



GP Companion Resource to the "12 questions to ask your doctor if you have been diagnosed with hepatitis C."

This resource provides General Practitioners with suggested answers to the consumer flyer "12 questions to ask your doctor if you have been diagnosed with hepatitis C". This resource has been developed for National Hepatitis Awareness Week, 18 May - 24 May 2009.

The GP Companion Resource is available for download from www.ashm.org.au/publications. The consumer flyer can be downloaded from www.hepatitisaustralia.com.

In Australia, over 207,000 people have chronic hepatitis C (about 1% of the population) and it is now the major reason for liver transplants in Australia.

1 What are the symptoms of hepatitis C and how will it affect my liver?

Symptoms of hepatitis C

Acute hepatitis C

- Hepatitis C involves an initial (acute) phase of infection
- Mostly asymptomatic infection or have flu-like symptoms
- Those who do have symptoms can experience nausea, dark urine, jaundice and abdominal discomfort

Chronic hepatitis C

Hepatitis C infection is called chronic when it has been present for longer than 6 months

- Many people with chronic HCV are asymptomatic
- Mostly non specific symptoms including malaise, fatigue, nausea, abdominal discomfort, anorexia, arthralgia, pruritus and intolerance to fatty foods
- Symptoms vary greatly from person to person
- Symptoms often take a long time to develop (up to 10-15 years)

Advanced chronic liver disease

- Increased lethargy
- Fluid retention – swollen ankles and abdomen
- Easy bruising
- Haematemesis and melaena
- Encephalopathy – reversal diurnal sleep pattern, forgetfulness, drowsiness, inappropriate behaviours and stigmata of chronic liver disease

15-35% successfully clear the hepatitis C virus (HCV) without treatment. Hepatitis C antibody (HCV Ab) will remain positive for life after the infection, even if the virus is cleared successfully. People who have cleared the virus can acquire HCV infection again.

How will chronic hepatitis C affect the liver?

Of 100 people with chronic hep C who remain untreated:

After 20 years:

- 45 will never develop serious liver damage
- 47 will develop mild or moderate liver damage
- 7 will develop liver cirrhosis
- 1 will develop liver failure or liver cancer

After 40 years:

- 45 will never develop serious liver damage
- 31 will develop mild or moderate liver damage
- 20 will develop liver cirrhosis
- 4 will develop liver failure or liver cancer

Factors associated with more rapid disease progression include:

Male gender, heavy alcohol and or cannabis intake, obesity, older age at time of initial infection (>40 yrs), co-infection with HIV and/or hepatitis B, longer duration of infection.

2 What do I need to know about transmission of hepatitis C?

How is hepatitis C transmitted?

- Hepatitis C transmission is predominantly parenteral
- 90% of cases in Australia are transmitted via injecting drug use. All injecting equipment can spread HCV including needles, syringes, water, spoons, filters, swabs, tourniquets and even blood on hands and in the preparation area. If your patient has ever injected drugs (even once) it is worth considering testing for HCV
- Unsterile tattooing and body piercing
- Blood transfusions and blood products before 1990 in Australia
- Mother to baby - vertical transmission is around 5%. Breastfeeding is not contraindicated unless nipples are cracked and bleeding
- Occupational (not common)- only 2-8 in every 100 high risk needle-stick injuries in a hospital setting will result in HCV transmission
- Household - very rare, only occurs when blood-to-blood contact e.g. sharing toothbrushes, razors, nail clippers, cuts/injuries
- Sexual transmission - rare although presence of blood (e.g. menstruation or active herpes ulcers) may increase the risk. No recommendation to use barrier protection in monogamous couples when blood is not present

Other risk factors include:

- Imprisonment – a past history of time in the justice system is a prompt to consider HCV testing
- HIV positive men - participating in activities which cause mucosal trauma or bleeding are at increased risk
- Born in high prevalence country (Asia, Africa, Middle East, Eastern and Southern Europe) where often acquired due to poor infection control practices during procedures e.g. vaccination or chemoprophylaxis programs for schistosomiasis

Patients may want to discuss how they may have got HCV, so try to allow time for discussion at the consultation when positive results from testing are discussed.

