

**Minites Viral Hepatitis Arctic Working Group  
Polar Center, Copenhagen  
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**Sponsors:**

**Statens Serum Institut  
WHO/EURO**

**Alaska Native Tribal Health Consortium**

**Arctic Investigations Program, Centers for Disease Control and Prevention**

**International Union and American Society for Circumpolar Health**

**Participants Attending the Circumpolar Hepatitis Meeting in Copenhagen 16-17 October 2007**

**WHO/**

**EURO**

Andrei Lobanov  
Chinara Aidyralieva

[ALO@euro.who.int](mailto:ALO@euro.who.int)  
[c.aidyralieva@who.org.ru](mailto:c.aidyralieva@who.org.ru)

**Russia**

Vladimir Chulanov  
Andrei Tulisov  
Abryutiva Larisa  
Dr. Elena Fast

[Vladimir.chulanov@pCr.ru](mailto:Vladimir.chulanov@pCr.ru)  
[Tandr@NET.RU](mailto:Tandr@NET.RU),  
[Labryut@yandex.ru](mailto:Labryut@yandex.ru)  
c/o Alexander Maslov  
[maslov@chukotnet.ru](mailto:maslov@chukotnet.ru)

**Greenland/  
Scandinavia/**

**Europe**

Karin Ladefoged  
Malene Borresen  
Anders Koch  
Henrik Krarup  
Peter Skinhoj  
Flemming Stenz  
Gert Mulvad  
Mads Melbye

[kala@glr.gl](mailto:kala@glr.gl)  
[MLB@SSI.DK](mailto:MLB@SSI.DK)  
[AKO@SSI.DK](mailto:AKO@SSI.DK)  
[aas.s6mu@nja.dk](mailto:aas.s6mu@nja.dk)  
[peter.skinhoej@rh.regionh.dk](mailto:peter.skinhoej@rh.regionh.dk)  
[FLST@gh.gl](mailto:FLST@gh.gl)  
[GM@gh.gl](mailto:GM@gh.gl)  
[mme@ssi.dk](mailto:mme@ssi.dk)

**Canada:**

Gerald Minuk  
Carla Osiowy  
Isaac Sobol  
Bryce Larke  
Dr. Jun Wu  
Tom Wong  
Andre Corriveau  
John Morse

[gminuk@ccunamitoba.ca](mailto:gminuk@ccunamitoba.ca)  
[Carla\\_osiowy@phac-aspc.ca](mailto:Carla_osiowy@phac-aspc.ca)  
[isobol@gov.nu.ca](mailto:isobol@gov.nu.ca)  
[bryce.larke@gov.yk.ca](mailto:bryce.larke@gov.yk.ca)  
[Jun\\_Wu@hc-sc.gc.ca](mailto:Jun_Wu@hc-sc.gc.ca)  
[tom\\_wong@phac-aspc.gc.ca](mailto:tom_wong@phac-aspc.gc.ca)  
[Andre\\_Corriveau@gov.nt.ca](mailto:Andre_Corriveau@gov.nt.ca)  
[john\\_morse@gov.nt.ca](mailto:john_morse@gov.nt.ca)

**Alaska/USA** Brian McMahon

[bdm9@cdc.gov](mailto:bdm9@cdc.gov)

Michael Bruce  
James Williams  
Jay Wenger  
Tom Hennessy  
Stephanie Bialek  
Chong Gee Teo

[zwa8@cdc.gov](mailto:zwa8@cdc.gov)  
[jwilliam@anthc.org](mailto:jwilliam@anthc.org)  
[jdw2@cdc.gov](mailto:jdw2@cdc.gov)  
[tbh0@cdc.gov](mailto:tbh0@cdc.gov)  
[zqg7@cdc.gov](mailto:zqg7@cdc.gov)  
[enz0@cdc.gov](mailto:enz0@cdc.gov)

The first annual meeting of the Viral Hepatitis Arctic Working Group was held in Novosibirsk in June of 2006. At the end of this meeting it was decided to focus efforts on collaborative research on hepatitis B virus (HBV) and defer projects on other forms of viral hepatitis until later. The second meeting focused on 1) a review of activities in research and public health in Hepatitis B in the Arctic between the 1st and 2nd meeting, 2) progress in collaborative research on hepatitis B accomplished between the 1st and 2nd meeting, 3) plans for collaborative research in hepatitis B for the next year and 4) a preliminary discussion of potential research topics in hepatitis C.

