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Diphtheria infection in North West Canada, 1969, 1970 and 1971

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SUMMARY

In three years, *Corynebacterium diphtheriae* was isolated from 1238 people, consisting of 820 North American Indians or Metis, 318 people of Caucasian origin, 97 Eskimos and 3 Asiatic Indians. Diphtheria infection of the throat, nose, ears and skin was common in the North American Indian and Metis people, but rarely caused severe symptoms. The infection occurred less often in white people but was more serious; of 27 cases of toxic respiratory diphtheria, 25 were white people. The public health significance of the endemic infection of the North American Indian and Metis people is discussed.

INTRODUCTION

When mass prophylactic immunization against diphtheria was introduced, there was concern that it would result in an increased number of carriers (Topley, 1933). Instead of this, *Corynebacterium diphtheriae* has almost disappeared from most countries where there is an immunization regime. This has not happened in North West Canada where, in spite of a high prophylactic immunization rate, diphtheria infections continue to occur.

A description of diphtheria infection diagnosed bacteriologically is given in this paper. Some features of the disease, which is widespread and endemic in this region, are unusual and of epidemiological interest.

The region and the people

Specimens come to this laboratory from an area extending northwards from latitude 52° N in Alberta, to the Arctic Coastal districts of the Northwest Territories. The climate is dry, with a long cold winter and short warm summer; the southern part of the region is in the cool temperate zone, but the winter is longer and colder to the north.

North West Canada is inhabited by the native people, which include pure bred and half bred (Metis) North American Indians, and white people of Caucasian origin. This region is very sparsely populated, with the exception of the city of Edmonton, population 435,500, where most of the inhabitants are white. Most of the native population live in scattered, often remote and isolated, villages, or in communities on reserves; in contrast to the white people, their socio-economic

conditions and standards of hygiene are low; they live in close personal contact in overcrowded houses without adequate washing facilities. Approximately 18,000 Indians live on reserves in Northern Alberta and an additional 6200 in the North-west Territories. Population figures for Metis are not available. Diphtheria-positive Eskimos are also included in this paper, but they are too few to be representative, and are not discussed as further investigations are being made. The mode of life and environment of the Eskimos are very different from those of the Indians and Metis.

MATERIALS AND METHODS

The results of bacteriological cultures reported in this paper were from unselected swabs, taken and submitted by physicians or nurses for diagnostic or public health purposes. Serum-coated cotton wool swabs were used for specimens from nose, throat, skin lesions, and ear discharges. Swabs from distant places were sent immersed in a modification of Stuart's transport medium (Amies, 1967). The swab was inoculated on 10% sheep blood nutrient agar, Hoyle's lysed sheep blood tellurite agar, and Billings' modification of Tinsdale's serum cystine tellurite agar. The procedures for culture and identification of *Corynebacterium diphtheriae* have been described (Jellard, 1971). All strains of *C. diphtheriae* were tested for toxin production by a modification of the plate diffusion test of Elek (1948); the technique was that described by King, Frobisher & Parsons (1949), except for the use of the serum substitute medium of Hermann, Moore & Parsons (1958). The tests were examined at 24, 48 and 72 hr. incubation. Fifty-nine strains of *C. diphtheriae* were also tested for toxin production by subcutaneous inoculation of guinea-pigs, which confirmed the results of the plate test on every occasion.

RESULTS

Corynebacterium diphtheriae was cultured from nose, throat, skin or ear swabs from 1238 people; of these 820 were North American Indian or Metis, 318 were white, 97 were Eskimo, and 3 were Asiatic Indian. Altogether there were 1272 cultures of *C. diphtheriae*, whose type and toxigenicity are given in Table 1; the additional 34 cultures came from infections of more than one site, simultaneous infection with more than one strain, or subsequent reinfection with a different strain of *C. diphtheriae*. The primary site of isolation and ethnic group are shown in Table 2. All cultures from Eskimos were non-toxigenic. No relationship between the site and the type or toxigenicity of the infecting strain of *C. diphtheriae* was found. (When a toxigenic strain was found, nose and throat swabs from contacts were taken, which would account for a higher proportion of toxigenic strains from the nose and throat, than from the ear or skin.) More ear and skin swabs from natives were diphtheria-positive than from white people.

