Use of skin substitutes in adult Canadian burn centres

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RA Hopper, J Knighton, J Fish, W Peters. Use of skin substitutes in adult Canadian burn centres. *Can J Plast Surg* 1997;5(2):112-117. Seventeen Canadian adult burn centres were surveyed to determine the pattern of use, cost and availability of nine skin substitutes. An equal number of centres in the United States with comparable bed capacities were approached for comparison. Eighty-eight per cent of the Canadian centres and 76% of the United States centres responded to the questionnaire. Human cadaver skin, pig skin and Biobrane were used by approximately twice as many United States centres as Canadian centres. Cultured epidermal autografts (CEAs) were used by 20% of the Canadian centres and 15% of the American centres. Opsite, Tegaderm and Duoderm were used widely in both countries. Alloderm was used only in the United States, and amnion was not used in either country. The most common use of each substitute varied among centres, however, the pattern of use was comparable between the two countries, with the exception that Biobrane was not used in Canada to cover donor site wounds. In the United States, 60% of cadaver skin and all CEAs were purchased from private companies, whereas use of these two relatively expensive skin substitutes in Canada was restricted to centres with access to hospital-affiliated skin banks or laboratories. With the dependence of Canadian centres on noncommercial sources of biological skin replacements, research development in established skin banks should be encouraged, and regional discrepancies regarding access to these facilities addressed.

Key Words: *Burn centres, Burn dressings, Burns, Canadian survey, Skin substitutes*

Utilisation de substituts cutanés dans les centres canadiens pour grand brûlés adultes

RÉSUMÉ : Dix-sept centre canadiens pour grands brûlés adultes ont fait l'objet d'un sondage afin de déterminer le mode d'utilisation, le coût et la disponibilité de neuf substituts de peau. Autant de centres des États-Unis dotés du même nombre de lits ont été approchés à des fins comparatives. Quatre-vingt-huit pour cent des centres canadiens et 76 % des centres américains ont répondu au questionnaire. La peau de cadavres humains, la peau de porc et Biobrane ont été utilisés par environ deux fois plus de centres américains que de centres canadiens. Les autogreffes d'épiderme cultivé ont été utilisées par 20 % des centres canadiens et 15 % des centres américains. Opsite, Tegaderm et Duoderm ont été utilisés couramment dans les deux pays. Alloderm a été utilisé aux États-Unis seulement et l'aminon n'a été utilisé ni dans un pays, ni dans l'autre. L'emploi de l'un des substituts au détriment des autres variait selon les centres. Toutefois, le mode d'utilisation était comparable entre les deux pays, à l'exception de Biobrane qui n'a pas été utilisé au Canada pour couvrir les sites des donneurs. Aux États-Unis, 60 % des greffons provenant de cadavres et toutes les autogreffes d'épiderme cultivé ont été achetés de sociétés privées, alors qu'au Canada, l'utilisation de ces deux substituts cutanés relativement coûteux a été limitée aux centres qui avaient accès à une banque ou à des laboratoires de greffes cutanées affiliés. Compte tenu de la dépendance des centres canadiens à l'endroit des sources non commerciales de substituts cutanés biologiques, la recherche et le développement doivent être encouragés dans les banques de produits cutanés établies et il faut tenter d'abolir les problèmes géographiques d'accessibilité à ces établissements.

Advances in the development of skin substitutes are frequent topics in current burn literature (1-4). The elusive goal of finding a skin replacement to mimic completely the interaction and functions of dermis and epidermis has yet to be achieved; however, a large number of synthetic and biological products are available that can serve important roles in caring for burn patients. Burn facilities in the United States have been surveyed to determine the extent of use of some of these products (5,6); however, Canadian centres have not been examined. To anticipate the role of future technology in Canadian burn

centres, it is first necessary to understand the pattern of use of the existing skin substitutes.

