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Routes of M. tuberculosis transmission among merchant seafarers

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Abstract
For centuries, tuberculosis has been identified as a burden to seafarers. In this study, we assessed the magnitude of tuberculosis among merchant seafarers today. Furthermore, we identified the most likely routes of M. tuberculosis transmission by the use of DNA fingerprinting. A database containing all culture-positive tuberculosis cases in Denmark in 1992–2003 was combined with a register on all seafarers and their employment periods aboard Danish ships. All strains of M. tuberculosis were analysed using DNA-subtyping. 64 cases of culture positive tuberculosis among seafarers were identified. The risk of tuberculosis among males was 1.51 (1.10–2.01) compared with the general population. Two of the 64 cases were likely to be shipping-related, 5 were possibly shipping-related, and 10 were less likely to be shipping-related. The remaining 47 cases were very unlikely to be shipping related. Including the 2 first categories, the incidence was 0.09 cases per 1000 y at sea. The excess risk of tuberculosis among active and former Danish seafarers is most probably due to infections acquired in Denmark. Despite multi-cultural crews aboard, including many from high-incidence countries, our study indicates that only limited transmission of M. tuberculosis takes place among crew aboard modern ships or during shore leaves.

Introduction
For centuries, tuberculosis has been recognized as an important disease among seafarers. Crowded quarters and long voyages have facilitated the spread of the disease, and in many places, special hospital facilities have been established to take care of seafarers with tuberculosis [1]. Merchant seafarers, especially ratings, were among the occupations with the highest burden of tuberculosis in Copenhagen during the beginning of the 20th century [2]. Also, during recent decades, outbreaks of tuberculosis have been documented aboard navy ships with large crews living under crowded conditions [3,4]. However, little is known about the extent of the problem in merchant shipping today.

Shortly after World War 2, mandatory annual tuberculosis screening of all Danish seafarers was initiated owing to the high burden of tuberculosis at sea, and due to the introduction of screening programmes in specific population groups in Denmark [5]. After the war, the general tuberculosis burden diminished rapidly in Denmark, but a considerable number of cases were still detected among seafarers. Around 1960, however, the situation changed and the number of active cases among seafarers declined rapidly [6]. After 1970, fewer than 10 new cases were detected per y in spite of more than 30,000 screenings annually. In August 1983 the mandatory specific tuberculosis screenings of Danish seafarers ceased [7], and after that date examinations for tuberculosis were only carried out if a seafarer had symptoms of active disease, e.g. at the mandatory general health examinations for seafarers carried out every second y. Active immunization with BCG of tuberculin-negative Danish schoolchildren ceased gradually around 1980.

In Denmark, during the last 2 decades of the 20th century, the burden of tuberculosis has increased again, mainly due to immigration from high-incidence countries [8]. At the end of the 1990s, approximately 500 cases were reported annually, and in 2000, for example, the overall incidence was 10.3 per 100,000 inhabitants. A large proportion of cases was diagnosed among immigrants, but significant M. tuberculosis transmission was also identified among Danish-born individuals, and it
was documented that an increasing proportion of the Danish-born cases was infected by a few dominant strains of M. tuberculosis, pointing in the direction of active transmission [9]. Recent DNA-fingerprinting studies also indicated that there was only limited transmission among the Danish- and foreign-born cases [8].

The purpose of this study was to access the magnitude of tuberculosis among seafarers and identify possible routes of M. tuberculosis transmission today. We wanted to clarify whether contact with foreigners, aboard or ashore, from high-incidence countries, influenced the magnitude of tuberculosis among seafarers born in low-incidence countries.

**Material and methods**

The study was a historic follow-up. Linking a register including all seafarers working aboard Danish ships since 1 April 1986 with a register including all culture-confirmed cases of tuberculosis from 1992 to October 2003, all culture positive cases of tuberculosis among seafarers were identified.

The Danish Maritime Authority administrates a register on seafarers. This register holds information on each individual seafarer, including information on all employment periods aboard Danish merchant ships. It was fully operational on 1 April 1986, but it also includes data on employment periods starting before 1 April if they ended after the operational date [10]. Danish shipping companies are legally bound to complete an employment form each time a seafarer is signed on, and a copy of this form has to be sent to the Danish Maritime Authority. Thus, for each case of culture-confirmed tuberculosis among seafarers, it was possible to obtain a detailed record of employment periods aboard different ships and check whether the case of interest had been working together with any other seafarers with tuberculosis. A total of 53,302 seafarers (14,264 F, 39,038 M) was included in this study. The cohort was open. They were included from the d of first employment on a ship until the end of the follow-up period, 31 October 2003.

