

ORIGINAL PAPER  
ΕΡΕΥΝΗΤΙΚΗ ΕΡΓΑΣΙΑ

## The prevalence of tuberculin skin positivity among Greek army recruits

**OBJECTIVE** Although the prevalence of tuberculosis (TB) is declining, it remains one of the leading causes of death among infectious diseases worldwide. In this study, the prevalence and predictors of tuberculin skin testing (TST) positivity were analyzed among Greek army recruits. **METHOD** The study population consisted of 3,684 men aged 18–43 years recruited into the Greek army between November 2010 and February 2011. TST was performed on all recruits on enrollment, according to established procedures. A TST reaction size  $\geq 15$  mm was considered positive. Anthropometric measurements (height, weight) were performed using standard techniques. Data on age, place of residence, and educational level were collected. **RESULTS** The mean age of the recruits was  $23.2 \pm 2.8$  years. TST positivity prevalence was 1.4% (52/3,684), and bivariable analysis and backward, stepwise multivariable logistic regression showed that the sociodemographic characteristics did not vary with TST positivity. **CONCLUSIONS** The prevalence of TST positivity among Greek male army recruits is very low (1.4%). The percentage of TST positivity has continued to decrease in Greece over the last 30 years in spite of a surge of immigrants from countries with high TB infection rates.

ARCHIVES OF HELLENIC MEDICINE 2012, 29(3):331–335  
ΑΡΧΕΙΑ ΕΛΛΗΝΙΚΗΣ ΙΑΤΡΙΚΗΣ 2012, 29(3):331–335

G. Michas,<sup>1</sup>  
I.A. Drosatos,<sup>2</sup>  
M. Kokolios,<sup>3</sup>  
A. Kampouras,<sup>4</sup>  
M. Schoina,<sup>5</sup>  
A. Asimakos,<sup>6</sup>  
R. Micha<sup>7</sup>

<sup>1</sup>Department of Internal Medicine,  
General Hospital of Kalamata, Kalamata

<sup>2</sup>Medical Service of the Hellenic Army,  
Artillery Training Center, Thiva

<sup>3</sup>Medical Service of the Hellenic  
Army, 523 Infantry Training Center,  
Mavrodendri, Kozani

<sup>4</sup>Medical Service of the Hellenic Army,  
XXIV Armored Brigade, Litochoro

<sup>5</sup>Department of Internal Medicine,  
General Hospital of Katerini, Katerini

<sup>6</sup>Department of Intensive Care Medicine,  
"Evangelismos" General Hospital,  
Athens, Greece

<sup>7</sup>Department of Epidemiology, Harvard  
School of Public Health, Boston, MA, USA

Επίπτωση θετικής  
δερμοαντίδρασης φυματίνης  
σε νεοσύλλεκτους οπλίτες  
του στρατού ξηράς

Περίληψη στο τέλος του άρθρου

### Key words

BMI  
Education  
Greek male recruits  
Place of residence  
Tuberculin skin test

Submitted 10.9.2011

Accepted 27.9.2011

According to the latest World Health Organization (WHO) report, the prevalence of tuberculosis (TB) is declining globally in all 6 WHO regions.<sup>1</sup> TB mortality is predicted to decline from the 8th position among the leading causes of death in 2002 to the 23rd in 2030.<sup>2</sup> The tuberculin skin test (TST) is an inexpensive and easy to use method for the diagnosis of latent TB infection (LTBI)<sup>3</sup> and although

the interferon- $\gamma$  release assay (IGRA) produces superior specificity in populations that have been vaccinated in childhood with the *Bacille Calmette-Guérin* (BCG) vaccine<sup>4</sup> (as in Greece) it is costly and cannot be implemented in large populations. The prevalence of TST positivity among Greek army recruits has been studied three times since 1981,<sup>5–7</sup> showing a reduction in the TST positivity rates

over the last 30 years. The purpose of this study was to evaluate the prevalence and sociodemographic predictors of TST positivity in Greek army recruits during the period November 2010 to February 2011.

## MATERIAL AND METHOD

### Study population

The study was conducted in Thiva and in Mavrodendri, Kozani, Greece, where the Artillery Training Center and the 523 Infantry Training Center, respectively, are currently based. The study population consisted of 3,684 male Greek army recruits (entering November 2010–February 2011), aged 18 to 43 years. All the recruits underwent chest X-ray, routine physical examination and a TST. The study protocol was approved by the Medical Directorate of the Greek Army General Staff.

