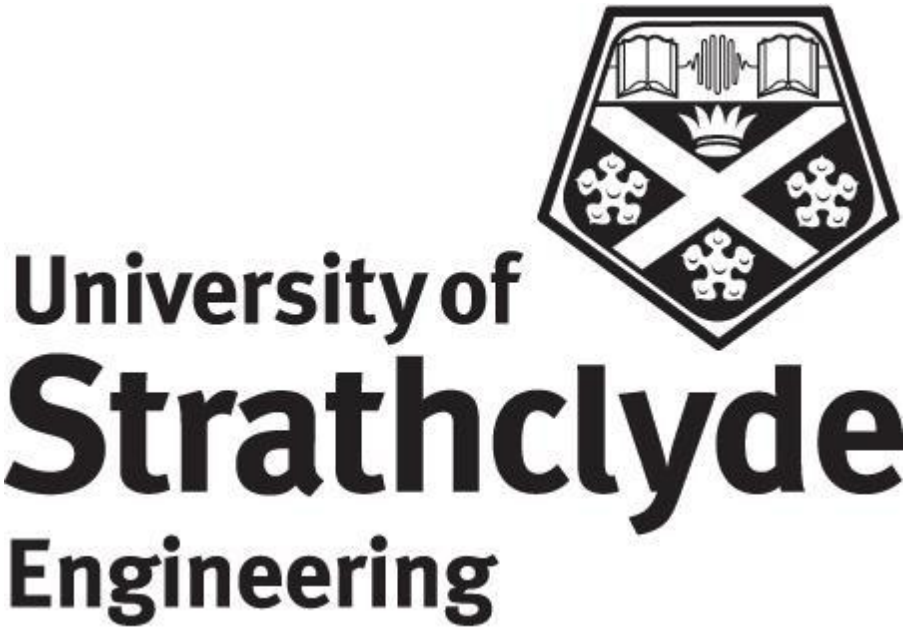
A review of the status of medical technology in wound management and wound healing.



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Signed:

Date:

Acknowledgements:

The satisfaction and happiness that accompanies the successful completion of the thesis would be incomplete without mentioning of the people who made it possible and whose constant guidance and encouragement have kept me going on.

I dedicate this study especially to my grandfather "Mukund kamath" who is not between us today and also dedicate this to my family for the support provided throughout my career.

It is difficult to overstate my gratitude to my MSc. supervisor, Prof. Patricia Conolly. With her enthusiasm, inspiration and her great efforts to explain things clearly and simply made this project fulfilling. Throughout my thesis-writing period, she provided encouragement, sound advice, good teaching and lots of good ideas.

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Without the support from friends, this project would not have been an enjoyable experience; I thank them for their love and faith in me.

Every day I remind myself that my inner and outer life are based on the labors of the other men, living and dead, and that I must exert myself in order to give in the same measure as I have received and still receiving……Albert Einstein.

ABSTRACT

The objective of this review will be to compare and contrast commercial and nearly-commercial skin substitutes and to also shed light on the wound healing therapies and illustrating their roles in wound management. Over last two to three decades bioengineered skin substitutes have been carefully studied and proven in advanced wound healing technologies. Understanding the stages of wound repair, wound bed preparation, pH, tissue viability, tissue management, moisture balance, epithelial advancement inflammation and infection helps clinicians in their approach removing barriers to healing and stimulating the process.

The advanced wound management market for dressing is divided in three, 1.Moist wound dressings such as hydrocolloid, foams, hydrogels etc. 2.Silver dressings such as Aactisorb, Aacticoat, contreet etc. and 3.Biomaterials dressings and skin substitutes such as hyalograft. Currently the field is undergoing an exciting growth and innovation driven by an increasing number of chronic wounds and new medical understanding of ways of operating both economically and clinically.

Individualization of each therapy based on particular patient and the wound helps in understanding of mechanisms of skin substitutes and accelerated healing. The review will also deal with the problems and key issues of the devices and techniques used such as the electrical stimulation, negative pressure technology, hyperbaric oxygenation and various others in medical diagnostics of wound management and healing.

The current challenges for the clinicians are to understand advanced wound healing technologies relative roles, merits and availability. Many non-healing chronic wound treatments, most commonly by systemic or topical antimicrobial therapy in many cases have proven non-effective. Treatment of many chronic cases of uncontrolled diabetes ulcers, ischemia, infections, burns wounds, venous ulcers, traumatic wounds, surgical wounds etc. is extremely challenging. Wound nursing, after cure precautions and various contraindications is therefore also the part of the challenge.

CONTENTS:

Research project chapters:

LIST OF FIGURES:

Figure Number Page

LIST OF TABLES:

Chapter 1: Skin structure- Necessary knowledge for understanding of wound healing process.

Evidence based care has been proven very helpful tool in the healing process of wounds within a reasonable time frame. But despite this there remains a category of chronic wounds which fail to heal with the highest level of standard care. Understanding of the process of wound healing requires knowledge of skin structure and stages of wound healing.

