Research/ Recherche

Transport and storage of vaccines in Hungary: the first cold chain monitor study in Europe

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With assistance from WHO the Hungarian Ministry of Health organized two cold chain studies: the first in three counties in summer (1 July to 30 September 1987), the second in six counties (including the previous three) in winter (1 January to 31 March 1988). The counties were chosen according to their distance (50–300 km) from Budapest, individual districts and child health centres being selected randomly. All participants were trained before beginning the studies. The vaccines (DPT, measles and BCG) for immunization, with attached cold chain monitors, were transported from the manufacturers to the child health centres using the normal distribution systems in the country. The whole cold chain process was analysed with regard to (1) actual exposures to adverse temperatures and delays in distribution; (2) the places where such exposure or delay occurred; (3) the percentage of vaccines at risk of deterioration (actual and predicted) at the end of the study; and (4) the performance of refrigerators of different types.

Evaluation of the results (using WHO's EPIC software) showed significant deviations from acceptable standards. This first cold chain study in a European country proves that even in a temperate climate and with a reasonably well-organized public health service there can be significant weaknesses in the transportation and storage of vaccines. Recommendations to overcome these deficiencies are given.

Introduction

Although the cold chain is a prerequisite in tropical countries, it had been assumed that temperate climates would not be a problem for vaccine distribution and that managerial and logistical difficulties in an industrialized country would be minimal.[a,b] However, it appears that countries with a temperate climate can experience serious cold chain failure and should take care to protect vaccines against extreme winter and summer temperatures and ensure that they are used within a specified period of time. Cold chain studies in such countries provide essential information on the efficiency of the managerial process and functioning of the cold chain. To monitor the conditions during transportation and storage of vaccines from the manufacturer to the child immunization centres a protocol for using the cold chain monitor (CCM) was introduced by WHO in 1979.[c]

The present paper describes the organization, implementation and results of the two Hungarian CCM studies which were carried out in 1987 and 1988.

Materials and methods

Hungary (93 030 km^2), a country with intermediate economic and technical development, has a total GNP of 900 × 10^9 forints for 10.7 million inhabitants (1 US$ = 50 forints). The adult to child ratio is about 3:1 and the live birth rate, 13 per 1000. Budapest has 2.1 million inhabitants in 22 districts; the rest of the

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[a] *Training for mid-level managers to manage the cold chain system.* Unpublished document WHO-EPI/MLM/CC/Rev.

[b] *WHO logistics and cold chain for primary health care. How to use the vaccine cold chain monitor.* Unpublished document WHO-EPI/Log 84/27, 1984.

[c] *WHO protocol for a cold chain review using vaccine cold chain monitors.* Unpublished document WHO-EPI/CCIS/85.2, 1985.

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Table 1: **Geographical and demographic features and details about the country**

Area	93 030 km^2
Location	Longitude 16° 05′ to 20° 55′ E Latitude 45° 45′ to 48° 35′ N
Altitude	From 78 to 1015 m above sea level
Temperature:	
Average	10°C
Minimum	−12°C
Maximum	35°C
Population:	
Total	10 700 000
Newborns	150 000 per annum
0–14 years old	2 400 000
In Budapest	2 100 000
No. of counties	19 + Metro Budapest
No. of districts	140 + 22 (in Budapest)
No. of health facilities	Approx. 3200 + 100 (in Budapest)

country is divided into 19 counties and 140 districts (Table 1). Fig. 1 shows the counties that participated in the study. The Hungarian climate is temperate continental with summer temperatures rarely exceeding 35 °C and a winter temperature which infrequently falls below −12 °C.

