Diphtheria in the Russian Federation in the 1990s

Svetlana S. Markina,1 Nina M. Maksimova,1
Charles R. Vitek,2 Erika Y. Bogatyreva,1,a
and Anatoly A. Monisov

Abstract

A resurgence of diphtheria spread throughout the Russian Federation in the early 1990s; diphtheria had been well controlled, but circulation of toxigenic strains of Corynebacterium diphtheriae had persisted since the implementation of universal childhood vaccination in the late 1950s. More than 115,000 cases and 3000 deaths were reported from 1990 to 1997, and, in contrast to the situation in the prevaccine era, most of the cases and deaths occurred among adults. Contributing factors included the accumulation of susceptible individuals among both adults and children and probably the introduction of new strains of C. diphtheriae. Vaccine quality, vaccine supply, or access to vaccine providers did not significantly contribute to the epidemic. Mass vaccination of adults and improved childhood immunization controlled the epidemic. High levels of population immunity, especially among children, will be needed to prevent and control similar outbreaks in the future.

Methods

Diphtheria surveillance system. From the 1920s to 1991, the Sanitary-Epidemiologic Service (SES) of the Ministry of Health (MOH) operated a highly organized system for surveillance and control of infectious diseases throughout the Soviet Union; this system was also used to monitor vaccination coverage [5]. In the 1990s, the Russian SES continued to operate public health stations in almost all county-level districts; diphtheria reporting was mandatory from all clinical and laboratory facilities. In 1995, a World Health Organization evaluation found diphtheria reporting in Russia to be highly complete [6].

From the mid-1960s until 1995, standardized report forms from individual diphtheria cases were sent to the MOH from almost all oblasts (states) and were analyzed by the Diphtheria Epidemiology Section at Gabrichevsky Institute (Moscow). After 1995, individual reports were sent to the MOH for clinically severe cases only; summary data were sent for other cases.

Population immunization coverage and immunization status of diphtheria cases. Childhood coverage was monitored by mandatory annual reviews of immunization records at all clinics [5]. Beginning in 1994, adult coverage was measured nationally from reports of all primary care internists; almost all adults were registered with physicians in state clinics. Adults were considered immunized if receipt of ≥1 dose of diphtheria toxoid in the last 10 years was recorded. Childhood vaccination records were retrievable for a small proportion of young adults.

Results

Diphtheria in the Russian Soviet Socialist Republic, 1920–1977. Diphtheria was a highly endemic childhood disease in the prevaccine era. In 1931, immunization against diphtheria began in the Soviet Union in Leningrad, and the next 3 decades saw an expansion and evolution in immunization practices. The initial schedule of three doses at intervals of 15–20 days did not produce immunity in 15% of children, and a revaccination after 3–6 months was added in 1935. In 1940, routine vaccination was recommended for children 1–8 years of age. In 1953, routine vaccination was recommended with two doses at 11 and 12 months of age and a revaccination 6 months later; in 1956, the age for the first dose was lowered to 5 months. Re-vaccinations were added at 4 and 8 years of age in 1947 and at 12 years of age in 1956. Adsorbed toxoid was first used in 1956. Diphtheria and tetanus toxoids with whole-cell pertussis (DTP) vaccine began to be used in 1962, and an adsorbed DTP vaccine with 15 limit of flocculation units (Lf) of diphtheria toxoid, which produced more reliable immunity, began to be used in 1964 [7].
During the 1950s, diphtheria declined sharply in many Russian cities due to immunization. In Leningrad, diphtheria incidence fell from 85 cases/100,000 population in 1952 to 1 case/100,000 in 1958. Mortality from diphtheria among the urban population in the Soviet Union declined >90% from 1949 to 1957. However, the overall incidence remained high in Russia (68 cases/100,000 population; figure 2) and other republics due to incomplete registration and immunization of children. Regional immunization coverage as high as 80%–85% was frequently associated with persistently high rates of diphtheria [8].

