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Resurgence of diphtheria

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Abstract. Following the introduction of routine immunization with diphtheria toxoid in the 1940s and 1950s, diphtheria incidence declined dramatically in countries of the industrialized world. At the beginning of the 1980s many of these countries were progressing toward elimination of the disease. However, since the mid-1980s there has been a striking resurgence of diphtheria in several countries of Eastern Europe. For 1993, WHO received reports of 15,211 diphtheria cases in Russia and 2,987 cases in Ukraine. The main reasons for the return of diphtheria in these countries were: decreasing immunization coverage among infants and children waning immunity to diphtheria in adults, movements of the population during the last few years, and an irregular supply of vaccines. The outbreak spread to neighboring countries and in 1993 cases were reported in Azerbaijan, Belarus, Estonia, Finland, Kazakhstan, Latvia, Lithuania, Poland, Tajikistan, Turkey, and Uzbekistan. Epidemiological patterns of diphtheria are changing in developing countries, and the disease seems to be following patterns seen in industrialized countries 30 to 40 years ago. In developing countries, routine immunization against diphtheria was introduced in the late 1970s with the Expanded Programme on Immunization. In these countries, coverage of infants with 3 doses of diphtheria toxoid reached 46% in 1985, and 79% in 1992. Recent diphtheria outbreaks in Algeria, China, Ecuator, Jordan, Lesotho and Sudan demonstrate a shift in the age distribution of cases to older children and adults. Rapid clinical and public health responses are required to control diphtheria outbreaks. Three major measures are indicated: high immunization coverage of target groups, prompt diagnosis and management of diphtheria cases, and rapid identification of close contacts with their effective management to prevent secondary cases.

Key words: Diphtheria, Diphtheria toxoid, Epidemic, Epidemiological surveillance, Russia, Ukraine

Introduction

Before the advent of routine immunization, diphtheria was a common cause of morbidity and mortality. In temperate zones, more than 1 in 20 inhabitants suffered from clinical diphtheria during their lifetime and 5–10% of the these died of the disease [1]. The implementation of immunization programmes has ensured that diphtheria has not been a public health problem for a generation in many industrialized countries. At the beginning of the 1980s, when diphtheria incidence rates reached their lowest levels, there was optimism that elimination of indigenous respiratory diphtheria could be achieved in the European Region by 1990 through maintenance and strengthening of immunization services [2].

At least three factors favor the elimination of diphtheria: (1) humans are the only reservoir; (2) an effective, safe, and inexpensive toxoid vaccine exists; and (3) diphtheria is a seasonal disease, making its transmission more vulnerable to interruption. However, other factors may hinder the elimination of diphtheria. These include: the presence of an asymptomatic carrier state; the need for 3 initial doses of vaccine and subsequent booster doses due to short-lived immunity following immunization; and finally the erosion of political, professional, and popular support for immunization efforts.

Paradoxically, in some countries great successes in controlling diphtheria have fostered apathy toward immunization on the part of parents and physicians, unjustified ideas about contraindications to immunization, and a wave of anti-immunization propaganda. Physicians who have not seen clinical diphtheria may easily miss the diagnosis. New generations of parents who have never even heard of diphtheria have become complacent about the need to immunize their infants. As a result, immunization coverage levels have fallen in a number of industrialized countries. Since the mid-1980s, diphtheria, a disease which appeared to have been nearly conquered, has returned to many countries in Europe. Further expansion to other industrialized countries is a definite threat.

The epidemiological patterns of diphtheria are also

changing in developing countries, where the disease seems to be following patterns similar to those seen in industrialized countries 30–40 years ago. In both industrialized and developing countries, there is a need to reconsider the epidemiology of this dangerous disease.

General trends in the incidence of diphtheria

The history of diphtheria is full of unanswered questions. One intriguing puzzle is the cyclic occurrence of diphtheria. The disease tends to skip long periods of time between outbreaks and historical evidence suggests that diphtheria has occurred in cycles that include gaps of 100 years or more [3].

During the 16th and 17th centuries, diphtheria epidemics occurred in Spain, where the disease was known as 'morbus suffocans' or 'garotillo' (Table 1). The disease occurred in distinct waves in 1583 to 1613, 1630, 1645, and 1666.

Table 1. Cyclic occurrence of diphtheria in the world

Century	Place, Dates	Forms and extent
XVI–XVII	Spain 1583–1613, 1630 1645, 1666	'garotillo' or 'morbus sufocans'
XVIII	New England 1735–1740	'Throat distemper' with high case fatality rates
XIX	Many countries in Europe and America 1847–1899	Pandemic with mortality up to 100 per 100,000 population
XX	Europe during and after World War II	Incidence > 200 per 100,000 population
	Russia, Ukraine 1990–1994	Next round in a diphtheria cycle?

After this, no major diphtheria outbreaks were reported until the mid-18th century. From 1735–1740 an epidemic raged in the New England colonies of the Americas. A curious characteristic of this epidemic was its predilection for rural populations, and Boston escaped the epidemic [3]. Many patients suffered severe complications and case fatality rates were high. At that time, diphtheria was popularly known as 'throat distemper', and its mysterious origin and the slow, suffocating death it caused, contributed to its terror [4]. In Kingston, New Hampshire most families lost at least one child and many families lost all their children. Mortality statistics from Hampton Falls, New Hampshire show that the disease burden fell disproportionately on children: of 210 persons who died from diphtheria in 1735, 200 were less than 20 years of age (Table 2).

