CHAPTER 1

Introduction

1.1 The Skin and its Functions [1,2]

The skin forms the outer covering of the body and with its accessories – hair, nails, subcutaneous tissue, and sweat, sebaceous, and memory glands – is more properly called the **integument**. To most people, the skin is simply the protective surface of the body. In fact, it is far more than that. Next only to the muscles, it is the largest organ system of the body [1].

The skin is considered to be an organ since it consists of several kinds of tissue that are structurally arranged to function together. It is a heavy organ, accounting for approximately 7% of our adult body weight. The skin is of variable thickness, averaging 1.5 mm. It is thickest on the parts of the body exposed to wear and abrasion, such as the soles of the feet and palms of the hands. In these areas, it is about 6 mm thick. It is thinnest on the eyelids, external genitalia, and on the tympanic membrane (eardrum) where it is approximately 0.5 mm thick [2].

Protection of the inner tissues is one of the most important functions of the skin. As anyone can testify who has lost skin by a burn, sunburn, or other means, exposure of these inner delicate tissues can cause agonizing pain. The retention of body fluids is equally important. In loss of skin as from a burn, the most serious, and sometimes fatal, complication is shock due to loss of body water and salt.

In addition to simple conservation, the skin is an active factor in the maintenance of water balance. Whereas a person under average conditions excretes up to 1.5 liters a day in their urine, 0.7 liters or more are excreted in unnoticed perspiration and may be several times this amount in conditions of heat and/or extreme exertion. Uncompensated loss of this kind can have serious effects. The skin is also a major organ in the excretion of excess salt, as can be appreciated from the salty taste of sweat. In this instance, the skin is serving to regulate the balance of salts. Even a relatively minor shift in the proportion of, for example, sodium and potassium salts can have serious, even fatal, effects.

The skin also functions in the regulation of body heat. It is well known that a rise of a few degrees in body temperature causes intense drowsiness, as experienced by a person overcome in hot weather. The skin helps to dissipate heat, first by the expansion of the rich web of capillary vessels near its surface, which act as a radiator, and second by the outpouring of sweat, which absorbs heat when it evaporates. Conversely, heat is conserved by shutting down the vessels and sweat glands.

Finally, the skin is a major sense organ. Covering an area of nearly two square yards in a large person, every square inch contains dozens to hundreds of tiny sense organs (nerve ends) to detect light touch, pressure, heat, cold, and painful injuries. Loss of this widespread sensation (actually several sensations) would be very disabling. When such loss is induced experimentally, it causes mental disorganization.

In summary, the main functions of the skin are [3]:

1. Keeps the body as a separate and enclosed aqueous, or watery, internal environment
2. Prevents bodily damage from solar radiation
3. Regulates temperature through expandable blood vessels and sweat
4. Stores water, fats, vitamins, and carbohydrates
5. Senses touch, temperature, pain, itchiness, and pressure
6. Excretes small amounts of water, salt, and oxygen
7. Synthesizes and produces vitamin D with solar radiation
8. Protects the body from excess water, bacteria, heat, injury and infection

1.2 The Structure of the Skin [1]

The skin is composed of three distinct layers: the epidermis, the dermis, and the subcutaneous tissue (or hypodermis), as shown in Figure 1.1 below.