In the first session, Brian McMahon reviewed the practice guidelines that have been published in the past few years on the management of chronic hepatitis B infection. Guidelines have been developed in the the US (AASLD; revised in 2007), Europe (EASL; 2002), Asia-Pacific (APASL; revused 2005) and Canada (CASL; revised 2007). While there are some differences in the guidelines, all guidelines agree that all persons who are chronically HBsAg-positive should be followed every 3-12 months for liver aminotransferase levels (ALT and AST). Persons with elevated ALT levels should be tested for HBV DNA and if  $> 2,000$  IU/ml ( $10^4$  copies/ml), be followed more frequently, considered for liver biopsy and if more than mild inflammation and/or fibrosis is present, evaluated for treatment. In addition, persons  $> 40$  years with high HBV DNA levels and normal ALT/AST levels should have a liver biopsy and evaluated for treatment if inflammation or fibrosis is present. Several effective antiviral agents that can be orally administered easily in remote Arctic areas are licensed plus injectable alpha interferons, which can not easily be used in remote areas. While antiviral resistance and cost remain barriers, treatment programs can be implemented in the Arctic. The working group agreed that these were appropriate recommendations and specific recommendations for the Arctic should be developed.

Factors that are associated with the progression of liver disease in HBV include viral, demographic, co-infection with other viruses and social/environmental. The most important viral factor is HBV genotype. In the Arctic to date, genotypes A, B, C, D and F have been identified. Genotypes C and F appear to have the highest risk of progression and genotypes A and D an intermediated risk. Age over 40 and male sex are demographic risk factors. Co-infection with hepatitis C (HCV), delta hepatitis (HDV) or HIV are associated with increased risk of development of cirrhosis and hepatocellular carcinoma (HCC). Alcohol and non-alcoholic fatty liver disease (NAFLD) may be associated with liver disease progression but more data is needed.

### **Programs for Managing Persons with Chronic HBV Infection in the Arctic:**

#### **Alaska:**

Alaska has had a program to follow all HBV infected persons since 1983. The program is computerized and letters are sent to all 1532 carriers and lists to village and local hospital providers every 6 months. Bloods on carriers are drawn in their respective villages/communities, spun down and sent to a centralized laboratory at the Alaska Native Medical Center (ANMC) for testing. Results are downloaded to the hospital computer and monitored by a physician and RN. Initially only alpha-fetoprotein was performed but since 2001, ALT and AST have been added. Persons >20 years old with elevated ALT/AST levels and HBV DNA > 2,000 IU/ml are brought to Anchorage for liver biopsy and evaluation for treatment. Results to date have shown the half of all carriers in Alaska have had at least one elevated ALT/AST levels in the past 6 years, 20% of those are due to chronic hepatitis B, 30% likely due to alcohol use and 30% to NAFLD with the rest due to a variety of causes. Those with more than mild inflammation and fibrosis have been put on oral antiviral therapy. Resistance to lamivudine has been a problem. Screening for HCC with US has not been possible due to remoteness of villages where most carriers reside. AFP screening, though, has resulted in early detection of ¾ of tumors and dramatically improved 5 and 10-year survival. HBV in Alaska is mainly found in rural residents whereas HCV is primarily found in urban residents. A program for HCV similar to the one for HBV is operated in Alaska to follow over 1,000 HCV infected persons.

### **Nunavut**

Isaac Sobol presented information on Nunavut. There are ~ 30 000 people (85% Inuit) in the region. Almost no programmes exist for chronic HBV although a few patients have been evaluated and treated. There is little knowledge and system capacity to address the population at risk. Problems include infrastructure problems and shortage of physician. Dr. Sobol thought that the Alaskan experience could be implemented.

