

EVALUATION OF MEASLES VACCINE COLD CHAIN IN LAGOS STATE, NIGERIA**Oyefolu, A.O.B.^{1,4*}, Nwaeke, A.C.², Audu, R.A.³, Akinyemi, K.O.¹, Salu, O.B.³, Muller, C.P.⁴, Omilabu, S.A.²**

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Abstract

The National (level 1), State (L2), and Local government vaccine cold stores (L3) as well as some vaccination centres (L4) were physically inspected in Lagos State, Nigeria and the potency of the live-attenuated measles vaccine was tested. Both the L1 and L2 storage facilities were formally adequately equipped and maintained. This was also reflected in the potency of the vaccines. However, many vaccines at L1 were within weeks from expiration. Considerable problems with refrigeration and delayed forwarding became apparent at level L3 causing loss in potency both at L3 and L4: although, all L4 stores check-listed met all the EPI/NPI accreditation criteria, ¾ of the vaccines were sub-potent and this situation did not improve over the three year study period (1996-98). Time to expiration did not seem to be the main cause of loss of potency but rather poor and delayed handling. It is recommended that vaccines are moved more rapidly through the system and used well before expiration. Because of frequent power failures despite standby generators, we further recommend to include in the WHO criteria, book-keeping of periods of power failures, running time of generators and a complete recording of fuel consumption. Attitudes among vaccinating staff and handling of vaccines should also be improved by continued training.

Keywords: Measles vaccine; cold stores; potency

Running Title: Cold chain in Nigeria.

INTRODUCTION

Despite improved vaccine coverage, measles remains endemic in many African and other tropical developing countries with staggering morbidity and mortality rates (1-3)). In these countries, the loss in vaccine (L2) and the downward distribution to all State-controlled Local Government Cold Stores (LGCS- L3), which in-turn organise the distribution of vaccines to the various Vaccination Centres (VC, L4) operated under the responsibility of the Local Government Areas (LGA) of the State. The vaccination centres

(L4) are the point of care at which vaccines are administered to the recipients.

The maintenance of the cold chain at all levels of vaccine storage and distribution is obviously an essential and critical part of immunisation programmes and its regular follow-up is the key to a successful vaccination system. Therefore, potency testing of live viral vaccines is an important component for evaluating the cold chain on its various levels (8). This study evaluates the cold chain of the live attenuated measles vaccines at the different levels of vaccine storage and distribution throughout Lagos State, Nigeria.

MATERIALS AND METHODS

VACCINE COLD STORES

The following stores representing the different levels (L1–L4) of vaccine storage participated in this study: National Central Cold Store (NCCS) Oshodi (L1); the Lagos State Cold Store (LSCS) Ikeja (L2) and 5 Local Government Cold Stores (LGCS): Ikorodu, Kosofe-Ketu, Ajeromi-Ifelodun, Eti-Osa and Alimosho LGAs of Lagos State (all L3). Primary Health Centres (PHC) which served as the Vaccination Centres (VC) (L4) were Palm Avenue PHC, Isolo Road PHC and Kajola PHC (in Mushin LGA), Saint Sabina PHC (in Agege LGA), Ikosi PHC (in Kosofe LGA), Layeni PHC (in Ajeromi-Ifelodun LGA), Lagos Island LGA-staff clinic (in Lagos Island LGA), Ita-Elewa PHC (in Ikorodu LGA), Isheri-Olofin PHC (in Alimosho LGA) and Muri-Okunola PHC (in Eti-Osa LGA). The VC attended mainly to the needs of the middle and low socio-economic class of the population.

The cold chain facilities of most cold stores were physically inspected in 1998. The material checklist included, the cold room equipment, type of cold chain monitors, availability of sufficient deep freezers, refrigerators, ice packs, adequacy of electric power supply, availability and functionality of standby generators as power supply alternatives to the National Electric Power Authority (NEPA). Assessment was done using the standard questionnaires of the Expanded Programme on Immunisation/National Programme for Immunisation (EPI/NPI) (10).

