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Epidemic diphtheria reemerged in the republic of Georgia in 1993. From 1993 to 1997, 1405 cases were reported (28 in 1993, 312 in 1994, 429 in 1995, 348 in 1996, and 288 in 1997), with a cumulative incidence of 25.8/100,000 and a case fatality ratio of 9.5%. During 1993–1997, 53% of the diphtheria cases occurred among persons ≥15 years of age. Unvaccinated patients were more likely to have toxic forms (relative risk = 2.24; 95% confidence interval = 1.69–2.96) or to die of diphtheria (relative risk = 2.24; 95% confidence interval = 1.36–3.68) than those who had received at least one dose of diphtheria toxoid. Improvement in routine childhood vaccination coverage and implementation of mass adult vaccination campaigns have been critical to bringing the epidemic under control. By mid-1998, the overall diphtheria situation in Georgia appeared to have been controlled. Only 53 cases were reported from January to June 1998, representing a 64% decrease from the 148 cases during the corresponding period in 1997.

Background

This report describes the diphtheria outbreak in the republic of Georgia in the 1990s and is based on data from the national communicable disease surveillance system of the Ministry of Health (MOH) of Georgia. Brief basic information on Georgia is presented in table 1.

Diphtheria was widespread in Georgia in the prevaccine era. The reported incidence throughout 1930 to the 1950s varied from 26 to 77 cases per 100,000 population.

Vaccination against diphtheria in Georgia was first introduced in 1927. Vaccination with 3 doses of Ramon toxoid was practiced beginning in 1932. Precipitated toxoid was also in use for a limited period of time (1935–1937). The targeted age group for diphtheria vaccination was those persons who were 1–8 years old. Two booster doses were added to the schedule in 1944; however, the scope of diphtheria vaccination efforts until 1958 was limited. No reliable coverage information for the early period is available [1].

In the 1950s, Georgia experienced a major diphtheria outbreak, resulting in >14,000 cases and >700 deaths during 1955–1960 (figure 1). This outbreak was effectively controlled with the implementation of universal routine childhood immunization against diphtheria beginning in 1958. The number of cases declined dramatically from a peak of 3160 (incidence, 77/100,000) in 1958 to 852 (incidence, 20/100,000) in 1961 and to 9 (incidence, 0.19/100,000) in 1967. As a consequence of this successful universal routine childhood vaccination program, diphtheria was virtually eliminated in Georgia. Only 23 cases were reported during 1970–1986.

The number of reported diphtheria cases in Georgia increased slightly beginning in 1987 (13 reported cases each in 1987 and 1990). This increase coincided with changes in immunization practices. Following a virtual absence of the disease for many years, the awareness of risks from diphtheria decreased, and concerns regarding potential adverse effects of vaccination led to elaboration of a long list of contraindications. This affected vaccination coverage rates, although the coverage decline was not always reflected in official data. In 1986, the age for administration of the fifth dose of diphtheria toxoid was increased from 6 to 9 years (table 2). Also in 1986, Td (tetanus-diphtheria toxoids; known in the former USSR under the name of ADS-m) was allowed for primary immunization of infants as an acceptable alternative to immunization with diphtheria-tetanus-pertussis or diphtheria-tetanus (DTP/DT) vaccine. In addition, in 1986, the MOH of the Union of Soviet Socialist Republics added adult decennialTd booster doses at the ages of 26, 36, 46, and 56 years to the immunization schedule (Order no. 450); however, this mandate was not implemented in Georgia.

The events in Georgia and other parts of the former Soviet Union in the early 1990s had a profound impact on the diphtheria situation as well. Georgia regained its independence in 1990, but two ethnic conflicts (in former South Ossetia [in present territory of Shida Kartli] and Abkhazia) resulting in ~300,000 refugees and internally displaced persons, a civil war, a catastrophic economic crisis, and a severe energy shortage caused significant damage to the health care system. The most
important consequences of these events, with relevance to the diphtheria outbreak, follow:

- No vaccines were supplied to Georgia for nearly 2 years in the early 1990s due to discontinuation of vaccine supplies from Russia and the absence of alternative sources; thus, routine infant immunization was severely affected. Reported coverage with three doses of DTP/DT (DTP3/DT3) was <60% for 1992–1995 (table 3).
- The severe energy shortage, together with the lack of necessary reagents, greatly reduced laboratory capacities.
- Disruption of communication services resulted in incomplete and delayed reporting.
- As a part of the major health reform in Georgia beginning in 1995, the Public Health Department was separated from the old Sanitary-Epidemiologic Service. The process of transition took >1 year, resulting in uncertainties about division of responsibilities and a loss of skilled personnel.
- Due to economic hardship and transportation problems, access to health care became difficult, particularly in remote rural places.

All of the above conditions facilitated the large-scale spread within Georgia of the diphtheria epidemic, which started in Russia in the early 1990s.

### Descriptive Epidemiology

Epidemic diphtheria reemerged in Georgia in 1993. Twenty-eight cases (incidence, 0.5/100,000), the highest number since 1966, were reported in Georgia in 1993 (figure 1). The number of reported cases increased 11-fold to 312 (incidence, 5.7/100,000) in 1994 and peaked to 429 cases (incidence, 7.9/100,000) in 1995. The number of cases declined by ~19% in both 1996 and 1997 to 348 (incidence, 6.4/100,000) and 288 (incidence, 5.3/100,000) cases, respectively. A total of 1405 cases were reported during 1993–1997 (cumulative incidence, 25.8/100,000). Fifty-three diphtheria cases and 2 deaths were reported in Georgia in January through June 1998 (preliminary data). No information is available since 1993 from Abkhazia and parts of the former Southern Ossetian Autonomous Oblast, which are now controlled by separatists.

Although sporadic cases of diphtheria have been reported in different regions of Georgia since May 1993, a large-scale outbreak began in Ajara. By 1994, the epidemic had spread throughout the country. During 1993–1997, cases were reported from all but one region (Racha-Lechkhumi and Kvemo Svaneti) of Georgia (figure 2). However, more than two-thirds of the cases each year occurred in either Ajara or the capital city of Tbilisi. Cumulative diphtheria incidence rates (per 100,000) for 1993–1997 were highest for Ajara (155), followed by Guria (47) and Tbilisi (30). The increased incidence of diphtheria in Guria (14% of all cases in 1997) and Imereti (9%) began in 1997. Overall, Ajara and Tbilisi were most affected by the outbreak.

During 1993–1994, diphtheria cases occurred predominantly among children ≤14 years old (79% of cases in 1993, 54% in 1994). As the epidemic evolved, the proportion of cases among adults gradually increased, and in 1997, adults accounted for 62% of all reported cases of diphtheria in Georgia (table 4.1). On a cumulative basis, more than half of all cases (747 or 53%) during 1993–1997 occurred among persons ≥15 years old. Forty-one per cent of all cases occurred among young adults (15–39 years old). Persons ≥40 years of age accounted for only 12% of all cases. The case fatality ratio was highest among children <10 years old (14%), followed by adults ≥40 years old (13%). The case fatality ratio was 9% among persons 10–19 years old and 3.6% among adults 20–39 years old.

During 1993–1995, severe, toxic forms of diphtheria accounted for 25%–31% of all cases. (Patients were classified as having toxic forms of diphtheria if they had anterior neck edema or symptoms of severe systemic toxicity.) The percent of toxic forms decreased to 17% by 1997. The overall case fatality ratio also decreased from 12.5% in 1994 to 5.9% in 1997. Tbilisi and Ajara have had consistently lower case fatality

### Table 2. Recommended vaccination schedules for diphtheria toxoid vaccination in the republic of Georgia.

<table>
<thead>
<tr>
<th>Diphtheria toxoid dose no.</th>
<th>Recommended age for each dose</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Order no. 450, 14 January 1996</td>
</tr>
<tr>
<td>1</td>
<td>3 months</td>
</tr>
<tr>
<td>2</td>
<td>4.5 months</td>
</tr>
<tr>
<td>3</td>
<td>6 months</td>
</tr>
<tr>
<td>4</td>
<td>24–36 months</td>
</tr>
<tr>
<td>5</td>
<td>9 years</td>
</tr>
<tr>
<td>6</td>
<td>16–17 years</td>
</tr>
<tr>
<td>≥7</td>
<td>Every 10 years</td>
</tr>
<tr>
<td></td>
<td>years (not implemented)</td>
</tr>
</tbody>
</table>
ratios than all other regions. For example, in 1994, the case fatality ratio was 8.3% in Tbilisi and 9.2% in Ajara, and in the other regions combined, it was 26.2%.