As a result of rapid expansion of knowledge at the molecular level the past two decades have produced more advances in wound care, there has been a co-ordinated process combining both technology and scientific knowledge thus improving wound healing and providing new wound care methods. Although wounds have different phases during the healing process in various degrees the phases remain the same across all the patients (Stadelmann et al., 1998). Here the skin is taken as representative tissue type. Different categories of wound both acute and chronic wounds will be dealt during the study review. This chapter will deal with skin structure.

There is always distinction between repair and regeneration. The term ‘Repair’ refers to physiological adaptation of an organ after an injury in an effort to re-establish continuity without regards to exact replacement of lost or damaged tissue. ‘True regeneration’ of the tissue refers to ‘exact’ copy replacement of the lost or damaged tissue such a way that both morphologically and functionally are completely restored from and after the injury.

An ‘injury’ is an interruption of morphology and functionality of given tissue. Therefore wound healing is a necessary process after injury. It is an intricate process in which the skin or any other organ tissue repairs itself after an injury during which the process of wound healing is immediately set into motion. In a normal skin, the ‘Epidermis’ which is the outermost layer and the ‘Dermis‘ the inner or deepest layer exists in a steady state equilibrium thus forming a protective barrier against the external environment. Once the protective layer is broken the healing process is set in process (Buck & Bensoulilah, 2007).

1.1 Skin or the integument:

The outer protective layer called integument or skin is the largest organ in the human body, this adds up to 16% to the total body weight covering a surface area of 1.8 square meters. Skin is a dynamic organ and is always in a state of change the entire time as the cells present in the outermost layer of the skin is continuously shedding at the same time being replaced by innermost cells towards the surface inversely (Buck & Bensoulilah, 2007). The three structural layers to the skin are as follows:

1. The Epidermis.
2. The Dermis.
3. Subcutis.

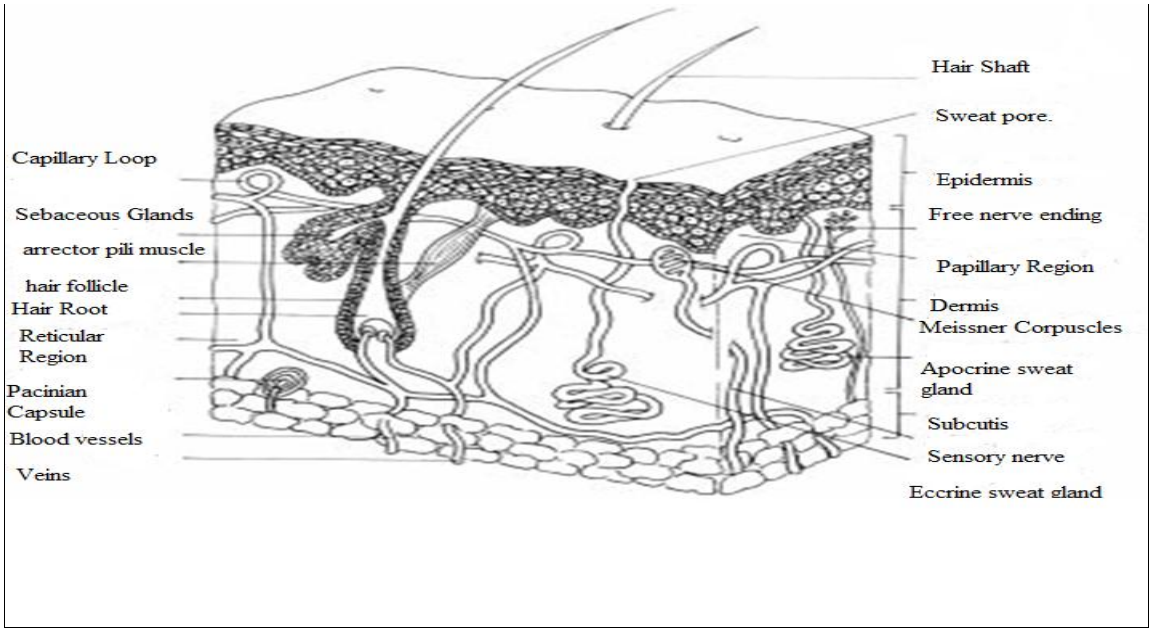


Fig 1.1: The figure shows cross sectional view of integument or skin (Taken from Buck & Bensoulilah, 2007).

Apart from these three layers there is also presence of different derivatives of skin like the hair, nails, sebaceous sweat and apocrine glands. The most important function of all is covering in the form of a physical barrier against the external environment for the human

body, being protective against the various harmful factors such as the micro-organisms, ultraviolet radiation, toxic agents and mechanical friction and also allowing and limiting the inward and outward passage of water, electrolytes and various substances (Buck & Bensoulilah, 2007).

1.2 Anatomy of the total skin:

The layers of the skin making up the total skin are epidermis, basement membrane, dermis, subcutis consistent throughout the body. The integument varies in thickness based on anatomical site and also depending on the age of the individual being measured (Buck & Bensoulilah, 2007).