### Tuberculin skin testing

Two tuberculin units (TU) of purified protein derivative (PPD) in 0.1 mL (RT 23 in Tween 80, SSI, Statens Serum Institute, Denmark) was injected into the dermis on the volar surface of the forearm. The reaction was evaluated 48 to 72 hours later by physicians who measured the maximum transverse diameter of the induration using the ballpoint pen-ruler method. A reaction size of  $\geq 15$  mm was characterized as positive. Study participants with a reaction size  $\geq 15$  mm were interviewed and examined by the staff of the departments of pulmonary medicine of either the 401 Army General Hospital of Athens or the 424 Army General Hospital of Thessaloniki, and were treated for LTBI, when indicated.

### Data collection

Measurement of body height (H) and weight (W) was performed by physicians using standard techniques, with the soldiers wearing no shoes and underwear only.

Body mass index (BMI) was calculated according to Quetelet's formula:<sup>8</sup>  $BMI=W/H^2$ . Weight status was classified according to the WHO definitions:<sup>9</sup> Underweight,  $BMI < 18.5$  kg/m<sup>2</sup>; normal weight,  $18.5 \leq BMI < 25$  kg/m<sup>2</sup>; overweight,  $25 \leq BMI < 30$  kg/m<sup>2</sup>; obese,  $BMI \geq 30$  kg/m<sup>2</sup>.

The place of residence of the recruits was classified as urban ( $\geq 10,000$  people) and rural ( $< 10,000$ ) areas, based on data from the National Statistical Service of Greece (2001 Census). For the purposes of this analysis, the residential areas were further divided into urban (cities with population  $> 100,000$ ), semi-urban (cities or towns with population  $\geq 10,000$  and  $< 100,000$ ), and rural (smaller cities, towns and villages with population  $< 10,000$ ).

Two categories of educational level of the recruits were created, depending on the years of education; individuals with  $> 9$  school years ("higher" education) and individuals with  $\leq 9$  school years ("lower" education).

As previous medical records were not available for review, no data on the recruits' BCG vaccination history could be obtained.

### Statistical analysis

Induration of  $\geq 15$  mm was characterized as positive. T-test and chi-square test were used in bivariable analysis to compare the prevalence of tuberculin reactivity for continuous and categorical variables, respectively. Backward stepwise multivariable logistic regression ( $p < 0.05$  for addition, and  $p < 0.1$  for removal) was used to assess the sociodemographic characteristics independently associated with tuberculin reactivity. All p-values were 2-tailed ( $\alpha = 0.05$ ). Analyses were performed using STATA 10.0 (STATA, College Station, TX).

## RESULTS

The mean age [ $\pm$ standard deviation (SD)] of the recruits was  $23.2 \pm 2.8$  years (tab. 1). The overall prevalence of TST positivity ( $\geq 15$  mm) was 1.4% (52 of the 3,684 recruits). Table 2 presents the results of the bivariable analysis performed to investigate possible associations of the epidemiological characteristics with the presence of TST reactivity. Sociodemographic characteristics did not vary with the presence of TST reactivity.

A backward, stepwise multivariable logistic regression model also showed that none of the sociodemographic characteristics investigated was statistically independently associated with presence of TST reactivity.

**Table 1.** Sociodemographic characteristics among 3,684 Greek male army recruits.

	Values*
Age (years)	23.2 $\pm$ 2.8
Height (m)	1.8 $\pm$ 0.1
Weight (kg)	80.4 $\pm$ 14.4
BMI (kg/m <sup>2</sup> )	25.2 $\pm$ 4.0
Education <sup>†</sup>	
Higher	1,594 (43.3)
Lower	2,090 (56.7)
Residence <sup>‡</sup>	
Rural	1,228 (33.3)
Semiurban	1,019 (27.7)
Urban	1,437 (39.0)

\* Values are mean $\pm$ SD for continuous variables, and n (%) for categorical variables

<sup>†</sup> Educational level was classified as lower ( $\leq 9$  school years) and higher ( $> 9$  school years)

<sup>‡</sup> Place of residence was classified as urban ( $\geq 10,000$  people) and rural ( $< 10,000$  people), based on the data from the National Statistical Service of Greece

BMI: Body mass index

**Table 2.** Bivariable analysis of risk factors associated with TST positivity (defined as induration  $\geq 15$  mm) among 3,684 Greek male army recruits.