National surveillance data provided more accurate information on vaccination status of cases beginning in 1996. Only the cases for whom the vaccination information (including vaccination dates) was obtained from their polyclinic records are included in this analysis. During 1993–1997, vaccination status was reported for 811 diphtheria cases (58%), including 64 fatal cases (48%). Overall, 372 of reported cases (46%) were unvaccinated, 224 (28%) had received one or two doses of diphtheria toxoid, and 215 (26%) had received three or more doses. There was a significant decrease in the percentage of unvaccinated cases in 1996–1997 (31%) compared with 1993–1995 (66%, \( P < .001 \)), which is related to successful vaccination efforts beginning in 1995.

Unvaccinated patients were more likely than those who had received at least one dose of diphtheria toxoid to have toxic forms of diphtheria (relative risk \( RR = 2.24 \), 95% confidence interval \( CI = 1.69–2.96 \)) (table 5). Vaccine-induced protection varied according to the age of patients. For patients \(<15\) years old, the receipt of \(\geq 2\) doses of diphtheria toxoid was needed to achieve significant protection from the development of toxic forms of the disease. Unvaccinated patients \(<15\) years old had a 3-fold increased risk of toxic forms of the disease compared with those who had received at least two doses of diphtheria toxoid \( RR = 3.42 \), 95% CI = 2.19–5.32). One dose of diphtheria toxoid provided significant protection from severe diphtheria for adult patients \(\geq 15\) years old \( RR = 1.85 \), 95% CI = 1.21–2.83). Unvaccinated adult patients were at a 4-fold increased risk of toxic forms of the disease compared with adult patients who received \(\geq 2\) doses of the vaccine \( RR = 4.17 \), 95% CI = 1.59–10.89). The greater protection among adults afforded by a single dose was most likely due to a priming effect from earlier childhood vaccination. Older adults may also have been primed naturally in the past when diphtheria was widespread. However, the verification of past immunization history for adults was extremely difficult, as their childhood immunization records were usually unavailable.

During 1993–1997, 41 fatal cases (64%) with known vaccination history occurred among unvaccinated persons; 11 fatal cases were in children \(<16\) years old. Nineteen deaths occurred in children \(\leq 4\) years old (one under \(1\) year old).

![Figure 1](image-url)  
Figure 1. No. of reported diphtheria cases and deaths (no. of deaths available beginning in 1955) in republic of Georgia, 1945–1998 (1998 = preliminary data for January to June).

### Table 3. National diphtheria toxoid vaccination (DTP3/DT3) coverage in republic of Georgia.

<table>
<thead>
<tr>
<th>Year</th>
<th>Coverage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1989</td>
<td>92.5</td>
</tr>
<tr>
<td>1990</td>
<td>91.4</td>
</tr>
<tr>
<td>1991</td>
<td>84.6</td>
</tr>
<tr>
<td>1992</td>
<td>58.3</td>
</tr>
<tr>
<td>1993</td>
<td>54.3</td>
</tr>
<tr>
<td>1994</td>
<td>58.3</td>
</tr>
<tr>
<td>1995</td>
<td>52.6</td>
</tr>
<tr>
<td>1996</td>
<td>83.2</td>
</tr>
<tr>
<td>1997</td>
<td>92.2</td>
</tr>
</tbody>
</table>

