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This edition of *Viral Hepatitis* is based on material presented at the Viral Hepatitis Prevention Board meeting on **Burden and Prevention of Viral Hepatitis in the Arctic Region** - Copenhagen, Denmark. March 22-23, 2012.

Editorial

This issue of *Viral Hepatitis* reviews topics covered at the VHPB's spring meeting held on March 22-23, 2012 in Copenhagen, Denmark. The main objectives of the meeting were to provide an overview of surveillance systems for viral hepatitis and review the epidemiological situation across the Arctic region, with particular focus on differences between indigenous and non-indigenous populations. The current prevention and control measures across the Arctic and sub-Arctic region were discussed, and the progress that has been made was highlighted. Future implementation of new prevention strategies, control measures and monitoring systems was explored. In addition, opportunities for further collaboration between countries in the Arctic were identified.

The Arctic and sub-Arctic region (territories above 60°N) is a very large area with very low population densities and remote communities, mostly with poor communications and road infrastructure, and extreme weather conditions. Socioeconomic living conditions are often poor and life expectancy is generally lower than in other populations. The region is populated by numerous diverse indigenous groups (e.g., Alaskan Natives, First Nations, Inuit, and Sámi), where traditional medicine often has a role in health care. In some of these indigenous communities, higher rates than the national average have been found for some infectious diseases.

There is a wide range of health care services, from tertiary care centres (with costly transport to centralized facilities) to community health centres. This variety in health care systems is related to population densities, involving different kinds of medical professionals and educational means, supplemented with programmes for village health practitioners, nurse practitioners, and other primary health care workers. The use of telemedicine tools, which is key in the area, is well established in some regions.

Epidemiological data were presented by country/region for hepatitis virus A (HAV), B (HBV) and C (HCV), and - when available - for hepatitis virus D (HDV) and E (HEV). The quality of collected data could be further improved in some Arctic regions by addressing the issue of under-reporting. Furthermore, harmonizing case definitions, and standardizing other surveillance parameters would facilitate comparison of data.

In many Arctic regions, HAV has become rare due to successful vaccination programmes coupled with improved water and sanitation, as well as preventive measures; but travellers to endemic areas still need vaccination.

Routine HBV vaccination has dramatically reduced HBV rates in several regions, such as Alaska, Canada, and the Russian Federation. Greenland is still a high endemic region where horizontal HBV transmission is a problem, indicating that the risk group vaccination approach has not been effective. However, after recently implementing routine HBV vaccination (in 2011), the possibly changing HBV epidemiology in Greenland deserves further evaluation.

High prevalences of HCV continue to be seen in the Arctic region and are linked to recent increases in drug use, mainly among the young population. The outcome of HCV disease is worsened by alcohol abuse.

HDV and HEV are not reportable in the Arctic region. HDV has been reported as a major contributing factor in liver cirrhosis in the Russian Federation. In Greenland, HBV/HDV co-infection, resulting in severe disease, is a concern; it is hoped that the recent introduction of universal HBV vaccination will improve this situation. Possibly due to infrequent testing, only a few cases of HEV (mainly imported) have been recorded across the Arctic Region.

Most countries in the Arctic region are confronted with similar challenges: enormous distances; extreme temperatures; low population densities in rural areas; logistical problems; high cost of transport; and patients in remote areas. Such challenges often demand creative solutions. Therefore international cooperation in the Arctic Region, such as the International Union for Circumpolar Health, International Circumpolar Surveillance (project under the Arctic Council) and EpiNorth network project, is important.

Brian McMahon and Hans Blystad on behalf of the Viral Hepatitis Prevention Board

VIRAL HEPATITIS PREVENTION BOARD**Advisers**

Dr Selim Badur
Microbiology Department, University of Istanbul, Turkey

Dr Hans Blystad
Norwegian Institute of Public Health, Oslo, Norway

Dr Paolo Bonanni
Public Health Department, University of Florence, Italy

Dr David Goldberg
Health Protection Scotland, Glasgow, Scotland

Dr Angela Dominguez
Department of Public Health, University of Barcelona, Spain

Dr Nedret Emiroglu
WHO Regional Office for Europe / EPI, WHO Copenhagen, Denmark

Dr Johannes Hallauer
Department of Health, Sozialministerium, Schwerin, Germany

Dr Wolfgang Jilg
Institute for Medical Microbiology and Hygiene
University of Regensburg, Germany

Dr Mira Kojouharova
Department Epidemiology and CD Surveillance
National Centre of Infectious and Parasitic Diseases, Sofia, Bulgaria

Dr H lene Norder
Department of Virology
Swedish Institute for Infectious Disease Control, Solna, Sweden

Dr Vassiliki Papaevangelou
Department of Pediatrics, University of Athens, Greece

Ms Tatjana Reic
European Liver Patients Association, ELPA

Dr Fran oise Roudot-Thoraval
Public Health, H pital Henri Mondor, Cr teil, France

Dr Daniel Shouval
Liver Unit, Hadassah University Hospital, Jerusalem, Israel

Dr Rui Tato Marinho
Liver Unit, University Hospital Santa Maria, Lisbon, Portugal

Dr Marita Van de Laar
European Centre for Disease Prevention and Control (ECDC),
Stockholm, Sweden

Dr Koen Van Herck
Centre for the Evaluation of Vaccination, Vaccine and Infectious Disease Institute, University of Antwerpen, Belgium

Dr John Ward
Liaison adviser, Division of Viral Hepatitis at
NCID, CDC, Atlanta, Georgia, USA

Dr Stefan Wiktor
Liaison adviser, Team lead, Global Hepatitis Programme
WHO, Geneva, Switzerland

Dr Alessandro Zanetti
Department of Public Health, Microbiology, Virology,
University of Milano, Italy

Honorary Advisers

Dr Pietro Crovari

Dr Alain Goudeau

Dr Peter Grob

Dr Nicole Gu rin

Dr Daniel Lavanchy

Dr Harold Margolis

Dr Mark Kane

Dr Eric Mast

Dr Elisabeth McCloy

Dr Andr  Meheus

Dr Colette Roure

Dr Craig Shapiro

Dr Steven Wiersma

Executive Secretary

Dr Pierre Van Damme
Centre for the Evaluation of Vaccination, Vaccine and
Infectious Disease Institute, University of Antwerpen, Belgium

Executive Secretariat

Ms Emmy Engelen

Ms Tinne Lernout

Ms Greet Hendrickx

Mr Alex Vorsters

Centre for the Evaluation of Vaccination, Vaccine and
Infectious Disease Institute, University of Antwerpen, Belgium

Rapporteur

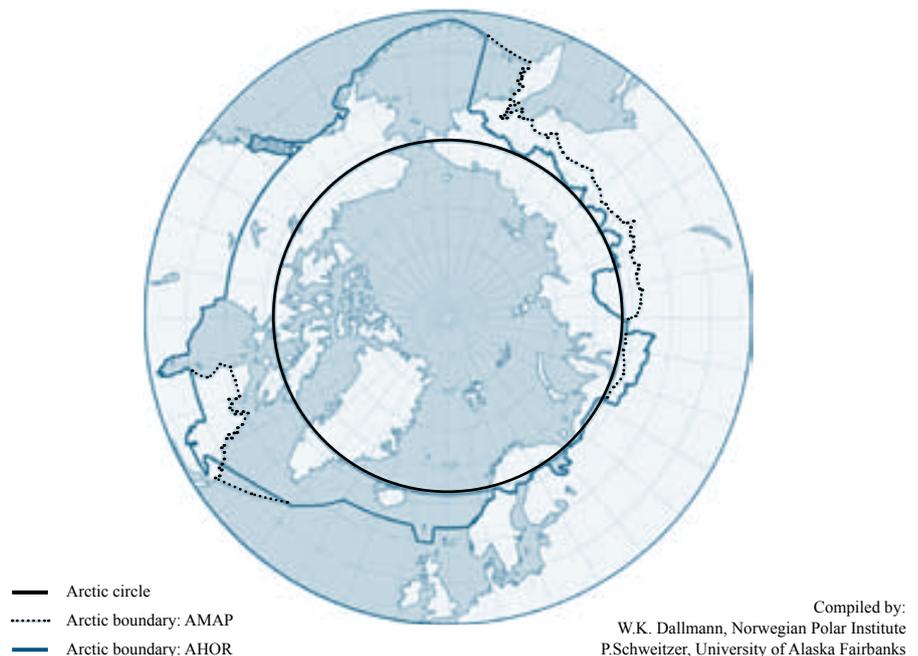
Mr David FitzSimons - Pr vessin, France

BURDEN AND PREVENTION OF VIRAL HEPATITIS IN THE ARCTIC REGION

Copenhagen, Denmark, March 22-23, 2012

General Introduction

The Arctic region includes territories north of the Arctic Circle (66 N) and the sub-Arctic territories above 60 N, bordering the Arctic Ocean, and all or northern parts of Canada, the USA (Alaska), Greenland, Iceland, Norway, Finland, Sweden, and the Russian Federation. For the purposes of studying populations, the Arctic can be defined as the administrative regions outlined in blue on the Figure below.

Map of the Arctic regions

Compiled by:
W.K. Dallmann, Norwegian Polar Institute
P.Schweitzer, University of Alaska Fairbanks

Source: Arctic Human Development Report, Stefansson Arctic Institute (www.svs.is)

The Arctic is home to 4 million people, half of whom reside in the Northern Russian Federation. Alaska, Canada, and Greenland contain approximately 45% of the total circumpolar land mass of the Arctic region, with human population densities in this region averaging fewer than one person per square km. Approximately 1 person in 10 is of indigenous ancestry.

The indigenous populations of Canada, Alaska and Greenland generally reside in remote isolated communities. They have little economic infrastructure and are still largely dependent on subsistence harvesting of wildlife resources for a significant proportion of their diet. In these remote regions, access to public health and acute care systems is often limited. Living conditions can be challenging, the climate is cold and housing is often sub-standard (in Western Alaska, 25% of homes do not have running water), with poor sanitation.

In general, the health and life expectancy of indigenous populations of Arctic regions has improved over the last 50 years. The increase in life expectancy can be attributed, not only to successful vaccination and education programmes, but also to the introduction of safe water supplies, sewage disposal, development of community-based medical providers, and improved health care and access to care.

Despite improvements, life expectancy is shorter and infant mortality rates are still higher among indigenous Arctic populations in Alaska, Northern Canada, and Greenland, than for Arctic residents of Nordic countries. Alaska Natives also have higher mortality rates following injury, often

related to hunting and increasingly to alcohol abuse (3.3 times the US rate); suicide (4.2 times the US rate); cancer (1.5 times the US rate); and higher rates of some infectious diseases, including hepatitis.

Other challenges to health in the Arctic region include the impact of rapid economic development, environmental contaminants, and climate change. These challenges pose serious threats to food and water security of many Arctic communities. Reduction in the traditional food supply and access to safe water will force many communities to depend increasingly on non-traditional foods, often less healthy western processed foods, leading to increasing rates of obesity, diabetes, cardiovascular diseases, and outbreaks of food-borne infectious diseases associated with fresh and processed foods.

There is cooperation between several organizations that focus on circumpolar health including:

- International Union for Circumpolar Health - a union of 5 circumpolar health organizations that has 13 working groups, and publishes the International Journal of Circumpolar Health (www.iuch.net).
- International Network for Circumpolar Health Research - includes several indigenous populations' organizations and regional health authorities, and encourages international collaboration on health research (www.inchr.com).
- Northern Dimension Partnership in Public Health and Social Well-being - includes 13 European countries and Canada and mainly focuses on implementing health programmes (www.ndphs.org).
- Barents Euro-Arctic Council - interests include tuberculosis (TB) prevention (www.beac.st).

- Northern Forum - involves governors from the Arctic countries (www.northernforum.org).
- Arctic Council - a ministerial forum which promotes co-operation between the 8 Arctic regions on a number of issues. Two of its 5 working groups focus on health issues (www.arctic-council.org).

Surveillance in the 8 Arctic nations was needed due to concerns over health disparities, in particular for infectious diseases. It is facilitated by well-established public health infrastructures in the Arctic region, including government and non-government health cooperatives and existing health surveillance systems. International Circumpolar Surveillance (ICS) was established in 1999 originally to investigate *Streptococcus pneumoniae* in Alaska and Northern Canada. Greenland joined in 2000; Iceland, Norway, Finland and Sweden in 2001; and the Russian Federation joined in 2011. The ICS provides standardized laboratory and epidemiologic data on invasive bacterial diseases, and identifies research needs and priorities in the region. At present, surveillance programmes include invasive bacterial disease and TB.

In addition to surveillance, the Arctic Council has working groups focused on research programmes, including *Helicobacter pylori*, sexually transmitted infections, climate sensitive infectious diseases, and viral hepatitis. The purpose of the Arctic Viral Hepatitis Working Group is to exchange information on research and public health programmes within the Arctic region and to conduct collaborative research and public health projects.

Based on a presentation by

A. Parkinson, Centers for Disease Control and Prevention, Anchorage, Alaska.

Health care systems in the Arctic region

Greenland

The ice sheet covers 85% of the total area of Greenland, therefore the population is small (56,000-57,000 people). Inuit account for 90% of the population and the remaining 10% are Danish or other nationalities. The centre of the West Greenland coast is most densely populated. Most people live in the 16 towns, of which Nuuk is the largest (16,000 people). Greenland was a Danish colony until 1953. In 1979, Greenland was granted Home Rule and became responsible for their own health care system in 1992. Greenland became self-governing in 2009, which meant that Greenlanders were recognized as an independent population.

It is not easy to run a healthcare system in Greenland, since towns are not connected by roads. Part of the local passenger transport within Greenland is by ship, but most people travel by air. Of the total budget for health care in Greenland, 7% is used just for transporting patients. For some specialist treatments, patients are transported to Copenhagen. Residents of Greenland receive free treatment (except travel-related vaccination), free medicines (except for non-prescription drugs), free physiotherapy, and free basic dental care.

Greenland is divided into 5 large health regions, each with regional hospitals and health centres. The rest of the cities have a health cen-

tre with at least one doctor, a number of beds and limited laboratory testing. The main hospital is Queen Ingrid's hospital in Nuuk where most laboratory testing takes place (liver biochemistry, HBV surface antigen [HBsAg], HBV "e" antigen [HBeAg], anti-HBs and anti-HBe antibodies). Testing for HBV DNA, HAV, HCV, and HDV is done at either Statens Serum Institut or Ålborg University Hospital, Denmark. Each settlement has a health care station staffed by a nurse or health assistant in the larger settlements, and by a local person with basic training in the smaller settlements. The regional hospitals, health centres, and the clinics of the larger settlements can all communicate patient consultations to specialists at Queen Ingrid's hospital or to the local regional hospitals/health center via telemedicine.

Based on presentations by

*F.K. Stenz, National Board of Health, Nuuk, Greenland;
K. Ladefoged, Queen Ingrid's Hospital, Nuuk, Greenland.*

The Canadian Arctic

The Arctic regions of Canada are geographically vast (half the total area of Canada), but sparsely populated (0.02–0.07 people/km²). The distribution of ethnic groups is shown in the Table on the next page. There is little interchange and integration between Inuit/Inuvialuit and First Nations/Dene.

Population of Canadian Arctic regions by ethnic group

Region	Population	Accessibility	First Nations, Dene or Innu	Inuit Inuvialuit	Metis	Non- Aboriginal
Nunavut	33,330 people (26 communities)	All communities dependent on air travel to access the south	-	80%	-	20%
Northwest Territories	43,485 people (33 communities)	Most communities dependent on air travel. Some communities accessible by road links that cross rivers; when rivers freeze up or thaw, the communities are only accessed by air	28%	11%	9%	52%
Yukon	34,891 people (16 communities)	All but 1 community is easily accessed by road	24%	-	76%	-
Nunavik	11,627 people (14 communities)	All communities dependent on air travel	-	90%	-	10%
Nunatsiavut (Labrador north coast)	2414 people (5 communities)	All communities dependent on air travel	5%	95%	-	-

Although federal government sets regulatory standards, health is primarily a provincial and territorial responsibility, including the administration of vaccination programmes, surveillance, and treatment. The Canada Health Act ensures that all Canadians have access to insured health care, regardless of their ability to pay. It is expensive to maintain this level of care in very remote regions, which rely on air evacuation of patients. The average health care costs for a person from Nunavut are nearly \$11,500 per year, which is twice the Canadian average [1].

