Frequent exposure to suboptimal temperatures in vaccine cold-chain system in India: results of temperature monitoring in 10 states

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Objective To estimate the proportion of time the vaccines in the cold-chain system in India are exposed to temperatures of < 0 or > 8 °C.
Methods In each of 10 states, the largest district and the one most distant from the state capital were selected for study. Four boxes, each containing an electronic temperature recorder and two vials of diphtheria, pertussis and tetanus vaccine, were placed in the state or regional vaccine store for each study state. Two of these boxes were then shipped – one per facility – towards the two most peripheral health facilities where vaccine was stored in each study district. The boxes were shipped, handled and stored as if they were routine vaccine supplies.
Findings In state, regional and district vaccine stores and peripheral health facilities, respectively, the temperatures in the boxes exceeded 8 °C for 14.3%, 13.2%, 8.3% and 14.7% of their combined storage times and fell below 0 °C for 1.5%, 0.2%, 0.6% and 10.5% of these times. The boxes also spent about 18% and 7% of their combined times in transit at < 0 and > 8 °C, respectively. In shake tests conducted at the end of the study, two thirds of the vaccine vials in the boxes showed evidence of freezing.
Conclusion While exposure to temperatures above 8 °C occurred at every level of vaccine storage, exposure to subzero temperatures was only frequent during vaccine storage at peripheral facilities and vaccine transportation. Systematic efforts are needed to improve temperature monitoring in the cold-chain system in India.

Abstracts in عربي, 中文, Français, Русский and Español at the end of each article.

Introduction

Childhood immunization is one of the most cost-effective health interventions.[1] Since most vaccines are sensitive to heat, an adequate cold-chain system often has to be created and maintained to preserve the quality of a vaccine before it is administered. Although emphasis has long been placed on avoiding high temperatures during vaccine storage and shipment,[2] exposure to "subzero" temperatures – i.e. temperatures < 0 °C – can also damage and reduce the potency of the diphtheria, tetanus and pertussis (DPT), diphtheria and tetanus, tetanus toxoid, hepatitis B and pentavalent vaccines.[3–9] The World Health Organization (WHO) recommends that all childhood vaccines except the oral polio vaccine be kept at 2–8 °C during their in-country distribution.[10]

In India, the Universal Immunization Programme targets 27 million infants and 30 million pregnant women every year.[10] The focus of the programme is on the vaccination of children aged less than 1 year against six vaccine-preventable diseases – tuberculosis, diphtheria, tetanus, pertussis, polio and measles – and the vaccination of pregnant women against tetanus. In some states, vaccines against hepatitis B and Japanese encephalitis are also included in the programme. There is a five-level supply chain for vaccines in India. This chain begins with government medical supply depots ($n = 4$). These depots supply state vaccine stores ($n = 35$), which, in turn, supply regional vaccine stores ($n = 116$). Vaccine is sent from the regional stores to district vaccine stores ($n = 626$), which, in turn, supply the last links in the chain: the primary or community health centres that act as peripheral vaccine stores ($n = 26\,439$).[10] Note that, in terms of the cold chain, a region is a subdivision of a state, not vice versa. Within this chain, all vaccines except the oral polio vaccine should be stored at 2–8 °C – either in walk-in coolers or ice-lined refrigerators – and be transported in cold boxes with ice packs that have been allowed to reach 0 °C. Although most of the cold-chain equipment in India is maintained by dedicated "cold-chain technicians" who are employed by the state-level departments of health, a few states buy such maintenance from the private sector. Immunization services in the public sector are mostly provided at district hospitals, urban health centres and

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primary or community health centres. However, outreach vaccination sessions at health subcentres or in remote villages are also conducted, using vaccine transported from the nearest primary or community health centre.

In India, several studies have assessed the exposure of vaccines to high temperatures.[11–13] However, there appears to be no information on vaccine exposure to subzero temperatures in the national cold-chain system. We therefore conducted a study to estimate the frequency of vaccine exposure to suboptimal temperatures – i.e. temperatures of < 0 or > 8 °C – at various levels in the cold chain.

Methods

Selection of study sites

The study was conducted, from February to August 2012, by following a WHO protocol for monitoring temperatures in a cold-chain system for vaccines.[2] Ten Indian states – Bihar and West Bengal in the east of the country, Arunachal Pradesh and Manipur in the north-east, Himachal Pradesh in the north, Andhra Pradesh, Karnataka and Tamil Nadu in the south, Gujarat in the west, and the central state of Madhya Pradesh – were selected to represent the main geographical regions of India (Appendix A, available at: http://www.nie.gov.in/Bulletin2013/Murhekar/AppendixA.pdf). In each of these 10 states, the district that was most distant from the state capital and the one that was largest in terms of either population ($n = 9$) or number of peripheral vaccine stores ($n = 1$) were selected for study. In each of the 20 selected districts, two peripheral health facilities where vaccine is stored – generally the two that were most distant from the district vaccine store – were selected, to give four peripheral vaccine stores – one urban and three rural – for investigation in each study state. We consulted with the managers of the Universal Immunization Programme to ensure that the peripheral vaccine stores that we selected for study were both accessible and staffed.[2] We also investigated the most distant outreach session run by each of the peripheral vaccine stores that we investigated. In each study state, one or two researchers were responsible for planning, coordinating and monitoring the study.

