



# **A MODEL OF CARE FOR THE MANAGEMENT OF HEPATITIS C INFECTION IN ADULTS**

**Prepared for the National Council on AIDS, Hepatitis C and Related  
Diseases by the ANCAHRD Hepatitis C Committee and Clinical Trial  
and Research Committee (CTARC)**

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## Table of Contents

|   |           |
|---|-----------|
| <b>1. INTRODUCTION.....</b>   | <b>5</b>  |
| <b>2.1 ALGORITHM: DIAGNOSIS AND TREATMENT OF HEPATITIS C.....</b>   | <b>6</b>  |
| <b>2.2 HEPATITIS C INFECTION – MANAGING THE PERSON NOT THE VIRUS.....</b>   | <b>7</b>  |
| Epidemiology.....   | 7         |
| Managing the Person not the Virus.....  | 7         |
| Natural history and progression.....  | 10        |
| Transmission risk.....  | 10        |
| Treatment.....  | 11        |
| <b>3.1. ALGORITHM: TESTING OF INDIVIDUALS FOR HEPATITIS C STATUS.....</b>   | <b>12</b> |
| <b>3.2. EXPLANATORY NOTES: TESTING OF INDIVIDUALS FOR HEPATITIS C STATUS.....</b>   | <b>13</b> |
| Assessing the Need for a Hepatitis C Test.....  | 13        |
| Pre-Test Discussion.....  | 14        |
| Hepatitis C Tests to Detect Past and Current Infection.....   | 15        |
| Post-Test Counselling.....  | 16        |
| Reporting Requirements and Client Confidentiality.....  | 17        |
| Accessing Testing.....  | 18        |
| <b>4.1. ALGORITHM: POSITIVE HEPATITIS C ANTIBODY TEST.....</b>  | <b>19</b> |
| <b>4.2. EXPLANATORY NOTES: POSITIVE HEPATITIS C ANTIBODY TEST.....</b>  | <b>20</b> |
| Liver Function Tests.....   | 20        |
| Referral to a Liver Clinic, HCV Specialist, Paramedical Specialists and Other Services.....   | 21        |
| <b>5.1. GENERAL PRACTITIONER PRE-REFERRAL CHECKLIST FOR CLIENTS WITH HEPATITIS C.....</b>   | <b>22</b> |
| History.....  | 22        |
| Physical Examination.....   | 23        |
| Blood Tests.....  | 23        |
| Hepatitis C with Normal Liver Tests.....  | 23        |
| <b>5.2. REFERRAL TO MEDICAL SPECIALISTS AND OTHER SERVICES.....</b>   | <b>24</b> |
| Referral to a Liver Specialist.....   | 24        |
| Referral to Hepatitis Councils, Injecting Drug User Organisations, Alcohol and other Drug Treatment Services, Counsellors, Social Workers, Psychiatrists & Psychologists..... | 24        |
| (Psychosocial Issues Associated with Hepatitis C Infection).....  | 24        |
| Referral to a Rheumatologist, Dermatologist or Renal Physician (Extrahepatic Manifestations of Hepatitis C Virus Infection).....  | 25        |
| Referral to a Nutritionist or Dietitian.....  | 25        |
| Referral to a Complementary or Alternative Therapist.....   | 26        |
| Hepatitis C and oral health.....  | 26        |
| <b>6.1. ALGORITHM: SERVICES PROVIDED BY A HCV SPECIALIST OR LIVER CLINIC.....</b>   | <b>27</b> |
| <b>6.2. EXPLANATORY NOTES: SERVICES PROVIDED BY A SPECIALIST OR LIVER CLINIC.....</b>   | <b>28</b> |
| Counselling and Information.....  | 28        |
| Preliminary Investigation.....  | 28        |
| Assessing Risk Factors for Developing Liver Damage.....   | 29        |
| <b>7.1. ALGORITHM: SELECTION OF CLIENTS WITH CHRONIC HEPATITIS C FOR TREATMENT.....</b>   | <b>31</b> |
| <b>7.2 EXPLANATORY NOTES: SELECTION OF CLIENTS WITH CHRONIC HEPATITIS C FOR TREATMENT.....</b>  | <b>32</b> |
| Deciding the Appropriateness and Necessity of Treatment.....  | 32        |
| Benefits of Treatment.....  | 32        |
| Liver Biopsy.....   | 33        |
| Assessing the Risk of Liver Disease Progression.....  | 33        |

|   |           |
|---|-----------|
| Treatment.....  | 34        |
| Accessing Treatment.....  | 34        |
| <b>8.1. ALGORITHM: MANAGEMENT AND TREATMENT FOR CLIENTS WITH HEPATITIS C.....</b>         | <b>37</b> |
| <b>8.2. EXPLANATORY NOTES: MANAGEMENT AND TREATMENT FOR CLIENTS WITH HEPATITIS C.....</b> | <b>38</b> |
| Treatment.....  | 38        |
| Duration and Effectiveness of Treatment.....  | 38        |
| Side Effects of Treatment and Routine Monitoring Required During Therapy.....             | 39        |
| <b>9.1. ALGORITHM: MONITORING AND MANAGEMENT POST THERAPY .....</b>                       | <b>41</b> |
| <b>9.2. EXPLANATORY NOTES: MONITORING AND MANAGEMENT POST THERAPY .....</b>               | <b>42</b> |
| End of Treatment Virological Response (ETR).....  | 42        |
| Sustained Virological Response (SVR).....   | 42        |
| Treatment Options for Clients Who Did Not Have a Sustained Virological Response .....     | 42        |
| <b>10.1. ALGORITHM: TRANSMISSION OF HEPATITIS C FROM MOTHER TO CHILD.....</b>             | <b>44</b> |
| <b>10.2. EXPLANATORY NOTES: TRANSMISSION OF HEPATITIS C FROM MOTHER TO CHILD.....</b>     | <b>45</b> |
| Who Should be Considered for Screening During Pregnancy? .....                            | 45        |
| Counselling.....  | 45        |
| Transmission risk.....  | 45        |
| Management of Pregnant Women who are Hepatitis C RNA Positive .....                       | 45        |
| Testing of Children of Women with Hepatitis C.....  | 46        |
| <b>11.1 ALGORITHM: HEPATITIS C HIV CO-INFECTION.....</b>                                  | <b>47</b> |
| <b>11.2 EXPLANATORY NOTES: HEPATITIS C HIV CO-INFECTION.....</b>                          | <b>48</b> |
| Screening.....  | 48        |
| Transmission of Hepatitis C.....  | 48        |
| Hepatitis C Progression .....   | 48        |
| HIV Progression.....  | 49        |
| Treatment and Drug Interactions.....  | 49        |
| <b>12. HEPATITIS C HBV CO-INFECTION.....</b>  | <b>50</b> |
| Detection of Virus.....   | 50        |
| Disease Progression .....   | 50        |
| Treatment and Drug Interactions.....  | 50        |
| Current Management of Hepatitis C / HBV Co-infection .....                                | 51        |
| <b>13. DIET AND HEPATITIS C .....</b>   | <b>52</b> |
| Referral to a Dietitian.....  | 52        |
| Alcohol.....  | 52        |
| Fats.....   | 53        |
| Sugar.....  | 53        |
| Vitamins.....   | 53        |
| Caffeine.....   | 54        |
| Food Colours and Preservatives.....   | 54        |
| <b>14. COMPLEMENTARY MEDICINE AND HEPATITIS C.....</b>                                    | <b>55</b> |
| Herbal Remedies.....  | 55        |
| <b>15. LIFESTYLE AND HEPATITIS C.....</b>   | <b>56</b> |
| Exercise .....  | 56        |
| Fatigue.....  | 56        |
| Stress.....   | 56        |
| <b>16. CONCURRENT DISEASE MANAGEMENT.....</b>   | <b>56</b> |
| <b>17. SUPPORT SERVICES .....</b>   | <b>57</b> |
| National.....   | 57        |

|   |           |
|---|-----------|
| Australian Capital Territory.....                 | 57        |
| New South Wales.....                              | 57        |
| Northern Territory.....                           | 58        |
| Queensland.....                                   | 58        |
| South Australia.....                              | 59        |
| Tasmania.....                                     | 59        |
| Victoria.....                                     | 60        |
| Western Australia.....                            | 60        |
| <b>18. USEFUL WEBSITES .....</b>                  | <b>61</b> |
| Government web sites.....                         | 61        |
| Hepatitis Councils.....                           | 61        |
| Diet, Medications, Lifestyle and Drugs.....       | 61        |
| Suicide/Crisis Helpline.....                      | 62        |
| <b>19. QUALITY OF EVIDENCE RATING (QER):.....</b> | <b>63</b> |
| <b>20. LIST OF ACRONYMS.....</b>                  | <b>64</b> |
| <b>21. REFERENCES.....</b>                        | <b>65</b> |

## 1. INTRODUCTION

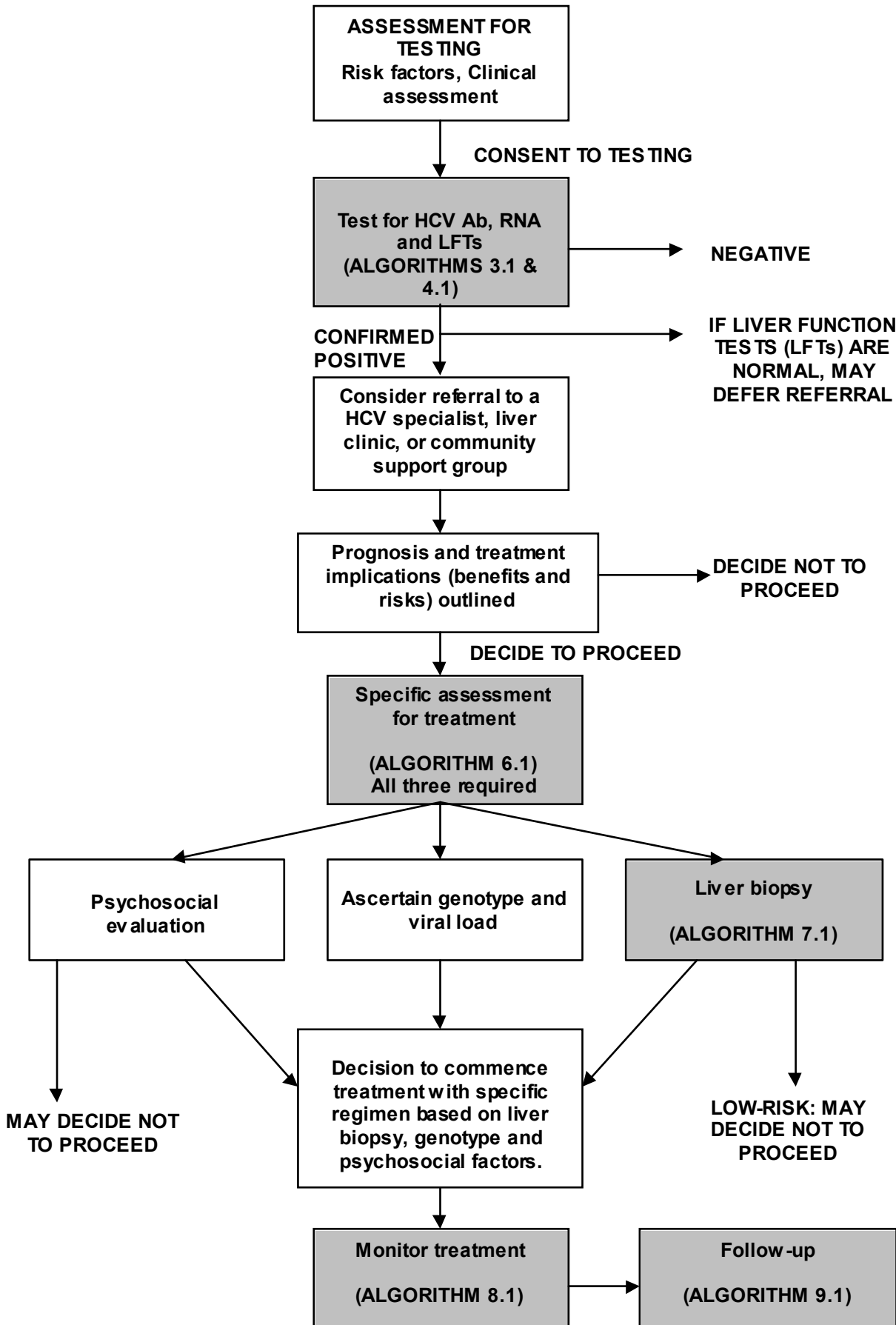
This Model of Care for Adults with Hepatitis C has been prepared by the Hepatitis C Committee and the Clinical Trials and Research Committee (CTARC) of the Australian National Council on AIDS, Hepatitis C and Related Diseases (ANCAHRD). It has been approved and authorised by ANCHARD as an official ANCHARD publication. Consultations occurred with a range of stakeholders including the Royal Australian College of General Practitioners (RACGP), the Australian Liver Association (ALA) of the Gastroenterological Society of Australia, the Australasian Society for HIV Medicine (ASHM), the Australian Hepatitis Council (AHC), the Australian Injecting and Illicit Drug Users League (AIVL), and Dr Margaret Hellard (Macfarlane Burnet Institute for Medical Research and Public Health). The Model of Care (MOC) has been written taking into account the National Hepatitis C Strategy 1999-2000 to 2003-2004<sup>1</sup> and the draft National Hepatitis C Testing Policy<sup>2</sup>.

The primary aim of this Model of Care (MOC) is to provide medical practitioners (both general practitioners and specialists) with best practice guidelines for the clinical care of people with hepatitis C. Paramedical groups, community support services and people with hepatitis C may also find the guide useful. The guideline, by providing best practice information to medical practitioners, seeks to provide a framework in which people with hepatitis C are clearly informed about the treatment and management options available to them. Improving the management of people with hepatitis C reduces the impact of this infection on the individual and the community. The model of care aims to enable both clients and clinicians to make informed decisions regarding management options, as well as facilitating client involvement and participation in the decisions about their health care.

It is recognised that many organisations do not currently have the capacity to reach the best practice standards in the model of care. It is also acknowledged that all individuals will not be able to access the services and supports described in the MOC due to a range of barriers such as remoteness, fee systems, and discrimination. The purpose of the current document is to set the benchmark for individuals, organisations and agencies providing care and support to people with hepatitis C. It is the role of Commonwealth and State authorities to address issues concerning the implementation of the MOC and individuals' capacity to access the recommended services and supports.

The algorithm presented in Section 2 provides an overview of the model of care. Further details concerning each step in the model of care is provided in following sections which consist of an algorithm and brief explanatory notes. The level of evidence has been documented for recommendations in the explanatory notes and where available is accompanied by the relevant reference(s). Published evidence is not always available to support the recommendations that are regarded by experts in the field as necessary or important for high quality care.

## 2.1 ALGORITHM: DIAGNOSIS AND TREATMENT OF HEPATITIS C



## 2.2 HEPATITIS C INFECTION – MANAGING THE PERSON NOT THE VIRUS

### Epidemiology

Hepatitis C is a blood-borne virus. The estimated prevalence of hepatitis C in Australia is 210,000 with 16,000 new infections estimated to have occurred in 2001<sup>3</sup>. Infection with the hepatitis C virus can lead to chronic infection with significant morbidity and mortality. A substantial proportion of people exposed to hepatitis C, however, will not develop chronic infection (estimates range between 20% and 30% for spontaneous clearance of the virus following acute infection)<sup>4</sup>. Estimates of people infected with hepatitis C who develop chronic disease vary due to gaps in current knowledge and the changing epidemiology of hepatitis C. Early studies reported a chronic rate of hepatitis C infection between 80%-85%. These studies were predominantly hospital based and involved people who became infected following a blood transfusion. More recent studies that report lower rates of chronic infection have been community based and involved injecting drug users or women who received small amount of virus from anti D immunoglobulin<sup>5-8</sup>. In these studies the rate of chronic infection was as low as 54%.

### Managing the Person not the Virus

Effective management of individuals undergoing screening and/or treatment for hepatitis C requires medical practitioners and clients to develop a partnership approach based on open communication, trust, shared decision making and information exchange<sup>9,10</sup>.

#### **A partnership approach between medical practitioners and clients involves:**

- Taking a holistic approach (treating the client as a whole person, with many potential interacting issues rather than a person with one disease)<sup>10</sup>.
- Non-judgmental and respectful attitude towards clients' needs, treatment preferences and lifestyle.
- Providing advice and information on the full range of medical and non-medical approaches to managing Hepatitis C.
- Empowering clients with sufficient information to make informed decisions that best suit their lifestyle, occupational and social responsibilities, personal needs and preferences.
- Developing rapport and mutual trust.