Prevention of HCV transmission:

- Using safer injecting practices
- Avoiding sharing and re-using contaminated objects that pierce the skin
- Using standard infection control procedures in a medical setting
- Practicing safe sex (where blood to blood contact is possible)

3 Do I have to tell anyone I have hepatitis C?

Hepatitis C is a notifiable disease.

Disclosure

In almost all cases, it is up to the individual whether or not to disclose their HCV infection.

Generally speaking, infected individuals do not have to tell anyone they have hepatitis C except:

- if they are giving blood or blood products to the Blood Bank (they will not be accepted as a donor)
- if they are a health care or dental worker involved in exposure-prone procedures
- if they are in or want to join the Australian Defence Force
- if they are applying for insurance and superannuation, especially life insurance

Practitioners who are uncertain about their statutory or common law obligations to patients or to the local Health Department, including privacy and reporting obligations, are strongly advised to contact their local health department, applicable privacy office or seek independent legal advice.

Discrimination

Australian Commonwealth law prohibits discrimination against someone with an infectious disease, unless the discrimination is necessary to protect public health. Most states and territories have corresponding laws.

Confidentiality

Practitioners have a duty of care to maintain the confidentiality of their patients. There are health specific laws requiring that medical practitioners not disclose any information regarding a person who has tested positive to an infectious disease.

Further information for patients and practitioners: Hepatitis Australia website: www.hepatitisaustralia.com Helpline 1300 437 222 (1300 HEP ABC) for your local hepatitis organisation. GPs can also refer to the ASHM website at: www.ashm.org.au.

4 What tests will I need to have to know how hepatitis C is affecting me?

Tests

When the initial screening antibody test is positive, further tests include:

- HCV RNA qualitative PCR - determines active infection or if the virus has been cleared
- Liver function tests (LFTs) – monitors condition of the liver

In some situations, the level of virus in the blood might be too low for the HCV RNA qualitative viral detection test to measure, therefore, a negative test may not always mean that the person has cleared HCV, and two HCV RNA tests, over a 6-12 month period are recommended. If both tests are negative, the person is said to have cleared HCV and further testing is not required, unless they are re-exposed to the virus e.g. restart unsafe injecting drug use.

If HCV RNA (PCR) is positive (indicating active infection), the following tests should be conducted:

- HCV RNA (PCR) viral genotyping – for treatment assessment
- HCV RNA (PCR) viral load – for treatment assessment
- LFTs (ALT most commonly elevated in viral hepatitis). If liver cell damage is present, LFTs may be raised but ALT is a poor indicator of disease stage or progression
- Full Blood Count (FBC)
- Electrolytes, urea, creatinine
- Fasting blood sugar level and lipids
- Hepatitis B tests (Hepatitis B core antibody, Hepatitis B surface antigen and Hepatitis B surface antibody)
- Hepatitis A antibodies
- HIV
- Thyroid function tests (interferon causes thyroid toxicity in 10-15%)
- Iron studies (transferrin saturation and ferritin) - to exclude haemochromatosis
- Autoimmune screening- ANA (antinuclear antibody), SMA (smooth muscle antibody) and LKMA (liver kidney microsomal antibody)– to exclude auto-immune liver disease
- Alpha-fetoprotein (AFP) – baseline hepatocellular carcinoma marker
- Alpha-1 – antitrypsin and copper, caeruloplasmin

Pathology tests indicating more severe fibrosis include

- An inverted AST/ALT ratio (where AST is higher than ALT)
- Low platelets
- Low albumin
- Raised prothrombin time
- Elevated direct bilirubin (severe liver injury indicated if ALT falls and bilirubin rises)

Other tests that may be undertaken during the workup for chronic HCV include:

- Abdominal ultrasound - to screen for hepatoma, portal hypertension, small amounts ascites and fatty liver. Does not assess degree of HCV liver damage and fibrosis
- Liver biopsy (no longer mandatory before treatment but can provide a more detailed and reliable indication of liver damage)
- Fibroscan (can be performed in selected outpatient clinics) determines the stiffness of the liver. A higher degree of stiffness correlates with a greater degree of hepatic fibrosis. Reliable in detecting little or no fibrosis in early cirrhosis and end stage liver disease but less sensitive when moderate fibrosis is present.

