Chronic hepatitis C is highly prevalent with prevalence rate of around 3% involving about 180 million people worldwide despite major advances in its understanding of viral pathogenesis and significant evolution in antiviral therapies. Most of the patients develop chronic infection because the virus evades the host immune response in majority of patients. Chronic HCV infection can lead to cirrhosis and hepatocellular carcinoma. Complications of HCV-related cirrhosis are the leading indication for liver transplantation in United States and Europe.

Chronic hepatitis C is the only chronic viral infection that can be cured by anti viral therapy. Currently only 40-50% of patients infected with HCV-genotype-I, treated with pegylated interferon and Ribavirin achieve a sustained virologic response (SVR). Till date pegylated interferon alfa and ribavirin are the standard treatment for treating chronic hepatitis C.

HCV genotype and early virologic response during treatment are important factors for individualization of antiviral therapy. Extended treatment duration of 72 weeks has been shown to reduce relapse rates significantly in patients who have chronic HCV genotype 1 infection and a slow virologic response compared with the standard duration of 48 weeks. Conversely, HCV genotype 1-infected patients with a low baseline HCV RNA concentration who become HCV RNA-negative at week 4 may be treated for 24 weeks without compromising sustained virologic response rates.

In patients who have HCV genotype 2 or 3 infection, who have better response to interferon alfa than patients infected with HCV genotype 1, the standard treatment duration is 24 weeks. Smaller trials showed that shorter treatment duration of 12 to 16 weeks is equally effective as the standard treatment duration in those patients infected with HCV genotype 2 or 3 who achieve a rapid virologic response after 4 weeks of therapy. Shorter course of therapy over 16 weeks has been shown to be as effective as a 24 weeks course in those patients who have genotype 2 or 3 infection, have a baseline viral load of 400,000 IU/mL or less, and achieve an early virologic response at week 4. In patients who have genotype 2 and 3 infection without a rapid virologic response at week 4, a longer treatment duration may be necessary to optimize sustained virologic response rates.

While the current treatment offers reasonable response rates there are enormous challenges that include therapy related adverse events, increasing population of non responders and special populations which includes patients of cirrhosis, immunosuppressed patients which includes patients on cancer chemotherapy, hemodialysis, thalassemics, patients of HIV infection and patients who get hepatitis-C after liver transplantation.

In this issue of the journal the author has described the recent progress made in the development of newer molecules in the management of chronic hepatitis C. Recent advances in structure determination of HCV proteins and development of a sub genomic replicon system besides cell culture infectious HCV clone has enabled the development of a specifically targeted antiviral therapy for hepatitis C (STAT-C). Numbers of molecules are under trial which are HCV-specific inhibitors and can improve treatment opportunities for patients who have chronic hepatitis C. New interferons and derivatives of ribavirin have been developed, and are currently being investigated in clinical trials.

Another recent area of interest has been the exploration of how genetics influence response to treatment. Individuals of European ancestry are more likely than those of African ancestry to attain SVR with peginterferon and ribavirin, and genetic studies have revealed that approximately half of this difference is explained by a polymorphism near the interleukin (IL)-28B gene, which encodes interferon-\(\lambda\). Recent studies have focused on assessing the role of IL-28B polymorphisms in determining response to therapy with these new agents.

The major challenge as these new agents are developed will be how to integrate these drugs into current treatment regimens to increase efficacy, improve tolerability and prevent the development of primary or secondary resistance to HCV.
specific inhibitors which is major problem to address. Combination of antiviral compounds inhibiting different viral and cellular mechanisms may reduce the problem of resistance. Future research should not only focus on the development of new compounds but on optimal drug combinations.

There is lot of diversity in different genotypes of hepatitis C virus and the large number of quasispecies in the infected individual leads to viral escape mutants leading to difficulties in development of effective vaccine. Therapeutic vaccination involves boosting the immune response in the already infected individual while as preventive vaccination helps in preventing establishment of chronic infection in exposed individual. Significant progress has been made in the development of effective vaccine against hepatitis C which is going to become a reality in coming years.\(^9\)

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References