1.2. a. Epidermis:

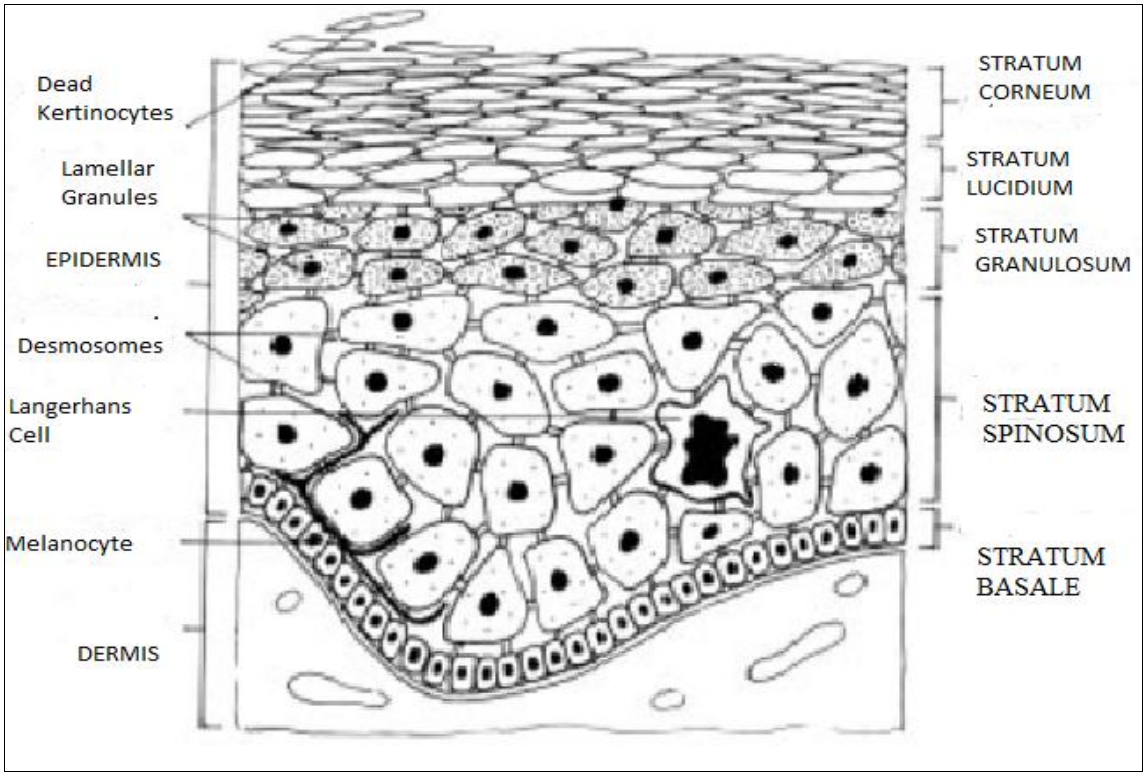


Fig 1.2: The figure shows the cross sectional view of the epidermis in the skin of the human body (Taken from Buck & Bensoulilah, 2007).

The main cells are keratinocytes which help in synthesizing a protein called as keratin. Desmosomes connect these cells. The cells are in constant transition from the superficial level towards the deeper layers of skin. This layer is stratified squamous epithelium,

thickness of this layer ranges from 0.05 mm in skin present on eyelids to 0.8-1.5 mm if measured on palms of hand and also soles of feet where layer being more thicker (Buck & Bensoulilah, 2007).

Based on the stages of keratin maturation the four layers of epidermis are as follows:

1. Stratum basale (Germination cell layer)

2. Stratum spinosum (Prickle cell layer)

3. Stratum granulosum (Granular cell layer)

4. Stratum corneum (Horny layer)

Stratum lucidium is seen in thick epidermis whereas stratum granulosum and corneum seen in the thinner epidermis layer. The layers spinosum and granulosum are together referred as Malphigm layer.

1.2. a.1. Stratum basale:

Attached to basal membrane by hemi desmosomes which are rivet- like structures and are present in keratinocytes in site of basal surface and helps in attaching one cell to the extra cellular matrix when two desmosomes attach to each other, Stratum basale is the inner most layer of the epidermis made up of mainly dividing and non-dividing forms of keratinocytes. During the stage when keratinocytes divide and differentiate them, they then constantly move up the surface from the deeper layer site. There is melanin producing melanocytes. They remain as in the form of granules in the site when melanosomes are transferred to adjacent keratin cells as melanin accumulates in melanosomes. These produce protection against ultraviolet radiations with light exposure increasing the ratio of melanocytes and keratinocytes (Ro & Dawson, 2005). Because of this reason there are more melanocytes on the facial skin and outer arm than inner arm and lower back. Furthermore, there is a different distribution of melanin in white and black skin.

Associated with cutaneous nerves and supposedly involved in light sensation and which are in large proportion in touch sensitive sites like finger tips and lips are the Merkel

cells or Merkel-Ranvier cells which have synaptic contact with the somatosensory afferents (Buck & Bensoulilah, 2007).

1.2. a.2. Stratum spinosum:

Appearing as ‘prickles’ at a microscopic level are the interconnecting bridges the desmosomes. This connects the basal cells as they move towards the outer layer of the skin forming the structure stratum spinosum. Located in the middle of their layers are the ‘Langerhans cells’. This cells acts as antigen-presenting cells during the immune reactions of the skin. These are dendritic, immunologically active cells and a derivative of the bone marrow.

