J. Hyg., Camb. (1984), **93**, 419–432
Printed in Great Britain

Diphtheria in North America

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SUMMARY

The incidence of diphtheria has declined in North America during the last fifty years until it is now an uncommon disease. This general pattern is similar to that seen in other developed countries with well-organized immunization programmes, but certain noteworthy characteristics have been observed in recent years: foci of infection lingered in two population groups of low socio-economic status, in both of which the skin has been an important reservoir. In central areas of certain cities, endemic diphtheria, chiefly cutaneous, has occurred amongst indigent adult males living in unhygienic conditions; and in the native Indian population of Northern Canada diphtheria infection has been endemic in infants and children, many of the infections being of the skin or ear and toxic disease being uncommon. During the last few years, diphtheria outbreaks have not been reported in urban areas and possibly endemicity is now restricted to northern native populations. The number of infections detected in these northern endemic areas is steadily decreasing.

INTRODUCTION

Classical naso-pharyngeal diphtheria is now rarely seen in North America. The site of infection is often the skin rather than the pharynx and toxic manifestations are unusual. The few endemic foci of diphtheria infection which still exist are in areas of poor socio-economic conditions, particularly among native populations in certain rural localities.

The almost complete absence of pharyngeal diphtheria is largely a consequence of antitoxic immunity and does not indicate eradication of the causative organism. Diphtheria bacilli are still detected, although increasingly rarely. The disease in North America is very well controlled but the diphtheria bacillus remains a threat to the non-immune; and, very rarely, sporadic cases of toxic disease still occur.

DIPHTHERIA PRIOR TO 1960

The history of diphtheria in the United States and Canada before 1960 resembles that in other countries in which mass immunization with toxoid was introduced during 1930–45. National morbidity statistics are available only from 1920 in the United States and from 1924 in Canada, but trends before then can be studied from other published data. Before 1920 there appears to have been a very gradual fall in incidence when measured over long periods although there were many short-term fluctuations. In the city of Montreal, for instance, the incidence rate per 100000 population between 1887 and 1920 was highest (572) in 1887–9 and lowest (140)

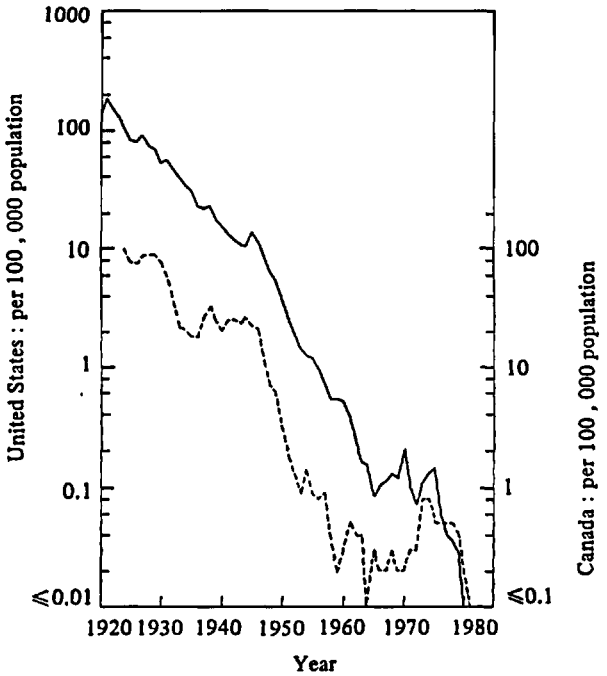

Fig. 1. Reported cases of diphtheria per 100000 population in the United States 1920–82 (——), and in Canada 1924–82 (– – –). (Data sources: National Office of Vital Statistics and the Centers for Disease Control, U.S.A.; and Health Division, Statistics Canada.)

in 1905–9, but rose to 222 in 1915–19 (Bourdon, 1945). A similar gradual but uneven decline in the morbidity rate between 1900 and 1920 was noted in Baltimore (Frost *et al.* 1936).

The fall in incidence began in the 1920s. At the beginning of the decade, diphtheria was a common disease in the United States and 147991 cases were reported in 1920 (Brooks, Bennett & Feldman, 1974). During 1921–4 it was the most common cause of death in Canadian children 2–14 years of age (Fitzgerald *et al.* 1932), and in 1924 9057 cases were reported in Canada. The morbidity rate then declined steadily from the 1920s to 1959 (Fig. 1), when only 934 cases were notified in the U.S.A. and 38 in Canada. As might be expected, the number of deaths reported annually declined in parallel with the falling morbidity rate (Fig. 2), but the case–fatality ratio for diphtheria in the United States remained constant (Fig. 3). One in ten of those who contracted the disease died (Munford *et al.* 1974). The Canadian experience was similar.