Test boxes

Forty test boxes – each of which contained a TRIX-8 electronic temperature recorder (LogTag Recorders, Auckland, New Zealand), two vials of DPT vaccine (procured from the state vaccine store for Tamil Nadu in Chennai), a FreezeAlert freeze-event indicator (Sensitech, Beverly, United States of America) and a TransTracker C freeze-event indicator (Temptime, Morris Plains, USA) – were prepared. The recorder used is a datalogger that records temperatures every 30 minutes. The DPT vials passed a shake test[14] – indicating they had never been frozen – before they were placed in the boxes.

Four of these test boxes – one for each of the peripheral vaccine stores that we investigated in the state – were placed in the state vaccine store – or regional vaccine store if no state store existed – in each study state. Each of these boxes was then stored, handled and transported, exactly as if it contained routine supplies of DPT vaccine, to one of the peripheral vaccine stores that we investigated. Each box was stored for at least 1 month in a state vaccine store (if present), 1 month in a regional vaccine store (if present), 1 month in a district vaccine store and 2 weeks in a peripheral vaccine store. Although the card boxes used for the study were the same as those used for routine vaccine shipments in India, they could be identified by the personnel involved in the cold chain. Each test box was accompanied by a monitoring sheet that was used by the staff in each store – or the research teams – to record when the box entered the store and when it left.

Temperature monitoring during outreach sessions

For outreach sessions, the vials of vaccines were routinely placed in polythene bags and transported from peripheral vaccine stores in vaccine carriers. For the present study, a TransTracker C freeze-event indicator was placed in the polythene bag containing the vaccine vials for each outreach session that we investigated. These indicators were checked at the end of the outreach sessions to see if these vials had been exposed to subzero temperatures after they had left the peripheral vaccine stores.

Interviews and store records

In interviews based on a structured questionnaire, the personnel who handled vaccine vials in the cold chain were asked about the maintenance of cold-chain equipment. Records of temperatures that had been routinely kept in each vaccine store were reviewed for the previous 3 months.

Data analysis

At the end of the study, test boxes were collected from the peripheral vaccine stores and transported – at room temperature – to the National Institute of Epidemiology in Chennai. The data from the dataloggers were downloaded and analysed. We calculated the proportions of the 40 boxes that had been exposed to a temperature of < 0 or > 8 °C at each level of the cold chain and while in transit and the percentages of the time that – while stored at each level of the cold chain or in transit – each datalogger had been exposed to a temperature of < 0 or > 8 °C. For each datalogger, we also estimated the longest period of exposure to a temperature of < 0 or > 8 °C, assuming that the datalogger had remained at a similar temperature between two consecutive temperature recordings of < 0 or > 8 °C. The freeze-event indicators in the test boxes were read after the boxes had been transported – unchilled – to Chennai. A shake test was conducted on all DPT vials retrieved from the peripheral vaccine stores.

Approvals

The study protocol was approved by the institutional ethics committee of the National Institute of Epidemiology. Permission to conduct the study was obtained from the Indian Ministry of Health and Family Welfare and the health authorities in each study state.

Results

The 40 dataloggers recorded temperatures over a total of 138 476 hours. The temperature data recorded while the test boxes were in vaccine stores and in transit accounted for > 99% and < 1% of this total time, respectively.

Proportions of boxes exposed to suboptimal temperatures

During their storage at state and regional vaccine stores, 11% (4/36) and 26% (5/19) of the test boxes were exposed to subzero temperatures while 89% and 58% of the boxes were exposed to temperatures of > 8 °C, respectively (Table 1). The corresponding proportions at peripheral vaccine stores were 63% (25/40) and 88% (35/40), respectively. During their transportation – and depending on the level of the cold chain at which the transport began – 18–36% of the test boxes were exposed to subzero

temperatures and 0 to 66% were exposed to temperatures of > 8 °C (Table 1).