### **Yukon Territories**

Bryce Larke presented data on Yukon Territories. There are 30,000 people residing in the Yukon and 24% are Indigenous natives. HBV is a reportable disease. Only 19 persons who are chronic carriers, mostly imported cases have been identified and 3 are on antiviral therapy. HBV DNA is performed every 6 months and liver function tests every 3-6 months. Liver US is done every 1-2 years. No liver biopsies have been done for hepatitis B but percutaneous biopsy is indicated for HCV patients.

### **North-West Territories (NWT)**

John Morris presented chronic HBV in NWT. There are 43 000 people in NWT, 50% are indigenous. There is no programme for follow-up of HBV infected persons. Few cases, mainly imported, have been identified. The HBV immunization programme has been a success. There is a high rate found for HCV hepatitis associated mainly with drug abuse and alcohol found.

### **Greenland**

Karin Ladefoged presented information on chronic HBV in Greenland. There are 56,000 people residing in Greenland. Greenland has 18 hospitals. Studies have shown a prevalence of HBV infection of 40-70% and HBV+HDV coinfection is common. Only 3 patients with chronic HBV needing treatment have been identified in 6 years. The incidence of Primary liver cancer is 2.6

per year. Between Jan2005 – Jun2007 89 HBsAg+ cases have been identified. Persons with HDV co-infection are treated with Peg-Interferon. There is almost no IDU in Greenland and < 1% of the population is infected with HCV.

## **Russia:**

Vladimir Chulanov presented data on HBV in the Russian federation. There are 2.5 cases per 100,000 in Russia with chronic HBV at 40 cases per 100,000. Both chronic and acute HBV are greater in Arctic and in some areas the incidence is >200 per 100,000. Inactive carriers are defined as normal ALT is high in some regions. In Yukutia, 32% of cirrhosis is due to HBV and of HBV infected persons 33% are co-infected with delta. The prevalence of HCV is as high as 12% in some areas and the incidence of HCC is 10-15 cases /100,000. The incidence of HAV is >50/100,000 and is higher in areas where outbreaks are occurring.

A Federal Targeted program Viral Hepatitis was begun in 2007. Goals are to provide additional vaccination programs for 25 million persons, provide additional diagnostic equipment and kits as well as antiviral drugs. Initially these programs were only provided for only HCV and HIV and HBV coinfection beginning in 2005, but now in 2007 the goals are strengthening laboratory diagnosis and viral hepatitis surveillance (26 regions will be provided with molecular biology equipment). Research and development and antiviral drugs will be starting in 2009. Drugs currently available for treatment include Interferons (IFN), Lamivudine, Peg- IFN, Entecavir in Oct 2007 and Telbivudine will be added.

Elena Fast presented information from Chukotka where the population is 50,000 people; 90% are indigenous people. The rate of chronic viral hepatitis from all causes peak at 60/100,000 per year in 2002, a rate 3-5 times higher than in Russia in general. There is a 5% prevalence of hepatitis B and C in Chukotka. There is high alcohol abuse in this area. Acute HAV epidemiology has been tracked since 2004 and there was an outbreak in 2005 with an incidence of 3,309 per 100,000 of hepatitis A in one district. Hepatitis A vaccine has been used since 2005

In 1992 hepatitis B vaccination was started with universal immunization of infants. The incidence of acute HBV has fallen to 2-9 cases/year from 10-20/100,000 per year between 2002-2006. Parenteral transmission and IDU rare. Since 2006 16-17 and from 2007 18-32 have been vaccinated and in one year persons up to age 55 years old will be vaccinated. 34% of total population vaccinated. No screening is done prior to vaccination.

Persons with chronic HBV are tested twice yearly. To date, 18 patients have been treated with hepatitis B or hepatitis C. Interferon's have been used in all patients. A computer-based system was begun this year managed by Elena. District doctors send data to her that includes demographic data, type of hepatitis and information on treatment if given. Testing for HBV by PCR is about to be introduced. Drugs are supplied under the national project cited above.

## **Vaccination Programs in the Arctic**

### **Alaska**

Screening pregnant women and administration of HBIG to infants of HBsAg-positive mothers began in 1980 in two hospitals. A vaccine demonstration project was begun in 1981 in 15 villages.