These general trends did not necessarily apply to all communities in the continent; the situation was patchy at the local level. The decline in morbidity between 1930 and 1955 was significantly slower in the southern states than in the remainder of the U.S.A. (Moore & Larsen, 1957). In one county of Georgia, for instance, there was no appreciable decline in disease incidence between 1935 and 1953, and an annual morbidity of about 47 cases per 100000 population was maintained despite an organized immunization programme (Murphy, Maley & Dick, 1956). Local variations were also noted in mortality, such as in Baltimore,

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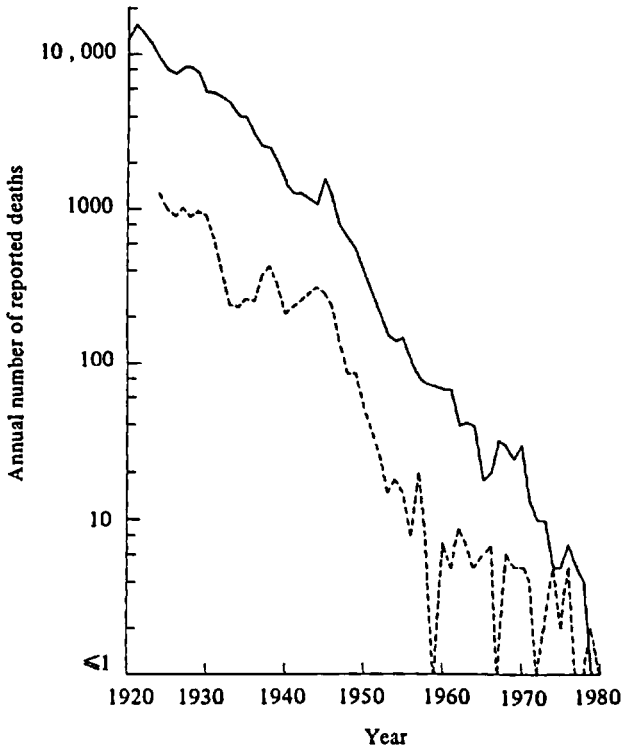

Fig. 2. Number of deaths from diphtheria reported annually in the United States 1920–82 (——), and in Canada 1924–1982 (---). (Data sources: National Office of Vital Statistics and the Centers for Disease Control, U.S.A.; and Health Division, Statistics Canada.)

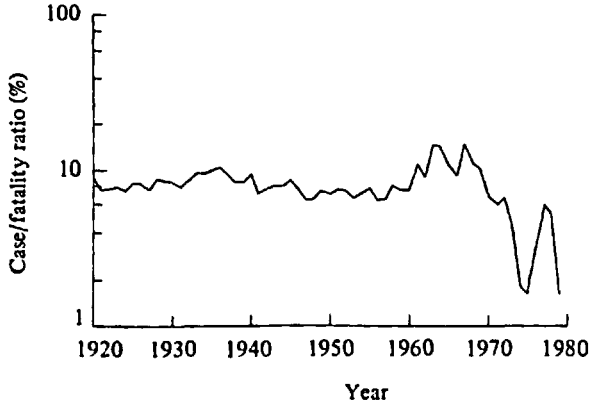

Fig. 3 Case–fatality ratio, expressed as a percentage, for diphtheria, United States 1920–79. (Data sources: National Office of Vital Statistics and the Centers for Disease Control, U.S.A.)

where the case–fatality ratio dropped from 8 % to 4 % between 1920 and 1936 (Frost *et al.* 1936) contrary to the unchanged ratio observed nationally.

The disease during this period occurred commonly in epidemics, primarily among children, and frequently presented in the toxic faucial form. An account of the clinical presentations, complications, and much fascinating detail of diphtheria in

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the 1940s is provided by Naiditch & Bower (1954), who reviewed 1433 cases occurring in Los Angeles County during the decade. Fifty-eight per cent of their patients were less than 10 years old. There was a trend in the 1940s and subsequently, however, for diphtheria increasingly to affect older persons than had been the case before childhood immunization was routinely practised. This was noted by Morton (1941), who reported on 891 cases of diphtheria in Halifax, Nova Scotia, during an 11-month period ending in June 1941. Among the 588 civilian cases, only 46% were less than 15 years old; and if 303 cases in the armed forces are included, only 30·8% of the 891 patients were under 15 years of age.

A substantial role in the decline of diphtheria must be attributed to the use of immunizing agents. Toxin–antitoxin mixture was used as a prophylactic in the early 1920s in New York state and its effect on the epidemiology of diphtheria was recorded by Godfrey (1932). Toxoid soon became the preferred preparation and a striking early example of its efficacy was noted during 1926–9, when there was a 75% reduction in cases among 27000 schoolchildren in Toronto who had been given toxoid compared with about 9000 who had not (McKinnon, Ross & Defries, 1931). By 1932, sufficient toxoid for more than a million persons had been distributed in Canada (Fitzgerald *et al.* 1932), but widespread use throughout the continent did not occur until the end of the decade.

THE TWO DECADES 1960–1979

During this period diphtheria was an uncommon disease but the decline in incidence, while continuing, was less regular (Fig. 1) because of occasional localized outbreaks that were superimposed upon an increasingly low endemicity. By 1971–3, however, the incidence in the United States had fallen to 0·11 per 100000, a rate comparable to that of malaria or typhoid fever; and if states reporting cases in American Indians are excluded, the incidence in the remainder of the country was only 0·01 per 100000 – lower than that for tetanus (Center for Disease Control, 1978). The majority (74%) of the 5048 cases reported in the United States during 1959–70 occurred in southern states, the highest rate (1·18 cases per 100000) being in Louisiana (Brooks, Bennett & Feldman, 1974). By 1970, 85% of reported cases were in states south of the 37th parallel of latitude (Center for Disease Control, 1971); but from 1971 to 1975 western states had the highest incidence (Center for Disease Control, 1978). The proportion of adult cases increased markedly in the 1960s. In 1960, 21% of reported cases in the United States were in persons over 15 years; by 1964 the figure was 36% (Communicable Disease Center, 1966) and during 1971–81, 48% of non-cutaneous cases were in persons aged 15 years or more (Centers for Disease Control, 1982*a*). The highest attack rate was in American Indians in Minnesota (13·4 per 100000); and for the entire U.S.A. the attack rate for Indians during 1959–70 was 20 times that for whites and three times that for black persons. This is believed to be a consequence of social and hygienic conditions associated with poverty rather than generic or racial factors (Brooks, Bennett & Feldman, 1974).

