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Improving access to antidotes in Thailand

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Improving access to antidotes and antivenoms, Thailand
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Abstract

\textbf{Problem} Historically in Thailand, access to poison antidotes was limited and antivenom stock management was inefficient.

\textbf{Approach} In 2010, the country established a national antidote programme, which created national and subnational antidote stocks, managed their distribution and trained health-care providers on clinical management and antidote use. In 2013, the programme incorporated antivenoms to improve stock management and avoid wastage due to stock expiry.

\textbf{Local setting} Before the programme, health-care providers consulted poison centres on clinical management of poisoning and some antidotes were not available. Individual hospitals stocked antivenoms, which often expired before use.

\textbf{Relevant changes} Today, the National Health Security Office finances and manages the centralized procurement of antidotes and antivenoms and all Thai patients have a right to antidotes regardless of health insurance. National and subnational stock levels are determined based on demand, treatment urgency and cost. A web-based system, which incorporates geographical information, was introduced for requesting antidotes and antivenoms. Poison centres provide training, 24-hour consultation services and outcome monitoring. Antidotes and antivenoms are now readily available and used correctly and clinical management has improved. Moreover, better stock and distribution control has helped avoid antivenom wastage and reduced antivenom costs, from US$ 2.23 million United States dollars (US$) to US$ 1.2 million.

\textbf{Lessons learnt} The programme’s success depended on strong and sustained policy support, adequate funding, improved operational capacity, training for health-care professionals and the provision of 24-hour online consultation services. A web-based centralized procurement and distribution ensured these essential medicines were available, minimized costs, reduced waste and saved lives.

Introduction

According to the Ramathibodi Poison Center in Thailand, there are more than 15 000 cases of poisoning in the country each year.\footnote{However, the true figure may be higher because}
consultations with poison centres are optional. Antidotes are important for treatment and, when they are unavailable, treatment efficacy may be reduced and outcomes compromised. Unfortunately, many antidotes are not readily available. In fact, they have been referred to as orphan drugs because of their scarcity.

In 2002, Thailand achieved universal health coverage when the whole population gained access to three public health insurance systems. The National Health Security Office was established by law to manage the Universal Health Coverage Scheme, which caters for 75% of the population and receives an annual budget funded through general taxation. Although the scheme is comprehensive and includes high-cost medicines, ensuring access to antidotes was initially a challenge because supplies were limited and there was no active management system. In contrast, antivenoms were readily available throughout the country because all hospitals had stocks. However, management was inefficient and some antivenoms passed their expiry dates before they could be used.

The need to improve access to antivenoms has been recognized as a major challenge for low- and middle-income countries and, in 2018, the World Health Assembly adopted a resolution on the burden of snakebite envenoming. Here we describe the lessons learnt in Thailand with a programme designed to increase access to both antidotes and antivenoms and to improve the efficiency of antivenom stock management.

Local setting
The market for antidotes is small, often their patents have expired, demand is unpredictable and profit margins are low. Consequently, the pharmaceutical industry has little incentive to develop and market these medicines, even though they are used for life-threatening conditions. Moreover, antidotes are expensive and have a short shelf life, which discourages individual hospitals from keeping large stocks. The World Health Organization (WHO) recommends establishing a central bank of antidotes as an effective and efficient way of ensuring prompt access to these drugs, thereby saving lives.

In 2002, the National Health Security Office in Thailand set up a special system to improve access to high-cost medicines. Medicines were selected and procured centrally and management of the supply chain was outsourced by the Government Pharmaceutical Organization to the private sector. This resulted in annual savings of a few billion Thai baht (i.e. 50 to 100 million United States dollars; US$). However, although this system improved access to high-cost medicines from 2009 onwards, access to antidotes remained a
major challenge. In contrast, access to antivenoms was not a problem but there was considerable wastage because all hospitals held stocks and drugs often expired before use.

National antidote programme
In 2010, the National Health Security Board established a national antidote programme to ensure equitable access to antidotes for the whole population – not only members of the Universal Health Coverage Scheme. The programme made extensive use of information and communications technology, not only to support procurement and supply chain management, but also for teleconsultations, which enabled frontline health professionals, particularly those in remote areas, to get advice on the proper use of antidotes and on clinical management.