	(-) Mantoux (n=3,632)	(+) Mantoux (n=52)	p†
	Values*		
Age (years)	23.3 $\pm$ 2.9	23.1 $\pm$ 2.3	0.61
Height (m)	1.8 $\pm$ 0.1	1.8 $\pm$ 0.1	0.52
Weight (kg)	80.3 $\pm$ 14.4	84.0 $\pm$ 15.9	0.07
BMI (kg/m <sup>2</sup> )	25.2 $\pm$ 4.0	26.1 $\pm$ 4.2	0.10
Education‡			
Higher	1,572 (43.3)	22 (42.3)	0.89
Lower	2,060 (56.7)	30 (57.7)	0.89
Residence§			
Rural	1,214 (33.4)	14 (26.9)	0.32
Semiurban	1,005 (27.7)	14 (26.9)	0.91
Urban	1,413 (38.9)	24 (46.2)	0.29

\* Values are mean $\pm$ SD for continuous variables, and n (%) for categorical variables

† t-test for continuous variables;  $\chi^2$  test for categorical variable

‡ Educational level was classified as lower ( $\leq 9$  school years) and higher ( $> 9$  school years)

§ Place of residence was classified as urban ( $\geq 10,000$  people) and rural ( $< 10,000$  people), based on the data from the National Statistical Service of Greece

In backward stepwise multivariable logistic regression ( $p < 0.05$  for addition, and  $p < 0.1$  for removal) none of the sociodemographic characteristics presented in the table was independently associated with tuberculin reactivity

BMI: Body mass index

## DISCUSSION

The main finding of this study is that, compared with previous similar Greek studies, there has been a decrease in the prevalence of TST positivity among Greek army recruits in the last 30 years. Bouros et al reported a decline of TST positivity from 14.2% in 1981 to 6.8% in 1991 (using the criterion of reactivity of  $\geq 10$  mm).<sup>5</sup> German et al reported in 2006 a TST positivity of 3.9% ( $> 15$  mm).<sup>6</sup> Similarly, Katsenos et al reported a TST positivity of 3.4% ( $\geq 15$  mm).<sup>7</sup> Here a further decline is documented of TST positivity to 1.4% ( $\geq 15$  mm), which reflects the progress towards TB elimination made over the past decades in Greece. The prevalence of TST positivity in Greek army recruits is close to or even less than that reported in other developed countries.<sup>10–14</sup>

A previous study that modeled the relevant epidemiological trends predicted a faster decrease of TST positivity in Greek army recruits, based on the success of the national anti-TB campaign.<sup>5</sup> However, immigration from developing countries with a high prevalence of TB (Iraq, Afghanistan, Pakistan, India, etc.) and repatriation of persons of Greek origin from the former Soviet Union and Balkan countries have probably challenged this declining trend during the last 20 years.<sup>15,16</sup>

A TST positivity threshold of 15 mm was used in this study. It has been suggested that if the BCG vaccination was administered more than 15 years previously, it should be ignored as a cause of a current positive TST result, especially if the induration is  $> 15$  mm.<sup>17</sup> The findings of the present study are in accordance with those of Katsenos et al in a similar population.<sup>7</sup> Dealing with the problem of previous BCG vaccination in Greek army recruits, the authors conducted IGRAs in all subjects with a TST  $> 0$  mm and found positive results only in those with TST indurations of  $\geq 15$  mm, but none in those with TST indurations of 10–14 mm.<sup>7</sup>

Potential limitations of the study should be considered. A positive TST reaction could possibly represent LTBI, previous BCG vaccination, or a cross reaction to non-tuberculous Mycobacteria (NTM). Although no data on prior BCG vaccination could be obtained, universal BCG vaccination of all children at school entry or in later school years (age of 5 to 7 years) continues to be compulsory in Greece.<sup>16</sup> However, when the induration is  $\geq 15$  mm, the likelihood that prior BCG vaccination, if performed more than 10 years previously, will interfere with the results of the TST has been shown to be small.<sup>18</sup> As far as the NTM infection rate in Greek army recruits is concerned, it is reported to be low (ranging from 4.1 to 7.1%), and it almost never causes induration  $\geq 15$  mm.<sup>19</sup>