Reference

[1] Canadian Institute for Health Information. *National Health Expenditure Trends, 1975–2008*. ISBN 978-1-55465-424-6 (www.cihi.ca, accessed 29 April 2013).

Based on a presentation by

B. Larke, Provincial Laboratory for Public Health, Edmonton, Alberta, Canada.

Alaska

In Alaska, the largest US state, around 710,231 people live in 200 communities. About half the residents of Alaska live in the Anchorage Metropolitan area. According to the 2010 US census, 19.1% of the population are Alaska Native/American Indian.

A fragmented health care system exists for the residents of Alaska, comprising: private practice; the Alaska Native Tribal Health Care statewide system (available to all resident Alaska Natives); the Veterans Administration programme (3 clinics cover 30,000 military veterans); and health care provision for those without health cover (>100,000 people).

The Alaska Native Tribal Health Care System has a village clinic in each community staffed by a community health practitioner (who follows a 16-week training period and exam) and/or mid-level practitioners. From these clinics, patients may be referred to the regional tribal hospitals. Besides these well-equipped regional hospitals, tertiary care for a large geographic area is provided by the Alaska Native Medical Center (ANMC) hospital in Anchorage, which also provides primary care for Anchorage residents.

Based on a presentation by

B. McMahon, Alaska Native Medical Center, Anchorage, Alaska.

Sámi population

The indigenous Sámi population includes: ~40,000 people in Norway; ~18,000 people in Sweden; ~7500 people in Finland; and

~2000 people in the Russian Federation. Sámi people are not recorded as a specific population group for infectious diseases and there is no register of Sámi people. However, there is an assembly of Sámi people, where they can voluntarily register. There are no specific infectious disease problems in the Sámi population.

Based on a presentation by

H. Blystad, Norwegian Institute of Public Health, Oslo, Norway.

The Nordic Arctic

About 80% of the funding for the Nordic health care system comes from public sources; however, the contribution made by the private sector is increasing (but not in the field of infectious diseases). All the Nordic countries have increased patient co-payments during the 1990s. The amounts of resources devoted to health care are about the same in the five Nordic countries (Denmark, Finland, Norway, Sweden and Iceland) when measured by the proportion of GDP devoted to health care, or by hospital beds or doctor/patient ratios.

Iceland

The area of Iceland is ~1000 km², and it has a population of 319,000. The population is young, with 88% under the age of 65 years. Most inhabitants live along the coast, as most of the inland area is uninhabitable. Central government provides most health care services. In 2010, 9% of Iceland's GDP was spent on health care (similar to other Nordic countries). There are 58 health care centres, 3 main hospitals (the largest is the University hospital in Reykjavik), and 17 other small institutions around the country. Hospitals and primary care, delivered by health care centres, are owned and run by the state. The cost of primary care provision is largely covered by the state, with patients only making minimal contributions. Specialists outside hospitals are private practitioners paid by patients and the state. Dentists, most nursing homes, and rehabilitation clinics are private. The health care system is comprehensive, covering all inhabitants.

Sweden

Regional government (county councils) is responsible for health care provision in Sweden. The county of Norrbotten in the North of Sweden is 25% of Sweden's total land area. The population in Norrbotten represents 3% of the Swedish population and contains 9.2% immigrants.

Although the definition of Sámi is not always clear, it is estimated that there are about 18,000 Sámi people in Norrbotten County. Compared to other native populations, the prevalence of infectious diseases appears to be low among the Sámi population [1]. There appears

to have been only one case of viral hepatitis (HCV) from 2002-2011. Intravenous drug use (IDU) amongst the Sámi population is low.

Norway

Norway is the second least densely populated country in Europe (~15 persons/km²). Central government determines health policy, but health care provision is the responsibility of the 4 health regions and the municipalities. The three counties north of the Arctic Circle constitute around 10% of the population in Norway. The Sámi people constitute around 1% of the Norwegian population. Most Sámi people live in the Arctic area. The largest Arctic island, Svalbard, has no indigenous people, but has a special status that allows settlers to make their homes there without permission. This makes the island attractive to asylum seekers, which could lead to an increase of the overall viral hepatitis disease burden in the future. The population of 4000 is mainly Norwegians, Russians and Ukrainians.

Finland

The population of Finland is around 5.4 million (16 people/km²). The region in northern Finland where Sámi people live, has an area of 86,000 km², with a low population density (~120,000 people).

In Finland, over 95% of the hospitals; the majority of outpatient services; and above 90% of clinical microbiology examinations are in the public sector. All primary health care responsibilities are managed at a municipal level. There are 183 municipalities and their populations range from 500–560,000 inhabitants. These municipalities form 20 health care districts and there is also a district for the Åland Islands; district populations vary from 50,000–1,500,000. Each health care district has hospitals providing specialist care (5 are university hospitals) and the main hospital in Northern Finland is in Rovaniemi.

Reference

- [1] Hassler S. *The health condition in the Sami population of Sweden, 1961-2002: causes of death and incidences of cancer and cardiovascular diseases*. PhD thesis, 2005, Umeå University, Sweden. ISBN 91-7305-869-6 (<http://urn.kb.se/resolve?urn=urn:nbn:se:umu:diva-519>, accessed 29 April 2013).

Based on presentations by

- H. Blystad, Norwegian Institute of Public Health, Oslo, Norway;
T. Gudnason, Directorate of Health, Reykjavik, Iceland;
A. Nystedt, Norrbotten County Council, Luleå, Sweden;
M. Kuusi, National Institute for Health and Welfare, Helsinki, Finland.

The Russian Arctic

The Russian Arctic comprises all the regions that are totally or partially within the Arctic Circle. The total population of the Russian Arctic region is 9339 (6.5% of the total Russian population ~143,000,000).

A mixture of private and state-financed provision of health care exists, but state provision predominates and, legally, every citizen is entitled to free health care. The system is organized at a regional level and, in addition to hospitals, there are rural health posts providing basic health facilities for about 4000 people (including vaccinations); health centres cover rural populations up to 7000 people with a range of primary care services; and urban polyclinics provide screening, in addition to general practice services.

Based on a presentation by

- A. Tulisov, UNICEF, Arkhangelsk, Russia.

Overview Table 1: Health care systems in the Arctic region

Country	Total population (Arctic/sub-Arctic)	Area (km ²)	Indigenous population	Health care (private, public – free or paid)	Decision level
Alaska	710,000	1.72 million	Alaska natives (Inupiat, Yupik, others)	Public/private Free/paid	-
Canada	150,000	4.99 million (50% of total Canadian area)	First Nations, Dene, Innu, Inuit+Inuvialuit, Metis	Public (Canada Health Act) - free	Provincial and territorial (although federal government sets standards)
Greenland	56,500	2.18 million (85% covered by ice)	Inuit (90% of total population)	Public - free treatment (except travel-related vaccination), free medicines (except for non-prescription drugs), free physiotherapy, and free basic dental care	National (Government of Greenland since 2009)
Iceland	319,000	103,000	Public Free (except minimal contribution for primary care)	Ministry of Health and Welfare	-
Russia	9,339,000	10.4 million (10 regions above or around Arctic circle)	Sámi, Nenets, Komi, Yakuts, Khanty, Evens, Sakha, Chukchi, others	Public/private	Regional level
Nordic countries	-	Homeland of Sámi people covers about 389,000 km ² of the Nordic countries and part of the Russian federation	-	Public (±80% Nordic health care centre)/ private	-
Finland	120,000	About 100,000	Sámi	Public/private	Municipal/ regional
Norway	470,000 (10% total population)	-	Sámi	-	Central government
Sweden	248,545	-	Sámi	-	Regional government

Viral hepatitis surveillance in the Arctic region

Greenland

In Greenland, there is HBV testing for pregnant women, children of mothers with chronic HBV, blood donors, and for clinical reasons. HAV and HCV are tested when there are clinical reasons.

There has been notification of clinical hepatitis since 1952 and notification of serologic testing since 1989. HAV, HBV and HCV are reportable by law to the Chief Medical Officer. Although laboratory tests are performed at Queen Ingrid's Hospital in Nuuk, reporting is the responsibility of local doctors and is hampered by under-reporting, perhaps due to the complexity of the notification system. Yearly reports from the Chief Medical Officer were stopped in 2003, due to the issue of under-reporting. Since 2007, yearly laboratory data from Queen Ingrid's Hospital have been reported to the Chief Medical Officer. However, there are no clinical data with the test results. For example, HBsAg positive results are reported, but no distinction is made between acute and chronic infection. Also, the reporting of multiple tests from the same person is possible. The laboratory results provide a lot of information, but data management is needed for reliable notification.

In Greenland and Denmark, a unique Civil Registration System assigns a central person registry (CPR) number to all Danish residents, which identifies them in nationwide registers [1, 2]. All persons born since 1968 in Denmark and 1972 in Greenland have a CPR number. In addition to registries of reportable infectious diseases and CPR, other important health registers in Greenland and Denmark are the: Birth Defect Registry, Cancer Registry, Childhood Vaccinations, Cause of Death Registry, Microbiological Test Results, National Inpatient Registry, and the Pathology Registry.

Whilst hepatitis cases are presently under-reported, opportunities for improved surveillance exist, by using: centralized hepatitis testing in Nuuk; CPR numbers to identify test results; and other registries, including morbidity information from hospital registers.

In 1998, Greenland began to participate in the International Circumpolar Surveillance system, hence it is important to report and discuss the Greenland data separately from Denmark because, for some health issues, there is commonality between Arctic regions.

The Danish Database for Hepatitis B and C (DANHEP)

A possible tool for registering data for patients with hepatitis that may be useful in Greenland is the DANHEP database. It was established in Denmark in 2002 as a national, clinical database for HBV and HCV, which can be used for clinical quality and for scientific and clinical trial purposes. Patients are registered into the database via the Internet and their unique CPR number by one dedicated person in each hospital. Completeness of registered data in DANHEP is confirmed by comparison with notified laboratory data. Informed patient consent is required for inclusion into the database and patients may refuse data being used for specific research purposes. The biobank at Ålborg University Hospital collects annual blood samples from the patients in the database.

The information that is entered into DANHEP for patients with chronic HBV and HCV infection followed at hospital departments in Denmark includes:

- Number of patients
- Gender and age

- Mode of transmission
- Country of origin
- For HBV: HBeAg and HBV DNA status and genotype
- For HCV: genotype
- HIV co-infection
- Liver biopsy results
- Treatment

References

- [1] Frank L. *When an Entire Country Is a Cohort*. *Science* 2000;287:2398-2399.
 [2] Frank L. *The Epidemiologist's Dream: Denmark*. *Science* 2003;301:163.

Based on presentations by

*A. Koch, Statens Serum Institut, Copenhagen, Denmark;
 F. Kleist Stenz, National Board of Health, Nuuk, Greenland;
 N Weis, Copenhagen University Hospital, Hvidovre, Denmark.*

The Canadian Arctic

Surveillance is a provincial and territorial responsibility in Canada, each jurisdiction has a formal agreement with federal government to provide statistics on notifiable diseases. Population-based viral hepatitis surveillance is conducted through routine (Canadian Notifiable Disease Surveillance System, CNDSS), and enhanced (Enhanced Hepatitis Strain & Surveillance System, EHSSS) surveillance. This enhanced surveillance started in 1998 and data have been gathered at 12 pilot sites in Canada, including the Northwest Territories, since 2009. As part of this surveillance, for each case there is contact follow-up and, where possible, the cause of infection is ascertained.

Based on a presentation by

B. Larke, Provincial Laboratory for Public Health, Edmonton, Alberta, Canada.

Alaska

The State of Alaska is responsible for its own disease surveillance. The State Epidemiology Programme records cases of diseases that are reportable by law, including acute HAV (since 1974); acute and chronic HCV; acute HBV; and chronic HBV (limited reporting from 2011). The perinatal HBV reporting programme was expanded in 2011. The State Section of Epidemiology receives mandatory notifications via electronic laboratory reporting, fax, and phone from laboratories and health care providers. There is no federal funding for enhanced surveillance of HBV or HCV, so only acute cases of HAV and HBV are investigated for contacts and exposures.

The Alaska State Virology Laboratory provides HAV, HBV and HCV enzyme immune assay (EIA) antibody testing and runs ~11,000 HBV tests and ~8000 HCV tests per year.

A large number of HCV cases have been identified (14,000), but no differentiation has been made between acute and chronic cases, due to the lack of confirmation and RNA results (discontinued in 2011). There is no enhanced surveillance for exposures, risk factors, and no cluster/outbreak investigations. Information is limited to laboratory reports which only include age and gender.

The blood donor screening programme works well; serology tests and nucleic acid test (NAT, for HIV and HCV) are performed. Test results are reported to the State, and the patient (via letter). In the

case of a positive test, the individual is advised to consult a doctor, but there is no further follow-up by the State of Alaska Department of Epidemiology.

The Arctic Investigations Program of the Centers for Disease Control and Prevention is a branch of the National Center for Emerging and Zoonotic Diseases located on the Alaska Native Medical Center campus in Anchorage. It conducts surveillance of certain infectious diseases in Alaska in collaboration with other Circumpolar nations and has a special interest in the indigenous population. For hepatitis research, it collaborates with the Alaska Native Tribal Health Consortium (ANTHC) and Division of Viral Hepatitis, CDC.

The Alaska Native Registries for HBV and HCV are more complete than the State database and are used for patient management and public health programmes for the Alaska Native population (see Prevention and Control of Viral Hepatitis in the Arctic Regions). Mortality data (HAV and HCV) based on death certificates are available from the State of Alaska. The ANTHC and CDC have information on causes of death on persons with chronic HCV and HBV that is updated every few years.

Based on presentations by

B. McMahon, Alaska Native Medical Center, Anchorage, Alaska;

T. Thomas, Alaska Native Medical Center, Anchorage, Alaska.

The Nordic Arctic

Infectious disease control is least centralized in Sweden (good regional control), and most centralized in Norway (no regional levels), leading to a homogenous policy for infectious disease strategies, control and vaccination programmes. Immigrants are recorded in surveillance registers. Surveillance data are collected through aggregated reports from laboratories (especially Finland) and individual patient identification notifications (especially Norway, Sweden). Electronic notifications through the Internet are well developed (except in Norway). Incidence surveillance data are of high quality in the Nordic countries, however there have been limited prevalence studies in risk groups. Surveillance data are disseminated via an interactive web. A surveillance collaboration exists between The Norwegian Institute of Public Health; the Swedish Institute for Communicable Disease Control; the National Institute for Health and Welfare (Finland); and the Statens Serum Institut (Denmark). Since 1998, all Nordic countries have been collaborating in the EpiNorth project. This project aims to improve communicable disease surveillance, control and communication in the Nordic and Baltic countries and Northwest Russia.

Iceland

Surveillance in Iceland is the responsibility of the chief epidemiologist from the Center for Health Security and Infectious Disease Control. Beside surveillance, he also supervises and organizes communicable disease (and other health threats) control and prevention, including coordination of official and public prevention measures and providing information to health care workers and broad public.

There are two types of reporting system, one for notifiable diseases (reported in aggregate numbers, without personal identifiers)

and one for reportable diseases, including viral hepatitis, reported with personal identifier. There are Central Registers of reportable diseases, notifiable diseases, national vaccinations (with personal identifiers) and antibiotic prescriptions (no personal identifiers).