Table 2. Mortality due to diphtheria, Hampton Falls, New Hampshire, 1735 (according to reference 3)

Age groups in years	Population		No. of deaths	Mortality rate in %
	N	%		
< 10	404	32.1	160	39.6
10–20	310	24.6	40	12.9
> 20	546	43.3	10	1.8
Total	1260	100	210	15.2

In the 19th century, diphtheria returned to America and Europe in a great pandemic. In 1881 in New York city, more than one per cent of children under 10 years of age died from diphtheria [5]. From 1880 through 1888, annual diphtheria case fatality rates in a large hospital in Boston ranged from 40% to 52% [6]. Statistics from large European cities like Hamburg and London showed mortality rates of 50 to 100 deaths per 100,000 population and the average mortality rates in European countries were about 40 per 100,000 population [7].

A huge epidemic of diphtheria was reported in Europe during and after the Second World War [8]. From 1937 to 1940, the diphtheria incidence rate was 29 per 100,000 population in Denmark and below 20 per 100,000 population in the Netherlands, Norway, Sweden and Switzerland, but it was 212 per 100,000 population in Germany [9]. In 1941, the diphtheria incidence rate in Germany rose even higher and this rise continued for the next 3 years. There were 173 161 cases in 1941, 237,037 cases in 1942 and 238,409 cases in 1943. The disease in its virulent form spread to the occupied countries of Norway and the Netherlands with disastrous results (Figure 1). In Norway, there was an increase in the incidence rate from 7 per 100,000 population in 1937–1940 to 760 in 1943, and in the Netherlands from 15 to 622 per 100,000 during the same years. Stowman estimated that in 1943 there must have been some one million cases of diphtheria and about 50,000 deaths due to diphtheria in Europe, outside of Russia [9]. Diphtheria turned out to be the leading epidemic disease of the War on the European continent both as a cause of morbidity and mortality. The epidemic spared England and Wales, where a steep decline in diphtheria incidence continued throughout the 1940s [8] (Figure 1). In some countries, such as Poland, the epidemic started after the Second World War and its spread was exacerbated by socio-economic changes, great population shifts from rural to urban areas, overcrowded housing conditions following wartime bombings, and high fertility rates [7].

In the industrialized countries of Europe and North

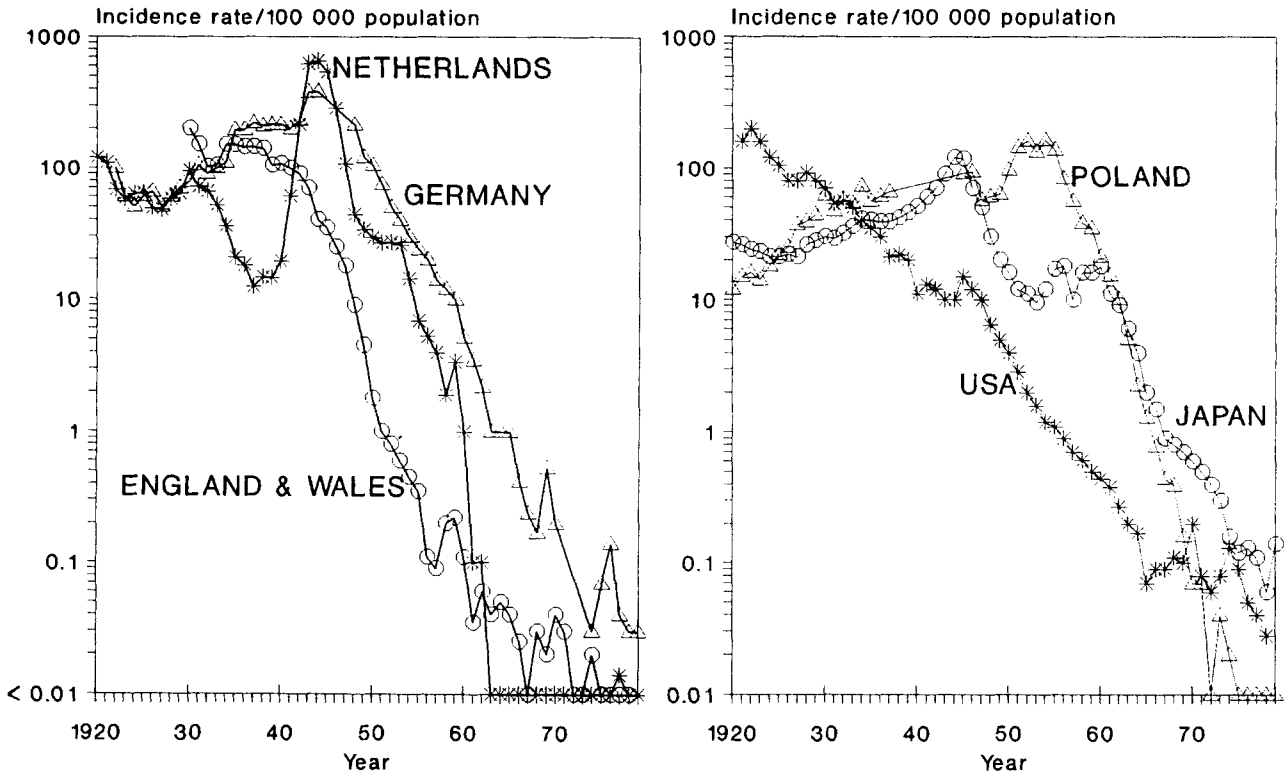

Figure 1. Diphtheria incidence rate per 100,000 population in several countries, 1920–1980 (updated from reference 7).