5 Is there a treatment for hepatitis C? How successful is it?

Treatment for HCV

The aim of treatment is hepatitis C viral eradication or sustained viral response (SVR). SVR is defined as undetectable virus (HCV RNA) (by PCR) in blood 24 weeks after completion of therapy, and equates to a cure. Once SVR has been achieved it is highly durable, with almost all patients (> 95%) remaining clear of the virus.

The standard treatment is a combination of pegylated interferon and ribavirin prescribed under the PBS S100 scheme. Pegylated interferon is given once weekly subcutaneously and ribavirin is taken twice daily orally.

The duration and chance of success of treatment is determined largely by HCV genotype and viral load before the start of treatment.

Genotype 2 or 3 patients require 24 weeks of therapy (unless advanced liver disease and then need 48 weeks). The SVR rate for Genotype 2 and 3 patients is high at 70-80%.

Genotype 1 or 4 patients require 48 weeks of therapy. The SVR rate for genotype 1 and 4 is much lower at approximately 40-45%.

The benefits of achieving SVR include:

- A reduced risk of progression of liver damage
- A lower incidence of hepatocellular carcinoma
- Significant regression in fibrosis (even in cirrhotic patients)
- Improvement in quality of life scores

Even unsuccessful treatments often have benefits as patients learn more about their illness, ways to keep their liver healthier, develop new support systems and receive information regarding new treatments.

Antiviral therapy is available (S100 PBS) to patients with chronic HCV infection who:

- Are 18 years or older
- Have no evidence of decompensated liver damage (complicated cirrhosis)
- Are not pregnant or breastfeeding or whose female partner is not pregnant; both patient and partner each to use an effective form of contraception if potential for pregnancy
- Are managed in an accredited treatment centre.

Re-treatment is also approved for patients who have had one prior course of interferon. Patients most likely to benefit are relapsers to previous therapy, failed previous treatment with non-pegylated interferon, have genotype 2 or 3 HCV infection, low fibrosis stage and low viral load.

Major contraindications to therapy include:

- Decompensated liver disease
- Less than 18 years

- Women who are pregnant or men whose female partners are pregnant (Ribavirin is teratogenic – patients and their partners must avoid pregnancy during therapy and for six months after cessation of treatment)
- Major psychiatric conditions, particularly severe depression (recent hospitalisation, self harm), unstable schizophrenia or bipolar disorder
- Autoimmune diseases
- Significant cardiac, renal disease, blood disorders, epilepsy (treatment lowers seizure threshold)

A specialist must start the treatment, and either the specialist, or an accredited GP S100 prescriber should review the patient regularly and write scripts throughout the treatment. Each patient should have a nominated GP throughout treatment who has all current management information.

Side effects of treatment are discussed in detail in Question 8.

Briefly, side effects are common, but don't usually require treatment to be ceased. Patients do require significant support and encouragement throughout the treatment and it is good to discuss if they have flexibility with work or can arrange the treatment at a time when their life is not too hectic. It is important to discuss how medication side effects may impact on the individual's quality of life, relationships and work life.

See Ribavirin/Interferon Combination Therapy Fact Sheet at http://www.hivhepsti.info/riba_inter.htm for more information.

6 Can I do treatment anytime; what factors make the treatment work better?

When should treatment commence?

There is a workup phase prior to treatment. Each hepatitis C treatment service will have its own team and workup protocols. It can take some months till the patient is ready for treatment. The specialist, team and patient make treatment decisions on a case-by-case basis. Several team members, including the doctor, nurse, social worker and dietician, undertake patient reviews. Often Drug and Alcohol and Mental Health services are involved. The specialist will discuss things in more detail with a patient once all the individual's details are known.

