

Self-reported history of vaccination and disease and immunity against hepatitis A, hepatitis B, tetanus, diphtheria and varicella among Spanish military recruits

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This study aims to evaluate the immune status against hepatitis A, hepatitis B, tetanus, diphtheria and varicella in military recruits and the validity of self-reporting of their disease and vaccination history. A total of 226 participants were studied (mean age, 20.2 years; SD 1.7). 10.4% presented antibodies to hepatitis A, 78.3% to hepatitis B, 94.2% to tetanus, 77.4% to diphtheria and 81.9% to varicella. The relationship between self-reporting of vaccination history and seroprotection showed a high positive predictive value for tetanus (98.8%) and a high negative predictive value for hepatitis A (91%). Hepatitis A vaccination and serology testing for varicella and Hepatitis B on joining the Spanish armed forces are recommended.

Introduction

Military personnel can become exposed to transmissible infectious diseases during the course of their duty,¹ especially when on missions abroad. Spanish military personnel are being sent to countries such as Afghanistan, where community outbreaks of diphtheria are common, the prevalence of hepatitis B is $\geq 8\%$, and poor hygiene standards favor the transmission of diseases such as hepatitis A or tetanus.² The Russian experience in Afghanistan in 1980, where 60% of the 'sanitary losses' of the army during their occupation of that country were due to infectious diseases,³ remind us that the protection of soldiers is not just providing them the best fighting equipment but also adequate vaccination. It is important to know the immune status of military personnel on joining the armed forces in order to determine their degree of protection and set up the necessary vaccination protocols.

Table 1 shows the Spanish Army Forces vaccination schedule.⁴ In Spain, general population has been vaccinated against tetanus and diphtheria since 1964.⁵ The last case of diphtheria was declared in 1986.⁵ From 1983 to 2006 the cases of tetanus decreased from 90 to 21. All of them were declared in adults.⁶

In 1992 the Spanish Ministry of Health recommended that the Autonomous Communities establish an HBV immunization program for adolescents.⁷ In 1996 HBV immunization was approved in newborns, this vaccination strategy was adopted nationwide in 2002 maintaining catch up campaigns for adolescents.⁷ The coverage of hepatitis B vaccination in adolescents is actually around 80% and over 96% in newborns. The incidence

of hepatitis B in Spain has decreased from 114 cases/100,000 inhabitants in 1985 to 2 cases/100,000 in 2006.⁶

The vaccine against hepatitis A is not universally recommended for the general population in Spain. As a prophylaxis, pre-exposure is recommended for people who have an increased risk of hepatitis A (travellers to high-endemic zones, relatives and nurses of HAV patients, homosexuals having multiple sexual partners, parenteral drug users) and those people in whom infection would cause serious consequences (chronic hepatic patients, haemophiliacs, HIV, patients that are candidates for an organ transplant).⁷ In 2006, the incidence of hepatitis A was 3.7 cases/100,000 inhabitants.⁶

The vaccine against varicella for susceptible adolescent between 10–14 years old was incorporated into the Spanish vaccination scheduler in 2006.⁸ The cases of varicella declared in 2006 were 177,728, which mean an incidence of 448 cases/100,000 inhabitants.⁶

This study aims to assess the immune status of a group of individuals applying for the Spanish armed forces and the validity of self-reporting by a questionnaire of their disease and vaccination history. The findings of the evaluation will enable us to determine the degree of protection against hepatitis A, hepatitis B, tetanus, diphtheria and varicella.

Results

A total of 226 participants (209 men and 17 women) aged between 18 and 26 years (mean 20.2 years; SD 1.7) were studied.

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Table 1. Spanish army forces vaccination schedule

Vaccines	Time (month)		
	0	I	6–12
Diphtheria, Tetanus	dT	dT	dT
Hepatitis A, Hepatitis B	HAB*	HAB	HAB
Measles, Mumps, Rubella	MMR		

Vaccines recommended for all those without adequate documentation proving correct previous vaccination.⁴ *HAB Combined Hepatitis A and Hepatitis B Vaccine; Diphtheria, Tetanus, Pertusis (dTaP) vaccination boosters are indicated every 10 years.

The participants were from all over Spain and all had completed their secondary education.