Hepatitis C is a condition that has implications not only for an individual's physical health, but also for their social, psychological and emotional well being<sup>11,12</sup>. Medical treatment of the hepatitis virus represents one response within a range of approaches an individual may use in living with hepatitis C. Education and information exchange, counselling, support services, complementary therapies and lifestyle management (e.g., diet, exercise, stress relief) are important elements in managing hepatitis C. The appropriate balance between medical treatment and non-medical management strategies will depend on personal circumstances and choice, community context and lifestyle.

### **Early Contact with a Health Professional**

The first few contacts between a client and a health professional are extremely important because they provide the individual with the context for understanding their illness. Key objectives of this interaction are maintaining quality of life, reducing risk of disease progression and preventing transmission of infection. The initial assessment of a person with hepatitis C should incorporate general psychosocial review and involve information and education concerning:

- the natural history and progression of hepatitis C infection
- transmission risk reduction strategies (not sharing blood contaminated sharps; needles, syringes, injection paraphernalia, razors, refraining from blood donation)
- treatment strategies
- prevention of diseases that may arise from the risks that gave rise to hepatitis C infection (vaccination against hepatitis B)
- practical measures to maintain a well balanced diet
- the use of alcohol and other drugs. An alcohol and drug assessment should elicit client concerns (or lack thereof) regarding their use of alcohol and other drugs. Recommendations regarding alcohol use should be consistent with NHMRC guidelines, that is, people with HCV should consider drinking alcohol infrequently and well below recommended levels for their gender<sup>13</sup>
- resources and supports available for the physical, social and psychological aspects of hepatitis C infection including ways of dealing with potential discrimination.

This information should be reinforced and tailored appropriately at future visits.

### **Available resources and supports**

A range of support services are available for people undergoing hepatitis C testing and for people living with hepatitis C. Information about relevant resources and services should be provided at the first visit, and depending on the client's lifestyle and circumstances, may include information

about services for people who inject drugs. Listed below are the main types of organisations and services that may benefit individuals with hepatitis C. For the locations of specific services refer to Sections 17 and 18.

General Practitioners should consider referral, organising contact or shared care arrangements with:

- A trained and experienced hepatitis C counsellor. Contact details can usually be obtained from either the local Hepatitis Council or a tertiary hospital with a specialised hepatitis unit or outpatient liver clinic.
- A local drug user organisation
- The local Hepatitis Council
- A psychiatrist or psychologist
- A dietitian
- A drug or alcohol treatment service and/or counsellor. Referral to an alcohol or other drug specialist is most appropriate if the person is alcohol or drug dependent. However, for a non-drug dependent person, much can be gained through open and honest discussion with the primary care practitioner to encourage and monitor harm reduction strategies.
- A gastroenterologist or infectious diseases physician, a general physician with an interest in hepatitis C, or a hepatitis clinic. Specialists play an important role in explaining the natural history of the disease, management options and behaviours to reduce the risk of progression and transmission. Hepatitis clinics often have access to counsellors, support groups and psychiatrists.
- A complementary or alternative therapist experienced in hepatitis C management

### **Addressing potential discrimination**

Discrimination is a significant issue for people with hepatitis C and is often associated with the relationship between hepatitis C and injecting drug use<sup>14</sup>. Discrimination can and does occur within the health care setting<sup>14-16</sup>. Under the Commonwealth Disability Discrimination Act 1992 it is illegal to discriminate on the basis of disability if the disability is an infectious disease, except where discrimination is necessary to protect public health. Similar laws exist in all States and Territories. People with hepatitis C are entitled to receive the same level of access to medical treatment as other members of the community. Clients should be made aware of their rights concerning freedom from discrimination. Information and advice concerning individuals' rights regarding discrimination and complaints processes are available from Hepatitis Councils, drug user organisations and anti-discrimination services in each State and Territory.

## Hepatitis C and Discrimination

Discrimination may result from conscious and overt decisions or unconscious beliefs and attitudes<sup>14</sup>. Discrimination may be direct or indirect:

- **Direct discrimination:** treating a person with Hepatitis C less favourably than others<sup>14</sup>.
- **Indirect discrimination:** a requirement, condition or practice which appears neutral has a disproportionate impact on an individual who has hepatitis C<sup>14</sup>.

## Natural history and progression

The rate of hepatitis C chronic infection and disease progression varies considerably. The majority of people with hepatitis C will not develop advanced liver disease. Of 100 people with the hepatitis C virus (HCV), approximately 25 people will spontaneously clear the virus. Between 30 and 40 people will continue to be infected with the virus but will not develop progressive liver disease. Thirty five to 45 will develop some level of progressive liver disease associated with their hepatitis C. Symptoms related to hepatitis C and quality of life impairment may be present in both people with and without progressive liver disease. Of the 35 to 45 people with progressive liver disease, without treatment approximately 5 to 10 will develop cirrhosis (10 – 20% life time risk) and 1-3 will develop hepatocellular carcinoma<sup>17</sup>. The heterogeneity in disease progression and symptomatic disease means that some people will require limited contact with the health profession and support systems associated with hepatitis C whereas others will require constant and on going contact. It is important to emphasise that high risk patterns of alcohol consumption can accelerate liver damage from hepatitis C, therefore alcohol consumption should be limited to reduce the likelihood of progressive liver disease.

## Transmission risk

Hepatitis C is a blood-borne virus affecting the liver. For successful transmission to occur the virus:

- must be present in the blood of a person with hepatitis C
- in sufficient concentrations to present an infection threat to another person (people with even low viral loads may transmit HCV, depending on the type of exposure), and
- directly enter the bloodstream of another person by blood-to-blood contact through a rupture or opening in the skin.

In Australia the greatest source of risk for transmission of HCV is through sharing or reusing needles, although other injecting equipment (such as swabs, tourniquets, or containers used for mixing drugs), hands, puncture sites and the preparation area may become contaminated and

pose a significant transmission risk. Although often present in other body fluids, the concentration of the virus in such fluids is considered too low for transmission to occur<sup>12</sup>. Worldwide prevalence of HCV among injecting drug users is estimated at 70%, whereas Australian studies have found prevalence rates of 60-68% amongst injecting drug users<sup>4</sup>.

The risk of transmission of hepatitis C through occupational needle stick injury is estimated at approximately 2% when the source is HCV antibody positive, and between 3-10% when the source is HCV RNA (Ribonucleic Acid) positive<sup>18</sup>. The risk of transmission via blood and blood product has become virtually negligible following the introduction of testing for hepatitis C in 1990. The risk of vertical transmission (mother to child) is estimated to be approximately 5-8%<sup>19</sup>. Sexual transmission of hepatitis C is uncommon (estimated to <1%) in both heterosexuals and homosexuals except where the individual and their partner are co-infected with HIV (Human Immuno-deficiency Virus) (QER III-3)<sup>20-22</sup>. Transmission can occur from sharing razors and toothbrushes.

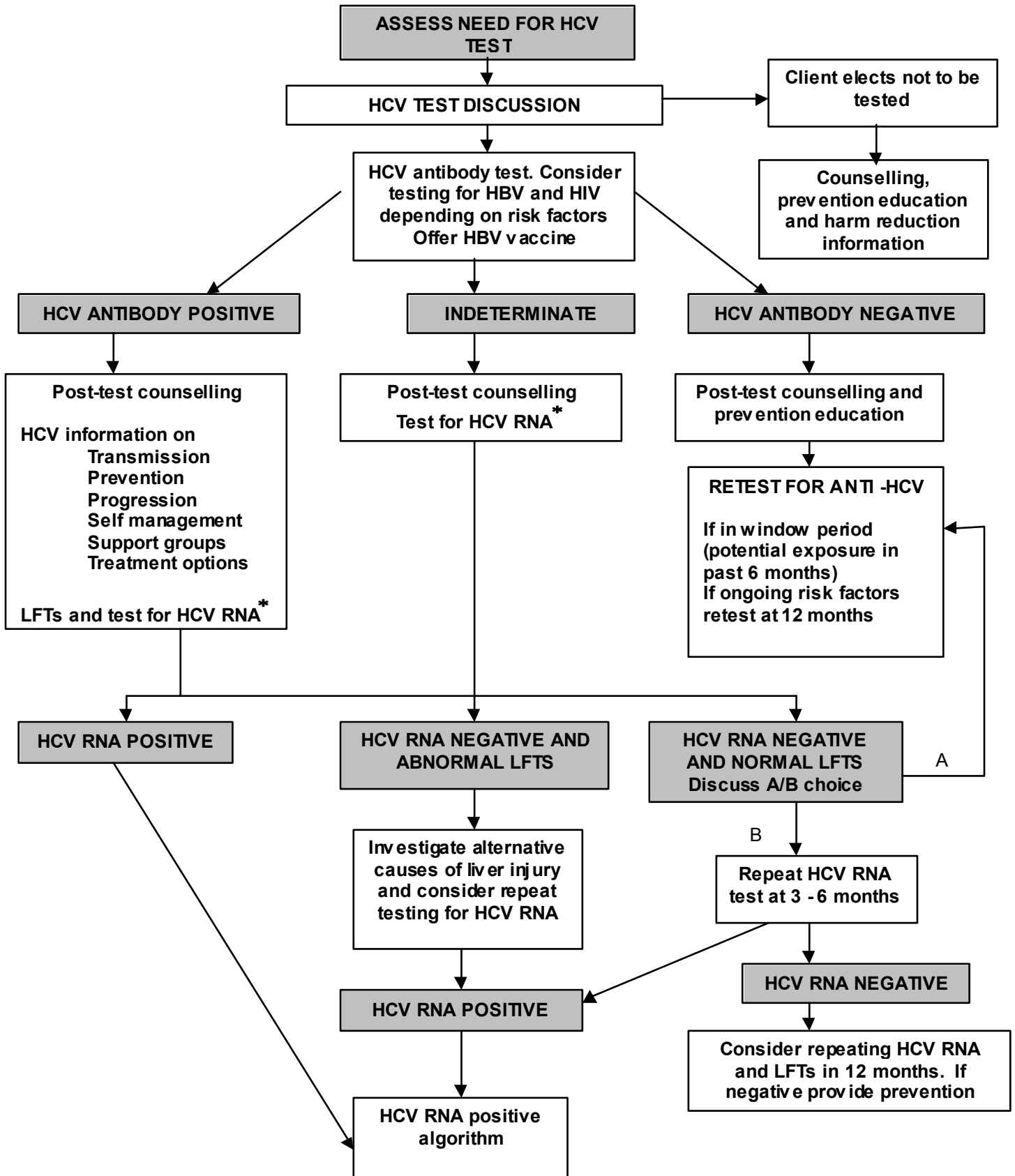
Although household transmission of hepatitis C would appear to be a rare event, it is an issue that often creates considerable anxiety for people living with hepatitis C, their families, and other household members. Clients should be provided with information on avoidance of potential situations of blood-to-blood contact such as sharing of razors and toothbrushes. The client should also be provided with information that dispels myths associated with transmission risk in the home and in the workplace (e.g., through aerosols, close contact, sharing of cutlery etc).

Clients should also be counselled about disclosing their diagnosis to others. There is no legal requirement for a person with hepatitis C to disclose their status except for blood and tissue donations. People who inject drugs should be encouraged to consider their current injecting practices and methods of needle and equipment disposal to prevent infection and cross-infection within their own using community, and to whom within this community they disclose their HCV status.

## **Treatment**

Treatment options are available and vary according to stage of infection and disease progression. However the majority of people will not be disadvantaged by delays in treatment and many people may never require treatment for the virus. Details of current treatments are given in Sections 7 and 8. Regardless of whether immediate treatment is initiated, people should be given information on relevant risk behaviours, transmission risks, infection from other strains and lifestyle management issues.

### 3.1. ALGORITHM: TESTING OF INDIVIDUALS FOR HEPATITIS C STATUS\*



\*Adapted by kind permission of Australian Family Physician, Royal Australian College of General Practitioners

\* Subject to compliance with MBS Schedule Specifications

## 3.2. EXPLANATORY NOTES: TESTING OF INDIVIDUALS FOR HEPATITIS C STATUS

### Assessing the Need for a Hepatitis C Test

A request for hepatitis C testing may be instigated by the client or medical practitioner. In assessing the need for a test the risk of likely infection should be considered based on potential hepatitis C exposures. In relation to injecting drug use, many people may not disclose their potential risk factors due to previous experiences of discrimination related to injecting drug use. It is also widely reported that a substantial number of people are simply unable to identify a likely risk factor<sup>23,24</sup>. This can be a source of significant distress and frustration for the client in the event that their test is positive.

The National Hepatitis C Testing Policy<sup>2</sup> recommends testing for hepatitis C antibodies should be routinely offered to the following groups:

- people who have ever injected drugs
- people who have been incarcerated in a custodial institution
- people who were transfused with blood or blood products before February 1990
- people who have been transfused with blood or blood products overseas
- people who have had a potential occupational or environmental exposure to hepatitis C (for example, a needle-stick injury) and, where possible, the exposure source—with their specific informed consent
- health care workers who engage in exposure-prone procedures
- people with abnormal liver function tests or evidence of liver disease with no apparent cause
- people with extrahepatic manifestations of hepatitis C infection
- renal dialysis patients
- people who request testing in the absence of an identified risk factor.

For some individuals and groups, testing for hepatitis C may be considered and offered on the basis of an individualised risk assessment. Among these groups are:

- people with a history of tattooing or body piercing, taking account of multiple tattoos or body piercings and the settings in which the procedures took place
- people born in countries where there may be a high prevalence of hepatitis C infection
- the sexual partners of people with hepatitis C.

## **Pre-Test Discussion**

Comprehensive discussion prior to testing is crucial to the effective management of people considering undergoing testing for hepatitis C. Information should be provided on the probability of a positive test based on risk status. Consideration of hepatitis C testing may raise significant emotional, social or psychological issues for clients<sup>12</sup>. Therefore, it is recommended that pre- and post-test counselling be conducted in person rather than over the telephone. In addition to face-to-face discussion, provision of written information, support and referral to additional support services (e.g., Hepatitis Councils) can assist clients to make an informed decision about testing.

### **Issues to consider during Hepatitis C pre-test discussion**

In the process of informing clients medical practitioners should provide clear descriptions of the process of testing and the meaning of positive, negative and indeterminate test results. Clients should be assisted to prepare for all possible test results. For example, clients should be encouraged to consider coping strategies and sources of support they can utilise in response to each possible test result<sup>10,12</sup>. Pre-test counselling should also address issues concerning confidentiality of tests results and requirements for medical practitioners to notify State/Territory health departments of positive test results.

The pre-test discussion provides an opportunity to:

- provide relevant, up-to-date information to assist in making a decision about testing
- discuss the testing procedure and provide the client with the option of not being tested
- explain the probability of a positive test based on risk status
- check the client's understanding of the information provided
- discuss the probability of spontaneously clearing the virus, factors affecting disease progression and options for treatment
- assess the possible response of the client to the test outcomes and review the level of support they have available
- provide and discuss information to prevent further transmission based on current lifestyle factors
- obtain informed consent.

Informed consent involves ensuring the client has information about and clearly understands the:

- likely risk factors for transmission
- implications of test results (such as positive, negative, false positives, indeterminate results)
- potential health outcomes relative to test results
- range of medical and other services available in the occurrence of a positive test result<sup>12</sup>.

To reduce the risk of further transmission, risk behaviours such as unsafe injecting practices that can lead to viral transmission should be discussed. It is important to emphasise that the risk of transmission through sexual contact and household transmission is low. Clients should be advised not to share razors and toothbrushes to reduce the risk of household transmission. The probability of spontaneously clearing the virus and the factors affecting disease progression should be discussed (refer to Section 2) as should treatment availability and options (refer to Sections 7 and 8).

### **Strategies to reduce further risk of transmission include:**

- adopt safer injecting practices:
  - always using new injecting equipment
  - ensure tabletops and preparation areas are clean to prevent microscopic transmission
  - always wash hands before and after injecting
  - do not assist others to inject, or share mix, spoons, tourniquets or filters
  - don't share equipment with others even if it has been cleaned
- avoid sharing razors and toothbrushes to reduce the risk of household transmission
- avoid giving blood
- avoid obtaining new tattoos or body piercing.

Other possible topics for discussion will depend on the client's situation, but may include vertical transmission (if pregnant), work issues, insurance, disclosure and discrimination. Not every issue needs to be discussed during the initial test discussion and each client will have different information needs (QER IV). As retention of information is often a significant issue for those receiving an initial diagnosis, post-test counselling should be considered an essential component of the assessment and treatment plan.