Additionally, the TST technique itself has certain drawbacks. It requires two visits and skilled personnel for administration and interpretation. However, these major issues were successfully dealt with in this study, since, in the army setting, all recruits came back for the second visit, and the placement and interpretation of the TST was conducted by trained physicians. The TST remains the standard test of choice for the diagnosis of LTBI in large and presumably healthy populations such as that of this study, at least until IGRAs testing becomes less expensive and/or more clinical data on IGRAs become available.<sup>20</sup>

Finally, these results cannot be extrapolated to other populations (e.g., the elderly, women, etc.), as this study included only healthy males between 18 and 43 years of age. All the study recruits had a normal chest X-ray, reported no recent close contact with a person with active TB, and they were generally in a good health; individuals with risk factors for TB (diabetes mellitus, HIV, immunodeficiency, hematological malignancies) are not recruited into the Greek army. Apart from that, the study recruits comprised a representative sample of the general male population of that age in Greece, since enrollment in the Greek Armed Forces is obligatory for all males above the

age of 18 years, and they came from all parts of Greece (urban, semi-urban, and rural) and from all social classes. Previous studies<sup>5-7</sup> conducted among Greek army recruits included populations with sociodemographic characteristics similar to the subjects in this study, mainly due to the fact that army recruitment procedure has not changed in Greece in the last 50 years.

In conclusion, these results show a further decline in the

prevalence of TST positivity (to 1.4%) among Greek army recruits compared to the findings of previous studies in this population over the last 30 years, confirming the progress that has been made towards TB elimination in Greece. The goal of TB elimination, however, can only be achieved if an efficient and effective countrywide TB surveillance system is implemented,<sup>21</sup> especially now that the immigration from countries with a high TB index is again escalating.

## ΠΕΡΙΛΗΨΗ

### Επίπτωση θετικής δερμοαντίδρασης φυματίνης σε νεοσύλλεκτους οπλίτες του στρατού ξηράς

Γ. ΜΙΧΑΣ,<sup>1</sup> Ι.Α. ΔΡΟΣΑΤΟΣ,<sup>2</sup> Μ. ΚΟΚΟΛΙΟΣ,<sup>3</sup> Α. ΚΑΜΠΟΥΡΑΣ,<sup>4</sup> Μ. ΣΧΟΙΝΑ,<sup>5</sup> Α. ΑΣΗΜΑΚΟΣ,<sup>6</sup> Ρ. ΜΙΧΑ<sup>7</sup>

<sup>1</sup>Τμήμα Εσωτερικής Παθολογίας, Α΄ Παθολογική Κλινική, Γενικό Νοσοκομείο Καλαμάτας, Καλαμάτα,

<sup>2</sup>Ιατρική Υπηρεσία Κέντρου Εκπαίδευσης Πυροβολικού, Θήβα, <sup>3</sup>Ιατρική Υπηρεσία 9ης Ταξιαρχίας Πεζικού,

Κοζάνη, <sup>4</sup>Ιατρική Υπηρεσία XXIV Τεθωρακισμένης Ταξιαρχίας, Λιτόχωρο Πιερίας, <sup>5</sup>Τμήμα Εσωτερικής Παθολογίας,

Γενικό Νοσοκομείο Κατερίνης, Κατερίνη, <sup>6</sup>Τμήμα Εντατικής Θεραπείας, Γενικό Νοσοκομείο Αθηνών «Ευαγγελισμός»,

Αθήνα, <sup>7</sup>Τμήμα Επιδημιολογίας, Harvard School of Public Health, Βοστώνη, ΗΠΑ

