Population-based epidemiological survey of hepatitis B, D and C among Inuit migrated to Denmark and in high endemic Greenland

I will talk

most about HBV
less about HDV and
least about HCV
Hepatitis B in Greenland

1973: 2900 cases screened, 7.1 % HBsAg positive
   P. Skinhøj Am J Epidemiol 1974

1985: 1893 cases screened in Sisimiut, 11.5 % HBsAg positive
   O Rosing Olsen UFL 1989

1997: 503 cases screened, 7.0 % HBsAg positive
   B C Langer J Viral Hepat 1997

2007: 8879 cases screened, 7.4 % HBsAg positive
   M. Børresen Phd afhandling 2010
Background

Greenland is an endemic area of hepatitis B infection (HBsAg > 7%)

Most transmission of hepatitis B virus (HBV) in Greenland takes place before the age of 20 years

Liver cirrhosis and liver cancer (HCC) are less frequent than expected

Until September 2010 HBV vaccination was not part of the national infant immunization programme in Greenland
Hepatitis B virus infection among Inuit in Greenland

Study 1:
Participants living in Greenland:
229 men and 205 women with both parents born in Greenland
Age 50 – 69 years
Participation rate 95 %

Study 2:
Participants living in Denmark:
33 men and 103 women of which 81% had both parents born in Greenland and 46 % had lived more than half of their life in DK
Age 40 – 69 years
Participation rate 52 %

Krarup H, Andersen S et al. SJG 2008
Results Study 1

Median age was 58 years with no gender difference

None had physical signs of liver disease

HBsAg was positive in 20.4%

Fewer were HBsAg positive in Nuuk compared to Tasiilaq and settlements in Eastgreenland (4% vs. 28.9%)

No difference between Eastgreenland town and settlements (28.6% vs. 29.4%)

More men than women were positive (26.4% vs. 13.7%)

97 % were anti-HBe positive

Krarup H, Andersen S et al. SJG 2008
Flowchart

- **HBsAg**
  - +ve
  - -ve
    - **anti-HBs**
    - **anti-HBc (tot)**
      - +ve
      - -ve
        - Stop
          - 27
          - 56/61
          - HDV-RNA
            - +ve
            - -ve
              - Stop
                - 325
                - 0/5
  - **HBeAg**
    - +ve
      - HBV-DNA
        - 61/88
        - +ve
          - HBV pre-C
        - -ve
          - Stop
            - 101
            - 5/330
            - 242/343
  - **anti-HBe**
    - +ve
    - -ve
      - Stop
        - 27
        - 52/61
        - HBV genotype
Past or present HBV infection among 50 – 70 years old

Krarup H, Andersen S et al. SJG 2008
Distribution of HBV genotypes

- B: 90%
- D: 8%
- B and D: 2%
Results

The C- and X-gene and most of the genome of 20 genotype B positive samples could be sequenced

The samples showed > 94 % homology with subtype Bj and < 92 % homology with Ba

The Greenlandic samples were > 97 % mutually homologous

Krarup H, Andersen S et al. SJG 2008
Results

Among the 343 HBsAg negative, 242 (56.1%) were anti-HBc and/or anti-HBs positive, 30 were anti-HBs positive only.

In adjusted comparisons, a marginal difference was found in Bilirubin, while differences were absent for AST, GGT and BASP.
Results

Of HBsAg positive HBV-DNA was positive in 70 % (median 40,000 copies/mL (10; 90 percentiles: 1,000; 404,000 copies/mL))

Pre-core mutation analysis was feasible in 64 %, all except one had pre-core mutation (G1896A), none had CP mutations

Genotype could be determined in 59 %, of which 90 % had HBV genotype B. 8 % genotype D

Samples sequenced from 20 persons showed HBV subtype Bj (now B6)
Results Study 2

5 women and 1 man were HBsAg positive

All were anti-HBe positive and viral load was low, 200 IU/mL being the highest

Detection of precore mutation and genotype was not possible in any of these subjects

None of HBsAg positive persons was anti-HDV or anti-HCV positive

One participant had been exposed to both hepatitis B and D virus and one had been exposed to both hepatitis B and C virus

Rex K et al. SJG 2012
Markers of HBV among Greenlanders who have migrated to Denmark

North (n=67)

Capital (n=18)

South (n=45)

East (n=5)
Hepatitis D

- In all 6 persons were anti-HDV positive
  - 4 were men and 4 were from Eastgreenland
  - All had markers of former HBV infection, but only one was HBsAg positive
  - None was HBV-DNA or HDV-RNA positive
  - All 6 had elevated GGT, but only one had elevated AST

- The exposure in both our studies is generally low and lower than reported from certain areas on the west coast of Greenland
  - B C Langer J Viral Hepat 1997
  - M Børresen J Viral Hepatitis 2010

- Based on our data hepatitis D is rare among Inuit in Greenland and Denmark, but with 7 % HBsAg positive HDV infection can pose a problem
Hepatitis C

- Of 434 Inuit in Greenland screened for anti-HCV
  - 35 (8.1%) were positive with anti-HCV 3.0 (Abbott Axsym™ System), when tested further
  - 2 of the 35 were positive with Ortho HCV 3.0 Elisa, while
  - 0 of 35 were positive using INNO-LIA™ HCV Score as confirmatory test.
  - HCV-RNA was negative in all 35 samples

- Of 136 Inuit in Denmark 2 were anti-HCV positive. One was a known IVDU, living in Denmark for 47 of his 50 years

- **Hepatitis C is rare among Inuit in Greenland and Denmark**
Conclusion

More than 75% had markers of present or previous hepatitis B infection

HBV genotype B6 with pre-core mutation was predominating

HBV viral load was generally low

Liver biochemistry did not differ with HBsAg status

None had hepatitis C or D

Hepatitis B infection, genotype B, with pre-core mutation, appears to be an indolent disease in Inuit in Greenland