National Hepatitis C Testing Policy

Australian National Council on AIDS, Hepatitis C and Related Diseases

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Disclaimer

This Testing Policy has been developed as a concise source of standardised information to assist government, health professionals, industry, hepatitis C-infected individuals, and the community in general, about matters associated with hepatitis C testing. The diagnosis and treatment of medical conditions such as hepatitis C require the consideration of an individual's particular circumstances by a qualified medical practitioner. This Testing Policy is not a substitute for medical advice, and should not be used to diagnose or prescribe treatment for any condition.

The views expressed in this Testing Policy are not necessarily those of the Commonwealth or the Australian National Council on AIDS, Hepatitis C and Related Diseases (ANCAHRD).

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Executive Summary

Hepatitis C is the most commonly diagnosed notifiable communicable infection in Australia. The Hepatitis C Virus Projections Working Group of the Australian National Council on AIDS, Hepatitis C and Related Diseases (ANCAHRD) released the report *Estimates and Projections of the Hepatitis C Epidemic in Australia 2002* which stated that in 2001 approximately 210 000 people in Australia had hepatitis C antibodies and approximately 16 000 new infections were occurring annually. Although the virus may be cleared after infection, it persists in 65–85 per cent of those infected. Of these cases, 5–10 per cent develop cirrhosis after 20 years and 3–5 per cent develop hepatocellular carcinoma. Thus, hepatitis C represents a significant public health concern.

A diagnosis of hepatitis C also has multiple implications in relation to an individual's work, family and quality of life. Caring for a person diagnosed with hepatitis C calls for informed and sensitive management. Health professionals, infected people and the community recognise that clear and rigorous guidelines for diagnosing and monitoring hepatitis C infection are needed and that the guidelines should take account of the life of the infected individual as well as of the populations at risk and their needs.

The National Hepatitis C Testing Policy has been formulated under the auspices of the Australian National Council on AIDS, Hepatitis C and Related Diseases (the Commonwealth's principal independent advisory body on hepatitis C) and the Intergovernmental Committee on AIDS, Hepatitis C and Related Diseases (the intergovernmental committee responsible for implementation of the National Hepatitis C Strategy). The policy is intended to provide advice to government, health professionals, industry, hepatitis C–infected individuals, and the community in general, about matters associated with testing.

Anti-HCV antibody testing first became available in 1990. The number of hepatitis C antibody tests carried out each year in Australia is approaching 2 million (including blood service and diagnostic testing) and about 50 000 for supplemental immuno-assay tests. New technologies have offered further dimensions in testing strategies. Qualitative and quantitative nucleic acid tests (NAT) are useful in detecting infection in the early stages and in assessing clearance of the virus and the effect of treatment. Qualitative NAT can be used to determine if infants of infected mothers have been infected. Genotype testing is useful in predicting the response to treatment because some hepatitis C subtypes are more sensitive to therapy than others. In addition to these tests, short incubation immuno-assays are available and home kits are being developed for marketing.

The National Hepatitis C Testing Policy offers clarification on the use of hepatitis C tests and the interpretation of diagnostic tests in the context of other laboratory tests and specific clinical situations.

There are 32 recommendations. Recommendations 1 to 19 outline the principles for hepatitis C testing and emphasise the need for individuals to be informed about testing and to be tested voluntarily. Testing must be of benefit to the individual, and

confidentiality must be maintained at all levels of testing. People with hepatitis C should have access to treatment and ongoing monitoring. Particular attention should be paid to groups such as Aboriginal and Torres Strait Islander peoples and people from culturally and linguistically diverse backgrounds, who may have difficulty gaining access to health services; populations at risk, such as injecting drug users and people in custodial settings, also warrant particular attention.

Recommendations 20 to 29 outline diagnostic strategies. Appropriate testing standards are to be applied by all laboratories undertaking testing for hepatitis C. Minimum practices, which should be adopted by all laboratories, include the need to confirm antibody reactivity by two separate immuno-assays based on different antigens and different immuno-assay formats. Discordant test results in two immuno-assays may require additional testing by qualitative NAT or referral to a reference laboratory, or both. The National Serology Reference Laboratory should keep laboratories up to date on appropriate combinations of immuno-assays, to avoid common cross-reactivity between tests. The utility of qualitative NAT in testing newly diagnosed hepatitis C sero-positive individuals and in testing infants born to hepatitis C sero-positive mothers is discussed in Chapter 6.

The use of short incubation tests is not supported—except in the case of screening potential organ donors, when the tests should be performed by suitably trained laboratory personnel. Home sampling or testing is not supported for the Australian situation.

The regulation of hepatitis C test kits and the supporting Quality Assurance Program are dealt with in Recommendations 30 to 32. An outline for a classification system for hepatitis C tests and test kits is presented; the system offers a choice of test protocols within a given situation and a framework for evaluation of test kits and for incorporating new technology as it emerges.

The policy recommends that it be a condition of registration of hepatitis C kits by the Therapeutic Goods Administration that laboratories using the kits participate in the National Serology Reference Laboratory's hepatitis C Quality Assurance Program. Standard and reference testing for hepatitis C should be provided by public and private sector laboratories that comply with the National Association of Testing Authorities – Royal College of Pathologists of Australasia audit and accreditation mechanisms, according to National Pathology Accreditation Advisory Committee guidelines.

The National Hepatitis C Testing Policy will clarify for all concerned the testing parameters for hepatitis C and guide the approach to diagnosis and management.

Recommendations

The guiding principles

1. The seven guiding principles for hepatitis C testing in Australia are as follows:

    - Testing is voluntary and should be accompanied by test discussion, post-test counselling and specific informed consent.
    - Testing should be of benefit, either directly or indirectly, to the person being tested.
    - Test results should remain confidential at the clinical level, in data management, and during the notification process.
    - Testing should be accessible to all who are or have been at risk of infection.
    - Appropriate standards must be applied by laboratories carrying out testing, to ensure a high level of accuracy in test results.
    - People with hepatitis C infection should have access to continued monitoring of their health status and to appropriate treatment.
    - Testing and notification are critical to determine the extent and location of hepatitis C infection in the community.

Implications of the principles

2. The benefits of testing will be maximised if the opportunity is taken to provide health promotion–based interventions related to minimising transmission and introducing lifestyle modifications that may limit the adverse consequences of infection. Health promotion messages to people who inject illicit drugs should include information on hepatitis A and hepatitis B vaccination, irrespective of the hepatitis C test result. Testing should be accompanied by referral to relevant agencies, such as hepatitis C councils and drug user organisations, as appropriate.

3. The benefits of hepatitis C testing will be maximised when a patient's other primary health care needs are taken into account. This particularly applies in the case of people who inject illicit drugs: they can have complex health care needs and often experience discrimination by health care providers.

4. Continued monitoring of health status should be available to all people infected with hepatitis C, with assessment for treatment taking place in accordance with current eligibility guidelines.

5. Anonymous, de-identified testing for surveillance purposes should occur only where there is no other feasible method for obtaining the necessary data. It should be scientifically justified and consistent with the Australian Hepatitis C Surveillance Strategy.

6. Mandatory and compulsory testing should be strictly limited to special, clearly sanctioned situations (as outlined in this document) and undertaken in an ethical and effective manner; test discussion and post-test counselling are essential.

Access to diagnostic testing

7. There is a need to improve access to hepatitis C testing, placing emphasis on health promotion principles—through discussion prior to testing and post-test counselling—for all people at risk of hepatitis C and particularly for people who inject illicit drugs. Testing will be most efficacious if it is part of a broader process that seeks to promote the health of people who inject illicit drugs, rather than being perceived as an isolated engagement. Peer-based user organisations are well placed to contribute to this process.

8. There is a need to continue education programs for health care professionals who deal with matters related to the testing and care of people with hepatitis C. In particular, these programs should be designed to develop professionals' skills in undertaking exposure assessments of drug use and should encourage appropriate attitudes to people who inject illicit drugs.

9. Access to testing for people from culturally and linguistically diverse backgrounds should be facilitated by targeted, sensitive community education, further training of health care workers, and ready access to interpreter services.

10. Access to testing for Aboriginal and Torres Strait Islander peoples with risk factors for hepatitis C should be facilitated by adopting good management practices for testing for other stigmatised diseases. This includes developing within organisations policies that outline the best approach to test discussion and post-test counselling, providing information to individuals in a culturally sensitive way and in a format they can understand, allowing individuals sufficient time to make their decision, ensuring confidentiality, and providing details of where the individual can go for more information.

11. Hepatitis C diagnostic testing should be available on a voluntary basis to all inmates of custodial institutions, as part of a comprehensive primary health care risk assessment and throughout the term of their incarceration. In keeping with the principle that inmates should have health care access equivalent to that available to the general community, testing should be accompanied by test discussion and post-test counselling, with an emphasis on health promotion. Inmates who have hepatitis C should have access to regular monitoring of their health status. Treatment should be available to those who meet standard eligibility criteria.

12. National protocols for the diagnosis and management of hepatitis C in custodial settings should be developed in consultation with the relevant stakeholders, including inmates.

13. There is a need for continuing education and training of health care professionals in relation to hepatitis C and non-judgmental attitudes to people who inject illicit drugs, particularly in rural and remote areas, where the choice of health services may be limited.

The recommended approach to diagnostic testing

14. Testing for hepatitis C antibodies should be offered to people who have an identified risk of infection. The decision to be tested is one for individuals to make on an informed basis, in consultation with health care professionals. Testing 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 needlestick 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.

15. 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 infected with hepatitis C.

16. Adherence to standard infection-control guidelines is the principal means of preventing transmission of hepatitis C infection in health care settings. Routine screening of health care workers for hepatitis C infection is inappropriate, but all health care workers involved in exposure-prone procedures have a responsibility to know their hepatitis C status.

17. Health care professionals in settings where pregnant women are evaluated or receive routine care should conduct a thorough risk assessment to determine the need for hepatitis C testing and other prevention measures. Pregnant women should receive specific information about the risk of vertical transmission and breastfeeding. Antenatal testing for hepatitis C should be undertaken only when the woman's history reveals a relevant risk exposure or the woman requests it: it should not be a routine diagnostic test.

18. Decisions about pre-operative testing of a patient for hepatitis C should be made on the basis of benefit to the patient. Medical practitioners are advised to ensure that a thorough risk assessment is carried out and the patient's informed consent is obtained before testing. Routine pre-operative testing cannot be justified.

19. In the absence of risk factors for infection, the offer of diagnostic hepatitis C testing for the following groups is not currently indicated:

    - health care workers
    - pregnant women
    - infants born to mothers infected with hepatitis C
    - household (non-sexual) contacts of hepatitis C–positive people—unless there is a history of direct exposure to blood
    - pre-operative patients
    - the general population.

Diagnostic strategies

20. The National Serology Reference Laboratory should periodically circulate to all laboratories advice about appropriate pairings of first and supplemental immuno-assays that provide independent results and pairings that are so similar that the supplemental result is of little value.

21. The following *minimum* practices should be adopted by all laboratories in determining whether a sample is hepatitis C antibody positive:

    - A sample negative on a single immuno-assay screen can be confidently reported as hepatitis C antibody negative.

- Samples with an initially reactive result should be subject to a minimum of one supplemental immuno-assay, using a different assay. 'Best practice' is to repeat the first assay in duplicate and, when samples are repeatedly reactive, to conduct supplemental testing.

- A sample that is reactive on two separate immuno-assays based on different antigens and different immuno-assay formats has a very high probability of containing true hepatitis C antibodies and can be reported as confirmed.

- When seeking to confirm a result, laboratories should use only appropriate pairings of first and supplemental immuno-assays, as recommended by the National Serology Reference Laboratory.

- Test results should not be reported until these minimum steps to confirm hepatitis C have been taken.

22. In the case of discordant antibody test results—the first test is repeatably reactive and the supplemental enzyme immuno-assay is negative—laboratories are advised to adopt *one or more* of the following strategies:

    - If there are no risk factors and there is no clinical suspicion, report that the individual is anti-HCV negative.

    - If risk factors are present, repeat the antibody test on a newly collected sample and/or conduct follow-up testing after a suitable interval. Then perform a qualitative nucleic acid test and report a 'confirmed' positive if the test is reactive—ideally on two separate samples.

    - If a discordant sample is negative by qualitative nucleic acid testing, perform an immunoblot and report the result according to the manufacturer's criteria.

    - If none of the above procedures is possible in the testing laboratory or if none is appropriate, the sample should be referred to a reference laboratory for further opinion.

23. The Australian National Council on AIDS, Hepatitis C and Related Diseases and the Intergovernmental Committee on AIDS, Hepatitis C and Related Diseases should convene a panel comprising the National Serology Reference Laboratory, the Public Health Laboratory Network, research and diagnostic virologists, clinical hepatologists and other experts to develop a consensus position on the most suitable approach by laboratories for confirming a diagnosis of hepatitis C.

24. Qualitative nucleic acid testing should be a standard component of the diagnostic work-up of all individuals who are hepatitis C antibody positive but have normal liver function.

Short incubation tests

25. If there is an urgent need to test, short incubation tests have potential. It may be that this method is suitable for screening possible organ donors. The testing should be done only by suitably trained laboratory personnel.

26. When a short incubation test is used, samples that show an initially reactive result for hepatitis C antibodies should always be subjected to testing with a conventional algorithm. Test results should not be communicated to patients until supplemental testing has been done.

27. The use of short incubation tests as part of an infection-control strategy is not supported.

28. The use of short incubation tests before elective surgery and before minor surgical procedures performed in non-hospital settings is not supported.

Home-based testing

29. Hepatitis C testing in Australia should be performed only when there is a good relationship between the person being tested and a suitably qualified health care professional and when test discussion and counselling may be carried out. The introduction of home-based testing and home collection is not supported**.**

A uniform national quality assurance program

30. It should be a condition of the Therapeutic Goods Administration's registration of hepatitis C test kits that sponsors supply only to laboratories participating in the National Serology Reference Laboratory's hepatitis C Quality Assurance Program. This requirement should not, however, preclude laboratories from participating in other quality assurance programs if they wish to do so.

Classification of test kits for regulatory purposes

31. The proposed classification system for hepatitis C test kits should be adopted (see Table 5, in Chapter 7).

Restrictions on the use of reference tests

32. Hepatitis C standard and reference tests should be performed by public and private sector laboratories that participate in the recommended quality assurance programs and comply with the National Pathology Accreditation Advisory Committee's guidelines. In the case of reference tests, it should be a requirement that public and private sector laboratories be authorised to conduct these tests; the authorisation should be contingent on compliance with

standardised criteria, as endorsed by the Intergovernmental Committee on AIDS, Hepatitis C and Related Diseases.

Introduction

Development of the policy

The development of the policy was at the instigation of the Australian National Council on AIDS, Hepatitis C and Related Diseases (ANCAHRD) and the Intergovernmental Committee on AIDS, Hepatitis C and Related Diseases (IGCAHRD). The process was overseen by the National Hepatitis C Testing Policy Steering Committee. The members of the National Hepatitis C Testing Policy Steering Committee are listed in Appendix A.

In finalising this document an extensive consultation process was undertaken. A wide range of organisations, professional bodies, and state and territory governments made submissions to the consultation process. These submissions were taken into account in finalising the policy.

The nature of the policy

This policy document constitutes an official joint statement by ANCAHRD (the Commonwealth Government's principal independent advisory body on hepatitis C) and IGCAHRD (the intergovernmental committee responsible for implementation of the National Hepatitis C Strategy). It makes a number of recommendations designed to facilitate policy implementation in important areas. Implementation of some recommendations will be a matter for particular bodies, but overall implementation will be the responsibility of governments, professional bodies and community organisations, working in partnership. ANCAHRD and IGCAHRD take responsibility for implementation of the policy within their respective domains and for promotion and monitoring of implementation. They will also develop and implement a process for reviewing the policy.

The scope of the policy

Although the primary focus of this policy is diagnostic testing for hepatitis C, it also deals with testing as it relates to continuing management for people living with hepatitis C and with screening of the blood supply. It seeks to set the agenda by recommending the desired approach to testing for both diagnosis and continuing patient management. The current situation in relation to testing is also outlined so as to place the recommended approach in context.

Policy relating to surveillance is covered by the Australian Hepatitis C Surveillance Strategy, developed in 1999 by the Hepatitis C Surveillance Committee of the Communicable Diseases Network of Australia.