As a GP you can perform a Chronic Care Plan; any pending dental work should be undertaken pre treatment. A Dental Health Care Plan often helps as can a Mental Health Care Plan, a Team Plan and an Allied Health Care Plan, depending on the individual circumstances and in conjunction with the hepatitis C treatment specialist and team.

Factors to consider in the timing of treatment include:

- Impact of the side effects on the individual, family and work, in particular exhaustion. Consider support networks available for the patient at this time in his or her life
- Severity of liver damage – those with more severe damage are encouraged to have treatment as soon as practicable; others can plan treatment around events in their lives such as work, social conditions, pregnancy plans
- Drug and alcohol factors – ideally patients should be alcohol and cannabis free during treatment; other recreational drug use should be well controlled. Patients on buprenorphine or methadone are not excluded from treatment and can be referred if stable on their medication. Consideration should be given to the level of drug dependence of current injecting drug users who may be eligible for treatment if they remain stable and use intermittently
- Mood and psychiatric disorders – often better to start antidepressants prior to treatment if any element of low mood. Patients with bipolar disorder or schizophrenia should be stable and have psychiatric review before treatment if possible
- Co-infections e.g. HIV or chronic hepatitis B
- Other medical conditions - especially renal impairment, diabetes and cardiac disease. Physician pre treatment review is recommended
- Overweight and obesity - encourage weight loss before commencing treatment

Predictors of a good response to treatment (SVR) include:

- HCV genotype is the most powerful predictor of response (genotypes 2 and 3 have a 70- 80% chance of SVR, while genotypes 1 and 4 have only a 40-45% chance of SVR)
- Low viral load: HCV RNA (by PCR) < 400 000 IU/mL pre treatment
- Milder degree of hepatic fibrosis
- Female
- Younger age (especially under 40 years)
- No alcohol or cannabis intake during treatment
- Lower body mass index and not insulin resistant
- Good adherence to treatment - especially in the first few months
- A rapid viral response (RPR): HCV RNA < 50 IU/mL 4 weeks into treatment is a good indication of SVR

Note: A number of treatments for HCV genotype 1 are currently in clinical trials and show great promise for increasing the chance of achieving an SVR and in reducing the length of treatment to 24 weeks. Recommendations for the most appropriate treatments may change, based on the future availability of these drugs and some people with HCV genotype 1 who do not need treatment urgently opt to wait for 2-3 years to see if the new regimes reach the PBS.

(See also <http://www.hepcaustralia.com.au/News/New-Directions-in-Hepatitis-C-Therapy-A-Look-at-the-Evolving-Therapeutic-Arsenal.php>).

Factors associated with accelerated disease progression include:

- Age of infection (> 40 years at age of infection)
- Heavy alcohol intake (> 40/50 gm/day) – promotes viral replication
- Daily cannabis use - likely to promote viral replication
- Male
- Duration of infection (> 20 years)
- Moderate-to-severe hepatic fibrosis at baseline liver biopsy
- Co-infection with HBV and HIV or both
- Obesity (especially if linked with steatosis and fatty liver on biopsy)

Patients at highest risk of liver disease progression should be encouraged to consider therapy as soon as practicable, especially if long duration of infection, haematological and biochemical markers of fibrosis (e.g. AST/ALT ratio > 1, low platelets) and moderate/severe fibrosis on liver biopsy or fibroscan).

If patients are on treatment and are remanded in custody or sentenced to prison, it is important that there is no interruption to treatment. Patients should be encouraged to take their medication with them.

A number of support networks are available for people with hepatitis C infection in Australia. The state Hepatitis C Councils and Hepatitis Australia provide support and resources to patients. Refer to www.hepatitisaustralia.com; The Hepatitis C Council of NSW: www.hepatitisc.org.au. or your local Hepatitis Council website.