It was not possible to determine the race of every person who was swabbed, but of 4948 consecutive nose, throat, skin and ear swabs 402 were from natives and 4546 from whites. Of the 402 swabs from natives, 19 (4·7%) were positive, whereas

Table 1. *Type and toxigenicity of* 1272 *cultures of* Corynebacterium diphtheriae

Type of *C. diphtheriae*	Toxigenic	Non-toxigenic
Gravis	274	193
Intermedius	261	23
Mitis	31	415
Atypical	19	56
	585 (46 %)	687 (54 %)

Table 2. *Primary site of isolation of* Corynebacterium diphtheriae *and the ethnic group of* 1238 *persons*

Site	Indian/Metis	Eskimo	Caucasian	Asiatic Indian	Total
Nose/throat	389	25	277	2	693
Ear	224	65	14	0	303
Skin	207	7	27	1	242
Total	820	97	318	3	1238

3 out of 4546 (0·07 %) of swabs from white persons were positive. In this small sample the incidence of diphtheria-positive swabs was more than 60 times greater in native than in white persons.

Age of diphtheria-positive persons

The age of 1197 diphtheria-positive persons is shown in Fig. 1. The highest incidence of diphtheria isolation was in the first year of life, and there was a transient rise at the age of 6 years, the school entry age.

Prophylactic immunization

An inquiry showed that the immunization rate of children from the different areas was satisfactory and that immunization was carefully maintained. This was confirmed by a small investigation of 208 Indian children aged 1–12 years, who were infected with toxigenic *C. diphtheriae*; 160 (77 %) had had a primary series of three inoculations, with or without a reinforcing dose, completed within 7 years of infection, and were therefore fully immunized; 19 were inadequately immunized; 29 were unimmunized.

Seasonal incidence of isolation of C. diphtheriae

In each autumn and winter there was an increase in the number of positive cultures (Fig. 2, Table 3). *C. diphtheriae* was isolated each week of the 3-year period.

Nose and throat swabs

Of 727 cultures of *C. diphtheriae* isolated from nose or throat swabs, 381 (52·4 %) were toxigenic and 346 (47·6 %) were non-toxigenic.

Haemolytic streptococci, mostly group A, were isolated from many of the diphtheria-positive nose and throat swabs. It is often impossible to determine the

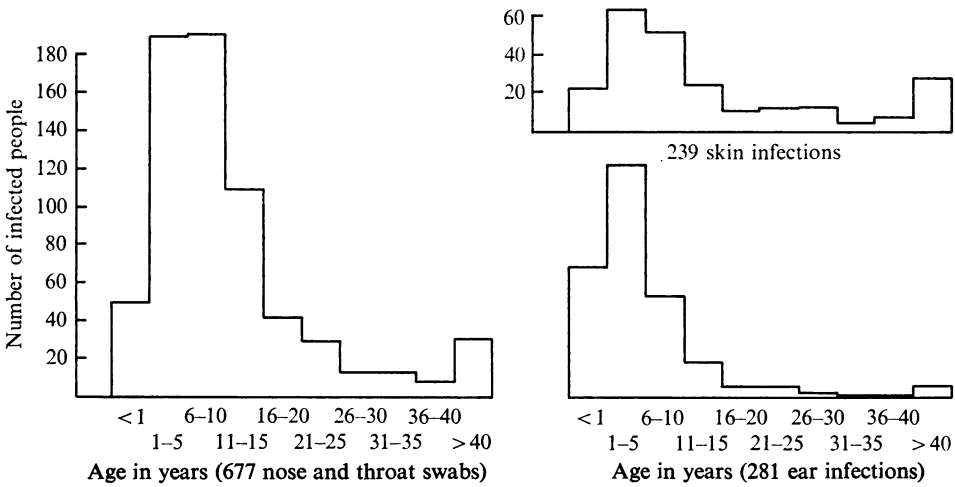

Fig. 1. *Corynebacterium diphtheriae* infections by age in swabs from skin, ear, nose and throat.

