The Application of Silicone Gel for Treatment of Hypertrophic Scars and Burn Wounds, and Consideration of t e "Ideal" Burr Dressing.

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ABSTRACT

This thesis describes the author's investigations into the design of a burn dressing; the use and mode of action of silicone gel when applied to hypertrophic scars, and its use as a burn dressing. This research was carried out at the Bioengineering Unit, Strathclyde University in conjunction with the Burns Units at Glasgow Royal Infirmary and the Royal Hospital for Sick Children, Glasgow, and the Dow Corning Corporation.

The Introduction provides a background to the history of burn dressings and hypertrophic scarring. The need to define the "ideal" burn dressing is emphasised, and the thesis objectives are stated.

Chapters 2,3 and 4 provide a background to the study by describing the anatomy and physiology of skin, wound healing, burns, hypertrophic scarring and burn dressings.

The limitations of presently available burn dressings is reviewed in Chapter 5. Quantitative, critical criteria, useful for defining the "ideal" burn dressing, are presented in the same chapter.

Chapter 6 is a literature review on the chemistry and medical applications of silicones.

The treatment of hypertrophic scars with silicone gel is discussed in Chapter 7. The mode of action of the material has been examined and a possible explanation is presented.

Chapter 8 explores the possibility of using silicone gel

as a burn dressing by examining its relevant properties and the application to burn wounds.

The results of the investigation are discussed in Chapter 9. Silicone gel has been found to be a very effective treatment for hypertrophic scars. However, more research is required to fully discover its potential as a burn dressing, and to completely define the "ideal" burn dressing quantitatively.

ACKNOWLEDGEMENTS

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CONTENTS

PAPERS RESULTING FROM THE WORK PRESENTED IN THIS THESIS

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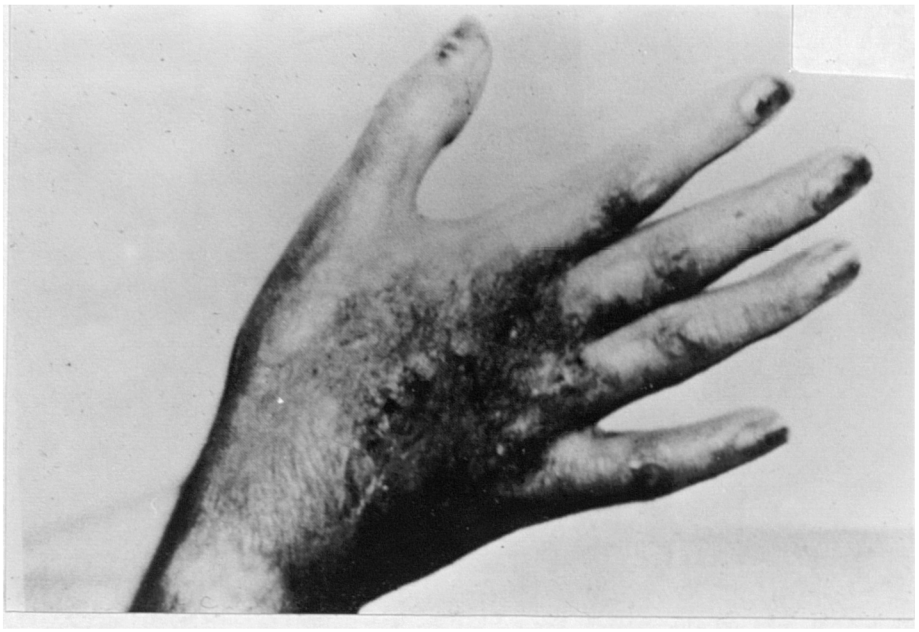


Figure 1.1 Spontaneously healed and grafted second and third degree burns of the dorsum of the hand demonstrates an apparently excellent cosmetic result 2 months post-burn (Larson, 1973).

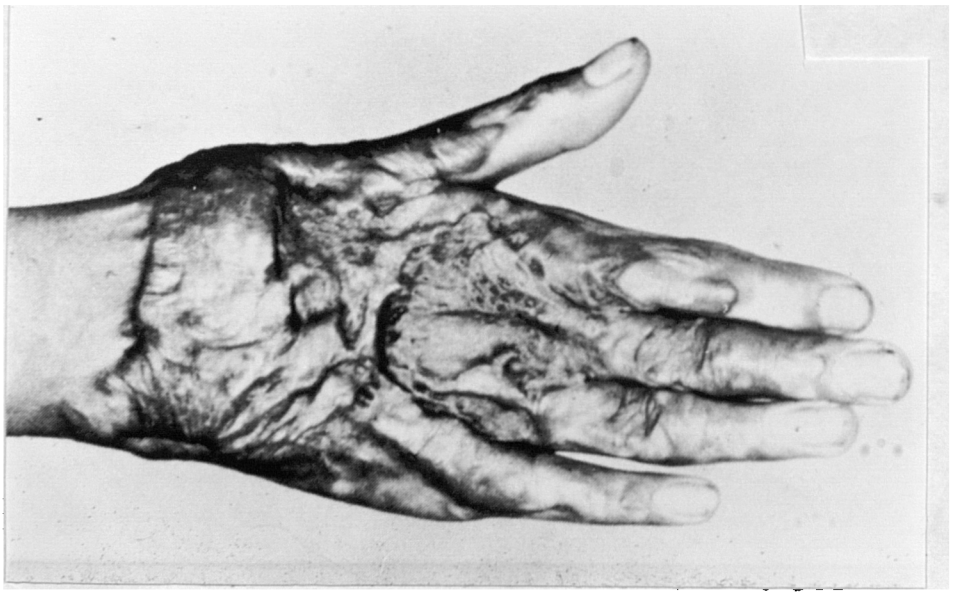


Figure 1.2 The same hand seen 6 months later showing severe hypertrophy (Larson, 1973)

CHAPTER 1

INTRODUCTION

Burn injuries have afflicted man since the discovery of fire, and many different methods of treatment have been advocated. Until the late sixteenth century, plants, boiled cow dung, milk from a woman who had just given birth to a son, honey, vinegar or wine are examples of the treatments applied to burn wounds (Artz & Moncrief, 1969; Artz, 1970). By 1607, the degrees of burn injury and the problems of contracture had been recognised, and early in the nineteenth century cotton wool was recommended for absorbing exudate (Artz & Moncrief, 1969; Artz, 1970). From this period in history to the present day, the pathophysiology of burns and the requirements for burn wound healing have become understood, although an "ideal" burn dressing has not been defined.

Hypertrophic scarring is a common sequela to burn injuries (Figures 1.1 and 1.2). These lesions are recognised by their thick, red appearance. Conventionally, pressure, in the form of custom-made pressure garments or splints, is applied to reduce these disfiguring scars. This form of treatment is not always effective, for example, pressure can be impossible to apply to scars located in anatomical depressions, over flexures or during movement.

In an effort to apply uniform pressure to any scar in any

position or during movement, Perkins and her colleagues (1982) used silicone gel sheets (Spenco Medical Corporation MD-3071). This group discovered that scars under pressure and silicone gel treatment regressed in a shorter time than those only under pressure. They later observed that silicone gel alone would encourage scar regression, however, the mode of action was not explained.

Dow Corning, the international manufacturers of silicone products, developed a similar silicone gel to be tested in Glasgow. The study was a joint venture between Dow Corning, the Burns Unit at the Royal Infirmary and the Bioengineering Unit, University of Strathclyde, and later included the Burns Unit at the Royal Hospital for Sick Children. This thesis reports the results of this study.

The objectives of the thesis are:

1. To determine whether or not silicone gel softened and reduced hypertrophic scarring, and if so by what mode of action;
2. To establish critical, clinical criteria in quantitative terms, and thus define the "ideal" burn dressing;
3. To explore the possibility of one material (silicone gel) being used to treat both open burn wounds and hypertrophic (and non-hypertrophic) scars.

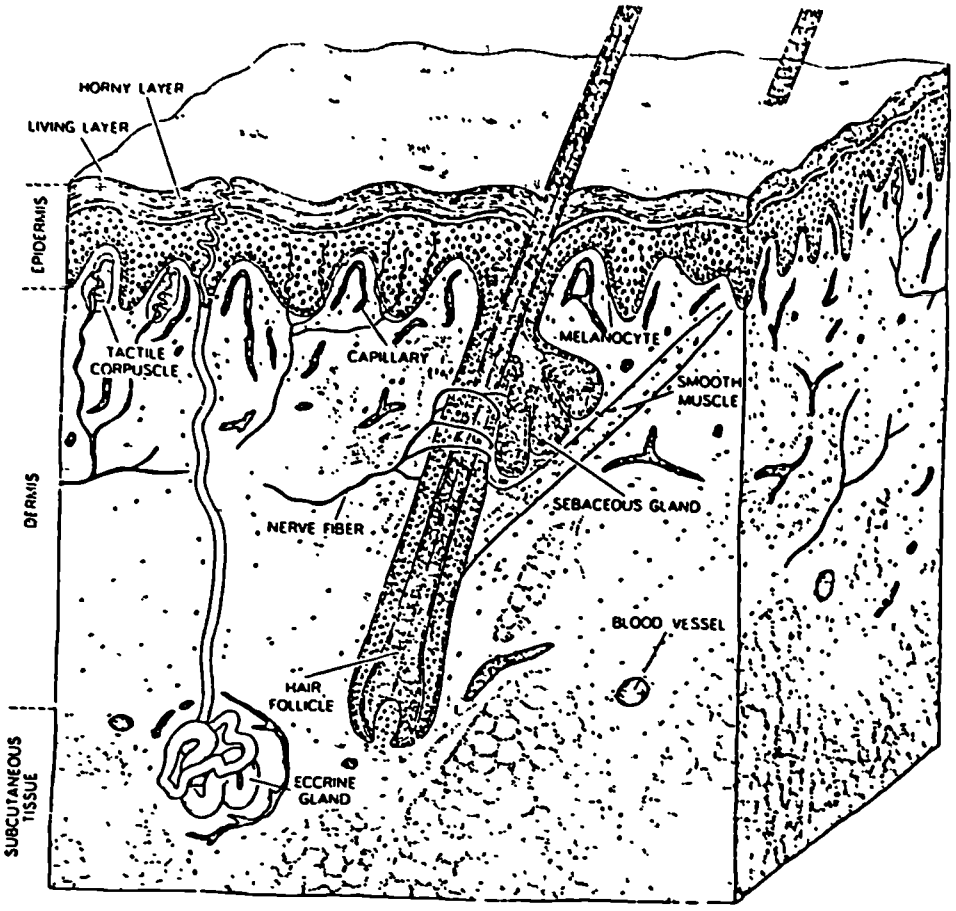


Figure 2.1 The skin (Montagna, 1965).

CHAPTER 2

HUMAN SKIN AND WOUND HEALING

2.1 INTRODUCTION

Skin is the largest and most versatile organ of the body. It is likewise the most exposed, and hence the organ most subject to trauma. However, the skin, along with bone and liver, has the reparative power and regenerating capacity to ulimately restore continuity and function to the traumatised area (Osment, 1975).

The skin acts as a protective sh eld against phvsical and chemical attack and wards off the harsh ultraviolet rays of the sun. It identifies each individual, by shaping the facial and body contours as well as by distinctive markings such as fingerprints (Montagna, 1965).

2.2 STRUCTURE OF SKIN

The skin is composed of layers, the two principal layers being the upper epidermis and the underlying dermis (Figure 2.1).

2.2.1 The Epidermis

The epidermis, the most superficial part of the skin which forms the selective barrier between the body and the environment, is composed of stratified squamous epithelium consisting of interconnected cells of ectodermal origin. These cells are joined together by modifications of the cell membrane called desmosomes which maintain the integrity of the tissue. The thickness of the

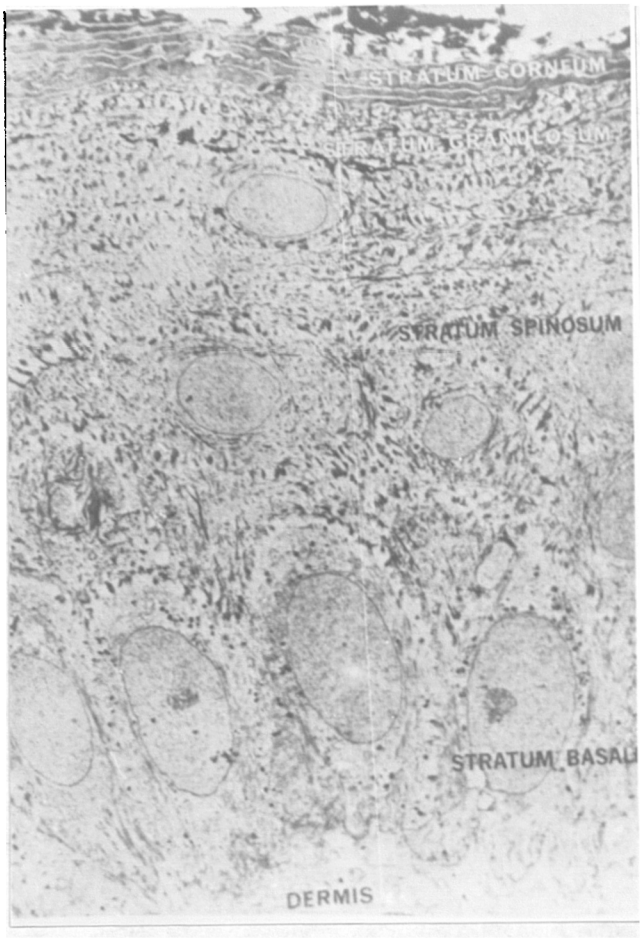


Figure 2.2 Structure of the epidermis (Ferguson, 1980).

epidermis varies in different parts of the body but is normally about 0.1 mm thick, although on the palms of the hands and soles of the feet it is between 2 and 3 mm thick.

The epidermis has two major layers, the stratum Malpighii (living cells) and the stratum corneum (dead, horny cells). The basal cell layer and spiny layer (Figure 2.2) are collectively known as the stratum Malpighii (Rhodin, 1974). The term stratum Malpighii is sometimes used to include the granular layer (Montagna & Parakkal, 1974; Lever & Schaumberger-Lever, 1975).

2.2.1.1 The stratum basale. Basal epidermal cells are cuboidal or low columnar in shape with the long axis aligned vertical to the skin surface (Montagna & Parakkal, 1974). The major function of these cells is division and to support this function the basal cell has an abundance of the cellular inclusions associated with an active metabolism, including the specialised markers of cell division, the centrioles (Odland & Reed, 1967). The basal cell layer also contains melanocytes which are capable of producing the pigment melanin, "which protects the dermis from the harmful effects of sunlight and overproduction of vitamin D" (Osment, 1975).

2.2.1.2 The stratum spinosum. The cells of the spiny layer nearest the basal layer are polyhedral in shape (Figure 2.2), while the successive one to three cells, before the stratum granulosum, are more flattened and elongated. In the cells just below the stratum granulosum, distinctive granules appear for the first time (Charles, 1959; Odland, 1960; Frei & Sheldon,

1961). They appear throughout the cytoplasm but are more numerous near the cell membrane. They are ovoids or short rods in configuration and their size ranges around 100-300μm, and they are called membrane-coating granules (Matoltsy & Parakkal, 1965), Odland bodies or keratinosomes. Their biochemical nature is not fully understood, but they do contain hydrolytic enzymes and therefore may play a role in exfoliation.

2.2.1.3 The stratum granulosum. This layer is 2-3 cells thick. these cells continue the process of flattening begun in the stratum spinosum, until they become almost as flat as keratinised cells in the stratum corneum. Their most distinguishing feature is the keratohyalin granules that they contain. Also present are the membrane-coating granules (M.C.G.s) of the stratum spinosum but their number decreases as the cells near the stratum corneum and as keratohyalin content increases. These M.C.G.s are thought to be discharged from the cell (Odland & Reed, 1967). In this layer the nuclei and other organelles start to disintegrate.

2.2.1.4 The stratum lucidum. This non-cellular layer is found in friction surfaces or in areas where the epidermis is very thick, and is rarely coloured with histological stains (Montagna, 1962).

2.2.1.5 The stratum corneum. The stratum corneum, or horny layer, consists of 25 or more layers of dead, horny, flattened cells, and represents the end of epidermal differentiation. The cells contain dense structures which may be either nuclear

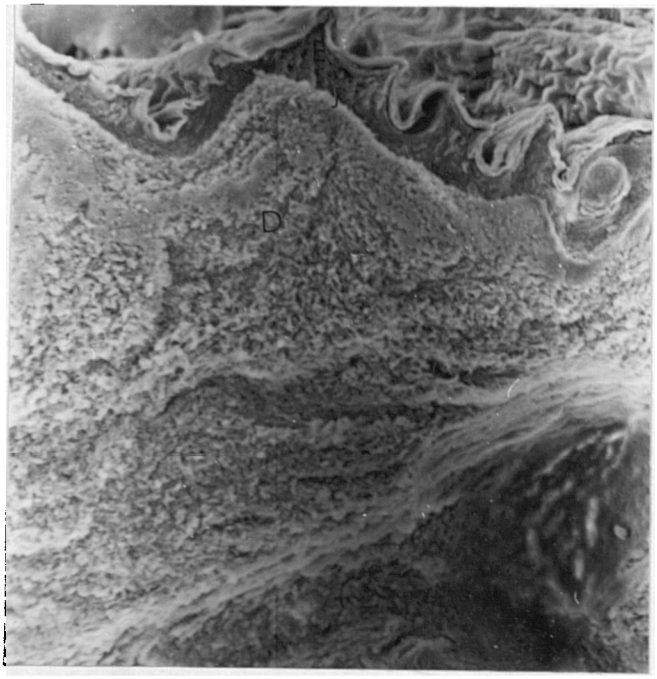


Figure 2.3 Scanning electron micrograph of the dermo-epidermal junction (J); E, epidermis; D, dermis.

or keratohyalin remnants or melanosomes without membranes. The matrix is filled with fibrils (Odland & Reed, 1967). In friction surfaces, the cells of this layer are firmly cemented together (Montagna & Parakkal, 1974).

Normally about two weeks is required for a cell which has just reached the innermost part of the stratum corneum to be shed from the surface. An almost equal amount of time is needed for a basal cell, the innermost epidermal cell, to reach the stratum corneum (Osment, 1975).

2.2.2 The Dermoepidermal Junction

This appears in micrographs (Figure 2.3) as an irregular, wavy line .5-1μm thick and follows the undulations of the boundary zone between the epidermis and the dermis.

Epidermal cones and ridges of different sizes, called rete pegs, project into the dermis, enclosing between them vascularised dermal papillae.

In mammals, including man, a submicroscopic, 35nm thick membrane follows the basal contours of the epidermal cells, and is separated from them by a space of 30nm. No filaments, either epidermal or dermal, cross this membrane, called the basement membrane (Montagna, 1962). This membrane comprises the epidermal basal cell plasma membrane, the lamina lucida, the basal lamina and the zona diffusa (Briggamen & Wheeler, 1975).

Though genetically determined, the dermoepidermal junction is morphologically adapted to the various shearing forces to which the skin is exposed. In the palms and soles, the basal

cytoplasmic processes of the epidermal cells are long and the development of the argyrophil reticulum between the processes is extensive. Moreover, the epidermal ridges and cones attain a great depth and complexity in these areas. In contrast, the epidermal ridges in the medial side of the thighs or the abdomen are shallower and the union of the epidermis with the dermal reticulum is less distinct.

2.2.3 The Dermis

In man, the whole mass of dermis constitutes between 15 and 20% of total body weight. The versatility of the dermis is seen in its range of functions, from ion exchange to protection from mechanical injury. The epidermis and the cutaneous appendages grow upon the dermis and take nourishment from it, also their growth and differentiation seem to guided by it. The dermis interacts with the epidermis during embryogenesis and morphogenesis and during repair and remodeling. Its various properties stem primarily from the matrix of extracellular connective tissue, the ground substance and the fibrous proteins, but being connective tissue, the dermis is unstable and undergoes change, breakdown and renewal (Montagna, 1962; Montagna & Parakkal, 1974).

The dermis consists of two layers at the light microscope level, a superficial papillary layer of thin fibres immediately underneath the epidermis, and a deep reticular layer composed of a network of thick collagen fibres. The dermal matrix contains few cells, more in the upper papillary layer than in the lower

reticular layer, which are predominantly fibroblasts with the potential to produce most, if not all, the components of the extracellular matrix. More abundant are the mast cells, in addition, histiocytes or macrophages, melanocytes, and extravasted leukocytes are often found (Montagna & Parakkal, 1974).

2.2.3.1 Ground substance. The dermal matrix consists of an amorphous, semi-fluid, non-fibrillar ground substance that cushions and lubricatates the dermal consitiuents, such as the collagen fibres, and helps nourish and support the epidermis. It contains proteins, soluble collagen, enzymes, immune bodies, metabolites, water, inorganic ions, blood sugars and proteins, urea, metabolic products of connective tissue cells, and complexes of mucopolysaccharides and proteoglycans (Dorfman, 1953; Montagna, 1962; Montagna & Parakkal, 1974). Proteoglycans consist of a central protein core with polysaccharide side chains (Mathews, 1967). The major polysaccharide moieties consist of three glycosoaminoglycans: hyaluronate, dermatan sulphate (chondroitin sulphate B) and chondroitin sulphate A. These are hydrophilic substances that bind water in the dermis. As mucopolysaccharides decrease in the dermis with age, and as collagen increases, the hydration of the dermis decreases, and the diffusion characteristics of the ground substance change (Worobec & Solomon, 1978).

2.2.3.2 Collagen. The most abundant fibrous protein in mammals is collagen, indeed, over 90% of the dry weight of dermal tissue consists of collagen. Amino acids, especially glycine (30% by

weight of collagen) and hydroxyproline (12% by weight of collagen), the latter being a relatively specific marker for collagen (Ross, 1968), condense to form a coiled structure which is the collagen molecule. However, hydroxyproline is not incorporated into the chain as such, but is formed from the hydroxylation of proline after proline has become part of the collagen molecule. Failure of the hydroxylation step specifically inhibits collagen synthesis and secretion from the fibroblast, resulting in deleterious effects on wound healing.

A protein can be identified as collagen if it possesses the following characteristics:

(i) The presence of three linear peptide chains of equal length in a right-handed helical configuration, the three chains being arranged parallel to each other, and the assembly being twisted into a left-handed "super helix" tropocollagen molecule. This rod-shaped triple helix is approximately 290nm long and 1.4nm in diameter.

(ii) The presence of glycine in every third position along the peptide chain, so that the chains, referred to as α chains whose rigidity is maintained mainly by hydrogen bonds (Ross, 1968; Montagna & Parakkal, 1974), consist of repeating triplets Gly-X-Y where X and Y may be any amino acid.

(iii) The presence of the unique amino acids, hydroxyproline and hydroxylysine. These occur only in the Y position of the tripeptide Gly-X-Y (Peacock & Van Winkle, 1976).

A number of α chains have been identified, each of which

Table 2.1 (Woodhead-Galloway, 1980).

COLLAGEN TYPE	MOLECULAR FORM
I	$(\alpha_1(I)_2)\alpha_2$
II	$(\alpha_1(II))_3$
III	$(\alpha_1(III))_3$
IV	$(\alpha_1(IV))_3$

is a specific gene product having a characteristic amino acid composition and sequence. Further analysis of the α chain (Woodhead & Galloway, 1980) has shown that it consists of two fractions (α_1 and α_2). These aggregate in a characteristic manner leading to the formation of molecules of several types (Table 2.1). It is now known that there are at least four types of collagen. The most common type (I) makes up the majority of skin, bone and tendon, while type II collagen is found in cartilage. Type III is found in embryonic tissues and in the cardiovascular system, while type IV makes up basement membranes (Cohen et al., 1979).

The three-dimensional arrangement of the collagen meshwork can be seen with the scanning electron microscope (SEM) at relatively low power. Collagen fibrils 10-15μm in diameter are woven into a mat of remarkable structural integrity and flexibility. At the level of the transmission electron microscope (TEM), the collagen in this network is seen to be arranged hierarchially. Collagen bundles that can be seen with the naked eye are reffered to as fibres, which under the light microscope consist of numerous smaller fibrils. Fibrils, by definition the smallest units that can be seen under the light microscope, are 10-15μm in diameter. Under the electron microscope, the fibrils themselves are seen to be composed of bundles of smaller, identical and parallel "micro-fibrils" 30-60nm diameter (Figure 2.4).

2.2.3.3 Elastin. Elastin makes up only 2% of the dry weight of

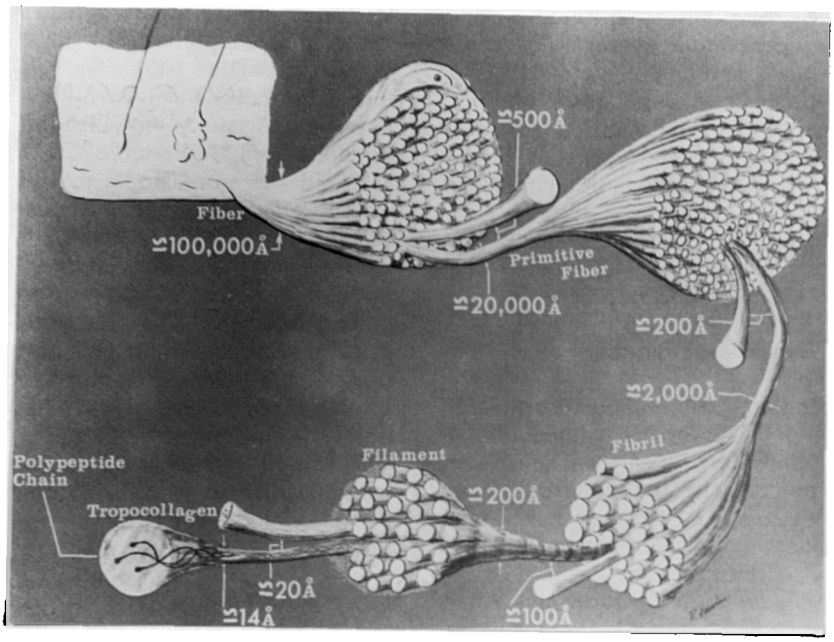


Figure 2.4 Schematic diagram of the assembly of components of a collagen fibre (Peacock & Van Winkle, 1976).

human skin. Elastic fibres, which impart to the skin the ability to resume its original shape after stretching, are coarse, branching, cylindrical, or flat ribbons entwined among the collagenous fibres in the dermis (Montagna, 1962). The abundance of elastin fibres varies from area to area; they are always more abundant in the scalp and face than elsewhere, even in newborn infants (Montagna & Parakkal, 1974).

The protein elastin is non-fibrillar and homogeneous. Elastic fibres consist of two components: and inner amorphous "medulla," the elastin, and an outer "cortex" consisting of non-elastin proteinaceous microfibrils 11nm in diameter. During early elastogenesis, the elastic fibres consist predominantly of the microfibrils. The fibrillar component has been found in grooves in the surface of fibroblasts where it appears to be a tubular mould into which the amorphous inner material is secreted (Ross & Bornstein, 1969). The sequence of appearance of the fibrillar and the amorphous components suggests that one is the precursor of the other. The two proteins differ markedly in amino acid composition and neither resembles collagen. The amorphous component has essentially the same amino acid composition as a soluble elastin precursor, tropoelastin, isolated from copper-deficient pigs. Thus, the elastin of the elastic fibre is the central amorphous material and is chemically unrelated to the outer microfibrillar component (Ross & Bornstein, 1969).

In the papillary layer, the probable function of the elastic

fibres is to anchor the epidermis to the dermis, also to anchor the origin of hair follicles to the surface of the reticular layer. They also form a skeleton around the secretory segments of eccrine and apocrine glands and anchor blood vessels to their environment by way of a loose reticulum (Montagna & Parakkal, 1974).

2.2.3.4 Reticulin. Reticulin can be identified in the dermis as fine-branching fibres which form a network. A dense bed of these fibres found in the upper part of the papillary layer either forms the basement membrane or is a component part of it. The greatest preponderance of reticular fibres is in the papillary layer and in its extentions around the cutaneous appendages, for example, around sweat glands and in the connective sheath of hair follicles. In the reticular layer they are only numerous around blood vessels (Montagna, 1962).

Physically and chemically reticulin is similar to collagen, however, the fibrils are thinner than collagen fibrils but they do show the same regular striations in the electron microscope. Montagna and Parakkal (1974) suggested that reticulin may provide a template for the extracellular aggregation of collagen fibrils, however, it is still the least well understood of the fibrous components of connective tissue.

2.2.3.5 Fibroblasts. Fibroblasts arise from tissue mesenchyme and not as originally believed from haematogenic precursors (Ross & Lillywhite, 1965; Ross et al., 1970). Their functions are the synthesis of collagenous and elastic fibres, the amorphous ground substance mucopolysaccharides, and the metabolism of

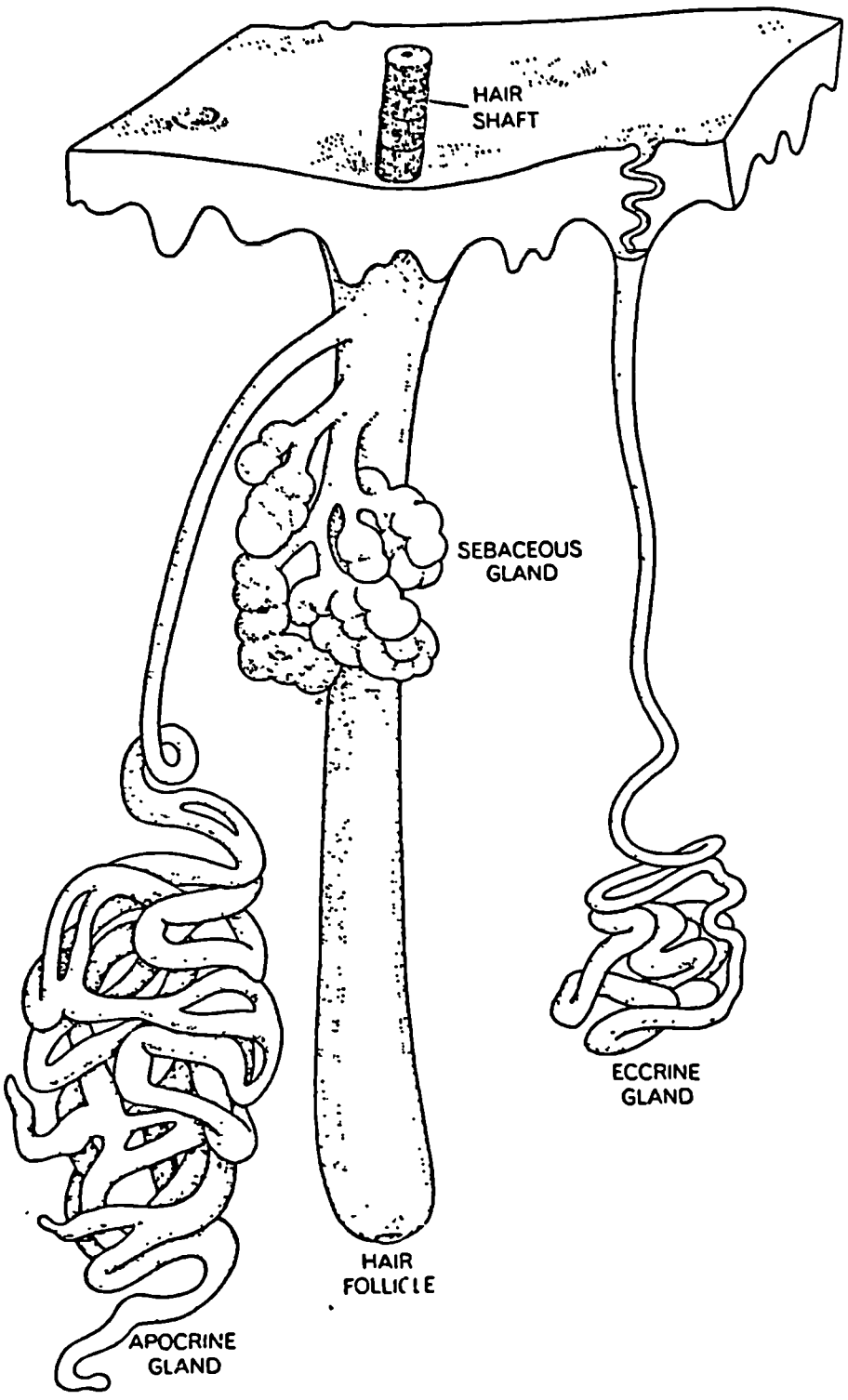


Figure 2.5 Sweat glands (Montagna, 1965).

steroids and cholesterol. In addition, they can release many proteolytic and collagenolytic enzymes, and thus may play a role in connective tissue remodeling (Montagna & Parakkal, 1974).

2.2.4 Skin Appendages

Sweat glands are found widely distributed throughout the skin. There are two types of sweat gland, the eccrine and the apocrine glands. The apocrine glands are usually associated with hair follicles and the eccrine glands are not. The two types have different origins, structures (Figure 2.5) and functions.

The eccrine glands are innervated by the sympathetic nervous system and secrete most of man's sweat that is mainly water but contains 0.1-0.4% sodium chloride. This has two main functions:

(i) cooling the body by evaporation,

(ii) moistening the friction surfaces, such as those of the palms and soles, which prevents flaking of the horny layer, improves grip and assists the tactile sensitivity (Montagna, 1962).

The apocrine glands have no nervous control, but are stimulated by circulating adrenalin. They produce a milky, odourless fluid which, due to bacterial activity, can subsequntly develop a characterisitc and sometimes offensive odour.

Eccrine glands are thought to have evolved more recently and that apocrine glands are primitive in terms of evolution (Green, 1976).

The sebaceous glands (Figures 2.1 & 2.5) are composed of secretory epithelial cells arranged to form alveoli. Sebaceous

glands secrete sebum, an oily substance containing fatty acids, triglycerides, waxes, cholesterol and cellular debris, into the hair follicles. On the skin it provides some waterproofing, acts as a bactericidal agent and prevents drying especially on exposure to heat and sunshine.

Hair follicles consist of a downward growth of epidermal cells into the dermis or even the subcutaneous tissue. At the base of the follicle there is a cluster of cells, called the bulb, from which the hair grows. The hair is formed by the multiplication of cells in the bulb and, as they are pushed upwards and away from their source of nutrition, the cells die and are converted into keratin.

2.2.5 Cutaneous Systems

The capillary blood vessels and lymphatic vessels lie in the connective tissue of the dermis. The kind of cutaneous vascular beds are determined by the kind of skin they perfuse, the thickness of the various dermal and hypodermal layers, the types and numbers of appendages present and the specific relation of the skin to the bones and muscle layer under it (Montagna & Parakkal, 1974).

2.2.5.1 Cutaneous vascular system. The cutaneous vasculature controls body temperature, affects blood pressure, and carries nutrients to the skin. Blood flow in the skin may vary from 0.5 ml/mg/100ml tissue during strong vasoconstriction caused by exposure to cold (Burton, 1961) to the 5.2 ml/mg/100ml tissue normally found (Ryan, 1973).

Formerly, the dermis was believed to contain superficial

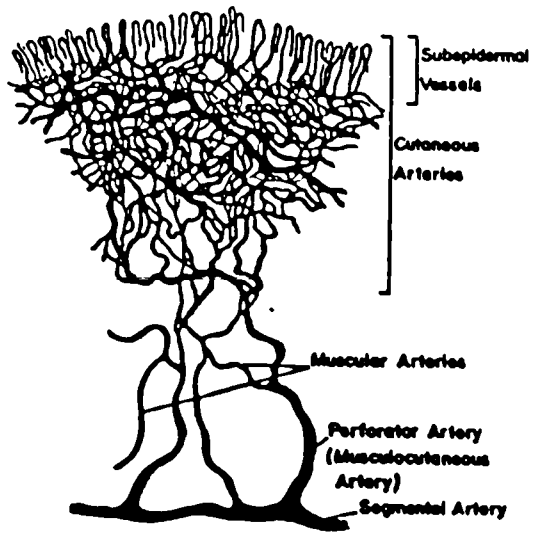


Figure 2.6 This figure shows the patternless cutaneous vascular system, the branching of the segmental artery into the perforator artery, and the latter, in turn, branching into muscular and cutaneous arteries (Montagna & Parakkal, 1974).

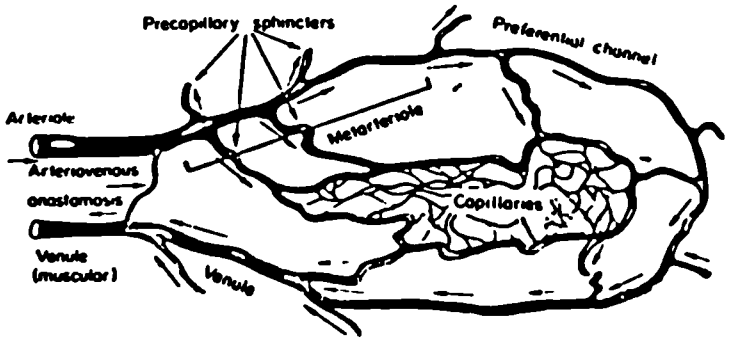


Figure 2.7 Zweibach's concept of the basic structural pattern of the terminal cutaneous vessels (Montagna & Parakkal, 1974).

and deep plexuses, but Winkleman (1961) and Saunders (1961) demonstated interconnecting vessels at all dermal levels (Figure 2.6). In addition to widespread dermal anastomoses, there is also a rich periappendageal vascular network. In areas where the papillae are long and narrow, long capillary loops run perpendicular to the skin surface.

Cutaneous terminal arterioles and metarterioles that have a muscular wall, form a preferential channel toward the venular circulation, and regulate flow to capillary beds through precapillary sphincters. Contraction of precapillary sphincters shunts blood through the preferential channel, bypassing the capillary bed (Figure 2.7). Venules also control capillary flow by their ability to dilate and constrict passively (Zweibach, 1959).

2.2.5.2 Cutaneous lymphatic system. Cutaneous lymphatics are probably as extensive as blood vessels, but have not been shown satisfactorily. The principal role of the lymphatic system is to remove plasma proteins from extracellular spaces. Secondarily, it removes particulate and antigenic materials from tissues (Montagna & Parakkal, 1974).

2.3 FUNCTIONS OF SKIN

Skin forms the boundary between the body and the external environment and as such has five main functions: protection, sensation, storage, absorption and heat regulation.

2.3.1 Protection

The primary role of skin is protection of the internal

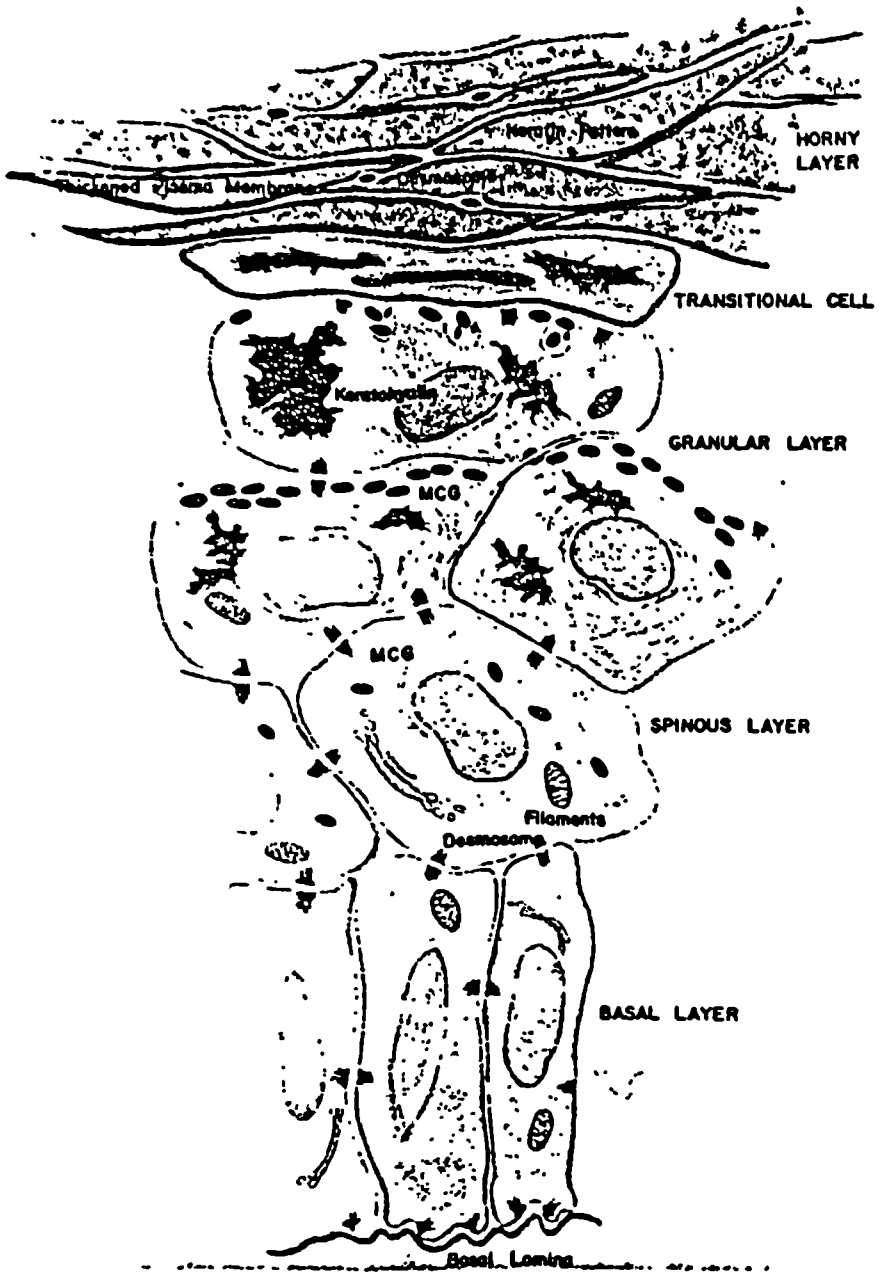


Figure 2.8 Schematic diagram showing the layering of the epidermis. The basal cells are mitotically active. The differentiation products - filaments, membrane-coating granules, keratohyalin and thickened plasma membrane are shown in the different layers. The fully cornified cells are packed with a filament-matrix and show the "keratin pattern" (Montagna & Parakkal, 1974).

structures from injury and from invasion of micro-organisms. The outer layer of the epidermis is composed of the horny protein keratin. Keratinisation (Figure 2.8) is a protective specialisation observed in stratified squamous epithelium where there is "wear and tear," for example, in the skin. This process, which begins in the stratum basal, is the chemical degredation of cells and is accomplished essentially through the oxidation of sulphydryl groups to disulphide linkages (Osment, 1975).

As epidermal cells migrate upward from the basal layer, they lose their mitotic potential to a great extent and begin to synthesise such specific constituents as fibrillar and amorphous proteins, keratohyalin and membrane-coating granules. The cell surface becomes modified, and finally the nuclei and cytoplasmic organelles are lost (Montagna & Parakkal, 1974). At the end of this process of differentiation, epidermal cells become constituents of the horny layer which shields us against damage from the environment and maintains the "internal milieu." Any mechanical or chemical alteration in this layer impairs its "barrier" function and can make the skin permeable to water and soluble substances (Winsor & Burch, 1944).

2.3.2 Sensation

Nerve endings which are sensitive to changes in temperature and pressure are widely distributed in the dermis and excessive changes in either may cause pain. Anyone with sensory loss may readily develop severe injuries (Green, 1976).

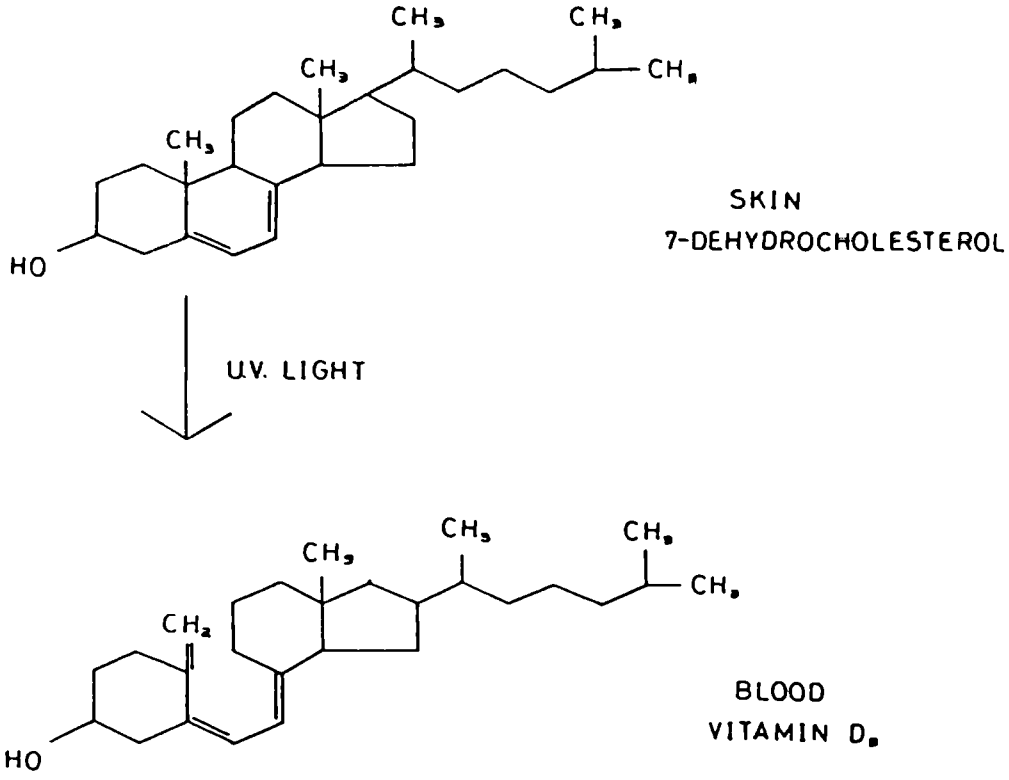


Figure 2.9 Skin synthesis of vitamin D_3.

2.3.3 Storage

The skin and subcutaneous tissues act as a store for water and fat. The adipose tissue under the skin is one of the main fat depots of the body. An accumulation of water under the skin leads to oedema.

2.3.4 Absorption

In the sebum there is a fatty substance present known as 7-dehydroxycholesterol. The skin absorbs ultra-violet radiation from the sun and this converts 7-dehydroxycholesterol to vitamin D_3 (cholecalciferol) (Figure 2.9). The vitamin D_3 thus formed is absorbed into the blood stream and is utilised within the body to ensure the satisfactory development and maintenance of bone tissue.

2.3.5 Temperature Regulation

Man maintains his central body temperature at a constant value which is independant of the environmental temperature. This is achieved by continuously maintaining a balance between heat gained (from metabolism, environment, shivering and eating hot food) and the heat lost (by conduction, convection, radiation and evaporation).

The heat lost from the skin is determined by the skin temperature, which is lower than the central body temperature. The higher the skin temperature the greater the heat loss, the lower the skin temperature the lower the heat loss. The skin temperature depends on the skin blood flow and this, in turn, depends on the activity of the sympathetic nerves to the skin.

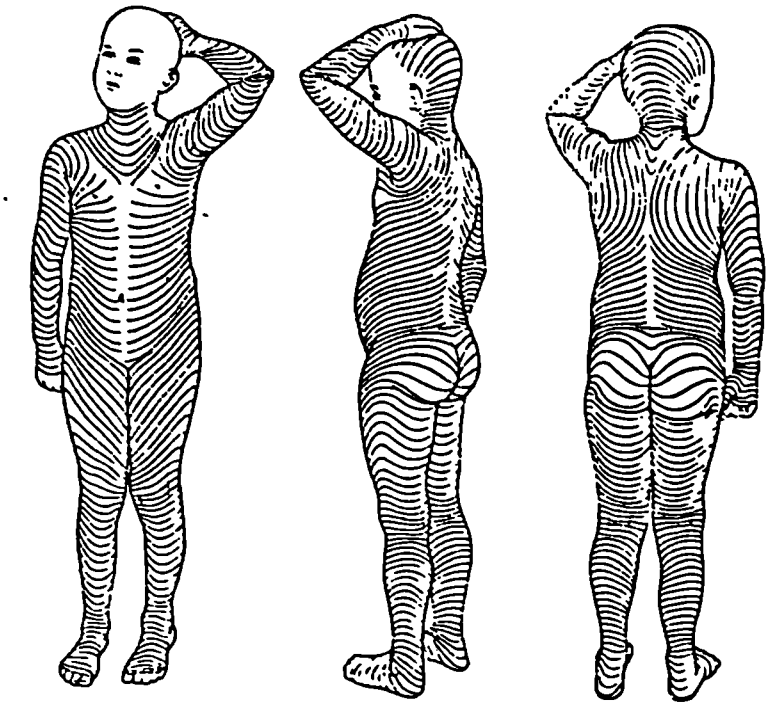


Figure 2.10 Normal relaxed skin tension lines (MacMillan & Lang, 1979).

The higher sympathetic vasoconstricter tone, the lower the skin blood flow, the lower the skin temperature and the lower the heat loss from the skin. The lower the vasoconstricter tone, the higher the skin blood flow, the higher the skin temperature and the higher the heat loss (Green, 1975).

If the temperature of the body is increased by 0.25-0.5°C the sweat glands are stimulated to secrete sweat. Sweat is conveyed to the body surface and sometimes evaporates into the atmosphere thus cooling the body. It cools the body because the heat which evaporates the water is taken from the skin. If the atmospheric air is humid the evaporation of sweat does not take place so readily and beads of sweat appear on the surface of the body (Ross & Wilson, 1973).

2.4 MECHANICS OF SKIN

The mechanical properties of skin are determined by the structure and components of the epidermis and dermis. These properties, which exist when skin is in its natural state of pretension, are important in plastic surgery.

2.4.1 Natural Lines of Skin Tension

When at rest, skin exhibits a biaxial tension (Figure 2.10). These lines of maximal local tension, called relaxed skin tension lines (Borges & Alexander, 1962; McMillan & Lang, 1979), "Langer's lines," lines of tension, cleavage lines, crease lines, "lines of election," lines of minimal tension, lines of minimal extensibility or "lines of elasticity" (Flint, 1976), which correspond to the directional pull which, in the skin

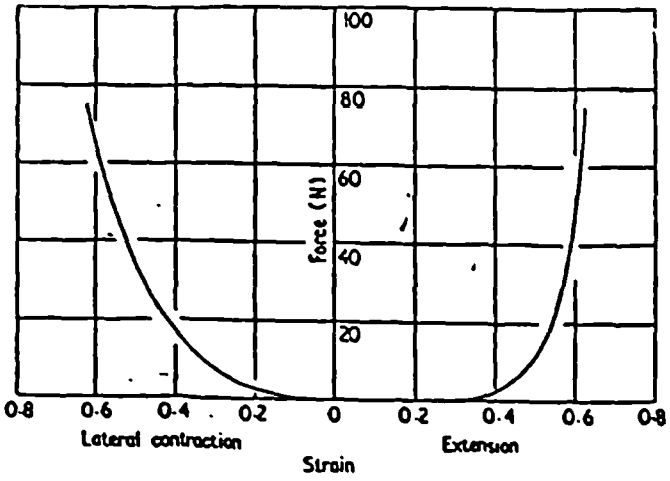


Figure 2.11 Force-deformation relations for excised human skin in uniaxial tension. Large extensional strain is accompanied by contraction of a similar magnitude (Kenedi et al., 1975).

in an area at rest, is determined largely by the protusion of the underlying skeleton and internal organs. These lines do not always coincide with the wrinkle lines, the lines of expression, or the ridges and furrows formed by muscle contraction or articular movements, however, they are very much the same in all individuals.

Some researchers (Cox, 1941; Ridge & Wright, 1965) accept that these lines should be those elected for surgical incision and excision while others (Kraissl, 1951; Gibson et al., 1965; Gibson & Kenedi, 1967; Gibson et al., 1969; Gibson et al., 1971) are unable to support this concept, and in fact, categorically state that Langer's lines are not lines of tension but are lines of minimum extensibility and may be useful in planning excisions but not incisions.

2.4.2 Mechanical Properties

Skin is an anisotropic, non-linear, viscoelastic, inhomogeneous material and it is likely that there is a correlation between major lines of blood supply and the biomechanical characteristics (Kenedi et al., 1975).

If tension is applied to skin there is a point at which the skin blanches as the capillary patency is obliterated. If allowed to persist it will cause necrosis of the skin. This is important in plastic surgery because in a skin flap with an impaired blood supply, a small degree of tension may cause blanching across the base of the flap and lead to necrosis of all of the distal area (Gibson, 1965). Increasing tension

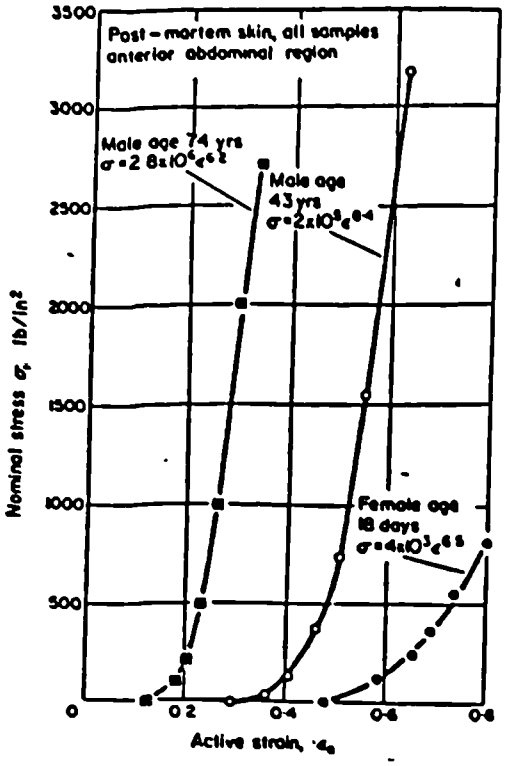


Figure 2.12 Comparison of uni-directional tensile test results for different ages (Kenedi et al., 1965).

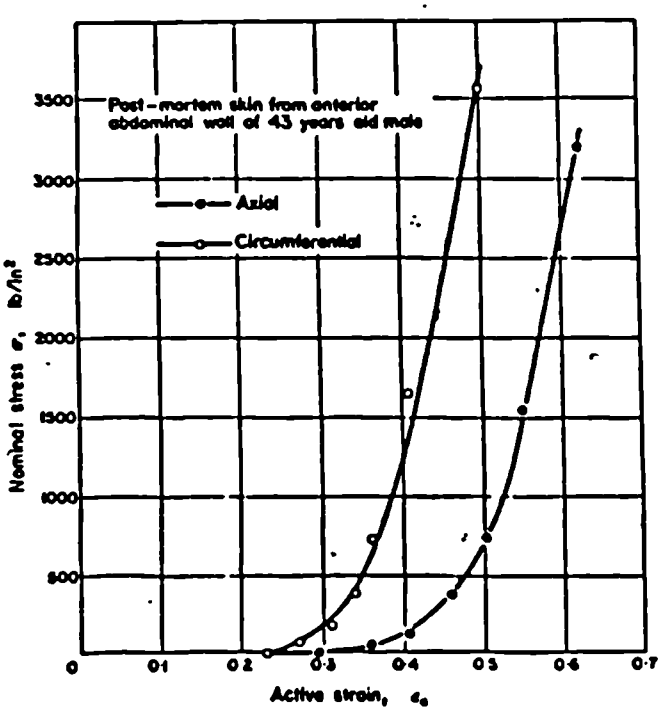


Figure 2.13 Comparison of uni-directional tensile test results in different directions on the same individual (Kenedi et al., 1965).

has four effects on skin:

(i) no effect on normal skin but stretching of immature scars,

(ii) stretching of skin,

(iii) necrosis of skin,

(iv) rupture of dermis.

When a force is applied to stretch skin *in situ* the skin extends in the direction of the applied force and at the same time contracts in a plane at right angles to the applied force. When stretched *in vitro*, there is a progressive decrease in the total volume of the stretched specimen of skin. Figure 2.11 shows a load-deformation test in uniaxial tension on human skin. The curve shape is concave to the load axis, showing a decrease in deformation with increase in load, and the contractions at a right angle to the applied load (the Poisson effect) are comparable in magnitude to the direct extensions.

Typical examples of stress-strain curves for different ages are shown in Figure 2.12. It can be seen that the curves consist essentially of two regions: a primary range showing large extensions for low loads and a "secondary" stage during which the increments of extension continue to decrease with increasing load up to failure. The curves are similar in form in that they may all be represented by the relationship $\sigma = A\xi^n$ where A and n are coeficients obtained from experimental results. The main effect of age as regards curve shape appears to be in the "primary" range, the extent of this gradually decreasing with increasing age. Such differences in the extent of the primary

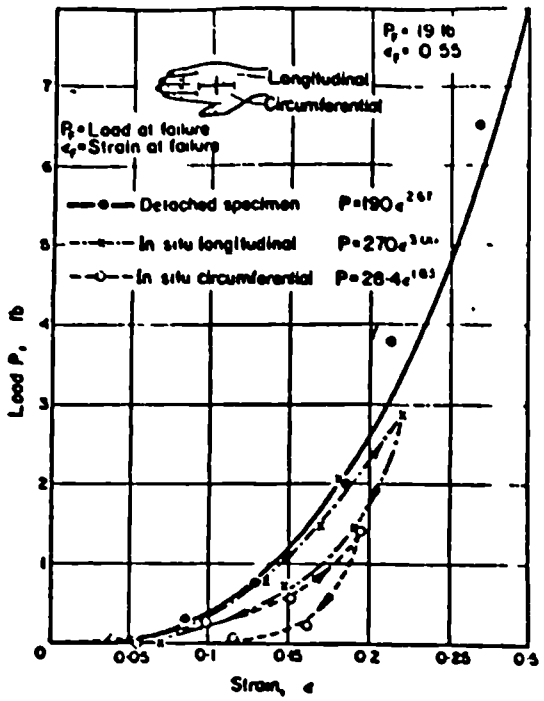


Figure 2.14 Comparison of tensile test on detached specimen with load-strain relationship obtained before removal of specimen of the skin from the back of the hand (Kenedi et al., 1965).

range are also indicated in Figure 2.13 which shows the comparison between specimens taken at right angles from the anterior abdominal wall of the same individual. It can be seen that abdominal skin in the direction of the longitudinal axis of the body appears more extensible at low loads than in the circumferential direction. These variations in the mechanical characteristics of skin observed at different ages, at different sites, and in different directions at the same sites are probably due to variations in the architecture of the collagen and elastin fibre networks (Gibson et al., 1965).

Kenedi and colleagues (1965) compared skin *in vivo* with detached skin from results obtained during and after a tattoo grafting operation (Figure 2.14). The results show that:
(i) the curve shapes are similar to those previously obtained,
(ii) the loading and unloading paths in the *in situ* tests do not coincide, hysteresis is present and residual extensions obtained on unloading recover with time,
(iii) the results obtained from the comparable *in situ* and detached specimen tests show good agreement and are correlatable.

2.4.3 Fibre Orientation

When load is applied to skin, the initial deformation mechanism, both *in vitro* and *in vivo* appears to be one of straightening and load orientation rotation of the collagen bundles, culminating at higher load levels in a fully oriented and virtually close-packed structure (Figures 2.15 & 2.16). This network deformation is the controlling factor in the

Figure 2.15 Scanning electron microscope picture of the dermis (Park, 1979).

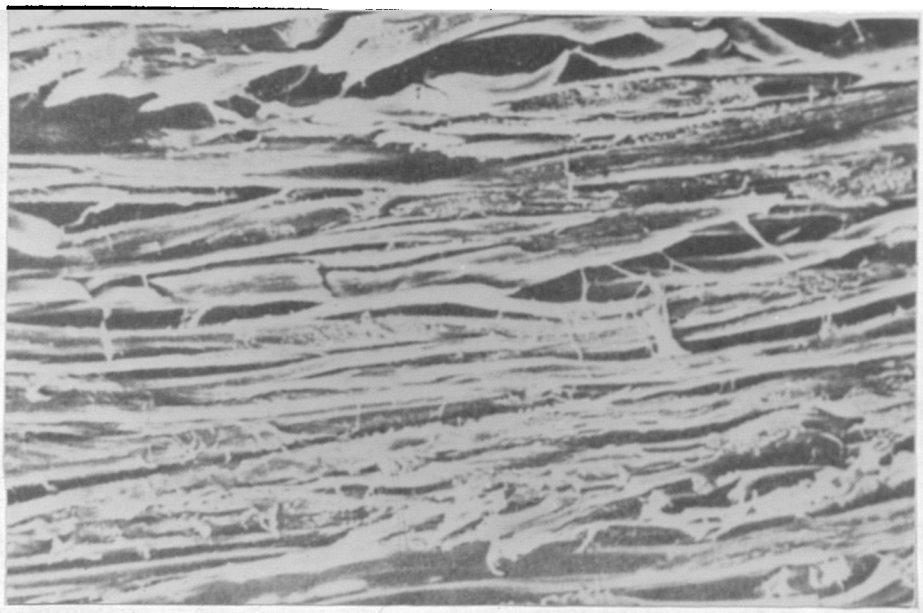


Figure 2.16 Scanning electron micrograph of the dermis after stretching. Stretch direction is horizontal (Park, 1979).

overall load-deformation relation of skin, since when the majority of the fibres are re-arranged parallel to the line of stretch the fibres resist further extension in that direction (Gibson et al., 1965), rather than the mechanical characteristics of the collagen itself (Kenedi et al., 1965).

Craik and McNeil (1965) carried out histological studies on post-mortem human abdominal skin and found that the collagen fibres of the dermis became oriented in the plane of stress, took on an affinity for the red dye of Masson's trichrome stain (a histological stain consisting of a red and a green dye, with which normal dermal collagen stains green), and eventually showed fracture lines and complete disruption. At low load levels relaxation allows the fibres to re-assemble themselves in their normal random fashion but they retain their red staining. At slightly greater loads, although the orientation and the affinity for the red dye remain on relaxation, the fibres assume a wavy pattern.

The elastic fibres in the dermis form a secondary network interconnected with that of collagen and probably act as stores of the energy required to return the collagen network to its relaxed state. Interstitial fluid is displaced from the network as the fibres are orientated and compacted parallel to each other and must be replaced before the relaxed pattern is re-established (Gibson et al., 1965).

2.4.4 Effect of Tension on Wound Healing

The ability of a wound to resist rupture can be expressed

as energy absorbed (energy absorbed is proportional to force x displacement, or extension). This property of wounds is only half that of normal tissue after five months of healing (Forrester et al., 1970). However, up to 13 weeks wounds continue to gain tensile strength at a relatively constant rate (Madden & Peacock, 1968).

Tape-closed wounds develop greater tensile strength than sutured wounds, but are more brittle and have, as a result, no greater ability to resist rupture (Forrester et al., 1970). However, Sommerlad and Creasey (1978) showed that a certain technique of suturing (in a comparison of four techniques of wound closure) produced a narrower scar than other techniques. They suggested that tapes only bring the skin surfaces together whereas subcuticular suturing approximates the middle dermis and obliterates any microspaces left by tapes, thus an earlier, stronger union occurs.

An important stage in wound healing is the formation of collagen by fibroblasts (see 2.5.4 and 2.5.5). Scar tissue is not arranged in a random fashion but is highly ordered and the connective tissue continues to be remodeled (broken down and re-synthesised) over many months after wounding. Hunter and Finlay (1976) found a difference in structure between the edge and the centre of a scar which they explained by considering the forces transmitted from the adjacent dermis and subdermis. At the edge of the wound the scar fibres are influenced directly by the fibres of the adjacent dermis and are, therefore,

orientated in a similar direction. However, in the centre of the wound the forces acting on the scar collagen arise not just from the adjacent dermis but also from the subdermis and, in certain situations, deeper tissues, for example, in vertical abdominal incisions the wound is brought under repetitive stresses by movement of the chest wall, diaphragm and abdominal muscles in breathing.

In wounds sited along Langer's lines most of the collagen should be orientated along the wound because tension is exerted along its axis. If the scar lies at right angles to Langer's lines i.e. where there is little tension along the scar, collagen is first laid down across the scar and thereafter in a random fashion Hunter & Finlay, 1976; Sommerlad & Creasey, 1978). Studies of animal wounds placed under tension support the idea that fibres are laid down along the lines of stress (Forrester et al., 1970). This basic property of connective tissue is, of course, mediated by the fibroblasts which are capable of sensing the orientational stresses and responding by laying down collagen fibres to resist them. t is a fundamental property of normal connective tissue cells, whose molecular basis is not understood, although it is possible that piezoelectric forces are involved.

