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# A cross-sectional study on vaccine coverage and seroprevalence in schoolchildren in Andorra

Eduard Portella [1,2], Josep Goicoechea [3], Joan Penella [3]

[1] Servei Andorrà d'Atenció Sanitària (SAAS), Andorra la Vella
[2] Departamento Salud Pública y Legislación Sanitaria, Universidad de Barcelona
[3] Servei de Planificació Sanitària, Conselleria de Treball i Benestar Social, Govern d'Andorra, Andorra la Vella

Immunization against certain specific diseases is commonly accepted as one of the more cost-effective procedures carried out by health services [1]. While there is no one single immunization schedule that suits all countries, experience acquired over recent decades shows that some basic principles generally apply: a careful evaluation of the epidemiological situation in the area, and an assessment of the human resources needed and available to perform the anticipated activities, have to be made before a programme is planned [2].

Vaccine coverage monitoring is the usual way to evaluate immunization programmes. Incidence of disease is used more rarely, and other types of studies may complement these methods [3,4,5].

For more than fifteen years the headquarters of the Expanded Programme of Immunization (EPI) Secretariat in Geneva has been acting as a coordinating centre for the exchange of information on immunization activities worldwide. Among its functions, it is entrusted with monitoring the efficacy of vaccine production and with providing training for immunization programme-planning. The EPI has used the results of evaluation and monitoring in order to discuss the strengths and weaknesses of programmes.

The slow improvement of national information systems seems to be a point of weakness; in many countries appropriate data are difficult, though not impossible to obtain, and the precision of vaccine coverage estimates is usually very low [4].

The Principality of Andorra is a small country in the Pyrenees, between France and Spain, which has had its own juridical personality since the XIII century. Within an area of 468 km$^2$, 75.5% of the population, 46166 in the 1989 census, is made up of immigrants (Spaniards 54.7%, French 6.5%, Portuguese 8.5%, British 1.6% and others 4.4%) [6]. A Systematic Immunization Plan running since September 1988 involves centralised vaccine import and supply and an explicit, clearly defined schedule of vaccinations for the population aged 16 and under against diphtheria, tetanus, pertussis, poliomyelitis, rubella, measles and mumps [7]. The Plan is carried out by the school health service and by independent general practitioners and paediatricians, who are paid for their work within the Plan. Before introducing the vaccination schedule there were some explicit local recommendations on the issue. A general description of the historical background of the present study follows [8].

Since the seventeenth century, patients have paid doctors directly, generally small amounts, for their services. Town councils also paid them for looking after members of the community who did not have the means to pay. Regulations for doctors' practice are not new. In 1898, when the population of the Principality was 5000, a *Reglament dels Metges* (Rules for care and to carry out legal or forensic tasks) was established. The first call to the town councils to caccinate members of the community dates from 1910. It was suggested that the services necessary for vaccination should be put at the public's disposal twice a year. In 1951 it was decreed for the first time that all children starting school should have a medical check and vaccinations, and in 1960 the Health and Hygiene Management Service was set up inside the Administrative Body, one of its functions being to supervise health in schools. Five years later anti-polio vaccination for children was declared obligatory and free of charge. This vaccination is administered by the town councils' health services.

In 1966 there were seven doctors; five general practitioners, and two in charge of surgery, one of whom dealt with obstetrics. A private clinic with fifteen beds for births and surgery was the only hospital service. The population was estimated at 14380, 14% of whom were of school age.

In 1967 the *Caixa Andorrana de Seguretat Social* (Andorra Social Security System) was set up, to which all salary earners are obligatorily affiliated. Patients pay doctors directly for services rendered, and the organization reimburses patients in part. Social Security regulations only cover curative services; preventive services are explicity excluded. In 1969, vaccination against smallpox, whooping-cough, poliomyelitis and tuberculosis was declared obligatory for all children entering school, and a medical certificate also had to be presented. Doctors who had trained at French or Spanish universities were conscious of the need for vaccination.

