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RE-EVALUATION OF THE BASIC PROCEDURES INVOLVED IN THE STORAGE OF MEASLES VACCINE IN PUBLIC HEALTH UNITS OF THE MUNICIPALITY OF NITERÓI, STATE OF RIO DE JANEIRO, BRAZIL

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Four years after the first visit seventeen public health units were visited again and evaluated as to standards of storage recommended by the Brazilian Immunization Programme. In 100% of the units, refrigerators and proper inside location of vaccines in the refrigerator were adequately or regularly maintained and checked, respectively. However, when control of temperature was checked, only 64.7% presented adequate storage conditions. In 94.1% of the units, health workers complained of lack of immediate technical support in emergency situations. In 55.2% the titers vaccine samples of were under the minimal recommended potency. It is necessary that the factors concerning the cold chain be continually evaluated so that the quality of the vaccines that will be used is not affected.

Key-words: Measles vaccine. Quality control. Community health services.

Although highly effective, live attenuated measles vaccines are biologically unstable, sensible to solar radiations and to high temperatures, so they need a complex system to protect them. This system, named cold chain, i.e. maintenance process, handling and distribution of the vaccines at central, regional and local levels, has the purpose of securing that these products arrive at the immunization sites in a potent state[1 2 4].

In spite of high levels of vaccinal coverage reached for measles in Brazil outbreaks of the disease continue to occur, suggesting the presence of other factors besides the known relation age of vaccination *versus* interference of maternal antibodies[6 9 10]. Probably, one of these factors is directly related to the conditions of the cold chain supplied by precarious installations and equipment, as well as insufficiently trained health personnel, which makes the control of the disease more difficult.

The necessity of knowing the influence of some of these factors in the immunization programmes made us carry out an investigation during the months of January and February - 1986, to evaluate the basic procedures involved in the storage of measles vaccine in public health units of the Municipalities of Niterói and São Gonçalo, State of Rio de Janeiro[10 11]. At regional and local levels, results of this research showed inadequacy and lack of uniformity, concerning conditions of vaccine storage as well as insufficient training of health workers. In 100% of the vaccine sample titers were well under the minimal recommended potency by the manufacturers.

According to the results described above, we agreed that it was necessary to make another evaluation of the cold chain. In January 1990 we visited all public health units of the Municipality of Niterói, State of Rio de Janeiro. We also visited, at National level, the Central Nacional de Estocagem e Distribuição de Vacinas (CENADE) and at State level the Departamento de Insumos Básicos (DIB).

MATERIALS AND METHODS

City description. In the 1991 census[3], the population of Brazil was estimated 146,154,502

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inhabitants and 8.5% of these lived in the State of Rio de Janeiro. Niterói is one of the greatest cities of this State (pop. 416,123 inhabitants) and is connected to the capital (Rio de Janeiro City) by ferry boat and a bridge. The city revenue comes from commerce and tourism as well as some governamental and industrial activities.

The immunization of the children of the Municipality of Niterói takes place at the public health units.

Objective of the visits. On each visit it was observed if the basic procedures involved in the storage of measles vaccine (Table 1), according to the standards recommended by the Brazilian Immunization Programme[4], were performed, and 3 - 5 samples of the vaccine supply in use or in stockpile were collected for viral titration. We used a protocol with the same questions presented in the former research[11], as follows:

- Refrigerators: conditions (in good working order and used only for vaccines); temperature control (recorded twice daily, thermometer functioning properly, charts to record all temperature measurement); arrangement (vaccines placed in middle shelves, bottles or other containers full of water stored in the lower shelves) and cleanliness.
- Maintenance of the vaccines in application rooms: reconstituted vaccine discarded after 4 hours and temperature control.
- Immediate technical support in emergency situations as power failure or defect of the refrigerators.

A grade was given for each evaluated item, which varied from adequate (100%) to regular ($\geq$70%) and insufficient (<70%), according to its accomplishment.