Under the programme, national and subnational stocks of antidotes were established as hubs for supplies. The hubs content is based on three criteria: (i) demand in the local area; (ii) whether an antidote had to be provided urgently; and (iii) cost. Today hospitals request antidotes through a web-based system with a high level of data integrity and security. This system includes data on real-time inventories at all hubs and on expiry dates. The distribution of antidotes to hospitals that request them is managed by the stocking centres and responsibility for replenishing stocks has been outsourced by the Government Pharmaceutical Organization to the private sector. The programme is also involved in training health-care providers on the appropriate use of antidotes: manuals and clinical guidelines have been circulated and in-service training is organized annually (Box 1).

The programme involves close collaboration between several agencies: (i) the National Health Security Office allocates the annual budget and steers and monitors the programme; (ii) the Queen Saovabha Memorial Institute produces antivenom and some antidotes; (iii) the Government Pharmaceutical Organization is responsible for procurement and for managing the supply chain; (iv) the Thai Food and Drug Administration registers medical products; (v) the Thai Society of Clinical Toxicology provides clinical expertise and training; (vi) poison centres at Siriraj and Ramathibodi Hospitals provide clinical consultations; and (vii) the Ramathibodi Poison Center is responsible for monitoring treatment outcomes.

Initially, six antidotes were selected using epidemiological data from the Ramathibodi Poison Center: sodium nitrite, sodium thiosulfate, methylene blue, dimercaprol, succimer and glucagon. Succimer, dimercaprol and glucagon were procured from abroad by the Government Pharmaceutical Organization. Methylene blue, sodium nitrite and sodium
thiosulfate were mainly manufactured by the Queen Saovabha Memorial Institute at a price per vial 30 times lower than imported equivalents.

Antidotes were divided into four categories: (i) critical antidotes, which must be administered in less than 1 hour; (ii) emergency antidotes, to be administered within 1 to 6 hours; (iii) urgent antidotes, to be administered within 6 to 24 hours; and (iv) non-urgent antidotes. In 2018, botulinum antitoxin was held at the Ramathibodi Poison Center only as demand was small and the antidote is very expensive (i.e. up to US$ 12 500 per treatment course), whereas cyanide antidotes were held in subnational stocks because demand was homogenous throughout the country and dimercaprol was held at only a few subnational centres because demand was low and patients were treated in well-equipped hospitals.

Before the programme, individual hospitals procured and stocked snake antivenom themselves without adequate data on poisonous snakes in their localities. Consequently, supply exceeded demand and antivenom was wasted. In response, antivenom was integrated into the programme in 2013 and subnational stocks were adjusted in accordance with local epidemiological data on snake bite cases. This improved the efficiency of stock management and minimized waste. The Queen Saovabha Memorial Institute plays a principal role in producing antivenoms.

General and regional hospitals were invited to serve as subnational centres for stocks of antidotes and antivenoms. In addition, these drugs were included in the national list of essential medicines, which means they are covered by all three public health insurance schemes and their cost is incorporated into annual budgets. As clinical management is as important as the availability of antidotes, annual training for health-care professionals on the use of antidotes was initiated and guidelines on antidote use were distributed. Importantly, poison centres were made responsible for supervising treatment with antidotes and for monitoring clinical outcomes. The operation of the programme is continually being improved with the help of evaluations and reviews. Currently, the programme covers nine antidotes and seven antivenoms.

**Relevant changes**

Since the programme was implemented in 2011, there has been no shortage of any antidote or antivenom covered. Previously, almost no antidotes were available and deaths occurred. Between 2011 and 2017, 1800 patients who were poisoned benefited from the programme. In addition, 25 636 patients exposed to snake venom had access to the appropriate antivenom
and lives were saved. Adjusting the subnational stocking and distribution of antivenom to match the local prevalence of snakebite cases resulted in more efficient stock management and reduced costs: the average annual procurement budget for antivenom decreased from US$ 2.23 million in 2012 when all hospitals purchased their own antivenom to US$ 1.2 million between 2013 and 2017 – a 46% cost saving despite relatively constant demand (Table 1). The effect on mortality was also favourable: mortality due to severe cyanide poisoning decreased from 52.0% before the programme to 28.3% after. There were increases in the overall and appropriate use of antidotes for severe cyanide poisoning, both of which are independently associated with lower mortality.  

