

**ASSESSMENT OF VACCINE EFFICACY FOR DISEASES INCLUDED
IN THE NATIONAL IMMUNIZATION PROGRAM FOR
PRESCHOOL CHILDREN**

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Abstract

OBJECTIVE: The periodical evaluation of the population specific protection against the diseases included in the National Immunization Program (NIP) is necessary in view of the strengthening strategies.

MATERIAL AND METHODS: The study was performed in 2001 y on a representative sample of 714 children aged less than 5 years old. The determination of antibody levels was made through the indirect ELISA (Diasorin kits) taking 0.1 IU/ml as basic level for diphteria and tetanus antitoxine, 10 IU/l for the HBs antibodies, and higher than 40 AU/ml for measles and pertussis antibodies.

RESULTS: Tetanus sero-protection was found in 96% of children (95% CI: 94.6–97.4) with an average geometrical mean of tetanus antitoxine antibodies of 1.49 IU/ml. The protection level of the diphteria antitoxine antibodies was about 10% lower than the level of antitetanus sero-protection of 87.4% (95% CI: 86.1-88.7). The children vaccinated with DTP3 have a medium level of seroprotection, while those who received 4 doses of vaccine have 91.8%. The Bordetella pertussis antibodies were present at a protector level in 76.1% children (95% CI: 72.9-79.2). The humoral antimeasles immunity reaches an average of 55.6% protected children (95% CI: 52.1-59.2) for a level of seropositive values of 62%. The percentage of the children protected against hepatitis B virus (HBV) infection had an average value of 59.5% (95% CI: 57.1-63.1) while the seropositive value was estimated to be 71.9%.

CONCLUSIONS: The specific immunity to tetanus in the children aged less than 5 years corresponds to the goal of the National Immunization Program, but it is lower for diphteria, measles and HBV indicating susceptibility to these diseases.

Key words: vaccination, prevalence, postvaccinal immunity

Rezumat

OBIECTIV: Evaluarea periodică a nivelului de protecție specifică a populației, față de bolile din Programul Național de Imunizări (PNI) este necesară în scopul optimizării strategiilor de supraveghere și control

MATERIAL SI METODA: Studiul s-a realizat în anul 2001, pe un eșantion reprezentativ de 714 copii cu vârsta sub 5 ani. Determinarea titrurilor de anticorpi s-a efectuat prin testul ELISA indirect (truse Diasorin) considerând valoarea prag de 0,1 UI/ml pentru antitoxina difterică și tetanică, 10 UI/l pentru Ac antiHBs și mai mare de 40 UA/ml pentru anticorpi antirujeolă și antipertussis.

REZULTATE: *Seroprotecția antitetanică* s-a evidențiat la 96% (95% IC: 94,6–97,4) din copii, cu o medie geometrică a anticorpilor antitoxină tetanică de 1,49 UI/ml. Prevalența titrului protector de anticorpi *antitoxină difterică* este mai mică cu aproximativ 10% decât nivelul seroprotecției antitetanice, 87,4% (95% IC: 86,1–88,7); vaccinații cu DTP3 prezintă

nivelul mediu de seroprotecție, iar cei cu 4 doze de vaccin, 91,8%. Anticorpii față de *Bordetella pertussis* s-au decelat în titru protector la 76,1% (95% IC: 72,9-79,2).

Imunitatea umorală antirujeolă se cifrează în medie la 55,6% (95% IC: 52,1-59,2%) din investigați, cu un nivel de seropozitivitate de 62%, iar seroprotecția față de *infecția cu virusul hepatitei B* are valoarea medie de 59,5% (95% IC: 57,1-63,1) și un nivel de seropozitivitate estimat la 71,9%.

CONCLUZII: Nivelurile de imunitate specifică antitetanică evidențiate la copiii sub 5 ani corespund țintelor din Programul Național de Imunizări, dar cele ale imunității față de difterie, rujeolă și hepatită virală B au valori mai mici, evidențiind susceptibilitate față de aceste boli.

