

Tetanus Epidemiology in Europe and in Italy: a review

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Key words

Tetanus • Epidemiology

Summary

A review of tetanus epidemiology in Europe and in Italy was undertaken.

To this purpose data were collected from the following sources:

- World Health Organization's Web page;*
- Eurosurveillance Weekly (Bulletin and Web page);*
- Italian Ministry of Health (Bulletin and Web page);*
- Publications from the National Institute of Statistics (ISTAT);*
- Tuscany Region Web page.*

Moreover, a seroepidemiological study was performed on a sample of 522 subjects belonging to the open population of Southern Tuscany using an ELISA test.

The results show: extensive vaccination coverage for both Europe and Italy; a clear trend towards reduction of incidence in Europe from 1985 to 1994; a persistence of neonatal tetanus on the European continent, especially in certain countries like Turkey; the end of declining incidence in Italy around 1987; high percentages of elderly subjects living in Tuscany without protective immunity, particularly among females.

The results suggest the need to implement European strategies to control tetanus, especially by actively offering vaccination to unprotected subjects.

Introduction

One the aims of the World Health Organization (WHO) project «Health for all for the year 2,000», concerns tetanus. The target to reach for the European Region was the elimination of neonatal tetanus within the year 1995 (morbidity rates lower than 1/1,000 live births)^{10 24 27}. This result was achieved by many countries (e.g.: Austria, Belgium, Bulgaria, Czech Republic, Denmark, Finland, etc.). However, WHO estimates suggest that, in 1997, 500 neonatal tetanus cases occurred in the Region²³ and the number of cases amounted to 400,000 worldwide. The number of neonatal tetanus notifications in the world decreased from 31,849 in 1988 to 11,974 in 1996, with a moderate increase in 1997 (15,716 notifications)²⁷.

In 1994, the total number of tetanus cases in subjects of all ages, reported to the WHO, amounted to 42,225, with 68% of Countries regularly transmitting notifications²². Tetanus-diphtheria immunization is compulsory for all newborns in Italy, starting from the third month of life and for all those employed in occupations at risk³. Recent provisions of law call for the implementation of preventive measures through the 1994-96 and 1998-2000 National Health Plans. A law issued in 1994 provided anti-tetanus immunization free of charge for the entire population.

In Italy, the disease has been subject to compulsory notification since 1955³.

The overall data show that, following a slow but constant reduction of tetanus incidence, there are signs of a moderate morbidity increase.

The aim of the study was to describe and compare the epidemiological trend of tetanus in Europe, Italy and Tuscany.

Materials and methods

STUDY DESIGN

The need for an updated picture of the current epidemiological situation is highlighted by the following events:

- social, political and economic upheavals that followed the dissolution of the former Soviet Union (leading to a breakdown of Public Health facilities in Eastern European countries, with severe consequences for the health of those citizens);
- a reverse in the trend towards reduction of tetanus incidence in Italy, with local signs of a moderate morbidity increase;
- the situation of Tuscany, where reported incidence is the highest in the Country.

The following indicators were used in order to evaluate tetanus epidemiology and protection:

- vaccination coverage, calculated as the percentage of children who had received at least three doses of vaccine (Europe, Italy and Tuscany) at 24 months of age;
- tetanus cases among those subject to compulsory vaccination (Italy);
- incidence of neonatal tetanus (Europe and Italy);
- incidence of Tetanus (Europe, Italy and Tuscany);

- incidence of Tetanus according to sex and age (Italy and Tuscany);
- case-fatality rate (CFR) for Tetanus according to age and sex (Italy and Tuscany);
- tetanus antitoxin immunity in the population of Southern Tuscany, evaluated by serum samples collected from a representative number of subjects.

This last part of the study aimed to: a) ascertain whether an improvement in the immune coverage had occurred by undertaking a comparison with other studies carried out in Tuscany in the past; b) evaluate the efficacy and effectiveness of vaccination services; c) verify the application of the scheduled and recommended booster dose administration; d) evaluate the percentage of subjects belonging to risk groups who lack protection.

DATA SOURCES

With regard to international data, we utilized the World Health Organization Web page²², its Web catalogues and the Eurosurveillance Weekly Bulletin^{5 21}. Denominators for calculation of morbidity in European Countries and of the chi-square for linear trend were obtained from the De Agostini General Encyclopaedia^{7 8}.

Since the WHO European Region does not correspond with the European Continent, we excluded data belonging to Israel and Jordan, whilst we kept those relative to Extra-European States such as: Armenia, Azerbaijan, Georgia, to make comparisons with the former Soviet Union.

