PERSISTENCE OF ANTIBODIES AGAINST TETANUS UPON REVACCINATION

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SUMMARY

To assess the interval since the last revaccination against tetanus the persistence of antibodies was determined using ELISA test in 128 subject. Levels of antibodies against tetanus higher than the protective level of 0.1 IU/ml were found not only in those revaccinated less than ten years ago, but also in those revaccinated more than ten years before. With increasing length of the interval since last revaccination the antibody levels against tetanus decreased gradually although they remained above the protective level. No basic dependence of that trend on gender or age has been found. In the whole series, antibodies against tetanus exceeded the protective level for up to 20–25 years post last revaccination. This finding together with a favorable epidemiological situation as regards the occurrence of tetanus could eventually enable to prolong the interval for revaccinating adults in the Czech Republic.

Key words: tetanus, antibodies, revaccination, persistence
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INTRODUCTION

Revaccination against tetanus in adults presents a certain problem for the general practitioner as regards the meeting of the prescribed interval since last revaccination against tetanus and as the case may be, whether it is necessary after expiry of that interval, to begin again with three doses of anatoxin of the basic vaccination scheme. This problem has not been resolved even by the latest legislative amendment prolonging that interval from the former ten years to 10–15 years (1).

Serological surveys carried out up to now revealed a good indiscriminate collective immunity in Czech population, and data in Czech and foreign publications (2, 3) point to a longer persistence of post-vaccination antibody levels exceeding the prescribed interval for revaccination.

The object of analysis is a group of individuals in whom blood has been tested for antibodies against tetanus, in the laboratory of the Regional Public Health Center Ostrava. The vaccination history of those subjects has been looked up and an evaluation of the interval since last vaccination in relation to antibody levels has been made, that being the objective of the present study.

MATERIAL AND METHODS

The series includes subjects in whom blood has been sampled for antibodies against tetanus in the laboratory of the Department of Immunology at the Regional Public Health Center Ostrava over the years 1996 through 2000. In all, 128 subjects have been investigated as presented in Table 1 and broken down by age and gender. The basic source of information was the database of the KHS Ostrava laboratory, which contains the name, surname, birth number, date of sampling, name of physician taking the sample, and the antibody titer. In those subjects there have been looked up anamnestic data from their healthcare documentation at the general practitioners, i.e. all data on vaccination against tetanus, reason for vaccination – whether it was the basic scheme, revaccination, or on treating an accident – as well as the reason for determining the antibody titer, and possibly why the then valid ten-year interval for revaccination had not been kept. As far as the blood sample came from another district, the District Public Health Center in question was asked to look up the necessary anamnestic data.

The data were put in, sub-grouped and computer processed with the aid of the programs Excel, Access, and Stata. The interval since last vaccination in relation to antibody titer has been evaluated. In view of that the distribution of the selection of *titer* data differs from the normal distribution, power transformation was performed: log titer = log(titer). For the calculation of the studied dependence of the antibody titer value on time that has passed since vaccination, regression analysis was applied.

Methodology of Investigating the Blood for Antibodies against Tetanus

For the demonstration of the anti-tetanus antibody titer the "TETANUS ELISA" set of Genzyme Virotech GmbH was applied following the instructions of the producer. Antibodies present

Table 1. *Breakdown of series by age and gender*

Age group	Males	Females	Total
0–14	2	0	2
15–49	24	60	84
50 +	14	28	42
Total	40	88	**128**

Table 2. Breakdown of series into subgroups by gender and interval between vaccination against tetanus and blood sampling for antibodies

Subgroup	Males		Females		Total	
	n	%	n	%	n	%
A Blood sampling within 10 years since vaccination	24	35.8	43	64.2	67	52.3
B Blood sampling 10 and more years since vaccination	16	26.2	45	73.8	61	47.7
Total	**40**	**31.2**	**88**	**68.8**	**128**	**100.0**

Table 3. Numbers of subjects and time interval between blood sampling and last vaccination in Subgroup A

Time interval between blood sampling and last vaccination	Number of subjects investigated
1 month	27
2 months	10
3–5 months	7
6–12 months	5
13 months–8 years	18
Total	**67**

Table 4. Numbers of subjects and time interval between blood sampling and last vaccination in Subgroup B

Time interval between blood sampling and last vaccination (years)	Number of subjects investigated
10–14	24
15–20	25
21–24	8
25–35	4
Total	**61**

Table 5. Protective effect and recommended vaccination according to levels of anti-tetanus IgG (after Schroeder et al.)