## **Hepatitis C Tests to Detect Past and Current Infection**

### **Antibody tests**

The hepatitis C antibody test detects past exposure to hepatitis C. In Australia very specific (third generation) serological assays are generally used<sup>25</sup> (QER - III-2). Antibodies can usually be detected after 8 weeks. The window period for antibody detection is 30-150 days. The rate of false positive and false negative tests varies; false positives are more likely in low risk groups.

False negatives can occur in clients who are HIV positive or have other deficiencies in humoral immunity. PCR (polymerase chain reaction) tests are indicated in these groups (QER III-2)<sup>26</sup>.

## **Hepatitis C RNA**

Detection of hepatitis C RNA indicates current infection. The test is used to differentiate between people who have been exposed but cleared the virus and people who have chronic infection<sup>5,6</sup>. It should be performed on all clients who are hepatitis C antibody positive. HCV RNA is also used to detect acute infection before seroconversion and in the management of people being treated for hepatitis C. Nucleic acid testing is performed either with the polymerase chain reaction (PCR) or with the branched DNA (bDNA) assay. PCR has a lower limit of detection than bDNA and can detect  $10^2$  to  $10^3$  copies/ml of virus<sup>26, 27</sup>.

## **Post-Test Counselling**

Post-test counselling provides medical practitioners with the opportunity to clarify information already provided to the clients, to reinforce information regarding risk factors for infection, and further establish the clinician-client relationship in the event that further contact is required, particularly in situations where a negative or indeterminate result is returned.

Following detection of hepatitis C RNA some clients may require additional support or time to discuss the implications of the test outcomes. It is important that information provided during the initial test discussion is reinforced, including reminders about the role of other support services available for people with HCV. Additional appointments, or arranging a direct referral to other support services (rather than merely providing someone with information) may be helpful to the client. Resist the temptation to overload the client with too much information, but provide specific information with regard to preventing further transmission, disease progression, self-care and treatment options (including non-pharmacological treatment)<sup>12</sup>. A management plan should be mapped in consultation with the client regarding frequency of follow-up appointments and testing. If the client is hepatitis C RNA negative, discuss the role of follow up testing, and strategies to reduce the risk of future exposure (QER IV).

Medical practitioners should also be aware that some people miss out on post-test counselling. It is important to check when seeing a new client who has been previously diagnosed that they have accessed information and/or counselling about hepatitis C.

## **Reporting Requirements and Client Confidentiality**

### **Reporting requirements**

Hepatitis C is one of the diseases reported to the National Notifiable Diseases Surveillance System (NNDSS) maintained at the Commonwealth Department of Health and Ageing, Canberra. The list of notifiable diseases is determined by the Communicable Diseases Network of Australia. NNDSS collates information on notifiable diseases collected in each State and Territory. Notifications of hepatitis C are classified either as incident (ie newly acquired) or unspecified (where the timing of infection is unknown). Enhanced surveillance for incident hepatitis C cases is undertaken in some jurisdictions.

Three jurisdictions undertake surveillance on all hepatitis C notifications to determine whether they are incident cases (Australian Capital Territory, South Australia and Tasmania); Victoria and Western Australia undertake enhanced surveillance on all cases initially identified as incident by the notifying laboratory or doctor, in addition to a random sample of all unspecified hepatitis C notifications (10 per cent sample in Victoria, and a 30 per cent sample in Western Australia); New South Wales has informed the Commonwealth Department of Health and Ageing it will cease state-wide enhanced surveillance for hepatitis C in 2003; No surveillance has ever been undertaken in Queensland; and enhanced surveillance ceased in the Northern Territory in 2001, and has not recommenced since that time.

### **Client confidentiality**

Clients should be informed of their rights to confidentiality concerning their hepatitis C status. The following guidelines are provided by the National Hepatitis C Testing Policy<sup>2</sup>.

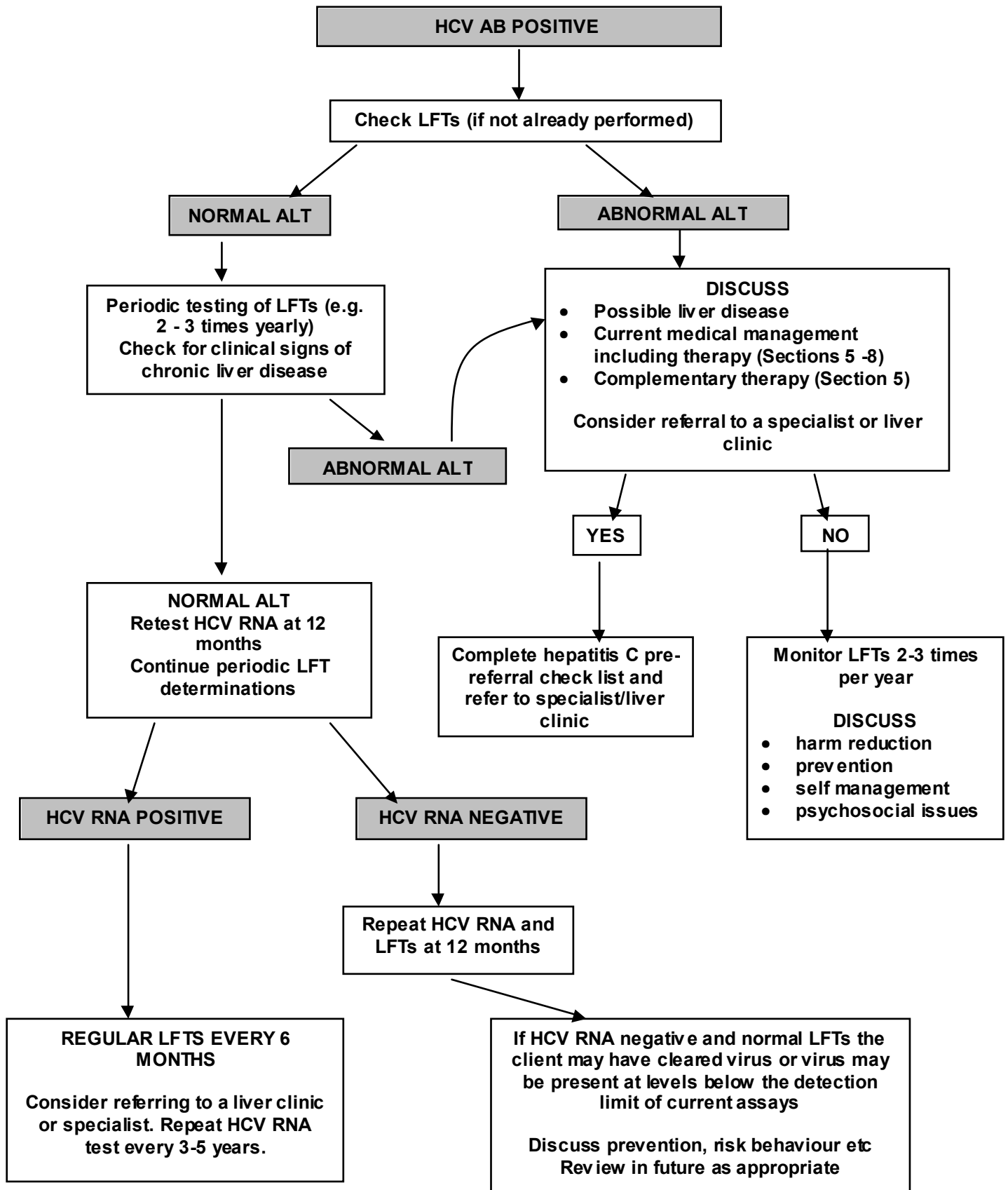
“If people who have been tested or are contemplating testing are to have confidence in the health system it is essential that adequate mechanisms exist to ensure the confidentiality of test results at all levels—clinical, data management, and the notification process. People who are considering testing are entitled to be told about how notification to health authorities of confirmed positive tests results occurs and the confidentiality safeguards that apply”<sup>2</sup>.

## Accessing Testing

Testing is available from private medical practitioners and through public health services. Medicare pays for testing from private practitioners and testing through public clinics is generally free for clients. The Medicare Benefits Schedule (March 2003) funds the following hepatitis C treatment assessment and monitoring tests from private practitioners:

- testing for hepatitis C using hepatitis C antibody test (Item No. 69438).
- supplementary testing for hepatitis C antibodies using a different hepatitis C antibody assay on the specimen which has a reactive result on the initial hepatitis C antibody test (Item No. 69441).
- quantitation of HCV RNA load in plasma or serum in the pre-treatment evaluation for antiviral therapy of a patient with chronic HCV hepatitis - where any request for the test is made by or on the advice of the specialist or consultant physician who manages the treatment of the patient with chronic HCV hepatitis (including a service in item 69444 or 69445) - not exceeding 1 episode in a 12 month period (Item No. 69442).
- nucleic acid amplification and determination of hepatitis C virus genotype if:(a) the patient is HCV RNA positive and is being evaluated for antiviral therapy of chronic HCV hepatitis; and (b) the request for the test is made by, or on the advice of, the specialist or consultant physician managing the treatment of the patient; No more than 1 episode in a 12 month period (Item No. 69443).
- detection of Hepatitis C viral RNA if at least 1 of the following criteria is satisfied: (a) the patient is hepatitis C seropositive and has normal liver function tests on 2 occasions at least 6 months apart; (b) the patient's serological status is uncertain after testing; (c) the test is performed for the purpose of: (i) determining the hepatitis C status of an immunosuppressed or immunocompromised patient; or (ii) the detection of acute hepatitis C prior to seroconversion where considered necessary for the clinical management of the patient; not exceeding 1 episode in a 12 month period (Item No. 69444).
- detection of hepatitis C viral RNA in a patient undertaking antiviral therapy for chronic HCV hepatitis (including a service described in item 69444) - not exceeding 4 episodes in a 12 month period (Item No. 69445).

## 4.1. ALGORITHM: POSITIVE HEPATITIS C ANTIBODY TEST\*



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## 4.2. EXPLANATORY NOTES: POSITIVE HEPATITIS C ANTIBODY TEST

Initial reports suggested that spontaneous clearance or resolution of hepatitis C infection occurred in the first six months following infection, with virus persisting beyond this point indicating lifelong infection. More recent studies suggest that hepatitis C viral clearance may continue for at least the first three years of infection (QER III-2)<sup>28,29</sup>. The factors associated with spontaneous viral clearance are unknown. Some studies suggest that acute clinically overt hepatitis, low peak hepatitis C RNA level, vigorous cytotoxic T lymphocyte (CTL) responses, and a lower rate of hepatitis C quasi-species development are associated with spontaneous hepatitis C clearance. There is also limited evidence for ethnicity, and alcohol or other drug use in determining hepatitis C clearance (QER III-2)<sup>5,29-31</sup>.

If an individual's previous HCV RNA status was positive or unknown, and his or her current HCV RNA status is negative, current knowledge is uncertain concerning the duration of RNA negative test results required before the individual can be considered to have cleared the virus. Currently, a minimum of two negative HCV RNA tests is required over a two-year period for a certain result. The uncertainty is due in part to the low sensitivity of the test when the virus is at low levels in the blood (QER – IV).

### **Liver Function Tests**

There is a variety of serum liver function tests (LFTs) which are used as markers of liver inflammation or disease (e.g., obstruction of bile ducts). Although indicative, LFTs cannot distinguish the specific cause of abnormal LFTs that arise from HCV infection, HBV infection, alcohol, cancer and infections like glandular fever. Nevertheless, LFTs provide valuable information on the estimated extent of liver disease and rate of progression (regardless of cause).

### **Normal liver function tests in people who are HCV antibody positive**

Clients with normal Alanine Aminotransferase (ALTs) are less likely to develop liver damage and are not recommended for treatment (QER III-3)<sup>32,33</sup>. The longer the period of antibody positivity with normal liver function tests (LFTs) the greater the likelihood that the disease will not progress (QER III-3)<sup>32</sup>.

A person with normal liver tests over many years should occasionally have their hepatitis C RNA checked to establish if they continue to be positive. There is no evidence guiding the frequency of such testing although every 3-5 years is suggested (QER IV).

### **Abnormal liver function tests**

LFTs, in particular the ALT, are useful markers when managing hepatitis C infection. Clients with abnormal liver function tests are more likely to be viraemic and are at increased risk of developing liver damage related to their hepatitis C. At the same time it is important to explain to clients that there is not a linear relationship between the ALT level and their level of liver injury, inflammation or fibrosis (QER III-3)<sup>32,34</sup>.

### **Referral to a Liver Clinic, HCV Specialist, Paramedical Specialists and Other Services**

Clients should be encouraged to attend a liver clinic or HCV specialist on at least one occasion. Effective ongoing management of clients with hepatitis C involves shared care with the general practitioner, liver specialist, paramedical specialists and community support services. Section 5.1 provides a pre-referral checklist indicating the types of information a GP should consider prior to referral to a liver clinic, HCV specialist, paramedical specialist and other services. Section 5.2 discusses the conditions and issues associated with hepatitis C addressed by each type of service. The services provided by liver clinics and HCV specialists are considered in Section 6.

## 5.1. GENERAL PRACTITIONER PRE-REFERRAL CHECKLIST FOR CLIENTS WITH HEPATITIS C

### History

Date of all hepatitis C antibody and RNA tests (if known)

Most likely mode of transmission

Alcohol and other drug history (for all drugs including prescribed medications and alcohol).

- type of drug/s used
- pattern of use (including how long the person has been using, establish pattern over the last 7 days, and whether this is 'typical', identify patterns of use on special occasions)
- frequency of use
- when the person last used (identify possible intoxication or withdrawal)
- route of administration (oral, snorting, swallowing, injecting, anal)

Risk behaviour related to injecting drug use:

- when first injected
- whether and how assistance was provided
- use of needles before or after other people (identify recent and previous episodes)
- sharing of injecting paraphernalia
- injecting in the company of others
- assisting others to inject (eg. snabbing for other people)

Transfusion or medical procedure – year in which the event took place.

Other exposure (e.g. needle stick injury in the workplace) and year in which the event took place

Country of birth/origin

Risk factors leading to increased likelihood of liver disease progression – high risk patterns of alcohol consumption, co-infection with HBV or HIV, re-infection with a second hepatitis C virus

History of hepatitis in the past – jaundice, right upper quadrant pain, fever, nausea

History of previous treatment for hepatitis C

History of other blood borne viruses

Other illness – diabetes etc

Cultural (e.g., context and location of drug use) and psychosocial (e.g., housing, finances, employment) issues

Medication, complementary therapies, allergies

Symptoms of impaired health related quality of life that may be due to chronic hepatitis C infection – fatigue, lethargy, malaise, depression, mood swings, sleep quality, nausea, right upper quadrant discomfort, food intolerance

History of depressive illness, epilepsy, psoriasis, autoimmune disease

## **Physical Examination**

Signs of chronic liver disease

## **Blood Tests**

### **Essential**

Hepatitis C antibody result; hepatitis C RNA result; LFTs

### **Important**

Hepatitis B serology; Hepatitis A serology; HIV serology (with pre- and post-test counselling); FBE (full blood examination), prothrombin time (PT) (INR – International Normalised Ratio)

### **Consider**

Alpha-fetoprotein (baseline for Hepatocellular Carcinoma), thyroid function test

Tests for other causes of chronic liver disease – nuclear, mitochondrial and smooth muscle antibodies, serum transferrin saturation and ferritin, serum copper and caeruloplasmin

Ultrasound (especially if clinical evidence suggestive of cirrhosis or age over 45 years)

## **Hepatitis C with Normal Liver Tests**

If a client has normal liver tests there is no need for blood tests looking for other causes of chronic liver injury or tests for cirrhosis or liver cell cancer (alpha-fetoprotein, ultrasound).

## **5.2. REFERRAL TO MEDICAL SPECIALISTS AND OTHER SERVICES**

The need to refer a client to other medical specialists and services varies depending on the impact of hepatitis C on the client's physical, psychological and social well being and also the client's preferences for accessing these services.

### **Referral to a Liver Specialist**

In order to assess the extent of liver disease, eligibility for treatment and complex medical management, referral to a HCV specialist or liver clinic should be considered. The activities undertaken by HCV specialists and liver clinics are described in Section 6.

### **Referral to Hepatitis Councils, Injecting Drug User Organisations, Alcohol and other Drug Treatment Services, Counsellors, Social Workers, Psychiatrists & Psychologists**

#### **(Psychosocial Issues Associated with Hepatitis C Infection)**

Following diagnosis, and regardless of the source of transmission, many clients with hepatitis C may feel extremely disappointed, frustrated or angry about contracting a chronic disease that has potentially severe morbidity and mortality. Most are likely to be concerned about the implications of the disease on their lifestyle, work or other commitments, recreational activities, and interpersonal relationships. Many may require specific counselling about these issues. Counselling is also strongly recommended for people who have acquired hepatitis C following a medical intervention, or those who have no identified risk factor.