With regard to national data, we made use of publications by the Ministry of Health^{12 17}, its Web page¹³, as well as publications of the Central Institute of Statistics (ISTAT) (Annuario Statistico Italiano and Annuario di Statistiche Sanitarie). Denominators for the calculation of morbidity and of chi-square for linear trend were obtained from census data and for Tuscany were drawn from the Tuscany Region WEB page²⁰ and the already mentioned national data.

Seroepidemiological studies

SAMPLE SIZE

To estimate the sample size required, we preliminarily studied 362 subjects stratified by sex and by the following age groups: 2-3, 13-14, 18-20, 23-24, 30-65 and > 65 years. Based on the percentages of protected subjects in each age group, (antitoxin titre > 0.1 IU/ml), we estimated the sample size, admitting a 5% risk of error, within each group, and a maximum of 10% inaccuracy. The total number of studied subjects was 522.

RECRUITMENT OF SUBJECTS

Subjects were recruited in 1997 by means of a systematic random sampling design. Blood samples were drawn from subjects of a healthy open population who applied to laboratories for screening purposes.

ANTITOXIN TITRATION

Sera were stored at -20°C until titration and were tested for tetanus antitoxin antibodies by enzyme linked immunosorbent assay (ELISA) (ARNIKA, Diagnostic Line, Milan, Italy).

The antibody titre was expressed in IU/ml in order to compare it with standard international serum.

For the interpretation of results, the following scheme was used¹⁸:

- < 0.1 IU/ml: no protection;
- 0.1-5 IU/ml: short term protection;
- > 5 IU/ml: long-term protection.

STATISTICAL ANALYSIS

The following softwares were utilized: [Excel-version 8 (Microsoft-Corporation, Redmond, WA); Statview-version 4 (Abacus-Concepts, Inc. Berkeley, CA) and EPINFO-version 6.04 (Center for Disease Control-CDC, Atlanta)].

Results

VACCINE COVERAGE

According to WHO data, worldwide children's vaccine coverage against tetanus exceeds 80%²⁶ and immunization coverage with 2 doses of tetanus toxoid among pregnant women catches up 64%²⁸. Coverage is generally high in Europe. In Finland and Hungary, for instance, it is virtually estimated at 100%, while in most States it ranges from 90% to 99% and is lower than 90% in the following Nations: Spain (88%), Armenia (87%), Russia (87%), Estonia (85%), Greece (85%), Malta (84%), Bosnia (79%), Turkey (79%), Latvia (75%), Belgium (62%) and Germany (45%).

Further data released by the European Union are in disagreement with those mentioned above; the Weekly Eurosurveillance Bulletin, for example, reports 94% and 85% vaccine coverage for Belgium and Germany, respectively.

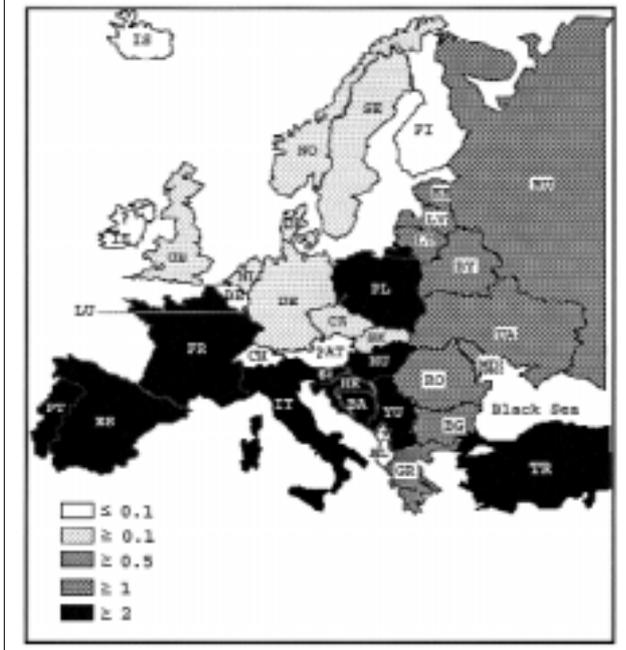
Italian vaccine coverage, as shown by a research of the Ministry of Health¹⁷, as well as by a study conducted by the «Italian Vaccine Coverage Survey Working Group»¹⁹ is around 95%. In particular, the initial results of the Icona project, achieved in 1998 by the Italian Ministry of Health, show levels of vaccine coverage for tetanus which range from a minimum of 88.6% in Campania to a maximum of 100% in Valle d'Aosta. The average coverage in the country amounts to 94.8% (95% CI = 93.6-96.0).