Cuvinte cheie : vaccinare, prevalență, imunitate postvaccinală

INTRODUCTION

Morbidity by infectious diseases was and still is a health care priority worldwide.

In 1974, when the Expanded Program on Immunization was launched, to offer a multilateral support for countries to develop the immunization programs, the vaccination was practically not in use in some developing countries. Less than 5 percent of the world's children were receiving three doses of diphtheria-tetanus-pertussis vaccine (DTP) and polio vaccine (OPV) during their first year of life. However, at the end of the 90's, the highest coverage was reached with 83 percent for BCG; 83 percent for DTP3; 84% for OPV and 82% for measles vaccine (1).

In the past two years, a decrease in global vaccine coverage by 7 percent for DTP3, 8 percent for measles vaccination and 6 percent for OPV3 was recorded (2).

Europe has the highest vaccine coverage rate, with 94 percent for OPV3, 94 percent for DTP3, 92 percent for measles vaccine, and 84 percent for BCG (3). The average regional coverage for hepatitis B was 37% since 32 out of 51 countries have

been implemented the universal hepatitis B immunization program (3).

In Romania, following the initiation of the generalized immunization program for seven preventable diseases no cases of diphtheria, poliomyelitis and tetanus neonatorum and a marked decrease in the number of measles and hepatitis B cases have been reported. Tetanus in the adult and old teenagers remained at an average of 20 cases per year. Less than 82 cases of whooping cough are reported every year, that is only 16 percent of the cases recorded in 1995 (2).

In spite of these improvements, a careful epidemiological surveillance based on case definition, modern diagnostic methods, and adequate amounts of vaccines properly stored and administered is essential (4).

The periodic assessment of the protection level by seroprevalence surveys measuring the immunity status of the target population to the diseases in the National Immunization Program (NIM) is necessary. A regional survey of the immune status of the children under 5 y has been developed in northeastern districts (Moldova) of Romania.

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MATERIAL AND METHOD

The study was performed in 2001 years. The sample consisted of 714 children aged less than 5 years (mean age 1.6 years), representative for an expected mean prevalence of specific immunity of 80 percent and an accepted error of 3 percent.

The titer of diphtheria and tetanus antitoxins, anti-HBs, measles and pertussis antibodies was measured by indirect ELISA (Diasorin kits). Titers higher than 0.1 IU/ml of diphtheria and tetanus antitoxins, 10 IU/l for the

HBs antibodies and 40 AU/ml for measles and pertussis antibodies were considered protective.

The seroprevalence data and their correlation with the level of vaccine coverage were processed in EPI Info 6 and Excell.

RESULTS AND DISCUSSION

Seroprotection against tetanus (titers higher than 0.1 IU/ml) was found in 96% (95% CI: 94.6–97.4) of cases, with district - to - district variations of 92.5% and 98% (fig.1).

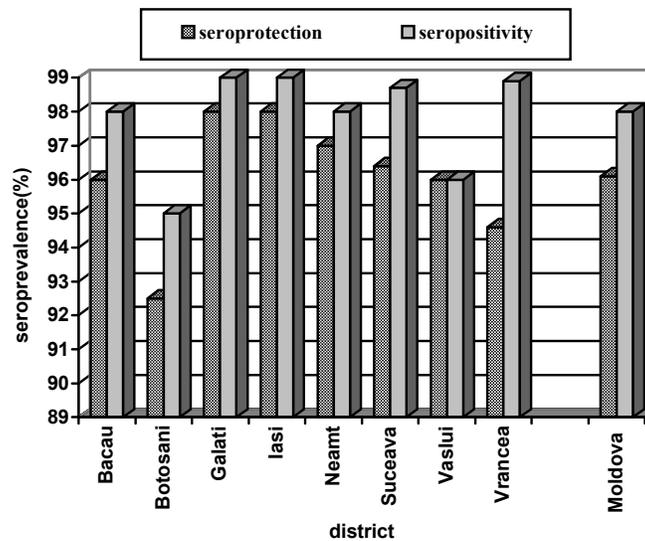


Fig. 1 Antitetanus protection prevalence in children from northeastern part of Romania

The geometrical mean of tetanus antitoxin titers was of 1.49 IU/ml (95% CI: 0.59-2.38).