The case–fatality ratio showed more fluctuation during this period than formerly, falling to 5% in Canada during 1971. This fall was probably due in large measure to an increase in the number and proportion of cases of cutaneous and

aural diphtheria, conditions with a very low case–fatality ratio, rather than to a change in the likelihood of death in patients with toxic respiratory diphtheria (Varughese, 1978). A similar fall in the case-fatality in the U.S.A. in 1973 (Fig. 3) coincided with an outbreak of clinically mild skin diphtheria (Center for Disease Control, 1978). Fatal diphtheria increased in frequency in the elderly but was most common in the young. The risk of dying of diphtheria in the United States during 1959–70 was four times greater in children under 5 years of age than in those aged 20 years or more (Munford *et al.* 1974). Of 51 deaths in the U.S.A. reported during 1971–5, 20 were in persons aged less than 10 years and 17 in persons of 50 years or more. An increase in the proportion of deaths in older persons was also evident in Canada; during 1960–8 70 % of deaths were in children under the age of 10 years but during 1969–76 only 27 % of the deaths were in children (Varughese, 1978).

Local outbreaks of respiratory-tract diphtheria in Texas accounted for much of the increase in cases reported in the United States during 1968 to 1970. In Austin 88 cases occurred during 1968–9 (Zalma, Older & Brooks, 1970) and there were 196 cases in San Antonio in 1970 (Marcuse & Grand, 1973). Cases occurred predominantly in urban areas with poor socio-economic conditions, and most of the patients were less than 15 years old. Other U.S. outbreaks of respiratory diphtheria included six adult cases in Omaha, Nebraska (Heath & Zusman, 1962), 11 children in Miami in 1969 (Hennekens & Saslaw, 1976), and outbreaks, some protracted, in the states of Alabama, Arizona, New Mexico and Washington reported by the Center for Disease Control (1978). An outbreak in Washington state in 1972–5 in which cutaneous infection predominated will be considered separately. The largest Canadian outbreak during this time was one of 50 cases among Inuit (Eskimos) in 1976 in Cambridge Bay, Northwest Territories (Forrest *et al.* 1977). Smaller incidents include 12 cases in adult forestry workers in Quebec in 1974 (Gauvreau *et al.* 1977), four cases associated with a residential school on Vancouver Island in 1976 (Reynolds, Bowmer & Carr, 1976) and nine cases in Fort Liard, N.W.T., in 1980 (Gourlai *et al.* 1981).

The most significant change in the character of the disease during this period was its localization to certain geographic areas and socio-economic groups. In 1960 the 918 reported cases occurred in 43 of the 50 United States; but by 1978 the 76 cases notified were from only nine states, 84 % being from the state of Washington (Center for Disease Control, 1980). Furthermore, in the localized areas where the disease remained endemic, infection of the skin became a noteworthy and significant feature.

Infection in three geographical areas

Many of the infections detected in North America between 1960 and 1979 occurred in the fringes of the continent. They have been studied in particular in three areas: Northern Canada, the Pacific Northwest and the Southern United States.

Northern Canada

In northern Alberta and the Northwest Territories (N.W.T.) of Canada, infection was widespread but toxic respiratory diphtheria uncommon. These infections were reported by Dixon & Thorsteinson (1969), who isolated 391 strains in the second

half of 1967, and were studied in more depth by Jellard (1972), who reported on 1238 infected persons diagnosed during 1969–71. The area is relatively dry, has a long cold winter and a short warm summer. Most of those infected were North American Indians or persons of mixed European and Indian descent (Metis). The organisms, between one-third and one-half of which were toxogenic, were recovered most often from the nose and throat, but infections of the ear and skin together accounted for almost an equal number. Infection was most common in children under the age of 10 years. In the diphtheritic skin infections, which generally took the form of impetigo or an infected wound or ulcer, haemolytic streptococci or *Staphylococcus aureus* or both, were usually present in the lesions.

There were striking differences between diphtheria infections in the white population and those in the native Indian people. Caucasian persons were less often infected, rarely suffered from skin and ear infections, but were liable to develop toxic respiratory-tract diphtheria. For example, of the 1238 infected persons reported by Jellard (1972), 318 (25·7%) were Caucasians; but of the 17 cases of toxic diphtheria that occurred, all but one were in white persons. Infection in Indians and Metis was endemic and generally presented as non-toxic infection of the nose and throat, as ear infections in infants and children, or as superficial skin infections, especially of the lower limbs.

It seems likely that although the diphtheria bacillus is widespread in rural native Indian populations of northern Canada, the population is protected by a high level of immunity gained from active immunization programmes. Natural immunity from frequent reinfection early in life may have reinforced the immunity from toxoid. The organism continues to circulate, together with streptococci and staphylococci, in conditions of poor personal hygiene and overcrowded housing. Unimmunized white adults who may come in contact with native people, either by visiting the north or by contact in urban areas, remain at risk of toxic diphtheria; and examples of this occurred in the Pacific Northwest.