Temperatures at vaccine stores

While at state, regional and district vaccine stores, the dataloggers only spent 1.5% (95% confidence interval, CI: 1.4–1.6), 0.2% (95% CI: 0.1–0.2) and 0.6% (95% CI: 0.5–0.7) of their time at subzero temperatures, respectively. Although exposure to such low temperatures was only recorded at one of the state vaccine stores that we investigated – the one for Tamil Nadu (Table 2) – temperatures of > 8 °C were recorded at all of the state stores that we investigated except the one for Tamil Nadu. At regional and district vaccine stores, the dataloggers spent 13.2% and 8.3% of their time at temperatures of > 8 °C, respectively. At the peripheral health facilities, exposure to temperatures of < 0 or > 8 °C was quite common and accounted for 10.5% (95% CI: 10.2–10.8) and 14.7% (95% CI: 14.3–15) of the time that the dataloggers spent in such facilities, respectively. Temperatures of > 8 °C were particularly common in the peripheral vaccine stores in the states of Manipur, Bihar and Madhya Pradesh (Table 3). Overall, temperatures of < 0 and > 8 °C were recorded for 4% and 13% of the combined time –137 519 hours – that the dataloggers recorded temperatures in vaccine stores.

In some vaccine stores, the members of the research team quickly identified the reasons for the suboptimal temperatures that had been recorded. At the state vaccine store in Tamil Nadu, for example, a thermostat had been turned too low, resulting in subzero temperatures, while gaps between the plates forming the walls of the walk-in cooler used by the state vaccine store in Manipur allowed the temperatures in the cooler to rise above the optimal values.

Table 1. **Suboptimal temperatures in the cold-chain system for vaccines, India, 2012**

Distribution stage	No. of test boxes (%)		
	Monitored	Exposed to	
		< 0 °C	> 8 °C
Vaccine storage			
State vaccine store	36	4 (11)	32 (89)
Regional vaccine store	19	5 (26)	11 (58)
District vaccine store	36	8 (22)	15 (42)
Community or primary health centre	40	25 (63)	35 (88)
Vaccine transportation			
State to regional store	15	5 (33)	2 (13)
State to district store	19	6 (32)	8 (42)
Regional to district store	17	3 (18)	6 (35)
District store to community or primary health centre	35	8 (23)	6 (17)
Community health to primary health centre	14	5 (36)	0 (0)
Other route	3	1 (33)	2 (67)

Temperatures during transit

Temperatures during transit between vaccine stores were recorded for a total of 957 hours. Exposures to temperatures of < 0 and > 8 °C were recorded for 173.5 (18.1%; 95% CI: 15.8–20.8) and 69.5 hours (7.3%; 95% CI: 5.8–9.2) in transit, respectively. Exposure to subzero temperatures was particularly frequent during the shipment of the vaccines in Himachal Pradesh (52.2% of transit time), Manipur (25.9%), Arunachal Pradesh (23.6%) and Bihar (18%), whereas exposure to a temperature of > 8 °C during transit was most common in Bihar (23.3% of transit time) and Andhra Pradesh (16.2%) (Table 3).

Temperatures during outreach sessions

Two of the 40 bags of vaccine vials investigated – both used in Tamil Nadu – were found to have been exposed to subzero temperatures during outreach sessions.

Duration of exposure to suboptimal temperatures

"Continuous spells" – that is, periods that covered at least two consecutive readings by a datalogger – accounted for about 85% of the exposure to subzero tempera-

Table 2. **Times that vaccines in state and regional stores spent at suboptimal temperatures, India, 2012**

State	State vaccine stores				Regional vaccine stores			
	OP[a]	% of OP spent at		TR (°C)	OP[a]	% of OP spent at		TR (°C)
		< 0 °C	> 8 °C			< 0 °C	> 8 °C	
Andhra Pradesh	6770.0	0	6	2.3 to 10.6	1769.0	0	0.1	0.3 to 9.8
Arunachal Pradesh	3082.0	0	1.9	3.0 to 14.2	–	–	–	–
Bihar	4733.5	0	16.6	1.0 to 16.2	–	–	–	–
Gujarat	–	–	–	–	3557.0	0	0.5	1.2 to 8.3
Himachal Pradesh	4855.5	0	0.2	3.8 to 17.4	4465.5	0.03	51.3	–3.6 to 15.0
Karnataka	4351.0	0	6.6	0.2 to 15.1	3176.0	0.2	3.5	–2.9 to 20.9
Madhya Pradesh	4522.0	0	28.8	1.9 to 17.0	2359.0	0	0.3	1.3 to 11.4
Manipur	4211.5	0	83.3	3.8 to 17.5	–	–	–	–
Tamil Nadu	6147.0	10.7	0	–2.1 to 7.2	2934.0	0.7	0	–0.8 to 7.1
West Bengal	5958.0	0	0.7	1.4 to 17.9	–	–	–	–
All	**44 630.5**	**1.5**	**14.3**	**–2.1 to 17.9**	**18 260.5**	**0.2**	**13.2**	**–3.6 to 15.0**

OP, observation period; TR, temperature range.
[a] In hours, rounded to the nearest 0.5 hour.