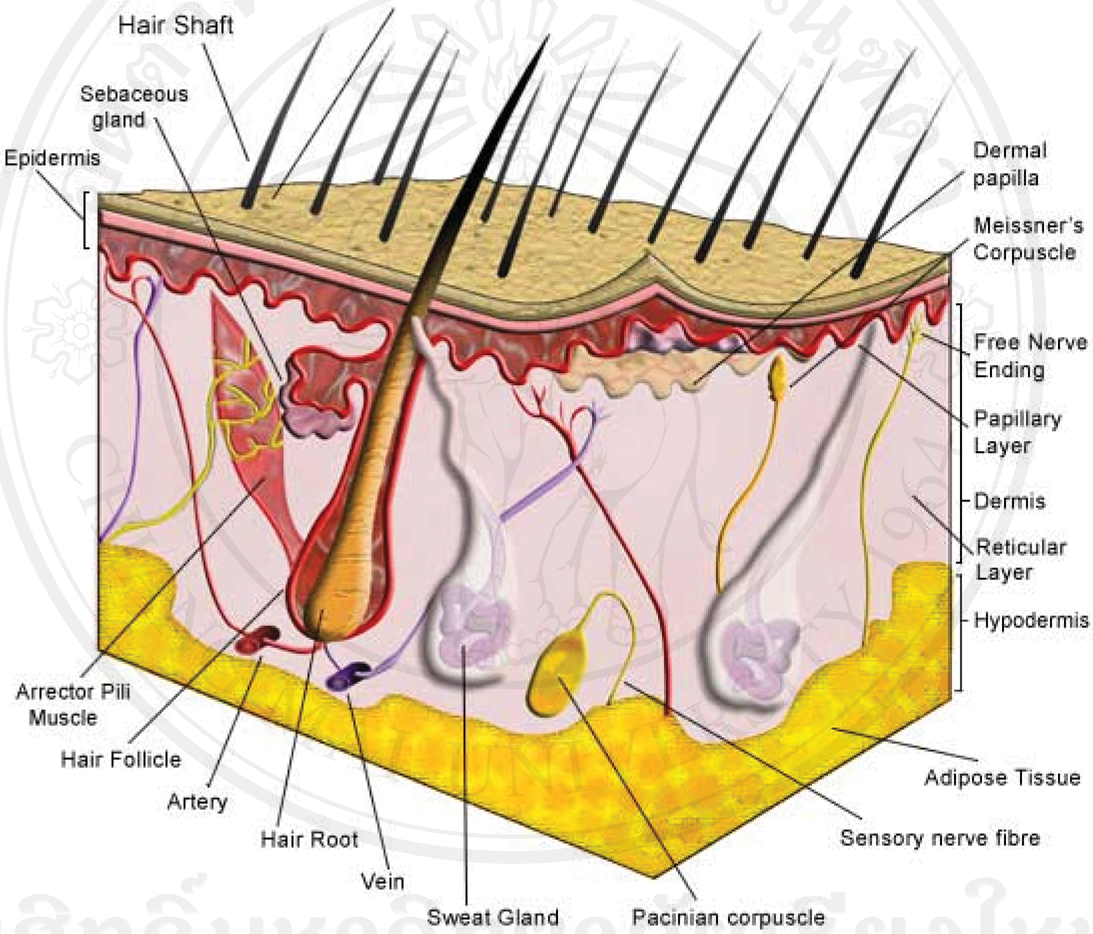

Figure 1.1: The structure of the skin [4].

(1) The Epidermis

The outer layer or epidermis is composed of many tiers of flattened cells which are continuously replaced at the bottommost layer and lost at the most superficial layer. As the cells move to more superficial positions, they become impregnated with a waterproofing material called keratin, become transparent, and die. Simple rubbing or washing of the skin removes patches of such dead cells. They seem to have a sticky nature when in water which causes them to adhere to glossy surfaces such as to the wall of the bathtub. The sheet of "skin" which peels off our arms following sunburn is actually several layers of such dead cells. Because there are no nerves or blood vessels in the epidermis, injuries restricted to this layer cause no bleeding and little or no pain.

(2) The Dermis

The dermis is a much thicker layer and much tougher than the epidermis. It is the "skin" from which leather is made and is visible only after the epidermis has been scraped off. Here are located the glands, nerves, and blood vessels as well as the tough connective tissue which gives skin its strength. This connective tissue consists of strong collagenous fibers, similar to those of tendons and ligaments, as well as a quantity of elastic fibers. These elastic fibers are responsible for the smoothness of the skin regardless of whether it is stretched or relaxed. The elastic fibers also cause the normal separation of the cut surfaces of a wound and necessitate suturing (stitching) of injuries deep into the dermis. Aging of the skin includes a gradual failure of these elastic fibers and the skin wrinkling which we associate with advancing age.

(3) Subcutaneous Tissue

Underlying the dermis is a layer of subcutaneous tissue. This layer of rather loose and liquid tissue separates the skin from the muscles. This loose, often fatty, layer makes possible the movement of the skin over the underlying muscle in such areas as the back of the forearm. In certain areas such as the small of the back, the subcutaneous tissue measures two or more inches in thickness, even in thin persons. In general, however, thin people have little fat in the subcutaneous layer, whereas most of the fat which we associate with obesity is deposited here. In this sense, all of us, fat or thin, are pretty much alike once the skin is removed.

