Name of Project: **CHRONIC INFLAMMATION RELATED TO HEPATITIS C AND RISK OF BONE DISEASE**

Investigator(s).
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Research question(s): Among patients with chronic hepatitis C infection without cirrhosis, what is the association between systemic inflammation related to HCV infection and bone mineral density?

Brief Background/Significance:
Over 4 million individuals in the United States are infected with chronic hepatitis C virus (HCV), and up to 30% of these patients will develop cirrhosis. Although metabolic bone disease is a well-recognized complication of cirrhosis, over half of HCV-infected patients will develop osteopenia or osteoporosis even in the absence of advanced liver disease. The pathogenesis of bone loss in chronic HCV infection is not clearly understood, but it is likely that the persistent inflammatory state induced by chronic HCV viremia plays a critical role in the progression of bone disease (Figure), as has been shown in other inflammatory disease such as rheumatoid arthritis and inflammatory bowel disease. As this association has not been well-defined in HCV infection, we have designed this cross-sectional study to compare bone mineral density in patients with chronic HCV infection *without* evidence of cirrhosis with historic age-, sex-, and race-matched controls without chronic liver disease and to evaluate the association between biochemical markers of bone turnover, markers of chronic inflammation and BMD in a well-characterized cohort of HCV-infected patients. Understanding the burden and pathogenesis of low bone mass in this population is key to developing strategies aimed at early identification of bone disease in this population, which will allow for the implementation of effective treatment options to prevent debilitating osteoporosis-related fractures.

Inclusion/exclusion criteria (list)

- **Inclusion:** Patients will be eligible if they have chronic HCV infection, as documented by HCV viremia within 1 year of enrollment in the study *without* evidence of cirrhosis (based on a combination of labs, imaging, and provider notes that are available in the electronic health record). Only patients between the ages of 40 and 60 years will be included.

- **Exclusion:**
  - Renal failure
  - Use of anti-resorptive or anabolic medications for known bone disease
  - Actively receiving treatment for HCV

Method of contact/recruitment: We have identified patients who are potentially eligible for our study through STOR and Apex searches and additional manual electronic health record review. We will then send the patient’s primary care physician an opt-out e-mail informing them that their patient may be eligible for our study and providing them with the opportunity to let us know that they do not want our patient to be contacted. We will then recruit the patient directly either on the phone or by mail.

Benefits/burden for participants:
Subjects may directly benefit from participating in this study by obtaining information
on their BMD. However, there may be no direct benefits to some study participants, although the information gained in this study may serve to benefit the future management of all HCV-infected patients. The potential risks of participating in this study are minimal: 1) risk of radiation exposure from the DXA scan including a potential increased risk of malignancy, 2) risk of infection or bleeding from venipuncture, and 3) accidental breach of privacy. However, the amount of radiation used in a DXA scan is approximately 2.5 microSieverts (µSv, which is significantly less than the average radiation exposure associated with an abdominal X-ray (100 µSv) and the worldwide average annual level of naturally occurring background radiation (2.4 mSv). Blood sampling will be conducted under the usual aseptic techniques. Strict measures, including password-protection of all data and limitation of access to all data to only study personnel, will be taken to minimize the risk of privacy breach.

Any benefits or burden to DGIM practitioners? DGIM practitioners may be burdened if laboratory or DEXA results are abnormal. However, we feel that the tests that are being performed are within reasonable clinical practice.

Timeline for recruitment: July 1, 2011 through June 30, 2013
Funding source: American College of Gastroenterology
Potential for DGIM collaborators? Cindy Lai
Do you agree to notify us when recruitment is completed? Yes
Date form completed: July 14, 2012