Level of anti-tetanus IgG IU / ml	Protective effect	Recommended vaccination
<0.03	non	basic vaccination
0.03–0.1	not sure	booster vaccination
0.1–0.5	exists	booster vaccination
0.6–1.0	sufficient	check up in 2 years
1.1–5.0	long-term	check up in 5–10 years
>5.0	extremely high	check up in 10 years

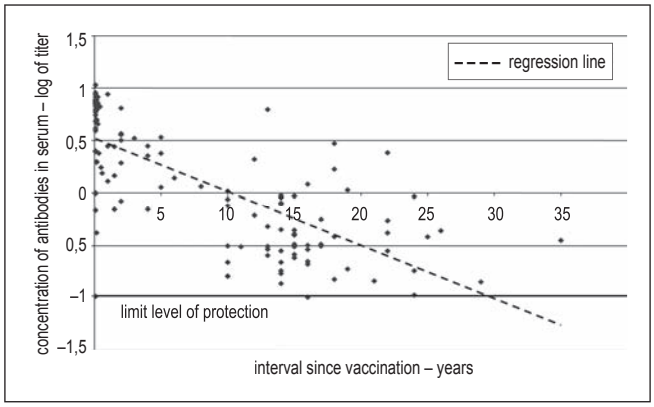

Fig. 1. Persistence of post-vaccination antibodies against tetanus

in the serum investigated form a complex with antigen that is bound in the wells of each strip. Unbound immunoglobulins are removed in the washing step. Added conjugate binds with the complex formed. On addition of substrate solution (TMB) there appears a blue color that turns yellow. Measuring of extinction (OD) was carried out at 450/620 nm wavelength within 60 minutes of addition of stop solution. The calibration curve and calculation of antibody level values in each sample was performed with the aid of a computer program. A table in the instructions for each set was used for interpreting the results.

In agreement with the information leaflet of the test, the value 0.1 IU/ml expressed as log titer = –1 was interpreted as the protective level.

RESULTS

The subjects investigated in whom there have been drawn blood samples for antibodies at various intervals since vaccination, were divided into subgroups: subgroup A – in whom blood samples were taken within 10 years after vaccination; and subgroup B – in whom blood was taken for antibody analysis more than 10 years after vaccination (Table 2).

In subgroup A there were 67 patients, of whom 24 (35.8%) were males and 43 (64.2%) were females, in whom blood was sampled for antibodies less than 10 years after last vaccination. Among them were even patients in whom those blood samples were taken within a very short period of time after vaccination. In 27 subjects blood was sampled one month after vaccination, in 10 subjects after 2 months since vaccination. The other time intervals are presented in Table 3. In subgroup B there were 61 subjects, of whom 16 (26.2%) were males and 45 (73.8%) were females, in whom blood was sampled ten or more years since their last vaccination (Table 4).

All of the subjects had antibody concentrations exceeding the protective level, i.e. greater than a titer value of –1 log. Serum antibody concentrations depended on the time that had elapsed since last application of tetanus anatoxin.

In Fig. 1 antitoxin concentration values in the serum of subjects are depicted who had been completely vaccinated and afterwards received at least one revaccination dose, in relation to the time that had elapsed since last vaccination. With increasing intervals since the last dose of tetanus anatoxin received a significant decrease in antibody titer has been registered ($p<0.001$; correlation coefficient: –0.7475). Equation of regression line: log titer = 0.5178–0.0513 x time.

Figure 2 illustrates that correlation in males, in whom with increasing intervals since time of last vaccination a significant decrease in antibody concentrations has also been noted ($p<0.001$; correlation coefficient: –0.8039). Equation of the regression line:

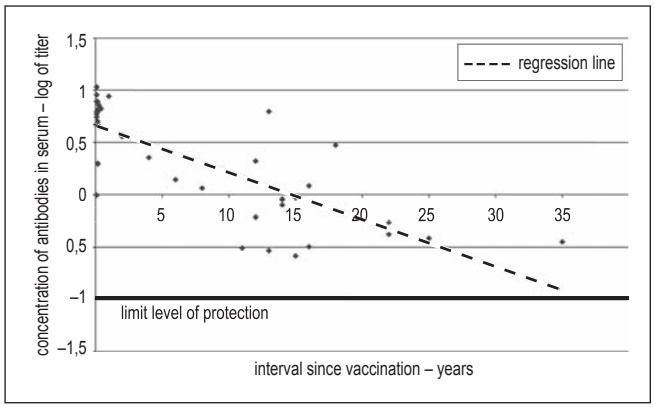

Fig. 2. *Persistence of post-vaccination antibodies against tetanus – in males.*

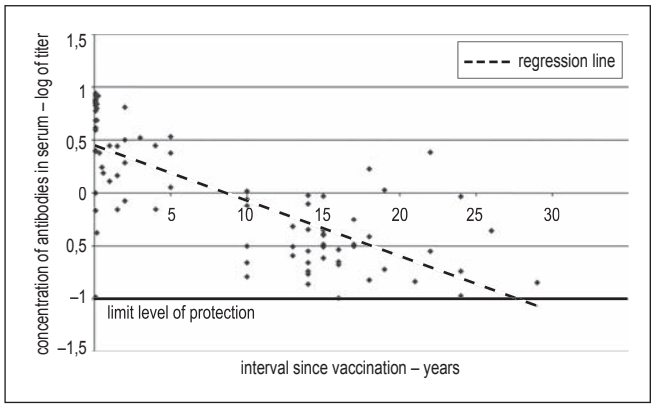

Fig. 3. *Persistence of post-vaccination antibodies against tetanus – in females.*

