested?

1. Anyone with an inherited bleeding disorder who was treated with a plasma-derived clotting factor replacement therapy or whole blood product prior to 1993 may have been exposed to hepatitis C, and to a lesser extent hepatitis B. This may include:
   - Males and females with haemophilia
   - Females with bleeding symptoms who carry the haemophilia gene
   - Males and females with von Willebrand disease (VWD)
   - Males and females with other rare inherited bleeding disorders.

The person may have had their first clotting factor treatment any time from infancy onwards, and may have been a child when initially exposed.\(^3,4\)

<table>
<thead>
<tr>
<th>Year</th>
<th>Initiative</th>
</tr>
</thead>
<tbody>
<tr>
<td>1990</td>
<td>HCV antibody testing of the blood supply</td>
</tr>
<tr>
<td>1990</td>
<td>HCV inactivation manufacturing processes for factor VIII plasma-derived products (treatment for haemophilia A and VWD)</td>
</tr>
<tr>
<td>1993</td>
<td>HCV inactivation manufacturing processes for factor IX products (treatment for haemophilia B)</td>
</tr>
<tr>
<td>2004</td>
<td>Universal access to recombinant products for all Australians with haemophilia. These are genetically engineered and contain little or no human material. There have been no reports of blood borne virus infection with recombinant products.</td>
</tr>
</tbody>
</table>

All individuals with bleeding disorders who had blood product or clotting factor treatments before 1993 should have HCV diagnostic testing consistent with Australian national policy (http://testingportal.ashm.org.au).

Most will have had HCV testing in the past and their HCV test documentation should be reviewed and confirmed with them.

Some will also have had unsuccessful HCV treatment with earlier interferon-based regimens and their treatment history should be reviewed and documented.

2. People with mild haemophilia or VWD, including females with bleeding problems, may have had few bleeding episodes requiring plasma-derived treatment and this may have occurred many years ago. Commonly these people may not have regular follow up with a Haemophilia Treatment Centre or be aware of their risks or possible exposure to hepatitis C from treatment.\(^4\)
3. If the person migrated to Australia after 1993 or is visiting Australia from another country and has had blood product treatments in their country of origin, they may have been exposed to HCV in their country of origin and their HCV status should be reviewed.

4. People with inherited bleeding disorders may also be at risk of HCV infection for reasons independent of their bleeding disorder and should be tested if they have risk factors. This includes people who have ever injected illicit drugs or steroids, who have tattoos or body piercing, or who have ever been in a custodial setting, before or after 1993.

   For the full list of risk factors, see Table 1, “Populations to consider for a hepatitis C virus screening test” in the Australian recommendations for the management of hepatitis C virus infection: a consensus statement.  

5. Approximately 15-20% of those exposed to HCV will have spontaneously cleared the virus, indicated by a negative HCV PCR test. People who were diagnosed as a child or adolescent may not have understood their viral status or its significance and this should be confirmed and clarified with them.

6. If an adult with a bleeding disorder has a current infection with HCV, infection is likely to be of at least 25 years’ duration - a significant risk factor for chronic liver disease or cirrhosis. This requires further assessment with referral to a hepatitis or liver clinic.

Accessibility and financial barriers

7. Those with severe disease relating to their bleeding disorder may live with the long term effects of chronic bleeding, such as arthritis, joint problems, and pain, as well as hepatitis C symptoms. Severe fatigue, depression and other mental health issues, pain and mobility problems can cause difficulty in accessing services. There may also be financial barriers.

8. Ensuring that clinic appointments and referrals take travel and accessibility into account may assist with attendance. Referral to a Haemophilia Social Worker or Counsellor at the regional Haemophilia Treatment Centre to provide support with accessing services may also be helpful.

HCV/HIV co-infection

9. In Australia all people with bleeding disorders who have HIV have been co-infected with hepatitis C. HCV is known to progress faster in the presence of HIV and therefore it is more likely that their HCV will result in advanced liver disease. If they are still HCV PCR positive, medical management of their hepatitis C is best undertaken in consultation with the person’s HIV and haemophilia teams.