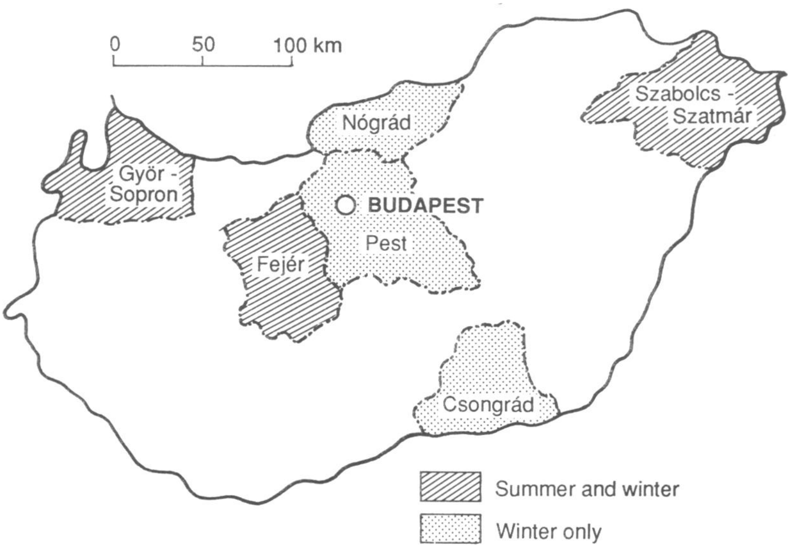
Public health organization

The public health policy is coordinated by the Epidemiological Division of the Ministry of Health in Budapest (EDMOH), and each of the 19 counties has a county public health headquarters (CPHH). Within Budapest and the 19 counties there are 162 district public health services (DPHS), and within the districts there are 3300 child health centres (CHC) with preventive and curative sections. The preventive section is responsible for the immunizations.

Vaccines. The triple DPT (diptheria, pertussis, tetanus) vaccine is manufactured and distributed every 3 months by the Human Institute (Budapest) to the DPHS using the normal postal system. Measles vaccine is manufactured in Moscow by the Viral Vaccine Institute and transported to Budapest where it is stored in the National Institute of Hygiene (NIH); after testing for potency it is distributed twice a year in cold boxes from the NIH to the county and district levels and finally to the child health centres. BCG vaccine is manufactured by the NIH in Budapest and distributed every 3 months to the maternity service clinics (MS) by post.

Cold chain monitors (CCM). These were supplied by WHO's Expanded Programme on Immunization (EPI) and, after activation by the Human Institute and the National Institute of Hygiene for their respective vaccines, were attached to the vaccine parcels according to the EPI guidelines and the studies' protocol. Each CCM records the cumulative effect of exposure to temperatures above 10°C ("ABC") and 34°C ("D"), the monitors changing colour at varying rates depending on the temperatures. The "ABC" monitor, which has four indexes (–, A, AB and ABC), will completely change colour in 11 days at 21°C or 14 days at 12°C. The "D" monitor, which has two indexes (– and D), changes within 2 hours at tem-

Fig. 1. **Map of Hungary showing selected counties in the study.**



peratures above 34°C. The monitors are not potency indicators, but show whether the vaccines had been exposed at or above the stated temperatures for longer than the stated time limits. This information is useful to the programme manager to find weaknesses in the cold chain and to decide whether a vaccine consignment may be used. The Freeze Watch monitor, which was used in the second study, has two indexes (– and F) changing below −3°C.[d]

Implementation of the studies

The counties were chosen according to their distance from Budapest: short (50–100 km: Fejér, Nógrád and Pest); medium (100–200 km: Györ-Sopron); and long (200–300 km: Csongrád and Szabolcs-Szatmár). These six counties cover 28% of the total population of Hungary. The district health services and the child health centres were selected randomly for the cold chain monitoring of the DPT and measles vaccines (40% of the selected counties' child health centres were chosen in summer, and 20% for the winter study); all the maternity services in the six counties were included for the BCG cold chain evaluation.

The basic principle and the technical aspects of the monitors were described and demonstrated to the participants during a preliminary consultation with an EPI consultant from WHO in February 1987 and at a meeting of the chiefs of the epidemiological departments of the county public health services in April 1987.[e]

The two studies were carried out from 1 July to 30 September 1987 in Fejér, Györ-Sopron and Szabolcs-Szatmár counties, and from 1 January to 31 March 1988 in these three as well as Pest, Nógrád and Csongrád counties. Follow-up and consultations during the studies were maintained by the national coordinator and the WHO consultant.