For each identified case of reportable diseases, by law, a report should be received from the clinician (either working in a health care centre, hospital or private practice), and from the laboratory. Clinician reporting is inconsistent, so the laboratory reports are relied upon. There is passive and active surveillance. Passive surveillance is disease reporting of acute HAV (mostly laboratory reporting); acute and chronic HBV; and acute and chronic HCV. HDV and HEV are also reportable, however, no cases of HDV or HEV have been identified, probably because these cannot be diagnosed in Iceland. Cases of acute HBV and HCV are under-reported and consequently data are unreliable. Active surveillance (screening of defined populations) is mainly for chronic HBV and HCV.

Sweden

For communicable diseases there is a double reporting system (laboratory and clinician) to the Department of Communicable Disease Control. Clinician compliance with reporting communicable diseases is good. When a case has been diagnosed a number of steps are taken in order to limit the chance of transmission, including contact tracing and free treatment. More than 60 infections, including HAV, HBV, HCV, HDV and HEV, are notifiable as part of communicable disease control.

Norway

HAV, HBV, HCV are notifiable diseases with full patient identification. There is double reporting, from laboratories and clinicians, to the Norwegian Institute of Public Health and Municipality Health Officer. Cases are under-reported by clinicians. Case definitions for HCV changed in 2008, but for HAV and HBV the case definitions have remained unchanged since 1975. There has been better distinguishing between cases of acute and chronic HBV since 1992.

Finland

Infectious disease control and epidemiology are mainly the responsibility of the National Institute for Health and Welfare, which has managed a National Register since 1995. There is daily or weekly electronic notification of diagnostic findings from microbiological laboratories to the National Register, with full person identification (similar to Denmark and Sweden). Clinicians also report cases, but this is far from complete. In order to improve the reliability of clinician notifications, if a laboratory makes a diagnosis of a notifiable disease, the clinician receives a reminder to notify the case. HAV, HBV, HCV are diseases notifiable by laboratory and physicians with full patient identity. The primary health care centres have access to data for their region from the Register.

Based on presentations by

H. Blystad, Norwegian Institute of Public Health, Oslo, Norway;

T. Gudnason, Directorate of Health, Reykjavik, Iceland;

A. Nystedt, Norrbotten County Council, Luleå, Sweden;

M. Kuusi, National Institute for Health and Welfare, Helsinki, Finland.

The Russian Arctic

Reporting of 'infectious hepatitis' was introduced in 1953 and as of 1975 'serum hepatitis' was also to be reported. Changes were implemented in the beginning of the 1990's: from 1991 to 1993 only acute HAV and HBV were reported; later on (1994) HCV was added to the surveillance system, and from 1999 chronic HBV and HCV were also reported. Reporting has been based mainly on laboratory surveillance in combination with clinical reports collected by the regions. Currently, recording of cases occurs on the regional level on a daily basis, and on a monthly basis aggregated data (number of

cases) are reported to the federal level. There is a potential problem of under-reporting and over-reporting of chronic cases when health care providers are not consciously reporting; or even multiple reporting may exist if patients are seeking medical care in different clinics (on federal level as well as regional level). At the moment, a federal registry for personal recording and follow-up of patients with chronic viral hepatitis is under pilot implementation.

*Based on a presentation by
A. Tulisov, UNICEF, Arkhangelsk, Russia.*

Overview Table 2: Summary of the viral hepatitis surveillance programmes in the different Arctic region nations

Country	Included in national surveillance HAV, HBV, HCV, ...	Mandatory/voluntary	Reported by	Including (acute HAV, acute and/or chronic HBV, acute and chronic HCV)	Screening for
Alaska	HAV HBV HCV	Mandatory	Laboratory Health care providers	Acute HAV Acute HBV/chronic HBV Acute and chronic HCV	<u>HBV</u> : pregnant women, sexual and household contacts of HBsAg+ women, blood donors <u>HCV</u> : blood donors
Canada	HAV HBV HCV*	Mandatory	Laboratory to public health authorities	Acute HAV Acute HBV/chronic HBV Acute and chronic HCV* Differences exist on regional and federal level	<u>HBV</u> : pregnant women, sexual and household contacts of HBsAg+ people, blood donors <u>HCV*</u> : blood donors; encouraged among all high-risk populations
Greenland	HAV HBV HCV HDV	Mandatory	Local doctors/ laboratory (Queen Ingrid's Hospital, Nuuk)	No classification	<u>HBV</u> : pregnant women, children of HBsAg+ mothers, blood donors, other clinical reasons. <u>HAV/HCV</u> : clinical reason
Iceland	HAV HBV HCV HDV HEV	Mandatory	Health care providers Laboratory	Acute HAV Acute HBV/chronic HBV Acute and chronic HCV	<u>HBV</u> : migrants outside Europe, pregnant women, blood donors, IDU <u>HCV</u> : migrants outside Europe, pregnant women, blood donors, IDU
Russia	HAV HBV HCV	Mandatory (regional level)	Laboratory Clinical reports	Acute HAV Acute HBV/chronic HBV Acute and chronic HCV	<u>HBV/HCV</u> : pregnant women; newborns of HBsAg+ or HCV+ mothers; blood donors; health care workers; chronic liver disease patients; inpatients and outpatients at drug and alcohol rehabilitation centres and STD clinics; patients on haemodialysis; children in orphanages; households and contacts of HBV/HCV patients; migrants; military personnel
Nordic countries					
Finland	HBV HCV	Mandatory**	Laboratory** Clinicians	Acute HBV/chronic HBV** HCV: anti-HCV+ or HCV RNA	<u>HBV**</u> : pregnant women, blood donors <u>HCV</u> : blood donors, haemodialysis patients
Norway	HAV HBV HCV	Mandatory**	Laboratory Clinicians	Acute HAV Acute HBV/chronic HBV Acute and chronic HCV	<u>HBV**</u> : blood donors, IDU, prisoners, haemodialysis patients <u>HCV</u> : blood donors, IDU, prisoners, haemodialysis patients
Sweden	HAV HBV HCV HDV HEV	Mandatory**	Laboratory Clinicians	Acute HAV** Acute HBV/chronic HBV Acute and chronic HCV	<u>HBV**</u> : pregnant women, blood donors, IDU, prisoners, haemodialysis patients <u>HCV</u> : blood donors, IDU, prisoners, haemodialysis patients, migrants

* http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/09vol35/35s2/Hep_C-eng.php

** ECDC Technical Report: Surveillance and prevention of hepatitis B and C in Europe (Oct, 2010)

http://ecdc.europa.eu/en/publications/Publications/101012_TER_HepBandC_survey.pdf

Epidemiology of viral hepatitis in the Arctic region

HAV

Greenland

The last reported important HAV outbreak in Greenland occurred from 1970-1974, affecting 11% of the population (4961 cases in 11 out of the 15 districts), mainly in young adults 0-25 years [1].

In 1994, seroprevalence studies in 2 regions in Greenland showed that the seroprevalence of anti-HAV antibodies significantly increased with age, from <10% in children less than 20 years old to >95% in adults older than 50 years of age [2]. Although there has been no HAV vaccination programme in Greenland, and a high proportion of the population is susceptible, no HAV outbreaks have been reported in recent years and the number of new cases recorded for the last decade is low [3]. However no studies on HAV incidence or prevalence have been performed since 1994.

The Canadian Arctic

Community-based studies conducted from 1980 to 2000, have documented the prevalence of anti-HAV in Arctic Canada [4-6]. The rates of anti-HAV prevalence in these studies have been between 75% and 95%. Since about 1995, the annual number of HAV cases is low (<5/100,000 of population) and mainly restricted to travelers to endemic countries.

Alaska

Prior to the availability of HAV vaccine, Alaska experienced large recurrent outbreaks of acute HAV, with the highest impact amongst Alaska Native people in rural areas. From 1950 to the 1990s, HAV epidemics have occurred in Alaska every 10-15 years. In 1990, Alaska was designated as a region of high anti-HAV prevalence, with similar prevalence rates to those found in Greenland, South America, Africa and Asia.

HAV vaccination programmes for all children in the State of Alaska started in 1996. The introduction of universal childhood vaccination has dramatically reduced the incidence of acute HAV in Alaska from the highest in the US, to the lowest in the world. Since 1997, rates of new infections have been fewer than 5 per 100,000 people. In 2002-2007, the Statewide incidence of HAV had fallen to 0.9/100,000, with the largest decrease observed in Alaska Native people, whose incidence in 2002-2007 was lower (0.3/100,000) than the overall US 2007 rate (1.0/100,000).

The Nordic Arctic

Except in an outbreak setting among IDU in 1987 (incidence of 6.0/100,000), the incidence of acute HAV has been very low in **Iceland** since 2000 (only 1 to 3 cases each year; or ~0.3-0.9/100,000). Risk groups include travellers, IDU, immigrants and foreigners. For 25% of the cases no specific risk factor has been identified. Acute HAV is more common in males and most common in the 20-40 year age group, followed by the 10-19 year age group. The average incidence of acute HAV cases in **Northern Sweden** (Norrbotten County) has been low over the last 10 years (0.36/100,000). In the past, most HAV cases were among people originating from Norrbotten, but now are mainly imported cases.

There was a large, nationwide outbreak of HAV among IDUs in **Norway** between 1995 and 1999 (corresponding to a concomitant outbreak of acute HBV). Norway is one of the countries in Europe where the most free needles are distributed to IDU, but it also has

one of the highest mortality rates from drug overdose. Small outbreaks of HAV have occurred among men who have sex with men. In 2011, 22 cases of HAV were notified (0.44/100,000 population), mostly imported food-borne cases [7]. Generally, notification rates for HAV for the North of Norway (Arctic area) are similar to the rest of the country.

In 1994, before the start of the National Register in **Finland**, there was a large outbreak of HAV in the vicinity of Helsinki among IDU, involving 500 cases. After another outbreak among IDU in 2002-2003, the vaccination policy was changed and free HAV vaccination was offered to IDU. Since 2004, the HAV incidence has been low (0.4/100,000 population in 2009) and most cases have been imported. However, there is evidence that the data on cases notified by clinicians are incomplete, because in about one third of the cases there is no record of the location of the patient. Nearly all HAV cases (99.3% out of the 15 cases) in 2011 were among the native Finnish population. Epidemiology of HAV in the Northern region where the Sámi people live, is similar to the rest of Finland. From 2007 to 2011, there were between 0 and 3 HAV cases reported annually.

The Russian Arctic

Compared to the rest of the Russian Federation, the incidence rate of HAV in the Arkhangelsk region was always lower and even seems to further decrease (to less than 3/100,000), although there have been periodic outbreaks (2004-2006).

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Based on presentations by

- M.L. Borresen, Statens Serum Institut, Copenhagen;**
B. Larke, Provincial Laboratory for Public Health, Edmonton, Alberta, Canada;
G. Minuk, University of Manitoba, Winnipeg, Canada;
B. McMahon, Alaska Native Medical Center, Anchorage, Alaska;
T. Thomas, Alaska Native Medical Center, Anchorage, Alaska;
T. Gudnason, Directorate of Health, Rykjavik, Iceland;
A. Nystedt, Norrbotten County Council, Lulea, Sweden;
H. Blystad, Norwegian Institute of Public Health, Oslo, Norway;
M. Kuusi, National Institute for Health and Welfare, Helsinki, Finland;
A. Tulisov, UNICEF, Arkhangelsk, Russia.

HBV

Greenland

Since the mid 1960s, HBV has been endemic in Greenland. Several studies have shown that around 7% of the population (~3-4,000 people) are HBsAg positive (chronic carriers) [1, 2, 3]. In Greenland, there does not seem to be perinatal transmission of HBV. Most transmission occurs before the age of 20 (mainly in adolescence or young adulthood), but after 5 years of age the incidence of chronic cases is rare. However, the proportion of infected adolescents and young adults that become chronic carriers was higher than expected.

A population-based epidemiological survey, published in 2008, of the Inuit population in Greenland included a random sample of 50-69 year olds (N=434) [4] which was compared with another group of Inuit people (40-69 year olds) who migrated to Denmark (N=136). This survey revealed that 20% (86 out of 434) of the group living in Greenland were HBsAg positive and 98.8% of these were anti-HBe positive. Among individuals who were HBsAg negative, 56.1% were anti-HBc and/or anti-HBs positive, and 12.3% of these were only anti-HBs positive [4]. This is unusual because the older population in this region have not been vaccinated, however, it is possible that they have lost anti-HBc but are still anti-HBs positive. In the Inuit group that had migrated to Denmark, only 4.4% (6 out of 136) were HBsAg positive. All 6 HBsAg positives were anti-HBe positive with a low viral load (200IU/ml) and none of the 6 HBsAg positive individuals were anti-HDV or anti-HCV positive [5]. More than 75% of the total study population in Greenland had markers of present or previous HBV infection. HBV viral load was generally low and liver biochemistry did not differ with HBsAg status.

Surprisingly, despite the high prevalence of HBV infection, liver cirrhosis and hepatocellular carcinoma (HCC) occur less frequently in Greenland than in other high endemic countries [3]. The reasons for the low HCC frequencies in Greenland are not well understood, but are perhaps due to genotypes that are associated with a less severe disease course, or due to the age of infection which might be later in life, with infected individuals not living long enough to develop symptoms.

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Based on presentations by

M.L. Børresen, Statens Serum Institut, Copenhagen, Denmark;
K. Ladefoged, Dronning Ingrid's Hospital, Nuuk, Greenland;
H. Krarup, Ålborg University Hospital, Ålborg, Denmark.

The Canadian Arctic

Community-based studies in the Canadian Arctic regions between 1980 and 2000 have reported HBsAg prevalences between 2% and 7% (mean 4%) [1-4]. More recent data show that HBV incidence is decreasing in Canada and is rare in Arctic Canada: 61 cases were reported in Northwest Territories from 2000-2011, 61% amongst non-Aboriginals [5-7]. Most new HBV cases are observed in Asian immigrants and in non-Canadian-born people coming from high endemic regions. More cases of HBV are found in women, but this could be a reflection of the screening policy in which all pregnant women are screened for HBsAg. Sexual transmission is the main route of transmission of HBV.

In order to understand the natural history of HBV infection in the Canadian Arctic, 144 HBsAg positive individuals were compared to 144 HBsAg negative individuals residing in the same communities of Baffin Island. The median follow-up period was 23 years for HBsAg positive individuals and 22 years for HBsAg negative individuals. No differences were found between the 2 groups in terms of liver enzyme tests, liver function tests, liver related morbidity, mortality rates, or age at death. The high mortality rates in both cohorts (38% in both) prevented the evaluation of the rate of complications due to HCC and cirrhosis, although no related bio-markers for HCC were found.

Prevalence of occult HBV

HBV DNA testing on sera collected in 1980 in a community in the Canadian Arctic has shown a prevalence of occult HBV of 10% (18% in anti-HBc positive individuals and 8% in anti-HBc negative individuals) [8]. In a more recent study using a more stringent definition for occult HBV (reverse transcriptase PCR and nested PCR combined), the prevalence of occult HBV in 706 samples was 1.3% [9]. In the early 1980s, 27 occult HBV carriers showed no clinical, biochemical or radiological evidence of disease during a 30-year follow-up. The high incidence of occult HBV should be further investigated. It could be possible that cases of occult HBV are chronic carriers that have cleared the virus.