Paediatricians and general practitioners vaccinated children, and the school health service probably heightened awareness about the need for vaccinations, among both families and doctors.
In 1988, basic medical attention was provided by 22 general practitioners, 3 paediatricians, 5 gynaecologists and 22 dentists. Medicines and vaccinations were available to the public at the 27 pharmacists' outlets. These were supplied mainly by 4 distributors, who had to make journeys of some two or three hours by road. No cold-chain system was used during this delivery process.
The aim of this study was to find out the vaccine coverage and the effectiveness of immunization practice before the introduction of the Plan, and to identify information that could be useful for improving and modifying aspects of the Plan.

## Methods

The study population was a cohort of all children born in 1983 attending school in Andorra in May 1988. A two-stage randomized sample was obtained. The first stage corresponded to the four school systems currently running in the country (Andorran, French, Spanish and confessional). The second was cluster selection, each cluster corresponding to an elementary school. Table 1 shows the proportion of school children in the sample.
Data on sociodemographic variables and past history were obtained by a questionnaire given to the parents of the selected children. Parental occupation was classified according to the British Occupation Classification.
The presentation of every child's vaccination card was required to assess vaccine administration. Minimal vaccination coverage was defined as that warranting a sufficient degree of immunization for every disease considered in the Plan. For DTP and OPV minimal vaccination coverage was attained when a child had received three doses of the vaccine. Vaccination coverage was considered optimal if the child had received four doses of DTP or OPV. One single dose of vaccine was considered as correct vaccination against measles, mumps and rubella.
Testing of serum antibody titers was performed on venous blood samples from the schoolchildren selected, at the Barcelona Hospital Clínic Microbiology Service. The following techniques were employed: a) diphtheric antitoxin: passive hemagglutination reaction (protective antibody titer > 0.01 IU/ml); b) tetanus antitoxin: passive hemagglutination reaction (protective antibody titer > 0.01 IU/ml); c) antipertussis antibodies: microplate agglutination (protective antibody titer greater than 1:320); d) antipoliomyelitis antibodies: neutralization reaction of microplate cell cultures (protective antibody titer > 1:4); e) antimeasles antibodies: hemagglutination antibody reaction and immunoassay reaction (ELISA) (protective antibody titer > 1:5); f) antiparotitis antibodies: indirect immunofluorescent reaction and ELISA (protective antibody titer > 1:8). Testing of antirubella antibodies was not performed owing to technical problems.
Confidence intervals for proportions were calculated using the normal approach of binomial distribution whenever n was big enough. Testing of hypotheses was performed using the normal approach of binomial distribution for proportions, the chi square test and Fischer's exact test[9]. Confidence intervals for odds ratios were calculated by the exact method[10]. The significance level used was 5 percent.

Tab. 1. Sample size in each school system.

| School Systems | Children | Sample | |
|---|---|---|---|
| Andorran | 85 | 14 | 16,5% |
| French | 232 | 39 | 16,8% |
| Spanish | 176 | 34 | 19,3% |
| Confessional | 103 | 12 | 11,7% |
| | 596 | 99 | 16,6% |

## Results

96 schoolchildren (51 boys and 45 girls) were selected from the cohort born in 1983. The questionnaire answer rate was 80% and the children's mean age was 5.5 years (SD 0.5). The children selected were attending different school systems: Spanish (39), French (34), Andorran (14) and confessional (12), and 43% were born in Andorra.
An optimal coverage (4 doses) was attained by 86.8% for DTP and 83.3% for OPV, while minimal coverage (3 doses) was attained by 97.8% for both DTP and OPV, the dropout percentage between the third and the fourth doses being 11.9% for DTP and 15.4% for OPV. Vaccine coverage for the diseases needing only one dose was 60.8% for measles and 27.8% for both mumps and rubella.
Protective levels of antitetanus antibodies were found in 93.6% of children, antimeasles antibodies in 86.7 percent and antidiphtheria antibodies in 88.5%. Protective levels of antipertussis and antiparotitis antibodies were found less frequently; the value in both cases was 78.7%. The lowest percentages of protective levels of antibodies were found against poliomyelitis viruses 1, 2 and 3: 59.1, 63.6 and 56.1% respectively (Table 2).
While most of the children showing serum protective antibody levels against diphtheria, tetanus, pertussis and polio had received four doses of the corresponding vaccine and were optimally covered, only 51% of those with protective levels against measles had been vaccinated. We were able to estimate the vaccine-protective effect in vaccinated

