

## Early diagnosis improves outcomes in hepatitis C

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Dr Michael H Miller  
MBChB MRCP PhD  
Clinical Lecturer in Gastroenterology and Hepatology

Professor John F Dillon  
MBBS MD FRCP  
Professor of Gastroenterology and Hepatology  
Medical Research Institute, University of Dundee, Dundee, UK



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**AUTHORS**

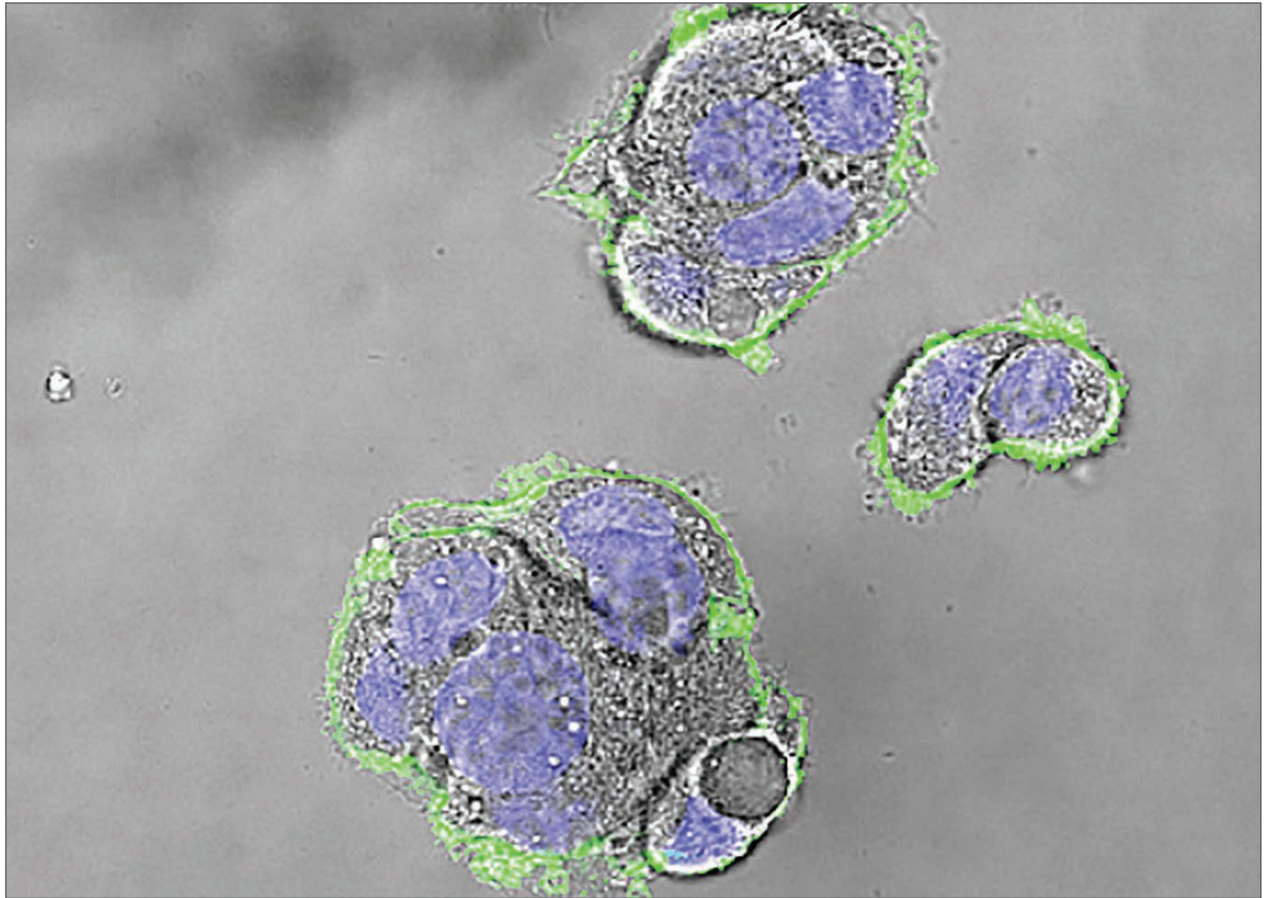
**Dr Michael H Miller**

MBChB MRCP PhD  
Clinical Lecturer in  
Gastroenterology and  
Hepatology

**Professor John F Dillon**

MBBS MD FRCP  
Professor of Gastroenterology  
and Hepatology

Medical Research Institute,  
University of Dundee,  
Dundee, UK



**FIGURE**  
HCV E2 molecule  
binding to cultured  
hepatocytes, the  
process of infection

## What are the risk factors?



**HEPATITIS C (HCV) AFFECTS 0.8-1% OF THE UK POPULATION, WITH UP TO 70% HAVING ONGOING**

chronic infection.<sup>1</sup> The prevalence is higher within certain ethnic, cultural and socioeconomic groups. HCV is curable but if left untreated can progress to end stage liver failure or cancer (hepatocellular carcinoma).

HCV has six known genotypes,<sup>2-7</sup> which show geographical variance. Genotypes 1 and 3 are most commonly seen in the UK.

Therapeutic breakthroughs over the past few years have led to cure rates of more than 90%. The challenge is to deliver the benefits of these new drugs.

## How should patients be diagnosed?

### RISK FACTORS

Several groups are at increased risk of HCV. People who inject drugs (PWID) are the main high-risk group in the UK. Blood to blood transmission is the main mode of infection, risk factors include:

- Sharing or reuse of needles for injection (and other drug paraphernalia)