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Based on presentations by

B. Larke, Provincial Laboratory for Public Health, Edmonton, Alberta, Canada;

G. Minuk, University of Manitoba, Winnipeg, Canada.

Alaska

Traditionally, a high HBV prevalence has been reported among the Alaska Native population before the implementation of the HBV vaccination programme. In the mid 1980s, approximately 75% of the Alaska Native population was screened for HBV. Serological testing of 52,022 Alaska Natives between 1983 and 1987 revealed a prevalence of HBsAg of 3.1% (1603) and 13.8% (7155) for total HBV seropositivity (any HBV marker) [1]. The highest rates of seroprevalence were reported for the Bristol Bay and Yukon Kuskokwim Delta regions of Alaska. Follow-up of the Alaska population-based HBV cohort showed that of 1550 patients identified between 1974 and 1987 with chronic HBV infection, in 2012, 1350 people are still alive. About 40,000 screened individuals with no markers of HBV infection were vaccinated. The introduction of universal HBV immunization programmes that combine infant and pre-adolescent vaccination have led to a marked decline in the incidence of acute and chronic HBV among the Alaska Native population. The number of HBsAg positive Alaska Native children (under 20 years of age) has fallen from 450 in 1988 to 2 in 2008. In 2012, there were no carriers in the <20 age group. In the mid 1980s, 45% were HBeAg positive and that number has now fallen to 2%. Since 1999, there have been no cases of HCC in children [2]. HBV vaccination has resulted in a generation of Alaska Native children who are free of HBV and its sequelae.

According to the 2010 US census, 6.6% of the population of Alaska originates from outside Alaska and an important proportion are from high risk areas (approximately 38,000 Asian and 7400 Pacific Islanders). Based on this information, if 5%-10% were infected it can be roughly estimated that about 2300-4600 non-Alaska Native people in Alaska would have chronic HBV.

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Based on presentations by

B. McMahon, Alaska Native Medical Center, Anchorage, Alaska;
L. Bulkow, Centers for Disease Control and Prevention, Anchorage, Alaska.

The Nordic Arctic

Iceland

In the past, no differentiation was made between acute and chronic HBV cases in Iceland, due to poor reporting by clinicians and also because, until 2010, measurement of IgM against core antigen was not possible.

There have been HBV outbreaks in Iceland from time to time, but generally 20-30 cases of acute and chronic HBV were diagnosed each year in 2009-2011 (7.5 to 9.1 cases per 100,000 population). Most cases were in males in the 20-40 year age group. With limited exceptions, such as an outbreak among IDU involving native Icelandic people, most of the cases of HBV are in immigrants. Most of the cases among immigrants are chronic HBV and it is thought that most of the native cases may be acute. Between 2009 and 2011, acute HBV incidence was approximately 1.77 cases per 100,000 population. Over the next few years, better laboratory differentiation between cases will be possible and higher quality data will be collected. For most cases the risk factors are unknown, probably due to poor reporting. Risk groups that have been identified include: IDU, homosexual contact, haemophiliacs, and mother to child transmission (2 cases). No cases have been reported for HCW or blood recipients.

Sweden

The average incidence of acute and chronic HBV cases over the last 10 years in Northern Sweden (Norrbotten County) was 19 cases/100,000. Around 90-95% of HBsAg positive cases reported are imported cases in immigrants who are chronic carriers. There are very few acute cases (approximately 5 cases in the last 10 years).

Norway

Generally, the incidence of acute and chronic HBV for the North of Norway (Arctic area) are similar to the rest of the country. There was a large, nationwide outbreak of acute HBV among IDUs in Norway between 1995 and 2008, but currently acute HBV incidence is low; 56 cases of acute HBV (1/100,000) were notified in 2011 [1]. Most cases occur via heterosexual transmission and in IDUs.

There are approximately 20,000-30,000 chronic HBV carriers in Norway and the majority (90-95%) of diagnosed chronic HBV cases are in immigrants. Testing is offered to all immigrants, weeks or a few months after arrival in the country. Follow-up, and treatment (if needed) of these chronic carriers is a current focus. In 2011, 707 cases of chronic HBV were notified (14 cases/100,000) [1]. More people are diagnosed in the north of the country as a result of testing of immigrants whilst they are in asylum centres in the north.

Finland

Acute and chronic HBV are distinguished in the National Register in Finland. The main modes of transmission of acute HBV are IDU and sexual contact, but in both groups the incidence of acute HBV has fallen over the years and is now very low. In 2011, 79.2% of acute HBV cases were in native Finns. The rates of chronic HBV have been slowly decreasing since 1995. In 2011, individuals born outside Finland represented 52.3% of the chronic HBV cases. Epidemiology of HBV in the Northern region where the Sámi people live, is similar to the rest of the country. Between 2007 and 2011, there were 4-11 chronic HBV cases annually in the Hospital District, resulting in an average annual incidence of 3.38-9.29 cases per 100,000 residents.

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www.msis.no

Based on presentations by

- T. Gudnason, Directorate of Health, Reykjavik, Iceland;**
A. Nystedt, Norrbotten County Council, Luleaa, Sweden;
H. Blystad, Norwegian Institute of Public Health, Oslo, Norway;
M. Kuusi, National Institute for Health and Welfare, Helsinki, Finland.

The Russian Arctic

As a result of vaccination, over the last decade the incidence of acute HBV has dramatically decreased; by 18-fold in the Russian Federation and by 27.4-fold in the Russian Arctic. Among children under 14 years of age, the incidence of acute HBV has also decreased 6-fold to around 1 case/100,000 population in both the Russian Federation and the Russian Arctic. Prior to vaccination, most cases of acute HBV were in 15-30 year olds. In 2010, the incidence was 2.2/100,000 in the Russian Federation and 1.6/100,000 in the Russian Arctic.

In 2011, in the Arkhangelsk region there were only 5 reported cases of acute HBV. In 2 other Russian Arctic regions (Khanty-Mansiysky and Chukotskaya), which are quite densely populated and in which 5-10% of the population are indigenous, incidences are still high (2.7 and 8.2 cases per 100,000, respectively). A study conducted in the Chukotskaya region in 2009 showed that among almost 500 people tested (of whom 84% were indigenous) the HBsAg positivity rate among the indigenous was 11.2%, which is much higher than among the non-indigenous (1.4%).

Chronic HBV, defined as the presence of clinical symptoms and/or elevated liver enzymes (alanine aminotransferase [ALT]) and HBeAg positivity, is stable or slightly decreasing in the Russian Arctic regions. In 2010, the incidence of chronic HBV in the Arctic regions was 22.2 cases per 100,000 (ranging from 5.2 to 122.8 per 100,000, depending on the region), compared to 13.3/100,000 in the rest of the Russian Federation. Due to vaccination, there has also been a 3.7-fold decrease in chronic carriage (HBsAg positive, but no clinical signs) in the Russian Federation and a 5.7-fold decrease in the Russian Arctic regions.

Based on a presentation by

A. Tulisov, UNICEF, Arkhangelsk, Russia.

HCV

Greenland

In West Greenland, the HCV seroprevalence among Inuits in 1994 was 0.8% [1], but none of the individuals were HCV RNA positive. In routine tests performed at Queen Ingrid's Hospital in Nuuk from 1992 to 2003, the HCV seroprevalence was 0.09%. Injectable drugs are not readily accessible, which is a key factor in the low incidence of HCV in Greenland.

In a population-based epidemiological survey among the Inuit population, after confirmed anti HCV testing and HCV RNA testing, no HCV cases were identified among 434 Inuit people living in Greenland [2], whereas only 2 out of 136 (1.5%) Inuit people that had migrated to Denmark were anti-HCV positive [3]. From these data it is possible to conclude that HCV is rare among Inuit living in Greenland and Denmark.

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Based on presentations by

- M.L. Borresen, Statens Serum Institut, Copenhagen, Denmark;**
H. Krarpur, Ålborg University Hospital, Ålborg, Denmark.

The Canadian Arctic

Community-based studies of the prevalence of HCV in Arctic Canada conducted between 1980 and 2000 have reported prevalences varying between 1% and 18% [1-3].

Serological evidence of HCV infection (anti-HCV) is more common in the Canadian Inuit and First Nations than the rest of the Canadian population, whereas viremia (HCV RNA positivity) is less common (less than 5% versus 75% of anti-HCV positive individuals, respectively) [3]. Investigations of the immunological response to HCV in First Nations populations has revealed that these populations are less susceptible at a cellular level to HCV-induced Interleukin 10 (IL10) synthesis, which might contribute to enhanced HCV clearance [4, 5]. Successful resolution of HCV viral infection in this population is not found in other parts of the world and may assist in the development of a vaccine against HCV. It is also possible that HCV-infected Inuit and First Nations populations are being exposed to the virus at a much younger age when rates of spontaneous clearance of HCV are greater.

Recent data show that the reported HCV incidence rates have slowly decreased in the Northwest Territories in the last 10 years. Rates in Yukon, whose population includes larger numbers of a younger generation who experimented with drugs, are the highest in the country, mainly a reflection of widespread, stringent testing and reporting. Incidence of HCV is higher in males and IDU is the main route of transmission of HCV. Incidence is highest in the 40-49 year age group and is largely due to injection drug use when these individuals were younger [6]. However, high HCV rates were also observed in the younger generation. More Aboriginals than non-Aboriginals in Northwest Territories are IDUs and, therefore, there are more cases of HCV (52%) in this group than amongst non-Aboriginals (48%) [7].

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Based on presentations by

B. Larke, Provincial Laboratory for Public Health, Edmonton, Alberta, Canada;

G. Minuk, University of Manitoba, Winnipeg, Canada.

Alaska

In the Alaska State database, 13,944 anti-HCV positive individuals have currently been identified, which includes 2300 Alaska Native individuals (an estimated 1.8% population prevalence) and 11,644 non-Alaska Natives (an estimated 1.6% population prevalence). Good HCV data are available for the Alaska Native/American Indian population in Alaska, due to intense screening. Alaska Natives have HCV prevalences, HCV genotype distribution and risk factors similar to the National Health and Nutrition Examination Survey (NHANES) estimates for the US. So far, 1300 anti-HCV positive Alaska Natives have been enrolled as an outcomes cohort. It was found that 78.4% of those tested were HCV RNA positive, and 21.1% were HCV RNA negative and had cleared the virus. HCV occurs mainly in urban areas and there is very little HCV in the rural areas, where IDU is uncommon. HCV prevalence in non-Alaska Natives is probably underestimated and might be higher than in the US population. Screening in non-Alaska Natives is poor, while they are more exposed to HCV because a larger proportion is living in urban areas where there is more IDU. Targeted screening of this population is necessary to provide reliable prevalence data. The most important risk factors in Alaska Natives with HCV are IDU, blood transfusion and risk behavior (including snorting, high risk occupation, multiple sexual partners, sexual partner with HCV, IDU sexual partner, HCV household contact, tattoo).

Mortality data reveal that the likelihood that Alaska Native individuals with chronic HCV die from liver related death (LRD) is 17 times higher than in the rest of the US population as a whole and is 12 times higher than in the general Alaska Native population. A model of survival probability for individuals with HCV at 25 years showed that if an individual is not a heavy drinker, the probability of dying over 30 years of a LRD is only about 10%, but for heavy drinkers the probability is 35%. Heavy alcohol use is associated with the incidence of LRD and end stage liver disease, regardless of whether patients are chronically infected or recover from HCV infection [1].

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Based on a presentation by

B. McMahon, Alaska Native Medical Center, Anchorage, Alaska.

The Nordic Arctic

Iceland

Reports of HCV do not distinguish between acute and chronic cases. Generally, the HCV incidence is higher than for HBV (40-60 cases per year). In 2011, around 45 cases (13.8/100,000 population) were reported. Similar to HBV, most cases are in males in the 20-40 age group. When risk factors are identified (60% of cases), the major reported risk factor is IDU (around 50% of cases). Other risk groups are blood recipients, haemophiliacs and people having heterosexual contacts. A very small number of infections occur via mother to child transmission, homosexual contact or in health care workers (HCW). Most HCV cases are among the native Icelandic population.

Sweden

In 2009, Norrbotten County had a very high incidence of HCV (80/100,000 among the 15-24 year age group) compared to other Nordic countries (35 to 50 per 100,000) [1]. The observed increase in HCV cases in Norrbotten County does not seem to be related to increased testing activity, but is likely related to a rise in the use of injectable morphine-based drugs among young people in Norrbotten County.

The high incidence among young people in Norrbotten County who become infected with HCV through IDU, shows an increasing trend since 2009 (6 cases on average before 2009 to 25 cases in 2009). This trend in cases among IDU is also observed in older age groups (see Figure below). The mean age of females and males was 20 and 22 years, respectively. In 2011, there were 7 cases of acute HCV reported and 4 were in the younger age groups.

New HCV cases in IDU in Norrbotten County, Sweden 1998-2011



Norway

High quality surveillance data for HCV in Norway were lacking in the past, partly due to difficulties in differentiation between acute and chronic cases. The quality of the data has been improving since 2008, when the HCV case definition changed. There are approximately 20,000 to 30,000 chronic HCV carriers. Follow-up and treatment (if needed) of these chronic carriers is a current focus. In 2011, 1675 HCV cases (acute and chronic) were notified (34/100,000 population). Generally, the number of acute and chronic HCV notifications for Arctic Norway are similar to the rest of the country.

Finland

The number of notifications of HCV has been very high since 2000, when notification of the disease began in Finland. In 2000, the total number of cases notified was 1739 and in 2010 the total notified was 1132 (21/100,000 population). There has been a slight decrease in all age groups over the 10 year period, but the burden of disease remains substantial. The recorded routes of transmission are: IDU (most common), sexual contact, perinatal, and blood products. In 2010, the

highest incidence of HCV was registered around Helsinki and 2 other counties. In 2011, native Finns represented 84.4% of the cases of HCV. HCV prevalence studies in the South/East of Finland among IDU in the needle exchange programme show stable rates of 70%.

The epidemiology of HCV in the Northern region where the Sámi people live, is similar to other parts of the country: between 2007-2011, there were between 22 and 25 HCV cases annually (annual incidence of 14 to 21 per 100,000) in the Hospital District.

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Based on presentations by

T. Gudnason, Directorate of Health, Reykjavik, Iceland;

A. Nystedt, Norrbotten County Council, Lulea, Sweden;

A.L. Lindqvist-Svedberg, Norrbotten County Council, Lulea, Sweden;

H. Blystad, Norwegian Institute of Public Health, Oslo, Norway;

M. Kuusi, National Institute for Health and Welfare, Helsinki, Finland.

The Russian Arctic

The number of acute HCV cases in Russia and the Russian Arctic appears to be decreasing, but this is likely due to a change in case definition - clinicians are reporting more cases as 'chronic' - resulting in a corresponding increase in the number of chronic cases. Overall, the incidence of HCV appears to be slowly increasing, especially in young adults. In 2010, the incidence of acute HCV was 2.1 and 2.2 cases per 100,000 population in the Russian Federation and the Russian Arctic, respectively. The respective incidence of chronic HCV in 2010 was 40.2 and 57.2 cases reported per 100,000. The Arctic region with the highest number of cases was Yamalo-Nenetsky, with an incidence of 129.3/100,000. The main route for HCV transmission is IDU (~50% of cases). Therefore, HCV is linked to areas where there is more IDU. Differences by regions can be explained by variation in the quality and completeness of reporting. A serological study conducted in 2009 (N=459) in the Chukotka region, which has a large indigenous population, showed that HCV occurred more frequently in the non-indigenous population: the anti-HCV positivity rate was 5.4% in the non-indigenous population and 2.3% among the indigenous.

Based on a presentation by

A Tulisov, UNICEF, Arkhangelsk, Russia.

HDV

Greenland

In a population-based epidemiological survey among the Inuit population living in Greenland (N=434, data collected in 1998 [1]) or Inuit that had migrated to Denmark (N=136, data collected in 2008) [2], 6 individuals were anti-HDV positive; 5 in Greenland (1.1%) and 1 in Denmark (0.7%). All had markers of former HBV infection, but only one was HBsAg positive and none was HBV DNA or HDV RNA positive. All 6 had elevated liver biochemistry. These figures show that the HDV exposure in this study was low and lower than reported from certain areas on the west coast of Greenland [2, 3], and suggest that HDV is rare among Inuit in Greenland and Denmark. However, with around 7% of the population of Greenland being HBsAg positive, HDV infection could become a more widespread problem.