If Hunter and Finlay's (1976) thesis was applicable to keloids it would suggest that excessive forces were acting on these wounds to produce the large amount of fibrous tissue present. This is unlikely but cannot be ruled out. Other

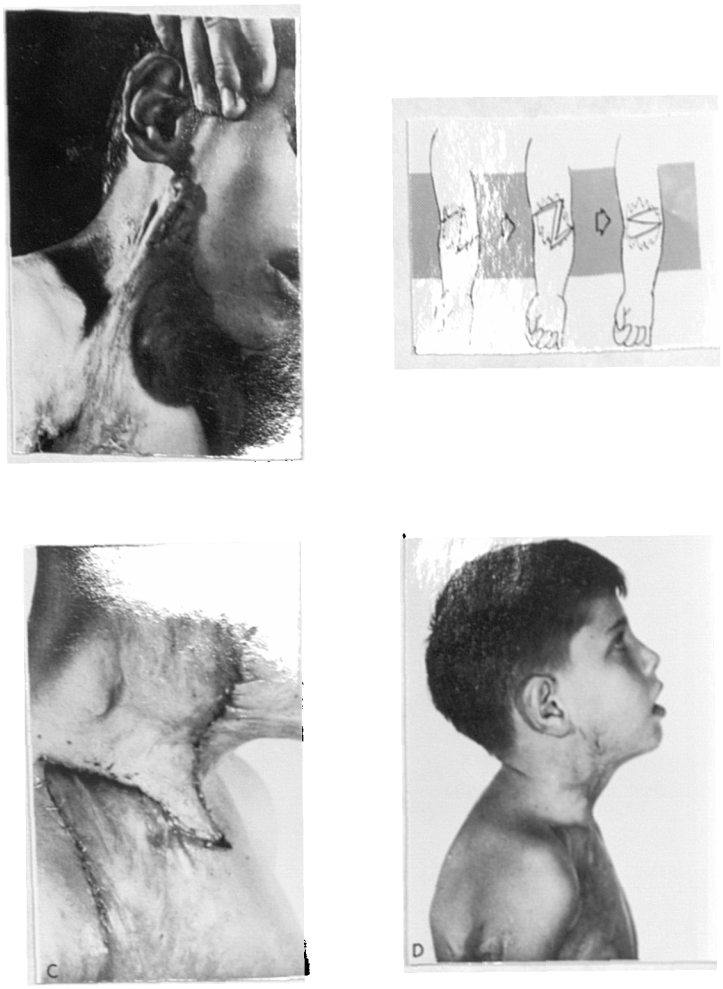


Figure 2.17 A, Scar contracture of neck. B, Z-plasty. Sixty-degree angles and flaps are interchanged. This increases length and decreases width, and also changes direction of the scar. C, Z-plasty completed. D, Later result of Z-plasty (Larson et al., 1979).

explanations proposed by Hunter and Finlay (1976) suggest that keloid cells initially proliferate like benign tumour cells and are capable of sensing the forces applied to them but are incapable of laying down collagen along the lines of force in order to counteract the stress thus more collagen synthesis than normal occurs resulting in a mass of scar tissue, or keloid fibroblasts try to make up in quantity of collagen what is lacking in mechanical quality.

Forrester and colleagues (1969) noted that the SEM appearance of hypertrophic scar supported the idea that hypertrophic scarring may depend on repeated rupturing and rehealing of small fibrils in a brittle scar. They suggest that it may be possible to control the structural organisation of collagen during healing, thus improving "scar performance."

There are techniques in plastic surgery employed to improve anti-tension line scars, these are the Z-plasty and the W-plasty. The W-plasty is used especially in long anti-tension line scars of the forehead (Borges & Alexander, 1962).

The Z-plasty (Figure 2.17) or reversed Z-plasty is used to correct scars 60° or more away from Langer's lines (Borges & Alexander, 1962; Larson et al., 1979).

2.5 WOUND HEALING

Few human tissues can regenerate themselves following an injury, and the process of wound healing repairs damaged skin. This is an intricate physiological process in which several different kinds of cells appear at successive intervals in

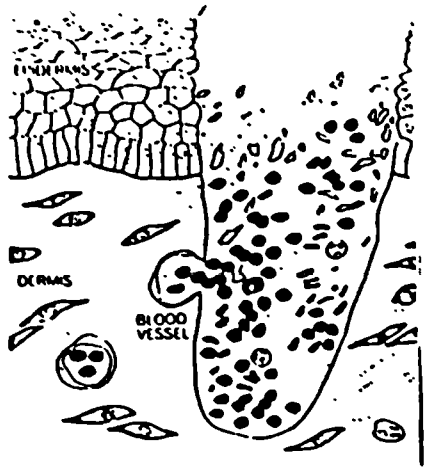
order to absorb foreign matter, destroy bacteria and repair the injury. Without this process complex multicellular organisms could neither survive nor evolve.

2.5.1 Scab Formation

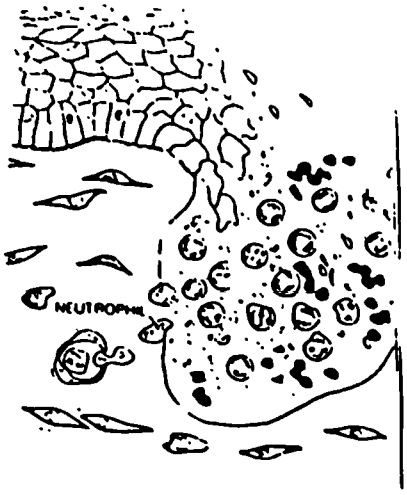
Immediately after injury blood flows into the wound, and wound healing in the dermal layer begins when a clot forms. As blood flows out of a damaged vessel, the platelets adhere to the inner surface of the vessel wall. The clotting factors released from blood and tissue collagen include Hageman factor, which serves a pivotal role in initiation of three events: the activation of complement components, activation of fibrinolytic agents of the plasmin group, and initiation of the clotting process. In the presence of calcium ions (Ca^{2+}) and additional clotting factors in the plasma, thromboplastin catalyses the conversion of prothrombin (a serum globulin continuously manufactured by the liver) to thrombin. Thrombin is an enzyme that catalyses the conversion of the soluble plasma protein fibrinogen to the insoluble protein fibrin. The fibrin gradually forms a mesh in which the blood cells become embedded and the clot is formed and stops blood loss from the damaged vessel. At the surface of the clot, fibrin and other proteins in the blood serum dehydrate and form the protective barrier or scab.

2.5.2 Inflammatory Response

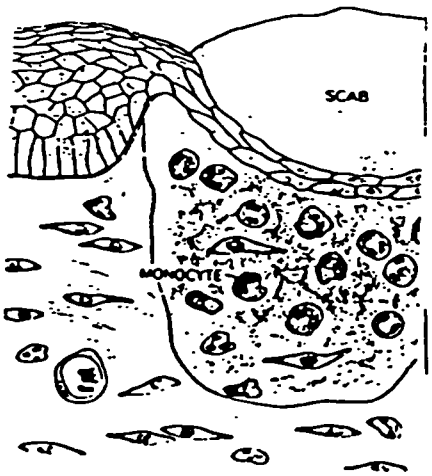
Initially, a new wound rapidly becomes the site of an inflammatory response which gradually covers the defect with a red inflammatory tissue (Remensnyder, 1982).



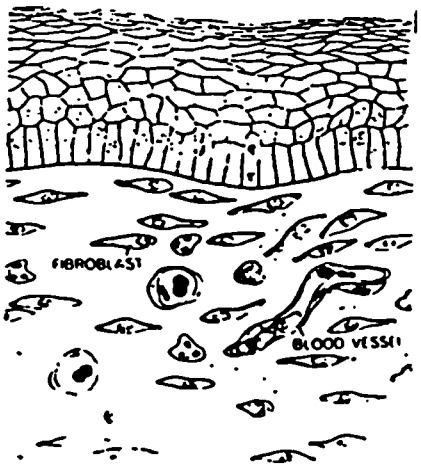
Time of wounding. Gap fills with blood. Blood contains red cells and fibrinogen.



One day later. Neutrophils enter the wound as do epidermal cells.



Two days later. Wedges of epidermis have met under scab. Fibroblasts have migrated into the defect.



Seven days later. Scab has sloughed off. A few monocytes and neutrophils remain in the wound.

Figure 2.18 Wound healing (Ross, 1969).

Inflammation, which is inextricably linked to coagulation, begins as fluids enter the wound around the scab. The fluid comes from leaking blood vessels in the nearby uninjured tissue. This fluid contains erythrocytes, platelets and a number of proteins such as globulin, albumin and antibodies. If the wound is infected, the globulin and antibodies may attack the infecting organisms but normally this fluid provides an environment for the white cells that follow it into the wound about six hours later.

The first of these cells are the neutrophils (polymorphonuclear leucocytes) (Figure 2.18). Once inside the wound they can destroy bacteria by phagocytosis. Most of them then move towards the surface and become trapped in the upper portion of the wound where dehydration is greatest and kills them (Pollack, 1979a). Also, if there are no bacteria present, the outer membrane of the neutrophil ruptures and enzyme-containing granules are released. Subsequently the enzymes attack the extracellular debris at the site of the injury; such material can then be more easily removed by the cells that later appear in the wound (Ross, 1969).

Within the first twelve hours after injury the monocyte begins to migrate into the wound. On entering the wound the monocyte becomes a macrophage (Ross, 1969). The macrophage is probably the key cell of the inflammatory response. It:

(i) debrides injured tissue,

(ii) processes macromolecules to useful amino acids and sugars,

(iii) attracts more macrophages,

(iv) probably signals for fibroblast formation and activation,

(v) may signal for neovascularisation, and

(vi) secretes lactate that in turn stimulates collagen synthesis by fibroblasts (Hunt & Van Winkle, 1979).

Towards the end of the inflammatory response another kind of cell, the fibroblast, appears and begins to repair the injury by secreting the collagen and protein polysaccharides that form scar tissue (Ross, 1969).

All these events are linked. Leibovich and Ross (1976) showed that the platelet, when stimulated by thrombin, produces a factor, called platelet factor (Antoniades - Kocher, 1977), that stimulates the growth of fibroblasts. Platelets and thrombin, as well as macrophages, stimulate both fibroplasia and angiogenesis in vivo (Greenburg & Hunt, 1978).

2.5.3 Role of Mast Cells

Mast cells have been found to increase significantly in number as the healing process progresses (Schilling, 1968) therefore they must play an important part in wound healing. However, these cells have been found to be ubiquitous throughout the body, mainly found in loose connective tissue (Schilling, 1968), and are found in hypertrophic scars (Kischer & Bailey, 1972).

These cells contain basophilic granules composed of sulphated mucopolysaccharides (e.g. heparin and chondroitin sulphate), histamine and other substances (Kischer & Bailey, 1972). They

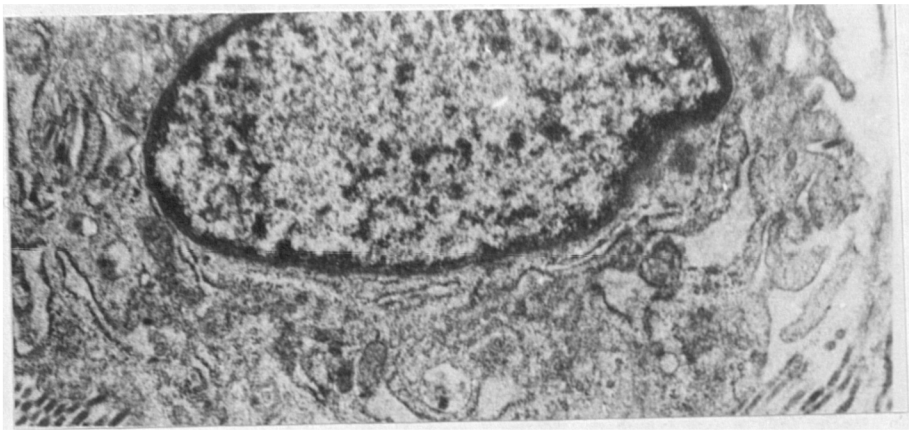


Figure 2.19 A fibroblast (Gabbiani et al., 1972).

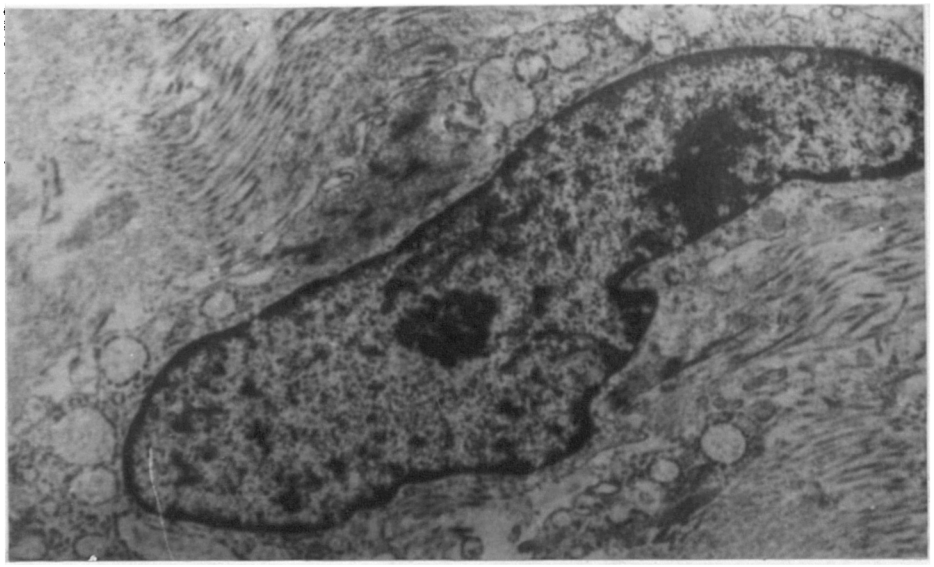


Figure 2.20 Transmission electron micrograph of a myofibroblast. Note the prominent microfilaments in the periphery of the cell just above the nucleolus (Hunt & Van Winkle, 1979).

degranulate and release these substances and this feature may be one of the key features in overt scar formation (Baur et al., 1977); for example, histamine, when released, can accelerate wound healing and vasodilation, and this vasodilation might account for the chronic inflammation of the wound or scar tissue.

2.5.4 Role of Fibroblasts and "Myofibroblasts"

The fibroblast (Figure 2.19) is identified on the basis of structure and utilisation of amino acids during collagen synthesis. Fibroblasts are present in wounds after 24 hours (Ross, 1964) or, more usually, three days (Peacock & Van Winkle, 1976) and rapidly increase in number.

Fibroblasts are cells which synthesise collagen. Ross (1964) added radioactively labelled proline (a marker for collagen) to fibroblasts and discovered the synthetic pathway through the fibroblast. The label was found initially in the endoplasmic reticulum, then in the Golgi complex, vesicles, filamentous aggregates and finally in extracellular collagen. However, Ross (1967) believes that other synthetic pathways exist.

These cells are also responsible for the formation of mucopolysaccharides (proteoglycans) and, at a later stage, the formation of elastic fibres (Ross, 1980). Initially, it was thought that elastic fibres did not form in the process of wound healing, but Williams (1970) has shown that new elastic fibres can be found in scars of 60 days or older.

In contracting granulation tissue, fibroblasts develop

contractile characteristics and resemble smooth muscle when tested by pharmacological agents, and by chemical and immunological means (Gabbiani et al., 1972). It has been suggested that the contraction of granulation tissue is dependent upon these modified fibroblasts, termed "myofibroblasts" (Figure 2.20) (Majno et al., 1971). Fibroblasts in granulating tissues are formed either locally from pre-existing cells of the same type or from more primitive mesenchymal cells (Ross, 1968; Ross et al., 1970) and it has been proposed that "myofibroblasts" originate from fibroblasts. The latter proposal is supported by the fact that fibroblasts cultivated in vitro normally develop extensive fibrillar systems (Goldberg & Green, 1964) and intercellular connections (Devis & James, 1964), both found in "myofibroblasts" (Gabbiani et al., 1972). However, what determines whether a cell becomes a fibroblast or a "myofibroblast" is not known, but, the fact that "myofibroblasts" are characteristically found in open granulating wounds whereas fibroblasts are found in closed incised wounds suggests that environmental factors, such as exposure to air, mi ht be the determining factor (Peacock & Van Winkle, 1976).

2.5.5 Role of Collagen

The importance of collagen in wound healing has been appreciated for a very long time because the ultimate result of the repair process is the formation of scar tissue composed mainly of collagenous fibres.

New collagen is found in healing wounds after two days

(Hunt & Van Winkle, 1980) and collagen fibrils approximately 50nm in diameter are present in the wounds of normal animals by the fifth day. In succeeding time periods the diameter of the fibrils increases, and by the ninth day there are two populations of fibrils, differing with respect to size (Ross & Benditt, 1961).

Using the SEM Forrester and colleagues (1969) noted that after 10 days the individual collagen fibrils were less discrete than normal unwounded tissue. Also, the fibrils were haphazard and showed little sign of coming together into bundles. At this stage the wound has very little tensile strength (5% of unwounded tissue) due to the small number of fibrils and their loose arrangement. However, after 100 days collagen is in the form of large irregular masses without the fibril substructure characteristic of normal skin. The tensile strength has increased to 70% of normal unwounded skin.

In addition to collagen synthesis, collagenolytic activity is present during wound repair (Grillo & Gross, 1967). Grillo and Gross (1967) found that collagenolysis is initially localised in the epithelium, although it is also present in the granulation tissue. Baur and colleagues (1979) observed fibroblast-like cells which appeared to be involved in collagen fibre and filament degredation. They named these cells "fibroclasts" (fibroblasts actively degrading collagen) or "myofibroclasts" (contractile fibroblasts actively degrading collagen) and suggested that these cells accelerate tissue remodeling especially in

Table 2.2 The involvement of the collagen-collagenase system in all the stages of tissue repair (Shoshan, 19 9 .

HAEMOSTASIS	Collagen brings about platelet adhesion to initiate clot formation;
INFLAMMATION	Collagenase and collagenolytic cathepsin B clear the wound area;
PROLIFERATION	(i) Fibroblast and plasma fibronectin bind to collagen, (ii) Collagen chemotactic properties induce fibroblast migration, (iii) Collagen synthesis provides adequate matrix for scar tissue, (iv) Procollagen extension peptides regulate collagen synthesis by a feed-back mechanism;
REMODELING	(i) Collagen matures and collagenase allows adequate removal of collagen, (ii) Enzyme-inhibitor complex may be a factor in connective tissue catabolism.

rises rapidly. Some of it comes from the local circulation, arriving as a result of microvascular permeability. As healing progresses, the hyaluronic acid decreases and chondroitin sulphate increases. As maturation occurs, the concentration of mucopolysaccharides falls, eventually to a low level. At some point, a small amount of mucopolysaccharide is incorporated into the collagen fibre. As mucopolysaccharides are lost, water is also lost; and the wound assumes its dense white appearance due to its high content of tightly packed collagen fibres (Hunt & Van Winkle, 1979).

2.5.8 Vascular and Lymphatic Proliferation

New blood capillaries are formed by budding or sprouting from existing capillaries, penetrate the wound and grow into loops. The loops then ramify throughout the wound by the division of their cells. As the capillaries from different sites migrate, they meet and form an interconnecting network (Ross, 1969). The electron microscope shows that the cells of the migrating endothelial buds have little contact with one another, and frequently there are considerable gaps between adjacent cells. This, together with the open-endedness of some sprouts obviously contributes to the extravascular accumulation of fluid and cells (Schoefl & Majno, 1964; McMinn, 1976).

The endothelial lining of vessels (both arterial and venous) larger than capillaries is capable of regenerating by migration and mitosis. In these larger vessels there is some evidence that new endothelial cells may arise by metaplasia of leucocytes

or other kinds of connective tissue cells migrating from the vessel wall.

Before the new capillary network forms there is a marked gradient of oxygen within the wound, the centre of the wound being the most deficient in oxygen. This gradient may be partially responsible for the branching of new vessels into the region. However, little is known about the factors that stimul te vascular growth. It has been postulated that, in addition to low p_{O_2}, reduced blood pressure, changes in the ground substances, metabolic changes, and mast cell stimulation all might be factors that promote the response (Schilling, 1968). More recently, however, Thakral and colleagues (1979) provided evidence that a factor derived from the wound macrophage has the potential to stimulate blood vessel growth.

Once the continuity of the connective tissue has been re-established, many of the new capillaries regress. Thus the wound changes from a tissue that is rich in blood vessels and actively dividing cells into one that has a much simpler structure (Ross, 1969).

New lymphatic capillaries form in a similar way to blood capillaries by sprouting from existing vessels (McGinn, 1976). The principal difference seems to be that the buds appear some days later than the vascular ones and they are less numerous.

2.5.9 Granulation Tissue and Epithelialisation

The macrophage, the endothelial cell and the fibroblast make up the majority of granulation tissue which has the key

role in the healing of all organs except those of epithelial origin. Granulation tissue is "purple, boggy tissue" which rises above the surface of surrounding skin (Peacock & Van Winkle, 1976). It is highly vascular, delicate and easily damaged, it is extremely resistant to infection and it will ultimately change to scar tissue (Silver, 1980). Granulation tissue can present a serious physical barrier to migrating epithelium and to reduce this either excess granulation tissue can be surgically excised or reduced by the skillful application of dressings.

Epithelialisation can progress at a maximal rate beneath a natural dressing (scab), therefore there is no biological reason for applying an artificial dressing to a first or second degree skin wound, provided a natural dressing can be maintained long enough for epithelialisation to occur (Peacock & Van Winkle, 1976).

Four to six hours after wounding, the epithelial cells at the edges of the wound accumulate glycogen granules, and, after a further four to six hours, mitoses appear in the basal layers of the epithelium and cells begin to migrate from these layers, either under the edges of the clot, which provides a guide to the migrating cells, or across or through it (Ross, 1969; Silver, 1980). The migration of the epithelium is well organised, involving the breaking and re-forming of desmosomes, and is by a "leap-frogging" process. As this occurs, the cells ingest and digest the strands of serum protein and fibrin

lying in their path. This activity clears the wound of debris and of the fibrin "scaffolding" which united the wound margins. When the leading edges of the sheets of epidermal cells meet and form a continuous layer beneath the scab, each cell regains its normal identity, and the thickness is restored to what it was before the injury (Ross, 1969). During the migration process, epithelial cells may cut through the collagen of the dermis, presumably by means of collagenases either secreted by themselves or activated in the tissues through which they are passing. Epithelial cells will migrate through intact established dermis but will not pass through healthy granulation tissue. When they meet granulation tissue, they become deflected over its surface (Silver, 1980).

2.5.10 Wound Contraction

Contraction may be defined as the process by which the size of a full-thickness open wound is diminished, and is characterised by the centripetal movement of the whole thickness of surrounding skin. In humans, contraction seldom goes to completion except in very small wounds, and it may result in deformity and loss of function, the extent of which depends upon size and location of the original wound (Peacock & Van Winkle, 1976).

The mechanism of wound contraction is found in the granulation tissue (James, 1964) and evidence suggests that it is a cell mediated phenomenon (James, 1964; McMinn, 1976; Peacock & Van Winkle, 1976). In 1956, Abercrombie and colleagues implicated

Table 2.3 Factors affecting wound contraction (Peacock & Van Winkle, 1976; Hunt & Van Winkle, 1980).

FACTOR	EFFECT
Cortisone.	RETARDED
Cyanide and dinitrophenol.	Movement of wound edges inhibited
Smooth muscle inhibitors.	INHIBITED
Colchicine and vinblastine.	INHIBITED
Adherent dressings.	DELAYED
Adherent dressings applied during lag phase.	INHIBITED
Application of a full-thickness skin graft to an excised wound before contraction.	INHIBITED
Application of a full-thickness skin graft to an excised wound after contraction has started.	Contraction proceeds for several days before being inhibited (mechanical blocking).

the fibroblast population of the granulation tissue mass as a whole, then Grillo and colleagues (1958) suggested that a zone of cells beneath the wound margins was responsible. However, the first report of contractile fibroblasts (myofibroblasts, see 2.5.4) in wound healing appeared in 1971 (Majno et al., 1971). Later studies have implicated that it is these cells which play the principal role in wound contraction (Baur et al., 1978). Myofibroblasts comprise 50-75% of the total cellular population in the dermis of active hypertrophic scars and are thought to play a role in the development of these disfiguring lesions (Baur et al., 1975).

Myofibroblasts are structurally similar to smooth muscle. The stimulus for contraction is unknown, but it has been suggested that exposure to a hostile environment, such as air, may stimulate contraction (Peacock & Van Winkle, 1976), although contraction and myofibroblasts are also found in certain diseases (e.g. Dupuytren's contracture) where the same conditions are not present as would be in an open wound (Gabbiani & Majno, 1972). The mechanism of contraction by myofibroblasts may be similar to that of smooth muscle since drugs which inhibit smooth muscle inhibit wound contraction (Peacock & Van Winkle, 1976), or it may be due to myofibroblasts utilising the motile force of microfilaments and involving the function of microtubules (Hunt & Van Winkle, 1980). Table 2.3 lists the factors which affect wound contraction.

Although many theories regarding the mechanism of wound

contraction have been discussed in the literature (e.g. Straile, 1958; Van Winkle, 1967b) the precise mechanism is still not fully understood.

2.5.11 Stimulus to Repair

A large number of theories have been proposed to account for this phenomenon:

2.5.11.1 Positive stimulus. This may result from the release of a factor by the wounding of tissue. These factors are called wound hormones or trephones (Abercombie, 1957; Hell, 1970). This theory has received a renewed impetus following recent observations on the possible functions of platelets in wounds.

2.5.11.2 Removal of an inhibitory feedback mechanism. Bullough and Lawrence (1966) have identif ed mitotic inhibitory substances in mature cells which they call chalones. They also propose that, as cells age and as part of normal metabolism, cells produce a mitotic inhibitory substance which not only prevents the ageing cell itself from dividing but may diffuse out from the cell when it dies or loses membrane integrity, thus reducing the mitotic activity of cells around it. Indeed, a substance can be extracted from the superficial layers of the epidermis which inhibits the activity of the basal cells (Silver, 1980).

2.5.11.3 Physical factors. Many physical factors have been suggested as being involved in stimulating repair. Among these have been altered gradients of oxygen tension, pH or ionic concentrations particularly potassium released from damaged cells (Maroudas, 1975; Silver, 1975), and mechanical effects, such

as changes of tension which may occur in damaged tissue.

2.5.11.4 Biological factors. Cell hypoxia has been a popular suggestion since it can be seen that new blood vessels tend to grow towards hypoxic areas (Silver, 1980). However, other evidence has suggested that the macrophage may be a very important part of the stimulus to repair and may indeed produce gradients in some way (Clark et al., 1976).

2.5.12 Scar Formation

The end result of the wound healing process is the formation of scar tissue from granulation tissue (Silver, 1980). The collagen arrangement in a scar is different from that in normal tissue, and, the collagen present in a normal scar is turned over by fibroblasts at a constant rate between 6 months and 20 years after the initial wounding whereas in both hypertrophic scars and keloids the rate of collagen synthesis was initially twice that in normal scars, and 2-3 years after wounding it fell to approximately the same level as in normal scars. During this turnover there is a long-term change in cross-linking of the fibre arrangement and there can be a re-organisation of the fibre direction of the scar, particularly in places where there are mechanical stresses placed on the wound.

2.5.13 Factors Affecting Wound Healing

Wound healing can be influenced by hormones, environmental conditions or systemic medications, therefore it is important in the design of wound dressings to be aware of these factors.

2.5.13.1 Effect of hormones. It has been found (Ahoner et al.,

1980) that glucocorticoids and female sex hormones delay wound repair by modifying the inflammatory reaction. Also, collagen synthesis, epithelialisation and contraction can all be inhibited and can thus cause serious clinical problems.

2.5.13.2 Environmental conditions. The three conditions affecting wound healing are temperature, humidity and oxygen tension.

Environmental temperature around wounds may play a role in healing since decreased environmental temperature significantly slows healing of superficial cutaneous wounds but not of deep wounds (Lofstrom & Zederfeldt, 1957; Lundgren, 1959). However, lowering the temperature of the entire body by the induction of hypothermia causes decreased tensile strength, even in deep wounds (Filston & Vennes, 1968).

Epithelialisation is more rapid under occluded conditions where the surface of the wound remains moist and epidermal cells are able to migrate more readily. Moisture in open wounds can be maintained using suitable dressings. However, the dressing must allow gas exchange and have an absorptive capacity otherwise the exudate builds up and becomes a source of infection (Pollack, 1979b).

Investigations have shown that healing of various types of wounds is enhanced by increased local oxygen tension, and that a reduction in available oxygen inhibits repair (Pai & Hunt, 1972; Silver, 1972). Winter (1972) studied the healing of open wounds in domestic pigs and found that wounds covered with oxygen-permeable polyethylene film epithelialised more

Table 2.4 Systemic medications affecting wound healing.

FACTOR	EFFECT ON WOUND HEALING	CAUSE
Corticosteroids	Suppressed	Anti-inflammatory, Anti-proliferative, Immunosuppresive, Vasoconstrictive.
Vitamin C	Enhanced	It is a cofactor for the enzymes responsible for the hydroxylation of lysine & proline in collagen, plays a role in the resistance to infection.
Aspirin	Decreases tensile strength of healing wounds.	Anti-inflammatory

rapidly than those covered with an oxygen-impermeable polyester membrane. Thus, it would seem that although most of the tissue oxygen involved in the healing of wounds is likely to be derived from the local circulating blood, at least a portion of it may come from the environment at the wound surface. Also, accelerated epithelialisation of open wounds under hyperbaric conditions has been reported (Fischer, 1969) and skin wounds in dogs close more rapidly at sea level than at an altitude of 3000 metres (Utinka, 1964). Thus, oxygen tension plays an important role in wound healing.

2.5.13.3 Systemic medications. Some drugs negatively influence wound healing, therefore it is important for surgeons to know what medications have been administered before surgery such that healing is not impaired.

For a detailed review of what drugs affect wound healing, the reader is reffered to Pollack (1982) since Table 2.4 only lists a few selected medications and their effect on wound healing.

CHAPTER 3

BURNS

A burn injury is probably the most traumatic injury afflicting man, and 7% of all accidents are burns and scalds. In England and Wales in a year 14,000 patients with burns were admitted to hospital, and 700 deaths occurred (Gowar, 1984).

Those people at greatest risk are "toddlers," the elderly, the sick (e.g. epileptics) and those under the influence of alcohol and/or drugs.

3.1 THE CAUSES OF BURN INJURIES

3.1.1 Thermal Injury

Thermal injury occurs as a result of heat transfer from a heat source to the body. This can occur by direct conduction or by electromagnetic radiation, and individual energy sources may produce thermal injury by single or multiple means. Flame, for example, can burn by direct contact or by superheating the ambient air or by a combination of both (Moncrief, 1979). The extent of injury is determined by the temperature of the burning object, the length of exposure, the thickness of skin exposed to the object, and the ability of skin to conduct the heat away (usually proportional to blood flow).

Thermal burns most commonly result from contact with hot liquids or metals, explosions or flames. Scald burns are most common in children under 3 years of age. In the 3-15 year age group, major burns usually result from the misuse of fire especially

matches. The ignition of clothing from open fires and heaters also accounts for a high percentage of burns in this age group. In adults, burns are usually flame-caused from home, car or industrial accidents (Artz & Yarbrough, 1973).

Freezing injuries, such as frostbite and those caused by freon gas, are similar to burn injuries and are treated in the same manner (Gowar, 1984).

3.1.2 Electrical Injury

Electrical injury is unique in the field of thermal trauma. The extreme heat generated by the resistance of tissues to the passage of high voltage electrical current (1000 volts or more), the unpredictable path of electricity through the body, and the variation in the response of individual tissues separates these injuries from other types of thermal injury (Baxter, 1970).

Although electrical injury is often classified with burn injuries it is more precisely a crush injury or vascular insufficiency accompanying the surface burn, therefore, the treatment is modified considerably from that of the usual thermal injury because tissue damage is much deeper (Artz, 1967; Artz, 1974; Rousse & Dimick, 1978).

Injuries associated with electricity may be categorised as follows: true electrical injury, electrothermal burns and flame burns (Artz, 1967; Artz & Moncrief, 1969; Artz, 1974; Quinby et al., 1978).

3.1.2.1 True electrical injury. This type of injury, caused by an electric current passing through the skin, is characterised

44A

Table 3.1 Pathophysiology of chemical burns (Artz & Moncrief, 1974).

AGENT	MECHANISM OF ACTION	APPEARANCE	TEXTURE
Acid Burns			
Sulfuric Nitric Hydrochloric Trichloroacetic Phenol	Exothermic reaction, cellular dehydration and protein precipitation	Gray, yellow, brown or black, depending on duration of exposure	Soft to leathery eschar, depending on duration of exposure
Hydrofluoric	Same as other acids plus liquefaction and decalcification	Erythema with central necrosis	Painful leathery eschar
Alkali Burns			
Potassium hydroxide Sodium hydroxide Lime	Exothermic reaction, hygroscopic cellular dehydration with saponification of fat and protein precipitation	Erythema with bullae	Painful, "soapy" or slick eschar
Ammonia	Same as other bases plus laryngeal and pulmonary edema	Gray, yellow, brown or black often very deep	Soft to leathery depending on duration
Phosphorus	Thermal effect, melts at body temperature, runs, ignites at 34°C., acid effect of H_3PO_4	Gray or blue green glows in dark	Depressed leathery eschar
Mustard gas	Vesicant, alkalization effect	Marked erythema with vesicles and bullae	Painful, soft vesicles and bullae
Tear gas	Weak acid effect	Similar to mild second-degree flame burn	Soft and wet

Table 3.2 Management of chemical burns (Artz & Moncrief, 1974).

AGENT	CLEANSING	NEUTRALIZATION	DEBRIDEMENT
Acid Burns			
Sulfuric Nitric Hydrochloric Trichloroacetic	Water	Sodium bicarbonate solution	Debride loose, nonviable tissue
Phenol	Ethyl alcohol	Sodium bicarbonate solution	Debride loose, nonviable tissue
Hydrofluoric	Water	Same as other acids plus magnesium oxide, glycerin paste, local injection, calcium gluconate	Debride loose, nonviable tissue
Alkali Burns			
Potassium hydroxide Sodium hydroxide Ammonia	Water	0.5–5.0% acetic acid or 5.0% ammonium chloride	Debride loose, nonviable tissue
Lime	Brush off powder	0.5–5.0% acetic acid or 5.0% ammonium chloride	Debride loose, nonviable tissue
Phosphorus	Water	Copper sulfate soaks	Debride and remove particles of phosphorus
Mustard gas	Water	M-5 ointment	Aspirate, then excise blebs during flushing with water
Tear gas	Water	Sodium bicarbonate solution	Debride loose tissue

by exit and entry cutaneous wounds which usually signify local destruction of deeper tissues. Current usually penetrates muscle, follows the path of blood vessels, and causes thrombosis at a site some distance from the original injury.

3.1.2.2 Electrothermal burns. Electrothermal burns such as flash or arc burns are the result of electrical generation of heat outside the skin. The burns that follow the leaping of an electric arc from the conductor to the skin are mainly associated with high tension current. They are severe and deep because an electric arc has a temperature of about 2500°C.

3.1.2.3 Flame burns. These result from the ignition of clothing by electrical sparks and arcing.

However, in many instances, all three types of electrical injury are present in the same patient.

3.1.3 Chemical Burns

Laboratory accidents, civilian assaults, industrial mishaps and inexpert application of agents used for medical purposes account for most of the chemical burns in a civilian population (Curreri, 1979).

Chemical agents do not "burn" in the sense that they destroy tissue by hyperthermic activity although selected ones can also act in this manner. Rather, as a class, they comprise entities which coagulate protein by reduction, oxidation, salt formation, corrosion, protoplasmic poisoning, metabolic competition/inhibition, dessication, or the ischemic concomitants of vesicant activity (Jelenko, 1974).

Tissue damage is dependent upon: strength or concentration of the agent, quantity of the agent, manner and duration of skin

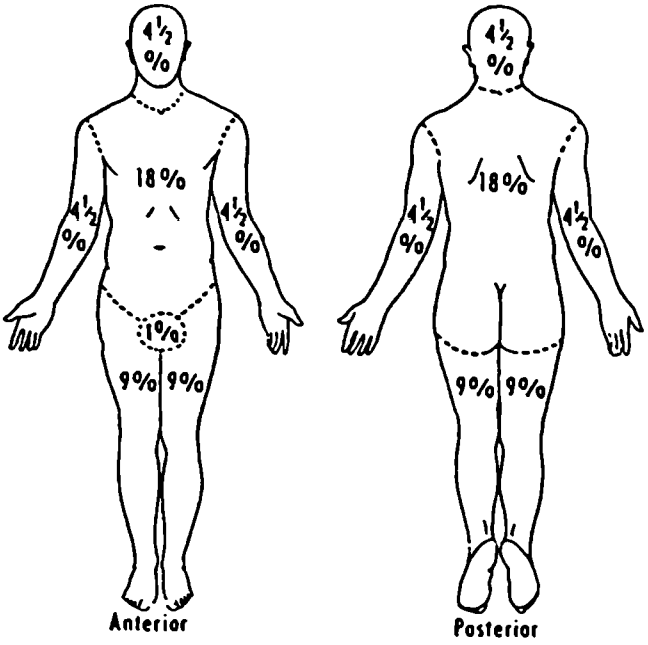


Figure 3.1 Rule of Nines (Moylan, 1979).

contact, extent of penetration into tissue, and, mechanism of action (Curreri et al., 1970), and an outline of the pathophysiology and management of such injuries is given in Tables 3.1 and 3.2.

3.2 CLASSIFICATION OF BURN INJURIES

A burn injury is classified on the basis of the extent of injury and the depth of injury.

The extent of injury is expressed as the amount of surface area injured in relation to the total body surface area. The most rapid and easiest technique used to estimate the extent of a burn injury is the Rule of Nines devised by Pulaski and Tennison (Moylan, 1979). This technique divides the body surface into areas representing 9% or multiples of 9% (Figure 3.1), and by totalling the areas of the body involved, the extent of the burn can be estimated.

Burn depth, previously described as first, second or third degree, indicating in increasing order the depth of tissue destruction, is now classified as follows:

partial thickness,

full thickness.

A partial thickness burn involves the loss of epidermis, a deep partial thickness burn involves some loss of dermis and a full thickness injury means that both the epidermis and the dermis have been lost.

The determination of burn depth is usually by inspection of the wound, a full thickness wound implies that both epidermis and dermis are destroyed but the partial thickness injury

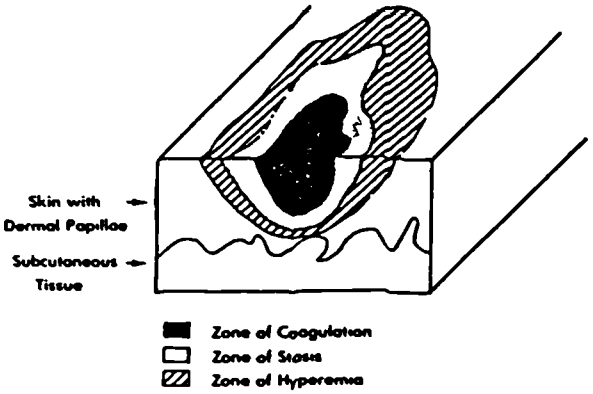


Figure 3.2 The burn wound is characteristically made up of several zones of tissue death, with confluent wounds of equal depth being unusual except in very deep burns (Moncrief, 1979).

characteristically takes two forms: the surface may be covered with blisters of varying sizes, and when these are removed the epidermis beneath it is weeping, glistening, bright pink, and is very sensitive to temperature changes, exposure to air and light touch; deeper partial thickness wounds are waxy white but still soft and elastic, and although they are sensitive to pressure, they are insensitive to light touch or soft pinprick.

Other methods employed to diagnose the depth of burn injuries include dye differentiation (Goulian & Conway, 1968) and thermography (Branemark et al., 1968; Hackett, 1974; Pollock, 1981).

"The determination of the extent and/or depth of burn injuries can be in error if estimated during the early post-burn period since tissue destruction may be progressive but other changes are reversible" (Hinshaw, 1963; Hinshaw, 1968).

3.3 THE APPEARANCE OF A BURN INJURY

The immediate effects of a burn injury are the cessation of capillary flow and the coagulation of cellular and tissue components (Zawacki, 1974a), and during the first week, three well-defined zones (Figure 3.2) can be observed in a typical thermal burn: the zone of coagulation surrounded by the zone of capillary stasis which, in turn, is bounded by the zone of hyperaemia (Lawrence, 1975). If coagulation occurs through the entire dermis or if the zone of stasis penetrates below the deepest epithelial structures (e.g. hair follicles or sweat glands) the burn will be full thickness (Lawrence, 1975; Baur et al., 1977), and an eschar will form. If, however, a less

destructive trauma occurs (partial thickness wound) a vesicle or blister will be produced.

3.3.1 The Zone of Hyperaemia

The zone of hyperaemia is the site of minimal cell involvement and early spontaneous recovery (Moncrief, 1979). This area has a circulation, and metabolism continues to occur. A biopsy of this zone shows almost complete loss of the epidermis without apparent structural damage to the dermis (Jackson, 1952).

3.3.2 The Zone of Stasis

The zone of stasis contains a patent sub-papillary plexus but metabolism is diminished or has ceased. Also, after 24 hours the circulation ceases and complete stasis has occurred (Jackson, 1952). This zone has been found to be reversible when drying, and when studied under these conditions, it may be divided into a zone of early stasis and a zone of delayed stasis (Zawacki, 1974a).

Injury is more severe in the more superficial zone of early stasis. Stasis is rapid in onset, is complete within 2-4 hours, is associated with maximum accumulated oedema, and is not reversed until after the second post-burn day. Since no epithelial cells survive within this zone, repopulation of hair follicle epithelium appears to be by migration of viable cells from deeper tissues.

Injury in the more deeply situated zone of delayed stasis is less severe. Stasis is delayed in onset until 4 hours post-burn, lasting until 16 hours post-burn; associated with little or no contribution to accumulated oedema; and begins to be

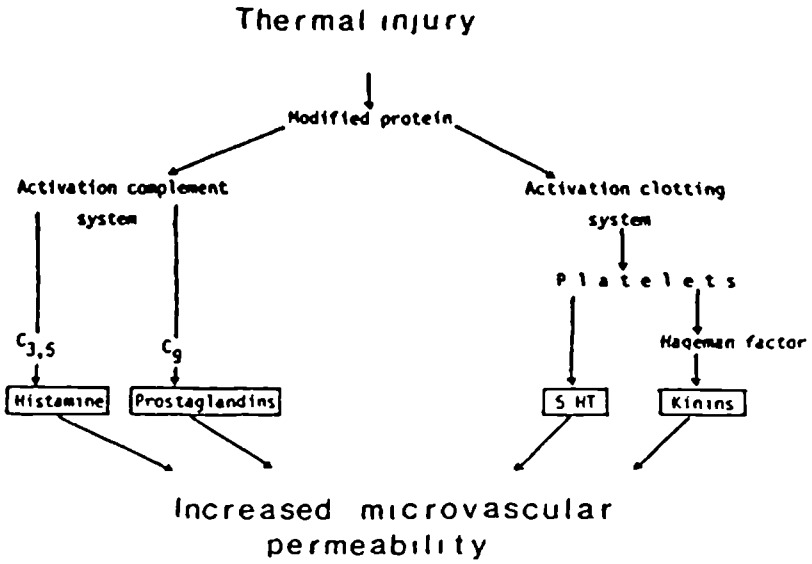


Figure 3.3 A scheme showing some of the inflammatory factors involved in the "acute phase" of the burn syndrome (Arturson, 1980)

reversed as early as 16-24 hours post-burn, about the time sensation returns. Some hair follicle epithelial cells may remain viable in this zone and are able to migrate and repopulate the hair follicles in all levels of the zone of stasis (Zawacki, 1974b).

3.3.3 The Zone of Coagulation

The zone of coagulation is the site of irrevesible skin death. Microscopically there is complete obliteration of the lumina of the vessels in the sub-papillary plexus and the capillary loops. Temporary blanching has frequently been observed as the first response of capillaries to heat and it is possible that this white skin of the central zone is produced by coagulation of the tissues during this transient period of spasm by some temperature over 70-80°C Jackson, 1952; Moncrief, 1979).

3.4 THE DAMAGE CAUSED BY BURN INJURIES

The pathophysiologic events observed in a burned individual are characterised by an inflammatory reaction leading to rapid oedema formation due to dilatation of blood vessels, increased extravascular osmotic activity and increased microvascular permeability to macromolecules Arturson, 1980). This may be stimulated in the acute phase of a thermal injury by the modified protein outside blood vessels Figure 3.3). The modified protein could serve to activate the complement cascade. Once the complement system is activated a host of permeability factors are liberated at the site of injury. These consist mainly of histamine and prostoglandins (mainly PGE_1, PGE_2 and PGF_{2a}) (Arturson, 1977).

The modified protein also activates the coagulation system which leads to the release of 5-hydroxytryptamine from the platelets and formation of the vasoactive polypeptides and the kinins via factor XII. All these mediators of the inflammatory reaction cause increased microvascular permeability.

3.4.1 Tissue Damage

The skin plays a very vital role in the body - that of a barrier. When the skin is damaged or lost, the underlying tissue becomes exposed to infection. The incidence and severity of burn wound infection depends on the size of the burn, the age of the patient (there is a dramatic increase of infection in patients over 60), the medical and nutritional state of the patient, and the type of infecting organism (Alexander, 1979). Indeed, infection causes about 60% of the deaths in burn patients today despite intensive therapy with topical and intravenous antibiotics (see 3.6.1).

Another feature related to loss of skin is increased evaporative water loss which will be discussed in chapter 5.

When skin is damaged, there is considerable upset in the circulatory system. Damage to the blood vessels and blood elements results in a loss of capillary integrity with a marked increase in local and systemic capillary permeability. Consequently, fluid and protein escape rapidly, resulting in a rapid diminution of blood volume and the characteristic shock phase of burn injuries seen during the first 48 hours (see 3.5.2.3) (Artz &

Yarbrough, 1973). Indeed, Robb (1967) suggested that treatment of burn injuries should be directed at the microcirculation to limit the depth of the burn and to lessen the need for skin grafting.

In an experimental study on scalded rats, Massiha and Monafo (1974) noted that changes leading to thrombotic occlusion appeared earlier and were more pronounced on the venular side of the vasculature than the arterial side, and concluded that venous occlusion may be the primary cause of the dermal ischemia that follows a burn injury.

3.4.2 Cellular Damage

In normal cells the transmembrane potential is about -90mV, even in non-burn areas in burned patients this is diminished by almost 20% (Baxter, 1974). Rapid and adequate resuscitation restores this transmembrane potential to only a 10% deficit therefore the changes are probably due to impaired circulatory support of the cellular metabolic processes. Also, due to the inadequate circulation is an increase in intracellular sodium and water and a 25% deficit in the extracellular fluid. These become near normal with fluid replacement therapy. Thus, without adequate fluid replacement to support the metabolism of local tissues, the transcellular transfer of ions and water would continue to occur at a progressive rate until cell membrane function ceased and the cell died (Baxter, 1974) and if enough cells die the body will also die.

3.5 BURN WOUND MANAGEMENT

The field of burn wound management is controversial and reflects vastly differing individual preferences in the handling of the burn wound. In addition to the burn wound other problems often arise from shock, obstructed airway, lung damage (due to inhalation of smoke), fractures, head or spinal injuries and internal bleeding. Such problems must be faced prior to treatment of the burn wound; shock and smoke inhalation will be discussed in detail in 3.5.2.

3.5.1 Burn Wound Healing

Consideration of wound healing (Van Winkle, 1967a; Van Winkle, 1967b; Schilling, 1968; Van Winkle, 1968; Ross, 1969; McMinn, 1976; Peacock & Van Winkle, 1976; Baur et al., 1977) indicates that the burn injury does not appear to be much more complex, with respect to healing, than other injuries to the integument. Likewise, the phases of burn repair, the cellular populations involved, the methodology of tissue reconstructions, and the regaining of integumentary tensile strength are similar, if not identical, to those observed in other large wounds (Larson et al., 1974a; Peacock & Van Winkle, 1976).

Following a burn trauma, in the areas of skin adjacent to or underlying the wound, the initial vasoconstriction occurs seconds after the onset of trauma and lasts for only a few minutes. Vasodilation then follows and maximises within 10 minutes. Several hours later leucocytes infiltrate the tissue, and these accompany vascular stasis and occasional haemorrhage (Schilling,

1968). The inflammatory response that follows the trauma is probably a response to the excessive quantities of devitalised and/or necrotic tissues or by microbial contaminants which are both characteristic of burn wounds.

The granulation tissue which is formed after a burn wound has stabilised consists of a complex tissue which is composed of fibroblasts, capillary networks, and other infiltrating cells (Schilling, 1968; McMinn, 1976). The initiation of the granulation phase of repair occurs at the time of trauma although the first visible signs of granulation do not appear for 2 or 3 days post-burn (Peacock & Van Winkle, 1976). The first indications are the proliferation of the capillary networks at the base and/or margins of the wound which result in the bright red colouration of the tissue (McMinn, 1976). Vascular proliferation is accompanied by fibroblasts migrating into the wound tissue and producing new extracellular materials (principally collagen but also some mucopolysaccharides initially) (Schilling, 1968). Likewise, macrophages from the blood migrate through the area and remove debris.

During the latter stages of granulation, the forming dermal components can be observed to assume bizarre configurations of collagen (Linares et al., 1972). These patterns continue to enlarge so that in early scar formations bundles or tracts of collagen begin to assume a whorl-like arrangement. As the scar continues its development characteristic nodules of fused collagen filaments and cells are observed in the deeper layers of the

dermis (Linares et al., 1972; Baur et al., 1975; Kischer, 1975; Baur et al., 1977; Tully, 1980) and these will be discussed in detail in 3.6.2.

3.5.1.1 Epithelialisation. The restoration of the epidermis is effected by the mitotic activity of basal cells located in the stratum spinosum of undamaged normal epithelium (Van Winkle, 1968). The cell division occurs at the wound margins and/or from areas of skin appendage (hair follicle or sweat gland) remnants located within the wound itself (McMinn, 1976). The epidermal mitotic activity becomes apparent within 48 hours after trauma with hair follicles appearing to be the most important source of epidermal cells (McMinn, 1976), and appears to demonstrate a diurnal rhythm with the greatest activity during rest and sleep (Van Winkle, 1968).

After cell division, new daughter cells appear to detach, flatten considerably, and migrate over the wound surface until they cover the entire wound. If a crust or blister is present, the cells migrate through the base of the blood and fibrin material of the crust or over the reticular layer of the dermis within the v sicle (Van Winkle, 1968; McMinn, 1976). The production of fibrinolytic or proteolytic enzymes by these cells allows them to migrate through the base of the crust material (McMinn, 1976).

The migration of the epidermal cells and their eventual coverage of the wound does not appear to depend upon the presence of a basement membrane which is later reformed by the epidermis

irrespective of dermal activity (Kallman et al., 1967; Odland & Ross, 1968). The differentiation of the migrated epidermal cells then reforms the scar epidermis (Van Winkle, 1968; McMinn, 1976).

If the entire integument has been destroyed (full thickness -wound) re-epithelialisation must await the reformation of the proper substrata (vascular beds, new collagen fibres etc.) produced by granulation tissue. Large full thickness burns lack skin appendages and must therefore be provided with sources of epidermal cells. This is usually accomplished by skin grafting procedures which are fruitful only after the vascular beds have been adequately reformed or earlier by excision of burned tissue to reveal viable tissue (Baur et al., 1977).

3.5.1.2 Dermal repair. The repair of the dermis is mediated primarily by the very numerous fibroblasts observed in wound healing tissue (Van Winkle, 1967a; Schilling, 1968; McMinn, 1976). Fibroblasts synthesise the collagen and mucopolysaccharides that comprise the dermal fibres which provide tensile strength to the integument (Grossfeld et al., 1957; Ross & Benditt, 1961; Van Winkle, 1967a; Schilling, 1968; McMinn, 1976). During the early stages of repair fibroblasts grow through the wound on fibrin strands found within the crust or clot but the fibrin network does not seem to be essential for this movement (Schilling, 1968). Later in the repair process the fibroblasts appear to move through the tissue on a network of collagen filaments synthesised by other fibroblasts.

The myofibroblasts are first observed in deep partial thickness

and full thickness burn granulation tissues 3-5 days after the trauma and represent only a small fraction of the total fibroblast population at that time. Their numbers continue to increase during the course of wound repair so that at the height of the wound contraction (the "drawing together" of the wound) phase of repair and up to 120 days post-burn their numbers may comprise the majority (50-75%) of the fibroblasts in the tissue. At the peak of a scar contracture (continued contraction) formation they may account for 100% of the total fibroblast population (Baur et al., 1978).

Mast cells are scarce in granulation tissues but their numbers increase significantly as healing progresses. These cells appear to increase in number during a chronic inflammatory reaction which is a persistent feature of a healing burn wound and its subsequent scar formation (Schilling, 1968). Degranulating mast cell configurations have been observed in active hypertrophic scar and granulation tissues (Baur et al., 1977b). The released mucopolysaccharides could then form a mucinous ground substance by the hydration of the acid glycosaminoglycans which may in turn provide the matrix for new collagen formation (Baur et al., 1977b). The histamine that is released appears to accelerate wound healing and vasodilation. This vasodilation of the wound or scar capillaries could account for the chronic inflammation of the tissues. In fact, the inflamed appearance of the tissue is the major clinical sign of active healing and/or scar formation. Thus, the mast cell activities (degranulation and release of

ground substances - histamine release and vasodilation) are both key features of overt scar formation and when one function is lost the other appears to be likewise halted (Baur et al., 1977a).

3.5.1.3 Contraction. Large burn wounds may be too extensive to be closed by normal wound contraction even though the phenomenon does occur to some extent (Van Winkle, 1967b; Peacock & Van Winkle, 1976). Many possible explanations have been proposed for this movement with the two most plausible being the "picture frame theory" and the "pull theory" (Baur et al., 1977a). The "picture frame theory" suggests that active cells within the margin of the wound migrate inward pulling on the material within the margins of the defect. The "pull theory" suggests that material (collagen fibres, cells etc.) within the defect pull on the wound margin (Van Winkle, 1967b), and is probably the better theory since myofibroblasts are present in large numbers within the wound.

Burn wound contractions often continue, with respect to time, beyond the actual closure of the wound. When this happens the scar becomes a disabilitating and/or disfiguring "scar contracture" especially if joints underlie the tissue.

3.5.2 Initial Treatment

3.5.2.1 First aid. Ideally, the burn wound should be treated immediately after injury. Obviously, the first action should be to extinguish the flames of burning clothing. Hot or smouldering clothing should be removed and cold water applied. Patients

who have been scalded should have their hot, soaked clothing removed because it will act as a continuing source of heat and produce a deeper burn. The burn wound should then be covered with a sterile dressing and the patient taken to hospital.

3.5.2.2 Smoke inhalation. The number of admissions to hospital and deaths of patients suffering from inhalation of smoke and toxic substances has increased in recent years (Carr, 1978). This may be due to the use of more flammable upholstery materials such as plastic foams which also produce toxic fumes and/or that more people are being rescued who would formerly have died and not been admitted to hospital (Cason, 1981).

Hot, dry air cools down rapidly by the time it has been inhaled as far as the vocal cords and hence could hardly cause damage to the lungs (Cason, 1981). Moist heat, however, because of its water content has a high heat capacity and retains this heat until it reaches the alveoli where it can cause damage and even necrosis of the alveolar epithelium. However, dry heat containing smoke and toxic products can cause damage to the lungs due to the irritant nature of the mixed gaseous and solid content. Such substances as carbon monoxide, nitrogen peroxide, hydrochloric acid, hydrocyanic acid, phosgene (carbonyl chloride), nitric oxide, sulphurous compounds, aldehydes etc. may be produced by combustion of modern plastic materials.

Even if inhalation of smoke does not cause early death from asphyxia it may produce sever acute damage to the lung and respiratory tract. Even apart from the specific toxic products

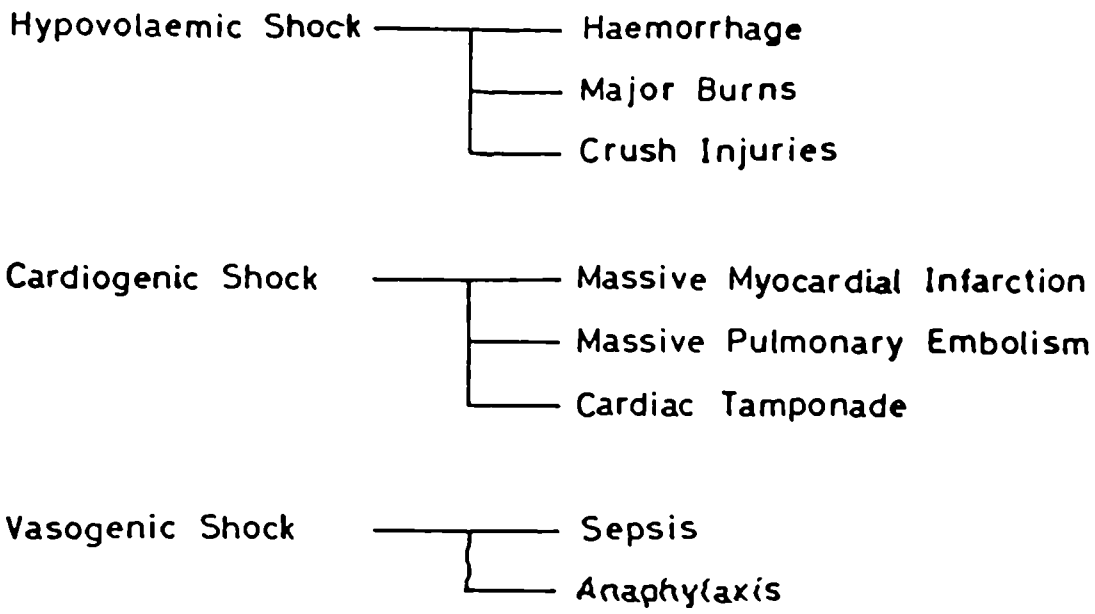


Figure 3.4 Classification of shock (Goode, 1984).

mentioned above, combustion in a confined space causes first of all anoxia due to depletion of oxygen; later, asphyxia, due to the production of carbon dioxide, and finally carbon monoxide poisoning from incomplete combustion.

The first concern is to ensure that there is a clear airway and either endotracheal intubation or tracheostomy may be required. Physiotherapy within the first 24-48 hours will allow most smoke inhalation patients to recover, but problems may occur e.g. pulmonary oedema, pulmonary collapse, pneumonia, ruptured lung etc. several hours after the injury and require specialist treatment.

3.5.2.3 Shock. The most precise and meaningful definition of shock is given by Dietzman and Lillehei (1968): "The inability of the circulatory system to meet the needs of tissues for oxygen and nutrients and the removal of their metabolites." This basic concept recognises that whatever the initial cause of the circulatory disorder, the final common pathway is inadequate perfusion of the tissues with blood.

The classification (Figure 3.4) implies that the cause of circulatory inadequacy lies in the function of the heart, the volume of fluid it circulates or the tone of the peripheral vasculature. Clinical shock, in the post-traumatic state, is nearly always a combination of two or three of these.

Reduction in the volume of blood in active circulation is a common denominator in shock and the central role of hypovolaemia in burns shock was first emphasised by Blalock in 1931 (Settle, 1974). He also showed that the hypovolaemia was correctable by

the infusion of plasma but it was not until the 1940's that the magnitude of the fluid shift (due to changes in capillary permeability in the affected tissues) in burns began to be elucidated. Prior to the work of Cope and Moore (1947), it was thought that the only loss of plasma from the circulation was that which could be seen leaving the surface of the wound. In the absence of a weeping surface, the systemic effects were passed off as "burns toxaemia."

In the shocked patient the underlying disorder leads to the arousal of sympathetic responses. These give shock its characteristic signs and symptoms: tachycardia with thready pulse, tachypnea, pallor, cold clammy skin, intense thirst and low urine output.

To prevent shock, fluid is given to replace what has been lost. If the burn is less than 10% body surface area (b.s.a.) fluid is given by increasing the oral intake. In adults with burns up to 15% b.s.a. oral fluid may be sufficient so long as it contains an adequate amount of sodium. Moyer's solution is an example of an oral replacement and it contains 4g NaCl and 1.5g $NaHCO_3$ per litre.

In larger burns fluid is given intravenously. There is, however, no general agreement on the type of fluid thought to be ideal for preventing burn shock - except that the essential ingredients are water and salt. Plasma is still the traditional replacement fluid and is still widely used in Britain due to the National Blood Transfusion Service making available a high

standard of product (although with recent fears about acquired immune deficiency syndrome it may be replaced by a synthetic product). The calculation of the amount of plasma required is:

$$\frac{\text{Total \% area of burn x weight in kg.}}{2} = \text{ml fluid}$$

however, this is only for the first 4 hours, thereafter the patient is reassessed and the plasma "ration" for the next 4 hours is given.

3.5.2.4 Metabolic changes in burns. Thermal injury initiates more rapid erosion of body mass than does any disease process. Negative nitrogen balance, loss of other intracellular constituents, and a rapid decrease in body weight are consequences of the increased metabolic activity, and extensive loss of protoplasmic mass may result in severe erosion of energy and protein stores essential to wound healing and optimal body function (Davies, 1982).

The rate of increase of metabolic rate following a burn injury and its peak values are related to a number of factors including the severity of the burn, the time after burning, the presence or absence of severe bacterial infection, whether the burned area is treated exposed or dressed or covered with a cream containing antibacterial agents or various synthetic skins or hetero-, homo-, or autograft skin, and the temperature of the environment surrounding the burn (Wilmore, 1974).

3.5.3 Burn Wound Care

Over the last two centuries local burn wound care has fallen into two categories: the closed method (application of dressings)

and the open (exposure) method. However, in many cases the two methods are used on one patient, or a patient may be left exposed until the depth of burn is established (48-72 hours post-burn) and then dressed accordingly.

3.5.3.1 Application of dressings. The use of a dressing to absorb the fluid exudate from the burn wound was first advocated by Syme in 1834, but covering burn wounds dates back to earliest times (Artz & Moncrief, 1969).

The principle of the "closed" method lies in the fact that the majority of burns are sterile or have no pathogenic organisms on their surface in the first few hours after burning. If the burn can be completely sealed off from its surroundings by means of sterile dressings then it should be possible to prevent cross infection occurring. Usually the covering of a burn wound is accompanied by the application of a local antibiotic, antiseptic cream or lotion to the surface of the burn.

There is no general rule governing the dressing of burn wounds. Variations occur between different burns units and, with a vast number of products on the market, there are variations in the types of dressings used (this will be discussed in chapter 4). However, the conventional method of dressing a burn wound can be described as follows:

1. The burned area is initially cleaned with a detergent antiseptic (e.g. Savlon or Hibiscrub).
2. A protective prophylactic barrier of cream (e.g. silver sulphadiazine) is spread onto sterile pieces of tulle gras which

are then applied to the surface of the burn.

3. A barrier and absorption layer is then added in the form of cotton wool or Gamgee (gauze & cotton tissue).

4. A crepe bandage holds the dressing in place.

3.5.3.2 Exposure method. Exposure of the burn wound has long been practiced, but it became unpopular in the 1800's McMillan, 1974). However, since 1949 (Wallace, 1949) this method has become widely used and accepted.

The principle of this method is that drying the area of the burn inhibits the growth of bacteria, also the cooler surroundings, and ultraviolet sunlight are hostile to bacterial growth. The surface of the burn is initially cleaned with a detergent (e.g. Hibiscrub or Savlon), all the blisters are removed, and the area is allowed to dry. This may take several days and reforming blisters have to be removed daily. Eventually a uniform dry surface is obtained and antiseptic powders or lotions may be applied as a further deterrent to bacterial growth.

The exudate of a partial thickness burn dries and forms a hard crust which acts as a natural occlusive, protective cover of the wound within the first 2-3 days post-burn. Epithelial regeneration proceeds beneath such a crust and is usually complete in 14-21 days. After this time desquamation occurs, i.e. the crust falls off, leaving behind the healed surface (Artz et al., 1953).