The objective of this study was to survey the pattern of use, cost and availability of nine skin substitutes in Canadian adult burn centres. An equal number of centres in the United States with comparable bed capacities were also reviewed for comparison.

PATIENTS AND METHODS

From July to November 1995, a questionnaire was sent to medical directors of the 17 adult burn centres in Canada listed in the American Burn Association's (ABA) *Directory of Burn Care Resources for North America 1993-1994* (7). Questionnaires were also sent to 17 adult burn centres in the

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TABLE 1: Estimated number of patients receiving skin substitutes in 15 Canadian burn centres over a one-year period

Burn unit location	Admissions per year	Human cadaver skin	Pig skin	Cultured epithelial skin	Biobrane*	Opsite [†] , Tegaderm [‡] or Duoderm [§]
Victoria, British Columbia	20-50	5-10	—	—	10-30	>30
Vancouver, British Columbia	100-200	10-30	—	5-10	5-10	10-30
Edmonton, Alberta	100-200	10-30	—	1	2-5	2-5
Calgary, Alberta	50-100	2-5	1	—	—	>30
Saskatoon, Saskatchewan	20-50	5-10	—	—	—	10-30
Regina, Saskatchewan	50-100	—	—	—	2-5	>30
Winnipeg, Manitoba	20-50	2-5	2-5	—	>30	>30
Windsor, Ontario	100-200	—	10-30	—	5-10	10-30
London, Ontario	20-50	—	—	—	—	2-5
Hamilton, Ontario	50-100	—	>30	—	—	10-30
Toronto, Ontario	100-200	—	—	—	10-30	—
Montreal, Quebec	<20	—	—	—	—	5-10
Montreal, Quebec	?	10-30	—	2-5	—	—
Saint John, New Brunswick	20-50	—	—	—	—	—
Halifax, Nova Scotia	20-50	2-5	—	—	—	>30

*Dow B Hickam Inc, Texas; [†]Smith and Nephew Inc; [‡]3M Canada Inc; [§]Bristol-Myers Squibb Canada Inc

United States with comparable bed capacities to the Canadian units. These centres were randomly selected from the directory and represented 17% of the United States units with listed bed capacities of fewer than 20.

Questions dealt with the use of five biological – human cadaver skin, pig skin, amnion, cultured epithelial autograft and Alloderm graft (LifeCell Corporation, Texas) – and four synthetic – Biobrane (Dow B Hickam Inc, Texas), OpSite (Smith and Nephew Inc), Tegaderm (3M Canada Inc) and Duoderm (Bristol-Myers Squibb Canada Inc) – skin substitutes during the one-year period preceding the survey. For each skin substitute, the directors were asked whether the product was used in their centre over the past year, and, if so, how many patients received it, where was it obtained, and what was its most common use. Nonresponders to the first questionnaire were sent a second request. Because of a relatively low response from the United States centres to the first questionnaire, responses to the second questionnaire were anonymous to increase the return.

Information on tissue banks and academic facilities offering skin products in Canada was obtained from telephone conversations with the contact persons listed in the directory or the facility director. Commercial product information and prices were obtained from company monographs, which were available in autumn 1995.

RESULTS

Sixty-five per cent (11 of 17) of Canadian units responded to the initial questionnaire. The percentage increased to 88% (15 of 17) after a second copy was mailed to nonresponders. Forty-seven per cent of the American centres responded to

the initial questionnaire, and the percentage increased to 76% (13 of 17) after the nonresponders were approached again.

The number of patients receiving skin substitutes in each surveyed centre is listed in Tables 1 and 2. Although the listed bed capacities of the centres were comparable between the two countries, the number of admissions per centre over the survey year tended to be greater in the United States. Approximate costs of each skin substitute at the time of the survey are listed in Table 3.