In 2005, a large HDV outbreak was identified in Itilleq on the West coast of Greenland, a HBV hyper-endemic settlement with a population of 133 inhabitants [4]. In 2006, there was very high chronic carriage (27% HBsAg positive), 56% were immune to HBV (indicating past infection), and 17% had not been exposed to HBV. Among the children tested, 29% were chronically infected, 35% were immune and 37% were never exposed. The burden of disease was very high in the 0-29 year age group. Of the chronically infected children, 53% were HBeAg positive and 73% had elevated ALT levels. Retesting of the chronic carriers in Itilleq showed ongoing liver involvement without virus clearance. HDV testing of all the HBsAg positive cases revealed that 5 (33%) children who were HBsAg positive in 2006 had HDV seroconverted between March 2006 and June 2007, indicating an HDV superinfection causing a much more severe disease course, and by September 2009 an additional 2 HBV chronically infected children had become HDV positive. HDV was the predictor for elevated ALT. The highest ALT levels were among HDV RNA positive individuals. The settlement children had high viral loads for HBV and HDV (higher than the adults), and horizontal transmission probably occurred via scratches and contaminated surfaces. It is hoped that HBV vaccination will help to control the ongoing HDV outbreak in Itilleq and reduce the incidence and spread of HBV/HDV superinfection.

The overall HDV prevalence in Greenland is uncertain (around 5-40% of HBsAg positive individuals, with regional differences). Some studies found HDV prevalences among HBsAg positives as high as 40% in West Greenland [3] and 15% of 390 HBsAg positive samples from South, West and East Greenland [5]. It would be interesting to study how HDV superinfection/co-infection influences anti-HBe seroconversion.

The Nordic Arctic

In Norrbotten County (Sweden), there have been 3 cases of HDV diagnosed in the last 15 years and they were all imported cases from individuals outside the area. Since 2002, HDV has no longer been notifiable in Norway. Prior to 2002, there were sporadic cases of HDV notified among IDUs.

The Russian Arctic

HDV is not reportable in the Russian Federation, but since there has been a reduction in the cases of HBV, the number of HDV cases is also likely to decrease. However, in some regions of Russia, the HDV prevalence among HBsAg positive persons is very high. In two regions of the Russian Arctic - Chukotka and Yakutia - it is as high as 36% and 28%, respectively. A study of liver cirrhosis aetiology in the Yakutia region of the Russian Arctic has revealed that HBV (32%) and HDV (33.1%) are the main causes of cirrhosis [6].

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Based on presentations by

H. Krarup, Ålborg University Hospital, Ålborg, Denmark;

M.L. Borresen, Statens Serum Institut, Copenhagen, Denmark;

A. Nystedt, Norrbotten County Council, Luleå, Sweden;

H. Blystad, Norwegian Institute of Public Health, Oslo, Norway;

A Tulisov, UNICEF, Arkhangelsk, Russia;

V. Chulanov, Central Research Institute of Epidemiology, Moscow, Russia.

Overview Table 3: Seroprevalence and incidence data for HAV, HBV/HDV and HCV in the Arctic region

Country	Seroprevalence %			Annual incidence/100,000 (period)		
	HAV	HBV/HDV	HCV	HAV	HBV	HCV
Alaska	-	HBsAg+ in Alaska Native children <0.01% (2003-2008) ^a 0% (2011)	1.8% in Alaska Natives 1.6% in non-Alaska Natives ^b	0.9 overall 0.3 in Alaska Natives 0.7 in non-Alaska Natives (2002-2007) ^c	0 acute (in children since 1992) ^d <1 in adults statewide	-
Canadian Arctic	-	-	2% in First Nations 18% in Inuit (in 2000) ^e	0-4 in Yukon and Northwest Territories (1998-2004) ^f	~7 in Northwest Territories (2008) ^g	~15 in Northwest Territories (2011) ^h ~100 in Yukon (2009) ^h
Greenland	Anti-HAV+ 54% overall, age dependent significant rise from 9% in second decade to 50% in third decade ⁱ	HBsAg+ 7.4% overall (2007) ^j 20% in Inuit ^k 4.1% in Inuit in DK ^l HDV ~5-40% of HBsAg+	0.09%	Low in Inuit ^l	-	-
Iceland	-	-	-	0.3-0.9 (2000-2011) ^m	7.5-9.1 acute+chronic (2009-2011)	13.8 (2011)
Russian Arctic	-	-	-	<3.0 ^p	Acute: 1.6 (regional var. 0 to 8.2) chronic: 22.3 (regional var. 5.2 to 122.8) (2010) ^q	Acute: 2.2 (2010) chronic: 57.2 (2010) ^r
Nordic countries						
Finland in Lapland Hospital district	-	-	-	0.4 (2009) tot. Finland 2.53 (2011) ⁿ	chronic 9.29 (2009) 3.38 (2011) ⁿ	14 (2009) 21 (2011) ⁿ
Norway	-	-	-	0.44 (2011) ^o	1 acute 14 chronic (2011) ^o	34 (2011) ^o
North Sweden	-	-	-	0.36 (in last 10 years)	19 mainly chronic (in last 10 years)	29 (in last 10 years)

a Long-term hepatitis B immunogenicity studies in Alaska and the impact of vaccination on cirrhosis, chronic hepatitis B and liver cancer. Data presented at the meeting by Lisa Bulkow, Alaska: slide 25 (see www.vhpb.org)

b Estimated population prevalence based on Alaska State database, but in this estimate probably 25-50% of HCV positives were not identified. Data presented at the meeting by Brian McMahon, Alaska. Epidemiology of Viral hepatitis in Alaska: slide 21 (see www.vhpb.org)

c Population estimates derived from 2000 US census data. Data presented at the meeting by Timothy Thomas, Alaska. Hepatitis Surveillance system in Alaska, including hepatitis A: slide 11 (see www.vhpb.org)

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e The Epidemiology and Natural History of Viral Hepatitis in the Canadian North. Data presented at the meeting by Gerald Minuk, Canada: slide 23 (see www.vhpb.org)

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http://dsol-smed.phac-aspc.gc.ca/dsol-smed/ndis/cgi-bin/ndischart?DATA_TYPE=R&YEAR_FROM=89&YEAR_TO=04&CAUSE=048&AREA=60&AREA=61&AGE=0&SEX=3&CTIME1=View+Chart

g The health care systems and communicable disease control and hepatitis Surveillance in Canada. Data presented at the meeting by Bryce Larke, Canada: slide 19 (see www.vhpb.org)

h The health care systems and communicable disease control and hepatitis Surveillance in Canada. Data from the Public Health Agency of Canada, presented at the meeting by Bryce Larke, Canada: slide 24 (2009); slide 20 (2011) (see www.vhpb.org)

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m Epidemiology of viral hepatitis in Iceland. Data presented at the meeting by Thorolfur Gudnason, Iceland: slide 4 (see www.vhpb.org)

n National Infectious Disease Register. <http://www3.thl.fi/stat/>

o Norwegian Surveillance System for Communicable Diseases (MSIS). www.msis.no

p Official bulletin of the Federal Gossaeptidnadzor Center, Russia

q Epidemiology of viral hepatitis in Russia (Arctic region). Data presented at the meeting by Andrey Tulisov, Russia: slides 4, 13 (see www.vhpb.org)

r Epidemiology of viral hepatitis in Russia (Arctic region). Data presented at the meeting by Andrey Tulisov, Russia: slides 20, 21 (see www.vhpb.org)

HEV

The Canadian Arctic

A study exploring the seroprevalence of HEV infection in an isolated Inuit community (393 serum samples) in the Canadian Arctic, found 11 samples (3%) positive for IgG anti-HEV [1]. Two of the 11 individuals had IgM anti-HEV, but none were HEV RNA positive. HEV cases did not seem more common for a particular age group or gender, but the number of positive samples is small. The source of HEV in the Northern Canadian regions is unclear, since there are no pigs, but HEV transmission following the consumption of karibou meat cannot be excluded, although in a separate limited study on karibou no HEV was detected. It should be taken into account that these HEV prevalence data are based on first generation anti-HEV assay kits and they require confirmation with more accurate serological testing, because disparities between old and more recent anti-HEV kits may result in different seroprevalence rates.

The Nordic Arctic

There have been no HEV cases reported in the last 15 years in Norrbotten, Sweden, but this may be due to infrequent testing. Dur-

ing testing, if HBV and HCV have been ruled out, HEV testing may be carried out. HEV is not notifiable in Norway, but there have been sporadic imported cases originating from the Indian subcontinent.

The Russian Arctic

In 2009 a seroprevalence study (N=459) performed in Chukotka region found that 4% were HEV positive, and non-indigenous people were twice as likely to be affected as indigenous.

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Based on presentations by

- G. Minuk, University of Manitoba, Winnipeg, Canada;
A. Nystedt, Norrbotten County Council, Lulea, Sweden;
H. Blystad, Norwegian Institute of Public Health, Oslo, Norway;
A Tulisov, UNICEF, Arkhangelsk, Russia;
V. Chulanov, Central Research Institute of Epidemiology, Moscow, Russia.

Molecular epidemiology of viral hepatitis in the Arctic region

HBV genotype distribution in the Arctic nations

	HBV genotype				
	A	B	C	D	F
Greenland [1] Krarup HB et al., 2008 (Inuit population) [2] Børresen M, 2011	24%	Predominant 90%	1%	8% 60%	-
Canadian Arctic [3] Osiovy C et al., 2011	-	B6 predominant in Eastern region	-	D3, D4 predominant in Western region	-
Alaska	9% (A2)	6%	15%	predominant 55% (D2, D3)	17%
Iceland [4] Björnsdóttir TB et al., 2005	30%	-	-	65%	-
Russian Arctic	Present	-	Present	Predominant	-

HBV genotypes

There are 8 major HBV genotypes (A-H) and a number of subgenotypes, that have a distinct geographic distribution worldwide. The distribution differs, even between Arctic nations; for example, there is less genotype B in Alaska compared to Greenland while genotype F, the native American genotype, is frequently found in Alaska, but not in Greenland (see Table above).

Two major subgenotypes of HBV genotype B exist: Bj (Japan, also designated B1 subgenotype) is non-recombinant with HBV genotype C and less commonly associated with HCC. Conversely, the Ba (Asia) subgenotype, which can be divided into B2, B3, B4, B5, is recombinant with HBV genotype C in the core promotor/pre-core/core genome region. This subgenotype is associated with a higher risk of HCC in HBV carriers [5-9].

A comparative study of B subgenotypes in the Arctic investigated 50 native HBV carriers with no evidence of HCV or HIV co-infection, compared with the sequencing results of 50 Bj and 50 Ba retrieved from an Asian databank [10]. After phylogenetic analysis all sequenced arctic strains formed a separate (unclassified) cluster, which was later classified as a new subgenotype B6, and were related to the non-recombinant Japanese Bj/B1 subgenotype. Based on disease severity markers, including HBeAg, HBV DNA, ALT, and clinical state (asymptomatic, chronic, liver cirrhosis or HCC), the non-recombinant B1 and B6 subgenotypes appear to be less severe than subtypes B2-B5 [10].

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Based on a presentation by

A. Koch, Statens Serum Institut, Copenhagen, Denmark.

Greenland

The distribution of HBV genotypes in Inuit populations living in Greenland is shown in the Table above [1]. A genome analysis of 20 genotype B positive samples of Inuit people in Greenland, confirmed that samples showed >94% homology with subtype Bj (Japan) and <92% homology with Ba [1].

It was suggested during the meeting that subgenotype B6 (or a mutual predecessor of B6 and B1) followed the Eskimos when they migrated from East Asia/Siberia to Alaska in 10,000 BC (see Figure below). The Eskimos later divided into 3 groups; Aleutians (Aleuts, West Alaska), Yupik (West Alaska), and Inuit (North Alaska, Canada & Greenland). The Inuit spread eastwards from Alaska to Greenland around 1000 AD.

HBV subgenotype B6, predominant in Greenland, seems to have a less severe clinical course, similar to the situation in Canada (see Epidemiology HBV: The Canadian Arctic). However, larger studies on the clinical course of subgenotype B6 are needed, particularly following individuals into later life, because even if the virus rep-



licates less, the carrier can still develop HCC at a lower incidence. Possibly this subgenotype appears less severe, because most infected individuals do not live long enough to develop the disease. In addition, the immune system of the host (depending on whether epitopes are recognized or not) also plays a role in disease severity. Further research into subgenotype B6, including the natural history of infection with HBV B6, is needed.

The extent to which HBV genotypes influence the behaviour of HDV over time is also not known. For instance, the disease course of HDV in cases of HBV genotype B3 is thought to be different than for other HBV genotypes. There was a higher prevalence of HDV with HBV genotype D, which explains the higher HDV incidence on the West coast of Greenland where HBV genotype D is predominant.

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Based on presentations by

H. Krarup, Ålborg University Hospital, Ålborg, Denmark;
M.L. Borresen, Statens Serum Institut, Copenhagen, Denmark.

The Canadian Arctic

A large study conducted in 1983-1985 and including >14,000 individuals representing 30% of the population in Northern Canada, found that in 227 HBV DNA positive samples genotype B6 predominates in the Eastern Arctic region of Canada whereas the D genotype (D3 and D4) is confined to the Western Arctic region of Canada [1].

The less severe disease course that seems to be associated with HBV genotype B6, compared to other genotypes, could be due to a difference in mutations between genotypes. Full genomic testing of samples from individuals with HBV over a 5-year period showed that subgenotype B6 has a greater mutation rate (4.1%) than genotype D (1.3%) or F (0.7%). The complication of cirrhosis is most associated with epitopes of the core gene, and the B6 subgenotype also had more mutations (1.9%) in the core gene than genotype D (1.5%) or F (1.1%). It could be possible that, over time, subgenotype B6 in the Eastern Canadian Arctic has reached a symbiotic relationship with the host, where it mutates readily and is able to evade the immune system.

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Based on presentations by
**B. Larke, Provincial Laboratory for Public Health,
 Alberta, Canada;**
G. Minuk, University of Manitoba, Winnipeg, Canada.

Alaska

Alaska is the only place in the world that has 5 different HBV genotypes in a population that is not ethnically diverse, being 95% Eskimo/Inuit. Genotype D is predominant (over 50%).

It is not clear how some of these genotypes arrived in Alaska, but it is likely that some of them are very old. Since Alaska is not ethnically diverse, it is the genotype and not ethnicity that determines the route of transmission. In northwest Alaska, where genotype C predominates, perinatal transmission of HBV was common prior to vaccination. In areas where genotype C was not found, such as southwest Alaska, the predominant transmission route was horizontal from child to child through open cuts and scratches. Transmission in adults through sexual exposure occurs less frequently.

Genotypes A and D are associated with HCC and active liver disease in older individuals. The HBV cohort study showed that all Alaskan genotype A strains belong to the A2 subtype, which is typical for Europe and North America. Two subtypes of genotype D were found in Alaska, D2 and D3. Their geographical distribution is separated by a mountain range. Genotype D3 is associated with HBV vasculitis following acute infection.

No serious sequelae associated with subgenotype B6 have been identified to date (see also sections HBV Greenland and HBV Canadian Arctic). The origin of genotype C2 is Southern China, and perinatal transmission rates are high. Unlike the other genotypes, most women infected with genotype C will still be HBeAg positive and have high viral loads during their child-bearing years, which explains the association of the genotype with perinatal transmission. Genotype C is also associated with higher rates of HCC compared to genotypes A2, B6, D2, and D3, with cirrhosis starting around the age of 40 years. Genotype F has 2 subtypes, F1 (from the Amazon) and F2. Genotype F was identified primarily in Southwest Alaska, located along the two main rivers and is associated with HCC in children and young adults.