Αρχεία Ελληνικής Ιατρικής 2012, 29(3):331–335

**ΣΚΟΠΟΣ** Η φυματίωση είναι λοιμώδης νόσος, η οποία οφείλεται στο *Mycobacterium tuberculosis* και παραμένει ένα σοβαρό πρόβλημα υγείας, ιδιαίτερα στις αναπτυσσόμενες χώρες. Η δερμοαντίδραση φυματίνης (Μαντουχ) αποτελεί ένα από τα κυριότερα μέσα για τη διάγνωση της φυματίωσης. Σκοπός της παρούσας μελέτης ήταν η ανάλυση της επίπτωσης της θετικής Μαντουχ σε νεοσύλλεκτους οπλίτες του στρατού ξηράς. **ΥΛΙΚΟ-ΜΕΘΟΔΟΣ** Εκπονήθηκε έρευνα σε 3.684 νεοσύλλεκτους οπλίτες που κατατάχθηκαν στο στρατό ξηράς κατά το χρονικό διάστημα Νοέμβριος 2010–Φεβρουάριος 2011. Οι οπλίτες ήταν ηλικίας 18–43 ετών. Η Μαντουχ χαρακτηρίστηκε θετική σε διήθηση  $\geq 15$  mm. Ανθρωπομετρικές μετρήσεις (ύψος, βάρος) πραγματοποιήθηκαν, χρησιμοποιώντας πρότυπες μεθόδους. Συλλέχθηκαν ακόμη δεδομένα για την ηλικία, τον τόπο κατοικίας και το εκπαιδευτικό επίπεδο των οπλιτών. **ΑΠΟΤΕΛΕΣΜΑΤΑ** Η μέση ηλικία των οπλιτών ήταν 23,2 ( $\pm 2,8$ ) έτη. Η επίπτωση της θετικής Μαντουχ ήταν 1,4% (52/3.684), ενώ η ανάλυση των δύο μεταβλητών που εφαρμόστηκε έδειξε ότι τα κοινωνικο-δημογραφικά χαρακτηριστικά δεν διέφεραν με την παρουσία θετικής Μαντουχ. Παρομοίως, στο μοντέλο πολυμεταβλητής γραμμικής παλινδρόμησης που χρησιμοποιήθηκε, τα κοινωνικο-δημογραφικά χαρακτηριστικά δεν συσχετίστηκαν με την παρουσία θετικής Μαντουχ. **ΣΥΜΠΕΡΑΣΜΑΤΑ** Τα αποτελέσματα που προέκυψαν, φανερώνουν ότι η επίπτωση της θετικής Μαντουχ στον άρρενα νεανικό ελληνικό πληθυσμό είναι πολύ μικρή (1,4%) και ακολουθεί μια πτωτική τάση τα τελευταία 30 έτη, παρά την αθρόα εισροή οικονομικών μεταναστών από χώρες με υψηλά ποσοστά φυματίωσης.

**Λέξεις ευρητηρίου:** Δείκτης μάζας σώματος, Δερμοαντίδραση φυματίνης, Εκπαίδευση, Νεοσύλλεκτοι οπλίτες, Τόπος κατοικίας

## References

1. WORLD HEALTH ORGANIZATION. *Global tuberculosis control report 2010*. WHO, 2010
2. MATHERS CD, LONCAR D. Projections of global mortality and burden of disease from 2002 to 2030. *PLoS Med* 2006, 3:e442
3. ANONYMOUS. Diagnostic standards and classification of tuberculosis in adults and children. This official statement of the American Thoracic Society and the Centers for Disease Control and Prevention was adopted by the ATS Board of Directors, July 1999. This statement was endorsed by the Council of the Infectious Disease Society of America, September 1999. *Am J Respir Crit Care Med* 2000, 161:1376–1395
4. MAZUREK GH, JEREB J, VERNON A, LOBUE P, GOLDBERG S, CASTRO K ET AL. Updated guidelines for using interferon gamma release assays to detect *Mycobacterium tuberculosis* infection – United States, 2010. *MMWR Recomm Rep* 2010, 59:1–25
5. BOUROS D, DEMOILIOPOULOS I, MOSCHOS M, PANAGOU P, DEMOILIOPOULOS D, KONSTANTOPOULOS S ET AL. Tuberculin sensitivity trends in Hellenic army recruits during the period 1981–1991.