In full thickness burns surface exudation is minimal, if present at all, therefore crust formation does not occur. Instead,

the parched, pearly white, dead skin is directly converted into an eschar which serves as a temporary cover. In 48-72 hours the eschar dehydrates and contracts and assumes a dark brown appearance. To delay the formation of cracks in the dry eschar those parts of the body should be splinted or immobilised as well as possible (Cason, 1981). The eschar remains essentially unchanged until liquifaction occurs beneath it due to the action of leucocyte tissue or bacterial enzymes. This usually begins in 10-14 days post-burn. However, after 10 days a cream antibiotic dressing may be applied to speed separation of the slough before grafting, or the eschar can be removed and grafted if there is full thickness skin loss (Cason, 1981).

The exposure method is commonly used on parts of the body which cannot easily be sealed off from the environment with dressings e.g. the face, buttocks and perineum. It can also be used when only one surface of the body is burned and becomes mandatory when hyperpyrexia (temperature above 40^{o}C) cannot be controlled. Environmental factors such as temperature and humidity influence the rate of crust or eschar formation, and a warm, dry environment hastens development of the protective cover (Cason, 1981).

3.6 COMPLICATIONS

3.6.1 Infection

A burn or scald may be said to be similar in many ways to any skin wound except that it commonly involves a much larger area of the body surface and there is a larger amount of necrotic

tissue. There is also much oedema and exudate, and these factors make an excellent nutrient medium in which many types of bacteria can grow freely. Bacteria reach a burn wound via the following routes:

1. Self contamination from the surrounding uninjured skin and the gastrointestinal tract.
2. Airborne i.e. dust, skin squames or droplets of aqueous fluid.
3. Contact with contaminated ob ects which include bedding, thermometers etc.

Resistance to infection may be diminished by shock, electrolyte disturbances, dehydration, anaemia, hypoproteinaemia, loss of immunoglobulins and high serum levels of corticosteroids which may be present in a burn patient. Whereas simple colonisation of the burned surface does not necessarily indicate infection it can be a danger because it may easily be followed by profuse growth of bacteria with invasion of healthy tissues followed by septicaemia and death. Infection is one of the commonest causes of death in burns, and over 50% of total burn patient deaths are due to septicaemia (Artz & Reiss, 1957). However, the incidence of burn wound sepsis has been more than halved since the introduction of topical antibacterial agents in the 1960's.

3.6.1.1 Topical agents. Topical therapy is aimed at the reduction of organisms in the burn wound rather than complete eradication of the bacterial flora. Effective topical therapy will reduce the bacterial population from 10^8-10^{10} organisms per gram of

tissue to a more desirable level of 10^4 organisms per gram of tissue, thus allowing eschar separation without invasion of surrounding healthy tissue. Therefore, topical chemotherapy must be used in association with active debridement of necrotic tissue to prepare the wound for skin grafting. Until the burn wound is closed by skin grafting, the potential for sepsis exists. Various topical agents are available, and each will be discussed.

Silver nitrate (0.5%), historically, was the first effective topical agent, introduced by Moyer and his colleagues in 1965. It markedly reduces evaporative water loss and has a broad antibacterial spectrum (Yarbrough, 1978). This agent has limited powers of penetration and is most effective in the management of recent previously untreated burn wounds. It is a chemical escharotic (Davies et al., 1981) and repeated application creates a hard eschar surface. This further impairs penetration and ultimately necessitates the use of early surgical debridement or a change in the antimicrobial agent used. Also, the nitrate ion in the presence of bacterial flora can be changed to a nitrite ion. This, with its strong oxidative property, could result in formation of methemoglobin (Lentz et al., 1966). In addition, the silver combines with chlorides, siphoning off Na ions and requiring substantial NaCl replacement to prevent hyponatremia (Fox & Quintiliani, 1982).

Silver nitrate is a very messy agent and, although it is relatively inexpensive, its social disadvantages (discolouration of the wound and bedding) have precluded its widespread use

(Reid, 1982).

A methylated sulphonamide (Mafenide or Sulphamylon) was introduced in 1966 (Moncrief et al., 1966) and has a wide spectrum of activity for both gram-negative and gram-positive organisms and rapidly penetrates to the sub-eschar tissues. An 11.1% concentration of the drug in a water miscible base is applied to the wound with a gloved hand, and is usually left without dressings. However, it has several disadvantages including allergic manifestations (Yaffe & Dressler, 1969), tachypnoea, hyperventilation, acidosis with increased serum chloride and decrease in arterial P_{CO_2} (Shuck & Moncrief, 1969). In addition to these problems, the application of this agent is extremely painful therefore patient tolerance is very low.

An aminoglycoside (Gentamicin or Garamycin), used as an 0.1% cream or ointment, was designed specifically for use against Pseudomonas spp. However, resistant strains develop early when the drug is used indiscriminately in large burn populations (Moncrief, 1979). For this reason it is only available in small quantities. Absorption of the drug varies according to whether it is applied in a cream base or an ointment base (Stone et al., 1968). In the cream base the drug is rapidly absorbed and in the ointment base absorption is slower and more constant. Also, absorption of gentamicin decreases as the water content of the eschar gradually diminishes, but as eschar separation occurs and granulations become prominent, the drug is rapidly absorbed. It is rarely used now because of these problems.

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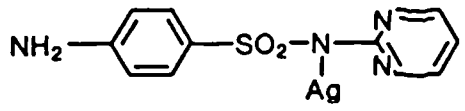

Figure 3.5 Structure of silver sulphadiazine (Fox, 1968).

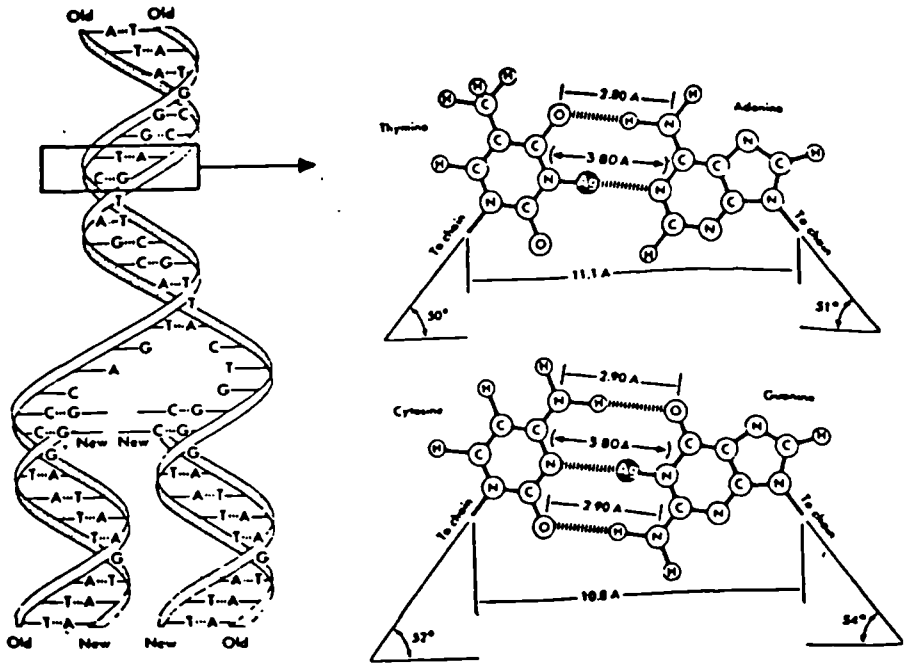

Figure 3.6 The binding of DNA. On the left is shown the double helix of DNA. The bases T...A and C...G are joined by hydrogen bonds. Cell replication is preceded by separation of the two strands as indicated. On the right is an enlarged view of one section of the model showing the site where silver is substituted for the hydrogen bond between the nitrogens of the bases (Jensen & Davidson, 1966). Since the N-Ag-N distance should be about 3.8Å whereas an N-N...H distance is about 3.0Å, a certain amount of distortion of the Watson-Crick structure would occur (Fox et al., 1969).

Silver sulphadiazine (1%) (Flamazine or Silvadine) was first introduced in 1968 by Fox and his colleagues (Figure 3.5). The combination of the bactericidal effect of silver with the bacteriostatic effect of sulphadiazine made the new compound particularly effective. It has a very broad antibacterial activity against gram-positive and gram-negative organisms particularly Pseudomonas aeruginosa, Proteus spp., Escherichia coli, Klebsiella spp., Staphylococcus spp., and Candida albicans (Fox et al., 1969). It penetrates through full thickness eschar and only minor discomfort is experienced when applied (Davies et al., 1981). It is, today, the most popular topical antibacterial agent used.

In contrast to silver nitrate, silver sulphadiazine does not react rapidly with chloride, SH groups or proteins: its antibacterial action is thereby not diminished. Although sulphonamides are competitively inhibited by para-aminobenzoic acid (PABA) (McManus, 1981), a component of folic acid, silver sulphadiazine activity is not reduced (Fox et al., 1969; Fox et al., 1976) which suggests an alternative mode of action.

Additional studies have shown that silver sulphadiazine reacts rapidly with deoxyribonucleic acid (DNA) and releases sulphadiazine. Bacteria incubated with radioactive silver-labelled silver sulphadiazine acquire radioactive silver in proportion to their content of DNA (Fox et al., 1969). Furthermore, when Pseudomonas aeruginosa were cultivated in media containing silver sulphadiazine and separated into protein, ribonucleic acid (RNA)

and DNA fractions, the maximum accumulation of silver occurred in the DNA fraction (Modak et al., 1973). Subsequently the role of the sulphadiazine was explored using sulphur-labelled (S-35) silver sulphadiazine in the growth medium. None of the labelled sulphadiazine was found in the bacteria or in the DNA fractions (Fox et al., 1974).

A possible location of silver in DNA is shown in Figure 3.6. Jensen and Davidson (1966) have shown that silver displaces the hydrogen bonds between adjacent nitrogens of the purines, adenine or guanine, and pyrimadines, thymine and cytosine, in the DNA molecule. Consequently, at those sites, the normal distance of 3 Angstroms between the pairs AT and GC is increased to 3.8 Angstroms, and, presumably the Watson-Crick model is distorted. The nitrogen-silver bonds appear to be stronger than the hydrogen bonds (nitrogen-hydrogen); bacteria with DNA-bound silver will presumably not divide and multiply (Fox et al., 1969b).

In recent years the high cost of silver and the development of bacterial strains resistant to silver sulphadiazine, other agents have been investigated. One of the most promising is cerium-nitrate silver sulphadiazine (Flammacerium). This was introduced in 1977 (Monafo et al., 1977) and has since been shown to be effective due to a synergistic effect between the two agents (Rosenkranz, 1979).

Zinc sulphadiazine has also been tried with limited success (Fox, 1984). Zinc oxide has been used in ointments and powders for centuries and, more recently, as a tape (Gang, 1981).

Antiseptics are used in many instances in preference to other agents as topical antimicrobials (Gilmore, 1977). The main reason behind this is that agents of this type do not exhibit the same ability in enhancing the development of resistant organisms commonly detected when antibiotic or chemotheraputic containing agents are applied topically (Lowbury et al., 1976; Prince et al., 1978).

Povidone iodine (Betadine or Disadine DP) is available as a solution, foam, ointment, cream or dry powder spray, and is a wide spectrum antiseptic. Betadine cream has been used as a second-line topical agent because of its broad antibacterial spectrum. However, this agent rapidly dessicates the eschar, making eschar removal difficult (Yarbrough, 1978). Betadine foam, which is difficult to apply evenly, has been noted to cause febrile responses in some patients with large thermal injuries. Another iodine-based antiseptic, Cadexomer iodine, is a powder which absorbs exudate and combats infection by releasing iodine. However, it has only recently been used on burns (Lawrence et al., 1984a).

Chlorhexidine (Hibitane) is available as a cream or antiseptic tulle and is very popular. This agent has also been reported in use as a cream with silver nitrate (Lowbury et al., 1976) or with phenoxetol (Lawrence et al., 1982).

Dextranomer (Debrisan) is a highly hydrophilic dextran polymer manufactured in the form of dry, spherical beads. The dry beads are placed on a wound and the wound secretions are sucked up

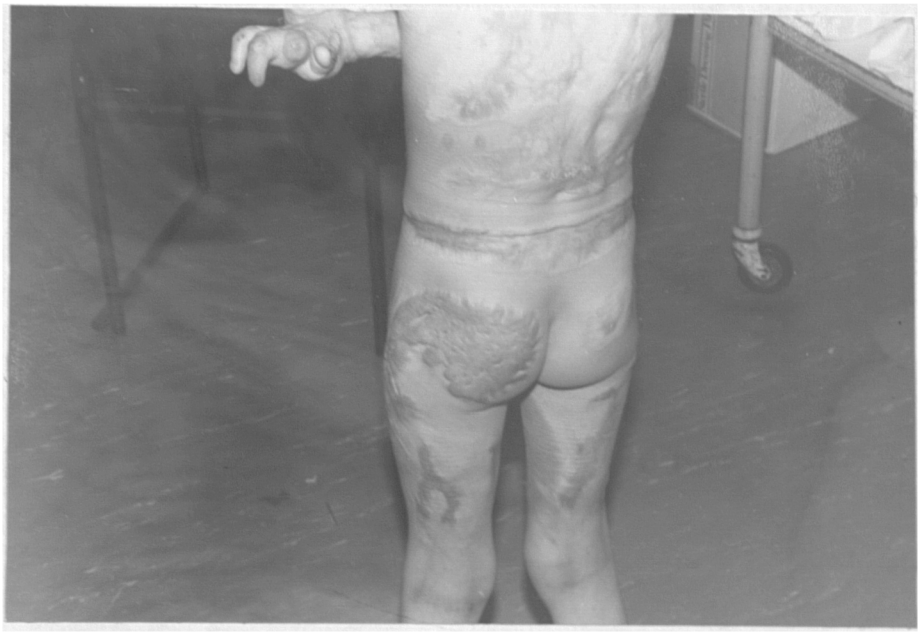

Figure 3.7 Hypertrophic scarring.

into and between the beads. No crust is formed and bacteria and granular substances are removed with the secretions. It has been used on burns (Paavolainen & Sundell, 1976; Arturson et al., 1978; Flamment, 1979; Angorn, 1982) and has been found to reduce infection and prevent sepsis, decrease inflammation and maintain mobility of joints. However, its major drawback is difficulty in handling.

3.6.2 Hypertrophic Scar and Keloid

Assuming that hypertrophic scars (Figure 3.7) and keloids have afflicted man since early times, it is strange that descriptions of these lesions did not appear in the literature until the end of the eighteenth century (Linares, 1977). The first description of keloid-like lesions was in a book on skin lesions in 1790 (Retz, 1790), and the term "cheloide" or "keloide" was not introduced until the early nineteenth century (Alibert, 1816; Alibert, 1817).

Very often the two lesions are difficult to distinguish. Keloids are defined as benign, proliferative, fibrous outgrowths, having their origin in the sub-papillary layer of the dermis, and develop as a result of trauma in certain individuals. Hypertrophic scarring is a consequence of a deep injury to the skin. It is recognised as a reddened, elevated, hard mass of skin occurring over a healed area, and can lead to severe contractures and loss of function. However, in some cultures they are produced for cosmetic purposes (Figure 3.8). The major difference between the two is that the keloid grows beyond the original wound

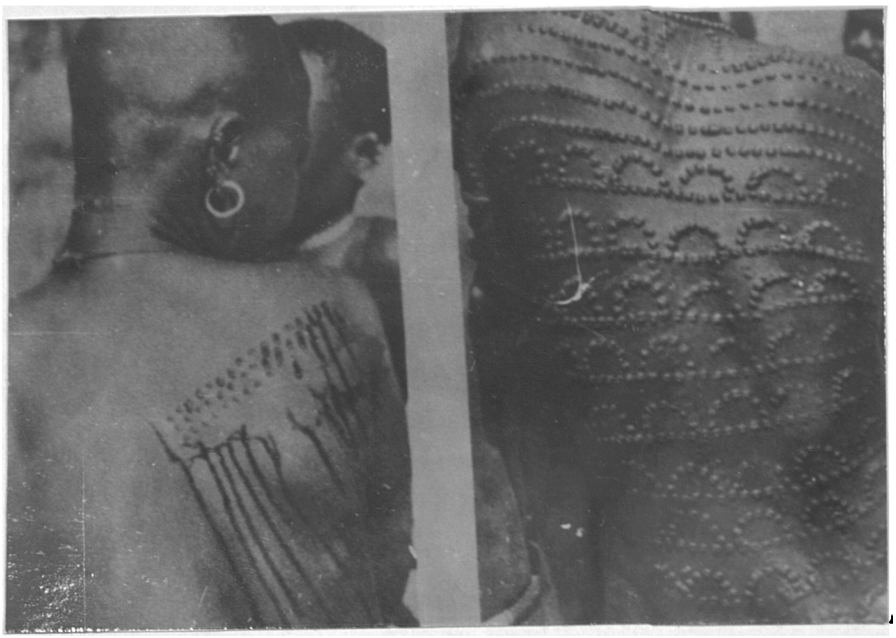

Figure 3.8 Hypertrophic scar being produced on Africans. The finished result is on the right (Hunt, 1979).

while the hypertrophic scar stays within the boundaries of the wound. Whereas keloids enlarge and rarely resolve spontaneously, hypertrophic scars tend to evolve to a peak size and often regress over a period of months or years.

Four main theories on the origin of the hypertrophic scar have been postulated:

1. Hypertrophy is a response to tension along or across the scar causing fibroblasts to contract, collagen "buckling" and later "nodule" formation (Larson et al., 1971).
2. "Myofibroblast anchoring substance" (MAS) provides the attachment of the contracting cell (myofibroblast) to an adjacent collagenous structure. The myofibroblast then foreshortens the collagenous matrix, which is then fused into the contracted mass by the mucopolysacchrides of the ground substance. The foreshortening raises and stiffens the scar (Baur et al., 1978).
3. There is continued inflammation or infection serving as a constant stimulus to connective tissue formation (Hunt, 1979).
4. An adhesive matrix of mucopolysaccharide entraps new collagen, which is buckled in response to the passive compression and buckling of skin resulting from joint flexion (Brody et al., 1981).

3.6.2.1 Aetiological factors. The reasons why certain people develop hypertrophic scars and/or keloids are not known, however, many constitutional factors have been cited in the literature and these may be listed as follows:

Sex. Some observers have found the sexes to be equally affected

(Koonin, 1964; Alhady & Sivanantharajah, 1969) while others have found females to predominate males in the ratio 1.8:1 (Cosman et al., 1961). However, this may be due to the fact that the female is more concious of the cosmetic effect of the scar and would therefore more readily have it treated (Cosman et al., 1961).

Age. The incidence of hypertrophic scar and keloid formation is higher in children and young people (Garb & Stone, 1942; Asboe-Hansen et al., 1956; Peacock et al., 1970; Larson et al., 1974). The reason for this variation is unknown. Several factors could account for this distribution such as: the young have a higher incidence of trauma (Kitlowski, 1953); the collagen turnover is accelerated in the young due to their growth spurts; there is a higher degree of elasticity and tension in young skin than in old skin (Ketchum et al., 1974).

Race. Keloids are more common in Negroes (Garb & Stone, 1942; Koonin, 1964) with other races also showing a marked disposition (Alhady & Sivanantharajah, 1969). The ratio of coloureds to whites with keloids varies between 2:1 and 19:1 (Bloom, 1956; Koonin, 1964).

Glucksman (1951) indicates that the tendency to scar hypertrophy is due to the presence of lanugo hair which is more common in coloured people and women and children of the white races. However, Koonin (1964) suggests that the high incidence of keloids in the dark-skinned races is due to an aberration of melanocyte stimulating hormone (MSH) because:

1. The high incidence of keloids in dark-skinned races, whose melanocytes are apparently more reactive to MSH.
2. The main sites of keloid formation occur in parts of the body where the concentration of melanocytes is greatest (keloid formation is rare on the palms and soles, where the concentration of melanocytes is minimal).
3. The incidence of keloids is higher during times of physiological hyperactivity of the pituitary, such as puberty and pregnancy - and pituitary hyperactivity is also associated with increased pigmentation.

Heredity. In 1956, Bloom reviewed 31 familial cases of keloids in the literature and studied an Italian family with 14 affected members in 5 generations. The pedigrees indicated that the predisposition to keloid formation is inherited according to a regular, dominant, autosomal gene.

Location. No part of the body is exempt from scar formation but some areas do seem more inclined to produce hypertrophic or keloid scars than others (Trusler & Bauer, 1948). These scars are rarely found on the sole of the foot, palm of the hand, genitalia or eyelids. However, they are commonly found over the neck, shoulder, thorax, extremities (Trusler & Bauer, 1948; Alhaqy & Sivanantharajah, 1969; Peacock et al., 1970; Ketchum et al., 1974), and three varieties have been observed on the ear lobe following ear piercing (Abdel-Fattah, 1978).

Tension. Keloids frequently occur in areas of increased skin tension, and Borges and Alexander (1962) suggested that tension

along or across a scar plays a significant role in hypertrophic scarring by producing a higher stimulus for fibroplasia. Tension may be caused by several factors, e.g. when there is a great loss of tissue or excision of a large skin tumour when tension is increased on attempting to close the wound. Scars parallel to the lines of relaxed skin tension are free of tension and are normal.

Local factors. In 69% of the cases studied by Glucksman (1951), scar hypertrophy was found when hair and/or other keratinised material contacted the dermis and caused a foreign body reaction.

Initiating trauma. Hypertrophic scarring is one of the most common and disabling sequelae following thermal injury (Larson et al., 1976). Burns, either chemical or thermal, therefore, are the real cause of scar and keloid formation (Konuralp, 1976). However, even minor trauma, for example ear piercing, can lead to the formation of keloids and hypertrophic scars (Garcia-Velasco, 1972), and the most common initiating factors, including burns, are surgery, lacerations, abrasions, acne, boils, B.C.G. inoculation (Alhady & Sivanantharajah, 1969) and smallpox vaccination (Bloom, 1956).

Enzymatic factors. The histoenzymological patterns of hypertrophic scar and keloid have been studied by many researchers and all have found that the activity of some enzymes in the individual fibroblast is similar in both types of lesion (Katatowski, 1968; Hoopes et al., 1971; Ketchum et al., 1974). The difference between the types of scar appears to reside in the growth potential of the process of fibroplasia - which is considerably increased

in keloids, bringing about a greater amount of tissue and a longer time for its development. Also, both keloids and hypertrophic scars have similar cytological and cytochemical features:

1. hyperplasia of immature fibroblasts;
2. an abundance of ribonucleic acids and glycoproteins accompanied by the production of mucopolysacchrides and collagen fibrils;
3. a vascular neoformation (Ketchum et al., 1974).

Biochemical factors. Hypertrophic scars have been shown to contain higher amounts of hexose, hexosamine, sialic acid, uronic acid and glycogen than normal scars and are thus more active metabolically (Shetlar et al., 1971). However, the main facet of hypertrophic scar and keloid formation is the disruption in collagen metabolism.

The collagen produced in response to an injury of human skin is initially stabilised by a cross-link derived from hydroxyallysine, and characteristic of embryonic skin. In normal healing there is a change over with time to the cross-link derived from allysine, which is typical of young skin collagen. In contrast, hypertrophic scars fail to follow the time-related changes of normal skin, but retain the characteristics of embryonic collagen, indicating a continued rapid turnover of the collagen. This is further supported by the high proportion of the embryonic Type III collagen present in hypertrophic scars (Bailey et al., 1975).

Although collagen synthesis in hypertrophic scars is twice that of normal scars (Craig et al., 1975), it drops to the same level after 2-3 years. In addition, inhibitors of human skin collagenase, α-1-antitrypsin and α-2-macroglobulin, are increased

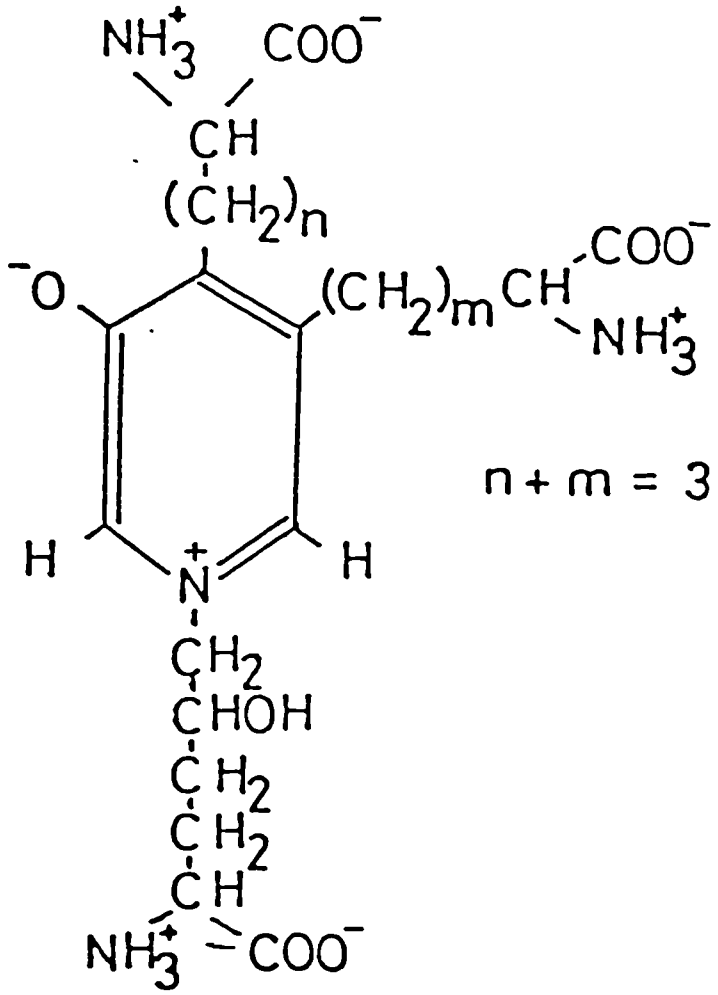

Figure 3.9 Structure of pyridinoline. The sum of n and m is 3, but the exact values of n and m have not yet been deduced by chemical methods (Moriguchi & Fujimoto, 1979).

in keloids and hypertrophic scars (Diegelmann et al., 1977; Jackson, 1980). In hypertrophic scars collagen fibres form nodules and whorls (see 3.6.2.2) which are coated with mucopolysaccharides, mainly chondroitin-4-sulphate (Craig et al., 1975). An increase in chondroitin-4-sulphate, due to the absence of hyaluronidase activity (Alexander & Donoff, 1980), either prevents collagenase action (Linares & Larson, 1978) or increases collagen production by increasing proline hydroxylase activity (Shetlar et al., 1972; Diegelmann et al., 1977). Knapp and his colleagues (1977) demonstrated that collagen fibres and fibre bundles display a decreasing level of organisation as the clinical degree of scar abnormality increases and that this structural gradient correlates with the gradient of intermolecular cross-linking in the same tissues, normal, mature scar, hypertrophic scar and keloid being successively less cross-linked. However, they also found that the enzyme which initiates intermolecular cross-links, lysyl oxidase, is normal or elevated in hypertrophic scar and keloid. Another interesting observation is that of Moriguchi and Fujimoto (1979) who isolated a new cross-linking amino acid from the collagen of hypertrophic scars (Figure 3.9) and called it pyridinoline, but it is virtually absent from the collagen in normal skin.

One of the common treatments used to reduce hypertrophic scars and keloids is the injection of triamcinolone (Maguire, 1965; Ketchum et al., 1966). This has been shown to reduce the amount of α_1-antitrypsin i.e. removes collagenase inhibitors

(Diegelmann et al., 1977) without interfering with collagen synthesis (Cohen & Keiser, 1973).

The partial pressure of oxygen in the hypertrophic scars of burned patients has been investigated. Sloan and his colleagues (1978) and Berry and his colleagues (1985) found that the P_{O_2} in scar tissue was significantly depressed when compared with normal dermis, however, Sherwin and his colleagues (1985) found the opposite i.e. that the P_{O_2} is elevated above that of the normal dermis.

Hormonal factors. There is an increased incidence of keloid formation during physiological hyperactivity of the pituitary gland, such as during puberty and pregnancy (Edgerton et al., 1951; Cosman, 1961; Ketchum et al., 1974).

Keloids have been observed to resorb after the menopause, and are rare in the elderly (Edgerton et al., 1951), but it is possible that they have followed the natural resorption process that takes place in time. However, Garb and Stone (1942) suggested that the resorption was due to the diminution or absence of a type of hormonal secretion.

Immunological factors. Laurentaci and Dioguardi (1977) published results of 40 patients and 131 controls which indicated that individuals with antigens HLA-B14 or HLA-Bw16 have a greater risk of developing keloids although neither of these antigens were found in patients with hypertrophic scars.

It has also been suggested that keloids are related to an immune reaction in the scar to sebum secreted from cut or damaged

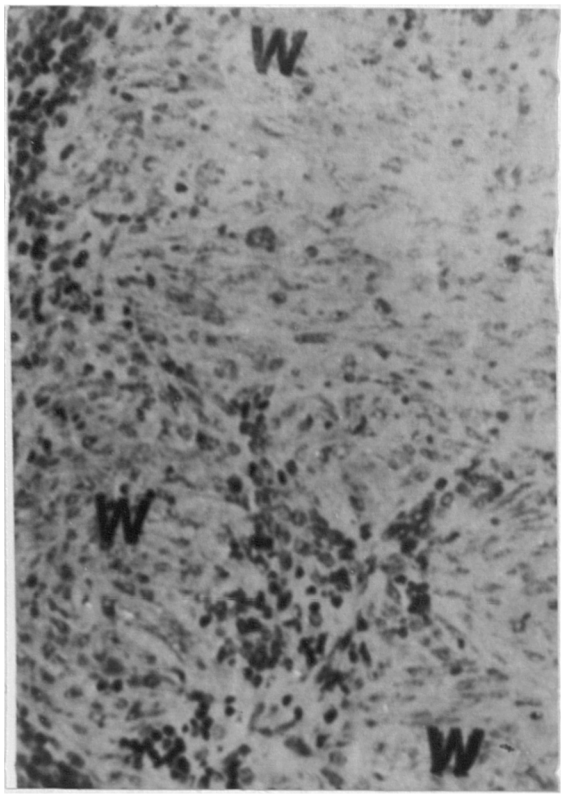

Figure 3.10 Whorl like formations of collagen fibres (W). (Linares et al., 1973).

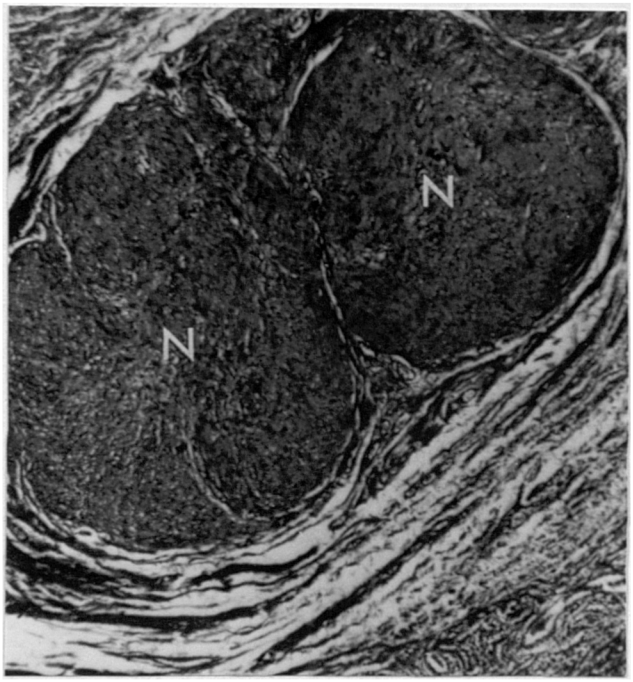

Figure 3.11 Reticular area of dermis of hypertrophic scar with two large discrete nodules (N). Note the peripheral layers of collagen forming a near septal-like capsule. Verhoeff's stain. (Linares et al., 1972).

sebaceous glands and ducts (Yagi et al., 1979), and this may explain the mysterious beneficial effect of corticosteroids which are immunosuppressors.

3.6.2.2 Histopathology. In both hypertrophic scars and keloids, the collagen fibres progress from whorl-like arrangements (Figure 3.10) to distinct nodular forms (Figure 3.11). The fibre bundles increase in thickness and the nodular area becomes highly compact. Because both types of lesion show this, they are indistinguishable from each other histologically (Conway et al., 1960; Mancini & Quaife, 1961; Linares et al., 1972; Linares et al., 1973). Thus, the difference between normal wound healing and healing with hypertrophic scarring or keloid formation lies not only in the length of time over which new collagen is being formed but also in the arrangement of newly formed collagen (compare Figures 3.12 and 3.13) (Mancini & Quaife, 1961). However, this arrangement of collagen fibres is found in the granulation tissue (Linares & Larson, 1974) and could therefore serve as a prognostic index to the type of scar that will develop.

In both hypertrophic scar and keloid there is also an increased amount of granulation tissue with capillaries, fibroblasts, mast cells, collagen, and there is a prolonged production of these elements in keloids. Linares (1971) reports that the whorls and nodules persist in keloids but ultimately flatten out in hypertrophic scars, and that nodular formation appears to reflect the most active and worst phase of hypertrophic scarring.

While the existence of a whorled pattern of collagen fibres

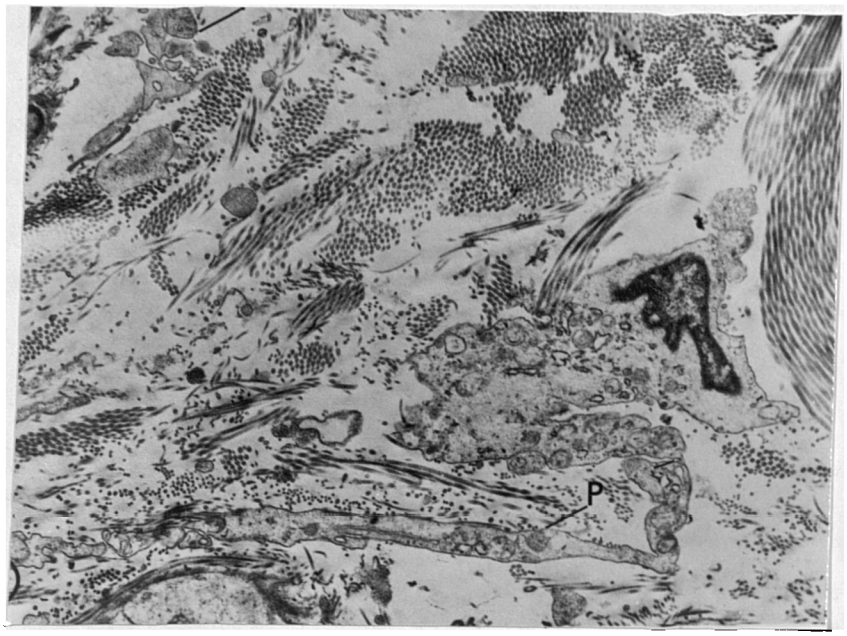

Figure 3.12 Area of reticular dermis from normal skin. Collagen is not closely packed and fibroblasts exhibit many processes (P), (Linares et al., 1972).

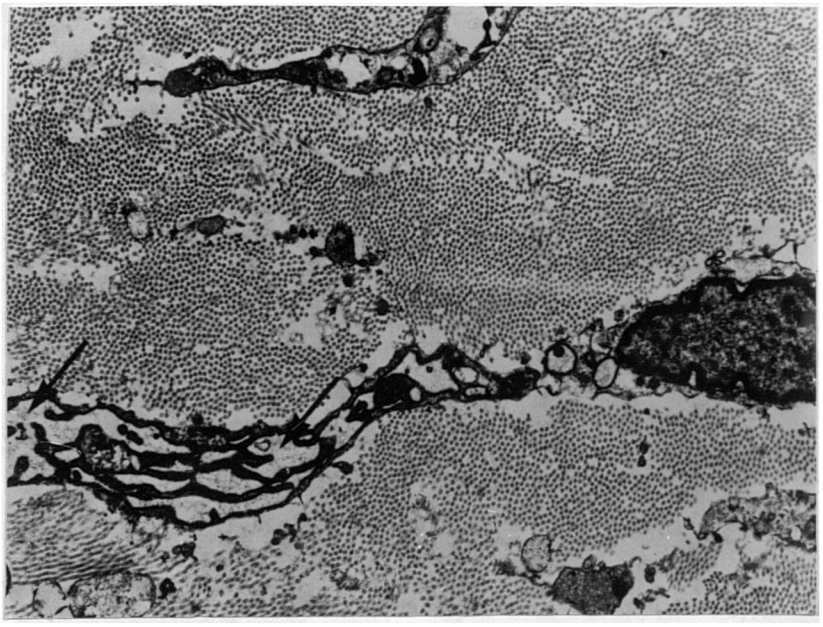

Figure 3.13 Area of reticular dermis within nodule of hypertrophic scar. Cytoplasmic processes with markedly dilated rough endoplasmic reticulum (arrows). Note tight packing of the collagen (Linares et al., 1972).

orientated around a central mass or nodule is well documented (Larson et al., 1974a; Larson et al., 1974b; Larson et al., 1976; Linares et al., 1972; Linares et al., 1973; Linares et al., 1976; Linares et al., 1977; Kischer et al., 1972; Kischer et al., 1975; Kischer et al., 1978) another explanation has been postulated. Tully (1980) also observed these nodules but whereas others described the centre of the nodule as being formed by a complete fusion of the fibres into a homogeneous mat of collagen, Tully (1980) shows that the nodules are the cut ends of extremely large (up to 1.5 mm diameter) bundles of collagen fine fibres or fibrils.

That hypertrophic scars show a temporary lack of elastin fibres has been known since the middle of the last century (Gray, 1850). Indeed, there is a progressive decline in the amount of elastin from atrophic scars (scars which are depressed, supple, and have a shiny surface) through normal scars (scars level with the skin surface), with a marked reduction in hypertrophic scars and a virtual absence in keloids (Bhangoo et al., 1976). In a histological investigation, Linares and Larson (1977) found fragmented and degenerated elastin-like fibres in patients who later developed hypertrophic scars. They suggested that this response could contribute to the persistency of the chronic inflammatory process usually present in immature hypertrophic scars, or that the immunological response elicited by the injured elastin fibres could also be interfering with the normal pathway of the biosynthesis of the elastin, resulting in a failure of

80A

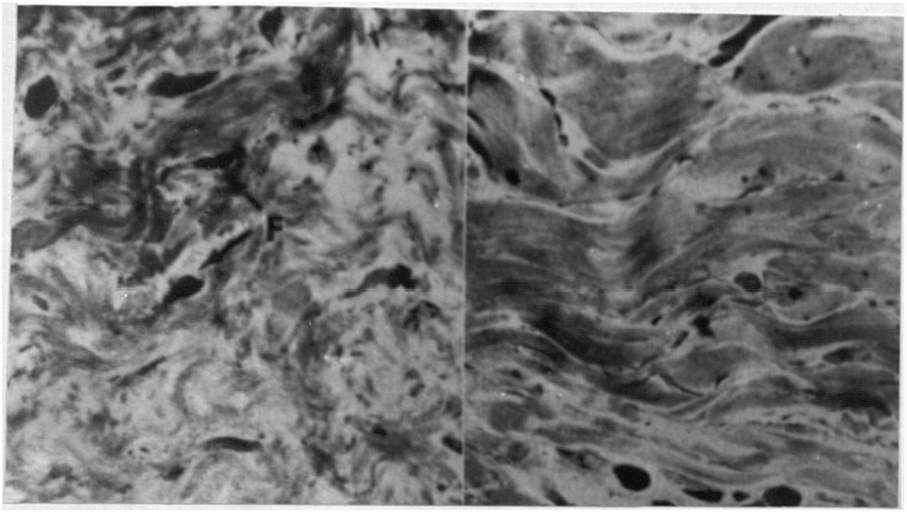

Figure 3.14 A, light micrograph of a hypertrophic scar with fibroblasts scattered throughout the collagen matrix. (F, fibroblasts). Methylene blue and azure II. B, light micrograph of a mature hypertrophic scar demonstrating the absence of fibroblasts in much the same area. Methylene blue and azure II. (Baur et al., 1975).

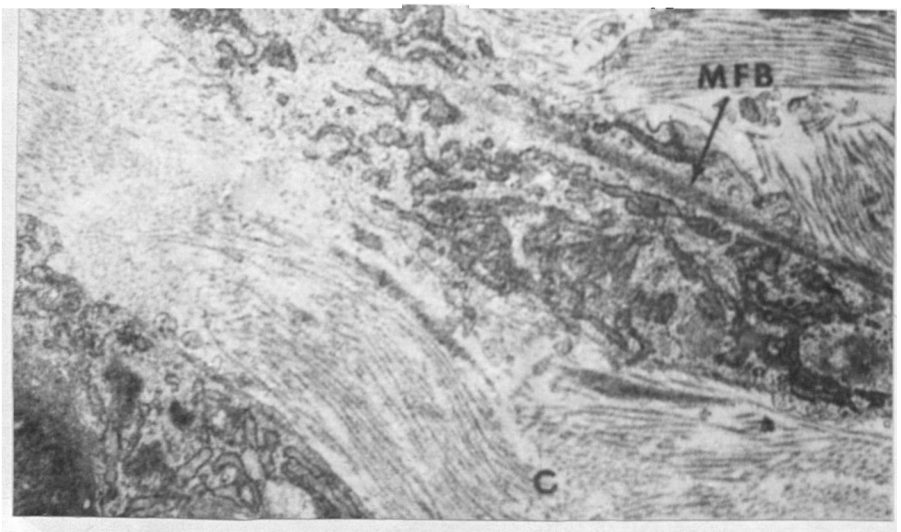

Figure 3.15 Myofibroblasts observed in an immature hypertrophic scar. The microfilament bundle is in parallel orientation to the majority of collagen filaments observed in the intracellular matrix. C, collagen filaments; MFB, microfilament bundle. Lead citrate and uranyl acetate. (Baur et al., 1975).

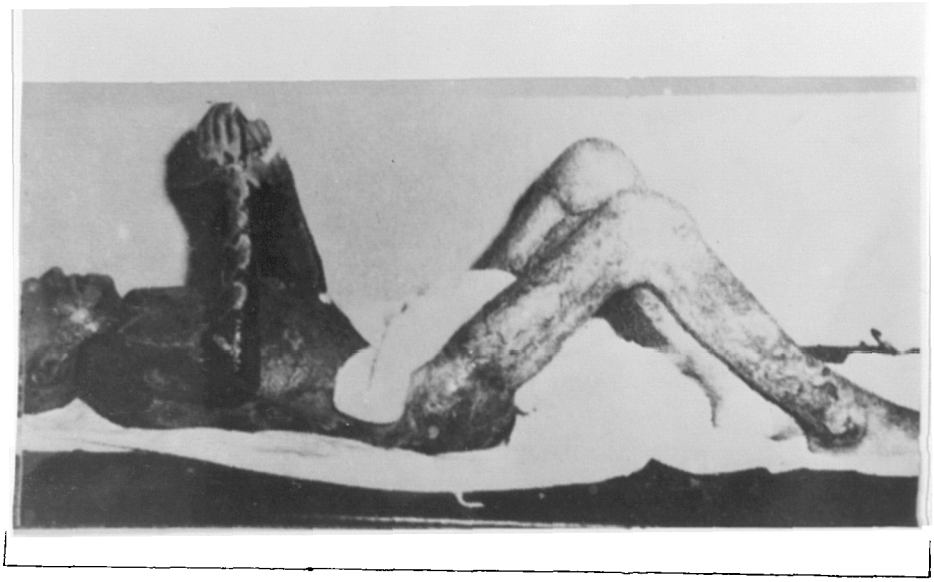

Figure 3.16 Child in the "position of comfort," (Larson et al., 1979).

elastogenesis.

Myofibroblasts have been found in immature hypertrophic scars (Figures 3.14 and 3.15). The contraction of these cells could play a significant role in the elevation of the scar tissue (Baur et al., 1975).

3.6.2.3 Prevention of hypertrophic scar and contracture. A burn wound will shorten until it meets an equal, "opposing force." It shortens by the action of myofibroblasts and the force exerted by these cells may be sufficient to dislocate joints. One of the major problems in post-burn management s that the position of comfort for most patients is the position of flexion (Figure 3.16) and they will assume this position if allowed to do so. This position permits the new collagen fibres in the wound to fuse together (Figure 3.17) and results in contracture formation, therefore the position of comfort is the position of contracture (Larson et al., 1979).

Larson and his colleagues (1979) have concluded that hypertrophic scar and contracture can be significantly altered, controlled, and markedly decreased with special techniques. These include proper positioning of the patient (Figure 3.18 , utilisation of splints to maintain good position of all joints (Figure 3.19), the use of skeletal traction to allow exposure of skin grafts and maintain proper positioning of joints (Figure 3.20), and the use of pressure garments after healing (Figures 3.21 and 3.22).

3.6.2.4 Treatment of hypertrophic scars.

Surgery. Surgery is usually not indicated during the active

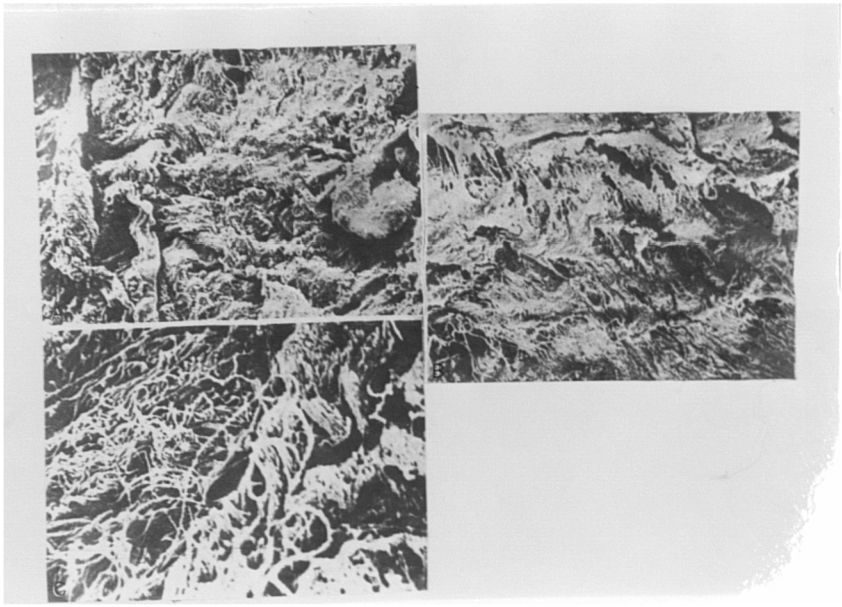

Figure 3.17 A, collagen fibres fused in a hypertrophic scar; B, after 3 weeks of pressure and serial splinting the compact collagen is beginning to lessen; C, after 6 weeks of therapy individual fibres are visible (Al-Rawi, 1980).

phase of scarring i.e. as long as the scar is highly vascular, the final results would be less than optimal because of the vigorous response of the local tissue to the additional trauma. Once the scar has lost its activity and matured, the local tissue response is less and an improved result can be anticipated. However, if contracture is too severe to respond to non-surgical means surgery must be carried out early (Larson et al., 1979).

To relieve scar contractures for a functional result the Z-plasty, skin flap or skin graft in most cases are very successful (see Figure 2.17). In 1976, Longacre reported successful application of the Z-plasty to the scar itself which changed the direction of the predominant collagen molecules in contracted and developing hypertrophic scar from the lines of tension to the normal crease lines and relaxed the tension. This was associated with softening, thinning, flattening, and blanching, and changes at the biochemical, ultrastructural and histological levels of organisation (Longacre et al., 1976).

Another similar surgical technique is the X-release (El-Otefy, 1981) which involves two v-shaped flaps and when combined with split-skin grafts consistently gives satisfactory results in a one-stage operation.

Surgery alone can often be ineffective in treating hypertrophic scars therefore other adjunctive measures are used simultaneously (Ketchum et al., 1974). For example, Garcia-Velasco (1972) advises surgery combined with radio-therapy or surgery combined with corticosteroids, while Babin and Ceilly (1979) suggest

Figure 3.18 Child positioned in bed to avoid contracture. Note elbow and knee extension (Larson et al., 1979).

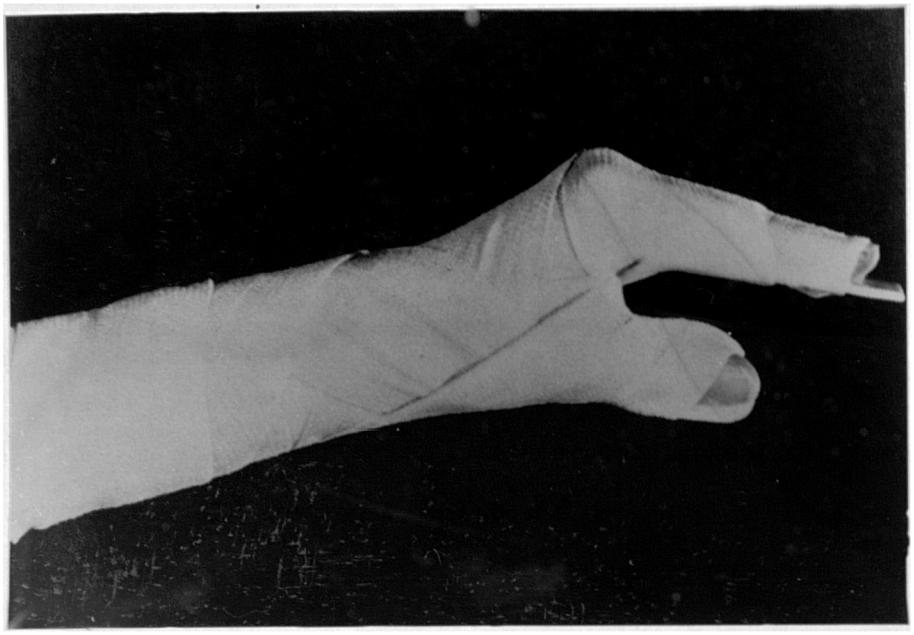

Figure 3.19 Isoprene hand splint retained with elastic wrap demonstrating wrist extension, metacarpophalangeal flexion, interphalangeal extension, and abduction and flexion of thumb (Larson et al., 1978).

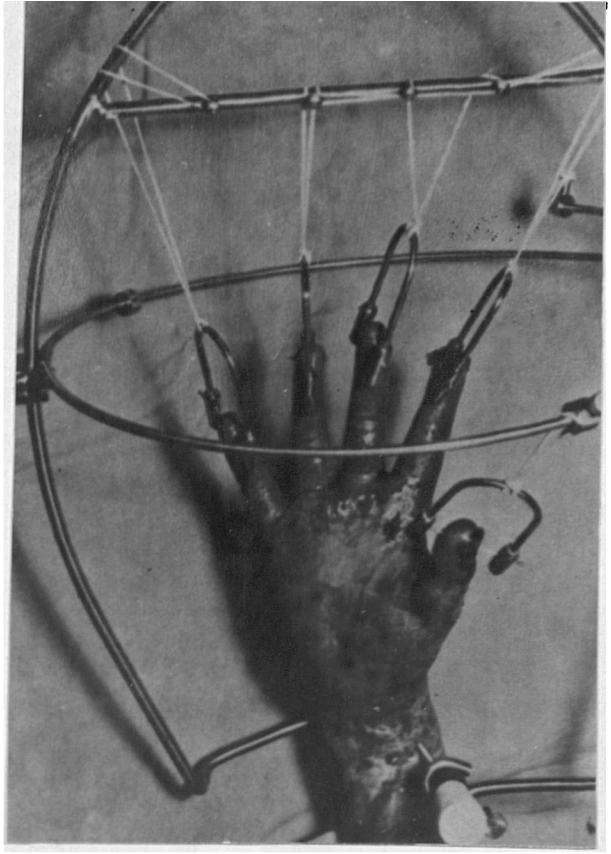

Figure 3.20 Skeletal suspension device demonstrating radial and digital threaded pins, traction bows, and elastic bands for positioning (Al-Rawi, 1980).

cryotherapy and low dose intralesional triamcinolone followed later by surgical excision.

Chemotherapy. Up to the 1950's, many agents were tr ed to soften and flatten keloids and hypertrophic scars. These included herbs, thiosinamine, formalin, oil of creosote or the use of iodine iontophotesis, nitrogen mustard, enzymes, pepsins, snake venom and hyaluronidase, with unsuccessful or uncertain results (Cosman et al., 1961).

The use of steroids was introduced in 1950 when Baker and Whitaker demonstrated that direct application of steroids over a prolonged period of time produced thinning of the dermis, limited to the area of treatment. Conway and Stark (1951) treated a series of keloids with excision followed by parenteral adrenocorticotrophic hormone (ACTH) but this was unsuccessful. In 1954, hypertrophic scars injected with hydrocortisone were arrested but did not regress (Griswold, 1954). However, in 1956, Asboe-Hansen and colleagues reported regression in 85% of hypertrophic scars treated with hydrocortisone.

In 1965, Maguire reported the first successful regression of a large keloid from intralesional treatment with triamcinolone, a 9-α-fluorohydrocortisone. Since then other authors have reported similar successes (Griffith, 1966; Ketchum et al., 1966; Ketchum et al., 1971). This agent also softens the scar, relieves pruritis, pain and paraęthesia (Alhady & Sivanantharajah, 1969), and increases the rate of collagen degredation (Cohen et al., 1974; Ketchum, 1976). However, Kiil (1977) reported partial recurrence after

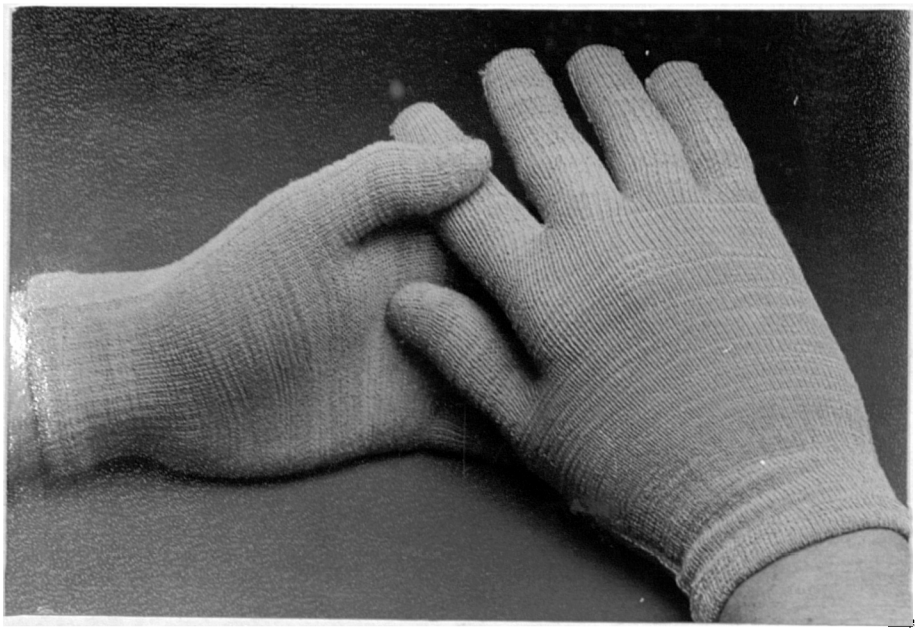

Figure 3.21 A "ready to wear" Tubigrip pressure garment.

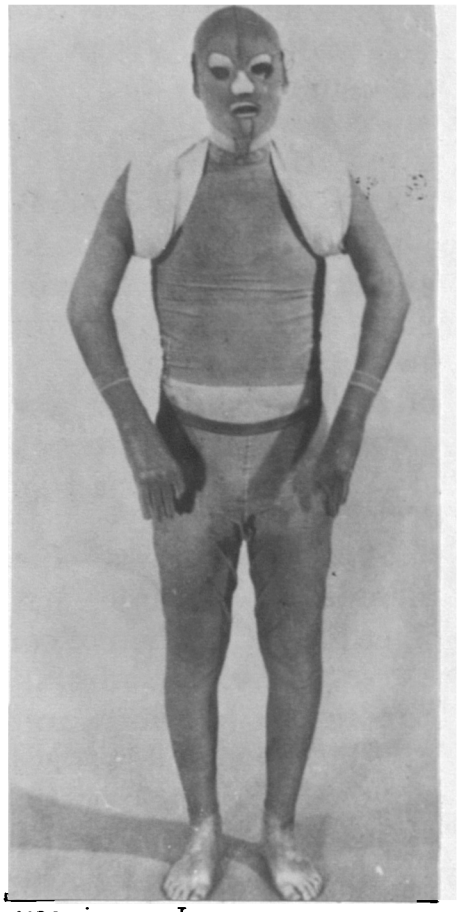

Figure 3.22 Patient wearing a Lycra pressure garment (Al-Rawi, 1980).

one year and after five years, the recurrence rate was 50%.

Cryotherapy. This involves carbon dioxide ice being placed on the scar tissue. This method is rarely used today since unsatisfactory results have been observed (Ketchum et al., 1974).

Radiotherapy. X-ray treatment for keloids was first introduced in 1906 by De Beurman and Gougerat, but it was not until 1961 that irradiation was proven to be non-effective in already established scars (Cosman, 1961). Thus, radiation treatment is not routinely used in the care of hypertrophic scars (Ketchum et al., 1974).

Ultrasonics. Wright (1971) reported that ultrasonics used in the treatment of abnormal scar tissue was unsuccessful.

Pressure. This is a brief discussion and for more detailed information, the reader is reffered to Al-Rawi (1980), Naismith (1980) and Tully (1980).

Many burns units use constant pressure and splinting with an excercise program to maintain a satisfactory range of motion in joints in cases of hypertrophic scar and contracture (Dobbs, 1979).

Constant pressure dressings or garments (Figures 3.21 and 3.22) exerting pressure of 25-40 mmHg for 4-6 months, will decrease the vascularity, decrease the amount of mucopolysaccharides, especially chondroitin sulphate A, decrease the cellular response as well as the collagen deposition and significantly lessen the localised lymphoedema (Larson et al., 1979), also it accelerates the natural remodeling of hypertrophic scar tissue (Tully, 1980). However, Naismith (1980) found the same features with pressures

in the range 15-40 mmHg. Therapy with constant pressure dressings is improved by the addition of conforming splints to oppose the forces of the myofibroblasts and voluntary muscle action, thereby maintaining the body structures in optimal position and giving the greatest benefit to the patient (Parks et al., 1978; Larson et al., 1979; Tully, 1980). Because the forces generated in this form of therapy are continuous and unrelenting, the splints should be worn at all times, except during periods of vigorous exercise. It has been suggested (Kischer, 1975; Kischer et al., 1975) that during this treatment biopsies should be checked in the scanning electron microscope for effectiveness.

Peacock and Van Winkle (1976) suggest that the pressure exerted by these dressings is sufficient to reduce the size of the scar because of the amount of water present, although it is more likely that pressure causes diminution of mass by accentuating the static condition and occluding the vascular bed to raise the level of hypoxia to the point of inducing degeneration of the fibroblasts leading to less production of collagen (Kischer et al., 1975).

The controversy regarding pO_2 in hypertrophic scars (see 3.6.2.1) continues. Sloan and his colleagues (1978) noted that when pressure was applied the pO_2 in hypertrophic scars decreased further, while the results obtained by Berry and his colleagues (1985) were initially similar to those of Sloan et al. for one third of their patients, however, the pO_2 in all patients eventually increased to near normal skin values as the scars matured. The

low tissue pO_2 values observed by Sloan and colleagues (1978) and Berry and co-workers (1985) have been attributed to compact collagen nodules and thickened capillary walls acting as a barrier to oxygen diffusion (Larson et al., 1976; Berry et al., 1985) and that since these are reduced with pressure therapy, the pO_2 increases. In contrast, Sherwin and his colleagues (1985) found that the elevated pO_2 in hypertrophic scars decreased as pressure was applied and concluded that the tissue remodeling changes found after pressure therapy could be due to alterations in oxygen supply to the proliferating scar tissue.

Silicone gel. Silicone gel has been observed to reduce hypertrophic scarring (Perkins et al., 1982; Quinn et al., 1985a) and this will be discussed in chapter 7.

3.7 CONCLUSION

The optimisation of treatment of burn wounds and hypertrophic scarring could be by materials which have certain common properties e.g. conformability, durability, ease of application and removal, elasticity, gaseous exchange, water vapour transmissibility, and which are non antigenic and non toxic.

CHAPTER 4

BURN DRESSINGS

4.1 INTRODUCTION

The field of burn wound management is controversial and reflects vastly differing individual preferences and experiences in the handling of the burn wound. The eventual goal in the treatment of burns is to cover the defect with the patient's own skin, i.e. the wound is either allowed to heal or is autografted. Due to the nature of these wounds, re-epithelialisation can be very slow and controversy remains as to whether or not wounds should be covered or left exposed for this period. In addition to the complications associated with the burn itself, other attendant injuries of varying severity may be present including shock, obstructed airway, lung damage (due to inhalation of smoke), fractures, head or spinal injuries, and internal bleeding. Such problems must be faced prior to treatment of the burn wound.

Although different materials have been used to cover burn wounds (reviewed by Artz, 1970; Park, 1978; Davies, 1983a; Davies, 1983b) the reasons for using many of these materials have not always been specified or clearly defined. Additionally, the terminology used to date has been inconsistent, e.g. burn wound covering (Park, 1978), short-term dressing (Davies, 1983a), long-term substitutes for skin (Davies, 1983b), burn covering (Schwope et al., 1974), skin substitute (Tavis et al., 1978;

Table 4.1 Properties of the "ideal" burn dressing.

Absorbency

Adherence

Bacterial barrier

Comfort

Conformability

Drug delivery

Durability

Ease of application and removal

Elasticity

Gaseous exchange

Haemostatic

Non antigenic and non toxic

Sterilisability

Tear resistance

Water vapour transmissibility

Bartlett, 1981), artificial skin (Yannas & Burke, 1980), synthetic skin (Lin et al., 1981) and burn dressing (Chvapil, 1982). The approach adopted in this thesis is to utilise the expression "burn dressing" to describe the material covering a burn wound irrespective of the duration of application.

4.2 REQUIREMENTS OF A BURN DRESSING

Table 4.1 (modified from Tavis et al., 1978; Chvapil, 1982; Lawrence, 1982; Pruitt & Levine, 1984) lists the relevant properties of the ideal burn dressing and these will be considered in more detail.

4.2.1 Ease of Application and Removal

Application of the dressing should be uncomplicated and should, ideally, not involve any prior material preparation such as mixing of components or thawing. The dressing should then adhere rapidly to the uninjured skin surrounding the wound with sufficient strength to resist lifting and slipping (leading to loss of the bacterial barrier), but must separate readily when removed. Adherence must be uniform, since small areas of non-adherence will lead to fluid-filled pockets where bacteria may proliferate. Adherence obtained by the drying of exudate on the dressing is undesirable since pain will be caused on removal and some or all of the regenerating epidermis or granulation tissue may be damaged (Tavis et al., 1978). Similarly, there should be no ingrowth of tissue into the dressing or other strong attachments that will prevent easy removal (unless adhering dressing remnants are biodegradable). Consideration of the patient dictates that removal of the dressing should be pain-free.

4.2.2 Fluid Balance

Fluid balance in burn injuries is very important since burn wounds lose vast amounts of fluid through evaporation and exudation, leading to a fall in body temperature and increase in metabolic rate. Dressings must absorb fluid, control its transmission and maintain a high humidity at the wound site since high humidity encourages granulation and assists epithelialisation. Normal skin allows water vapour to pass through it at a rate of approximately 8.5 +/- 0.5 g $m^{-2}h^{-1}$ while retaining protein and electrolytes (Lamke et al., 1977). Burn wounds lose water at a much greater rate even when covered by the natural dressings, the crust and eschar, (178.1 +/- 5.5 and 143.2 +/- 4.5 g $m^{-2}h^{-1}$ for partial and full thickness burns respectively (Lamke et al., 1977)). Water lost by evaporation from burned tissues causes surface cooling because of the latent heat of evaporation (2.42 MJ/l) and body temperature will fall unless there is a compensatory increase in heat production or the environment provides a substantial amount of energy to compensate for both the evaporative heat loss and that required for other metabolic purposes, for example, the increased rate of turnover of total body protein (Kien et al., 1978a,b,c). When the daily evaporative water loss exceeds three litres the energy requirements for evaporation are greater than the basal heat production of a normal adult. It has been suggested that the increased rate of heat production is related to surface cooling secondary to increased evaporative water loss from the burned tissues because both the increased rate of oxygen consumption

and the quantities of water lost by evaporation are directly related to the extent of the burn (Roe & Kinney, 1964; Caldwell, 1976; Davies, 1982). Indeed, the application of occlusive dressings or skin substitutes or homo-, hetero-, or autograft skin rapidly reduced both the rate of water loss and the metabolic rate to near normal values (Caldwell, 1976; Lamke et al., 1977). However, the optimal water vapour transmission properties of burn dressings have not been deduced. But, the rate should not be so great that the tissue dries, capillaries thrombose and "excess water" is lost (Tavis et al., 1978) nor should it be so limiting that the wound is macerated, the healing process delayed and increased risk of bacterial growth (Chvapil, 1982). Similarly, the absorptive properties need to be characterised (Quinn et al., 1985b). Ideally, the dressing should also be permeable to other gases such as oxygen and carbon dioxide. The levels of these gases directly affect the cellular and humoral activities, indeed, the rate of epithelialisation is directly related to oxygen availability (Turner, 1983).