The intended readership

The intended readership of this policy document is broad—Commonwealth, state and territory health authorities; members of professional bodies; members of the medical

technology industry; health care professionals; and members of community organisations. Many people at risk of or with hepatitis C will also be vitally interested in a policy of this nature, but this document is not intended as means of communication with them: specific resources have been, and will continue to be, developed for these people.

The structure of this document

Chapter 1 of this document outlines the broader policy context and summarises the epidemiology of hepatitis C in Australia and the natural history of the disease. It also briefly describes the different types of hepatitis C tests and their uses and presents data on the extent of hepatitis C testing in Australia.

Chapter 2—'Guiding principles for hepatitis C testing'—identifies the seven core principles that should govern how hepatitis C testing is carried out in Australia and discusses the implications of these principles.

Chapter 3—'Access to diagnostic testing'—provides policy advice on how to maximise access to testing for people who inject illicit drugs, people from culturally and linguistically diverse backgrounds, Aboriginal and Torres Strait Islander peoples, people in custodial settings, and people in rural and remote areas.

Chapter 4—'The recommended approach to diagnostic testing'—outlines the benefits and risks of hepatitis C testing and the steps that can be taken to maximise the benefits and minimise the risks. It sets out the indications (risk factors) that result in recommendations for offering diagnostic testing, plus recommendations for when testing may be offered and when the need for testing requires consideration in light of risk factors for infection. The rationale for whether or not testing should be encouraged in particular population groups or settings is also discussed. Among the areas covered are antenatal testing; testing of infants born to mothers infected with hepatitis C; testing of household (non-sexual) contacts; sexual partners; pre-operative testing; health care workers; recipients of blood transfusions and blood products; blood, body tissue and organ donors; and testing following environmental or occupational exposure.

Chapter 5—'Diagnostic strategies'—provides advice on minimum standards for laboratory diagnosis and investigation of hepatitis C. The policy approach to short incubation tests and home-based testing is also set out.

Chapter 6—'Funding'—discusses the current funding arrangements for hepatitis C testing under the Medicare Benefits Schedule.

Chapter 7—'Regulatory matters and quality assurance'—provides the policy framework for evaluating the performance of hepatitis C test kits, post-marketing surveillance of quality assurance, participation in a uniform national quality assurance program, and the categorisation of test kits for regulatory purposes and restrictions on the use of certain test kits.

1 The context

This chapter outlines the broader policy context and summarises the epidemiology of hepatitis C in Australia and the natural history of the disease. It also describes the different types of hepatitis C tests and their uses and presents data on the extent of hepatitis C testing in Australia.

1.1 The broader policy context

In Australia there has already been a substantial amount of policy development of relevance to hepatitis C testing. This National Hepatitis C Testing Policy was developed by drawing on existing policy where applicable. The following documents are of particular importance in providing a broad policy framework and guidance on particular matters:

- the *National Hepatitis C Strategy 1999–2000 to 2003–04*, which provides the overall framework for Australia's response to the hepatitis C epidemic
- the National Health and Medical Research Council's March 1997 report *A Strategy for the Detection and Management of Hepatitis C in Australia*, which has had a major influence on the approach to hepatitis C testing in Australia
- the 1999 *Australian Hepatitis C Surveillance Strategy*, developed by the Hepatitis C Surveillance Committee of the Communicable Diseases Network of Australia
- the Communicable Diseases Network of Australia's July 2000 draft for public consultation, *Infection Control in the Health Care Setting: guidelines for prevention of transmission of infectious diseases*, which recommends revisions to existing policy
- the Medical Services Advisory Committee's March 2000 *Hepatitis C Viral Load Testing Assessment Report*, which provides the basis for extension of Medicare funding to cover the use of viral load tests in relation to treatment
- the ANCARD–IGCARD September 1998 *HIV Testing Policy*, which deals with many similar matters.

1.2 The epidemiology of hepatitis C in Australia

Hepatitis C is the most commonly diagnosed notifiable communicable infection in Australia. There have been more than 165 000 notifications of hepatitis C infection since 1990, when antibody testing became available in Australia. The number of notifications remained very stable, at 18 000–20 000 a year, between 1994 and 2000.

It is estimated that there were approximately 210 000 people living with hepatitis C infection in Australia in 2001 and that around 16 000 new infections are occurring

each year.[1] The total number of notified cases represents approximately 60 per cent of the estimated number of people living with the virus.[2] This is probably one of the highest rates of diagnosis in the world. The actual rate of undiagnosed people may be lower, depending on the extent of multiple notifications.

Hepatitis C is transmitted through blood-to-blood contact. Studies of risk factors in Australia indicate that around 80 per cent of infections have been caused by sharing of injecting equipment or other forms of blood exposure among people who inject illicit drugs. Five to 10 per cent of cases may have been exposed through receipt of blood or blood products, primarily prior to 1990.[3] A further 10–15 per cent may have become infected through:

- non-sterile medical or dental procedures, particularly for people born in countries where the prevalence of hepatitis C is relatively high
- non-sterile tattooing, body-piercing and other skin-incision procedures
- mother-to-infant transmission during pregnancy or delivery
- needlestick injuries received in occupational and health care settings and other accidental exposure to blood or blood products.

A small number of people who test hepatitis C antibody positive do not have a recognised risk factor.

Because the risk is considered very low, hepatitis C is not defined as a sexually transmissible infection, although sexual transmission is possible and has been documented. Hepatitis C is not transmitted through social or casual contact.

There are nine main genotypes, or strains, of hepatitis C. The most common genotypes present in Australia are types 1 and 3. Type 3 occurs more often in younger and more recently infected individuals. Previous infection with one strain of the virus does not protect against reinfection with the same strain or a different one.

The response to antiviral therapy is poorer in individuals with higher circulating viral loads, those infected with genotype 1, those in older age groups, and those with cirrhosis.

1.3 The natural history of hepatitis C infection

As a result of recent studies, we now have a better understanding of the natural history of hepatitis C.[4] People with acute infection usually display no symptoms. As a result,

[1] ANCAHRD Hepatitis C Sub-committee 2002, *Hepatitis C Virus Projections Working Group: estimates and projections of the hepatitis C virus epidemic in Australia,* Australian National Council on AIDS Hepatitis C and Related Diseases, Sydney, p. 1.
[2] National Centre in HIV Epidemiology and Clinical Research 2002, *HIV/AIDS, Hepatitis C & Sexually Transmissible Infections in Australia: annual surveillance report 2002*, NCHECR, Sydney, p. 11.
[3] ANCARD Hepatitis C Sub-committee, op. cit.
[4] Dore G 2000, 'Natural history of hepatitis C infection', *Hepatitis C: informing Australia's national response*, Department of Health and Ageing, Canberra.

acute infection is unlikely to be recognised unless hepatitis C or liver function testing is performed for some other reason or the patient is being monitored following a needlestick injury or some other risk exposure.

Infection persists for many years, and possibly indefinitely, in at least 65–85 per cent of those infected. Approximately 5–10 per cent may progress to cirrhosis after 20 years and perhaps 15–20 per cent after 40 years. Among those with cirrhosis, there is an approximately 3–5 per cent long-term risk of development of hepatocellular carcinoma.

Progression of liver damage is relatively slow and can be assessed by the degree of fibrosis in liver biopsies. Progression is faster in males, people infected at age 40 or older, people with a high alcohol intake, people with consistently raised alanine aminotransferase levels, the obese, and people co-infected with HIV or hepatitis B.[5] Progression can be slowly reversed, at least in part, with successful antiviral therapy.

1.4 Types of hepatitis C tests

This section provides a brief overview of the main types of hepatitis C tests used for donor testing, diagnostic testing, and the monitoring and management of infected people. Matters associated with diagnostic strategies, particularly in relation to confirmation of sero-positive status and resolution of discrepant test results, are dealt with in Chapter 5.

1.4.1 Serological tests

On the whole, serological tests are easy to perform, relatively inexpensive, can be automated and produce low variability. They are used to indirectly diagnose the presence of hepatitis C infection by identifying the presence of hepatitis C antibodies.

The antibody test

An individual's immune system produces array of antibodies in response to the presence of any invading substance or organism. The hepatitis C antibody test (an immuno-assay) looks for the presence of hepatitis C antibodies. It is most commonly used to diagnose whether a person has been infected with hepatitis C.

Although antibodies to hepatitis C can usually be detected 10 weeks after infection, the seroconversion 'window period' has a wide range (quoted to be from 54 to 192 days), during which antibodies may not be detected by an antibody test. When a person recently exposed to the risk of hepatitis C infection tests negative, they should be retested after the window period and then retested if there are clinical signs or symptoms.

The tests are carried out mechanically in large numbers or batches, resulting in cost efficiencies. The cost of antibody testing is about $15.

[5] Deuffics S, Buffat L, Poynard T& Vallerian A-J 1999, 'Modeling the hepatitis C virus epidemic in France', *Hepatology*, vol. 29, pp. 1596–601.

Antibody test kits generally perform well in infected and uninfected individuals. Negative results are accurate and can be relied upon, but false-positive and indeterminate test results do occur. Where reactive results are produced on initial testing, other testing should be conducted before any result is made known. Confirmation of all initially reactive results is essential and should be completed before the results are conveyed to the requesting doctor and patient.

About 15–35 per cent of people clear the virus without any therapeutic intervention. But these people have residual antibodies, so the antibody test does not determine whether a person is still carrying the virus.

Short incubation assays

Immuno-assay technology has been adapted so that reactions can take place within minutes. This type of immuno-assay is known as a 'short incubation test', and it can be used on a single sample and with little or no laboratory equipment. It is suitable for use where rapid diagnosis is needed under conditions other than normal diagnostic testing or screening. The potential for false results is higher in short incubation tests compared with conventional immuno-assays. The test results should be interpreted by experienced people in a laboratory setting.

Particle agglutination assays

Particle agglutination assays are similar to immuno-assays. They are used to great advantage in countries where there is limited funding for testing because they do not require sophisticated equipment and are highly reliable. They are not as reliable as immuno-assays and at present are not carried out in Australia.

Immunoblot assays

Immunoblots are supplemental assays that can be used to further test a specimen that has produced a reactive result in an antibody test kit. They are another type of immuno-assay.[6]

Immunoblots are considered by some as a de facto 'gold standard' test for the purpose of confirming the presence of hepatitis C antibodies and therefore hepatitis C infection. There is debate in scientific circles about the merits of immunoblots in supplemental testing. They may be less sensitive than other immuno-assays and so can be negative or indeterminate after an antibody becomes reactive very soon after infection. There is also debate about how much new information is gained by an immunoblot, since the antigen used is usually of a construction similar to that used for corresponding antibody tests, although manufacturers have made efforts to avoid this.

The Centres for Disease Control and Prevention, USA have recently recommended that all samples repeatably negative in an enzyme immuno-assay be subjected to supplemental testing by immunoblot.

[6] The immunoblot assay is sometimes called a 'RIBA test'. Because 'RIBA' is a manufacturer's brand name, the generic term 'immunoblot assay' is used here.

Use of immunoblots has been quite limited in Australia, partly because of their expense: a test costs about $70 to $100.

Liver function tests

Liver function tests (such as alanine aminotransferase and aspartate aminotransferase tests) are used to determine if there is current or ongoing liver damage. The results are generally reliable, but aminotransferase levels can vary with fluctuations in disease activity, so repeated testing is advisable. Liver damage can occur even with minimal elevation of aminotransferase.

Aminotransferase levels can also be elevated for reasons other than hepatitis C—for example, if the liver is damaged by excessive alcohol intake or the presence of other viruses. They are a non-specific marker of liver damage. Further, although there is a general correlation between alanine aminotransferase elevation and liver biopsy showing evidence of continuing liver damage, this is not absolute. Thus, a normal ALT result does not fully exclude continuing liver damage.

Liver function tests cost about $20.

1.4.2 Nucleic acid tests

Nucleic acid tests, such as polymerase chain reaction tests, are widely used in the diagnosis and management of hepatitis C infection. They are extremely sensitive in detecting low viral levels, making them very useful for early detection (on average, within 23 days of exposure) of the virus. Techniques involving nucleic acid testing are more complex, time consuming and expensive than most serological testing techniques other than immunoblots. The qualitative NAT, the quantitative NAT, and genotype testing are three types of nucleic acid testing used for detecting hepatitis C.

Qualitative nucleic acid testing

The qualitative NAT detects hepatitis C viral RNA sequences directly. A true positive result confirms that infection is present. This type of test is used for the following purposes:

- to investigate an antibody-reactive individual for evidence of current infection—the main purpose
- within the window period following a risk incident, to check whether a person has contracted hepatitis C, since there may be insufficient antibodies present to be detected using an antibody test. If infection has occurred, for the vast majority of people it would be detectable by qualitative NAT within 23 days, on average, of exposure
- to determine if the virus is detectable when consistently normal liver function tests and no symptoms are found in an antibody-positive individual
- for patients who have had a first negative qualitative NAT result and are thought to have cleared the virus—that is, to confirm the result of the test

- to determine whether infants of infected mothers have been infected, rather than waiting the 18 months it may take for the child to clear maternal antibodies

- in immuno-compromised patients who have elevated ALT levels concurrent with a negative hepatitis C antibody test—because false negative antibody tests are more likely in this group

- to detect the response to treatment because a negative qualitative NAT result may indicate that the patient has been effectively treated or has cleared the infection

- to screen donated blood.

Despite improvements in NAT technology, false positive and false negative results are possible. False negative results can be caused by fluctuations in the level of hepatitis C virus in the bloodstream: the level may be low and undetectable. A true negative test indicates viral clearance from the blood or a low viral load but provides no indication of whether the virus is still present in liver cells or lymphocytes. With current knowledge, complete viral clearance cannot be determined with certainty.[7]

Newer generation tests are constantly achieving greater sensitivity and specificity. For this reason, people who appear to have spontaneously cleared infection, based on a negative qualitative NAT, should continue to be monitored at intervals for the presence of liver disease. This could take the form of a second qualitative NAT a year after the initial negative test or in the context of the patient's clinical indications. If the second test is also negative and continued exposure or risk practices can be ruled out, the patient could be informed of the strong probability that they do not have and will not develop chronic hepatitis C. As a precaution, they could be advised to have a liver function test every two years.

There is a high correlation between repeated positive qualitative NAT results and repeated abnormal liver function test results. Some practitioners perform repeated liver function tests and if these continue to be abnormal qualitative NAT is considered to add very little information.

With our evolving understanding of the natural history of the hepatitis C virus—we now know that 15–35 per cent of people spontaneously resolve their infection—it is important for people who have cleared hepatitis C infection to be informed.

False negative and false positive results can also occur as a result of inappropriate handling or storage of the specimen, although this problem is minimised when appropriate handling and testing guidelines are adhered to.

The cost of a qualitative NAT is about $90 in diagnostic testing but substantially lower when used for screening donated blood.

[7] Canadian Association for the Study of the Liver 1999, *The Management of Viral Hepatitis: proceedings of a consensus conference held in Montreal*, <http://www.lhsc.on.ca/casl/cont.htm>.

Quantitative nucleic acid testing

A quantitative NAT quantifies the level of hepatitis C RNA (the viral load) in the blood. The higher the viral load, the higher the level of infectiousness. People with higher viral loads are less likely to respond to treatment with interferon or other therapies. The test may be used to monitor the response to antiviral therapy. It costs about $175.

Genotype testing

Genotype testing (and virus sub-typing) is used to determine the type of hepatitis C virus with which an individual is infected. Genotype determination is important when therapy is being considered: it has been shown that the relative likelihood of a successful response to therapy depends on the particular genotype present. Numerous methods are available for this determination (serotyping, nucleic acid methods, and blotting methods). The cost of this type of testing is about $110. The MBS benefit is $200; this includes the NAT component of the test, which is about $90.

1.5 The extent of hepatitis C testing in Australia

1.5.1 Antibody testing

In 1999 in Australia, 1 485 361 specimens were screened for antibodies to hepatitis C (see Table 1). Of these, 885 465 were screened by blood transfusion services; the remainder of the tests were conducted by diagnostic and reference laboratories.[8] In the same year 599 896 hepatitis C antibody specimens were tested for purposes other than blood banking; in 2000 and 2001 the numbers were 722 702 and 769 891 respectively.

Data from the Commonwealth Department of Health and Aged Care for the financial year 1998–99 show that 313 358 hepatitis C tests attracted a benefit under the Medicare Benefits Schedule. This included 5 796 supplemental tests on specimens that proved reactive on an initial antibody test. Although the time period for the purpose of comparison is different, these data indicate that a high proportion of hepatitis C tests are being conducted in settings or for reasons that do not attract a benefit under the Medicare Benefits Schedule or that results are being reported without supplemental testing. This would include tests requested for patients receiving treatment in public hospitals and other public sector services (such as sexual health clinics and methadone clinics) and when the test is done as part of a screening program.

