MALARIA RAPID DIAGNOSTIC TESTS IN TROPICAL CLIMATES: THE NEED FOR A COOL CHAIN

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Abstract. Malaria control programs in endemic countries increasingly rely on early case detection and treatment at village level. The rapid diagnostic tests (RDTs) and accompanying drugs on which the success of these programs depends deteriorate to varying degrees at high temperatures. To assess the ability of health systems to maintain RDTs within manufacturers’ specifications, we monitored temperatures in the delivery chain from manufacturer through to the village health worker in Cambodia and the Philippines. In both countries, storage temperatures regularly exceeded those recommended for most RDTs intended for field use, whereas temperatures during transport greatly exceeded the lower and upper limits. These results emphasize the need for good logistical planning during the introduction of point-of-care tests in tropical countries and the importance of considering the stability of diagnostic tests during procurement.

INTRODUCTION

The storage and use of malaria rapid diagnostic tests (RDTs) in remote areas presents a new challenge to many health systems. These devices, with limited shelf life and subject to degradation by the environment, are increasingly being deployed to remote and poorly resourced areas where users have limited supervision. In these settings, health personnel will rely on the RDTs to make potentially life-saving treatment decisions.

Exposure to high temperatures has the potential to degrade RDTs. Most manufacturers recommend storage between 4°C to 30°C, and shelf life is based on this assumption, but refrigeration and air-conditioning is commonly unavailable in malaria endemic areas where RDTs are intended for use. To document the conditions to which malaria RDTs are likely to be subjected in operational use, we monitored the temperatures during storage and routine transport in two countries where they are currently widely used: Cambodia and the Philippines. Drugs, including artemisinin-combination therapy (ACT), are transported and stored under similar conditions, and appreciating the environment to which RDTs and ACT are subject during routine use has important implications for the design of early case detection and treatment programs.

MATERIALS AND METHODS

Temperature monitoring. All temperatures were recorded using electronic temperature monitors (Smart Button Temperature Logger; ACR Systems, Surrey, Canada; range −10°C to +85°C, accuracy ±0.5°C) stored with the RDTs and programmed to record every 20 or 30 minutes during inter-country and in-country transport and every hour during long-term storage. Whenever the RDTs were moved, the date and information on the type of transport (aircraft, car, boat, foot) were recorded. Monitors in storage facilities were replaced every 10 weeks. Stored data was downloaded from the monitors, and daily and monthly temperature averages were calculated using Microsoft Excel.

Cambodia. Cambodia has a tropical climate with a mean annual temperature of 27°C. During the hot season, daytime temperatures may exceed 38°C (Department of Meteorology, Ministry of Water Resources and Meteorology, unpublished data, 2004).

Malaria rapid diagnostic tests arriving in Cambodia are stored at the air-conditioned central medical store (CMS) in the capital, Phnom Penh, before distribution. At the peripheral level, RDTs are commonly stored in rural health centers or in provincial storage facilities with no temperature control. In this study, temperatures were monitored for 12 months (January 2003 to December 2003) in the CMS and two peripheral locations, Sampove Loun hospital and Ankor Ban Health Center, and during road transport between these locations.

The Philippines. The Philippine climate is tropical and has a mean annual temperature of 26.6°C. During the hot season, temperatures rise above 36°C (Philippine Atmospheric, Geophysical and Astronomical Services Administration, Climate Data Section, unpublished data, 2004). RDTs and drugs are stored in the central storage facility of the Department of Health (DoH) in Manila, a building without air-conditioning. In rural malaria-endemic areas, RDTs are typically stored in the home of the village health worker or in the rural health center.

Temperature monitoring was conducted for a consignment of RDTs stored at the central storeroom of DoH for 5 months (April 2003 to August 2003) and for RDTs stored in six remote villages in Palawan Province for 13 months (May 2003 to June 2004). In the villages, the RDTs were stored in the village health workers’ homes, traditional thatched-roofed huts. Temperatures were recorded during transport from DoH to the six villages by aircraft, car, boat, and foot.

Inter-country shipment. Manufacturers of malaria RDTs agreed to include a temperature monitor with the RDTs before sending the consignments to the World Health Organization in the Philippines. Temperatures were monitored every hour during nine shipments.