1.2. a.3. Stratum granulosum:

Appear in the form of granules when these layers are seen on the surface area of the skin. Losing of nuclei and their cytoplasm gives this appearance. The cells in this layer is a dense collection of basophilic keratohyalin granules which contain lipids with interconnection of desmosomes helping in the waterproofing functions and prevention of fluid loss from the body.

1.2. a. 4. Stratum corneum:

Corneocytes are hexagonal shaped, cornified cells forming the layers of the stratum corneum as a result of keratinocytes maturation. Soles of feet and palms of hands have the most number of layers ranging from 10-30. These cells are enveloped in a protein layer and water retaining keratin proteins.

1.2. b. Basement membrane:

Rare disease such as Bullous pernphigoid which involves formation of blisters and is acute or chronic form of autoimmune skin disease and Epidermolysis bullosa which is form of inherited skin disease involving blister formation in mucosal membranes and skin are a result of abnormalities of this two layer complex structure. The layer is highly irregular, in which dermal papillae from papillary dermis projects perpendicular to skin surface. As a part of ageing signs seen visually this functional surface flattens and is also known as the dermoepidermal junction.

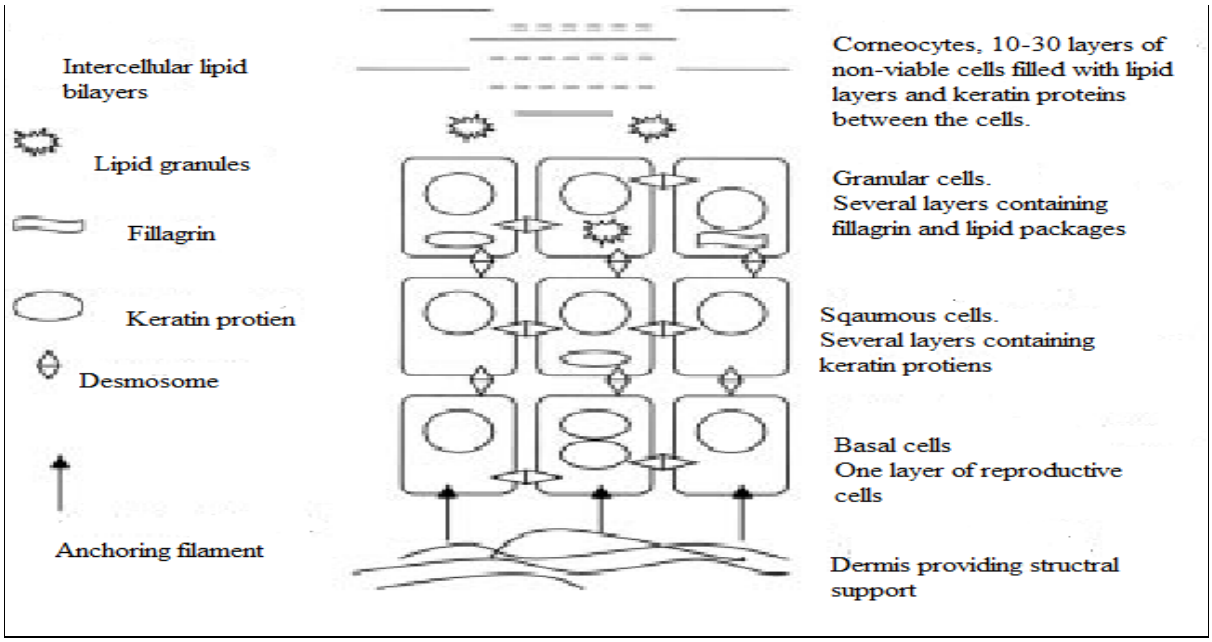


Fig 1.3: The figure explains the barrier function of epidermis (Taken from Buck & Bensoulilah, 2007).

The cellular shape and orientation of keratin proteins add strength. Rest of the cellular space is filled with lipid bilayers. If the water content drops below 10% these cells no longer remain intact and crack. But whereas can retain water three times more its weight. The movement of epidermal cells to this layer the duration is called 'epidermal transit time' and generally takes 28 days (Buck & Bensoulilah, 2007).

1.2. c. Dermis:

Located below the epidermis and made of tough supportive cell matrix with two layers are

1. Thin papillary layer.
2. Thicker reticular layer.

The dermis may be 0.6 mm on the eyelids and 3 mm on the back, palms and soles. Loosely arranged collagen fibres connect with the epidermis. From the base of the papillary layer to the subcutis tissue, extending from deeper reticular layer is a thick column of collagen running parallel to skin surface and include fibroblasts immune competent mast cells and macrophages. Fibroblasts produce collagen, elastin and structural proteoglycans. 70% of the dermis is collagen which gives strength and toughness. Elasticity and flexibility

is maintained by elastin and the proteoglycans maintains hydration providing viscosity. Within these is small quantity of striated muscle, hair roots, nerve cells, fibres, lymphatic's and dermal vasculature (Buck & Bensoulilah, 2007).