Table 3. **Times that vaccines in district and peripheral stores and in transit spent at suboptimal temperatures, India, 2012**

State	District vaccine stores				Primary or community health centres				In transit			
	OP[a]	% of OP spent at		TR (°C)	OP[a]	% of OP spent at		TR (°C)	OP[a]	% of OP spent at		TR (°C)
		< 0 °C	> 8 °C			< 0 °C	> 8 °C			< 0 °C	> 8 °C	
Andhra Pradesh	3164.0	0	3.3	1.6 to 14.4	2074.0	38.4	2.2	−10.3 to 16.1	89.5	0	16.2	2.7 to 14.1
Arunachal Pradesh	5576.5	3.1	7.4	−2.7 to 16.9	2711.0	0.2	3.1	−4.1 to 22.1	101.5	23.6	0	−5.8 to 7.8
Bihar	4652.5	0	49	1.8 to 24	6056.5	2.6	39.5	−1.9 to 30.6	122.5	18.0	23.3	−2.3 to 16.1
Gujarat	3576.0	0	0	2.6 to 7.9	4404.5	11.4	1.3	−4.8 to 26.9	52.0	0	0	0.5 to 7.6
Himachal Pradesh	745.0	0	0	2.1 to 4.6	4527.5	4.8	1.5	−6.5 to 18.5	189.5	52.2	5.3	−9.1 to 20.2
Karnataka	3366.5	0	0	0.7 to 10.2	4121.5	21.6	0.2	−8.2 to 16.6	76.0	8.6	6.6	−15.0 to 13.5
Madhya Pradesh	4273.0	0	0	0.1 to 9.2	4770.0	11.4	17.4	−8.9 to 26.7	35.5	12.7	8.5	−7.2 to 9.6
Manipur	2323.0	0.1	0	−0.4 to 7.1	5462.0	0.7	40.6	−6.4 to 27.8	13.5	25.9	0	−4.3 to 7.8
Tamil Nadu	2956.0	0	0	0.5 to 5.5	2060.0	0.2	0	−2.6 to 5.3	145.5	8.2	0	−6.7 to 6.0
West Bengal	4047.5	0.8	1.7	−2.4 to 18.2	3761.0	27.8	4.4	−21.3 to 30.6	131.5	1.5	6.5	−0.9 to 15.8
All	**34 680.0**	**0.6**	**8.3**	**−2.7 to 18.2**	**39 948.0**	**10.5**	**14.7**	**−21.3 to 30.6**	**957.0**	**18.1**	**7.3**	**−15.0 to 20.2**

OP, observation period; TR, temperature range.
[a] In hours, rounded to the nearest 0.5 hour.

tures (Table 4) and 94% of the exposure to temperatures of > 8 °C (Table 5) that we recorded.

Temperature monitoring with freeze-event indicators

Although subzero temperatures were recorded by the dataloggers in 34 of the 40 test boxes, the freeze-event indicators in 31 boxes showed evidence of freezing at any point during the study. The results seen with the two types of freeze-event indicators were identical.

Shake test

At the end of the study period, 67 of the 80 DPT vials that had been transported to peripheral vaccine stores were sent to the National Institute of Epidemiology for shake tests. Fifty-one (76%) of these 67 vials failed the test, indicating that the vaccines they contained had been frozen during the study period (Table 4).

Routine temperature monitoring and equipment maintenance

In five of the state vaccine stores that we investigated – those in Andhra Pradesh, Bihar, Madhya Pradesh, Tamil Nadu and West Bengal – wireless dataloggers were being used routinely for temperature monitoring. The staff in the other state vaccine stores – and most of those in vaccine stores at lower levels of the cold chain – relied on the temperatures displayed on the control panels of coolers and refrigerators or on dial thermometers. There was no evidence that any of the devices used for routine temperature monitoring in the vaccine stores had ever been calibrated. Although every vaccine store that we investigated could provide records of the temperatures in the stores for the previous 3 months, there was no evidence to show that these records were routinely reviewed to identify any deviations from the recommended temperatures. Almost all of the routine records of temperature indicated values of 2–8 °C.