Based on a presentation by
B. McMahon, Alaska Native Medical Center, Anchorage, Alaska.

Iceland and The Russian Arctic

There has been little focus on genotyping HBV in Iceland; one study found 65% genotype D and 30% genotype A [1].

Samples from 9 out of 86 regions in the Russian Federation are being genotyped at the Reference Center for Viral Hepatitis in Moscow. Samples tested were mainly HBV genotype D in all 9 regions, followed by genotypes A and C.

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Based on presentations by
T. Gudnason, Directorate of Health, Reykjavik, Iceland;
A. Tulisov, UNICEF, Arkhangelsk, Russia.

HCV genotypes

A study of HCV genotype distribution among 55 IDU in Iceland, found 58% genotype 1a, 38% genotype 3a, 2.5% genotype 1b [1]. Genetic fingerprinting of samples from 11 HCV cases in the 15-25 year age group who were infected in 2009-2010 in a small town called Piteå, in Norrbotten County (Sweden), revealed 5 different HCV subgenotypes (1a and 3a were most common), which is surprising because it was expected that HCV strains among IDU would be more homogenous.

In the Russian Federation, genotype 1b is the most common HCV genotype, followed by 3a, 2a and 1a.

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Based on presentations by
T. Gudnason, Directorate of Health, Reykjavik, Iceland;
A.L. Lindqvist-Svedberg, Norrbotten County Council, Luleå, Sweden;
A. Tulisov, UNICEF, Arkhangelsk, Russia;
V. Chulanov, Central Research Institute of Epidemiology, Moscow, Russia.

HDV genotypes

Worldwide, there are currently 8 HDV clades (genotypes) identified and infection with clade 1 has the most adverse outcomes. In Greenland, in Itilleq, 3 different clusters of clade 1 were found, and aligned with sequences from Mongolia, Iran, Turkey, US, Canada, Taiwan, France and Italy.

Based on a presentation by
M.L. Børresen, Statens Serum Institut, Copenhagen, Denmark.

Prevention and control of viral hepatitis

Greenland

HAV

The last nationwide HAV outbreak in Greenland was between 1970 and 1974 [1]. Although there has been no HAV vaccination programme, and a high proportion of the population younger than 35 years of age is susceptible, there are currently no outbreaks of HAV. However experience from Alaska suggests that childhood

HAV vaccination could be an effective way of controlling HAV in Greenland [2].

HBV

In 1987, the National Board of Health concluded that HBV was endemic in Greenland and recommended targeted screening of all pregnant women for HBsAg; and vaccination of children born to

HBsAg positive mothers; household and sexual contacts of carriers; and vaccination of other groups at risk.

Effectiveness of the targeted HBV vaccination programme for children born to HBsAg positive mothers in Greenland

HBV screening of pregnant women in Greenland was included in the Greenlandic Hepatitis B database since 1992. The result of HBsAg testing at the first pregnancy examination was recorded and vaccination for children born to HBsAg positive mothers recommended, according to National Guidelines at the time (before 2010: Hepatitis B Immune Globulin [HBIG] and 10µg recombinant vaccine at birth, 1, 2, and 12 months).

A study investigated the effectiveness of this targeted approach to screening and vaccination [3]. Of the 4050 women tested (from 1992-1999 and 2005-2009), 135 (3.2%) were found to be chronic carriers (HBsAg positive). Of the 248 children included in the study, information on vaccination coverage was available for 207 (83%). Despite being born to HBsAg positive mothers, 42 children (20.3%) received no vaccination or HBIG, and only 70 (33.8%) received the complete 4-dose schedule. No difference in vaccination strategies was found between high endemic and low endemic regions. A follow-up study of 140 of the children born to HBsAg positive mothers revealed that 8 children had evidence of breakthrough infection: 4 (3%) were chronic carriers; and 4 (3%) had been infected and cleared the virus. Of the 8 children positive for antibody against HBV core antigen (anti-HBc), 7 had received at least 3 HBV vaccinations, but only half of them had received HBIG. Of the anti-HBc negative children who had received at least 3 doses, 59% had anti-HBs <10mIU/ml and 73% of all included children had anti-HBs <10mIU/ml. Perhaps not all children initially responded to the vaccination course, and this finding could explain why breakthrough infections occurred. Low response rates could be explained by factors related to the cold chain, e.g., freezing of vaccines in the Arctic region. Ongoing studies are investigating the possible impact on response rates of perfluorinated compounds (from contaminated fish consumption).

Universal newborn HBV vaccination

It was clear from the above study that the targeted approach of vaccination for children born to HBsAg positive mothers was not effective. In 2009, the National Board of Health approved universal newborn HBV vaccination and in September 2010 a 4-dose schedule (at birth, 3, 5, and 12 months) was added to the childhood immunization programme in Greenland. In addition to routine HBV vaccination of newborns (approximately 800 children/year), pregnant women are still screened for HBsAg so that newborns from positive mothers can also be given HBIG and followed up. The large majority of deliveries occur in a hospital setting, allowing for the timely administration of the first dose, given within 24 hours of birth, or at least before the baby leaves the hospital. However, administering the other doses once babies have returned home, sometimes to remote settlements, can be problematic and vaccination schedules are often delayed up to 3-6 months. It remains to be investigated whether a 4-dose HBV vaccination schedule improves long-term immunity. There is also a catch-up HBV vaccination programme for children at 12 years of age.

The current screening programme in Greenland

Currently, restricted screening for HBsAg and anti-HBs is performed in pregnant women, contacts of HBsAg positive individuals, blood donors, patients prior to chemo- and immunosuppressive therapy, HIV positive persons, and patients with elevated ALT. Vaccination is re-

commended for all patients found to be HBsAg and anti-HBs negative. It is recommended that HBsAg positive patients are tested further (HBeAg, anti-HBe, anti-HCV, anti-HDV; HBV DNA in case of increased ALT; When positive for anti-HDV also test HDV RNA), as shown below, but it is not clear how closely these recommendations are followed.

Indications for treatment of chronic HBV

All cases of HBsAg positive cirrhosis (irrespective of viral load) are eligible for treatment with Tenofovir or Entecavir. Patients with chronic HBV are eligible for the same treatment if they fulfil 2 of the following 3 criteria: HBV DNA >2000IU/ml; ALT above upper normal limit; or liver biopsy with inflammation (score A2) and/or fibrosis (score F2). Follow-up of the 3000-4000 patients with chronic HBV will have a substantial impact on the health care system. Recommendations for follow-up are shown below, however at present very few carriers are actually followed up. Telemedicine tools have been implemented recently, but are not used for follow-up of patients with viral hepatitis.

Chronic HBV patient follow-up in Greenland:

For untreated patients:

HBsAg, anti-HBs, and ALT testing every 6-12 months
Alpha-fetoprotein (AFP) once a year

For treated patients:

HBsAg, anti-HBs, ALT, and HBV DNA testing every 3-6 months
AFP once a year

The Central Patient Registry records all hospital admissions. Between 2002 and 2011, 17 cases of acute HBV (3/100,000 a year) were recorded. This is probably an underestimation as many cases are treated in outpatient clinics, not in hospital. Among chronic HBV patients that are eligible for treatment, only a small number are treated (also true for HDV); of 14 chronic HBV cases admitted to hospital, 7 fulfilled treatment criteria, but only 2 were treated and neither completed the treatment course.

Many of the 31 HBsAg positive individuals identified during the HDV outbreak at Itilleq [4] (see Epidemiology HBV Greenland and HDV Greenland) were not followed up, but a review of the files revealed that at least 3 patients not co-infected with HDV fulfilled the criteria for HBV treatment (high levels of ALT and HBV DNA). Of the HBsAg positive patients, 21(68%) were co-/superinfected with HDV [4].

Barriers to treatment in Greenland include the scattered populations, many living in small settlements with poor access to hospital facilities. Other treatment barriers include the rapid turn-over of hospital staff and the lack of specialists; the need for courier transportation for blood samples (for viral load testing); and low compliance.

In order to improve surveillance and treatment of viral hepatitis in Greenland, there is a need for centralized guidance from Queen Ingrid's Hospital in Nuuk and a national database. Viral hepatitis should be a priority in the health care system and commitment to this issue is needed. These improvements will be a challenge in Greenland, since it is a country with poor resources and limited manpower.

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Based on presentations by
M.L. Borresen, Statens Serum Institut, Copenhagen, Denmark;
F.K. Stenz, National Board of Health, Nuuk, Greenland;
K. Ladefoged, Queen Ingrid's Hospital, Nuuk, Greenland.

The Canadian Arctic

HAV

In the North of Canada, improvements in the quality of drinking water and sewage disposal systems, and education for food handlers on safety precautions, together with promotion of HAV vaccination for all travellers to endemic countries, has brought about an almost complete eradication of HAV, similar to Alaska.

HBV

The prevention and control measures for HBV in Canada include:

- Promoting and maintaining a high coverage of universal HBV immunization beginning in early infancy. Three doses are given within the first year of life and vaccine coverage is high (e.g., 89% in Northwest Territories [1]). Due to routine HBV vaccination (since 1998), a decrease in HBV incidence has been observed in all 3 Canadian Arctic territories;
- Screening of all pregnant women for HBsAg and providing HBIG and vaccine to newborns at birth if the mother tests positive;
- Ensuring that all health care providers have protective anti-HBs levels;
- Enforcing blood and body fluid precautions in health care settings and also settings such as tattooists;
- Developing public education programmes regarding sexual transmission of HBV and promotion of safer sexual practices (educational materials may need to be provided in several languages: the Northwest Territories recognizes 11 different official languages [1]); and
- Implementing harm reduction strategies for users of street drugs.

HCV

The prevention and control measures for HCV in Canada include:

- Taking every opportunity to screen at-risk individuals for anti-HCV. For example, in Yukon HCV rates appear higher than in other territories in Northern Canada, but this reflects active screening and testing for HCV over several years. Screening for HCV is strongly encouraged in Yukon for anyone using street drugs by injection or inhalation, inmates upon entry to correctional facilities, anyone presenting with an STI and their contacts, pregnant women, and anyone who received blood or blood products before 1992. Efforts are also made to follow up Yukon residents diagnosed with HCV outside the territory, representing 16.5% of the 504 total cases of HCV between 2000 and 2011;
- Enforcing blood and body fluid precautions in health care settings, as well as in tattoo and body piercing sites;
- Developing and implementing culturally-sensitive educational programmes and community-acceptable harm reduction

strategies for users of street drugs, e.g., needle exchange programmes, and distribution of other drug equipment; and

- Providing antiviral drug treatment and monitoring programmes for suitable, eligible individuals chronically infected with HCV. In Yukon and other territories, there is an incentive for the patient to be screened because treatment is provided for free to eligible HCV positive patients.

In the past few years, the use of drugs in Canada has escalated which, in turn, has influenced rates of HCV. For example, in Northwest Territories among individuals aged 15 years and older that were surveyed in 2002, 16% had ever used illicit drugs, while in 2009, 24% reported that they had ever used illicit drugs [1]. The data also reflect increases in injection drug use among women, youths/young adults, and the First Nations population.

HDV

In Canada, HDV testing is only done for individuals who are HBsAg positive.

Reference

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Based on a presentation by
B. Larke, Provincial Laboratory for Public Health, Edmonton,
Alberta, Canada.

Alaska

The State of Alaska is responsible for immunization coordination and provides via the federal government vaccines against infectious diseases, including HAV and HBV, at no cost to children. Vaccination policy in Alaska follows the US Advisory Committee on Immunization Practices (ACIP) recommendations. State public health nurses travel to communities to provide immunizations, which can also be given by the community health practitioners.

HAV

In Alaska, HAV vaccine was licensed in 1995 and ACIP recommended routine vaccination for US children in populations with high HAV rates, including American Indian/Alaska Native communities. In January 1996, universal HAV vaccination was implemented for all Alaskan children 2-14 years of age. This was expanded to 2-18 year olds in 1997, and to 1-18 year olds in 2006. From 2001, HAV vaccination was made a requirement in Alaska for daycare and school attendance. In 2010, 44.7% of Alaskan children (native and non-native) received at least 2 doses of HAV vaccine [1]. Vaccination coverage of 24-35 month old American Indian/Alaska Native children was the highest among all racial/ethnic groups in the US.

Targeted vaccination of children in high incidence areas between 1996 and 1997 resulted in a 20-fold decrease in HAV incidence from 1997-2001 in the American Indian/Alaska Native population to a rate similar to the overall US rate and this decrease continued between 2001 and 2007, classifying Alaska as a country of low HAV prevalence. The decrease in HAV rate was most pronounced among children aged 0-14 years: from 112/100,000 to 0.2/100,000 [2]. There is no general HAV vaccination programme targeting adults in Alaska. Experience from Alaska, and also from Israel, has shown that universal childhood HAV vaccination programmes can be effective in eradicating HAV infection in adults, if children are the main

route of transmission. This consequently reduces the need for catch-up programmes, unless transmission includes other routes such as contaminated water.

The results for long-term immunogenicity after administration of HAV vaccine in children are in line with long-term data in adults, with no change in geometric mean titre (GMT) at 10 years post-vaccination. Only a few children became seronegative, but this number was not significant enough to consider the introduction of a booster dose. Modelling suggests that depending on the age of administration and the different schedules used, immunogenicity may last longer than 15-32 years post-vaccination [3,4]. Continued observation of these cohorts is necessary to understand the duration of antibody persistence and protection given by HAV vaccination.

HBV

Different measures, summarized below, were taken in Alaska to reduce HBV among Alaska Native population.

Alaska Native HBV control programme:

- 1978: Establishment of a registry of HBsAg positive persons
- 1980: Screening of pregnant women for HBsAg with HBIG given to exposed infants at birth
- 1981-82: HBV vaccine demonstration project

Alaska Native HBV mass screening and vaccination programme:

- 1984-87: 52,000 Alaska Native persons screened; 40,000 susceptible persons vaccinated
- since 1984: Vaccination of all infants starting at birth
- since 1982: Screening of HBsAg positive persons using AFP every 6 months; follow-up of elevations
- since 2001: ALT and aspartate aminotransferase (AST) testing added; HBV DNA testing of persons with elevated levels; persons with HBV DNA >2000IU/ml evaluated for treatment
- 2007-2010: Vaccination of non-native high risk groups

Universal HBV vaccination for children was introduced in 1984. In 2010, 71.2% of Alaskan children (native and non-native) received the universal HBV birth dose, and 91.8% of children received at least 3 doses of HBV vaccine [1].

Furthermore, between 2007 and 2010, the State of Alaska received CDC funding to vaccinate high risk adults against HBV and, by January 2012, ~5000 doses had been administered. A collaborative project vaccinated clients of the Anchorage Syringe Exchange Program, offering HCV antibody testing as an incentive. All adult HBV vaccinations ceased in 2012 due to lack of funding.

Since 1980, all pregnant women are screened for HBV and infants born to HBsAg positive mothers are given HBIG and HBV vaccine within 12 hours of birth and are followed up. Sexual and household contacts of the HBsAg positive women are identified, tested, and vaccinated when appropriate.

Studies of the long-term efficacy of HBV vaccine in Alaska have shown that the vaccine protects completely against acute symptomatic HBV and chronic HBV for up to 22 years in those immunized as children and adults (results from 30 year study pending) [6] and up to 15 years in those immunized as infants [7]. Breakthrough infections are rare and do not seem to be affecting public health,

even when immune memory wanes. There is currently no scientific evidence that vaccines do not protect against disease; therefore introduction of an HBV booster dose in the routine vaccination programme is not recommended [8]. Long-term follow-up of a cohort of children from HBsAg positive mothers, vaccinated with a 4-dose (0, 2, 4, 12 months) HBV schedule (starting at birth) is ongoing and will provide valuable data.

The Alaska Native HBV Program is well supported by the population. There is no social stigma in Alaska surrounding HBV, and substantial resources are provided by the US. The role of primary care physicians and village health aids is essential to the success of the programme.