7 When do I need to see a liver specialist; will I have to pay for tests and treatment?

When to refer:

- For treatment consideration after pre treatment assessment
- For assessment of the severity of disease, especially if evidence of chronic liver disease or extra hepatic manifestations (e.g. lichen planus, cryoglobulinaemia, glomerulonephritis, porphyria cutanea tarda, vasculitis, lymphoma, thyroid dysfunction)
- At patient request

A list of local specialists and hepatitis C treatment services are available from the ASHM Directory 2008 – 2009 at: www.ashm.org.au/directory

Cost:

Costs for medications, specialist appointments and investigations will vary depending on whether the patient has a health care concession card, is a private patient or is receiving care under Medicare or is treated at a public hospital liver unit. For HCV treatment medication, patients will be charged the normal PBS prescription cost by

the dispensing hospital pharmacy. The amount for each item (at March 2009) is \$5.30 for concession cardholders and \$26.30 for all others. If the patient does not receive Medicare benefits, the cost for medications will exceed \$1000 per month.

8 Are there any side effects to treatment?

Treatment side effects:

Side effects must be monitored closely and the patient supported throughout treatment. Side effects are common but don't usually require treatment to be ceased. Treatment dosage may need to be changed by the specialist.

Common side effects include:

- Flu like symptoms 8-48 hours after first few pegylated interferon injections; tend to become less severe over first month; manage with adequate hydration and paracetamol
- Nausea, weight loss, (often 10% body weight loss, sometimes more – Sustagen and dietician input often required)
- Mood disorders - especially irritability, anxiety, low libido and depression (20-50% experience depression, often from serotonin depletion due to interferon). Irritability and depression respond rapidly to antidepressant medication, in particular SSRIs. Social worker and/or psychologist input can be very helpful pre, during and post treatment
- Alopecia
- Skin eruptions including very dry skin, mild rash
- Dry cough
- Myelosuppression with low white cell count, neutrophils and platelets during treatment
- Induction of autoimmunity, particularly thyroid disease
- Ribavirin can induce a dose-dependent anaemia with a fall in haemoglobin - often causes shortness of breath and increased tiredness
- Some patients return to injecting drug use during treatment

Rarer side effects but ones not to be missed include:

- Retinitis - visual changes should be assessed immediately (same day) by an ophthalmologist or optometrist – retinitis requires cessation of treatment
- Pneumonia
- Interstitial lung disease
- Myocardial infarction or arrhythmia
- Worsening diabetes
- Sepsis – more common in patients with cirrhosis
- Severe autoimmune disorders - interferon can flare, at times permanently, immune disease e.g. psoriasis, thyroid (Graves' disease, Hashimoto's disease) and inflammatory bowel disease
- Potential bleeding – cerebral haemorrhage
- Severe depression and suicide
- Decompensation into advanced liver failure

Ribavirin is a teratogenic Category X drug. Both male sperm and female ova are affected during treatment and for 6 months after treatment. This risk requires the use of double contraception throughout the treatment period and for up to 6 months after treatment. Termination is strongly advised for pregnancy during this time.

9 What can I do to look after my health?

Ways to protect the liver and prevent disease progression include:

- Limit or cease alcohol intake: excessive alcohol consumption > 50 g/day and likely less leads to disease progression and increased risk of hepatocellular carcinoma. Referral to local Drug and Alcohol Services can assist in reduction/cessation
- Limit or cease cannabis use
- Cease current medical or complementary medicines that may harm the liver
- Vaccinations – make sure fully vaccinated for hepatitis A and B
- Healthy eating and reduction in abdominal obesity and Body Mass

Index to normal range. Overweight patients should be encouraged to reduce weight gradually, often under the guidance of their GP or dietician