Biological substitutes

The eight Canadian centres that used human cadaver skin employed it to cover excised burn wounds, either as a temporary dressing before autografting or when there was lack of autograft. Five centres had their own local source of cadaver skin and the other three were situated in cities close to a Canadian tissue bank. Cadaver skin was used in all except one of the surveyed United States centres. Forty per cent of these centres obtained the skin from local hospitals or laboratory-affiliated skin banks, whereas the remaining 60% obtained the skin from a commercial company.

Pig skin was used in 27% of the Canadian centres and 46% of the American centres surveyed. The primary use of pig skin was temporary coverage of excised burns. One Canadian centre and two American centres used xenograft as a temporary dressing for treating partial-thickness burns, and two Canadian centres reported that they use xenograft to treat severe cases of toxic epidermal necrolysis.

Twenty per cent of the Canadian and 15% of the American centres used cultured epidermal autograft (CEA) during the survey year. Patients grafted with CEA in Vancou-

TABLE 2: Estimated number of patients receiving skin substitutes in 13 United States burn centres over a one-year period

Admissions per year*	Human cadaver skin	Pig skin	Cultured epithelial autograft	Alloderm†	Biobrane‡	Opsite§, Tegaderm¶ or Duoderm**
>200	>30	2-5	—	—	>30	>30
>200	10-30	5-10	—	—	2-5	>30
100-200	10-30	—	—	—	—	>30
100-200	10-30	—	—	1	>30	10-30
100-200	2-5	—	1	—	2-5	—
100-200	10-30	5-10	—	—	—	—
50-100	5-10	2-5	—	—	10-30	5-10
50-100	5-10	—	1	2-5	—	—
50-100	10-30	5-10	—	10-30	5-10	2-5
50-100	10-30	—	—	—	5-10	>30
50-100	2-5	—	—	1	5-10	—
50-100	—	—	—	—	2-5	5-10
50-100	1	10-30	—	—	2-5	—

*Responses from the centres were anonymous; †LifeCell Corporation, Texas; ‡Dow B Hickam Inc, Texas; §Smith and Nephew Inc; ¶3M Canada Inc; **Bristol-Myers Squibb Canada Inc

TABLE 3: Approximate cost of various skin substitutes for coverage of 10% total body surface area wound*

Skin substitutes	Source	Price (CDN\$)†
Human cadaver skin‡	The British Columbia Tissue Bank§	—
	Firefighter's Burn Unit Skin Bank§	270
	Foothill's Hospital Skin Bank§	—
	Nova Scotia's Firefighter's Burn Treatment Society Skin bank§	1000
	New York Firefighters Skin Bank	1660
Pig skin‡	Brennen Medical Inc, Minnesota	—
	Frozen, sterile	260
	EZ-Derm	340
Cultured epithelial allograft	Vancouver Skin Bank§	13,500
	Laboratoire des grands brûlés§	11,000
	Genzyme Corporation, Massachusetts	44,800
Alloderm	Lifecell Corporation, Texas	6,700
Lifeskin	Culture Technology Inc, California	29,200
Biobrane‡	Dow B Hickam, Texas	310
Duoderm‡	Bristol-Myers Squibb Inc	46
Opsite‡	Smith and Nephew Inc	40
Tegaderm‡	3M Canada Inc	26

*Calculated from estimated total body surface area of 1.88 m² for a man of height 178 cm, weight 70 kg; †Prices as of autumn 1995. Conversion ratio of US\$1.00=CDN\$1.37 where applicable, which does not take into consideration discounts offered due to hospital contacts, quantity purchased, etc. Additional costs such as for transportation, biopsy processing or additional dressings are not included. ‡Average cost of different sizes and shapes available; §Availability depends on local demand, and transfers are done on a nonprofit basis

ver, British Columbia and Edmonton, Alberta obtained the tissue from the British Columbia Tissue Bank in Vancouver, British Columbia. Patients grafted at the Hôtel-Dieu de Montréal, Québec, received their tissue from the Laboratoire d'Organogénèse Expérimentale (LOEX) in Québec City,

Québec. The two American units that reported use of CEA obtained the graft commercially.