Time spent aboard for each employment period between 1 January 1992 and 31 October 2003 was calculated and summarized. Employment periods that started before 1 January 1992 were only counted from 1 January 1992, and employment periods continuing after 31 October 2003 were only counted until the end of October 2003. A total of 75,680 y was spent aboard in the mentioned period corresponding to a mean of 6396 y at risk per calendar y.

In the period between 1992 and 2003, the Danish merchant fleet consisted of approximately 500 merchant ships. The majority of these ships were employed in overseas trade. The number of foreign-born seafarers has steadily increased since establishment of the Danish International Ships Register (DIS) in 1988, and in 2003, 40% of the crewmembers were foreign-born. The largest group was from the Philippines followed by Polish citizens. The foreign-born seafarers are normally screened for tuberculosis in their country of origin before embarking.

In Denmark, during the last 2 decades, approximately 80% of all tuberculosis cases have been culture verified [11]. The proportion of culture-verified cases is higher among adults and lower among children. Since 1992, all cultures of M. tuberculosis from these culture-verified cases have been DNA-subtyped by the gold standard method of 'IS6110 Restricted Fragment Length Polymorphism' (RFLP), as described in detail elsewhere [12]. Strains of M. tuberculosis from different patients who share identical IS6110 DNA-fingerprint patterns are referred to as 'clustered', and these patients might be part of the same transmission chain. Conversely, it is highly unlikely that patients harbouring strains with different IS6110 DNA-fingerprint patterns are part of the same transmission chain. Information on IS6110 DNA-fingerprint patterns has been stored in a register at the State Serum Institute together with additional epidemiological linkage information.

Before linking the DIS and tuberculosis registers, both were linked with the Central Population Register (CPR). Only individuals who, according to CPR, had or still enjoyed residence in Denmark, and who were employed at sea after they were diagnosed, were included in the calculation of standardized incidence ratios (SIR). SIRs were calculated using the whole population in 1997 as numerator [13]. Time at risk was calculated from the d of inclusion to death, emigration, or the end of the follow-up period.

Additional information on seafarers and former seafarers with tuberculosis was retrieved from the files of Department of Epidemiology, at Statens Serum Institute. This department administers an archive of mandatory tuberculosis notifications retrieved from clinicians, including contact tracing information. In all except 1 case, the notification information was available. Notification information on any non-seafarers belonging to the same cluster as a seafarer was also available.

To evaluate whether a case of tuberculosis in a seafarer was shipping-related or not, the cases were divided into 5 different categories depending on the likelihood of transmission. This categorization was based on the DNA-subtyping result, information on
exposure from known contacts, and the history at sea including contacts with foreign-born seamen.

The definition of each category is described in Table II. Category 0 ‘not shipping related’ includes those who had their first employment period after they were diagnosed with a tuberculosis episode. However, they may in theory have been to sea before 1 April 1986 when the register was created. Also, they may have been employed aboard foreign flagged ships. The definition ‘possibly shipping related’ and ‘less likely to be shipping-related’ included a 5-y limit since last employment aboard a ship. This 5-y limit is arbitrary, but it is chosen because approximately half of all tuberculosis patients develop active disease within 2 to 5 y after the primary infection [14–16]. Thus, the chance of an infection being shipping-related is less than 50%.

Results

In total, 64 cases of culture-positive tuberculosis among seafarers were identified (14F, 50M). 38 (59%) were born in Denmark, 10 (16%) in Greenland or the Faroe Islands, and 16 (25%) outside the Danish Kingdom.

One seafarer lived in Greenland at time of diagnosis and another lived abroad. These 2 seafarers were excluded from the incidence calculations, as well as 7 seafarers who had tuberculosis before their first recorded employment period at sea. The incidence of culture-verified tuberculosis among male seafarers and former seafarers is shown in Table I. The age-standardized incidence ratio among female seafarers was 1.16 (0.56–2.14).

In Table II, the results of the transmission classification are presented. In total, 7 seafarers were classified as ‘likely’ or ‘possibly’ shipping-related. Using this figure, the risk of tuberculosis per 1000 y at sea could be calculated to 0.09. If the category ‘less likely’ was included, the theoretical incidence could be calculated to 0.22 cases per 1000 y at sea.

14 of the 64 seafarers with tuberculosis had been working on the same ship as another seafarer who also developed tuberculosis within the follow-up period. However, in only 1 of these cases, the seafarers were infected with strains of M. tuberculosis with identical IS6110 DNA-fingerprint patterns. In the remainder of cases, the IS6110 DNA-fingerprint patterns were completely different from each other rendering transmission highly unlikely.