The protective response in tetanus antitoxin was detected in 94.4% of

recipients after the administration of the first dose of DTP vaccine, increasing to 96.0% in those who received three doses, and to 96.5% in

the children who received four doses of vaccine.

The prevalence of sera with **protective diphtheria antitoxin** titer (> 0.1 mIU/ml) was lower than the seroprotection against tetanus by about 10%, 87.4% (95% CI: 86.1-88.7) of the DTP3 recipients being protected against diphtheria. The administration of an additional dose, DTP4, induced an increase of 3.4% in the rate of protective titers, thus a value of 91.8% being reached. District-to-district

variations of diphtheria protection rate were noticed (fig. 2).

The geometric mean of diphtheria antitoxin levels was estimated at 0.33 IU/ml (95% CI: 0.29-0.36) (fig. 3).

Immunity to *Bordetella pertussis* (titers higher than 40 AU/ml), the third antigenic component of diphtheria-tetanus-pertussis vaccine, was found in 76.1% of children (95% CI: 72.9-79.2), with significant district-to-district variations - between 61% and 89% (fig. 4).

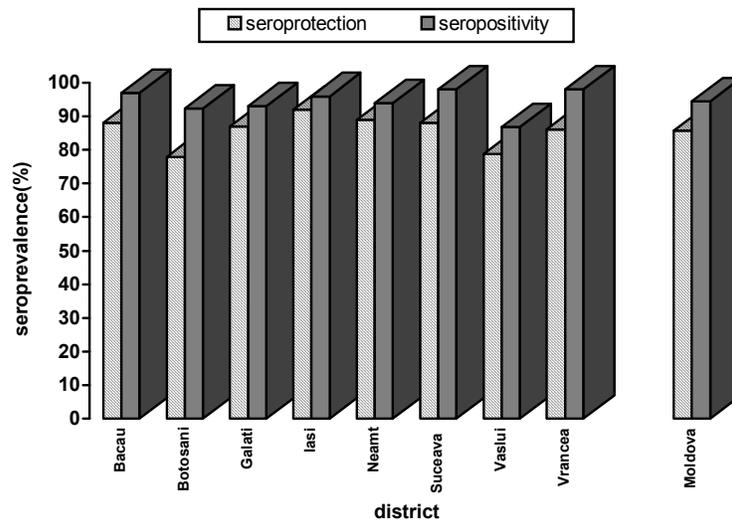


Fig. 2 Antidiphtheria immunological status in children from northeastern part of Romania

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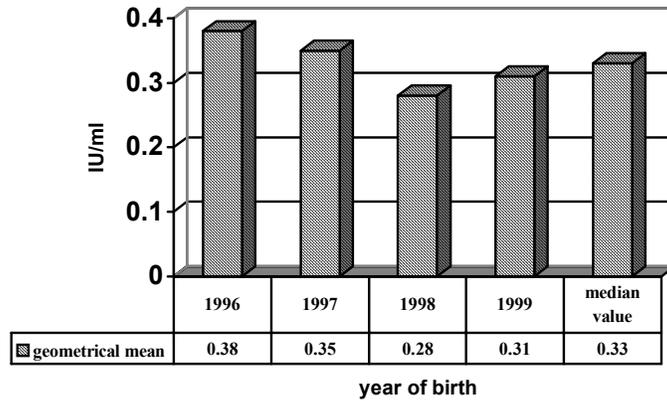