Maintenance of the cold-chain equipment in the states of Karnataka, Himachal Pradesh and West Bengal was outsourced to the private sector. In the other states that we investigated, such maintenance was the responsibility of cold-chain technicians employed by the states' health departments. In all of the states, the mean frequency of defrosting of ice-lined refrigerators in primary or community health centres varied from once a week to once a month. The median ages of the walk-in coolers found

Table 4. **Spells of continuous exposure of vaccines to temperatures of < 0 °C and results of shake tests, India, 2012**

State	Exposure to temperatures of < 0 °C						Shake test[a]	
	Total duration[b]	Continuous spells[c]					No. of vials tested	No. of vials that failed
		Combined duration[b]	Total no.	No. of spells lasting (hours)				
				≤ 1	2–9	≥ 10		
Andhra Pradesh	796.5	786.0	23	2	6	15	8	7
Arunachal Pradesh	200.5	166.5	55	9	44	2	1	0
Bihar	181.5	134.5	63	35	26	2	6	2
Gujarat	503.5	487.5	20	1	4	15	8	2
Himachal Pradesh	316.0	254.5	58	42	6	10	8	8
Karnataka	903.5	871.5	44	23	3	18	8	6
Madhya Pradesh	547.0	517.0	54	15	24	15	4	4
Manipur	41.0	34.0	14	4	10	0	8	6
Tamil Nadu	697.0	113.0	178	168	10	0	8	8
West Bengal	1080.5	1041.0	56	15	24	17	8	8
All	**5267.0**	**4404.5**	**565**	**314**	**157**	**94**	**67**	**51**

[a] A vial that failed a shake test at the end of the study was presumed to have been frozen at some point – or points – in the cold chain.
[b] In hours, rounded to the nearest 0.5 hour.
[c] A "continuous spell" at < 0 °C was indicated by a datalogger that showed two or more consecutive readings of < 0 °C.

in state and regional vaccine stores was 12 years (range: 2–27 years) while the median age of the ice-lined refrigerators – which were generally found at lower levels of the cold chain – was 11 years (range: 1–23 years). The irregularity of the power supply was a major issue in all of the facilities that we investigated and especially in the primary or community health centres of Manipur, Bihar, Madhya Pradesh and Tamil Nadu.

Table 5. **Spells of continuous exposure of vaccines to temperatures of > 8 °C, India, 2012**

State	Exposure to temperatures of > 8 °C					
	Total duration[a]	Continuous spells[b]				
		Combined duration[a]	Total no.	No. of spells lasting (hours)		
				≤ 1	2–9	≥ 10
Andhra Pradesh	573.5	468.5	78	24	33	21
Arunachal Pradesh	557.5	491.0	39	4	17	18
Bihar	5488.0	5368.5	194	50	69	75
Gujarat	56.5	53.5	4	1	2	1
Himachal Pradesh	2374.5	2256.5	141	49	59	33
Karnataka	410.0	357.5	70	38	26	6
Madhya Pradesh	2140.5	1833.5	662	490	135	37
Manipur	5726.5	5514.5	249	44	104	101
Tamil Nadu	0.0	0.0	0	0	0	0
West Bengal	284.5	239.5	45	23	14	8
All	**17 611.5**	**16 583.0**	**1482**	**723**	**459**	**300**

[a] In hours, rounded to the nearest 0.5 hour.
[b] A "continuous spell" at > 8 °C was indicated by a datalogger that showed two or more consecutive readings of > 8 °C.

Discussion

In terms of the quantity of vaccines used, numbers of beneficiaries, geographical spread, personnel and cold-chain equipment involved, India has one of the largest immunization programmes in the world.[10] Each year, the country spends more than 500 million United States dollars on its national immunization programme. Several new or underused vaccines are likely to be introduced in this programme in the near future. Maintenance of an adequate cold-chain system is essential if vaccines of good quality are to reach each child or woman to be vaccinated. The present study indicates that – as they work their way from state vaccine stores to the children needing them – the vaccines are frequently exposed to temperatures that are lower or higher than the recommended values, with presumably adverse effects on the quality of the vaccines.

During their storage in the vaccine stores in most of the study states, the vials of vaccine in the test boxes were more frequently exposed to temperatures that were higher than the recommended values than to subzero temperatures. The problem of exposure to high temperatures during storage appeared to be particularly acute in the states of Manipur, Madhya Pradesh, Bihar and Himachal Pradesh. In general, exposure to subzero temperatures was found to be common only during storage at peripheral health facilities and in the relatively short periods that the vaccines were in transit between storage facilities. In a systematic review of the results of 14 investigations on cold-chain systems in developing countries, the summary findings were that 21.9% (95% CI: 10.3–33.6) of the refrigerators used for storage and 35.3% (14.8–55.8) of shipments were exposed to freezing temperatures.[15] Freezing during transportation is usually the result of the use of ice packs that have not been properly "conditioned" – that is, allowed to warm to 0 °C before use.[16,17]

In general, vaccine stability and potency are both temperature-dependent. Excessive heat can alter the protein structure and/or chemical stability of a vaccine and result in loss of potency.