[8] Australia's National Serology Reference Laboratory collects the data from laboratories participating in its Quality Assurance Program. Data for blood transfusion services are complete, but there may be missing data for diagnostic and reference laboratories, although the numbers are not thought to be significant. The figures for 2001 in Table 1 are a best estimate.

Table 1 Number of specimens tested for antibodies to hepatitis C: Australia, 1997 to 2000

Year	Blood transfusion services	Diagnostic and reference laboratories	Total
1997	819 983	326 210	1 146 193
1998	930 782	541 884	1 472 666
1999	885 465	599 896	1 485 361
2000	920 322	722 702	1 643 024*
2001	977 436	769 891	1 742 081*

Notes: The number of specimens tested by diagnostic laboratories and reference laboratories was not separately identified until 1999. Figures for 2000 and 2001 may be an under-estimate because not all data were reported to the NRL.Source: National Serology Reference Laboratory, Australia.

The number of hepatitis C antibody tests performed each year is comparable with the number of HIV antibody tests: in 1999 in Australia 1 577 661 specimens were screened for antibodies to HIV; for 2000 and 2001 the figures were 1 708 525 and 1 806 246 respectively.

There is some evidence that high levels of repeat testing for hepatitis C antibodies occur in people who have already tested sero-positive. There are several circumstances in which this can occur:

- where a patient is referred to another health service (for example, from general practitioner to specialist) without copies of their pathology report and it is not possible to obtain copies of the report—the health service may feel obliged to repeat the relevant tests (including to establish the person's hepatitis C sero-status) to determine the diagnosis beyond doubt or for medico-legal reasons

- in situations where routine screening is offered to a population subgroup—for example, screening of all entrants to a drug treatment program

- where there have been indeterminate or discrepant test results.

In the case of the first and second circumstances just listed, there may be opportunities to reduce the amount of repeat testing by improving referral practices and assessing whether retesting for people entering drug treatment programs is needed if they report that they have already tested positive. Jurisdictions should examine opportunities to reduce the extent of unnecessary repeat testing.

Frequent patient-initiated repeat testing may suggest a need for counselling. Of relevance here might be continued engagement in risk practices and testing sought by the 'worried well' in the absence of an identified risk.

Table 2 shows the number of specimens tested for antibodies to hepatitis C by diagnostic and reference laboratories in each state and territory in 1999 and the number tested by diagnostic laboratories in 2000 and 2001.

Table 2 Number of specimens tested for antibodies to hepatitis C: Australia, 1999 to 2001

State	Testing by diagnostic and reference laboratories—1999		Testing by diagnostic and reference laboratories—2000		Testing by diagnostic and reference laboratories—2001	
	No. of tests	% of national total	No. of tests	% of national total	No. of tests	% of national total
NSW	223 503	37.3	254 699	035.2	220 886	28.7
Vic	118 401	19.7	135 825	18.8	177 631	23.1
Qld	122 200	20.4	151 225	20.9	173 128	22.5
WA	63.092	10.5	93 236	12.9	93 324	12.1
SA	43 798	7.3	57 654	8.0	76 051	9.9
Tas	12 046	2.0	13 643	1.9	11 715	1.5
ACT	9 379	1.6	10 563	1.5	11 112	1.4
NT	7 477	1.3	5 857	0.80	6 044	0.8
Total	599 896	100.0	722 702	100.00	769 891	100.0

Source: National Serology Reference Laboratory, Australia.

1.5.2 Hepatitis C supplemental testing

In 1999 in Australia 47 370 supplemental tests for hepatitis C were reported as having been conducted (see Table 3). Supplemental tests include second antibody tests, immunoblots and nucleic acid RNA tests (both quantitative and qualitative). The data set does not provide information about the type of test that was used, although that information is available. Caution has been used in interpreting the data because some laboratories may not have returned data to the National Serology Reference Laboratory. The number of specimens tested for antibodies has remained quite stable in recent years, yet there appears to have been a significant increase in the number of supplemental tests, particularly in 1999. The reason for this is not readily apparent, although during 1999 there was a vigorous campaign to make sure that all hepatitis C testing laboratories were enrolled in the National Serology Reference Laboratory's Quality Assurance Program.

In 1998–99, 3 355 qualitative NATs attracted a benefit under the Medicare Benefits Schedule. However, not all of these tests would have been used for the purpose of diagnosis.

Table 3 Supplemental tests for hepatitis C: Australia, 1997 to 1999

Year	Blood transfusion services	Diagnostic laboratories	Reference laboratories	Total
1997	2 565	10 920	n.a.	13 485
1998	636	17 642	n.a.	18 278
1999	552	16 617	30 201	47 370

n.a. Not available.

Note: The number of specimens tested by diagnostic laboratories and reference laboratories was not separately identified until 1999. Such data were not collected after 1999.

Source: National Serology Reference Laboratory, Australia.

1.6 The location and process of testing

Diagnostic testing for hepatitis C can be done in a variety of locations. In Australia the most common location is general practice, which offers the advantage of placing testing within a broader primary health care context. Testing is also done in sexual health clinics, often as part of an overall risk assessment for a range of infectious diseases. Because of the non-judgmental stance of clinic workers, these locations are seen as accessible to people who inject illicit drugs. Some peer-based user organisations provide on-site testing for hepatitis C through collaborative arrangements with local health services. This can facilitate access to testing and places testing within a broader health promotion and support context. Testing also occurs through drug and alcohol services, which can have the benefit of appropriate targeting and facilitation of access.

There are four distinct steps in the process of testing for hepatitis C:

- *considering whether to be tested*, which includes 'test discussion'[9] between health care professional and patient on the need for testing and its implications and the provision of specific informed consent if testing proceeds
- *sample collection* by taking blood from the patient
- *testing of the sample* by the laboratory
- *communication of the result* by the health care professional to the patient in the context of post-test counselling and referral to suitable support agencies.

[9] Test discussion is defined and described in section 4.1.3.

2 Guiding principles for hepatitis C testing

This chapter identifies the seven core principles that should govern how hepatitis C testing is carried out in Australia and discusses the implications of these principles.

2.1 The guiding principles

The following seven guiding principles should form the basis for how hepatitis C testing is carried out in Australia:

- Testing is voluntary and should be accompanied by test discussion, post-test counselling and specific informed consent.
- Testing should be of benefit, either directly or indirectly, to the person being tested.
- Test results should remain confidential at the clinical level, in data management, and during the notification process.
- Testing should be accessible to all who are or have been at risk of infection.
- Appropriate standards must be applied by laboratories carrying out testing, to ensure a high level of accuracy in test results.
- People with hepatitis C infection should have access to continued monitoring of their health status and to appropriate treatment.
- Testing and notification are critical to determine the extent and location of hepatitis C infection in the community.

2.2 Implications of the principles

The following points amplify the guiding principles:

- *Test discussion and post-test counselling.* Appropriate test discussion and post-test counselling should be an integral part of all voluntary, mandatory and compulsory testing (see Section 4.1.3). People with antibody-positive results will need continuing support and information, which may involve referral to community agencies such as hepatitis C councils and drug user organisations.
- *Informed consent.* Particular care should be taken to obtain specific informed consent from marginalised groups. The process of obtaining that consent may need to take account of cultural and language barriers and matters associated with discrimination.

- *Confidentiality.* 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.

- *Access.* People who have been at risk of exposure to hepatitis C infection should have ready access to testing. Where barriers to testing exist—especially for marginalised groups—special provisions may need to be made to facilitate access. Funding arrangements should be such that the cost of testing does not discourage people at risk of infection from being tested.

- *Anonymous testing.* To facilitate access for people who might be reluctant to seek hepatitis C testing, anonymous testing should be available from a number of health care settings in each jurisdiction.

- *Health promotion.* The benefits of testing should be maximised by using the opportunity to deliver health promotion messages aimed at minimising transmission and encouraging lifestyle modifications that may limit the adverse consequences of infection.

- *The primary health care context.* The benefits of hepatitis C testing will be maximised when a patient's other primary health care needs are taken into account. This applies particularly to people who inject illicit drugs, who may have complex health care needs and often experience discrimination by health care providers.

- *Monitoring and treatment.* Continuous monitoring of their health status should be available to all people infected with hepatitis C, with assessment for treatment occurring in accordance with current eligibility guidelines.

- *Regulation and quality assurance.* Requirements for the registration and supply of hepatitis C test kits by the Therapeutic Goods Administration and for their use (as outlined in Chapter 7) should be adhered to. The role of the National Serology Reference Laboratory is important in ensuring high-quality hepatitis C testing.

- *Cost-effectiveness.* Testing should be carried out in a cost-effective manner.

- *Human rights.* Testing practices must comply with federal and state or territory anti-discrimination legislation and other relevant laws. This could mean that it is unlawful to require a person, on the basis of actual or imputed hepatitis C infection, to undergo a hepatitis C test as a pre-condition of any medical treatment or that it is unlawful to refuse, delay or defer treatment if the patient refuses the test.

- *Remedies.* Effective, practical and accessible redress (apart from recourse to the law) should be available for unauthorised hepatitis C testing—for example, a health care complaints mechanism.

- *Mandatory and compulsory testing.* Mandatory or compulsory testing is appropriate only in specific circumstances:

  - Compulsory testing is appropriate in some rare situations (as provided for in public health legislation) where the welfare of others in the community depends on the testing of an individual—for example, if a person suspected on reasonable grounds of being hepatitis C positive persistently behaves in a way that places others at risk of infection. Adequate safeguards should exist to ensure that compulsory testing is used only when there are no alternatives. The right of appeal against a decision or order to be tested should always exist.

  - Mandatory testing, where a person may be prohibited from participation in certain activities unless they undergo testing and are found to be hepatitis C negative, is appropriate in some circumstances—for example, homologous blood donation. Any mandatory testing must be firmly based on scientific knowledge of how the virus is transmitted and on ethical considerations. To protect against potential abuse, any requirements for mandatory testing should be fully documented in guidelines that describe the justification, the procedure to be followed, and safeguards to ensure protection against abuse and compliance with ethical standards.

  Mandatory and compulsory testing should always be accompanied by test discussion and post-test counselling.[10]

- *Surveillance.* Information from hepatitis C testing contributes to an improved understanding of epidemiology and allows for targeting of health promotion interventions and planning of care and treatment services.

- *Anonymous de-identified testing.* For surveillance purposes anonymous de-identified testing may be considered in special circumstances. It must, however, comply with the National Health and Medical Research Council's *National Statement on Ethical Conduct in Research Involving Humans*[11], include full scientific justification (as for all research), and be consistent with the Australian Hepatitis C Surveillance Strategy.

- *Infection control.* Testing does not diminish the need for standard precautions in handling blood and body fluids in any health care setting.

[10] Test discussion, as outlined in this policy, is not required for blood donors. Post-test counselling is not required for blood donors who test negative for hepatitis C. Blood services should either provide post-test counselling for donors who test positive or refer these people to appropriate services.
[11] National Health and Medical Research Council 1999, *National Statement on Ethical Conduct in Research Involving Humans*, NHMRC, Canberra.

Recommendations

1. The seven guiding principles for hepatitis C testing in Australia are as follows:
   - Testing is voluntary and should be accompanied by test discussion, post-test counselling and specific informed consent.
   - Testing should be of benefit, either directly or indirectly, to the person being tested.
   - Test results should remain confidential at the clinical level, in data management, and during the notification process.
   - Testing is accessible to all who are or have been at risk of infection.
   - Appropriate standards must be applied by laboratories carrying out testing, to ensure a high level of accuracy in test results.
   - People with hepatitis C infection should have access to continued monitoring of their health status and to appropriate treatment.
   - Testing and notification are critical to determine the extent and location of hepatitis C infection in the community.

2. The benefits of testing will be maximised if the opportunity is taken to provide health promotion–based interventions related to minimising transmission and introducing lifestyle modifications that may limit the adverse consequences of infection. Health promotion messages to people who inject illicit drugs should include information on hepatitis A and hepatitis B vaccination, irrespective of the hepatitis C test result. Testing should be accompanied by referral to relevant agencies, such as hepatitis C councils and drug user organisations, as appropriate.

3. The benefits of hepatitis C testing will be maximised when a patient's other primary health care needs are taken into account. This particularly applies in the case of people who inject illicit drugs: they can have complex health care needs and often experience discrimination by health care providers.

4. Continued monitoring of health status should be available to all people infected with hepatitis C, with assessment for treatment taking place in accordance with current eligibility guidelines.

5. Anonymous, de-identified testing for surveillance purposes should occur only where there is no other feasible method for obtaining the necessary data. It should be scientifically justified and consistent with the Australian Hepatitis C Surveillance Strategy.

6. Mandatory and compulsory testing should be strictly limited to special, clearly sanctioned situations (as outlined in this document) and undertaken in an ethical and effective manner; test discussion and post-test counselling are essential.

3 Access to diagnostic testing

This chapter provides policy advice on how to maximise access to testing for people who inject illicit drugs, people from culturally and linguistically diverse backgrounds, Aboriginal and Torres Strait Islander peoples, people in custodial settings, and people in rural and remote areas.

A central principle of this National Hepatitis C Testing Policy is that people at risk of hepatitis C should have equitable access to good-quality testing in an appropriate setting. The *National Hepatitis C Strategy 1999–2000 to 2003–20* states, 'People affected by hepatitis C do not make up a homogeneous group or community. In the design, implementation and evaluation of interventions and services, attention must be paid to the diverse cultural, geographic, social and economic circumstances of people affected by the virus'.[12] Considering that the extent to which some groups have ready access to testing varies, it is vital that attention be given to exploring all the available options for improving people's access to testing.

Gaining access to testing itself may not actually present problems. The associated costs may, however, prevent many people from coming forward. Factors such as discrimination also need careful consideration and suitable responses. Testing is not an isolated health intervention: it should be seen within the broader context of both health and human rights in achieving positive health outcomes for individuals. Partnerships with those affected by hepatitis C, such as drug user organisations, provide cost-effective and appropriate access to testing for injecting drug users who may be at risk of hepatitis C. These types of partnerships ensure that a more holistic and empowering model of health care is offered, with peer-based monitoring and health maintenance being an integral part. Such service provision is likely to increase the uptake of testing and improve the health of those affected by hepatitis C.

3.1 People who inject illicit drugs

For people who inject illicit drugs, the accessibility of hepatitis C testing varies. Although they might be discouraged from seeking testing because of the stigma associated with their behaviour, many have been tested on multiple occasions and testing is often done as part of a battery of tests.[13] Routine screening is common at the time of entry to drug treatment programs such as methadone programs, although this is by no means universal.

There is a lack of information about the characteristics of people who inject illicit drugs and who have been tested, although younger people appear less likely to be tested than older people.[14] It has also been speculated that those in contact with drug

[12] Department of Health and Ageing 2000, *National Hepatitis C Strategy 1999–2000 to 2003–04*, DoHA, Canberra.
[13] Loxley W, Davidson P, Heale P & Sullivan P 2000, *Drawing Blood: injecting drug users, blood borne viruses, testing and vaccination*. National Drug Research Institute, Curtin University of Technology, Perth. Seventy per cent of a Perth-based sample of 200 people who inject drugs had been tested for hepatitis C and other blood-borne viruses an average of seven times (p. v).
[14] ibid., p. 10.

treatment agencies are more likely to have been tested. On this basis, it has been hypothesised that users of opiates are more likely to have been tested than users of non-opiate substances.

It seems that testing is often done in a routine way, without regard to maximising its potential benefits. When testing is done without a purpose—beyond simply making a diagnosis—the benefits will be limited. In one Australian study of people who inject illicit drugs, three-quarters of respondents claimed to have received no test discussion. Post-test counselling was even less common, but there was a higher likelihood of it occurring for those who tested sero-positive.[15] Post-test counselling that focused on prevention appeared to be rare, the focus usually being on medical advice.

In some places access to testing has been facilitated by the co-location of primary health clinical services with drug user organisations and needle and syringe outlets. Where services are able to meet the full range of primary health care needs of people who inject illicit drugs, hepatitis C diagnosis is placed in this broader context. Testing through drug user organisations also has the advantage of being strongly linked to continuing health promotion and peer support and counselling.