**NOTE.** DTP3/DT3, coverage with 3 doses of diphtheria-tetanus-pertussis or diphtheria-tetanus vaccine.
cases (17%) had received 1 or 2 doses of diphtheria toxoid, and
12 (19%) had received three or more doses. The distribution of
fatal cases by vaccination status did not change significantly
over time. Of the 11 fatal cases among children who had re-
portedly received three or more doses of vaccine, 8 had either
received their last dose of vaccine >5 years previously or been
hospitalized ≥4 days after disease onset. Among children, the
receipt of at least 3 doses of diphtheria toxoid was necessary
for significant reduction of the risk of fatal outcome. Unvac-
cinated children with diphtheria were at >3-fold increased risk
of fatal outcome than children who had received ≥3 doses
(RR = 3.57, 95% CI = 1.81–7.05). The effectiveness of diph-
theria toxoid in preventing death was even higher among adults.
No fatal cases were reported among adults who had received
more than one dose of diphtheria toxoid. The RR of diphtheria
death for unvaccinated adult patients compared with those who
had received at least 1 dose of the vaccine was 4.82 (95%
CI = 1.45–15.97).

Laboratory Results

For extended periods of time during 1993–1995, laboratories
were not able to routinely perform cultures for Corynebacterium
diphtheriae. Since 1996, culture has been routinely available in
major centers, such as the National Reference Laboratory at
the National Center for Disease Control (Tbilisi), the Infectious
Disease Hospital laboratory in Tbilisi, and the public health
laboratory in Batumi.

For the whole period of the epidemic, 725 patients underwent
laboratory testing for diphtheria. C. diphtheriae was isolated in
samples from 392 cases (54% of those tested; 28% of all cases).
In 1997, 158 diphtheria patients (55%) had bacteriologic testing.
C. diphtheriae was isolated in 116 cases (73% of those tested;
40% of all cases in 1997). Overall in 1997, 2775 samples were
cultured for diphtheria patients, contacts, and other persons:
The cultures were positive for C. diphtheriae in 254 instances.

Control Measures

The diphtheria epidemic in the republic of Georgia occurred
during the most difficult period in the recent history of the
country, coinciding with the peak of the political and socio-
economic crisis, and diphtheria epidemic control measures were
implemented with the extensive support from the international
donor community.

In late 1993, a workshop held by the World Health Organiza-
tion (WHO) and the REACH (Resources for Children’s
Health) project was instrumental in revising the vaccination

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Figure 2. No. of diphtheria cases (in parentheses) in republic of Georgia by region, 1993–1997. *, no reporting since October 1993.
Table 4. Reported diphtheria cases and deaths by age group, republic of Georgia, 1993–1997.

<table>
<thead>
<tr>
<th>Year</th>
<th>0–4 years</th>
<th>5–9 years</th>
<th>10–14 years</th>
<th>15–19 years</th>
<th>20–29 years</th>
<th>30–39 years</th>
<th>40–49 years</th>
<th>50–59 years</th>
<th>60–69 years</th>
<th>&gt;70 years</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1993</td>
<td>9 (2)</td>
<td>9 (0)</td>
<td>4 (0)</td>
<td>1 (0)</td>
<td>5 (1)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>28 (3)</td>
</tr>
<tr>
<td>1994</td>
<td>50 (9)</td>
<td>68 (10)</td>
<td>49 (7)</td>
<td>30 (3)</td>
<td>38 (4)</td>
<td>39 (1)</td>
<td>22 (2)</td>
<td>14 (3)</td>
<td>2 (0)</td>
<td>0</td>
<td>312 (39)</td>
</tr>
<tr>
<td>1995</td>
<td>55 (12)</td>
<td>65 (14)</td>
<td>87 (10)</td>
<td>42 (5)</td>
<td>83 (3)</td>
<td>56 (1)</td>
<td>30 (5)</td>
<td>8 (0)</td>
<td>2 (0)</td>
<td>1 (1)</td>
<td>429 (51)</td>
</tr>
<tr>
<td>1996</td>
<td>50 (4)</td>
<td>52 (2)</td>
<td>48 (1)</td>
<td>54 (5)</td>
<td>63 (0)</td>
<td>35 (3)</td>
<td>26 (3)</td>
<td>16 (3)</td>
<td>4 (2)</td>
<td>0</td>
<td>348 (23)</td>
</tr>
<tr>
<td>1997</td>
<td>45 (3)</td>
<td>39 (5)</td>
<td>28 (3)</td>
<td>43 (1)</td>
<td>58 (1)</td>
<td>35 (1)</td>
<td>23 (1)</td>
<td>13 (1)</td>
<td>2 (1)</td>
<td>0</td>
<td>288 (17)</td>
</tr>
<tr>
<td>Total for 1993–1997</td>
<td>209 (30)</td>
<td>233 (31)</td>
<td>216 (21)</td>
<td>170 (14)</td>
<td>247 (9)</td>
<td>163 (6)</td>
<td>101 (11)</td>
<td>53 (7)</td>
<td>10 (3)</td>
<td>1 (1)</td>
<td>1405 (133)</td>
</tr>
</tbody>
</table>

