Chapter 9: Physiology of Cutaneous Tissue Expansion

George S. Goding, Jr.

The ability of the skin to adapt to an expanding mass beneath its surface is well demonstrated by pregnancy and slowly growing subcutaneous tumors. Interest in the effects of expansion on skin has resulted from the clinical application of this phenomenon. The principal use of cutaneous tissue expansion has been to "create" additional skin that would be available for coverage of nearby defects.

Effect of Tissue Expansion on Skin

The different layers of the skin and subcutaneous tissue appear to respond differently to expansion. The epidermis reacts to cutaneous expansion most productively. In histologic studies the epidermis is found at least to maintain its thickness and often to increase its thickness, despite the increased surface area it is required to cover (Pasyk, Argenta, and Hassett, 1988; van Rappard et al, 1988). In normal skin the superficial keratinized cells of the epidermis are continually replaced by cells from the basal layer. The mitotic activity of the basal layer ensures a constant supply of cells to the epidermis during normal activity and appears to increase in response to tissue expansion. In the guinea pig, inflation of a subcutaneous implant resulted in a three-fold increase of mitotic activity in the epidermal layer within 24 hours (Austad, Thomas and Pasyk, 1986). Within 1 week the epidermal mitotic activity returned to baseline levels. With intermittent expansion no difference in the histologically defined layers of the epidermis was seen in the minipig model (van Rappard et al, 19880. With more rapid expansion histologic changes do occur, such as flattening of the rete ridge, which persisted for up to 12 months after the expansion was complete (van Rappard et al, 1988).

In most studies, the dermis has been found to be less tolerant of tissue expansion than the epidermis (Pasyk, Argenta, and Hassett, 1988; van Rappard et al, 1988). In the guinea pig model, a decrease in the dermal thickness has been found as early as 1 week after initiation of tissue expansion (Austad et al, 1982). Dermal thickness was also found to be significantly decreased in human skin 5 weeks to 5 months after expansion was initiated (Pasyk, Argenta, and Hassett, 1988). In contrast to these results, Mustoe et al (1989) found dermal thickness to be increased after expansion in the canine model. Bartell and Mustoe (1989) thought the canine to be a superior model for cutaneous tissue expansion because of its biochemical similarities with human skin. Timmenga et al (1990) studying the rabbit, found the dermis to be thickened in both expanded and sham-operated skin. Histologic examination revealed thickened dermal collagen bundles with loosely packed fibers that were felt to explain the increased dermal thickness (Timmenga et al, 1990). In a study of biopsies from expanded human skin (Pasyk, Argenta, and Hassett, 1990), the dermis was found to be significantly thinner than that of biopsies from control skin. In rapidly expanded skin, dermal changes include an alteration of the angle of cross-linkage of the collagen bundles (van Rappard et al, 1988). The angle, normally around 70 degrees, is reduced in an amount proportional to the rapidity of expansion. Eventually, collagen fibers will run nearly parallel to the surface.

The subcutaneous fat and muscle are the layers least tolerant of expansion. Experiments in guinea pig, swine, and canine models have demonstrated marked thinning of

expanded subcutaneous fat and muscle (Austad et al, 1982; Mustoe, Bartell, and Garner, 1989; van Rappard et al, 1988). With rapid expansion in the minipig, fat cell necrosis and atrophy of muscle fibers was a common finding (van Rappard et al, 1988).

Because the tissue expander is a foreign body, a capsule begins to develop soon after its placement. In a study using minipigs, two layers of the capsule could be distinguished after 1 week (van Rappard et al, 1988). The inner layer consisted of macrophages, and the outer layer was composed mainly of fibroblasts. With time the outer layer becomes predominantly collagen. Studies of collagen in breast implants have found a predominance of type 1 collagen with lesser quantities of type 3 and type 5 collagen in descending order (Lee, Squier, and Bardach, 1985). The pattern of collagen types in these capsules is similar to that found in cutaneous scar tissue.

Hair, sebaceous glands, and sweat glands do not appear to respond actively to tissue expansion (von Rappard et al, 1988). The density of these dermal appendages simply decreases to an extent proportional to the surface area gained by expansion.

Effect on Nerves and Blood Vessels

Elongation of peripheral nerves occurs with tissue expansion. In the rat model the increase in nerve length is proportional to the degree of expansion (Milner, 1989). A slow rate of expansion is better tolerated than rapid expansion. All expanded nerves showed a decrease in conduction velocity, with the greatest decreases occurring in nerves elongated by greater than 50% of their original length.