America, and in Australia and Japan, routine immunization of infants and children with diphtheria toxoid has been carried out since the 1940s and 1950s. This resulted in a dramatic decline in both clinical disease and carriage rates. In addition, the proportion of cases occurring in older children and adults increased. In developing countries, the introduction of diphtheria toxoid within the Expanded Programme on Immunization started in the late 1970s. Coverage of infants in developing countries with 3 doses of diphtheria toxoid rose from less than 5% in 1974 to 46% by 1985 and 79% by 1992.

Since 1974, countries have reported the annual incidence of diphtheria to the World Health Organization. The worldwide total number of reported diphtheria cases ranged from 70,000–90,000 per year in the 1970s to 22,000–27,000 per year in the 1990s (Figure 2). This represents a global decrease in diphtheria morbidity of about 70% over a 20 year period. The majority of diphtheria cases were reported from developing countries, but the contribution of these countries to the global total slowly declined from 97% of all cases in 1974 to 79% in 1992. This contrasts sharply with increasing diphtheria incidence in industrialized countries (Figure 2). This unfavorable trend for the industrialized countries is largely due to an abrupt increase in the number of diphtheria cases reported since 1990 from the European Region.

There are differences in reported diphtheria incidence in various regions of the world. Since the mid-1980s significant declines in diphtheria morbidity have occurred in the American, Eastern Mediterranean, and Western Pacific Regions. A smaller

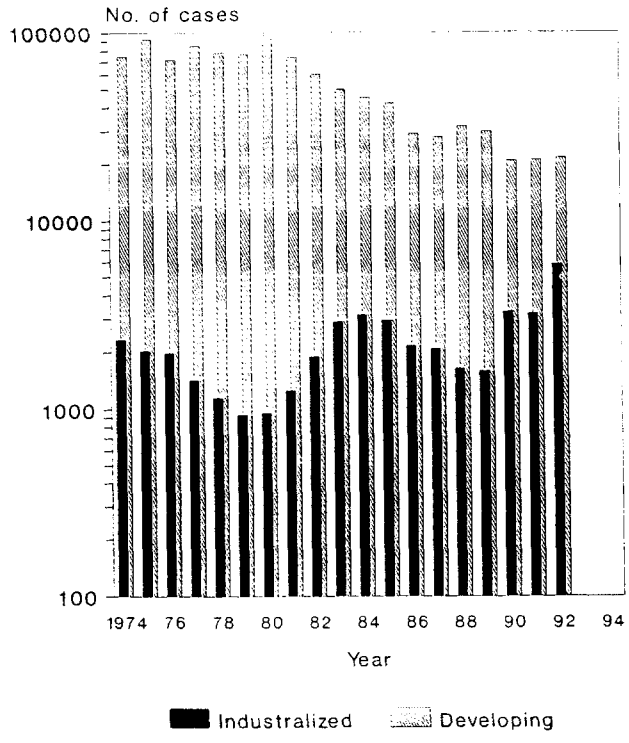

Figure 2. Number diphtheria cases reported from developing countries and industrialized countries, 1974–1993. Based on data reported to WHO as of 1 March 1994.

decline occurred in the South East Asia Region. No clear change is apparent in the African Region, reflecting the later start of immunization programmes and the lower coverage levels achieved. In the European Region diphtheria morbidity has been stable for many years, but starting 1990 in rose sharply.

Recent epidemics of diphtheria in Europe

The recent rise in diphtheria in Europe is largely the result of a massive epidemic in the Russian Federation and Ukraine. There is evidence that this epidemic is spreading to other European countries.

Diphtheria epidemic in the Russian Federation

From the late 1950s to the mid 1970s, there was a steady decrease in diphtheria incidence in the USSR. In 1975 and 1976, only 199 and 198 cases were reported from the USSR, for the lowest-ever incidence rate of 0.04 per 100,000 population (Table 3). The country was progressing towards elimination of the disease.

After 1976, diphtheria incidence began to increase in the USSR [10, 11], reaching its first peak during 1983–1985, when the number of cases exceeded 1,400 for each of these years. Most of the diphtheria cases were reported from the Russian Socialist Republic (now the Russian Federation). A second wave of the epidemic started in 1990 and as of November 1994, the incidence was still rising. The Russian Federation reported 1876 cases in 1991, 3987 cases in 1992, and 15,211 cases in 1993. In the first eleven months of 1994, 34,408 cases of diphtheria were reported. The incidence rate exceeded 1 per 100,000 population in 1991 and 10 and 20 per 100,000 population in 1993 and 1994, respectively (Table 3). In 1992, diphtheria incidence in the Russian Federation exceeded 10 per 100,000 in Moscow and St. Petersburg, but 20 regions surpassed this incidence level in 1993 [12]. The number of deaths due to diphtheria increased from 80 in 1991 to 388 in 1993.