In 1984 hepatitis B vaccination was introduced into all infants beginning at birth. From 1983-1987 a catchup program that resulted in 52,000 Alaska Natives undergoing screening for HBV markers and the vaccination of 40,000 persons. The incidence of acute symptomatic HBV fell from over 200/100,000 in 1981 to 0 in the Yukon-Kuskokwim Delta and < 1/100,000 in the rest of the state in 2005. Long-term studies have shown that HBV vaccine is protective for at least 22 years in children above 1 year of age and adults and 15 years in newborns. Long-term protection studies are planned to continue.

### **Canada:**

In Canada's NWT 95% of children have been vaccinated beginning at 2 months of age with the second and third doses at 4 and 6 months. Passive surveillance programs for acute HBV are in place in Yukon and NWT. Nunavut does not have a surveillance program. Follow-up of vaccination programs have demonstrated that anti-HBs GMT are very good in adolescence. Some areas are considering delaying hepatitis B vaccine until later in life and instead of infant vaccination, developing a school based program and giving HBV vaccine at the same time with human papilloma vaccine which theoretically might give longer protection during adult years. However, the disadvantage could be poorer compliance and failure to prevent transmission in infancy and childhood which could increase the risk of chronic infection and the number of chronic carriers.

### **Greenland**

Flemming Stenz presented the Greenland program. Since 1987, it has been recommended that pregnant women be screened for HBsAg and HBIG and vaccine be administered to infants of positive mothers at birth. Also high risk groups including household and sexual contacts be vaccinated; hospital staff are offered vaccine but not required to be immunized. In 1989 and 1991 universal infant and school entry hepatitis B vaccination was recommended by medical authorities in Greenland but failed to gain political support. Dr. Stenz is currently working on a proposal to add HBV, HPV and pneumococcal vaccine to the childhood immunization program. In 1987 a registry for HBsAg-positive carriers was initiated but those identified have not been followed until recently, when the registry was again initiated.

### **Russia**

Andrei Tulisov presented information on the epidemiology and vaccination program in the Russian North where 12-13 million people live, 7% of the Russian population. Between 1994 and 2006 there has been a drop in the rates of acute HBV and chronic HBV carriage and chronic hepatitis due to vaccination. However the incidence of acute and chronic HCV is increasing. Hepatitis B vaccine is offered to all newborns at months 0, 1 and 6 and the coverage for children is 97 % coverage. The 2006 goal is to decrease incidence of HBV by 3 times and to immunize those above 35 years old. In the future the goal is to provide vaccine coverage for 55% of the population. Future challenges include how to deal with target risk groups such as injecting drug users (IDU), commercial sex workers, sexual contacts of carriers as well as immigrants and seasonal workers from HBV endemic areas.

**An orientation of the Danish Polar Center /DPC) was given.**

## **Current Hep B research in the Arctic**

### **Research in HBV in Arctic Countries:**

#### **Alaska:**

In Alaska, research in HBV has focused on the description of HBV genotypes and their role in disease progression. The five HBV genotypes found in Alaska are A2, B6, C2, D and F1. Genotype F1 has been found to be strongly associated with HCC, especially in young adults and genotype C with HCC in older adults with cirrhosis. Genotype D has been found to be associated with HBV vasculitis. Compared to the other 4 genotypes, genotype C is associated with a much higher mean age of seroconversion from HBeAg to anti-HBe, age 47 years compared to < 20 years for the other 4 genotypes.

#### **Greenland:**

Henrik Krarup reported that the HBV genotypes found in Denmark were predominantly B and D. He performed a survey to determine hepatitis markers and HBV genotypes in a group of elderly Inuits (ages 50-69 years, median 58) from Nuuk and Tasiilaq in Eastern Greenland. None had physical signs of liver disease. The prevalence of HBsAg was 20.4%. The prevalence of any HBV seromarker was 60% in Nuuk and 90% in Tasiilaq and surrounding settlements. Surprisingly, 30 persons were anti-HBs positive only and vaccination had not been used in this area. ALT levels were not done because only AST can be used in frozen material. HBV DNA was positive in 61 persons with a median value of 40,000 copies/ml (range 1,000 to 404,000; 55/56 had Precore mutation G1896A. Genotype B was found in 47 and 5 were infected with genotype D. Approximately 25% of HBV infected persons had  $>10^4$  copies/ml of HBV in their sera. In Denmark HBV genotypes found are genotype D (primarily in Turks), B and C in Asians and A in Africans.