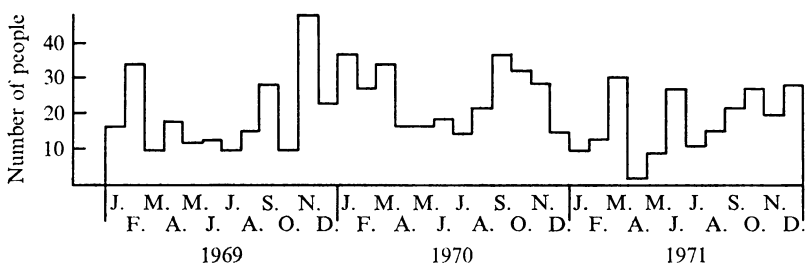

Fig. 2. 1969–1971, monthly isolations of *Corynebacterium diphtheriae* from nose and throat swabs of 693 persons.

causative or primary pathogen in a mixed streptococcal and diphtheritic infection. For the purpose of this paper, the diagnosis of toxic diphtheria of the upper respiratory tract is restricted to those people who were bacteriologically positive for *C. diphtheriae*, who had a diphtheritic membrane or clinical signs of diphtheria. Details are given in Table 4 of the 27 cases of toxic respiratory diphtheria; 25 of these people were white. In addition, an unimmunized white girl aged 2 years died from acute clinical diphtheria which was not confirmed by culture, because tonsillar tissue, excised at autopsy, was immersed in formalin; toxigenic *C. diphtheriae* mitis was isolated from two sibling carriers. All these cases came from rural areas, where white people were more liable to have contact with Indians or Metis than in urban districts.

Skin lesions

The skin lesions of 242 persons were diphtheria-positive; 27 of these were white. Eighty-six (35·5 %) were infected with toxigenic *C. diphtheriae*, and 156 (64·5 %) were infected with non-toxigenic strains. There were no toxic effects from these infections. Of the 242 lesions, 230 (95 %) were associated with haemolytic strepto-

Table 3. 1969–1971, *monthly isolations of* Corynebacterium diphtheriae *from (a) skin lesions:* 242 *people and (b) ear swabs:* 303 *people*

	1969		1970		1971	
	(*a*) Skin	(*b*) Ear	(*a*) Skin	(*b*) Ear	(*a*) Skin	(*b*) Ear
Jan.	3	9	5	7	4	10
Feb.	4	7	4	5	6	8
Mar.	5	8	5	7	7	20
Apr.	2	5	4	9	2	5
May	5	2	5	5	6	6
June	2	4	6	8	9	6
July	7	6	1	4	5	4
Aug.	6	5	6	11	6	5
Sept.	5	11	13	16	16	18
Oct.	7	13	12	15	18	11
Nov.	5	11	9	9	14	12
Dec.	9	6	11	7	9	8

Total (*a*) skin: 242.
Total (*b*) ear: 303.

Table 4. *Twenty-seven cases of toxic respiratory diphtheria*

Race	Age	Sex	Type of *C. diph.*	Toxigenicity	Prophylactic Immunization State
White	2	F	Intermedius	+	Nil
White	2	M	Gravis	+	Nil
White	2	M	Intermedius	+	Nil
White	4	F	Gravis	+	Nil
White	5	M	Intermedius	+	Nil
White	5	M	Intermedius	+	Nil
White	6	F	Intermedius	+	Nil
White	6	M	Gravis	+	Incomplete
White	7	M	Mitis	+	Incomplete
White	7	F	Mitis	+	Nil
White	7	M	Gravis	+	Nil
White	7	M	Intermedius	+	Incomplete
Indian	10	F	Gravis	+	Not known
White	10	F	Mitis	+	Full
White	12	M	Gravis	+	Not known
Metis	12	M	Gravis	+	Full
White	13	F	Intermedius	+	Full
White	13	M	Mitis	+	Incomplete
White	13	M	Gravis	+	Not known
White	14	F	Intermedius	+	Full
White	32	F	Gravis	+	Not known
White	42	M	Gravis	+	Not known
White*	45	M	Intermedius	+	Not known
White	47	M	Intermedius	+	Not known
White	50	M	Gravis	+	Nil
White	50	M	Gravis	+	Not known
White	52	F	Gravis	+	Not known

* Fatal.