**‘HCV is curable but if left untreated can progress to end stage liver failure or cancer’**

## What are the treatment options?

- Tattooing or acupuncture with non-sterile equipment
- Needlestick injuries
- Blood and blood products (before 1991 in the UK)
- Medical procedures
- Contact with blood from an infected person

Male circumcision and childhood inoculations are also potential modes of transmission in the developing world.

Sexual transmission of HCV is uncommon with studies suggesting an incidence of 0-2/1,000 years of sexual contact,<sup>2</sup> although this rate is higher in cases of co-infection with HIV and men who have sex with men.<sup>3</sup> Infected individuals should be advised to take »

# SPECIAL REPORT

## HEPATITIS C INFECTION

precautionary measures; the sharing of razors and toothbrushes should be discouraged and safe sexual practices encouraged.

Acute hepatitis C infection has mild symptoms only and is likely to go undiagnosed. The estimated diagnosis rate in England is 35%, suggesting that 65% of the total HCV-positive population remains undiagnosed.<sup>8</sup> Symptomatic presentation is uncommon.

HCV is often detected in response to abnormal liver enzymes and a subsequent liver screen. In this situation, patients usually only have a mild rise in transaminases. The most common method of detecting HCV is case finding in high-risk groups:

- Both current and former PWID
- Patients on opiate substitution therapy
- Patients who have received overseas healthcare
- Recipients of blood products before 1991 in the UK
- Certain immigrant groups (e.g. Eastern Europeans, Pakistanis,<sup>4</sup> Egyptians<sup>5</sup>)

GPs can play a major role in identifying those at risk of the disease providing information and arranging testing.

### DIAGNOSIS

Maintaining a high index of suspicion is paramount. Offering HCV testing to at-risk groups will allow early detection and referral.