Fig. 3 The geometrical mean of antidiphtherie antibodies titers

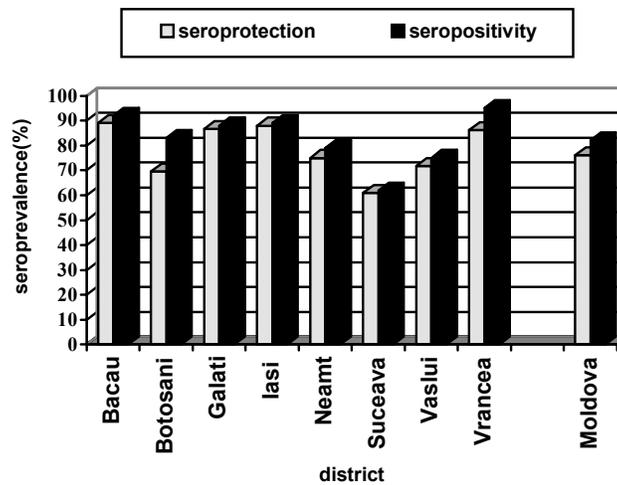


Fig. 4 Antipertussis immunity seroprevalence in children from northeastern part of Romania

Protective titers of pertussis antibodies were found in 76.1% of the investigated children after the first dose of DTP. An increase by about 1.5-1.7% was recorded following the administration of the next two doses,

and reached 84.1% in those receiving four doses (DTP4).

The present immunization schedule includes four doses of diphtheria-tetanus-pertussis vaccine until the age of 1 year and other three doses administered at the age of 30-35

months, 7 and 14 years. The 5-year-old child gains immunity with five vaccine doses, the last two/three administration with the bivalent diphtheria- tetanus (DT) vaccine. The analysis of data revealed susceptibility rates to tetanus, diphtheria

and pertussis of 4%, 8.8% and 23.9% respectively.

The prevalence of measles humoral immunity, expressed in arbitrary units (AU) with antibody titers higher than 40 AU/ml, was on average of 55.6 percent (95% CI: 52.1-59.2) (fig. 5).

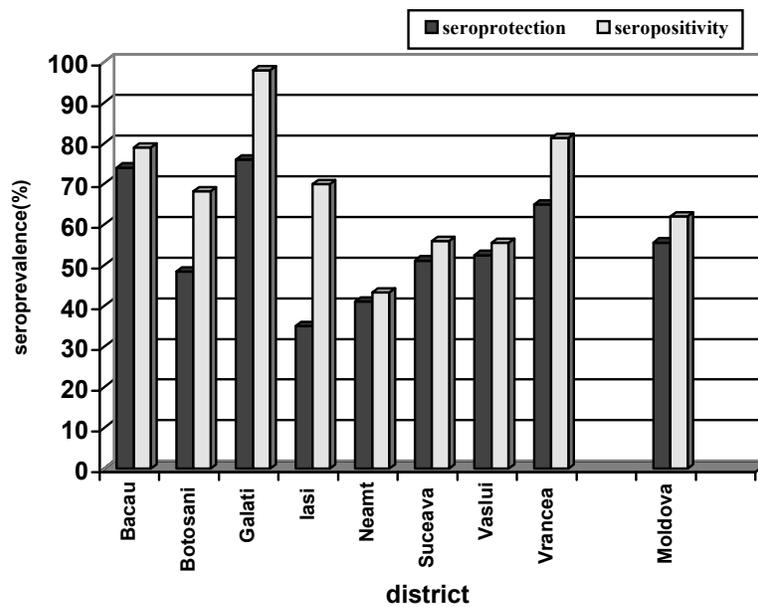


Fig. 5 Children immunological anti-measles status in northeastern part of Romania

The geometric mean of titer was of 68.55AU/ml and ranged between 46.07 AU/ml in the children born in

1999 and 105.79 in those born in 1998 (fig. 6).

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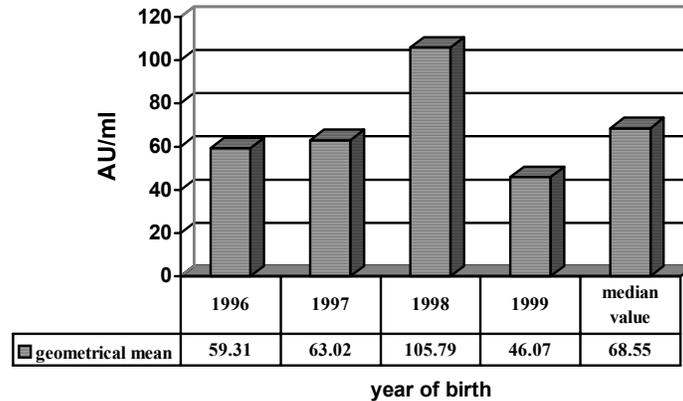


Fig. 6 The geometrical mean of anti-measles antibodies titers

The higher level of mean titer of children born in 1998 could be explained by an increased immunity due to the wide circulation of measles virus during the 1997-1998 epidemic.