People who have established high-risk patterns of alcohol use, or who choose to inject drugs, tend to have quite complex life issues associated with their alcohol or other drug use. Maintaining injecting drug use involves a complex and to others a seemingly chaotic lifestyle in which, for example, the cycle of using and obtaining drugs to prevent or treat withdrawal symptoms may seem to take priority over issues related to health and HCV. An apparent lack of concern or reluctance to become involved in treatment does not necessarily suggest the client is uninterested or concerned about their health, rather that other issues may take priority at that point in time. A reluctance to immediately engage or continue with care may be a source of greater frustration for the health professional than the client. Establishing rapport, negotiating level of care, and ensuring opportunities for the client to return will provide the basis for creating ongoing opportunities for engaging the client in future care.

Managing psychosocial aspects of care (e.g., continued drug use, emotions such as anger, frustration, depression) are as important as managing hepatitis C. Involving other parties and engaging in shared care relationships ensures that clients have quality support in areas where their primary care professionals may have less confidence. Depending on the concerns raised by the client referrals and links may be made with rehabilitation or welfare services, social workers, psychologists, counsellors, psychiatrists, Hepatitis Councils and peer based user groups. Information about needle and syringe programs or chemists who supply clean needles can also be useful. As discussed previously, issues of discrimination particularly in relation to health care and work are important for people with hepatitis C. Information and advice concerning individuals' rights regarding discrimination and complaints processes are available from Hepatitis Councils, drug user organisations and anti-discrimination services in each State and Territory.

### **Referral to a Rheumatologist, Dermatologist or Renal Physician (Extrahepatic Manifestations of Hepatitis C Virus Infection)**

People with hepatitis C may suffer from a variety of symptoms (including fatigue, non-specific malaise, depression and joint pain) in the absence of signs of chronic liver disease, which can give rise to a great deal of frustration for the affected individual. Studies have reported 40 - 50% of people with hepatitis C report significant fatigue<sup>35</sup>. Hepatitis C infection is also associated with mixed cryoglobulinaemia, membranoproliferative glomerulonephritis and other auto-immune conditions. Over a third of clients with hepatitis C have cryoglobulins<sup>35</sup> but only 1-2% develop EMC (essential mixed cryoglobulinemia). Conversely approximately 80% of mixed cryoglobulinaemia is secondary to hepatitis C infection. Mixed cryoglobulinaemia is associated with the presence of serum immunoglobulins that precipitate in the cold and lead to a vasculitis of varying severity. Symptoms can range from palpable purpura, arthralgia and weakness to involvement of vital organs. Nephrotic syndrome can also occur. Glomerulonephritis is thought to be due to the deposition of immune complexes of the viral antigen or antibody or both within the glomerular basement membrane. This can lead to both membranous and membranoproliferative glomerulonephritis. Other conditions reported to be associated with chronic hepatitis C infection include Sjogrens syndrome, Hashimoto's thyroiditis, hypothyroidism, lichen planus, porphyria cutanea tarda (PCT), corneal ulcers and idiopathic pulmonary fibrosis.

### **Referral to a Nutritionist or Dietitian**

The evidence supporting the need for a specific diet for hepatitis C is far from clear and is discussed in more detail in Section 13. Although the majority of clients do not need to change their diet because of hepatitis C, many want independent information from a dietitian or nutritionist. There are some circumstances (such as severe liver disease and in some cases, cirrhosis) when specialised dietary advice may be essential. Referral to a nutritionist or dietitian working in the

hepatitis/gastroenterology field or specific written information on this aspect of their management may be worthwhile. Most Hepatitis Councils have healthy eating and nutrition guidelines for people with hepatitis C<sup>36</sup>.

## **Referral to a Complementary or Alternative Therapist**

Many clients want information about naturopathic treatments and complementary therapy for hepatitis C. The Hepatitis Councils often have information about complementary therapies as do some hepatitis clinics at referral hospitals. These therapies are discussed in more detail in Section 14.

## **Hepatitis C and oral health<sup>1</sup>**

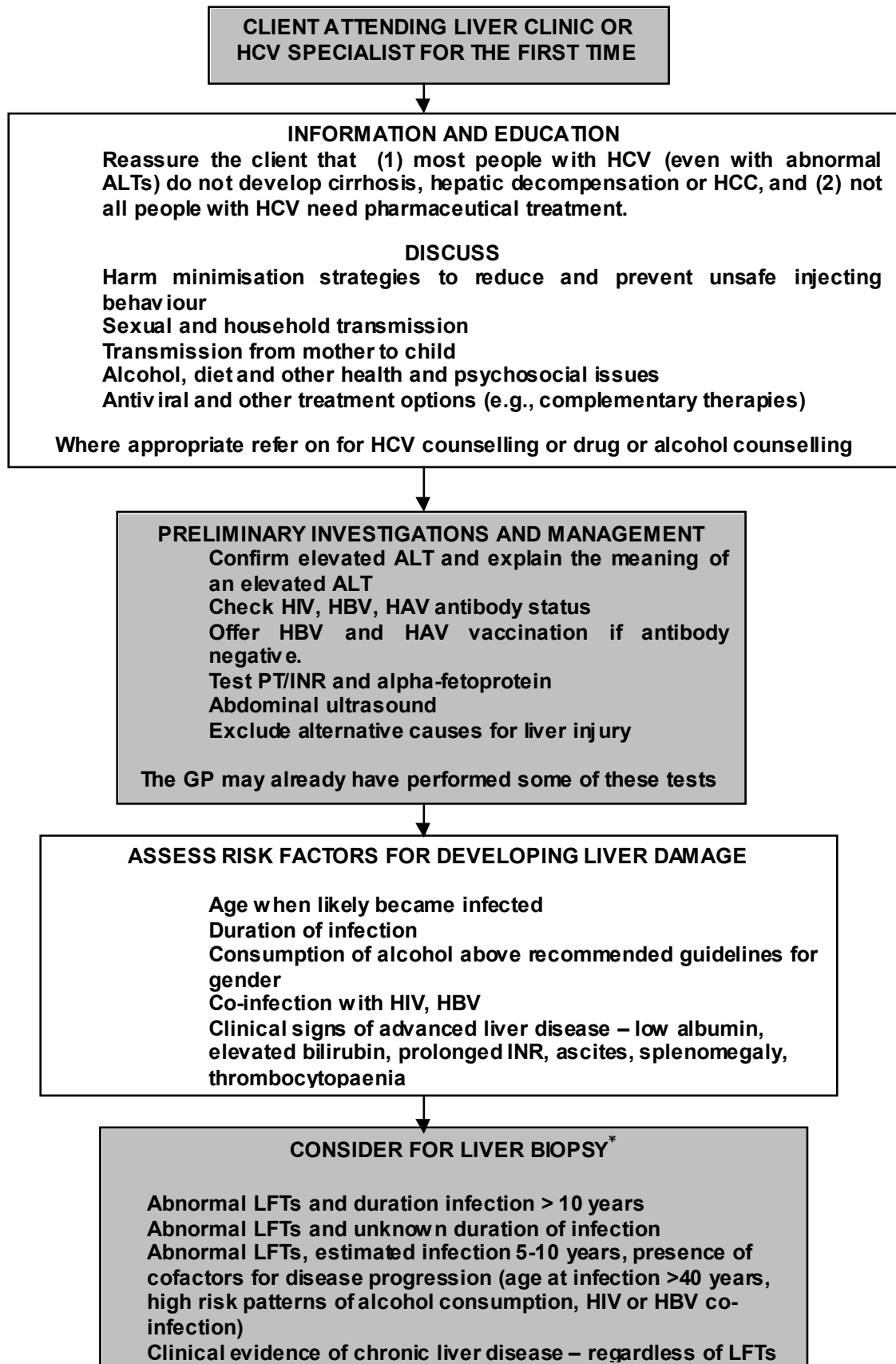
Dental cavities, number of missing teeth and periodontal health for people with hepatitis C are significantly worse than comparable groups in the community. People with hepatitis C infection suffer loss of esteem due to poor oral aesthetics and also have difficulty with diet due to poor oral health and dental pain. It is now evident that much of the dental disease suffered by people with hepatitis C can be attributed to dry mouth syndrome associated with the hepatitis C infection although factors such as injecting drug use, methadone and other prescription medications, cigarette smoking and poor diet may all contribute to their poor oral health.

Sporadic intermittent dental care will not address the oral health needs of those people with hepatitis C infection with dry mouths or periodontal disease. If oral health and prognosis for dental treatment is to be improved, then oral care treatment plans incorporating long term prevention components should be developed such that the influences of infection with a chronic virus, medication and for some individuals injecting drug use will be overcome. This entails the use of home fluoride applications, oral hygiene instruction, antiplaque mouth rinses where appropriate, dry mouth toothpastes, dietary counselling and regular reviews by the dentist and hygienist for monitoring of oral hygiene. Additionally people with hepatitis C may require extensive restorative and prosthetic dental treatment to restore function and aesthetics that has deteriorated because of their condition. Management of periodontal needs is a more complex issue. The success of the comprehensive treatment protocol outlined above needs to be established as this may impact on the periodontal disease pattern eliminating the need for invasive periodontal treatment.

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<sup>1</sup> Information in this section was provided by Liz Coates MDS (Adel), FICD, FPFA, FADI, Senior Consultant, Coordinator Special Needs Unit, Adelaide Dental Hospital.

## 6.1. ALGORITHM: SERVICES PROVIDED BY A HCV SPECIALIST OR LIVER CLINIC



\* Based on Dore, G. (2001, p. 137). Initial assessment and clinical monitoring. In Crofts, N., Dore, G., & Locarnini, S. (2001) (Eds). Hepatitis C: An Australian Perspective. Melbourne: IP Communications.

## 6.2. EXPLANATORY NOTES: SERVICES PROVIDED BY A SPECIALIST OR LIVER CLINIC

### Counselling and Information

Referring a client with chronic hepatitis C infection to a specialist or liver clinic on at least one occasion is worthwhile. Referral to a specialist is required for consideration of eligibility for S100 drugs (see Section 7.2). Specialists can also provide additional advice, guidance and clarification of information on hepatitis C previously provided to clients in post-test counselling. Clients are often concerned about the risk of transmitting the virus to their family or friends. As well as the issues of injecting and blood-to-blood spread, clients are often concerned about sexual and perinatal transmission risk. As discussed earlier, the risk of sexual transmission is generally low except where the client and the partner are co-infected with HIV (QER III-3)<sup>20-22</sup>. The risk of vertical transmission (discussed in Section 10) is around 5-8%<sup>2</sup>. The low risk of household transmission should also be emphasised. In discussion about liver disease progression it is important to encourage clients to adopt low-risk patterns of drinking or to consider abstinence. (QER III-3)<sup>5,37,38</sup>. Treatment options should also be discussed.

### Preliminary Investigation

#### Liver function tests

Clients must currently have abnormal ALTs in conjunction with documented hepatitis C infection before they are eligible to receive government-supported treatment (see Section 7.2).

#### Hepatitis A, hepatitis B and HIV

Determine client's exposure to hepatitis A, hepatitis B and HIV. Hepatitis A and B vaccines should be offered to clients with no evidence of previous exposure or vaccination. HBV and HIV are reported to impact on hepatitis C progression and response to treatment<sup>38,39</sup>. Refer to Sections 11 and 12.

#### Other blood tests

Exclude other potential causes of liver injury. FBE, albumin and PT/INR are useful markers of liver synthetic function and an alpha-fetoprotein is a marker of hepatocellular cancer.

#### Ultrasound

Opinion varies on the usefulness of abdominal ultrasound. Ultrasound can be useful for detecting lesions but is less helpful for detecting cirrhosis. Clients with hepatitis C infection rarely develop a hepatocellular carcinoma without already having cirrhosis.

## **Liver Biopsy**

Liver biopsy is an important tool for assessing the severity of a client's disease and is more reliable than either blood tests or ultrasound in predicting fibrosis or cirrhosis. Combined with other information such as duration of infection and risk factors such as high risk patterns of alcohol consumption or co-infection with HIV, biopsy provides important information about the rate of progression of hepatitis C related liver injury and the need for treatment. A biopsy result is useful for planning future management strategies regardless of whether the client wants treatment immediately or at some possible time in the future. Further information on liver biopsy is provided in Section 7.2.

## **Assessing Risk Factors for Developing Liver Damage**

### **Age**

The age at which a client became infected has been considered an important predictor of disease progression. Recent data suggest that this association may not be as great as previously thought and the association with hepatitis C and disease progression may be associated with other confounding factors.

### **Alcohol**

It has been well established that people with HCV who drink at risky or high-risk levels are likely to have poorer health outcomes than those who do not drink alcohol. There is no evidence to suggest that people with HCV should totally abstain from using alcohol. However, to reduce the risk of harm it is recommended that alcohol is limited to infrequent low-risk levels to limit disease progression or that total abstinence is considered<sup>13</sup>.

### **Duration of infection**

The longer the duration of the infection the greater the likelihood of a person having chronic liver disease (CLD). At the same time if a person has been infected for more than 10 years and they have no histological or biochemical evidence of necroinflammatory changes his or her chance of developing CLD is reduced.

### **Genotype**

Uncertainty surrounds the role of virus genotype (genetic structure) in liver disease progression. Some studies report genotype 1 increases the risk of developing CLD but this is confounded by the fact that people with genotype 1 were on average infected at an older age and for a longer duration. Genotype does not have a significant role when assessing the risk of liver disease progression.

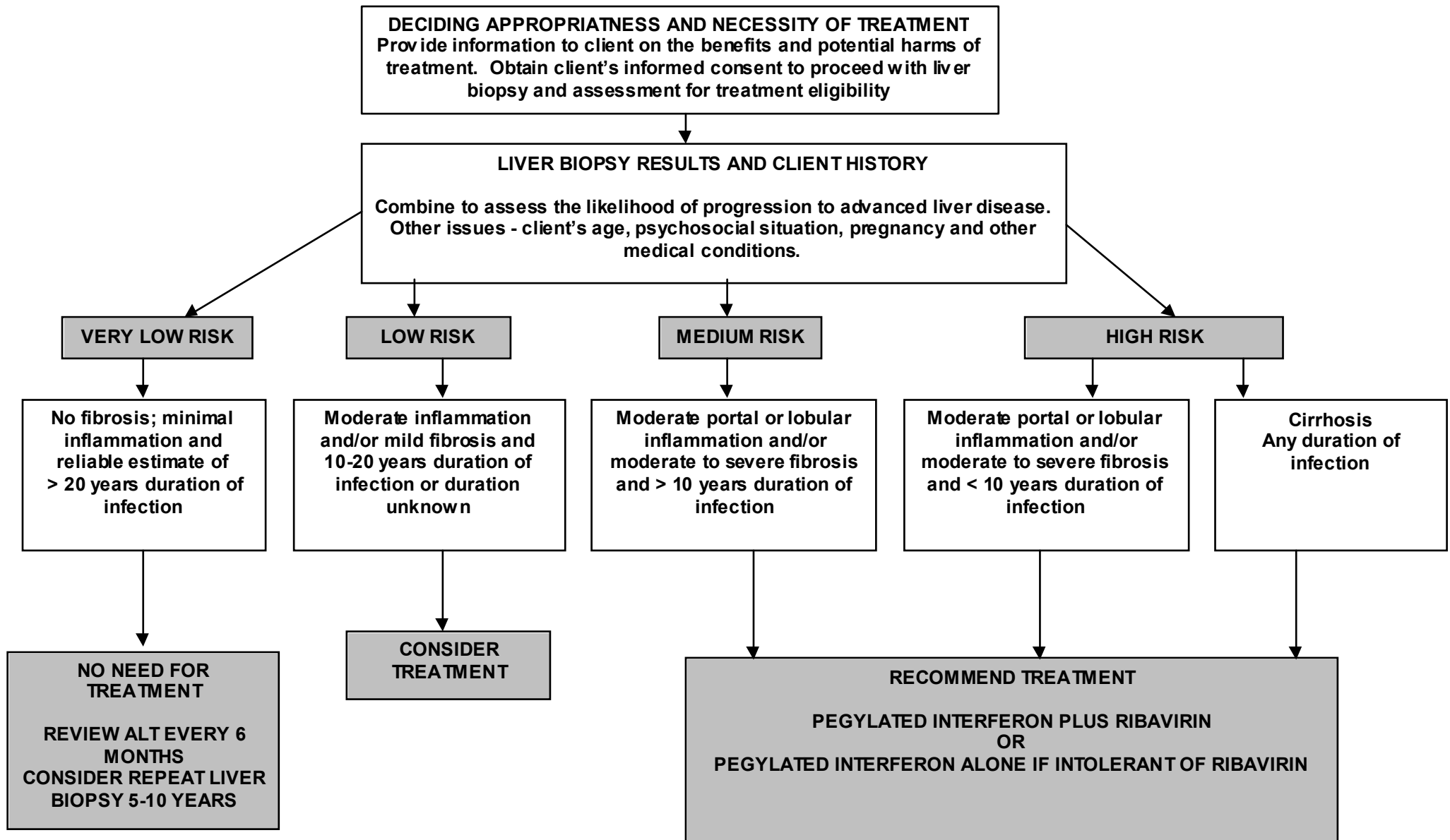
**Blood transfusion**

Clients infected by a blood transfusion may be at greater risk of progressing than clients infected via injecting drug use (possibly due to the amount of virus to which the individual was exposed and the number of quasi species), although age may be a confounding factor.