No Canadian centres reported using Alloderm, whereas four surveyed American centres used it when there was minimal autograft to harvest.

Synthetic substitutes

Biobrane was used by 47% of the Canadian centres and 77% of the American centres. The primary use in most centres was coverage of superficial partial-thickness burns, although two centres in each country used it to cover excised burns or treat severe toxic epidermal necrolysis and two of the American centres used Biobrane for donor site dressing.

Synthetic dressings were used by 80% of Canadian centres and 62% of American centres. Although donor site coverage was the most common use in both countries, synthetic dressings were also used frequently in Canada as temporary dressings for superficial partial-thickness burns. One Canadian centre mentioned on the questionnaire that it used these products to treat toxic epidermal necrolysis. No centres reported using amnion to treat burn wounds.

DISCUSSION

Wound closure is a key goal in managing the burn patient. Not only does it help to halt or reverse infectious, metabolic and fluid-electrolyte abnormalities, it also serves to minimize wound pain and aid in recovery of function. Skin substitutes achieve wound closure when autologous skin is not available. The ideal skin substitute would be durable, storable, inexpensive and nonallergenic, and should adhere quickly to the wound, simulating the functions of the skin that it replaces (8,9). None of the available skin substitutes possess all these properties; however, they each have particular strengths and weaknesses that suit them for different roles in burn wound care.

Human cadaver skin

Some consider fresh human cadaver skin (allograft) to be the 'gold standard' for temporary closure of burn wounds (10). It adheres well to a healthy wound bed, resulting in reduced contamination and reduced protein, heat and water loss. In a recent survey of 54 United States burn unit medical directors, cost, rejection and disease transmission were the most commonly perceived disadvantages of human cadaver skin, whereas surveyed skin bank directors listed availability as the most significant shortcoming (6).

Four Canadian skin banks are listed in the current ABA directory. The British Columbia Tissue Bank is funded through the Vancouver Hospital and Health Sciences Centre operating budget, with the burn unit providing supplemental equipment and education funding through external fundraising. All skin is frozen unless it is needed immediately by the hospital burn unit, in which case fresh skin is preferred. Fresh skin can be stored for up to three weeks at 4°C, and the frozen form for up to five years in liquid nitrogen. Priority is given to the provincial demand for skin, although in the past, allograft has been provided to units across western Canada. In the latter case, no fee has been charged except to cover the cost of transportation.

The Firefighter's Burn Unit Skin Bank in Edmonton, Alberta is funded through the burn centre at the University of Alberta Hospital, and the Red Cross provides the site. It is the only Canadian facility to be accredited by the American Association of Tissue Banks. Fresh and frozen cadaver skin is provided primarily to the two provincial burn units; however, it has been supplied to patients in Manitoba and Toronto, Ontario in the past. Out-of-province units are charged \$25 per piece of skin ranging from 5 by 10 cm to 10 by 30 cm.

The Foothills Hospital Skin Bank in Calgary, Alberta, established in 1986, is part of a larger transplantation committee. Initially, funding was developed through private donations from the Shriner's organization but is now covered by the hospital operating budget. All skin is frozen unless immediately needed by the unit. To date, no outside units have been supplied; however, the bank organizers would consider providing cadaver skin to other Canadian units if the need became apparent.

The Nova Scotia Firefighter's Burn Treatment Society Skin Bank in Halifax, Nova Scotia is funded through the Victoria General Hospital operating budget. All harvested skin is frozen. Although the Maritime and Atlantic provinces are the most common recipients, skin has been supplied to units as far away as California. Out-of-province hospitals are charged according to a proportion of the graft budget for that year. The cost per unit is approximately \$100 per 6 by 30 cm carrier.