People who have a history of injecting illicit drugs, often some years previously and without subsequent use, may be unlikely to be tested because of their unwillingness to disclose participation in an illicit practice or because of inadequate skills on the part of many health care professionals in taking drug-use histories. Although these people might pose little or no risk of transmission, they may be progressing to a point where treatment is a useful option or where lifestyle changes may be of benefit to their health and wellbeing. They are also likely to receive the bulk of their health care in the general practice setting; there is thus a need to continue existing programs to educate general practitioners about hepatitis C, eliciting drug-taking histories, and attitudes to injecting drug use. This, of course, does not preclude the need for education of other health care professionals.

[15] ibid., pp. vi–vii.

Recommendations

7. There is a need to improve access to hepatitis C testing, placing emphasis on health promotion principles—through discussion prior to testing and post-test counselling—for all people at risk of hepatitis C and particularly for people who inject illicit drugs. Testing will be most efficacious if it is part of a broader process that seeks to promote the health of people who inject illicit drugs, rather than being perceived as an isolated engagement. Peer-based user organisations are well placed to contribute to this process.

8. There is a need to continue education programs for health care professionals who deal with matters related to the testing and care of people with hepatitis C. In particular, these programs should be designed to develop professionals' skills in undertaking exposure assessments of drug use and should encourage appropriate attitudes to people who inject illicit drugs.

3.2 People from culturally and linguistically diverse backgrounds

People now living in Australia who were born in countries where there is a higher prevalence of hepatitis C infection, mainly as a result of unsterile medical procedures, may have unknowingly been at risk of infection. These people are mainly from culturally and linguistically diverse backgrounds.

The extent to which people from culturally and linguistically diverse backgrounds have been tested for hepatitis C is not known. There is no information available about the circumstances that result in testing, but anecdotal information suggests that it occurs as a result of symptoms suggestive of hepatitis and in pre-operative screening. Compared with other health care workers, general practitioners are likely to have more contact with this population group.

Access to testing for people from culturally and linguistically diverse backgrounds may be limited by several factors:

- lack of knowledge of and inability to, understand health care messages
- difficulty in finding culturally and linguistically appropriate health care in their local areas
- fear of the stigma associated with a diagnosis of hepatitis C
- a lack of perceived risk on the part of either the patients or their doctors.

There is a need to ensure that people from culturally and linguistically diverse backgrounds have access to information and support that are culturally appropriate. This includes developing resources in languages other than English and delivering

cross-cultural awareness training for hepatitis C organisations and relevant health care workers.

Recommendation

9. Access to testing for people from culturally and linguistically diverse backgrounds should be facilitated by targeted, sensitive community education, further training of health care workers, and ready access to interpreter services.

3.3 Aboriginal and Torres Strait Islander peoples

There is a lack of information with which to gain an indication of the prevalence of hepatitis C infection among Aboriginal and Torres Strait Islander peoples. It is probable that the prevalence of infection would reflect the prevalence of injecting drug use. Evidence of a high prevalence of hepatitis C in custodial settings and the disproportionately high representation of Aboriginal and Torres Strait Islander peoples in these settings give cause for concern.

Considering the overall lower health status of Aboriginal and Torres Strait Islander peoples and the burden of other social and health problems they bear, measures for dealing with hepatitis C infection should be placed in the context of primary health programs designed to improve health outcomes in general for this population group.

Limited access to health care has been identified as one factor that contributes to the poorer health status of Aboriginal and Torres Strait Islander peoples. The National Indigenous Australians' Sexual Health Strategy canvassed the mechanisms that need to be developed to encourage Aboriginal and Torres Strait Islander people to be tested for HIV. Stigma is associated with both HIV and hepatitis C, so these mechanisms have broader applicability. Relevant factors identified by that strategy are:

- in collaboration with organisations and regions, developing policies that outline the best way to approach test discussion and post-test counselling
- providing information in a format that individuals can understand and use
- allowing individuals sufficient time to make their decisions
- ensuring complete discretion and confidentiality
- providing details of where the individual can go for more information.

Several other points are also important in relation to testing Aboriginal and Torres Strait Islander people:

- The way information is provided and how and where services are developed must be culturally acceptable.

- There is a need to involve Aboriginal and Torres Strait Islander peoples' health and community organisations.
- Test discussion, seeking informed consent and post-test counselling need to be undertaken in culturally appropriate ways. This requires special attention in mainstream settings.
- Hepatitis C testing should take place in the broader context of general and targeted community education programs dealing with hepatitis C and other health concerns.

Recommendation

10. Access to testing for Aboriginal and Torres Strait Islander peoples with risk factors for hepatitis C should be facilitated by adopting good management practices for testing for other stigmatised diseases. This includes developing within organisations policies that outline the best approach to test discussion and post-test counselling, providing information to individuals in a culturally sensitive way and in a format they can understand, allowing individuals sufficient time to make their decision, ensuring confidentiality, and providing details of where the individual can go for more information.

3.4 Custodial settings

The prevalence of hepatitis C among inmates of custodial institutions is high because of the high level of injecting drug use and unregulated tattooing in this population, both inside and outside prison. In the Northern Territory testing of inmates for hepatitis C is mandatory, but neither mandatory nor compulsory testing is practised in any other jurisdiction in Australia. Voluntary testing is available to inmates in all jurisdictions. Some jurisdictions routinely offer testing to new inmates at the time of reception, although the merit of this approach has been questioned since this is a highly stressful time for inmates. It is unlikely that any health promotion messages or understanding of the meaning of the test would be retained—assuming that testing is accompanied by such interventions.

The extent to which inmates are adequately assessed for a range of primary health care risks varies but is generally limited by resource constraints. In all jurisdictions inmates are able to seek hepatitis C testing from a correctional health service at any time during their imprisonment, although they may encounter problems of access resulting from resource constraints and restrictions on their movement that impede access to health services. The other situation in which inmates can be tested is if they display symptoms that appear consistent with hepatitis.

Because of the high prevalence of hepatitis C infection among inmates, correctional health services in all jurisdictions view hepatitis C as an important public health concern. The proportion of inmates tested for the virus is not known: there is no consistent data collection across jurisdictions. Estimates of testing vary between

jurisdictions. In one jurisdiction the estimate has been as high as 66 per cent, but other jurisdictions estimate that only around 10 per cent of inmates are tested. Given the high prevalence of both risk factors and hepatitis C infection, a testing rate of 10 per cent is low.

If, as a result of resource constraints, the purpose of testing inmates is practically limited to making a diagnosis, the usefulness of the testing can be questioned. The benefits of hepatitis C testing in custodial settings will be maximised if a number of criteria are met:

- There is test discussion and informed consent is obtained before testing—to maximise understanding of hepatitis C and how transmission is prevented.
- For those found to be infected, there is post-test counselling in relation to transmission, lifestyle and the virus's natural history.
- There are measures in place that help to prevent transmission of hepatitis C.
- The health status of infected inmates is regularly monitored.
- Treatment is offered to those inmates for whom it is indicated.

In the case of Aboriginal and Torres Strait Islander inmates, methods of conducting effective test discussion and post-test counselling and providing continuing support should be developed in collaboration with Indigenous health services.

The particular circumstances applying in juvenile justice centres require that the process of consultation with detainees and other stakeholders (including parents, guardians, health care workers and advocates) be further considered and that mechanisms be incorporated in hepatitis C testing procedures when developing protocols and models of care.

If national protocols for the testing of inmates were developed it would have the benefit of encouraging best practice in relation to the diagnosis of hepatitis C in custodial settings.

Recommendations

11. Hepatitis C diagnostic testing should be available on a voluntary basis to all inmates of custodial institutions, as part of a comprehensive primary health care risk assessment and throughout the term of their incarceration. In keeping with the principle that inmates should have health care access equivalent to that available to the general community, testing should be accompanied by test discussion and post-test counselling, with an emphasis on health promotion. Inmates who have hepatitis C should have access to regular monitoring of their health status. Treatment should be available to those who meet standard eligibility criteria.

12. National protocols for the diagnosis and management of hepatitis C in custodial settings should be developed in consultation with the relevant stakeholders, including inmates.

3.5 Rural and remote areas

People who live in rural and remote areas and who are at risk of hepatitis C may be reluctant to seek testing through local health facilities because of concerns about the stigma, discrimination on the part of health care professionals, and the possibility of breaches of confidentiality. They may seek testing in other towns, but distance and a lack of transport can pose difficulties.

Although hepatitis C is not a sexually transmissible disease, sexual health clinics have a history of seeing people with risk factors for hepatitis C and are experienced in providing non-judgmental services. Where sexual health clinics exist in rural areas, they provide an important point of access to testing. Nonetheless, it needs to be recognised that the majority of testing in rural areas will be done by general practitioners, who should be supported in this role.

Recommendation

13. There is a need for continuing education and training of health care professionals in relation to hepatitis C and non-judgmental attitudes to people who inject illicit drugs, particularly in rural and remote areas, where the choice of health services may be limited.

4 The recommended approach to diagnostic testing

This chapter outlines the benefits and risks of hepatitis C testing and the steps that can be taken to maximise the benefits and minimise the risks. It also sets out the indications (risk factors) that result in recommendations for offering diagnostic testing, recommendations for when testing may be offered and when the need for testing requires consideration in light of risk factors for infection. The rationale for whether or not testing should be encouraged in particular population groups or settings is also discussed. Among the areas covered are antenatal testing; testing of infants born to mothers infected with hepatitis C; testing of household (non-sexual) contacts; sexual partners; pre-operative testing; health care workers; recipients of blood transfusions and blood products; blood, body tissue and organ donors; and testing following environmental or occupational exposure.

4.1 The benefits and risks of diagnostic testing

The National Health and Medical Research Council makes the following comments in relation to the benefits and risks of screening:

> Active screening for early detection of disease in affected individuals is widely applied in preventive medicine and public health practice. Where an unequivocal benefit accrues to the person being screened, from a negative or positive result, the justification for screening is incontrovertible ... Where the benefits of screening accrue largely to the public or to a third party, and the benefits to a person being screened are equivocal, the justification for case detection through screening is more contentious. This is particularly so for diseases where a diagnosis may confer psychological and social disadvantages.[16]

This raises the question of what are the benefits and risks—at the level of public health and for individuals—in relation to hepatitis C testing.

4.1.1 The benefits

The following potential benefits have been identified in relation to hepatitis C testing:

- Testing provides an opportunity for the delivery of prevention messages on a one-to-one basis. This could help uninfected individuals who are engaging in risk practices to personalise the risk of infection. The importance of not infecting others can also be emphasised to those who are infected, thus offering potential benefits in terms of public health.

- Diagnosis of hepatitis C might encourage individuals to adjust their lifestyle in such a way as to reduce the risk of liver damage—for example, a reduced alcohol intake, dietary modification and stress reduction.

[16] National Health and Medical Research Council 1997, *A Strategy for the Detection and Management of Hepatitis C in Australia*, NHMRC, Canberra, p. 18

- Infected individuals can be monitored, and treatment can be offered to those who meet the clinical eligibility criteria. There is benefit in starting treatment before cirrhosis develops; this results in a higher response rate and lowers the risk of progression to cancer of the liver. Cirrhosis can develop in the absence of symptoms, so it is possible to progress to this stage without any indications that would prompt testing.

- Testing provides the opportunity to collect data that can be used to monitor the extent of, and patterns and trends in, hepatitis C infection. This offers potential benefits in terms of public health.

4.1.2 The risks

A number of risks have been associated with hepatitis C testing, among them the following:

- People who are identified as infected with hepatitis C often report experiences of prejudice and discrimination.

- Seeking testing may involve disclosure of risk factors, which could have adverse consequences for the individual.

- A diagnosis of hepatitis C can diminish an individual's quality of life because of the worry and fear of the consequences it engenders. When the data on the number of people who achieve spontaneous viral clearance and the slow progression rates for others are taken into account, it can be argued that awareness of hepatitis C infection causes more detriment for some people than do the actual physical effects of the infection.

- Only a proportion of patients (about 41 per cent with combination therapy) gain a long-term response with the currently available treatments.

- The current treatments are limited in their variety, accessibility and availability and are demanding for individuals.

- Support services for people with hepatitis C are limited by the available resources.

- There is a low risk of a false positive result in an appropriate testing strategy and an even lower risk of a false negative test result.

4.1.3 Maximising the benefits and minimising the risks

When deciding whether to be tested, individuals should be well informed, so that they can weigh up the potential benefits and risks. As well as this, action can be taken to maximise the benefits and minimise the risks; this involves health promotion, test discussion and post-test counselling, provision of information and support, and ongoing health monitoring.

Health promotion opportunities

At present the greatest public health benefit of testing lies in the potential to modify risk behaviour by offering testing in the context of an education and prevention intervention. If testing is coupled with effective education and prevention interventions, its public health benefits will be maximised by targeting people engaging in practices that pose a risk of hepatitis C transmission. This particularly applies to people who inject illicit drugs.

From a public health perspective, there is little benefit in testing people who do not engage in behaviours that pose a risk of transmission of hepatitis C. Nevertheless, sentinel testing of particular populations or in specific settings can play an important part in determining the extent of the epidemic and monitoring trends.[17]

Test discussion and post-test counselling

Provision of accurate, suitably presented information before testing and when revealing test results is essential if individuals are to make informed decisions about the benefits and risks of hepatitis C testing.[18] This is particularly important in view of the widespread misunderstanding about the natural history of hepatitis C infection. Accurate information can help reassure people about the likelihood of immediate and longer term consequences and place hepatitis C infection in a realistic context.

Test discussion

The health care professional and the patient should thoroughly discuss the matter before testing for hepatitis C infection.[19] This process is called 'test discussion' rather than 'counselling' because the health care professional may, in addition to counselling, be required to assess risk, obtain consent, arrange follow-up, and identify referral needs. 'Counselling' does not encompass this broader role. Use of the term 'discussion' is not intended to diminish in any way the importance of the process. The term 'test discussion' is used in preference to 'pre-test discussion' because the latter assumes that testing will follow the discussion, which is not necessarily the case.

The hepatitis C test discussion should provide accurate information about safe practices that are appropriate to a person's gender, culture, language and behaviour. The complexity of the discussion will vary from person to person, depending on their risk factors and other variables. At minimum, however, the discussion should cover the following:

- risk assessment and the reason for testing
- how to reduce the risk of becoming infected or infecting others—for example, information about safe injecting when this is relevant

[17] Sentinel testing is not dealt with in this policy because it comes within the scope of the 1999 Australian Hepatitis C Surveillance Strategy.
[18] The *Australian Family Physician* special issue on hepatitis C (1999, vol. 28, December) provides guidance on test discussion and post-test counselling.
[19] The requirements for hepatitis C test discussion do not apply to blood donors.

- the testing process, including how test results are provided, the reliability of the results and the window period
- what positive, negative and indeterminate results mean
- the natural history of hepatitis C infection
- confidentiality and privacy
- what happens to test results—that is, the notification procedure
- the person's willingness to be tested
- support mechanisms while waiting for the test result and if the result is positive
- seeking of informed consent if testing is to occur.

Post-test counselling[20]

It is important for *all* test results—negative, positive or indeterminate—to be conveyed in person and in a manner that is sensitive to gender, culture, language and behaviour.

A negative test result provides an opportunity to reinforce information and education messages about safe behaviours and to examine any difficulties or concerns the individual may have in relation to practising safe behaviour. Regardless of the test result, there should also be discussion of the benefits of hepatitis A and hepatitis B vaccination for people who inject illicit drugs.

If the result is positive, post-test counselling should include discussion—at an appropriate time—of matters such as the following[21]:

- immediate needs and supports
- safe behaviours—education, information and support
- who to tell and how
- understanding and managing strong emotions, feelings, reactions and changes
- the natural history of hepatitis C infection
- determining the person's current health status in relation to hepatitis C and continuing monitoring
- available treatments

[20] A guide to the initial management of hepatitis C is provided in the hepatitis C supplement to the *Australian Family Physician* (1999, vol. 28, December).

[21] There is no need for post-test counselling of blood donors who test negative. While blood services may not conduct post-test counselling for donors who are positive, they have a responsibility to refer these people to health care professionals with appropriate skills.

- complementary and alternative management options
- ways of dealing with loss and grief, depression, anger and anxiety
- the benefits of vaccination against hepatitis A and hepatitis B
- strategies for managing hepatitis C infection that are flexible and appropriate to the person's needs and circumstances
- legislative requirements in connection with notification.

Referral information should also be provided, as should written information for the person to take away.

Provision of information and support

In addition to post-test counselling, people diagnosed with hepatitis C infection may need continuing support, particularly in the period immediately after they learn their test result. The purpose is to provide reassurance, to help them work through any difficulties (such as telling others they are infected) and to help place the infection in context. This is also another opportunity to reinforce messages about the natural history of hepatitis C and to inform people of the available treatments, should treatment become necessary.

