

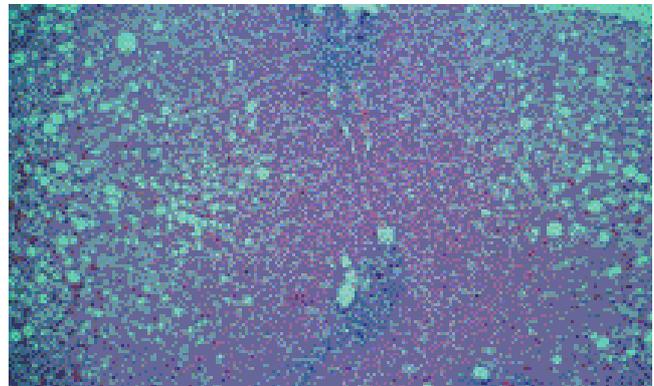
Chronic hepatitis C

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Chronic hepatitis C is a major public health issue.

Of acutely affected people with hepatitis C virus infection, about 80% will eventually develop chronic infection.



COURTESY OF DR TECH AND DR GEORGE, SYDNEY, NSW

Figure. Histological changes seen in progressive liver disease due to chronic hepatitis C virus infection. Early fibrosis can be seen.

Remember

- Over 200,000 Australians are living with chronic hepatitis C virus (HCV) infection. They incur a 20-year risk of cirrhosis of 7% and a lifetime risk of hepatocellular carcinoma of 2 to 3%.
- Those with a current or past history of intravenous drug use represent the most prevalent subgroup (50 to 80%).
- About 80% of people with acute HCV infection eventually develop chronic infection.
- The incidence of newly identified cases is predicted to increase in future years. Chronic HCV infection is, therefore, a major public health issue.
- Combined therapy with peginterferon alfa-2a or 2b and ribavirin (Pegasys RBV Combination Therapy and Pegatron Combination Therapy [with PEG-Intron Redipen Injector], respectively) can achieve sustained virological response rates of 50 to 60% for all genotype infections of HCV.

Assessment

- Initial assessment should include the duration of infection, its probable source (from the patient's risk factors), and the presence of symptoms of chronic liver disease and other comorbidities, including autoimmune disorders or endocrinopathy.
- The history should include medication use, social activities, occupation and any psychiatric disorders. Current reproductive status must be determined as ribavirin is a potent teratogen.
- An examination should be performed to assess for features of chronic liver disease, including clubbing, leuconychia, jaundice, spider naevi, gynaecomastia, ascites, testicular atrophy and peripheral oedema.
- Initial investigations include a full blood count, electrolytes, liver function tests and clotting assessment, serology for hepatitis A, B and C viruses and HIV, HCV genotype determination, thyroid function tests and a liver ultrasound.
- Preclinical cirrhosis may be identified by a prolonged International Normalised Ratio (INR), reduced platelet count or reduced albumin level. Liver ultrasound may detect early nodularity indicating more advanced fibrosis.
- Antibody to HCV (anti-HCV) is detected by ELISA immunoassay, with a sensitivity of 90 to 95%. A qualitative HCV RNA test (by polymerase chain reaction [PCR]) can help to exclude false-positive results (Table).
- Liver biopsy is the gold standard for determining the histological grade of inflammation and stage of fibrosis. This is not essential for patients infected with HCV genotypes 2 or 3 who have a high likelihood of treatment response. However, patients with HCV genotype 1 should be offered a liver

Table. Hepatitis C virus (HCV) infection: summary of common diagnostic tests

| Diagnosis | Anti-HCV test | HCV RNA test |
|----------------------|----------------------|--------------|
| Acute hepatitis C | Positive or negative | Positive |
| Chronic hepatitis C | Positive | Positive |
| Resolved hepatitis C | Positive or negative | Negative |

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Useful online hepatitis C resources

Hepatitis Australia

www.hepatitisaustralia.com

Australasian Society for HIV Medicine

www.ashm.org.au

Gastroenterological Society of Australia

www.gesa.org.au

biopsy to help plan future therapy. Additionally, if there is concern over other diagnoses (e.g. fatty liver, alcohol excess or clinical suspicion of cirrhosis) then a biopsy is indicated.

Management

- General measures for management of patients with HCV infection are pre- and post-test counselling, psychological support and education, maintenance of good health, reduction of potential hepatotoxins (including medications and alcohol) and hepatitis B vaccination. Vigilant surveillance for signs of hepatic failure (e.g. encephalopathy, jaundice, ascites, hypoglycaemia, coagulopathy) should also be carried out.
- After exposure to HCV, blood should be tested for anti-HCV and HCV RNA. Liver function and anti-HCV tests should be carried out at one, three and six months postexposure. There is currently no postexposure prophylaxis.
- In acute HCV infection, a number of small studies have suggested that early treatment with peginterferon alfa therapy may improve clearance rates and normalise serum alanine aminotransferase levels.¹ However, peginterferon alfa therapy is not currently approved for acute HCV infection and clinical trials to assess response are under way.
- In chronic HCV infection, the goal of treatment is to achieve a sustained virological response. This is determined by HCV RNA clearance and normalisation of serum alanine aminotransferase levels six months following completion of treatment. This reduces progression in all stages of chronic liver disease.
- Favourable factors of a sustained virological response in hepatitis C treatment include infection with HCV genotypes 2 or 3, a low pretreatment viral load, minimal hepatic fibrosis, female gender and a young age (less than 40 years). Combined therapy with weekly peginterferon alfa-2a or -2b and daily ribavirin is effective in achieving a sustained virological response. Peginterferon monotherapy (Pegasys, PEG-Intron Redipen Injector) is occasionally used in specialised centres in patients who cannot tolerate ribavirin (e.g. those with renal impairment). Standard interferon monotherapy is generally no longer used in clinical practice to treat patients with hepatitis C.
- Overall, 50 to 60% of all patients with hepatitis C achieve a sustained virological response after combined therapy; patients with HCV genotypes 1 and 4 have a lower rate (40 to 50%), and those with HCV genotypes 2 and 3 have a slightly higher rate (60 to 70%). Treatment duration can range from 24 to 48 weeks.
- Patients with early, well-compensated cirrhosis may also benefit from combined therapy. Annual or six-monthly screening with liver ultrasound and a serum alpha-fetoprotein (AFP) test should be offered to cirrhotic patients to screen for the development of hepatoma.
- Future therapies may include other antiviral agents (e.g. amantadine) or

protease inhibitors. Individualised treatment programs may evolve with wider use of earlier quantitative PCR analysis to predict individual response rates (rapid responders and poor responders). This may improve sustained virological response rates, safety, compliance, costs and quality of life for individual patients.

- Useful online resources for patients with hepatitis C are listed in the box on this page.

References

1. Calleri G, Cariti G, Gaiottino F, et al. A short course of pegylated interferon-alpha in acute HCV hepatitis. *J Viral Hepat* 2007; 14: 116-121.

Further reading

1. Dienstag JL, McHutchison JG. American Gastroenterological Association medical position statement on the management of hepatitis C. *Gastroenterology* 2006; 130: 225-230.

DECLARATION OF INTEREST: Dr Watson has acted as a Principal Site Investigator in studies on the treatment of hepatitis C virus infection. Studies he has been involved in have been partly or completely sponsored by research funding from Schering-Plough, Roche and Genome Sciences Inc. Dr Hair: None.

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