Less information is available about diphtheria in the Inuit (Eskimos). An outbreak occurred in Cambridge Bay, N.W.T., during 1976 and 1977. All but one of 50 cases in the community occurred in Inuit; most of the patients were children, 31 being between 5 and 14 years old (Forrest *et al.* 1977; Gully *et al.* 1977). Diphtheritic infection of the ear often occurred in Inuit. Among 97 infected Inuit reported by Jellard (1972), the site of infection was the ear in 65 (67%).

The Pacific Northwest

This area, comprising the Canadian province of British Columbia and the adjacent state of Washington, has a temperate climate and high rainfall. Diphtheria has been reported particularly from the two major cities, Seattle and Vancouver.

In Seattle, Wash., from 1972 to 1975 there was a focus of persistent skin diphtheria in a decaying central area of the city termed 'skid road' (Pedersen *et al.* 1977). This term, which originated in Seattle, although it is now widely used and sometimes modified to 'skid row', originally denoted a place where logs were skidded into the water, but is now applied to the central areas of large cities where destitute males, often alcoholic, exist in poor crowded housing. The Seattle outbreak comprised 558 infected persons, 334 being from the Skid Road area; three white men, all over 47 years of age, died from respiratory diphtheria, but the

noteworthy feature was that 74 % of the infections were cutaneous. Adults formed 93 % of the infected persons, 70 % were classed as heavy drinkers, 84 % were male, and 39 % were American Indians. The continuing nature of the 3-year outbreak is believed to have been the result of environmental contamination from cutaneous lesions combined with poor personal hygiene. One patient suffered from chronic intermittent cutaneous diphtheria with multiple skin lesions for 3 years (Bader *et al* 1978).

A smaller outbreak of cutaneous diphtheria occurred in Vancouver, B.C., 175 kilometres north of Seattle, during a 16-month period ending April 1972 (Cockroft, Boyko & Allen, 1973). Forty-four cases were reported, and staphylococci or haemolytic streptococci were present in the diphtheritic skin lesions of all the patients. Ulcerating lesions, mostly indolent and deep, occurred in 24 patients, and infected lacerations or abrasions in 11. As in Seattle, the patients were mostly middle-aged indigent alcoholics, generally males. The strains belonged to both *gravis* and *intermedius* biotypes, but all were toxinogenic.

Whereas in the urban Pacific Northwest, diphtheria infections, mostly cutaneous, occurred in destitute alcoholic males, an outbreak in 1973 in a rural area of Washington state caused by biotype *intermedius* mostly affected children, predominantly Indians (Koopman & Campbell, 1975). The primary focus of infection is believed to have been four children with cutaneous diphtheria from whom 20 other cases and 48 carriers eventually became infected, mainly in school classrooms, during a period of about a month. There was epidemiological evidence that persons with skin infections were more contagious than those with respiratory infections, infection spreading from Indian children with skin infections to the rest of the Indian community and thence to the Caucasian community.

The southern United States

The majority of diphtheria cases reported in the U.S.A. during 1959–70 occurred in southern states, and during 1969–70 the attack rate in states south of the 37th parallel of latitude was 35 times greater than in states to the north (Center for Disease Control, 1971). Attention was drawn by Belsey *et al.* (1969) to the importance of skin infections as a significant reservoir of diphtheria in Louisiana and Alabama, and to the occurrence of skin carriage in areas that had been free from clinical disease for many years. The study was stimulated by the fortuitous culturing of *C. diphtheriae* from skin lesions of a child with typical impetigo during a survey of respiratory-tract carriers. Diphtheria bacilli were isolated from skin lesions of 30 % of 268 otherwise healthy persons, and the authors showed an association between infection of the skin and of the respiratory tract. *C. diphtheriae* was found in skin lesions of 3 of 33 persons living in a rural region in which clinical diphtheria had not been observed for 8 years. Infection was more common in children under 9 years of age than in older persons; and a history of immunization was equally common in the infected and the uninfected.

THE NINETEEN-EIGHTIES

Since 1980 very few cases of diphtheria have been reported in North America. To some extent this may have been a consequence of a change in reporting

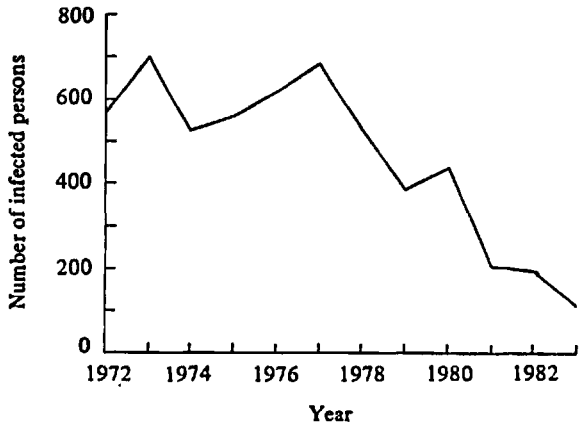

Fig. 4. Annual number of persons in Alberta and Northwest Territories from whom *C. diphtheriae* was isolated during 1972–83. (Data from Provincial Laboratory, University of Alberta.)

practices, since in the United States cutaneous diphtheria has not been consistently reported since 1979 (Centers for Disease Control, 1982*b*). Nevertheless the figures are noteworthy: in the U.S.A., 3 cases were reported in 1980 and 5 cases in 1981; in Canada, 7 cases in 1981 and 11 cases in 1982. But the death of an unimmunized 9-year-old girl in the United States in 1982 is a reminder of the continuing danger to the unprotected (Centers for Disease Control, 1982*a*). That not only the number of cases but also the number of infected persons has fallen in some localities is suggested by figures for diphtheria bacilli identified at the author's laboratory in Edmonton, Alberta. The mean annual number of isolations of *C. diphtheriae* from patients in Alberta and the N.W.T. fell from 612 during 1976-8 to 178 during 1981-3 (Fig. 4).