Tab. 2. World Health Organisation standards [12], vaccine coverage and seroprevalence Cross-sectional study in schoolchildren born in 1983. Principality of Andorra, 1988.

| Diseases studied | WHO standards (%) | Vaccine coverage (4 doses) (%) | Seroprevalence (%) | 95% CI |
|---|---|---|---|---|
| Diphtheria | 95.0 | 86.8 | 88.5 | 80.8–96.5 |
| Tetanus | 95.0 | 86.8 | 93.6 | 87.8–99.6 |
| Pertussis | 80.0 | 86.8 | 78.7 | 68.9–89.2 |
| Polio-1 | 95.0 | 83.3 | 59.1 | 48.8–72.4 |
| Polio-2 | 95.0 | 83.3 | 63.6 | 52.0–75.2 |
| Polio-3 | 95.0 | 83.3 | 56.1 | 42.5–66.5 |
| Measles | 90–95 | 60.8 | 86.7 | 78.7–95.4 |
| Rubella | 90–95 | 27.2 | – | |
| Mumps | 90–95 | 27.2 | 78.7 | 72.3–91.6 |

against non-vaccinated schoolchildren for this disease (OR = 0.11, 95% CI 0.01–0.80, $p < 0.003$). This was not the case for the other diseases studied, owing to the small numbers involved and the lack of reported disease antecedents in the sample.

## Discussion

The vaccine coverage found shows that schoolchildren aged 5–6 years in Andorra have attained a high level of coverage [7], slightly higher than that observed in most developed countries [4]. This type of study depends on the accuracy of vaccination records (vaccination cards) as well as on information obtained from the children's parents. In this study data were obtained from the children's vaccination cards to a somewhat larger extent (89.9%) than in other studies [12, 13].

Serum antibody testing has the additional advantage of measuring the clinical protection level attained among the schoolchildren studied. However, results of seroprevalence studies are difficult to interpret because the absence of antibodies does not necessarily mean susceptibility to the disease, and because vaccination is not the only possible cause of the presence of the antibodies detected [3]. These statements do not apply to tetanus, where protective antibodies are produced almost exclusively through vaccination [5]. Consequently, we believe that antibody presence is a good indicator of vaccine effectiveness with regard to tetanus, and their prevalence in our study was 93.6%, which may be considered high. More difficult to interpret are the results obtained for diphtheria (88.7%) and pertussis (79.0%), both diseases with a high degree of natural immunity. Yet we believe that vaccination may well have been the cause of this high serum antibody prevalence, since no history of disease was reported in the questionnaire answered by parents.

Vaccination against mumps and measles has been introduced more recently in Andorra, and vaccine coverage was low for both diseases (Table 2). However, a protective level of antibodies was present in a high percentage of the children studied, suggesting that there is a high degree of natural immunity to these conditions.

Antipolio vaccine shows a coverage of 83.3%, but serum antibody prevalence is considerably lower than for other diseases with similar levels of vaccination coverage. This might be due to a lesser natural immunity, decreased vaccine effectiveness, or both. OPV is made with live attenuated polio viruses, and it is extremely sensitive to variations in temperature. Poor supervision of the cold chain during transportation and delivery may well have contributed to these results [14]. It is unusual to think of cold chain failures in our developed countries, but the results of this study show that the preservation of the cold-chain is the one single measure that could be expected to improve seroprevalence of antibodies, as vaccine coverage has already attained fairly acceptable levels.

No association was found between protective antibody levels and the other variables studied such as sex, social class or place of residence, but a statistically significant association was found between the country of origin or the school system and the presence of protective levels of antipolio antibodies. This suggests that there may be groups of schoolchildren who are not correctly vaccinated, and this may be related to social class. This possibility should be investigated in further studies.

## Conclusion

The evaluation of an immunization programme may be of benefit to other elements of the health care system, and in particular those that are difficult to evaluate directly [4]. We suggest that the findings of this study show how the lack of an official vaccination schedule or the lack of a formal organisation of immunisation services have not had a great impact on vaccine coverage levels. However, our findings also show that more attention should be paid to factors that determine vaccine effectiveness, however elementary they are. For example, the need to preserve the cold-chain during transportation and delivery may not seem such an obvious problem in our European latitudes, but it is nevertheless important. Needs like this may be better covered through the implementation of programs that include centralisation of vaccine import, transportation and supply in well-defined areas.