## ‘Dry blood spot testing is highly sensitive and specific’

Testing is usually on blood, the presence of HCV antibodies indicates exposure to HCV, but does not confirm active HCV infection. Once exposed to the virus the patient will have HCV antibodies lifelong. An HCV-positive individual should have their HCV PCR checked to confirm active infection.<sup>9</sup>

In groups who are difficult to reach, dried spot blood testing is a convenient method of delivering HCV testing.<sup>6</sup>

It allows blood sampling in the community from patients who often have difficulties with traditional phlebotomy. In addition, non-clinical workers can carry out dry blood spot testing. It is a useful screening test which has been shown to be highly sensitive and specific.<sup>7</sup>

### REFERRAL

All patients with evidence of active HCV infection (HCV RNA positive) should be considered for referral to local specialist hepatology or infectious diseases services. In addition, most local services will have developed referral pathways with access to clinics. Many units will offer community-based clinics using nurse specialists and treatment networks at the point of contact attempting to engage the difficult to reach cohorts.

Traditionally, active drug injection was regarded as a barrier to HCV services and treatment. This is no longer the case. Evidence suggests that engaging active PWID and providing education, awareness and support will increase their treatment success rates to those of non-injecting drug users/previous users.<sup>10</sup>

## ‘Fibroscan provides an additional means of non-invasive assessment of liver fibrosis’

At the point of referral an assessment of the stage of disease will be made. This can be done using noninvasive serum fibrosis markers such as the FIB4 panel, AST:ALT ratio and APRI.<sup>11</sup> Fibroscan is a useful adjunct, providing an additional means of non-invasive assessment of liver fibrosis,<sup>12</sup> this is accessed via specialist services.

### MANAGEMENT

The objective of HCV treatment is to achieve cure. This is measured as undetectable virus RNA measured three or more months after the end of a planned treatment programme, and is known as a sustained virological response (SVR).

HCV management options have changed dramatically over the past five years, with improvement in patient experience, cure rates and tolerability. The first treatment for HCV was interferon alpha which was very poorly

**Table 1**

### Treatment options for HCV genotypes 1, 2 and 3

HCV genotype	Drug treatment	Duration
<b>Genotype 1</b>		
Treatment naive (non-cirrhotic)	Sofosbuvir, ledipasvir	8 weeks
	Ombitasvir, paritaprevir, ritonavir, dasabuvir	12 weeks
	Sofosbuvir, daclatasvir	12 weeks
	Sofosbuvir, simeprevir	12 weeks
Treatment experienced (non-cirrhotic)	Sofosbuvir, ledipasvir	12 weeks
	Ombitasvir, paritaprevir, ritonavir, dasabuvir	12 weeks
	Sofosbuvir, daclatasvir	12 weeks
Cirrhotic irrespective of previous treatment	Sofosbuvir, ledipasvir +/- ribavirin	12 weeks
	Ombitasvir, paritaprevir, ritonavir, dasabuvir, ribavirin	12 weeks
	Sofosbuvir, daclatasvir, ribavirin	12 weeks
<b>Genotype 2</b>		
Interferon eligible	PEG interferon alpha with ribavirin	16-24 weeks
Interferon ineligible or treatment experienced	Sofosbuvir, ribavirin	12 weeks
<b>Genotype 3</b>		
Low viral load, mild to moderate fibrosis	PEG interferon alpha, ribavirin	16-24 weeks
Non-cirrhotic*	Sofosbuvir, PEG interferon alpha, ribavirin	12 weeks
	Sofosbuvir, daclatasvir, ribavirin,	12 weeks
	Sofosbuvir, ledipasvir, ribavirin,	12 weeks
Cirrhotic*	Sofosbuvir, PEG interferon alpha, ribavirin	12 weeks
Cirrhotic interferon ineligible *	Sofosbuvir, daclatasvir, ribavirin	12 weeks
	Sofosbuvir, ledipasvir, ribavirin	12 weeks

# key points

## SELECTED BY

Dr Jez Thompson

GPwSI Addiction Leeds, RCGP Regional Substance Misuse Clinical Lead Yorkshire and the Humber