In 1959, the Soviet MOH ordered the implementation of a set of diphtheria control measures; major efforts were made to monitor implementation. Immunization was mandatory for all children 5 months to 12 years of age. By 1963, only sporadic cases of diphtheria were reported in most regions of Russia; by 1970, only 0.5 cases/100,000 population were reported. Diphtheria incidence reached a nadir in 1975 (0.03 cases/100,000; figure 2). Despite good surveillance, there were periods of several years in many cities and oblasts in the 1960s and 1970s during which no cases or carriers of diphtheria were reported. Some cities continued to report occasional cases, and ongoing surveillance of selected groups found persistent low-level circulation of toxigenic strains even in the absence of disease [8–9]. Incidence rates in rural areas were higher than in cities [8]; lower levels of immunity among rural children were tied to incomplete immunization coverage [10].

In the mid-1970s, immunization programs had resulted in good control of diphtheria throughout Russia for more than a decade and for 2 decades in some urban areas; elimination of the disease seemed possible. Although circulation of toxigenic strains continued at low levels in some areas, most individuals born since 1950 had not been exposed to diphtheria.

First vaccine era resurgence—1978–1989. Beginning in 1978, an increase in diphtheria was noted. A majority of cases occurred among adults, among whom incidence rates rose more rapidly and to higher levels than among children [11–12]. The
resurgence of diphtheria was associated with a change in the predominant circulating biotype of *Corynebacterium diphtheriae* from gravis (75% of cases in 1975–1976) to mitis (60% of cases in 1977–1981 and 80% of cases in 1982–1986) [11–12]. In response to the resurgence, the SES introduced a more intensive system for control of diphtheria, which included closely following the incidence of disease, the level of population immunity, and the circulation of *C. diphtheriae*. To find even mild diphtheria cases, bacteriologic examination of all cases of pharyngitis was recommended. In 1983, adult immunization was introduced for contacts of diphtheria cases or carriers, for adults in occupational groups found to be at higher risk, and for all adults in some communities with outbreaks [12–13]; however, adult coverage did not exceed 10% in the 1980s.

Other trends resulted in drops in early childhood immunization coverage in the 1980s in many areas, and a small but increasing percentage of children went unvaccinated. The control of many infectious diseases resulted in complacency among pediatricians, who became increasingly concerned about adverse events from vaccination; accepted contraindications were greatly expanded. A study of 1688 3-year-old children in Moscow in 1980–1981 found that 28% of the children were unvaccinated and another 44% had not received the recommended fourth dose of DTP [14]. Medical contraindications were the reason for failure to vaccinate more than two-thirds of the children; parental refusal accounted for <5%. Medical contraindications also resulted in low coverage in other areas [15]. Studies showed that reduced-potency diphtheria-tetanus toxoids (Td) vaccine with 5 Lf of diphtheria toxoid was immunogenic when given for the primary series [16], and Td vaccine was used widely instead of DTP or diphtheria-tetanus toxoids vaccines despite recommendations to limit its use. Later in the 1980s, public support for vaccination fell due to a widely publicized anti-immunization movement.

The peak of the 1980s resurgence occurred in Russia in 1983 (1284 cases) and 1984 (1319 cases; 0.9 cases/100,000 population in each year). Reported cases then gradually decreased to 555 (0.4/100,000) in 1988 and 593 in 1989. During the 1980s, the incidence of diphtheria in Moscow followed a similar trend until 1989 when Moscow reported 94 cases of diphtheria, double the 46 cases reported in 1988. Strains of gravis biotype were isolated from 49% of cases in 1989, compared with 23% of cases in 1988. Six deaths due to diphtheria were reported in Moscow in 1988–1989, although only six total deaths had been reported in 1981–1987 [1].