Clinical management

10. Clinical management of the person with a bleeding disorder and HCV should be the same as for the general population of people with HCV, and follow the current Australian recommendations for the management of hepatitis C virus infection: a consensus statement, with some further considerations to manage potential bleeding complications in people with advanced liver disease.

11. Where the safety and efficacy of direct acting antiviral (DAA) treatments have been studied in a cohort of people with inherited bleeding disorders, the studies found that the DAA treatment was safe and well-tolerated in people with haemophilia and VWD, did not appear to worsen the underlying bleeding disorder, and demonstrated efficacy consistent with clinical trials in the general population with hepatitis C.
As with the general population of people with HCV,


13. People with cirrhosis/advanced liver disease should be managed in conjunction with a liver specialist.

14. People with treatment failure usually have developed antiviral drug resistance. New regimens undergoing approval and in development are likely to be effective treatment for many of these patients.

If the person with a bleeding disorder experiences treatment failure with a first-line DAA therapy, it is recommended that they be referred to a specialist centre where HCV resistance testing is available and there is greater access to evolving salvage treatment strategies through clinical trials.1

**Bleeding disorder-related medical complications**

15. Cirrhosis as a complication of HCV infection may result in bleeding which could be worsened due to the presence of the inherited bleeding disorder.

16. Invasive tests or procedures such as liver biopsies or dental or surgical procedures can also be complicated by bleeding disorder-related bleeding. Where possible, non-invasive assessment methods such as Fibroscan® or serum biomarkers for liver fibrosis should be used instead of a liver biopsy. If invasive procedures are indicated in the individual’s HCV management, they should be undertaken in consultation with the person’s Haemophilia Treatment Centre.

17. If the person has advanced liver disease, it is important to liaise with their Haemophilia Treatment Centre as well as a liver specialist for information on their individual bleeding problems and to manage any potential bleeding complications encountered with HCV treatment or management.

18. Where HCV eradication cannot be achieved, regular monitoring (every 6 months) for end-stage liver complication is recommended. Clear communication is required between Haemophilia Treatment Centre staff, hepatologists and other liver clinic staff, and the patient’s general practitioner regarding planned monitoring and the delegation of responsibility for following up of results.12

**When to liaise with the local Haemophilia Treatment Centre**

- When the person has advanced liver disease
- If invasive medical or dental procedures or surgery are indicated
- Where HCV eradication cannot be achieved
- If the individual requires support with accessing medical services
MORE INFORMATION

Haemophilia Treatment Centres provide comprehensive care for people with bleeding disorders -
www.haemophilia.org.au/support-services/treatment-services

Peer support and information for people with bleeding disorders is available from Haemophilia Foundations –
www.haemophilia.org.au

Australian Haemophilia Centre Directors’ Organisation – www.ahcdo.org.au

Haemophilia Foundation Australia – www.haemophilia.org.au

T: 03 9885 7800
E: hfaust@haemophilia.org.au

ACKNOWLEDGEMENTS

Prepared by the Australian Haemophilia Centre Directors’ Organisation (AHildo) and Haemophilia Foundation Australia (HFA),
August 2017.

Reviewed by Dr John Rowell and Dr Simon McRae, AHCDO; A/Prof Joe Sasadeusz, Infectious Diseases Service,
The Alfred hospital, Melbourne; A/Prof Simone Strasser, AW Morrow Gastroenterology and Liver Centre,
Royal Prince Alfred Hospital, Sydney.

REFERENCES

   Latest edition available on the website < http://www.hepcguidelines.org.au>


People with bleeding disorders and hepatitis C

Disclaimer
This document is a general guide to appropriate practice, to be followed subject to the circumstances, clinician’s judgement and patient’s preferences in each individual case. It is designed to provide information to assist decision making. The relevance and appropriateness of the information and recommendations in this document depend on the individual circumstances. Moreover, the recommendations and guidelines are subject to change over time.

Each of the parties involved in developing this document expressly disclaims and accepts no responsibility for any undesirable consequences arising from relying on the information or recommendations contained herein.