RESULTS

Storage and transport in Cambodia. Temperatures recorded in the CMS, Phnom Penh, ranged from 18°C to 30°C (mean, 24.2°C). At the provincial locations, temperature...
ranged from 15°C to 42.5°C. The mean annual storage temperature was 23.8°C and 29.3°C at Ankor Ban and Sampove Loun, respectively. Temperatures were more than 30°C for 39% of the recording period at Ankor Ban and 14% at Sampove Loun (Table 1) and were particularly high at Ankor Ban Health Center, where temperatures between 35°C and 40°C were recorded every month (Figure 1).

The transport time from CMS to Ankor Ban Health Center through Sampov Loun was approximately 4 days. During transport, temperatures ranged from 22.5°C to 38.5°C (mean, 29.5°C). Temperature was more than 30°C for 37 hours, which was more than one third of this period (Table 1).

**Storage and transport temperatures the Philippines.** The temperatures in the central storeroom at DoH in Manila ranged from 26°C to 34.5°C (mean, 29.4°C; Table 2). Temperatures were above the recommended 30°C for almost 30% of the monitoring period (Figure 2). In the six villages, temperatures ranged from 19°C to 38.5°C. The mean temperature in the six sites was similar, ranging from 19°C to 38.5°C. The mean temperature in the six sites was similar, ranging from 19°C to 38.5°C. Temperatures more than 30°C were recorded in all locations for a mean 12% of the recording period, but they rarely exceeded 35°C (Table 2). The two RDT distributions rounds from the central storage to the remote health facilities in Palawan took 11 and 16 days in May 2003 and March–April 2004, respectively. The mean temperature during transport was 30°C and 29.3°C, respectively, with a maximum of 49.5°C recorded when the transport vehicle was parked in the shade. During the first distribution round, the RDTs were exposed to temperatures more than 30°C for 114 cumulative hours (>4 days). In the second round, the temperature was above the recommended range for 127 cumulative hours (~5 days; Figure 3).

**Temperatures during inter-country shipment.** The recorded temperatures exceeded 30°C during all the shipments, before or after air shipment or both. In most cases, this was transient, and temperatures rarely surpassed 35°C. In-flight temperatures remained less than 30°C. One consignment of RDTs was frozen during shipment and stored at the airport of arrival in a freezer facility at an average of −3°C (minimum, −5°C), although no markings or documentation requested frozen storage.

**DISCUSSION**

The malaria rapid diagnostic tests monitored in this study were frequently exposed to conditions outside the 4–30°C limits recommended by most manufacturers. Excessive temperatures were documented in all storage facilities except the

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**Table 1**

<table>
<thead>
<tr>
<th>Location</th>
<th>Temperature (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≤ 30°C</td>
</tr>
<tr>
<td>Storage</td>
<td></td>
</tr>
<tr>
<td>CMS</td>
<td>8,520</td>
</tr>
<tr>
<td>Sampove Loun</td>
<td>8,752</td>
</tr>
<tr>
<td>Ankor Ban</td>
<td>8,923</td>
</tr>
<tr>
<td>Transport</td>
<td></td>
</tr>
<tr>
<td>Transport CMS-Ankor Ban*</td>
<td>104</td>
</tr>
</tbody>
</table>

* The RDTs passed through Sampove Loun during transport.

**Figure 1.** Monthly average, maximum, and minimum temperatures in two remote RDT storage facilities, Cambodia.
air-conditioned central storeroom in Cambodia. Excessive heat exposure occurred during transport of RDTs in Cambodia and the Philippines. The temperatures recorded in Cambodia and the Philippines are likely to have a significant impact on performance during the shelf life of some RDTs. Similar or more extreme conditions can be expected in other malaria endemic areas, where seasonal temperatures can reach 45–50°C, and exposure to such conditions may explain published reports of reduced sensitivity or failure of RDTs that performed well in other studies.\(^1\)–\(^9\)

Development of a “cool chain” for RDTs is therefore essential.\(^10,11\) Most health services have experience with short-term requirements for cold chains in remote areas for vaccines. However, while malaria RDTs do not require such stringent temperature control, the requirement to maintain control for prolonged periods at the most peripheral levels will be new to many health services. Temperature control of central storage facilities should be a basic requirement if storage is prolonged.\(^12\) In remote health facilities, simple and inexpensive evaporative cooling boxes may offer a solution to the problem of high temperatures during long-term storage, and thatch roofs are likely to be cooler than iron roofs. Recent unpublished trials in Cambodia with evaporative cooling boxes designed for RDT storage indicate that storage temperatures can be reduced considerably (National Malaria Center, Cambodia). The use of cheap temperature monitors, such as vaccine vial monitors (VVMs), to indicate if the product is damaged, should also be studied.\(^13\) However, the effect of cumulative high temperatures on the shelf life of different RDT products needs to be studied to determine the specifications of the appropriate VVMs.