## Summary

A cross-sectional study on vaccine coverage and vaccine effectivenes was carried out on a randomized sample of the cohort of schoolchildren born

in 1983 attending school in Andorra, prior to the introduction of a Systematic Immunisation Plan that included centralised import and delivery of vaccines to vaccinating clinics, surveillance of the cold-chain during vaccine delivery, and a clearly-defined immunization schedule against diphtheria, tetanus, pertussis, polio, mumps, rubella and measles.
Vaccine coverage was estimated from vaccination card records; history of disease and sociodemographic variables were obtained through a questionnaire to the children's parents and vaccine effectiveness was estimated through serum antibody testing.
Vaccine coverage levels for DTP and OPV were 97.8% for both. Protective serum antibody prevalence was correspondingly high except for the polio viruses. The authors suggest that decreased vaccine effectiveness, probably due to poor preservation of the cold chain, might be the cause of this finding. In countries or regions with an otherwise developed organisation of health services, an important issue like this can still be overlooked.

**Résumé**

**Etude transversale de la couverture vaccinale et de la séroprévalence chez des écoliers d'Andorre**
Cette étude a été réalisée sur un échantillon aléatoire de la cohorte d'écoliers d'Andorre née en 1983, avant l'établissement d'un Plan de Vaccinations Systématiques comprenant l'importation et la distribution centralisées des vaccins, la surveillance de la chaîne du froid et la définition d'un calendrier vaccinal contre les maladies suivantes: diphtérie, tétanos, coqueluche, poliomyélite, rubéole, oreillons et rougeole. La couverture vaccinale a été estimée à partir des carnets de vaccination; les antécédents de ces maladies et les variables sociodémographiques ont été obtenus par un entretien avec les parents des écoliers et l'efficacité des vaccins est estimée par la détermination d'anticorps sériques protecteurs. La couverture vaccinale par la DTCoq et VPO est de 97,8%. La prévalence d'anticorps sériques protecteurs correspond à la couverture, à l'exception des trois virus de la polio. Les auteurs suggèrent que la diminution de l'efficacité vaccinale serait provoquée par une faible surveillance de la chaîne du froid. Dans des pays ou régions qui, par ailleurs, ont une organisation de services de santé de style occidental, l'importance de cet aspect ne devrait pas être négligée.

**Zusammenfassung**

**Querschnittstudie zur Durchimpfung und Serumprävalenz von Schulkindern in Andorra**
Eine Querschnittstudie zur Durchimpfung und Wirksamkeit der Impfung wurde an einer zufälligen Stichprobe von Schulkindern des Jahrganges 1983 in andorranischen Schulen durchgeführt. Diese fand vor der Einführung eines systematischen Impfprogrammes statt, welches zentralisierten Import und Abgabe des Impfstoffes an Kliniken, die Überwachung der Kältekette und einen klar definierten Impfplan gegen Diphterie, Tetanus, Pertussis, Polio, Mumps, Röteln und Masern beinhaltete. Die Durchimpfung wurde aus den Impfkarten geschätzt, anamnestische Daten zu durchgemachten Krankheiten und soziodemokratische Variablen wurden in einem Fragebogen an die Eltern erfasst und die Wirksamkeit der Impfung durch Serumantikörpertests bestimmt. Die Durchimpfung für DTP und orale Polio lag bei 97,8%, entsprechend hoch war die Prävalenz von Serumantikörpern ausser für Polio. Die Autoren nehmen an, dass verminderte Wirksamkeit der Impfung wahrscheinlich aufgrund schlechter Kälteketten die Ursache dieses Befundes sind. In Ländern oder Regionen mit einer sonst gut entwickelten Organisation der Gesundheitsdienste kann ein wichtiger Schritt wie dieser leicht übersehen werden.

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**Address for correspondence:**
Dr. Eduard Portella
Santa Fe de Nuevo México, 13
E-08017 Barcelona/Spain