Arteries and veins can also tolerate expansion. In the rat model, all vessels in expanded saphenous neurovascular bundles remained patent with elongation of up to 10% per day (Stark, Hong, and Futrell, 1987). Histologic examination of the elongated vessels showed preservation of wall thickness. Microvascular anastomosis using the elongated vessels had a patency rate as good as control vessels. Electron microscopy of guinea pig skin that expanded for up to 8 months was unable to demonstrate any change in the vessels of the dermis or subcutaneous layer (Pasyk et al, 1982). Using tritiated thymidine, increased mitotic activity has been detected in endothelial cells, pericytes, and smooth-muscle cells of expanded guinea pig arteries (Austad and Pasyk, 1987). Thus, arteries appear to respond to expansion in a manner similar to epidermis - by developing additional tissue.

Effect on Blood Flow and Flap Survival

Cutaneous blood flow varies indirectly with skin tension (Larrabee, Holloway, and Sutton, 1984; Marks, Mackenzie, and Burney, 1985). With expander inflation there is a temporary decrease in cutaneous blood flow (Goding, Cummings, and Tachy, 1988; Ricciarelli et al, 1989). When the expander is deflated or removed the blood flow is temporarily greater than in sham operated controls (Goding et al, 1988; Marks et al, 1986; Ricciarelli et al, 1989). In the pig model, the increased blood flow seen with expander deflation was not present after 24 hours (Ricciarelli et al, 1989). This initial rise in blood flow with expander deflation is seen even after creation of a random cutaneous flap from the expanded skin (Marks et al, 1986). Blood flow has been detected in the capsule that forms around the tissue expander (Manders et al, 1984). The presence of a capsule, however, did not increase cutaneous blood

flow in subcutaneous pockets with inflated or noninflated tissue expanders as compared to pockets created without expander placement (Goding, Cummings, and Trachy, 1988). Capsulotomy was also found not to affect survival length of flaps created from expanded skin (Morris et al, 1989).

Flaps created from expanded skin have increased blood flow and viability when compared to acutely raised flaps (Cherry et al, 1983; Morris et al, 1989; Sasaki and Pang, 1984). The increased blood flow and survival length are similar to that seen with delay or implantation of an expander without subsequent inflation. The surgical manipulation required to place the expander, therefore, appears to bestow the advantages represented by the "delay phenomenon".

The advantage of tissue expansion over simple delay is that more donor tissue is available. A permanent gain in skin was found after expansion was studied in the pig buttock flap model (Vanderkolk et al, 1988). After 5 weeks of expansion there was a 53% increase in surface area. Over half of the tissue remained 29% larger than controls. The increase in area was relatively stable 3 months after flap replacement. The gain in donor tissue with expansion allows the surgeon to create larger flaps or permits easier closure of the donor site.

Attempts to Enhance Tissue Expansion

Attempts have been made to improve on the process of tissue expansion with the use of pharmacologic agents. The anticontractile agents papaverine and cytochalasin D were found to enhance the rate and extent of cutaneous tissue expansion in the guinea pig when delivered via a separate catheter to the area of the expander. The use of anticontractile agents was felt to result in a decrease in the ability of contractile fibroblasts in the capsule to resist expansion. Interference with collagen cross-links by topical administration of dimethylsulfoxide (Lang, Dick, and Narayanan, 1987) and beta-aminopropionitrile (Cohen and Dunn, 1988) have also enhanced cutaneous tissue expansion.

Netscher, Spira, and Peterson (1989) studied the effect of three chemical agents (prostaglandin E_2, hyaluronidase, and colchicine) on tissue expansion in the rat model. Each agent is known to have multiple physiologic effects. The pharmacologic effects of greatest interest to the investigators were the vasodilatation with prostaglandin E_2 the enzymatic activity on ground substance mucopolysaccharides with hyaluronidase, and the stimulation of tissue collagenase and inhibition of mitosis with colchicine. Hyaluronidase and colchicine were found to enhance the rate of tissue expansion whereas prostaglandin E_2 enhanced the tissue oxygen tension of expanded tissue immediately after inflation. Further investigation of pharmacologic manipulation with tissue expansion may result in increased safety and decreased time associated with clinical application of the technique.