The epidemic spread to most of the regions of the Russian Federation. In 1992 the highest incidence rates were registered in the European part of the country [13]. For 1993, detailed analysis shows that incidence rates for diphtheria were highest in St. Petersburg City (51.7/100,000), St. Petersburg Region (36.9), and Moscow City (28.3). Rates were high in Tver (25.2), Novgorod (23.5), and Pskov (19.6), three regions situated between Moscow and St. Petersburg. High incidence was also reported in Kaliningrad (20.6), the region separated from the rest of Russia by Lithuania and Poland [12]. Other areas with high incidence rates in 1993 were Siberia and several regions in the far eastern part of Russia – Krasnoyarsk (22.6), Irkutsk (13.1), and Vladivostok (42.5).

Table 3. Reported number of diphtheria cases and incidence rate per 100,000 population, USSR 1965–1990 and Russia 1991–1993

Year	Number of cases	Rate per 100,000
1965	4,691	2.00
1966	3,102	1.30
1967	2,595	1.10
1968	2,235	0.93
1969	1,710	0.71
1970	1,101	0.45
1971	765	0.31
1972	516	0.20
1973	319	0.13
1974	285	0.11
1975	199	0.08
1976	198	0.08
1977	238	0.09
1978	270	0.10
1979	270	0.10
1980	345	0.13
1981	560	0.21
1982	917	0.34
1983	1,411	0.51
1984	1,609	0.59
1985	1,511	0.54
1986	1,156	0.41
1987	1,076	0.38
1988	870	0.30
1989	839	0.29
1990	1,431	0.49
1991	1,876	1.30
1992	3,897	2.60
1993	15,211	10.20

Analysis of the age and geographic distribution of diphtheria cases provides clues to the causes of the epidemic. Before 1980, diphtheria incidence among children under 5 years of age was low and diphtheria occurred mostly in older children, adolescents, and adults (Figure 3). By the mid-1980s, in the first wave of the epidemic, there was a major change in the age distribution of cases, with a dramatic increase of diphtheria morbidity in preschool-aged children. Such changes were clearly seen in Moscow, where the epidemic started (Figure 3). By 1992, the epidemic was characterized by an increased incidence in all age groups, with peak incidence in children aged 5–10 years and adults aged 30–50 years (Figure 4).

Some data suggest that military staff played an important role in spreading the epidemic. In 1988, in the Lenin Kzyl-Ordinskoi Region of the Kazakh Republic (now Kazahkstan) where 58 cases of diphtheria were reported, 39 (67%) occurred in military personnel [14]. At the beginning of the 1990–1993 outbreak in Moscow, increased morbidity was reported among young adult members of paramilitary

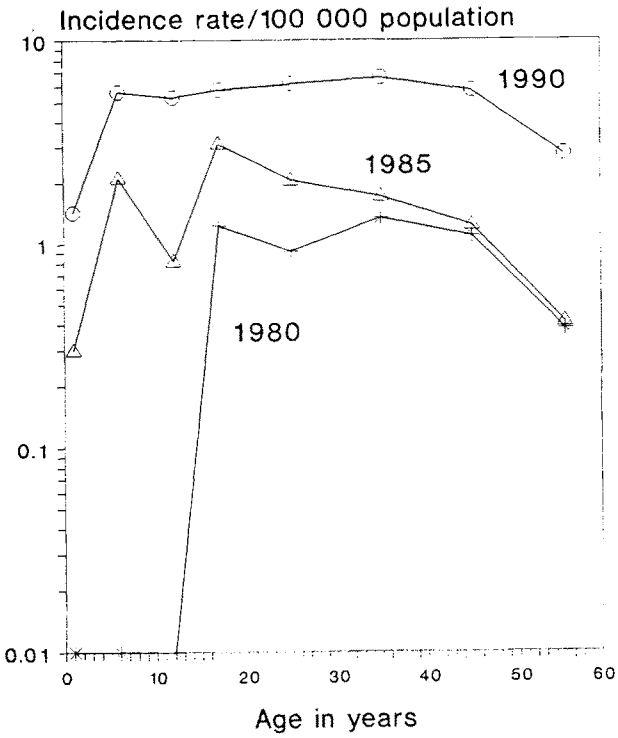

Figure 3. Diphtheria incidence rate per 100,000 population, by age group, Moscow, 1980, 1985, and 1990. Reported by Ministry of Health, USSR.

construction units [15, 16]. In 1992 and 1993, the diphtheria incidence was among the highest in the country in Kaliningrad Region, where large numbers of military troops are stationed [13].

In the period of low incidence prior to 1980, diphtheria incidence was higher in the former Central Asian Republics of the USSR (now the countries of Turkmenistan, Tajikistan, Uzbekistan, Kirgizstan, and Khazakhstan) than in the Russian Federation, Ukraine, and Belarus. From 1990 through 1992, the incidence in Russia and Ukraine was substantially higher than in the former Central Asian Republics (Table 4). This suggests that diphtheria infection spread from south to north. In the south, it had an endemic character and attacked mostly young children. In the north, diphtheria appeared first in Moscow and then in St. Petersburg, where adults with waning immunity and unimmunized children created a susceptible population. From these northern cities, the epidemic spread to other parts of Russia and, later, to Ukraine and Belarus.

In the Russian Federation, seasonality of diphtheria was apparent, with a higher number of cases in the late autumn and winter. From September 1993 through October 1994, the number of reported cases has continued to increase dramatically and there are no signs that the epidemic is waning (Figure 5).

Diphtheria epidemic in Ukraine

In Ukraine, the annual reported number of diphtheria cases remained below 100 from 1970 through 1989. Then there was a rapid increase, with 109 cases reported in 1990, 1103 cases in 1991, 1553 cases in 1992, 2987 cases in 1993, and 2325 in the first eleven months of 1994. The incidence rate increased more than 200-fold between 1976 and 1993 (Table 4).