schedule and list of contraindications to conform to WHO standards. The revised schedule for routine childhood immunization and the list of contraindications was endorsed by Order number 41 of the MOH of Georgia on 16 February 1994 (table 2).

With vaccine provided by international donors and an improved supply of electricity and completion of the reorganization of the public health service, vaccination (DTP3/DT3) coverage increased from 54% in 1993 to 92% in 1997. However, the reported coverage estimates may not be completely reliable because available population data are inaccurate due to major population shifts that occurred early in the 1990s (there has been no national census since 1989).

Adult vaccination against diphtheria was not implemented in Georgia in the pre-epidemic period. Beginning with 1994, limited adult vaccination was done in Georgia as part of outbreak control measures and contact management. In accordance with the WHO/UNICEF strategy for diphtheria control in the Newly Independent States [2], a mass campaign of immunization with single doses of diphtheria toxoid was targeted at the entire population (those 3–60 years of age). This campaign was implemented on a region-by-region basis from July 1995 through March 1996, starting with Ajara and ending with Tbilisi; it resulted in 83% overall coverage. However, the initial campaign in Tbilisi (December 1995 to March 1996) was inadequate and resulted in a reported coverage of only 66% among 15- to 60-year-old adults. In response, mopping-up vaccination efforts were conducted in Tbilisi in April and May 1997, increasing the percentage of coverage with one dose of Td among adults to 83%.

Serologic studies done by the Tbilisi office of the US Centers for Disease Control and Prevention (CDC) during the 1995 mass immunization campaign in Kakheti region demonstrated high overall immunogenicity with one dose of Td vaccine among 18- to 59-year-old adults. However, these serologic results indicated that after one dose of Td vaccine, many 40- to 59-year-old adults, especially those 40–49 years old, were still susceptible to diphtheria [3]. After serologic and epidemiologic data (the age distribution of cases and deaths) were considered, a decision was made to administer a second dose of Td to 30- to 49-year-old adults. This second-round mass campaign was conducted in September and October 1997 and resulted in 86% reported coverage. A local mopping-up campaign was conducted in Guria region in 1997 in response to the increase in reported cases of diphtheria.

In 1997, routine adult Td booster doses every 10 years (at 24, 34, 44, and 54 years of age) were added to the vaccination schedule. However, due to recent immunization of most adults during mass campaigns, this is not yet being implemented.

In addition to the vaccination efforts directed toward raising population immunity, other control strategies aimed at improvement of case and contact management and surveillance were implemented:

- The timely identification, quarantine, and treatment of patients with diphtheria antitoxin and antibiotic (penicillin G and erythromycin are recommended)
- Identification of close contacts of diphtheria cases
- Vaccination of diphtheria patients (at hospital discharge) and their close contacts
- Bacteriologic investigation of close contacts of diphtheria patients
- Antibiotic treatment of contacts of diphtheria cases (however, antibiotics are sometimes given to culture-positive contacts only)
- Adoption of the WHO case definition for diphtheria and implementation of a standardized diphtheria case report form beginning 1 January 1997
- Introduction of the review of each reported case by an expert national panel for final classification beginning in 1998

Since the beginning of the epidemic, especially since 1995, the MOH had been implementing educational measures on diphtheria diagnosis, treatment, immunization, and surveillance. Training sessions and various publications, including regular reports in the Epidemiology Bulletin of the Ministry, were the most common means of disseminating information. The contact management room, established in 1996 at the Tbilisi Infectious Disease Hospital with the assistance of UNICEF and CDC, was a useful demonstration project on implementation of WHO guidelines on the management of contacts of diphtheria cases.