**Second vaccine era resurgence—1990–1998.** In 1990, Moscow reported 399 cases of diphtheria, a further 4-fold rise; 1211 cases were reported throughout Russia. In 1990, ~25% of cases among children and >95% of cases among adults were among individuals without recorded diphtheria immunization. An increase in internal travel and migration during the early 1990s and a stream of refugees from NIS countries made diphtheria more difficult to control; in 1990, 24 of the 89 Russian oblasts reported cases imported from other oblasts or NIS countries.

In 1991, 1876 cases (1.3/100,000 population) were reported in Russia, and in 1992, the number of cases doubled to 3897 (2.6/100,000). Moscow City and Moscow Oblast (2172 cases) and St. Petersburg City and St. Petersburg Oblast (1210 cases) accounted for almost half of all cases in 1990–1992; these two cities were transportation and economic centers and were the initial destination for most refugees and migrants. In 1992, sharp rises in incidence were reported from almost all regions, especially from European regions, such as Saratov and Kalinin-grad Oblasts and the Northern Caucasus. The incidence rate

---

**Figure 2.** Reported diphtheria cases and incidence in the Russian Federation, 1950–1998
among children exceeded the rate among adults (2.9 vs. 2.5 cases/100,000), and an autumn peak in incidence among both adults and children occurred [16]. This seasonality was characteristic of the prevaccine era and had continued among childhood cases during the 1980s [12]. In 1993, cases increased nearly 3-fold to 15,209 (12.5 cases/100,000), with steep increases in Eastern Siberia. The incidence rate among children exceeded the rate among adults by 60%, and the seasonal rise in cases was pronounced. The epidemic peaked in 1994, when 39,582 cases were reported (26.9 cases/100,000), with 1104 deaths. In 1994, very high rates of diphtheria were reported in Northern European Russia (Karelia, Komi, Leningrad, Novgorod, and Pskov Oblasts), and in Eastern (Irkutsk) and Far Eastern (Primorsky and Magadan) Siberia.

A decrease in the epidemic began in 1995, when the number of cases fell by ~10% to 35,652. In 1996, 13,604 diphtheria cases (9.3/100,000 population, a 62% decrease) were reported, and in 1997, 4057 cases (2.8/100,000) were reported. Nevertheless, in 1996–1997, several oblasts in northwestern European Russia and Eastern Siberia continued to report high rates of diphtheria. In 1996, the incidence in Magadan was 8-fold higher than the national average, and in 1997, it was ~6-fold higher (17 cases/100,000). In 1998, a provisional total of 1436 cases was reported throughout the Russian Federation.

Descriptive epidemiology: In the years 1990–1997, a total of 115,088 cases of diphtheria were reported in Russia, with 3078 fatalities. The Gabrichevsky Institute received detailed age information for 99,861 cases (86.6%) and vaccination history for 52,710 cases (45.7%); age and vaccination information was available for 2967 (96.4%) of the fatal cases. During 1990–1997, 58%–68% of cases reported annually occurred among adults, 6%–8% among adolescents 14–17 years of age, and 27%–32% among children <14 years of age. Overall, ~85% of cases had a mild clinical course.

Among adults, the highest incidence of diphtheria was among those 18–19 years of age and those 40–49 years of age (table 1). The clinical course of diphtheria was mild among >90% of adult cases 18–29 years of age. Childhood coverage among this age group had been very high, and records of adolescent or adult vaccination were found for 61% and 76% of cases in 1994 and 1995, respectively. The highest proportion of severe cases and 40% of all fatalities occurred among adults 40–49 years of age; childhood coverage among these adults had been incomplete, and some of these individuals were not reached by the vaccination efforts in the 1990s. Among adults 40–49 years of age, 74% of cases in 1994 and 46% of cases in 1996 were unimmunized; 28%–30% of unimmunized cases had a severe clinical course.

