

PhD thesis

Host immunity to tuberculosis in Greenland

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SUMMARIES

Summary in English

Tuberculosis is still a major global health challenge with an estimated two billion individuals infected worldwide. Many of these will progress to TB unless preventive measures are identified. Currently the Bacillus Calmette-Guérin vaccine (BCG) is the only licensed vaccine against TB. To control the development and spread of TB a new and effective vaccine is much needed. It is well established that understanding how the immune system responds to tuberculosis infection and to TB is necessary to develop a new and effective vaccine. Hence, knowledge on protective immunity to both infection and disease is needed.

In recent years, Greenland has experienced an increase in number of TB cases and in 2012 the TB incidence was comparable to other TB-high-endemic countries. BCG vaccination of newborns has been a part of the childhood vaccination programme in Greenland since 1955, however it was discontinued in 1991 and reintroduced in 1997. In three studies from East Greenland, we evaluated the BCG vaccine's ability to protect against both infection and TB. Furthermore, we investigated immunity to infection and disease by evaluating how the immune system recognised antigens derived from the tuberculosis bacteria.

In the first study we evaluated the effect of BCG vaccination and found that BCG vaccination reduced the risk of infection with 20% and the risk of disease with 50%.

In the second and third study we evaluated immunity to the tuberculosis bacteria. The second study measured immunity to infection caused by the tuberculosis bacteria in its dormant stage where the individual is only infected but has not developed TB. The study was based on data from the entire East Greenlandic population in the age groups 5-31 years. Our results documented that immunity to the dormant stage of infection was the same as among individuals with previous TB. The study also documented that immunity to the dormant stage of infection did not offer the individual protection from later TB development. In the third study, we evaluated the sustainability of immunity to the infection. The study was based on measurements from 65 young adults from East Greenland and documented that immunity to tuberculosis infection is very versatile and not sustained over time.

Our findings contribute with important knowledge on the preventive ability of the BCG vaccine in the Arctic and show that BCG vaccination is still important in the prevention of TB. Furthermore, TB immunity characterised in an Arctic setting, seems to have a different pattern compared with other geographic regions. This and information on sustainability of immunity over time, contributes with new knowledge of importance for the development of a new and effective TB vaccine.

Summary in Danish - Dansk sammendrag

Tuberkulose er stadig et stort problem for den globale folkesundhed og anslået to milliarder individer er smittet. Uden forebyggende foranstaltninger vil mange af disse udvikle tuberkulose sygdom (TB). Bacillus Calmette-Guérin vaccinen (BCG) er den eneste vaccine til forebyggelse af TB, men udvikling af en ny TB vaccine er nødvendig for fremtidig effektiv forebyggelse af såvel infektion forårsaget af tuberkulose bakterien og til forebyggelse af videreudvikling til TB. For at kunne udvikle en ny og effektiv TB vaccine er det afgørende at forstå hvordan immun systemet reagere på infektion med tuberkulose bakterien og på TB.

Igennem de senere år har Grønland oplevet en stigning i antallet af nye TB tilfælde og i 2012 var TB forekomsten så høj at den var sammenlignelig med andre TB-høj-endemiske lande. BCG vaccination af nyfødte har været en del af børnevaccinationsprogrammet i Grønland siden 1955, dog med en midlertidig afbrydelse i 1991 efterfulgt af genindførelse i 1997. I tre undersøgelser udført i Østgrønland, har vi undersøgt hvor godt BCG vaccination beskytter mod infektion med tuberkulose bakterien og overfor TB. Herudover har vi undersøgt immunitet overfor både tuberkulose infektion og overfor TB ved at måle hvordan immunsystemet genkender antigener afledt af tuberkulose bakterien.

I det første studie undersøgte vi virkningen af BCG vaccination og fandt at BCG vaccination reducerede risikoen for smitte med tuberkulose bakterien med 20% og risikoen for TB med 50%.

I det andet og tredje studie undersøgte vi tuberkulose immunitet. I det andet studie målte vi immunitet over for infektion med tuberkulose bakterien i bakteriens hvilende tilstand, hvor den enkelte kun er inficeret men ikke har udviklet sygdom. Studiet byggede på målinger fra hele den østgrønlandske befolkning i alders grupperne fra 5 til 31 år. Vi fandt at immunitet overfor hvilende tuberkulose infektion uden symptomer på TB var den samme som hos dem der havde TB. Vi fandt også at immunitet over for hvilende tuberkulose infektion ikke gav beskyttelse mod senere udvikling af TB. I det tredje studie undersøgte vi immunitet over for tuberkulose infektion over tid og over for senere udvikling af TB. Dette studie byggede på målinger blandt 65 unge fra Østgrønland og vi fandt at immunitet over for infektion og TB er meget svingede over tid.

Vores studier bidrager med vigtig viden om hvor godt BCG vaccination beskytter mod tuberkulose infektion og TB i Arktis og fastslår at BCG vaccination stadig er vigtig i forebyggelsen af TB. Herudover ser det ud til at tuberkulose immunitet i Arktis har nogle andre karakteristika end det man finder andre steder i verden. Dette og den fundne alsidighed af tuberkulose immunitet er ny viden af betydning for udviklingen af en ny og effektiv TB vaccine.

Summary in Greenlandic – Naalisarnera

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