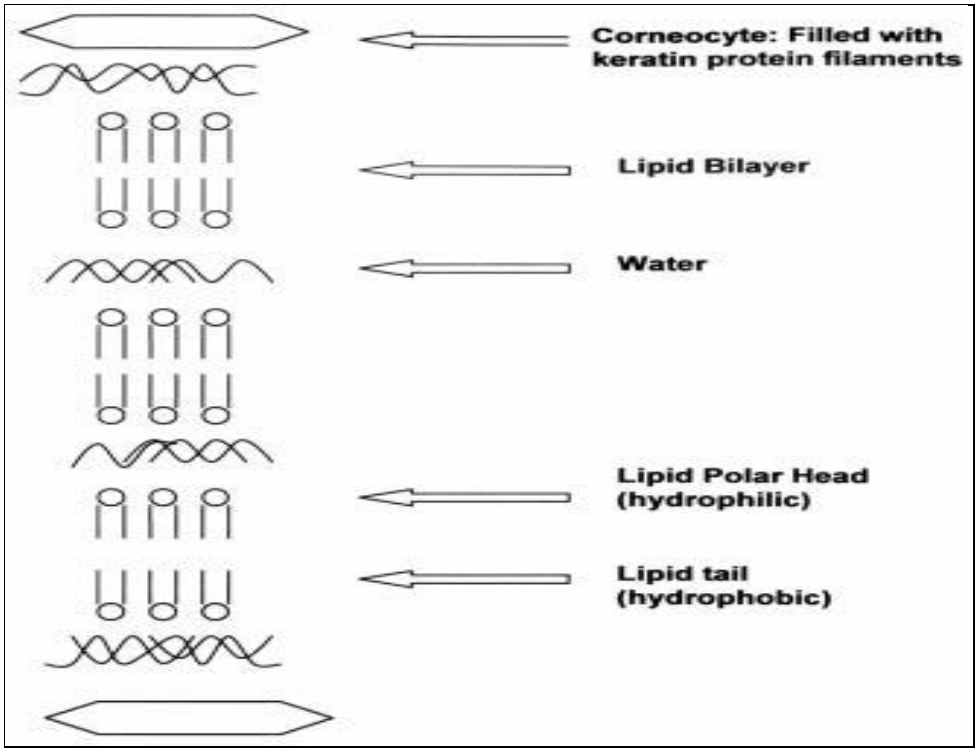


Fig 1.4: The figure shows the coenocyte's lipid bilayers (Taken from Buck & Bensoulilah, 2007).

1.2. d. Subcutis:

Can be 3 cm thick on abdomen and is a form of loose connective tissue and fat. Is the deepest layer of the skin and is also known as the subcutaneous layer. This consists of a continuous network involving collagen and fat cells. The layers helps in conserving body heat balance also in turn protecting other organs from injury by acting as what is known as "shock absorber".

1.3 Blood and lymphatic vessels:

Branches of subcutis artery form a superficial artery plexus at the papillary and reticular dermal boundary. Thus the dermis gets a rich blood supply. Each capillary loop formed by

the branches of plexus in papillae of the dermis has the single loop of capillary vessels, one arterial and one venous. The thermoregulation of the skin depends on the dilation and constriction of the capillary loops.

1.3. a. Nerve supply:

Free nerve endings lie in the dermis where they detect pain, itching and temperature of the body. In both the case of myelinated and unmyelinated fibres the cell bodies are found in the dorsal root ganglia in case of all cutaneous nerves.

The innervation with respect to hands, face and genitalia are in their highest ratio. The pressure and vibration are received by Pacinian corpuscles and the touch sensations are by Meissner's corpuscles. These are the specialized corpuscles receptors lying in the dermis. Motar innervations of the skin are adrenergic fibres which innervate blood vessels, apocrine glands, hair and the erector muscles. While, cholinergic fibres do the same in case of eccrine sweat glands (Buck & Bensoulilah, 2007).

1.4 Derivatives of the skin:

1.4. a. Hair:

Germinative cells line each follicle of hair to produce keratin and melanocytes which help in synthesizing pigment. An erector pill muscle is associated with pulling the hair erect during cold, fear and emotion. Found in varying densities of growth on surface of body, follicles are dense on scalps and face. These are derived from epidermis and dermis.

1.4. b. Nails:

Aid in grasping and protecting the fingertip are nails which are 0.3 mm to 0.5 mm thick keratin hardened to form dense plate. Keratinocytes divides and matures to harden to form a nail plate, below which lies the nail bed. The white lunular is base of plate. This is the distal and visible plate of the matrix. Because of dermal capillaries on bed nail plate appears to be pink in color. Refer figure 1.5 in the following page for structure of nail.

1.4. c. Sweat glands:

Urea, fatty acids, lactic acid, chloride, glycoproteins and mucopolysaccharides are the contents of the watery fluid secreted by sweat glands. These glands are coiled tubes secreting these fluids and are located within the dermis 2.5 million on the skin surface. Classified into two

1. Eccrine glands
2. Apocrine glands.

Eccrine glands present in palms and soles, forehead and axillae and apocrine glands are present in hair follicles (Buck & Bensoulilah, 2007).