log titer = 0.6579–0.0462 x time. In females that correlation is expressed in Fig. 3, likewise demonstrating a significant decrease ($p<0.001$; correlation coefficient: –0.7396). Equation of the regression line: 0.4473–0.0522 x time.

An analysis of the decrease in antibody titer in two age groups, has been carried out, namely under 50 years (Fig. 4) and over 50 years of age (Fig. 5). No significant difference in antibody decrease between the two age groups has been found.

Figure 6 depicts the correlation of antibody concentration in subjects who had their blood sampled for antibodies within 10 years since last vaccination. No significant decrease in serum antibodies has been observed, however, there is an apparent decreasing tendency with increasing time since last vaccination.

In Fig. 7 are values of antibody concentrations in the serum of subjects who had their blood sampled for antibodies more than ten years since last vaccination. No significant decrease in serum antibody levels has been observed, the dip in the regression line being gradual.

DISCUSSION

It has been presented in the literature (4, 5, 6) that basic immunization against tetanus confers protection for less than ten years, and that the first revaccination should be carried out within ten years so that immunity be preserved. It has been calculated, that 25 years after primary vaccination, 10% of vaccinate would be unprotected (5).

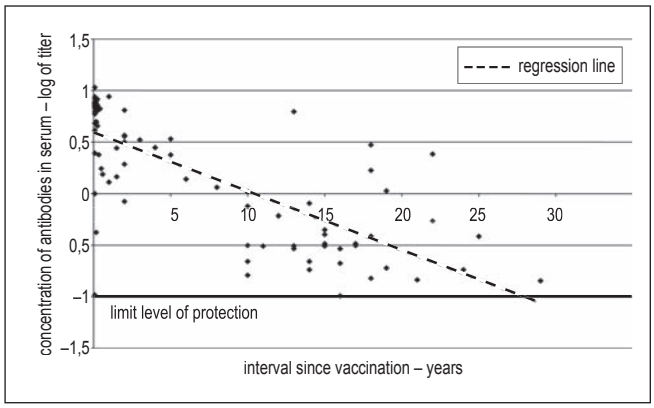

Fig. 4. *Persistence of post-vaccination antibodies against tetanus – in age group of under 50 years.*

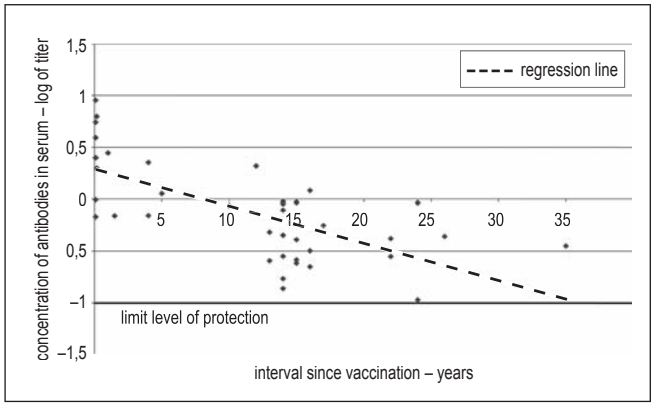

Fig. 5. *Persistence of post-vaccination antibodies against tetanus – in age group of over 50 years.*

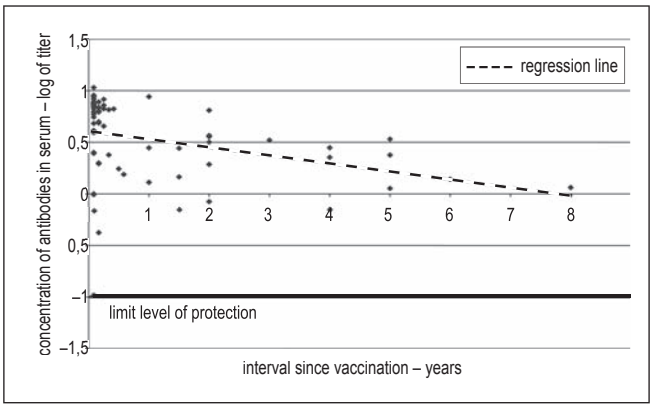

Fig. 6. *Persistence of post-vaccination antibodies against tetanus – at intervals within 10 years since last vaccination.*