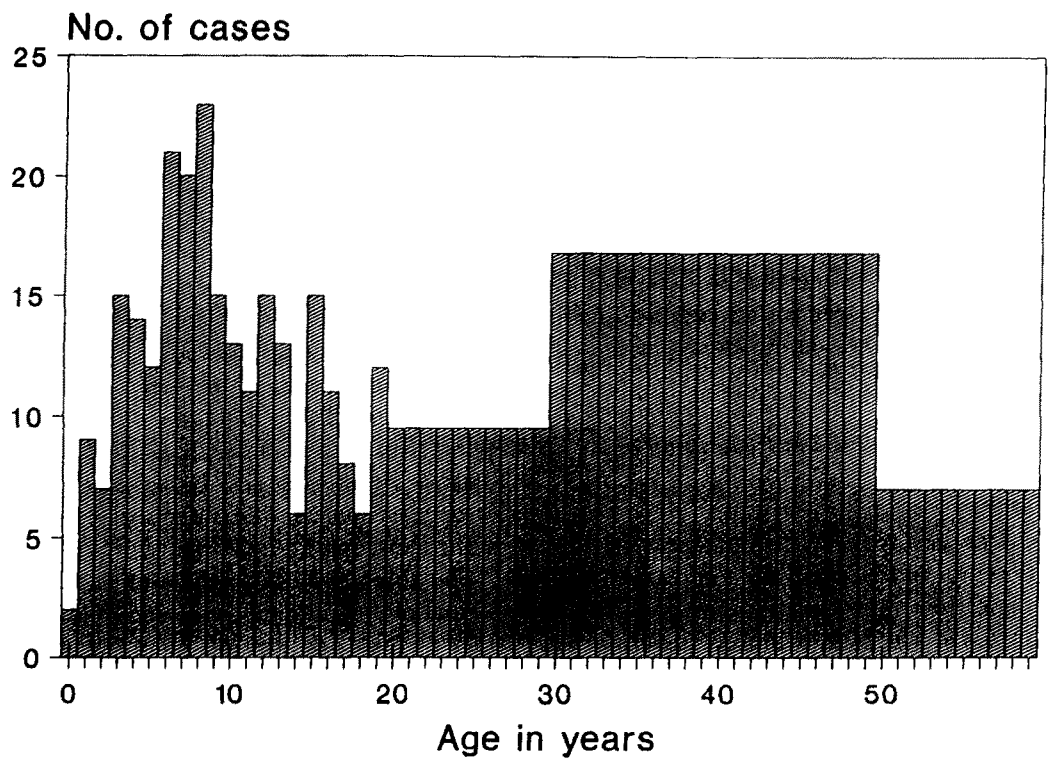

Figure 4. Number of diphtheria cases, by age group, Moscow, 1992 (according to reference 13).

Table 4. Diphtheria incidence rates per 100,000 population in Russian Federation, Ukraine, Belarus, Turkmenistan, Tajikistan, Uzbekistan, Kirgizstan, and Kazakhstan, 1976–1993

Year	Russia	Ukraine	Belarus	Turkmenistan	Tajikistan	Uzbekistan	Kirgizstan	Kazakhstan
1976	0.04	0.02	NA	1.37	0.31	0.27	0.11	0.09
1977	0.04	0.06	0.02	1.60	0.21	0.25	0.17	0.15
1978	0.10	0.04	0.01	1.68	0.42	0.18	0.00	0.11
1979	0.09	0.04	0.03	0.57	0.31	0.23	0.61	0.18
1980	0.18	0.05	0.02	0.21	0.10	0.17	0.47	0.09
1981	0.34	0.06	NA	0.37	0.12	0.15	0.22	0.06
1982	0.56	0.08	0.07	0.39	0.19	0.13	0.34	0.13
1983	0.91	0.11	0.07	0.91	0.07	0.12	0.10	0.03
1984	0.93	0.12	0.18	1.95	0.26	0.64	0.02	0.07
1985	0.82	0.14	0.18	1.29	0.80	0.68	0.09	0.11
1986	0.53	0.19	0.23	1.38	2.07	0.42	0.10	0.19
1987	0.51	0.17	0.33	0.93	0.44	0.44	0.21	0.20
1988	0.37	0.15	0.11	1.11	0.43	0.31	0.09	0.38
1989	0.40	0.11	0.16	2.10	0.35	0.08	0.09	0.18
1990	0.80	0.19	0.22	0.11	0.22	0.06	0.14	0.14
1991	1.30	2.12	0.25	0.11	0.09	0.04	0.23	0.18
1992	2.62	2.98	0.64	0.57	0.29	0.14	0.09	0.26
1993	10.20	5.72	1.09	0.08	3.26	0.63	0.13	0.48

NA = Not available.

Cases were reported from all regions, but the incidence rates were almost twice as high in urban areas compared with rural areas. In 1993, 34% of cases were reported from 3 areas – Kiev City (570 cases), Kharkov Region (311 cases), and Lvov Region (149 cases) [17]. An additional 16% of cases in 1993 were reported from the main industrialized areas – Dniepropietrovsk, Donieck, and Zaporozhe.