Community organisations such as hepatitis C councils and drug user organisations are well placed to provide information and support. People diagnosed with hepatitis C infection should be told how to contact these organisations.

Ongoing health monitoring

For people infected with hepatitis C, the usefulness of testing will be maximised if their health status is regularly monitored.

Some groups of people infected with hepatitis C (such as people who inject illicit drugs) may have other, more pressing, health concerns. In this situation it is preferable that their overall primary health care needs, including their hepatitis C infection, be approached in a comprehensive way and in a setting that is non-discriminatory and sensitive to their situation. This will also assist in facilitating access to suitable health care, which is often limited for this group of people.

In population groups for which it is likely that infection with hepatitis C occurred a considerable time ago, there may be additional benefit in being tested: if infected, these people are more likely than those relatively recently infected to have progressed to the point where treatment might be indicated. This is most likely to apply to people infected in their country of birth, people who were infected through the receipt of blood or blood products in Australia before 1990, and people who previously injected illicit drugs.

4.2 When diagnostic hepatitis C testing should be offered

The recommendation for who should be offered diagnostic hepatitis C testing is based on:

- a known epidemiological relationship between a risk factor and acquiring hepatitis C infection
- the prevalence of risk behaviours or characteristics in the population being tested
- the prevalence of infection among people with a particular risk behaviour or characteristic
- the need for people with an identified exposure to be evaluated for infection.

Indications for testing may change in the future, as more becomes known about the epidemiology and transmission of hepatitis C.

Recommendation

14. Testing for hepatitis C antibodies should be offered to people who have an identified risk of infection. The decision to be tested is one for individuals to make on an informed basis, in consultation with health care professionals. Testing 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 needlestick 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—these conditions are listed in Appendix B
    - renal dialysis patients
    - people who request testing in the absence of an identified risk factor.

4.3 When diagnostic hepatitis C testing might be offered

For some individuals and groups, diagnostic testing for hepatitis C might be offered on the basis of an individualised risk assessment. The following groups warrant consideration:

- people with history of tattooing or body piercing, or both
- people born in countries where there is a high prevalence of hepatitis C infection
- the sexual partners of people infected with hepatitis C.

4.3.1 Tattooing and body piercing

For people with a history of tattooing or body piercing, or both, the risk of infection will probably be greater if there have been multiple tattoos or body piercings; it will also be influenced by the setting in which the tattooing or piercing was done. In settings that deal with a high proportion of hepatitis C–infected people and where tattooing or body piercing is done without adequate infection-control procedures (for example, in custodial institutions) the risk of infection is high.

4.3.2 People born in countries with a high prevalence of hepatitis C infection

For people born in countries where there is a high prevalence of hepatitis C infection (for example, Egypt and Vietnam) the risk of hepatitis C infection may be greater than it is for people born in Australia. For people born in regions such as Asia initial investigation of possible liver disease, using liver function testing, may be more appropriate because of the relatively high hepatitis B prevalence in these regions. Hepatitis B and C antibody testing can then be offered to those with abnormal test results.

4.3.3 Sexual partners of infected people

Sexual partners of people infected with hepatitis C should be told about the available information on the risk of transmission through sexual activity, to help them make decisions about testing and precautions. The risk of transmission is low, but it seems that sexual transmission does occur at a rate of up to 3 per cent among long-term partners of hepatitis C–infected people.[22]

Co-infection with HIV is associated with some increase in the risk of sexual transmission of hepatitis C.

Recommendation

15. 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 infected with hepatitis C.

[22] Crofts N, Thompson S & Kaldor J 1999, *Epidemiology of the Hepatitis C Virus*, Technical report series no. 3, Communicable Diseases Network of Australia and New Zealand, p. 46.

4.4 When diagnostic hepatitis C testing might be considered

The currently available evidence suggests that hepatitis C testing should be offered to the following groups only if they have risk factors for infection:

- health care workers other than those who are involved in exposure-prone procedures or who have had a specific risk exposure
- pregnant women
- household (non-sexual) contacts of hepatitis C–positive people—unless there is a history of direct exposure to blood
- pre-operative patients
- the general population. The absence of a risk history for hepatitis C infection characterises the vast majority of the Australian population. There is no reason to encourage testing in the absence of risk factors.

4.4.1 Health care workers

The Communicable Diseases Network of Australia's *Infection Control Guidelines for the prevention of transmission of infectious diseases in the health care setting*, adherence to standard infection-control procedures should be the principal means of preventing the transmission of hepatitis C in health care settings. The Guidelines are at: http://www.health.gov.au/pubhlth/strateg/communic/review/draft.htm

For health care workers, routine screening for hepatitis C infection is inappropriate. Testing might identify a risk, but it does not diminish the risk and is no substitute for standard infection control. Reliance on testing may lead to diminished emphasis on the importance of standard precautions to prevent cross-infection.

Because there is a remote possibility of transmission from heath care worker to patient during exposure-prone procedures, all health care workers involved in such procedures have a continuing responsibility to know their hepatitis C status. Health care workers with hepatitis C viraemia (that is, who have hepatitis antibodies and are shown to be positive by qualitative nucleic acid testing) should not perform exposure-prone procedures.

There is no consensus on how often regular testing should be carried out, but health care workers involved in exposure-prone procedures should be tested after an incident—such as a sharps injury. Health care workers with hepatitis C infection should be assessed by their medical practitioner and an advisory panel or board in relation to their continued involvement in direct patient care that may involve exposure-prone procedures. The various jurisdictions in Australia have policies that define the professional and ethical obligations of health care workers.

Health care workers with indeterminate hepatitis C test results should not be excluded from performing exposure-prone procedures on the basis of the test results alone. If test results are positive or indeterminate, health care workers should be assessed by an

experienced medical practitioner over a reasonable period for any signs of current or active infection. Where there is insufficient evidence of current or active infection, the treating medical practitioner or the individual concerned should seek the advice of the state or territory advisory panel or registration board.

Recommendation

16. Adherence to standard infection-control guidelines is the principal means of preventing transmission of hepatitis C infection in health care settings. Routine screening of health care workers for hepatitis C infection is inappropriate, but all health care workers involved in exposure-prone procedures have a responsibility to know their hepatitis C status.

4.4.2 Antenatal testing

The general risk of hepatitis C transmission from mother to child during pregnancy or at birth is estimated to be 5–8 per cent. Several factors increase the risk:

- HIV co-infection in the mother
- a high viral load—although this is not exclusively predictive and no cut-off point at which transmission will occur has been identified
- an increased duration between membrane rupture and delivery
- the use of invasive devices such as foetal monitors.

Factors not associated with a higher risk of transmission are the mode of delivery, hepatitis B co-infection and breastfeeding. At present there are no drug therapies that reduce the risk of mother-to-child transmission.

There is no evidence that the prevalence of hepatitis C among pregnant women is significantly higher than for the general population, since sexual transmission of hepatitis C is known to occur relatively infrequently.

Taking account of the factors that follow, it is concluded that there is no good basis for offering hepatitis C screening to all pregnant women:

- The prevalence of hepatitis C among pregnant women is thought to be very low, so the positive predictive value of screening would be low. It would be difficult to justify the cost of routine screening on the basis of the number of new positive cases that would be found.
- The additional number of pregnant women who would be diagnosed as hepatitis C infected as a result of routine screening may not be significantly higher than the number diagnosed by offering testing on the basis of identified risk factors.

- A high number of indeterminate and false positive results would be diagnosed in a low-prevalence population, causing unnecessary anxiety.

- The risk of transmission to the infant is low, and knowledge of hepatitis C status is unlikely to affect a mother's decision about her current pregnancy.

- Interventions to minimise the risk of transmission are very limited. (Recent evidence from an observational study suggests that the mode of delivery may influence transmission, with a lower risk being observed in the case of elective caesarean section.[23] However, the researchers caution against using this information to change antenatal screening policy: the results need to be confirmed in a randomised controlled trial.)

Nonetheless, any woman identified as being at risk of hepatitis C infection should be offered testing. The process should involve a thorough assessment of potential exposure through the recognised means of transmission. Testing should always be associated with specific informed consent, the provision of information about the meaning of the results (particularly in relation to pregnancy) and post-test counselling.

This aspect of the National Hepatitis C Testing Policy should be regularly reviewed, to take account of any therapeutic advances that could minimise the risk of transmission and other new information, including information on hepatitis C sero-prevalence.

A review of antenatal testing policies and practices for HIV and hepatitis C infection, conducted in 2001 by the National Centre in HIV Epidemiology and Clinical Research[24], found a high rate of screening for hepatitis C in pregnant women. The Australian National Council on AIDS, Hepatitis C and Related Diseases and the Intergovernmental Committee on AIDS, Hepatitis C and Related Diseases should examine findings of this study to determine whether any action needs to be taken to reduce the rate of routine screening.

Transmission from mother to child will not occur if the mother has spontaneously cleared viral infection, so all pregnant women who test positive for hepatitis C antibodies should be offered qualitative nucleic acid testing to determine if they are still infectious. This indication for qualitative NAT is not currently covered under the Medicare Benefits Schedule (see Chapter 6).

[23] Gibb DM, Goodall RL, Dunn DT, Healy M, Neave P, Cafferkey M & Butler K 2000, 'Mother to child transmission of hepatitis C virus: evidence for preventable peripartum transmission', *Lancet*, vol. 356, no. 9233, pp. 904–7.
[24] National Centre in HIV Epidemiology and Clinical Research 2001, 'Review of antenatal testing policies and practice for HIV and hepatitis C infection'.

Recommendation

17. Health care professionals in settings where pregnant women are evaluated or receive routine care should conduct a thorough risk assessment to determine the need for hepatitis C testing and other prevention measures. Pregnant women should receive specific information about the risk of vertical transmission and breastfeeding. Antenatal testing for hepatitis C should be undertaken only when the woman's history reveals a relevant risk exposure or the woman requests it: it should not be a routine diagnostic test.

4.4.3 Testing of infants born to mothers infected with hepatitis C

The decision whether to seek testing for a child is a matter for the parents, in consultation with health care professionals. 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.[25] 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. (See Chapter 6 for a discussion of the funding implications of this.)

4.4.4 Household (non-sexual) contacts

Routine social or casual non-sexual contact carries no risk of transmission of hepatitis C. Household transmission is rare and does not occur through the usual family and domestic contact—such as sharing drinking and eating utensils, hugging and kissing. With the exception of direct exposure to blood, the risk of transmission is small, but not non-existent, and can be significantly reduced by adhering to basic infection-control principles in the home. The main way of reducing the risk of transmission in the home is to prevent infected blood from coming into contact with an uninfected person.

People are not always aware that they are infected: they may not exhibit or be aware of the signs and symptoms. Hepatitis C diagnostic testing should be considered if any exposure to or transfer of blood has occurred.

4.4.5 Pre-operative testing

Adherence to standard infection-control procedures offers the best protection against infection for both health care professionals and patients. Pre-operative hepatitis C

[25] Srivastava A, Smith AL & Hardikar W 2000, 'Natural history of hepatitis C acquired in infancy', *Journal of Gastroenterology and Hepatology*, vol. 15, p. J67.

testing should be performed only if it will benefit the patient. Testing for hepatitis C is rarely an urgent need in a clinical situation.

Medical practitioners are advised to conduct a thorough risk assessment of the patient and to obtain the patient's informed consent before recommending a test. Routine pre-operative testing cannot be justified. In any situation where a patient is unable to give consent or withholds it, the patient should be managed as if he or she were infectious.

Recommendation

18. Decisions about pre-operative testing of a patient for hepatitis C should be made on the basis of benefit to the patient. Medical practitioners are advised to ensure that a thorough risk assessment is carried out and the patient's informed consent is obtained before testing. Routine pre-operative testing cannot be justified.

19. In the absence of risk factors for infection, the offer of diagnostic hepatitis C testing for the following groups is not currently indicated:

    - health care workers
    - pregnant women
    - infants born to mothers infected with hepatitis C
    - household (non-sexual) contacts of hepatitis C–positive people—unless there is a history of direct exposure to blood
    - pre-operative patients
    - the general population.

4.5 Recipients of blood transfusions and blood products

When the hepatitis C antibody test became available in 1990 Australia responded promptly by introducing screening of the blood supply. Since that time the risk of acquiring hepatitis C through blood transfusion has become minimal.

All state and territory governments have funded hepatitis C 'look-back' programs designed to identify and offer testing to people who may have received a transfusion of a fresh blood product that was potentially infected with hepatitis C. Although this job is largely complete, the Australian Red Cross Blood Service recognises that there may, from time to time, be cases that require look-back and has developed a national policy to guide the process. Look-back programs cannot locate all people who might have been infected through the blood supply because hospital records before 1990 are incomplete. For this reason, people who were transfused with fresh blood products before 1990 should be routinely offered hepatitis C testing.

4.6 Blood, body tissue and organ donors

Since June 2000 qualitative nucleic acid testing has been the standard for screening fresh blood products for hepatitis C and HIV. Use of this technology reduces the window period for detecting infection from 66 days to 23, on average, providing a further level of protection for the blood supply. Antibody tests will also continue to be used in the screening of blood since some people can test qualitative NAT negative and antibody positive. The risk of transmission through transfusion is now considered very low.

In addition, potential donors with risk factors for hepatitis C and other blood-borne infections are excluded through the use of donor declaration forms. To deal with the rare instances when a blood donor does test positive to hepatitis C or other blood-borne pathogens, the Australian Red Cross Blood Service now uses a standardised assessment process to collect information about the person and the circumstances of their donation. This is used in reviewing the adequacy of the risk assessment form.

Blood donors who are repeatedly reactive in screening tests (antibody or qualitative NAT) are informed that they cannot donate blood. They are provided with oral and written information about hepatitis C and are referred to a medical practitioner in a non–blood service situation for assessment and care. They are also made aware of support agencies such as hepatitis C councils.

Pressing time frames associated with the allocation of organ and tissue donations preclude the use of NAT. The Australian National Organ Allocation protocols state that before organ or tissue allocation an accredited laboratory must complete currently acceptable hepatitis C antibody testing procedures. Under these protocols, people with a relevant medical history, known risk behaviours, known injecting drug use, or positive hepatitis C antibody test results are excluded from donating.

4.7 Exposure in health care settings

4.7.1 Exposure to blood known to be infectious

Patients and health care workers exposed to blood that is known to be infectious should be informed of the exposure by a designated professional. Where possible, confidentiality about the individual who is the source of the blood should be maintained. Baseline serum should be collected from the exposed person, to establish their sero-status at the time of exposure. Expert counselling on the implications of the incident should be provided, and follow-up should be offered. If the exposed person refuses testing and serum storage, this should be documented.

4.7.2 Exposure to blood of unknown sero-status

A person whose blood or body fluids are the source of an exposure in a health care setting should be evaluated for infection with hepatitis C. The available information (such as a medical record) on the source person may rule out infection. If the source person’s hepatitis C status is unknown, that person should be informed of the incident and their consent to hepatitis C testing should be sought. Test discussion and post-test

counselling should be available. If consent cannot be obtained—for example, if the patient is unconscious—procedures complying with relevant state or territory legislation should be followed.

If the source person is found to be hepatitis C negative, there is generally no need for further follow-up of the exposed person. There is, however, a need for follow-up if there is any likelihood that the source person is sero-converting or was at high risk of blood-borne viral infection at the time of exposure.

If the source person is hepatitis C antibody positive, a qualitative NAT should be done. The risk of transmission is negligible if the source tests negative on qualitative NAT.[26] However, until there is general agreement that negative hepatitis C qualitative NAT means there is *no* risk of transmission, a negative result will not eliminate the need to follow up the person who has been exposed. Nonetheless, a negative test result should help considerably with counselling and reassurance.

Reasonable efforts should be made to identify the source of the exposure. If the source remains unknown, appropriate follow-up should be determined on the basis of the level of risk posed by the exposure, the likelihood of the source being infected with hepatitis C, and the prevalence of hepatitis C in the community in which the exposure occurred.[27]

[26] Dore GJ, Kaldor JM & McCaughan GW 1997, 'Systematic review of the role of PCR in defining infectiousness among people infected with hepatitis C virus', *British Medical Journal*, vol. 315, pp. 333–7.

[27] The policy on testing where an exposure has occurred in a health care setting and on the testing of health care workers is based on the recommended approach in *Infection Control in the Health Care Setting: guidelines for the prevention of transmission of infectious diseases* (Communicable Diseases Network of Australia and New Zealand 2000, Draft for public consultation, CDNANZ, Canberra).