Lyophilized vaccines such as measles vaccines need to be kept cold and to be used within 4 hours after they have been reconstituted. Otherwise, such vaccines lose stability and are at increased risk of bacterial contamination. Exposure to freezing causes agglomeration of the aluminium salt adjuvants used in DPT and hepatitis vaccines[4,18] and – since the size of the granules that form increases on repeated freezing and thawing[19] – exposure to freezing probably has a cumulative adverse effect. In laboratory studies, the freezing of a vaccine has been found to cause the antigen to become disassociated from the adjuvant and reduce immunogenicity.[3] DPT, diphtheria and tetanus and tetanus toxoid vaccines that have been frozen are more likely to cause local reactions than vaccines that have never been frozen.[3] Although there is little direct evidence of vaccine failure in the field as the result of exposure of the vaccine to subzero temperatures, there have been a few reports from Mongolia of lower antibody responses to hepatitis B vaccine as the result of vaccine freezing.[20,21]

The main aim of the present study was to evaluate the extremes of temperature that occurred in India's national cold-chain system for vaccines. However, the members of the research team sometimes easily identified the reasons why vaccines were being exposed to suboptimal temperatures – such as an incorrectly set thermostat. The causes of the suboptimal temperatures recorded in all of the vaccine stores need to be identified. There seemed to be a general lack of attention to detail: the devices used for the routine monitoring of the temperatures in vaccine stores had never been calibrated, the temperature measurements that were made routinely were not regularly reviewed, and there was rarely a fixed schedule for the defrosting of refrigerators. Power cuts, shortages of trained personnel and irregular defrosting of refrigerators appeared to be the key issues affecting the maintenance of the cold chain at the district and subdistrict vaccine stores. The evidence for vaccine freezing during transport pointed towards the need for the conditioning of the ice packs used to keep the vaccines cool while in transit.[16,17]

Our study has certain limitations. Temperatures during the transport of vaccine from the peripheral stores to outreach sessions were only monitored with freeze-event indicators and not with the more informative dataloggers. Although the dataloggers were often exposed to temperatures of > 8 °C, we were not able to determine if such temperatures damaged the vaccine and we made no attempt to test the potency of the vaccine in each of the vials in the test boxes at the end of the study. Unfortunately, all of the DPT vials used in the study had been procured from the state vaccine store in Tamil Nadu – the only state vaccine store where our dataloggers recorded subzero temperatures. Although shake testing of these DPT vials indicated that none had been frozen before the start of our study, it remains possible – and perhaps probable – that they had already been exposed to subzero temperatures at that stage. The high number of DPT vials that failed the shake test at the end of our study may therefore have reflected the cumulative effect of exposures to subzero temperatures in the cold-chain system during our study and similar exposures at the state vaccine store at Tamil Nadu before the study began.

Based on the findings of our study, we propose several recommendations for improving the maintenance of the Indian cold chain. Briefly, there is an urgent need to identify the reasons for the suboptimal temperatures recorded in state, regional and district vaccine stores and to ensure the continuous and accurate monitoring of temperatures in these stores, using digital devices. There is a need to conduct refresher training of the staff of the peripheral stores, with emphasis on the regular defrosting of refrigerators. All staff involved in the transport of vaccines need to be taught how to condition ice packs, and the supervision of the monitoring of cold-chain temperatures needs to be improved. At all levels, there is a need for regular calibration of the devices used to record temperatures. Programme managers at all levels of the cold chain need to review temperature records regularly. The recording of a suboptimal temperature should prompt a rapid corrective response, such as a request for a visit from a cold-chain technician. Although a good cold-chain system may appear expensive, it is likely to be cost-effective, especially whenever costly combination vaccines need to be used in developing countries. Although the development of thermostable vaccines could improve vaccine effectiveness and decrease the need for a cold chain,[22,23] such vaccines will probably be expensive, at least when they are initially marketed. Developing countries are therefore likely to need effective cold-chain systems for many more years. ■

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ملخص

التعرض المتكرر لدرجات حرارة دون المستوى الأمثل في نظام سلسلة تبريد اللقاحات في الهند: نتائج رصد درجة الحرارة في 10 ولايات

الغرض تقدير نسبة الوقت الذي تتعرض خلاله اللقاحات في نظام سلسلة التبريد في الهند لدرجات حرارة < 0 أو > 8 درجات مئوية.