Overall, the incidence of diphtheria was higher among children than adults; however, the clinical course was mild in ~90% of the infected children. Among children ≤2 years of age, diphtheria incidence was 2- to 4-fold lower than among other children, but the proportion of severe forms of illness and the case fatality rate was much higher (table 1). The proportion of clinically severe cases in this age group decreased as vaccination coverage improved. However, a substantial proportion of the cases were unvaccinated through most years of the resurgence; for example, in 1997, 71% of cases among children <1 year of age and 17% of cases among children 1–2 years of age were unimmunized.

Beginning in 1993, the incidence of diphtheria among children 4–6 years of age matched that among young school-aged children (7–8 years of age). Even as the overall incidence in the population declined in 1996, children 4–8 years of age continued to have the highest rates of diphtheria. The clinical course of illness was mild in ~90% of cases who had received a primary series and one revaccination of diphtheria toxoid, regardless of the type of vaccine (DTP or Td) used in the pri-

### Table 1. Cumulative incidence of, mortality from, and case fatality ratio for diphtheria, by age group, Russian Federation, 1990–1997.

<table>
<thead>
<tr>
<th>Age group, years</th>
<th>Population in 1990–1997 (to nearest thousand)</th>
<th>No. of cases, 1990–1997</th>
<th>Cumulative incidencea (per 100,000)</th>
<th>No. of fatalities, 1990–1997</th>
<th>Cumulative mortalitya (per 100,000)</th>
<th>Case fatality ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1</td>
<td>1,480,000</td>
<td>431</td>
<td>29.1</td>
<td>33</td>
<td>2.2</td>
<td>7.7</td>
</tr>
<tr>
<td>1–2</td>
<td>3,555,000</td>
<td>2280</td>
<td>64.1</td>
<td>156</td>
<td>4.4</td>
<td>6.8</td>
</tr>
<tr>
<td>3–6</td>
<td>9,121,000</td>
<td>10,673</td>
<td>117.0</td>
<td>342</td>
<td>3.8</td>
<td>3.2</td>
</tr>
<tr>
<td>7–14</td>
<td>18,555,000</td>
<td>18,681</td>
<td>100.2</td>
<td>228</td>
<td>1.2</td>
<td>1.2</td>
</tr>
<tr>
<td>15–17</td>
<td>6,320,000</td>
<td>7057</td>
<td>111.7</td>
<td>41</td>
<td>0.7</td>
<td>0.6</td>
</tr>
<tr>
<td>18–19</td>
<td>4,213,000</td>
<td>3935</td>
<td>93.4</td>
<td>25</td>
<td>0.6</td>
<td>0.6</td>
</tr>
<tr>
<td>20–29</td>
<td>19,703,000</td>
<td>13,366</td>
<td>67.8</td>
<td>72</td>
<td>0.4</td>
<td>0.5</td>
</tr>
<tr>
<td>30–39</td>
<td>25,245,000</td>
<td>16,658</td>
<td>66.0</td>
<td>295</td>
<td>1.2</td>
<td>1.8</td>
</tr>
<tr>
<td>40–49</td>
<td>18,144,000</td>
<td>18,136</td>
<td>100.0</td>
<td>1172</td>
<td>6.5</td>
<td>6.5</td>
</tr>
<tr>
<td>50–59</td>
<td>17,038,000</td>
<td>6577</td>
<td>38.6</td>
<td>460</td>
<td>2.7</td>
<td>7.0</td>
</tr>
<tr>
<td>≥60</td>
<td>24,771,000</td>
<td>2242</td>
<td>9.1</td>
<td>143</td>
<td>0.6</td>
<td>6.4</td>
</tr>
<tr>
<td>Total</td>
<td>148,146,000</td>
<td>99,861</td>
<td>67.4b</td>
<td>2967</td>
<td>2.0</td>
<td>3.0</td>
</tr>
</tbody>
</table>

**NOTE.** No. of cases and fatalities were obtained from reports sent to Gabrichevsky Institute, Moscow, in 1990–1997. Reports cover 87% of 115,284 reported diphtheria cases and 96.4% of fatalities in Russian Federation in this period.