Four criteria were evaluated:

(1) exposures to adverse temperatures and delays in distribution;

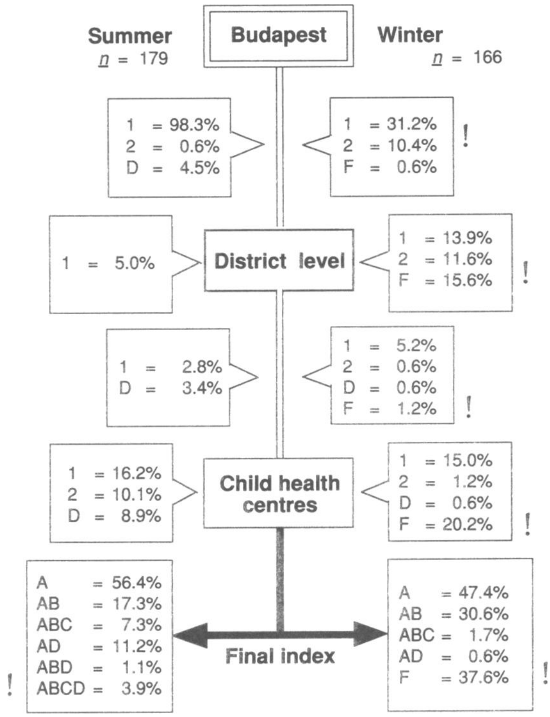
(2) places where such exposure or delay occurred;

(3) Percentage of vaccines at risk of deterioration because of such exposure or delay (actual and predicted); and

(4) the performance of refrigerators of different types.

At the end of the study the cold chain monitors were collected at the county level and sent to NIH in Budapest. Because at the time a suitable computer was not available in the Ministry of Health the monitors were sent to WHO headquarters for computerized analysis using the EPIC software. Data on stock levels, vaccine consumption and type of refrigerator were also collected.

Fig. 2. **DPT vaccine cold chain.**



Results

This paper presents only the main results, the detailed analysis of the studies appearing in the full report which is available on request.[f]

DPT vaccine

Adsorbed DPT vaccine has to be protected against extreme heat and freezing; it is distributed by the postal service every 3 months to the district level.

Fig. 2 shows in diagrammatic form the changes

[d] Freeze Watch manufactured by PyMatt Corp., Somerville, NJ, USA.