**Co-infection with HIV and/or HBV**

Clients co-infected with HIV and/or HBV are at greater risk of progression to cirrhosis (refer to Sections 11 and 12).

## 7.1. ALGORITHM: SELECTION OF CLIENTS WITH CHRONIC HEPATITIS C FOR TREATMENT\*



\*Based on Dore, G. (2001). Therapy decision making. In Crofts, N., Dore, G., & Locarnini, S. (Eds). Hepatitis C: An Australian Perspective. Melbourne: IP Communications.

## 7.2 EXPLANATORY NOTES: SELECTION OF CLIENTS WITH CHRONIC HEPATITIS C FOR TREATMENT

### Deciding the Appropriateness and Necessity of Treatment

As discussed in Section 5.2 the ongoing management of hepatitis C involves a variety of strategies including treatment. It is important to recognise that not every client wants or requires treatment. Clients' decisions concerning treatment and the extent to which they utilise other non-treatment strategies will depend on their personal needs, preferences, social responsibilities, occupation and lifestyle. Some clients with mild disease want treatment so they are free of the virus. Other clients at high risk of progressing to CLD do not want treatment because of concerns of the side effects of treatment or because their life style makes it difficult to comply with the treatment regime.

If treatment is considered necessary and appropriate, it is important that clients understand the serious commitment they are making before commencing treatment. Treatment takes up to 12 months, can have debilitating side effects (both physical and neuro-psychiatric), and requires a significant time commitment due to requirements to regularly monitor clients during treatment and for 6 months post treatment.

Clients may also choose to pursue other approaches to managing hepatitis C such as complementary and alternative therapies and changes to lifestyle and diet. Further detail is provided in Sections 5, 13, and 14.

### Benefits of Treatment

Treatment can lead to long term clearance of the hepatitis C virus with accompanying improvement in the ALT and histological improvement of the liver and improved quality of life. Clients with undetectable serum hepatitis C RNA six months following the end of treatment fulfil the definition of a sustained virological response (SVR). This response is associated with histological improvement in the liver<sup>40,41</sup> with reports of clients who achieve a SVR showing regression of fibrosis even in clients with cirrhosis<sup>42</sup>.

There is evidence that clients who have fibrosis with or without cirrhosis are less likely to develop HCC (hepatocellular carcinoma) if treatment with interferon is successful (QER III 2)<sup>43,44</sup>. One study reported a 15% reduction in HCC in cirrhotic clients who received treatment (QER I).

## **Liver Biopsy**

A liver biopsy should be used to assess the risk of a client progressing to advanced liver disease. The results should be used when weighing up the likely risks and benefits of treatment. Only after determining the severity (or lack of severity) of a client's disease can an informed discussion with the client occur about the necessity for treatment and the time frame in which treatment should occur.

A biopsy is not usually recommended in clients with normal ALTs. In individuals who do not wish to have treatment or who may not be suitable for treatment the need for a biopsy should be carefully discussed. Evidence of cirrhosis in such people has the potential to change the management of their condition due to the increased risk of hepatocellular cancer. A liver biopsy showing evidence of fibrosis or significant inflammatory disease is necessary for clients to receive treatment via government-funded schemes.

Many people with hepatitis C are anxious about a liver biopsy despite the risks associated with a biopsy being extremely low. Minor complications after percutaneous liver biopsy include transient, localized discomfort at the biopsy site, mild transient hypotension, and pain in the right upper quadrant or right shoulder after the biopsy (approximately 25%)<sup>45</sup>. Three to four percent of people may have a small amount of bleeding. Less than 1% of clients will require a transfusion and 1/1000 to 1/10000 may require surgery. The mortality rate for liver biopsy is approximately 1 in 10,000-12,000, but it should be noted that the highest mortality is in people who undergo biopsy of a malignant lesion<sup>45</sup>. There have been issues for some people with hepatitis C accessing pain relief after receiving a biopsy. Pain relief needs to be provided to any client regardless of injecting drug use behaviour.

## **Assessing the Risk of Liver Disease Progression**

There is limited evidence to guide decisions concerning those clients who should receive treatment versus those clients who, based on the risk of progression, do not require treatment but rather can wait and be reassessed. Clinical judgement and an understanding of other medical or non-medical issues affecting the client are important. For example, some clients with only minimal liver disease may wish to have treatment because of the ongoing social issues of being infected with a blood borne virus associated with injecting drug use.

The risk of progression of liver disease is based on a combination of factors. The duration of infection and the degree of necroinflammatory and fibrotic change on the liver biopsy are important. High risk patterns of alcohol intake affects the rate of progression. Uncertainty surrounds the relationship between genotype and viral load and progression of liver disease. However, infection with genotype 1 is associated with a lower SVR to treatment than genotypes 2 or 3.

Clients are at very low risk of progression to CLD if they have no fibrosis or minimal inflammation and have been infected for greater than 20 years. These clients should be monitored but do not require treatment at that time. Clients who have been infected for less than 20 years and have abnormal liver tests but minimal fibrosis or inflammation are at low risk of progression but could be considered for treatment especially if other factors, such as an impaired health related quality of life, are present. Clients who have moderate portal or lobular inflammation or moderate fibrosis or worse are at medium to high risk of progression and should be offered treatment.

## **Treatment**

The different treatment regimens are discussed in Section 8.

## **Accessing Treatment**

Clients may choose to finance their treatment. In order to be eligible for government supported treatment under Section 100 of the National Health Act clients must meet the following criteria (March 2003):

### **PEGINTERFERON ALFA-2b**

#### **CAUTION:**

Treatment with peginterferon alfa has been associated with depression and suicide in some patients. Patients with a history of suicidal ideation or depressive illness should be warned of the risks. Psychiatric status during therapy should be monitored.

Chronic hepatitis C in patients 18 years or older who have compensated liver disease and who have received no prior interferon therapy and have a contraindication to ribavirin, who satisfy all of the following criteria:

- (1) Histological evidence of chronic hepatitis on liver biopsy (except in patients with coagulation disorders considered severe enough to prevent liver biopsy);
- (2) Abnormal serum ALT levels in conjunction with documented chronic hepatitis C infection (repeatedly anti-HCV positive and/or HCV RNA positive);
- (3) No other forms of chronic liver disease;
- (4) Female patients of child-bearing age are not pregnant, not breast-feeding, and are using an effective form of contraception.

The treatment course is limited to 0.5 to 1 microgram per kilogram weekly for up to 52 weeks.

Treatment is to cease if plasma HCV RNA remains detectable by an HCV RNA qualitative assay after 24 weeks of therapy.

## **RIBAVIRIN and INTERFERON ALFA-2b**

### **CAUTION:**

Treatment with interferon alfa has been associated with depression and suicide in some patients. Patients with a history of suicidal ideation or depressive illness should be warned of the risks. Psychiatric status during therapy should be monitored.

### **CAUTION:**

Ribavirin is a category X drug and must not be given to pregnant women. Pregnancy in female patients or in the partners of male patients must be avoided during treatment and during the 6 month period after cessation of treatment.

Treatment of chronic hepatitis C in patients who have relapsed following interferon alfa-2a/2b monotherapy where the monotherapy treatment would have complied with the criteria for PBS subsidy and who satisfy all of the following criteria:

- (1) Histological evidence of chronic hepatitis on liver biopsy (except in patients with coagulation disorders considered severe enough to prevent liver biopsy);
- (2) Abnormal serum ALT levels in conjunction with documented chronic hepatitis C infection (repeatedly anti-HCV positive and/or HCV RNA positive);
- (3) Female patients of child-bearing age are not pregnant, not breast-feeding, and both patient and their partner are using effective forms of contraception (one for each partner). Male patients and their partners are using effective forms of contraception (one for each partner). Female partners of male patients are not pregnant.

The treatment course is limited to 24 weeks.

Treatment is to cease if plasma HCV RNA remains detectable by an HCV RNA qualitative assay after 12 weeks of therapy;

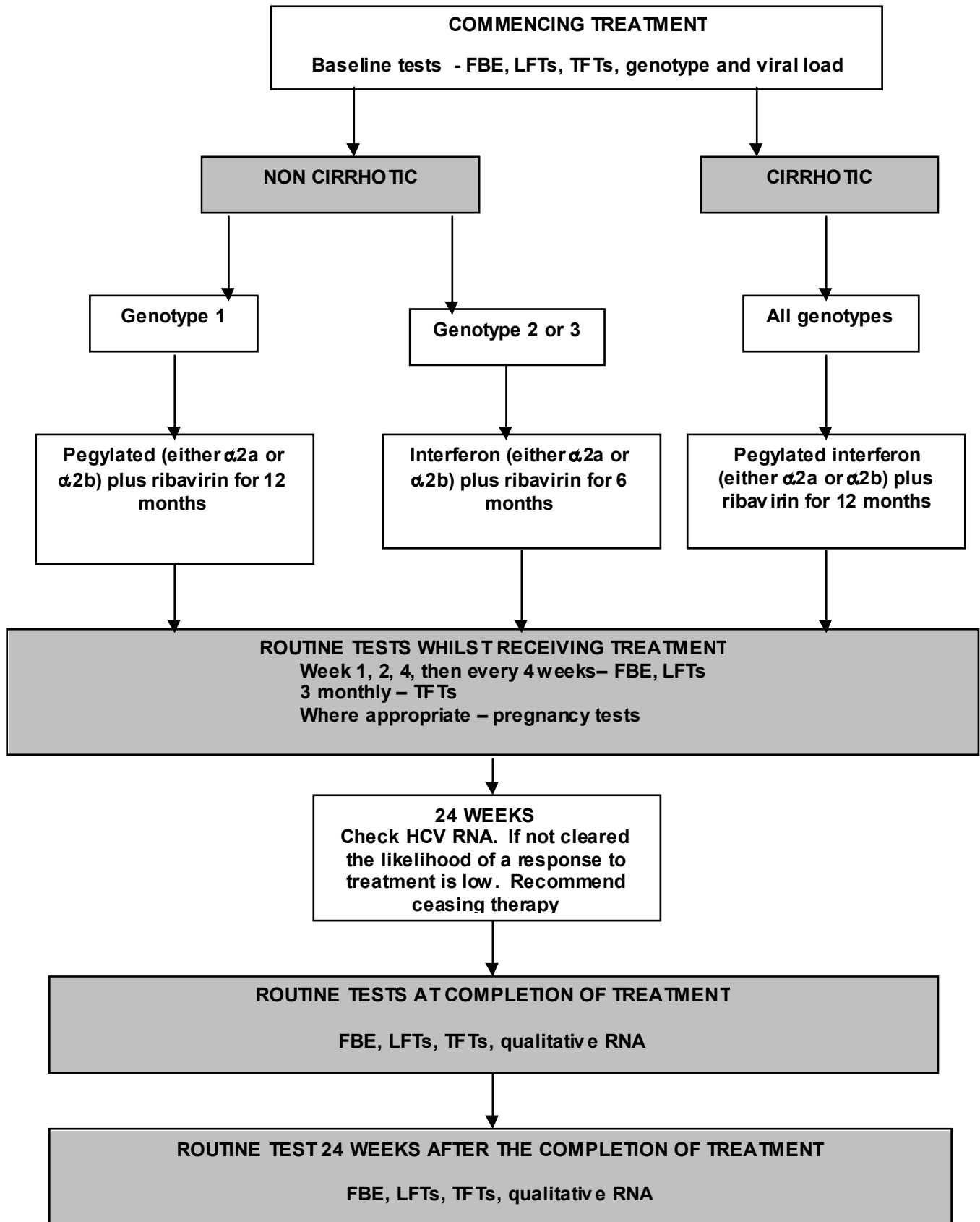
Treatment of chronic hepatitis C in patients previously untreated with interferon alfa-2a/2b and who satisfy all of the following criteria:

- (1) Histological evidence of Metavir (or equivalent index) stage 2, 3 or 4 fibrosis or stage 1 with grade A2 or A3 inflammation, i.e. moderate to severe inflammation evident on liver biopsy (except in patients with coagulation disorders considered severe enough to prevent liver biopsy);
- (2) Abnormal serum ALT levels in conjunction with documented chronic hepatitis C infection (repeatedly anti-HCV positive and/or HCV RNA positive);
- (3) Female patients of child-bearing age are not pregnant, not breast-feeding, and both patient and their partner are using effective forms of contraception (one for each partner). Male patients and their partners are using effective forms of contraception (one for each partner). Female partners of male patients are not pregnant.

The treatment course is limited to 24 weeks, except for patients with genotype 1 hepatitis C and patients with hepatic cirrhosis or bridging fibrosis regardless of genotype, for whom the treatment course is limited to 48 weeks.

Patients eligible for 48 weeks treatment may only continue therapy if plasma HCV RNA is not detectable by an HCV RNA qualitative assay after the first 24 weeks of therapy.

## 8.1. ALGORITHM: MANAGEMENT AND TREATMENT FOR CLIENTS WITH HEPATITIS C\*



\*Adapted by kind permission of Australian Family Physician, Royal Australian College of General Practitioners

## 8.2. EXPLANATORY NOTES: MANAGEMENT AND TREATMENT FOR CLIENTS WITH HEPATITIS C\*

### Treatment

The combination of interferon and ribavirin is the current treatment standard and is available under the government funded S100 scheme. Compared to interferon alone, combination therapy does not affect the initial response rate but reduces the relapse rate thereby increasing the rate of SVR (40 - 45% SVR). Recent trials comparing pegylated interferon plus ribavirin to standard interferon plus ribavirin or pegylated interferon alone report the SVR following the combination of pegylated interferon plus ribavirin ranges from 54%<sup>46</sup> to 56%<sup>47,48</sup>. It is likely that the combination of pegylated interferon and ribavirin will become the new standard of treatment.

**Interferon** is a glycoprotein produced by white blood cells in response to viral infections. It has a direct antiviral effect (thought to be its primary action) and it amplifies specific and non-specific T cell responses. Standard interferon is self injected 3 times weekly<sup>49</sup>.

**Pegylated interferon** is interferon bound to a polyethylene glycol moiety. It has sustained absorption, a slower clearance and a longer half-life than unmodified interferons<sup>50</sup>. Pegylated interferon is self injected once weekly.

**Ribavirin** is a synthetic nucleoside analogue structurally resembles guanosine with *in vitro* activity against several DNA and RNA viruses including the flaviviridae. Ribavirin is used in combination with interferon because when given as monotherapy it can lower serum ALT but does not reduce the hepatitis C RNA level. Ribavirin is taken orally daily; it has a half-life of 44-49 hours<sup>49</sup>.

### Duration and Effectiveness of Treatment

Genotype, baseline viral load<sup>51,52</sup> and cirrhosis<sup>50,53</sup> affect the success of treatment. Hepatitis C RNA should be measured at baseline and 24 weeks. Early loss of RNA is associated with a greater probability of achieving a SVR<sup>54</sup>. Clients with detectable RNA at 24 weeks have less than 2% chance of achieving a SVR and are unlikely to benefit from continued therapy.

### Non cirrhotic clients

Interferon monotherapy is no longer used for treating hepatitis C infection. Interferon plus ribavirin or pegylated interferon alone leads to a higher SVR rate (QER II)<sup>50,52,53</sup>. Standard interferon plus ribavirin in non-cirrhotic clients with genotypes 2 and 3 should be given for 24 weeks (with a reported SVR in 65%). Clients with genotype 1 should receive 48 weeks of treatment (reported SVR is around 30%) (QER

II)<sup>26,49,53</sup>. As outlined earlier, Pegylated interferon plus ribavirin leads to a higher SVR than either standard interferon plus ribavirin or pegylated interferon alone with reports of clients with genotype 1 treated for 48 weeks having a SVR of 42% (QER II)<sup>48</sup>.