Malene Børresen reported on surveys in a population-based cohort of Inuit from Greenland conducted by SSI, DIH, Nuuk, & Sisimiut Health Center. Blood samples from 6500 persons (1987) and 2500 persons (1998) were tested; 6% were found to have chronic HBV infection and 28% were immune. Nine were HBeAg and 115 were anti-HBe positive. Most had genotype D (60%), the rest were infected by genotypes A and B. She also reported on an HDV outbreak in a hyper-endemic settlement in Greenland south of Sisimiut of 160 inhabitants. In March 2005, 3 patients from the settlement were hospitalized with acute hepatitis. A serosurvey in this settlement showed that 90% had HBV markers with 25% HBsAg-positive, of which 15/31 persons were seropositive for HDV. Elevated ALT levels were found in 70%, with 50% having ALT levels of more than twice upper limits of normal. Of the HBsAg-positive children, 70% of were also HDV-IgG positive. This outbreak appeared to be a superinfection of HDV on chronic HBV as 30% of 15 children HDV experienced seroconversion from March 2006 to 2007 with increased levels of HBV DNA and Delta RNA. Dr. Børresen also reported on a follow up study of children to HBsAg seropositive mothers. Overall in Greenland, 3.4% of 6,000 mothers tested were HBsAg-positive. Only 33% of children born to HBsAg positive mothers received their 4 HBV vaccinations, while every fifth child did not get receive HBV vaccination at all. Thus the strategy in Greenland of vaccination only children of HBsAg-positive mothers is not working, similar to the experience in the US and elsewhere prior to universal HBV infant vaccination.

#### **Canada:**

Gerry Minuk reported he has received an IPY grant to determine:

1. Rate, nature and regional HBV genomic susceptibility to mutations in paired serum samples over a 25 year period
  - a. 60 persons are surviving from the 1983-85 study of HBsAg carriers
2. Prevalence of occult HBV in stored sera derived from community-based, Northern Canadian Population
  - a. 14,198 sera samples from 42 communities all 5 geographical regions of the NWT, ages from 6 month to 95 years, 52% are females
  - b. He believes that occult infection is real and can be in two forms – replication and non-replicative or low-replicative forms.
3. Relative risk of liver-related death in occult HBV, HBsAg positive, resolved HBV and HBV naive patients

Other Project he is planning includes:

- The pathogenesis of HBV-B6 will be investigated in stem cells transfected with genotypes Ba and B6 to examine the viral X region and possible connection to HCC
- Spontaneous HCV clearance appears to be higher in Indigenous persons and may be due to IL 10 suppression during the innate immune response after HCV infection.
- Health care access to HBV and HCV followup and treatment: First Nation compared to other ethnic groups.
- A high rate of autoimmune hepatitis was found in Indigenous people of Canada and vitamin D levels, associated with immune modulating effects, will be investigated in persons with autoimmune hepatitis

*Carla Osiowy* reported preliminary data on the HBV Genotypic characterization of HBsAg positive carriers in the Arctic. Past surveys from 51 communities in Canada with a population of 50% Inuit found that the HBsAg positivity rate was 3% and varied from 0 to 11%. Of 423 HBsAg-positive specimens, 300 are completed; 74% are positive for HBV DNA with range varying from 2 to 6.7 log IU/ml by PCR. Phylogenetic analysis in conjunction with Professor Mizokami's lab in Nagoya Japan showed that all genotype B sequences clustered together into a new, subgenotype B6. In some settlements genotype D was also found. Pre-core G1896A was found in approximately 80% and basal core promoter was present in 40%, always associated with pre-core mutation.

Further discussion future studies on genotype B6 was conducted and all agreed to pool their HBV genotype B6 samples. One suggestion was to ask Professor Mizokami to examine all B6 samples from the Arctic using his molecular clock technique.