5 Diagnostic strategies

This chapter provides advice on minimum standards for laboratory diagnosis and investigation of hepatitis C. The policy approach to short incubation tests and home-based testing is also set out.

It should be noted that, because of their unique requirements, blood services have developed their own strategies for screening donations. This part of the National Hepatitis C Testing Policy does not apply to blood services.

5.1 Laboratory investigation of hepatitis C infection

Laboratory investigations are usually directed towards answering one or more of the following questions:

- Has the patient been infected with hepatitis C?
- Is the patient currently infected?
- Has the patient recently undergone acute infection?
- What is the current level of virus replication?
- Is there current ongoing liver damage?
- How much cumulative liver damage has been sustained?
- What is the infecting virus genotype?
- What testing should be performed for epidemiological surveillance?

In many instances, a specific answer to one of these questions (for example, Is the patient currently infected?) raises implications in relation to other questions (such as the question about ongoing liver damage). A full clinical interpretation of the significance of serological results will depend on the results' correlation with a number of other factors, including clinical history, ALT levels and risk factors.

For accurate diagnosis in different populations it is important that laboratory criteria that are independent of the clinical context of the test be developed.

5.1.1 Has the patient been infected with hepatitis C?

The question of whether the patient has been infected with hepatitis C is usually answered by performing an immuno-assay for hepatitis C antibody in serum or plasma. The presence of true antibody indicates that the patient has been infected with the virus. In a majority of cases (65–85 per cent) an individual with true hepatitis C antibody is probably still infected. The absence of antibody usually means the patient has never been infected, although antibody may become undetectable years after the

infection has been cleared. Furthermore, antibody may not be detectable very early in the course of infection or in people who are immuno-suppressed—for example, some people who inject illicit drugs and people undergoing therapies such as chemotherapy and dialysis. The proportion of infection in this group without antibody is unknown, but it is very small.

There is general consensus among reference laboratories in Australia that, where a serum sample is non-reactive in a single approved immuno-assay for hepatitis C antibody, it can be reported that the sample is antibody negative. In contrast, there are varying opinions about the best way for a laboratory to confirm an initially reactive immuno-assay. Because of the appreciable rate of false reactive results and the need to distinguish them from antibody-positive results, supplemental testing of all screen-reactive results is essential. Supplemental testing to confirm hepatitis C infection should be completed before test results are conveyed to the requesting doctor and patient.

Current approaches to confirmatory testing

Current practice in Australia for confirming the presence of hepatitis C antibody has been strongly influenced by the protocols set out in *A Strategy for the Detection and Management of Hepatitis C in Australia*.[28] This document stipulated that all samples initially reactive in one immuno-assay should be retested with a second, independent immuno-assay, to confirm specificity. A sample is not considered to be positive for hepatitis C antibody until the supplemental immuno-assays have been performed and have been found to be reactive. However, the algorithms so generated have created difficulties with samples that are reactive in the initial immuno-assay and not the secondary one. Furthermore, tests that are reactive for technical reasons are then tested in the second enzyme immuno-assay and it is known that some combinations of immuno-assays can share false reactivity.

In Australia there is no scientific consensus about the optimal way to confirm the presence of hepatitis C antibody. There is continuing debate about whether it is preferable to repeat an initially reactive screening test (singly or in duplicate) before confirming with a second enzyme immuno-assay and only confirm those samples that are repeatedly reactive in the initial screening procedure or whether it is better to proceed directly to confirmation. All manufacturers of test kits recommend the latter approach. The choice will depend, at least in part, on the type of population being tested (and hence the positive predictive value of the reactive result). In practice, most laboratories have used variations on one or both of the following approaches to confirm an initially reactive result:

- testing with another immuno-assay that uses antigen combinations that differ from those used in the first assay

- use of or referral to a reference laboratory for testing with one of several immunoblot assays or by qualitative NAT.

[28] National Health and Medical Research Council 1997, *A Strategy for the Detection and Management of Hepatitis C in Australia*, NHMRC, Canberra.

Note: In the case of initially reactive results, it is important to follow the manufacturer's instructions on the package insert. These instructions are assessed by the Therapeutic Goods Administration as part of the performance evaluation for the test kit. Responsibility for any deviation from the instructions rests with the user of the test kit: non-compliance is considered a failure to perform the test as intended.

Appropriate combinations of assays

The hepatitis C virus cannot be cultured and, because there is a patent covering its genomic sequence, access to hepatitis C antigens is limited. As a result, the same or very similar antigens are used by a number of immuno-assays and also in immunoblot assays that involve a different type of test format. Collection of laboratories' testing data and extensive additional testing by the National Serology Reference Laboratory (NRL) have allowed the identification of immuno-assays that share common false reactivity—that is, false positive results in accordance with the NHMRC guidelines. Using this information, the NRL has advised which combinations of immuno-assay kits are likely to provide the most reliable results. Although this information has been widely used in Australia, the NRL reports that some laboratories still use inappropriate combinations of immuno-assays for supplemental testing. This can result in reporting of falsely positive results, and it is important that laboratories use the appropriate combination of assays in confirming a diagnosis.

Recommendation

20. The National Serology Reference Laboratory should periodically circulate to all laboratories advice about appropriate pairings of first and supplemental immuno-assays that provide independent results and pairings that are so similar that the supplemental result is of little value.

Use of alternative immuno-assays is cheaper than using an immunoblot for the supplemental test. Immunoblots are less sensitive than immuno-assays and so may be negative or equivocal for longer in very early infection. There is debate about how much new information is gained by immunoblot, given that the source of antigen is often identical to that used in the corresponding immuno-assay. On the other hand, immunoblots are considered by some as a de facto 'gold standard' for anti-HCV immuno-positivity. Their use has been quite limited in Australia and is declining in United States.

There is general agreement in the Public Health Laboratory Network (PHLN) that samples reactive in both the initial immuno-assay and a separate secondary immuno-assay based on different antigens and a different format have a very high probability of being true antibody positive for hepatitis C and can therefore be reported as a confirmed positive. But not all dually reactive samples will contain true hepatitis C antibody: a small percentage of results will still be false positive, since no single protocol using immuno-assays only can be relied upon as a gold standard in all situations.

Best practice dictates that for all new positive diagnoses a second round of testing—using a newly collected sample—be performed to avoid erroneous reporting resulting from transcription or labelling errors. This is not current practice in all laboratories.

Individual laboratories may wish to perform additional confirmatory tests, beyond the recommended minimum standard of practice, which is one confirmatory test using a different assay. Funding under the Medicare Benefits Schedule is consistent with the NHRMC minimum standard; that is, reimbursement is provided for one supplemental test.

Discordant results

At present there is a diversity in practice for dealing with 'discordant' test results—samples that are reactive in one immuno-assay and non-reactive or negative in another. As a minimum, the first assay should be shown to be repeatably reactive, to ensure that the reactivity is reproducible and the initial reactivity is not a result of technical factors. Current practice in the various laboratories includes the following:

- reporting the result as anti-HCV negative
- reporting the result as discordant, equivocal or 'indeterminate' and retesting the patient in three to six months
- repeating the immuno-assay using a newly collected sample
- performing an immunoblot and reporting the result according to the manufacturer's criteria
- performing a qualitative NAT and reporting the sample as a 'confirmed' positive if the test is reactive (ideally on two separate occasions) or 'indeterminate' if negative. Because of the risk of contamination, qualitative NAT should always be performed on a dedicated sample and never on the sample submitted for serology. If the qualitative NAT result is negative, the antibody result is reported as 'indeterminate' because a negative NAT result does not adequately distinguish between a true or false antibody result
- where a 'discordant' sample is negative on qualitative NAT, performing an immunoblot.

In practice, if the second immuno-assay is negative on a person's sample and the person is without risk of infection with the virus, the test result may be deemed anti-HCV negative. Some laboratories are reluctant to follow this course, however, and will conduct further testing using one of the procedures just listed. Reliably performed qualitative NAT with a positive result can be used to support the authenticity of a reactive or positive antibody result, but a negative NAT cannot be used to exclude a true antibody result.

Under the Medicare Benefits Schedule, qualitative NAT attracts a payment if two different immuno-assay results have been inconclusive. This is currently restricted to one test a year for any patient. There is general agreement in the PHLN that it is

highly preferable to perform two qualitative NATs, if the first result is reactive, to guard against the danger of a false positive through contamination either upon collection or in the laboratory. When the patient is antibody positive in two assays and qualitative NAT positive on the first test, repeat NAT testing is not warranted. (Medicare does not cover qualitative NAT if the patient is antibody positive in two assays.)

At present no Medicare benefit is payable for the use of an immunoblot to confirm a hepatitis C diagnosis.

There are four main reasons for the diversity in approaches to supplemental testing to confirm hepatitis C infection:

- There is no test that represents a gold standard.
- Following an initially reactive immuno-assay result, in some contexts it may be more cost effective to repeat the initial test while in other contexts laboratories choose to go straight to a second immuno-assay for reasons of cost (this is also a minimum standard in the NHMRC protocol).
- Formal scientific studies comparing different approaches are not necessarily definitive because conclusions from one study may not apply equally to other settings using different primary assays, population groups with a different hepatitis C prevalence or disease spectrum, or different virus genotypes.
- There are valid but competing technical arguments in favour of a number of the approaches to supplemental testing to confirm hepatitis C–positive status.

In spite of this, minimum guidelines for confirmation of hepatitis C infection need to be provided, so that all laboratories are aware of acceptable standards of practice. Beyond that, individual laboratories can vary how they confirm positive results, provided that the minimum standards are met.

Recommendations

21. The following *minimum* practices should be adopted by all laboratories in determining whether a sample is hepatitis C antibody positive:

    - A sample negative on a single immuno-assay screen can be confidently reported as hepatitis C antibody negative.
    - Samples with an initially reactive result should be subject to a minimum of one supplemental immuno-assay, using a different assay. 'Best practice' is to repeat the first assay in duplicate and, when samples are repeatedly reactive, to conduct supplemental testing.
    - A sample that is reactive on two separate immuno-assays based on different antigens and different immuno-assay formats has a very high probability of containing true hepatitis C antibodies and can be reported as confirmed.
    - When seeking to confirm a result, laboratories should use only appropriate pairings of first and supplemental immuno-assays, as recommended by the National Serology Reference Laboratory.
    - Test results should not be reported until these minimum steps to confirm hepatitis C have been taken.

22. In the case of discordant antibody test results—the first test is repeatably reactive and the supplemental enzyme immuno-assay is negative—laboratories are advised to adopt *one or more* of the following strategies:

    - If there are no risk factors and there is no clinical suspicion, report that the individual is anti-HCV negative.
    - If risk factors are present, repeat the antibody test on a newly collected sample and/or conduct follow-up testing after a suitable interval. Then perform a qualitative nucleic acid test and report a 'confirmed' positive if the test is reactive—ideally on two separate samples.
    - If a discordant sample is negative by qualitative nucleic acid testing, perform an immunoblot and report the result according to the manufacturer's criteria.
    - If none of the above procedures is possible in the testing laboratory or if none is appropriate, the sample should be referred to a reference laboratory for further opinion.

False reactivity in immuno-assays is common—0.5–4.0 per cent of cases, depending on the type of immuno-assay and the population being tested. Testing strategies

should be formulated in order to distinguish false from true reactivity. The supplemental test should be selected to make this distinction. Repeatably reactive samples subjected to supplemental testing with registered assays and found to be non-reactive in the supplemental immuno-assay, should be called 'anti-HCV negative'. Registered immuno-assays are equally sensitive, so a negative result, whether the immuno-assay is used as a screening or a supplemental assay, should be taken as showing no hepatitis C antibody is detectable; that is, the sample is anti-HCV negative. If it is decided on clinical grounds to test the sample further using other tests, a result should not be reported until the testing is complete. Thus, discordant results should not be reported as such.

5.1.2 Is the patient currently infected?

Between 15 and 35 per cent of people infected with the hepatitis C virus will spontaneously resolve their infection, although the predictors of this spontaneous resolution are not yet clear. This specific population group may be hepatitis C antibody positive but hepatitis C RNA negative; the question of whether someone falls into this group is thus best answered by qualitative NAT to detect hepatitis C RNA. A single negative test for hepatitis C RNA does not, however, definitively exclude the presence of infection.

In the past, nucleic acid tests have suffered from false positive results because either the sample was contaminated with virus or PCR product was inadvertently introduced from other samples. This problem has been diminished by improved test design and greater laboratory skill. It is nevertheless still essential that a fresh blood sample be taken specifically for PCR or other NAT to obtain as reliable a result as possible. Adequate positive and negative quality controls should be used to ensure that each run maintains its specified sensitivity, and internal controls should always be used to detect inhibition. A positive result from a correctly performed NAT provides a high degree of certainty that the patient is currently infected; a negative result, however, does not exclude infection.

Emerging technology for hepatitis C RNA testing, using advanced nucleic amplification methods, has higher sensitivity and a low contamination risk, which increases the probability of reliable results.

Until recently, nucleic acid testing was to some extent discouraged because of problems with specificity and the cost. These problems are now less significant. It is also clear now that the majority of patients with reactive antibody results are aware of the importance of NAT and want to know their current infection status.

It is now recommended, therefore, that qualitative NAT be considered a standard component in the diagnostic work-up for all individuals who are hepatitis C antibody positive. Such a step requires that payment under the Medicare Benefits Schedule be considered; in particular, the frequency of testing authorised for reimbursement will need to be re-examined (see also Section 6.2).

Recommendation

24. Qualitative nucleic acid testing should be a standard component of the diagnostic work-up of all individuals who are hepatitis C antibody positive but have normal liver function.

5.1.3 Has the patient recently undergone acute infection?

Seroconversion from antibody negative to antibody positive is the most definitive evidence for acute infection. In practice, however, this evidence is difficult to obtain outside regularly monitored populations because most acute infections are clinically silent and patients therefore do not seek testing. An exception to this is the individual who has recently been exposed in an identifiable event and is then monitored for infection. If infection has occurred, tests become positive usually in the order nucleic acid test, enzyme immuno-assay, then immunoblot.

Although a number of serological assays for acute-phase IgM antibody have been described—which would allow diagnosis of recent infection from a single sample—none has yet been adequately evaluated and determined to be sufficiently reliable.

5.1.4 What is the current level of virus replication?

There are two main molecular testing techniques for the quantification of hepatitis C RNA: amplification of nucleic acid (quantitative PCR or NASBA); and signal amplification (for example, bDNA). Most laboratories use commercially manufactured kits for this testing.

Nucleic acid test assays have generally reached higher sensitivity (in terms of numbers of genomes detected per millilitre) than signal amplification assays. Newer versions of NAT assay are achieving even higher sensitivities. In contrast, bDNA methods have lower sensitivity—for example, 5–10 x 10^3 copies per millilitre, which is being improved upon—but are more robust and not as prone to contamination.

There have been reports of bias between different nucleic acid tests in determining the viral load in patients with different viral genotypes and of discrepant results between different assay procedures on the same sample. This has two important implications:

- Continued monitoring of different commercial assays and between laboratories is essential for quality control and identifying problems.

- Comparisons between *relative* values for different patients obtained using the same assay are likely to be more meaningful than absolute numbers obtained using different procedures.

5.1.5 Is there current ongoing liver damage?

The question of whether there is current ongoing liver damage is usually answered by conducting serum liver function tests (that is, aminotransferase tests) or by liver

biopsy. For people with anti-HCV positive immuno-assay results and abnormal liver function tests, it may be useful to progress to quantitative NAT and genotyping, bypassing qualitative NAT.

Levels of aminotransferase rise fairly rapidly after hepatocellular injury but can vary with fluctuations in disease activity, so repeated testing is advisable. They can also be elevated coincidentally for reasons other than hepatitis C infection—such as excess alcohol consumption and other viruses.

There is a general correlation between elevated aminotransferase and histological evidence of ongoing liver damage on liver biopsy. This is not absolute, though, and a normal aminotransferase result does not fully exclude ongoing liver damage.

5.1.6 How much cumulative liver damage has been sustained?

The best way of determining the extent of cumulative liver damage is to carry out a liver biopsy. Indications for liver biopsy and its interpretation are beyond the scope of this document.

