The changing age structure of diphtheria patients: evidence for the effectiveness of EPI in the Sudan

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During an outbreak of diphtheria in Khartoum, Sudan, in 1988, only 19.1% of patients admitted to hospital were under 5 years of age. This is considerably less than the proportion of such patients seen during a similar outbreak in Khartoum in 1978 (49.5%) and also less than the proportion (55.2%) of under-5-year-olds reported for all inpatients with diphtheria in the Sudan during 1979–86. Cluster surveys carried out between 1981 and 1989 demonstrate that vaccination coverage was much higher for under-5-year-olds (about 65% for the third dose of diphtheria-pertussis-tetanus vaccine (DPT3)) than for children of school age (< 20% for DPT3) at the time of the 1988 outbreak.

These results indicate that improved vaccination coverage led to the shift in the age distribution of diphtheria patients seen during the 1988 outbreak. It is unlikely that these data are affected by the type of biases that usually plague disease surveillance systems and can therefore be used as a simple way of assessing the effectiveness of the Expanded Programme on Immunization (EPI).

In the search for evidence of the effectiveness of the Expanded Programme on Immunization (EPI) in reducing disease-specific morbidity and mortality, much attention has focused on the use of clinic-based surveillance data. Such data are, however, subject to biases that can affect the number of cases reported. One way of using clinic-based data that may avoid such biases is to examine changes in the proportion of patients with characteristics (such as age) that are associated with different levels of vaccination coverage. The present article describes on outbreak of diphtheria in Khartoum, Sudan, in 1988, during which preschool-age children were underrepresented among the cases admitted to hospital. The data from this outbreak are compared with available archival data on diphtheria.

Observations and results

The 1988 outbreak

From 1 August 1988 until 31 December 1988, 209 suspected cases of diphtheria were admitted to two teaching hospitals (Omdurman and Khartoum North) in Khartoum (Fig. 1). Attention to the outbreak was drawn by an EPI staff member in one of the hospitals who noticed a sharp increase in the number of cases admitted to the quarantine unit.

In almost all instances, diphtheria was diagnosed on the basis of clinical presentation rather than on the results of throat swab cultures. Because of the lack of culture medium, only six throat swabs were taken and all were negative. Whether this was due to poor specimen handling, prior treatment of the children with antibiotics, or misdiagnosis could not be determined. None the less, there is considerable evidence that most of the diagnoses were correct. First, all the patients were seen by consultant paediatricians who had a great deal of experience with the disease. Second, an internationally recognized expert in diphtheria confirmed the clinical diagnosis in four suspected patients that he examined. Last, of the six children who died (all the deaths involved children greater than 5 years of age who had not been vaccinated) four exhibited sequelae commonly associated with diphtheria—three died from myocarditis and one from laryngeal obstruction. The causes of death of the other two children were not known.

There was no single focus for the outbreak. Patients came from all parts of Khartoum Province, including rural areas, and no individual neighbour-hood contributed more than 9% of the cases. The two teaching hospitals from where the data in the present study originated were the only hospitals in Khartoum that had functional quarantine units during the outbreak and which also had the facilities to store diphtheria antitoxin.

Age distribution

Cases recorded during the outbreak. The most striking aspect of the 1988 outbreak was the age distribution

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of the patients. As shown in Fig. 2, only 19.1% of the patients were under 5 years of age. The median age of all patients was 8 years, and only 2.8% of cases were infants.

The proportion of cases aged under 5 years in the two study hospitals was very similar (20.6% in Omdurman and 17.8% in Khartoum North).

**Cases from the disease reporting system.** The annual statistics of the Ministry of Health were examined to determine the age distribution of reported cases of diphtheria in the Sudan. Data were available for inpatients from 1979 to 1986. Of the 4202 cases admitted to hospital and reported during these 8 years, 55.2% involved children under 5 years of age. It should be noted that the proportion of cases reported among under-5-year-olds began to decrease in 1984, even though the actual number of cases did not decline consistently (Fig. 3).

Ministry of Health statistics were also available for 1970–77 but these were aggregates of data for in- and outpatients. None the less, the data are consistent with those for 1979–86, with 54.8% of the 8917 reported cases being under 5 years of age.

*Fig. 1. Monthly distribution of the number of cases of diphtheria admitted to two teaching hospitals in Khartoum during the 1988 outbreak.*

*Fig. 2. Age distribution of cases of diphtheria during the 1988 outbreak in Khartoum and for the whole of the Sudan in 1979–86.*
**Fig. 3. Proportion of cases of diphtheria among under-5-year-olds, compared with all cases (all age groups) reported for the whole of the Sudan, 1979–86.**

### Discussion

The 1988 outbreak of diphtheria in Khartoum demonstrates the effectiveness of EPI. That so few of the cases were under 5 years of age indicates that this age group reaped the benefit of high vaccination coverage. Also, since the outbreak involved all areas of the city, many more cases would have been reported among under-5-year-olds had it not been for the success of EPI since 1985.

A well-documented outbreak of diphtheria occurred in Khartoum from early August to mid-November 1978, approximately the same time of year as the 1988 outbreak (1). Of the 107 children who were admitted to one hospital during the 1978 epidemic, 49.5% were under 5 years of age and 1.8% were infants (Table 1). Also, significantly more under-5-year-olds suffered postdiphtheritic complications than did older children (odds ratio, 3.03; 95% confidence interval, 1.13–8.50) (2).

Apart from increased immunization coverage, it is important to examine some of the alternative explanations for the considerably greater proportion of older children among the cases seen during the 1988 outbreak.