While it is impossible to be certain of the reason for the welcome reduction in both reported cases and infected persons, it has coincided with intensive immunization programmes against infectious diseases of childhood in both countries. In 1978 it was estimated that over 70% of the U.S. population under 14 years of age had received three or more doses of toxoid (Center for Disease Control, 1980), and this figure has almost certainly increased since then. There is now a legal requirement in all 50 U.S. states and in two Canadian provinces (Ontario and New Brunswick) that all children be immunized against diphtheria before beginning school.

CHARACTERISTICS OF THE ORGANISM

Biotype

The *mitis* biotype has predominated in the U.S.A. in recent years. During 1959-70, 53% of 1888 reported typed isolates were *mitis*, 27% *gravis*, 15% *intermedius* and 4% indeterminate (Brooks, Bennett & Feldman, 1974). *Mitis* predominated in the south and north, but *gravis* in the west, where it represented 65% of strains. *Gravis* strains have been somewhat more common in northern Canada, where of 1633 strains isolated during 1967–71, 36% were *gravis*, 35% *mitis*, 24% *intermedius* and 5% indeterminate (Dixon & Thorsteinson, 1969; Jellard, 1972).

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Toxogenicity

Among the 1633 Canadian strains, about half (52%) the *gravis* strains were toxogenic, almost all (92%) the *intermedius* strains, but very few (5%) of the *mitis* strains. In the United States during 1959–70, considerable variation was noted in the proportions of toxogenic isolates: during 1959–64 more than 95% of *gravis* strains were toxogenic, but in 1965–7 the percentage was less than 44. *Intermedius* strains were almost all (99%) toxogenic, and *mitis* varied widely from 99% in 1962 to 74% in 1969–70 and to 14% in 1971–5 (Brooks, Bennett & Feldman, 1974; Center for Disease Control, 1978).

Phage type

The phage-typing method of Saragea & Maximescu (1964, 1969) has been used by a few North American investigators. Strains from Texas and adjacent states were examined by McCloskey, Saragea & Maximescu (1972), who found the majority of strains isolated during 1968–71 to belong to a previously undescribed *intermedius* type designated K, while most of the others belonged to *gravis* phage type XIV. In Canada, Toshach, Valentine & Sigurdson (1977) examined 3077 strains from Alberta with a limited set of the Saragea and Maximescu phages. Among the 1824 typable strains, 42 types were recognized but 20 of them were uncommon. Strains from other provinces showed a similar type distribution. The *gravis* strains all belonged to two related types, the *intermedius* strains to a handful of types, including K, and while a larger number of types were represented among the *mitis* strains, most *mitis* strains were resistant to all the phages. Phage typing has been of some value in differentiating strains in defined outbreaks in northern communities in which a variety of types were circulating.

Antibiotic resistance

Unusual resistance of diphtheria bacilli to antibiotics has been reported in recent years. The first two strains reported with resistance to erythromycin and lincomycin were detected among 950 strains from the Northwest Territories of Canada by Jellard & Lipinski (1973). The minimum inhibitory concentration (MIC) of each antibiotic was 1000 μg or more per ml. Subsequently strains resistant to erythromycin (MICs 32–256 μg/ml) and clindamycin (MIC more than 512 μg/ml) were isolated in Seattle, Wash. (Coyle *et al.* 1979). During the 12 years 1972 to 1983, 105 (1·9%) of 5672 strains of Canadian origin examined in the author's laboratory were resistant to erythromycin and lincomycin. Of these, 83 were non-toxogenic *mitis* strains and 16 were toxogenic *intermedius*.

Tetracycline resistance, although common in some countries (Rockhill *et al.* 1982), is very rare in North America, and among the 5672 Canadian strains only two (0·04%), both non-toxogenic *mitis*, were resistant to tetracycline, one isolated in 1979 and the other in 1983.

CUTANEOUS DIPHTHERIA

A striking change in the pattern of occurrence of diphtheria in the last fifteen years has been the increase in the reported cases of skin infection. Previously, skin diphtheria was regarded as essentially a disease of the tropics, although occasional

cases had been reported in North America (Flor-Henry, 1961), often as complications of diseases of the respiratory tract. The increased incidence has been associated with poor socio-economic conditions, particularly overcrowded housing and poor standards of hygiene. The majority of cases have been either in young native people in certain rural areas, particularly northern Canada, or among middle-aged destitute males in the centre of cities, notably Seattle and Vancouver.