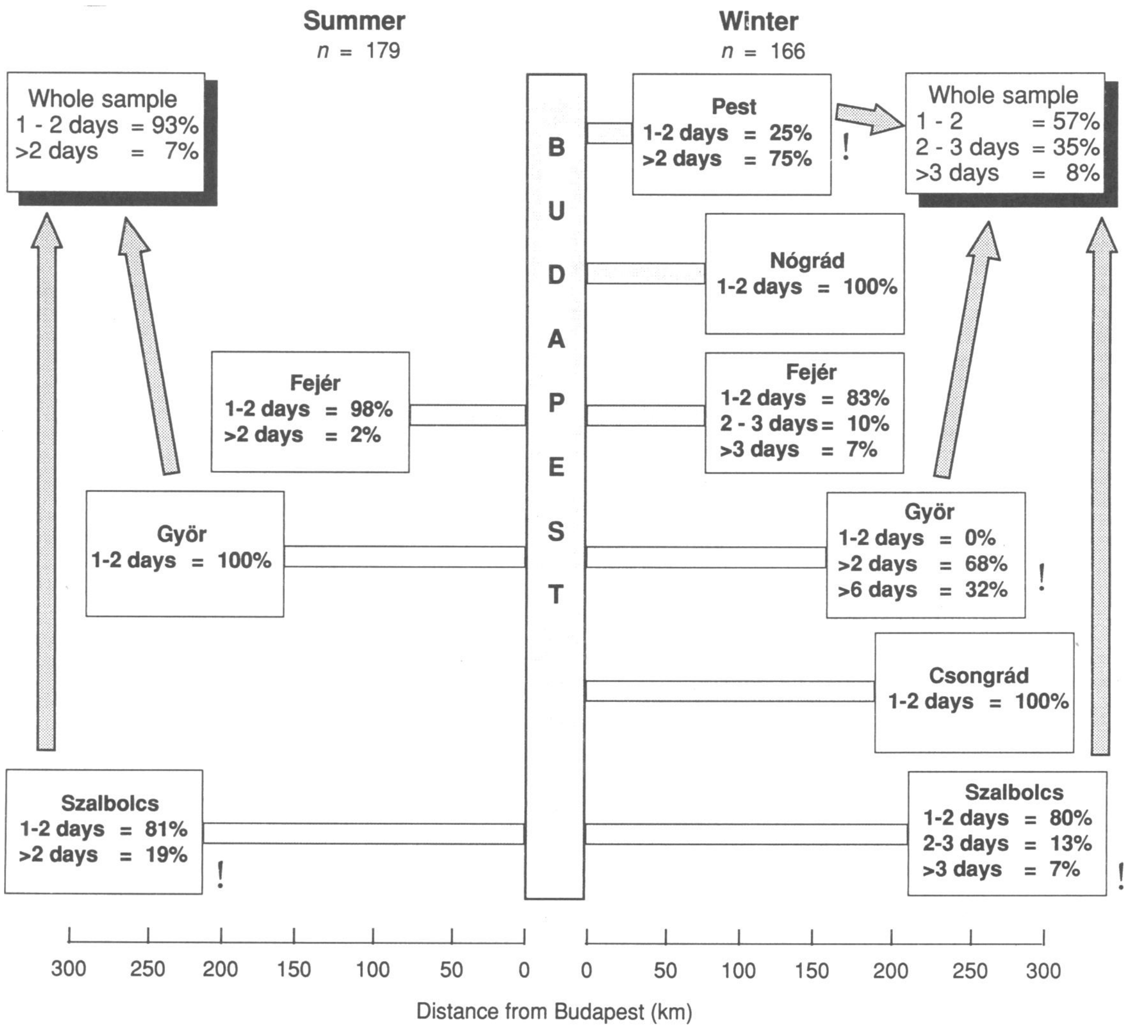
[e] **WHO Expanded Programme on Immunization.** *Vaccine cold chain monitor.* Unpublished document WHO-EPI/CCIS/85.1/Rev. 4, 1985.

[f] **Battersby, A. & Lugosi, L.** *Report on the storage and transport of vaccines in Hungary. Analysis of cold chain monitors used between 1.7.87 and 30.9.87 and between 1.1.88 and 31.3.88.* Unpublished document WHO-CD, Copenhagen, 1989.

observed in the cold chain monitors attached to the DPT vaccine between Budapest and the destinations. The summer exposures are shown on the left and the winter exposures on the right. The ! symbol indicates exposures that could seriously affect the potency of the vaccine. For the ABC monitor the exposure is shown as a rate of change, with a maximum of three changes. One single change may be from – to A, or A to AB, or AB to ABC. It is important to remember that these monitors recorded the cumulative effect; thus, one change during storage in a child health centre could have been from AB to ABC while that during transport from Budapest to the district level could have been from – to A. With the D and F indicators, only one change is possible and this is recorded as D and F, respectively.

The final index (Fig. 2) gives the percentage of monitors that recorded changes by the end of the study period. The results show that, for both summer and winter periods, the cold chain for DPT was not satisfactory. Almost all the vaccine was exposed to heat during transport between Budapest and the districts. At the district stores the exposure to heat was much less, but exposure to cold during the winter was considerable. Excessive hot and cold temperatures were experienced during storage at the child health centres so that, by the end of the summer, 4% of the vaccines were seriously compromised;

Fig. 3. **Delays during distribution of DPT vaccines from Budapest.**



in the winter; 38% had been exposed to below freezing temperatures.

Fig. 3 shows the time in days for transport of DPT by the postal service from Budapest to the district level in summer and winter. The ! symbol indicates a problem. The fact that 10.4% of the winter samples recorded two changes in index (Fig. 2) may be attributed to delays of over two days in the post, which is unacceptable considering the relatively short distances involved.