1.3 Burns

1.3.1 Causes of Burns [5-6]

Each year, burn or scald injuries account for many patients who seek medical or hospital treatment and advice. In the United States alone, it is estimated that up to 2.5 million individuals per year will receive medical treatment for their burns or have at least 1 day of restricted activity because of their injuries. Furthermore, at least 150,000 of these patients will be hospitalized, with an estimated 10% mortality rate [6]. Approximately 1% of the Australian and New Zealand population will suffer from a burn each year. Of these people affected, 50% will suffer from some daily restriction of activity and 10% will require admission to hospital. Exposure to heat is the most common cause of a burn accounting for over half of all burn cases. Chemical exposure accounts for 2.1-6.5% of all admissions to burns units. Electrical burns are estimated to account for 3-4% of burn–related injuries [4]. "Burn" is a broader term than many people think. Most people believe that only heat causes burns but the medical definition of a burn has more to do with the depth of damage rather than the actual cause. Amongst the many causes of burns are:

1. Flames from a fire
2. Hot gases, liquids or solids
3. Electric or gas fires or coming into contact with live electric wire
4. Sunburn
5. Friction burns, for example from a revolving wheel
6. Chemical burns such as from strong acids or alkalis
7. Radiation burns

1.3.2 Burns Classification [7-10]

Burns are generally classified into "degrees" depending on the depth of damage.

(1) First Degree Burns

First degree burns, which are limited to the top layer of the skin (epidermis), are moist and red in colour and are usually not very painful. Sunburn is a typical first degree (also called superficial) burn. A first degree burn is usually red and blanches (turns white) if pressed. First degree burns do not produce blisters and they usually heal themselves without specialist medical treatment in 3-6 days.

(2) Second Degree Burns

Second degree burns involve the entire epidermis and some portion of the dermis (second layer of the skin) and are sub-classified as either superficial or deep.

- **Superficial partial-thickness burns** cause blistering and are painful. Under the blister, they are red and moist. They heal within 3 weeks with minimal cosmetic defects (hardly noticeable scarring) and with usually only a change in the skin colour. They require medical treatment but usually not hospitalization.
- **Deep partial-thickness burns** are dry and may appear ivory or pearly white. They involve tissue destruction to the deeper layers of the dermis. Healing takes up to 4-6 weeks and may leave hypertrophic or thick scars. These burns usually require hospitalization, at least during the initial healing period.

(3) Third Degree Burns

Third degree burns destroy the full thickness of the epidermis, dermis and extend down to the subcutaneous tissue. With these burns, the skin is charred and leathery and often depressed from the surrounding tissue. Third degree burns are usually not painful simply because the nerve endings have been destroyed. These burns are by far the most serious and require hospitalization and skin grafting over extended periods (months) of time.

First Degree Burn

Second Degree Burn

Third Degree Burn

Figure 1.2: Classification of burns according to depth (degree) of damage [11].

1.4 Exudate [12-13]

An **exudate** is any fluid that filters from the circulatory system into lesions or areas of inflammation. Its composition varies but generally includes water and the dissolved solutes of the blood, some or all plasma proteins, white blood cells, platelets and (in the case of local vascular damage) red blood cells [12]. A typical definition of exudate is:

"Fluid, cells or other substances that have been slowly exuded, or discharged, from cells or blood vessels through small pores or breaks in cell membranes." [13]

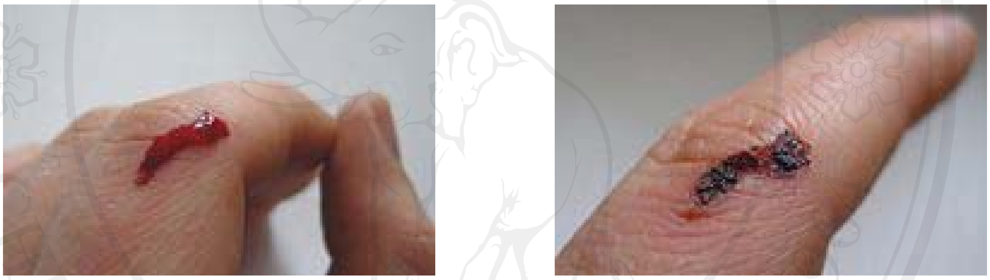

Figure 1.3 : Moist and dried exudate from a finger wound [12].