In Tuscany, 92.8% coverage (95% CI = 86.4-99.2) was detected at 12 months (subjects vaccinated in time) with an increase to 95.7% (95% CI = 92.7-98.5) at 24 months.

ASSESSMENT OF THE NUMBER OF CASES IN COHORTS SUBJECT TO COMPULSORY VACCINATION

Data from the Ministry of Health regarding reported tetanus cases show that, during the period 1992-96, 64%

Fig. 1. Tetanus incidence in Europe, rate per 1,000,000 inhabitants in 1985.

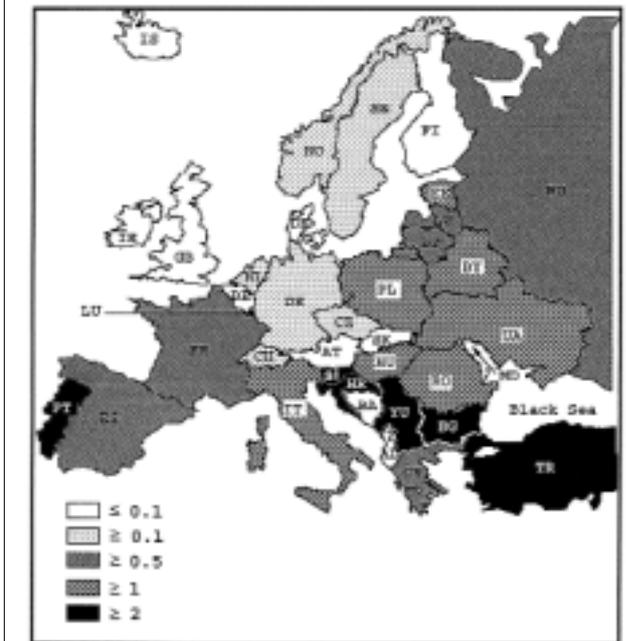


occurred in unvaccinated individuals, 33% in subjects whose vaccination history was unknown and 3% among incompletely vaccinated subjects¹².

INCIDENCE OF NEONATAL TETANUS

The following countries of the WHO European Region (EURO) have reported cases of neonatal tetanus in recent years: Albania (1 case in 1990 and 1991, 3 in 1992

Fig. 2. Tetanus incidence in Europe, rate per 1,000,000 inhabitants during 1993 or 1994.



and 1993, 6 in 1994 and 1995), Azerbaijan (1 case in 1993), Romania (3 cases in 1992 and 1 in 1993, 1994 and 1995 respectively), Turkey (127 cases in 1995, 61 in 1996 and 33 in 1997), the United Kingdom (1 case in 1994) and Yugoslavian Republic (4 cases in 1994 and 3 in 1997)²⁸.

In Italy²⁸ the average number of cases decreased from 23.6 cases annually (s.d. = 7.5) during the period 1960-66 to 3.4 cases annually (s.d. = 1.3) during 1971-75. The most recent cases occurred in 1977 (two) and 1980 (one) (ISTAT - Annuario di Statistiche Sanitarie 1960-1980).

TETANUS MORBIDITY (OVERALL)

Data on tetanus incidence in Europe for the years 1985 and 1993-1994 are illustrated in Figures 1 and 2. It may be noted that there was a slight decline in the incidence rate of some countries: Italy, Poland, Turkey and the former Soviet Union. More evident improvements were accomplished in France and Spain. In other countries, such as the United Kingdom, Germany, Denmark, Finland and The Netherlands, the incidence remained very low, as in the past, and sometimes declined further.

Overall, in Europe there is an evident trend towards tetanus incidence reduction. As a matter of fact, the chi square for linear trend shows a highly statistically significant decrease (chi square = 2295.779; $p < 0.00001$) during 1975-1994.

The trend of the disease in Italy shows a clear decline of tetanus incidence during 1955-1987 (chi square for linear trend = 4450.81; $p < 0.000001$), although, this trend seems to have slowed down since 1988 (chi square for linear trend = 0.035; $p = 0.85058$, during 1988-1997).