2.2 Collection of vaccine samples and potency testing

From 1996 through 1998, a total of 56 vaccine samples were collected from 7 cold stores (L1-L3) and 9 vaccination centres in Lagos State. All the vaccines were of the lyophilised type (10 doses per

vial; Edmonston-Zagreb strain, Pasteur Merieux) and were delivered by UNICEF to the L1 store. At the vaccination centers (L4) aliquots (0.5ml) of the reconstituted vaccines were collected into sterile vials when ready for administration to children. Aliquoted samples were transported to the laboratory in well-insulated cold-boxes and either immediately titrated for potency or stored at -70°C until titration within 24 hours. The vaccine manufacturer, lot and batch numbers, date of collection and the expiry date were recorded for each sample. The 50% Cell Culture Infectious Dose (CCID₅₀) per human dose was determined according to WHO guidelines on quadruplicate wells on confluent monolayers of B95a cells (1×10^5 cells/ml) in 24-well Costar® tissue culture plates (11). The CCID₅₀ was calculated as described by Reed & Muench (12).

RESULTS

ASSESSMENT OF COLD STORES

On physical inspection of the NCCS (L1) and the LSCS (L2), all criteria of the EPI/NPI accreditation checklist for a National and State cold store were met. In accordance with WHO recommendation, all vaccines showed expiry dates; both L1 and L2 had adequate refrigerated main and sub-stores with functioning standby generators to ensure uninterrupted power supply; requisition forms and functioning refrigerated vans for transportation of vaccines to L3 stores were also available. In addition, criteria of *Table 1* were fulfilled as applicable. Of the five L3 stores inspected, only two (Ikorodu- and Eti-Osa LGCS) met all EPI/NPI cold chain accreditation criteria; the others satisfied 69 – 81% of the criteria

applicable to L3 stores. *Table 1* shows that proper storage of diluents was the most frequently encountered problem among the L3 stores inspected. The 5 vaccination centres checklisted met all EPI/NPI accreditation criteria applicable to L4 stores: availability of adequate thermometers, cold boxes, ice packs, vaccine carriers, strict adherence to vaccine expiry dates, standard keeping of vaccine ledgers and records.

VACCINE POTENCY

Only 29 (52.7%) of the 55 vaccines titrated from L1 – L4 met the WHO recommended virus titre of $3.0 \pm 0.5 \text{ Log}_{10}$ (i.e. ± 1000 infectious viral particles per human dose) for a potent measles vaccine and one vaccine vial was contaminated at source. *Figure 1* shows that both the percent of potent vials as well as the CCID_{50} decreases as the vaccine were handed down from L1 to L4 and that this decrease is particularly strong for L4.

Overall, only 8 (25.8%) of the 31 vaccine vials titrated from the L4 met the WHO requirement. Expired vaccines were only found in one of the L3-stores (Ajeromi-Ifelodun LGCS) but only one of the three expired vaccine samples was sub-potent. In 1996, none of the 6 titrated measles vaccines collected at the three L4 facilities met the WHO recommended virus titre. In 1997, only 7 (31.8%) of the 22 vaccine vials collected from L4 met this WHO standard, although the three vaccines tested the same year from L1 were potent. In 1998, vaccine potency did not improve at the L4 level (1/4) but at the L3 level, 12/15 vaccine vials and 1/1 at the L2 level met the potency criteria. The vaccines titrated from the L1 and L2 facilities over a 2-year period had titres ≥ 3.0 . *Figure 2* shows that

many vaccines (31/56) of all levels were within 14 weeks from expiration dates. The median time to expiration of vaccine vials and batches were 6 and 16 weeks respectively at L1/L2 with some within 1-2 months from expiry. At L3 median time to expiration was 3 weeks including some vaccines, which were expired. On average vaccines became sub-potent around the expiration date at L3, and much earlier at L4.