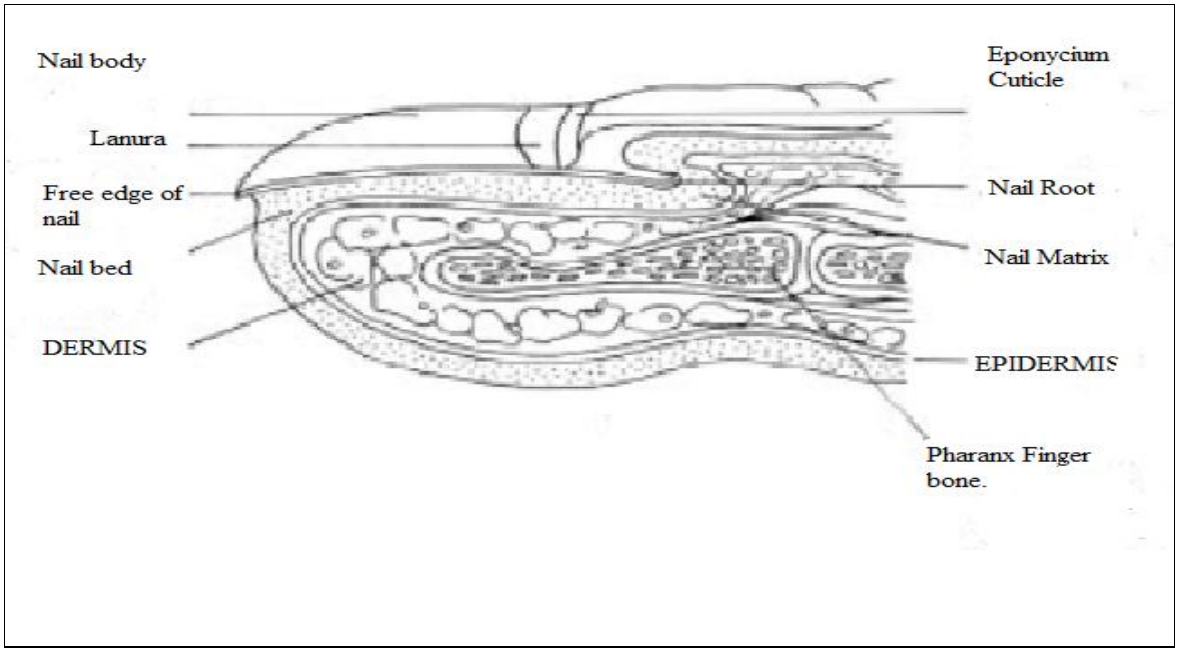


Fig1.5: The figure shows the structure of nail (Taken from Buck & Bensoulilah, 2007).

1.4. d. Subaceous glands:

Oily sebum arrives by holocrine secretion, during this process the cells breakdown and release lipid cytoplasm. These plays following role maintain differentiation, structure and permeability barrier. Apart from this the gland protect from ultraviolet radiation, antioxidants transport to skin surface and hormonal signaling (Gawkrodger, 2002).

1.5 Important physiological functions of skin:

1.5. a. Barrier function:

During the reduction of moisture content of skin granules which are filled with the protein fillagrin there is a breakdown to free amino acids in stratum corneum. As degenerating cells move towards the outer layer the enzymes breaks the complex of keratin and fillagrin and thus leaves fillagrin outside while keratin, which is water retaining forms inside. In order to control osmotic pressure and amount of water content during dry skin the fillagrin breaks down. NMF are the Natural Moisturizing Factors and these consist of lactic acid, urea and salts. Also refer figure 1.3 in this chapter.

Table 1.1: The table describes important functions of skin (Buck & Bensoulilah, 2007).

- Mechanical, thermal, physical injury and noxious agents are various factors against which skin plays a barrier role.
- Useful factor in the conservation of moisture content present in the skin.
- Reduces the effect of ultraviolet radiation.
- Acts as a sensory organ.
- Thermoregulatory factor.
- Immunological surveillance.
- Synthesizes vitamin D called Cholecalciferol.

1.5.2. Shedding of cells:

Skin integrity and smoothness are maintained by shedding of cells also known as desquamation of the stratum corneum. This process happens as dissolving bridges of protein, the desmosomes. The absence of water the skin cells do not shed but become roughened, dry, thick and scaly. For Example in psoriasis which is disease involving less shedding of skin and accumulation of skin. Thus knowledge of skin is useful in the process of wound healing. Individualization of each therapy based on particular patient and the wound helps in accelerated healing and in understanding of mechanisms of skin substitutes The review will also deal with the problems and key issues of the devices and technique used in wound healing such as the electrical stimulation, negative pressure technology, ultrasound, and hyperbaric oxygenation in medical diagnostics of wound management and healing. Stages of wound healing and an overview on advanced dressing with devices and diagnostics will be dealt in further chapters

Chapter 2: Phases of wound repair, role of growth factors with and 'TIME' framework.

The classic model of wound healing is divided into three or four stages sequentially but with overlapping phases (Ruszcak, 2003).

