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**EFFECT OF ACEXAMIC ACID  
ON SPLIT THICKNESS SKIN GRAFT TAKING  
A CLINICAL & HISTOPATHOLOGIC STUDY**

THESIS

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To

*My Parents*

and

*Prof. Dr. N.M. Souelem*



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***INTRODUCTION***

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## INTRODUCTION

Every plastic surgeon has met one time or another in his career, problems of healing of full thickness skin defects. He resorts in the majority of cases, to the use of skin grafts or flaps and in some cases he may be obliged to accept the natural process of wound healing.

Whatever method he uses, the end result is more or less satisfactory; but in some cases he may be faced with such problems as delayed wound healing, excess fibrous tissue formation, bad quality of skin grafts, and other problems. Although the study of wound healing has progressed greatly in the last years, together with stability of surgical techniques of skin grafting, yet still many problems are not solved and it is because of that, any new tool added to these fields is worth to be studied for its value.

In this thesis, a review of the pathology of wound healing, together with a review of literature on the topic of skin grafting is presented as an introduction to the study of the drug acexamic acid and its effect on healing or skin grafting of a full thickness defect of skin.

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***REVIEW OF LITERATURE***

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### ANATOMY OF THE SKIN

As animal life evolved from aquatic to terrestrial forms, skin evolved as an adaptation to the changing environment, providing protection against certain physical and chemical hazards, controlling the exchange of water between organism and surroundings, aiding in the regulation of body temperature, and serving as an extensive receptor for tactile and thermal stimuli. This surface covering consists of a single sheet-like organ whose population of cells is derived from somatic ectoderm and mesoderm and from the specialized ectoderm known as neural crest tissue.

The skin is composed of two layers, an outer epidermis of stratified squamous epithelium and an inner dermis or corium of relatively acellular fibrous tissue which forms the bulk of the skin thickness. The skin is attached to the underlying structures by the subcutaneous tissue, which is a superficial fascia infiltrated by varying amounts of fat and is responsible for the mobility of the skin on the deeper structures. The degree of mobility varies from one place to another on the body according to the density of the subcutaneous tissue and also roughly correlates with the thickness of the skin, thin skin being generally looser than thick skin. Skin thickness itself varies considerably, ranging from 0.5 mm on the eyelids to more than 5 mm in the interscapular region of the back. Average skin thickness is 1 - 2 mm. Skin is usually thicker on the posterior body

surfaces, but on the palms and soles the skin is thicker than almost any dorsal surface (on palms and soles, both epidermis and dermis are substantially thicker than in other locations and differ histologically as well). The interface between epidermis and dermis is characterized by downward projections of epidermis called rete pegs alternating with upward projections of dermis known as dermal papillae. The dermal papillae tend to be taller and more numerous in areas where mechanical stress is higher, such as the palms and soles, lips, nipples and external genitalia.

The epidermis is a cornified, stratified, squamous epithelium which consists of several layers of cells, the most important of which is the stratum basale, the deepest layer and the chief site of mitosis. Also found in this layer are the pigment containing melanocytes; neural crest derivatives that help determine skin color by virtue of the amount of melamin they contain.

The dermis is composed of irregularly arranged dense connective tissue containing both collagen and elastin but with a great preponderance of the former. The cellular elements are mostly fibroblasts and histiocytes. The collagen and elastin are organized into individual fibres and fibre bundles which form networks parallel to the surface.

The blood supply to the skin originates either through direct cutaneous arteries or mostly in arteries of the muscles that penetrate the superficial fascia and form

subcutaneous networks, from which arise branches that form plexi in both the reticular and papillary layers of the dermis. Branches from these plexi supply the epidermis and its appendages. There are roughly parallel sets of venous plexis.

There are efferent sympathetic nerves that supply vascular smooth muscle, the errectores pilorum of the hairs and the sweat glands, but most of the nervous supply of the skin is somatic sensory. Like the blood vessels, these fibres arise from trunks in the subcutaneous tissue and form a subpapillary plexus. The fibres that arise from this plexus terminate either as free nerve endings among the cells of the epidermis or as specialized tactile receptors, such as Pacinian corpuscles, Meissner's corpuscles, and the end-bulbs of Krause.

There are three epidermal appendages in human skin: the hair follicles, sweat glands and sebaceous glands. These epithelial structures usually extend down into the reticular dermis and subcutaneous tissue (Copenhaver et al., 1971).

## WOUND HEALING

### Types of Wounds

Wounds are either closed where the skin is not broken or open where the continuity of the skin is lost.

#### Closed Wounds:

1) *Abrasions*: These are classified as closed wounds because the superficial layers of the skin only are scraped away due to forcible friction with a rough object. Blood comes out as oozing droplets. The condition is painful due to exposure of the nerve ends.

2) *Ecchymosis or bruising*: This usually results from trauma by a blunt object. Extravasation of blood occurs in the subcutaneous tissues due to rupture of small vessels. The skin becomes discolored (first red then yellow) then the blood is absorbed and the color returns to normal.

3) *Haematoma*: If blood is poured out and enclosed by fascia or membrane a haematoma results. The collection of blood may be subcutaneous, subfascial, subperiosteal or intramuscular.

Open Wounds:

1) *Incised Wounds:* These are clean cut wounds. They are caused by sharp instruments (as surgical wounds) or sometimes by blunt instruments hitting the skin which is stretched over a bone e.g. the scalp or the skin over the shin of the tibia.

2) *Contused Wounds:* These are wounds associated with contusions. Their edges are irregular and they are very liable to infection. They are caused by blunt trauma or gross forms of violence.

3) *Lacerated wounds:* These are similar to contused wounds but more extensive and the tissues are more severely crushed.

Major crushing injury is accompanied by a degree of tissue necrosis. The wound may be heavily contaminated by bacteria and organic matter. In the presence of devitalised tissue, especially muscle, the risk of infection is increased. Industrial and road traffic accidents account for the majority of the crushed and devitalised wounds.

4) *Punctured wounds:* These are deep wounds with a small orifice. There is a liability of injury to deep structures e.g. blood vessels, nerves, viscera, serous cavities, joints, etc. They are caused by pointed instruments e.g. daggers, nails, knives etc.

### **Types of healing**

Wound healing is customarily divided into first, second and third intention healing (Hunt, 1983).

**First intention (primary) healing:** It occurs when tissue is cleanly incised and reapproximated and repair occurs without complication.

**Second intention (secondary) healing:** This is the healing of an open wound (or a closed [dead] space) through formation of granulation tissue and eventual coverage of the defect by spontaneous migration of epithelial cells. Most infected wounds and burns heal in this manner. One can easily see that primary healing is simpler and requires less time and material than secondary healing. It sometimes happens that primary healing is possible but insufficient reserve is present to allow secondary healing. For example, an ischemic limb may heal primarily, but if the wound opens or becomes infected, the wound might not heal.

**Third intention healing:** This is usually called delayed primary closure. It occurs when the surgeon leaves a wound open to accomplish the first phases of healing and then closes it to finish healing as if by first intention. The wound is less likely to become infected while open than if the wound is closed primarily. The closed wound is most susceptible to infection in the first 4 days. Closure of a wound by skin graft is also an example of third intention healing.