### **Russia:**

Vladimir Chulanov revealed that the distribution of HBV genotypes in Yakutsk found were 50% genotype D, 47% with genotype A and the rest genotype C. HBV genotype D predominates in the rest of the Russian Federation. The subtype of genotype A is A2 with no clustering and the subtypes of genotype D are D1, D2 and D3 with no definite clustering. In Alaska only D1 and D2 were found with no D3 found. Co-infection with HDV (Delta) was commonly found. In Yakutsk 50% Of HDV is genotype I and 50 % genotype II. In the rest of Russia only HDV genotype I is found. Genotype II is unique in the Indigenous population in Yakutsk. There are approximately 1500 Siberian

Eskimos in Chakutka. A possible survey would be to conduct a serosurvey of the Siberian Eskimos to see if HBV genotype B6 is found.

Regarding HAV, Genotypes: IIIa is the most prevalent (65%) found in Yakutsk as in Kurdistan and Kirgizstan. In the rest of Russia the HAV genotype found was genotype Ia.

## **Conducting research in remote communities: Logistics problems, Motivating Community providers and residents to participate, IRB and Ethical Concerns**

### **Research in Greenland:**

Anders Koch reported that each person in Denmark and Greenland has a unique personal registration number. For research studies informed consent is required and approval from KVUG – Committee of ethical research projects in Greenland, as well as acceptance from the local hospital. Information regarding the study is supplied to local authorities. For studies using the Country wide Registry, consent is not required. Methods used for recruiting persons for studies include television, radio, posters and newspaper ads. Communicating results of studies are very important. Communication back to the community is in the form of a letter. Reporting back at individual level is required if the results have any consequences for the participant. Publication of findings in International journals is usually sought. Logistical problems include travel to remote communities, weather and cost. Most towns have basic diagnostic and laboratory facilities. It is important to maintain goodwill with the local hospital and staff.

### **Alaska**

Mike Bruce reported on Alaska. The first question asked in regards to a research project: Is this project something the tribal board is interested in. Meeting with the local Tribal Health Board is usually done even before the protocol has been written. Once written, the protocol is sent to the CDC IRB and the Alaska Native Area IRB if Indigenous people are involved. This process of approval can take over 6 months. Afterwards approval from tribal council approval is sought. Thereafter consent from the patient both to be included in the study and a second consent to have blood stored in blood banks, otherwise sera must be disposed of when the study is complete. To communicate the results back to the patient, usually a letter with a summary of the findings is sent back to the participants. Other ways of communicating results include posters, newsletters etc.

### **Canada**

Bryce Larke discussed obstacles to research in the Canadian Arctic.

Around CANADA there are different specific “rules” involving research. Usually, if no blood is drawn research can be done without consent. A major problem is access to “aboriginal” settlements. Sometimes it is difficult to differentiate between “Research vs. public health” For recruitment, advertisements, posters and other means are utilized.

Isaac Sobol stated that there are no local ethic boards in Nunavut. So if the central IRB has accepted a protocol, the local authorities will defer to the Central Board.

### **Russia:**



In Russia, any human research requires ethical approval. Approval authority rests with the local committee, where the researchers are located. Thereafter Indigenous people associations are the organizations contacted for approval authority in their regions. Logistical difficulties in conducting research in the Russian Arctic include: high costs, sample collection and transport (only one company is licensed to transport human materials), delays due to weather, lack of local qualified staff, and lack of statistical data on Indigenous people in Russia. Finally the relevance as well practical outcome for those who participate is important.

## **Collaborative projects**

The most important part of this meeting was to select and design collaborative research projects that would involve all countries in the Arctic. It was stressed that the members of Viral Hepatitis Arctic Working group are the ones who will decide which projects to develop, which groups will conduct the specific parts of each project and what individuals will draft the manuscripts for publication. The following collaborative research projects were developed by this Working Group.

### 1) Characterization of HBV genotype B6:

HBV genotype B6 appears to be a unique HBV genotype that has only been found in the Arctic regions of Greenland, Canada and Alaska. It is also possible that this genotype might be found in Russia but surveys of indigenous populations such as Siberian Eskimos, who are close to Alaska, need to be done first in order to determine this.