### **Cirrhotic clients**

Clients with cirrhosis have lower rates of SVR compared to non-cirrhotic clients following treatment with interferon and ribavirin or pegylated interferon (QER 1)<sup>50,53</sup>. Despite low response rates these clients had improved ALTs and histological improvement with reduced mortality and morbidity following treatment (QER 1)<sup>55</sup>. Pegylated interferon with ribavirin has been found to improve the outcome of cirrhotic clients (30% SVR) although the numbers studied are small (QER III-1)<sup>48,51</sup>. It is generally recommended that clients with cirrhosis receive 12 months of treatment regardless of genotype (QER III-1)<sup>49,51</sup>.

### **Side Effects of Treatment and Routine Monitoring Required During Therapy**

Baseline LFTs and FBE should be performed before commencing treatment and monthly throughout treatment.

#### **Interferon/pegylated interferon**

Common side effects are viral like illness with associated fever, aches and pains, fatigue and lethargy. Decreased appetite and nausea and vomiting and diarrhoea can occur as can hair loss, weight loss, dry skin and rashes. Clients can be irritable and have considerable psychosocial stress. Depression and mood change is an important side effect and should be monitored closely throughout the course of treatment. Suicidal ideation is an important toxicity to identify and manage (see text box). Interferon can be associated with altered thyroid function and therefore TFTs (Thyroid Function Tests) should be performed prior to treatment commencing and at 3 monthly intervals. Interferon has an anti-proliferative effect that can lead to a decrease in white cells, especially neutrophils, and platelets. Visual disturbance such as optic neuropathy is rare.

#### **Interferon and suicide risk**

It is important for clients and medical practitioners to be aware that side effects commonly associated with Interferon include mood swings and depression. There are rare documented cases of individuals on Interferon treatment committing suicide due to mood swings and depression associated with the treatment<sup>56,57</sup>. Client's mental health should be closely monitored by their medical practitioner. The listing of support services listed in Section 17 of this document includes suicide support services in each state.

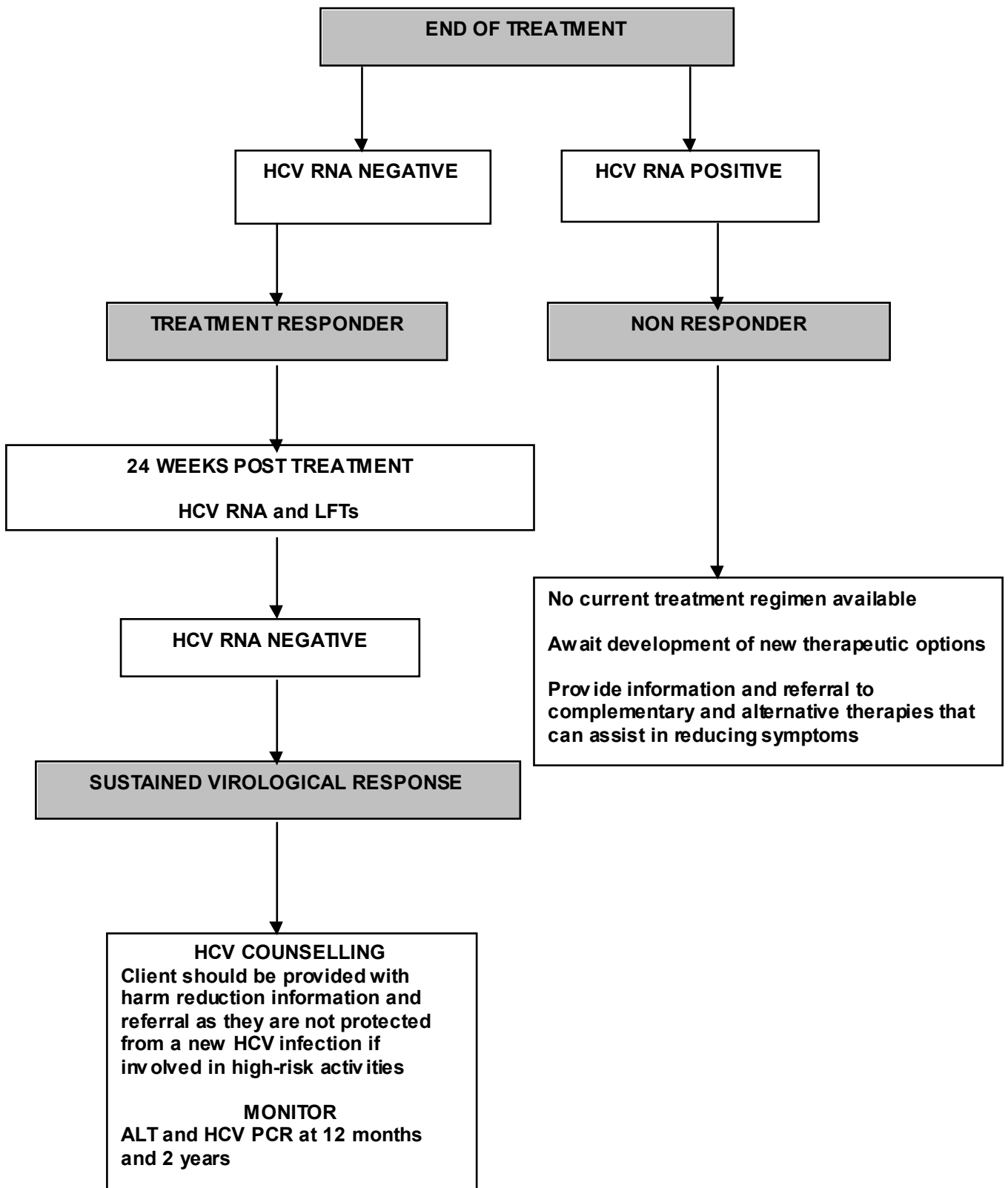
## **Ribavirin**

**Ribavirin** is a known teratogen. Clients and their partners should use adequate contraception (both oral contraception and a barrier method) during treatment and for six months following the completion of therapy. Clinicians should ensure clients understand the necessity and importance of using dual methods of contraception to ensure pregnancy does not occur prior, during or 6 months following treatment. Ribavirin causes a predictable dose dependent haemolysis and is also associated with pruritus and skin rash.

## **Management of side effects**

Management of side effects can include the use of paracetamol for mild aches and pains and selected non-steroidal drugs for severe arthralgia. Clients with depression and anxiety should be closely monitored and can be treated with antidepressants and anti-anxiolytic drugs. Clients who develop thyroid dysfunction should be reviewed by an endocrine specialist. Clients with dry skin can be treated with creams and when particularly problematic referred to a dermatologist. Many Hepatitis Councils also provide treatment support groups which can assist clients to deal with side effects.

## 9.1. ALGORITHM: MONITORING AND MANAGEMENT POST THERAPY\*



\*Adapted by kind permission of Australian Family Physician, Royal Australian College of General Practitioners`

## 9.2. EXPLANATORY NOTES: MONITORING AND MANAGEMENT POST THERAPY

### End of Treatment Virological Response (ETR)

Clients should have LFTs, FBE and a qualitative hepatitis C RNA at the end of a course of treatment. The earlier a client becomes hepatitis C RNA negative during treatment the greater the likelihood they will have a sustained viral response (SVR)<sup>54</sup>. If a client is hepatitis C RNA positive at the completion of therapy they have failed to respond to treatment.

### Sustained Virological Response (SVR)

A SVR is defined as undetectable hepatitis C RNA by a sensitive test such as PCR at 24 weeks post treatment. Clients with normal ALTs and SVR are unlikely to relapse. There is evidence that long term sustained viral clearance is associated with histological improvement in the liver<sup>40 41</sup>.

Factors affecting the rate of SVR are genotype, base line hepatitis C RNA and the degree of fibrosis. Genotype 1 is associated with a lower SVR than genotypes 2 or 3. A lower base line hepatitis C RNA (<2 million copies/ml) increases the likelihood of a SVR. Clients with lesser degrees of fibrosis are more likely to have a SVR (QER – II)<sup>52,53,58</sup>.

### Treatment Options for Clients Who Did Not Have a Sustained Virological Response

Information is limited about the benefits of further treatment after clients fail to have a SVR. Clients who did not respond to interferon monotherapy do not benefit from re-treatment with interferon at the same dose<sup>49</sup>. Earlier studies reported that clients benefit from longer or higher doses of interferon<sup>59</sup> but current practice would be to offer such clients combined therapy, preferably with pegylated interferon plus ribavirin. Clients who responded to prior interferon therapy and then relapse do better than clients who had no response to initial therapy<sup>49,59</sup>.

### Responded but relapsed (did not have a SVR)

As with previously untreated clients, the hepatitis C genotype is the most important factor affecting the rate of SVR in clients being retreated. Treatment of clients who responded to therapy but did not maintain a SVR is similar to treatment for naive clients. Standard treatment of interferon and ribavirin should be offered for 6 months except in clients with genotype 1 or in genotypes 2 and 3 with advanced fibrosis/cirrhosis who should be offered 12 months of treatment<sup>49</sup>.

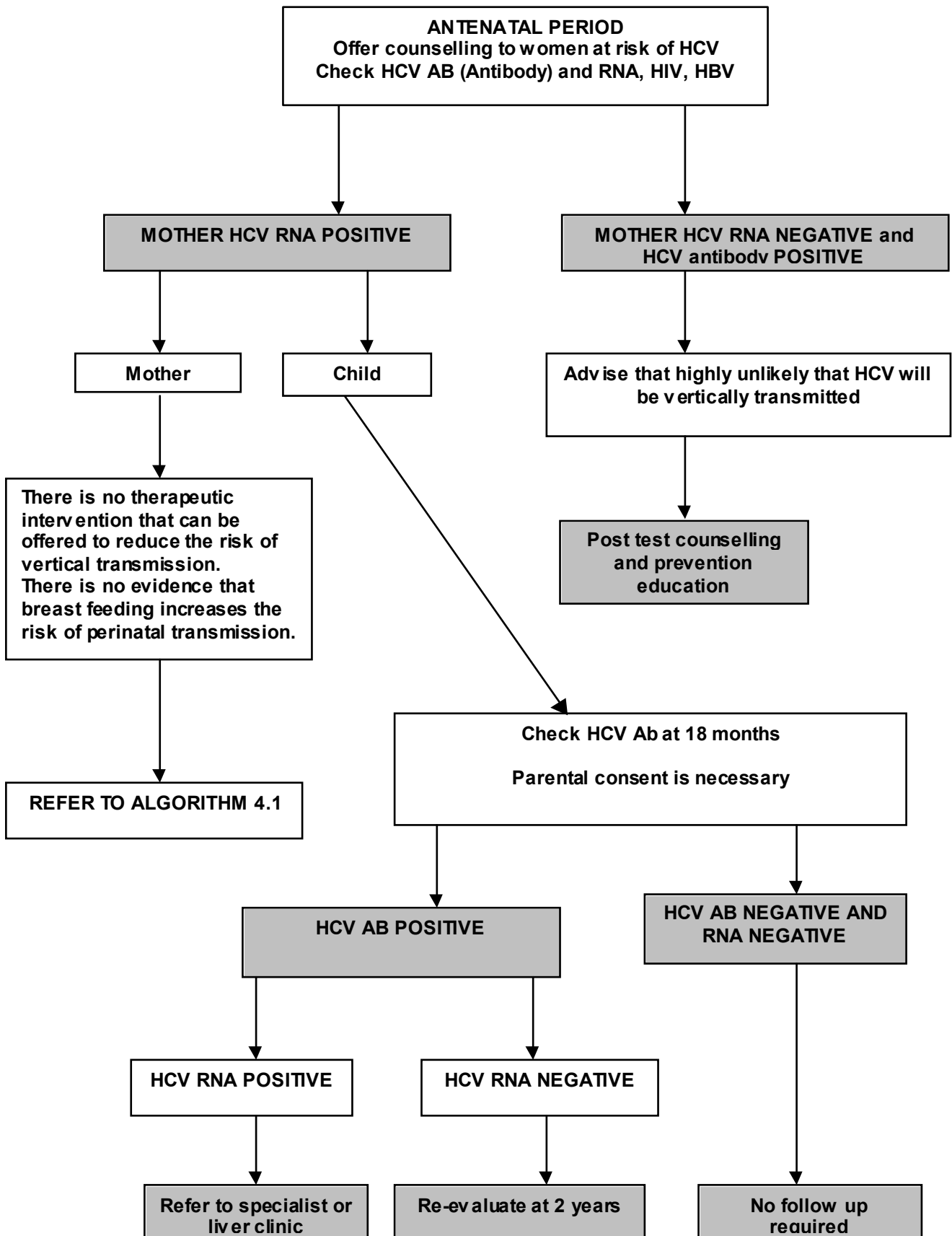
Clients who relapsed after interferon monotherapy will become less common and will be replaced by clients relapsing after standard interferon plus ribavirin therapy. Currently there are no data to guide re-treatment, but it is likely that these clients will be offered pegylated interferon plus ribavirin.

### **Nonresponders to combined interferon and ribavirin**

Limited data is available concerning the best treatment strategy for managing clients who did not respond to interferon and ribavirin. The recently conducted trials of pegylated interferon plus ribavirin studied only previously untreated clients. It is likely that combined pegylated interferon and ribavirin may prove useful in a percentage of clients who do not respond to standard combination therapy.

A few studies have examined the response to amantadine in clients who failed to have a sustained response to interferon alone. The combinations of interferon and ribavirin versus interferon and amantadine were compared. The SVR was 3.9% in the ribavirin arm and 0% in the amantadine arm. It should be noted that treatment was only given for 24 weeks and clients were predominantly genotype 1 with high pre-treatment viral loads<sup>60</sup>. Studies are currently under way investigating the benefits of interferon, ribavirin and amantadine.

## 10.1. ALGORITHM: TRANSMISSION OF HEPATITIS C FROM MOTHER TO CHILD\*



\*Adapted by kind permission of Australian Family Physician, Royal Australian College of General Practitioners

## 10.2. EXPLANATORY NOTES: TRANSMISSION OF HEPATITIS C FROM MOTHER TO CHILD

### Who Should be Considered for Screening During Pregnancy?

Pregnant women should not be routinely screened for hepatitis C. Testing for Hepatitis C antibodies should be conducted if a pregnant woman has an identified risk of infection as described in Section 3.2.

### Counselling

It is important to offer specific counselling to women with hepatitis C who are pregnant. The level of experience and expertise counselling pregnant women concerning hepatitis C varies between medical practitioners; some practitioners will be comfortable offering advice, others should consider referring the client to a specialist clinic or another medical practitioner.

### Transmission risk

The risk of vertical transmission of hepatitis C is approximately 5-8%<sup>2</sup> and transmission only occurs if the mother is hepatitis C RNA positive<sup>19,61</sup> (QER III3). The risk of transmission increases with co-infection of HIV. There is no known intervention that reduces the transmission of hepatitis C from mother to child. The risk of transmission, interventions to reduce transmission (currently none proven – see below) and postnatal issues such as breast-feeding and testing of their child should be discussed with the client.

### Management of Pregnant Women who are Hepatitis C RNA Positive

#### Caesarean section

Studies on the benefit of caesarean section are mixed. A number of studies have suggested no benefit but many studies were underpowered (i.e. sample sizes may not have been sufficient to detect the effect of caesarean section). A recent case control study has suggested that caesarean section may be beneficial but more research is needed<sup>61-64</sup> (QER III-2).

#### Intrauterine scalp monitoring

There is speculation that intrauterine scalp monitoring may increase the risk of transmission but there is not specific evidence for this. Some hospitals recommend scalp monitoring should not be performed where women are known to be hepatitis C infected<sup>65</sup> (QER III-2).

#### Breast feeding

There is no evidence that hepatitis C is passed from mother to child via breast-feeding although these studies are underpowered. Some studies have shown hepatitis C in breast milk but not in levels leading to transmission<sup>66-68</sup> (QER III-2).

## **Viral transmission during pregnancy**

There is some suggestion that the risk of transmission is related to the level of hepatitis C RNA in the mother's blood during pregnancy. Due to the lack of available interventions and the fact that treatment cannot be offered during pregnancy (because current treatments are teratogenic) this is currently of little practical use to the medical practitioner<sup>61,69</sup> (QER III-2).