1. Hemostasis.
2. Inflammatory.
3. Proliferative.
4. Remodeling.

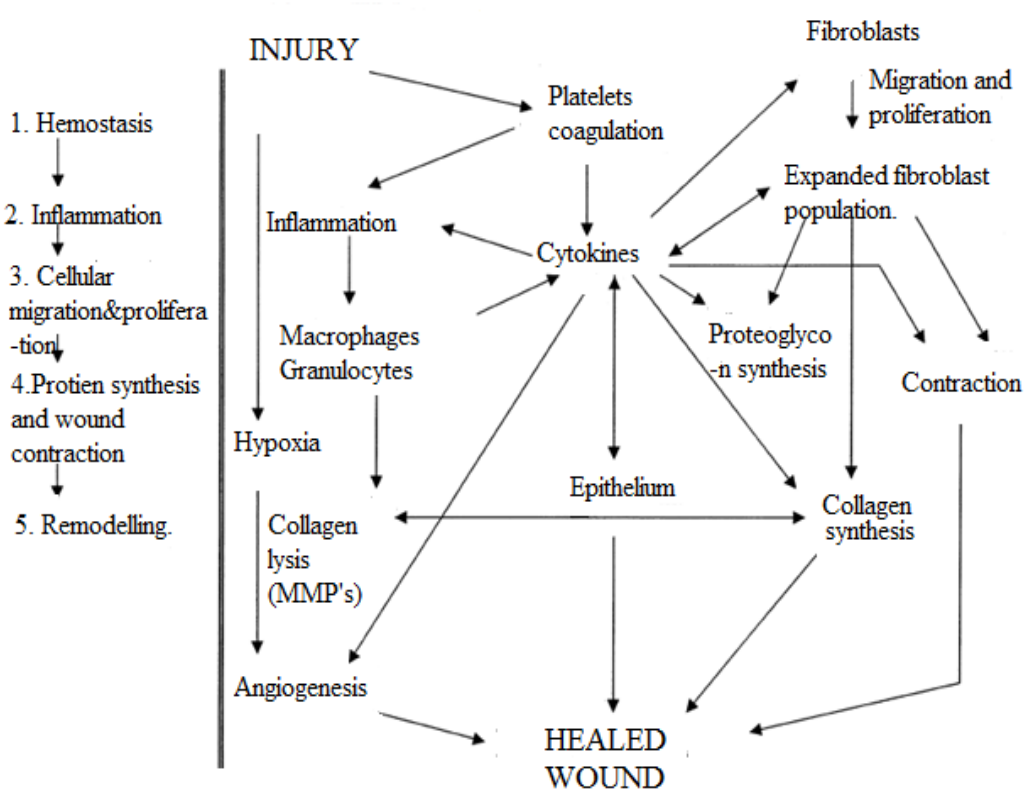


Fig 2.1: This figure shows sequential wound healing stages. (Taken from Ruszcak, 2003); Explains the flow describing acute wound healing cascade, the progression of acute wound healing hemostasis to the final phases of remodeling dependent on a complex interplay of varied acute wound healing events.

Once the protective skin barrier is broken biochemical events takes place with an orchestrated cascade to repair the damage. Platelets (Thrombocytes) aggregates at the injury site and because of the aggregation a fibrin clot is formed thus controlling the active bleeding. This is the process of hemostasis. The bacteria and debris are phagocytized and removed, Also there is a release of factors that cause the migration and division of cells involved during the proliferative phase. This process takes place in the second stage of the cascade called the inflammatory phase.

Characterized by angiogenesis, granulation tissue formation, epithelization, wound contraction and collagen deposition is the proliferative phase. Vascular endothelial cells form the new blood vessels during the process of angiogenesis. Fibronectin and excreting collagen forms a new extracellular matrix which is provisional during granulation tissue formation and fibroplasia epithelial tissue cells crawl and proliferate on this wound bed providing the new tissue covering (Stadelmann et al., 1998).

The size of the wound is reduced by a contraction process forming a firm grip on all the edges of the damaged tissue. This is due to the action of myofibroblasts. Collagen then is remodeled and realigned and unwanted cells are removed by apoptosis during maturation and the remodeling phase. These stages vary in the time lap and all the phases are overlapping during the repair. Along with the healing process depend on different factors including diabetes, arterial disease, age and infection etc. (Enoch & Price, 2004).

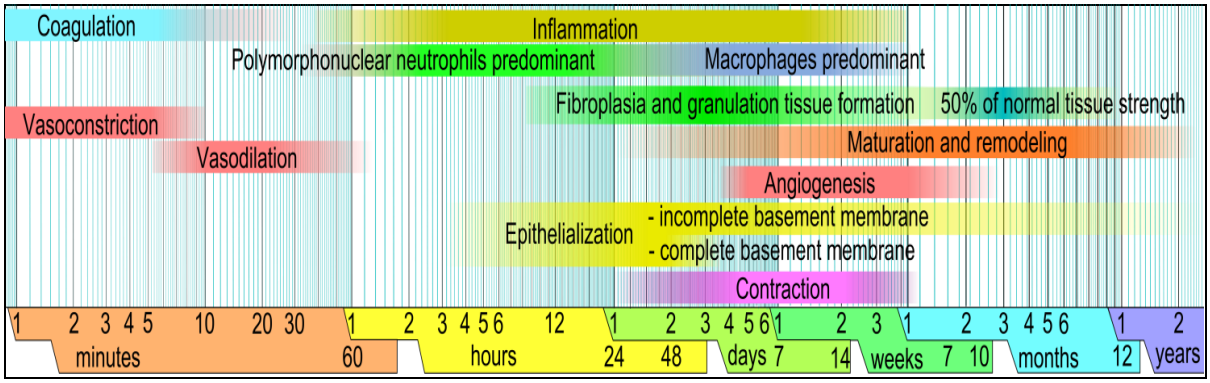


Fig 2.2: The figure above shows different process with time variance during healing processes (Taken from Sollner & Asmussen, 1993).