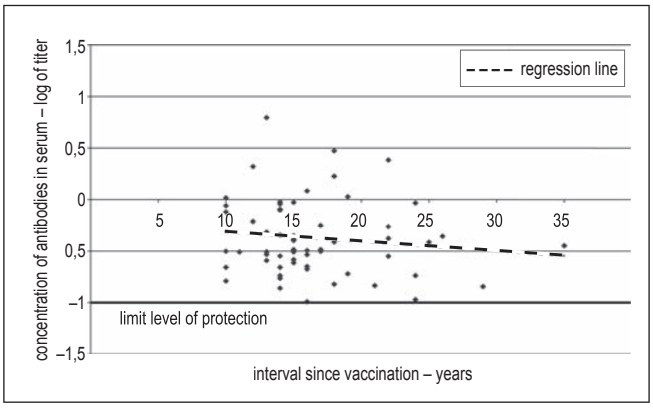

Fig. 7. *Persistence of post-vaccination antibodies against tetanus – at intervals of over 10 years since last vaccination.*

Revaccination provides substantially longer protection than the basic vaccination. That could be explained by a greater response upon revaccination than that what follows basic vaccination. Repeated vaccination is essential for a persisting immunity throughout life, and according to a number of domestic and foreign studies, revaccination at 20-year intervals should be sufficient to offer lasting protection (2, 3).

Also results in the presented series reveal that with years passing after last revaccination the antibody titer gradually decreases, nevertheless remaining above the protective level of 0.1 IU/ml (–1 log titer) for at least up to 20–25 years after last revaccination. Such a situation remained analogous not only for the whole series but also upon breaking it down by males and females. Likewise, no significant difference has been found between subjects under 50 years of age and those over 50. Only on comparison of subjects revaccinated less than 10 years ago and those revaccinated more than 10 years ago, was it apparent that antibody levels were lower by one order in the latter as against those in subjects revaccinated less than ten years ago.

Revaccination at shorter intervals may be connected with a risk of post-vaccination side effects (7, 8). Therefore, it is necessary to consider the urgency of the risk of developing the given disease against which the vaccination program is aimed. From the epidemiological point of view the best proof of the effectiveness of the vaccination program is the incidence of tetanus in any given region. In the Czech Republic tetanus is a rare sporadic disease since the later half of the 1980s, that documenting best the good level of immunity in the Czech population (Fig. 8), namely even in the elderly (9). As far as doubts regarding the immunity of any given patient against tetanus exist, it is proper to investigate his/her antibody level against tetanus, and then proceed, e.g. according to the scheme presented by Schroeder *et al*. (10) as presented in Table 5.

CONCLUSIONS

By investigation 128 serum samples it has been found that not only in subjects who had been revaccinated less than ten years ago but also those that had been revaccinated more than ten years before, antibody levels against tetanus remained higher than the protective level of 0.1 IU/ml.

With increasing time since last revaccination gradually the antibody level against tetanus decreases although it remains above the protective level.

In principle, any correlation with gender or age in the antibody trend has not been found. Only in subjects in whom the interval since last revaccination was longer than ten years, was the antibody titer lower by one order, nevertheless still above the protective level.

In the whole series antibodies against tetanus were found to be above the protective level for up to 20–25 years since last revaccination. This finding, together with the favorable epidemiological situation regarding tetanus incidence, could render possible to still prolong the interval for revaccination of adults in the Czech Republic.

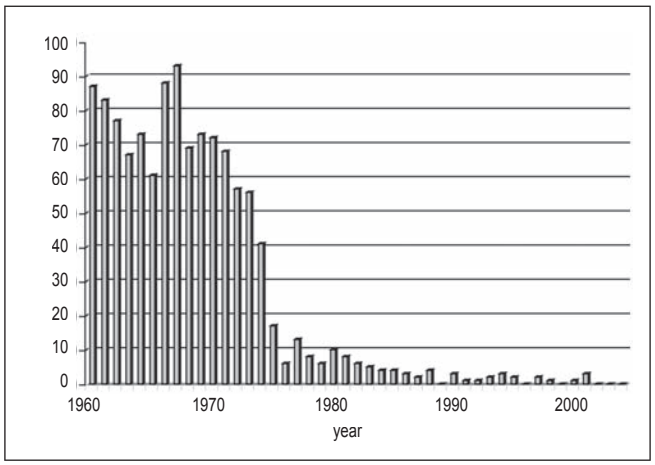

Fig. 8. *Incidence of tetanus in the Czech Republic over the years 1960 through 2004 (number of cases).*

Acknowledgements

The authors wish to thank the staff of the Departments of Epidemiology at the Regional Public Health Center Ostrava and at the former District Public Health Centers in the North Moravian Region for assistance in data collection, and the staff of the Department of Immunology at the Regional Public Health Center Ostrava for the testing for antibodies against tetanus.

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Received and accepted March 10, 2005