## **Testing of Children of Women with Hepatitis C**

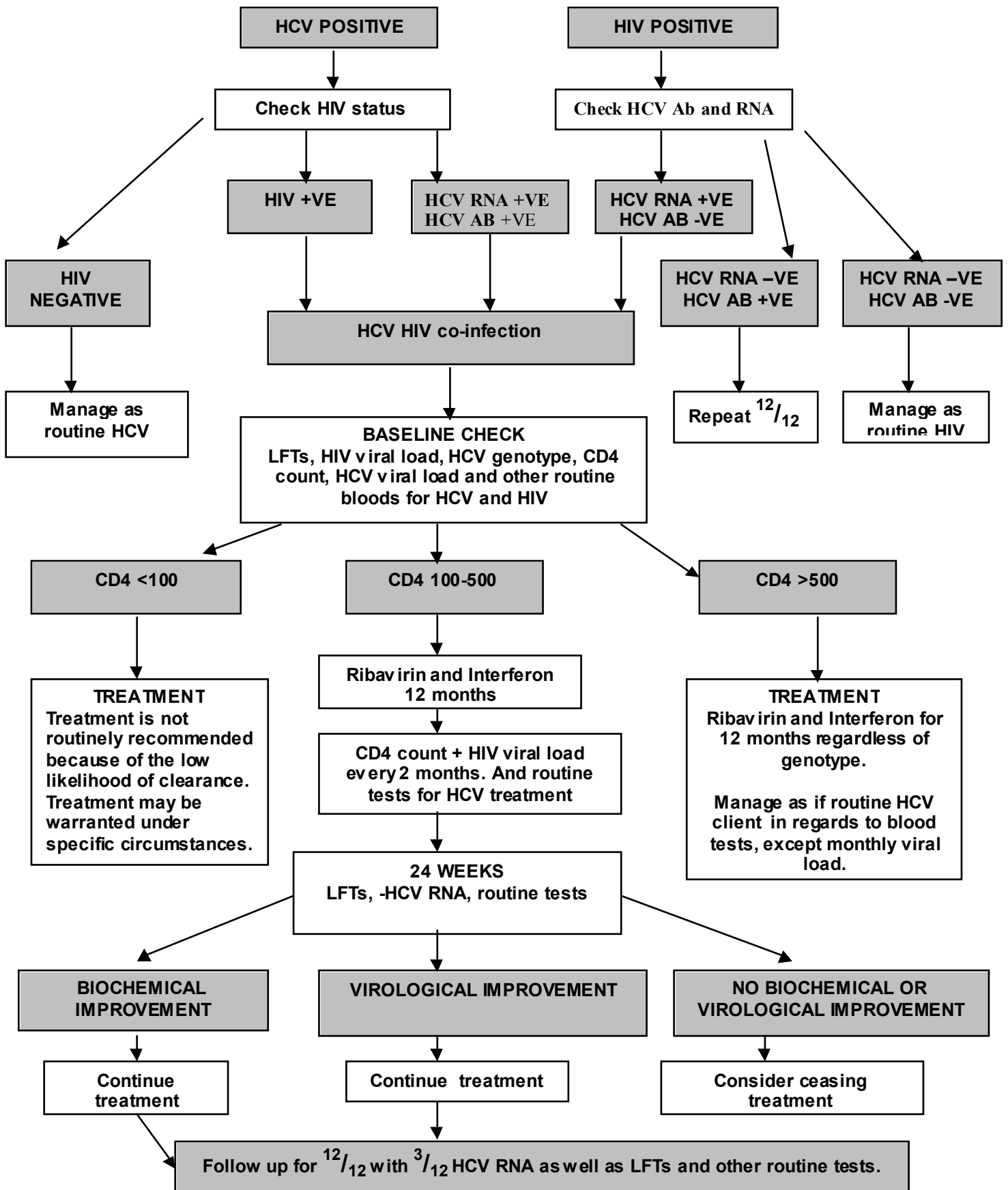
The progression of hepatitis C in children is reported to be slower compared to adults, with children demonstrating lower rates of progression to chronic liver disease at 20 years. There are few long-term cohorts of children with hepatitis C, therefore it is unknown if progression to chronic liver disease is lower or simply slower than in adults.

It is important to offer parents the opportunity for testing of children who were at potential risk of acquiring vertically transmitted hepatitis C. It is also important to understand that some parents do not want their children tested for hepatitis C despite the increased risk if the mother has hepatitis C.

The following recommendations are taken from the National Hepatitis C Testing Policy<sup>2</sup>.

“Although there is no approved treatment for hepatitis C in children or adolescents, they can be monitored for the presence or development of liver disease, and those with persistently elevated ALT levels can be referred to specialists for management. Hepatitis A and hepatitis B vaccination should be offered along with other steps that may be taken to limit liver damage. Infants born to hepatitis C-positive mothers will retain maternal antibodies up to the age of 18 months. Before this age, antibody testing may be difficult to interpret. If earlier diagnosis of hepatitis C infection is desired, a qualitative NAT can be performed at or after the infant's first post-natal visit, at age 1–2 months.”

## 11.1 ALGORITHM: HEPATITIS C HIV CO-INFECTION\*



\*Adapted by kind permission of Australian Family Physician, Royal Australian College of General Practitioners

## 11.2 EXPLANATORY NOTES: HEPATITIS C HIV CO-INFECTION

HIV and hepatitis C share common routes of transmission with the exception of sexual transmission for which the risk of HCV infection is low. Following the introduction of hepatitis C screening in 1991 unsafe injecting practices are currently the most common mode of co-infection. In Australia the prevalence of HIV amongst people who inject is relatively low, therefore hepatitis C HIV co-infection is less of a problem compared to many countries in the world. Further information is available in the ASHM publication Dore & Sasaduez (2003)<sup>70</sup> *Co-infection HIV and viral hepatitis: A guide for clinical management*.

### Screening

All HIV positive clients should have their hepatitis C status assessed with an antibody test. Medical practitioners should be aware that in the setting of immunosuppression due to HIV the hepatitis C antibody test is unreliable and has a high rate of negative and indeterminate results. Recommendations vary as to whether all HIV positive clients should have a hepatitis C RNA test. At a minimum all HIV positive clients with abnormal LFTs should have hepatitis C RNA test.

### Transmission of Hepatitis C

Hepatitis C can be transmitted sexually in the setting of HIV infection. Reports vary but the increased risk in transmission appears to be related to a higher hepatitis C viral load and a high level of immunosuppression in the person transmitting the virus. The rate of transmission appears to be higher if the partner is already HIV infected<sup>22,71</sup> (QER III-3). There is also an increase in perinatal transmission of hepatitis C in co-infected women<sup>19</sup>. Vertical transmission of hepatitis C occurs in 16% of cases when the mother is co-infected with HIV<sup>19</sup>.

### Hepatitis C Progression

Clients co-infected with HIV are at greater risk of progression to cirrhosis and liver failure compared with clients infected with hepatitis C alone. Immune restoration that occurs with antiretroviral treatment can exacerbate immune mediated tissue damage from other infections such as hepatitis C, PCP (Pneumocystis Carinii Pneumonia) and TB (tuberculosis). The mean time from the onset of hepatitis C infection to cirrhosis has been found to be longer in HIV negative clients (> 15 years versus < ten years)<sup>72</sup> (QER III-3). The level of immunosuppression due to HIV affects the progression of liver disease; cirrhosis is reported to be more common in people with CD4 counts of less than 200. Another study reported the hepatitis C viral load was higher in clients with lower CD4 but reported no direct effect on progression<sup>72</sup> (QER III-3).

## HIV Progression

Evidence is mixed about the impact of hepatitis C on HIV progression. There is some suggestion that hepatitis C/HIV co-infected individuals are at increased risk of non-liver disease related death. Other studies have suggested hepatitis C does not impact on the progression of HIV<sup>73-75</sup> (QER III-2).

## Treatment and Drug Interactions

Treatment of hepatitis C in the presence of HIV can be effective. In the limited number of studies available the response rates are better in clients with high CD4 counts. In clients with lower CD4 counts it may not be possible to clear virus and the aim is to delay disease progression. Interferon and ribavirin is currently the treatment of choice but it is likely that the combination of ribavirin with pegylated interferon will be preferred in the future<sup>76</sup> (QER III-1).

Commencement of cARV (combination antiretroviral treatment) can result in a hepatic flare most likely due to virus-virus interference as seen in hepatitis C/HBV co-infection. The hepatitis C RNA usually returns to normal after a few weeks to months. There is no evidence that treating HIV decreases the hepatitis C viral load<sup>77</sup>.

Treatment of hepatitis C in clients with low CD4 counts can be problematic because interferon can reduce the white blood cell count that in turn can lead to a fall in CD4 counts. This problem may be compounded when clients are on a cARV regimen that decreases the white blood cell count. Ribavirin can lead to a decrease in haemoglobin through haemolysis of the red blood cell. Therefore there may be drug interactions with cARV regimens containing zidovudine (ZDV) that can lead to a further decrease in haemoglobin.

Another theoretical concern with combination therapy is that ribavirin may impair the phosphorylation of thymidine analogues used to treat HIV (ZDV and d4T particularly) leading to inactivation of the drug and potential monotherapy<sup>78</sup>. *In vitro* data suggests this may be the case but recent studies suggest neither rebound HIV viraemia nor viral resistance develops.

Ribavirin increases phosphorylation of didanosine (DDI), which could be expected to increase levels of active DDI metabolites. Recent case reports of lactic acidosis associated with combination interferon and ribavirin therapy in people with HIV/hepatitis C coinfection receiving DDI-containing regimens supports increased DDI toxicity<sup>79</sup>. The product information for DDI now states that it should be used with extreme caution in people receiving ribavirin therapy.

Hepatotoxicity is a concern with HIV therapy. Nevirapine and ritonavir have been associated with hepatotoxicity, however, low-boosting doses of ritonavir do not appear to increase the risk.

## 12. HEPATITIS C HBV CO-INFECTION

The natural history of hepatitis C and HBV co-infection is far from clear. The general view is that one virus tends to dominate the other virus leading to decreased viral replication of the less dominant virus<sup>80</sup>. Although the evidence is limited, some studies suggest that hepatitis C is the dominant virus on most occasions. Furthermore, some reports suggest hepatitis C viral replication is increased in the presence of HBV co-infection (QER III-3).

It is important to emphasise to clients that co-infection is when they have chronic hepatitis C and chronic hepatitis B infection. If the person had been infected with hepatitis B but spontaneously cleared the virus they do not have co-infection.

### Detection of Virus

The hepatitis C antibody test appears to be unaffected by co-infection with HBV but the converse is not true. The sensitivity of the HBV serological testing appears to be diminished by co-infection with hepatitis C. There are reports of clients being co-infected with hepatitis C and HBV despite being HBsAg (Hepatitis B pre-surface antigen) negative. This is known as co-infection by “serologically silent” hepatitis B<sup>81</sup>. It has been suggested that hepatitis C core protein may impair the polymerase activity of HBV *in vitro*, potentially lowering HBV titre in co-infected clients. Therefore routine enzyme immunoassay may not detect HBV in spite of the presence of HBV viraemia in low titres (QER III-2).

### Disease Progression

Several reports suggested the severity of liver disease is increased both clinically and pathologically in co-infected clients. Individuals with hepatitis C who are anti-HBc (Antibody to hepatitis B core) positive are reported to have a higher prevalence of cirrhosis. There are reports that at a molecular level hepatitis C (particularly genotype 1) interferes with HBV viral replication. Whether this leads to a decrease or increase in disease severity is questionable with reports suggesting an increase in liver disease and HCC<sup>43</sup> (QER III-2).

### Treatment and Drug Interactions

There are reports that co-infection with HBV can lead to a decrease response to interferon therapy in hepatitis C. It is postulated that co-infection leads to down regulation of the interferon receptors in the liver<sup>82</sup> (QER III-3).

## **Current Management of Hepatitis C / HBV Co-Infection**

Clients with hepatitis C should routinely have a HBV serology as outlined in Section 6. There is insufficient evidence to suggest that all hepatitis C clients should be tested for HBV DNA. It may be worthwhile testing for HBV DNA in clients with hepatitis C who have rapidly progressive liver disease, HCC, who have failed previous treatment or who come from a country with a high level of endemic HBV.

Clients with hepatitis C/ HBV co-infection should be treated for their hepatitis C based on the selection criteria for clients who have hepatitis C infection alone. The issues of drug interactions and the possibility of a reduced likelihood of having a SVR should be discussed with the client. In addition, clients should be carefully monitored.

## 13. DIET AND HEPATITIS C

There is a great deal written about diet and hepatitis C with very little substantiated information about specific dietary requirements for people with hepatitis C. Despite the lack of evidence, many people follow strict diets excluding red meats, dairy food, foods containing added sugars, caffeine and artificial colours and preservatives. This can be time consuming, stressful and involve substantial lifestyle changes. At the same time diet is an area where many clients feel they can have direct control over the management of their hepatitis C.

Therefore despite the limited evidence of the benefits of exclusion diets it is important to offer support for clients as they investigate dietary strategies to improve their everyday sense of well being, as well as exploring the impact various dietary strategies may have on their disease progression.

Medical practitioners unsure of appropriate dietary advice should refer clients to a qualified dietitian who has experience in the area. Dietitians are usually located at most major hospitals. A useful web site is [www.daa.asn.au](http://www.daa.asn.au). Much of the information in this section has been drawn from the document "Nutrition and Hepatitis C – Information for Health Care Workers" available at this site<sup>83</sup>. The Australian Hepatitis Council have also produced the "Healthy Eating Guide for People with Hepatitis C" available through Hepatitis Councils<sup>36</sup>.

### Referral to a Dietitian

Consider a referral if the client:

- is experiencing symptoms such as nausea, anorexia or unexplained weight change (this can be seen with clients on combination therapy)
- has advanced liver disease
- has another condition which requires a specialised diet

The majority of clients with hepatitis C infection will not develop advanced liver disease and the dietary recommendation for these people is to have a healthy diet which involves high fibre and low fats. A web site providing information on the dietary guidelines for Australians is

<http://www.health.gov.au/pubhlth/strateg/food/guide/index.htm>.

### Alcohol

Safe alcohol consumption is one of the most important lifestyle considerations for people with hepatitis C infection. There is good evidence that an alcohol intake exceeding 4 standard drinks per day increases the risk of progression of liver disease in association with hepatitis C infection<sup>37,38</sup> (QER III2).

The NHMRC Australian Alcohol Guidelines<sup>13</sup> recommend that to minimise harm amongst the general population:

**Males:** consume 6 drinks or less on any one occasion, or no more than 4 standard drinks per day, with at least 2 alcohol free days per week

**Females:** consume 4 drinks or less on any one occasion, or no more than two standard drinks per day, with at least 2 alcohol free days per week

The NHMRC guidelines identify people who have HCV to consider drinking at levels less than those recommended for the general population to prevent further harm, and may consider not drinking at all.

Strategies to reduce alcohol consumption include:

- Alternate alcoholic drinks with non-alcoholic spacers.
- If thirsty, quench thirst with water, then have an alcoholic drink.
- Eat when, or before you drink as it helps to slow down the rate of absorption.
- Plan your drinking time – begin drinking later and go home earlier.
- Avoid salty snacks, no matter how tempting.

## Fats

The majority of people with hepatitis C infection do not need to follow a very low fat diet. A moderately low fat diet (as recommended for all Australians) is usually appropriate. Clients who are not tolerating fats may require specialised advice from a dietitian. There is no scientific evidence that people with hepatitis C need to avoid dairy foods.

## Sugar

There is little specific data relating to hepatitis C and the need for a diet low in sugars. As part of a healthy diet it is important not to have so high a sugar intake that it displaces more useful foods. People with hepatitis C infection should not have difficulty metabolising sugar.

## Vitamins

There is a lack of high quality trials measuring the benefit of specific vitamins in relation to objective measures of hepatitis C progression such as ALT levels or viral titre. Most people who eat a balanced diet do not need vitamin supplementation. People taking vitamin supplements should be warned not to exceed the recommended doses.

## **Vitamin E**

Studies have been conducted using Vitamin E on clients who have failed traditional treatment for hepatitis C. The results are variable; some have reported a benefit from vitamin E supplements while others have not observed a benefit. (QER - IV)

## **Selenium**

Low plasma selenium levels may be associated with increased risk of hepatocellular carcinoma in people with HBV but there is not direct evidence of a relationship between selenium levels and hepatitis C.

## **Vitamin B12**

Vitamin B12 has been reported to reduce anorexia and jaundice and symptoms associated with acute viral hepatitis, however the evidence is uncertain and its relevance in the management of chronic hepatitis C is questionable.