Any increase in the enrolment rates in schools between 1978 and 1988 would have meant that proportionally more school-age children were exposed to diphtheria and hence were more likely to catch the disease. However, the available data show that gross school enrolment rates remained essentially constant from 1979–80 (51.5%) to 1985–86 (50%) (3, 4, 6, 7).

It is also unlikely that the commencement of the school term in September could account for the overrepresentation of school-age children among the cases of diphtheria. The term began after the outbreak was well under way, and the age distribution of the patients seen in August 1988 did not differ from that observed after the schools opened (in August, 10 of 47 (21%) cases involved under-5-year-olds; after August, under-5-year-olds represented 18.5% of cases). Also, in 1978, the school term began at approximately the same time, and there was a much lower proportion of cases aged over 5 years.

An improvement in living conditions could have explained the change in the age distribution of the cases of diphtheria in the two outbreaks. However, no such improvement has occurred in the Sudan. For example, the per capita gross national product (GNP) fell by 4.2% per annum over the period 1980–86 (3).

A possible source of bias in our data is that during the 1988 epidemic the diagnosis of diphtheria was not confirmed by culture of throat swabs, whereas during the 1978 outbreak confirmatory diagnosis was routinely carried out.
Data from other countries also support the conclusion that the average age of diphtheria cases increases, in general, as vaccination coverage improves (Table 1). A significant change in the morbidity rates for diphtheria among children under 5 years of age has been reported for Indonesia (5) in a province where vaccination coverage was similar to the current level in Khartoum. Also, a study in Jordan indicates that a comparable change in the age distribution of diphtheria cases occurred when the

Table 1: Comparison of the age distribution of cases of diphtheria in selected developing countries

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>% distribution of cases</th>
<th>Incidence (per 100 000)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sudan (Khartoum)</td>
<td>Yemen Arab Republic</td>
</tr>
<tr>
<td>0–4</td>
<td>19 1</td>
<td>49.5</td>
</tr>
<tr>
<td>5–9</td>
<td>52 1</td>
<td>39.3</td>
</tr>
<tr>
<td>10–14</td>
<td>25 4</td>
<td>11.2</td>
</tr>
<tr>
<td>&gt; 15</td>
<td>3 3</td>
<td>–</td>
</tr>
<tr>
<td>Total number of cases</td>
<td>209</td>
<td>107</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>% DPT1 coverage (age group)</th>
<th>86</th>
<th>&lt;25</th>
<th>40</th>
<th>?</th>
<th>&gt;70</th>
<th>65</th>
<th>85</th>
</tr>
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<tbody>
<tr>
<td>(12–23 months)</td>
<td>(&lt;5 years)</td>
<td>(&lt;5 years)</td>
<td>(15–20 months)</td>
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</tbody>
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*See ref. (2)
*See ref. (3)
*See ref. (6).
*See ref. (5).
vaccination coverage improved (6). Furthermore, in the USA, where vaccination programmes have been operating for many years, less than 25% of cases of diphtheria are under 9 years of age (7).

The shift in the age distribution of cases of diphtheria that we have reported is probably not affected by the biases that usually complicate disease surveillance studies. Changes in the level of reporting effort, in the use of and access to health facilities, or in the accuracy of diagnoses are unlikely to account for any change in the proportion of patients from a particular age group, since an age-specific change in any of these factors is improbable. For example, the proportion of under-5-year-olds admitted to hospital for diseases other than diphtheria was the same both during and before the outbreak.

While diphtheria is not the most common of the EPI target diseases, a decrease in its incidence would be a good marker for the overall success of the programme in reducing overall morbidity and mortality. Monitoring the change in the age distribution of cases of diphtheria is therefore a straightforward, and probably unbiased, way of demonstrating the impact of EPI efforts.

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Résumé

Modification de la répartition par âge des malades atteints de diphtérie: confirmation de l'efficacité du PEV au Soudan

Au cours d'une épidémie de diphtérie survenue à Khartoum, au Soudan, en 1988, seuls 19,1% des malades admis à l'hôpital avaient moins de 5 ans. Ce chiffre est très nettement inférieur à la proportion de malades de cet âge enregistrée au cours d'une épidémie semblable en 1978 (49,5%). Les données du Ministère soudanais de la Santé indiquent que 55,2% des malades hospitalisés pour diphtérie dans l'ensemble du pays au cours de la période 1979-1986 étaient âgés de moins de 5 ans. Les données globales provenant de la même source montrent que 54,8% des sujets atteints de diphtérie, qu'ils aient été ou non hospitalisés, pendant la période 1970-1977, étaient des enfants d'âge préscolaire.

Des sondages par grappes effectués entre 1981 et 1989 ont montré que la couverture par le vaccin antitétanique-antitétanique-anticoquelucheux progressait régulièrement. Au moment de l'épidémie de 1988, la couverture des moins de 5 ans par la troisième dose de vaccin était de 65%, alors que celle des enfants d'âge scolaire était de moins de 20%.

Ces résultats indiquent que l'amélioration de la couverture vaccinale a provoqué un déplacement vers le haut de la répartition par âge des malades atteints de diphtérie. Il est peu probable que ces données aient été influencées par les biais généralement rencontrés dans les systèmes de surveillance des maladies. Ces biais courants, qui sont, par exemple, des modifications dans le taux de notification, dans l'utilisation des services de santé ou dans les critères diagnostiques retenus, sont peu susceptibles d'avoir eu une influence sur la proportion des malades dans le groupe des moins de 5 ans.

Aux États-Unis d'Amérique, en Indonésie et en Jordanie on a observé le même glissement de la répartition par âge des malades atteints de diphtérie, lié à l'augmentation du taux de couverture vaccinale. L'analyse de la distribution par âge des malades atteints de diphtérie constitue donc une manière simple d'évaluer l'efficacité du Programme élargi de Vaccination (PEV).

References
