

Study name: International Collaboration on Viral Hepatitis

Project number: EOI 1109

Contact:

Brian McMahon

Liver Disease and Hepatitis Program, Alaska Native Tribal Health Consortium and Arctic Investigations Program Centers for Disease Control and Prevention

4315 Diplomacy Drive

Anchorage Alaska

99508

USA

Tel: 907-729-3419

Fax: 907-729-3429

Email: bdm9@cdc.gov

Abstract:

High rates of hepatitis A, B have been found in Alaska, Canada, Greenland and Russia, especially in indigenous populations. In addition, high rates of hepatitis C are seen in Alaska Native Peoples, Canadian indigenous populations and Russians, especially those living in the Arctic regions. Also, co-infection of hepatitis B and D are found in parts of Greenland and Russia. These viral infections have had an adverse effect on the peoples of the Arctic. Although liver disease is the 12th leading cause of death in Americans, it is the 6th leading cause of death in American Indians and Alaska Natives. Similarly in Canada, deaths from liver disease are also the fifth leading cause of deaths in the 45-65 year age group. Chronic viral hepatitis due to hepatitis B and C are believed to be major contributors to liver disease in these populations. Greenland has one of the highest rates of HBV infection in the world and HBV and HCV are felt to be a major health problem in Russia, especially in remote populations. At the ICCH in Novosibirsk in 2006, a Viral Hepatitis Workshop was held and from that meeting, a group of interested researchers and public health workers and administrators formed the Viral Hepatitis Arctic Research Group which has been included as a part of the Infectious Disease Working Group of the International Union for Circumpolar Health. The group has met twice more in Copenhagen in October of 2007 and September of 2008. Collaborative studies have been formed among researchers in the Arctic.

Project Status: Active

Project Progress 2007-2008:

1. Determine the prevalence of active hepatitis B infection in Greenland: The prevalence of HBsAg, the marker for chronic hepatitis B, varies from 8% to 12% in Greenland. To determine what proportion of persons have active liver disease from hepatitis B defined as an ALT level above 40 U/L and an HBV DNA level > 2,000 IU/ml 200 persons who were HBsAg-positive were tested and approximately 15% were found to have met the definition of active liver disease and another 5% had elevated HBV DNA levels but normal ALT levels demonstrating that transmission was ongoing in Greenland and asymptomatic liver disease due to HBV was present.
2. Determine the HBV genotypes present in the Arctic. HBV genotype testing was performed in laboratories in Alaska, Canada, Russia and Denmark. Five HBV genotypes: A2, B6, C, D and F1 were found in Alaska Natives. In Canada, genotypes A, D and B6

- were found. In Greenland, genotypes A, B6 and D were found and in Russia, genotypes A, D and C were found.
3. Characterization of a hepatitis Delta (HDV) outbreak in Greenland in persons, predominantly children with chronic HBV infection. An outbreak of severe acute hepatitis was discovered to be due to HDV superimposed on HBV resulting in severe not fatal hepatitis in several children. Epidemiologic investigations by the Statens Serum Institute and laboratory investigations in Denmark and in Alaska were conducted. A paper for publication is being prepared. This investigation led to the introduction of hepatitis B vaccine into the community to try to stop the epidemic.
 4. Comparison of the sequences between the same HBV genotypes found in Arctic Countries.
 - a. HBV genotype B6. A new subgenotype has been found in Alaska, Canada and Greenland that appears to be less virulent than other HBV genotypes and is related to genotype B1 found in Japan but many centuries distant. These findings were published in the Journal of Infectious Diseases 2007;196:1487-92.
 - b. Comparison of HBV genotype D between Russia, Canada, Alaska and Greenland. A study to compare sequences and disease associations between those infected with HBV genotype D in Alaska, Greenland, Canada and Russia will be performed in laboratories in each of these countries and sequences will be sent to a collaborating laboratory in Nagoya Japan which has software to do sophisticated comparison of HBV sequences. Project has started in 2008 and will be completed in 2009.
 - c. Planning for projects to compare sequences of HBV genotypes C and A found in different Arctic Countries. Plans were drawn up to compare the sequences of HBV genotypes D found in Alaska, Canada, Greenland and Russia; Genotypes A found in Alaska, Greenland and Canada and finally genotype C found in Alaska and Russia in 2009-2010.
 5. Advocacy for the introduction of routine newborn and childhood immunization with hepatitis B vaccine in Greenland. Greenland is the only country endemic for hepatitis B infection where routine vaccination is not done. Routine vaccination is done in Alaska, Canada and Russia. The group passed a resolution to urge the Danish and Greenland governments to implement routine vaccination. In addition, members of the working group from Denmark and Alaska attending a meeting in Copenhagen also pushed for routine immunization to be started.
 6. Studies on Hepatitis C virus (HCV) in the Arctic. A separate subgroup for hepatitis C was organized at the meeting in 2007. The first task is to examine strain differences between HCV in Russia, Alaska and Canada (very low rates of HCV are found in Greenland).

Plans 2009:

1. Continue to determine the prevalence of active hepatitis B infection in Greenland but screening more HBsAg-positive persons for ALT and HBV DNA and determine candidates for antiviral therapy
2. Publish descriptive study of hepatitis Delta/HBV outbreak in Greenland
3. Finish study on comparison of HBV genotype D in the Arctic and draft a manuscript
4. Conduct study on comparison of HBV genotypes A and C in the Arctic.
5. Continue to actively advocate for introduction of hepatitis B vaccine in Greenland until this is done.
6. Expand study of hepatitis B in Arctic.
7. Meet for the fourth time at the ICCH conference in July 2009 in Yellowknife.

Expected Completion Date: Ongoing