* Cumulative incidence and mortality for each age group are defined as sum of all cases or deaths in age group during 1990–1997 divided by population (in 1994) of age group.

* Cumulative incidence based on 115,284 cases reported in Russia overall between 1990 and 1997 was 77.8 cases/100,000 population.
mary series. Among adolescents (15–17 years old), the incidence of diphtheria was similar to the incidence among school-aged children (7–14 years old), and most cases were mild.

Of the 2967 fatalities in 1990–1997, 759 were among children, 41 were among adolescents, and 2167 were among adults. Diphtheria mortality reached 0.6 deaths/100,000 population in 1995 (20-fold higher than in 1990) and then rapidly declined to 0.07/100,000 in 1997. The highest mortality was among preschool-aged children and adults 40–59 years of age (table 1). Most fatalities (85%) were in unimmunized persons (table 2); 11% of patients had received 1 or 2 doses of diphtheria toxoid. Although 17% of fatalities among children 3–14 years of age were among individuals with records of receipt of ≥3 doses of vaccine, virtually none of these children had received booster doses at the recommended intervals.

During 1990–1997, outbreak investigations and screening examinations detected 91,385 carriers of toxigenic strains of C. diphtheriae. Almost 40% of carriers were detected among children 7–14 years of age.

Laboratory: Since the 1960s, the vast majority of diphtheria cases have been confirmed by culture. More than 91% of diphtheria cases in 1982–1986 [12] and ≥89% of diphtheria cases in 1993–1994 were confirmed by isolation of toxigenic strains of C. diphtheriae. The proportion of C. diphtheriae strains that were gravis biotype began to increase after 1985. By 1989, 52% of the strains isolated from diphtheria cases were the gravis biotype, and in 1990, this proportion jumped to 64% as cases increased in the 1990s (table 3), reaching highly related, as determined by ribotyping and multilocus enzyme electrophoresis [18]. Ten gravis strains from the period 1986–1989 were in this sample and were isolated from patients in four widely separated oblasts. Seven of these strains from three oblasts (Vladimir in 1987 and 1988, Murmansk in 1987, and Krasnoyarsk in 1989) (figure 1) belong to the “epidemic clone.”

Outbreak control. In late 1993, immunization against diphtheria was mandated for all adults; at that time, an estimated 30% of adults had received one or more doses of diphtheria toxoid in the previous 10 years. Adult coverage reached 67% by the end of 1994 and 91% by the end of 1997. As of 1 January 1998, >99 million adults had received at least one dose in the previous 10 years, and >89 million had received more than one dose.

Between January 1993 and December 1995 alone, nearly 70 million adults were vaccinated [19]. To meet the unprecedented demand for adult-formulation vaccine, Russian vaccine production was rapidly increased: During 1994–1995, nearly 80 million doses of adult-formulation vaccine were produced, compared with <6 million doses in 1992.

From 1990 to 1993, strenuous efforts were made to improve compliance with existing immunization recommendations for children. In November 1994, the diphtheria immunization schedule was revised. Revaccinations were recommended at 6, 11, and 16 years of age, replacing the recommendation from 1986–1994 for two revaccinations at 9 and 16 years of age. The number of contraindications that were accepted was sharply reduced, and the use of Td vaccine in the primary series was discouraged. Immunization coverage with diphtheria toxoid increased in the 1990s (table 3), reaching ≥95% for recommended doses among children ≤3 years of age in 1996.