TETANUS INCIDENCE ACCORDING TO SEX AND AGE

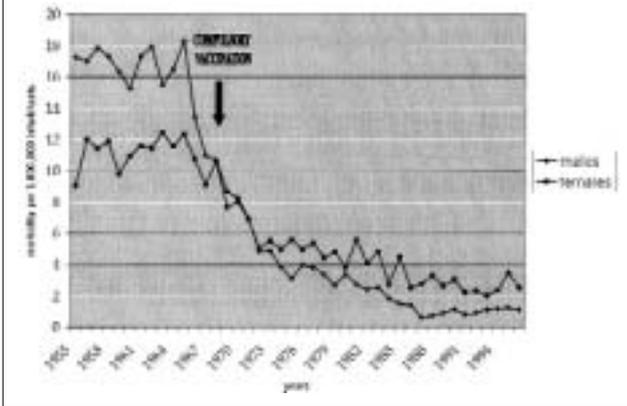
Figure 3 shows tetanus cases reported to the Italian Ministry of Health during the period 1955-1995, divided according to sex. The chi-square for linear trend shows a clear trend towards reduction of incidence during 1955-1987 in both sexes (males: 3458.149, $p < 0.000001$; females: 1071.911; $p < 0.000001$). By contrast, the analysis shows a moderate increase of cases in males (chi square for trend = 4.045; $p = 0.04430$) and a pause trend in females (chi square for trend = 0.718; $p = 0.39686$) during the period 1988-95.

The decline of tetanus incidence registered in Tuscany, as well as in the entire country since 1955, has been reversed in recent years. In fact, there is a trend towards increase during the period 1986-1997 (10 cases in 1986 and 24 in 1995) (chi square for trend = 6.117; $p = 0.01399$). Thirty-one out of the 33 cases occurring during 1996-1997 affected subjects over 65, and 28 subjects were female.

CASE FATALITY RATE FOR TETANUS BY SEX AND AGE

In Italy the case-fatality rate for tetanus is clearly still very high at present (52% and 33% in 1993 and 1994, respectively). The trend is towards an increase during

Fig. 3. Tetanus morbidity in Italy according to gender from 1955 to 1996.



1964-1990 for both males and females (chi square for linear trend in males = 43.381; $p < 0.000001$; chi square for linear trend for females = 53.368; $p < 0.00001$; in both sexes = 176.776; $p < 0.000001$).

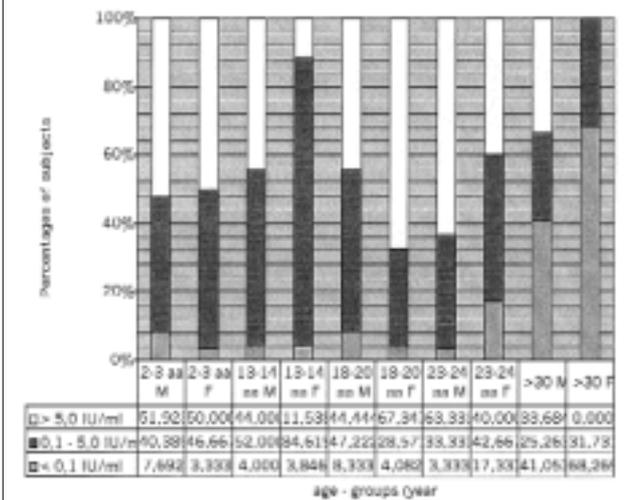
During 1991-1994, the trend of the case-fatality rate was stable, with a non-significant reduction in females (chi square for linear trend in females = 3.362; $p = 0.06668$; in males = 0.429; $p = 0.629$; in both sexes = 3.654; $p = 0.05593$).

In Tuscany, during 1996 and 1997, lower case-fatality rates were reported (25% and 17% in the two years respectively).

ANTI-TETANUS IMMUNITY IN THE POPULATION OF SOUTHERN TUSCANY

Figure 4 shows the results of the seroepidemiological study. Males of 2-3 years of age were protected in 92.3% of cases (95% CI: 85.0-99.6%) and females of the same age in 96.7% of cases (95% CI: 88.3-100%). Among adolescents, 96.0% of males (95% CI: 88.3-

Fig. 4. Tetanus immunity: percentages of protected subjects according to gender and age-group, Southern Tuscany, 1997.



100%) and 96.1% of females (95% CI: 88.3-100%) were protected.

In the 18-20 years age group, 91.7% of males (95% CI: 82.6-100%) and 95.9% of females (95% CI: 90.4-100%) were protected.

Before the third booster dose (at 23-24 years of age), an increasing percentage of females lacking protection were detected (17.3%) (95% CI: 8.8-25.9%), as compared to males (3.3%) (95% CI: 0-9.7%).

Finally, only 58.9% of males (95% CI: 49.1-68.8%) and 31.7% of females (95% CI: 22.8-40.7%) over 30 showed tetanus antitoxin levels higher than 0.1IU/ml.

Discussion

In Europe, improvements in the prevention of tetanus have been striking in past decades. At the beginning of the century, more than 5,000 died from this disease each year, and the number decreased to 1,000 during 1971-1980². Immunization campaigns and improvements in childbirth and neonatal care have had an essential role in such improvements.