Table 1

EPI/NPI accreditation criteria met by L1-L3 cold stores in Lagos State, Nigeria

Storage Level	1	2	3	4	5	6	7	8	9	10	Total score (%)
	Adequacy of fridge for vaccine storage	Normal fridge t°	Diluent in fridge	Freezer for ice-packs only	Daily am & pm t°	Functioning standby generator	Adequacy of freezer for vaccine storage	Normal freezer t°	Normal vaccine spacing in fridge/freezer	Vaccine within expiry date	
L1	YES	YES	NA	YES	YES	YES	YES	YES	YES	YES	100
L2	YES	YES	NA	YES	YES	YES	YES	YES	YES	YES	100
L3 (IKR)	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	100
L3 (KSF)	NO	NO	NO	YES	YES	YES	YES	YES	YES	YES	81
L3 (AJE)	YES	YES	NO	NO	NO	NO	YES	YES	YES	NO	69
L3 (ETD)	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	100
L3 (ALD)	NO	NO	NO	YES	YES	NO	YES	YES	YES	YES	75
Total (%)	71	71	40	86	86	71	100	100	100	92	

NA = Not Applicable

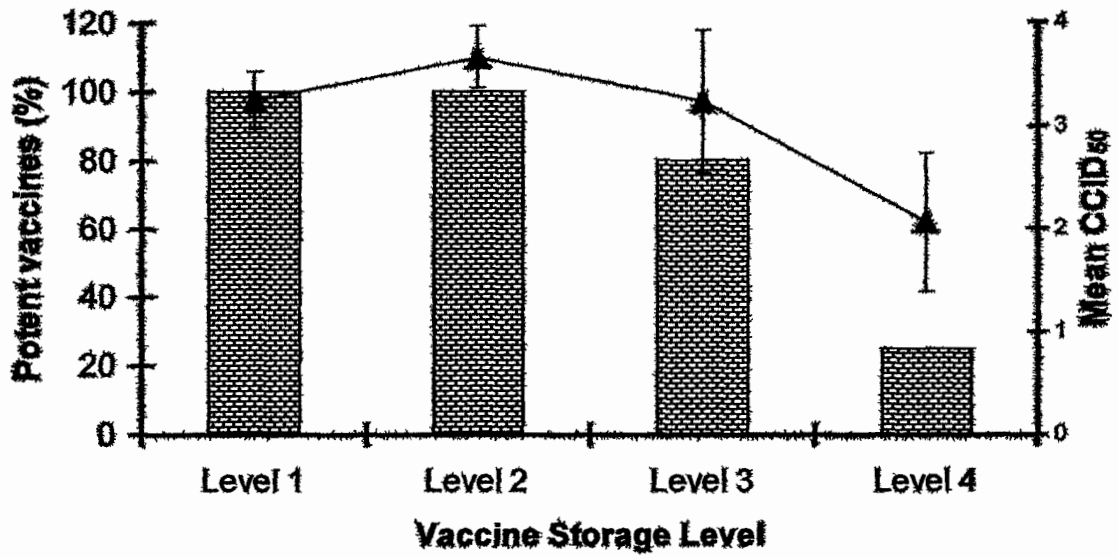


Fig. 1. (Oyefolu *et al.*)

