Hepatitis C virus (HCV) infection is often found in the setting of co-existent liver disease to include nonalcoholic fatty liver disease (NAFLD), hepatitis B virus (HBV) and autoimmune hepatitis. The most common co-existent liver disease is NAFLD, by a wide margin. The association of these diseases with chronic hepatitis C (CHC) infection has historically meant potential decreased responses to pegylated interferon and ribavirin therapy, particularly with NAFLD, and increased progression of fibrosis. With the dawn of new antiviral therapy that target HCV directly, treatment trials focusing on these special populations are eagerly needed. There is a plethora of data linking insulin resistance, hepatic steatosis and nonalcoholic steatohepatitis (NASH) with diminished response to pegylated interferon and ribavirin therapy. In fact, some data suggest that sustained virologic response may be diminished by 40-50%. In addition, this metabolic derangement is linked to disease severity and progressive fibrosis. Interestingly, recent treatment data with protease inhibitors suggest that insulin resistance is improved with therapy and does not impair response to treatment. Intuitively this makes sense as these agents target HCV directly, rather than affecting innate immune function. However, we are still lacking treatment efficacy data with the new direct acting antiviral agents (DAAs) in the setting of NASH. Furthermore, given that these diseases are seen commonly together, we anxiously await data showing that eradication of CHC has a positive impact on disease progression in those patients who still have underlying NASH. To date, trials have specifically excluded patients with this co-existent disease, supposedly in an effort to optimize cure rates and mitigate side effects. Moving forward, it seems prudent to make this group a priority for treatment given the significant risk of disease progression and the propensity to progress to hepatocellular carcinoma (HCC) outside the setting of cirrhosis in some cases.

HBV and HCV co-infection is relatively common in regions of the world where both diseases are endemic and among high-risk groups such as intravenous drug users. Data suggest that there is more rapid disease progression compared with mono-infection. In addition, progression to HCC is significantly increased. By one estimate, the cumulative HCC risk at 10 years was 45%, compared to 28% for HCV mono-infection. Efficacy studies in patients with co-infection treated with DAAs are lacking. In addition, there are no published data to my knowledge on the long-term prognosis in patients achieving a sustained virologic response to HCV infection. Subsequently, co-infection with HBV provides an area that is ripe for investigation with the new DAA regimens.

The association of autoantibodies such as antinuclear antibody (ANA) and anti smooth muscle antibody (ASMA) with CHC is relatively common and does not necessarily imply a co-existent autoimmune hepatitis. Nor is the presence of autoantibodies required to make the diagnosis of co-existent autoimmune hepatitis. Subsequently, it is often necessary to consider both clinical data as well as histopathologic data in making the diagnosis of co-existent disease. Treatment of autoimmune hepatitis and co-existent CHC can be challenging. Steroids may exacerbate HCV replication and treatment of CHC with a pegylated interferon based regimen may lead to
an exacerbation of the autoimmune hepatitis. While no DAA studies exist that address this issue to date, it would seem that this would be an area that would be ideal for an all-oral DAA regimen. Eliminating interferon from the treatment paradigm would mitigate the concern for an AIH flare while on treatment.

References