Depending on vaccination status, the children sample was divided into three categories: vaccinated (67%), unvaccinated (20%), unknown status (13%) (fig. 7).

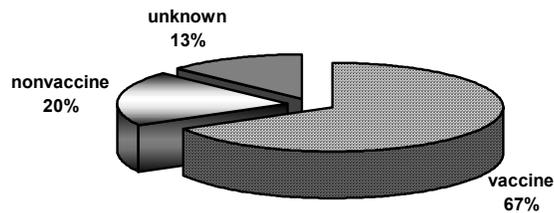


Fig. 7 The vaccinal anti-measles status in children from northeastern part of Romania

According to the timing of **measles vaccination**, 85.3% of the children in this study received it when aged 9 to 12 months age. In this group of children, the protective response in

measles antibodies ranged between 62.3% and 64.4%.

It was noticed that in 41.5% of the vaccinated children without measles protection the lapse of time between vaccination and immunity testing was

less than 1 year, and in 33% of them less than 6 months. The decrease in measles antibody titer, known to as a vaccine failure (6) was also found, but the high percentage of unprotected children after a short lapse of time raise out the question of the quality of vaccination (transportation, storage, administration).
The 20% of **unvaccinated** children included:

- 12% children younger than the minimum recommended vaccination age of 9 months;
- 8% eligible children not vaccinated for different reasons.

Immunologically, 4.3% of these children were protected against measles (passive or acquired immunity). The serological tests of children with **unknown** vaccination history revealed that 3.3% of them presented measles protection (fig. 8).

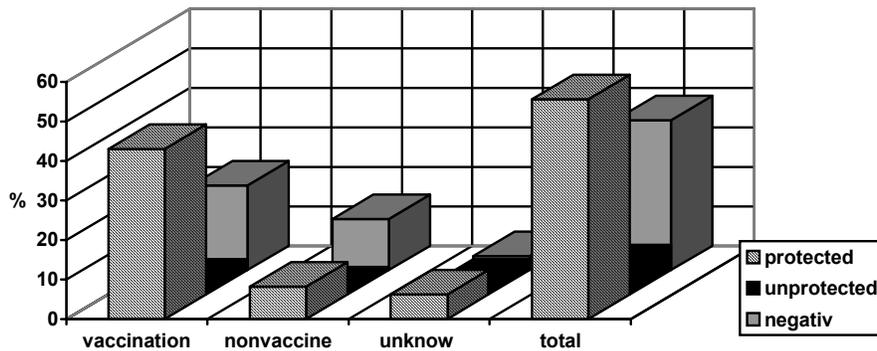


Fig. 8 The immunological antimeasles status for vaccinal antecedents

The high rate of children (44.4%) without measles protection found in our survey requires immediate improvements of the prevention and control strategies.

The goal of **measles** elimination by 2007-2010 requires both the adjustment of vaccination scheme (7), knowing the fact that the efficacy is 85% in the child vaccinated at the age of 9 months, and sustained efforts to assure ensuring a safe administration.

Seroprotection against hepatitis B virus infection, expressed in titers of anti-HBs antibodies > 10 IU/l induced by hepatitis B vaccine introduced in the national immunization program in 1995, was found in 59.5% of children (95% CI: 57.1-63.1) with district-to-district variations ranging between 55% and 73%. As figure 9 presents 72% of them were found seropositive.