Le Centre des Grands Brûlés in the Hôtel-Dieu de Montréal has organized a skin harvesting program to meet the needs of its own unit. Human cadaver skin is also available to Canadian units from American sources. Two estimates given were US\$150 per quarter square foot (7.5 by 30 cm) for the New York Firefighters Lifelink and US\$450 for a 6 by 30 cm carrier from a source in Seattle, Washington.

Human cadaver skin was used less often in Canadian centres than in their American counterparts. Although the percentage of centres affiliated with a local hospital-based skin bank was roughly equal between the two countries, 60% of the American centres bought their tissue from private sources. Regular purchase of commercial human cadaver skin, instead of less expensive alternative products, is likely more difficult to justify in the publically funded Canadian hospital budget than in the private insurance-based system found in the United States.

Pig skin

Pig skin (xenograft) has gained acceptance as a temporary dressing alternative to allograft due to its lower cost and greater availability. Frozen pig skin has a storage life in a less than 0°C freezer of 6 to 18 months from the date of manufacture. Like allograft, it has the desirable properties of being able to adhere initially to a clean wound; to cover nerve endings to decrease pain; to function as an autograft test graft; and to diminish heat, protein and electrolyte loss (11,12). A premeshed, de-epithelialized shelf-stored form is available (EZ-Derm, Brennen Medical Inc, Minnesota), which is reported to be more resistant to bacterial degradation because the collagen is chemically cross-linked with an aldehyde group.

In both countries, pig skin was used by about half as many centres as those that used human cadaver skin. The two Canadian centres reporting the most frequent use of pig skin used it to the exclusion of human cadaver skin, whereas in the United States centres, both tissues were used. All pig skin was purchased from private industry. Price varied depending on the form, dimension and quantity purchased. Frozen, sterile, perforated pig skin costs around US\$65 for an 8 by 61 cm roll, whereas the perforated shelf-stored form of the same dimensions costs US\$73.85.

CEA

The technique of culturing human epidermal cells into confluent keratinizing sheets suitable for grafting was first described by Green and colleagues in 1979 (13) and first described for use in burn patients by O'Connor et al in 1981 (14). By 1992, it had been used to graft more than 240 patients in the United States (15).

At present, lack of mechanical stability of cultured epithelium is a major concern (16-18), therefore, the use of a dermal substitute in combination with CEA is receiving increased interest (3,19-21). Laboratory work is also underway to enhance genetically the function of the cultured keratinocytes to promote tissue regeneration (22).

All CEAs used by the Canadian centres were obtained from one of two academic facilities, whereas in the United States the grafts were grown by a private company. Eight to 16 patients were grafted in the surveyed Canadian centres over a one-year period, compared with only two in the United States centres. The expense of commercial CEA and the

greater use of less expensive allodermal substitutes in the United States may be two reasons for this discrepancy.

The British Columbia Tissue Bank and LOEX are the only facilities in Canada providing CEA on a regular basis to Canadian burn centres. Up to two years ago, CEA was supplied by the British Columbia Tissue Bank to western Canadian units at a cost of \$1,500 per flask (10 by 20 cm sheet). This fee was designed to cover only the cost of supplies, of which the medium was the most expensive. More recently, the bank has supplied CEA primarily to its affiliated burn unit. It is investigating using a dermal substitute in conjunction with CEA to increase mechanical stability and decrease wound contracture.

Clinical activities of LOEX are funded on a nonprofit fee-for-service basis, with additional support from the local Fireman's Fund. Research efforts of the laboratory are funded by peer-reviewed grants. Unfortunately, a questionnaire could not be obtained from the burn centre at the Hôpital du St-Sacrement in Québec City, Québec, which uses most of the CEA produced by the laboratory. LOEX has also supplied CEA to units in Montréal, Québec and Halifax, Nova Scotia and more recently to a hospital in Ottawa (following the survey). Fifteen to 20 patients per year are biopsied for culture, with about 10 patients surviving for grafting. After receiving a 4 to 6 cm² full-thickness biopsy, the laboratory can supply CEA to a unit within 15 to 24 days, depending on the rate of division of the cells, which is largely determined by the patient's age. The autograft is transported in 35 cm² flasks, accompanied by two of the laboratory's technicians for assistance during the grafting procedure. An initial processing fee of \$2,700 followed by \$5.50 to \$6.25 per cm² of graft is designed to cover the laboratory's processing expenses on a nonprofit basis.