Table 5. *Clinical diagnosis of* 198 Corynebacterium diphtheriae *positive skin lesions*

Impetigo	102
Trauma	39
Ulcer, leg	23
Burn	16
Eczema	15
Ulcer, hand	3

cocci of groups A, B, C or G and 209 (86·3%) with *Staphylococcus aureus*. The clinical diagnosis of 198 persons with diphtheria-positive skin lesions is given in Table 5. With the exception of the ulcers, the lesions were superficial and did not suggest diphtheria infection. The ulcers were on the leg or arm, oval or circular, up to 4 × 3 cm. and 1 cm. deep, with a sero-purulent base and well-defined raised margin.

Ear swabs

All 303 diphtheria-positive ear swabs were from persons with acute or chronic otitis media and aural discharge; 14 were from white people; 102 (33·7%) were infected with toxigenic *C. diphtheriae*, and 201 (66·3%) with non-toxigenic strains. Information was available for 281 persons, and of these 130 (46·3%) were children in the first 2 years of life (Fig. 1); the youngest was 4 weeks old. Toxic symptoms due to diphtheria were not found. Haemolytic streptococci of groups A, B, C or G were present in 247/303 (81·1%) of these swabs, *Streptococcus pneumoniae* in 14/303 (4·6%), *Staph. aureus* in 234/303 (77·2%) and on only two occasions was there a pure growth of *C. diphtheriae*.

DISCUSSION

These findings confirm the observation of Dixon & Thorsteinson (1969) that diphtheria infection is common in the native and Metis people of North West Canada. It is much less common in white people, though when they are infected they may be seriously ill. The difference in the disease in native and white people is very striking. In the natives, the infection is endemic and may present as uncomplicated infection of the nose and throat, superficial skin infection, and ear infections in babies and young children. Classical toxic diphtheria nearly always occurs in white people, and with them skin and ear infections are rare.

The different nature of the disease in white people and the natives of tropical countries has been known for many years. It was suggested that racial factors contributed to the difference (Frost, 1928; Dudley, 1929), but this has been difficult to prove. Dudley thought that the domestic environment was important, and that the rarity of clinical diphtheria in natives was due to natural infection immunity, acquired early in life, in the close contact of the home. This was supported by Liebow, MacLean, Bumstead & Welt (1946) in the South Pacific Islands, and by Gunatillake & Taylor (1968) in Ceylon, who found that skin diphtheria was common and led to an effective herd immunity. The epidemiological signifi-

cance of diphtheritic skin lesions has also been shown by Belsey, Sinclair, Roder & LeBlanc (1969).

The endemic skin diseases of the natives of tropical countries and North West Canada are comparable; conditions in the overcrowded homes are suitable for cross-infection with diphtheria bacilli and the associated pathogenic haemolytic streptococci; this may occur by skin-to-skin contact or indirectly by articles contaminated with the discharges from infected superficial skin lesions and nasopharyngeal secretions. The conditions in North West Canada are probably more favourable for cross-infection; the severe northern winters confine the people indoors and prolong the time of exposure to infection, and the discharging ears of the babies and young children also contribute to the high incidence of the disease.

Because of the frequent association of non-toxigenic and toxigenic *C. diphtheriae* with haemolytic streptococci and *Staphylococcus aureus*, the role of *C. diphtheriae* as the primary pathogen in the skin and ear infections is questionable. The elimination of this mixed endemic infection is difficult, but the aim should be an improvement in the living conditions and education in personal hygiene. Previous immunization had no apparent effect on the skin and ear infections. In fact, Grasset (1952) doubted the need for prophylactic immunization of African natives, while he stressed its importance for white people who lived in contact with them. It is just as important that white people in North West Canada should continue to be fully immunized against diphtheria.

Little is known about the relationship of toxigenic and non-toxigenic strains of *C. diphtheriae* in nature, but the scarcity of non-toxigenic strains in many places where diphtheria does not exist does suggest a close association. The coexistence of non-toxigenic and toxigenic strains in endemic areas is interesting; non-toxigenic strains should not be ignored, but regarded as an indication that the conditions are also suitable for toxigenic strains. In the laboratory, non-toxigenic *C. diphtheriae* has been converted to toxigenicity by the acquisition of lysogenic bacteriophage (Freeman, 1951; Groman, 1953), but no such transformation has yet been shown to occur in natural conditions.

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