HCV

There is no organized screening for chronic HCV for the Alaskan population, however the blood donor screening programme which includes tests for HBV, HCV and HIV works well. Positive results are reported to the State and a letter is sent to the patient advising them to consult a doctor, but no further follow-up is done.

Treatment and follow-up of patients with HBV and HCV

In remote populations the primary care providers are responsible for treatment (via telemedicine with the Alaska Native Medical Center [ANMC]), so it is important that a level of education is maintained. Information for health care providers on viral hepatitis and liver disease, including treatment, is available from the Alaska Native Tribal Health Consortium (ANTHC) [9]. Due to the fact that the health care system in Alaska is fragmented, there is no referral for treatment for HCV in non-native persons; it is up to the provider to offer it.

Viral hepatitis registries

In addition to their application for research, computerized registries of patients with HBV and HCV can be useful tools for implementing into clinical practice evidence-based practice guidelines, such as those of the European Association for the Study of the Liver (EASL) and the American Association for the Study of Liver Diseases (AASLD). Personal identification of cases can be used, because in the US it is allowed for the purposes of patient management. Such a legal framework would be useful in other countries. Through public health registries, reminder letters can be generated to prompt patients to go for testing, specific tests and vaccination can be recommended and educational material can be disseminated (including information for family members/close contacts).

The ANTHC HBV and HCV registries are used for patient tracking, generating reminders for laboratory testing, summarizing clinical information for reports and clinical research.

Every 6 months, the ANTHC HBV registry generates a letter which is sent to 1350 HBV carriers to remind them to have a blood test and a list of patients (including lab slips with barcodes) that have been contacted is sent to the health practitioner of each community. Blood is taken in the village clinic or hospital. Patients who fail to have blood drawn (within 3 months of the first letter), receive a reminder letter. Compliance is good; overall, 70-80% are being followed up at least every 2 years.

Baseline HBV DNA testing was performed for all carriers in 2001. Follow-up HBV DNA testing is performed for patients with elevated ALT or AST; those with a personal or family history of HCC; and those with previous HBV DNA elevations above 2000IU/ml. Patients with HBV DNA between 2000 and 20,000IU/ml have repeated

HBV DNA levels performed at each visit. Patients that are evaluated further are described below.

HBV patients that receive further evaluation:

- Patients with AFP levels >10ng/ml are referred to nearest hospital for ultrasound or triphasic CT scan, reviewed by teleradiography at ANMC
- Patients over the age of 40, or with persistently elevated ALT levels or ALT levels >twice upper limit of normal and HBV DNA >2000IU/ml are recommended a liver biopsy at ANMC to see if they need treatment. Patients under 40 years of age with elevated ALT and HBV DNA >20,000IU/ml are also recommended a liver biopsy at ANMC
- Patients with moderate or severe inflammation or fibrosis (Metavir/Ishak score ≥ 2) are treated with anti-viral therapy

Data from the ANTHC HBV registry show that individuals with immune active HBV who are HBeAg negative and who have HBV DNA over time between >2000 and 20,000IU/ml, are unlikely to have moderate to severe liver fibrosis. However, if the HBV DNA level exceeds 20,000IU/ml on at least one occasion over time there is a 75% chance that individuals will develop moderate to severe inflammation and/or fibrosis. Therefore, the threshold of 20,000IU/ml appears to be a good marker to indicate treatment without biopsy. In contrast, HBsAg titres do not appear to correlate with the degree of liver inflammation or fibrosis that are found in biopsy.

The ANTHC HCV registry generates reminder letters that are sent to HCV patients every 6 months to take to their nearest health care provider with a list of laboratory tests to be done. Patients with clinical evidence of advanced fibrosis (Metavir 3 or 4 on biopsy), clinical evidence of cirrhosis, or AFP levels persistently >10ng/ml are sent a separate letter every 6 months to take to their health care provider recommending liver ultrasound. Follow-up compliance is low (half of the HCV patients do not keep appointments), which may be explained by the fact that the primary risk factor for infected individuals is IDU, and many have some mental health problems. However, this

phenomenon is not observed with the same population in Denmark. HCV patients with higher risk for HCC are recommended to have an ultrasound every 6 months. As most of these patients live in cities where ultrasound is available, compliance is good. In contrast, 80% of HBV patients live in remote areas, therefore testing AFP seems more useful for detecting patients with HBV who are at risk of developing HCC. Those with AFP >10ng/ml are referred to the nearest hospital for liver ultrasound.

Patients with small tumors may have surgical resection or radiofrequency ablation. Patients are referred to Seattle if liver transplantation is necessary.

HCV outcomes study

From 1994-2005, 960 HCV patients were followed in a retrospective-prospective population-based study (mean 7.2 years prospectively, mean 12.1 years retrospectively) [10]. The characteristics and outcomes updated through 2011 of this cohort are shown in the Table below.

Outcomes for PegIFN/RBV treatment

HCV treatment was given to 156 patients (167 courses): 110 with pegylated interferon and Ribavirin (PegIFN/RBV); 34 with standard IFN/RBV; 15 with standard IFN; 12 with Telaprevir or Boceprevir/PegIFN/RBV and 1 with interferon lambda (Infergen).

The outcomes (up until August 2011) for 102 patients treated with pegIFN/RBV are shown in the Table on next page. A good response to treatment is found with genotypes 2 and 3. Although selection of patients is careful and treatment is free, the drop-out rate is high. If a patient misses more than 1 week, treatment is stopped. HCV treatment requires substantial infrastructure and manpower resources. Newer antiviral drugs with fewer side-effects could help improve treatment compliance rates.

Treatment with Telaprevir and Boceprevir has recently started in Alaska. However, with these drugs intense patient monitoring for side effects is required. HCV genotype 1 patients with moderate to severe fibrosis will be offered triple therapy if they have a compatible liver biopsy or FIBROSpect2 above 80 and those with

Characteristics of 960 Alaskan HCV patient followed from 1994-2005, updated 2011

Characteristic/outcome	N (%) or mean (range)	
Age	50.6 years (13-88)	
Sex	Male 603 (46%)	Female 696 (54%)
HCV genotype	1(66%); 2(20%); 3(13%); 4(0.4%)	
Co-infections	HIV (n=38; 16 living); HBV (n=15)	
Risk behaviours	History of IDU (57%)	Blood transfusion (20%)
Diabetes type II	83 cases known	
% BMI ≥ 30	27%	
Treated for HCV	150 (14% of PCR +)	
Liver biopsy	361 patients (28%); 69% Ishak 0-2 and 31% Ishak 3-6	
Estimated length of HCV infection	24.4 years (4-60)	
End stage liver disease (ESLD)	121; 74 Ascites, 69 Varices, 59 Coagulopathy, 32 Hepatic encephalopathy	
HCC	36	
Death	266 (66 [24%]) Liver related death [LRD]	

Outcomes for PegIFN/RBV treatment in 156 Alaskan HCV patients

Genotype	Treated	Discontinued	Failed	Relapsed	SVR*	SVR in those who completed treatment
1	47	22 (47%)	11	4	15 (32%)	10/25 (40%)
2	37	7 (19%)	3	3	27 (73%)	24/27 (89%)
3	18	6 (33%)	1	2	9 (50%)	9/12 (75%)
Total	102	35 (34%)	15	9	51 (50%)	43/64 (67%)

*SVR: Sustained Virologic Response

bridging fibrosis or cirrhosis will be prioritized. Genotype 1 patients with mild or no fibrosis will be encouraged to wait for oral combinations. Genotype 2 and 3 patients will be offered PegIFN/RBV regardless of disease stage.

Alaska Native children are followed and treated for HCV when appropriate. Of 20-25 children with HCV, it was only felt that treatment was appropriate for 1 child. This 13-year-old has cirrhosis, responded to treatment, but then relapsed. The child is currently waiting for new drugs with fewer side effects to become available.

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Based on presentations by

T. Thomas, Alaska Native Medical Center, Anchorage, Alaska;
L. Bulkow, Centers for Disease Control and Prevention, Anchorage, Alaska;
B. McMahon, Alaska Native Medical Center, Anchorage, Alaska.

The Nordic Arctic

The Nordic countries have selective programmes for vaccination against HBV, rather than universal infant vaccination. A survey conducted by ECDC revealed that there is variance between the different countries in the population groups that are targeted for HBV vaccination, as shown in the Table on the next page:

Iceland

HAV

There are recommendations for HAV vaccination for travellers, IDU, and homosexuals. The number vaccinated is high: in 2010, 3879 individuals were vaccinated against HAV.

HBV/HCV

In Iceland, there is screening (active surveillance) for chronic HBV and HCV for the following groups:

- for immigrants from outside the EU, screening is mandatory (along with HIV and TB) and effective because it forms part of the health assessment before a person is allowed to stay in Iceland. Those found positive are offered treatment, if eligible. It should be noted that many Icelanders found HCV screening of immigrant children and during pregnancy controversial, as there is no effective treatment;
- for pregnant women to identify children at risk and ensure follow-up and treatment of infected mothers. Participation is only 25% and needs to be improved; 3-8 HBsAg positive cases are identified each year, mainly originating from Asia;
- blood donors (100% participation); and
- drug users (participation unknown).

In addition to the groups listed above, HBV vaccination is also recommended for blood recipients, travellers, and for those wanting a tattoo or body piercing [2]. There is no active screening programme for prisoners, but they are offered vaccination. Vaccination coverage needs to be improved within the IDU population. A needle exchange programme has recently started. Diagnosis and registration of acute disease also requires improvement, to differentiate it from chronic HBV. Treatment for HBV is being centralized (there is 1 gastroenterologist in Iceland that takes care of the treatment).

Every year, around 3000 people are vaccinated against HBV in Iceland. Vaccinations are registered in the central vaccination database, with personal identifiers, at vaccination sites (health centres,

HBV risk group vaccination programmes in Nordic countries

	Finland	Norway	Sweden	Iceland
Neonates born to HBsAg+ mothers	✓	✓	✓	✓
Individuals at risk for HBV due to occupation	✓	✓	✓	✓
Haemodialysis patients		✓	✓	✓
Chronic liver disease patients		✓	✓	
Household contacts of injecting drug users	✓			
Intravenous drug users	✓	✓	✓	✓
Household contacts of HBsAg+ patients	✓	✓	✓	✓
Homosexuals		✓	✓	✓
Immigrants (high/middle endemic countries)		✓	✓	
Newborns with at least one parent from an HBV-endemic country		✓	✓	
Prisoners			✓	
Commercial sex workers	✓	✓		

Source: Surveillance and prevention of hepatitis B and C in Europe. Stockholm: ECDC 2010 [1]

hospitals, with private physicians/subspecialists, and other places). Since 2007, there has been an electronic real time interactive central vaccination database - the Vaccination Register - which records all vaccinations from 2002, and to which all health centres and hospitals are connected (not yet to private health offices). Health centres and hospitals, as well as individuals, can access information from the database. The central vaccination database can be linked to other databases, for example to the International Classification of Diseases 10th revision (ICD-10) diagnosis registers, and can also be used to study coverage and vaccine effectiveness. Whilst vaccination data are not considered sensitive in Iceland, there have been individual privacy issues that have arisen during international collaborative projects investigating adverse effects following vaccination.

The introduction of universal childhood vaccination with hexavalent vaccine containing HBV antigen into the childhood vaccination programme is under consideration. Although it is perceived to be more expensive, there are currently no plans to perform a cost-effectiveness analysis for HBV vaccination in Iceland.

Sweden

A number of measures are helping to reduce the spread of HBV and HCV in Norrbotten County including: risk group screening campaigns (including immigrants); screening of pregnant women; contact tracing for all diagnosed cases; and vaccination. In Sweden, many health care decisions, including the implementation of vaccination programmes, can be made at a county level.

HBV

In addition to vaccination of risk groups (including children), routine HBV vaccination for children has been in place in Norrbotten County since 2011, although universal HBV vaccination has not been implemented at national level.

HCV

The Swedish Communicable Diseases Act of 2004 requires HCV infected patients to have personal guidelines to prevent spread of the disease. Infected individuals should be given support and treatment for HCV and also for drug dependence (when applicable). Contact tracing is mandatory for every case.

Norrbotten County Council conducted a survey in 2008 to evaluate reduction of the risk of spreading HCV and other blood-borne diseases among HCV patients. A questionnaire was sent to physicians who had reported new cases of HCV during 2005-2006 in Norrbotten County. Results revealed that contact tracing was mostly done by the physicians themselves and had only been done for about 20% of the cases; only partners and children were traced, but not drug-sharing contacts. Following this survey, new strategies for contact tracing have been put into practice: patients are to be referred to a counsellor who is responsible for tracing contacts. It is important that the counsellor has good knowledge about blood-borne diseases, health promotion, and psychosocial support. Clear guidelines on how to deal with young people who are at risk, using drugs, and/or HCV positive are needed. Through a 3-year project, education about blood-borne diseases and prevention will be provided to personnel who meet people at risk; motivational interviewing techniques will be taught; better information will be provided for young people and those with cognitive problems; and collaboration will be established between drug departments, social services, mental health departments, and infectious disease clinics.

In Norrbotten County from 2005-2010, young people were generally being tested for HCV under their own initiative at community health centres or youth counselling services. Drug dependence treatment centres and mental health care services rarely tested for HCV. There is no free needle exchange programme in Norrbotten county.

Norway

Selective HBV vaccination only reaches 20-25% of susceptible IDUs. Several working groups in Norway are currently advocating routine HBV vaccination, because risk group vaccination is expensive and has proven inefficient. Health economics analyses are needed, because of competing priorities and the availability of new vaccines for HPV and influenza.

Finland

There is a very complete HBV screening programme for pregnant women and a needle exchange programme is in place for IDU. HBV vaccination is only offered free to certain risk groups.

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Based on presentations by

H. Blystad, Norwegian Institute of Public Health, Oslo, Norway;

T. Gudnason, Directorate of Health, Reykjavik, Iceland;

A. Nystedt, Norrbotten County Council, Lulea, Sweden;

A.L. Lindqvist-Svedberg, Norrbotten County Council, Lulea, Sweden.

The Russian Federation

HAV

There is no universal HAV vaccination programme in Russia at the federal level, however it is included in vaccination calendars in some regions. HAV vaccination is also used when outbreaks occur and for risk groups.

HBV

HBV testing is stringent in the Russian Federation, for example, all

immigrants and anyone admitted to hospital are tested. Screening for HBV and HCV is mandatory for targeted groups (including blood donors, pregnant women, HCW, immigrants, newborns of mothers with HBV or HCV; chronic liver disease patients, inpatients; outpatients, e.g., at drug and alcohol rehabilitation centres and STD clinics; patients on haemodialysis; children in orphanages; households and contacts of HBV/HCV patients; and military personnel). As a result, 10% of the population in the Russian Federation have been screened for HBV. In the Arkhangelsk region, 160,000 tests are performed annually, representing 15% of the population tested every year.

The decreasing trend in HBV is due to a successful routine vaccination programme. The HBV vaccination programme is not mandatory, but refusal can lead to limitations, such as school entry refusal. In 1998, the Russian Federation started a programme of universal immunization of newborns, but due to a problem in availability of imported vaccines, good coverage above 93% was only achieved as of 2003. Currently most vaccines used are produced in Russia. In 2010, coverage in newborns was 97.9%. From 2006, coverage >92.7% has been achieved for teenagers (14-19 years of age). At present, around 80% of people up to the age of 35, and 60% of people up to the age of 65 have been vaccinated. In 2011, the total number of vaccinated people in the Russian Federation was ~81 million (total population is ~142 million). In addition to universal newborn immunization, risk groups are also vaccinated.

Overview Table 4: Hepatitis prevention programmes in Arctic region: HAV and HBV vaccination, HBV and HCV screening.