Initial reports that cutaneous diphtheria was more common and of more significance than previously reported in Canada (Dixon & Thorsteinson, 1969) and the United States (Belsey *et al.* 1969), were followed by a report by Jellard (1972), who noted 242 skin infections among 1238 persons infected with *C. diphtheriae* in northern Alberta and in the Northwest Territories of Canada. Indian or Metis persons contributed 207 (85%) of these cases and the majority of patients were children. The increase in incidence in the United States was recognized during the period 1971–5, when 431 cases were reported, compared to 31 cases during 1959–70 (Center for Disease Control, 1978); however, 420 of these were from an outbreak in Washington state. By 1975, cutaneous diphtheria accounted for 67% of reported cases of diphtheria in the U.S.A., having exceeded reported respiratory cases in 1974 for the first time (Center for Disease Control, 1978). The disease in the United States primarily affected destitute adults, many of whom were American Indians.

Instead of the deep ulcerative lesions typical of primary cutaneous diphtheria, especially in the tropics (Liebow *et al.* 1946; Livingood, Perry & Forrester, 1946), most of the lesions in Canadian patients were superficial and unaccompanied by toxic complications. Among 198 diphtheritic skin lesions with a known clinical diagnosis, 102 were classed as impetigo whereas only 26 were ulcers, mostly occurring on the legs (Jellard, 1972). Reviewing 1415 cutaneous diphtheria infections, Jellard (1982) noted that, except for ulcers, skin diphtheria was not recognizable clinically. Diphtheria infection was associated with infection with pyogenic cocci and presented in such forms as impetigo, septic abrasions, infected burns or insect bites and infected scabies.

The clinical presentation has varied somewhat between regions. In Louisiana, superficial lesions indistinguishable from infections associated with pyogenic bacteria were common and ulcers uncommon (Belsey *et al.* 1969); but in Vancouver, 24 of 44 cases had ulcerating lesions, mostly indolent and deep (Cockroft, Boyko & Allen, 1973).

A very large proportion of skin lesions infected with diphtheria bacilli also harbour *Staphylococcus aureus* and haemolytic streptococci. Thirty-six of 44 patients with cutaneous diphtheria in Vancouver (Cockroft, Bokyo & Allen, 1973) harboured all three organisms, and in northern Canada 95% of diphtheria skin lesions were associated with haemolytic streptococci of groups A, B, C or G and 86% with staphylococci. In this laboratory during 1980–3, 75% of all skin swabs in which *C. diphtheriae* was present also harboured *Streptococcus pyogenes*, whereas only 30% of nasopharyngeal swabs positive for diphtheria also contained *S. pyogenes*. It seems likely that skin infections caused or secondarily infected by streptococci or staphylococci predispose to secondary infection with diphtheria bacilli, and that poor personal hygiene is an important contributing factor.

The superficial lesion infected with both toxinogenic diphtheria bacilli and various pyogenic cocci is a potential source of serious disease to the community,

but is unlikely to cause the patient toxic complications. In these respects it resembles the respiratory-tract carrier state. The local severity of the skin lesion will vary with the extent and site of infection, but often the response to therapy is slow and the course protracted. The widespread dissemination of diphtheria bacilli from skin lesions into the environment was demonstrated by Belsey (1970) and the epidemiological role of cutaneous diphtheria in a rural diphtheria epidemic, which included respiratory cases, was demonstrated by Koopman & Campbell (1975).

Reports of skin diphtheria in Canada and the United States are now decreasing annually. Since 1979, cutaneous diphtheria has not been consistently reported in the United States, probably contributing to the decrease in cases reported in 1980 and 1981 (Centers for Disease Control, 1982*b*).

INFECTIONS OF THE EAR

Diphtheritic infections of the ear have been reported with surprising frequency in young Indian children in northern Canada. From 1967 to 1981, 1162 isolations of *C. diphtheriae* were reported from swabs of ear discharge from patients in northern Alberta and the Northwest Territories of Canada (Dixon & Thorsteinson, 1969; Jellard, 1982). Jellard (1972) noted that 95 % of the patients were of North American Indian, Metis or Inuit origin, that 46 % were less than 2 years of age, and that concurrent infection with haemolytic streptococci (81 %) or *S. aureus* (77 %) was usual.

The primary disease of these children was probably otitis media, caused generally by haemolytic streptococci. As with cutaneous infection, the clinical findings were similar whether or not diphtheria bacilli were present. The corynebacteria appear to be secondary and to play no significant pathogenic role. The biotype and toxogenicity of the strains from the ear (18 % toxogenic *gravis*; 51 % non-toxogenic *mitis*) were very similar to those isolated from patients with skin lesions (19 % toxogenic *gravis*; 53 % non-toxogenic *mitis*) and substantially different in these respects from strains from patients with respiratory infections (29 % toxogenic *gravis*; 37 % non-toxogenic *mitis*). This is suggestive that the diphtheria bacilli reach the middle ear by way of the external auditory canal rather than the nasopharynx (Jellard, 1982).

In the United States aural diphtheria has been much less commonly reported. During 1959 to 1970, 16 of the 3916 bacteriologically confirmed reported cases of diphtheria were ear infections and 11 of these were secondary to nasopharyngeal diphtheria (Center for Disease Control, 1971). Among 1433 diphtheria cases in Los Angeles from 1940 to 1950, the ear was infected in only five patients (Naiditch & Bower, 1954). Primary diphtheritic otitis media was reported in two patients by Drury (1925) and in one by Downes (1959).