At the end of the study not all the vaccines had been utilized. By comparing the final exposure index and the rate of utilization of the vaccines with the quantities in stock, it was possible to predict how much of the remaining vaccine would be exposed to unacceptable conditions by the time it was used. This is described as vaccine which is at risk in Table 2. A long period of storage has two consequences:

- qualitative, if there is a loss of potency of the vaccine; and
- economic, if excess unused quantities of vaccine are wasted.

Table 2: **DPT vaccine: percentage of remaining vaccine at risk after the end of the studies**

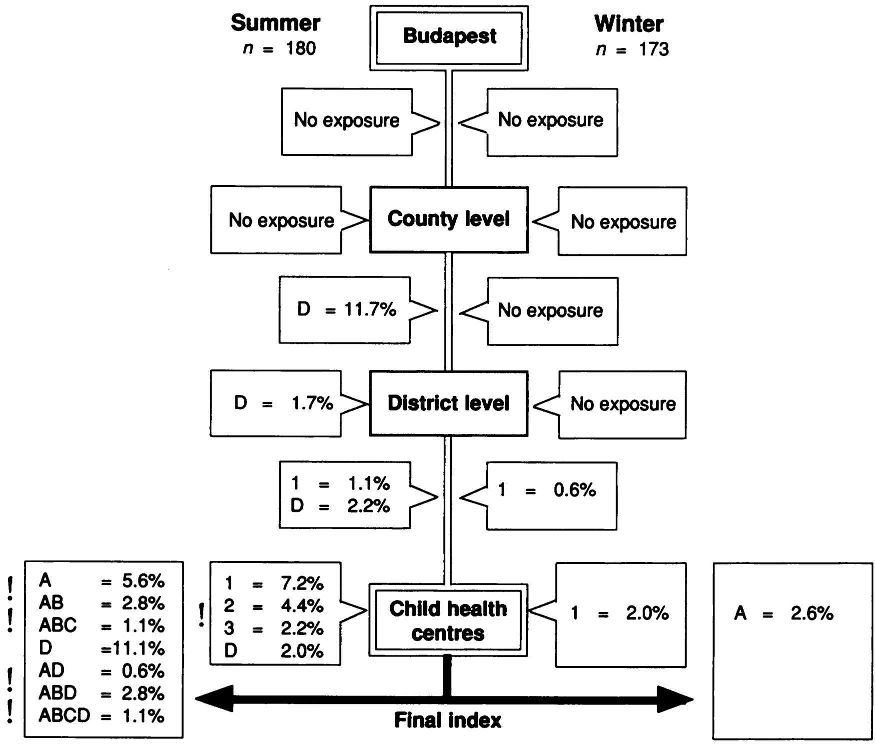
Summer (n=179):	
Minimal exposures (no risk)	88%
Exposures at risk	12%
ABCD+ for >3 months	1.7%
ABD+ for >3 months	2.2%
ABC+ for >3 months	2.2%
AB+ for >6 months	1.7%
A+ for >9 months	4.5%
Winter (n=166):	
Nil exposure	20%
Minimal exposures (no risk)	21%
Exposures at risk	59%
Frozen	38%
AB+ for >6 months	13.5%
A+ for >9 months	7.6%

Measles vaccine

Measles vaccine, which is more heat sensitive than DPT but not susceptible to damage by freezing, is distributed twice a year to the district level.

Fig. 4 summarizes the cold chain for measles

Fig. 4. **Measles vaccine cold chain.**



vaccine. In the summer, during transport and storage of vaccines from the county to district and then to the child health centres, 8% of the monitors recorded changes to "AB" or more, indicating exposures to 21°C or higher for >6 days. In the winter study the only change recorded was 3% for the "A" index.

During the summer, delays in transport were slight, with 3% of the monitors taking more than one day to reach their destination. During the winter, delays were longer, with 4% taking more than two days to reach the district level and 7% taking more than 2 days to reach the child health centres; these delays were concentrated in Csongrád (30% of the subsample) for the former and in Pest (30% of the subsample) for the latter. The delay in transportation was much less than for DPT and BCG vaccines, both of which were sent through the postal service. Given the relatively short distances in Hungary a delay of more than one day is not acceptable.