الطريقة في كل ولاية من الولايات العشر، تم اختيار المنطقة الأكبر والأبعد عن عاصمة الولاية من أجل الدراسة. وتم وضع أربعة صناديق، يحتوي كل منها على مسجل إلكتروني لدرجة الحرارة وقنينتين من لقاح الخناق والشاهوق والكزاز في مخزن اللقاحات في الولاية أو الإقليم لكل ولاية من ولايات الدراسة. وبعد ذلك يتم شحن اثنين من تلك الصناديق – واحد لكل مرفق – إلى أبعد مرفقين من المرافق الصحية الطرفية حيث يتم تخزين اللقاحات في كل منطقة من مناطق الدراسة. وتم شحن الصناديق ومناولتها وتخزينها كما لو كانت إمدادات لقاحات روتينية.

النتائج في مخازن الولاية والإقليم والمنطقة والمرافق الصحية

الاستنتاج رغم أن التعرض لدرجات حرارة فوق 8 درجات مئوية قد حدث في كل مستوى من مستويات تخزين اللقاح، إلا أن التعرض لدرجات حرارة تحت الصفر تكرر فقط خلال تخزين اللقاحات في المرافق الطرفية ونقل اللقاحات. وهناك حاجة لجهود منظمة لتحسين رصد درجة الحرارة والتحكم فيها في نظام سلسلة التبريد في الهند.

الطرفية، على التوالي، تجاوزت درجات الحرارة في الصناديق 8 درجات مئوية بالنسبة إلى 14.3 ٪ و13.2 ٪ و8.3 ٪ و14.7 ٪ من أوقات تخزينها المجمعة وانخفضت دون 0 درجة مئوية بالنسبة إلى 1.5 ٪ و0.2 ٪ و0.6 ٪ و10.5 ٪ من تلك الأوقات. وقضت الصناديق أيضاً حوالي 18 ٪ و7 ٪ من أوقاتها المجمعة أثناء النقل في درجة حرارة < 0 و> 8 درجات مئوية على التوالي. وفي اختبارات الاهتزاز التي تم إجراؤها في نهاية الدراسة، أظهر ثلثا قناني اللقاحات في الصناديق علامات على التجمد.

摘要

印度疫苗冷链系统频繁处于次优温度：十个邦的温度监控结果

目的 估计印度冷链系统中疫苗处于<0或>8 ° C温度的时间比例。

方法 在十个邦中，选择每个邦最大的县和距离邦首府最远的县进行研究。在每个研究邦的邦或区域疫苗储放点中放置四个盒子，每个盒子包含一个电子温度记录器和两瓶白喉、百日咳和破伤风疫苗试剂。然后将其中两个盒子运送到每个研究县储存疫苗的两个最外围卫生设施处，每个设施一盒。将这些盒子按常规疫苗供应一样运送、处理和储存。

结果 在邦、区域和县疫苗存放点以及外围卫生设施中，盒子中的温度超过8 ° C的时间占其组合储存时间的比例分别为14.3%、13.2%、8.3%和14.7%，低于0 ° C的时间比例为1.5%、0.2%、0.6%和10.5%。在运输过程中，这些盒子处于< 0 和> 8 ° C温度的时间占组合时间的比例也分别是18%和7%。在研究结束时执行的振荡测试中，盒子中三分之二的疫苗试剂显示出冻结的证据。

结论 在各级疫苗储存中都有温度超过 8 ° C 的情况发生，但频繁出现温度低于零度的情况仅在外围设施疫苗储存和疫苗运输过程中出现。要改善印度冷链系统中的温度监控和控制，需要付出系统性的努力。

Résumé

Exposition fréquente à des températures suboptimales dans la chaîne du froid des vaccins en Inde: résultats du suivi des températures dans 10 états

Objectif Estimer le pourcentage du temps d'exposition des vaccins à des températures inférieures à 0°C ou supérieures à 8°C dans la chaîne du froid en Inde.

Méthodes Dans chacun des 10 états, le district le plus grand et le district le plus éloigné de la capitale de l'état ont été sélectionnés pour cette étude. Quatre boîtes, contenant chacune un enregistreur de température électronique et deux flacons de vaccin contre la diphtérie, la coqueluche et le tétanos, ont été placées dans le dépôt des vaccins de la région ou de l'état pour chaque état étudié. Deux de ces boîtes – une par centre – ont été ensuite expédiées vers les deux centres de santé les plus périphériques où les vaccins sont stockés dans chaque district de l'étude. Les boîtes ont été expédiées, manipulées et stockées comme des boîtes de vaccins habituelles.

Résultats Dans les dépôts de vaccins de l'état, de la région et du district et dans les centres de santé périphériques, les températures à l'intérieur des boîtes ont été supérieures à 8°C pour, respectivement, 14,3%, 13,2%, 8,3% et 14,7% de leurs temps de stockage combinés et inférieures à 0°C pour, respectivement, 1,5%, 0,2%, 0,6% et 10,5% de ces durées. Les boîtes ont également passé environ 18% et 7% de leurs temps combinés en transit à des températures inférieures à 0°C ou supérieures à 8°C, respectivement. Dans les tests d'agitation menés à la fin de l'étude, deux tiers des flacons de vaccins dans les boîtes ont présenté des signes de congélation.