Among the 57 seafarers and former seafarers with tuberculosis after starting working at sea, 10 had records of active employment at sea within 6 months before diagnosis. Among these, 7 had a sputum smear-positive tuberculosis. Six out of the 7 had been working aboard a ship within 1 month before diagnosis.

Additional investigations of a cluster of 2 persons, 1 of whom was a seafarer included in the study, identified a male seafarer from the semi-independent Faroe Islands, who had not been found by linkage of the 2 registers due to an incompletely recorded ‘personal identification number’ (Danish CPR number). This seafarer had a history of recent close contact with a Philippine seafarer with symptoms of tuberculosis aboard a Danish merchant ship. This case is not included in the tables which only include cases found by linkage of the registers.

Discussion

This study is based on data retrieved from 2 registers assumed to be highly representative in their respective fields [10,11]. Therefore, we believe that we have identified the majority, if not all, of the culture confirmed cases of tuberculosis among Danes who have been working as seafarers aboard Danish ships from 1986 and onwards.

The crude incidence of tuberculosis among seafarers is higher than that identified in this study as

<table>
<thead>
<tr>
<th>Age group</th>
<th>Y of observation</th>
<th>No. of cases</th>
<th>Expected no. of cases among seafarers</th>
<th>SIR 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 to 19</td>
<td>3,817,227</td>
<td>8558</td>
<td>0.38</td>
<td>0.0 (0.0–9.8)</td>
</tr>
<tr>
<td>20 to 29</td>
<td>4,958,299</td>
<td>98,116</td>
<td>8.47</td>
<td>0.8 (0.3–1.7)</td>
</tr>
<tr>
<td>30 to 39</td>
<td>5,279,137</td>
<td>101,986</td>
<td>10.35</td>
<td>1.2 (0.6–2.0)</td>
</tr>
<tr>
<td>40 to 49</td>
<td>4,916,309</td>
<td>61,781</td>
<td>5.57</td>
<td>2.5 (1.4–4.2)</td>
</tr>
<tr>
<td>50 to 59</td>
<td>4,382,996</td>
<td>52,126</td>
<td>3.33</td>
<td>2.1 (0.9–4.3)</td>
</tr>
<tr>
<td>60 to 69</td>
<td>2,844,357</td>
<td>24,619</td>
<td>1.37</td>
<td>3.7 (1.2–8.5)</td>
</tr>
<tr>
<td>Total</td>
<td>28,211,888</td>
<td>352,566</td>
<td>29.9</td>
<td>1.51 (1.10–2.01)</td>
</tr>
</tbody>
</table>
Table II. Likelihood of cases being shipping-related. The classification of each case is based on identified subtype, epidemiological data on exposure and on history at sea.

<table>
<thead>
<tr>
<th>Classification</th>
<th>Description of the group</th>
<th>Number of cases</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category 0. Not shipping related.</td>
<td>Tuberculosis before first recorded employment at sea.</td>
<td>7</td>
<td>Some may theoretically have been employed aboard foreign flagged ships or been at sea before 1986.</td>
</tr>
<tr>
<td>Category 1. Likely to be shipping-related.</td>
<td>Danes with clinical tuberculosis within 1 y after possible specific exposure at sea.</td>
<td>2</td>
<td>One of the cases had clustered DNA fingerprints.</td>
</tr>
<tr>
<td>Category 2. Possibly shipping-related.</td>
<td>Danes infected with a unique strain or belonging to a cluster where according to the epidemiological information were likely to be the index case.</td>
<td>5</td>
<td>Three of the 5 cases have also had residence abroad in the 5-y period before diagnosis.</td>
</tr>
<tr>
<td>Category 3. Less likely to be shipping-related</td>
<td>They should have been working at sea within 5 y before diagnosis.</td>
<td>10</td>
<td>Two of the seafarers were infected with unique strains and the remaining 3 belonged to clusters with only 2 cases. The seafarers were the index case in these cluster.</td>
</tr>
<tr>
<td></td>
<td>Danes infected with unique strains but more than 5 y between diagnosis and the possible exposure at sea or with known exposure ashore.</td>
<td></td>
<td>Among the 7 Danes, 5 were infected with unique strains. They were possibly infected before DNA-subtyping was introduced in 1992.</td>
</tr>
<tr>
<td></td>
<td>Foreign born residents in Denmark infected with unique strains but with a long career (several y) at sea.</td>
<td></td>
<td>Two seafarers belonged to clusters with only 2 cases. In both cases, they were the index case, but at time of diagnosis not been at sea for more than 7 and 13 years, respectively.</td>
</tr>
<tr>
<td>Category 4. Very unlikely to be shipping-related</td>
<td>Danes infected with strains in clusters commonly occurring in Denmark or Greenland and no known contacts aboard ships.</td>
<td>40</td>
<td>Foreign born residents totalled 3 persons including 1 from the Faroe islands.</td>
</tr>
<tr>
<td></td>
<td>Foreign born residents in Denmark infected with unique strains or a strain known to be common in their country of origin.</td>
<td></td>
<td>20 of the 40 seafarers in this category were Danes and 11 of these were infected with 1 of the 2 most frequent clusters in Denmark including 1 seafarer infected with a strain which was only 1 band different from a very frequent cluster in Denmark. The remaining 9 Danes also belonged to well known clusters.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Nine of the remaining seafarers were Danish citizens but originated from Greenland or the Faroe Islands and belonged to clusters frequent in Greenland or Denmark.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Four of the foreigners were infected with strains frequent in Denmark and 2 Somalis and 1 from Sudan belonged to clusters well known among these nationalities. The remaining 5 foreign born seafarers belonged to unique clusters and had a history of a short career at sea and no known exposure aboard a ship.</td>
</tr>
</tbody>
</table>
not all cases of tuberculosis are confirmed by a positive culture. In the general population in Denmark, nearly 20% of all notified cases were not culture confirmed [11], but as this study only includes adults, the figure is likely to be lower.