Table 3 shows the percentage of measles vaccine at risk after the end of the studies. It should be noted that although the percentage of critical exposure at the end of the summer study was only 8%, the gross overstocking of vaccine resulted in 21% of the vaccine being at risk of deterioration before use.

Table 3: **Measles vaccine: percentage of remaining vaccine at risk after the end of the studies**

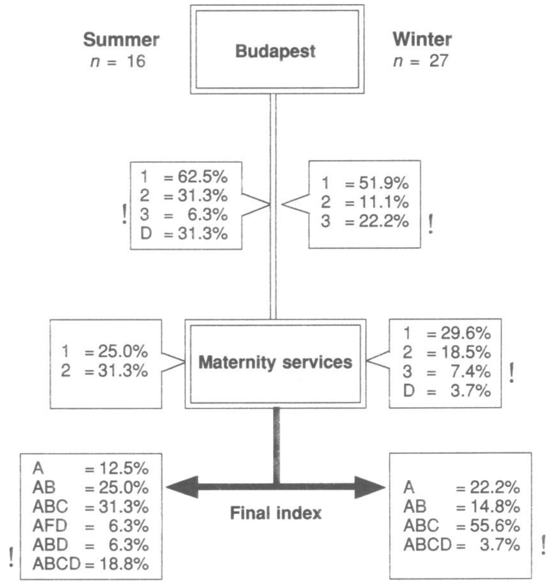
Summer (n=180)	
Nil exposure	64%
Minimal exposures (no risk)	15%
Exposures at risk	21%
ABCD+ for any duration	1.1%
ABD+ for >3 months	2.8%
AD+ for >3 months	0.6%
D+ for >6 months	3.9%
AB+ for >6 months	0.6%
A+ for >6 months	1.7%
Nil+ for >12 months	9.7%
ABC+ for any duration	0.6%
Winter (n=173)	
Nil exposure	96%
Minimal exposures (no risk)	3%
Exposures at risk	1%
Nil+ for >12 months	1.2%

BCG vaccine

The Hungarian BCG vaccine, when new, is able to tolerate temperatures of 25°C for 60 days without loss of potency below the minimum effective viable units (VU) per dose (100 000 VU/0.1 ml intradermally). This vaccine is distributed through the postal service direct to the maternity services (MS).

Fig. 5 illustrates the cold chain for BCG vaccine. In summer, all the monitors recorded changes by the time of their arrival at the maternity services; 31.3% had reached temperatures in excess of 34°C and 6.3% also recorded an exposure equivalent to 11 days at 21°C. In winter, 85.2% of the monitors recorded changes; 22.2% were due to exposures in excess of 21°C for at least 11 days.

Fig. 5. **BCG vaccine cold chain.**



By the end of the summer study 31.3% of the monitors recorded changes to the "D" index; of these, 18.8% also recorded a change of "ABC". An additional 31.2% had been exposed above 21°C for at least 11 days (ABC). During the winter, by the end of the study 3.7% had been exposed to temperatures above 34°C and 59.3% had experienced temperatures above 21°C for at least 11 days. The effect of heat on a vaccine of low thermal mass, during unprotected transportation, is very marked both in summer and in winter. This suggests that the effects of central heating in postal sorting offices is at least as significant as the summer ambient temperatures.

Table 4 shows the percentage of the BCG vaccine at risk of deterioration after the end of the studies. The length of time the vaccine is likely to remain in the maternal services results in a very high percentage of the vaccine (50%) being at risk before use.