Transport of the vaccines. The vaccines collected from the public health units had been produced by three different manufacturers: Vaccine Bio-Manguinhos (strain BIKEN CAM - 70), in 5-dose vials, produced by Laboratório de Bio-Manguinhos, Fundação Oswaldo Cruz, State of Rio de Janeiro, Brazil; Vaccine Instituto Butantan (strain Moraten), in 5-dose vials, produced by Instituto Butantan, State of São Paulo, Brazil; Vaccine Rouvax (strain Schwarz), 10-dose vials, produced by Institute Mérieux - Lyon, France. All vaccines had been delivered by CENADE. The lyophilized vaccines were kept in insulated cold boxes with ice and taken to the Laboratório de Controle Microbiológico de Bio-Manguinhos, where they were tested on the same day of collection.

Vaccines Titration. After their reconstitution, the vaccines were diluted in 199 medium, containing 3% inactivated calf serum and tested in VERO cells by micro - titration technique in plate[10 16]. After incubation at 37°C in a CO_2 incubator for 7 days, the plates were examined for cytopathic effects with an inverted microscope and the vaccine titers were calculated by the Reed - Müench method[13]. In accordance to the manufacturer the minimal recommended potency for the product is:

- Vaccine Bio-Manguinhos: 5000 $TCID_{50}$/0.5ml ($10^{3.7}$ $TCID_{50}$).
- Vaccine Instituto Butantan: 1000 $TCID_{50}$/0.5ml ($10^{3.0}$ $TCID_{50}$).
- Vaccine Rouvax: 1000 $TCID_{50}$/0.5ml ($10^{3.0}$ $TCID_{50}$).

RESULTS

At National level (CENADE), no irregularity was found in the storage conditions of measles vaccine. All the standards recommended by the Brazilian Immunization Programme[4] had been kept. However, at State level (DIB), several irregularities were found, such as defect of equipment of the cold room at - 20°C, lack of immediate technical support in emergency situations, lack of thermometers and charts to record the daily temperature of the freezer. The vials of the vaccine were stored inside their own packages, one on top of the other, and kept inside a horizontal freezer maintained in an inappropiate room.

The Municipal Health Secretary Office of Niterói kept two refrigerators in a regional health unit store room to store the products in order to centralize the delivery of the vaccines. Irregularities were also found there, such as: lack of charts to record the daily temperature of the refrigerators and immediate technical support in emergency situations, and also, vaccines incorrectly placed on the lower shelves of the refrigerators.

The evaluation of the cold chain of the public health units in Niterói (Table 1) showed that the

majority did not fulfil the standards recommended by the Brazilian Immunization Programme[4], where a predomination of grades R and I was found.

The results of the titration of the vaccines are presented in Table 2 in accordance to their origin and expiration dates. In 74.4% of the national samples tested, the dates indicate that vaccine titers were not only under the minimal recommended potency but also presented different sample titers in the same lot. However, this loss of potency did not occur in imported vaccines, where all samples tested were above the minimal potency recommended.

DISCUSSION

This research showed that the situation of the cold chain of the Municipality of Niterói had improved compared to the former evaluation done in 1986[10 11], in spite of the still existing problems. It was shown that in 100% of the health units, the conditions of the refrigerators and proper inside location of the vaccines in this equipment were adequate or regular although this percentage was higher than the one found (86.4%) during the former work. Also, it was verified that the control of the temperature of the refrigerators had improved;

Table 1 - Evaluation of the cold chain of the Public Health Units of the Municipality of Niterói, State of Rio de Janeiro (1990).

Health units	Conditions	Refrigerators		Temperature control	Vaccines in application room	Immediate technical support
		arrangement	cleanliness			
1	R	A	R	R	R	I
2	A	A	A	R	A	I
3	A	A	A	R	A	I
4	R	A	A	R	A	I
5	R	A	A	R	A	I
6	R	R	I	R	R	I
7	R	R	A	I	R	I
8	A	A	A	R	A	I
9	A	R	I	I	A	I
10	R	R	I	I	R	I
11	A	A	R	A	A	A
12	A	R	A	I	A	I
13	R	R	A	R	A	I
14	A	R	R	A	A	I
15	A	R	A	I	A	I
16	A	A	A	I	A	I
17	A	R	A	A	A	I

A: adequate (100%) R: regular (⩾70%) I: insufficient (<70%)

Table 2 - Results of titration of measles vaccines collected from public health units of the Municipality of Niterói, State of Rio de Janeiro (January/1990).