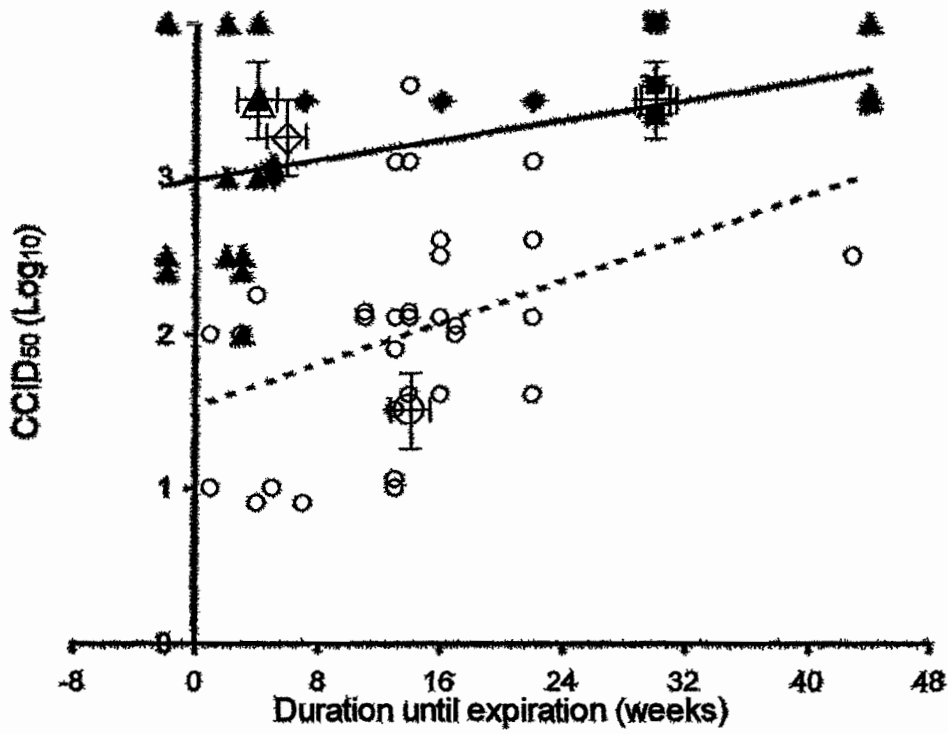


Fig. 2. (Oyefolu *et al.*)

DISCUSSION

When administrated under optimal conditions seroconversion rates to current measles vaccines (Edmonston-Zagreb strain) are >95% (13). With the exception of a small percentage of secondary vaccine failures, all of those who seroconvert are protected by long-lasting and robust immunity (13,14). However, the live-attenuated vaccine is highly sensitive to temperature, and a defective cold chain severely reduces vaccine efficacy (15). The WHO has a catalogue of recommendations as minimal requirements for maintaining a cold-chain at the different levels.

Both the L1 and L2 storage facilities were formally well equipped and maintained and this was reflected in the potency testing of the vaccines. However, many vaccines at L1 were within weeks from expiration. At L3 delayed forwarding was aggravated by considerable problems with refrigeration causing loss in potency both at L3 and L4. Expiration or time to expiration did not seem to be the main cause of loss of potency but rather delayed and inadequate handling.

It is therefore recommended here that vaccines are moved more rapidly through the system and that they are used at least 4 months before expiration. In fact, recommendations should be made for each level with respect to the allowed time to expiration for each batch, to avoid that batches close to expiration leave central stores. Batches that are close to their expiry date should have their potency recertified through laboratory testing before leaving the central stores as was suggested before (5,6).

Interruption of electricity supplied by the National Electric Power Authority (NEPA) was another general problem reported at all levels of vaccine storage and distribution, as has been reported before (5,6,8). Power failures are

notoriously paired with the lack of fuel for standby generators and their indiscriminate diversion at L3 for personal or other unrelated use by officials. While this must stop, we strongly recommend here to include to the WHO criteria, book-keeping of the exact periods of power failures, running time of generators and a complete inventory of fuel consumption.

Although, all L4 stores check-listed met all the EPI/NPI accreditation criteria, ¾ of the vaccines were sub-potent and this situation did not improve over the three year study period. In most vaccination centres (L4) this was due to inadequate handling of vaccines and attitudes among vaccinating staff. Personnel kept vaccines on thawed ice-packs at ambient temperatures and/or in their palms during conversations. Therefore there is an urgent need for continued training and education of vaccinating staff. Reprinting and redistribution of the summarised WHO-guidelines (14) for vaccinators could be a first step.

Although this study is relatively limited in scope and in some ways anecdotal rather than representative, it revealed considerable discrepancies between formal accreditation criteria and vaccine quality. More stringent recommendations are suggested with respect to moving of vaccines through the cold-chain and with respect to the closer monitoring of main and accessory power supplies and failures.

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Legends to Figures

Fig. 1. Vaccine potency at the different storage levels of the cold chain. At level L4 an aliquot of reconstituted vaccine taken just before injection was used for potency testing. Bars are percent of potent vaccines; mean CCID₅₀ (▲—▲).

Fig. 2. Vaccine potency (CCID₅₀) and time to expiration of vaccine sampled at the different storage levels L1 (◆); L2 (■); L3 (▲); L4 (●); potency trend line at L3 (—) and L4 (---). Large open symbols represent median potency ± S.D. of batches at the different storage levels L1 (◇); L2 (□); L3 (△); L4 (O). As in Fig. 1 potency testing at level L4 was performed on reconstituted vaccine just before injection.