**Conclusions**

Beginning in 1996, the number of reported cases and deaths in Georgia began to decline, and the proportion of toxic forms...
Table 5. Severity and outcome of diphtheria cases by vaccination status, Georgia, 1993–1997.

<table>
<thead>
<tr>
<th>No. of vaccine doses</th>
<th>Severity</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Toxic</td>
<td>Nontoxic</td>
</tr>
<tr>
<td>0–14 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 doses</td>
<td>33</td>
<td>30</td>
</tr>
<tr>
<td>1 dose</td>
<td>9</td>
<td>11</td>
</tr>
<tr>
<td>2 doses</td>
<td>3</td>
<td>15</td>
</tr>
<tr>
<td>≥3 doses</td>
<td>20</td>
<td>112</td>
</tr>
<tr>
<td>&gt;15 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 doses</td>
<td>66</td>
<td>132</td>
</tr>
<tr>
<td>1 dose</td>
<td>22</td>
<td>100</td>
</tr>
<tr>
<td>≥2 doses</td>
<td>4</td>
<td>46</td>
</tr>
<tr>
<td>All ages</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 doses</td>
<td>99</td>
<td>162</td>
</tr>
<tr>
<td>≥1 dose</td>
<td>58</td>
<td>284</td>
</tr>
</tbody>
</table>

NOTE. RR, relative risk; CI, confidence interval.
<sup>a</sup> Nonsignificant.
<sup>b</sup> P < .05 (Fisher’s test).

...of diphtheria also decreased. The improvement of routine childhood vaccination coverage and implementation of mass adult vaccination campaigns have been critical to bringing the epidemic under control. However, only a 33% decrease in diphtheria cases in 1997 compared with 1995 was achieved in Georgia, compared with a >75% decrease in some other Newly Independent States of the former Soviet Union where mass immunization campaigns were implemented more promptly. This difference can partially be explained by coincidence of the peak of the epidemic with the maximum disruption of the public health system and considerable under-reporting of cases during the early phase of the epidemic.

The sensitivity of diphtheria surveillance in Georgia has improved considerably since 1996. As a result, the actual decline of cases is likely underestimated. In addition, the mass vaccination campaign stretched over a long period of time, and this may have decreased its overall impact. The carrying out of the adult mass vaccination program proved to be most difficult in Tbilisi, with its large, mobile, urban population and dysfunctional polyclinic system. It is now recognized that it was a mistake that Tbilisi, one of the major foci of the epidemic, was the very last site in which the campaign was conducted. The recognition of the crucial importance of adequate social mobilization for the success of the mass immunization campaign was yet another lesson learned from the experience in Tbilisi.

This epidemic affected the entire population of Georgia, including adults. The experience of the present epidemic in Georgia has clearly demonstrated the effectiveness of adult vaccination in preventing severe diphtheria cases and, especially, deaths from diphtheria. Therefore, the future implementation of routine adult diphtheria toxoid immunization must become a priority for the immunization program in Georgia.

Over the past 2 years, diphtheria surveillance in Georgia has improved. The quality and completeness of information on diphtheria cases following the introduction of standardized case report forms have increased considerably. Expert panel review of cases is expected to increase the specificity of the diphtheria surveillance system and address concerns regarding potential over-reporting of diphtheria cases from certain regions with recent increases in the number of predominantly mild cases (e.g., Guria and Imereti). This is especially important because bacteriologic confirmation of cases is not always feasible, and diagnosis is often made on clinical grounds only.

At present, the overall diphtheria situation in Georgia appears to have been controlled. According to the preliminary data for January to June 1998, numbers of reported cases of diphtheria began to decline faster than they had in prior years. Only 53 cases and 2 deaths were reported during this time period, representing a 64% decrease from the 148 cases that occurred during the corresponding period in 1997 and possibly indicating the approaching end of the epidemic.

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References