The reported number of deaths due to diphtheria was 50 in 1991, 68 in 1992, and 78 in 1993. Case fatality rates were high, especially in rural areas, and this was largely due to delays in diagnosis and treatment [17]. For 1992, the case fatality rate was 8.8% in rural areas and 2.9% in urban areas. For 1993, the case fatality rate fell to 5.4% in rural areas and 1.9% in urban areas.

Diphtheria shows a clear seasonality in Ukraine, with the highest numbers of cases in September, October, and November. In the first two quarters of 1994, the epidemic appeared to be coming under control but in autumn 1994 the incidence increased sharply (Figure 5).

Why an epidemic in the Russian Federation and Ukraine?

Reasons for the resurgence of diphtheria in the Russian Federation and Ukraine are complex. Major reasons include: low immunization coverage rates among infants and children, waning immunity to diphtheria among adults, and large movements of the population during the last few years.

The most critical factor was the drop in immunization coverage in children. In the Russian Federation, coverage levels plummeted from highs of more than 80% before 1980 to 68% by 1990 [18]. In many urban areas, including Moscow and St. Petersburg, the diphtheria immunization coverage rates in infants were very low, ranging from 18% to 59% [16, 19–21]. In Ukraine, national coverage of infants with the primary series of DPT vaccine was 85% in 1981, but fell to 46% in 1982 and remained below 50% through 1987 [17].

Many factors contributed to these drops in immunization coverage. An excessive list of contraindications, indicating more than 50 specific diagnoses where DPT vaccine should not be given, led many physicians not to immunize children [22]. A series of unbalanced statements about the danger and ineffectiveness of vaccines appeared in medical journals, the popular press, radio, and television. These media statements damaged the confidence of the public and medical workers in immunization [23]. The drop in immunization coverage was compounded by irregular supplies of vaccines in 1992 and 1993 in some parts of the Russian Federation [22] and Ukraine.

A second critical factor was increasing susceptibility of the adult population. Waning immunity is apparent in persons older than 20 years of age in the Russian Federation and Ukraine, as seen in other European countries [24]. These adults added to the pool of susceptible individuals.

The third critical factor was movement of the population, facilitating the spread of infection. As the USSR broke up into the countries of the Newly Independent States, considerable population migration occurred, particularly into Moscow.

Other factors probably contributed to spread of the epidemic. Once toxigenic strains of *Corynebacterium diphtheriae* are introduced in sufficient numbers to

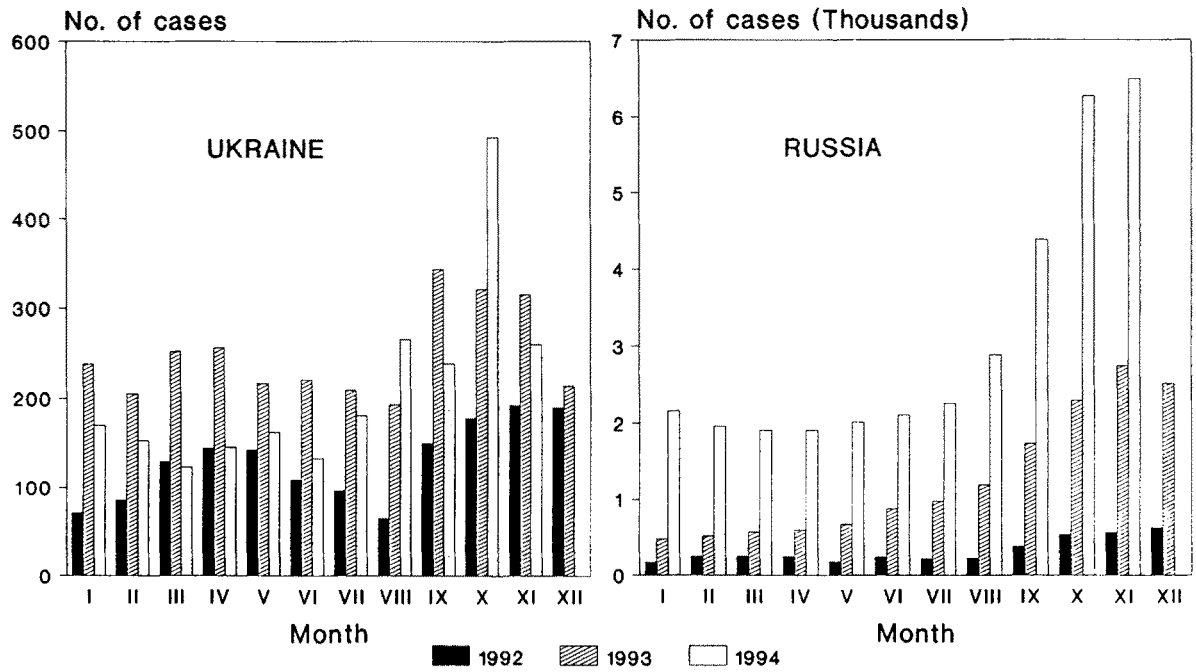

Figure 5. Number of diphtheria cases, by month, Russia and Ukraine, January 1992 through November 1994. Data from the State Committee for Sanitary Epidemiological Surveillance, Russian Federation and Ministry of Health Ukraine.

establish multiple foci of infection, control may be difficult. In St. Petersburg, biotype gravis accounted for 30% of cases in 1986 and 90% in 1990 through 1992. In Ukraine, biotype gravis was isolated in 82% of cases [25].

