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No Mechanism Found for Spontaneous Tetanus Immunity in Rural Cambodia

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ABSTRACT

Introduction: It has been recorded as hypothesis that, in tropics, being repeatedly contaminated by cow's dung containing *Clostridium Tetani*, administered through open wounds in sole feet, you may benefit from a non-vaccination spontaneous protective immunity against tetanus, obviating tetanus immunization.

Methods: A catch-up adult tetanus vaccination, with two sessions one year apart, was organized in 1992-4 for 13,600 EPI and post-EPI population, in a rural district of Cambodia, with very low vaccine coverage and with peasants experiencing often untreated open sole wounds and breeding cattle resting under the floor of their home, thus being possibly infected by *Clostridium tetani*. Volunteers were asked about occurrence of these factors supposed to give protective antibodies against tetanus. They provided their sera, taken before and after first vaccine injection, and tested for tetanus by mouse-protection method.

Results: No relation was found between contact with cattle and/or presence of feet open cracks and level of tetanus antibodies, before or after injection of first dose of tetanus vaccine.

Conclusion: No mechanism for spontaneous protection against tetanus was shown in this prospective study.

INTRODUCTION

Spontaneous antibodies against tetanus, without known vaccination administration, has been often described. It was suspected that, being repeatedly contaminated by cows dung, containing *Clostridium Tetani* spores [1] penetrating through cracks in sole feet [2,3], non-vaccine spontaneous protective immunity against tetanus is produced, obviating tetanus immunization [4,5]. This has been always asserted in retrospective studies [1, 2,4-9]. We took the opportunity, during a large, catch-up tetanus vaccination, to investigate, in adults and prospectively, production of these spontaneous antibodies and their impact on tetanus immunity [8,9].

PLACE, POPULATION AND METHODS

Place, time and population

The catch-up tetanus vaccination took place in 1991-4, in a rural district (Angkor Thom) with a mostly rural population of 14,900, in Siem-Reap medical region, Cambodia, near Angkor tourist site [10,11].

Methods

After clearance of Siem Reap Authorities, enrollment and signature of 18-59 years-old, physically apt, volunteers was obtained, giving informed consent for blood

testing. They were questioned about factors thought to bring spontaneous tetanus antibodies: owning cattle resting under their high-floor houses and suffering often from open cracked sole, due to not wearing shoes. Anti-tetanus serum in case of open wound was unavailable in this district. Volunteer's serum samples, taken during inclusion in the study and 6 months after first vaccination, were titrated at Ho Chi Minh Pasteur Institute (HCMPI) following Ipsen's mouse-protection method [12].

RESULTS

There has been no correlation found between presence of tetanus antibodies, and presence of looked-after risk factors for spontaneous tetanus antibodies at first sample, before first dose of tetanus vaccine (Table 1).

Table 1: Prevalence of risk factors and spontaneous tetanus antibodies in volunteers tested by mouse-protection method before vaccination, Angkor Thom tetanus study, 1991-4.

Risk factor	Total	Showing spontaneous tetanus immunity		RR	p
		Yes	%		
foot ulceration					
Total	194	35	18%		
Yes	27	6	22%	1.28	-
No	167	29	13%	1	0.54
Raising cattle					
Total	194	35	18%		
Yes	35	6	20%	1.09	-
No	159	27	16%	1	0.83

After administration of first dose of vaccine, volunteers with spontaneous tetanus antibodies were more protected against the disease (Table 2).

With memory bias of previous female immunization, often vaccinated for neonatal tetanus prevention by Minister of Health, there was a significant increase in tetanus antibodies compared to males in the older age-group (Table 3).

DISCUSSION

Methods

The mouse-protection method developed by Ipsen has been considered the best technique to test tetanus protection in humans [13]. This labor-intensive method, requesting high provision of mice, could only be provided by HCMPI. Compared to quick serological testing, in terms of sensitivity and specificity, the mouse-protection method has been shown more specific [13]. The pre-examination of volunteers excluded females suspect of gravity and adults suspect of acute or chronic disease [14].

Table 2: Seroconversion through mouse-protection testing, after having received one dose of vaccine, in seronegative volunteers with no memory of vaccination before study, in comparison with other groups. Angkor Thom tetanus study, 1991-4.

Group of volunteers	N	Mean and Confidence Interval of tetanus antibodies
With spontaneous antibodies without memory of immunization	35 (14%)	0.016<0.095<0.94
No tetanus antibodies shown and without memory of vaccination	159 (66%)	0.0020<0.0026<0.0090
One vaccination recorded before titration	5 (2%)	0.0023<0.018<0.056
Two vaccinations recorded before titration	20 (8%)	0.002<11.95<45.46
Three vaccinations recorded before titration	22 (9%)	0.203<33.78<200

Table 3: Seroconversion titers in mouse-protection testing, after one tetanus dose in seronegative volunteers. Angkor Thom tetanus study, 1991-4.

sex	Total	N with tetanus titers over 0.01 IU/mL	%	RR	p
M	71	36	50.7%	1	-
F	21	17	80.9%	1.60 (95% CI: 1;17-2.18)	4

Results

This study shows the benefits of a prospective study, conducted in a region characterized by a low prevalence of tetanus vaccination and a high prevalence of risks factors for spontaneous seroconversion. Memory bias, as shown by Table 3, give some doubts on validity of results. A randomized study is however, for such a lethal disease, unacceptable ethically.

CONCLUSION AND RECOMMENDATIONS

Naturally acquired antibodies to tetanus have been also shown in this study. Better follow-up of vaccine records in tropical countries will have to be set-up to better ascertain these antibodies and their mechanism of production. Computerized register of vaccinations, when readily available, will allow better follow-up of vaccine status and naturally acquired antibodies against tetanus [15].

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