Simple measures during transport from manufacturer and within countries can help avoid exposure of RDTs to high temperatures. These include notifying the shipper/air carrier of storage requirements, notification of arrival, avoid leaving RDTs inside a vehicle in the sun or on an airport tarmac, and transporting the RDTs in vehicles with air-conditioning whenever possible. Transport of RDTs in insulated containers could further reduce large temperature fluctuations. Clear temperature specifications should be displayed on packaging;

<table>
<thead>
<tr>
<th>Location</th>
<th>Total</th>
<th>≤ 30°C</th>
<th>30.1–35°C</th>
<th>35.1–40°C</th>
<th>40.1–45°C</th>
<th>&gt; 45°C</th>
</tr>
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<tbody>
<tr>
<td>Storage</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DoH</td>
<td>2,305</td>
<td>1,665 (72)</td>
<td>640 (28)</td>
<td>0</td>
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<td>0</td>
</tr>
<tr>
<td>Bay Bay Daraga</td>
<td>8,632</td>
<td>7,774 (90)</td>
<td>856 (10)</td>
<td>2 (&lt; 1)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Gugnan I</td>
<td>8,699</td>
<td>7,909 (91)</td>
<td>776 (9)</td>
<td>14 (&lt; 1)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Gugnan II</td>
<td>8,652</td>
<td>7,581 (88)</td>
<td>1,061 (12)</td>
<td>10 (&lt; 1)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Kasuyan</td>
<td>8,608</td>
<td>7,356 (86)</td>
<td>1,246 (14)</td>
<td>6 (&lt; 1)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Marufinas</td>
<td>8,274</td>
<td>7,265 (88)</td>
<td>991 (12)</td>
<td>18 (&lt; 1)</td>
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<td>0</td>
</tr>
<tr>
<td>Tagusao</td>
<td>8,708</td>
<td>8,196 (94)</td>
<td>487 (6)</td>
<td>25 (&lt; 1)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Transport</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Manila-Palawan*</td>
<td>255</td>
<td>141 (55)</td>
<td>103 (40)</td>
<td>6 (2)</td>
<td>2 (&lt; 1)</td>
<td>3 (1)</td>
</tr>
<tr>
<td>Manila-Palawan†</td>
<td>362</td>
<td>235 (65)</td>
<td>110 (30)</td>
<td>11 (3)</td>
<td>6 (2)</td>
<td>0</td>
</tr>
</tbody>
</table>

* May 2003.
† March to April 2004.
the frozen storage recorded in one shipment in this study could destroy some RDTs.

Maintaining transport and storage of RDTs less than 30°C may be impossible in many malaria endemic countries, as shown in this study. Therefore, besides ensuring and monitoring proper transport and storage, it is clearly important to regularly test the sensitivity of the RDTs. Test wells containing recombinant parasite antigen are commercially available and under development, whereas comparison with microscopy in representative sentinel sites may be a useful alternative.

The temperatures documented in Cambodia and in the Philippines have implications beyond the performance of malaria RDTs. Antimalarials and other essential drugs are commonly stored under the same conditions, thus exposing them to temperatures above the recommended maximum storage (e.g., 25°C for artemether-lumefantrine), with the likelihood of reduced drug efficacy. Rapid tests for detection of other diseases are sometimes used and transported in similar conditions, with little quality monitoring, and the implications of low sensitivity of tests for HIV and viral hepatitis to blood banking and case management are clear. Careful planning of distribution and storage, purchasing policies that take product stability and intended conditions of use into account, and consideration of staggered procurement to minimize post-purchase storage time should be part of a national policy for malaria and for other diseases requiring diagnosis and treatment at the periphery of the health service.

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REFERENCES