The occurrence of an epidemic raises questions about vaccine potency and the quality of the cold chain. The diphtheria component of Russian diphtheria-pertussis-tetanus (DPT) vaccines appears to meet WHO requirements of potency [26]. Two retrospective case-control studies of vaccine efficacy were conducted during the outbreak. A study in Kiev showed that 3 doses of diphtheria toxoid had a clinical protective efficacy of 82% (95% confidence interval: 63% to 91%) [25]. A study in Moscow determined that 3 or more doses of diphtheria toxoid had a clinical protective efficacy of 96% (95% confidence interval: 92% to 97%) [27]. The Moscow study also showed that interval since vaccination was important: children whose last vaccine dose was 4–7 years earlier were 2.5 times more likely to get diphtheria compared with those who last dose of diphtheria toxoid was received during the previous 12 months [27]. However, in the early 1990s some areas young children received their primary immunizations with diphtheria vaccine that had a reduced amount of diphtheria toxoid (standard DPT vaccine was replaced by adult-strength Td vaccine) [23].

Diphtheria in other countries in Europe

The epidemic spread to other European countries. In Belarus, 66 cases were reported in 1992 and 120 cases in 1993 [28]. An increased number of cases was reported in Estonia (3 in 1992 and 11 cases in 1993), Latvia (8 and 12 cases), and Lithuania (9 and 8 cases).

Finland reported 4 cases in 1993, following 30 years of zero reporting. Three of the Finnish cases had epidemiological links with cases in the Russian Federation. One was a 43 year old male who fell ill after a visit to St. Petersburg [29].

In Poland one cases was reported in 1992 and 10 cases in 1993. Five of these cases occurred in men 22 to 26 years of age who were fully immunized as children, but visited or had contacts with visitors from Ukraine or Belarus [30].

In 1993, increased numbers of diphtheria cases were reported from Azerbaijan (141 cases), Kazakhstan (82), Tajikistan (187) and Uzbekistan (137). In these countries, this was mostly attributable to shortages of vaccine for several years leading to decreasing coverage.

Turkey, which reported 13 cases in 1992 and 49 cases in 1993, has also had problems in achieving high coverage in the eastern parts of the country.

Diphtheria in developing countries

It is commonly stated that diphtheria has not been a major health problem in developing countries. In these countries, the warm climate encourages children to be out-of-doors and skin abrasions are readily infected with *C. diphtheriae*. The high prevalence of such skin sores contributes to the early development of natural immunity against diphtheria.

However, since the 1980s outbreaks of respiratory diphtheria with high case fatality rates and high rates of complications have been reported from developing countries in Africa, Asia, and the Eastern Mediterraneans and Latin America.

In Yemen, an epidemic in 1981 and 1982 produced 149 cases, with an overall attack rate of 118 per 100,000 population, several times higher than the rates reported in Eastern Europe in the 1990s [31]. Immuniza-tion coverage was very low in Yemen at this time (less than 10%) and the outbreak was typical of outbreaks seen in the prevaccine era. Preschool-aged children were most frequently affected and the incidence rate was 557 per 100,000 for male under 5 years of age. The case fatality rate was 14% [31].

In Jordan, two diphtheria outbreaks have been reported: one in 1977 to 1978 and the second in 1982 to 1983 [32, 33]. The first epidemic occurred when the immunization coverage did not exceed 20% and the age group most affected was children below 10 years of age. In 1979, Jordan embarked on a comprehensive immunization programme and the coverage rate in infants increased to 70%. Nevertheless, an outbreak of diphtheria occurred in December 1982 and January 1983. The age groups most affected in 1982 and 1983 were quite different from the age distribution in the earlier outbreak. Adolescents and young adults were largely involved, with nearly half of all patients hospitalized in the Jordan University Hospital above 20 years of age; about 65% of the patients were older than 15 years of age. Two of the hospitalized patients were school teachers, and three of their pupils were identified as carriers [33].

In Sudan, an outbreak with 107 cases of respiratory diphtheria occurred in Khartoum in 1978. Forty-eight percent of the 107 diphtheria cases admitted to the two main hospitals were preschool aged [34]. Twenty-nine patients (27%) suffered severe complications. Neurological complications were the most common; however, 5 of 6 deaths were due to cardiovascular complications [35]. An accelerated immunization programme was started in Khartoum in 1985 and by 1988 coverage of infants with 3 doses of DPT vaccine reached 60% to 70%. In a second epidemic in 1988, a shift in the age distribution of cases was observed, with only 19% preschool-aged, 52% aged 5–9 years, and 29% aged 10 years or older [36].

In an outbreak in Hubei Province, China in 1988 to 1989, 103 cases of diphtheria were reported [37]. The epidemic primarily involved adults (70% of cases were in persons above 20 years of age) and the overall case fatality rate was low, 1.9%. As the immunization coverage rates in Hubei Province rose gradually from 53% in 1984 to 82% in 1988, the diphtheria incidence rate dropped from 157 per 100,000 population in 1966 to 0.2 in 1984. No diphtheria cases were reported from 1985 through 1987. The epidemic started in urban areas and later spread to rural areas, but transmission of infection in rural areas was not as widespread as in urban areas, presumably because of less crowding. Increased migration of the population and waning diphtheria immunity among adults were considered as reasons for this mainly adult epidemic [37].

