What has this cost? Estimates only are possible, because costs of laboratory procedures, hospital care, medical care and special diets have all changed over the period of study. It has not been possible to include any estimate of the cost of the hospitals' part in the program, i.e. staff time and mailing charges to the laboratory (Table II).

Identification costs include the cost of the screening procedure per case. Hospitalization is the cost of hospital care during diagnostic assessment and initiation of dietary treatment. Medical care includes medical care during hospitalization as well as follow-up care for five years. Laboratory tests are those performed on an out-patient basis during five years of follow-up. Diet consists of a synthetic food which is low in phenylalanine and is provided by the program. The diagnosis and special care of the child with PKU therefore costs $6800 or about $7000 more than the care of a normal child. Most of these costs are carried by the province as insured health services. In contrast is the estimated cost of $250,000 of caring for an untreated severely retarded child in an institution. It would be impossible to put a price on the benefits to the child and his family of the prevention of retardation.

Résumé

Le dépistage de la phénylcétonurie en vaut-il la peine?

Le plan de dépistage de la phénylcétonurie (PCU) chez les nouveaunés mis sur pied par les autorités ontariennes a permis de toucher 94.5% des nouveau-nés entre 1966 et 1971. Il a permis d'identifier 70 nourrissons, dont 47 étaient des cas classiques et 23 étaient des cas atypiques de PCU. La fréquence était de 1 cas par 16,700 naissances d'enfants vivants pour les cas classiques et de 1 cas sur 34,000 naissances d'enfants vivants pour les cas atypiques. Depuis le début du programme, un diagnostic de PCU a été posé chez 44 enfants durant la première enfance de le traitement qui leur a été appliqué a été couronnée de succès. Trois nourrissons seulement ont subi une arriération mentale, dont deux avaient échappé au cours du plan de dépistage.

Le coût de l'identification et du traitement pour un enfant durant cinq ans est d'environ $7000, se qui est évidemment très inférieur à la somme de $250,000 nécessaire pour couvrir les soins hospitaliers, la vie durant, d'un individu dont l'arriération mentale est sévère.

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Cutaneous infections due to Corynebacterium diphtheriae

W. H. Cockcroft, M.D., C.R.C.P. [C], W. J. Boyko, B.SC., M.D. and D. E. Allen, M.SC., *Vancouver, B.C.*

Summary: Toxigenic *Corynebacterium diphtheriae* was grown from skin lesions of 44 indigent patients seen at the emergency or out-patient departments of this hospital, 43 of them within the last 16 months of the study period. In all cases staphylococci or hemolytic streptococci were also present in the wounds. An increase in the incidence of clinical diphtheria occurred in the few months preceding and overlapping the period of recognition of the cutaneous infections. The *gravis* strains, which accounted for the majority of the infections, were sensitive to erythromycin and to penicillin, but were relatively resistant to cloxacillin.

Cutaneous diphtheria is not uncommonly seen in tropical countries[1, 2] and extensive outbreaks occurred in some prisoner-of-war camps during World War II,[3] but in North America diphtheritic skin infections have been recorded infrequently.[4-6] In Vancouver diphtheria has been very uncommon in recent years: no cases were seen in the Vancouver General Hospital during the years 1963 to 1967, nor were any toxigenic strains isolated in the hospital laboratory during that period. However, in June 1968 a patient with a septic lesion on the foot due to *C. diphtheriae* was seen in the out-patient department. Between that time and April 1972, 43 other patients, most of whom live in the skid-row area of Vancouver, have been treated for similar cutaneous lesions infected with toxigenic strains of *C. diphtheriae*. All 43 additional cases were seen in the last 16 months of this period. Since 1968 the number of cases of faucial diphtheria seen in this hospital has also increased sharply.

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From The Division of Bacteriology, Department of Pathology, Vancouver General Hospital, and The Division of Medical Microbiology, University of British Columbia, Vancouver, B.C.
Reprint requests to: Dr. W. H. Cockcroft, Division of Bacteriology, Vancouver General Hospital, 855 West 12th Avenue, Vancouver 9, B.C.

Patients and methods

The patients, for the most part, were unemployed adults who presented themselves to the out-patient or emergency departments of the hospital for the treatment of septic lesions. Most lived in small hotels or rooming houses in a restricted area of the older part of the city. Many had no fixed address and a history of alcoholism was common. Swabs from the cutaneous lesions were sent to the hospital laboratory for culture. The clinical records of all patients whose wounds yielded toxigenic organisms were reviewed.

In the laboratory, blood-agar, mannitol salt agar and trypticase soy broth containing 0.1% agar were the media used routinely. If diphtheroids were seen in the gram-stained smear of the exudate, tellurite blood-agar was also used as a

primary plating medium. Gram-positive bacilli which had characteristic sugar reactions and morphology when grown on Loeffler's serum slopes were sent to the B.C. Provincial Division of Laboratories for confirmation of identity and for guinea pig virulence tests. Toxigenic strains were sent to the Laboratory of Hygiene in Ottawa for serologic typing. Staphylococci and streptococci were identified by conventional methods. Bacitracin discs (Taxos A, BBL) were used to detect Group A streptococci.