5.1.7 What is the infecting virus genotype?

The infecting virus genotype (as well as viral load) is an important factor in predicting the response to treatment. To determine the genotype, one of the following two methods can be used:

- NAT-based (specifically PCR) methods are most commonly used but are applicable only to viraemic patients from whom a PCR product can be obtained. PCR-based methods use one of five approaches
  - RT–PCR using type-specific primers
  - sequencing of PCR products
  - RT–PCR followed by restriction fragment length polymorphism analysis
  - amplification of viral material followed by heteroduplex mobility analysis
  - RT–PCR with universal primers followed by hybridisation to type-specific probes.

  For the last of these approaches, PCR product analysis uses a commercially available system; the others use in-house methods. Each approach has advantages and disadvantages, which are discussed more fully elsewhere.[29]

- Serotyping methods use peptides that represent genotype-specific regions of the core, or NS4, region of the hepatitis C genome to detect circulating genotype-specific antibody that reflects the infecting virus genotype. As a result, this approach does not require the presence of viraemia at the time of the assay. The

[29] See Medical Services Advisory Committee 2000, *Hepatitis C Viral Load Testing: assessment report*, Commonwealth of Australia, Canberra.

disadvantage is that it does not distinguish between subtypes and is not as useful in immuno-suppressed individuals, in individuals with multiple infections of different genotypes, or soon after infection.

With either of the approaches a minority of infections cannot be genotyped for different reasons. In addition, infections with multiple hepatitis C subtypes present a particular problem.

5.1.8 Epidemiological surveillance

Data from the assays just discussed, in particular immuno-assay data, are regularly analysed to assess the extent and distribution of hepatitis C infection in the community. For this purpose, it is critical that each confirmed positive result is classified as:

- a repeat sample from a known infected individual who has already been entered on the appropriate database

  or

- the first test on an individual who has not previously been tested—that is, a newly notified individual for whom the date of acquisition of infection is not necessarily known

  or

- a repeat test on an individual who previously tested negative— that is, a new infection or seroconversion where the time boundaries of the transmission event may be estimated.

If these categories are not distinguished, the analysis for epidemiological purposes is of little value.

5.2 Short incubation testing

'Short incubation testing' refers to hepatitis C antibody testing that usually can be performed more quickly than the standard antibody test. To date, only one short incubation test is registered by the Therapeutic Goods Administration for use in Australia; it is registered for supplemental testing only, not for screening, and there are a number of restrictions on its use.

5.2.1 Interpretation of short incubation testing

Short incubation tests are manually done and the results read visually, which introduces the element of subjective interpretation. The tests are easy to carry out but, like other assays, are subject to error if protocols are not followed exactly.

The negative predictive values of short incubation tests are such that infection can be reasonably excluded if the test result is negative. These tests are, however, more likely to miss seroconversion because they are less able to detect low levels of antibody.

Their positive predictive value is low in populations where hepatitis C infection is uncommon. For low-prevalence populations, the vast majority of reactive tests will be falsely reactive. Supplemental testing with a different test must always be performed on each reactive sample before the test results are communicated to patients.

5.2.2 Possible uses of short incubation tests

Transplantation

A negative short incubation test provides reasonable evidence for excluding established hepatitis C infection but, as noted, may miss a sample from a seroconverter. A negative result facilitates rapid initial assessment of organs for transplantation while standard testing is being carried out.

Clinical management

For some diseases, urgent confirmation of diagnosis is needed so that therapy can begin immediately. The nature of the clinical consequences of hepatitis C infection and the currently available therapies mean there is no benefit in a rapid diagnosis compared with the time taken to do a standard antibody test.

There is no need to use short incubation tests for elective surgery patients: clinical assessment of hepatitis C status, if needed, can be done using standard antibody tests well before hospital admission.

Infection control

Use of short incubation tests as part of an infection-control strategy is not supported. Adoption of standard precautions in relation to blood-borne viruses is a more effective approach. Reliance on negative hepatitis C test results may give health care professionals false confidence since they could be at risk of contracting other blood-borne pathogens that have not been tested for. The possibility of false negative results in seroconverters also needs to be considered.

Occupational exposure

With HIV, short incubation testing can be used to confirm or exclude the presence of infection in the source of the exposure: this will aid decision making about whether to initiate prophylactic therapy. Anti-viral therapy for hepatitis C exposure is not practised, so possible occupational exposure is not currently an indication for the use of short incubation tests.

Recommendation

25. If there is an urgent need to test, short incubation tests have potential. It may be that this method is suitable for screening possible organ donors. The testing should be done only by suitably trained laboratory personnel.

26. When a short incubation test is used, samples that show an initially reactive result for hepatitis C antibodies should always be subjected to testing with a conventional algorithm. Test results should not be communicated to patients until supplemental testing has been done.

27. The use of short incubation tests as part of an infection-control strategy is not supported.

28. The use of short incubation tests before elective surgery and before minor surgical procedures performed in non-hospital settings is not supported.

5.3 Home-based testing

There are two types of home-based testing. 'Home testing' means testing done and interpreted by an individual in a domestic setting. 'Home collection' refers to an individual collecting a sample at home and sending it to a laboratory dedicated to testing and interpretation of these results. Kits for either method are not available in Australia, and there are no such dedicated laboratories.

5.3.1 Home testing

Home-use testing should be distinguished from point-of-care testing. There are two common uses of home-use in vitro diagnostic devices in Australia. The first is for home collection, self-diagnosis and management; the second is for home collection of a sample to be tested at a second facility and/or interpreted without the involvement of a health care practitioner.

In home testing, the person buys a test kit from an outlet such as a pharmacy, by mail order or via the internet. After reading the instructions, they collect a sample (usually a finger-prick specimen of blood) and carry out the test. It is up to them to interpret the result.

Two main reasons are put forward in support of this form of testing:

- the inability of some groups to afford medical consultations and testing
- a reluctance to attend medical services because of concerns about confidentiality or a mistrust of health services.

There are, however, a number of factors that bring the value and practicality of home testing into question:

- People testing at home are removed from any clinical intervention. They may not be aware of the limitations of the test (for example, the possibility of false positive results) or of the concept of the window period.

- There is no chance of either test discussion or post-test counselling, and the opportunity to use testing for health promotion is lost.

- Proper storage and use within the shelf life of the test kit cannot be guaranteed.

- Home kits are currently unable to reproduce the sensitivity and specificity of laboratory tests.

- The positive predictive value of the test kit results will be low. This means there will be a higher ratio of false positive results compared with true positive results. It is most usually the 'worried well' who use this type of testing.

- Reading of such tests by untrained individuals with a personal stake in the results is fraught with danger.

- Vital epidemiological data are lost.

5.3.2 Home collection

In the case of home collection, the individual obtains a sample collection kit from an outlet such as a pharmacy, by mail order or via the internet. A finger-prick sample of blood is placed on filter paper and sent to a designated laboratory. The sample is coded and the individual waits for a prescribed period before telephoning for the results. After providing their code number, the individual hears a pre-recorded message (which includes prevention information) if the test is negative or is transferred to a telephone counsellor if the result is positive. The counsellor makes an assessment and refers the person to the nearest health service provider.

Compared with home testing, home collection has the following advantages:

- The precision of the testing procedure, in adequate samples, appears similar to that achieved with clinically based testing.

- There is laboratory involvement in performing the test, and confirmatory testing is performed before the release of positive results. This eliminates the majority of false positive results.

- Individuals must have contact with a health service to obtain their test results.

There are, however, two important disadvantages. First, the opportunity for test discussion is lost. Second, people with positive results may find themselves in a vulnerable position since the opportunity to provide immediate support may be limited by the nature of the telephone interaction with the counsellor; this raises the risk of self-harm.

In the United States, where home collection has been approved as a means of HIV and hepatitis C testing, the sponsoring companies have been required to establish considerable infrastructure, including telephone hot lines, trained counsellors and access to laboratory facilities. Similar infrastructure would be required if home collection testing were to be approved in Australia.

Hepatitis C testing is widely available in Australia and cost is not often an impediment to obtaining this type of health care, so it is unlikely that home collection would have a significant market. In fact, it would cost a person more than testing performed through the normal health care system.

There is currently only limited demand for home-collection testing in Australia and the establishment and running costs for a sponsoring company would be prohibitive.

Recommendation

29. Hepatitis C testing in Australia should be performed only when there is a good relationship between the person being tested and a suitably qualified health care professional and when test discussion and counselling may be carried out. The introduction of home-based testing and home collection is not supported**.**

6 Funding

This chapter discusses the current funding arrangements for hepatitis C testing under the Medicare Benefits Schedule.

6.1 Antibody testing

The hepatitis C antibody test is reimbursable under the Medicare Benefits Schedule. If the test result is reactive a benefit is payable for supplemental testing using a different hepatitis C antibody assay. If, however, the laboratory chooses to repeat the initial test procedure before proceeding to a different test (as recommended by the National Serology Reference Laboratory), the repeat of the initial test is not funded. When the initial test result is negative, no benefit is payable for a supplemental antibody test because such a test is not considered necessary; that is, the test result is considered a true negative and thus not in need of confirmation.

Following an initially reactive immuno-assay result, in some contexts it may be more cost effective to repeat the initial test while in other contexts laboratories choose to go straight to a second immuno-assay for reasons of cost (this is also a minimum standard in the NHMRC protocol.

As discussed in Chapter 5, it is essential that laboratories do not report positive hepatitis C antibody test results if they have not been appropriately confirmed.

6.2 Qualitative nucleic acid testing

Qualitative nucleic acid testing for the presence of hepatitis C virus RNA is currently reimbursable under the Medicare Benefits Schedule in the following circumstances:

- The patient is hepatitis C sero-positive[30] and has normal liver function tests on two occasions at least six months apart.
- The patient's serological status is uncertain[31] after testing.
- The test is performed for the purpose of
  - determining the hepatitis C status of an immuno-suppressed or immuno-compromised patient

    or
  - detecting acute hepatitis C before seroconversion where this is considered necessary for clinical management of the patient.

[30] 'Hepatitis C sero-positive' means that the results of two different assays of hepatitis C antibodies have been positive.
[31] 'Uncertain' means any result where two different assays of hepatitis C antibodies are inconclusive.

MBS reimbursement for qualitative nucleic acid testing is restricted to one test per person in any 12-month period. There are three reasons for qualitative nucleic acid tests for antibody positive individuals:

- Only 65–85 per cent of antibody-positive individuals are positive for hepatitis C RNA.
- Demonstration of RNA status carries significant implications for prognosis, infectivity and suitability for therapy.
- Increasingly, patients and practitioners are seeking a direct answer to the question of current infection status, independently of antibody status.

Individuals who are still infected may have levels of viraemia that fluctuate around the limit of sensitivity of the assay, so a second qualitative NAT may be indicated after an interval. Subsequent management will depend on the full picture produced by laboratory investigations, clinical features and epidemiological factors.

Under the current arrangements qualitative nucleic acid testing of pregnant women known to be hepatitis C sero-positive attracts a benefit only if the patient has had normal liver function tests on two occasions at least six months apart. The risk of transmission from infected mother to child is low but may be related to the actual quantitative level of virus. When a qualitative NAT is negative the woman can be assured that it is probable that she has cleared viral infection, eliminating the possibility of transmission. Notwithstanding, consideration should be given to qualitative nucleic acid testing of all infants born to mothers who are hepatitis C sero-positive.

6.3 Patients undergoing antiviral therapy

The Medicare Benefits Schedule provides reimbursement for genotyping and qualitative and quantitative NAT when interferon therapy is being monitored in patients with chronic hepatitis C. These tests can be used to provide evidence on which to base a decision to initiate or continue antiviral treatment. They might also provide additional information that could help both patients and clinicians make such decisions.

Both the infecting viral genotype and the viral load are factors in predicting the response to treatment. The predictive value of the tests is, however, not sufficiently high to be used as a justification for excluding a patient from treatment. Even among patients with a high viral load or a specific genotype a proportion will respond to therapy, and an empirical trial of this form of treatment should be allowed. Detection of viraemia in the course of treatment has a higher predictive value and can be used to guide decision making about the continuation of therapy.[32] Qualitative NAT can also be used to assess the response to treatment.

[32] Medical Services Advisory Committee 2000, *Hepatitis C Viral Load Testing: assessment report*, Commonwealth of Australia, Canberra, p. vi.

Although the cost of testing based on nucleic acid is relatively high, the Medical Services Advisory Committee concluded that, with careful patient selection, quantitative viral load testing and genotyping are cost-effective.[33]

6.3.1 Quantitative nucleic acid testing

MBS reimbursement for quantitative NAT is available only for patients considering antiviral therapy—as opposed to all patients infected with hepatitis C. This restriction is based on the premise that quantitative testing should provide for clinicians and patients information about the probability of achieving a sustained response to antiviral therapy. The tests are to be done only when a patient has confirmed hepatitis C, as confirmed by qualitative NAT.

The RNA-based tests may be requested by or on the advice of the specialist or consultant physician or by a primary care practitioner involved in a shared-care arrangement with a consultant physician, for the purpose of informing decision making about treatment.

6.3.2 Qualitative nucleic acid testing

In addition to the current indications for use in the diagnosis of hepatitis C infection, qualitative NAT can be used once, if needed, before treatment and up to three times in the following 12 months to assess the response to treatment. The maximum number of qualitative tests for any course of treatment is four, including those provided under the existing Medicare Benefits Schedule item that relates to the diagnosis of hepatitis C.

In addition to assessing the response to interferon alpha, a negative qualitative NAT is required under the Highly Specialised Drugs Program after 12 weeks of combination interferon–ribavirin therapy for continued eligibility for reimbursement for this form of treatment.

6.3.3 Genotype testing

Genotype testing is restricted to one test for each patient. It would usually be done when considering whether to initiate treatment and to determine the duration of therapy.

Because of reinfection, the frequency of genotype testing is currently under review; further studies will need to examine the extent of use of the test.

6.3.4 Viral load testing

Viral load testing is used prior to treatment and is restricted to one test per patient in any 12-month period.

[33] ibid.

7 Regulatory matters and quality assurance

This chapter provides the policy framework for evaluating the performance of hepatitis C test kits, post-marketing quality assurance, participation in a uniform national quality assurance program, and the categorisation of test kits for regulatory purposes and restrictions on the use of certain test kits.

7.1 Performance evaluation

The Therapeutic Goods Administration has regulatory responsibility for hepatitis C test kits through the *Therapeutic Goods Act 1989* and its associated regulations. The TGA is responsible for ensuring that in vitro diagnostic test kits undergo a full pre-market evaluation to demonstrate that they meet the quality, safety and efficacy standards required for registration in Australia. The TGA contracts out the performance section of this evaluation to the National Serology Reference Laboratory.

The TGA is developing a new regulatory framework for in vitro diagnostic devices that is in keeping with international best practice. The IVD framework will be based on the Global Harmonization Task Force's principles and will complement the new regulatory system for medical devices.

7.2 Post-marketing quality assurance

The Therapeutic Goods Administration also has responsibility for post-marketing surveillance. It has the power to remove from the market any test kit that is not performing to the expected standard or that is known or demonstrated to be defective. It also monitors overseas reports and incident reports in relation to hepatitis C test kits.

The TGA is assisted in its post-market surveillance by the National Serology Reference Laboratory, through its Quality Assurance Program and its laboratory information network. The NRL has been contracted by the Commonwealth Government to perform this function, which involves implementing and reporting on a number of quality assurance methodologies.

7.2.1 Specificity monitoring

The National Serology Reference Laboratory conducts specificity monitoring of the ongoing performance of test kits. If the level of false reactivity in tests in large numbers of samples is monitored, both assay and laboratory problems can be detected. There is usually a low rate of false reactivity, but the accumulated data are used as a measure of an assay's continued performance. A sudden increase in the false reactivity rate could suggest a problem.

7.2.2 Quality assessment programs

The National Serology Reference Laboratory's quality assessment programs are designed to assess the accuracy of the entire laboratory testing process, from receipt of the specimen to delivery of the test result. A panel of specimens is provided at regular intervals to participating laboratories for testing. The laboratories are able to compare their results with reference results and with the results of similar laboratories. This allows problems to be identified and resolved. It also creates a networking ability across laboratories, so they can help each other with performance evaluation.

7.2.3 Quality-control samples

The National Serology Reference Laboratory distributes quality-control samples that laboratories can use to continually monitor the precision of hepatitis C antibody and nucleic acid tests. When used in every assay run, the samples allow for confirmation that the test results are reproducible and reliable. Monitoring the reactivity of a quality-control sample, which should deliver consistent results across runs and batches, means that intra-laboratory and batch-to-batch variability can be tracked and aberrations in performance can be assessed as laboratory or test-based.