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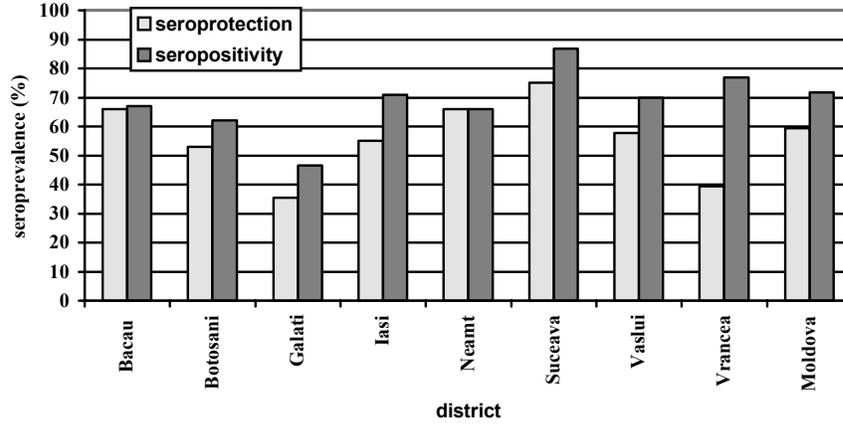


Fig. 9 Antihepatitis B immunity prevalence in children from northeastern part of Romania

A 95.8% of vaccine coverage rate in investigated children was found after two doses of hepatitis B vaccine, and 92.3% after the third dose administration. The immunizing course of hepatitis B vaccine consists in three doses given at birth, 2 and 6 months age.

The geometric mean level of anti-HBs antibodies in the investigated series was of 44.4 IU/l, being lower in the children with a longer lapse of time between vaccination and immunity testing (from 70.97 to 34.64 IU/l at 2 years following vaccination) (fig. 10).

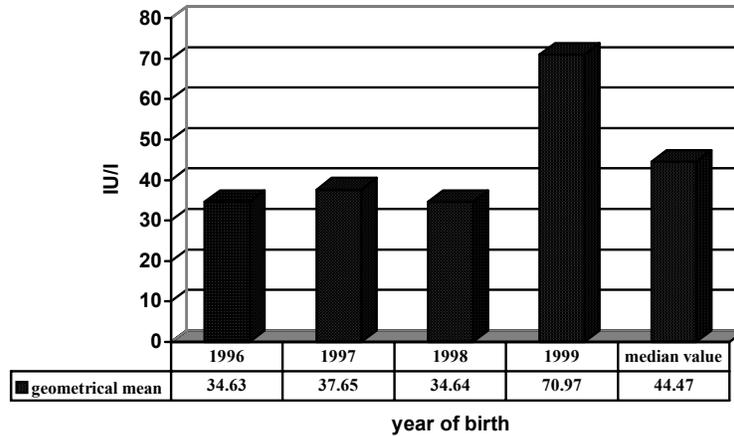


Fig. 10 The geometrical mean of anti-HBs antibodies titers

The decrease of anti-HBs antibodies related to the interval since vaccination requires the following of postvaccinal immunity trend to evaluate the opportunity of a booster dose.

European Consensus Group on Hepatitis B Immunity shows the persistent protection against symptomatic infection and carriage of HBs antigen up to 15 y after primary immunization (5).

The immunological survey revealed comparable results in children from northeastern and western part of Romania (8). These data prove the low protective level of the immunity for measles (65.8%) and HBV infection (52.3%).

The monitories of the population immunological protective status help to identify the receptive groups and to elaborate additional strategies to improve the propose objectives.

CONCLUSIONS

- The specific immunity to tetanus in the children aged less 5 y corresponds with the goal of the National Immunization Program, but the lower levels for diphtheria, pertussis, measles and viral hepatitis B, indicate the susceptibility to these diseases.
- The following are essentially for complete elimination of measles:
 - implementation of a system of vaccine administration with preserved immunogenic potential and in full safety conditions

- additional vaccinations (resumption of the periodical vaccination in children aged 0-4 years)

- The decrease of anti-HBs titer needs a research about the booster necessity.

ACKNOWLEDGMENTS

We wish to thank the following supplying the microbiological product: Ecaterina Chihaiia, Anca Dancau, Mihaela Debita, Marina Maiorov, Odette Nicolae, Roxana Pipirigeanu.

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