	HAV vaccination	HBV vaccination	Screening HBV	Screening HCV
Alaska	Universal vaccination (2-18 years)	Universal vaccination of infants starting at birth (min 3 doses) Vaccination of risk groups	State follows CDC guidelines: recommends screening of persons born in endemic countries and other high risk groups	Recommends screening for high risk groups as per CDC guidelines
Canadian Arctic	Recommended for high risk groups (e.g., travellers to endemic countries)	Universal vaccination: early infancy (3 doses) or pre-teens (3 doses); health care workers	Recommended for: pregnant women, contacts of HBsAg+ persons. Mandatory for all Canadian blood donors	Recommended for (in Yukon): pregnant women, IDU, persons with STD and their contacts, recipients of blood products before 1992. Mandatory for all Canadian blood donors
Greenland	No	Universal vaccination (0, 3, 5, 12 months) Catch-up programme for children 12 years of age	Recommended for: pregnant women, contacts to HBsAg+ persons, blood donors, patients prior to chemo- and immunosuppressive therapy, HIV+ persons, patients with elevated ALT	No
Iceland	Recommendations for travellers, IDU, homosexuals	Risk group vaccination*	Screening for chronic HBV-HCV: migrants from outside EU, pregnant women, blood donors, drug users	
Russian Federation	No vaccination programme; only for outbreak control and certain risk groups	Universal newborn vaccination and vaccination of risk groups	Screening for HBsAg mandatory for specific target groups (incl. blood donors, pregnant women, HCW, migrants)	
Nordic countries				
Finland	Drug users	Risk group vaccination*	Programme for pregnant women	-
Norway	-	Risk group vaccination*	-	-
Sweden	-	Risk group vaccination* Universal vaccination of infants in Norrbotten County	Risk group screening campaigns for HBV-HCV (including immigrants); pregnant women, contact tracing for all diagnosed cases	

*see Table page 24: Risk group vaccination programmes for HBV in Nordic countries

Globally, 2% of the Russian population is HBsAg positive. Long-term analyses of vaccinated cohorts will need to take into account that chronic infection might have occurred before vaccination, and thus should not be viewed as vaccine failure.

Annually, 12% of the population of the Arkhangelsk region have been vaccinated against HBV. The main vaccination cohorts were firstly teenagers, then young adults (18-35 yrs) and, because there was still vaccine available, some older people were also vaccinated. Since 2004, coverage for children under the age of 1 year has been >95%. From 2007-2010, coverage for the age group 1-17 years in the Arkhangelsk region was around 95%. Coverage for the 18-35 year

age group was initially low in 2007, but in 2010 was around 82.5%. For adults up to 65 years old, coverage is >60%.

HCV

In 2008, due to the availability of new tests and equipment, the frequency of HCV testing increased. Testing for HCV in Arkhangelsk region is slightly less frequent than for HBV, but still high: around 12.5% of the population were tested between 2009 and 2011.

*Based on presentations by
A. Tulisov, UNICEF, Arkhangelsk, Russia; V. Chulanov,
Central Research Institute of Epidemiology, Moscow, Russia.*

Conclusions

The Arctic region is large, comprising the northern parts of 8 countries (northern parts of the United States of America (Alaska), Canada, Greenland, Iceland, Norway, Finland, Sweden and the Russian Federation), but it is scarcely populated, with a total of around 4 million people and a proportionally high number of young people. In addition to non-indigenous populations, the Arctic is home to numerous diverse, indigenous populations, including Alaska Native, First Nation, Inuit, and Sámi. Indigenous populations have their own languages and traditions, including the use of healers. Many communities live remotely and can be difficult to access due to poor transport infrastructure and challenging weather conditions. Access to public health and acute care systems can be limited and costly, particularly if air transportation is required to reach remote communities. Often these communities live in substandard conditions, with poor housing, water supplies, and sanitation. Although there have been improvements in health and life expectancy of indigenous populations in the Arctic over the last 50 years, life expectancy is shorter and infant mortality rates are still higher than in the southerly parts of these countries. Higher rates of some infectious diseases, including HBV, have been found in some indigenous communities of the Arctic.

Health care systems

A broad variety of health care systems exists across the Arctic region, involving socialized medicine (Greenland, Canada, Alaska, Iceland, Finland, Sweden, Norway, Russian Federation) besides private provision. In some countries the health system is centralized (Norway, Iceland); for others it is decentralized and organized at a regional level (Sweden, Finland); or a mixed system of central government and regional organization exists. In some countries the systems are very co-ordinated, while in others there is a fragmented system (Alaska).

A range of primary, secondary and tertiary health care services exists across the Arctic region. Generally, the more remote Arctic communities have community health centres/clinics (e.g., in Greenland, Alaska, Iceland). Primary health care workers in the communities have a pivotal role in public health. Telemedicine linked to referral centres can be a very valuable resource to remote primary care clinics. Larger towns or regions are often serviced by small hospitals. Specialist care is sometimes only available at one main hospital and transportation costs for tertiary referral can be considerable.

Surveillance

In the Arctic region HAV, HBV and HCV are reportable diseases, whilst HDV and HEV are not reportable, and the diagnostic testing of the latter are in most Arctic countries incomplete or even non-existent. Reporting is mostly based on clinical and laboratory data, enhanced with patient follow-up. Limited funds are available for analysis and use of the data for public health purposes. Some prevalence data need updating (e.g., Canada), taking advantage of new assays.

Under-reporting of cases was mentioned as an issue in most of

the countries of the Arctic region, and clinicians in particular are seen as the weak link in the reporting system. Several approaches for improved reporting were suggested:

- educating medical school students about the importance of reliable data;
- focusing on epidemiology, clinical medicine and public health in medical school programmes;
- providing clinicians with feedback, showing added value of notification;
- using electronic and automatic systems to transfer clinician's diagnosis directly to a registry;
- possible incentives;
- clarifying appropriate timing for reporting process to clinicians with regards to availability of lab confirmation; and
- enhanced reporting by hospitals, allowing for improved discrimination between acute and chronic infections.

A variety of systems (registries and databases) exist for the collection of viral hepatitis data. Hepatitis databases, such as DAN-HEP which makes use of unique coded identifiers, could be valuable tools with a broad application, including the follow-up of treatment for patients with chronic viral hepatitis. The Alaska Native Tribal Health Consortium's HBV and HCV registries are well-established and are used effectively to benefit clinical practice, as well as research. Automated reporting and notification systems are well developed in Nordic countries and could be applicable elsewhere, but issues of privacy and confidentiality need consideration.

International co-operation

The Arctic regions of countries often have common health issues and socioeconomic conditions, therefore collaboration between these regions is important. The International Union for Circumpolar Health is an NGO comprising several bodies that focus on health in the Arctic, with 18 working groups, including infectious diseases, environmental health, health policy and food security. Other organizations include the Arctic Council ministerial forum, networks, expert groups and bodies bringing together different countries and groups; health aspects covered range from health inequities and diet to mental health and surveillance. The EpiNorth surveillance project involves the collaboration of different countries of the northern part of Europe including the three Arctic Nordic countries and the western part of the Russian Federation. This project is generating useful data; including evidence of the dramatic reduction in the notification of acute HBV in the north-west of the Russian Federation.

Epidemiology

In some of the Indigenous Arctic communities, higher rates than the national average have been found for some infectious diseases. The prevalence of infectious diseases appears to be low in the Sámi population. Immigrants from highly endemic countries increase prevalence rates and may account for the high rates of viral hepatitis seen in Arctic regions. In countries with small indigenous populations, immigrants may also account for most

chronic infections. Vaccination is widely accepted and has dramatically reduced incidence rates of vaccine preventable disease.

HAV

Vaccination, coupled with improved water quality, sanitation and preventive measures (food handling), have made symptomatic HAV rare or quasi-non-existent in most Arctic countries. Most HAV infection is now confined to travellers to endemic countries, who require vaccination. HAV vaccination of children has been shown to reduce the incidence of HAV infection in adults. Experience from Alaska, in line with the experience from Israel, has shown that universal childhood HAV vaccination programmes can be effective in eradicating HAV infection in adults, if children are the main route of transmission. This consequently reduces the need for catch-up programmes, unless transmission includes other routes such as contaminated water. Protective immunity against HAV has been demonstrated up to 17 years post-vaccination (with 2 doses) and administering 1 dose has been shown to be effective in an HAV outbreak situation, but more evidence is needed to use 1 dose generally.

HBV

In the Arctic region, universal HBV vaccination has dramatically reduced rates of HBV, particularly in Canada, the Russian Federation and Alaska (no HCC has been found in Alaskan children since 1999). HBV vaccination has resulted in a generation of Alaska Native children who are free of HBV and its sequelae. Risk group vaccination is costly and it was mentioned during the meeting that this approach is often not effective; more cost-effectiveness data are needed to drive policy development and assist decision-making. The introduction of universal HBV vaccination at national level is currently under consideration in Iceland and Norway. There is presently no evidence to support the introduction of a HBV booster dose.

Research has shown that the predominant route of HBV transmission is genotype-dependent. The Alaska Native population is not ethnically diverse, yet a defined distribution of 5 of the 8 genotypes of the HBV virus is found. A new B6 subgenotype has been identified in Greenland, Canada, and Alaska; it seems to be associated with a less severe disease course, but the natural history of infection with this subgenotype requires further investigation. Occult HBV has been documented in Northern Canada in 4% of HBsAg negative individuals. The clinical course of cases of occult HBV needs to be studied further.

HCV

There is a high prevalence of HCV in the Russian Federation, Iceland, northern Sweden, and northern Finland, which correlates with increases in injecting drug use among the younger generation. Such rise of HCV infection in young people due to increased drug abuse is also seen globally, e.g., in the US reports from rural areas and small cities in Massachusetts, Wisconsin and South Florida. Despite extensive prevention programmes, HCV outbreaks among IDU continue to occur (e.g., in Norway). HCV is less common in remote areas (e.g., in Greenland) since it is linked to the accessibility of injectable drugs. It is important to bear in mind that sometimes higher rates of reported HCV are a reflection of successful screening and follow-up (including contact tracing), as has been found in the Yukon, northern Canada. Research in Alaska has shown that alcohol is a strong cofactor for adverse outcomes in patients with HCV. Indigenous populations generally have similar prevalences, genotypes and risk factors for HCV infection as populations in the non-Arctic regions of countries.

Spontaneous clearance of HCV has been reported in 18% of patients in Canada. If this resolution of the virus could be understood, it could assist in the development of a HCV vaccine.

In Alaska (Alaska Native Program), Canada (First Nations programmes), Iceland, Greenland and Sweden, HCV antivirals are offered to patients for free; while in Russia, patients have to pay for anti-viral treatment.

HDV

In some communities in Greenland that are endemic with HBV, superinfection with HDV is a problem. HDV has also been re-

ported in the Russian Federation as major contributing factor to liver cirrhosis, but is uncommon or non-existent in most other countries.

HEV

Possibly due to infrequent testing, only a few sporadic cases of HEV, mostly imported, have been reported. Karibou/reindeer in Canada may be a reservoir of the virus but currently no serological evidence has been found.

Prevention and treatment

Varied hepatitis vaccination policies exist across the Arctic region. A universal HAV vaccination policy exists in Alaska, while in Canada, Finland, Iceland, Norway, Sweden and the Russian Federation there is a selective HAV vaccination policy. There is universal HBV vaccination in Greenland (since 2010), the Russian Federation, Canada, and Alaska; and selective HBV vaccination in Finland, Norway, Sweden, and Iceland. In most countries vaccinations are provided free of charge. In Alaska, vaccination against HAV and HBV is provided to all children at no cost. A decentralized health care system, such as the one in Sweden, can enable regional decisions to be made about health care programmes, including the introduction of universal vaccination.

In addition to vaccination, continued screening and improvements in living conditions and access to care, the continued need for education was emphasized. In Alaska, registers of HBV and HCV patients are used to send reminders for testing, provide test results, and disseminate culturally sensitive educational material. Often it is necessary to provide information in a number of different languages. Educational programmes targeting at-risk groups (e.g., IDU), such as the approach used in northern Sweden, can be particularly useful for HCV prevention. Moreover, new and successful approaches like contact tracing (e.g., those demonstrated in the Yukon and northern Sweden) are also important for prevention and control of viral hepatitis.

Future activities

- There should be continued surveillance and follow-up of HAV and HBV vaccination, focusing on vaccinated cohorts and the long-term public health impact on populations.
- Research to demonstrate immunological memory and duration of protection is also needed. Education about persistence of HBV in the environment is needed in order to persuade the public about the value of prevention of viral hepatitis, such as the vaccination of children before the commencement of sexual activity. Culturally sensitive and multi-language education and trainings material need to be developed.
- Further investigation of non-responders to HBV vaccination is needed to determine whether not responding is due to host or administrative factors (e.g., in communities in Greenland).
- More research is needed on the natural history of specific genotypes (e.g., B6) as well as studies to understand the interaction between HBV and HDV in Greenland, as well as an evaluation of the recent introduction of universal HBV immunization there.
- Lifestyle factors (such as alcoholism, drug abuse, HPV infection) should be considered as potential confounders of HBV and HCV disease. It would be interesting to understand why IDUs are infected with HCV and not HIV in some countries.
- The quality of reported data could be improved for some Arctic regions by addressing the issue of under-reporting. Furthermore, harmonizing case definitions and standardizing other surveillance parameters (e.g., risk factors, transmission routes) would facilitate comparison of data.
- Analysis of the available data in the existing databases and extra economic studies on the impact of vaccination and screening should be utilized to inform public health decisions, in addition to being used for research.
- The ongoing evaluation of the availability and the impact of treatment for HBV and HCV on the incidence of HCC and cirrhosis is important.

These multiple challenges and opportunities emphasize the need to further enhance circumpolar collaboration, in order to benefit from shared experience and data within the Arctic region.

List of Participants

Blystad Hans	Norway	Lindqvist-Svedberg Ann-Louise	Sweden
Børresen Malene L	Denmark	Marano Cinzia	Belgium
Bulkow Lisa	Alaska, USA	Marinho Rui Tato	Portugal
Canuel Ed	Denmark	McMahon Brian	USA
Delpire Véronique	Belgium	Minuk Gerald	Canada
Dominguez Angela	Spain	Norder Helene	Sweden
Donoghoe Martin	Denmark	Nystedt Anders	Sweden
Duffel Erika	Sweden	Olivieri Antonio	Belgium
Engelen Emmy	Belgium	Parkinson Alan	Alaska, USA
FitzSimons David	Switzerland	Pfeifer Dina	Denmark
Gregersen Bo	Denmark	Reic Tatjana	Croatia
Gudnason Thorolfur	Iceland	Roudot-Thoraval Françoise	France
Hendrickx Greet	Belgium	Shouval Daniel	Israel
Hallauer Johannes	Germany	Stenz Flemming Kleist	Greenland
Harmanci Hande	Switzerland	Thomas Timothy	Alaska, USA
Hauser Natalie	Denmark	Tulisov Andrey	Russia
Koch Anders	Denmark	Van Damme Pierre	Belgium
Kojouharova Mira	Bulgaria	Vanderpooten Anita	Belgium
Krarup Henrick	Denmark	Vorstens Alex	Belgium
Kuusi Markku	Finland	Ward John	USA
Ladefoged Karin	Greenland	Weis Nina	Denmark
Larke Bryce	Canada	Zanetti Alessandro	Italy
Lavanchy Daniel	Switzerland		

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For further information, please contact:
VHPB Executive Secretariat
Centre for the Evaluation of Vaccination
Vaccine and Infectious Disease Institute
Faculty of Medicine and Health Sciences
University of Antwerpen (Campus 'Drie Eiken')
Universiteitsplein 1, B-2610 Antwerpen, Belgium
Tel +32 (0)3 265 25 23, Fax +32 (0)3 265 26 40
E-mail: info@vhpb.org