Wide geographic variations of sensitivity to MOTT sensitins in Greece

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ABSTRACT: Several studies have suggested that large bodies of water are a main source of infection with mycobacteria other than tuberculosis (MOTT). If this is correct, there should be a gradient in the infection rate with MOTT between mountainous and seaside areas.

To test this hypothesis, we performed skin testing with tuberculin and sensitins in 19,470 Greek Armed Forces recruits. Initially, several MOTT sensitins were used, but when it became clear that the Mycobacterium scrofulaceum sensitin was the most appropriate, the study was continued with it alone in 17,403 recruits. Finally, in order to evaluate the geographical distribution of sensitivity to sensitins, we studied the results of 8,507 of these recruits living in or near their birthplace. They were divided into three geophysical areas: seaside 3,389 recruits; mountains 2,692 recruits; and inland plains 2,426 recruits.

MOTT sensitivity rates were 4.1% in mountainous areas and 7.1% in seaside areas. All small Aegean islands had high MOTT rates (above 8%). In inland plains, high MOTT rates (above 8%) were observed among those living near big rivers. This geographical distribution of MOTT sensitivity supports the theory that large bodies of water are a main source of infection with MOTT.


Keywords: Mycobacteria other than tuberculosis, mycobacterium tuberculosis sensitin, tuberculin

Presented in part at the 1st ERS meeting in Brussels, 1991.

Previous studies have suggested that large bodies of water, such as coastal and inland waters, may be a significant source of infection with mycobacteria other than tuberculosis (MOTT). This was first suggested by Edwards et al. [1] almost four decades ago. In their study, over 670,000 US Navy recruits were skin tested with purified protein derivative-standard (PPD-S) and PPD-B (Battey) and the highest reaction rates to PPD-B sensitin (70% or more) were found amongst residents of the Southeast States [1]. Several recent studies, again mainly from the US, have examined various environmental sources, and all indicate natural water as the primary source of human infection with MOTT [2–5].

Unlike Southeastern US and some European countries, such as Sweden [8, 9] and the Netherlands [10], where sensitivity to sensitins has been examined, Greece has still a serious tuberculosis problem [11, 12]. Therefore, bacille Calmette-Guérin (BCG) vaccination is widely applied, and we had to take this into consideration. Finally, since MOTT have only been studied once, more than 20 yrs ago in Greece [13], a preliminary phase was required to determine which sensitin was the most representative.

Population and methods

The study was conducted among Greek Armed Forces recruits, aged 19–21 yrs. Recruits with possible previous BCG vaccination (according to history, records or obvious vaccination scar) were excluded, although we and others [14–17] have shown that even successful previous BCG vaccination interferes very little with Mantoux readings.

The reactions (size of skin induration) were read after 48–72 h. The study was approved by the Scientific Ethics Committee of the Greek Armed Forces and was completed in two phases.

Phase One

Several sensitins were used to establish which was the most representative of MOTT infection. Thus, we performed

Phase Two

The study was continued with the most appropriate sensitin, Mycobacterium scrofulaceum sensitin, in 17,403 recruits. Finally, in order to evaluate the geographical distribution of sensitivity to sensitins, we studied the results of 8,507 of these recruits living in or near their birthplace. They were divided into three geophysical areas: seaside 3,389 recruits; mountains 2,692 recruits; and inland plains 2,426 recruits.

MOTT sensitivity rates were 4.1% in mountainous areas and 7.1% in seaside areas. All small Aegean islands had high MOTT rates (above 8%). In inland plains, high MOTT rates (above 8%) were observed among those living near big rivers. This geographical distribution of MOTT sensitivity supports the theory that large bodies of water are a main source of infection with MOTT.


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In a multinomial population, was derived:

\[
\frac{p_1-p_2}{\sqrt{p_1(1-p_1)(n_1/n)(n_2/n)}}
\]

employing classical statistical procedures.

Results

Phase Two

When it became obvious (see Results) that PPD-scrufalaceum was the most appropriate sensitin, the study was continued with this sensitin only (and tuberculin) in 17,403 recruits.

Finally, in order to study the geographical distribution, 8,896 recruits not living in, or near, their birthplace, or living in large metropolitan areas (Athens, Thessaloniki) were excluded. These two metropolises have a very mixed population of natives and inhabitants from other parts of Greece and this could create confusion. Thus, the population was limited to 8,507 recruits. These were divided into three geophysical areas (seaside 3,389 recruits; mountains 2,692 recruits; and inland plains 2,426 recruits). As mentioned previously, for the evaluation of geographical distribution, only 8,507 of the 17,403 recruits were included; namely those living in their place of birth and outside the two major metropolises (Athens and Thessaloniki). Of 2,692 recruits living in mountainous areas, 110 (4.08%) were considered infected with MOTT and MTB infection [18–20] i.e. those with a reaction to tuberculin larger than to the sensitin, but <5 mm difference.