- Maintain good overall health, reinforcing need for relaxation and stress reduction – if low mood is a problem, consider cognitive behavioural therapy, referral to a psychologist and antidepressant medication
- Monitor for symptoms/signs of liver progression (6 – 12 monthly examination) with GP
- Patients with HCV who continue to inject drugs unsafely remain at risk of overdose, viral infections and other health problems Drug use should be stabilised before referral for HCV treatment – referral to local Drug and Alcohol Services is recommended
- Nutrition: strong recommendation against restrictive calorie diets. A well balanced diet is recommended. For most people with HCV, dietary recommendations are the same as for the general population (encouraging: grilled rather than fried food; lean meats and fish; reduced-fat products; wholemeal bread; vegetables and fruit; pasta; minimising fat for spreading and cooking)
- Symptoms of fatigue, headache, aching muscles and joints may be reduced by planning rest periods and incorporating light-to-moderate exercise
- There is little evidence that herbal medicines have a profound antiviral effect despite many patients reporting some symptomatic improvement and the ability of some agents to induce a fall in ALT. Most preparations are safe but some have reported hepatotoxicity and should be avoided (e.g. mistletoe, valerian, heliotropium, kombucha tea). Close monitoring of liver biochemistry is recommended at the commencement of any herbal medicine course

For more information, refer to Hepatitis Australia website www.hepatitisaustralia.com or call the helpline 1300 437 222 (1300 HEP ABC). Refer to ASHM website: www.ashm.org.au or call (02) 8204 0700.

10 Should I be vaccinated/tested for other forms of hepatitis?

Yes, all HCV patients should be tested for other forms of hepatitis (the specific tests are nominated in Question 4) and HAV and HBV vaccination should be offered to all patients with chronic hepatitis C, unless they are already immune

Why?

- Co-infection with more than one hepatitis virus may be associated with more severe liver disease
- Super infection with hepatitis A (HAV) in a patient with chronic hepatitis B or C, or acute hepatitis B in a patient with chronic hepatitis C may precipitate acute liver failure
- Patients with HBV and HCV co-infection are more likely to progress to cirrhosis and to develop hepatocellular carcinoma

11 How often should I come back and see you?

The aims of follow-up in patients with chronic hepatitis C are to:

- Reinforce the need for lifestyle changes, if needed, and support patients making changes
- Discuss treatment options with patients
- Determine appropriate timing of referral to a specialist
- Monitor patients with cirrhosis for complications, such as hepatic decompensation and hepatocellular carcinoma. For patients with chronic hepatitis C, ongoing monitoring is recommended every 6 to 12 months, unless there are specific reasons for more frequent monitoring (e.g. encouraging behaviour change).

Tests to be conducted include:

- LFTs
- Full blood count
- Prothrombin time or international normalised ratio (INR)

If cirrhosis present, then also do 6-12 monthly monitoring (as advised by your specialist)

- Hepatic ultrasound to screen for hepatocellular carcinoma
- Serum alpha-fetoprotein (AFP) to screen for hepatocellular carcinoma (If raised AFP, abdominal CT to look for hepatocellular carcinoma)

Signs of decompensated liver failure or complications of cirrhosis

include:

- Peripheral oedema
- Ascites
- Splenomegaly
- Jaundice
- Bruising, alopecia, gynaecomastia
- Encephalopathy

Once complications or decompensation have developed, liver transplantation is the only effective treatment. The specialist will refer to the liver transplant unit as indicated.

12 Where can I go for more information and support?

Patients should see their regular GP for more information. GPs can obtain contact details for local specialists and Hepatitis Treatment Services from the ASHM Directory 2008 – 2009 at: www.ashm.org.au/directory

GPs can also refer patients to:

- Hepatitis Australia website: www.hepatitisaustralia.com or call the helpline 1300 437 222 (1300 HEP ABC) or www.hepc.com.au, an interactive website for young people

References

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- ASHM, (2008). *B positive: All You Wanted to Know About Hepatitis B.*
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The resources above are available to order or download from the ASHM website at: www.ashm.org.au/publications

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ABN 48 264 545 457
 © Australasian Society for HIV Medicine 2009

ISBN 978 1 920773 70 3

Funded by the:
Australian Government, Department of Health and Ageing.

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