7.2.4 The Tertiary Reference Testing Laboratory

The National Serology Reference Laboratory's Tertiary Reference Testing Laboratory serves as a reference point for hepatitis C serology samples whose status cannot be resolved at the screening or reference laboratory level. Specialised testing strategies are used, among them selected tests not used by other laboratories. This provides an extra layer of testing for samples that are difficult to diagnose using screening laboratories' normal strategies.

7.2.5 Blood and tissue services

The Therapeutic Goods Administration audits the Australian Red Cross Blood Service for compliance with the Code of Good Manufacturing Practice for Human Blood and Tissues. The purpose is to ensure that the Blood Service operates in accordance with best international practice. Laboratories testing tissue for transplantation must also be audited for compliance with the Code of Good Manufacturing Practice.

7.3 Participation in a uniform national quality assurance program

A uniform national quality assurance program for hepatitis C testing, in which all laboratories participate, offers a number of advantages:

- the availability of a comprehensive national database that allows for monitoring of the performance of hepatitis C test kits
- appropriate and efficient use of test kits by screening and reference laboratories, facilitating collection and assessment of the accuracy of epidemiological data
- verification that laboratories' performance is accurate and complete

- assurance that test kits can be tracked after sale and that investigation of any problems can be coordinated as a result of data supplied to the National Serology Reference Laboratory

- over time, promotion of uniform testing strategies and test-interpretation criteria. (In the case of HIV testing this has served Australia well by establishing international benchmark standards for HIV serology.)

The National Serology Reference Laboratory is best placed to implement a uniform national quality assurance program for hepatitis C testing. The utility of the existing NRL Quality Assurance Program is limited because not every laboratory that tests for anti-HCV participates. Participation in the NRL Quality Assurance Program is a requirement for HIV kit registration, so that the laboratories can receive the kits from the sponsors. This provision should be extended to cover the registration of hepatitis C test kits.

The National Serology Reference Laboratory has demonstrated its ability in quality assurance for high–risk disease testing through its development and management of the HIV testing quality assurance system. It is contracted through the Therapeutic Goods Administration to monitor the quality of hepatitis C test kits and liaises closely with the laboratories and the TGA. The TGA has strongly endorsed the NRL as the preferred provider of quality assurance for hepatitis C testing.

It should be noted that the National Hepatitis C Testing Policy Steering Committee was unable to reach agreement in relation to the need for a single preferred reference laboratory for the purpose of quality assurance. It did agree, however, that this status should be reviewed, along with the policy document, as changes in other policies and in technology occur.

Although there is a strong case for a registration requirement to ensure that all laboratories participate in the National Serology Reference Laboratory's Quality Assurance Program for hepatitis C test kits and testing, this should not preclude laboratories from participating in additional quality assurance programs if they wish to do so.

Recommendation

30. It should be a condition of the Therapeutic Goods Administration's registration of hepatitis C test kits that sponsors supply only to laboratories participating in the National Serology Reference Laboratory's hepatitis C Quality Assurance Program. This requirement should not, however, preclude laboratories from participating in other quality assurance programs if they wish to do so.

7.4 Categorisation of hepatitis C test kits for regulatory purposes

The Therapeutic Goods Administration has the power to impose conditions on the registration of products; among them in the case of hepatitis C kits is the categorisation of the kit according to its intended use. Hepatitis C test kits are currently approved as being suitable either for routine screening or for supplemental purposes only. Screening tests have a performance capability that is suitable for blood donor screening, and supplemental tests are those capable of clarifying sero-status. There is no restriction on the supply of hepatitis C kits approved for screening. In contrast, test kits approved for use in supplemental assays and those using newer technologies such as PCR or amplification may be supplied only to laboratories approved by the state or territory health authority in question.

Technological advances have led to the production of test kits that are suitable for purposes other than screening and confirmation of diagnosis—that is, for surveillance, prognosis, monitoring and, possibly, urgent use. The Therapeutic Goods Administration has adopted an alternative classification system that recognises this wider range of purposes for the registration of HIV test kits. This system, which was developed as part of the HIV Testing Policy, could also be applied to hepatitis C test kits. The advantages of the HIV testing classification system are that it provides the following:

- a wider choice of testing protocols
- indications of current usage
- a possible model for accommodating new technologies
- a framework for establishing the extent of evaluation for each type of test kit
- a classification that can be generalised to other areas of serology.

Table 5 provides details of the proposed classification system for hepatitis C test kits.

Table 5 Proposed categorisation of hepatitis C test kits

	Test categories	
Purpose or use of kit	Standard	Reference
Donor testing—screening of blood and tissue donations	Enzyme immuno-assay Closed system immuno-assay NAT screening assay *Level 1*[a]	Enzyme immuno-assay Immunoblot
Diagnostic testing—to determine the infection status of a sample for clinical purposes; for example, for diagnosis, antenatal, pre-operative, visa, insurance, emergency, bio-hazard, supplemental and confirmatory purposes	Enzyme immuno-assay Particle agglutination assay Closed system immuno-assay Short incubation test Alternative sample assay *Level 2*[a]	Qualitative amplification assays *Level 3*[a]
Unlinked epidemiological surveillance—definition of the infection status of a population where no results are conveyed to individuals from whom samples are taken	Short incubation test Alternative sample assay Incidence assay *Level 3*[a]	
Monitoring and management—quantify or characterise the virus for clinical management		Amplification assay (qualitative and quantitative) Enzyme immuno-assay Typing assay Assay for the detection of anti-viral drug resistance *Level 4*[a]

a. Denotes the minimum level of evaluation (see Section 7.4.2).

Note: The test categories are described in Section 7.4.1. Assays used for screening samples from tissue donors must be evaluated to Level 1.

7.4.1 The test categories

Standard tests

Standard tests can be used by laboratories to perform diagnostic or screening testing to identify the hepatitis C antibody status of samples using ‘screening’ or ‘standard’ assays. In the case of non-reactive results, further testing is necessary only if clinical considerations demand it. Reactive samples must be confirmed before the result is accepted as a true positive. Supplemental testing, using a different test or test kit, may be conducted in the laboratory that conducted the initial test.

Reference tests

Reference tests are used for confirmatory or additional special (supplemental) testing. This testing is done to identify true positive status by distinguishing true from false reactivity. The type of test used depends on the situation that gave rise to the need for testing—for example, in a setting of possible seroconversion, when the first supplemental test used might be an amplification assay. Usually this testing is done as part of a diagnostic strategy. Any test can be used for supplemental or confirmatory purposes, provided it is evaluated to the appropriate level. Another category of reference tests might be used once hepatitis C infection has been confirmed, to determine whether infection is still present, to quantify the viral load, to characterise the genotype, or to determine the virus’s sensitivity to antiviral agents.

7.4.2 Proposed levels of test kit evaluations

The level of evaluation for any test kit is commensurate with the risk of delivering a false result associated with its use.

- Level 1 requires that a sufficient number of samples be selected to fully determine all characteristics of the assay in a statistically valid manner. It involves estimation of sensitivity and specificity in sufficient samples to yield statistically valid assay comparison. Samples for estimation of sensitivity should include samples from infected people through the entire course of infection, including during seroconversion.

- Level 2 requires full evaluation of sensitivity within a multi-site protocol and with more limited determination of specificity—that is, in fewer samples than for Level 1 and therefore with a wider confidence interval around the estimation.

- Level 3 requires evaluation only in a characterised sensitivity panel, with testing in a limited number of negative samples that have the potential for or established false reactivity. Short incubation tests or alternative sample assays, if used for screening, should be evaluated as screening tests—that is, at Level 1.

- Level 4 calls for an evaluation protocol developed upon submission of the assay. Post-market monitoring or collection of data that show how the test is performing while it is being used will be required as a condition of the supply of the kits. The requirements will be listed on the TGA registration certificate.

Recommendation

31. The proposed classification system for hepatitis C test kits should be adopted (see Table 5).

7.4.3 Restrictions on the use of reference tests

Hepatitis C is the most commonly diagnosed notifiable infectious disease in Australia. Testing volumes are relatively high and have been so for a number of years. It is important that timely access to test results be facilitated through the participation of both public and private sector laboratories in diagnosis. Any restrictions on which laboratories can perform particular tests should be related to quality assurance.

Consistent with existing policy, all hepatitis C kits approved for use as reference assays may be supplied only to laboratories approved by the state or territory health authority concerned.

Laboratories involved in reference testing for hepatitis C should meet specific criteria to ensure appropriate standards. The criteria, as previously endorsed by IGCAHRD, are as follows:

- Be accredited under the joint National Association of Testing Authorities – Royal College of Pathologists of Australasia medical testing program, including having access to the expertise needed to evaluate test results.

- Undertake testing only at sites designated by state and territory health authorities and not pass test kits to a laboratory without such designation.

- Participate and continue to demonstrate performance to an acceptable standard in the national Quality Assurance Program of the National Serology Reference Laboratory.

- Adhere to the application of a scientifically validated testing methodology by following the manufacturer's instructions or validating in-house kits.

- Use testing strategies consistent with the guidelines outlined in this document.

- Comply with any laboratory standards for nucleic acid amplification, as required by the joint NATA–RCPA medical testing program.

- Provide statistical data as required to the National Serology Reference Laboratory for national collating and reporting of test results.

- In the case of hepatitis C RNA, run sufficient samples to be competent and comply with National Pathology Accreditation Advisory Committee guidelines for training of staff performing nucleic acid testing. NPAAC has developed guidelines for the accreditation of laboratories wishing to do NAT. The guidelines are comprehensive—covering facilities, equipment, staff qualifications and quality assurance. Testing laboratories' adherence to the guidelines would result in standardised, reliable and accurate hepatitis C testing in Australia. Adherence will be a requirement for payment of benefits under the Medicare Benefits Schedule.

Recommendation

32. Hepatitis C standard and reference tests should be performed by public and private sector laboratories that participate in the recommended quality assurance programs and comply with the National Pathology Accreditation Advisory Committee's guidelines. In the case of reference tests, it should be a requirement that public and private sector laboratories be authorised to conduct these tests; the authorisation should be contingent on compliance with standardised criteria, as endorsed by the Intergovernmental Committee on AIDS, Hepatitis C and Related Diseases.

Appendix A Membership of the National Hepatitis C Testing Policy Steering Committee

Development of the National Hepatitis C Testing Policy was overseen by a Steering Committee comprising the following people:

Ms Lorraine Breust (Chair)
Director
Hepatitis C Section
Commonwealth Department of Health and Ageing

Professor Chris Burrell
University of Adelaide
(representing the Australian National Council on AIDS, Hepatitis C and Related Diseases and the Public Health Laboratory Network)

Ms Susan Carruthers
National Drug Research Institute
Curtin University of Technology
(representing the Australian National Council on AIDS, Hepatitis C and Related Diseases)

Associate Professor Elizabeth M Dax
Director
National Serology Reference Laboratory, Australia

Ms Kirsty Hammet
South Australian Department of Human Services
(representing the Intergovernmental Committee on AIDS, Hepatitis C and Related Diseases)

Dr Charlotte Hespe
Royal Australian College of General Practitioners

Ms Jude Byrne
Australian Injecting and Illicit Drug Users League

Ms Shelley Tang
Therapeutic Goods Administration
Commonwealth Department of Health and Ageing

Mr Jack Wallace
Australian Hepatitis Council

Ms Kim Stewart
NSW Health
(representing the Intergovernmental Committee on AIDS, Hepatitis C and Related Diseases)

Appendix B Extrahepatic manifestations of chronic hepatitis C

In an article entitled 'Hepatitis C: a management guide for general practitioners' (*Australian Family Physician* 1999, vol. 28, Special issue, December, p. SI29), the following conditions are listed as extrahepatic manifestations of chronic hepatitis C:

- cryoglobulinaemia
- glomerulonephritis—usually membranoproliferative
- polyarteritis nodosa
- vasculitis
- lichen planus
- peripheral neuropathy
- Sjogren's syndrome
- porphyria cutanea tarda
- thrombocytopenia—more often a complication of portal hypertension
- non-Hodgkin's lymphoma
- thyroid dysfunction.

Glossary

Anonymous de-linked test	Testing of samples that have been irreversibly de-identified.
Compulsory testing	Testing when a person has no choice about being tested.
Confirmatory testing	Testing that leads to a diagnosis being confirmed. A confirmatory test is the test that gives the diagnosis.
Custodial settings	Includes the various settings in which adults and juveniles can be detained or imprisoned—prisons, juvenile justice centres, and remand and other detention centres.
Discordant EIA results	Results produced when two enzyme immuno-assays that are carried out consecutively give a reactive and a non-reactive result. Also referred to as 'equivocal' and 'indeterminate' results.
Gold-standard test	A test that unequivocally identifies the presence of an infection.
Heteroduplex mobility analysis	Method by which nucleic acid species of similar composition are separated in a gel on the basis of mass or charge, or both, to demonstrate differences in sequence or structure.
Home collection	Taking blood or another type of sample in a non–health care environment without the supervision of trained personnel and then forwarding the sample to a laboratory for analysis.
Home-based testing	Testing conducted in a non-laboratory or non–health care environment without the supervision of trained personnel.
Home-use in vitro diagnostic devices	Devices used for testing in the home, as distinct from point-of-care testing. Two common reasons for using home-use in vitro diagnostic devices in Australia are for home collection, self-diagnosis and management and for home collection of a sample to be tested elsewhere and/or interpreted without the involvement of a health care practitioner.
Indeterminate test result	A result that is neither clearly negative nor clearly positive.

In-house tests — A test that is developed or modified from another source within the confines of a laboratory, validated for use within that laboratory only, and not supplied for use outside that laboratory. For the purposes of this document, 'laboratory' means an Approved Pathology Laboratory, as defined in section 23D of the Commonwealth's *Health Insurance Act 1973*; the term 'supplied' is used with reference to the definition of the term 'supply' in the *Therapeutic Goods Act 1989*—that is,

> 'supply' includes (a) supply by way of sale, exchange, gift, lease, loan, hire or hire-purchase; and (b) supply, whether free of charge of otherwise, by way of sample or advertisement; and (c) supply, whether free of charge or otherwise, in the course of testing the safety or efficacy of therapeutic goods in persons or animals; and (d) supply, by way of administration to, or application in the treatment of, a person or animal.

Mandatory testing — Where testing is pre-condition of obtaining a service or benefit.

PCR testing — A technique whereby nucleic acid (cell genetic material) is amplified in order to detect the presence of particular and specific nucleic acid sequences.

Predictive values — Parameters that define the chance of a reactive test being truly positive (the positive predictive value) or a non-reactive test being truly negative (the negative predictive value) for the substance that a test is designed to detect.

Quality assurance — The means by which the integrity of tests and testing is assured.

Qualitative test — A test that detects the presence or absence of an agent or substance without measuring the level or quantity of that agent or substance.

Quantitative test — A test that not only detects the presence of an agent or substance but also gives the level or amount of the agent or substance.

Reference laboratory — A laboratory that conducts tests to clarify the nature of samples' reactivity or status following initial tests conducted either by standard laboratories or by the reference laboratory.

Sensitivity	The proportion of reactive results found by a given test in a known positive population. Indicates the potential false negative rate of a test.
Serology	Scientific testing to determine the presence, evidence or quantity of antibodies specific for infectious or other agents, chemicals or substances in blood.
Specificity	The proportion of non-reactive results found by a given test in a known population of negative samples. Indicates the potential false positive rate for a test.
Supplemental test	A test performed after initial, standard or screening testing, usually to clarify the sero-status of a reactive sample.

Abbreviations

ALT	alanine aminotransferase
ANCAHRD	Australian National Council on AIDS, Hepatitis C and Related Diseases
CDNA	Communicable Diseases Network of Australia
EIA	enzyme immuno-assay
HCV	hepatitis C virus
HIV	human immunodeficiency virus
IDU	injecting drug use
IGCAHRD	Intergovernmental Committee on AIDS, Hepatitis C and Related Diseases
IVD	in vitro diagnostic device
LFT	liver function test
MBS	Medicare Benefits Schedule
MSAC	Medicare Services Advisory Committee
NASBA	
NAT	nucleic acid test/testing
NATA	National Association of Testing Authorities
NHMRC	National Health and Medical Research Council
NPAAC	National Pathology Accreditation Advisory Committee
NRL	National Serology Reference Laboratory, Australia
PCR	polymerase chain reaction
PHLN	Public Health Laboratory Network
RCPA	Royal College of Pathologists of Australasia
RNA	ribonucleic acid
TGA	Therapeutic Goods Administration