Phase One

In order to establish the most suitable sensitin, dual skin tests were performed on 19,470 recruits with the following results. 1) from 4,742 recruits tested with PPD-avium (and tuberculin), 319 were considered infected with MOTT (2.2%), 519 with MTB, and 183 with either or both; 2) from 4,551 recruits tested with PPD-intracellulare (and tuberculin), 88 were considered infected with MOTT (1.9%), 589 with MTB, and 124 with either or both; 3) from 5,330 recruits tested with PPD-kansasii (and tuberculin), 57 were considered infected with MOTT (1.08%), 702 with MTB, and 88 with either or both; and 4) from 4,847 recruits tested with PPD-scrufalaceum (and tuberculin), 346 were considered infected with MOTT (7.1%), 586 with MTB, and 207 with either or both.

In addition, 508 recruits were tested with all five sensitins. Ninety four recruits (18.5%) had at least one reaction ≥5 mm; and half of these (49 out of 94 = 51%) had the largest reaction to PPD-scrufalaceum. Respective results with the other four sensitins were as follows: 21 (22%) had the largest reaction to PPD-intracellulare, 13 (14%) to PPD-kansasii, and 12 (13%) to PPD-avium. PPD-intracellulare was positive in 38 out of 94 (40%), PPD-kansasii in 37 out of 94 (39%) and PPD-avium in 24 out of 94 (26%).

Thus, positive reactions to PPD-scrufalaceum were more common than to any other sensitin (all Z≥10.44; p<0.001 for comparison in dual skin testing; and x²=190.3; p<0.001 for comparison in test with all five sensitins). Since 70 of the 94 recruits with any positive skin test to a sensitin were positive to PPD-scrufalaceum (74%), one can assume that roughly 3 out of 4 previous infections with MOTT were diagnosed using PPD-scrufalaceum.

Discussion

The main aim of our study was to test the dominant theory of the source of infection with MOTT. These mycobacteria are commonly found in house dust, tap water, coastal waters, soil and milk [5]. The infection...
is not spread by person-to-person contact [5]. Environmental reservoirs are considered to be the primary source of infection, more specifically contaminated waters. The main studies have been carried out in the Eastern United States. They have shown that the distribution of contaminated coastal and inland waters corresponds well with data from skin test sensitivity to MOTT sensitins [5].

Our study strongly supports this theory. The sensitivity to \( M. \) scrofulaceum sensitin was much higher among recruits born and living in the coastal areas of Greece than those living on the mountains. The phenomenon was very clear in the small Aegean islands, where the sensitivity to MOTT sensitin was highest, being in almost all islands >8%. A similar finding was observed in those recruits living in inland plains, where the sub-group living near big rivers also had relatively high rates of MOTT sensitivity (>8%). The geographical distribution of the sensitivity to tuberculin showed no preference for seaside or mountainous areas.

Several previous studies have pointed out variations in sensitin reactivity in the same country, mainly as a result of climate, distance from the sea and altitude [1, 22, 23]. In the most recent study [24] it was shown that the sensitivity to sensitins in the coastal area of Gotepborg, Sweden was much higher than that of the inland rural area of Jamtland, in agreement with our findings.

Other results of this study are interesting from the Greek Public Health point of view. The most significant being the fall in tuberculin sensitivity (from 25% 20 yrs ago to 10.6% [11], with a concomitant slight increase in the sensitivity to sensitins, from 5.8 to 7.0%) [13]. This is in agreement with the universal trend in Europe [10].

In conclusion, these data and those of other studies suggest that large bodies of water are a significant source of infection with MOTT. This seems to be true whether we examine children, as in Sweden, or young adults as in Greece. It is true whether we study countries with very high tuberculosic infection rates (India) [21], very low rates (Sweden) [23], or an intermediate situation (Greece). It is true whether we study countries with tropical climate (India), subtropical climate (Greece) or arctic climate (Jamtland, Sweden).

Acknowledgements: The authors wish to thank S. Chaparas for his guidance, H.M. Moutsopoulos for valuable comments and H.N. Prevezianou for excellent secretarial assistance.

References

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