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- 內文：
- **Introduction**

  About 170 million people in the world are infected withhepatitis C virus (HCV).

  Since the discovery of HCV in 1989, the number of acute HCV cases has fallen by more than 80%

  The major routes of transmission are injection drug use, blood transfusion hemodialysis, organ transplantation and less frequently sexual intercourse.

  Six major genotypes (1–6) of HCV have been identified
- **Natural history**

  Acute hepatitis usually is asymptomatic and rarely leads to hepatic failure.

  Approximately one fifth (20–30%) of patients with chronic HCV develop cirrhosis over a time period of 10–30 years

  advanced age (>40–55 years), male sex, HIV co-infection, higher body mass index, presence of hepatic steatosis and consumption of alcohol.

  Decompensated cirrhosis results in portal hypertension
- **Natural history**

  Among those with cirrhosis, 1–4% per year develop hepatocellular carcinoma

  The 5-year survival rate for patients with compensated cirrhosis is as high as 90% as compared to 50%for those with decompensated cirrhosis
- **Clinical features and diagnostic evaluation**

  Most patients with chronic HCV are asymptomatic or may present with nonspecific symptoms such as fatigue or malaise.

  Patients with decompensated disease may display peripheral manifestations of cirrhosis

  The diagnosis of HCV is made by the presence f anti-HCV antibody and HCV RNA in the blood.

  Liver function tests, prothrombin time and hepatitis B, HIV serologies

  Liver biopsy
- **Treatment**

  Treatment considerations for hepatitis C are based on the presentation of the disease (acute vs chronic), genotype, laboratory values, presence of co-infection (HIV, hepatitis B) and co-morbidities.

  The main goal of treatment of HCV is to achieve sustained virologic response (SVR), defined as the absence of HCV RNA in serum at least 6 months after the discontinuation of therapy.
- **Chronic hepatitis C**

  Treatment of chronic hepatitis C in adults is recommended for those who have detectable HCV RNA levels, elevated aminotransferase (ALT) levels, liver biopsy findings suggestive of progressive liver disease and the absence of any serious co-morbid conditions or contraindications as listed in Table 1

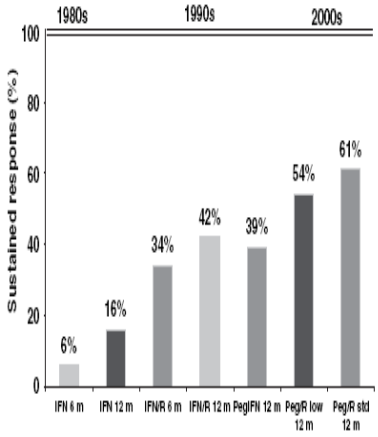
  The current recommended treatment of chronic HCV is the combination of peginterferon and ribavirin.

α-Interferon was first shown to have a benefit in chronic hepatitis C infection in 1986 Five to fifteen percent of patients achieved SVR after a 6- to 12-month course of IFN-α.

With peginterferon and ribavirin, 70–80% of patients with genotype 2 or 3 infection and 42–45% of those with genotype 1 infection can achieve a SVR.

Table 1 Contraindications to treatment with peginterferon and ribavirin

Absolute contraindications
1. Pregnancy
2. Breast feeding
3. Allergic reaction to either drug
Relative contraindications
1. Decompensated liver disease as defined by bilirubin >1.5 mg dl^{-1}, prothrombin time >15 s or INR ≥ 1.7, albumin <3.4 g dl^{-1}, ascites, bleeding esophageal varices, hepatic encephalopathy
2. Neuropsychiatric diseases
3. Coronary artery disease
4. Cerebrovascular disease
5. Renal failure
6. Previous organ transplantation
Close monitoring and dose adjustment might be required in patients with anemia, thrombocytopenia or leucopenia. Patients with renal dysfunction might need adjustment of ribavirin dose.



- **Acute hepatitis C**

  Up to 50% of patients with acute HCV spontaneously clear the virus.

  A delay of treatment for 8–12 weeks after the onset of acute hepatitis C has been suggested.

  Studies with IFN-a have reported SVR rates of as high as 95% when patients are treated for 24 weeks

  Studies of peginterferon with or without ribavirin have reported SVR rates of 80–89% with 24 weeks of treatment

- **Treatment response**

  In patients with SVR, HCV RNA levels become undetectable in 4–24 weeks and remain negative for the entire duration of follow-up. ALT levels return to normal and liver histology shows improvement. In those with relapse (20%), the HCV RNA levels reappear after therapy is stopped, usually within a few weeks of the end of treatment.

  In those with breakthrough (10%), HCV RNA levels initially become undetectable but reappear during therapy.

  In patients with non-response, HCV RNA levels never become undetectable during treatment.

- Predictors of treatment response

  Various factors have been associated with lower response rates in patients undergoing treatment with peginterferon and ribavirin. They are genotype 1, African American race, pretreatment HCV RNA levels of >800 000 IU ml)1, male sex, higher body mass index and advanced fibrosis

- **Adverse effects of treatment**

Adverse effects of peginterferon	*Comments*
Influenza like symptoms: Fever	Typically after the first injection.
Gastrointestinal symptoms: Nausea	
Hair loss:	20–25% of patients, usually temporary.
Bone marrow suppression: Leucopenia, thrombocytopenia	Typically 30–50% reduction in counts, may treat with G-CSF.
CNS toxicity: headache, depression, irritability, psychological changes	10% of patients, use of anti-depressants, dose reduction if severe.
Seizures	1–2% of patients, dose discontinuation.
Autoimmune thyroid disease: Hypothyroidism, hyperthyroidism	1–2% of patients, treat if symptomatic.
Others: cardiac side effects, interstitial nephritis, vision and hearing disturbances, elevation in serum aminotransferases	

Adverse effects of Ribavirin	*Comments*
Hemolytic anemia	Dose reduction if symptomatic or Hct < 30%, dose discontinuation if Hct drops further, may use erythropoietin.
Lymphopenia	Lymphocyte counts may decrease by 10–15%.
Gout: Increase in uric acid	Discontinue if attack severe/prolonged.
Pruritis	20% of patients, discontinue if severe.
Nasal stuffiness, sinusitis	20% of patients, treat if symptomatic.
Teratogenicity	Discontinue if pregnancy test positive.
Others: Hepatic iron accumulation, cholelithiasis, retinal changes	

- **Future advances in therapy**

  Ribavirin in high doses (1400–2400 mg) has been shown to achieve higher SVR rates in a small trial at the expense of a higher toxicity profile

  New forms of IFN are being tested clinically. A new generation of small molecule inhibitors targeting the viral-encoded enzymes, such as the proteases and polymerases is being developed. Although some of them are quite promising in suppressing HCV levels in HCVinfected people, drug resistant mutants emerge rapidly after the initiation of therapy. Therefore they would have to be used in combination with IFN-based therapy.

- Conclusion

  The current combination therapy of peginterferon and ribavirin will remain the mainstay treatment of hepatitis C for the next 3–5 years.

題號	**題目**
1	C型肝炎的主要傳染途徑 (A) 血液及血液製品的輸用 (B) 糞口傳染 (C) 空氣傳染 (D) 接觸傳染
答案(A)	出處：Dental management of the medically compromised patient P304
題號	**題目**
2	下列何者非肝臟代謝的牙科用藥?
	(A) Lidocaine (B) Aspirin (C) Tetracycline (D) Acyclovir
答案(D)	出處：Dental management of the medically compromised patient P.311