Discussion

Despite economic difficulties in the 1990s, Russia succeeded in controlling this epidemic, using a strong system of scientific

Table 2. Vaccination status of diphtheria cases and fatalities reported to Gabrichevsky Institute, Moscow, by age group, Russian Federation, 1990–1997.

| Age group, years | No. of reported nonfatal cases | Vaccination status | | | No. of reported fatal cases | Vaccination status |
|------------------|-----------------------------|------------------|---|------------------|------------------|
|                  | Total | Unvaccinated | 1–2 doses | ≥3 doses | Total | Unvaccinated | 1–2 doses | ≥3 doses |
| <1               | 169   | 149        | 7        | 13      | 33    | 33         | 0        | 0        |
| 1–2              | 1107  | 710        | 86       | 411     | 156   | 151        | 1        | 4        |
| 3–6              | 4749  | 1316       | 151      | 3282    | 342   | 304        | 3        | 35       |
| 7–14             | 10,617| 1535       | 108      | 8974    | 228   | 161        | 5        | 62       |
| 15–17            | 3342  | 1188       | 75       | 2079    | 41    | 28         | 3        | 10       |
| 18–19            | 1727  | 882        | 825      | 20      | 25    | 22         | 0        | 3        |
| 20–29            | 6330  | 4625       | 1505     | —       | 72    | 58         | 14       | 0        |
| 30–39            | 8866  | 6944       | 1742     | —       | 295   | 265        | 30       | 0        |
| 40–49            | 9014  | 7479       | 1535     | —       | 1172  | 1000       | 167      | 5        |
| 50–59            | 3171  | 2697       | 474      | —       | 460   | 380        | 80       | 0        |
| ≥60              | 1031  | 1979       | 83       | —       | 143   | 126        | 15       | 2        |
| Total            | 49,743| 28,404     | 6591     | 14,779  | 2967  | 2528       | 318      | 121      |

NOTE. Data are from case investigation reports sent to Gabrichevsky Institute in 1990–1997. Beginning in 1995, reports on mild cases of diphtheria were not sent and, thus, are not included in this analysis.
research, vaccine production, and public and clinical health care systems. This success reflects the work of thousands of medical professionals. When the previous diphtheria-control strategy proved inadequate in the 1990s, Russia changed its strategy and was then able to rapidly increase the production of diphtheria vaccines and antitoxin, deliver the supplies to medical providers, and administer vaccine to the population. The vaccination of nearly 70 million adults in 1993–1995 was the largest adult immunization outbreak-control campaign since global smallpox eradication efforts in the 1960s, which had also been supported by massive amounts of Russian vaccine.

Some lessons from the epidemic are obvious: The epidemic could have been prevented or limited by maintaining full vaccination of children and initiating earlier vaccination of adults. Other important questions regarding the outbreak remain incompletely answered: Why did this resurgence occur; which control measures were essential; and what lessons should other countries learn from the Russian experience?

Why did this resurgence occur? Three factors did not play significant roles in the diphtheria outbreak in Russia, namely vaccine quality, vaccine supply, and access to vaccine providers. The effectiveness of Russian-produced vaccine was demonstrated by international researchers in reviews of surveillance data [20] and in case-control studies [21]. Vaccine supply for children was always adequate, and production of adult vaccine quickly rose to meet the demand. Russian adult and pediatric clinics continued to operate and to provide free immunizations.

Two primary causes of the resurgence were the accumulation of susceptible individuals among both adults and children and the large-scale introduction of a new biotype of *C. diphtheriae*. Both of these factors have been linked to periodic upsurges of diphtheria in the past. For example, during World War II, the introduction of gravis strains by German troops resulted in outbreaks of diphtheria in Western countries where strains of mitis and intermedius had been endemic at low levels [22–23]. Social factors also contributed to increased spread of the epidemic and increased difficulty in controlling it; these factors included increased numbers of migrants due to the breakup of the Soviet Union, crowded living conditions, large numbers of susceptible military personnel, and increased numbers of homeless and traveling traders.

