

Fig. 2 Ferritin levels in responders and non-responders to interferon α treatment of chronic hepatitis C. * $P < 0.02$, non-responders vs responders. (Reproduced from 24).

tion and fibrosis in chronic hepatitis C, suggesting that the iron came from damaged hepatocytes.^{41,42} In contrast, the absence of stainable iron is associated with a higher likelihood of response.^{43,44} Other groups have suggested that iron may be a more significant factor in certain genotypes, in particular genotype 1b. In a study by D'Alba *et al.*,⁴⁵ patients with chronic hepatitis C and genotype 1b had higher hepatic iron concentrations compared with other genotypes. Genotype and hepatic iron concentration remained predictive factors of non-responsiveness on multivariate analysis.

HFE Mutations and Hepatitis C

The recent discovery of the *HFE* gene containing two missense mutations (C282Y and H63D) which are strongly associated with disordered iron metabolism raises the possibility that abnormal *HFE* genotypes could contribute to iron-related cell injury in chronic hepatitis C.⁴⁶ Recent studies have analysed the relationship of *HFE* mutations and iron overload in chronic

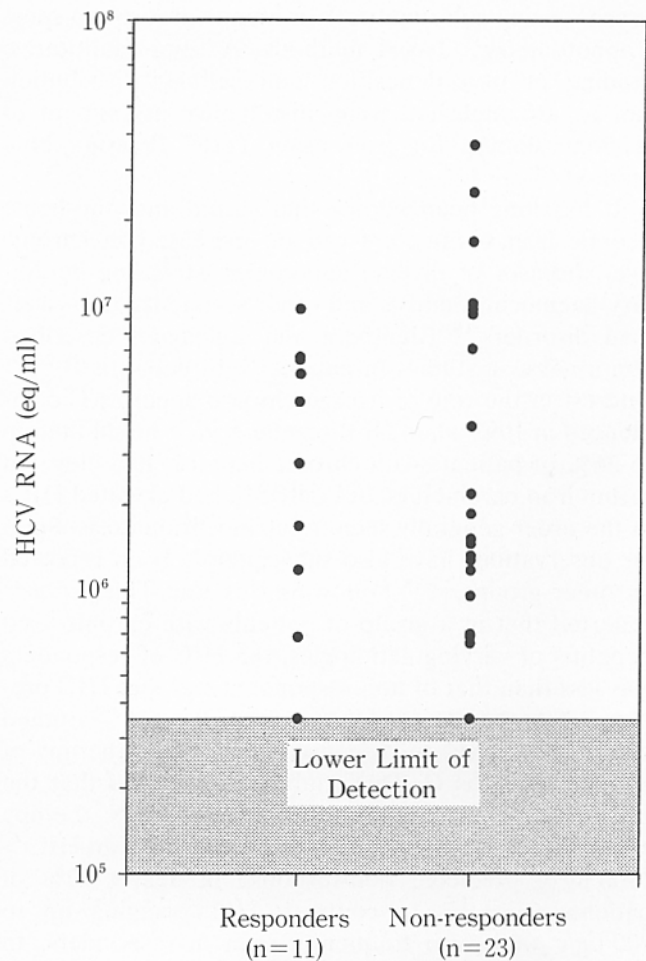


Fig. 3 Serum HCV RNA levels determined by branched DNA assay in responders and non-responders to interferon α treatment of chronic hepatitis C. The shaded region represents viral titers lower than 350,000 eq/ml, the lower limit of detection. (Reproduced from 24).

hepatitis C.⁴⁶⁻⁴⁹ Patients with hepatitis C have frequencies of *HFE* mutations that are no different than the general population. However, heterozygosity for the C282Y mutation is often associated with increased iron stores and with more advanced liver fibrosis.⁵⁰ There is a much stronger association between *HFE* gene mutations, abnormal iron status and HCV infection in patients with porphyria cutanea tarda.^{47,51,52} Thus in this group of patients it is possible that iron could play a more significant role in the pathogenesis of hepatitis C-related liver injury, but this remains to be confirmed in prospective studies.

Pathophysiology of Iron Toxicity in Hepatitis C

The mechanisms by which iron may cause liver disease have been recently reviewed.¹² The concept that iron can act in a synergistic fashion with other hepato-