**Lesson learnt**

The programme ensured timely access to essential antidotes and antivenoms, which saved lives even though the production and supply of these orphan drugs were limited and there were few clinical toxicologists in the country. Three factors contributed to the programme’s success (Box 2).

First, government policy was strong and sustained across different administrations – annual national budgets allocated full funding to the National Health Security Office for antidotes and antivenoms, which ensured an adequate supply of these essential medicines.

Second, the availability of antidotes and antivenoms was improved operationally by: (i) the use of central procurement; (ii) direct delivery from suppliers to national and subnational stocks; (iii) the creation of a management information system that included the number of doses available and their expiry dates; (iv) use of a web-based system to deal with requests from hospitals; and (v) timely delivery from stocks. These factors combined to ensure the timely use of antidotes and antivenoms and saved lives, even in very remote areas. In addition, the programme discouraged individual hospitals from purchasing and stocking these medicines, thereby decreasing wastage and substantially reducing costs.

Third, the manuals and clinical guidelines produced by poison centres and the annual training provided for clinicians improved case management and confidence in the use of antidotes and antivenoms. In addition, these centres provided 24-hour online consultation services to support case management remotely – clinical toxicologists at the centres could observe patients’ clinical symptoms in real time.
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Competing interests:

None declared.

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Box 1. Components of the Thai national antidote programme, 2010

Financing

• Continued political support ensured that the National Health Security Office received full funding for antidotes and antivenoms for the whole population, thereby protecting against financial risks and saving lives.

Design and operations

• Antidotes and antivenoms were stocked nationally and subnationally, as guided by epidemiological evidence.

• Procurement and supply chain management became more efficient: antidotes and antivenoms were provided rapidly following web-based requests and delivered through vendor-managed inventory systems.

• Efficient procurement and management of antivenoms resulted in substantial cost savings compared with the previous system in which individual hospitals purchased and stocked antivenoms, with the danger of stock expiring.

Capacity building

• Staff capacity was increased through: (i) the circulation of manuals and guidelines; (ii) annual in-service training for health-care professionals; (iii) the establishment of a 24-hour, online, real-time, clinical consultation service to support case management remotely; and (iv) outcome monitoring.

Box 2 Summary of main lessons learnt

• Strong and sustained policy support and full funding from the national budget ensured adequate supplies of essential antidotes and antivenoms.

• Improvements in operational capacity, which included central procurement, national and subnational antidote and antivenom stocks, and distribution aided by information and communication technologies, ensured these medicines were rapidly available for patients and minimized waste due to expired products.

• In-service training and 24-hour online consultations provided by poison centres improved clinical management and helped ensure antidotes and antivenoms were used correctly.
Table 1. **Patients treated and annual budget of the Thai national antidote programme, 2011–2017**

<table>
<thead>
<tr>
<th>Year</th>
<th>Antidotes</th>
<th>Antivenoms</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of patients treated</td>
<td>Budget, US$</td>
<td>No. of patients treated</td>
</tr>
<tr>
<td>2011</td>
<td>49</td>
<td>142 000</td>
<td>NA</td>
</tr>
<tr>
<td>2012</td>
<td>106</td>
<td>422 000</td>
<td>NA</td>
</tr>
<tr>
<td>2013</td>
<td>402</td>
<td>407 000</td>
<td>964</td>
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<td>204 000</td>
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<tr>
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<tr>
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<td>317</td>
<td>283 000</td>
<td>6824</td>
</tr>
<tr>
<td>2017</td>
<td>269</td>
<td>223 000</td>
<td>6648</td>
</tr>
</tbody>
</table>

NA: not applicable; ND: not determined; US$: United States dollar.

<sup>a</sup> One United States dollar was equivalent to approximately 35 Thai baht between 2011 and 2017.

<sup>b</sup> The average total annual cost of individual hospitals purchasing antivenoms during 2011 and 2012.