Refrigerator performance

There are three main types of refrigerator used for the storage of vaccines in Hungary and their perfor-

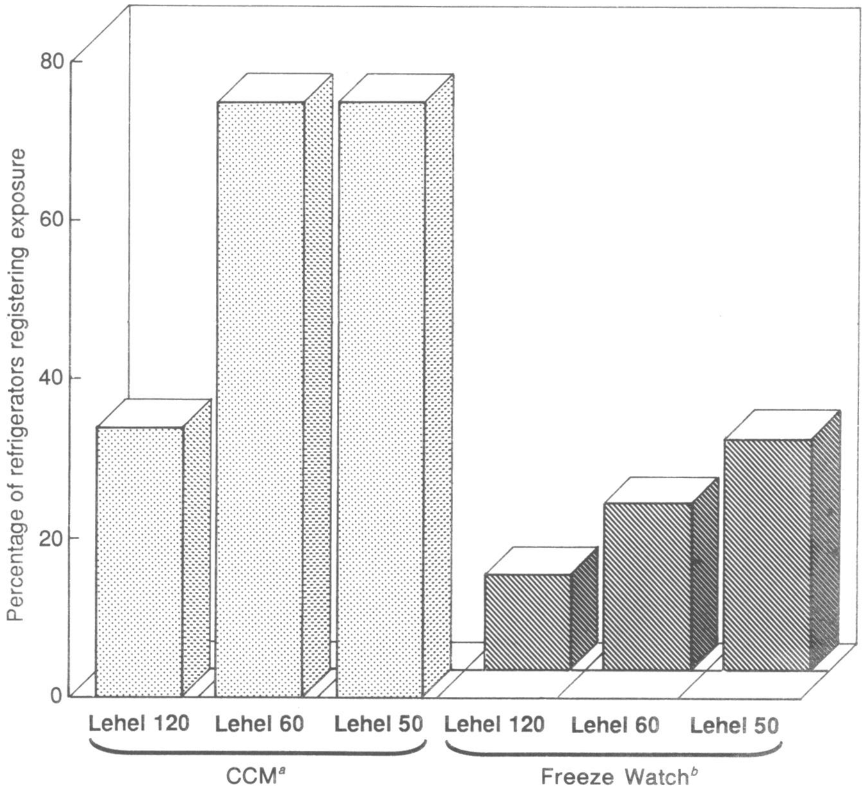
Table 4: **BCG vaccine: percentage of remaining vaccine at risk after the end of the studies**

Summer (n=16)	
Minimal exposures (no risk)	50%
Exposures at risk	50%
ABCD+ for >3 months	18.8%
ABC+ for >3 months	12.5%
AB+ for >6 months	12.5%
A+ for >9 months	6.3%
Winter (n=27)	
Nil exposure	4%
Minimal exposures (no risk)	79%
Exposures at risk	17%
ABCD+ for >3 months	3.7%
ABC+ for >3 months	11.1%
A+ for <9 months	3.7%

mance was assessed by measuring the percentage of monitors that underwent change while stored in the refrigerators. Data were combined from the two studies; the freezer compartment was monitored with the CCM and the main compartment with both the CCM and Freeze Watch. The results are summarized in Fig. 6.

The Lehel model 50 and 60 refrigerators were not able to ensure safe temperatures. While replacement of these models should be the ultimate objective, in the short term their performance could be improved by ensuring that water bottles are kept in the lower part of the refrigerator, thus providing an energy store when the refrigerator is only partly full.

Fig. 6. **Performance of three models of refrigerator for vaccines in the cold chain (change of index in CCM and Freeze Watch).**



[a] At least one change in index.
[b] CCM was placed in the main compartment and the freezer; Freeze Watch was placed in the main compartment only.

Discussion and conclusions

This first cold chain study in a European country with a temperate climate has provided information to the Hungarian Ministry of Health and to WHO on the quality of vaccine transportation and storage. The introduction of the cold chain monitor showed that it could strengthen the management of the cold chain, especially in countries with developed programmes.

The immunization policy in Hungary is conducted according to the guidelines for the WHO European Region,[g,h] but the results of the present study show considerable weaknesses in the cold chain during transportation and storage of the vaccines. The main matters for concern are as follows:

(1) The temperatures the vaccines are exposed to are sufficiently high to cause loss of potency for DPT, measles and BCG vaccines; DPT is also damaged by freezing.

(2) The delays and exposures during transportation of BCG and DPT vaccines are sufficient to put them at risk of deterioration.

(3) The quality of two models of refrigerators and the method of storage cannot ensure safe storage of the vaccines at all times.