**Chronic hepatitis C (HCV) infection affects 0.8-1.0% of the UK population, with up to 70% having ongoing chronic infection. HCV has six known genotypes (1-6), which show geographical variance. Genotypes 1 and 3 are most commonly seen in the UK. HCV is curable but if left untreated can progress to end stage liver disease and potentially hepatocellular carcinoma. HCV management options have changed dramatically over the past five years, with improvement in cure rates and tolerability; cure rates of more than 90% can now be achieved.**

**The main risk factors for acquiring HCV infection in the UK are injecting drug use and sharing drug using equipment. Other risk factors include receipt of blood products in the UK before 1991; tattooing or acupuncture with non-sterile equipment; medical procedures; needlestick injuries and contact with blood from an infected person. Some migrant groups, Egyptians, Pakistanis and some Eastern Europeans, have a higher prevalence of HCV infection than the indigenous UK population.**

**Acute hepatitis C infection has mild symptoms only and is likely to go undiagnosed. The estimated diagnosis rate in England is 35%, suggesting that 65% of the total HCV-positive population remains undiagnosed. The most common method of detecting HCV is case finding in high-risk groups. Blood testing is the cornerstone of diagnosis. Once exposed to the virus, the patient will have HCV antibodies lifelong. Those who test positive for HCV antibodies should be tested for persisting viral presence through HCV PCR testing – a positive result confirms active infection.**

**GPs can play a major role in identifying those at risk of the disease, which includes patients with known risk factors and those with unexplained abnormal liver function tests, providing information and arranging testing. Patients with confirmed active HCV infection should be referred to the local specialist hepatology or infectious disease service in accordance with locally agreed pathways.**

**Treatment of hepatitis C infection is with a range of combinations of antivirals, depending on the patient, the severity of liver disease and the virus genotype. Drugs used include pegylated interferon, ribavirin and a range of newer drugs: protease inhibitors (e.g. simprevir, boceprevir), NS5a inhibitors (e.g. daclatasvir, ledipasvir) and NS5b inhibitors (e.g. sofosbuvir, dasabuvir). Treatment is initiated in specialist centres, though primary care and community-based services are increasingly involved in the delivery of treatment in shared care arrangements.**

tolerated and associated with a less than 10% success rate.

The addition of ribavirin and then the pegylation of interferon improved cure rates throughout the 1990s and early 2000s. However, side effects remained an issue, with treatment courses lasting up to 48 weeks for HCV genotype 1.

In the past five years the fruits of unravelling the HCV genome and identifying target proteins have led to a plethora of new drugs in three classes:

- Protease inhibitors (e.g. simprevir, boceprevir)
- NS5a inhibitors (e.g. daclatasvir, ledipasvir)
- NS5b inhibitors (e.g. sofosbuvir, dasabuvir)

The combination of two or three drugs from these classes has led to treatment cure rates of up to 97%,<sup>13</sup> with treatment duration as short as eight weeks for some patients.<sup>14</sup>

An additional benefit of these agents, in particular if used without interferon, is a very good tolerability as there are few side effects.

## 'Therapeutic breakthroughs over the past few years have led to cure rates of more than 90%'

A number of patient characteristics influence the response to therapy, perhaps the most important of which is the presence of cirrhosis. Previous treatment history also has an impact on choice and duration of therapy.

Table 1, p26, opposite, summarises treatment options based on genotype, treatment experience and presence of cirrhosis.

Given the rapid changes, complexities of the different drugs, the impact of genotype and patient characteristics as well as drug costs treatment is initiated in specialist centres, although primary care and community-based services are increasingly involved in the delivery of treatment in shared care arrangements.

The excellent safety and tolerability of these new drugs means that a move towards more community-based treatment is highly likely, given that the main challenge is no longer curing the virus but delivering therapy to the patient.

## CONCLUSION

HCV is a common virus affecting the liver, with the potential to lead to liver failure and cancer. This virus can now be cured in most patients and complications prevented with early identification and treatment.

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## Useful information

### British Liver Trust

The website has a good patient-focused section on HCV  
[www.britishlivertrust.org.uk](http://www.britishlivertrust.org.uk)

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