- Tuber Lung Dis* 1995, 76:126–129
6. GERMAN V, GIANNAKOS G, KOPTERIDES P, FALAGAS ME. Prevalence and predictors of tuberculin skin positivity in Hellenic army recruits. *BMC Infect Dis* 2006, 6:102
  7. KATSELOS S, NIKOLOPOULOU M, KONSTANTINIDIS AK, GARTZONIKA C, GOGALI A, MARGELIS I ET AL. Interferon-gamma release assay clarifies the effect of bacille Calmette-Guérin vaccination in Greek army recruits. *Int J Tuberc Lung Dis* 2010, 14:545–550
  8. GARROW JS, WEBSTER J. Quetelet's index ( $W/H^2$ ) as a measure of fatness. *Int J Obes* 1985, 9:147–153
  9. ANONYMOUS. Obesity: Preventing and managing the global epidemic. Report of a WHO consultation. *World Health Organ Tech Rep Ser* 2000, 894:i–xii, 1–253
  10. D'AMELIO R, STROFFOLINI T, BISELLI R, MOLICA C, COTICHINI R, BERNARDINI G ET AL. Tuberculin skin reactivity in Italian military recruits tested in 1996–1997. *Eur J Clin Microbiol Infect Dis* 2000, 19:200–204
  11. JENTOFT HF, OMENAAS E, EIDE GE, GULSVIK A. Tuberculin reactivity: Prevalence and predictors in BCG-vaccinated young Norwegian adults. *Respir Med* 2002, 96:1033–1039
  12. FRANKEN WP, TIMMERMANS JF, PRINS C, SLOOTMAN EJ, DREVERMAN J, BRUINS H ET AL. Comparison of Mantoux and QuantiFERON TB Gold tests for diagnosis of latent tuberculosis infection in Army personnel. *Clin Vaccine Immunol* 2007, 14:477–480
  13. SMITH B, RYAN MA, GRAY GC, POLONSKY JM, TRUMP DH. Tuberculosis infection among young adults enlisting in the United States Navy. *Int J Epidemiol* 2002, 31:934–939
  14. MAZUREK GH, ZAJDOWICZ MJ, HANKINSON AL, COSTIGAN DJ, TONEY SR, ROTHEL JS ET AL. Detection of *Mycobacterium tuberculosis* infection in United States Navy recruits using the tuberculin skin test or whole-blood interferon-gamma release assays. *Clin Infect Dis* 2007, 45:826–836
  15. DANDOULAKIS M, ROUSSOS N, KARAGEORGOPOULOS DE, YATROMANOLAKIS N, FALAGAS ME. Trends of tuberculin skin test positivity rate among schoolchildren in Attica, Greece. *Scand J Infect Dis* 2009, 41:195–200
  16. MANTADAKIS E, ARVANITIDOU V, TSALKIDIS A, RAMATANI A, TRIANTAFILLIDOU E, TRYPSIANIS G ET AL. Changes in tuberculin sensitivity among first-grade students of elementary schools in Evros, Greece due to immigration. *Public Health* 2009, 123:618–622
  17. WANG L, TURNER MO, ELWOOD RK, SCHULZER M, FITZGERALD JM. A meta-analysis of the effect of Bacille Calmette Guérin vaccination on tuberculin skin test measurements. *Thorax* 2002, 57:804–809
  18. FARHAT M, GREENAWAY C, PAI M, MENZIES D. False-positive tuberculin skin tests: What is the absolute effect of BCG and non-tuberculous mycobacteria? *Int J Tuberc Lung Dis* 2006, 10:1192–1204
  19. DASCALOPOULOS GA, LOUKASS, CONSTANTOPOULOS SH. Wide geographic variations of sensitivity to MOTT sensitins in Greece. *Eur Respir J* 1995, 8:715–717
  20. HORSBURGH CR Jr, RUBIN EJ. Clinical practice. Latent tuberculosis infection in the United States. *N Engl J Med* 2011, 364:1441–1448
  21. PAPAVENTSIS D, NIKOLAOU S, KARABELA S, IOANNIDIS P, KONSTANTINIDOU E, MARINOI I ET AL. Tuberculosis in Greece: Bacteriologically confirmed cases and anti-tuberculosis drug resistance, 1995–2009. *Euro Surveill* 2010, 15; pii:19614
- Corresponding author:*
- G. Michas, Department of Internal Medicine, General Hospital of Kalamata, Antikalamos, GR-241 00 Kalamata, Greece  
e-mail: gv.michas@gmail.com
-