Table 2 shows the serology results for the diseases studied, as well as the self-reported vaccination and disease histories. Of the 226 participants studied, only 10.4% presented antibodies against hepatitis A, whereas 78.3% presented antibodies against hepatitis B, 94.2% against tetanus, 77.4% against diphtheria and 81.9% against varicella. There were no statistically significant differences in the serology results according to age or sex.

The anti-hepatitis B core antigen and hepatitis B surface antigen (HBsAg) titers were all negative and none of the subject's transaminases levels were over the normal range.

The self-reported disease history revealed that most participants had not suffered the diseases studied except varicella (61.1%). In the case of hepatitis A, 21.2% of participants said they had been vaccinated; for hepatitis B the proportion was 30.5%, for tetanus it was 36.6%, and for diphtheria it was 3.1%. When mean age and distribution by sex were analyzed according to disease and vaccination history, there were no statistically significant differences.

An analysis of the relationship between self-reporting of vaccination history and determination of the titers of antibodies to the diseases studied (Table 3) showed a greater positive predictive value (PPV) for tetanus (98.8%) and a greater negative predictive value (NPV) for hepatitis A (91%). The self-reported disease history gave the highest results for varicella (PPV 86.2%) and hepatitis A (NPV 89.8%). Protection against these diseases was not related to age nor to sex. The highest overall PV was found for Hepatitis A for either history of vaccination and disease.

Discussion

Several studies have tried to determine whether the self-reported disease or vaccination history could prove useful as a predictive value for immunity.^{9–11} In our study population, it is important to guarantee adequate protection against the diseases studied due to the greater risk of workplace exposure.

In Spain, the epidemiology of HAV infection has changed, and now tends to affect older people; therefore, a high percentage of young adults remain susceptible.^{12,13} Actually more than 65% of individuals aged less than 40 years are thought to be susceptible to HAV.¹⁴ Data from our study confirm this trend. The seroprevalence of anti-HAV antibodies was only 10.4%. When participants were asked if they had been vaccinated against

hepatitis A, 48 (21.2%) said that they had. Of these, only 7 were protected; therefore, the PPV (14.6%) of the questionnaire for vaccination history was too low to enable us to determine the number of participants who had been vaccinated. However, the questionnaire was valid for determining which of the participants who said they had not been vaccinated really were not immunized (NPV 96.2%).

Related to the hepatitis B, chronic cases were not detected and 78.3% were protected against the disease. We think that, with the age of the participants, possibly most of them had been vaccinated against hepatitis B in the catch up campaigns for adolescents conducted in Spain according to their vaccination schedule.^{6,15} However, when they were asked if they had been vaccinated, only 30.5% said that they had, showing that a large proportion of the study population did not know which vaccinations they had received. Of those who claimed they had not been vaccinated, 80.2% had antibodies. The PPV of the questionnaire for vaccination history was 73.9%, and the NPV was 33%, both of which are too low to provide a valid picture of the participants' immune status using the questionnaire.

On the other hand, the PPV of the questionnaire for tetanus vaccination history was high—98.8% of the respondents who said that they had been vaccinated were immune—whereas the NPV was low (8.3%). We agree with other authors that the questionnaire is a useful method of evaluating immunity in those respondents who said that they had been vaccinated against tetanus.¹⁶

As for diphtheria, the seroprevalence study carried out in Spain in 1996,⁵ revealed a prevalence of 98% in children aged less than 14 years and a decrease in antibody concentrations as age increased: the prevalence of antibodies in participants aged 30 to 39 years was 54%. In our study, 81.4% of participants were immune. When the participants were asked if they had been vaccinated against diphtheria, only 7 (3.1%) said they had, thus confirming the lack of knowledge about this vaccine reported by other authors.¹⁷

In Spain, seroprevalence studies for varicella show that 94% of adolescents and 99% of individuals aged more than 30 years are immune.^{5,18} Participants were not asked if they had been vaccinated against varicella, as their age meant that this vaccination was not included in their vaccination schedule.⁸ The data on local sales prior to the introduction of universal vaccination has not yet been published in Spain. In our opinion most of varicella vaccines prior to the introduction of universal vaccination were administered to children not to adolescents (pediatricians but not family doctors were recommending the vaccine) so we think that the possible effect in our results would be small.⁶ Although when they were asked if they had suffered the disease: 86.2% who said they did suffer the disease had antibodies, whereas 25% of those who said no were susceptible. The PPV was high, and the questionnaire was a valid tool for predicting participant immune status.