Using the above specified classification criteria, it seems that the majority of seafarers were infected ashore in Denmark. The risk of being infected on voyages to tuberculosis high-incidence countries as well as on ships with international crews from high-incidence countries seems limited, although this study also documented few cases where such transmission took place. The tradition for seafarers for taking up residence abroad in tuberculosis high-burden countries may increase the risk of tuberculosis infection among seafarers due to their more intensive exposure over prolonged periods of time.

When including all cases classified as 'likely', 'possible' and 'less likely', the calculated risk of tuberculosis while at sea was 0.22 cases per 1000 y at risk. This calculation should be interpreted with caution. Although all cases in these categories theoretically could be shipping-related, it is statistically and epidemiologically unlikely that they are, and thus the estimated figure should be seen as the maximum upper limit of the risk. For a period, 3 of the seafarers in the category 'possible' have had residence in a high endemic country. Also, being infected with strains of M. tuberculosis with a unique IS6110 DNA-fingerprint pattern does not necessarily imply that the primary infection occurred abroad. The person may have been infected in Denmark before DNA-subtyping was introduced in 1992. Also, his or her IS6110 DNA-fingerprint pattern may be unique due to genetic drift, although this is less likely because the patterns differed by several bands [17]. Compared to international travellers in general [18], the observed risk among seafarers is limited.

The reasons for the low observed overall risk, and the risk compared to travellers in general, may be several. Today, time in port is very limited and contact with the local populations therefore scarce. In addition, the foreign-born aboard ships are screened before embarking, and they are known to have limited social contact with Danish-born crew members [19]. Although today most have their own cabin, there may, however, occur some transmission among the foreign-born aboard Danish merchant ships, as they sometimes live under crowded conditions.

The majority of seafarers with tuberculosis in this study had not been active seafarers for quite some time before they developed active disease (Table II). A large proportion was infected with subtypes seen among groups of people ashore characterized by social problems such as homelessness and abuse of alcohol [9]. The most important risk factor for developing tuberculosis among the seafarers appears to be contacts with such groups ashore. Some former seafarers thus seem to be socially marginalized after leaving the occupation, in accordance with data from some of the individual notifications. Due to increased employment of foreign seafarers from low-income countries, it has become very difficult for Danish able-bodied seafarers to find employment at sea.

It is noteworthy that 7 out of 57 seafarers and former seafarers were employed aboard a ship within 6 months before they were diagnosed with sputum smear-positive tuberculosis. Despite this, no secondary cases of tuberculosis connected to these 7 cases were found in the cohort. However, they may have caused secondary cases aboard not included in the register. Aboard crowded navy ships, sputum smear-positive cases have caused outbreaks of tuberculosis [3,4] with 1 single index case resulting in up to 21 secondary cases. It seems, however, that modern merchant ships with single cabins for all crew members and limited social contact prevent massive spread of the disease.

In conclusion, seafarers from a low-incidence country such as Denmark have a low risk of being infected with tuberculosis while serving as seafarers in international trade, often with international crews. The excess risk of tuberculosis in this group is mainly caused by close contacts to certain risk groups in Denmark where tuberculosis is frequent. The tuberculosis problem among seafarers from a country such as Denmark is limited and no further prophylactic measurements seem justified. The abolition of mandatory screening 20 y ago still seems justified. However, health care personnel involved in pre-employment health examinations of seafarers should still be aware of symptoms of the disease.

Acknowledgements
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