CEA is available commercially from Genzyme Corporation (Massachusetts) at a cost of US\$435 per 25 cm² flask. Additional costs include biopsy analysis US\$500 US and transportation (variable, approximately US\$2,000).

Allodermal grafts

Unlike the epidermis, the dermis can be rendered acellular and still perform its basic protective and supportive functions. With removal of the dermal cells, the antigenic elements are also eliminated, and, therefore, alloplastic transplant can occur without rejection. Alloderm is a shelf-stored, freeze-dried, acellular human cadaveric dermal matrix. The principle of allodermal grafting is that ultra-thin (0.01 cm) meshed autograft laid on top of the allodermis will provide skin quality comparable to that obtained from thick partial-thickness grafts. The present cost is US\$2.60 per cm² with transportation cost, via air express, around US\$30.

None of the surveyed Canadian units used a processed allodermis at the time of the questionnaire; however, in late November 1995, Alloderm was used on a burn patient in Toronto, Ontario. For this patient, the cost of the product was covered by private donations to the Burn Centre Development Fund. Alloderm was used more widely than CEA in the surveyed United States centres.

Biobrane

Biobrane is a bilaminar, semisynthetic, temporary skin substitute made of silicone bonded to nylon mesh. Its adherence is facilitated by collagen peptides bonded to the nylon underlayer. Two comparative studies concluded that Biobrane was as effective as frozen human allograft for the temporary coverage of freshly excised full-thickness burn wounds before autografting (23,24). Retail cost of a 13 by 13 cm sheet of Biobrane is approximately \$28.

Although more United States centres used Biobrane the pattern of use was similar between the two countries, with the exception that it was not commonly used in Canada for coverage of donor site wounds.

Synthetic dressings

Opsite, Duoderm and Tegaderm were grouped for this survey. Duoderm is a hydrocolloid dressing, whereas Opsite and Tegaderm are elastomeric polyurethane films. Costs vary with size and make, from \$1.88 for a 10 by 14 cm sheet to \$2.65 for a 10 by 10 cm sheet. These three synthetic dressings were the most frequently used skin substitutes in the survey.

The future of skin substitutes in Canada

Health care funding in Canada is primarily a provincial concern. As hospital budgets become increasingly constrained, frequent free transfer of tissue between provinces will become unfeasible. To avoid this potential regional discrepancy in patient care, each province will require an established system of providing skin replacements to its units, either by expanding and formalizing the distribution by existing provincial banks or by selectively establishing new regional facilities. In the present climate of global fiscal constraints, such growth can only occur if burn unit administrators are dedicated to expanding their arsenal of burn treatments and if they can justify the associated expenditure by cost-benefit analysis.

Canadian centres appear to be more dependent on local nonprofit sources for their skin substitutes, compared with United States centres of comparable size. With the exception of the three relatively inexpensive synthetic dressings, the commercially available products were less widely used by the Canadian centres. Whereas the majority of the United States centres purchased cultured and cadaver skin from commercial sources, the Canadian centres obtained them from hospital-affiliated facilities.

Results of this questionnaire demonstrate that some regions of Canada are not affiliated on a regular basis with one of the four provincial skin banks. The populous provinces of Ontario and Quebec do not possess regional skin banks, and only British Columbia and Quebec have academic research laboratories actively providing cultured skin products. As the evolution of skin replacements continues, only those units with access to well established skin banks with up-to-date research interests will be able to provide the benefit of these advances to their patients.

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