(4) Vaccines, especially for measles immunization, are stored for too long at child health centres.

(5) Detailed analysis of the results shows that there are wide variations between the best and worst counties in the present study.

The main positive points are:

- The cold chain monitors can be used to monitor the cold chain accurately and efficiently. The cost of using them is approximately one tenth of that of conducting comparable serological studies.
- The use of the monitors has revealed deficiencies which could not have been observed during routine managerial visits and increased the awareness of the need for efficient cold chain management.
- In some counties the quality of cold chain management is high.
- The inadequacies of the cold chain can be pinpointed to specific locations, at particular levels of each cold chain, thus making the task of taking remedial action easier.
- It is now possible, using the cold chain monitors, to assess the level of risk of vaccine deterioration during transport and storage.

In order to improve the Hungarian cold chain system the following are recommended:

(1) Improve the quality of vaccine storage during transport with better packaging or by using more ice packs (*1, 2*).

(2) Minimize delays during dispatch through the postal service by mailing at the beginning of the week and using express delivery.

(3) Improve the performance of the existing refrigerators by following the WHO guidelines on maintaining refrigerators; when replacing existing refrigerators, choose the model with the best performance.

(4) Provide sufficient storage space at county and district levels to accommodate the whole of the vaccine stock for one supply period, thus enabling the storage time at health centres to be no longer than six weeks.

(5) Provide refresher training for staff concerning the storage and handling of vaccines, maintenance of the cold chain, and estimation of vaccine requirements.

(6) Assess the quality of the cold chain in the remaining counties.

(7) Request the Ministry of Health (Division of Epidemiology), which is responsible for the coordination of the Public Health Services, to organize random cold chain monitor studies to evaluate the progress being made in improving the cold chain. This progress should be reported to the Expanded Programme on Immunization at the WHO Regional Office for Europe in Copenhagen.

[g] *WHO Immunization policies in Europe. Report on a WHO meeting, Karlovy Vary, Czechoslovakia, 10–12 December 1984.* Unpublished document WHO-EURO ICP/EPI 001, Copenhagen, 1986.

[h] **Vass, A.** The Hungarian practice of immunization and its results. In: Fillastre, C., ed. *Childhood immunization acceptability. Seminar on 24–26 February 1986, International Children's Centre, Paris.*

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Résumé

Transport et stockage des vaccins en Hongrie: première étude sur la chaîne du froid en Europe

Avec l'aide de l'OMS, le Ministère hongrois de la Santé a organisé deux études de la chaîne du froid: la première a eu lieu dans trois départements en été (1er juillet au 30 septembre 1987), et la seconde dans six départements (y compris les trois précédents) en hiver (1er janvier au 31 mars 1988). Les départements ont été choisis en fonction de leur éloignement de Budapest (50–300 km). A l'intérieur de chaque département, un certain nombre de districts et de centres de santé infantile ont été choisis au hasard. Tous les participants ont reçu une formation avant le début des études. Les vaccins (DCT, anti-rougeoleux et BCG), munis d'indicateurs de contrôle de la chaîne du froid, ont été transportés depuis les établissements producteurs jusqu'aux centres de santé infantile grâce au système normal de distribution existant dans le pays. L'efficacité de la chaîne du froid a été analysée en ce qui concerne: 1) les cas réels d'exposition à des températures anormales et les retards de distribution; 2) les endroits où ces expositions du retards se sont produits; 3) le pourcentage de vaccins présentant un risque de détérioration (réel ou prévu) à la fin de l'étude; et 4) l'efficacité des différents types de réfrigérateurs utilisés.

L'évaluation des résultats à l'aide du logiciel EPIC de l'OMS a permis de constater des écarts significatifs par rapport aux normes considérées comme acceptables. La première étude de la chaîne du froid réalisée en Europe montre que, même dans un pays au climat tempéré où les services de santé publique sont relativement bien organisés, le transport et le stockage des vaccins peuvent présenter des points faibles. Des recommandations visant à corriger la situation ont été formulées.

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2. **Battersby, A. & Jansdaal, P.** *How to choose and make a cold box.* London, AHRTAG, 1983.