Vaccine origin	Samples tested	Samples with recommended potency	Samples with lost of potency
National(1)	43	11 (25.6%)	32 (74.4%)
Imported(2)	15	15 (100.0%)	-
Total	58	26 (44.8%)	32 (55.2%)

(1) Expiration date: January/1990: 32 samples; August/1990: 2 samples; April/1990: 9 samples.
(2) Expiration date: July/1991.

64.7% of the Units were considered adequate or regular. However, the immediate technical support in emergency situations continues being the most problematic item. It was considered insufficient in 94.1% of the health units evaluated and this percentage was considered higher than that found in the former research (90%).

After its production, measles vaccine is submitted to several tests of quality control by the manufacturer. Moreover, before the release of each lot, other tests are also performed by Instituto Nacional de Controle de Qualidade em Saúde (INCQS) to confirm its quality. After that, vaccine is stored at National level, where all the standards recommended by the Brazilian Immunization Programme[4] are kept. Although it was verified that the conditions of the cold chain of the Municipality had improved compared to the former evaluation in 1986, the results of this research show that the conditions of storage of measles vaccine, as much at State level as at Regional and Local levels, are still not adequate enough, which may have contributed to the deterioration observed when these products were analyzed. In 55.2% (32 samples) of 58 vaccine samples tested, without considering the manufactures, titers were under the minimal recommended potency at the time of their administration to the patient.

This evidence indicates that the vaccines tested probably lost potency after their distribution from the Central Site (CENADE). Whether the loss occurred during the transport from the State level (DIB) to the Public Health Units or in the DIB or in the Units themselves could not be determined within the limitations of this study.

Probably, the variations observed in titers of the three vaccines tested may be related to different thermostabilizers used by each manufacturer. These products are added during the production of the vaccine to increase the resistance to deterioration in prolonged storage and accidental exposure to higher temperatures[5 12 14 15]. The use of vaccines resistant to thermodegradation is important for the success of the immunization programmes, specially in countries with a hot climate and an inadequate cold chain system[12].

The expiration dates of the products may also have contributed to the variations observed in potency of the vaccines tested. As it is shown in Table 2, 32 from 43 samples of vaccines of National origin were analyzed at the end of the expiration date.

Also, it was verified that, without considering the manufacturer, the titers of the vaccines from the same lot varied according to their origin, suggesting lack of uniformity in the conditions of storage and distribution of these products.

Problems in the storage of measles vaccines presented in the research are not exclusive of our country. They were also found by Krugman et alii[8] and Carrasco et alii[1]. Consequently, the quality of the products is altered, decreasing the potency of vaccines, and then contributing to the development of "pockets" of susceptible children.

The results of this research show the importance of the use and maintenance of equipment, training of health personnel and, mainly, the necessity of a continuous evaluation of the cold chain.

RESUMO

Quatro anos após a primeira visita, dezessete Unidades Sanitárias do Município de Niterói - RJ foram visitadas novamente e reavaliadas de acordo com as normas técnicas específicas estabelecidas pelo Programa Nacional de Imunização. Constatou-se que em 100% das Unidades visitadas os cuidados com os refrigeradores e a arrumação das vacinas no interior dos aparelhos eram adequados ou regulares mas quanto ao controle de temperatura dos refrigeradores este percentual caía para 64,7%. De todos os itens avaliados, o mais problemático foi o apoio técnico imediato frente a situações de emergência, considerado insuficiente em 94,1% dos casos. Em 55,2% das amostras vacinais recolhidas das unidades sanitárias, os títulos estavam abaixo da potência mínima preconizada para tal produto no momento da aplicação. Verifica-se, deste modo, a necessidade de uma contínua avaliação dos fatores que intervêm na cadeia de frio evitando-se, assim, que seja comprometida a qualidade das vacinas a serem utilizadas.

Palavras-chaves: Vacina contra o sarampo. Controle de qualidade. Serviços de saúde pública.

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