Conclusion Alors que l'exposition à des températures supérieures à 8°C s'est produite à tous les niveaux du stockage des vaccins, l'exposition à des températures inférieures à 0°C n'a été fréquente que pendant le stockage des vaccins dans les centres de santé périphérique et au cours du transport des vaccins. Des efforts systématiques sont nécessaires pour améliorer le suivi et le contrôle des températures dans la chaîne du froid en Inde.

Резюме

Частое воздействие субоптимальных температур в холодовой цепи для вакцин в Индии: результаты температурного мониторинга в 10 штатах

Цель Определить время воздействия температур ниже 0 °C и выше 8 °C на вакцину в системе холодовой цепи Индии.

Методы В каждом из 10 исследуемых штатов был выбран самый крупный и один из самых отдаленных от административного центра округ. В каждом исследуемом штате в хранилище региона или штата были помещены четыре контейнера с электронными регистраторами температуры, в которых находились по две ампулы с вакциной от дифтерии, вакцина от коклюша и вакцина от столбняка. Два контейнера из четырех были отправлены в два наиболее удаленных учреждения здравоохранения (по одному контейнеру в каждое), где хранятся вакцины для исследуемых округов. Погрузка, отправка и хранение контейнеров осуществлялись в соответствии с обычными условиями поставки вакцин.

Результаты В хранилищах штатов, регионов и округов, а также в удаленных здравоохранительных учреждениях среднее время воздействия температуры выше 8 °C составило 14,3%, 13,2%, 8,3% и 14,7% от общего количества времени соответственно, а время воздействия температуры ниже 0 °C составило 1,5%, 0,2%, 0,6% и 10,5% от общего количества времени. Кроме того, во время транспортировки контейнеры подверглись воздействию температур ниже 0 °C и выше 8 °C в течение 18% и 7% от общего

количества времени соответственно. Во время испытаний на пенообразование, проведенных в конце исследования, две трети всех ампул с вакцинами имели признаки замерзания.

Вывод Воздействие температуры, превышающей 8 °C, было обнаружено на всех уровнях хранения вакцин, в то время как воздействие температуры ниже 0 °C было обнаружено во время хранения вакцин в удаленных медицинских учреждениях и во время транспортировки. Для улучшения качества наблюдения и контроля температурного режима холодовой цепи в Индии необходимо приложить планомерные усилия.

Resumen

Exposición frecuente a temperaturas subóptimas en el sistema de la cadena de frío para las vacunas en India: resultados de la monitorización de la temperatura en 10 estados

Objetivo Estimar la proporción de tiempo que las vacunas están expuestas a temperaturas inferiores a 0 o superiores a 8 °C en el sistema de la cadena de frío en India.

Métodos En cada uno de los 10 estados, se seleccionó para el estudio el distrito más extenso y el más distante a la capital del estado. Cuatro cajas, cada una de las cuales contenía un dispositivo electrónico de registro de la temperatura y dos viales de vacunas contra la difteria, tos ferina y tétanos se colocaron en el almacén de vacunas estatal o regional de cada uno de los estados del estudio. Dos de estas cajas se enviaron después – una por cada centro – hacia los centros sanitarios más periféricos, donde la vacuna se almacenó en cada distrito del estudio. Las cajas se enviaron, manipularon y almacenaron como si se tratara de suministros de vacunas rutinarios

Resultados En los almacenes de vacunas estatales, regionales y de distrito, así como en los centros sanitarios periféricos, respectivamente, las temperaturas en el interior de las cajas superaron los 8 °C durante el 14,3%, 13,2%, 8,3% y 14,7% de los períodos de almacenamiento combinados y bajaron de 0 °C durante el 1,5%, 0,2%, 0,6% y 10,5% de dichos períodos. Las cajas también estuvieron por debajo de 0 y por encima de 8 °C, respectivamente, alrededor del 18% y 7% del tiempo de los períodos combinados en tránsito. En las pruebas de agitación realizadas al final del estudio, dos tercios de los viales de vacunas de las cajas mostraron evidencias de congelación.

Conclusión Aunque la exposición a temperaturas superiores a 8 °C se produjo a todos los niveles del almacenamiento de las vacunas, la exposición a temperaturas bajo cero solo fue frecuente durante el almacenamiento en centros periféricos y el transporte. Es preciso realizar esfuerzos sistemáticos para mejorar la monitorización y el control de la temperatura en el sistema de la cadena de frío en India.

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