Members who volunteered or were nominated to be part of this project include:

- Alaska: Brian McMahan and Carol Jones
- Canada: Carla Osioya and Gerry Minuk
- Greenland: Henrik Krarup, Malene Børresen and Anders Koch
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Specific aims of the project could be

- Long-term follow up of patients infected with B6 to determine clinical outcome
- Molecular studies: Full genetic sequencing of B6 strains from different regions of each country to identify specific mutations and sequence differences.
- Examination of serial specimens from Greenland, Canada and Alaska to determine the rate of mutations in B6

### 2) Examination of Genotypes A and D in Russia, Greenland, Canada (D only?) and Alaska.

Progression of chronic HBV and rate of mutations

- Hypothesis: Differences in the core and X genes that explain the different outcomes in these genotypes other than B6. Are there specific core gene changes that allow HBV to evade immune system and is there stability to mutations in the X gene so that B6 is less likely to be carcinogenic.
- Phylogenetic analysis of genotypes A and D from all regions of the Arctic
- Clinical outcome of persons infected with genotype A or D (and in Alaska also C and F) compared to those infected with HBV genotype B6.

Members who volunteered or were nominated to be part of this project include:

- Alaska: Brian McMahon and Carol Jones
- Canada: Carla Osioya and Gerry Minuk
- Greenland: Henrik Krarup, Malene Børresen and Anders Koch
- Russia: Vladimir Chulanov, Elena Fast

### 3) Clinical outcome and HBV genotypes in the Arctic

- Determine the age specific prevalence and incidence of chronic liver disease due to chronic hepatitis B defined by the presence of elevated DNA  $>10^4$  (2,000 IU/ml) plus an elevated ALT level for each HBV genotype
- Determine prevalence and incidence of HBV related Cirrhosis defined by clinical liver decompensation (ascites, oesophageal varices, hepatic encephalopathy, coagulopathy or platelet count below 100,000) or liver biopsy )
- Determine the prevalence and incidence of HCC in HBsAg infected persons
- Determine the incidence of liver related death in HBsAg-positive persons
- Determine the number of patients put on antiviral therapy each year.
- Determine long-term outcome in healthy persons in the inactive HBV phase: HBsAg positive, DNA  $<10^4$  copies/ml ( $<2,000$  IU/ml) and normal ALT
- Determine the effect of confounders in the incidence and prevalence of active liver disease in HBV: Alcohol, BMI, diabetes, hyperlipidemia, co-infection with HBC, HDV or HIV

Members who volunteered or were nominated to be part of this project include:

- Alaska: Brian McMahon, Jim Williams, Mike Bruce, Tom Hennessy
- Canada: Gerry Minuk, John Morris, Isaac Sobol
- Greenland: Anders Koch, Karin Ladefoged
- Russia: Vladimir Chulanov, Elena Fast, Andrei Tulisov

### 4) Study of Delta agent (HDV) in Greenland and Russia

- Determine molecular sequencing and genotypes in regions in Russia and Greenland
- Determine clinical outcome of HBV-HDV co-infection

Members who volunteered or were nominated to be part of this project include:

- Greenland: Henrik Krarup, Karin Malene Børresen and Anders Koch
- Russia: Vladimir Chulanov, Elena Fast

- For molecular studies, Henrik Krarup volunteered to do the HDV genotyping for Greenland and Vladimir Chulanov agreed to do sequencing for both Russia and Greenland in addition to genotyping for Russia.

### 5) Development of a Common prospective database for HBV in the Arctic:

- There was an agreement on developing common minimum information for HBV clinical databases for the Arctic

- Each country and region would keep their own database which would include the minimum information agreed upon and any other information the individual centers would want to have for the own usage.
- Information collected would include:
  - Clinical and Laboratory data
  - Treatment database
    - Medications used
    - Resistance patterns
    - Outcome responses
- Each country and region would keep their own stored sera and tissue.
- Which information would be shared would be agreed upon by the entire group and any shared information would have identifiers removed to insure patient privacy.