4.2.3 Bacterial Barrier

The burn dressing should provide a bacterial barrier to prevent bacterial entry into the wound from the environment and vice versa, leading to cross infection. This bacterial barrier may be achieved by the dressing and/or by topical antibacterial agents. Where a burn dressing is used in association with a topical antibacterial agent, one option is to design the dressing to permit a controlled release of the agent. Since 1975 (Nathan et al.) antibacterial drugs have been added to dressings

in the manufacturing process. This technology can be used to incorporate other agents, for example, debriding agents such as "Travase", bromelain or N-acetyl cystein (Levinson, 1978) or "growth factors" (de Riel, 1984) such as epidermal growth factor, fibroblast growth factor and tumour angiogenesis factor to encourage wound healing.

4.2.4 Mechanical Properties

Burn dressings should posses mechanical characteristics to accomodate movement. This is dependant upon the site of application i.e. when a dressing is applied over a joint it should stretch and deform to allow flexion and extension of that joint. These mechanical characteristics can be defined as elasticity and conformability. Elasticity is neccessary if the dressing is to stretch freely over joints without causing shear stresses that will break the adhesive bond between the material and the skin's surface. Conformability, which can be defined as the ability to conform to the contours of the body and maintain position (without fluting or wrinkling) over the injured part even when wet and when joints are mobilised, is related to elasticity since compliant materials are more conformable (Queen - personal communication). In addition, any dressing should be durable enough to allow sitting, lying, bathing, wearing of clothes and should remain intact until changed.

4.2.5 Other Considerations

Materials to be used as dressings should be tested for potentially toxic substances (Lawrence, 1982) since local sensitisation

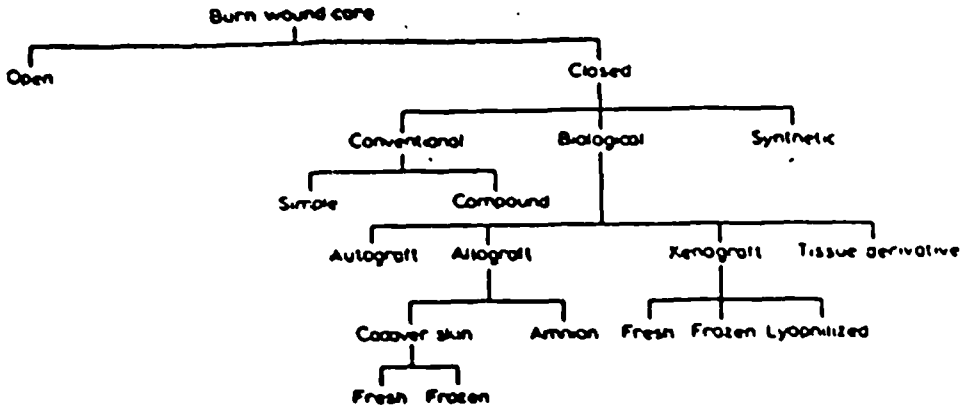

Figure 4.1 The choice of treatment of burns (Quinn et al., 1985b).

can occur, and both dressings and any adhesives used to attach them can sometimes cause a local dermatitis (Herniman, 1971). While biological dressings can be used with immune suppresion, elimination of antigenicity is a more desirable approach (Tavis et al., 1978). A dressing material possessing haemostatic properties would be desirable (when the wound is naturally bleeding or has been excised) since the time expenditure and tissue destruction inherent in electrocoagulation and other formms of haemostasis would be minimised (McMillan, 1970). Obviously, any material used to treat wounds should be sterilisable without adversely influencing its properties.

4.3 DRESSING DESIGN AND STRUCTURE

The choice of treatment for burns is outlined in Figure 4.1, which indicates the many different types of dressings available. Two separate types of burn dressing have emerged; the short-term dressing and the long-term skin substitute, with short-term dressings being preferable. This is because "use of serial excision and short-term dressings (while partial thickness wounds heal spontaneously or donor sites regenerate) has been successful even in 90%-plus full thickness burns" (Salisbury, 1983).

Dressings fall into three categories: conventional, biological and synthetic.

4.3.1 Conventional Dressings

Cotton wool, gauze, lint and Gamgee (gauze and cotton tissue) are still widely used for dressing all types of wounds including burns. The biggest advantage is their absorptive capacity. Wide-mesh

gauze impregnated with paraffin ("tulle gras") is commonly applied to the wound (usually with a topical antimicrobial agent), a layer of Gamgee or cotton wool acts as the absorbent portion, and a crepe bandage holds it in place.

4.3.2 Biological Dressings

The best cover for a wound is skin itself, and plastic surgery makes this possible. By means of a split-thickness skin graft, full thickness skin loss can be healed within a few days and the donor site within ten days. Unfortunately, there is a limited supply of viable skin available for autografting. To optimise the use of available skin for autografting, mesh grafting has proved successful (Tanner et al., 1964). A mesh, made from ordinary split-thickness sheet graft, by rolling it through cutters, is sutured onto the wound site and can cover an area of more than three times that of the donor site. This intensifies re-epithelialisation by migration.

Cutaneous allograft is the most frequently used and most effective biological dressing. Allograft skin can be obtained from a family member or other living volunteer, but is most commonly harvested from cadavers. Since fresh cadaver skin is not always available when required, it can be protected with glycerin, and with controlled freezing, be stored at -160^{o}C. Thus, allograft can be used for as long as six months after harvesting (Tavis et al., 1978; Salibury, 1983). Either fresh or frozen allograft is capable of decreasing bacterial counts

on the wound and diminishing evaporative water loss, protecting vital structures including the wound from dessication, decreasing pain and facilitating movement of involved joints (Salisbury, 1983; Pruitt & Levine, 1984).

Amnion, which has also been used as a biological wound dressing, is readily available from the delivery room and is inexpensive to prepare (Robson et al., 1973). It provides an adequate coverage with moderate adherence, elasticity and decreases bacterial counts, but it is so thin that it is not very durable and does not reduce evaporative water loss. However, amnion lacks antigenicity both on the body surface and inside the body (Trelford et al., 1972; Seashore et al., 1975). It has been noted (Mattews et al., 1981) that amniotic cells have high levels of transferrin glycoproteins which may have a dual function: isolation from the immune system and angiogenic factors. This is not a surface phenomenon, since even when finely minced, the cell particles do not elicit any immune response (Trelford & Trelford-Sauder, 1979). Also, it is not a species dependent phenomena, since human amnion works very well on laboratory animals and bovine amnion is equally effective on human burn wounds (Walker, 1984).

Xenograft is a graft of tissue obtained from an animal of a species different from the recipient. Although many different types of animal skin have been tried (Park, 1978), the only

xenograft in common use is pigskin. Porcine xenograft is commercially available in fresh, fresh-frozen and lyophilised conditions, but the sterility and viability of some commercially available fresh and fresh-frozen porcine skins have been questioned (Levine et al., 1976). Frozen and lyophilised xenografts present problems in handling. Fresh-frozen skin must be kept refrigerated and thawed before use. Lyophilised xenograft has had moisture removed by freeze drying, and although it can be stored normally it must be reconstituted by soaking in sterile saline or Ringer's solution. Despite these problems, porcine xenograft is used commonly (Elliot & Hoehn, 1973) and is especially effective when applied early in partial thickness burns, provided that deep dermal and full thickness areas are not covered (Bromberg, 1983). Evaporative water loss can be reduced by over 80% (Lamke, 1971), pain is diminished and meshed porcine grafts are now being produced which are not as effective in reducing evaporative water loss but are preferable in the more heavily contaminated wounds because meshing allows for mechanical egress of the bacteria into the dressing (Bromberg, 1983).

Tissue-derived type dressings are the most recent addition in the biological category. Collagen has been used because it has the unique advantages that it can be isolated and purified in large amounts and manufactured into a variety of physical structures, its structure and immunological chemistry are well characterised, the antigenicity can be altered and it has haemostatic

properties. Collagen has been used in dressings as a collagen-fabric composite film (Guldallian et al., 1973), reconstituted collagen fibres (Peacock, 1961), reconstituted extruded strips (Copenhagen, 1965), reconstituted sheets on "Dacron" mesh (Tavis et al., 1975), reconstituted pure sheets (Abbenhaus & Donald, 1971), microcrystalline porous mats (Lorenzetti et al., 1972), microcrystalline sheets (Lorenzetti et al., 1973), dermal collagen allografts (Oliver et al., 1977), microcrystalline powder (Hait et al., 1969) and collagen sponge grafts (Chvapil, 1977).

"Biobrane" (Woodroof Laboratories, U.S.A.) is a bilaminate membrane with an outer layer of ultrathin silicone rubber (allowing water vapour transmission but impermeable to bacteria), mechanically bonded to a fine-knit, flexible nylon fabric. Type I porcine collagen is covalently bonded to the fabric to provide an inert hydrophilic mesh inner layer into which granulation tissue can grow. "Biobrane" has been used as both a burn wound and donor site dressing and has some relevant properties: control of evaporative water loss (by thickness), elasticity and it decreases pain (Woodroof, 1984). However, in a comparative study, Billiet and his colleagues (1984) found that "Biobrane" was not superior to "tulle gras," also many precautions must be taken, for example, creams have to be applied over the dressing, and it should not be used on infected wounds with bacterial counts greater than 10^5.

Yannas, Burke and their colleagues (1981) have developed an "artifical skin" composed of a temporary "Silastic" epidermis

and a porous bovine collagen-shark cartilage chondroitin-6-sulphate fibrillar dermis, which is not removed, but is slowly biodegraded and serves as a template for growth of host connective tissue to form a "neodermis." The dermal layer is readily populated with fibroblasts and capillaries from the wound bed. The glycosaminoglycan content is claimed to control the physical and biochemical properties (e.g. pore size, cross-link density, helical structure of collagen and collagenase resistance) and the epidermal analogue permits water flux at levels similar to normal skin and protects the wound from mechanical trauma and microbial invasion. The developers report successful use in the treatment of extensive burns (Burke et al., 1981), and they are now developing a modified version which will reduce the incidence of scarring or contraction (Yannas et al., 1981) and which could be used for indefintie periods of time.

"Dermodress" (Sagi et al., 1984) is prepared by removing the epidermis, hair and other components from bovine skin leaving a "dermis" composed of collagen type I. This is irradiated and preserved in collagen solution. It has been kept on wounds for up to 56 days, then replaced with autograft. This dressing is said to have good adherence, no infection, no rejection, no vascular ingrowth and may prove successful when more clinical trials are carried out.

The most recent line of development has been the tissue culture growth of epidermal cells obtained from the prospective recipient who will require grafting. Single cell suspensions of

Type	Material	Trade Name
Preformed films	3% Sulphadiazine (or 3% sulphanilamide), 2 5% methyl cellulose, 3% triethanolamine and 0.5% sorbitol	
	Poly(vinyl chloride)	Clingfilm Stretch n Seal Vitafilm
	Poly-2-hydroxyethyl methacrylate and poly(ethylene glycol) 400	Hydron
	Polyurethane	Op-site Tegaderm
	Polytetrafluoroethylene	
	Polyacrylonitrile	
	Polyethylene	
	Polypropylene	
	Poly(lactic acid)	
	Polycaprolactone	PCL 700
	Silicone rubber, polyvinyl cord	Saran Wrap
	60% Acrylic copolymer, 30% gelatin, 10% glycerol	Cynthaskin
Spray-on films	Poly-1-hydroxyethyl methacrylate and (polyethylene glycol)	Hydron
	Poly(vinyl chloride) dissolved in ethyl acetate and propanone	
	2-Ethoxyethyl methacrylate dissloved in ethyl acetate	Nobecutane
	Poly-ε-caprolactone in tetrahydrofuran	
Gels	Partially hydrolysed casein, sodium lactate and sodium lauryl sulphate polymerized in the presence of zinc acetate	
	Polypropylene and ethylene oxides	Pluronic F127
	Agar and polyacrylamide	Geliperm
	Hydrated poly(ethylene oxide)	Vigilon
Foams and sponges	Poly(vinyl alcohol)	Ivalon
	Polysiloxane	Silastic Foam
	Polyurethane	Lyofoam, Synthaderm
	Polyesterurethane, polyetherurethane and acrylic	
	Poly(vinyl alcohol) and formaldehyde	
Composites	Polyurethane foam/polypropylene film	Epigard
	Polydimethylsiloxane/nylon fabric	Biobrane
	Silicone rubber/nylon	IP-758
	Poly-ε-caprolactone film/poly-ε-caprolactone foam	
	Collagen/caprolactone	

Table 4.2 Synthetic dressings (Quinn et al., 1985b).

epidermal cells can be cultured on collagen film into mulilayered sheets (Eisinger et al., 1980), epidermal cells can be cultured until confluent sheets fill a 50 mm tissue culture disc (14-21 days), and be applied to full thickness burns (O'Conner et al., 1981), and Bell and colleagues have developed a "living skin equivalent" which is a composite consisting of a fibroblast-seeded collagen fibrillar lattice upon which dissociated epidermal cells are cultured and proliferate (Bell et al., 1981). However, the major disadvantage of these techniques is the time required to culture the cells, during which short-term dressings will be used, and further donor sites may become available (Quinn et al., 1985b).

4.3.3 Synthetic Dressings

The history of efforts to develop a purely synthetic non-biological dressing has been one of frustration. Beginning with the early work of Pickrell (1942) who made sulphonamide films, a vast array of materials has been studied (Table 4.2). Synthetic dressings can be classified into four categories: films (preformed and spray-on), gels, foams and composites (Figure 4.2).

4.3.3.1 Films. Films represent the most extensive group of synthetic dressings. The intention is to cover the wound such that bacterial invasion is prevented while water loss is controlled. Many of the early preformed films and sprays (Table 4.2) have been found to have poor adherence and high counts of bacteria (Salisbury, 1983), but three types have remained popular.

Poly (vinyl chloride) films ("Clingfilm," "Stretch'n Seal"

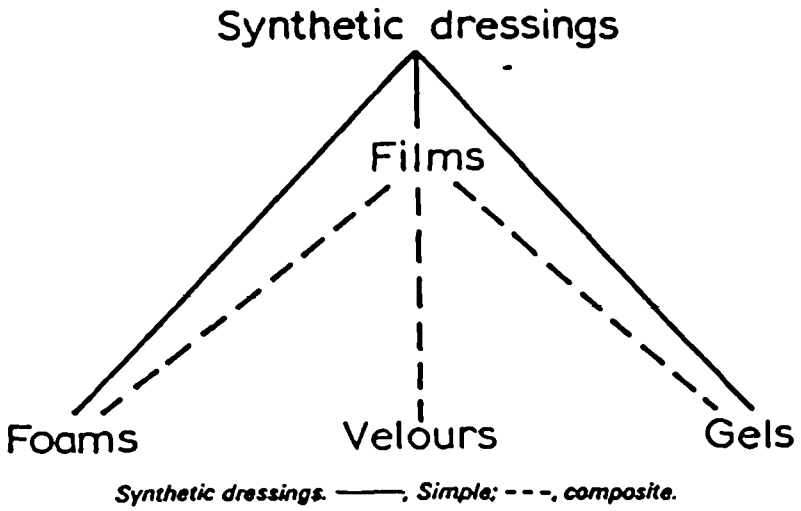

Figure 4.2 Synthetic dressings (Quinn et al., 1985b).

and "Vitafilm") have the desired flexibility and mechanical properties, however, their low water vapour transmission rates will lead to pooling of exudate under the dressing. Although these films are recommended for use on donor sites and partial thickness burns (Lendrum & Bowen-Jones, 1976; Townsend, 1976), they are probably more suitable as a "first-aid" temporary dressing.

The hydrophilic polyurethane film "Op-site" (Smith & Nephew, U.K.) has been used on partial thickness burns and donor sites. The film is impermeable to bacteria and, in addition to a reduction in pain, the rate of epithelialisation is increased (Neal et al., 1981). However, its water vapour transmission rate is low (Lamke et al., 1977) leading to fluid build up beneath the dressing (Townsend, 1976), and the film is very difficult to handle. Recently, the 3M company (U.K.) produced a polyurethane film ("Tegaderm") bounded by a frame to ease handling, but it has similar water vapour transmission characteristics to "Op-site" (Queen - personal communication). "Omiderm" is also composed of polyurethane with other hydrophilic components which confer a number of advantages (Golan et al., 1984), but because it has no absorptive capacity, fluid must be drained off, making it impractical in certain cases. Polyurethane films in the form of "gloves" have been used in the care of the burned hands because they are non-constrictive and allow free movement of the joints. Reid (1974) has reported on the care of hand burns using this technique with antibacterial creams inside the "glove" to control the

growth of bacteria in the wound.

"Cynthaskin" is a thin, flexible film prepared by mixing gelatine and glycerol in hot water and then stirring the mixture into an aqueous emulsion of acrylic copolymers; the mixture is then "evaporated" (Walliczek et al., 1982). The film has been used on donor sites and partial thickness burns. The films are durable, stable, reproducible, easily handled, control evaporative water loss, have high water phase permeability and act as a bacterial barrier. However, there is very little information available about the use of "Cynthaskin" clinically.

Spray-on films have been in existence since the 1950's and probably are most advantageous as first-aid dressings. However, only one has remained in use. "Hydron" dressing (Hydro Med Sciences & Hydron Laboratories, U.S.A.) is formed in situ on the burn wound by spraying the surface alternately with poly-1-hydroxyethylmethacrylate powder and liquid poly (ethylene glycol) 400 (Nathan et al., 1974; Nathan et al., 1975). Because it is formed on the wound there are no voids for exudate to accumulate and for bacteria to proliferate. Warren and Snelling (1980) found that the film frequently cracked, peeled or did not dry effectively leading to infection, but antimicrobial agents have now been incorporated into the film during preparation (Nathan et al., 1982). "Hydron" is also available as a preformed film.

Recently, a new composite dressing composed of poly-2-hydroxyethylmethacrylate, poly (ethylene glycol) 400, 5% dimethyl

sulphoxide has been developed with or without 2% silver sulphadiazine ("Dimac +" or "Dimac" respectively) and with a nylon backing (Nathan et al., 1984). However, there are little clinical data available to suggest whether or not it will become successful.

4.3.3.2 Gels. The advantages of the hydrophilic gels (silicone gel, discussed in chapters 7 & 8, is hydrophobic) are that they conform to the wound surface, they are impermeable to bacteria but are permeable to oxygen and water vapour, and antimicrobial agents can be incorporated within the material. However, the major disadvantage of the gels is their lack of durability, although for short-term coverage their ease of removal makes them appear very useful. Two gels have shown promise in the treatment of burns.

"Vigilon" (Bard, U.K.) is an inert, cross-linked hydrogel consisting of 96% water and poly (ethylene oxide). There is a thin polyethylene film over each surface of the gel; the film is removed from the side which is applied to the wound. "Vigilon" is permeable to oxygen and water vapour, and is absorbent (Mandy, 1983). However, it is recommended only for minor partial thickness burns (Spenc & Bates, 1981).

"Geliperm" (Geistlich, U.K.), a hydrophilic gel composed of agar and polyamide, was developed in 1977 by Wokalek and his colleagues (Wokalek et al., 1979) and has many properties similar to the ideal dressing (Myres, 1983), for example, absorbency, conformability, non-adherency, permeability to oxygen and water vapour. However, it should not be used on infected or necrotic

wounds, it must be kept hydrated with saline and must be kept covered with an absorptive compress (even though the gel is absorbent) and be held in place with a self-adhesive bandage (Geistlich product information).

4.3.3.3 Foams and sponges. The advantages of foams and sponges are threefold: they are absorbent, their thickness provides protection against mechanical injury and they are less expensive (and easier to apply) than conventional dressings (Davies, 1983a).

The "Ivalon Sponge," composed of poly (vinyl alcohol), was intensively studied and used in the 1960's by Chardack (Chardack, 1962; Chardack et al., 1962) and more recently by Mutschler and his colleagues (1979), but many problems arose from its use in animal studies. Autograft "take" was poor and fragments of "Ivalon" were found in the underlying tissue. Even though newer versions of the sponge have been produced it remains only for use in mass disaster situations because of the ease of stockpiling in sterile form, ease of application and low cost (Davies, 1983a).

"Lyofoam" (Ultra Laboratories, U.K.) is a polyurethane foam manufactured from a soft polyether foam which is subjected to further processes of heat and pressure to form a smooth, hydrophilic, porous surface membrane designed to be placed next the wound. Burn wounds on pigs healed more rapidly when "Lyofoam" was compared with dry cotton gauze (Winter, 1975), and, partial thickness wounds and donor sites have been found to heal without interruption beneath "Lyofoam" (Davenport et al., 1977). Unfortunately, very little clinical data are available to show whether or not

this dressing could be used successfully on human burn wounds.

4.3.3.4 Composites. Velour fabrics bonded to films have been widely used (Table 4.2), but they allow fluid to become trapped where bacteria can proliferate.

"Epigard" (Parke-Davies & Company, U.S.A.) is composed of an inner layer of reticulated polyurethane foam laminated to an outer sheet of microporous polypropylene film. The dressing firmly adheres to the wound bed and debrides the wound when removed leaving clean granulation tissue onto which autograft skin can be applied (Alexander et al., 1973; Mahnke et al., 1980). However, this form of debridement can be disadvantageous since the granulation tissue may also be removed. The other disadvantage appears to be that the foam does not absorb "toxic factors" from the burn wound (Scholmerich et al., 1981). Varients of "Epigard" using polytetrafluoroethylene film (Kleine-Natrop & Sebastian, 1979) or polyurethane film (Silverstein & McDonough, 1977) have also been recommended.

"Melolin" (Smith & Nephew, U.K.), is a non-adherent dressing comprising three bonded layers: a perforated clear polyester film, an absorbent pad of cotton and acrylic and a low linting non-woven fabric backing. It has been used in burn treatment with silver sulphadiazine spread on its surface (Settle, 1974).

A dressing which has just become available comprises an outer protective layer of pectin, methyl cellulose and other materials. The dressing, "Granuflex" (Squibb Surgicare, U.K.), is absorbent, impermeable to bacteria and adhesive, and may

prove to be useful in the treatment of small burns (Lawrence & Shah, 1984).

CHAPTER 5

DESIGN OF A BURN DRESSING

5.1 OBJECTIVES

The primary objectives in the management of burn wounds are to prevent infection and to (permanently) close the wound. Large full thickness burns rarely heal spontaneously and therefore require a new permanent cover. This permanent cover should be a piece of the patient's own skin, harvested as a sheet of split-thickness skin from an unburned site. However, before grafting, the wound bed must be ready to accept the graft. Therefore some other cover is required to prepare the wound for grafting. Similarly, dressings should allow healing of partial thickness burns to occur without interference. Dressings should therefore create an environment to allow the wound healing processes such as formation of granulation tissue, wound contraction and epithelialisation to occur.

5.2 CRITERIA

The requirements of a burn dressing are reviewed in chapter 4. In this chapter, the requirements are discussed with a view to establishing the critical criteria in quantitative terms, thus defining the "ideal" burn dressing.

5.2.1 Fluid Balance

The wound surface should be kept just damp to obtain the benefits of accelerated healing (Winter, 1970), but there should

be no pooling of fluid between the wound and the dressing because of the risk of infection. These factors can be obtained by materials with both absorptive and water vapour transmission properties and are considered in detail in 5.4. However, the quantity of fluid lost from a burn by exudation has not been clearly defined since previous data were obtained by repeatedly weighing the patient (Davies et al., 1974) therefore how absorptive a dressing should be has yet to be defined.

Similarly, although the evaporative water loss from a burn wound has been measured in situ (Lamke et al., 1977), the ideal water vapour transmission rate of a dressing is not known. The rate should be limiting to partially concentrate the exudate, but should not dessicate the wound. The claim that the water vapour transmission rate should be equal to that of normal skin (Lamke et al., 1977) applies only to long-term skin substitutes rather than short-term dressings.

5.2.2 Mechanical Characteristics

The mechanical properties of the "ideal" dressing also need to be defined, although it requires to be as elastic as normal skin (Quinn et al., 1985b) to cover joints and allow movement. Obviously, the dressing should be durable enough to allow normal activities without breaking down.

5.2.3 Gas Transmission

The importance of oxygen in wound healing has not been universally recognised. However, it has been observed that wounds heal poorly and are difficult to infect at high altitude where the oxygen tension is low, and heal quickly in oxygen enriched atmospheres

(Silver, 1985).

It has been noted (Silver, 1972) that when the wound surface is moist and relatively free of exudate, epidermal healing is faster under oxygen-permeable occlusive dressings in the presence of oxygen than in hypoxic conditions. However, in venous stasis ulcers where commonly there is gross bacterial contamination and large amounts of exudate, Silver (1972) found that, irrespective of dressing oxygen-permeability, almost all the oxygen disappeared from the surface of the lesion within one hour of dressing application. This is due to bacterial and inflammatory cell oxygen uptake preventing oxygen reaching the wound surface. This rate of uptake is such that even the most oxygen-permeable dressing was unable to transmit enough gas to penetrate the epidermis

Fibroblasts are aerobic cells and require oxygen for division and collagen synthesis. Both collagen synthesis and the development of early wound strength are critically dependent on oxygen supply (Silver, 1985) but, unlike the epidermis, fibroblast activity is stimulated by moderately elevated pO_2 only, and is reduced if the tension is increased further. However, this may be associated with the reduced blood supply (capillaries proliferate towards low pO_2 regions) and therefore substrate limitation which occurs in hyper-oxygenated tissue, rather than a direct effect of oxygen on fibroblasts (Silver, 1985).

In conclusion, oxygen is a necessary component for rapid and effective wound healing although it has a greater influence on epidermal cells than on those of the connective tissue. Excessive

amounts of oxygen may inhibit connective tissue repair, and the oxygen-permeability of a dressing will have little influence on the conditions at the wound surface unless the surface is kept relatively free of exudate, particularly if the exudate contains large numbers of inflammatory and bacterial cells.

5.2.4 Other Considerations

The other requirements of the "ideal" burn dressing (ease of application and removal, adherence, comfort, haemostatic, non antigenic and non toxic, and sterilisable) cannot be quantified but must be considered in the design of a dressing. However, the importance of the bacterial barrier cannot be over emphasised, and the incorporation of antibacterial agents will depend upon the structure and material of the dressing.

5.3 LIMITATIONS OF THE DRESSINGS AVAILABLE TODAY

All the dressings available today cater for some of the requirements of an "ideal" burn dressing. Conventional gauzes and fabrics have excellent absorptive properties, protect the wound from mechanical damage and will remain in use because of their low cost and ease of storage.

Biological dressings, because of their nature, approach the ideal coverage, but porcine xenografts have been found to have problems in handling, viability and cost (Bromberg, 1983). Similarly, amnion is too thin to be durable. Thus, cadaver allograft remains the optimum biological dressing (Pruitt & Levine, 1984) but it to has problems such as availability, immune rejection and infection.

The recent developments where biological derivatives are combined with synthetic materials may prove to be very useful in the future. Yannas and Burkes' artificial skin is promising although its preparation might preclude its use on economic grounds, whereas clinical data have suggested that "Biobrane" has limited application (Billiet et al., 1984). "Dermodress" may become beneficial since it is relatively easy to prepare and store. However, the tissue culture type dressing, which can be defined as a type of skin graft, may be advantageous in the future, but the time taken to "grow" dressings is the major drawback as is the lack of clinical data at the present time.

The vast range of synthetic dressings that has been tried reflects the interest in this subject. The earliest type of synthetic dressings, the films, provide gaseous exchange, elasticity, bacterial barrier, but their water vapour transmission characteristics are not sufficient to halt pooling beneath the dressing leading to infection. Gels will take the shape of the wound, adhere with easy removal, are absorbent and can be used as vehicles for antimicrobial agents, but they lack durability. Foams and sponges have absorbent qualities and water vapour transmission characteristics, but they allow ingrowth of epithelium which leads to secondary trauma when removed. Composites comprising different layers appear to be the best solution, and some, such as "Melolin" (Smith & Nephew, U.K.) which have different layers with different properties, are leading in the right direction in the development of the "ideal" dressing.

Table 5.1 Non renal water loss from patients with burns (Davies et al., 1974).

	RATE OF LOSS ml $cm^{-2}day^{-1}$		
WOUND	WEEK 1	WEEK 2	WEEK 3
Partial Thickness	0.45	0.30	0.25
Full Thickness	0.35	0.30	0.30

Table 5.2 Evaporative water loss from burn injuries (Lamke et al., 1977).

	E.W.L.		
WOUND	g $m^{-2}h^{-1}$	ml $cm^{-2}day^{-1}$	
Normal Skin	8.5	0.020	
First Degree	11.6	0.028	
Second Degree	178.1	0.427	(Deep partial thickness)
Third Degree	143.2	0.344	(Full thickness)

5.4 ABSORBENCY AND WATER VAPOUR TRANSMISSION CHARACTERISTICS OF THE "IDEAL" BURN DRESSING

Previous researchers (Davies et al., 1974:; Lamke et al., 1977) have described the non-renal, non-respiratory fluid loss in burned patients (Tables 5.1 & 5.2). Although the results were obtained by different means (see 5.2.1) there is a similarity between them. However, neither describes the accurate day-to-day fluid loss nor the area of burn nor the time of dressing application.

The fluid lost from a burn can be absorbed or evaporated (or both) by a dressing. However, up to three litres/day of fluid loss by evaporation can be accepted. If the loss exceeds three litres/day, the energy requirements for evaporation are greater than the basal heat production of a normal adult (Davies, 1982). This can be overcome by controlling room temperature and other external energy sources.

The influence of dressing characteristics on the extent of burn injury that can be tolerated without exceeding the maximum allowable evaporative fluid loss of 3 litres/day will be determined. Deep partial thickness and full thickness burns will be considered. The amount of fluid produced by the injury is assumed to be equal to the corresponding evaporative water loss value from Lamke and colleagues (1977). Two types of dressing are considered:

1. A dressing with no absorptive property i.e. it possesses only a water vapour transmission characteristic. This situation is typical of hydrophobic film type dressings.
2. A dressing with a nominal absorptive capacity of 0.1 ml $cm^{-2}day^{-1}$

and a water vapour transmission rate (WVTR) that is not affected by the hydration state of the dressing. This condition is approached by hydrogel materials with a rate limiting cover film. This absorptive capacity is approximately three times that of both "Vigilon" and "Geliperm" (Bard and Geistlich product information).

5.4.1 Dressing With No Absorptive Characteristics

In this case the rate of fluid production by the burn must be evaporated via the dressing otherwise pooling of fluid would occur. The dressing WVTR is thus:

1. For partial thickness injury (PT) WVTR = 0.427 ml $cm^{-2}day^{-1}$
2. For full thickness injury (FT WVTR = 0.344 ml $cm^{-2}day^{-1}$

The fluid loss from the body is thus the sum of the evaporative water loss through the intact skin (EWL_s) and the water vapour transmitted via the burn wound i.e. through the dressing. Therefore, for a total body surface area of A_T the fluid loss is related to the extent of burn, B (% of total area) by:

$$\text{Fluid loss} = EWL_s \times A_T \left(1 - \frac{B}{100}\right) + WVTR \times A_T \times \frac{B}{100}$$

For an adult of 2.0 m^2 surface area and EWL_s = 0.02 ml $cm^{-2}day^{-1}$ (Table 5.2) the fluid loss is therefore:

For PT injury, fluid loss = 0.4 + 0.0814B l/day

For FT injury, fluid loss = 0.4 + 0.0648B l/day

These relationships are shown by the solid lines in Figure 5.1 (PT injury) and Figure 5.2 (FT injury). If the evaporative loss is not to exceed 3l/day the maximum extent of burn injury is limited to 32% and 40% for partial thickness and full thickness respectively.

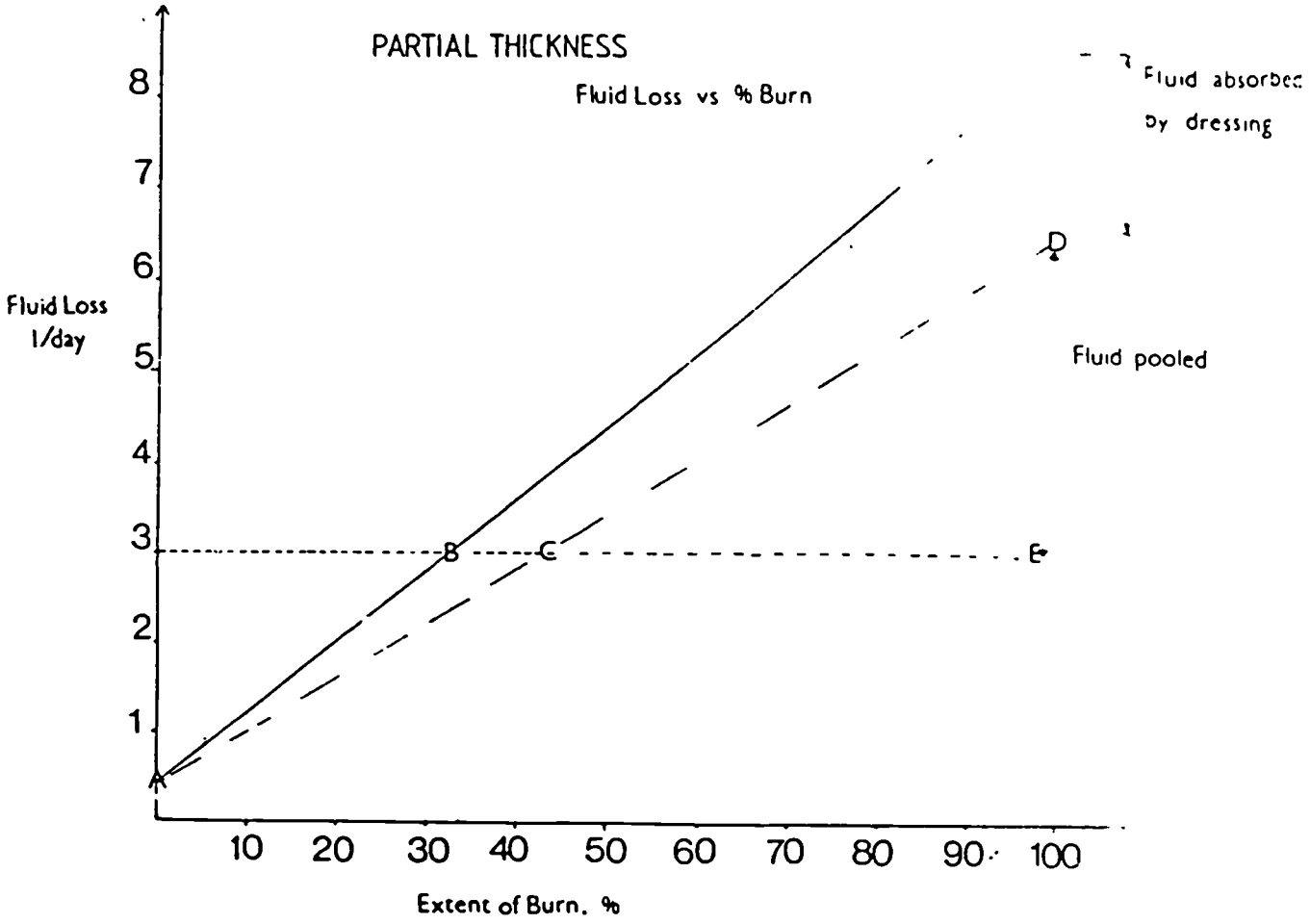

Figure 5.1 Graph of fluid loss vs. extent of burn for a partial thickness injury. Also plotted is the graph of fluid loss after a dressing with an absorptive capacity of 0.1 ml $cm^{-2}day^{-1}$ has been applied.

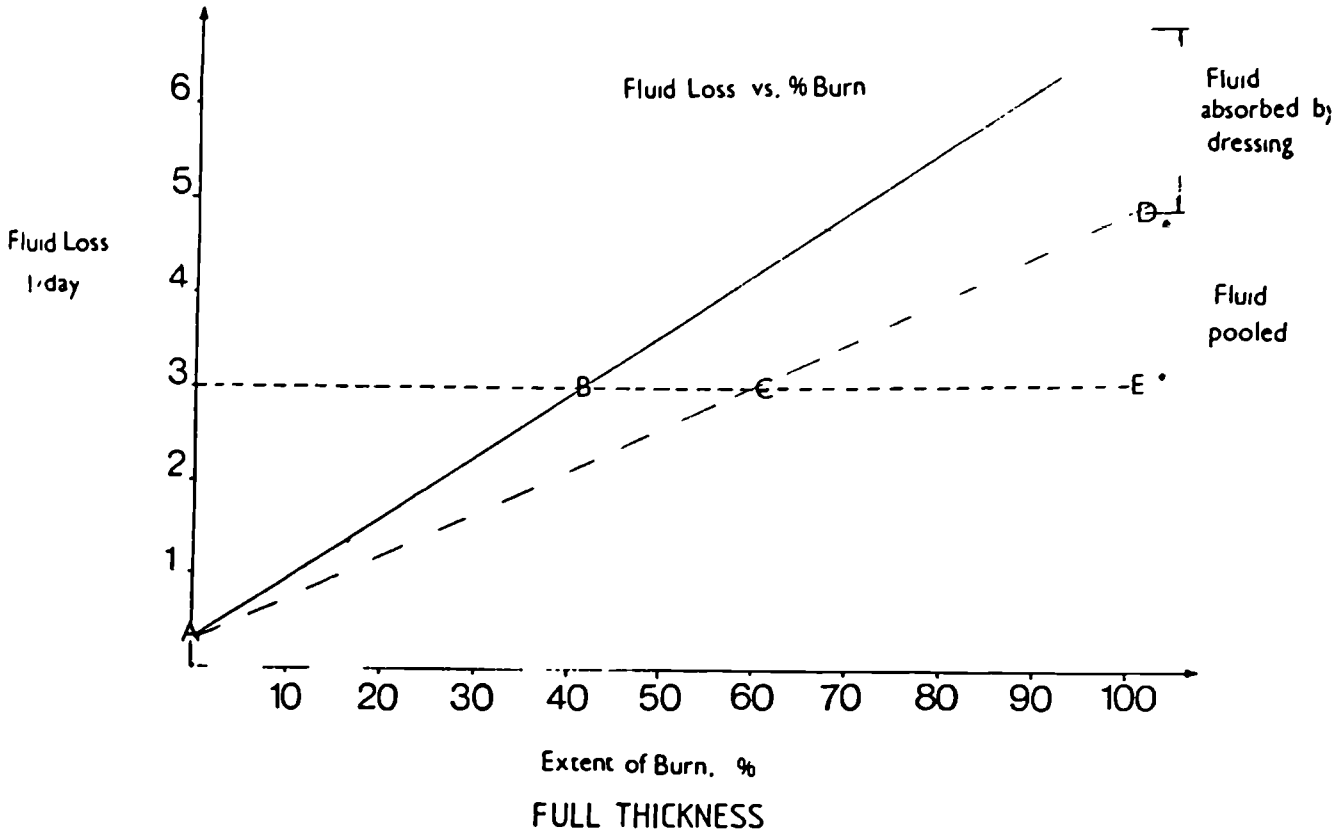

Figure 5.2 Graph of fluid loss vs. extent of burn injury for a full thickness wound. Also plotted is the graph of fluid loss after a dressing with an absorptive capacity of 0.1 ml $cm^{-2}day^{-1}$ has been applied.

5.4.2 Dressing With An Absorptive Rate of 0.1 ml $cm^{-2}day^{-1}$

The amount of fluid produced for evaporative loss (solid lines in Figures 5.1 & 5.2) is reduced to a level shown by the dotted lines in these Figures due to the absorption of fluid by the dressing. The amount absorbed varies linearly with extent of burn and is 2.0 l/day for 100% burn.

The effect of dressing absorptive capacity is to increase the burn area consitent with limiting the evaporative fluid loss to 3 l/day. For PT and FT injuries the liriting burn extents are 42% and 58% respectively. At these levels corresponding WVTR's of the dressing should be 0.327 ml $cm^{-2}day^{-1}$ and 0.244 ml $cm^{-2}day^{-1}$ respectively. Comparison with the WVTR's for the dressing with no absorptive capacity (5.4.1) shows a reduction in the WVTR requirement.

5.4.2.1 Partial thickness injury. From Figure 5.1 four regions may be identified:

1. Along line AB, burns not exceeding 32% can be left exposed without an unacceptable energy loss (or covered with a dressing with WVTR = burn EWL).
2. Along line AC, burns not exceeding 42% can be dressed with materials with an absorbent capacity of 0.1 ml $cm^{-2}day^{-1}$ and a WVTR sufficient to remove remaining fluid, with no unacceptable energy loss.
3. Along line CE, burns greater than 42% can be dressed with materials with an absorbent capacity of 0.1 ml $cm^{-2}day^{-1}$ and WVTR characteristics which will restrict the loss to

Table 5.3 WVTR of a dressing with an absorptive capacity of 0.1 ml $cm^{-2}day^{-1}$ associated with a 3 l/day evaporative water loss (total body surface area) for a PT injury.

% BURN	AMOUNT ABSORBED ml/day	FLUID LOSS INTACT SKIN ml/day	WVTR $ml/cm^2/day$	AMOUNT POOLED ml/day
42*	840	232	0.327	0
75	1500	100	0.193	2000
100	2000	0	0.150	3540

* Limit for pooling

Table 5.4 WVTR of a dressing with an absorptive capacity of 0.1 ml $cm^{-2}day^{-1}$ which will remove all fluid exudate from partial thickness burns.

% BURN	AMOUNT TO BE EVAPORATED* ml/day	FLUID LOSS INTACT SKIN ml/day	WVTR $ml/cm^2/day$
42+	3000	232	0.327
75	5000	100	0.327
100	6540	0	0.327

* Through intact skin and dressing

\+ Limit for acceptable energy loss

Table 5.5 WVTR of a dressing with an absorptive capacity of 0.1 ml $cm^{-2}day^{-1}$ associated with a 3 l/day evaporative water loss (total body surfacc area) for a FT injury.

% BURN	AMOUNT ABSORBED	FLUID LOSS INTACT SKIN	WVTR	AMOUNT POOLED
	ml/day	ml/day	$ml/cm^2/day$	ml/day
58*	1160	168	0.244	0
75	1500	100	0.193	760
100	2000	0	0.150	1880

* Limit for pooling

Table 5.6 WVTR of a dressing with an absorptive capacity of 0.1 ml $cm^{-2}day^{-1}$ which will remove all fluid exudate from full thickness burns.

% BURN	AMOUNT TO BE EVAPORATED*	FLUID LOSS INTACT SKIN	WVTR
	ml/day	ml/day	$ml/cm^2/day$
58+	3000	168	0.244
75	3760	100	0.244
100	4880	0	0.244

* Through intact skin and dressing

\+ Limit for acceptable energy loss

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three litres/day (Table 5.3), but pooling will be present.

4. Along line CD, burns greater than 42% can be dressed with materials which remove all fluid exudate (Table 5.4). No pooling will be present but there will be an unacceptable energy loss.

5.4.2.2 Full thickness injury. From Figure 5.2 the same deductions can be made as in 5.4.2.1, only the figures vary:

1. Burns not exceeding 40% can be left exposed without an unacceptable energy loss (or covered with a dressing with WVTR = burn EWL).
2. Burns not exceeding 58% can be dressed with materials with an absorbent capacity of 0.1 ml $cm^{-2}day^{-1}$ and a WVTR to remove remaining fluid, with no unacceptable energy loss.
3. Burns greater than 58% can be dressed with materials with an absorbent capacity of 0.1 ml $cm^{-2}day^{-1}$ and WVTR characteristics which will restrict the loss to 3 l/day (Table 5.5), but pooling will be present.
4. Burns greater than 58% can be dressed with materials which remove all fluid exudate (Table 5.6). No pooling will be present, but an unacceptable energy loss will be incurred.

5.4.3 Conclusion

The calculations demonstrate that dressings with different properties are required for different degrees of burn injury. However, they do not allow for the presence of mixed depth burns. Also, neither environmental conditions nor the application of topical antibacterial agents have been accounted for. Since the figures available are for adults, the type of dressing described may not be entirely relevant to the management of burned children.

Further clinical investigations are necessary to determine the day-to-day fluid loss from both adults and children in different environmental conditions before the "ideal" dressing can be accurately quantified.

Figure 6.1.

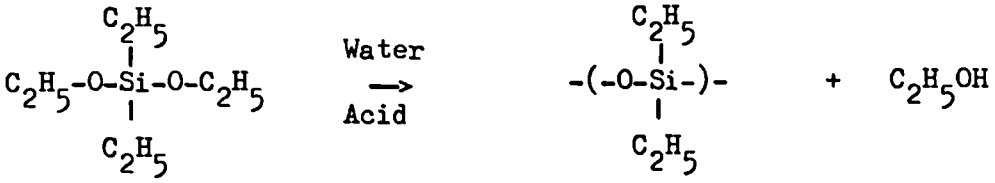


Figure 6.2.

CHAPTER 6

SILICONES

6.1 INTRODUCTION

An important feature of polymer develpoment has been the emergence of the polysiloxanes or silicones. Because of their general thermal stability, good electrical insulation characteristic consistency of properties over a wide temperature range, water-repellency and anti-adhesive properties, the silicone polymers have a wide diversity of applications, ranging from gaskets for jet engines to various medical applications. The polymers are available in a number of forms such as fluids, greases, rubbers and foams.

The original preparations of organosilicone compounds involved the reaction of hydrochloric acid with silicon and carbon to produce trichlorosilane, and the reaction of zinc diethyl with silicon tetrachloride to produce tetraethylsilane (Figure 6.1). The first silicone polymer was produced by reacting diethoxydiethylsilane with water in the presence of acid (Figure 6.2) (Brydson, 1982).

Although the basis of modern silicone chemistry was laid by Professor F.S. Kipping at the University College, Nottingham between 1899 and 1944, who made a number of valuable contributions to the modern silicone industry, he did not forsee the commercial value of his researches (Brydson, 1982).

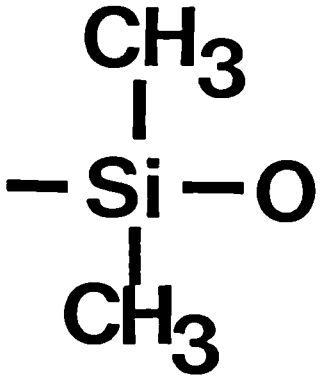


Figure 6.3 The dimethylsiloxane unit.

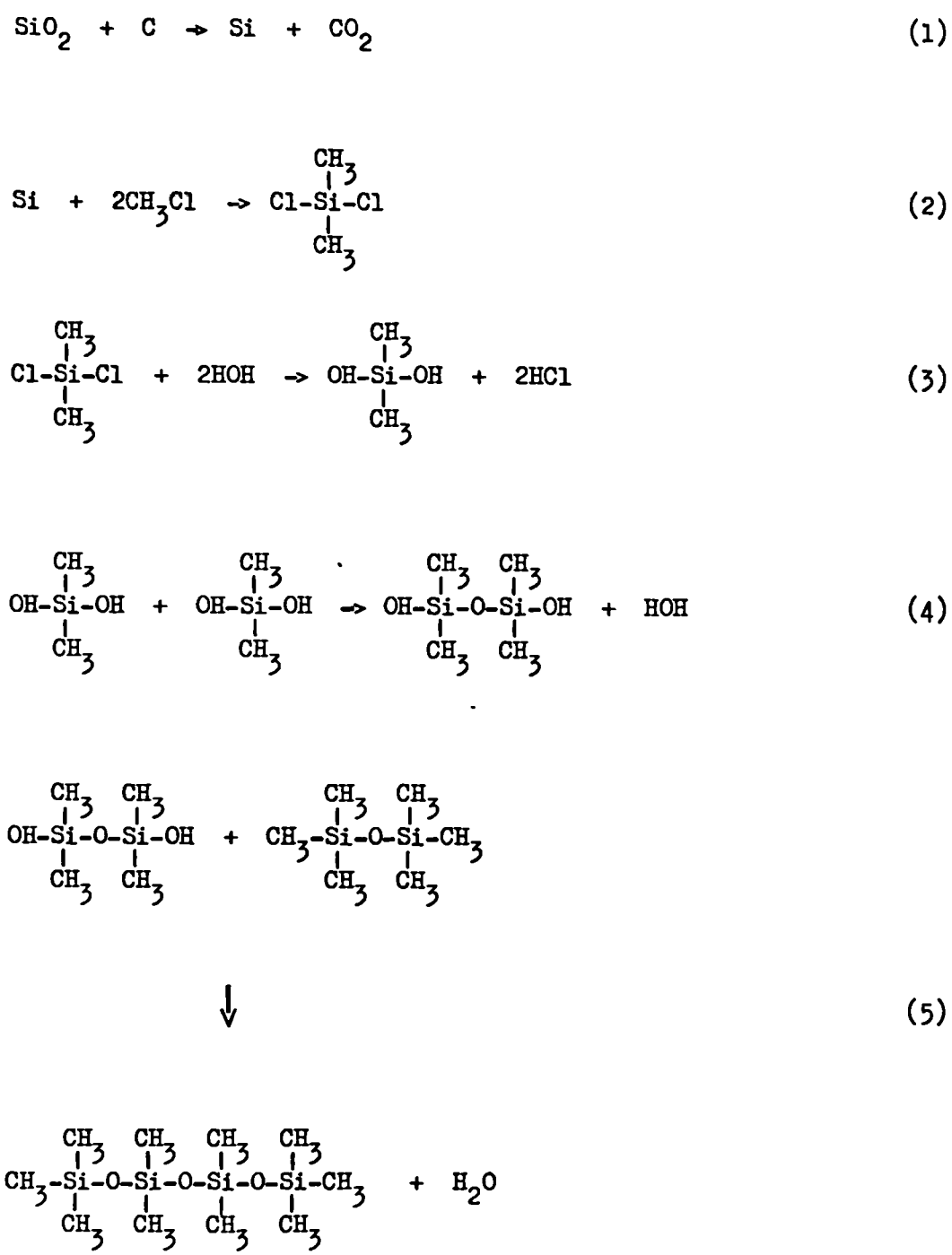


Figure 6.4 (Braley, 1968; Braley, 1970).

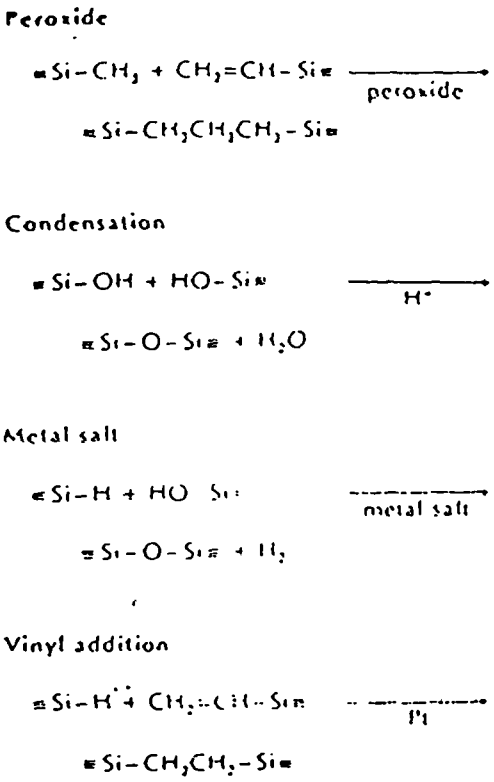


Figure 6.5 Silicone curing systems (Arkles & Redinger, 1983).

Table 6.1 Viscosity of polydimethylsiloxane as determined by the length of polymer chain (Braley, 1968).

Viscosity	Approximate $\left[\begin{matrix} CH_3 \\ | \\ -SiO- \\ | \\ CH_3 \end{matrix} \right]$ Units
.65 cs	2
1.00 cs	3
2 cs	5
10 cs	16
50 cs	46
100 cs	70
350 cs	130
1,000 cs	200
10 million cs	3,000

Table 6.2 Silicone substitutions (Arkles & Redinger, 1983).

Name	Structure	Application
methyl	CH_3	Basic substitution found in virtually all silicones: a crosslinking point with peroxide cures.
silicone	HO ≡	Crosslinking point for condensation and metal catalysed crosslinking.
hydride	H ≡	Introduces metal - catalysed and vinyl addition crosslink sites.
vinyl	CH_2=CH -	Increases peroxide reactivity; introduces crosslink points for vinyl addition.
phenyl	C_6H_5-	Increases modulus, thermal stability and UV stability; decreases reactivity with peroxides.
trifluoropropyl	$CF_3CH_2CH_2$-	Increases stability; increases solvent resistance.

6.2 CHEMISTRY

The basic structure of the medical silicones consists, essentially, of repeating linear chains of dimethyl-siloxane polymers (Figure 6.3). They are produced by converting silica to silicon (Figure 6.4.1) which is then treated with methyl chloride to form dimethyl dichlorosilane (Figure 6.4.2). The latter reacts with water to form an unstable diol (Figure 6.4.3) which spontaneously condenses to form a silicone polymer terminated by hydroxyl groups (Figure 6.4.4). If hexamethyl-disiloxane is added and the mixture equilibrated, polymers endblocked by methyl groups (Figure 6.4.5) and with predetermined average molecular weights can be obtained. These materials are clear water-white fluids, with the length of the polymer chain determining the viscosity of the group (Table 6.1) (Braley, 1968; Braley, 1970a).

A variety of groups, including phenyl, vinyl and hydrogen can be substituted for the methyl group in a silicone (Table 6.2). This is significant since the substitution, branching and molecular weight of a silicone polymer dictate the method by which curing or crosslinking can be accomplished. Fundamentally, there are four processes employed to cure silicones (Figure 6.5). In high temperature vulcanizing (HTV) systems, polymers containing methyl or vinyl groups are crosslinked with peroxides. In room temperature vulcanizing (RTV) systems, two cure methods are used. In the older methods, silanols are condensed with a moisture sensitive silane crosslinker or a metal salt catalyzed reaction

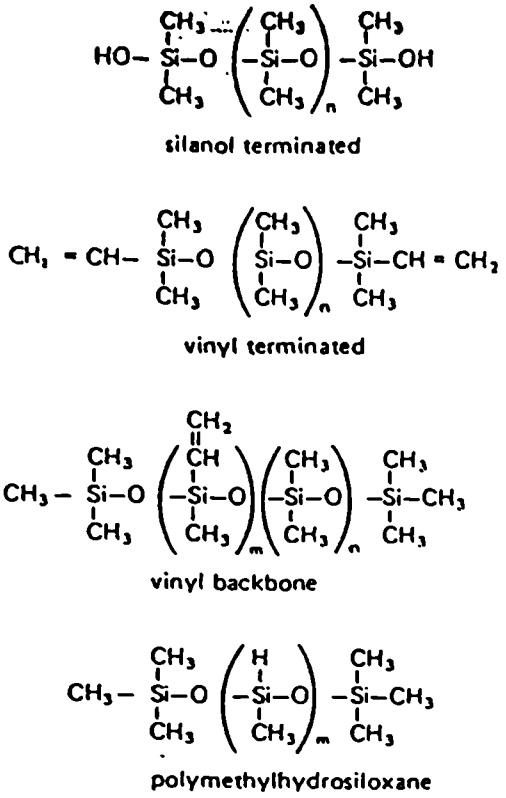


Figure 6.6 Silicone prepolymers (Arkles & Redinger, 1983).

between silicon hydrides and silanols takes place. The latter reaction liberates hydrogen which can be used to produce foamed products. Vinyl addition systems, in which a platinum complex catalyses the addition of silicone hydrides to vinyl substituted silanes, was initially used in low temperature vulcanising (LTV) systems but has been gradually extended to RTV's and HTV's (Arkles & Redinger, 1983).

Two general methods are used to produce silicone polymers. Gums and non-silanol terminated fluids are produced by base catalyzed (anionic) polymerization. Under typical conditions, potassium, sodium, or tetramethylammonium silanolate catalysts are introduced into a mixture of monomers and terminators. The mixtures are equilibrated by heating under moderate conditions (60-150°C). Silanol terminated polymers are produced by a variety of techniques including hydrolysis of chlorosilanes with water or indirectly with methanol and metal salt catalysed telomerisation of cyclics with low molecular weight silanol fluids which act as chain terminators (Sorenson & Campbell, 1968). Typical reactive silicone polymers are shown in Figure 6.6. They include silanol, vinyl and hydride functional materials of various degrees of polymerization.

Most silicones are filled with particulate silica, which has a reinforcing effect on silicone elastomers resulting in increased modulus, tensile strength, tear strength and abrasion resistance. The reinforcing effect depends on three properties of the filler: particle size, structure and surface interaction.

The particle size, together with the filler loading, determines the area available for surface interaction. The structure determines the extent polymer movement is restricted under deformation. The surface interaction determines the effectiveness with which particle size and structure control elastomer properties. Parameters associated with surface interaction include population and type of hydroxyl groups, adsorbed moisture and chemical treatment. It is postulated that the redistribution of stress among polymer chains in reinforced systems is accomplished by two-dimensional mobility of polymer chains that are otherwise bound tightly to the silica surface.

Chemical treatment of silica may greatly change its interaction with silicone polymers. Fumed silica behaviour can be altered by inactivating the isolated silanol groups with various silanes. Materials used to modify surface characteristics include hexamethyldisilazane, divinyltetramethylsilazane and cyclic and short linear siloxanes. Under-treatment of silica results in "crepe hardening," a characteristic condition in which uncured elastomer exhibits crumbling rather than plasticity under applied stress. Over-treatment of filler results in non-responsive or "dead" elastomers. High tear strength elastomers result from filler treatments which introduce vinyl groups.

6.3 PROPERTIES

The term "silicone rubber," widely used to describe silicone polymers, covers a range of materials with an equally broad range of properties. The properties of silicone rubbers depend

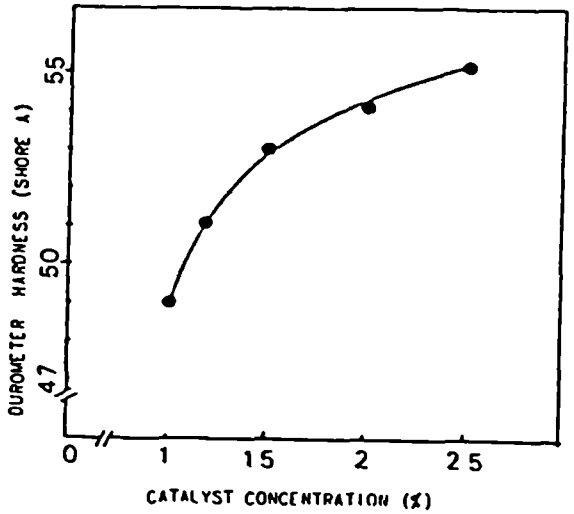


Figure 6.7 The effect of catalyst concentration on the durometer hardness of silicone elatomer (Devanathan, 1983).

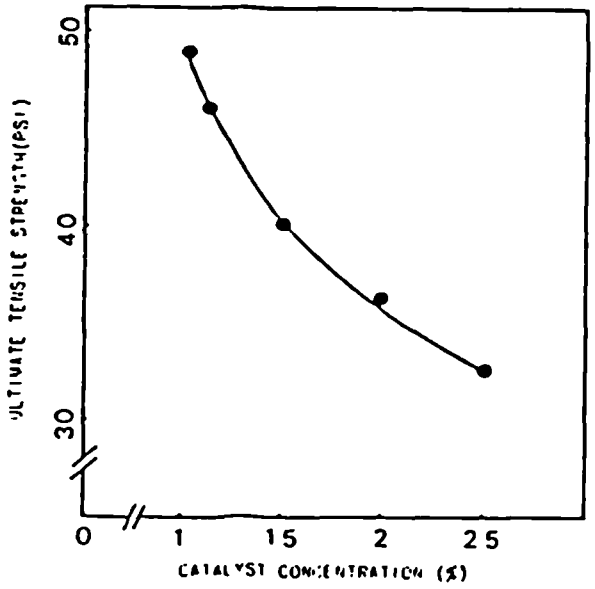


Figure 6.8 The effect of catalyst concentration on the ultimate tensile strength of silicone elastomer (Devanathan, 1983).

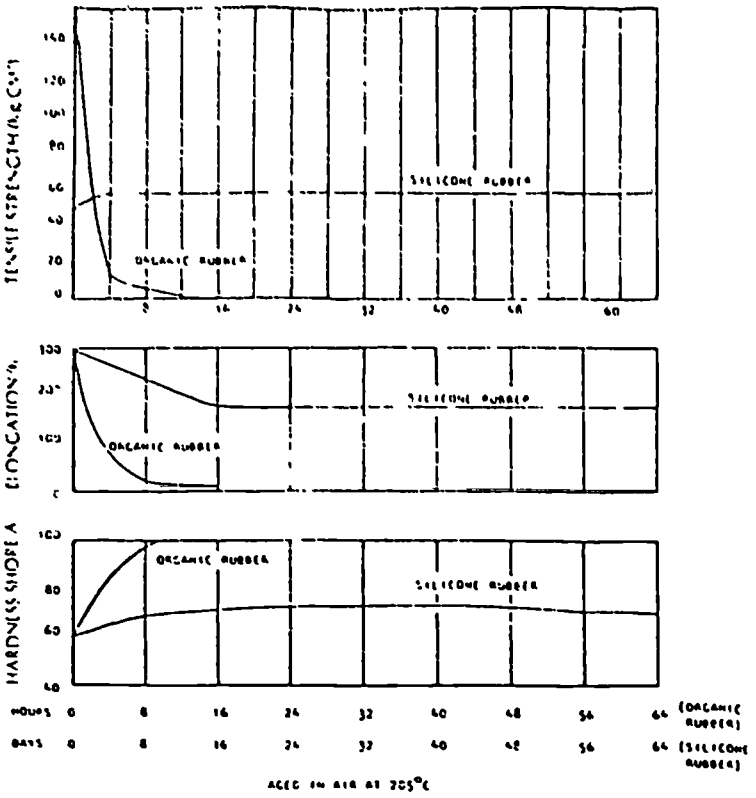


Figure 6.9 Effects of heat ageing on a "heat resistant" organic rubber and a silicone rubber of identical initial hardness (Gajewski, 1983).

upon the composition and conditions of the curing procedure (van Noort et al., 1977).

6.3.1 Mechanical Properties

In general, silicone rubbers are not as strong as organic elastomers. However, in addition to the utilisation of reinforcing filler, properties such as hardness, ultimate tensile strength and ultimate elongation can be enhanced by control of catalyst concentration (Figures 6.7 & 6.8) and cross-linking density (Gajewski, 1983; Devanathan, 1983).

6.3.2 Thermal Properties

In contrast to the mechanical properties, silicone polymers are superior to organic elastomers with respect to thermal properties (Figure 6.9).

Silicone rubbers are outstanding in their ability to retain their properties after exposure to heat. After heating to 150°C, there is little or no change in the properties when then stored at room temperature (Hampson, 1969). This means that they can be autoclaved or dry-heat sterilised without adversely affecting their properties (van Noort et al., 1977).

Flexibility at low temperatures can be enhanced by using silicone gums containing phenyl groups. Silicone rubber is superior to commonly used "low temperature" organic rubbers.

6.3.3 Chemical Properties

The chemical resistance of silicone rubber is excellent for aqueous systems, i.e. acids, bases and salts at room temperature.