Our study has a number of limitations. First, it may be affected by a selection bias, as the participants were predominantly male young adults in good health with an educational level possibly higher than the general population. Therefore, the result can not be extended to the Spanish general population but are possibly

Table 2. Self-reported history and vaccination and results of serological tests for detection of hepatitis A, hepatitis B, tetanus, diphtheria and varicella antibodies

Disease	Self-reported history % (n)				Serological result % (n)	
	Disease		Vaccination		Positive	Negative
	Yes	No	Yes	No		
Hepatitis A	0.4 (1)	99.6 (225)	21.2 (48)	78.8 (178)	10.2 (23)	89.8 (203)
Hepatitis B	0.4 (1)	99.6 (225)	30.5 (69)	69.5 (157)	78.3 (177)	21.7 (49)
Tetanus	1.3 (3)	98.7 (223)	36.3 (82)	63.7 (144)	94.2 (213)	5.8 (13)
Diphtheria	0.4 (1)	99.6 (225)	3.1 (7)	96.9 (219)	77.4 (175)	22.6 (51)
Varicella*	61.1 (138)	38.9 (88)	NA	NA	81.9 (185)	18.1 (41)

(N 226). *Participants were not asked if they had been vaccinated against varicella, as their age meant that this vaccination was not included in their vaccination schedule;⁸ NA, Not available.

Table 3. Seroprotection against hepatitis A, hepatitis B, tetanus, diphtheria and varicella, according to self-reported history of vaccination and history of disease and positive, negative and overall predictive values

Seroprotection	Anti VHA		Anti VHB		Anti TT		Anti DT		Anti VZ*		
	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	
History of Vaccination	Yes	7	41	51	18	81	1	6	1	NA	NA
	No	16	162	126	31	132	12	169	50	NA	NA
	PPV % (95% CI)	14.6 (4.9–25.1)		73.9 (63.7–84.3)		98.8 (96.8–100)		85.7 (60.3–100)		NA	
	NPV % (95% CI)	91 (86.8–95.2)		19.7 (13.7–26.3)		8.3 (3.6–12.4)		22.8 (17.4–28.6)		NA	
	PV % (95% CI)	74.8 (69.1–80.5)		36.3 (30.0–42.6)		41.1 (34.6–47.4)		24.8 (19.4–30.6)		NA	
	Yes No	0 23	1 202	0 177	1 48	3 210	0 13	0 175	1 50	119 66	19 22
History of Disease	PPV % (95% CI)	0 NA		0 NA		100 NA		0 NA		86.2 (80.2–91.8)	
	NPV % (95% CI)	89.8 (86.1–93.9)		21.3 (15.7–26.3)		5.8 (2.9–9.1)		22.2 (16.6–27.4)		25 (16.0–34.0)	
	PV % (95% CI)	89.3 (84.9–93.1)		21.2 (15.7–26.3)		7.1 (3.7–10.3)		22.1 (16.6–27.4)		62.4 (55.7–68.3)	

(N 226). VHA, hepatitis A; VHB, hepatitis B; TT, tetanus; DT, diphtheria; VZ, varicella; PPV, positive predictive value; NPV, negative predictive value; PV, overall predictive value; NA, not available; *Participants were not asked if they had been vaccinated against varicella, as their age meant that this vaccination was not included in their vaccination schedule.⁸

valid for other specific groups such as male university entrants. Furthermore, self-reporting of disease history and vaccination history can also be affected by memory bias and in our population we have observed that confusion between hepatitis A and hepatitis B has occurred. Future investigations must be aware of this confusion between hepatitis A and B when using questionnaires. Second, the laboratory determinations do not specify whether immunity was acquired actively or passively. However, the specificity and sensitivity of the techniques used are high and do not detract from the validity of the study.