Members who volunteered or were nominated to be part of this project include:

- Greenland: Karin Ladefoged and Anders Koch
- Russia: Vladimir Chulanov, Elena Fast. Andrei Tulisov
- Canada: John Morris and Isaac Sobol
- Alaska: Brian McMahan, Jim Williams, Tom Hennessy and Michael Bruce

Tasks to be done:

- Gerry Minuk will disseminates a draft of treatment guidelines for review
  - Brian M. Karin Ladefoged, Andrei Tulisov/Vladimir Chulanov, John Morris and Elena Fast will send around copies of what information they collect and will coordinate the development of which information will be collected by all sites.
  - Data input and registration of participants will depend on the individual country and region:
    - In Canada nurses perform data input
    - In Greenland data input is centralized
    - In Alaska data input is computerized and centralized.
    - In Chakutka, data input is done by Elena Fast
- Carla Osiowy is willing to test for drug resistance on sera from any country

## **Other Topics Discussed**

### **Endorsement for Universal Vaccination against Hepatitis B in Greenland**

- The group endorsed its support for Flemming Stenz in his effort to urge the authorities from Greenland and Denmark to introduce universal infant vaccination for hepatitis B in Greenland. WHO/Euro also added its support and Chinara Aidyralieva noted that the cost of the vaccine for WHO was approximately 30 cents US/dose and could be purchased for under \$1 per dose in most countries.

## **Website for the Viral Hepatitis Arctic Working Group**

The group endorsed the development of a website. Anders Koch, Jay Wegner, Tom Hennessy, Mike Bruce and Andrei Tulisov will explore possibilities for a website and how to develop and implement it.

#### **Next meeting of the Viral Hepatitis Arctic Working Group:**

The group agreed on to hold the next meeting in Copenhagen in September or early October. On October 20-22 the National Institutes of Health will hold a Consensus Conference on Hepatitis B in Washington DC. It was agreed the Working Group meeting should be at least 2 weeks prior to this meeting as some members were planning to attend. The group also endorsed having the 2009 meeting in Yellowknife NWT to be held in conjunction with the International Congress for Circumpolar Health.

#### **New Chair and Co-Chair for the Viral Hepatitis Arctic Working Group:**

The group unanimously endorsed Anders Koch to be chair for the next year and Carla Osiowy and Gerry Minuk would be co-chairs.

#### **Financial Support for the Meeting in 2008:**

CDC and WHO will be asked again to help with financial support. Drug company support was discussed, but the general consensus was that pharmaceutical support not be sought due to possible conflicts of interest. However, the group agreed that individual participants could ask local companies to support their individual participation in the meeting.

#### **Other Hepatitis Virus**

Tom Wong and Mike Bruce chaired this session. Several members of the group wanted to expand to other viral hepatitis diseases besides hepatitis B and D. The group felt that hepatitis C was the next disease to expand to, although there was discussion of adding hepatitis A in the future, especially regarding HAV genotype studies.

HCV is a major problem in Canada. In NWT Andrei Corriveau stated that there are more cases appearing in younger age groups, in women and from prisons. In Nunavut a community study found a 0.25% seroprevalence suggesting that it may not be as big of a problem there. Gerry Minuk reported on an interesting finding of a higher rate of spontaneous clearance of HCV in aboriginals. He speculated that this may represent a new 7<sup>th</sup> genotype of HCV. In Alaska a study is following 1000 HCV positive Alaska Native persons with 7 years of prospective and 17 years retrospective follow-up thus far; 100 have developed decompensated cirrhosis and 22 HCC or a total of 12% developing serious complications from HCV. A poor outcome has been found in HCV patients in Alaska with diabetes. The heavy use of alcohol is the dominant the factor associated with death from liver disease found in HCV positive persons in Alaska. A study on the immunology of HCV in Alaska is underway. In Greenland there is only a 1% seroprevalence of HCV likely due to little IV drug use there. In Russia, HCV is a big problem but few epidemiologic studies have been done to outline the extent of the problem.

Possible studies in HCV for the future could include:

- Studies to determine why do some people choose treatment while others do not
- Short term treatment studies using new antiviral agents compared with standard treatment
- Studies on patient and community awareness of viral hepatitis. Develop parallel studies in the different Arctic countries
  - HCV vs. HCV in both indigenous/non-indigenous people
  - HBV among indigenous people

Mike Bruce and Tom Wong will develop an agenda on hepatitis C for the next Working Group meeting in 2008.