DISCUSSION

Although pharyngeal diphtheria and its fatal complications are now rare in North America the causative organism has not been eradicated. This is indicated by the very occasional cases which still occur in the unimmunized and by

continuing detection of infected persons in remote areas. The extent of symptomless carriage is unknown. Special selective cultural techniques for the detection of *C. diphtheriae* are seldom used nowadays unless there is clinical suspicion of the disease. Consequently small numbers of diphtheria bacilli may be unrecognized during cultural examinations, particularly in the presence of streptococci or some other microbial cause for the lesion under investigation, and in such an instance infection will not be diagnosed. Nevertheless it seems likely that the number of persons harbouring *C. diphtheriae*, with or without lesions or symptoms, is falling. In the author's laboratory, where all swabs are examined by selective techniques for diphtheria bacilli, the organism is isolated exceedingly rarely in patients living in urban areas, and the number detected in northern rural areas is steadily decreasing (Fig. 4). Unimmunized persons continue to be at risk of serious illness, but the few data available suggest that the number of infected persons, who are the only source of new infections, is continually declining. Diphtheria still exists in North America but if the downward trend continues it may soon become a disease of historical record.

I am grateful to Dr Roger A. Feldman, Centers for Disease Control, Atlanta, for helpful discussions and advice. I also thank Dr Alan Hinman, C.D.C. Atlanta, and Dr Stanley Acres, Laboratory Centre for Disease Control, Ottawa, for providing statistical information.

REFERENCES

Bader, M., Pedersen, A. H. B., Spearman, J. & Harnisch, J. P. (1978). An unusual case of cutaneous diphtheria. *Journal of the American Medical Association* **240**, 1382–1383.

Belsey, M. A. (1970). Isolation of *Corynebacterium diphtheriae* in the environment of skin carriers. *American Journal of Epidemiology* **91**, 294–299.

Belsey, M. A., Sinclair, M., Roder, M. R. & Le Blanc, D. R. (1969). *Corynebacterium diphtheriae* skin infections in Alabama and Louisiana, a factor in the epidemiology of diphtheria. *New England Journal of Medicine* **280**, 135–141.

Bourdon, C. A. (1945). The diphtheria situation in Montreal and immunization. *Canadian Journal of Public Health* **36**, 305–311.

Brooks, G. F., Bennett, J. V. & Feldman, R. A. (1974). Diphtheria in the United States, 1959–1970. *Journal of Infectious Diseases* **129**, 172–178.

Center for Disease Control (1971). *Diphtheria Surveillance Report*, No. 11.

Center for Disease Control (1978). *Diphtheria Surveillance Report*, No. 12.

Center for Disease Control (1980). *Immunization Against Disease 1980*.

Centers for Disease Control (1982*a*). Fatal diphtheria – Wisconsin. *Morbidity and Mortality Weekly Report* **31**, 553–555.

Centers for Disease Control (1982*b*). Annual Summary 1981: reported morbidity and mortality in the United States. *Morbidity and Mortality Weekly Report* **30**, 32.

Cockroft, W. H., Boyko, W. J. & Allen, D. E. (1973). Cutaneous infections due to *Corynebacterium diphtheriae*. *Canadian Medical Association Journal* **108**, 329–331.

Communicable Disease Center (1966). *Diphtheria Surveillance Report*, No. 7.

Coyle, M. B., Minshew, B. H., Bland, J. A. & Hsu, P. C. (1979). Erythromycin and clindamycin resistance in *Corynebacterium diphtheriae* from skin lesions. *Antimicrobial Agents and Chemotherapy* **16**, 525–527.

Dixon, J. M. S. & Thorsteinson, S. (1969). Diphtheria bacilli isolated in Alberta in 1967 from the throat, nose, ears and skin. *Canadian Medical Association Journal* **101**, 204–207.

Downes, J. J. (1959). Primary diphtheritic otitis media. *Archives of Otology* **70**, 27–31.

Drury, D. W. (1925). Diphtheria of the ear. *Archives of Otology* **1**, 221–230.

FITZGERALD, J. G., DEFRIES, R. D., FRASER, D. T., MOLONEY, P. J. & MCKINNON, N. E. (1932). Experiences with diphtheria toxoid in Canada. *American Journal of Public Health* **22**, 25–28.

FLOR-HENRY, P. (1961). Cutaneous diphtheria. A brief historical review and discussion of recent literature, with presentation of two cases. *Medical Services Journal of Canada* **17**, 823–830.

FORREST, C. R., GULLY, P. R., ALDRICH, M. & JELLARD, C. H. (1977). Diphtheria – Cambridge Bay, N.W.T. *Canada Diseases Weekly Report* **3**, 45.

FROST, W. H., FROBISHER, M. JR., VAN VOLKENBURGH, V. A. & LEVIN, M. L. (1936). Diphtheria in Baltimore: A comparative study of morbidity, carrier prevalence and antitoxic immunity in 1921–24 and 1933–36. *American Journal of Hygiene* **24**, 568–586.

GAUVREAU, L., BRETON, J. P., BERGERON, M. G., DORVAL, J., MARTINEAU, G. & FRENETTE, G. (1977). Epidémie de diphtérie survenue sur la Côte Nord du St-Laurent à l'automne de 1974. *Canadian Medical Association Journal* **116**, 1279–1283.

GODFREY, E. S. (1932). Study in the epidemiology of diphtheria in relation to the active immunization of certain age groups. *American Journal of Public Health* **22**, 137–156.