Third, the Hepatitis A vaccine has been universally available in Catalonia since 1999.¹⁹ In our study population of the 226 recruits who participated only 3 (1.3%) were from Catalonia. So given this small sample comparison with recruits from other regions was not possible and in any case we think that the influence on the overall results would be minimal.

An analysis of the relationship between the responses to the questionnaire and the serology results reveals contradictions suggesting that the questionnaire may be an unsuitable tool for determining immunity, and serology testing becomes necessary to complete the information and apply the vaccination protocols. In agreement with the accepted recommendations for professional risk groups,^{7,10} military personnel should undergo serology testing for varicella on joining the armed forces if their clinical history raises doubts about whether they have been vaccinated. This recommendation will have to be reviewed in 2012, when the first cohorts of vaccinated reach the average age of recruitment.

We agree that all recruits should be vaccinated against hepatitis A. As shown in Table 1 the Spanish Army Forces vaccination schedule actually recommends vaccination against hepatitis A and B using the combined vaccine for all those without adequate documentation proving correct previous vaccination.⁴ Given the

high prevalence of antibodies against HVB, we think that in this specific population group an economical analysis is mandatory to decide which the more appropriate strategy is. Previous studies have shown that serology testing for hepatitis B is more cost effective than systematic vaccination in groups with a high likelihood of having been vaccinated.²⁰ Lastly, diphtheria, tetanus, pertussis (dTaP) vaccination boosters are indicated every 10 years in Spanish troops.⁴ Reinforced application of the current booster strategy is needed and further investigation required to analyze Pertussis disease burden.

Materials and Methods

We studied 226 randomly selected participants from the 584 recruits who presented at the Centro de Instrucción de Medicina Aeroespacial in June 2006 to undergo the necessary medical examinations for admission to the Officer Training School of the Spanish armed forces. An epidemiologic study of all participants was carried out, and the data collected were as follows: sociodemographic data (age, gender, place of residence and educational level), clinical history of infectious diseases (hepatitis A, hepatitis B, tetanus, diphtheria and varicella) and vaccinations received against these diseases.

A 10-mL blood sample was taken from each participant for the determination of antibodies. Hematological and biochemistry parameters were measured including transaminases levels. Informed consent was obtained and the reference hospital's ethics committee approved the study.

Serum samples were stored at -80°C until serological analysis at the laboratory of the Department of Public Health School of Health Sciences, University Rey Juan Carlos. Total anti-hepatitis A antibodies (anti-HAV) were determined using the microparticle enzyme immunoassay (MEIA) AXSYM HAVAB 2.0 (Abbott Diagnostics Division, Wiesbaden, Germany) in an automatic

SYSMEX reader. The total hepatitis B surface antibody (anti-HBs), the anti-hepatitis B core antigen (anti-HBc), and the hepatitis B surface antigen (HBsAg) titers were determined using the MEIA IMX SYSTEM AUSAB (Abbott Diagnostics Division, Wiesbaden, Germany) in an automatic IMX reader. Anti-HAV antibody titers of between 1.001 and 3.000 were considered non-reactive, and those between 0.000 and 1.000 were considered reactive. According to international criteria, anti-HBs titers above 10.0 IU/mL were considered protective.²¹

Varicella and tetanus were analyzed using the enzyme-linked immunosorbent assay (ELISA) of IgG antibodies (VARICELLA-ZOSTER ELISA IgG and TETANUS ELISA IgG; VIRCELL, S.L. Santa Fe, Granada, Spain). If the antibody index was less than 9, the result was considered negative. For diphtheria, IgG antibodies were determined using ELISA (Diphtheria ELISA IgG Testkit, Genzyme Virotech GMBH, Rüsselsheim, Germany), and values of less than 1 were considered negative.

A descriptive study was performed, expressing quantitative variables as the mean and standard deviation (SD) and the qualitative variables as proportions. Goodness of fit was determined using the Kolmogorov-Smirnov test, and means were compared using the t test or the corresponding non-parametric test. Differences in proportions were assessed using the Chi-square test, considering a two tail p value of <.05 as statistically significant. Positive, negative and overall predictive values of the self-reported history of disease or vaccination were calculated [95% confidence interval (CI)]. Statistical analysis was performed using SPSS version 16.0 (SPSS Inc., Chicago, IL).

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