Table 6.3 Chemical resistance of methyl-vinyl silicone

(Cajewski, 1983

Material	Weight Change %	Volume Change %	Durometer Change Points
ACIDS			
Nitric conc	+10	+10	-30
Nitric 7%	-1	-1	-2
Sulfuric conc.		DISINTEGRATES	
Sulfuric 10%	-1	<1	-2
Acetic conc.	+2	+3	-4
Acetic 5%	+4	+4	-8
Hydrochloric conc.	+1	+1	-6
Hydrochloric 10%	+2	+4	-4
Hydrochloric 3%	-1	+1	-2
BASES			
Sodium Hydroxide 20%	<1	<1	-2
Sodium Hydroxide 1%	<1	<1	-4
Ammonium Hydroxide conc.	+2	+2	-4
Ammonium Hydroxide 10%	+3	+2	-6
SALTS			
Sodium Chloride 10%	<1	<1	-2
Sodium Carbonate 2%	<1	<1	0
SOLVENTS			
Ethyl Alcohol	+5	+6	-10
Acetone	+5	+15	-15
Toluene	+75	+120	-30
Gasoline, Regular	+65	+130	-25
Gasoline, Aviation	+60	+110	-30
Mineral Spirits	+65	+110	-30
Carbon Tetrachloride	+130	+110	-25
OILS			
Caster Oil	<1	<1	-4
Lard Oil	<1	<1	-4
Linseed Oil	<1	<1	-2
Mineral Oil	+5	+6	-6
ASTM #1 Oil[2]	+3	+5	-6
ASTM #3 Oil[2]	+20	+31	-20
Silicone Oil SF96 (100)[2]	+25	-35	-25
Silicone Oil 42,000 cstk.[2]	+9	+10	-12
OTHER			
Water	<1	<1	<1
Hydrogen Peroxide 3%	<1	<1	<1
Pyranol 1476	+4	+4	-8

Table 6.4 Gas permeabilities in dimethyl silicone rubber (25°) (Robb, 1968).

Gas	$P_r \times 10^6$ $\left[\frac{\text{cc gas (RTP) cm}}{\text{sec, sq cm, cm Hg } \Delta P}\right]$	Gas	$P_r \times 10^6$ $\left[\frac{\text{cc gas (RTP) cm}}{\text{sec, sq cm, cm Hg } \Delta P}\right]$
H_2	65	C_2H_4	135
He	35	C_2H_2	2640
NH_3	590	C_3H_6	410
H_2O	3600	$n\text{-}C_4H_{10}$	900
CO	34	$n\text{-}C_5H_{12}$	2000
N_2	28	$n\text{-}C_6H_{14}$	940
NO	60	$n\text{-}C_7H_{16}$	860
O_2	60	$n\text{-}C_8H_{18}$	430
H_2S	1000	HCHO	1110
Ar	60	CH_3OH	1390
CO_2	325	$COCl_2$	1500
N_2O	435	Acetone	586
NO_2	760	Pyridine	1910
SO_2	1500	Benzene	1080
CS_2	9000	Phenol	2100
CH_4	95	Toluene	913
C_2H_6	250		

Data on weight change, volume change and hardness change (durometer) are shown in Table 6.3 after one week immersion of the test specimen at 25°C.

Silicone rubber, however, has an affinity for certain organic solvents such as ether, chloroform and toluene which cause it to swell. This phenomenon of swelling is complex and depends upon factors such as degree of cure, the amount and kind of filler, the nature of the solvent, and the duration of exposure (van Noort et al., 1977).

6.3.4 Permeability

At room temperature, silicone rubber has a high permeability to gases (Table 6.4). This high permeability is applied in the design of membrane oxygenators and other gas separation devices.

6.3.5 Biocompatibility

The common use of additives to achieve specific properties in most industrial elastomers has the disadvantage of potential adverse effects of eluting components. Therefore, in tailoring silicones for medical use, the approach has been to minimise complications by keeping the system as simple and inert as possible. Crosslinking agents must be chosen carefully since they significantly infuence the properties of the finished rubber.

6.3.5.1 Toxicity. Laboratory tests on a wide variety of animals have shown that silicones in general have an insignificant toxicity (Rowe et al., 1948; Kern et al., 1949; MacDonald et al., 1960; McGregor, 1960). A study of the toxicity of silicone rubbers compared with catgut, cotton, polythene and poly (vinyl acetate)

in animal tissues showed silicone rubbers to have the least irritation (Curreri et al., 1952). However, the low molecular weight methyl siloxanes can be irritating to the eyes. Some residual low molecular weight polymer is invariably present in silicone rubbers but various studies have shown that this does not leach out of the material (Swanson & LeBeau, 1974; van Noort et al., 1979). In general, the high molecular weight silicones exhibit no toxic effects and any toxicity resulting from their use is likely to be due to the presence of additives or the incomplete removal of catalyst byproducts than to the rubber itself (van Noort & Black, 1981).

6.3.5.2 Tissue compatibility. Experimental evidence has established that silicone rubbers are biologically inert in that no adverse tissue response is produced when used for prostheses (Braley, 1963; Mullison, 1964; Geha et al., 1970). Fibrous connective tissue grows in response to the foreign material and completely encapsulates the prosthesis in a fibrous sheath. No adhesion of the fibrous sheath to the silicone rubber takes place. Two different layers of the fibrous sheath can be discerned (Pablo et al., 1974); an inner layer composed of polyhedric cells, irregularly orientated and arranged in a single row at the surface of the implant, and an outer layer composed of fibroblasts, collagen, and reticular fibres. This fibrous tissue reaches maturation at approximately 4-6 weeks with numerous discrete thick bundles of collagen and reticular fibres. By this stage, the inner surface has a glistening, smooth, white appearance

and the fibrous sheath is highly flexible and elastic. This property of silicone rubber has been used in an effort to produce autogenous grafts for replacement of the aortic valve (Geha et al., 1970) and vena cava (Padula et al., 1969).

Although it is seemingly inert, there have been a number of recent reports of adverse tissue reaction to silicone rubber. This tissue reaction has been associated with the presence of small granules of the rubber between collagen bundles and within the cytoplasm of histiocytes around the implant. This is most commonly a complication of mammary augmentation resulting in constrictive fibrosis, requiring surgical correction (Smahel, 1977; Wilflingseder et al., 1978). Some believe it to be caused by the abrading of small particles off the rubber envelope of the prosthesis (Wilflingseder et al., 1974; Domanskis & Owsley, 1976). Others suggest it is due to silicone gel escaping from the silicone rubber envelope (Hausher et al., 1978; Rudolph et al., 1978). There has also been a report of an inflammatory response resulting from the presence of particulate silicone rubber in relation to broken prostheses after implantation of metacarpophalangeal joints (Aptekar et al., 1974; Christie et al., 1977). The growth of a calcific deposit around and on implanted silicone rubber prostheses has also been observed and can result in the need to replace the implant (Bayston, 1978).

6.3.5.3 Blood compatibility. The problem of finding suitable materials for use in the cardiovascular system is that when blood comes in contact with foreign surfaces biochemical reactions

occur at the material-blood interface which lead to thrombus formation.

Although silicone rubber has been shown to have a blood compatibility superior to most other materials, it too will ultimately cause thrombus formation (Akutsu et al., 1963; Nose et al., 1964; Gradel et al., 1966; Nosé, 1967; Mason et al., 1969; Honda et al., 1975; Mason et al., 1976). Platelet adhesion is the first observable stage in the reaction sequence leading to the formation of a thrombus. In the natural system the heart and blood vessels have a lining of endothelial cells which prevent the initiation of the clotting mechanism. However, when a foreign surface is placed in contact with the blood, platelets from the blood start adhering almost immediately. Aggregation of the platelets occurs and results in the formation of a thrombus.

When a material is in contact with blood for relatively short periods of time, as in renal dialysis and haemoperfusion, the problem has been alleviated by administering anticoagulants to the patient or heparinizing the blood contacting surfaces (Whiffen & Gott, 1964; Whiffen et al., 1964). The heparinization of silicone rubber surfaces resulted in prostheses remaining nonthrombogenic for several weeks but ultimately these prostheses failed since the heparin gradually leached out (Leininger, 1966; Uy & Kammermeyer, 1969; Leininger et al., 1972).

It has been observed that for certain polymers there is a correlation between surface tension and blood compatibility i.e. the lower the critical surface tension, the more blood

compatible the material (Baier et al., 1968; Baier, 1972; Newman et al., 1975). It has been suggested that the low surface tension for silicone rubber, due to the closely packed methyl side groups at the surface, is the reason for its superior blood compatibility (Olsen et al., 1973). This is apparently confirmed by observations which show that silica filler, which has a high critical surface tension when exposed on the surface, reduces the blood compatibility of silicone rubber (Nyilas et al., 1970), and a number of reports have established beyond doubt that superior blood compatibility is achieved when silicone rubber free of silica filler is used (Kolobow, 1974; Weatherby et al., 1975; Zapol et al., 1975; Chawla, 1976). Modification of the surface properties by developing copolymers of dimethyl siloxane with trifluoropropylmethyl siloxane, phenyl methyl siloxane, and others have shown that the polydimethyl siloxane is superior in terms of blood compatibility (Hoffman et al., 1970; Ratner & Hoffman, 1973; Fredecki, 1974; Hoffman, 1974).

It has now been well established that when a synthetic material contacts blood a layer of protein is adsorbed onto the surface within a matter of seconds (Brash, 1969; Dutton et al., 1969). This adsorption of protein is a critical step in the interaction of blood with an artificial surface (Szycher, 1983) since platelets cannot adhere to a nonphysiological substrate without this preconditioning layer of proteins (Scarborough et al., 1969). In general, contact of blood with an artificial surface leads to protein adsorption, platelet adhesion and activation of the intrinsic coagulation, with the response of

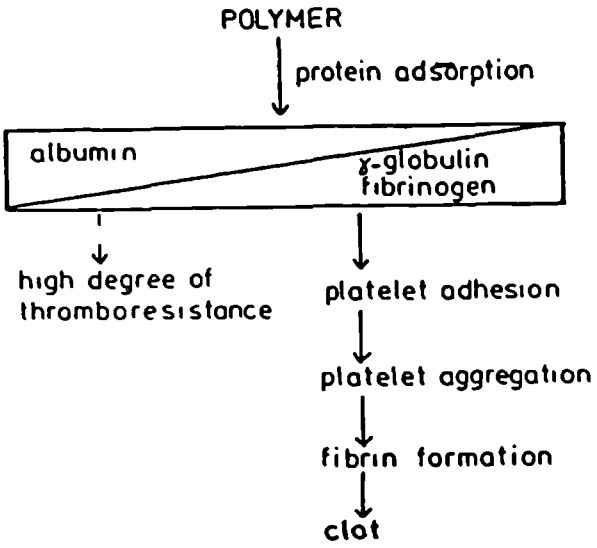


Figure 6.10 Suggested sequence of events at the blood-polymer interface leading to the formation of a thrombus (van Noort & Black, 1981).

platelets and coagulation factors influenced by the nature of the adsorbed protein layer (Feijen, 1977).

The composition of the adsorbed protein layer has a controlling influence on subsequent blood-material interactions (Baier et al., 1971; Lyman et al., 1974). With respect to the influence on platelets, the proteins which have received most attention are albumin, fibrinogen and γ globulin. The consensus drawn from numerous investigations is that platelet accumulation onto surfaces is enhanced by prior adsorption of fibrinogen or γ globulin and inhibited by prior adsorption of albumin (Figure 6.10) (Packham et al., 1969; Salzman et al., 1969; Zucker & Vroman, 1969; Lyman et al., 1970; Jenkins et al., 1973; Whicher & Brash, 1978; Absolom et al., 1979; Neumann et al., 1979; Adams & Feurstein, 1980). When blood comes into contact with a foreign surface, plasma proteins are adsorbed onto the surface rapidly and selectively to form a layer about 100nm thick. Fibrinogen is preferentially adsorbed as compared to albumin, globulin, lipoproteins and coagulation factors (Vroman et al., 1972). Fibrinogen strongly attracts platelets but it soon undergoes conformational change and becomes less reactive (Vroman et al., 1980).

Silicone rubber has been shown to have a preferential affinity for albumin adsorption as have the segmented polyurethanes, suggesting that the superior blood compatibility of these materials over others is related to the adsorbed protein layer which itself is determined by the surface structure and properties of the silicone rubber (Lee & Kim, 1974; Lyman et al., 1974). This

has been taken a step further by chemically coating silicone rubber with albumin in order to improve the blood compatibility and results so far are encouraging (Guidoin et al., 1976).

6.3.5.4 Stability. In addition to being acceptable to the physiological environment, silicone rubber should not deteriorate in this environment. A lack of acute toxicological or inflammatory response is not necessarily indicative of long-term viability in the physiological environment.

There have been many reports suggesting that gradual deterioration of silicone rubber can occur, leading to serious failure of prostheses such as artificial heart valves (Starr et al., 1966; McHenry, 1970; Hawher, 1971; Hylen et al., 1972; Morgan, 1973; Oparah et al., 1975) and finger joints (Swanson, 1968; Meesters & Swanson, 1972). It has been shown that silicone rubber absorbs lipids from the blood (Chin et al., 1971) and it has been suggested that failure of implants may be due to the uptake of lipids (Boone & Braley, 1966; Raible et al., 1966; Kien, 1974). McHenry and colleagues (1970) found an average increase in the weight of silicone rubber balls, as used in Starr-Edwards heart valve prostheses, of 10% for 5 patients with occluded valves. All occluders analysed showed yellowing, opacity and swelling, commonly referred to as ball-variance. These observations have been confirmed by others (Mayshan & Biolsi, 1973; Moacanin et al., 1973). In vitro techniques to test for lipid absorption could only reproduce low levels of this phenomenon. A study of the surface of silicone rubber occluders by Allwork and Norton (1976) revealed the presence

of microscopic cracks in both new and used occluders. It is possible that these microscopic cracks provide a route whereby the lipids can enter the occluders. This suggests that ball-variance can be eliminated by removing the surface microcracks, although it is likely that microcracks will ultimately occur due to abrasive wear. This would explain why ball-variance tends to be a late post-operative complication, the abrasive wear producing and expanding microcracks, which are subsequntely invaded by lipids (Boone & Braley, 1966; Homsey, 1970).

In subdermal implants such as artificial finger joints, the high levels of lipid absorption have not been encountered (Meesters & Swanson, 1972). Nevertheless, a significant number of prostheses have failed due to cracking or complete fracture, although in vitro test data predicted extreme longevity for these prostheses (Weightman et al., 1972). These results would suggest that lipid absorption is not the cause of failure in these cases, and that abrasive wear is more likely (Aptekar et al., 1974). This seems to be confirmed by studies carried out by Swanson and LeBeau (1974) and van Noort and his colleagues (1979) which showed that the increase in sample weight due to lipid absorption stabilized after 4 weeks of implantation, while properties did not change until 6 months after implantation. Both studies showed a significant change in properties after 9 months of subcutaneous implantation suggesting that the silicone rubber is attacked by the physiological environment. It has also been shown that when the calcific deposit which often occurs

Table 6.5 Examples of the medical applications of silicones.

MEDICAL SPECIALITY	APPLICATION	REFERENCES
Nervous system	Hydrocephalus shunt	Nulsen & Spitz, 1952; Pudenz et al., 1957; Anderson, 1959; Overton & Snodgrass, 1965; Rayport & Reiss, 1969; Kirsch et al., 1970; Bayston, 1976; Swanson, 1977; van Noort & Bayston, 1979; Frisch, 1983.
	Nerve cap	Swanson, 1977.
Cardiovascular & Respiratory Systems.	Aortic valve	van Noort & Black, 1981.
	Arterial prostheses	Ashton, 1969; McCaughan, 1969.
	Femoro-popliteal arterial grafts	Sparkes, 1973.
	Membrane lung	Burns, 1969; Bruck, 1973; Kolobow, 1974; Weatherby et al., 1975; Kolobow et al., 1976; Kolobow & Spragg, 1978.
Uro-genital system	Artificial ureter	de Nicola, 1950; Djurhuus et al., 1974.
	Penile implants	Loeffler & Sayegh, 1959; Lash et al., 1964; Loeffler et al., 1964; Lash, 1968; Small et al., 1975; Small, 1976; Finney, 1977.
	Artificial bladder	Peters, 1970; Stanley, 1972.
	Artificial sphincter	Kaufman & Raz, 1975; Rosen, 1976.
	Catheters	Seabury & Boyarsky, 1968; Gibbons et al., 1974.

Table 6.5 continued.

MEDICAL SPECIALITY	APPLICATION	REFERENCES
Orthopaedics	Finger joint implants	Swanson, 1968; Niebauer et al., 1969; Beckenbaugh et al., 1976; Swanson & Herendon, 1977; Wenger & Whalley, 1978.
	Carpal bone implant	Roca et al., 1976; Eiken & Holmqvist, 1977.
	Temporomandibular joint cap	Sanders et al., 1977.
	Tendon replacement	Hunter, 1965; Bader & Curtin, 1968.
	Development of a tendon sheath prior to tendon grafting	Urbaniak et al., 1976; Mahoney et al., 1976; Eskeland et al., 1977.
Ophthalmics	Contact lenses	Arkles & Redinger, 1983.

on silicone rubber is removed, a badly pitted surface is revealed (van Noort et al., 1979) and since silicone rubber is extremely sensitive to the presence of surface flaws, this could cause a substantial reduction in mechanical properties. The form of this attack is not clear, but it is possible that phospholipids or phosphatides may be involved since these can react with the Si-O bond in the backbone of the silicone rubber (Chan, 1973). It is this interaction of the physiological environment with the silicone rubber which may contribute to the failure of a large number of silicone rubber subdermal prostheses (van Noort & Black, 1981).

6.4 MEDICAL APPLICATIONS OF SILICONES

The advantages of using silicones for medical applications are:

1. Suitability for autoclaving
2. Minimal deterioration of properties with time
3. Adhesion only with the use of silicone adhesives
4. Minimal tissue reaction caused by medical grade silicones
5. Ability to resist attack by the body and metabolism by other organisms (Braley, 1968).

These advantageous properties of silicones have led to a widespread medical use. Examples of medical applications are listed in Table 6.5 and illustrated in Figures 6.11 to 6.16. The utilisation of silicones in this thesis is related to controlled release systems and plastic and reconstructive applications, and these are considered in more detail.

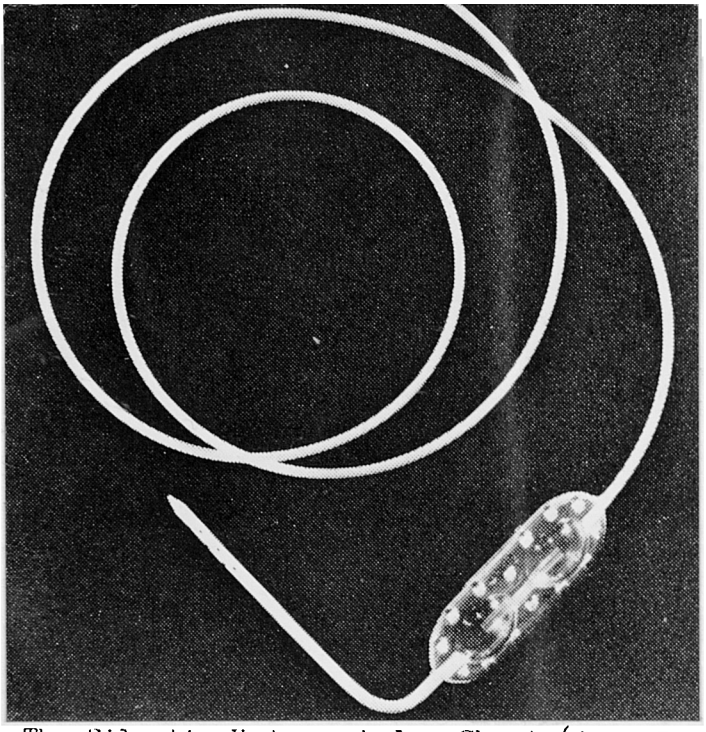


Figure 6.11 The Silastic Hydrocephalus Shunt (Ames Design) is designed to maintain proper intracranial pressure by serving as a drain for excess cerebrospinal fluid.

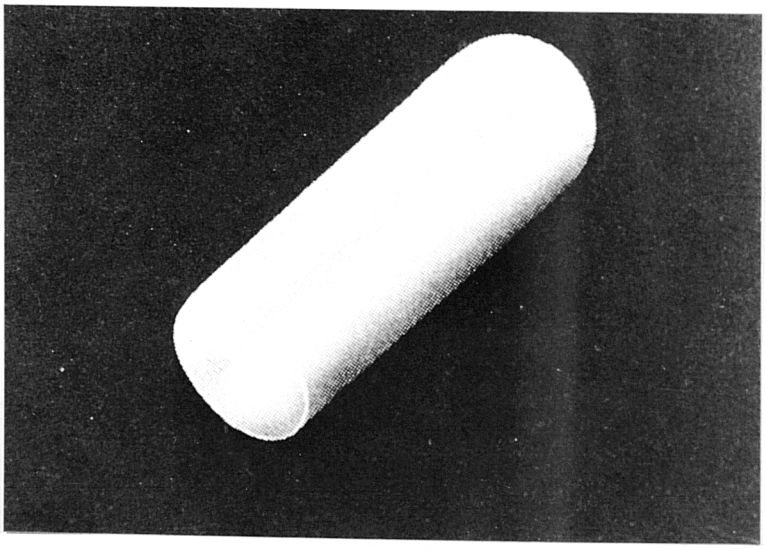


Figure 6.12 The Silastic Nerve Cap (Swanson-Ducher Design).

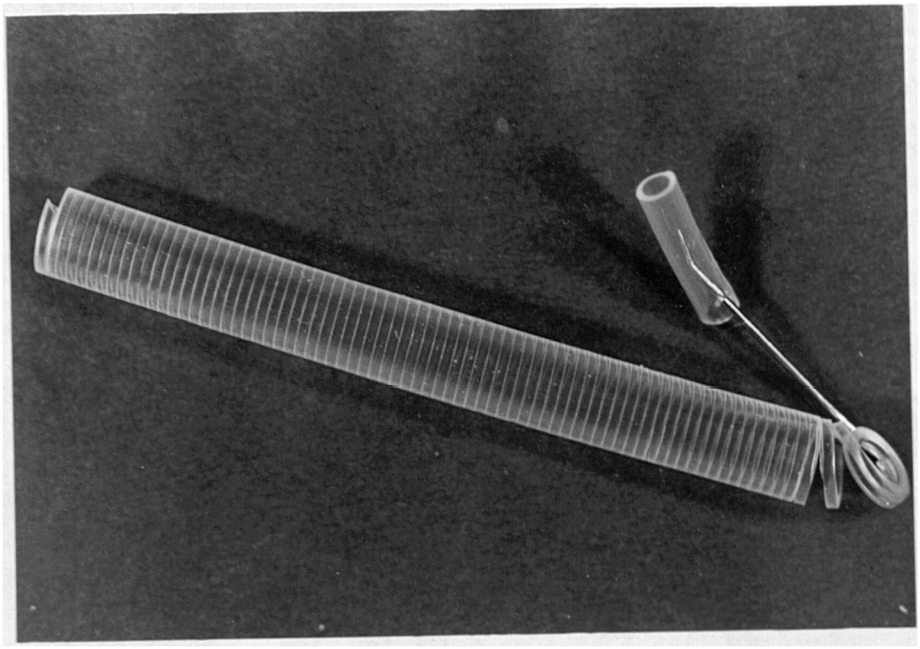


Figure 6.13 The Vascutek Shunt (Helix).

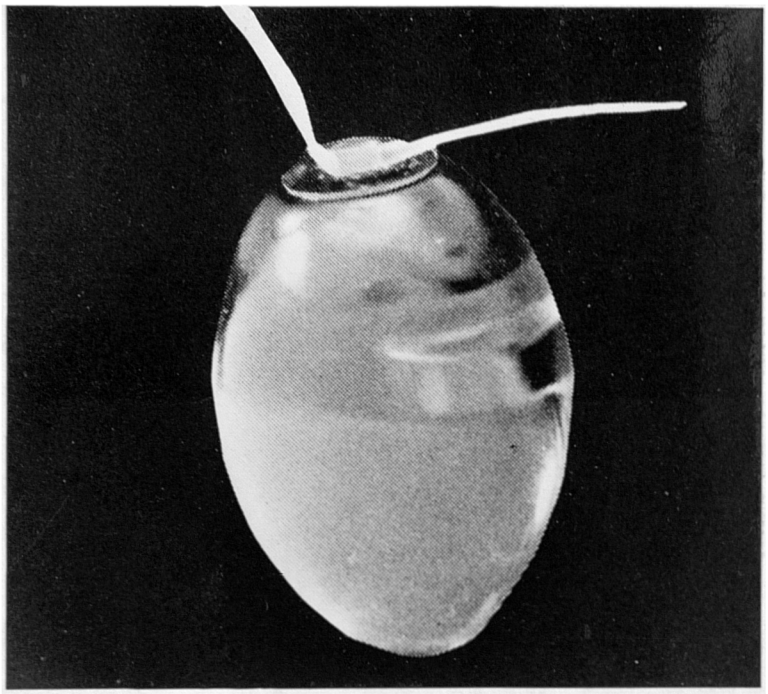


Figure 6.14 The Silastic Gel-Filled Testicular Implant (Lattimer Design) is a natural feeling medical grade implant which approximates the weight, size and soft consistency of the normal testicle.

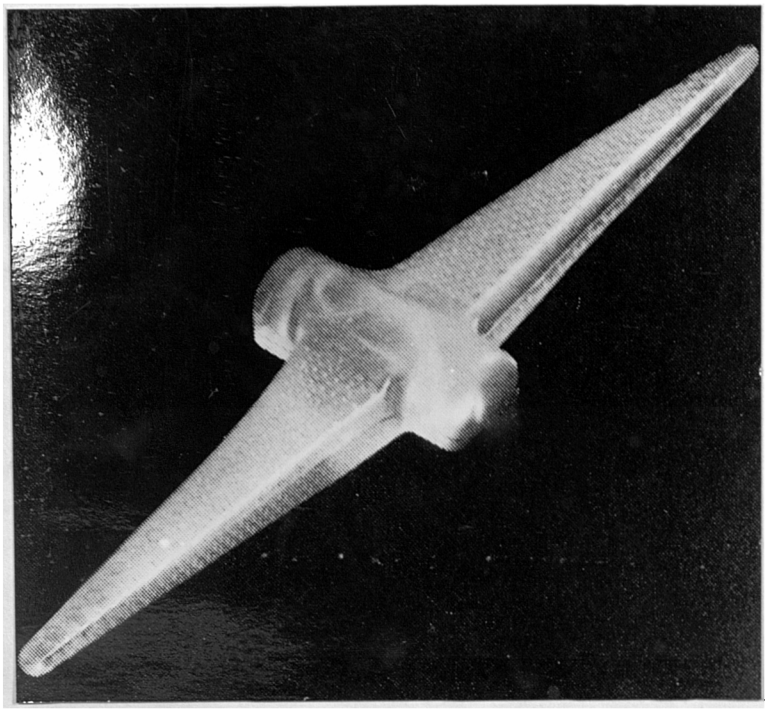


Figure 6.15 The Silastic Finger Joint Implant (Swanson Design).

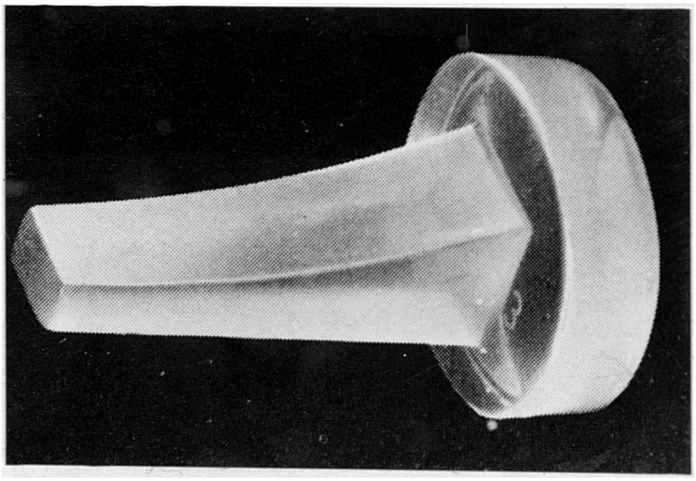


Figure 6.16 The Silastic Great Toe Implant (Swanson Design) is a pliable, one-piece, intramedullary-stemmed implant developed to overcome the disadvantage of shortening, occasional instability or painful stiffening which may follow standard arthroplasty procedures of the great toe.

6.4.1 Controlled Release Systems

In 1964, Folkman and Long reported the use of silicone rubber in sustained release formulations (Folkman & Long, 1964; Long & Folkman, 1966). Sustained release delivery systems based on the remarkable diffusion properties of silicone polymers have been shown to have many applications in medicine. A variety of chemical substances e.g. atropine and histamine (Bass et al., 1965), anaesthetics (Folkman & Mark, 1968), steroids (Roseman, 1972), chlorquine (Fu et al., 1973), indomethacin (Gaginella & Vallner, 1975), antibacterial agents (Morain & Vistnes, 1976) and pyrimethamine (Graham & Wood, 1984) have been administered both locally and systemically via silicone-releasing systems in a number of clinical situations.

6.4.2 Plastic and Reconstructive Surgical Applications

The employment of silicones in plastic surgery has become standard practice for certian procedures and their potential uses are increasing.

6.4.2.1 Silicone fluid. Silicone fluids have been used for soft tissue augmentation by injection. This technique has been used to treat patients with hemifacial atrophy, mandibular hypoplasia, depressed facial scars, superior maxillary retrusion, facial lipodystrophy, post-traumatic facial depression, pectus excavatum and frown lines (Blocksma, 1972);scars on soles and digits (Balkin, 1977); breast augmentation (Kopf, 1966); age associated furrows, perioral radial creases, wrinkled and thinned skin of the neck and of the dorsal surfaces of the hands that have

undergone age and actinically associated changes (Selmanowitz & Orentreich, 1977).

The response of tissue to silicone fluid injection has been characterised by Rees and Colleagues (1965). Microscopically, there is a mild inflammatory reaction, characterised by a round cell infiltration which subsides within six months. After massive doses, the injected material becomes encapsulated in delicate thin-walled spherical or ellipsoid spaces lined with flattened endothelium-like cells of connective tissue. Moderate fibrosis persists around these cyst-like structures for six months, and occasionally giant cells are observed. In terms of long-term effect, microscopic examination has revealed no significant chronic inflammatory response, though there has been evidence of varying degrees of mild chronic inflammation, including an apparent increase in the collagen content of dermal fibrous tissue, some disruption of dermal and subdermal architecture, a moderate number of macrophages, some lymphocytes and an occasional giant cell (Rees, 1983).

There are problems associated with injections of silicone fluid. These include infection, migration of fluid, cyst formation, and degrees of skin involvement from pigmentation to gangrene (Kopf et al., 1976). Many of these problems are, however, commonly associated with impure silicone fluid (Chaplin, 1969; Braley, 1970b; Kopf et al., 1976; Selmanowitz & Orentreich, 1977). These complications led to Dow Corning only supplying the material to approved investigators (Braley, 1971).

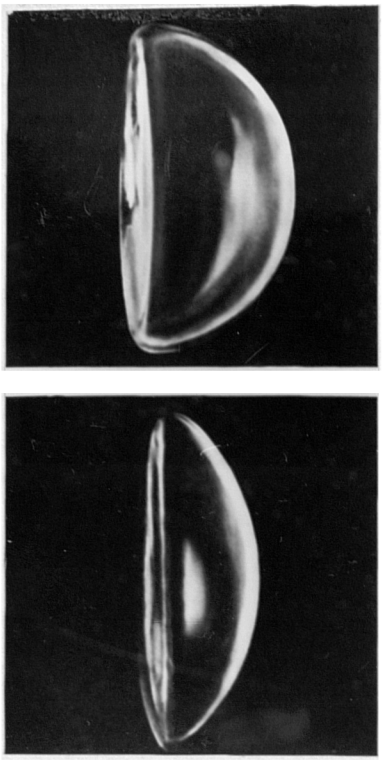


Figure 6.17 The Silastic Mammary Implant (Gel-Filled Round Design) is used in cosmetic augmentation mammoplasy or prosthetic restoration following subcutaneous mastectomy. The silicones are formulated to provide an implant that most approximates the weight, softness and mobility of the normal breast while conforming to the desired surgical pocket and overlying tissue.

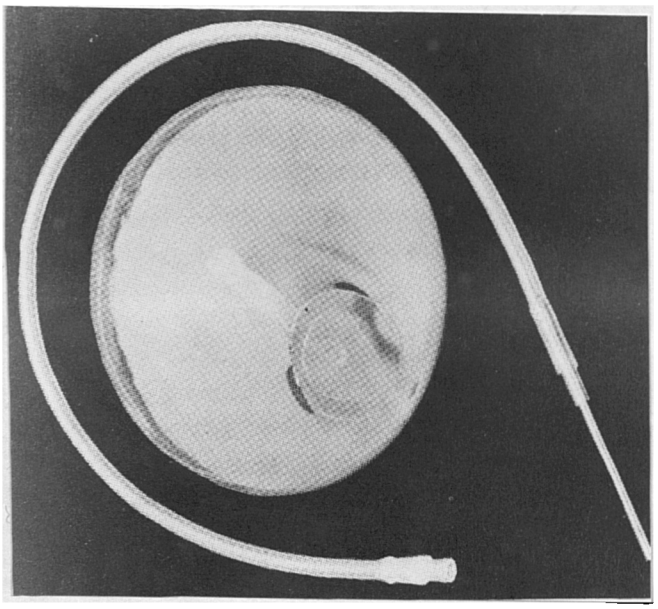


Figure 6.18 The Silastic Varifil Mammary Implant (Inflatable Design) is made from high performance silicone elastomer. It is designed to be filled with sterile isotonic saline through a self-sealing silicone valve. When implanted, the implant approximates the feel, mobility and weight of natural breast tissue.

Silicone fluids have been used in the treatment of burns (Maciejczyk & Sadowski, 1961; Gerow et al., 1963; Miller et al., 1965; Spira et al., 1967; Weeder et al., 1967; Batdorf et al., 1969; Jonsson & Lasson, 1981). In particular, burned hands have either been enclosed in plastic bags containing silicone fluid or pads soaked in silicone fluid (Miller et al., 1965; Spira et al., 1967; Batdorf et al., 1969), or immersed in a bath of silicone fluid (Weeder et al., 1967). These techniques led to early mobilisation, early debridement, early removal of the eschar and control of infection (Batdorf et al., 1969). This application of silicone fluid was also halted following use of impure types.

6.4.2.2 Silicone rubber. Silicone rubber has been used to manufacture a variety of implantable prostheses, and the tissues never become a herent to the rubber (Mullison, 1965). Reaction is minimal, the implant becomes encapsulated by a fibrous sheath which is always non-adherent to the rubber.

Silicone rubber prostheses have been used as breast implants, and gel-filled, saline-filled or inflatable types are available (Figures 6.17 & 6.18). The results have been very good (Williams, 1972). However, problems exist with implant "bleed" where material within the implant can pass through the silicone rubber envelope (Brody, 1977); and this may be responsible for constrictive fibrosis (see 6.3.5.2).

There have been many applications of silicone rubber maxillofacial prostheses for the reconstruction and replacement of cartilage or bone (Brown et al., 1960). These can be nasal

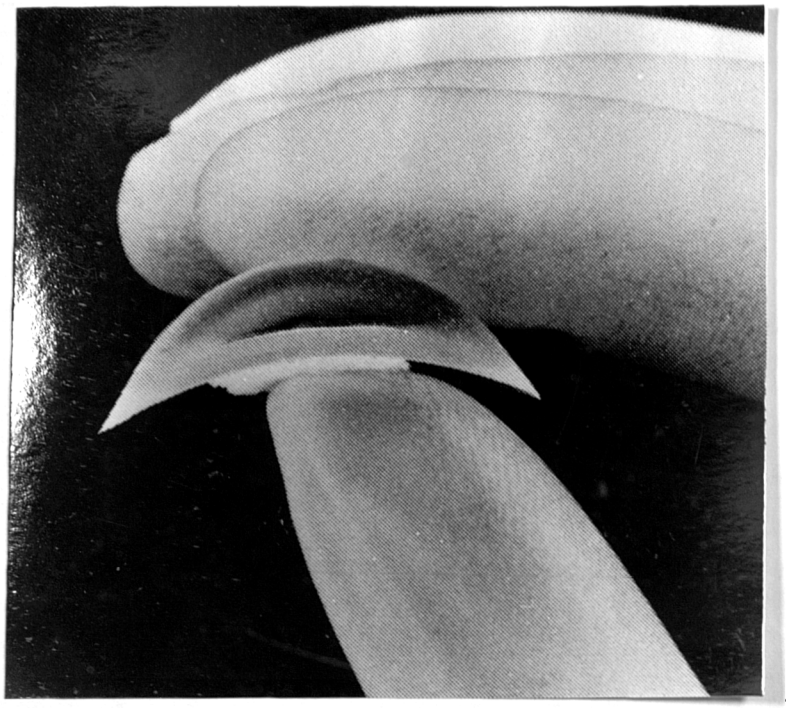


Figure 6.19 The Silastic Gel-Filled Chin Implant (Snyder Design), used in augmentation mentoplasty (microgenia) is fabricated from medical grade silicone gel contained within a uniqueley designed silicone elastomer envelope.

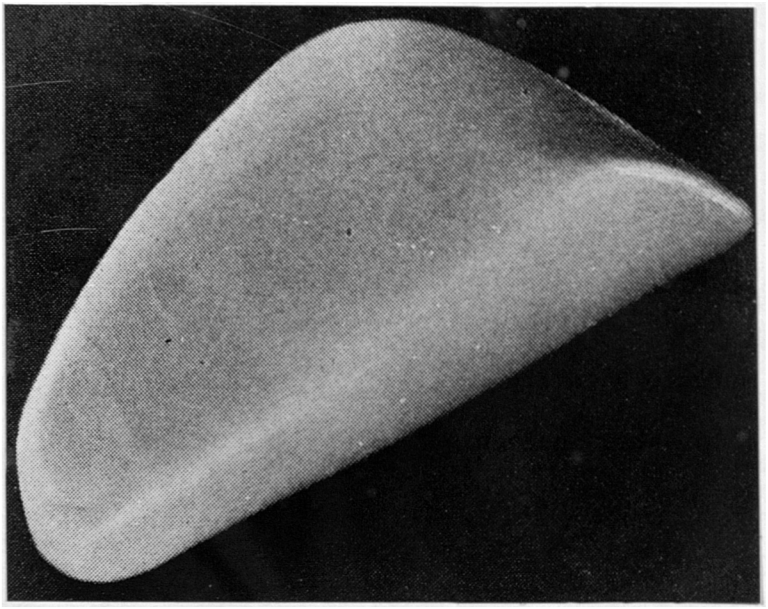


Figure 6.20 The Silastic Rhinoplasty Implant (Safian Technique) is a resilient, preformed, silicone elastomer implant designed for augmenting the sunken bridge of the nose.

supports (Farrior, 1966), jaw augmentation (Brown, 1963; Small et al., 1964), orbital floor repair (Kumpf, 1975; Borghouts & Otto, 1978) and chin augmentation (Feurstein, 1978; Ridley & Jones, 1978). These can either be carved from a block of silicone rubber (Mohler et al., 1976) or provided as prefabricated prostheses available in different sizes (Figures 6.19 & 6.20). The problem with the latter is that perfect adaptation is not always achieved, resulting in the presence of voids. Such dead spaces are potential sites for infection and many surgeons prefer to use cold curing silicone rubbers to provide better adaptation since they can be individually fabricated (Mohler et al., 1976; Wladen, 1983).. This type of elastomer has found use in the treatment of open granulating wounds (Wood & Hughes, 1975; Wood et al., 1977; Harding & Richardson, 1979; Smith et al., 1981), skin graft donor sites (Harding et al., 1980), open perineal wounds (Macfie & McMahon, 1980), hidradentis suppurativa (Morgan et al., 1980), malignant oral-cutaneous fistula (Regnard & Meehan, 1982), epidermoid cancer of the cheek (Shulka, 1982), open infected surgical wounds (Young & Wheeler, 1982) and pectus excavatum (Walden, 1983).

6.4.2.3 Silicone gel. Silicone gels have recently found use in the management of hypertrophic scars (Perkins et al., 1982; Quinn et al., 1985a) and this will be discussed in detail in chapter 7, and the use of silicone gel as a burn dressing will be discussed in chapter 8.

NOTE. Dow Corning silicone gel was originally supplied 1.5 mm thick, this was increased to 3.5 mm towards the end of the duration of this study. Both thicknesses of silicone gel were reinforced with a Dacron mesh.

CHAPTER 7

SILICONE GEL TREATMENT OF HYPERTROPHIC SCARS

7.1 INTRODUCTION

A silicone gel (Spenco Medical Corporation MD-3071) has been reported to soften and reduce hypertrophic scarring and contractures (Perkins et al., 1982), but the mode of action of this material was not explained.

Following this, Dow Corning developed an alternative silicone gel (Dow Corning X7-9119) which has been investigated with the co-operation of the Burns Units at both the Royal Infirmary and the Royal Hospital for Sick Children in Glasgow. The effect on scars and the mode of action were investigated.

7.2 EFFECT ON HYPERTROPHIC SCARS

Patients were selected by Professor W.H. Reid at the Burns Unit, Royal Infirmary, or by Mr P. Raine and Mr A. Azmy at the Royal Hospital for Sick Children.

Silicone gel is held in position by means of a crepe bandage, adhesive tape ("Elastoplast" (Smith & Nephew, U.K.) or "Micropore" (3M, U.K.)), a silicone adhesive (Dow Corning Medical Adhesive B) or a pressure garment; the site of the scar determines which method should be employed. Patients were evaluated every 1-2 months after commencing silicone gel treatment.

The material can be removed for bathing and can be washed in warm water and be re-applied. Ideally, silicone gel should

Table 7.1 The patients studied in the clinical trial of silicone gel. Scar score is based on the appearance of the scar after two months of treatment.

PATIENT	AGE	SEX	CAUSE	DURATION (M)	SITE	ATTACHMENT	SCORE
1. S.C.	5	M	FIRE	16	HANDS	CB	+
2. D.J.	13	M	FIRE	1	HAND	CB	++
3. F.H.	65	M	FIRE	1	HAND	CB	+
4. J.F.	45	M	FAT	2	HAND	CB	+++
5. R.M.	49	M	MOLTEN SULPHUR	1	HAND	CB	+
6. L.O.	17	F	SCALD	144	SHOULDER	TAPE	++
7. J.K.	72	M	FAT	1	ELBOW	TAPE	?
8. J.W.	15	F	GLASS	96	ARM	CB	+
9. S.L.	12	M	FIRE	3	HAND	CB	BROKE DOWN
10. S.D.	22	F	RTA	66	THIGH	DCB	NON HYPERTROPHIC SCAR (see 7.4.3)
11. C.M.	16	M	ELECTROCUTION	6	SHOULDER	P/DCB	+
12. L.J.	16	F	FAT	12	GROIN	P	+
13. L.W.	16	M	FIRE	1	ARM	CB	+++
14. C.G.	20	F	SCALD	12	GROIN	DCB	+
15. D.D.	SEE CHAPTER 8						
16. J.P.	24	F	SURGERY	240	BACK	DCB	NON HYPERTROPHIC SCAR (see 7.4.3)
17. D.A.	21	M	FIRE	8	ARM	CB	+
18. M.B.	56	F	HOT SUGAR	24	ARMS	P	++
19. L.M.	18	M	ELECTROCUTION	4	ARM	CB	?
20. I.G.	15	M	SCALD	54	SHOULDER	P	++
21. R.M.	11/12	M	FIRE	2	LEGS	TAPE	++
22. J.G.	16	M	BCG VACCINATION	30	ARM	TAPE	+
23. G.W.	16	M	FALL	5	SHOULDER	TAPE	+
24. A.M.	10	F	SCALD	7	GROIN	TAPE	?
25. J.F.	63	M	FIRE	6	BACK/ARM	TAPE/P	+++/+
26. M.L.	28	F	FIRE	1	ABDOMEN	TAPE	?
27. M.D.	31	F	FIRE	18	ABDOMEN	TAPE	?

PATIENT	AGE	SEX	CAUSE	DURATION (M)	SITE	ATTACHMENT	SCORE
28. M.M.	47	F	SCALD	2	FOOT/ABDOMEN	CB/TAPE	++/+++
29. C.R.	14/12	F	SCALD	5	CHEST	TAPE	++
30. S.J.	2	M	SCALD	9	ARM	CB	++
31. T.S.	67	M	SCALD	6	ARM	CB	++
32. C.R.	2	M	SCALD	14	CHEST	P	+
33. C.C.	18/12	M	SURGERY	12	LIP	TAPE	DIFFICULT TO ATTACH
34. T.W.	17	M	ELECTROCUTION	36	CHEST	P	?
35. J.M.	23	F	FIRE	72	FACE	P	BIOPSY OBTAINED FROM THIS PATIENT
36. L.D.	2	F	SCALD	3	ARM	CB	++
37. P.L.	17/12	M	SCALD	7	CHEST	P	++
38. D.M.	3	F	SCALD	4	BACK	P	?
39. F.J.	31	F	FAT	3	NECK/ARM	TAPE/CB	+++/+
40. G.R.	28	M	FIRE	3	THIGH	CB	BROKE DOWN
41. A.C.	35	F	SURGERY	11	ARM	CB	+++
42. T.M.	2	M	SCALD	2	SHOULDER	TAPE	+
43. A.K.	14	F	HOT ASH	9	FOOT	P	+
44. G.M.	17/12	F	SCALD	5	CHEST	DCB	+
45. D.H.	19/12	M	SCALD	9	ARM	CB	++
46. R.A.	23	M	INCISION	72	FACE	TAPE	?
47. W.M.	3	M	FAT	12	FOOT	CB	++
48. J.T.	4	M	SCALD	8	ARM	CB	+
49. M.S.	57	F	FIRE	6	NECK	TAPE	BIOPSY OBTAINED FROM THIS PATIENT
50. E.R.	31	M	KELOID	36	CHEST	TAPE	++
51. A.B.	22	M	RTA	19	ARM	CB	+
52. J.M.	5	M	SCALD	48	SHOULDER	TAPE	?
53. M.M.	2	M	FIRE	1	FACE	P	NOT A SCAR (see 7.4.3)
54. M.P.	20/12	M	SCALD	12	ARM	CB	++
55. A.G.	20/12	F	SCALD	6	NECK	TAPE	?
56. S.L.	9/12	F	SCALD	2	CHEST	TAPE	BROKE DOWN; WHEN RE-APPLIED ++
57. S.G.	15	F	SCALD	96	ARM	CB	+
58. L.W.	18/12	F	SCALD	11	CHEST	P	RASH DEVELOPED
59. M.H.	3	M	SCALD	28	ARM	TAPE	++
60. N.O.	2	M	SCALD	11	ARM	CB	+++

PATIENT	AGE	SEX	CAUSE	DURATION (M)	SITE	ATTACHMENT	SCORE
61. L.S.	17/12	F	SCALD	2	ARM	CB	?
62. K.M.	53	F	FAT	5	ARM	CB	++
63. G.E.	32	F	SCALD	6	ARM	CB	?
64. A.B.	7	F	FIRE	18	ARM	CB	?
65. S.M.	21/12	M	SCALD	4	CHEST	TAPE	++
66. D.M.	12/12	M	SCALD	1	CHEST	TAPE	RASH DEVELOPED
67. A.C.	2	M	SCALD	4	CHEST	TAPE	?
68. E.C.	20/12	F	SCALD	9	ARM	P	RASH DEVELOPED
69. K.M.	34	M	SURGERY	2	FOREHEAD	TAPE	NON HYPERTROPHIC SCAR (see 7.4.3)
70. E.C.	19	F	KELOID	84	SHOULDER	TAPE	+
71. R.T.	SEE CHAPTER 8						
72. S.F.	2	M	SCALD	11	CHEST	TAPE	++
73. D.B.	4	M	SCALD	8	SHOULDER	TAPE	++
74. W.Y.	SEE CHAPTER 8						
75. N.R.	SEE CHAPTER 8						
76. J.M.	24	F	SKIN GRAFT	240	ANKLE	P	++
77. M.K.	5	M	SCALD	36	SHOULDER/NECK	TAPE	RASH DEVELOPED
78. N.M.	14	F	INCISION	72	CHEST	TAPE	++
79. H.M.	74	M	INCISION	120	CHEST	TAPE	+
80. W.D.	17	M	FALL	12	FACE	TAPE	++
81. A.F.	17	M	INCISION	18	FACE	TAPE	+
82. G.P.	12/12	M	SCALD	3	CHEST	P	RASH DEVELOPED

be *in situ* for 24 hours, but this is not always practical and 12 hours per day may be adequate.

The only adverse effects found with silicone gel were pruritis (which generally occurred in warm weather) and a rash which appeared when regular hygiene was not observed (although in the under 5 age group, where this problem was more apparent, it is more likely due to a lack of tolerance). Both problems were eliminated with daily (or more frequent) washing of both the scar and the gel. Commonly, with careful attention to hygiene, silicone gel eliminates the pruritis usually associated with immature hypertrophic scars.

In three patients, the newly healed burn area (expected to become hypertrophic) broke down. This is probably due to the fact that the water vapour transmission rate of silicone gel is lower than that of skin (see 8.2.5) and that water collects below the gel and macerates the tissues. Since these occurences, care was taken with out-patients to ensure that the epidermis had completely healed, no scabs were present, and that patients were informed that frequent washing of both scar and gel was essential.

Silicone gel has been applied to 74 patients (Table 7.1) with hypertrophic or keloid scars. Scar improvement was rated after 2 months (for this thesis), and three aspects were measured: texture i.e. the scar became softer and more extensible (see 7.4), colour i.e. the scar became blanched, and how raised the scar was (both measured by comparative photography). Rating of the

scars was based on any change, i.e. if only one improvement, for example, a colour change, was observed the scar scored +, and if all three types of improvement were observed the scar scored +++ (the individual changes have not been recorded in Table 7.1, only that improvement was evident). All patients who returned to follow-up assessment showed an improvement in their scar after two months, although some patients had problems such as development of a rash.

The effect of silicone gel does not appear to be age-related or related to the method of attachment.

7.3 MODE OF ACTION OF SILICONE GEL

The effect of silicone gel on scars can be due to either physical (pressure, temperature, oxygen tension, hydration or occlusion) or chemical parameters. Each of these has been investigated.

7.3.1 Pressure

Pressure is the conventional method employed to reduce hypertrophic scarring. Pressures of 15-40 mmHg (Naismith, 1980) applied by custom-made garments will reduce the colour, and flatten and soften the scar in 6-12 months. Since pressure is known to be an effective treatment for hypertrophic scars, it was the first parameter to be studied.

When silicone gel has been applied to either a scar or normal skin, there appears to be an indentation, corresponding to the position of the material, on the skin giving the impression that pressure has been applied (see 7.4.2). However, when pressure transducers (MFP I, Appendix III) were placed on the skin and

Table 7.2 Pressure transducer results.

DRESSING	PRESSURE (mmHg)
Silicone gel	less than 1
Silicone gel + gauze + tape	less than 1
Silicone gel + crepe bandage	3.1 +/- 3.3

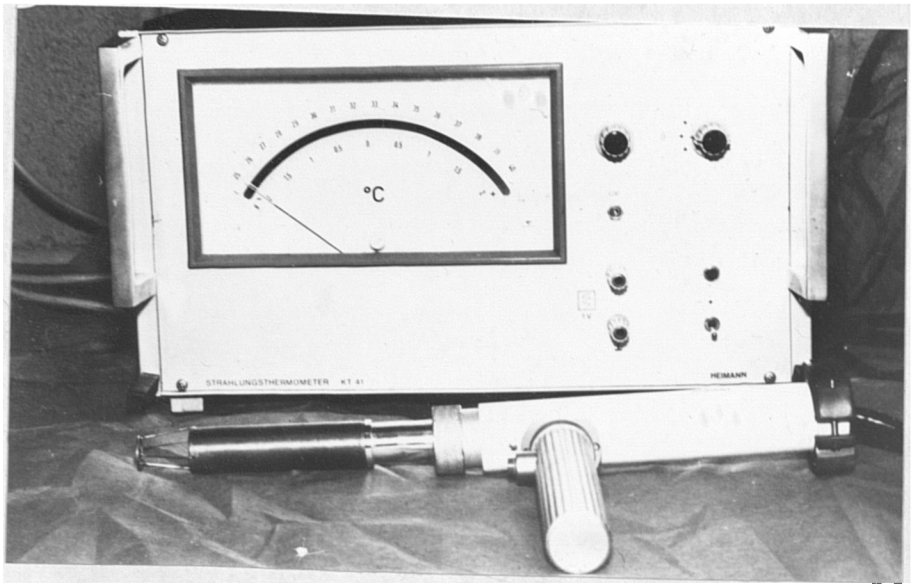


Figure 7.1 The Heiman KT41 radiometer.

Table 7.3 Radiometer results.

LAYER	TEMPERATURE °C
Scar	32.9 +/- 0.68
Silicone gel	32.1 +/- 0.45
Crepe bandage	27.4 +/- 4.8
Pressure glove	31.5 +/- 0.6
Skin control	31.3 +/- 1.7
Room temperature	22.8 +/- 1.7

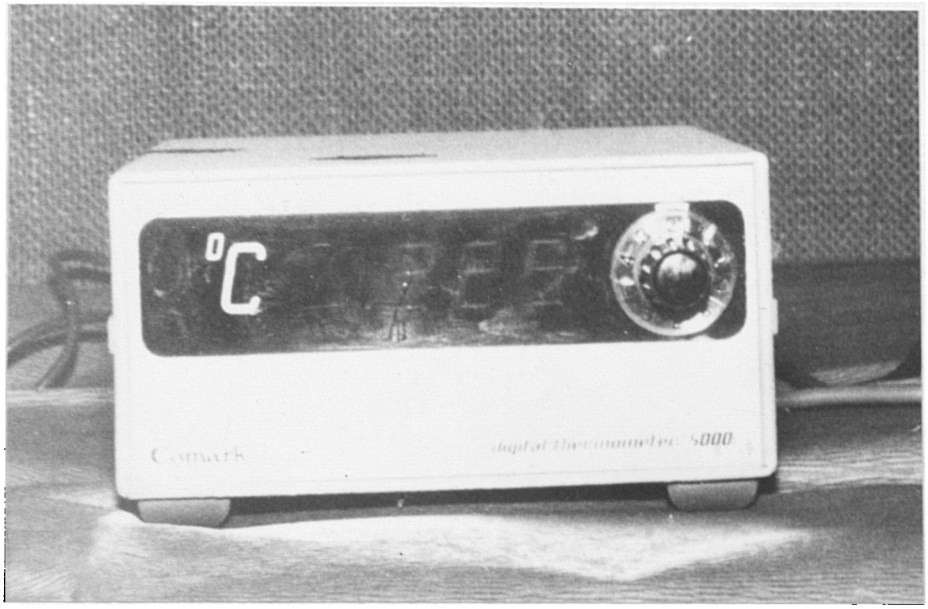


Figure 7.2 The Comark 5335 digital thermometer.

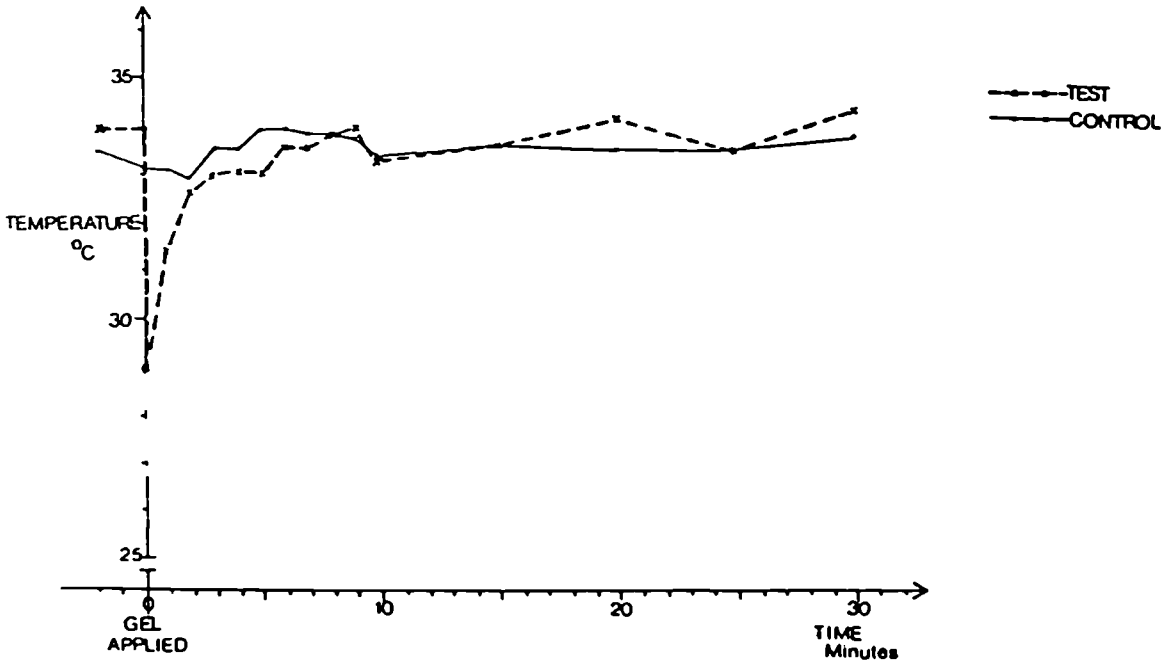


Figure 7.3 Thermocouple results.

silicone gel was applied and positioned by a variety of methods, pressures less than those required by pressure garments were observed (Table 7.2).

When silicone gel was positioned by a crepe bandage, pressures between 1 and 12.8 mmHg were recorded. Although this variation was found to be due to: 1. the person applying the crepe bandage, 2. the site of the bandage, 3. patient movement, the upper levels are pressures which may reduce hypertrophic scarring. However, these values were recorded so infrequently and without consistency that pressure is not required for the therapeutic action of silicone gel. Although when used under a pressure garment, pressure will be applied to the scar.

7.3.2 Temperature

To determine whether the temperature under silicone gel was significantly different from that of normal skin, two studies were undertaken. The first, using a radiometer (Heiman KT 41, Figure 7.1, Appendix III), involved measuring the temperature of the surfaces covering the scar by detecting infra-red radiation. Secondly, thermocouples were placed in contact with the skin to determine, over a period of time, what happened to the skin surface temperature beneath silicone gel.

Table 7.3 shows the radiometer results, and, as might be expected, the surface of the scar is slightly warmer than the outer coverings.

The Comark 5335 Digital Thermometer (Figure 7.2, Appendix III)

Table 7.4 Temperature of the scar treated with silicone gel.

TIME (mins.) / TEST NO.	1	2	3	4	5	6	MEAN	+/- 1 S.D.
Before application	34.6	33.5	33.6	32.9	34.5	34.5	33.9	0.6
Application of gel	29.4	29.2	29.3	29.6	28.8	30.0	29.4	0.4
1	31.3	31.2	31.2	31.5	31.3	31.2	31.3	0.1
2	33.1	31.5	32.9	31.3	32.8	34.8	32.7	1.2
3	33.3	31.5	32.9	31.8	33.0	34.9	32.9	1.1
4	33.2	31.5	32.9	31.9	33.1	34.8	32.9	1.1
5	33.3	31.6	32.8	31.9	33.0	34.8	32.9	1.0
6	33.9	32.3	33.5	32.6	33.8	35.4	33.6	1.0
7	34.0	32.2	33.5	32.7	33.8	35.3	33.6	1.0
8	34.3	32.9	34.2	32.4	33.6	35.4	33.8	1.0
9	34.3	33.0	34.1	32.5	33.6	35.3	33.8	0.9
10	33.8	32.6	33.7	32.1	33.1	34.9	33.4	0.9
15	34.1	32.6	33.8	32.2	33.2	35.0	33.5	0.9
20	34.0	32.3	33.4	32.6	33.7	35.3	22.6	1.0
25	33.8	32.6	33.7	32.1	33.1	34.9	33.4	0.9
30	34.0	32.3	33.4	32.6	33.7	35.3	33.6	1.0

Table 7.5 Temperature of the control site.

TIME (mins.) / TEST NO.	1	2	3	4	5	6	MEAN +/- 1 S.D.	
Before application	33.8	31.9	34.1	34.2	33.5	33.7	33.5	0.8
Application of gel	33.5	30.2	34.0	34.2	33.3	33.4	33.1	1.3
1	33.5	30.2	34.0	34.3	33.3	33.5	33.1	1.4
2	33.5	30.1	34.0	34.1	33.2	33.3	33.0	1.3
3	33.5	30.4	34.6	34.8	33.9	34.2	33.6	1.5
4	33.9	30.5	34.6	34.6	34.0	34.2	33.6	1.4
5	33.9	31.0	34.8	34.8	34.5	34.5	33.9	1.3
6	33.9	31.1	34.8	34.8	34.4	34.6	33.9	1.3
7	34.0	31.2	34.6	34.7	34.2	34.2	33.8	1.2
8	33.9	31.2	34.5	34.7	34.4	34.3	33.8	1.2
9	33.9	31.1	34.4	34.5	34.3	34.2	33.7	1.2
10	33.7	31.2	34.0	34.1	33.9	33.7	33.4	1.0
15	33.9	31.1	34.1	34.1	34.0	33.9	33.5	1.1
20	33.8	31.1	34.1	34.2	34.1	34.0	33.6	1.1
25	33.9	31.1	34.1	34.1	34.0	33.9	33.5	1.1
30	33.9	31.1	34.1	34.0	34.1	33.9	33.5	1.1

has two thermocouple elements. One was placed on the scar and the other on the control comparable symmetric site. The temperature was allowed to stabilise before readings were taken. Silicone gel was applied to the scar, and readings were taken every minute for the first ten minutes after application of silicone gel, and every five minutes thereafter. The results (Tables 7.4 & 7.5 and Figure 7.3) show that immediately after application of silicone gel, the temperature of the scarred skin drops since the gel is kept at room temperature (approx. 22°C), but within eight minutes scar surface temperature returns to normal levels.

These experiments show that temperature does not play a role in the therapeutic action of silicone gel.

7.3.3 Oxygen Tension

Skin respiration is approximately 0.5% that of the lungs (Milne, 1968). This varies with sex, age and height, but if a 34 year old man, 1.75m tall is considered:

Basal metabolic rate = 37 kcal/m^2/h

Calorific value of oxygen consumption = 4.825 kcal/l(STP)

therefore, $\dot{v}_{O_2}$ = 37/4.825 = 7.668 l(STP)/m^2/h

= 7.668 x 10^3/60 = 127.8 ml(STP)/min/m^2

Skin respiration = 0.005 x 127.8 = 0.639 ml(STP)/min/m^2.

This oxygen flux may be compared with that achievable through the silicone gel by considering the permeability and thickness of the gel together with the available P_{O2} driving force.

Initial calculations were based on the assumption that

Permeability of polydimethylsiloxane with 33% w/w silica filler to O_2

$$P_m O_2 = 6.0 \times 10^{-8} \quad cm^3(STP)cm/cm^2.s.cmHg \quad \text{(Robb, 1968)}$$

Available O_2 partial pressure driving force (ΔP_{O2})

$\Delta P_{O2\ skin} = (P_{O2\ ATMOS} - P_{O2\ SKIN})$ $\Delta P_{O2\ scar} = (P_{O2\ ATMOS} - P_{O2\ SCAR})$

$= 13 - 5.49$ $= 13 - 4.18$

$= 7.51$ cmHg $= 8.82$ cmHg

(Evans - personal communication).

Thickness of silicone gel, t_g, = 0.151 cm

Silicone gel on Skin

$$\text{Gas transmission rate} = \frac{P_m O_2}{t_g} \times \Delta P_{O2}$$

$$= \frac{6.0 \times 10^{-8} \times 7.51 \times 60}{0.151} \quad \frac{cm^3(STP)}{cm^2.min}$$

$$= 1.78 \times 10^{-4}$$

$$= 1.78 \quad \frac{cm^3(STP)}{m^2.min}$$

Silicone gel on Scar

$$\text{Gas transmission rate} = \frac{6.0 \times 10^{-8} \times 8.82 \times 60}{0.151} \quad \frac{cm^3(STP)}{cm^2.min}$$

$$= 2.1 \times 10^{-4}$$

$$= 2.1 \quad \frac{cm^3(STP)}{m^2 min}$$

Figure 7.4 Gas transmission through silicone gel (based on similar O_2 permeability to polydimethylsiloxane).