## **N-acetyl cysteine (NAC)**

NAC was reported in some early studies to have a role in clients who had not responded to interferon therapy, however recent studies have not shown an end therapy biochemical response or a sustained biochemical response rate. Clearance of the virus from serum was not observed in these studies.

## **Vitamin A**

People with damaged livers who drink alcohol should be warned to ensure their vitamin A intake is not excessive since alcohol and vitamin A utilise the same metabolic pathway. There have been reports of Vitamin A induced hepatotoxicity.

## **Caffeine**

There is no published evidence that the consumption of tea, coffee or caffeine containing drinks (cola) or foods (chocolate) lead to the progression of liver disease in people with hepatitis C. Some people with hepatitis C suffer fatigue and moderation of caffeine intake may be important so as not to exacerbate this fatigue, however this is an individual issue.

## **Food Colours and Preservatives**

There is no published evidence to suggest people with hepatitis C infection have difficulty metabolising artificial colours or preservatives.

## 14. COMPLEMENTARY MEDICINE AND HEPATITIS C

Many people with hepatitis C use complementary therapies, however few clinical trials and studies have been conducted therefore evidence for the effectiveness of such therapies is limited. Medical practitioners should be informed about complementary and alternative medicines being promoted and used by clients with hepatitis C. It is important that clients are provided with information concerning complementary and alternative therapies, and feel confident in discussing the use of these medicines with their treating medical practitioner even if he or she is not prescribing the complementary medicine.

### Herbal Remedies

#### St Mary's thistle (milk thistle)

Silymarin is thought to be the main active component in St Mary's thistle. It is suggested that silymarin increases the levels of endogenous antioxidants as well as having a variety of other actions. Evidence of its benefit in cirrhosis is mixed. Despite much anecdotal evidence of its benefits on liver disease symptoms, there is no direct evidence of it being of benefit in hepatitis C. Trials are currently underway.

#### St John's wort

Hypericin is thought to be the active ingredient in St John's wort with suggestions it has an antiviral effect. A recent study showed little benefit with no detectable antiviral activity when used by people with hepatitis C infection (QER – III2).

#### Ayurvedic herbs and Chinese Medicine.

Ayurvedic medicine is well established in India but little known in western cultures. Picrorhiza kurroa and LIV 52 are used in the management of liver disease but no direct virological evidence is available showing the benefit in chronic hepatitis C. Chinese herbs are often used as a mixture of herbs rather than one specific herb. A number of therapies are used and accepted as useful in China, but the direct evidence of their benefit in hepatitis C is limited.

It should be noted that the above list is far from exhaustive. Some herbal medicines have been shown to be hepatotoxic, therefore it is important clients are aware that this needs to be discussed with their complementary or alternative therapist. Hepatitis Councils have further information about complementary and alternative therapies and recommend that people seeking to use these therapies contact a qualified physician. The Australian Hepatitis Council has also produced a resource, "Complementary and Alternative Therapies for Hepatitis C", which is available through Hepatitis Councils.

## 15. LIFESTYLE AND HEPATITIS C

### **Exercise**

Exercise is part of a healthy lifestyle. Exercise elevates mood, improves the appetite and is useful for stress management. Moderate exercise may enhance immune function whereas exhaustive exercise may result in immune suppression (QER IV).

### **Participation in contact sports**

Having hepatitis C should not preclude someone from participating in contact sports because the risk of transmitting the virus this way is extremely low. Standard infection control procedures when managing a bleeding injury should be followed.

### **Fatigue**

Although an unreliable measure of disease progression or disease severity, people with HCV commonly experience fatigue. Managing fatigue includes prioritising daily activities, seeking and accepting assistance for some tasks, relaxing rather than sleeping (to ensure sleeping patterns are not disrupted), exercising, and having small frequent meals. Adequate sleep is important for health as evidence suggests that a lack of sleep is associated with changes in immune function. There is no direct evidence that sleep improves hepatitis C but it can improve overall health (QER IV).

### **Stress**

There is increasing evidence that psychological stress has a metabolic and immunological effect that can affect disease outcomes (QER IV). Hepatitis C support groups can be helpful for some people in managing their stress.

## 16. CONCURRENT DISEASE MANAGEMENT

Conditions such as diabetes that cause fatty liver disease may be a co-factor for HCV progression. As with alcohol and smoking it is important that co-existing chronic health conditions are well managed.

## 17. SUPPORT SERVICES

### National

|   |              |
|---|--------------|
| Australian Hepatitis Council                        | 02 6261 1600 |
| Australian Injecting and Illicit Drug Users' League | 02 6279 1600 |
| Lifeline  | 13 11 44     |

### Australian Capital Territory

#### Hepatitis Council

|                         |                |
|-------------------------|----------------|
| ACT Hepatitis C Council | (02) 6253 9999 |
| ACT Hepline             | 1300 301 383   |

#### Government Health Department

|   |                |
|---|----------------|
| ACT Department of Health and Community Services | (02) 6205 5111 |
|---|----------------|

#### Drug User Organisation

|                                |                |
|--------------------------------|----------------|
| CAHMA (Drug User Organisation) | (02) 6262 5299 |
|--------------------------------|----------------|

#### Alcohol and Other Drugs

|   |                |
|---|----------------|
| Alcohol and Drug Services 24 Hour Help line | (02) 6205 4545 |
|---|----------------|

#### Suicide/Crisis Helpline

|                                   |                                |
|-----------------------------------|--------------------------------|
| ACT Crisis Assessment & Treatment | (02) 6205 1065<br>1800 629 354 |
|-----------------------------------|--------------------------------|

### New South Wales

#### Hepatitis Council

|                            |   |
|----------------------------|---|
| Hepatitis C Council of NSW | (02) 9332 1853  |
| NSW Hep C Helpline         | Sydney callers: (02) 9332 1599<br>Other NSW callers: 1800 803 990 |

#### Government Health Department

|                       |                |
|-----------------------|----------------|
| NSW Health Department | (02) 9391 9000 |
|-----------------------|----------------|

#### Drug User Organisation

|                               |                                |
|-------------------------------|--------------------------------|
| NUAA (Drug User Organisation) | (02) 8354 7300<br>1800 644 413 |
|-------------------------------|--------------------------------|

#### Alcohol and Other Drugs

|   |                |
|---|----------------|
| ADIS (Alcohol and Drug Information Service) | (02) 9361 2111 |
|---|----------------|

## **Suicide/Crisis Helpline**

Salvo Care Line Counselling (02) 9331 6000  
(Regional) 1800 674 200

## **Northern Territory**

### **Hepatitis Council**

NTAHC (Northern Territory AIDS and Hepatitis Council) (08) 8941 1711

Hepatitis Helpline (08) 8922 8007

### **Government Health Department**

NT Department of Health and Community Services (08) 8999 2400

### **Drug User Organisation**

TUF (Territory Users Forum) (08) 8941 2308

## **Suicide/Crisis Helpline**

Crisis Line 1800 019 116

## **Queensland**

### **Hepatitis Council**

Hepatitis C Council of Queensland (07) 3229 3767

(Regional) 1800 648 491

### **Government Health Department**

Queensland Department of Health (07) 3234 0111

### **Drug User Organisations**

DUNES (Drug Users Network Education and Support) (07) 5520 7900

QuIVAA (Brisbane, Queensland Intravenous AIDS Organisation) (07) 3252 5390

1800 172 076

SCMAA (Sunshine Coast Injectors Voice & Action Association Inc.) (07) 5443 9576

### **Alcohol and Other Drugs**

ADIS (Alcohol and Drug Information Services) (07) 3236 2414

1800 177 833

## **Suicide/Crisis Helpline**

Salvo Care Line Counselling (Brisbane) (07) 3831 9016

(Sunshine Coast) 1300 363 622

## **South Australia**

### **Hepatitis Council**

Hepatitis C Council of SA (08) 8362 8443

(Regional) 1800 021 133

Hepatitis Helpline 1800 621 780

### **Government Health Department**

South Australian Department of Human Services (08) 8226 8800

### **Drug User Organisation**

SAVIVE (South Australian Voice for Intravenous Education ) (08) 8362 9299

### **Alcohol and Other Drugs**

ADIS (Alcohol and Drug Information Service) 1300 13 1340

DASC (Drug and Alcohol Services Council) (08) 8274 3333

### **Suicide/Crisis Helpline**

SA Mental Health 24Hr Assessment & Crisis

Intervention Service (ACIS) 13 14 65

(Regional) 1800 182 232

## **Tasmania**

### **Hepatitis Council**

TasCAHRD (Tasmanian Council on AIDS

Hepatitis and Related Diseases) (03) 6234 1242

1800 005 900

### **Government Health Department**

Department of Community and Health Services (03) 6233 3185

1800 067 415

### **Alcohol and Other Drugs**

ADIS (Alcohol and Drug Information Service) (03) 6228 2880

1800 811 994

### **Suicide/Crisis Helpline**

Mobile Intensive Support Team (03) 6233 7856

## **Victoria**

### **Hepatitis Council**

|                                  |                |
|----------------------------------|----------------|
| Hepatitis C Council of Victoria  | (03) 9380 4644 |
|                                  | 1800 703 003   |
| Helpline for Health Care Workers | (03) 9288 3586 |
| Hepatitis C Helpline             | (03) 9349 1111 |
|                                  | 1800 800 241   |
| TTY for hearing impaired         | 1800 032 665   |

### **Government Health Department**

|                              |                |
|------------------------------|----------------|
| Department of Human Services | (03) 9616 7777 |
|------------------------------|----------------|

### **Drug User Organisation**

|                                  |                |
|----------------------------------|----------------|
| VIVAIDS (Drug User Organisation) | (03) 9381 2211 |
|----------------------------------|----------------|

### **Alcohol and Other Drugs**

|                              |                |
|------------------------------|----------------|
| Alcohol and Drug Direct Line | (03) 9416 1818 |
|------------------------------|----------------|

### **Suicide/Crisis Helpline**

|           |          |
|-----------|----------|
| Care Ring | 13 61 69 |
|-----------|----------|

## **Western Australia**

### **Hepatitis Council**

|                         |                         |
|-------------------------|-------------------------|
| Hepatitis Council of WA | (08) 9328 8538          |
|                         | (Regional) 1800 800 070 |

### **Government Health Department**

|                      |                |
|----------------------|----------------|
| Department of Health | (08) 9227 7866 |
|----------------------|----------------|

### **Drug User Organisation**

|                                |                |
|--------------------------------|----------------|
| WASUA (Drug User Organisation) | (08) 9227 7866 |
|--------------------------------|----------------|

### **Alcohol and Other Drugs**

|   |                |
|---|----------------|
| ADIS (Alcohol and Drug Information Service) | (08) 9442 5000 |
|   | 1800 198 024   |

### **Suicide/Crisis Helpline**

|                              |                         |
|------------------------------|-------------------------|
| WA Mental Health Crisis Team | 1300 555 788            |
|                              | (Regional) 1800 676 822 |

## 18. USEFUL WEBSITES

### Government web sites

[http://partners.health.gov.au/pubhlth/strateg/hiv\\_hepc/hepc/manual.htm](http://partners.health.gov.au/pubhlth/strateg/hiv_hepc/hepc/manual.htm)

Hepatitis C: Resource manual. Information about hepatitis C and telephone numbers of various support services throughout Australia.

<http://www.dhs.sa.gov.au/pehs/topics/topic-hep-c-book.htm>

Information for people with hepatitis C from the Department of Human Services in South Australia.

[http://www.hepatitisaustralia.com/pages/Directory\\_of\\_Hep\\_Resources.htm](http://www.hepatitisaustralia.com/pages/Directory_of_Hep_Resources.htm)

National Hepatitis C Resource Directory.

[www.health.qld.gov.au/sexhealth](http://www.health.qld.gov.au/sexhealth)

Queensland Health website for hepatitis C, HIV and sexual health issues.

[http://www.humanrights.gov.au/disability\\_rights/index.html](http://www.humanrights.gov.au/disability_rights/index.html)

Information about disability discrimination from the Human Rights and Equal Opportunity Commission.

### Hepatitis Councils

<http://www.hepatitisaustralia.com> Australian Hepatitis Council

<http://www.hepatitisc.org.au/> Hepatitis C Council of NSW

<http://www.hepatitisc.asn.au> Hepatitis C Council of Queensland

<http://www.hepccouncilsa.asn.au/> Hepatitis C Council of SA

<http://www.tascahrd.org.au/> TasCAHRD (Tasmanian Council on AIDS Hepatitis and Related Diseases)

<http://www.hepcvic.org.au/> Hepatitis C Council of Victoria

[http://www.nevdgp.org.au/geninf/std\\_misc/hepc\\_contact\\_list.htm](http://www.nevdgp.org.au/geninf/std_misc/hepc_contact_list.htm) Hepatitis C Council of Vic. contact list

<http://www.hepatitiswa.com.au/> Hepatitis Council of WA

### Diet, Medications, Lifestyle and Drugs

<http://www.daa.asn.au/>

<http://www.health.gov.au/pubhlth/strateg/food/guide/index.htm>

<http://www.an.pfinance.yahoo.com/insurance/health> (useful information about insurance)

<http://hepccwa.highway1.com.au/6pie2.htm> Western Australia Substance Users Association

<http://www.aivl.org.au> Australian Injecting and Illicit Drug Users League (AIVL)

<http://www.drugsafe.org/>

[http://www.drugsafe.org/html/body\\_drugfactslea.asp](http://www.drugsafe.org/html/body_drugfactslea.asp)

[http://www.sesahs.nsw.gov.au/albionstcentre/nutrition\\_hepatitis%20C.htm](http://www.sesahs.nsw.gov.au/albionstcentre/nutrition_hepatitis%20C.htm)

## **Suicide/Crisis Helpline**

<http://www.lifeline.org.au> Lifeline

It is important to be aware that websites can change and some of the information on the websites is not consistent with this Model of Care.

## 19. QUALITY OF EVIDENCE RATING (QER):

- I Evidence obtained from a systematic review of all relevant randomised trials
- II Evidence obtained from at least one properly designed randomised controlled trial.
- III-1 Evidence obtained from well designed controlled trials without randomisation.
- III-2 Evidence obtained from well-designed cohort or case control analytic studies preferably from more than one centre or research group.
- III-3 Evidence obtained from multiple time series with or without intervention
- IV Opinions of respected authorities, based on clinical experience, descriptive studies or report of expert committees.

Quality of evidence ratings were developed by the NHMRC Quality of Care and Health Outcomes Committee (QCHOC), and aim to provide guidance on quality of evidence. The guidelines give greater weight to studies that, for methodological reasons, are less subject to error or bias. Well designed randomised controlled trials are likely to produce results with the least amount of error, and hence evidence gained from such trials is more compelling than studies with less randomisation or control (eg descriptive studies).

## 20. LIST OF ACRONYMS

|          |   |
|----------|---|
| AB       | Antibody  |
| AHC      | Australian Hepatitis Council  |
| AIVL     | Australian Injecting and Illicit Drug Users League                  |
| ALT      | Alanine Aminotransferase  |
| ANCAHRD  | Australian Nation Council on AIDS, Hepatitis C and Related Diseases |
| Anti-HBc | Antibody to hepatitis B core  |
| bDNA     | Branched Chain DNA  |
| cARV     | Combination Antiretroviral Treatment                                |
| CLD      | Chronic Liver Disease   |
| CTARC    | ANCAHRD Clinical Trials and Research Committee                      |
| CTL      | Cytotoxic T Lymphocyte  |
| DNA      | Deoxyribonucleic Acid   |
| EMC      | Essential Mixed Cryoglobulinemia                                    |
| ETR      | End of Treatment Virological Response                               |
| FBE      | Full Blood Examination  |
| HAV      | Hepatitis A Virus   |
| HbsAg    | Hepatitis B Pre-surface Antigen                                     |
| HBV      | Hepatitis B Virus   |
| HCC      | Hepatocellular Carcinoma  |
| HCV      | Hepatitis C Virus   |
| HIV      | Human Immuno-deficiency Virus                                       |
| INR      | International Normalised Ratio                                      |
| LFT      | Liver Function Test   |
| PCR      | Polymerase Chain Reaction   |
| PCP      | Pneumocystis Carinii Pneumonia                                      |
| PCT      | Porphyria Cutanea Tarda   |
| PT       | Prothrombin Time  |
| QER      | Quality of Evidence Rating  |
| RNA      | Ribonucleic Acid  |
| SVR      | Sustained Virological Response                                      |
| TB       | Tuberculosis  |
| TFT      | Thymol Flocculation Test  |
| WBC      | White Blood Cell  |
| ZDV      | Zidovudine  |

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