The basic concept behind moist wound healing is that the presence of exudate in a wound will provide an environment that stimulates healing. Exudate contains various components including lysosomal enzymes, white blood cells, lymphokines and growth factors. Many of the advanced wound dressings currently available are designed to keep the wound bed moist with exudate. There are clinical studies which have shown that wounds kept in a moist environment have lower infection rates than wounds treated with agents that tend to dry the wound bed. The concept of “moist wound healing” has been with us since the 1960s but only in the last few years has it become the accepted treatment philosophy for chronic wound care. Based on this philosophy, the most successful outcome is the one that produces wound closure in the shortest amount of time, along with the fewest number of treatments. As doctors often say: “Spending a few dollars more on the appropriate dressing is insignificant when compared to the cost of additional treatments.” [14]

1.5 Phases of Wound Healing [14]

The entire wound healing process is a complex series of events that begins at the moment of injury and can continue for months to years. The various stages of wound healing can be identified as follows:

1. **Inflammatory Phase**
   1.1 Immediate to 2-5 days
   1.2 Hemostasis
   - Vascoconstriction
   - Platelet aggregation
   - Thromboplastin makes clot

   1.3 Inflammation
   - Vascodilation
   - Phagocytosis

2. **Proliferative Phase**
   2.1 3 days to 3 weeks
   2.2 Granulation
   - Fibroblasts lay bed of collagen
   - Fills defect and produces new capillaries

   2.3 Contraction
   - Wound edges pull together to reduce defect

   2.4 Epithelialization
   - Crosses moist surface
   - Cells travel about 3 cm from point of origin in all directions

3. **Remodeling Phase (Maturation)**
   3.1 3 weeks to 2 years
   3.2 New collagen forms which increases tensile strength of wound
   3.3 Scar tissue is only about 80 percent as strong as the original tissue

These 3 main phases are summarized graphically in Figure 1.4 below.

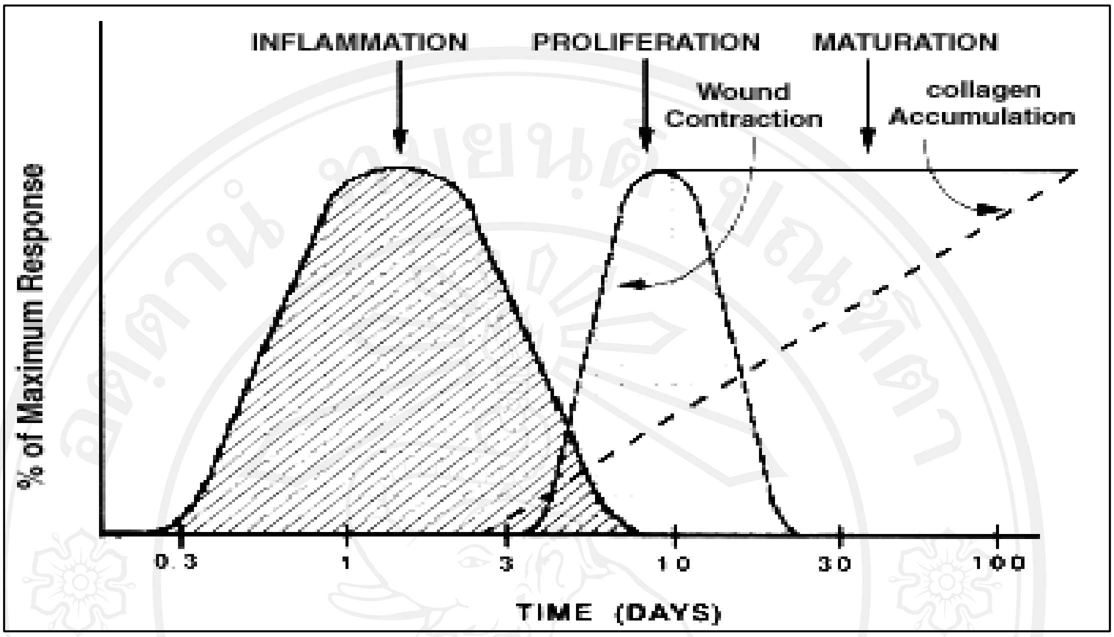

Figure 1.4 : The various stages involved in the wound healing process [15].