The accumulation of a large number of susceptible adults who lacked immunity was due to the effects of previous vaccination programs. In 1990, most Russian adults >60 years of age retained immunity to diphtheria from childhood infections prior to widespread vaccination; however, these immune individuals were a shrinking proportion of the population in the 1990s. In Russia, cohorts of middle-aged adults who had been born in the 1940s and 1950s had high rates of susceptibility to diphtheria, as documented in serologic investigations [13, 24–25]. Many had neither been immunized during the early years of vaccination programs nor had acquired natural immunity because circulation of toxigenic strains decreased after vaccination programs were introduced. These individuals were completely susceptible to diphtheria; birth cohorts from the 1940s and 1950s suffered most of the severe cases and fatalities in the resurgences of the 1990s and 1980s. Another group whose numbers were increasing consisted of young and middle-aged adults who had been immunized in childhood but whose immunity had waned. These adults were susceptible to diphtheria but retained some immunologic memory to diphtheria toxin; severe cases and fatalities were uncommon in the group.

Low immunization coverage among preschool-aged children was responsible for the high rate of severe disease among this age group. Among older children and adolescents, the incidence of mild diphtheria and carriage of *C. diphtheriae* was very high. It is likely that close contact and high rates of transmission in these groups played a critical role in amplifying the epidemic, although high coverage with ≥3 doses of vaccine prevented most severe disease.

While the accumulation of large numbers of susceptible persons was a necessary factor for the resurgence of diphtheria, the introduction of “new” strains was probably an important cofactor. Gravis strains predominated during this epidemic in Russia, and the molecular data suggest that most of these strains belonged to an epidemic clone. These strains explosively spread throughout Russia in the 1990s, while the mitis strains that circulated previously did not. This association suggests a role for microbial factors in the epidemic. No data have been published to suggest that strains of the epidemic clone possess a different exotoxin, the primary virulence factor for diphtheria; the epidemiologic data from this outbreak also support the effectiveness of diphtheria toxoid against the new strains. However, other virulence factors exist in *C. diphtheriae* [26], and additional investigation of the epidemic clone is needed. Immunity to diphtheria antigens other than exotoxin is poorly understood [26–27]; biotype-specific antibacterial immunity may play a role in periodic changes in circulating biotypes of *C. diphtheriae*.


<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1 year of age, primary series</td>
<td>82.7</td>
<td>68.5</td>
<td>68.7</td>
<td>72.6</td>
<td>79.2</td>
<td>88.1</td>
<td>92.7</td>
<td>95.1</td>
<td>95.6</td>
<td></td>
</tr>
<tr>
<td>3 years of age, first revaccination</td>
<td>77.3</td>
<td>77.3</td>
<td>71.4</td>
<td>81.3</td>
<td>83.0</td>
<td>88.0</td>
<td>92.4</td>
<td>94.7</td>
<td>96.6</td>
<td></td>
</tr>
<tr>
<td>7 years of age, second revaccination</td>
<td>88.3</td>
<td>89.3</td>
<td>84.9</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10 years of age, second revaccination</td>
<td>86.1</td>
<td>87.5</td>
<td>87.7</td>
<td>88.3</td>
<td>92.4</td>
<td>94.3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16 years of age</td>
<td>82.8</td>
<td>80.2</td>
<td>86.5</td>
<td>89.1</td>
<td>89.3</td>
<td>89.4</td>
<td>92.8</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NOTE. Data are from Russian Ministry of Health.

*a* Age groups include children up to next year of age (i.e., 1 year = children 12–23 months of age).
Although the molecular data have contributed significantly to understanding the evolution of the outbreak, the origin of the epidemic clone of gravis strains remains unclear. These strains were present in at least several sites in European Russia and Siberia by 1987–1989 [18]. However, conclusions are limited by the small numbers of years and regions studied; for example, strains from any years in both the 1980s and 1990s were available from only four geographic areas in the study. The rise in the proportion of gravis strains among diphtheria cases nationally from 1986–1989 suggests that the epidemic clone was gradually spreading during this period; in Moscow, the increasing incidence and fatalities and the abrupt rise in the proportion of gravis strains isolated from cases indicate that the resurgence was already underway in 1989.