GOURLAI, B., BOYLAND, B., VON HEITZ, R., KING, M. & JELLARD, C. H. (1981). Diphtheria – Northwest Territories (Mackenzie and Inuvik Zones). *Canada Diseases Weekly Report* **7**, 53–54.

GULLY, P. R., ALDRICH, M., REID, J. & JELLARD, C. H. (1977). Diphtheria – Cambridge Bay and Coppermine, N.W.T. *Canada Diseases Weekly Report* **3**, 202–203.

HEATH, C. W. JR., & ZUSMAN, J. (1962). An outbreak of diphtheria among skid-row men. *New England Journal of Medicine* **267**, 809–812.

HENNEKENS, C. H. & SASLAW, M. S. (1976). A diphtheria outbreak in Dade County, Florida. *Southern Medical Journal* **69**, 759–763.

JELLARD, C. H. (1972). Diphtheria infection in North West Canada, 1969, 1970 and 1971. *Journal of Hygiene* **70**, 503–510.

JELLARD, C. H. (1982). Diphtheria in Northern Alberta and the Mackenzie and Inuvik Zones of the Northwest Territories, 1969–1981. *Canada Diseases Weekly Report* **8**, 57–59.

JELLARD, C. H. & LIPINSKI, A. E. (1973). *Corynebacterium diphtheriae* resistant to erythromycin and lincomycin. *Lancet* i, 156.

KOOPMAN, J. S. & CAMPBELL, J. (1975). The role of cutaneous diphtheria infections in a diphtheria epidemic. *Journal of Infectious Diseases* **131**, 239–244.

LIEBOW, A. A., MACLEAN, R. D., BUMSTEAD, J. H. & WELT, L. G. (1946). Tropical ulcers and cutaneous diphtheria. *Archives of Internal Medicine* **78**, 255–295.

LIVINGOOD, C. S., PERRY, D. J. & FORRESTER, J. S. (1946). Cutaneous diphtheria: a report of 140 cases. *Journal of Investigative Dermatology* **7**, 341–364.

MARCUSE, E. K. & GRAND, M. G. (1973). Epidemiology of diphtheria in San Antonio, Tex., 1970. *Journal of the American Medical Association* **224**, 305–310.

MCCLOSKEY, R. V., SARAGEA, A., & MAXIMESCU, P. (1972). Phage typing in outbreaks in the Southwestern United States, 1968–71. *Journal of Infectious Diseases* **126**, 196–199.

MCKINNON, N. W., ROSS, M. A. & DEFRIES, R. D. (1931). Reduction in diphtheria in 36,000 Toronto school children as a result of an immunization campaign. *Canadian Journal of Public Health* **22**, 217–223.

MOORE, H. A. & LARSEN, G. I. (1957). Present distribution of diphtheria in the United States. *Public Health Reports* **72**, 537–542.

MORTON, A. R. (1941). The diphtheria epidemic in Halifax. *Canadian Medical Association Journal* **45**, 171–174.

MUNFORD, R. S., ORY, H. W., BROOKS, G. F. & FELDMAN, R. A. (1974). Diphtheria deaths in the United States, 1959–1970. *Journal of the American Medical Association* **229**, 1890–1893.

MURPHY, W. J., MALEY, V. H. & DICK, L. (1956). Continued high incidence of diphtheria in a well-immunized community. *Public Health Reports* **71**, 481–486.

NAIDITCH, M. J. & BOWER, A. G. (1954). Diphtheria. A study of 1,433 cases observed during a ten-year period at the Los Angeles County Hospital. *American Journal of Medicine* **17**, 229–245.

PEDERSEN, A. H. B., SPEARMAN, J., TRONCA, E., BADER, M. & HARNISCH, J. (1977). Diphtheria on Skid Road, Seattle, Wash., 1972–1975. *Public Health Reports* **92**, 336–342.

REYNOLDS, P. J., BOWMER, E. & CARR, W. G. L. (1976). A localized outbreak of diphtheria – Vancouver Island. *Canada Diseases Weekly Report* **2**, 141–142.

ROCKHILL, R. C., SUMARMO, HADIPUTRANTO, H., SIREGAR, S. P. & MUSLIHUN, B. (1982).

Tetracycline resistance of *Corynebacterium diphtheriae* isolated from diphtheria patients in Jakarta, Indonesia. *Antimicrobial Agents and Chemotherapy* **21**, 842–843.

SARAGEA, A. & MAXIMESCU, P. (1964). Schéma provisoire de lysotypie pour *Corynebacterium diphtheriae*. *Archives Roumaines de Pathologie Expérimentale et de Microbiologie* **23**, 817–838.

SARAGEA, A. & MAXIMESCU, P. (1969). Nouveaux types phagiques dans le schéma de lysotypie de *C. diphtheriae*. *Archives Roumaines de Pathologie Expérimentale et de Microbiologie* **28**, 1053–1058.

TOSHIACH, S., VALENTINE, A. & SIGURDSON, S. (1977). Bacteriophage typing of *Corynebacterium diphtheriae*. *Journal of Infectious Diseases* **136**, 655–660.

VARUGHESE, P. (1978). Diphtheria in Canada. *Canada Diseases Weekly Report* **4**, 65–68.

ZALMA, V. M., OLDER, J. J. & BROOKS, G. F. (1970). The Austin, Texas, diphtheria outbreak. Clinical and epidemiological aspects. *Journal of the American Medical Association* **211**, 2125–2129.