Thus, wound recovery is a complicated biological course which happens when the body responds to a skin injury. The change in local environment includes the interactions of cells, cell matrix and growth factors, which is very important for wound healing. Some of the main landmark events in the history of wound healing which have taken place in the past 60 years are [16]:

- In 1948, Doctor Bull of the Birmingham Emergency Center, UK, brought forward the application of a moist preservation dressing in wound healing for the first time.

- In 1958, Professor Odland discovered that, if the epidermal water blister was kept as a whole after the skin was injuried, the wound would heal more quickly than if it was broken.

- In 1962, Doctor Winter at London University, UK, proved that a wound covered with a moist preservation dressing healed faster than a wound exposed to the air.

- In 1963, Professor Hinman at the San Francisco Medical College of California University, USA, demonstrated in clinical trials on human patients that a wound covered with an aseptic polyethylene thin film healed faster than a wound exposed to the air.

- In the mid-1970s, occlusive dressings first introduced by Doctor Bull began to appear in the market.

Nowadays, therapies that keep the wound moist are accepted as being the most effective. Occlusive dressings provide the wound with a low oxygen environment which helps the formation of epithelium and collagen.

1.6 Materials for Wound Dressings

Nowadays, there are many different kinds of materials for use as wound dressings currently available in world markets. These materials can be classified as [17]:

1. Films

Film dressings are homogeneous dressings composed of a polymer sheet coated on one side with an adhesive. They are usually highly elastic and transparent. The most commonly used polymers include polyurethane, polyethylene, polytetrafluoroethylene and poly(dimethyl aminoethyl methacrylate) and are marketed under trade names such as ***Tegaderm, Dermafilm, OpSite*** and ***Oparaflex***. Film dressings are well suited for superficial wounds but, owing to their lack of absorbing capacity and impermeability to water vapour and gases, cause accumulation of wound fluid beneath the dressing and hence allow leakage of exudates and entry of exogeneous bacteria to the wound surface.

2. Foams and Sprays

Foam dressings are sheets of foamed solutions of polymers such as poly(vinly alcohol) and polyurethane. They are superior to film dressings in that they provide thermal insulation and help to maintain a moist environment at the surface of the wound. Furthermore, they are gas-permeable, non-adherent, light and comfortable.

Examples are silastic foam and lyofoam which have the advantage of being formable *in situ* to treat irregular cavity wounds. However, these dressings are difficult to use in certain anatomical areas, Spray dressings are also light and comfortable to the wound surface and are totally portable. Most sprays are copolymers such as ***Aeroplast*** which is a hydroxy vinyl chloride acetate-modified maleic ester resin. Further studies have resulted in the development of dressings composed of spray-foam combinations such as gelatin-based sprayable foam.

3. Composite Dressings

Composite dressings are composed of laminates of two or more layers. The outer layer is designed for durability and elasticity and may serve as a rate controller for water evaporation while the inner layer is designed for maximum adherence and elasticity. Composite dressings may be further classified as follows:

3.1 Hydrocolloid Dressings

Hydrocolloid dressings are composite formulations containing a cocktail of elastomeric, adhesive and gelling agents. Carboxymethyl cellulose is the most commonly used absorbent for wound fluid in hydrocolloids. Commercial examples of hydrocolloid wound dressings include:

- ***Granuflex*** : This material consists of an outer protective layer of polyurethane foam and an inner layer consisting of a hydrocolloid-polymer complex.
- ***Epigard*** : This is a composite of an inner layer of reticulated polyurethane laminated to an outer sheet of microporous polytetra fluoroethylene (PTFE). Adherence, availability, sterility, long shelf-life and low cost are its major advantages.
- ***Biobran*** : This is a composite of an ultra-thin porous membrane of polydimethylsiloxane bonded to an inner nylon mesh. Roberts et al. [18] and Stein [19] successfully used this material for both superficial and deep donor sites but Lim et al., [20] reported that bacterial infection was a common problem with this dressing.

3.2 Hydrogel Sheets

Hydrogel sheets consist of 3-dimensional network crosslinked hydrophilic polymers which interact with aqueous solutions. The most commonly used polymers are poly(ethylene oxide), polyacrylamide and poly(N-vinylpyrrolidone). Owing to their unique cooling ability, they are particularly beneficial for thermal burns. An example is ***Vigilon*** which is a crosslinked poly(ethylene oxide) hydrogel containing 96% water and supported on a net of low-density polyethylene [21]. The main disadvantage of hydrogel sheets is that they tend to be slippery in use and are difficult to keep in place in regions where there is movement and shear stress.