In France, where vaccination has been applied to all children since 1946, the reduction of mortality has been slow but continuous, ranging from 1,000 deaths in 1947 to 135 in 1977 (226 cases: CFR = 60%)¹⁶. More recently, French doctors reported 117 cases of tetanus with a CFR of 30% to the services of Public Health during the 1993-1995 period¹⁵.

The data show a trend towards an improvement of the epidemiological situation in Europe and in Italy. In particular, vaccine coverage is high in almost all countries of the Continent except for Turkey, where an implementation of vaccination strategies is needed. With regard to Italy, the degree of vaccination coverage is satisfactory, although improvements are needed in regions such as Campania.

Data relative to tetanus incidence in Italy among those subject to compulsory vaccination during 1992-96, show that no patient was completely vaccinated and only 3% reported partial immunization. This further supports vaccination efficacy.

Turkey and, in some way, the Yugoslavian Federation, are unable to report favourable data for neonatal tetanus. For the latter, war has surely affected delivery care conditions.

Tetanus morbidity reduction in Europe is clearly shown by statistical data; in some Countries, like Sweden, Finland, Norway and The Netherlands, the situation is extremely satisfactory.

In Italy there was a clear improvement from 1955 to 1987, but since 1988 the trend towards decline seems to have been reversed. In particular, among males there seems to be a moderate increase. This finding may be explained by the fact that most cases occur in non-immunized elderly subjects. However, females, are still predominantly affected in our country; moreover, their higher life expectancy leads to an increased risk with age. It is noteworthy that elderly women often dedicate

themselves to gardening which places them in a well-known risk situation.

The geographical distribution of tetanus in Italy shows higher morbidity levels in Northern and Central Regions compared to the South and the Isles. This is explained by the documented under-reporting of tetanus cases through routine reporting systems in the South.

In Italy, during 1964-92, CFR for tetanus was very high with a time trend towards increase, due to a rise in the mean age of case-patients. In fact, in the United States, fatality has declined to 11% because health measures have improved immunity in the elderly⁴. It should also be noted that in Italy, the medical treatment available to patients with tetanus should be improved. As matter of fact, not all patients admitted to hospital are treated in resuscitation rooms. In 1994, only 39.2% cases were admitted to emergency departments, whilst 37.3% and 5.9% were admitted to infectious disease and general medicine departments, respectively. Recently, CFRs relative to Tuscany (1996-1997) showed a reduction (25% and 17% respectively). This finding is consistent with the work from Prospero et al.¹⁴ conducted in the Marche Region during 1992-95, which showed low fatality levels (11%).

The data obtained from the seroepidemiological study allow some considerations. The immune protection of subjects aged 23-24 years improved in comparison with other studies carried out in 1985⁶. This is partially explained by the fact that at present, the companions of vaccinated subjects include those up to 30 years of age. The fact that relatively high percentages of subjects between 18 and 20 years of age (92% males and 96% females) show antibody levels 0.1 IU/ml and often > 5.0 IU/ml (44% males and 67% females) means that the booster at 16 is usually carried out but that its administration should be ensured in some way. Finally, high

percentages of subjects over 30, mainly belonging to older age groups, were found to be unprotected. As observed by Gergen et al.⁹ in American subjects, the prevalence of immunity declined rapidly starting by the age of 40 years, although the majority of cases reported in the last years in Italy and Tuscany, occurred in subjects 60 years of aged or older.

Improvements of prevention policies against tetanus, apart from savings lives, would also allow great economic savings. A study carried out by the Italian Ministry of Health¹² shows that, in 1994, the economic damage due to hospitalisation ranged from Lit. 4 to 5.8 thousand million (between Euro 2 and 2.9 million).

In conclusion it is clear that we must implement more effective strategies for the prevention of tetanus. They should aim to:

- offer all the elderly who seek medical assistance the opportunity to be vaccinated or to perform booster doses on various occasions (for instance when they undergo influenza vaccination)¹⁴;
- offer all women the opportunity to be immunized or to perform booster doses after delivery;
- offer all subjects at increased risk due to occupational exposure the opportunity to be vaccinated or to perform booster doses at the time of annual check-ups;
- improve the efficiency and effectiveness of vaccination services (i.e. total computerization);
- improve the efficiency and effectiveness of first aid services, in order to treat subjects with severe trauma with a complete primary course of vaccination.
- improve medical care to case-patients by admitting them to resuscitation rooms and intensive care units;
- promote health education campaigns through mass media such as television, which may reach a great number of elderly subjects.

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