

# Tuberculosis infection among children in Greenland - Use of new TB diagnostics

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## Dansk resumé

Nærværende ph.d.-afhandling bygger på epidemiologiske studier af forskellige aspekter af tuberkulosesmitte. Det overordnede formål med afhandlingen er at beskrive forekomst og risikofaktorer for tuberkulosesmitte blandt børn i Grønland med henblik på optimering af forebyggende tiltag. Delformålet er at beskrive anvendelsen af et nyt tuberkulosedagnostisk redskab i forskellige populationer.

Første studie 'The Comparison of Screening Procedures for *Mycobacterium tuberculosis* Infection Among Patients with Inflammatory Diseases' har til hensigt at teste, hvorvidt screeningsresultater for tuberkuloseinfektion blandt patienter med autoimmune lidelser adskiller sig, alt efter om den nye diagnostiske test Quantiferon TB-Gold test (QFT) eller den nuværende test, tuberkulin hudtesten (TST), bliver brugt. Studiet evaluerer ydermere, hvorvidt mulige forskelle i testresultat afspejler kendte risikofaktorer for tuberkuloseinfektion eller immunsuppression. Studiet dokumenterer en høj andel af diskordante QFT- og TST-resultater, hvor et positivt QFT-resultat fandtes at være tættere associeret med kendte risikofaktorer for tuberkuloseinfektion end tilfældet var for TST-resultatet. Brug af corticosteroider påvirkede testresultatet i begge tests ved at øge risikoen for et inkonklusivt QFT- og mindske sandsynligheden for et positivt TST-resultat. Uoverensstemmelse mellem de to tests understreger vigtigheden af, at begge test bruges ved screening for tuberkuloseinfektion blandt patienter med autoimmun sygdom.

Andet studie 'Ongoing Tuberculosis Transmission to Children in Greenland' er et populationsbaseret tværsnitstudie af tuberkulosesmitte blandt 2,231 grønlandske skolebørn (25% af hele den grønlandske population i den relevante aldersgruppe). Formålet med studiet er at estimere tuberkuloseoverførelsen til grønlandske børn samt risikoen for tuberkuloseinfektion pr. leveår. Børnene blev testet for tuberkuloseinfektion ved brug af QFT og TST, og kun børn med et dobbelt-positivt testresultat blev defineret som tuberkulosesmittede. 8,1% af børnene var tuberkulosesmittede og den årlige tuberkulosesmitterisiko blev estimeret til 0,8%. Smitterisikoen varierede med etnicitet og geografisk lokalitet. Studiet påviser at tuberkuloseoverførelse pågår i vidt omfang til Inuit-børn i Grønland, om end med en udtalt geografisk variation imellem studieregionerne.

Tredje studie 'Risk factors for tuberculosis infection among children in Greenland' bygger på data fra 1.797 af børnene i studie to. Formålet med studiet er at evaluere potentielle risikofaktorer for tuberkuloseinfektion i Grønland. Oplysninger om mulige risikofaktorer blev indhentet fra selvudfyldte spørgeskemaer og fra nationale registre. Tuberkuloseinfektion blev defineret som positivitet i både QFT og TST. I alt var 8,4% af børnene smittede med tuberkulose, og 10% rapporterede kontakt til en tuberkulosepatient. Overordnet set var stigende alder, det at være af Inuit-herkomst samt at have snæver aldersforskel til nærmeste ældre søskende signifikante risikofaktorer for tuberkulosesmitte blandt børnene. Smitemønstret for visse risikofaktorer ændrede sig markant alt efter om man havde kendt kontakt til en tuberkulosepatient. De påviste risikofaktorer for tuberkulosesmitte blandt grønlandske børn kan bruges til at målrette den tuberkulosebekæmpende indsats mod de børn der er i størst risiko for smitte.

## Summary in English

The PhD thesis is based on epidemiological studies which deal with different aspects of tuberculosis infection. The primary goal of the thesis is to describe the prevalence of and risk factors for tuberculosis infection among children in Greenland in order to optimize preventive interventions. Secondly, a partial aim is to describe the usefulness of a new TB diagnostic tool among different populations.

The first study 'The Comparison of Screening Procedures for *Mycobacterium tuberculosis* Infection Among Patients with Inflammatory Diseases' aims to determine if screening results for tuberculosis infection differ among patients with inflammatory disease depending on whether the new diagnostic tool, the Quantiferon TB-Gold test (QFT), or the current tool, the tuberculin skin test (TST), are used. It also evaluates if a possible difference are influenced by the presence of known risk factors for tuberculosis infection or by immunosuppression. The study documents a high degree of discordant positive QFT and TST results in subjects with inflammatory diseases and immunosuppressive therapy. In this population a positive QFT result was more closely associated with risk factors for tuberculosis infection than the TST result. The use of corticosteroids affected test outcome in both tests by increasing the risk of an inconclusive QFT result and decreasing the risk of a positive TST result. The divergence between the two tests underlines the importance for both tests to be taken into consideration when screening for tuberculosis infection among patients with inflammatory diseases.

The second study 'Ongoing Tuberculosis Transmission to Children in Greenland' is a population based cross-sectional survey of tuberculosis infection among 2,231 apparently healthy Greenlandic school children (~25% of the Greenlandic population in the relevant age group). The aims were to measure the tuberculosis transmission to children in Greenland and to estimate the annual risk of tuberculosis infection. The children were tested for Mtb infection using the TST and the QFT, and, conservatively, only subjects with dual-positive results were defined as tuberculosis-infected. 8.1% were tuberculosis-infected and the annual risk of tuberculosis infection was estimated to 0.8 % per year. The risk of infection varied by ethnicity and by location. The study highlights the fact that tuberculosis transmission occurs at a high level to Inuit children in Greenland with pronounced geographic differences between study locations.

The third study 'Risk factors for tuberculosis infection among children in Greenland' is based on data from 1,797 of the Greenlandic school children studied in Study II. The aim of the study was to evaluate potential risk factors for tuberculosis infection in Greenland. Questionnaires and nationwide registries were used to obtain information on potential risk factors. Tuberculosis infection, defined as positivity in both the QFT and in the TST was found in 8.4% of the children. 10% of the participating children reported known contact to a TB patient. Overall, increasing age, being of Inuit ethnicity and narrow age gap to closest older sibling were significant risk factors for tuberculosis infection among the children. Self-reported TB-contact significantly modified some of the additional risk factors. Clustering within siblings suggested the strong possibility of TB contact within the household, even when this was unknown to the family. The risk factors for tuberculosis infection identified among children in Greenland can help focus the tuberculosis intervention towards the children at highest risk of infection.