Case reports

1. V.S., a 68-year-old unemployed man living in the skid-row area, came to the out-patient department with multiple infected fissures on the foot and pre-tibial ulcerations from which *C. diphtheriae*, Group A streptococci and penicillin-resistant *Staph. aureus* were cultured. He was treated with saline compresses and erythromycin for 13 days. After six days *C. diphtheriae* was still present in the wound but was absent 10 days later. He was readmitted six weeks after discharge; lesions on both legs again grew *C. diphtheriae*.

2. R.P., a 29-year-old male skid-row resident, presented with infected lacerations on the plantar and flexor aspects of the foot, cellulitis and lymphangitis. A heavy growth of *C. diphtheriae* and penicillin-resistant *Staph. aureus* was obtained from the wounds. He was treated with antitoxin, penicillin for 13 days and erythromycin for 10 days, as well as saline compresses. The lesions were very slow to heal, with formation of eschars with erythematous margins. Cultures of wound material 22 days after admission grew *C. diphtheriae*.

3. F.H., a 46-year-old female North American Indian with a history of alcoholism, was seen in the emergency department with a 5-cm.-diameter indolent ulcer on the left medial malleolus. The ulcer had progressively enlarged following laceration by broken glass. She was treated with cloxacillin and saline compresses. She signed herself out of hospital and did not return for follow-up. Cultures from the ulcer yielded *C. diphtheriae*, penicillin-resistant *Staph. aureus* and Group A streptococci.

The patients were a heterogeneous group of middle-aged indigent alcoholics and younger transient unemployed individuals, 35 of whom were men and nine women. Two patients were known to be drug (heroin) addicts. Ten patients, five men and five women, were North American Indians.

The locations of the lesions are presented in Table I. Twenty-four patients had ulcerating lesions, most of which were indolent and deep. Ulcers on the feet were commonly multiple, but the clinical appearance of the lesions suggested no specific bacterial etiology. Infected lacerations and abrasions occurred in 11 patients, and a miscellaneous group included infected burns, eczema, an infected postoperative incision and one case of acute conjunctivitis. Erythromycin and penicillin were the antibiotics most frequently used for the initial treatment, and all but five patients received some antibacterial agent. In those patients who returned to the clinic for follow-up and in the six who were admitted to the hospital for treatment, healing of the lesions was slow, and in several instances *C. diphtheriae* could still be grown from the wounds after eight or more days of antibiotic therapy; none of the organisms had altered in their sensitivity to antibiotics. Neither myocarditis nor neuritis was recognized in any of the hospitalized patients, or in any of those who returned to the out-patient clinic.

Bacteriology of lesions

C. diphtheriae, Staphylococcus aureus and streptococci were isolated from the lesions of 36 of the 44 patients. In four cases *C. diphtheriae* was found in association with *Staph. aureus* and in a further four with streptococci. *Gravis* strains of *C. diphtheriae* were found in 40 of the 44 cases, the other four being *intermedius*, and all isolates had posi-

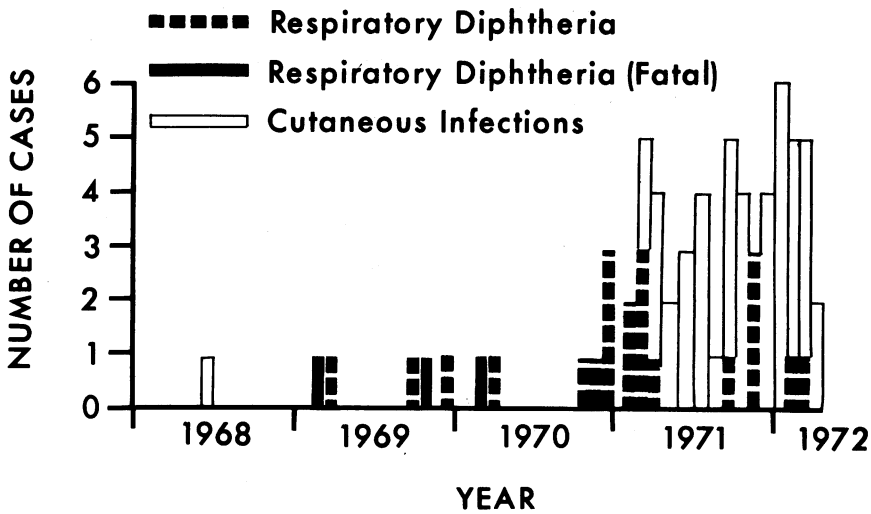

FIG. 1.—Occurrence of cutaneous and respiratory diphtheria, Vancouver General Hospital, June 1968 to April 1972.