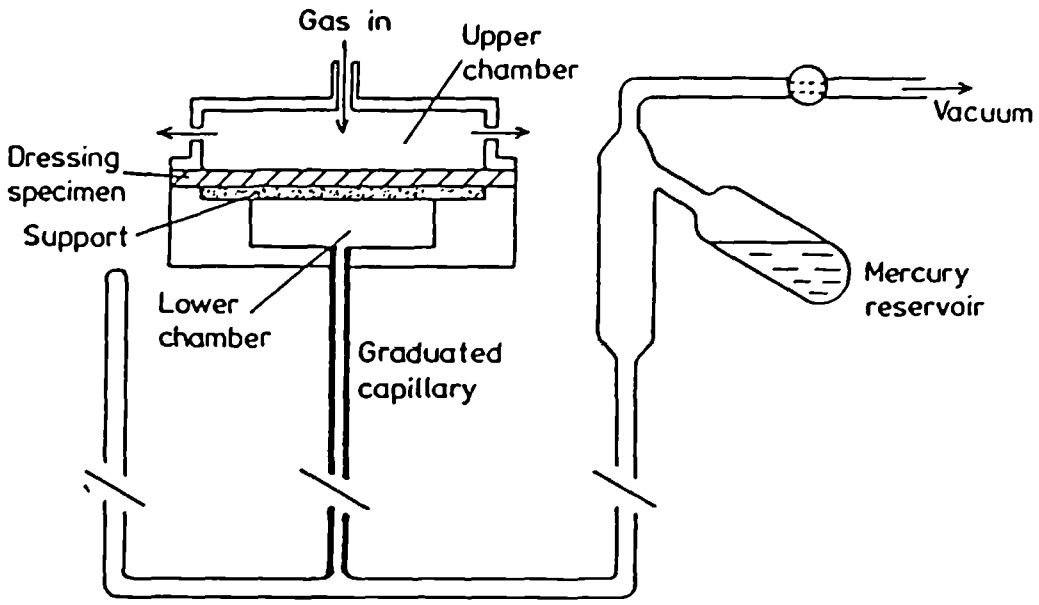


Figure 7.5 Apparatus used to determine the gas transmission of silicone gel

the silicone gel possesses a similar permeability as Dow Corning "Silastic" sheet (polydimethylsiloxane with 33% w/w silica filler). The results, shown in Figure 7.4, give gas transmission rates of 1.78 and 2.1 $cm^3O_2(STP)/(m^2min)$ for skin and scar P_{O2} conditions respectively, when a gel of thickness 0.151 cm is considered.

To corroberate these calculations, the oxygen permeability of silicone gel was measured according to British Standard BS 2782, 1965 method 514A. In this test (Figure 7.5) oxygen was passed at atmospheric pressure into the upper chamber. The lower chamber was separated from the upper one by the test material and was evacuated to a pressure of approximately 0.5 mmHg by a vacuum pump. When the required pressure was attained in the lower chamber, the apparatus was tilted until mercury filled both side tubes and the central capillary tube. At this instance, the pressure in the lower chamber was taken as the vacuum gauge pressure and the level of mercury in the capillary was noted. Change in the mercury level was recorded at one minute intervals. The gas transmission rate, G, was calculated from a linear portion of the level vs. time plot during which the level changes by a value h over time interval t. Specifically, the transmission rate is given by:

$$G = K/t\ (-2a_c - (v_o+a_c(2P_A-P_o))\log_e(1-h/s_o))$$

where:

$K = 273 \times 10^4 \times 24 / T \times A$

A = area of membrane (38.3 cm^2)

T = ambient temperature (^oK)

Table 7.6 Gas transmission (oxygen) through silicone gel.

TEST NO.	P_A(cmHg)	T (^{o}C)	Thickness (cm)	G (cm^3(STP) / m^2.day.atm)	Pr (cm^3(STP)cm / cm^2.s.cmHg)
1:1	75.8	16.5	0.35	1.637×10^4	8.75×10^{-8}
1:2	75.8	16.5	0.35	1.419×10^4	7.59×10^{-8}
1:3	75.8	16.5	0.35	1.130×10^4	6.04×10^{-8}
2:1	73.3	20	0.31	1.720×10^4	8.12×10^{-8}
2:2	73.3	20	0.31	1.661×10^4	7.84×10^{-8}
2:3	73.3	20	0.31	1.475×10^4	6.96×10^{-8}
3:1	75.4	20	0.32	1.701×10^4	8.27×10^{-8}
3:2	75.4	20	0.32	1.703×10^4	8.28×10^{-8}
3:3	75.4	20	0.32	1.704×10^4	8.29×10^{-8}
4:1	75.3	21	0.37	1.443×10^4	8.04×10^{-8}
4:2	75.3	21	0.37	1.472×10^4	8.20×10^{-8}
4:3	75.3	21	0.37	1.337×10^4	7.45×10^{-8}
MEAN	74.5	19.4	0.34	1.534×10^4	7.82×10^{-8}
+/- 1 S.D.	0.97	1.7	0.02	0.177×10^4	0.70×10^{-8}

t = time (h); a_c = cross-sectional area of capillary ($0.0175 cm^2$); h = distance moved by Hg over time t, = $h_t - h_o$ (cmHg); h_o = level in capillary at zero time; v_o = volume in chamber 2 at zero time (cm^3); P_A = pressure in chamber 1 at zero time (cmHg); P_o = pressure in chamber 2 at zero time = $P_{vac} + (h_o - h_{vac})$ (cmHg); P_{vac} = vacuum pressure (cmHg); h_{vac} = level of Hg in capillary tube corresponding to P_{vac}; s_o = pressure difference across membrane at zero time = $P_A - P_o$.

The results are summarised in Table 7.6 (see also Appendix IV). The oxygen permeability of silicone gel is higher than that quoted in Figure 7.4 because silicone gel is silica filler-free.

With this value, the skin and scar transmission rates for the 0.151 cm thick gel are 2.32 and 2.74 $cm^3 O_2 (STP)/(m^2 min)$ respectively. These rates are approximately 4 times greater than the skin respiration flux. Thus, although silicone gel is a barrier, sufficient oxygen reaches the skin for respiration.

The oxygen tension in scars was measures using a Radiometer TCM1 Transcutaneous Oxygen Monitor (Appendix III). The values recorded for silicone gel-treated and untreated scars were no different once the electrode had stabilised (10-15 minutes after starting the test).

7.3.4 Hydration and Occlusion

Any covering is occlusive to a certain extent and may alter the hydration of the skin. Studies, using an evaporimeter (ServoMed Ep1, Figure 7.6, Appendix III) which measures the rate of water vapour transmission from a surface, were carried out to determine what effect silicone gel ha on the hydration properties of the skin.

During the study, readings were taken from silicone gel in situ,

Table 7.7 Evaporimeter results from the test site on case no. 2. Units are g $m^{-2}h^{-1}$.

	TEST NO.								
TIME (mins)	1	2	3	4	5	6	7	8	Mean +/- 1 S.D.
Gel in situ	2	3	1	2	2	3	3	2	2.3 +/- 0.7
Gel removed	55	59	27	44	42	46	48	34	44.4 +/- 9.7
Gel off 5	26	35	13	30	21	31	23	9	23.5 +/- 8.4
Gel off 10	12	20	13	21	15	15	7	9	14.0 +/- 4.6
Gel off 15	12	18	8	18	9	14	7	9	11.9 +/- 4.1
Gel off 20	11	15	7	14	15	12	7	9	11.3 +/- 3.1

Table 7.8 Evaporimeter results for the control site on case no. 2. Units are g $m^{-2}h^{-1}$.

	TEST NO.								
TIME (mins)	1	2	3	4	5	6	7	8	Mean +/- 1 S.D.
Gel in situ	4	7	7	5	7	7	3	7	5.9 +/- 1.5
Gel removed	15	16	15	7	9	13	11	15	12.6 +/- 3.1
Gel off 5	10	9	8	7	10	10	7	9	8.8 +/- 1.2
Gel off 10	8	11	8	9	13	13	9	9	10.0 +/- 1.9
Gel off 15	6	11	8	6	8	9	7	7	7.8 +/- 1.6
Gel off 20	8	11	7	6	13	9	7	9	8.8 +/- 2.2

The relative humidity during these tests ranged from 29% to 58%, with a mean value +/- 1 standard deviation of 46.3 +/- 9.9%.

Figure 7.6 The Servo Med Epl evaporimeter.

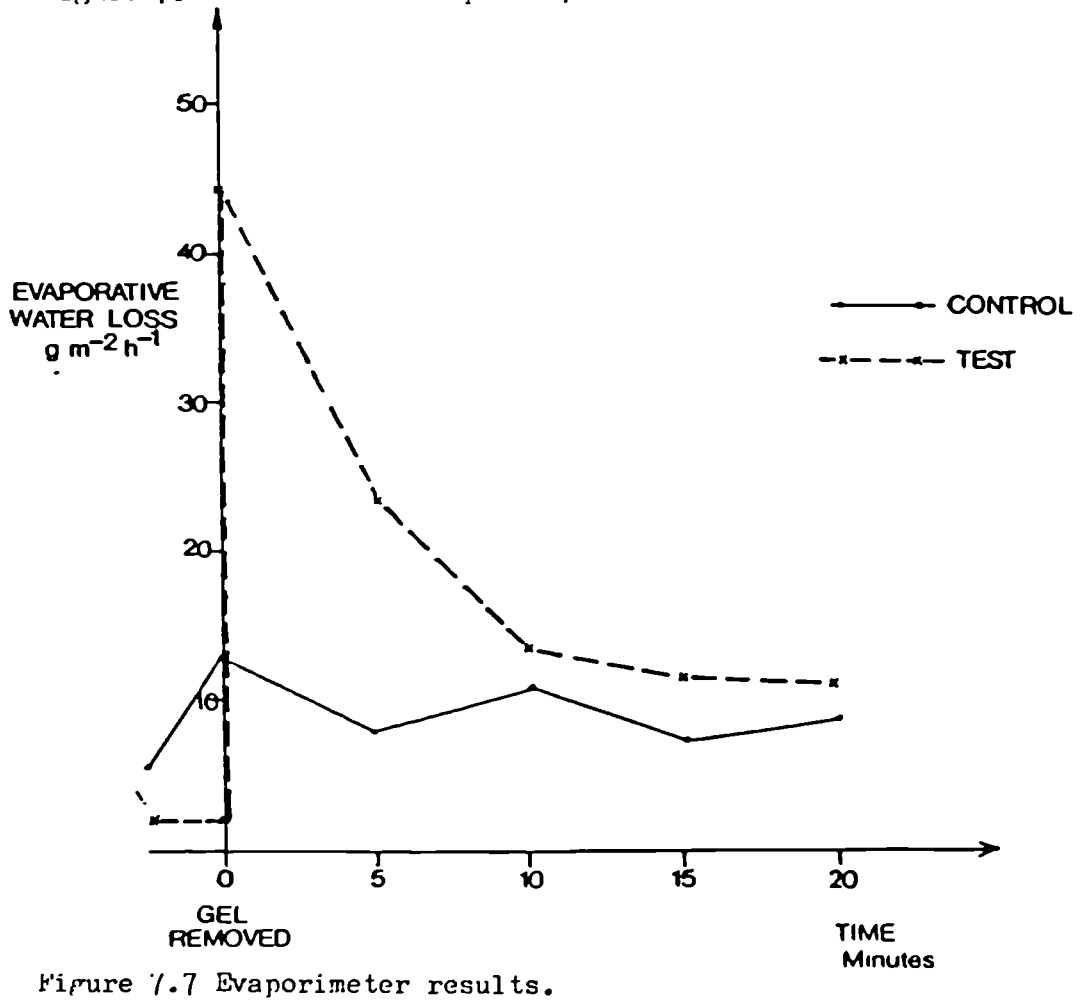


Figure 7.7 Evaporimeter results.

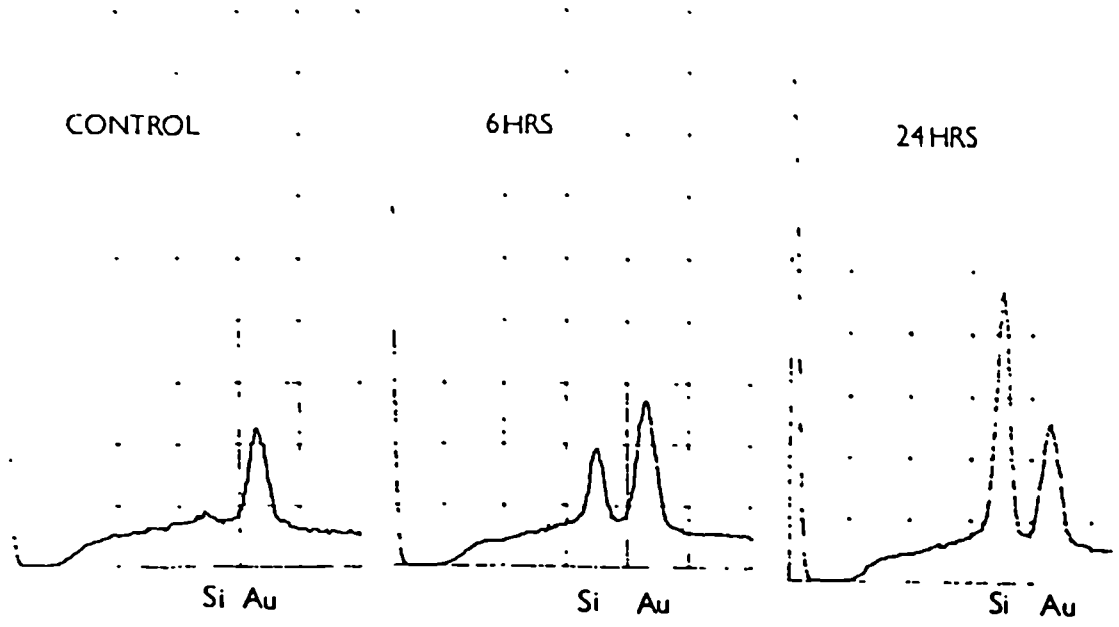


Figure 7.8 Chemical analysis of the oily fluid on filter paper after different times.

the scar on removal of the gel, and at 5 minute intervals thereafter until a stable reading was obtained. Corresponding readings were taken of the control comparable symmetric site. The results (Tables 7.7 & 7.8, Figure 7.7) for one patient show the pattern which was found in all patients and normal controls (who wore silicone gel).

The results show that when *in situ* the gel has a WVTR almost half that of skin (see 8.2.5) and when removed, the water loss from the scar increases dramatically. This effect of removing water from the scar is lost within 15-20 minutes. The build-up of fluid below the gel is not apparent, i.e. the scar does not look or feel wet, therefore there must be a water reservoir within the skin and it is likely to be in the stratum corneum (Inoue et al., 1983).

This effect (Figure 7.7) was mimicked by covering silicone gel with a polyurethane film (0.06 mm thick) such that this film was between the scar and the gel. This "occlusive" covering ("occlusive" to migration of silicone fluid) was applied to scars for two months. However, although the "occlusive" covering was physically identical in weight and thickness, and WVTR (see Appendix V), to silicone gel, its therapeutic action was not.

7.3.5 Chemical

To determine whether silicone gel released any material, pieces of silicone gel were placed on filter paper and left for 24 hours. After this time, the filter paper was observed to have an oily print of the sample. When this was analysed in the scanning electron microscope (SEM) X-ray analyser Phillips-Link system), which can determine what elements are present in a sample, silicon was found, and the experiment repeated over different time periods (Figure 7.8). There is a peak corresponding to gold because the sample was gold-coated to make it electrically conductive. Quantitative

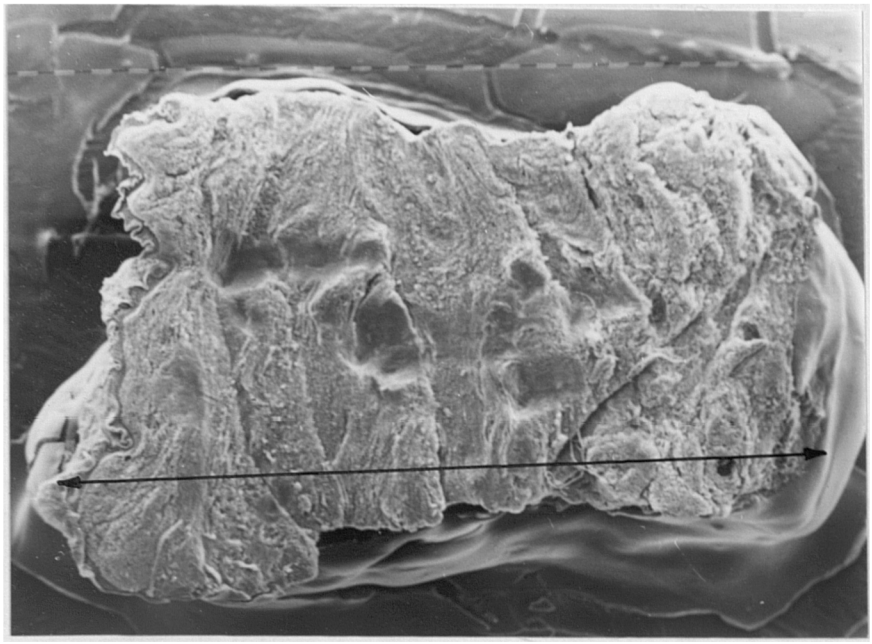


Figure 7.9 SEM micrograph (x32) of scar tissue that has been exposed to silicone gel. The axis marked on the micrograph indicates the path that was analysed for the presence of silicon.

results were difficult to obtain by this method, but the results do show a trend of increasing silicon with time.

To determine whether this low molecular weight silicone fluid entered the skin, skin samples were obtained from patients (Table 7.1) who wore silicone gel on their scars for two weeks prior to corrective surgery. The skin was placed in 10% formal saline buffered with phosphate (in the operating theatre) and fixed for two weeks. In the laboratory, the samples were removed from the fixative and were sectioned, with a scalpel, in distilled water. Sections 2 mm thick were obtained and a note of the orientation was recorded. The specimens were then placed in 10% acetone for one hour, and were dehydrated by immersion in three successive baths of 100% acetone, each for 24 hours. Drying was completed using a Critical Point Drying (CPD) apparatus. After complete dehydration, each specimen was mounted on an SEM specimen stub with double sided adhesive tape. The specimen was coated with carbon (to facilitate analysis to determine whether platinum, the catalyst employed in the preparation of silicone gel, was present), since no platinum was found the samples were re-coated with gold, and a conducting material (colloidal graphite) was painted around the specimen, next to the stub, to complete the path to earth.

The specimens were then viewed in the SEM X-ray microprobe (Phillips-Link system) to determine where silicon is located, if present, in the skin.

7.3.5.1 Results. Figure 7.9 shows a section of scar tissue

that had been exposed to silicone gel for two weeks. This was examined for the presence of silicon by probing along the axis marked on the Figure. The following Figures (7.10-7.17) show representative areas and their analytical results. The area under analysis in each micrograph is the intersection of the two white lines.

A control sample was examined in the same manner, and Figures 7.18 & 7.19 show typical results.

These results show, not quantitatively, that silicon is present in hypertrophic scar tissue and that this appears to be reduced in hypertrophic scars treated with silicone gel.

Specimens and their fixative media were analysed for the presence of polydimethylsiloxane (the repeat unit of silicone gel) by Dow Corning. Their results indicate that polydimethylsiloxane is present in untreated hypertrophic scar tissue and that it is reduced in treated scar tissue. No polydimethylsiloxane was found in the fixative media.

7.4 CASE STUDIES

Patients were requested to return every 1-2 months after commencing treatment for assessment. At each visit, the scar was photographed and tests were carried out, for example, determination of temperature and evaporative water loss.

To characterise treatment, an extensometer (Figure 7.20) was used. This device was used to determine the mechanical properties of the scar by "stretching" the skin. The strain (ϵ), corresponding to the magnitude of the lax phase of response, was measured under a constant tensile force (Stark, 1971).

Figure 7.10 Epidermis of hypertrophic scar treated with silicone gel (x120).

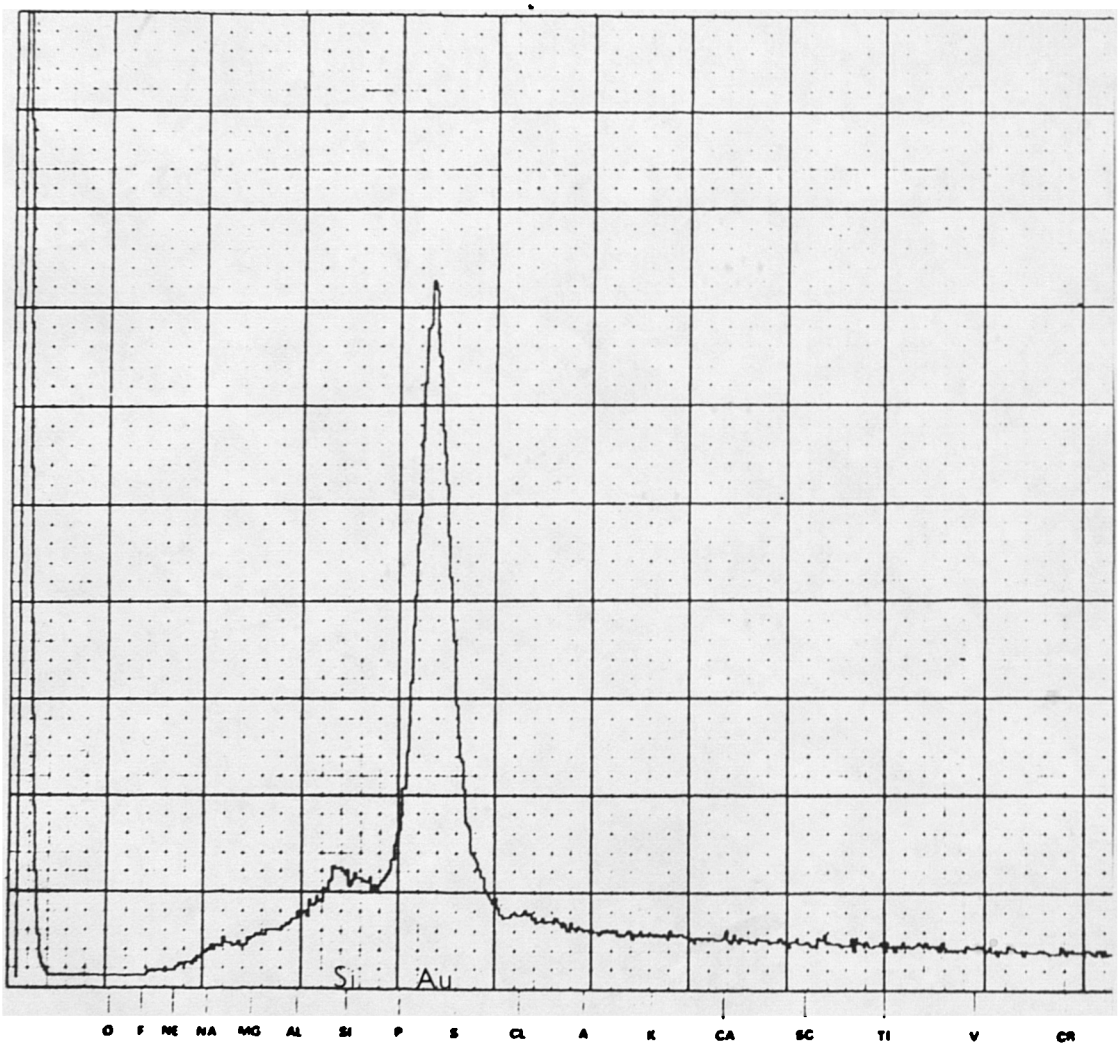


Figure 7.11 Analysis of the intersection point on Figure 7.10.

140B

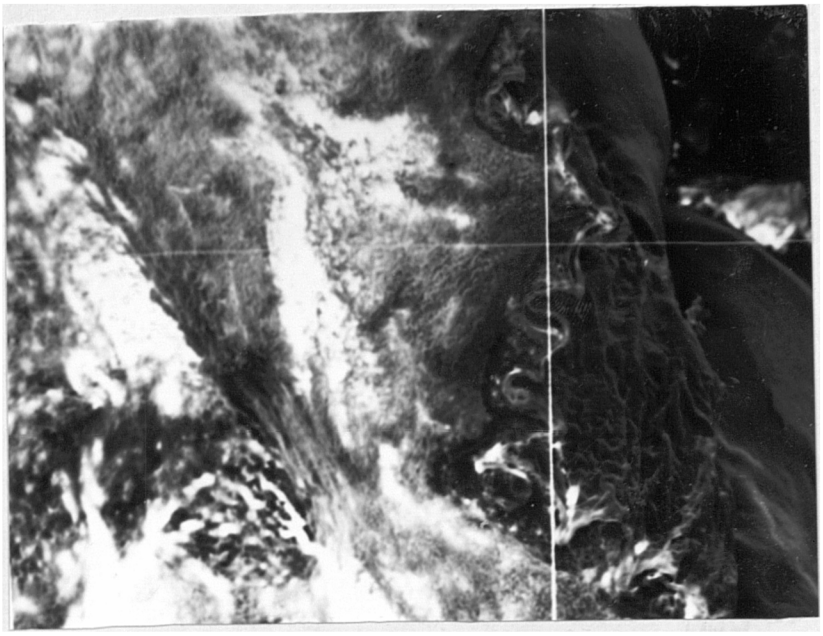


Figure 7.12 The epidermo-dermal junction in a hypertrophic scar that had been treated with silicone gel (x120).

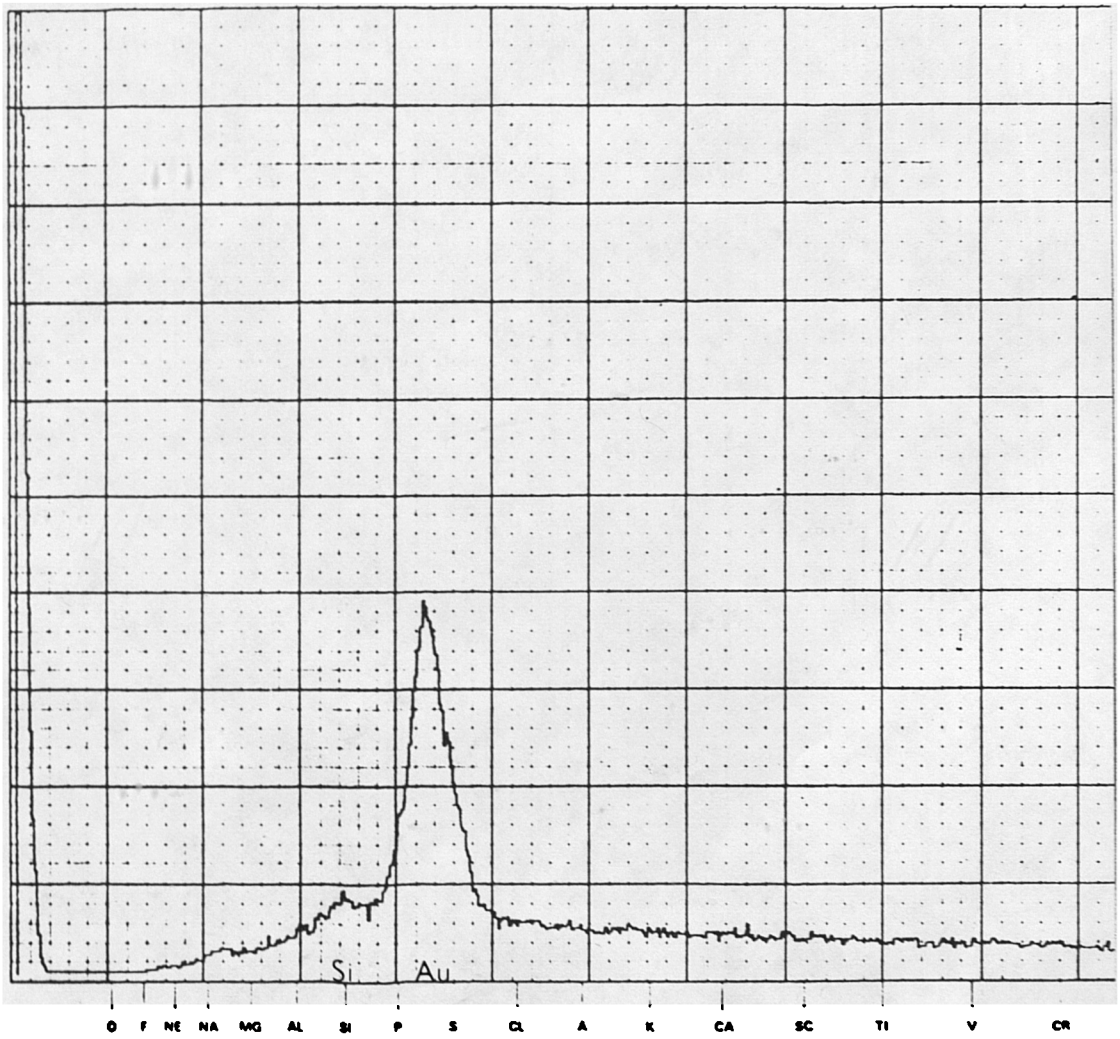


Figure 7.13 Analysis of the point of intersection of the two lines on Figure 7.12.

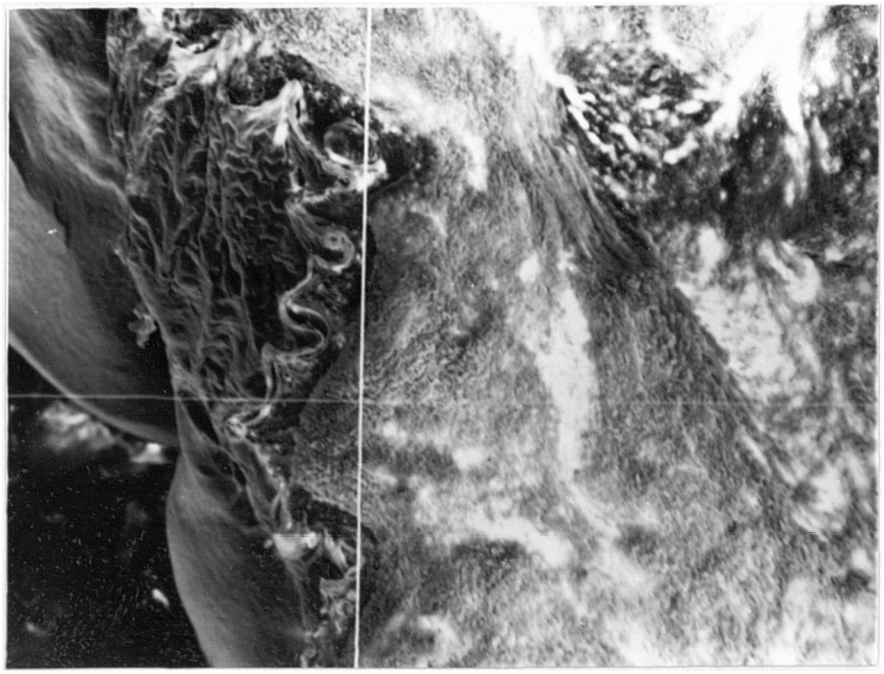


Figure 7.14 Area of dermis of hypertrophic scar treated with silicone gel (x120)

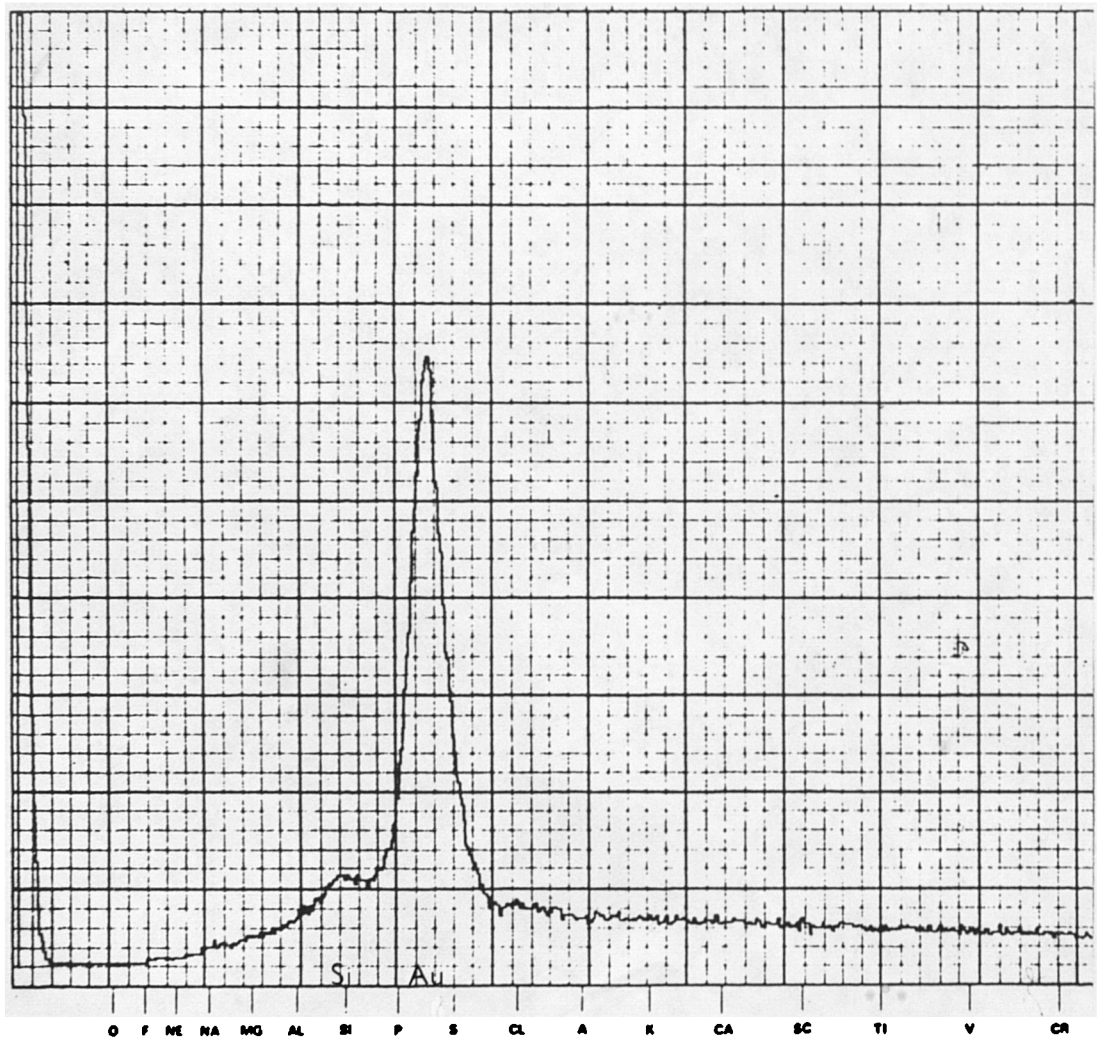


Figure 7.15 Analysis of the point of intersection of the two lines on Figure 7.14.

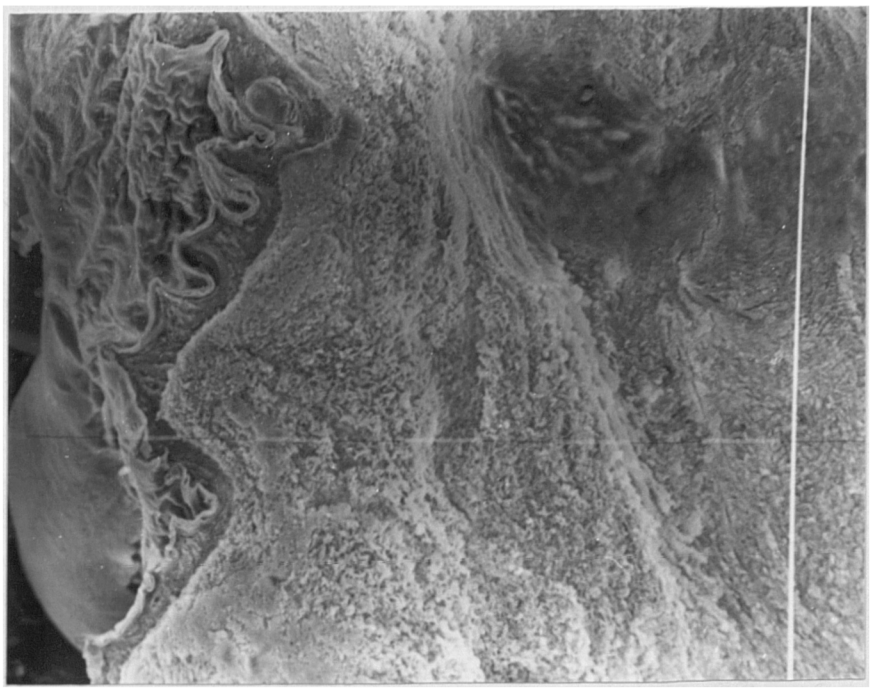


Figure 7.16 Area of deep dermis in a hypertrophic scar that has been treated with silicone gel (x120).

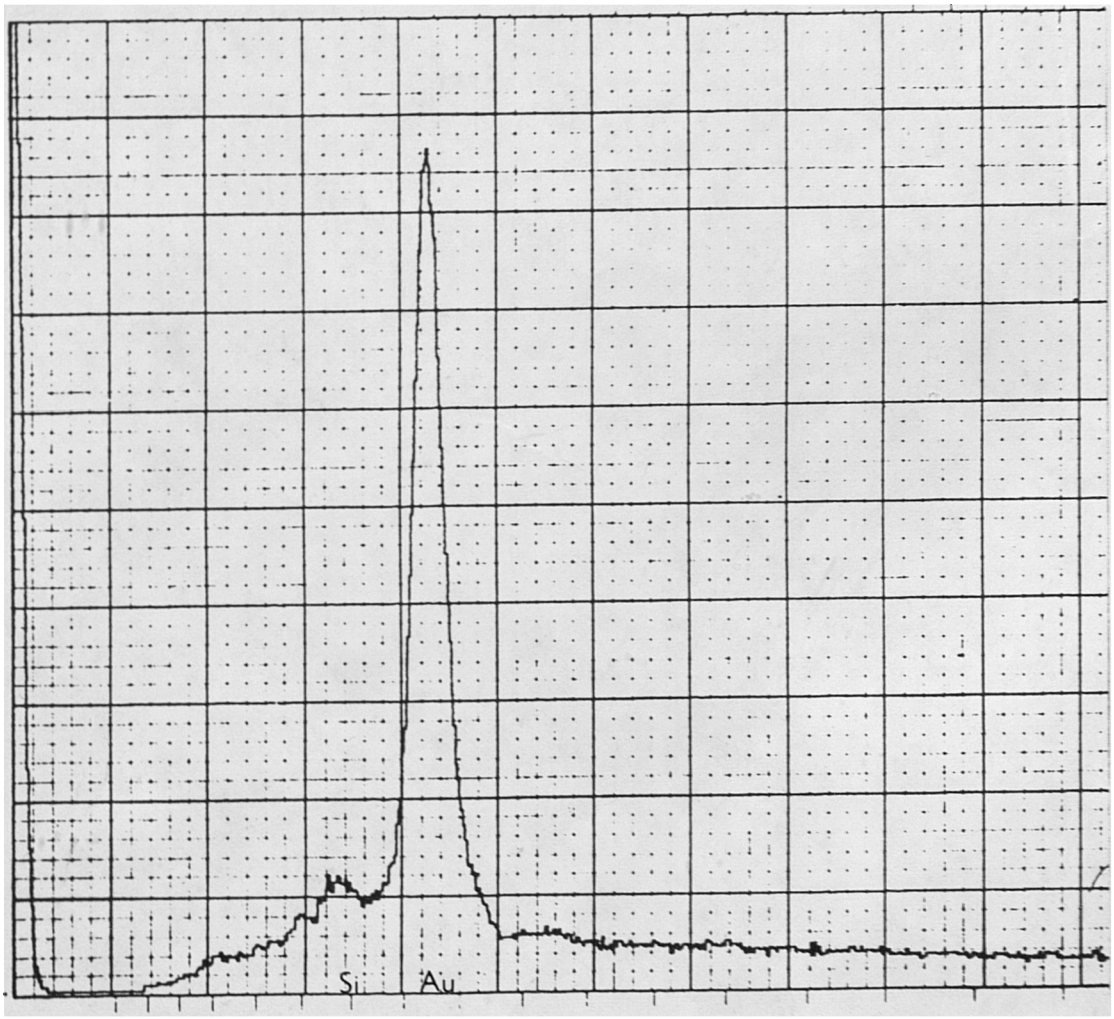


Figure 7.17 Analysis of the point of intersection of the two lines on Figure 7.16.

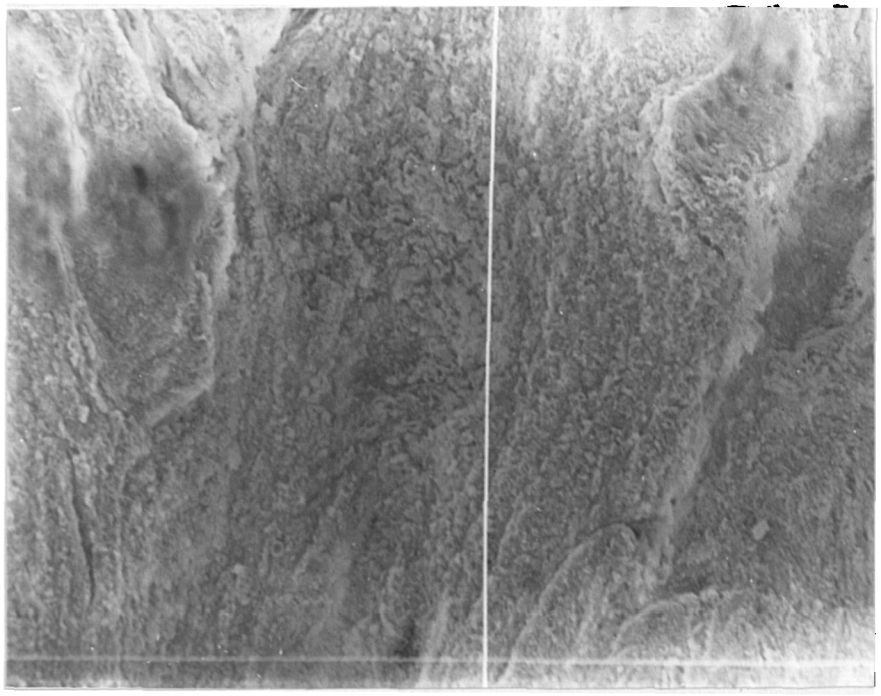


Figure 7.18 Area of the dermis of a control hypertrophic scar (x120).

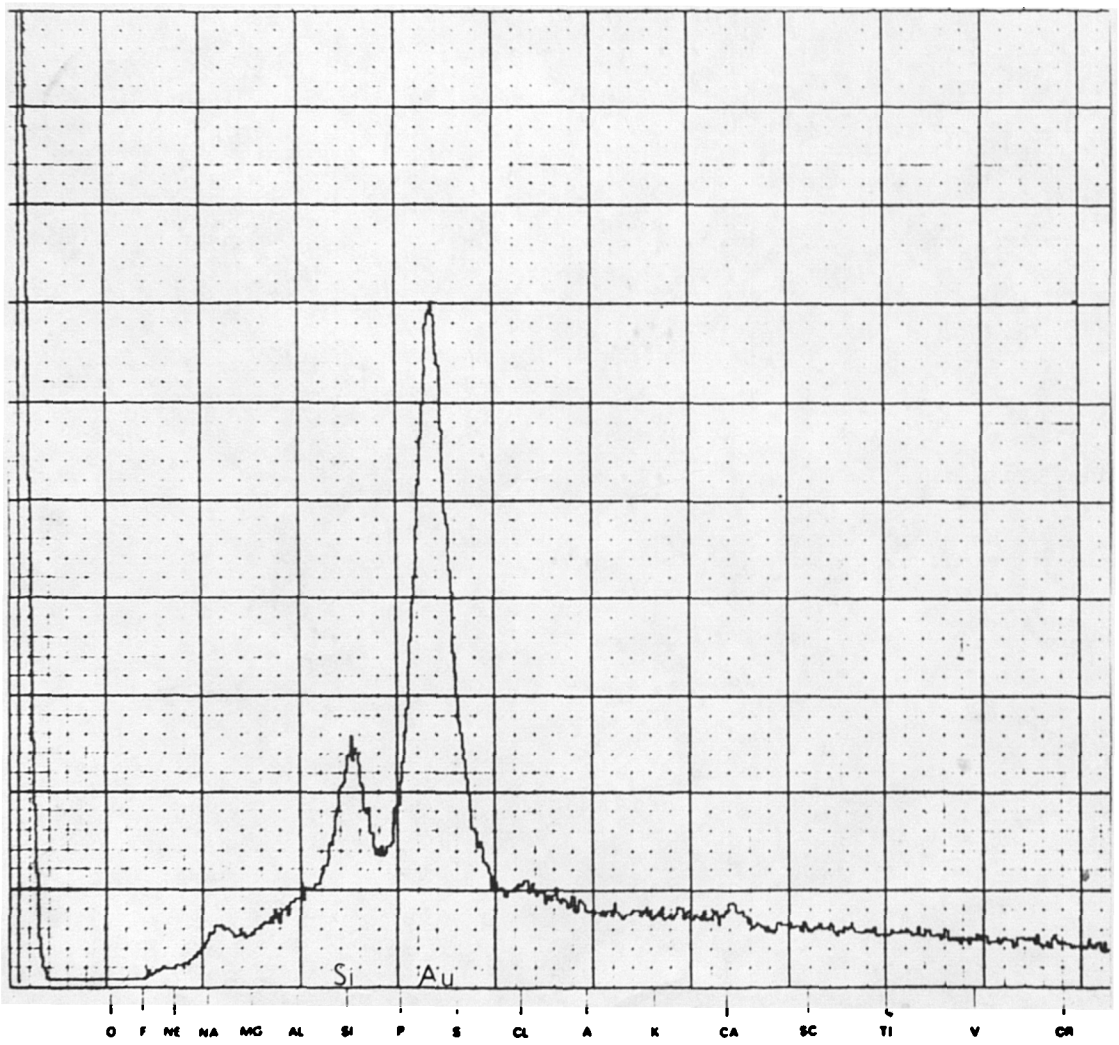


Figure 7.19 Analysis of the point at the intersection of the two lines on Figure 7.18.

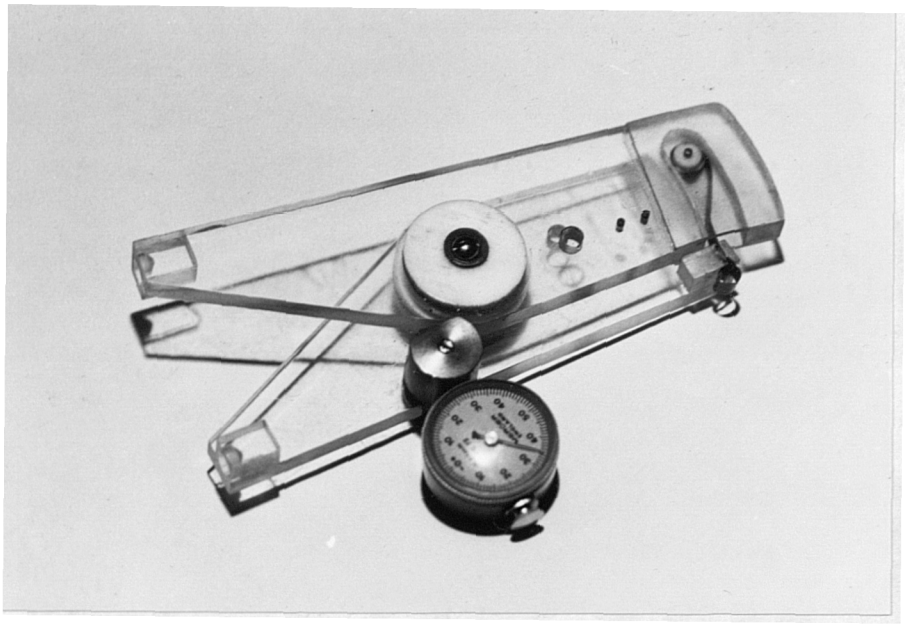


Figure 7.20 The extensometer used to determine the elasticity of hypertrophic scars.

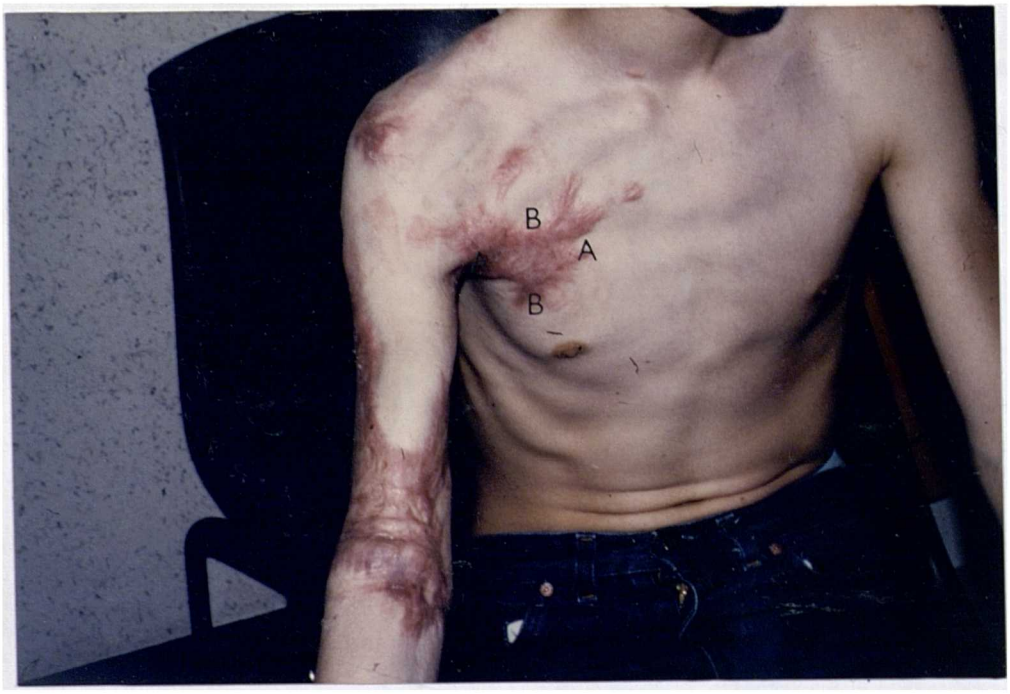


Figure 7.21 Case no. 11 before silicone gel treatment. (Note A-A is direction 1; B-B is direction 2).

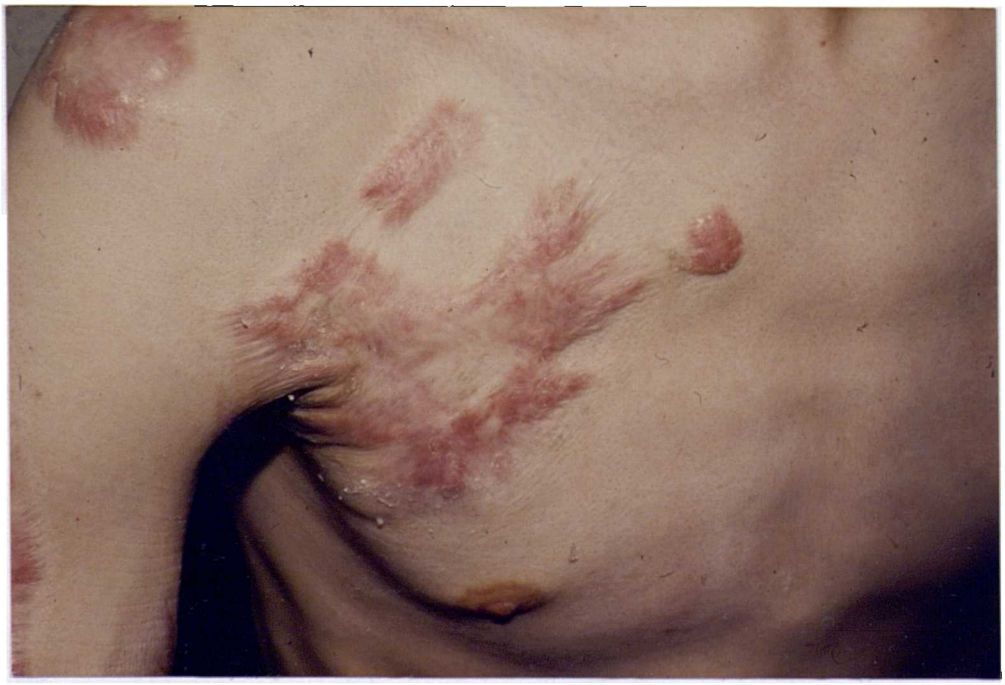


Figure 7.22 Case no. 11, 1 year after application of silicone gel. The centr of the scar is blanched and the edges have been flattened.

Case Study No. 11

C.M., a 16 year old boy, sustained a deep electrical injury and developed hypertrophic scarring on his right arm and chest. Pressure therapy was advised, however, the area on his chest (Figure 7.21, arrowed) did not benefit from this form of treatment and silicone gel was applied (six months after injury). The extensometer, which was only available five months after silicone gel application, results are summarised below:

Time After Silicone Gel Treatment (months)	Direction 1 $\%_\varepsilon$	Direction 2 $\%_\varepsilon$
5	7.35	7.85
6	8.47	12.67
7	4.94	11.40
9	6.97	12.67
10	8.23	11.27
11	12.03	10.77
12	12.03	14.57
13	17.10	17.10
14	17.10	17.10

Note that for the purpose of this thesis the extensometer limit was 17.10%. This could be altered for future studies characterising the mechanics of scar tissue. However, these results show that scar mobility is increased with silicone gel treatment.

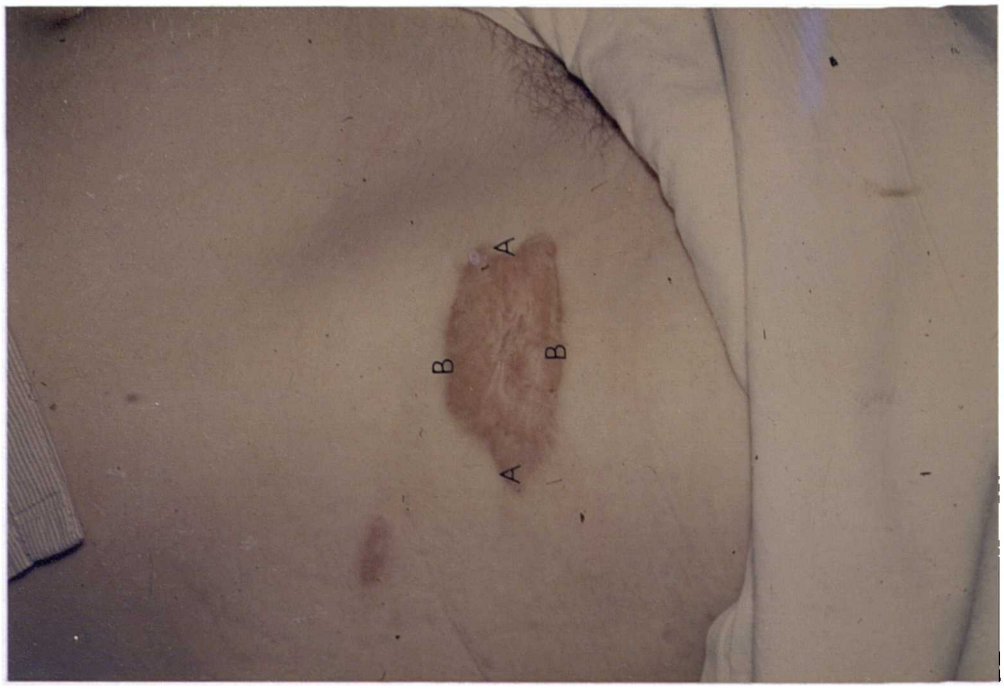


Figure 7.23 Case no. 14 before silicone gel treatment.

(Note A-A is direction 1; B-B is direction 2).

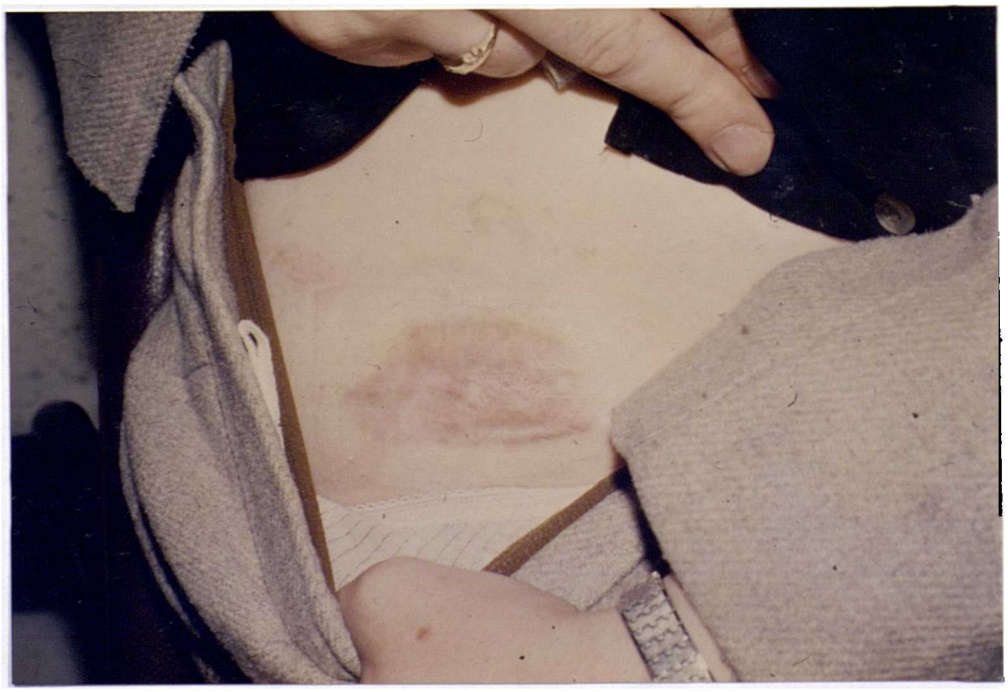


Figure 7.24 Case no. 14, 10 months after silicone gel treatment, the scar is flatter and blanched.

Case Study No. 14

C.G., a 20 year old female, suffered a scald injury to her groin which developed into a hypertrophic scar (Figure 7.23). Characterisation by extensometer was carried out four weeks after commencing silicone gel treatment:

Time After Silicone Gel Treatment (Weeks)	Direction 1 % ε	Direction 2 % ε
4	9.75	14.69
10	6.71	8.87
18	6.33	11.40
22	10.51	14.31
26	16.85	16.85
32	17.10	17.10
36	17.10	17.10

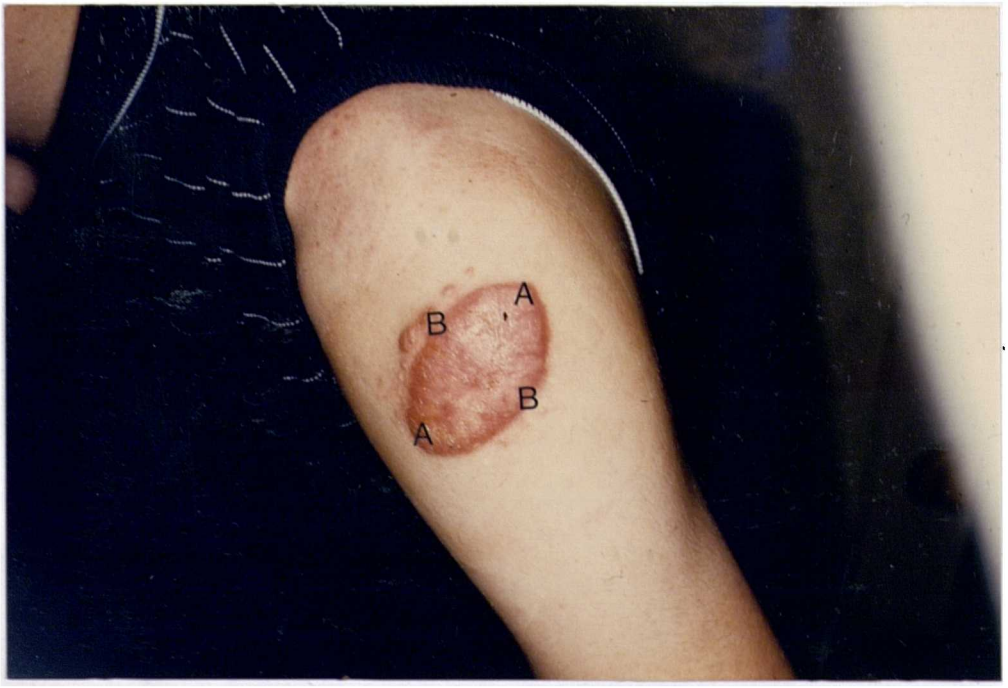


Figure 7.25 Case no. 22, 5 months after treatment, the scar is markedly raised and coloured. (Note A-A is direction 1; B-B is direction 2).

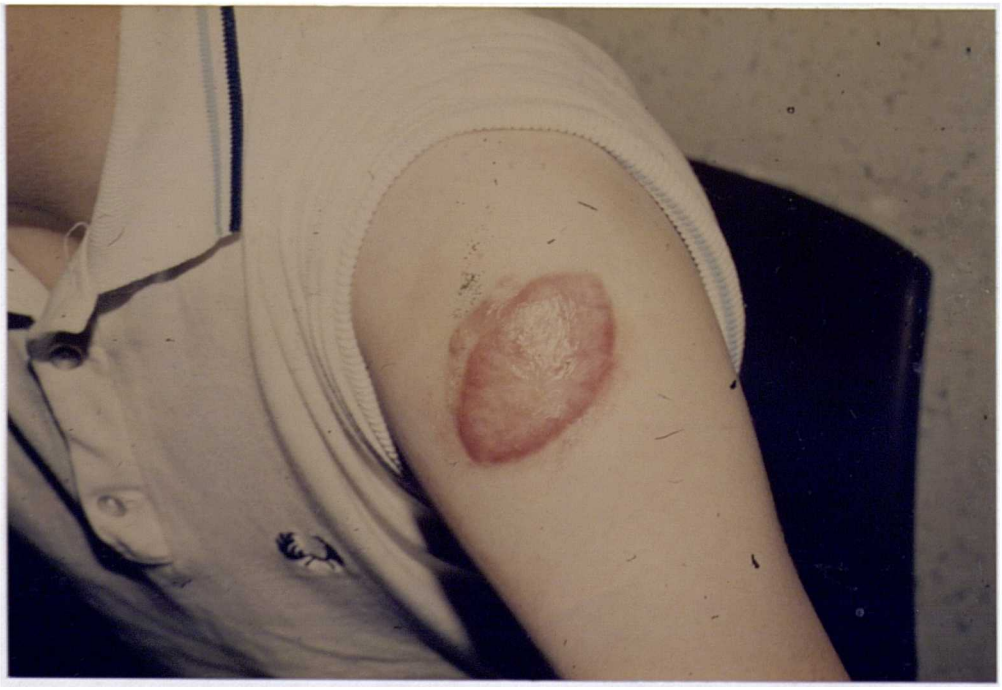


Figure 7.26 Case no. 22, 8 months after treatment, the colour has been reduced.

Case Study No. 22

J.G., a 16 year old boy, developed a hypertrophic scar (Figure 7.25) after a BCG vaccination. The scar had been injected with triamcinolone with no effect. Silicone gel was applied 30 months after the scar developed, and the scar initially became softer to touch. The treatment was characterised by extensometer:

Time	Direction 1 $\%\varepsilon$	Direction 2 $\%\varepsilon$
Before silicone gel treatment	5.57	6.97
4 weeks after treatment	6.59	12.92-
8 weeks after treatment	6.84	-
14 weeks after treatment	13.55	-
20 weeks after treatment	17.10	-

The extensometer became difficult to use in direction 2 due to the height of the scar and the two results obtained in this direction differ vastly because of this.