3.3 Amorphous Hydrogels

Amorphous hydrogels are similar in composition to sheet hydrogels except that the polymer has not been crosslinked to form a sheet. They contain small quantities of collagen alginate or complex carbohydrates. They are unique in their ability to donate moisture to a dry wound eschar and facilitate autolytic debridement in wounds. But owing to the viscosity of the amorphous hydrogel, it may be difficult to retain it in the wound bed. However, hydrogel dressings exhibit a more rapid rate of closure and re-epithelialization as compared with hydrocolloid dressings [22].

3.4 Gels

Several types of gel-based dressings have been developed. For example, Wichterlie and Lim [23] produced a poly(2-hydroxyethyl methacrylate) (PHEMA) hydrogel which was biocompatible and non-toxic. Subsequently, Nathan et al. [24] developed a PHEMA-PEG (Hydran) hydrogel which could be formed directly on the wound surface. Later still, a new type of wound covering marketed under the trade name of ***Geliperm*** was developed by Wokalek et al. [25] which was formed by the polymerisation of agarose and acrylamide. Further modification resulted in the development of a crosslinked poly(ethylene oxide) hydrogel [26].

3.5 Super-absorbents

Finally, super-absorbent dressings have an island configuration consisting of an extra-thin hydrocolloid as the adhesive portion with a central area of non-woven absorbent covering the super-absorbent particles encased inside. Commercial examples include ***Combiderm*** and ***Conva Tec***.

1.7 Property Requirements of Wound Dressings for Second Degree Burns [27,28]

Burn injuries are probably the most traumatic and most difficult to tend of all external injuries with many complications arising from the initial loss of skin. The number of burns accidents is currently increasing. Currently available wound coverings, such as those shown in Figure 1.5 below, have improved patient care significantly. The properties that serve to produce an ideal wound dressing for discard and replacement as needed during wound care require very careful consideration.

Figure 1.5 : Various types of wound dressing for treating second degree burns [28].

Firstly, the dressing must be rapidly and uniformly adherent and conform to the wound bed topography and contours so as to prevent air or fluid pocket formation. Good adherence reduces pain, facilitates decontamination, prevents peripheral channeling into the wound by bacteria, and promotes bonding to tissues. The dressing must be an absolute barrier to bacteria ingress, resist bacterial degradation, and prevent egress of wound organisms to the dressing's surface. It must also be permeable to water vapour to the extent that a moist exudate under the dressing is maintained without pooling, but excess fluid absorption and evaporation leading to desiccation of the wound bed are prevented. Restricting the rate to that of normal water transmission through skin may by insufficient to prevent pooling over a wound area. The dressing must be compatible with body tissue (e.g., permit ingrowth of vascular tissue), be non-toxic, non-antigenic, and non-allergenic.

The dressing should be a durable, stress-resistant (flexible and pliable) elastic material, and should be easy to apply and remove without trauma during dressing changes, non-adherent over healed areas in the wound bed, or be sloughed off with the scab. It is advantageous for the material to be antiseptic in nature and not only stop bacterial growth but reduce bacterial density in the wound, or at least be permeable to applied antibacterials. It is also an advantage for the material to be hemostatic, transparent (in order to indicate the presence of infection), able to provide thermal insulation, accelerate healing, minimize scar formation and, finally, in some special cases, be incorporated by the body (biodegradable) as it restores normal function to the skin.

The mode of development of hypoxic conditions in wound fluid has been studied. Although the partial pressure of oxygen under an air-permeable dressing is low, oxygen permeability is still deemed to be an important attribute for wound dressings. Leukocyte viability and function under an air-permeable cover is significantly greater than under an air-impermeable one. As for non-medical virtues, the wound cover should be an inexpensive, readily available, sterile material with minimal storage requirements and indefinite shelf-life.

Although many of the criteria for an ideal dressing have already been realized to a greater or lesser extent in currently produced materials, there is no one material or composite that serves for all types of wound, including donor sites, burns (large and small: superficial, deep partial, or full thickness), chronic ulcers, and various other pathologies of interest to medical practitioners. Clinicians, faced with a given lesion, may therefore pursue differing therapeutic modalities.