Table I
Distribution of lesions in 44 patients

Foot	13
Leg	13
Hand	9
Arm	3
Head	3
Trunk	2
Eye (conjunctivitis)	1

Table II
Organisms found in cutaneous lesions and antibiotic sensitivity in 44 patients

	Total isolates	Number of strains resistant to penicillin G*	tetracycline	erythromycin
C. diphtheriae gravis	40	0	0	0
intermedius	4	0	0	0
Staph. aureus	40	38	13	0
Group A streptococci	29	0	0	0
Non-group A streptococci	11	0	5	0

*Antibiotic discs: penicillin G 2 units, tetracycline 5 μg., erythromycin 2 μg.

tive virulence tests. Serologic typing of the first 22 strains of *C. diphtheriae* revealed that 16 were *gravis*, type II, two were *gravis* non-typable and four were *intermedius*. The last 22 isolates have all been *gravis* strains (starch positive) but are untyped as yet.

All cultures of *C. diphtheriae* were judged sensitive to penicillin G and erythromycin, using 2-unit penicillin G discs and 2-μg. erythromycin discs. Inhibitory zones produced by 5-μg. methicillin discs averaged 14 to 19 mm., and the MIC for this agent using four *gravis* isolates was 1 μg. However, with 1-μg. cloxacillin discs inhibitory zones were small or absent entirely, and the MIC for cloxacillin was 2 μg. for two strains and 4 μg. for a further two strains. The bacteriologic findings in the 44 cutaneous infections are summarized in Table II.

The incidence of tetracycline resistance in the *Staph. aureus* strains was higher than the 10 to 11% figure that we have found in hospitalized patients in 1971-1972. Although tetracycline resistance was not found in any of the cultures of Group A streptococci, it was found in almost half of the non-group A streptococci. It is believed that most or all of the latter are Group B streptococci and our local experience is that serologically proven Group B streptococci are frequently resistant to tetracycline.

Faucial diphtheria

The occurrence of faucial diphtheria in relation to the cutaneous infections is shown in Fig. 1. There were, in all, 25 cases of respiratory diphtheria. Only six of the 25 had a severe illness but three of these patients died, two with *gravis* infections and one with an *intermedius* strain infection.

Discussion

In Ceylon[2] and in the islands of the South Pacific[3] a high incidence of *C. diphtheriae* in skin ulcers in native children has been reported, and the early Schick conversion found in this population has been attributed to the cutaneous lesions. Liebow[3] observed both faucial and cutaneous diphtheria in American servicemen stationed in the South Pacific in areas where skin infections amongst the native children were common. He and others[5] seldom saw myocardial or neurological complications following cutaneous infections, but in British prisoners of war in Singapore in 1943[1] a severe outbreak of cutaneous diphtheria followed closely an epidemic of faucial diphtheria. Neuritis or myocarditis developed in 28% of the cases, a figure similar to that seen in cutaneous infections in troops in Burma.[4] The severity of these cases was thought to be due to a humid climate, lack of facilities for personal hygiene, and in the case of the prisoners of war, malnutrition.

Cutaneous diphtheria in North America, although less common, has been reported from Alabama and Louisiana[5] and from the northern areas of Canada.[6, 7] The majority of cases in the Canadian reports have been among North American Indians. Both toxigenic and nontoxigenic strains have been noted in cutaneous infections.[2, 6]

An outbreak of diphtheria in skid-row men was seen in Omaha, Nebraska in 1962,[8] but skin infections were not mentioned in that report, nor were they common during or following the San Antonio, Texas outbreak in 1970.[11]

The number of cutaneous diphtheritic infections seen in our clinic must represent only a fraction of the cases that are actually occurring, indicating a large reservoir of toxigenic strains in this population. It is uncertain whether transmission is primarily from the respiratory tract to skin or from skin to skin, but it has been shown that *C. diphtheriae* can survive in floor dust for at least 14 weeks.[9] Contaminated blankets were thought to be the source of the dust. This aspect deserves further investigation.

The finding that our isolates were relatively resistant to cloxacillin is in keeping with McCloskey's observation[10] that oxacillin was evaluated as ineffective for the strains of *C. diphtheriae* isolated during the San Antonio epidemic of 1970. Antibiotic sensitivity tests on the various organisms found in the cutaneous lesions in our patients suggested that erythromycin might be useful as a single oral antibiotic, but neither this drug nor combinations of penicillins were able to eradicate *C. diphtheriae* rapidly from the lesions in those patients where follow-up cultures were carried out.

Our recent experience has emphasized that the presence of staphylococci or hemolytic streptococci in a wound culture should not deter one from identifying fully any "diphtheroid" which may also be present.

Résumé

Chez 44 malades indigents examinés à l'urgence du service externe de l'hôpital, dont 43 avaient été vus durant les 16 derniers mois de la période de l'étude, on a cultivé le *Corynebacterium diphtheriae* (bacille de Löffler) à partir des isolats prélevés des lésions cutanées. Dans tous les cas, coexistaient également dans les plaies des staphylocoques ou des streptocoques hémolytiques. La fréquence des cas de diphtérie clinique avait augmenté durant les quelques mois précédant et chevauchant la période de la découverte des lésions cutanées. Les souches du type *gravis*, responsables de la majorité des infections, étaient sensibles à l'érythromycine et à la pénicilline, mais relativement résistantes à la cloxacilline.

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