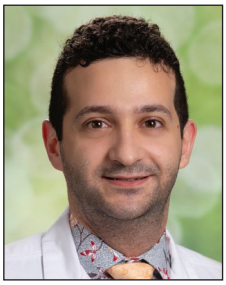
Overview of skin substitutes for secondary intention healing in dermatologic surgery

By Mohammad Fardos, DO, Vixey Silva, DO, and Anna Bar, MD, FAAD



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There is no universally accepted classification system for categorizing all commercially available skin substitutes.

Skin substitutes are indicated for temporary or permanent coverage of wounds requiring delayed reconstruction, large or secondary intention defects, cosmetically or functionally sensitive areas, poorly vascularized sites, impaired healing due to comorbidities, burns, or as adjuvants to skin grafting to optimize healing and outcomes.

Terminology

Acellular substitutes: Serve as dermal scaffolds without living cells to promote granulation tissue formation and revascularization.
Cellular substitutes: Composed of cells secreting extracellular matrix proteins and growth factors.
Allograft: Refers to tissue grafts (e.g., skin) taken from another human, typically a cadaver, used to cover wounds or burns temporarily or assist in healing.
Autograft: Refers to skin grafts harvested from the patient's own body, often from a donor site like the thigh or buttocks, for wound coverage or repair.
Xenograft: Refers to a tissue graft (e.g., collagen and extracellular proteins) obtained from an animal species, commonly pigs (porcine), cows (bovine), or fish.

Tissue type	Composition	Preparation	Advantages	Disadvantages
Amnion	Acellular substitute composed of human amniotic/chorionic membrane, composed of single-layer epithelial cells, basement membrane, and avascular connective tissue matrix.	Derived from placenta of screened donors. Can be applied directly to wound beds. For dry wound beds, the graft requires moistening (i.e., with saline) prior to application.	Non-immunogenic Long shelf life (up to 5 years) and some can be stored at room temperature Analgesic effect (reduces pain in the wound)	Typically requires multiple reapplications until wound is healed
Cultured epithelial autografts/ epidermal substitutes	Cohesive sheets of autologous keratinocytes, 2-8 cell layers thick.	Created by taking a small skin biopsy from the patient, isolating keratinocytes, expanding cells *in vitro*, and culturing them into sheets of epidermis (after 3-4 weeks). Sheets are then applied to wounds to promote skin regeneration.	Can be used on large area wounds Reduces need for harvesting multiple skin grafts as it can be regrown and reapplied as needed No need for reapplication	Fragile Does not contain dermal components Graft contraction Time-intensive process to create Costly
Acellular/ dermal allografts	Acellular substitute composed of dermal extracellular matrix proteins (collagen, elastin, glycosaminoglycans, hyaluronic acid).	Derived from cadaveric human dermis. Through a sequential decellularization process, the epidermis and all cells are removed, leaving behind a collagen-rich dermal scaffold. Scaffold integrates into the wound bed to regenerate normal skin. Must be rehydrated in a warm sterile solution prior to application. Apply within 4 hours with the dermal side facing down and basement membrane side facing up.	Ready to use Long shelf life (up to 5 years for some products) When used on superficial partial-thickness wounds, it can reduce pain. Pliability No need for reapplication	Time-intensive process to create

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Tissue type	Composition	Preparation	Advantages	Disadvantages
Cellular allografts	Cellular substitute composed of keratinocytes, fibroblasts, growth factors, and collagen.	Derived from cadaveric skin or human fetal foreskin. Can cause redness which is normal (not considered infection).	Promotes biological activity and tissue regeneration Supports reepithelialization	More costly than acellular grafts Requires proper storage (often cryopreserved or refrigerated) to maintain cell viability Higher risk of immunogenicity Reapplications often necessary
Xenografts	Collagen and extracellular matrix proteins derived from animal tissue (e.g., porcine, bovine, fish, frog)	Are sterilized to remove potential infectious agents. Applied directly to the wound bed in most cases. Used for deep wound beds with exposed bone, tendon, or cartilage. For dry wound beds, some xenografts (e.g., Kerecis) require moistening.	Readily available Low antigenicity Biodegradable Long shelf life Analgesic effect (reduces pain in the wound)	Defects healed by bovine xenografts may result in thinner skin that is vulnerable to traumatic injury Possible religious concerns for some patients
Bilayered living cellular construct/ composites epidermal and dermal	Two components: Epidermal: cultured human keratinocytes, often allogeneic (e.g., from neonatal foreskin) Dermal: Bovine type I collagen with human neonatal foreskin fibroblasts	Resemble the structure of human skin and serve as a scaffold for neovascularization and cellular infiltration. Should be handled aseptically and applied directly to a clean, debrided wound bed with adequate hemostasis. Do not require thawing or soaking. Secure in place using sutures, staples, or dressings as needed to ensure proper adherence	Ready to use Good for full-thickness defects (melanoma defect) Less vascular scars Low antigenicity Mimics natural skin structure; promotes neovascularization and cellular infiltration	Fragile Costly Requires proper handling and storage Short shelf-life
Synthetics	Hyaluronic acid-derived substitutes/ silicone	A synthetic, bi-layered, bioresorbable dermal substitute made from a hyaluronic acid derivative. The outer membrane features a transparent, semipermeable silicone layer that provides a protective barrier against fluid loss and external contaminants.	Bioresorbable Immunologically inert Ready to use Supports angiogenesis and fibroblast colonization	Characteristic smell (foul-odor) Requires proper handling and wound preparation for optimal results

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References

1. Davis M, Dugan K, Neill B, Shive M, Tolkachjov S. The Role of Skin Substitutes in Dermatologic Surgery: A Practical Review. *J Drugs Dermatol.* 2023;22(5):475-480. doi:10.36849/JDD.7132
2. Lu KW, Khachemoune A. Skin substitutes for the management of Mohs micrographic surgery wounds: a systematic review. *Arch Dermatol Res.* 2023;315(1):17-31. doi:10.1007/s00403-022-02327-1
3. Shahrokhi, S. (2023) Skin substitutes. *UpToDate.* Edited by M.G. Jeschke and K.A. Collins. Available at: www.uptodate.com/contents/skin-substitutes#H2091737136 (Accessed: 13 Jan. 2025).

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