7.4.1 Comment

These results show that the extensometer is not an accurate method of determining the mechanics of scar tissue. It has many disadvantages, for example, it cannot be used on very thick scars, or on certain parts of the body (particularly hairy regions because it is attached to the skin with adhesive tape), and it requires a great deal of practice before use in the clinic. However, these results do show a trend of increasing elasticity of the scar with silicone gel treatment.

The following case studies demonstrate the beneficial effect of silicone gel photographically.

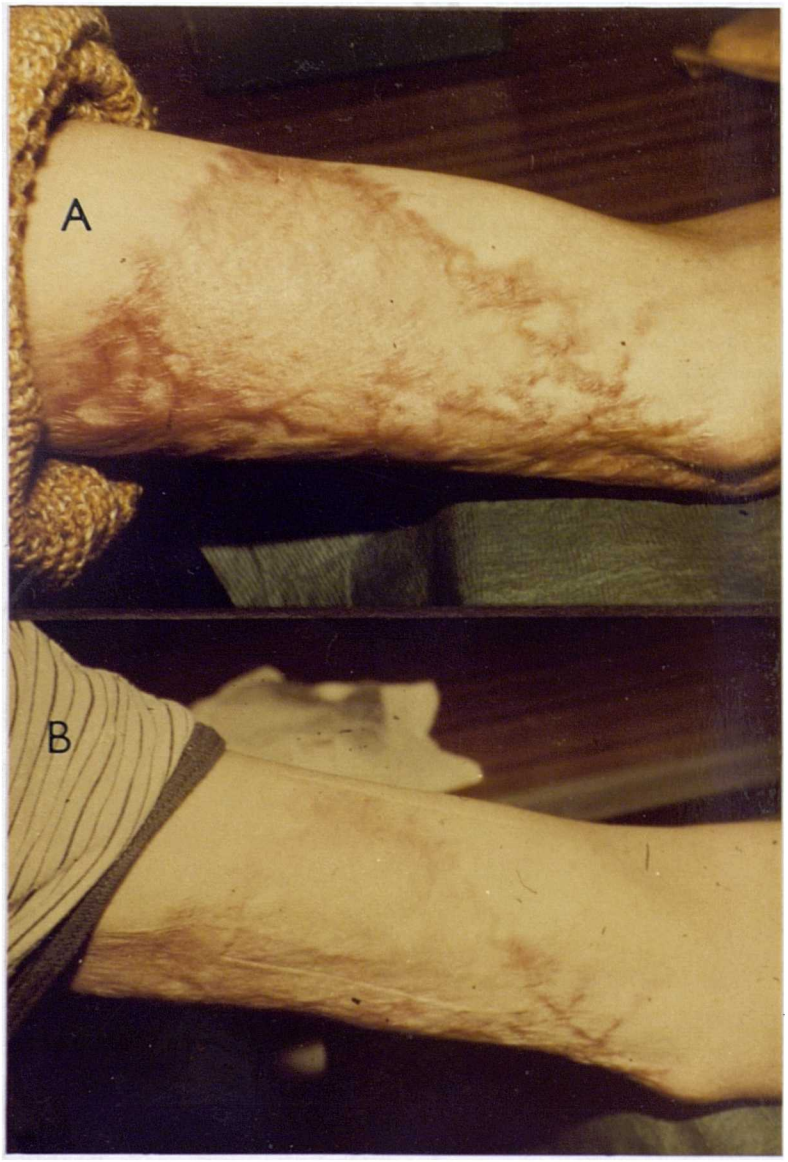


Figure 7.27 Case no. 13. A, before treatment with silicone gel; B, 3 months after application of silicone gel.

Case Study No. 13

L.W., a 16 year old boy, sustained a burn injury to his torso, and the resultant hypertrophic scar on his left arm was treated with silicone gel 6 weeks after injury. Figure 7.27 shows his scar before treatment, and after 3 months of silicone gel application.

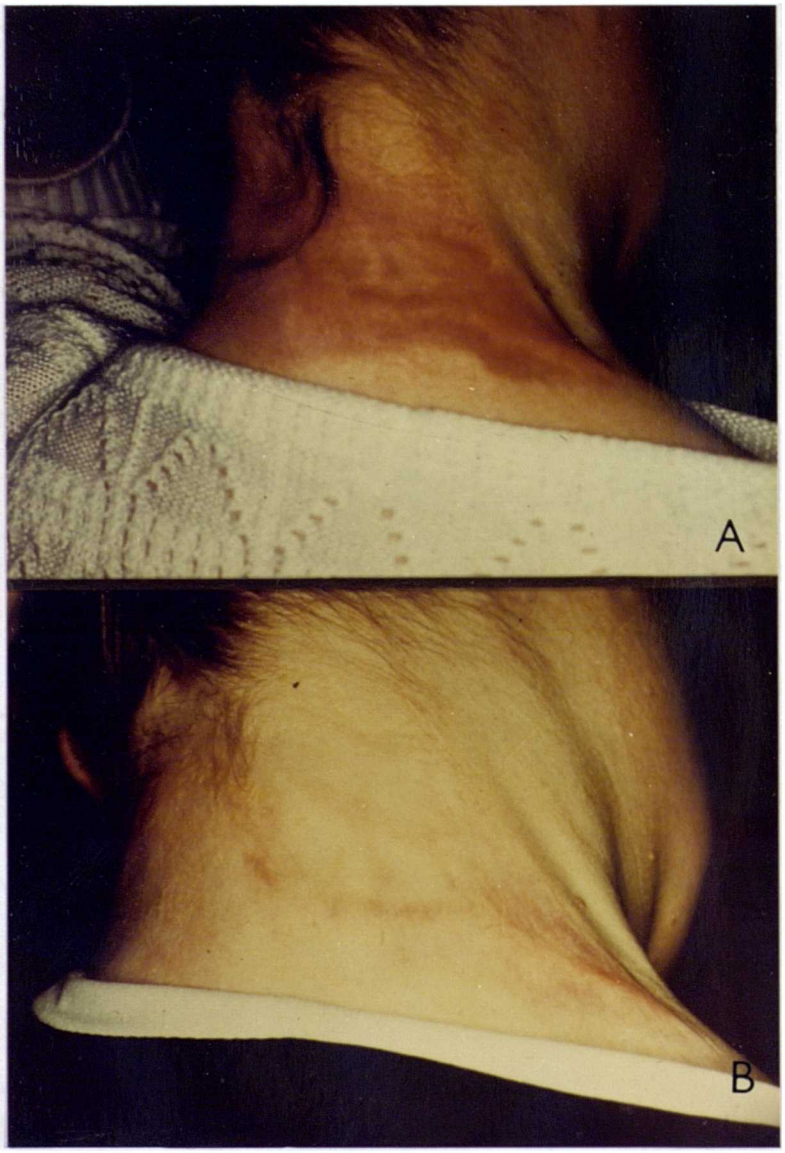


Figure 7.28 Case no. 39. A, 3 months after injury the edges are beginning to thicken; B, after 4 weeks of silicone gel treatment the area is completely flattened and blanched.

Case Study No. 39

F.J., a 31 year old woman, suffered a partial thickness burn injury to her neck. The healed area (Figure 7.28A) started to become hypertrophic 3 months after injury. Silicone gel was applied and after 4 weeks (Figure 7.28B) the scar has become softer, flatter and completely blanched.

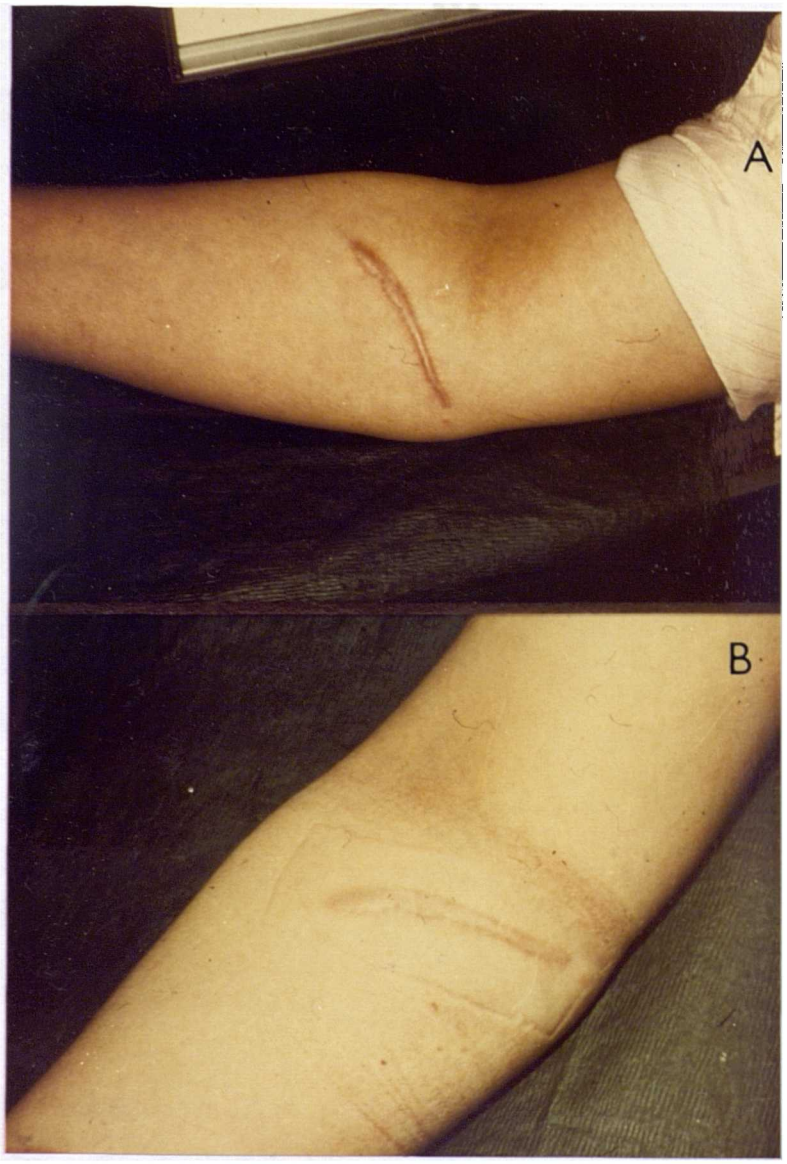


Figure 7.29 Case no. 41. A, 11 months after surgery; B, 6 weeks after silicone gel treatment the scar is flatter and blanched.

Case Study No. 41

A.C., a 35 year old woman, developed a hypertrophic scar on her forearm 11 months after a surgical incision (Figure 7.29A). Silicone gel was applied, and after 6 weeks (Figure 7.29B) the scar has become softer, flatter and blanched.

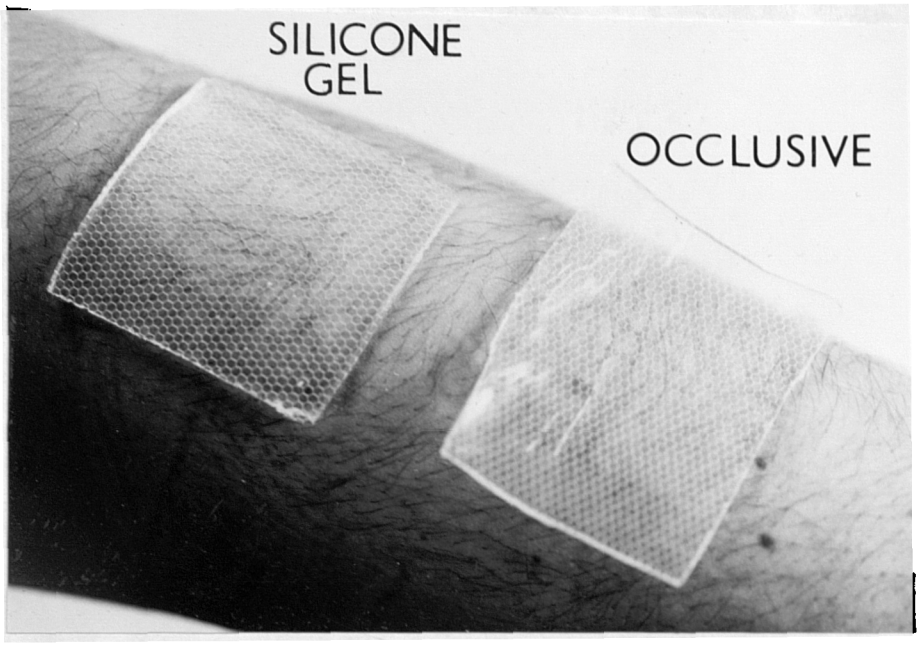


Figure 7.30 Volunteer wearing silicone gel and the "occlusive" covering.

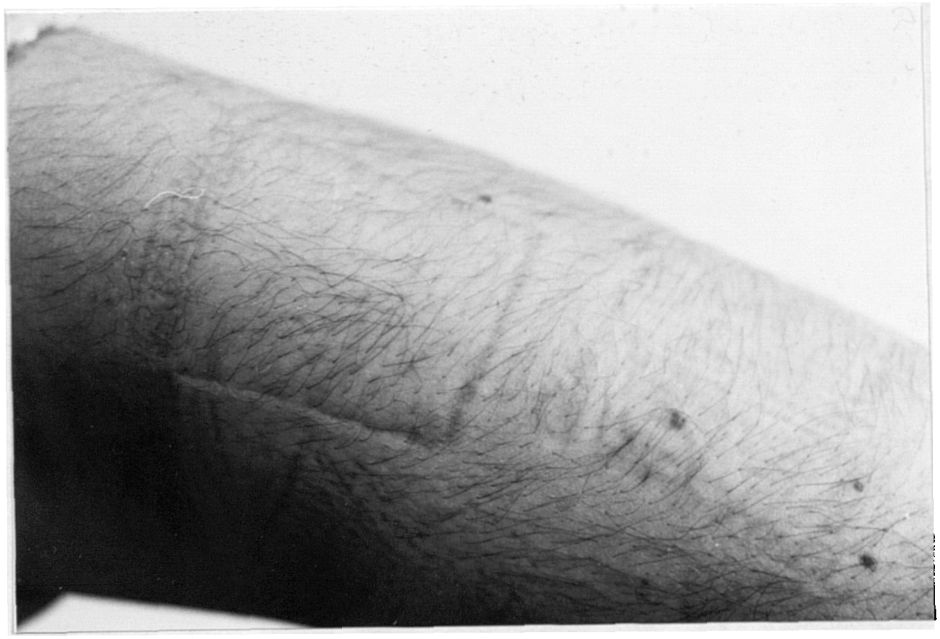


Figure 7.31 Removal of the above after 24 hours. Note the outline where silicone gel was positioned.

7.4.2 Comment.

In Figure 7.29B the outline of silicone gel is clearly visible, and it was suggested that this was evidence that silicone gel applied pressure. However, when silicone gel and the "occlusive" covering (see 7.3.4) were worn for 24 hours, both held in position with a crepe bandage, the outline can be observed where silicone gel had been applied (Figures 7.30 & 7.31) but not where the "occlusive" covering had been applied. It is thought that the outline is the impression obtained by the weight of silicone gel on the leached silicone fluid.

7.4.3 Other Scars Treated With Silicone Gel

Four patients with non-hypertrophic scar were successfully treated with silicone gel (Table 7.1).

Case No. 10 S.D., a 22 year old woman, had a linear, flat scar on her thigh which was discoloured. Application of silicone gel reduced this discolouration.

Case No. 53 M.M., a 2 year old boy, sustained deep burns to his face. His injuries required skin grafting. After the skin grafting operation, a pressure garment was advised to reduce the possibility of hypertrophic scarring. To prevent friction between the pressure garment and his grafted face, silicone gel was also applied. Silicone gel kept the grafted skin soft and supple.

Case No. 69 K.M., a 34 year old man, required a surgical

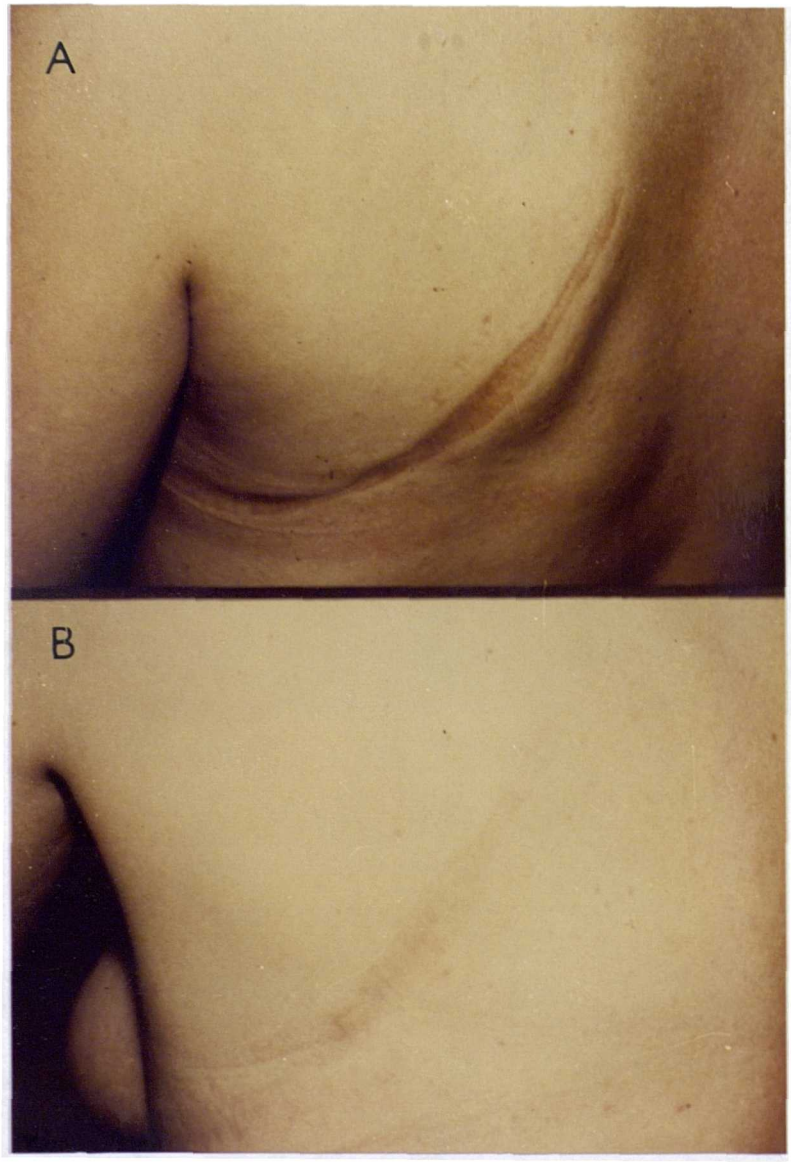


Figure 7.32 Case no. 16. A, depressed scar 20 years after surgery; B, 2 months after silicone gel treatment.

operation to remove a growth from his forehead. Since this patient is a Negro, there were fears that the scar would become hypertrophic. Silicone gel was applied 2 weeks after removal of sutures to prevent hypertrophy occurring. Three months after silicone gel application, the scar shows no sign of hypertrophy.

Case No. 16 J.P., a 24 year old woman, had a depressed scar on her back (Figure 7.32A) which was the result of an operation 20 years previously. Silicone gel was applied, and after 2 months (Figure 7.32B) there has been a dramatic improvement in the cosmetic appearance of her scar.

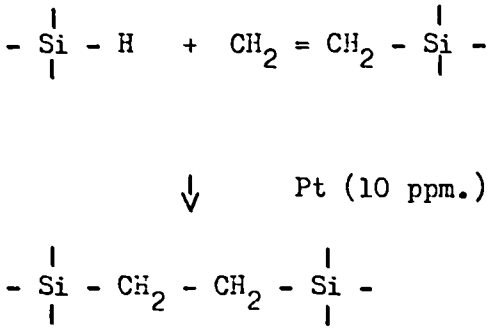


Figure 8.1 The vinyl addition curing system employed to manufacture silicone gel.

CHAPTER 8

USE OF SILICONE GEL AS A BURN DRESSING

8.1 INTRODUCTION

Before a material is applied to burn wounds it should be tested in the laboratory to determine whether it possesses similar properties to the "ideal" burn dressing (see chapters 4 & 5). Thus, the properties of silicone gel were investigated prior to use on open wounds.

8.2 PROPERTIES OF SILICONE GEL

8.2.1 Chemistry

Silicone gel is manufactured by employing the vinyl addition curing system (Figure 8.1) with a platinum catalyst (10 ppm.). The repeat unit of the gel is $(Si(CH_3)_2O)_n$, where n is approximately 100 and the molecular weight approximately 9000.

8.2.2 Mechanics

8.2.2.1 Tensile testing. A tensile test, a modification of the international ASTM D882-67 test, was carried out on an Instron TTCM Materials Testing Machine. Samples of silicone gel were cut into strips 1 cm wide, with a test length of 5 cm. Pneumatic grips provide a constant gripping force and can be used at low pressure for soft materials. However, the nature of the material proved to be difficult to grip and, even at very low pressure, the material broke down around the grips. To overcome this, "Perspex" strips were placed parallel to the test strips and

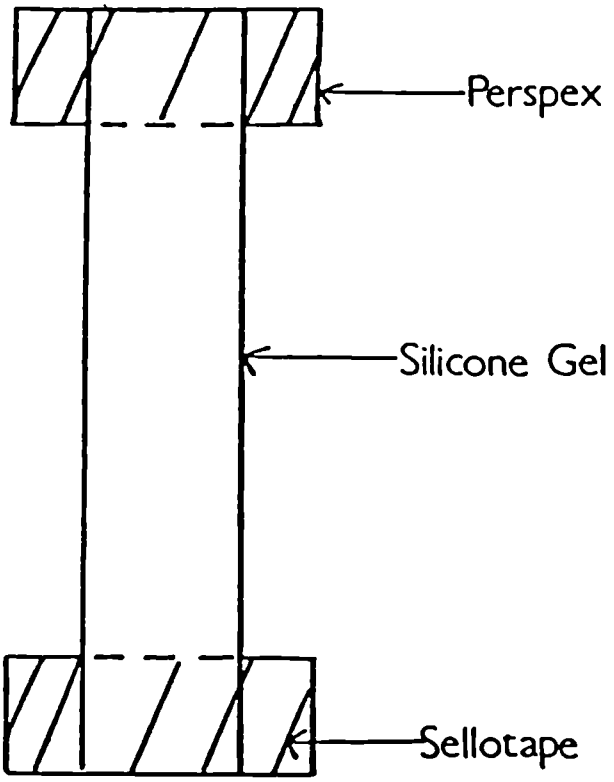


Figure 8.2 The test sample used in the mechanical testing of silicone gel.

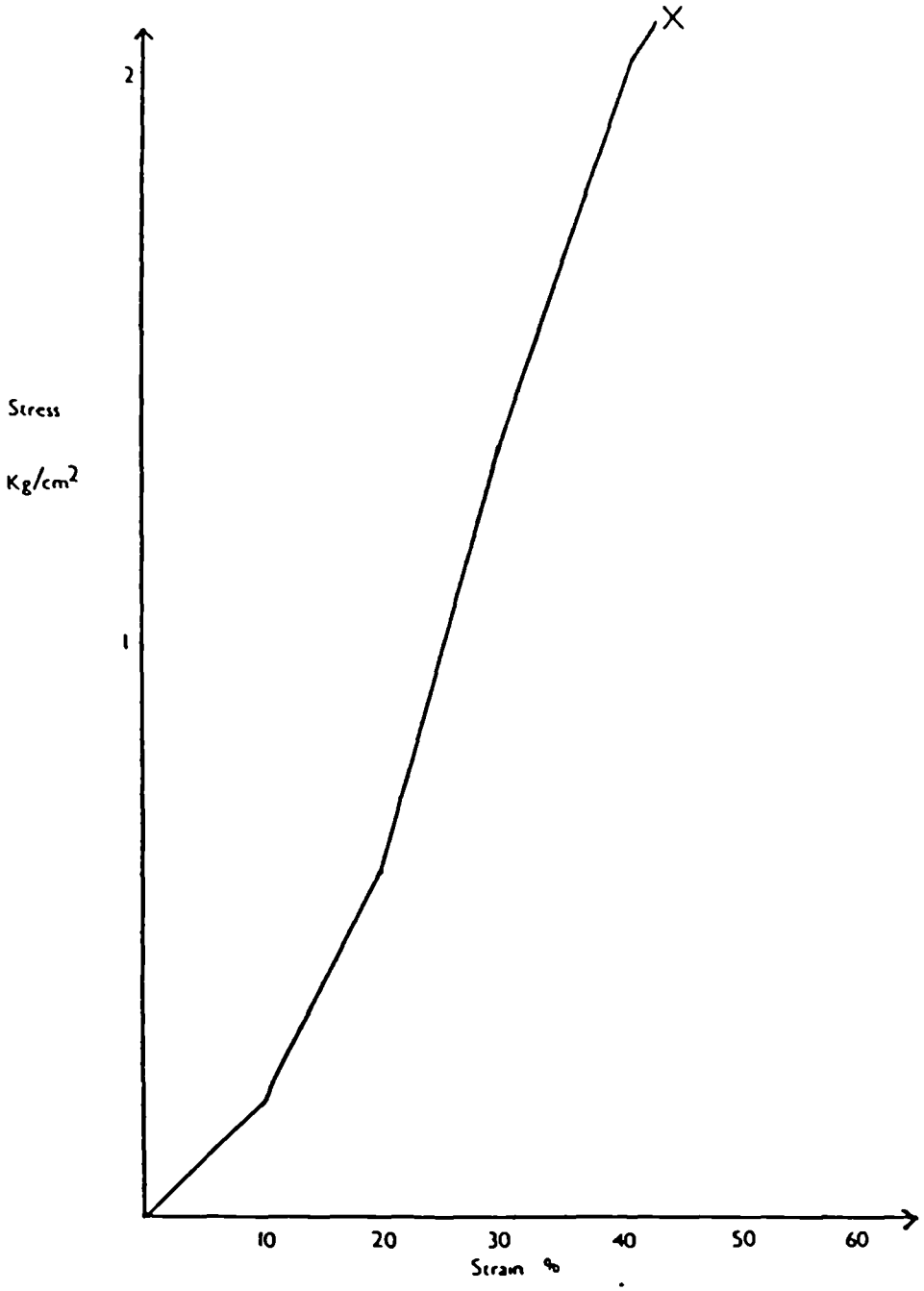


Figure 8.3 Tensile testing results. From the graph:

Breaking load = 225 g

Elongation at break = 41.8%

Tensile strength = 2073 g/cm^2 = 2.073 kg/cm^2

Figure 8.4 The test cell used in experiments to determine the conformability of silicone gel.

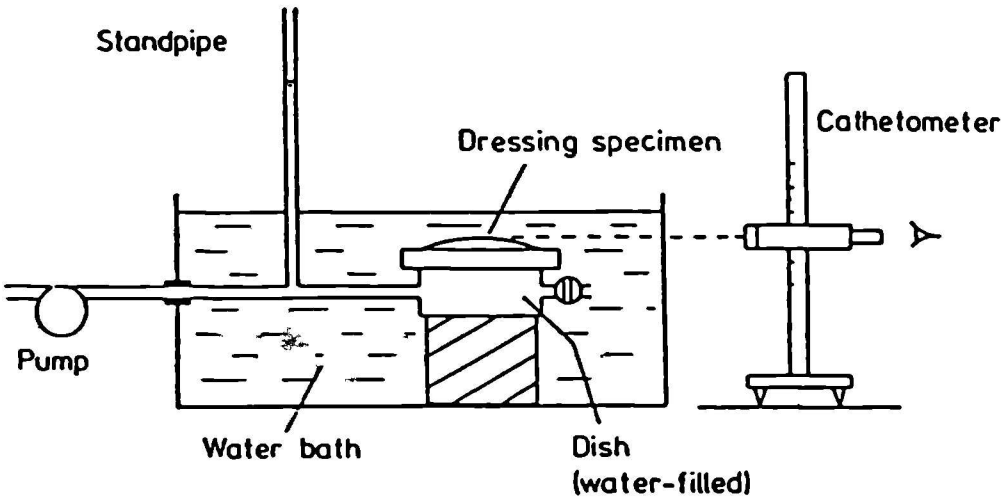


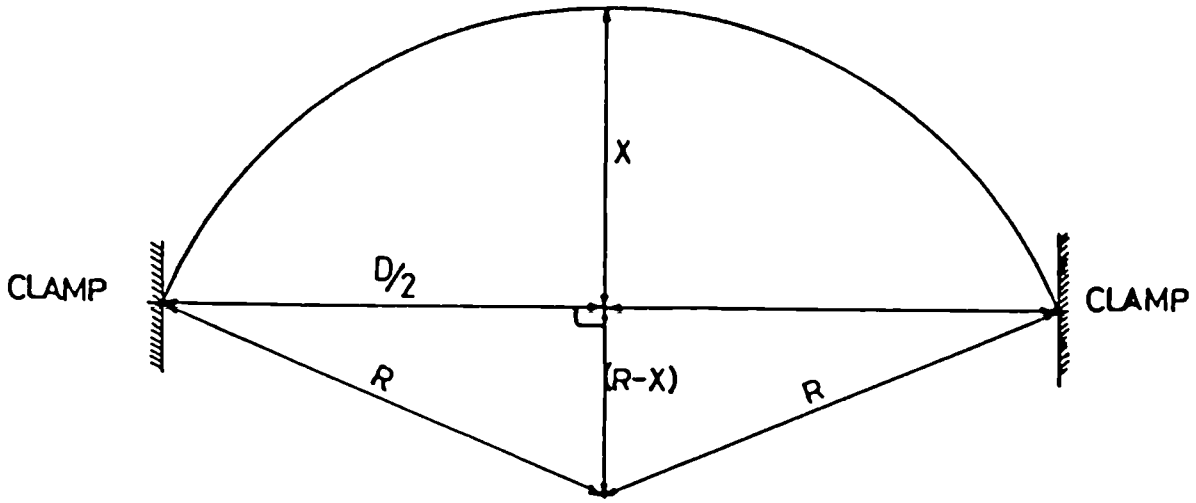
Figure 8.5 Apparatus used to determine conformability.

the system was held with "Sellotape" (Figure 8.2). The material could then be gripped.

Testing was carried out at a strain rate of 40%/minute ($0.008s^{-1}$) and the results are summarised in Figure 8.3. Problems arose, at the point X on the graph, when the gel just below the grips broke down and testing could not be carried out beyond this point.

Biaxial tests are necessary to determine the ability of a dressing to adapt. However, the nature of silicone gel is such that pure shear (constrained biaxial) tests cannot be carried out.

8.2.2.2 Conformability. An inflation test, devised to determine the conformability of dressing materials (Queen et al., 1985), was utilised. The test cell (Figure 8.4) was filled with distilled water and the lower wet/dry emery (grade P150C) cloth gasket was placed on the test cell rim. The prepared sample was carefully placed on top of the water surface and the test cell cap was screwed down to clamp the material in position. Any residual air trapped below the test material was removed, via the outlet port, using a syringe. Additional water may be added, via the inlet port, to bring the material to its neutral position (i.e. flat). Both the inlet and outlet ports were closed. Assessment was carried out in a submerged position (Figure 8.5) to counteract any sagging by buoyancy effects. When placed in the tank, the test pressure was applied to the specimen via the inlet port. It was essential that the inlet port remained closed until the



Change in height (X) = maximum height - reference height

$R^2 = D^2/4 + (R - X)^2$

$R^2 = D^2/4 + R^2 - 2RX + X^2$

$R = D^2/8 + X/2$

R = radius of curvature (cm)

D = diameter of exposed area of disc (cm)

X = change in height

Figure 8.6 Derivation of the formula used to calculate the radius of curvature from experimental data (Queen - personal communication).

Table 8.1 The radii of curvature of different body regions (Queen et al., 1985).

REGION	RADIUS OF CURVATURE (cm)
Buttocks	14.5
Head	10.2
Knee	9.3
Shoulder	7.5
Elbow	5.5
Heel	5.0
Knuckle	1.5
Finger joint	1.0

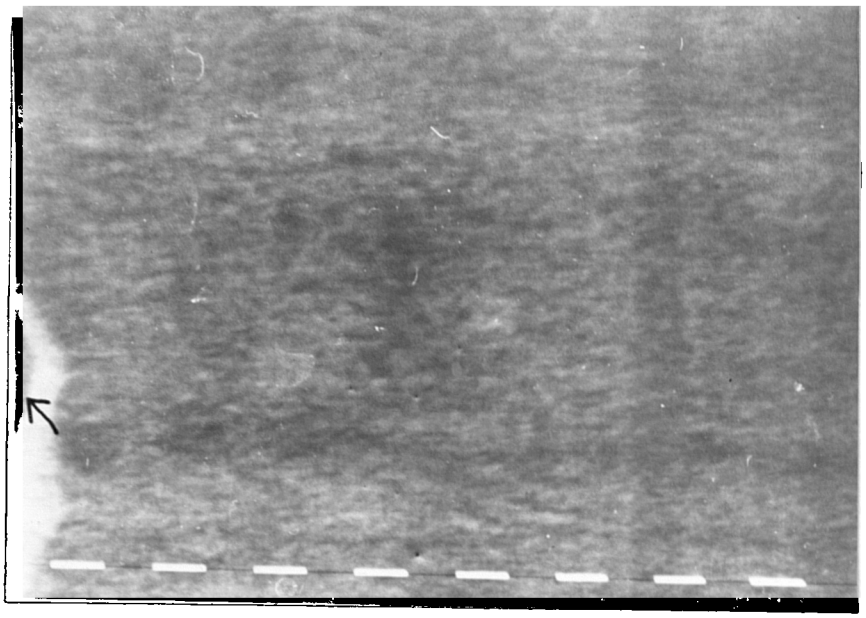


Figure 8.7 SEM micrograph of silicone gel (x5000). The surface is smooth; dirt is arrowed.

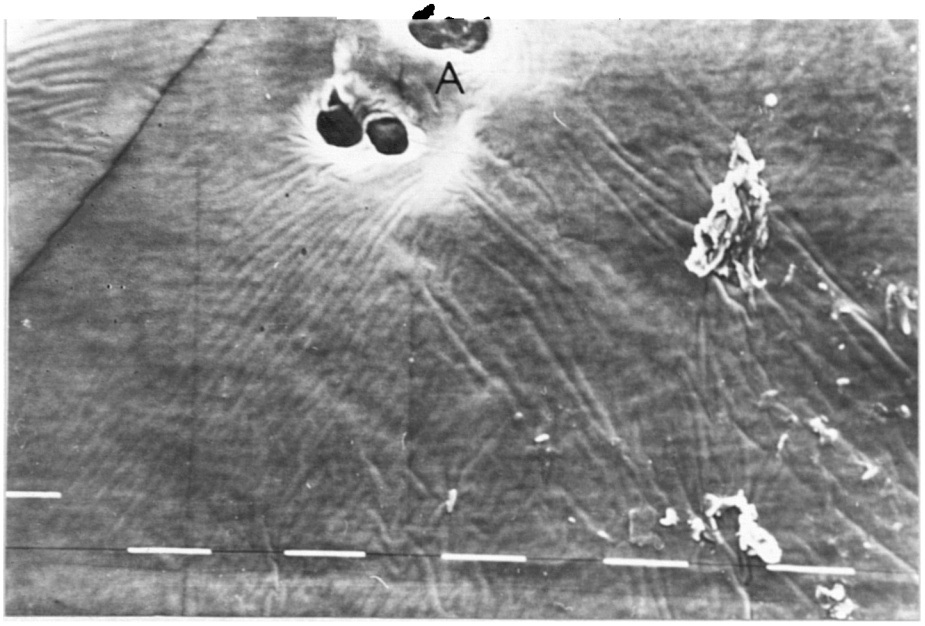


Figure 8.8 SEM micrograph of silicone gel (x2500). The surface is wrinkled; the pits (A) are artefacts of the preparative procedure.

Figure 8.9 SEM micrograph of silicone gel (x2500). Arrows indicate disolved gases.

height measurement had been recorded. Height was measured using a free standing travelling microscope (Griffen & George Ltd.). The inlet tap was opened to allow water to enter the test cell and closed one minute later, when the height was recorded. The radius of curvature was calculated from the formula (Figure 8.6) and compared with the radii of curvature for different regions of the body surface (Table 8.1).

Silicone gel was assessed in the above manner. However, clamping the material was problematic since it continually broke down and no results could be obtained using this method. However, since the material is as extensible as skin (Quinn et al., 1985a) silicone gel has adequate mechanical characteristics to cover joints and allow joint motion.

8.2.3 Appearance in the Scanning Electron Microscope. Pieces (2x2 mm) of silicone gel were attached to sample holders with double sided adhesive tape. The specimens were coated with gold. and a conducting material (Colloidal Graphite) was painted around the specimen, next to the stub, to complete the path to earth. The samples were then examined in a Phillips 501 Scanning Electron Microscope (SEM).

Silicone gel appears to have a relatively smooth surface (Figure 8.7), although "wrinkles" may be present (Figures 8.8 & 8.9).

8.2.4 Bacteriology

To test whether silicone gel is permeable to bacteria, two types of experiment were carried out.

1. Isosensitest agar was inoculated with the test organism

Table 8.2 The organisms used to determine the bacterial barrier effect of silicone gel.

Standard organisms:

Oxford *Staphylococcus aureus*

NCTC *Escherichia coli*

Wild strains:

Staphylococcus aureus 1

S. aureus 2

S. aureus 3

S. aureus 4

Staphylococcus spp. 1

Staphylococcus spp. 2

Streptococcus faecalis

Streptococcus mitis

Catalase negative Streptococcus spp.

Streptococcus spp.

Escherichia coli 1

E. coli 2

Candida albicans 1

C. albicans 2

C. albicans 3

C. albicans 4

Pseudomonas spp. 1

Pseudomonas spp. 2

Klebsiella spp.

Figure 8.10a The test cell used in the experiments to determine the water vapour transmission rate of silicone gel.

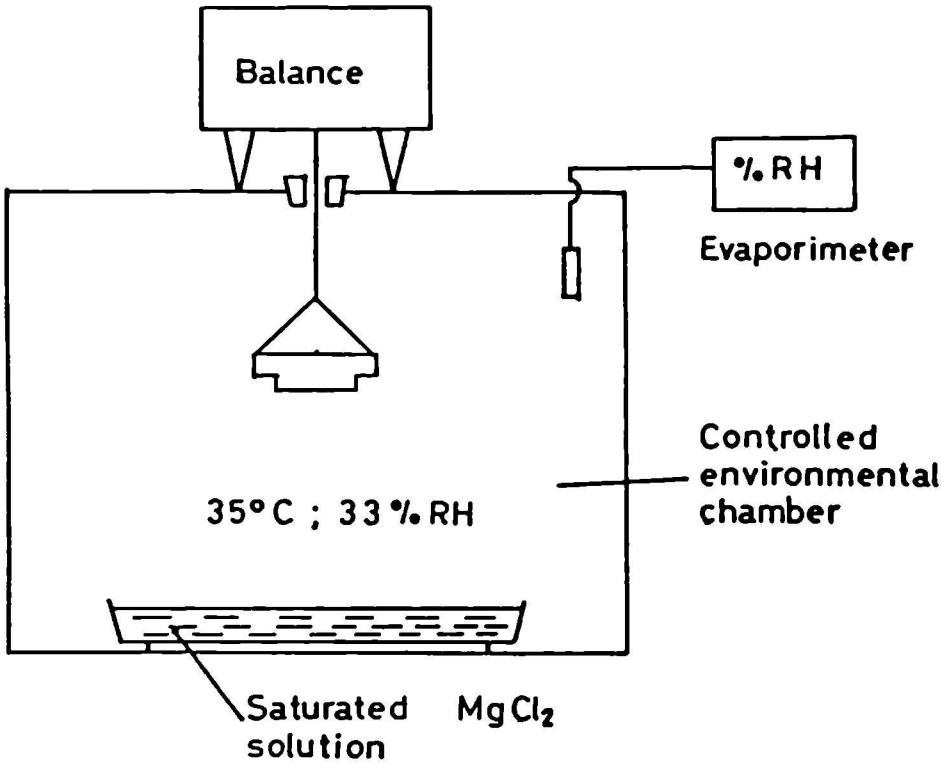


Figure 8.11 The apparatus used to determine water vapour transmission rate.

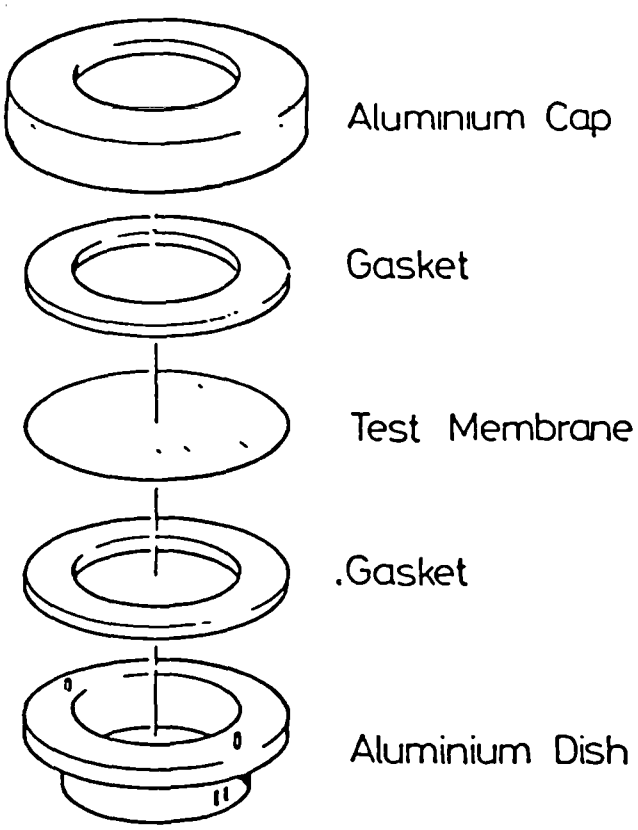


Figure 8.10b

(Table 8.2) and covered with silicone gel. The plates were incubated for 48 hours at 37°C in air. After the incubation period, colonies were observed growing under the material. To test whether organisms had grown through the gel, swabs were taken from the surface and were introduced into Columbia blood agar and Oxoid brain, heart infusion broth. After incubation, for 24 hours in air at 37°C, no growth was observed.

2. Pieces of silicone gel were placed on Isosensitest agar and the surface of the material was inoculated with the test organism. Following incubation, in air at 37°C for 48 hours, no colonies were observed. However, pure cultures of the organisms were recovered from the deliberately contaminated surface of silicone gel by the method described above.

These results show that silicone gel is impermeable to the organisms tested. Also, the material appears to be inert since it neither inhibits microbial growth nor alters it in any way.

8.2.5 Water Vapour Transmission Rate

Water vapour transmission through silicone gel was evaluated using a modification of the ASTM method E96-66. The material was mounted in a circular dish (Figures 8.10a & 8.10b), between two gaskets, containing 20 ml distilled water and with a test area of either 4.42×10^{-3} or 4.36×10^{-3} m^2. The dish was placed in an environmental chamber (Figure 8.11) in which the circulated air was kept at 35 +/- 1°C and the relative humidity at 33 +/- 1% (controlled by a saturated solution of magnesium chloride). The dish was orientated within the environmental

Table 8.3 Water vapour transmission rate of silicone gel.

TEST NO.	THICKNESS (cm)	RELATIVE HUMIDITY (%)	TEMPERATURE (°C)	SLOPE (g/h)	AREA (m^2)	WVTR ($g/m^2/h$)
1	0.135	32	35	0.022	0.00442	5.0
2	0.150	33	35	0.019	0.00442	4.3
3	0.151	33	35	0.018	0.00442	4.1
4	0.152	33	35	0.020	0.00442	4.5
5	0.135	33	34	0.020	0.00442	4.5
6	0.151	33	35	0.020	0.00442	4.5
7	0.118	33	34	0.029	0.00442	6.6
8	0.135	32	35	0.018	0.00442	4.1
9	0.116	33	35	0.033	0.00442	7.5
10	0.189	33	35	0.016	0.00442	3.6
11	0.132	33	35	0.018	0.00442	4.1
12	0.132	33	35	0.018	0.00442	4.1
13	0.220	33	34	0.012	0.00442	2.7
14	0.138	33	35	0.025	0.00442	5.7
15	0.148	33	35	0.017	0.00442	3.8
16	0.217	33	35	0.013	0.00442	2.9
MEAN +/- 1 S.D.	0.151 +/- 0.030					4.5 +/- 1.2

TIME POINTS AND WEIGHT LOSS VALUES FOR SILICONE GEL 5.000
30/7/84

POINT NO.1.000	1.000	0.030
POINT NO.2.000	2.000	0.051
POINT NO.3.000	3.000	0.073
POINT NO.4.000	4.000	0.101
POINT NO.5.000	5.000	0.116
POINT NO.6.000	6.000	0.127

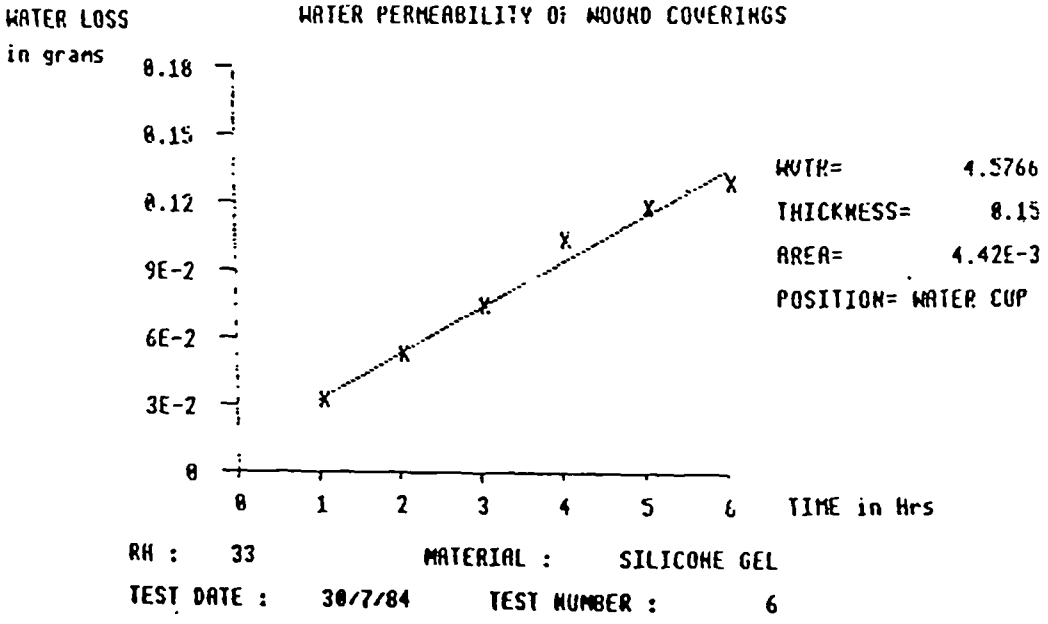


Figure 8.12 Water vapour transmission rate result of one test.

to have a saturated air space and the test material uppermost. By periodically weighing the dish, the rate of water loss and hence the water vapour transmission rate were determined.

The results are calculated from the gradient of the straight line in the graph of weight loss vs. time, divided by the surface area of the test sample. A computer program (D. Queen - personal communication) has been developed to calculate the water vapour transmission rate from the raw experimental data (Appendix II).

The results obtained (Table 8.3) indicate a WVTR of 4.5 +/- 1.2 (n=16) g $m^{-2}h^{-1}$ for silicone gel of thickness 1.51 +/- 0.30 mm (Figure 8.12).

Other silicone and non-silicone materials were tested by this method and the results are summarised in Appendix V.

8.2.6 Comment

The requirements of a burn dressing are discussed in chapters 4 and 5. From the investigation into the properties of silicone gel, it can be noted that the material fulfils some of the requirements i.e. it forms an effective bacterial barrier, it has the desired mechanical characteristics, it is permeable to water vapour, and allows gaseous exchange (see 7.3.3). Also, use of silicone gel on hypertrophic scars indicates that the material is comfortable, durable, easy to apply and remove, non antigenic and non toxic. Thus, silicone gel can be applied to burn wounds which have no exudate loss or are bleeding.

8.3 EFFECT OF SILICONE GEL ON BURN WOUNDS

8.3.1 Application of Silicone Gel

Patients were selected by Professor W.H. Reid at the Burns

Unit, Royal Infirmary, Glasgow, and were closely monitored by the nursing staff.

Silicone gel was applied to the wounds after the patient had bathed. Gauze swabs were placed over it to prevent slipping of the material after a crepe bandage was positioned.

The dressing was changed every alternate day, and the first advantage observed using silicone gel was that it can be washed and replaced. Also, it has soothing properties and removal is pain-free.

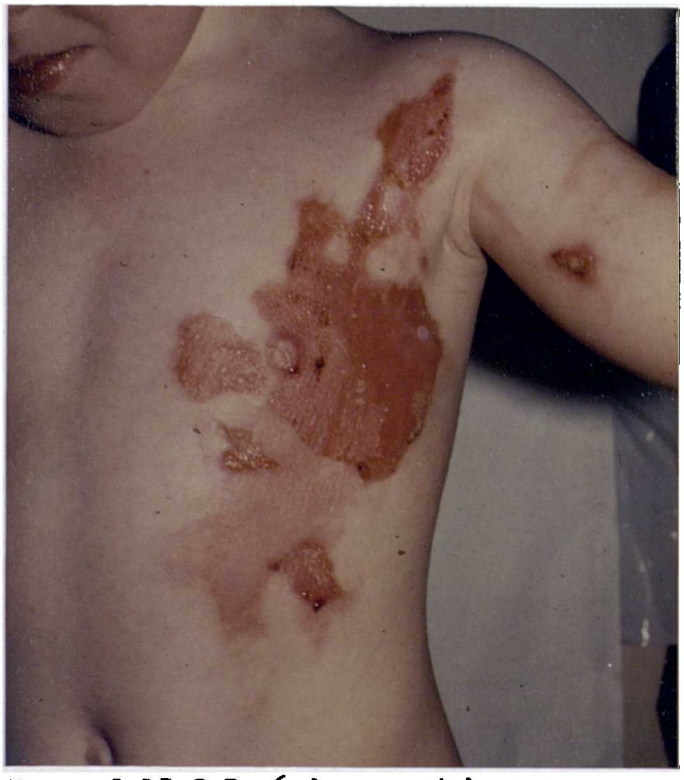


Figure 8.13 D.D. 6 days post-burn.

Figure 8.14 D.D. 38 days post-burn.

8.3.2 Case Studies

Case Study No. 15

D.D., a 3 year old boy, suffered a scald injury to his chest and right shoulder. He was initially treated with Hibitane soaks and "Jelonet" and "Teracotryl" dressings. Six days post-burn (Figure 8.13), since the wound was clean, Professor I.H. Reid suggested applying silicone gel. The following day, the wound had healed and the patient discharged (staff expected the wound to heal after a further 4 days with conventional dressings). Silicone gel application was continued for a month, after which (Figure 8.14) no scarring was evident.

Case Study No. 71

R.T., a 9 month old boy, sustained a 6% scald ($\frac{1}{2}$ full thickness) to his anterior chest and right arm. Before admission to the Royal Infirmary, ready dressings were applied, thereafter "Flamazine" dressings were administered. Three days post-burn silicone gel was applied (Figure 8.15). Two days after application of silicone gel there was no weeping of the wound (Figure 8.16). He was discharged the following day, silicone gel was advised to be used until evaluation at the out-patient clinic. Four days later, only a small area (Figure 8.17, arrow) at the axilla had not healed thus silicon gel treatment continued. After a further month, only the slower healing area was erythematous (Figure 8.18).

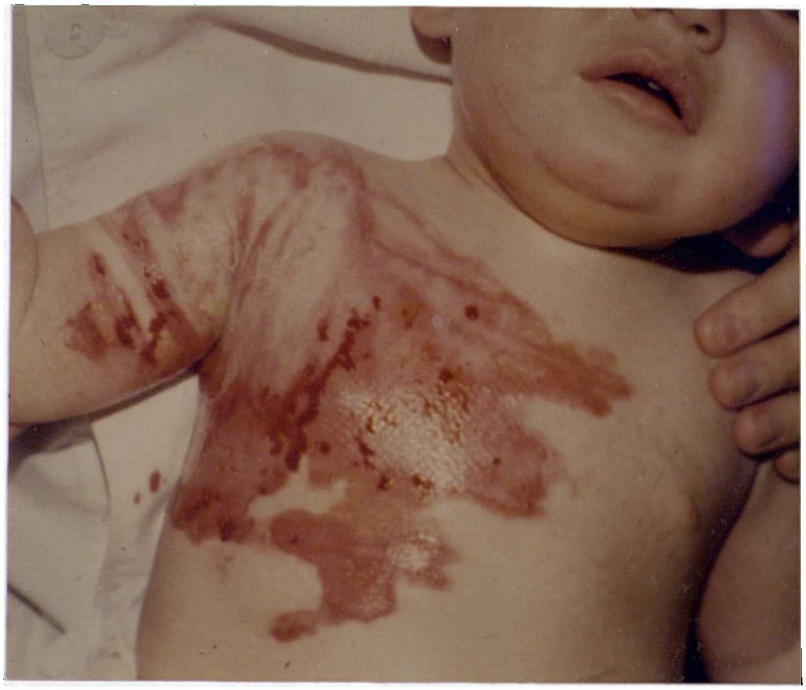


Figure 8.15 R.T. 3 days post-burn.

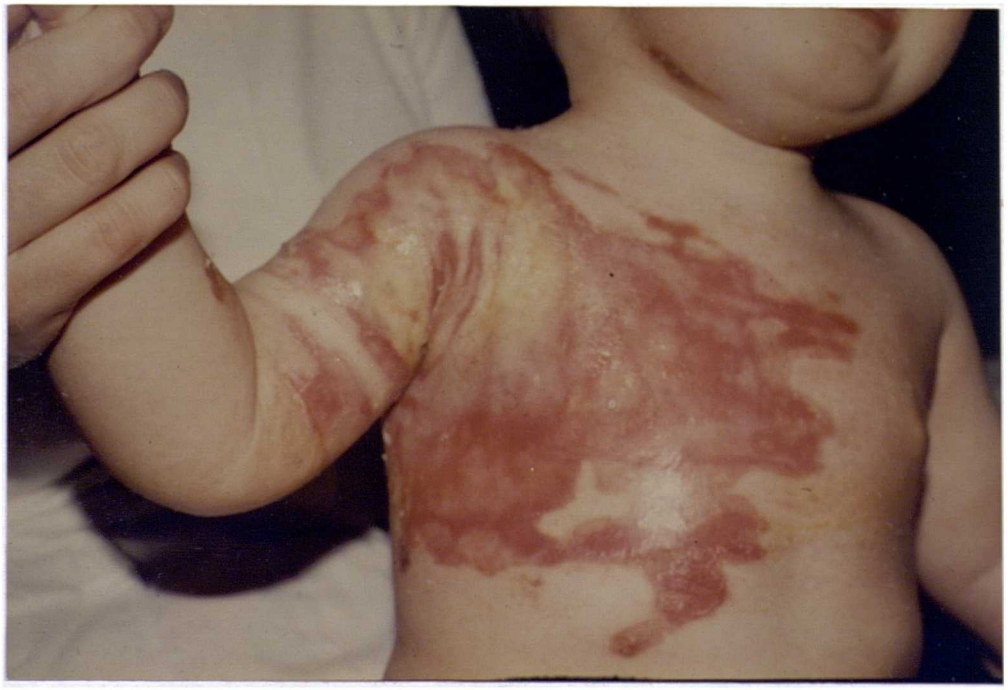


Figure 8.16 R.T. 5 days post-burn.

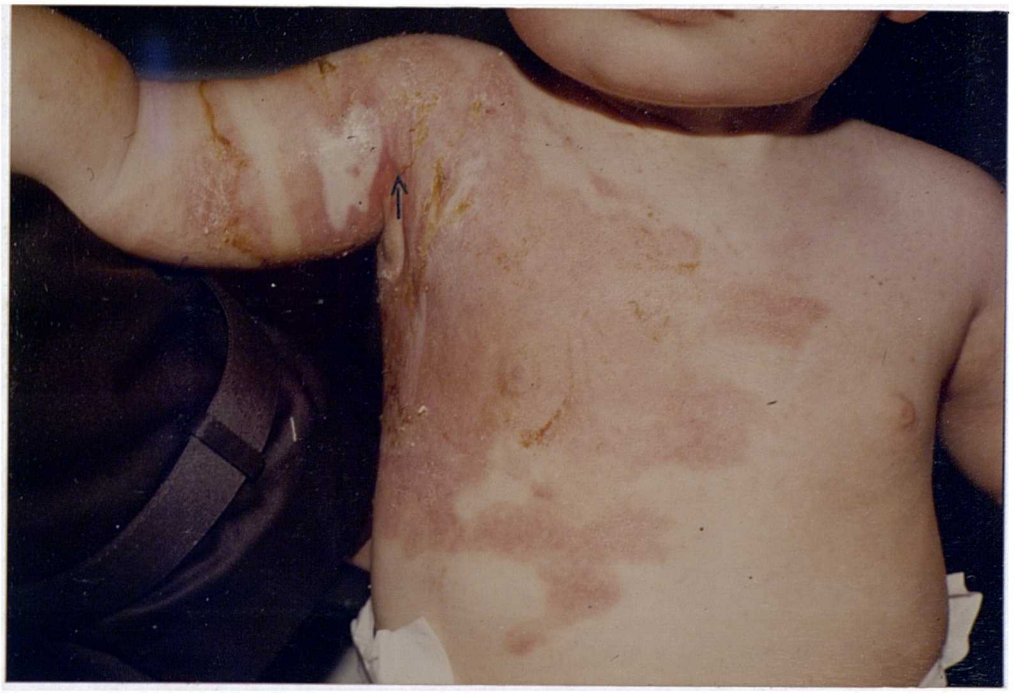


Figure 8.17 R.T. 9 days post-burn; arrow indicates unhealed area.

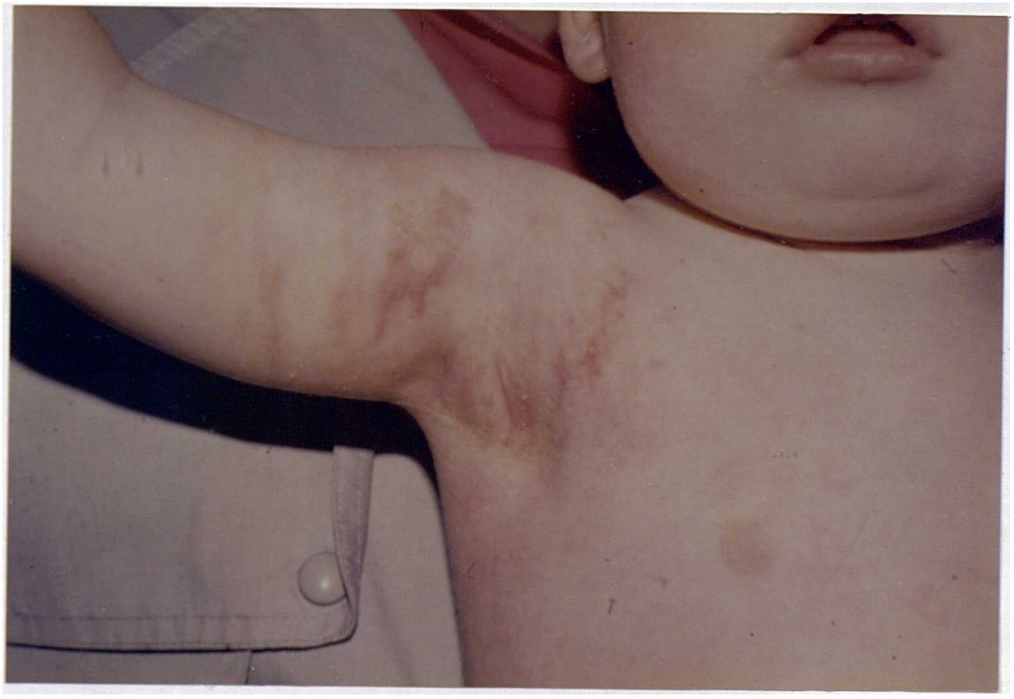


Figure 8.18 R.T. 38 days post-burn.

Case Study No. 74

W.Y., a 64 year old man, fell onto an electric fire and sustained 8% burns (6% full thickness) to his back and left arm. "Jelonet" and "Teracotryl" and later, "Flamazine" dressings were applied. Skin grafting was carried out 14 weeks post-burn, but there was no skin "take." Silicone gel was applied 23 weeks post-burn to the slow healing area on his back and arm (Figures 8.19 & 8.20). He was discharged 2 weeks after application of silicone gel (Figures 8.21 & 8.22). When discharged "Teracotryl," "Fucidin H," "Jelonet" and "Teracotryl" dressings were administered because nursing staff noticed that unless silicone gel was fitted only to the open wound, the newly healed areas surrounding it broke down.

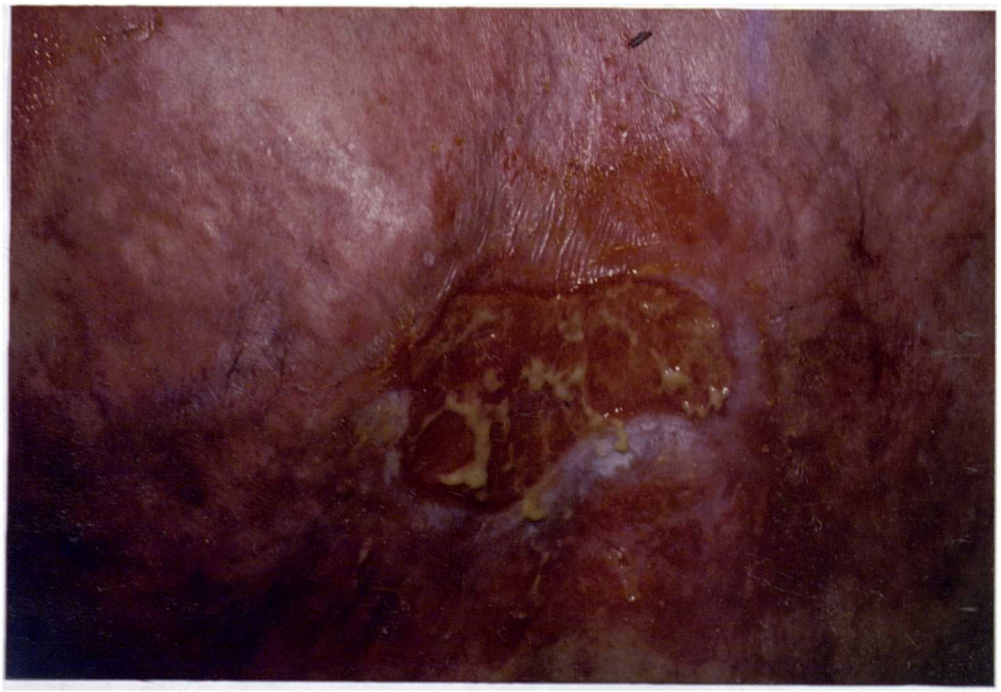


Figure 8.19 W.Y. 23 weeks post-burn.

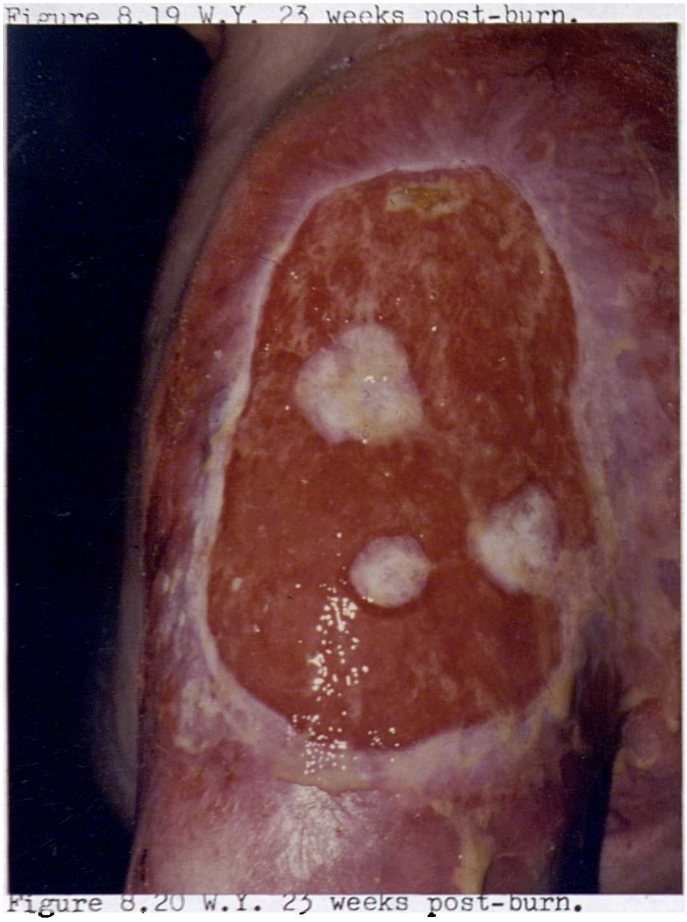


Figure 8.20 W.Y. 23 weeks post-burn.