In Quthing District of Lesotho, coverage with 3 doses of DPT in infants was above 90% since 1984. In 1989, there was a diphtheria outbreak with a total of 68 cases [38]. As seen in other outbreaks following a period of high immunization coverage, most cases were older, with 38% aged 10 to 14 years and 26% aged 15 to 20 years. The case fatality rate was 23%.

Diphtheria immunization coverage levels have been high in Algeria for many years, and coverage with 3 doses of DPT vaccine was reported as 81% for 1989. Algeria reported only 4 to 30 diphtheria cases per year from 1988 through 1992. In 1993 there was an epidemic with 291 cases [39]. It continued in January 1994, when 206 cases occurred. Three-quarters of the cases occurred in older age groups, with 44% aged 10 to 19 years, 20% aged 20 to 29 years, and 11% aged 30 years or older.

In Ecuator, a diphtheria outbreak began in week 39 of 1993. For the first 26 weeks of 1994 there were 411 cases reported and most cases were in persons 15–44 years age group [40].

The appearance of diphtheria outbreaks in older age groups in developing countries, especially where infant coverage levels have been relatively high for 5 to 10 years, repeats an epidemiological pattern seen in industrialized countries 30 to 40 years ago [24]. In the first stage, the disease shifts to school-aged children. In the second stage, it shifts to adolescents and adults. In response to these changes in disease patterns, countries need to consider adding booster doses of diphtheria toxoid to the immunization schedule. Where disease is documented in school-children, a preschool booster dose is appropriate. When the pattern shifts to mostly adult cases, a school leaving booster may be appropriate and periodic booster doses of diphtheria vaccine may be considered for the adult population.

Control of diphtheria outbreaks

When outbreaks occur, rapid clinical and public health responses are essential. Diphtheria outbreaks can be quickly controlled by the proper use of three major measures: (1) achieving a high immunization coverage in groups at risk, (2) prompt recognition and management of diphtheria cases, and (3) rapid identification of close contacts and their effective management to prevent secondary cases. Useful guidelines for case management, contact tracing, and preventive measures have been published recently [41, 42].

Failure to implement such guidelines can result in delayed diagnosis, delayed treatment, and increased morbidity and mortality. Delayed diagnosis and treatment are associated with high case fatality rates. In Kazakhstan, only 20% to 30% of cases were accurately diagnosed at the start of the outbreak, others were diagnosed only after bacteriological results were available, or classical complications occurred, or at autopsy [25]. In St. Petersburg, 88% of cases were not hospitalized until 4 to 10 days after onset [43].

One of the most important measures for preventing diphtheria is reaching and maintaining high levels of immunization in the community. In all countries a primary series of diphtheria toxoid is recommended for infants. Most industrialized countries and a number of developing countries where age shifts in incidence have occurred have added booster doses to the routine schedule. There is a growing body of evidence that the duration of immunity against diphtheria in persons not continually exposed to diphtheria may be shorter than in similar groups of persons from countries where diphtheria is prevalent. Therefore, in countries where diphtheria has been successfully controlled, immunity levels should be maintained by administering booster doses of diphtheria toxoid. The routine use of Td vaccine booster doses in adults at intervals 10–20 years is recommended in many countries although the implementation of such a programme is difficult to monitor [24].

In addition health authorities in some countries have called for immunization of high risk groups. Risk groups need to be defined locally. Alcoholics, drug addicts, the homeless, and minority populations can be heavily affected. In Sweden, localized outbreaks of diphtheria in Gothenburg and Stockholm were reported in 1984 involving a subpopulation of alcohol-abusers [44, 45]. Diphtheria outbreaks in urban alcoholics have been associated with poor hygiene, crowding, season, contaminated fomites, underlying skin disease, hyperendemic streptococcal pyoderma, and introduction of new strains from exogenous reservoirs [46]. In the USA, seven outbreaks of diphtheria were reported during 1971 through 1981, mostly involving persons from poor socioeconomic conditions with incomplete immunization status; high attack rates for American Indians were characteristic for many of these outbreaks [47].

Even in the 19th century, it was documented that diphtheria posed a special risk for medical personnel [6]. In the current outbreak in the Russian Federation and Ukraine, medical and nursing staff, teachers, preschool staff, vendors, transport employees, and food handlers have been identified as belonging to high risk groups [13, 17]. Epidemiological data indicate that military personnel in Russian Federation are also at risk [14–16].

However, professional high risk groups include only about 20% of all diphtheria cases in the epidemic in the Russian Federation, and campaigns of mass immunization of all children, adolescents and adults and conducted in affected countries.

In response to the diphtheria epidemic in The Russian Federation and Ukraine, the WHO Regional Office for Europe has worked closely with Member States to assure prompt investigation and reporting. A Plan of Action for Diphtheria Control in the European Region was completed [48]. Guidelines for case investigation, treatment of suspect cases, and laboratory testing have been prepared [42, 49]. WHO and UNICEF have worked with donors to ensure that necessary supplies of vaccines, antitoxin, and antibiotics are made available. Meetings on diphtheria have been sponsored by WHO in St. Petersburg in July 1993 and in Moscow in May 1994. A European Task Force on Diphtheria Control has been formed by the WHO Office in Copenhagen. The aim of the Task Force is to accelerate progress toward controlling the diphtheria epidemic in Eastern Europe and to reduce the danger of the spread of diphtheria beyond these countries. Strategies are being monitored on the basis of epidemiological, surveillance, and laboratory data with the aim of rapidly bringing the epidemic under control.

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