In addition, strains isolated during the epidemic period from most geographic regions have not been analyzed by molecular or other methods, leaving many important epidemiologic questions unanswered. For example, although gravis strains of the epidemic clone were isolated in Krasnoyarsk in 1989, disease activity remained low in the region until 1992–1993, when an explosive outbreak began that was associated with mitis strains. These mitis strains were not available for molecular analysis or other analysis; therefore, it is unknown whether they share molecular characteristics or virulence factors with strains of the epidemic clone.

Control—what worked. By 1995, the proportion of immune individuals in the Russian population (adult coverage: 70%; childhood coverage with primary series and booster: ~90%) had risen enough to limit the epidemic by directly decreasing the number of individuals susceptible to disease and by limiting transmission of the organism. The vaccination of adults played a critical role, and the Russian example helped other NIS countries to plan diphtheria-control efforts in the mid-1990s. Individuals also acquired immunity from clinical diphtheria or from carriage of toxigenic strains; naturally acquired immunity might have played an important role in some subpopulations, such as homeless alcoholics, who had high levels of disease and were difficult to reach with vaccination efforts. It is difficult to evaluate the relative contribution of other changes in the vaccination schedule to the decrease in diphtheria among all age groups in 1995. Implementation of the recommendation that lowered the age for the second revaccination from 9 years to 6 years in 1995 coincided with achievement of high levels of coverage among preschool-aged children and rapidly increasing levels of adult coverage.

Lessons for other countries. During the vaccine era, the experience with diphtheria in Russia diverged from that of Western, highly industrialized countries: For many industrializing countries, the Russian experience is relevant. In Western countries, high rates of coverage with diphtheria toxoid among children led to the elimination of indigenous cases of diphtheria and to an apparent interruption of circulation of toxigenic strains of C. diphtheriae, regardless of whether adults in these countries received revaccinations. These developments led to a belief among Western epidemiologists that high rates of immunization alone will interrupt circulation of toxigenic C. diphtheriae. However, several foci of toxigenic C. diphtheriae have been documented in recent years in these countries among subpopulations with low socioeconomic status, even though only limited surveillance has been conducted [28–30]. The persistence of toxigenic strains in lower socioeconomic populations suggests that the apparent success in interrupting circulation is partly due to the extremely high living standards enjoyed by the majority of the population in these countries; these living conditions stand in stark contrast to those of the rest of the world’s population.

The Soviet and Russian experience has been that of persistent circulation of toxigenic strains of C. diphtheriae and at least two resurgences of diphtheria despite fairly high levels of vaccine coverage among most childhood age groups. Studies in 1969–1970 documented that reintroduction of toxigenic strains into schools with 100% coverage of children produced widespread transmission of the organism for months despite an absence of cases [31]. A study in several oblasts in 1980–1981 found low-level circulation of toxigenic strains despite immunity in ≥97% of 20,000 children who were 4–14 years of age, as measured by Schick testing [12]. While inadequate implementation of immunization played a role in permitting circulation of diphtheria organisms to continue, the experience in Russia and elsewhere suggests that circulation is likely to persist in areas of lesser economic development even with good overall immunization levels.

Other countries also might take note of the combined effect of the diminished morbidity from childhood infectious diseases and of a vocal anti-immunization effort in eroding support for vaccination both among clinicians and the population; the parallels with trends in some Western countries have been noted [32].

Final lessons cannot yet be drawn from the 1990s’ diphtheria epidemic for the Russian Federation. Despite the marked decline in the incidence of diphtheria since 1995, diphtheria in Russia is still not adequately controlled. Toxigenic C. diphtheriae continues to circulate throughout the Russian Federation, and interruption of circulation in most areas is unlikely in the near future. Unimmunized individuals persist among all age groups, and the proportion of severe disease and fatalities among residual cases is still high. Continued efforts to achieve universal coverage of children and to increase adult coverage are needed.

References