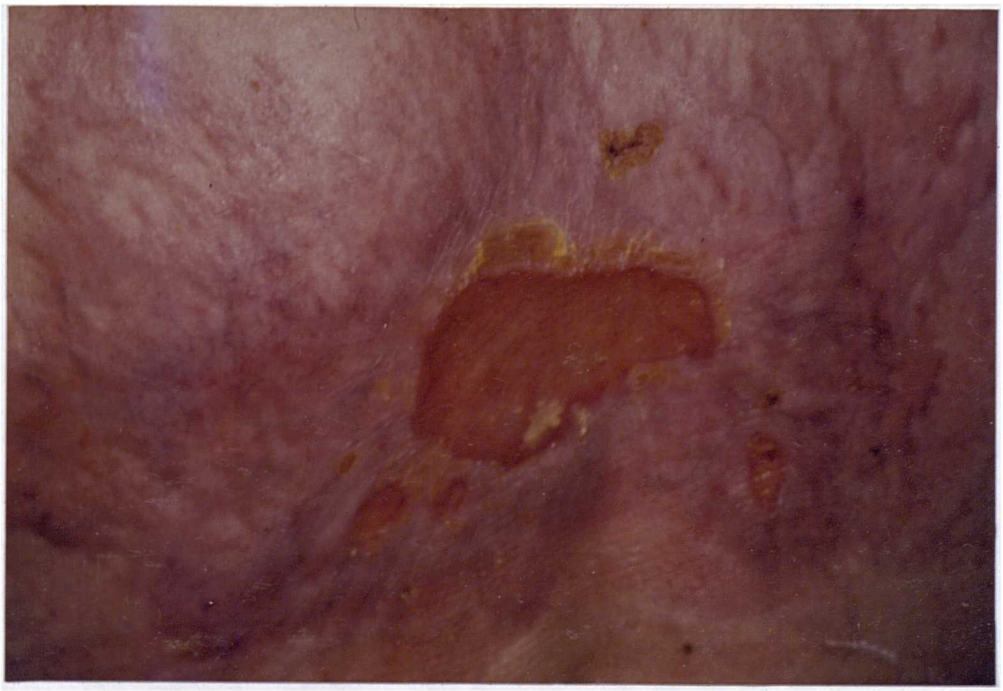


Figure 8.21 W.Y. 25 weeks post-burn.

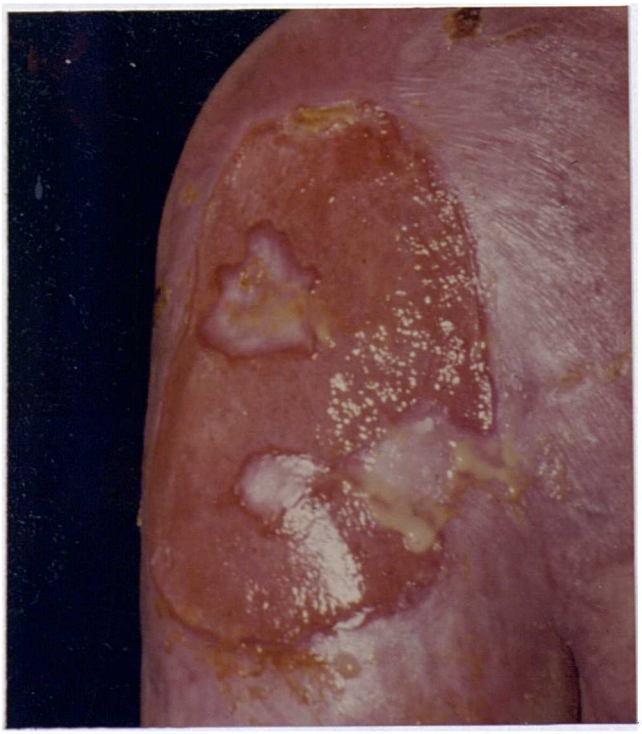


Figure 8.22 W.Y. 25 weeks post-burn.

Both open areas are not as extensive since the application of silicone gel.

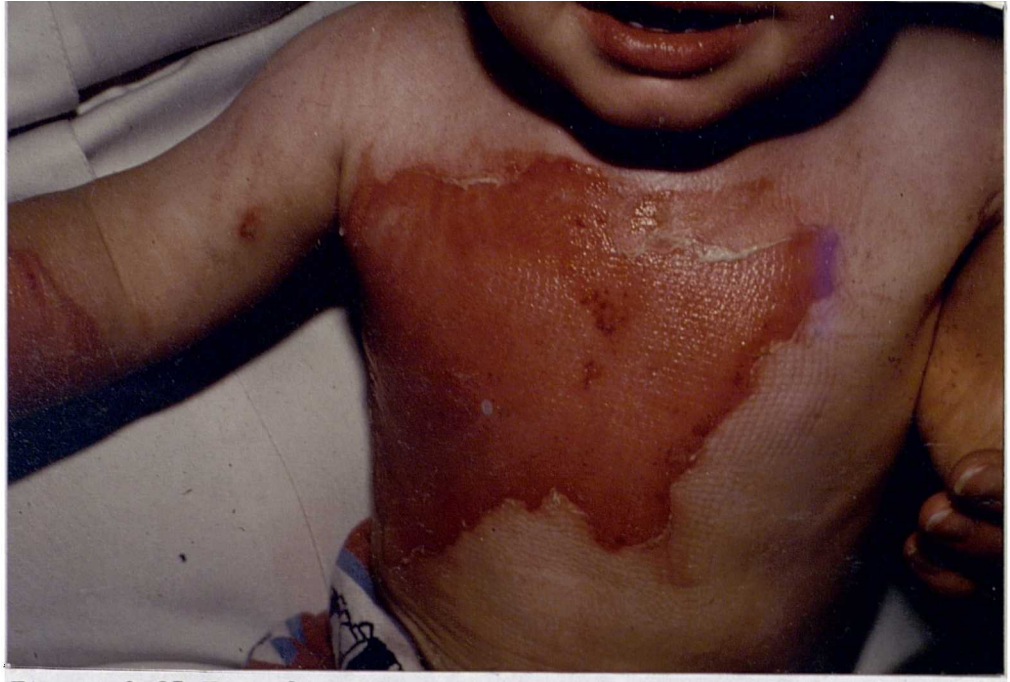


Figure 8.23 N.R. One day post-burn.

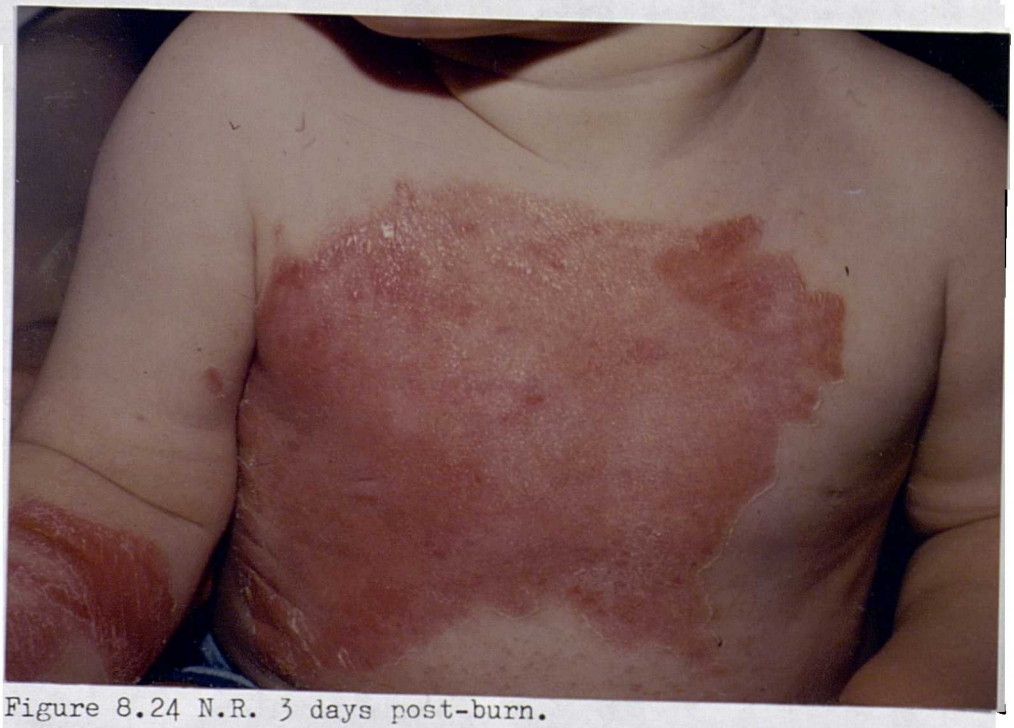


Figure 8.24 N.R. 3 days post-burn.

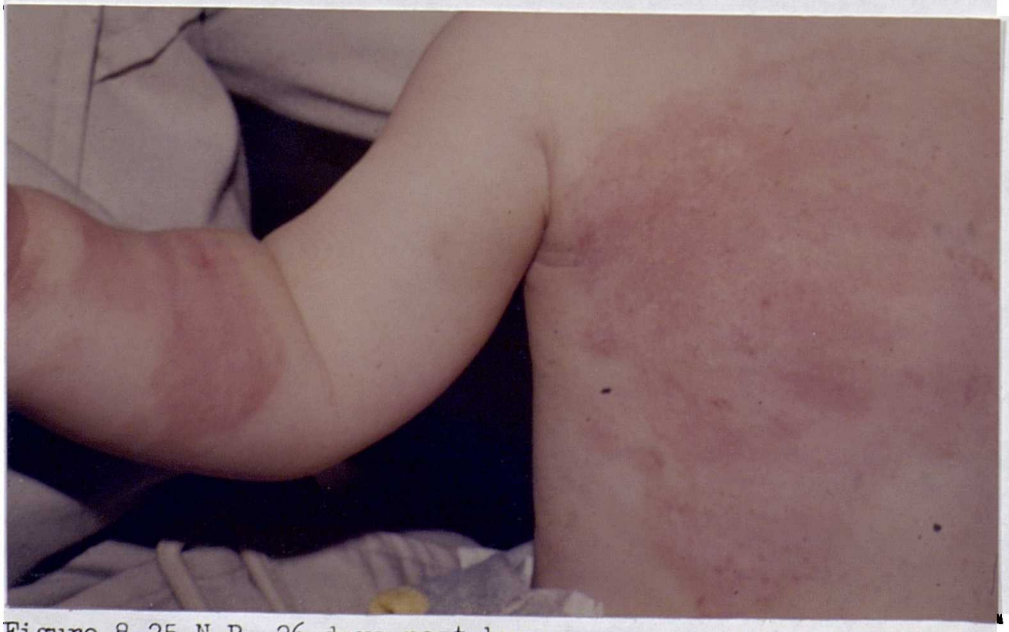


Figure 8.25 N.R. 26 days post-burn.

Case Study No. 75

N.R., a 17 month old boy, sustained a 9% partial thickness scald to his anterior chest, right forearm and hand. Initially, "Hibitane" soaks were applied, then "Jelonet" and "Hibitane" were administered, although "Flamazine" was applied to his hand. One day post-burn it was thought that the chest wound would become deeper, therefore silicone gel was applied the following day (Figure 8.23). Three days after silicone gel treatment most of the weeping had ceased, and had completely ceased after a further two days treatment (Figure 8.24) at which time the surface was flat but erythematous. He was evaluated at the out-patient clinic one week later when his chest was still erythematous. Silicone gel treatment continued for a further 2 weeks when the area became blanched (Figure 8.25). Silicone gel application was discontinued at this time because the patient's mother had difficulty in applying the material.

8.3.2 Comment

The number of patients evaluated in this trial is too small to draw any firm conclusions. However, the results do indicate that silicone gel is an easy to apply, comfortable dressing material which may be beneficial in the treatment of partial thickness wounds.

Table 9.1 Summary of the scar scores of 72 patients with 75 hypertrophic scars.

+	29.3%
++	30.7%
+++	9.3%
PROBLEM	12%
?	18.7%

CHAPTER 9

DISCUSSION

The work presented in this thesis is innovative in that the Dow Corning X7-9119 silicone gel had not previously been applied to either hypertrophic scars or burn wounds.

9.1 TREATMENT OF HYPERTROPHIC SCARS

The clinical trial of silicone gel treatment of hypertrophic scars (72 patients with 75 hypertrophic scars) has been very successful. 81.3% of the patients returned to follow-up assessment, and of these 69.3% (Table 9.1) demonstrated some improvement after 2 months of treatment. The remaining 12%, those with either a rash or break down of the surrounding skin, could have avoided their problems if proper attention to hygiene had been observed. The surrounding skin may break down because of the lower water vapour transmission rate of silicone gel compared to normal skin (4.5 vs. 8.5 g $m^{-2}h^{-1}$). Water will accumulate below the gel and, if the gel is not removed frequently during the application time, the tissue will be macerated. In the under-5 age group, the percentage of patients with these problems was doubled compared to older patients. This may be due either to a lack of tolerance of any dressing in general, or that the application of pressure garments with silicone gel speeds up the maceration process. Indeed, it is now recommended that when both pressure and silicone gel are applied, only one

should be used (usually pressure) for 24 hours/day and both for 12 hours/day.

The mode of action of silicone gel on hypertrophic scars was investigated with the co-operation of the patients. This can be attributed to either a physical effect (e.g. pressure, te perature, oxygen tension, hydration or occlusion) or a chemical effect. Pressure is known to reduce hypertrophic scarring, temperature is important in wound healing (Turner, 1985), an oxygen tension may be present if the aterial is permeable to oxygen (Davey - personal communication), and hydration and occlusion are both important criteria to be considered hen a material could be used on open or recently healed wounds. Each parameter was studied.

The influence of pressure was eliminated because the material exerts practically no pressure; no significant temperature change was found at the scar surface when the material was applied, thus temperature is not important; the permeability of silicone gel to oxygen means that skin respiration is not affected, also, the oxygen tension is not altered by wearing the gel; occlusion is not a contributing factor because the application of a physically identical material (the only difference being that a thin sheet of polyurethane was in contact with the scar) does not improve scar appearance or texture.

Evaporimeter studies have shown that the scar becomes hydrated due to the lower water vapour transmission rate of the gel in comparison to that of normal skin. Although this water

can be detrimental and break down newly healed areas, it may alter the hydration state of the stratum corneum to such an extent that the scar becomes softer to touch, more supple and more extensible.

By elimination, the mode of action of silicone gel must involve a chemical factor. Previous studies (Swanson & LeBeau, 1974; van Noort et al., 1979) have shown that the low molecular weight polymer, which is invariably present in silicone elastomers, does not leach out of the material. This investigation has demonstrated that a low molecular weight silicone fluid is leached from the Dow Corning silicone gel. Two patients wore silicone gel on their hypertrophic scars prior to corrective surgery. Scar samples from these patients and from one patient who did not wear silicone gel were available for chemical analysis. Both SEM-microprobe and chemical analysis indicate that the control scar contained silicon whereas silicone gel-treated scars had a reduced amount. Unfortunately, the techniques employed to detect silicon are inaccurate and no conclusions can be drawn from these results. Thus, this study has neither proved nor disproved the theory that silicone fluid enters the skin and acts in some way to reduce hypertrophic scarring. Further research is required to fully explain this phenomenon.

9.2 USE OF SILICONE GEL AS A BURN DRESSING

The properties of silicone gel suggest that it is an elastic, conformable effective bacterial barrier. However, mechanical testing of silicone gel was problematic. The material has a

reinforcing mesh within its structure which allows silicone gel to be handled under tension, but under compression it crumbles. This feature was also found clinically. Although the material can readily be applied, removed, washed and is durable for normal activities, it does crumble when manhandled. There is no in vitro test for the fragility of materials and this should be investigated.

Silicone gel was applied to relatively superficial burn wounds for short periods of time and therefore did not require the design criteria suggested in Chapter 5 for the "ideal" burn dressing. In particular, silicone gel has no absorptive properties and its water vapour transmission rate is lower than that of normal skin.

Although silicone gel was only applied to four patients during this study, the results are very encouraging. The material has a soothing effect on the wound thus patient co-operation is high, it is also easier to apply and remove than conventional dressings. Its mode of action must be investigated, and, since the study on hypertrophic scars suggests the release of a silicone fluid, silicon levels in the wound should be measured. Also, a wider, controlled clinical trial is essential to determine whether re-epithelialisation is enhanced. Because of the soothing effect of silicone gel, it should be applied, under trial conditions, to donor sites which can be painful and pruritic.

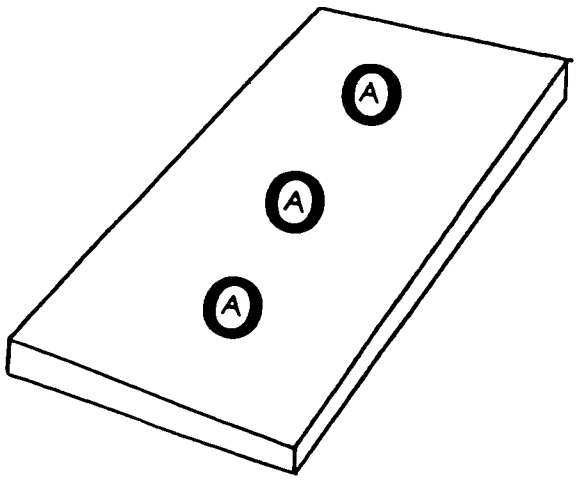


Figure 9.1 Sheet of absorptive material containing pre-cut, pre-weighed discs (A) which can be removed, weighed and returned without disturbing the whole dressing.

9.3 THE "IDEAL" BURN DRESSING

Burn dressings are manufactured from a wide variety of materials into various forms, and although the general properties of the "ideal" dressing are well documented, quantitative values have not yet been determined for those properties which could be so described.

Previous studies (Davies et al., 1974; Lamke et al., 1977) describe the fluid loss from burn patients. However, Davies and his colleagues (1974) present figures for weeks 1,2 & 3 after injury, whereas Lamke and co-workers (1977) describe an average evaporative water loss for an unspecified time after injury. Since these results do not indicate the day-to-day fluid loss nor the effect of factors such as temperature, humidity or the application of dressings, one of the objectives of this thesis was to determine the day-to-day fluid loss from burn wounds under varying conditions.

An experiment, using an absorptive material which did not change shape when hydrated, was devised. A sheet of material containing pre-cut, pre-weighed discs (Figure 9.1) could be applied to wounds and such discs could be removed, weighed and returned to the sheet at various time intervals until the dressing is changed. This could be carried out from the time the patient arrived in the Burns Unit until healing was complete to give an accurate indication of fluid loss over both short and long periods of time. Unfortunately, the hydrophobic nature of silicone materials ruled out their use in such experiments. However, Dow Corning did

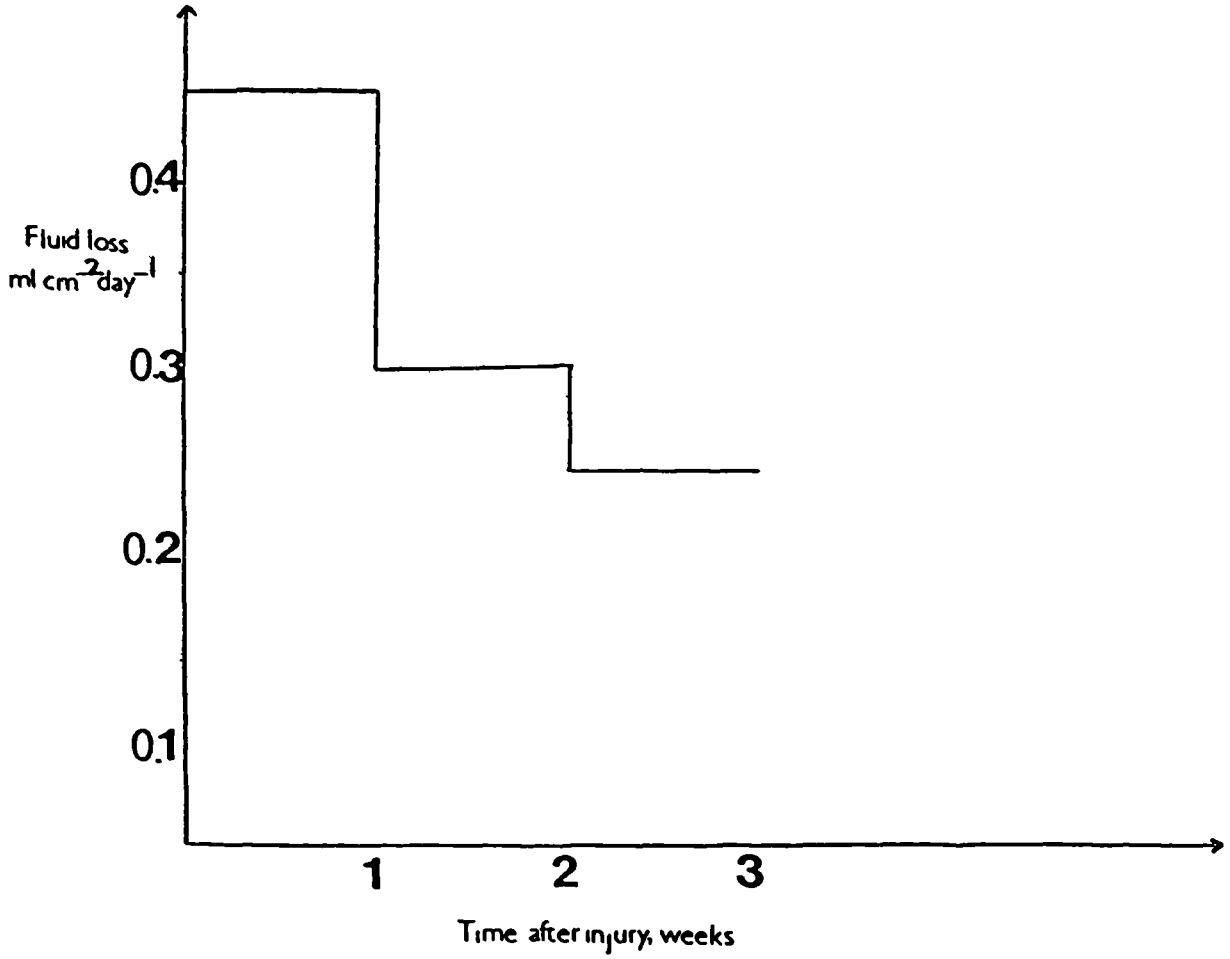


Figure 9.2 Graph of fluid loss from a partial thickness burn vs. time (Davies et al., 1974).

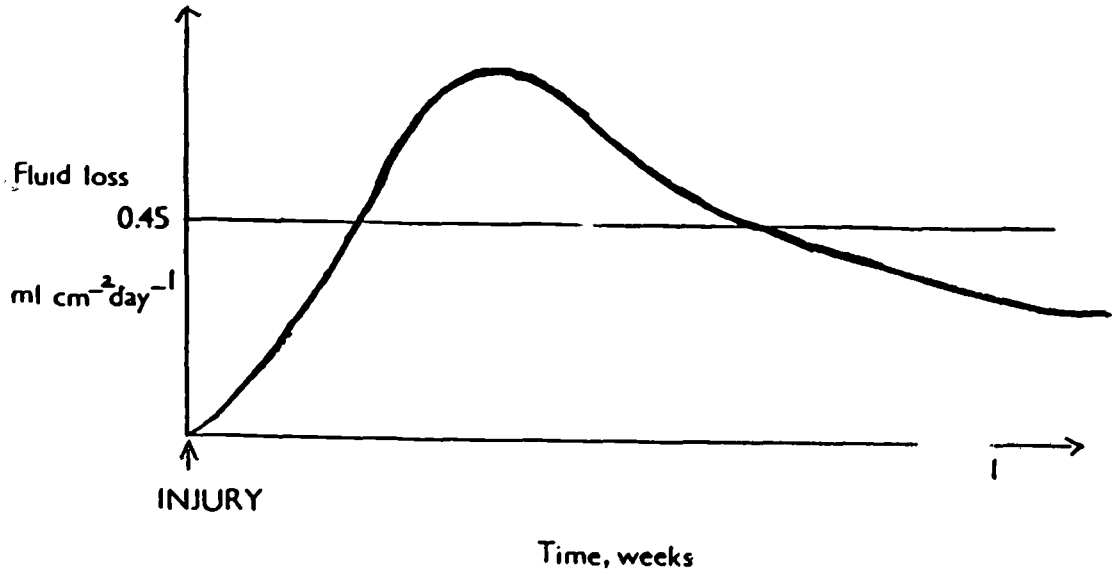


Figure 9.3 Hypothetical graph of fluid loss vs. time for a partial thickness injury.

attempt to manufacture a hydrophilic foam for this study but were unsuccessful.

From the results of Davies and his colleagues (1974), Figure 9.2 indicates the fluid loss from a partial thickness burn over three weeks. However, it is possible that in the first week after injury the fluid loss vs. time graph is more like that in Figure 9.3. If so, it would be desirable to discover the time of peak fluid loss to modify the dressing regime, such that different dressings with varying absorptive and WVTR properties would be required for different times after injury. Accomodating this transient peak may be achieved by various methods, for example, spreading the evaporative water loss over a large time period (if energy loss permits) or by absorption and discarding the dressing, or by a combination of these. Other factors may affect the results, e.g. shock, administration of drugs, room temperature and humidity, and these must also be investigated.

In the future, dressings will enhance their bacterial barrier function by releasing antibacterial drugs, and may directly enhance wound healing by the release of "growth factors" such as epidermal growth factor and fibroblast growth factor, and release of capillary stimulants. However, it is unlikely that any one-dressing will be "ideal" for all burn wounds, and specific dressings will be applied after consideration of the extent and depth of injury. Different dressings are also required for the different phases of injury i.e. first aid, temporary and "permanent" dressings. A first aid dressing must be readily available in

ambulances, be easy to apply, and be removed without causing further injury. One such material which fulfills these criteria is "Clingfilm." A temporary dressing would be one applied on a day-to-day or alternate day basis. It would control fluid loss and protect the wound from infection, and may lead to a dressing which could be kept in postion for several days at a time. Finally, a "permanent" dressing would ideally be the patient's own skin either from healing or grafting or, in the future, from epithelial expansion techniqes.

9.4 CONCLUSIONS AND RECOMMENDATIONS

In conclusion, this thesis presents silicone gel as a new, effective treatment for hypertrophic scars which lessens the time conventionally required to reduce these disfiguring lesions. Investigations into the mode of action indicate that this probably involves the penetration of skin by a low molecular weight silicone fluid and hydration of the stratum corneum. Future chemical analyses of scar tissue treated and untreated with silicone gel are necessary to fully explain this phenomena. Consideration should also be given to an investigation of silicone gels of different composition and different rates of release of the low molecular weight fluid.

Silicone gel also appears to be a useful dressing for burn wounds, although a larger clinical trial is essential to fully determine its advantages and limitations.

With respect to the "ideal" burn dressing, further clinical investigations of the fluid loss from burn wounds of patients

of different ages and under different conditions are necessary to accurately define the absorptive and water vapour transmission characteristics.

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APPENDICES

APPENDIX I

Patient details noted before commencing sil'cone gel treatment (over).

CASE STUDY NO.

NAME:

DATE OF BIRTH:

RACE:

CAUSE OF LESION:

DURATION OF LESION:

PREVIOUS TREATMENT:

SITE OF LESION:

DATE OF APPLICATION OF SILICONE GEL:

SITE OF SILICONE GEL:

COMMENTS:

APPENDIX II

The computer programs used to calculate the water vapour transmission rate from experimental data (over) (Queen -personal communication).

```
10REM FILENAME "WATIFA"
20REM VERSION NO.1 WHICH FILES DATA
30REM STATUS : DEVELOPMENT
40REM DATE :12 FEB 85
50REM PROGRAMMER :D.QUEEN
60 CLS
70 PRINT TAB(1,1) "ENTER NUMBER OF DATA POINTS"
80 INPUT TAB(30,1) NPTS%
90DIM X(NPTS%) : DIM R(NPTS%)
100MODE 7 :CLOSE#0
110  *FX200.1
120 REM DISABLE THE ESCAPE KEY
130 *FX6.0
140 CLS
150 M$=STRING$(15," ")
160 D$=M$:G$=M$
170 PRINT TAB(1.6) "ENTER THE NAME OF THE NEW DATA FILE (7 chars ...   .   max
"
180 INPUT TAB 25.7)F$
190 F$ (F$(F$.7)
200 H1-OPENUP(F$)
21? F CH1 0 PRINT"FIL ALREADY EXISTS":TIN ...       ...
220 CH1=OPENOUT(F$)
230 REPEAT
240 PROC data input
260 PROC store
270 UNTIL TA$="Y"
280 CLOSE#0
290 *FX200.0
300END
310
320DEF PROC data_input
330 CLS
340PRINT TAB(1,3) "MATERIAL?":INPUT TAB(25,3)M$
350PRINT TAB(1.4) "TEST DATE?":INPUT TAB(25,4)D$
360 PRINT TAB(1.5) "TEST NUMBER?":INPUT TAB(25.5)TN%
370 PRINT TAB(1.6) "RELATIVE HUMIDITY?":INPUT TAB(25.6)RH
380  PRINT TAB(1.8) "TEST POSITION?":INPUT TAB(30.8)N$
390 PRINT TAB(1,10) "INITIAL WEIGHT READING?":INPUT TAB(30.10)WSTART
400 PRINT TAB(1.12) "THICKNESS(cm)?":INPUT TAB(30.12)Z
410 PRINT TAB(1.14) "MEMBRANE AREA (m2)?":INPUT TAB(30.14)A
420 PRINT TAB(1.18)"IS THIS DATA CORRECT ?"," (Y/N)":INPUT TAB(39,18)A$
430 IF A$="N" CLS: GOTO 340
440 CLS : PRINT''
450 REM choice_of_X_values
460 PRINT TAB(1.1) "ENTER THE COORDINATES AS X,Y VALUES"
470 CLS:PRINT''
480 FOR I% = 1 TO NPTS%
490 PRINT "POINT NO.".I%
500 INPUT X(I%), R(I%)
510 PRINT
520 NEXT I%

530 PRINT TAB (1,23) "IS THIS DATA CORRECT?","(Y/N)":INPUT TAB(38,23)As
540 IF As = "N" GOTO 440

550 CLS:PRINT TAB(1.15) "IS THIS THE LAST TEST"
560 INPUT TAB(38.15)TA$
570 ENDPROC
580
590 DEF PROC_store
600PRINT#CH1,M$:PRINT#CH1,D$:PRINT#CH1,TN%
610 PRINT#CH1.RH:PRINT#CH1 N$:PRINT#CH1.WSTART:PRINT#CH1.Z
620 PRINT#CH1.A
630 FOR I%=1 TO NPTS%
640 PRINT#CH1,X(I%):PRINT#CH1,R(I%)
650 NEXT I%
660 ENDPROC
```

```
10REM FILENAME "WATERA"
20REM VERSION NO.1 WHICH ANALYSES STORED DATA
30REM STATUS : DEVELOPMENT
40REM DATE :12 FEB 85
50REM PROGRAMMER :D.QUEEN
60MODE 7 :CLOSE#0
 70 PRINT TAB(1,1)"ENTER NUMBER OF DATA POINTS?"
 80 INPUT TAB(30,1)NPTS%
 90 DIM X(NPTS%):DIM R(NPTS%):DIM Y(NPTS%)
100 REM *FX200,1
110 REM DISABLE THE ESCAPE KEY
120  *FX6,0
130 REG%=0
140 CLS
150 M$=STRING$(15," ")
160 D$=M$:G$=M$
170 PRINT TAB(1,6)"ENTER THE NAME OF THE DATA FILE FOR ANALYSIS  :INPUT TAB(
8)F$
180 CH1=OPENUP(F$)
190 IF CH1=0 PRINT "FILE NOT FOUND":PRINT TAB(1,6)"     ":GOTO 17
200 PRINT TAB(1,8) "ENTER THE TEST NUMBER REQUIRED":INPUT TAB(1,9 test%
210 PTR#CH1=0
220 REPEAT
230 PROC_read_file
240 UNTIL TN%=test% OR EOF#CH1
250 IF TN%<>test% PRINT "TEST NOT ON FILE" :PRINT TAB(1,9)"      ": GOTO 200
260 CLS
270 PROC_data display
280 MODE 0
290 PROC_processing_of_raw_data
300 DUM=GET
310 INPUT "HARDCOPY REQUIRED(Y/N)",B$
320 IF B$="Y" HCOPY%=1 ELSE HCOPY%=0
330 CLS
340 PROC_processing_of_raw_data
350 IF HCOPY%=1 THEN *SDUMP
360 CLS
370 PROC_choice_of Y_axis
380 PROC_choice_of_X_axis
390PROC_plot
400PRINT TAB(27,28)"PRESS SPACEBAR TO CONTINUE"
410DUM=GET
420MODE 7
430PROC_regression
440MODE 0
450PROC_calculate
460INPUT"HARDCOPY REQUIRED(Y/N)",H$
470IF H$="Y" HCOPY%=1 ELSE HCOPY%=0
480CLS
490PROC_plot
500 PROC_results
510IF HCOPY%=1 THEN *SDUMP
520 CLOSE#0
530 END
540
```

```
  550 DEF PROC_choice of_Y_axis
  560 REM this chooses the desired Y axis scale
  570 REM this program uses data line 510
  580 RESTORE630
  590 REPEAT
  600 READ YMAX
  610 UNTIL YMAX>=Y(NPTS%) OR YMAX=24
  620 stepY=YMAX/6
  630 DATA 0.03,0.06,0.18,0.6,3,6,12,18,24
  640 REM SFY=scaling factor for the Y axis
  650 SFY=600/(6*stepY)
  660 ENDPROC
  670
  680 DEF PROC_choice of_X_axis
  690 REM this repeat chooses the X axis scale
  700 REM this program uses data statement 620.
  710 RESTORE760
  720 REPEAT
  730 READ XMAX
  740 UNTIL XMAX>=X(NPTS%) OR XMAX=30
  750 stepX=XMAX/6
  760 DATA 3,6,9,12
  770 REM SFX=scaling factor for X_axis
  780 SFX=600/(6*stepX)
  790 ENDPROC
  800
  810 DEF PROC plot
  820 VDU5
  830 REM PLOTS PRESSURE VS TIME
  840 FOR I% = 1 TO NPTS%
  850 MOVE X(I%)*SFX+300,Y(I%)*SFY+320
  860 PRINT"X"
  870 NEXT I%
  880 IF REG%=1 THEN MOVE X(1)*SFX+300,YSTART*SFY+300 : DRAW X(NPTS%)*SFX+300,YE
ND*SFY+300
  890 REM DRAW X AXIS
  900 VDU5
  910 MOVE 300,300
  920 FOR J%=0 TO 6
  930 A%= 300+J%*100
  940 DRAW A%,300
  950 DRAW A%,285
  960 MOVE A%-150,265
  970 PRINT J%*stepX
  980 MOVE A%,300
  990 NEXT J%
 1000 MOVE 970,270
 1010 PRINT "TIME in Hrs"
 1020 REM DRAW Y AXIS
 1030 MOVE 300,300
 1040 FOR J% =0 TO 6
 1050 A%= 300 + J%*100
 1060 DRAW 300,A%
 1070 DRAW 280,A%
 1080 MOVE 90,A%+8
 1090 PRINT J%*stepY
 1100 MOVE 300,A%
 1110 NEXT J%
 1120 MOVE 10,980
 1130 PRINT "WATER LOSS"
 1140 MOVE 10,930
 1150 PRINT "in grams"
 1160 VDU4
 1170 PRINT TAB(24,1) "WATER PERMEABILITY OF WOUND COVERINGS"

 1180 ENDPROC
 1190
 1200 DEF PROC regression
```

```
1210 REG%=1
1220 PRINT TAB(1,3)"ENTER NUMBER OF POINTS TO BE"
1230 PRINT TAB(1,4)CHR$(129)"EXCLUDED"CHR$(135)"FROM THE REGRESSION ":INPUT TAB
(38,4)N%
1240 IF N%>9 OR N%<0 PRINT "INVALID DATA":GOTO 1220
1250@%=131850
1260 XSUM=0:X2SUM=0:YSUM=0:Y2SUM=0:CROSS=0:M%=NPTS%-N%
1270 FOR K%=N%+1 TO NPTS%
1280 XSUM = XSUM + X(K%)
1290 X2SUM = X2SUM + X(K%)*X(K%)
1300 YSUM = YSUM +Y(K%)
1310  Y2SUM =Y2SUM +Y(K%)*Y(K%)
1320 CROSS = X(K%)*Y(K%)+CROSS
1330 NEXT K%
1340 X2=X2SUM-XSUM*XSUM/M%
1350 Y2=Y2SUM-YSUM*YSUM/M%
1360 C2=CROSS-XSUM*YSUM/M%
1370 GRAD =C2/X2
1380 inter=YSUM/M%-GRAD*XSUM/M%
1390R=C2/SQR(X2*Y2)
1400 PRINT "GRADIENT    ",GRAD
1410 PRINT "INTERCEPT   ",inter
1420 PRINT "CORRELATION COEFF    ",R
1430PRINT
1440 PRINT TAB(1,15)CHR$(134)"REGRESSION  OK  '",CHR$(129),"(Y/N) "  INPUT TAB(3
7,15)A$
1450  IF A$="N" CLS :GOTO 1220
1460 FOR I%=1 TO NPTS%
1470 YSTART=X(1)*GRAD+inter
1480 YEND=X(NPTS%)*GRAD+inter
1490 HO=Y(N%+1):HT=Y(NPTS%)
1500 @%=10
1510 ENDPROC
1520
1530 DEF PROC_calculate
1540 @%=&50A
1550 WVTR=GRAD/A
1560 @%=10
1570 ENDPROC
1580
1590 DEF PROC_processing_of_raw_data
1600CLS:PRINT''
1610 PRINT"TIME POINTS AND WEIGHT LOSS VALUES FOR",M$"  ",TN%"  ",D$
1620 @%=10
1630 PRINT''
1640 FOR I%=1 TO NPTS%
1650 @%=&50A
1660 Y(I%)=WSTART-R(I%)
1670 @%=131850
1680 PRINT "POINT NO.";I%"    ",X(I%)"    ",Y(I%)
1690 PRINT
1700 NEXT I%
1710 ENDPROC
1720
1730 DEF PROC_read_file
1740 INPUT#CH1,M$:INPUT#CH1,D$:INPUT#CH1,TN%
1750 INPUT#CH1,RH:INPUT#CH1,N$:INPUT#CH1,WSTAR(
1760 INPUT#CH1,Z:INPUT#CH1,A
1770 FOR I%=1 TO NPTS%
1780 INPUT#CH1,X(I%):INPUT#CH1,R(I%)
1790 NEXT I%
1800 ENDPROC
1810

1820 DEF PROC_data_display
```

```
1840 PRINT TAB(1,3) "MATERIAL":PRINT TAB(25,3)M$
1850 PRINT TAB(1,4) "TEST DATE":PRINT TAB(25,4)D$
1860 PRINT TAB(1,5) "TEST NUMBER":PRINT TAB(25,5)TN%
1870 PRINT TAB(1,6) "RELATIVE HUMIDITY":PRINT TAB(25,6)RH
1880 PRINT TAB(1,8) "TEST POSITION":PRINT TAB(30,8)N$
1890 PRINT TAB(1,10) "INITIAL WEIGHT READING":PRINT TAB(30,10)WSTART
1900 PRINT TAB(1,12) "THICKNESS(cm)":PRINT TAB(30,12)Z
1910 PRINT TAB(1,14) "MEMBRANE AREA (m2)":PRINT TAB(30,14)A
1920 DUM=GET
1930 @%=10
1940 CLS : PRINT '
1950 PRINT CHR$(134)"THE COORDINATES ARE AS FOLLOWS' :PRINT
1960 FOR I% = 1 TO NPTS%
1970 PRINT "POINT NO.",I%,X(I%),R(I%)
1980 NEXT I%
1990 DUM=GET
2000 ENDPROC
2010
2020DEF PROC_results
2030 @%=&50A
2040 PRINT TAB(60,8) "WVTR=",WVTR
2050 PRINT TAB(60,10) "THICKNESS=",Z
2060 PRINT TAB(60,12) "AREA=",A
2070 PRINT TAB(60,14)"POSITION=",N$
2080 @%=5
2090 PRINT TAB(33,26) "MATERIAL : ",M$
2100PRINT TAB(10,28) "TEST DATE : ",D$,"    TEST NUMBER : ",TN%
2110 PRINT TAB(10,26) "RH : ",RH
2120 PRINT TAB(28,31) "KAREN J. QUINN"
2130 @%=10
2140 ENDPROC
```

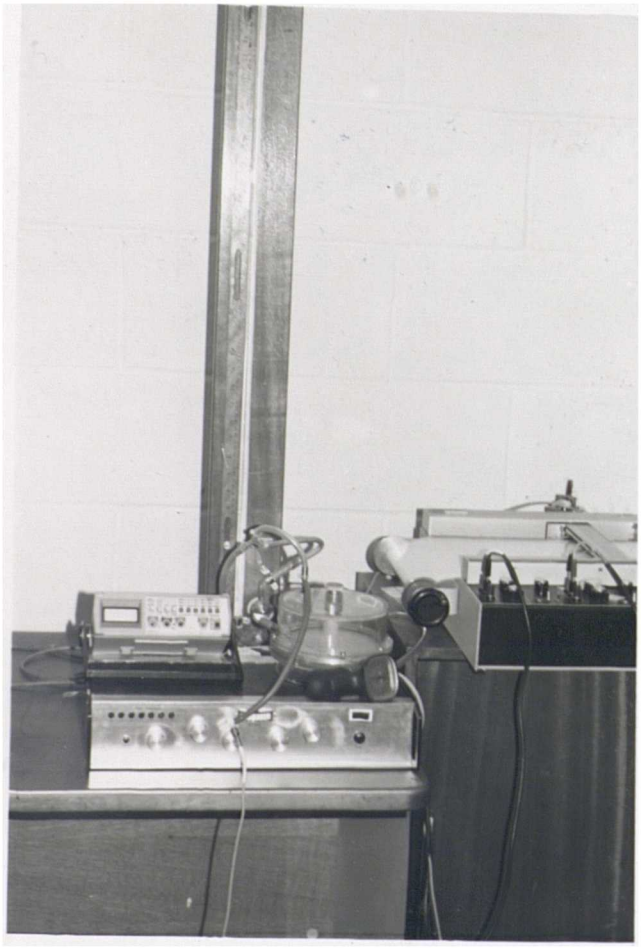


Figure AIII.1 Pressure transducer calibration unit.

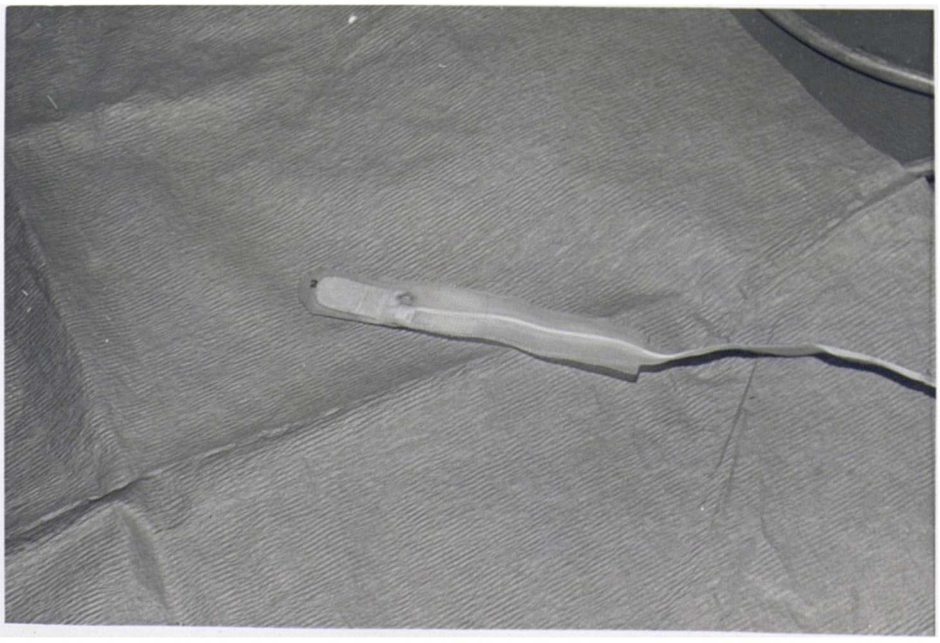


Figure AIII.2 Pressure transducer.

APPENDIX III INSTRUMENTATION

PRESSURE TRANSDUCERS

The pressure transducers used in this investigation were designed and manufactured at the Bioengineering Unit, University of Strathclyde. Figure AIII.1 shows the calibration unit and Figure AIII.2 the transducer itself. The transducer is flat and was therefore easy to attach to the skin with silicone gel and the positioning bandages.

For further information about these transducers, the reader is reffered to:

Ferguson-Pell, M.W., Bell, F. and Evans, J.H. (1976) Interface pressure sensors: existing devices, their suitability and limitations. In: "Bed Sore Biomechanics," R.M. Kenedi, J.M. Cowden and J.T. Scales, eds., pp189-198, MacMillan Press Ltd., London.

RADIOMETER

The Heiman KT 41 Radiometer was specifically designed as a non-contacting temperature measuring device for medical use. It has an optical sensing head, with a test area of 1.5 cm^2, attached by a lead to the amplifier unit.

Objects with a temperature above absolute zero radiate electromagnetic energy. The effect is not visible below 800°C, but at physiological temperatures there is measurable emission in the infra-red region. The radiometer detects this electromagnetic energy with thermal detectors. These are a pair of

small thermistors, one of which is exposed to the incident radiation and the other is shielded. The temperatures of the thermistors are compared to determine the increase in temperature due to radiation falling on the exposed thermistor.

COMARK DIGITAL THERMOMETE 5335

This instrument uses thermoelectric effects with two metallic conductors (Cu/CuNi). If two dissimilar metallic conductors are joined to form a loop, and one junction is at a different temperature from the other, an electric current will flow in th circuit. This current is produced by an electromagnetic force whose value depends upon the temperature difference as well as the material of the wires. The source of the thermal e.m.f. is the contact potential at the junctions of the two conductors. The "Fermi level" is the electronic energy level at which there is a 50% probability of finding an electron. This depends upon the number of electrons in the conduction band per cubic metre, which depends upon the temperature and the material. When two different materials are brought together, electrons move across the junction until the Fermi levels in the two materials are equal. This causes a potential difference between the materials. If a loop is formed by joining the materials at two places, the potentials will act in opposite directions. The difference in the potentials which occurs if the junctions are at different temperatures gives rise to the thermoelectric effect.

SERVOMED EVAPORIMETER Ep1

The ServoMed Evaporimeter Ep1 is an instrument for the quantitative determination of water evaporation i.e. water transport through diffusion, from or to surfaces in contact with the atmosphere. The transport of water by diffusion close to a surface (within approximately 1 cm), is determined by Fick's law:

$$\frac{1}{A}\frac{dm}{dt} = -D\frac{dp}{dx}$$

where:

A = the area of the surface (m^2)

m = the weight of transported water (g)

t = time (h)

D = a constant, 0.0877 g $m^{-1}h^{-1}$ $(mmHg)^{-1}$, related to the diffusion coefficient

p = partial pressure of water vapour in the air (mmHg)

x = distance from the surface

The formula indicates that the evaporation rate $\frac{dm}{dt}$ is proportional to the partial pressure gradient $\frac{dp}{dx}$, and thus can be determined by measuring the latter.

The evaporimeter probe contains, at two different distances from the surface, a pair of transducers, one for relative humidity the other a thermistor. From the signals from these transducers, the instrument first computes the partial pressure of water vapour at the two distances from the surface; then the partial pressure gradient; and the evaporation rate.

RADIOMETER TCM1 TC OXYGEN MONITOR

Under normal conditions, the diffusion of oxygen from the capillaries to the outermost layers of the tissue is very low, and the skin oxygen tension is therefore negligibly small. However, if the skin at the measuring site is heated, the capillaries will become dilated and allow for an increased flow of blood (hyperaemia). As a result of this induced hyperaemia, the permeability of the skin to oxygen will increase to such an extent that the skin oxygen tension ($tc\text{-}P_{02}$) becomes closely correlated with the arterial oxygen tension (P_aO_2). After equilibrium is established between the oxygen tension of the central arteries and that of the skin capillaries and surrounding tissue, $tc\text{-}P_{02}$ values reflecting changes in P_aO_2 values can then be measured with a transcutaneous electrode.

The TCM1 TC Oxygen Monitoring System is based on the use of a E5240 $tc\text{-}P_{02}$ electrode and a E5241 $tc\text{-}P_{02}$ scalp elecrode which combine in one unit a heating element, a temperature sensor and an oxygen electrode.

APPENDIX IV

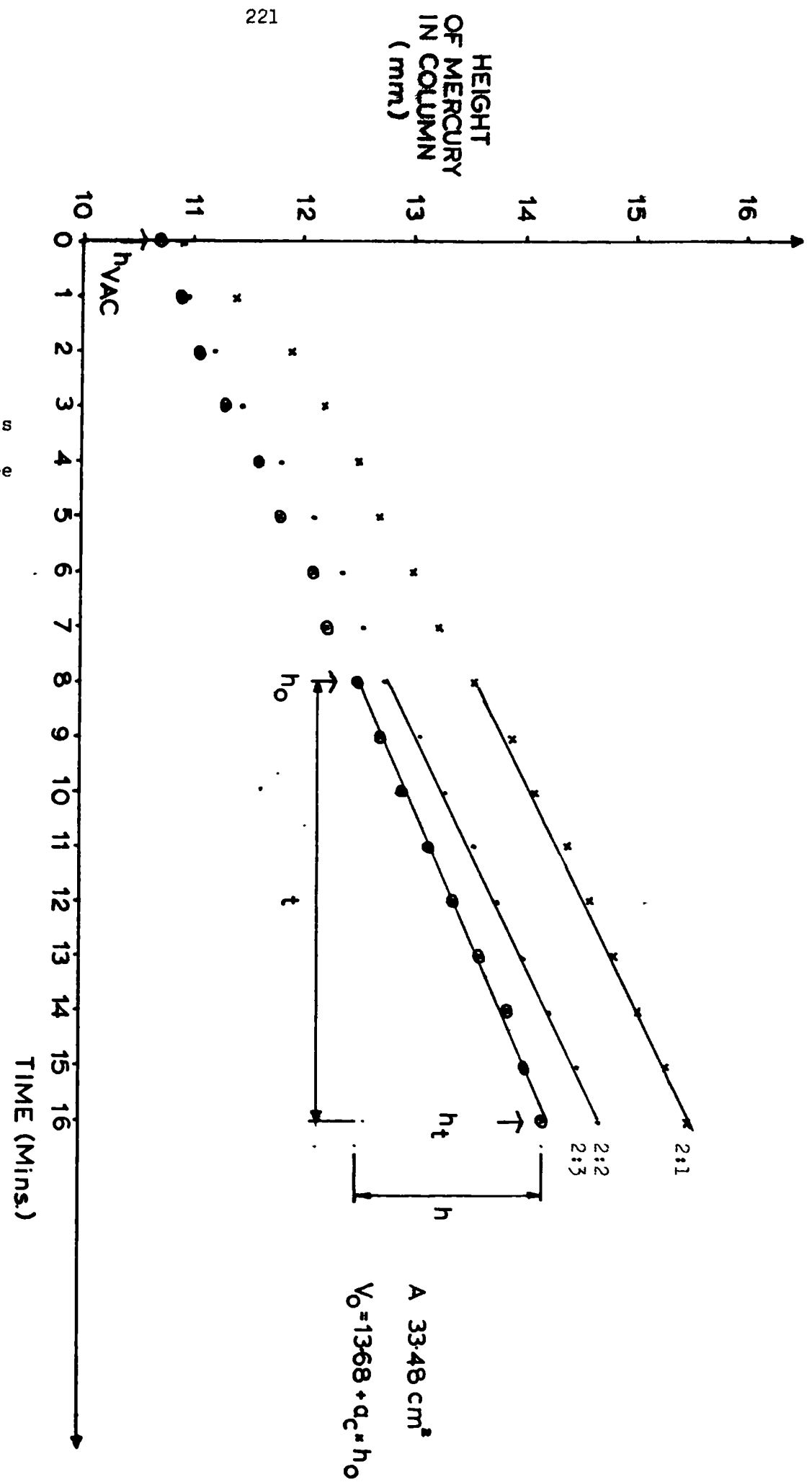
This appendix contains the results of thermocouple studies of two case studies, the results of three oxygen transmission through silicone gel tests, and evaporimeter studies of two case studies.

Thermocouple results from the test site of two cases.

TIME (mins.) / TEST NO.	1	2	3	4	5	MEAN +/- 1S.D.	
Before application	34.2	34.4	32.7	33.5	34.0	33.8	0.6
Application of gel	29.1	29.9	28.6	29.3	29.6	29.3	0.4
1	32.5	31.8	32.1	30.5	31.5	31.7	0.7
2	33.0	33.4	32.8	30.4	34.1	32.7	1.3
3	33.0	33.3	32.6	30.2	33.8	32.6	1.3
4	33.1	33.5	32.7	30.3	34.1	32.7	1.3
5	33.1	33.6	32.9	30.2	33.8	32.7	1.3
6	33.0	34.5	33.5	30.4	33.8	33.0	1.4
7	32.9	34.5	33.6	30.5	33.7	33.0	1.4
8	32.9	34.5	33.4	30.8	33.9	33.1	1.3
9	32.9	34.5	33.5	31.3	35.2	33.5	1.4
10	32.7	34.4	33.2	30.7	35.2	33.2	1.5
15	32.8	34.4				33.6	0.8
20	33.1	34.7				33.9	0.8
25	33.7	34.1				33.9	0.2
30	33.8	33.9				33.9	0.05

Thermocouple results from the control site of two case studies.

TIME (mins) / TEST NO.	1	2	3	4	5	MEAN +/- 1 S.D.	
Before application	32.5	32.2	30.5	31.4	33.8	32.1	1.1
Application of gel	32.5	32.2	30.5	31.3	34.2	32.1	1.2
1	32.6	32.2	30.3	31.3	34.4	32.2	1.4
2	32.6	32.3	31.1	31.4	34.5	32.4	1.2
3	33.0	32.4	31.4	31.8	34.6	32.6	1.1
4	33.2	32.4	32.1	31.8	34.7	32.8	1.0
5	31.5	32.4	31.9	31.8	34.8	32.5	1.2
6	31.5	32.5	32.3	32.0	34.8	32.6	1.1
7	31.7	32.5	32.7	32.1	34.8	32.8	1.1
8	32.0	32.5	33.0	32.1	34.8	32.9	1.0
9	32.0	32.7	32.7	32.2	34.8	32.9	1,0
10	32.3	32.7	33.0	32.3	34.7	33.0	0.9
15	34.7	33.2				34.0	0.8
20	34.1	33.5				33.8	0.3
25	34.8	33.7				34.3	0.6
30	34.7	34.1				34.4	0.3



plot of mercury

ion vs. time for gas

ility test cell (see

Evaporimeter results from the test site of three case studies. Note that units are g $m^{-2}h^{-1}$.

	TEST NO.																					
TIME (mins)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	Mean +/- 1 S.D.
Gel in situ	2	2	0	2	1	2	1	4	7	5	1	3	2	3	3	2	3	4	2	1	2	2.5 +/- 1.5
Gel removed	25	62	30	52	28	40	23	34	55	40	15	37	44	15	21	45	21	30	31	31	16	33.1 12.9
Gel off 5	12	18	15	12	8	15	10	15	27	23	9	15	23	8	9	26	13	18	14	14	12	15.0 5.5
Gel off 10	8	14	7	12	6	12	8	10	19	18	6	9	22	8	7	23	8	14	13	14	12	11.9 5.0
Gel off 15	8	13	7	9	5	12	7	8	18	18	6	7	15	8	8	14	8	12	6	10	12	10.0 3.7
Gel off 20	8	11	7	8	4	7	7	8	14	13	5	8	8	8	7	6	8	11	6	10	15	8.5 2.8

Evaporimeter results from the control site of three case studies. Note that units are $g\ m^{-2}h^{-1}$.

	TEST NO.																					
TIME (mins)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	Mean +/- 1 S.D.
Gel in situ	5	5	5	8	3	5	7	7	7	8	6	6	6	4	6	6	14	11	5	8	4	6.5 +/- 2.4
Gel removed	8	10	7	8	5	8	8	13	13	14	6	10	9	5	6	7	13	13	4	7	4	8.5 3.1
Gel off 5	8	10	7	9	6	8	10	12	13	9	5	8	7	4	6	11	11	13	8	7	4	8.4 2.6
Gel off 10	8	9	7	8	4	7	7	7	11	9	5	8	9	5	5	13	11	13	10	8	5	8.0 2.5
Gel off 15	8	8	7	9	5	6	6	7	10	8	5	5	10	4	5	6	11	9	11	8	5	7.3 2.1
Gel off 20	8	8	7	8	6	6	8	7	8	8	5	6	7	5	6	6	11	9	11	8	5	7.3 1.7

The relative humidity during these tests ranged from 37% to 58%, with a mean value +/- 1 standard deviation of 50.8 +/- 6.3%.

APPENDIX V

This appendix contains results of water vapour transmission experiments on silicone foams, rubbers, "occlusive" covering and polyurethane film.

"OCCLUSIVE" COVERING (SILICONE GEL COVERED WITH POLYURETHANE).

TEST NO.	THICKNESS (cm)	RELATIVE HUMIDITY (%)	TEMPERATURE (^{o}C)	SLOPE (g/h)	AREA (m^2)	WVTR ($g\ m^{-2}h^{-1}$)
1	0.217	33	35	0.009	0.00442	2.0
2	0.161	33	35	0.018	0.00442	4.1
3	0.231	33	35	0.010	0.00442	2.3
4	0.221	33	35	0.009	0.00442	2.0
5	0.226	33	35	0.010	0.00442	2.3
6	0.223	33	35	0.010	0.00442	2.3
7	0.147	33	35	0.017	0.00442	3.9
8	0.153	33	35	0.018	0.00442	4.1
MEAN +/- 1 S.D.	0.197 +/- 0.034					2.9 +/- 0.9

Student's "t" test indicates that there is no difference in the means of silicone gel and the "occlusive" covering WVTR, $t_{22,\ 0.025}$ = 2.058 and the value calculated for the data is 0.389.

SILASTIC RUBBER SHEETING OF THICKNESS 10 THOU'.

TEST NO.	THICKNESS (cm)	RELATIVE HUMIDITY (%)	TEMPERATURE (°C)	SLOPE (g/h)	AREA (m^2)	WVTR ($g/m^2/h$)
1	0.0253	33	35	0.059	0.00436	13.5
2	0.0253	33	35	0.055	0.00436	12.6
3	0.0254	33	35	0.054	0.00436	12.4
4	0.0254	33	35	0.049	0.00436	11.2
5	0.0254	33	34	0.047	0.00436	10.8
6	0.0254	33	35	0.035	0.00436	8.0
7	0.0254	33	35	0.034	0.00436	7.8
MEAN +/- 1 S.D.	0.0254 +/- 0.00005					10.9 +/- 2.1

SILICONE RUBBER OF THICKNESS 7 THOU'.

TEST NO.	THICKNESS (cm)	RELATIVE HUMIDITY (%)	TEMPERATURE (^{o}C)	SLOPE (g/h)	AREA (m^2)	WVTR ($g\ m^{-2}h^{-1}$)
1	0.0178	33	35	0.0628	0.00436	14.4
2	0.0177	33	35	0.0473	0.00442	10.7
3	0.0177	33	35	0.0579	0.00442	13.1
4	0.0178	33	35	0.0530	0.00442	12.0
5	0.0178	33	35	0.0558	0.00436	12.8
6	0.0178	33	35	0.0606	0.00436	13.9
7	0.0177	33	35	0.0458	0.00436	10.5
8	0.0178	33	35	0.0506	0.00436	11.6
MEAN +/- 1 S.D.	0.01778 +/- 0.00005					12.4 +/- 1.3

Student's "t" test indicates that there is no difference in the means of these two test samples (12.4 +/- 1.3 c.f. 10.9 +/- 2.1)

$t_{13,0.025}$ = 2.160 and the value calculated for the data is 0.422.

SILICONE FOAM WITH ONE SKINNED SIDE WHICH FACED THE WATER.

TEST NO.	THICKNESS (cm)	RELATIVE HUMIDITY (%)	TEMPERATURE (°C)	SLOPE (g/h)	AREA (m^2)	WVTR ($g/m^2/h$)
1	0.497	33	35	0.431	0.00442	97.5
2	0.472	33	35	0.497	0.00442	112.4
3	0.491	33	35	0.417	0.00442	94.3
4	0.469	33	35	0.506	0.00442	114.5
5	0.495	33	35	0.437	0.00442	98.7
6	0.512	33	35	0.360	0.00442	81.4
7	0.520	33	35	0.381	0.00442	86.2
8	0.510	33	35	0.445	0.00442	100.7
MEAN +/- 1 S.D.	0.496 +/- 0.017					98.2 +/- 11.3

SILICONE FOAM WITH ONE SKINNED SIDE WHICH FACED THE ENVIRONMENTAL CHAMBER.

TEST NO.	THICKNESS (cm)	RELATIVE HUMIDITY (%)	TEMPERATURE (^{o}C)	SLOPE (g/h)	AREA (m^2)	WVTR ($g/m^2/h$)
1	0.487	33	35	0.395	0.00442	89.4
2	0.484	33	35	0.416	0.00442	94.1
3	0.466	33	35	0.459	0.00442	103.8
4	0.462	33	35	0.482	0.00442	109.0
5	0.470	33	35	0.455	0.00442	102.9
6	0.463	32	35	0.477	0.00442	107.9
7	0.489	33	35	0.440	0.00442	99.5
8	0.465	33	34	0.475	0.00442	107.5
9	0.471	33	35	0.442	0.00442	100.0
MEAN +/- 1 S.D.	0.473 +/- 0.010					101.6 +/- 6.2

Student's "t" test indicates that there is no difference in the means of these two test samples (101.6 +/- 6.2 c.f. 98.2 +/- 11.3), $t_{15,0.025}$ = 2.131 and the calculated value for the data is 0.18.

SILICONE FOAM WITH BOTH SIDES SKINNED.

TEST NO.	THICKNESS (cm)	RELATIVE HUMIDITY (%)	TEMPERATURE (°C)	SLOPE (g/h)	AREA (m^2)	WVTR ($g/m^2/h$)
1	0.401	33	35	0.241	0.00442	54.5
2	0.406	33	35	0.226	0.00442	51.1
3	0.415	33	35	0.214	0.00442	48.4
4	0.412	33	35	0.210	0.00442	47.5
5	0.412	33	34	0.199	0.00442	45.0
6	0.407	33	35	0.233	0.00442	52.7
7	0.409	33	35	0.243	0.00442	55.0
8	0.407	32	35	0.227	0.00442	51.4
MEAN +/- 1 S.D.	0.409 +/- 0.004					50.7 +/- 3.3

POLYURETHANE SHEETING.

TEST NO.	THICKNESS (cm)	RELATIVE HUMIDITY (%)	TEMPERATURE (°C)	SLOPE (g/h)	AREA (m^2)	WVTR ($g/m^2/h$)
1	0.005	33	35	0.114	0.00442	25.8
2	0.006	33	35	0.096	0.00442	21.7
3	0.005	33	34	0.115	0.00442	26.0
4	0.006	33	35	0.095	0.00442	21.5
5	0.006	33	35	0.095	0.00442	21.5
6	0.006	33	35	0.094	0.00442	21.3
7	0.005	33	35	0.127	0.00442	28.7
MEAN +/- 1 S.D.	0.006 +/- 0.0005					23.8 +/- 2.8