Vasodilation and vasoconstriction during coagulation process may take 1-60 minutes and with other different time processes shown below with varying time. The faded time lap showed substantial variation based on wound size and healing conditions.

\This chapter deals with wound bed preparation focused on improving the healing rates of subjects with different chronic wounds, healing levels and optimization.

Active and aggressive measures should be applied to the underlying excessive buildup in wound base while providing proper wound care, because of this wound may remain unhealed. Chronic wound can be stagnant during first phase because of perfusion, nutrition etc. may be poor.

Proper wound healing condition for wounds after plastic surgery, amputation or disease or burn makes differences in the timeline of healing.

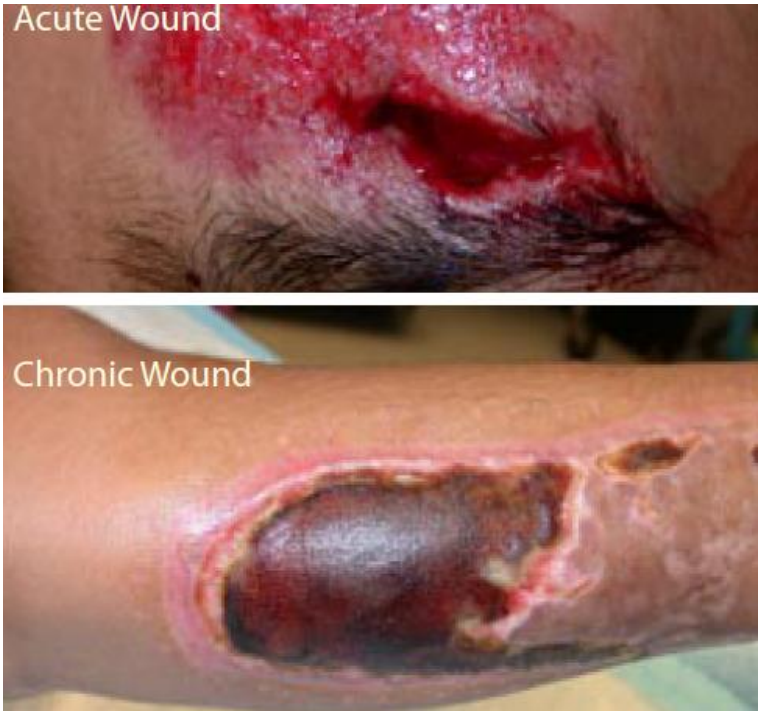


Fig 2.3: Images of Acute and chronic wound (Taken from Semer, 2003).

2.1 'TIME' in wound bed preparation: Wound bed preparation is a diagnostic and evolving concept. An internationally accepted guideline known as the "TIME" guideline explains it as not a static concept and the four components of model being as follow (EWMA, 2004).

1. Tissue management.
2. Inflammation and Infection.
3. Moisture balance.
4. Epithelial (edge) advancement.

Table 2.1: This table explains the "Evolution of TIME framework" (EWMA, 2004)

TIME acronym:	**Terms proposed by EWMA advisory**
Tissue non-viable or deficient.	Tissue management.
Infection or inflammation.	Inflammation and infection control.
Moisture imbalance	Moisture balance.
Edge of the wound, non-advancing or undetermined.	Epithelial (Edge) advancement

This concept should be adopted by clinicians increasing the potential of wound healing. This type of wound bed preparation offers chances in healing of chronic wounds ranging from aspects such as infection maintenance, necrotic tissue and exudate to also complex problems, for an example, as in phenotypic alterations in wound cells. This is site where a cell has become aged and is nonresponsive to treatments and there is need to re-engineer the chronic wound using such treatments, for an example cell therapy to reconstitute the dermal structure.

1. Tissue management:

Removal of necrotic or compromised tissue which are most common in chronic wound type may have positive effects, this removal takes out bacteria, non-vascularized tissue and cells that interrupt in the healing process commonly known as cellular burden thus helping in formation of a healthy tissue. This process of debridement helps in removal of cellular burden and creates stimulating environment which is particularly important. The Acute wounds on the other hand may require a single debridement process but chronic wound may require repeated debridement in the process of healing (EWMA, 2004)

2. Inflammation and Infection:

Colonies of bacterial and fungal organisms are commonly found in chronic wounds, this is because of the fact the chronic wound remains open for a of long time and also because of these factors which influence the colonization process such as underlying cause of disease, poor oxygen and blood supply. Bacterial colonies surrounded by a protective form of layer made of polysaccharides are known as bio films. The bio films form an early stage resistance against the antimicrobials (EWMA, 2004)

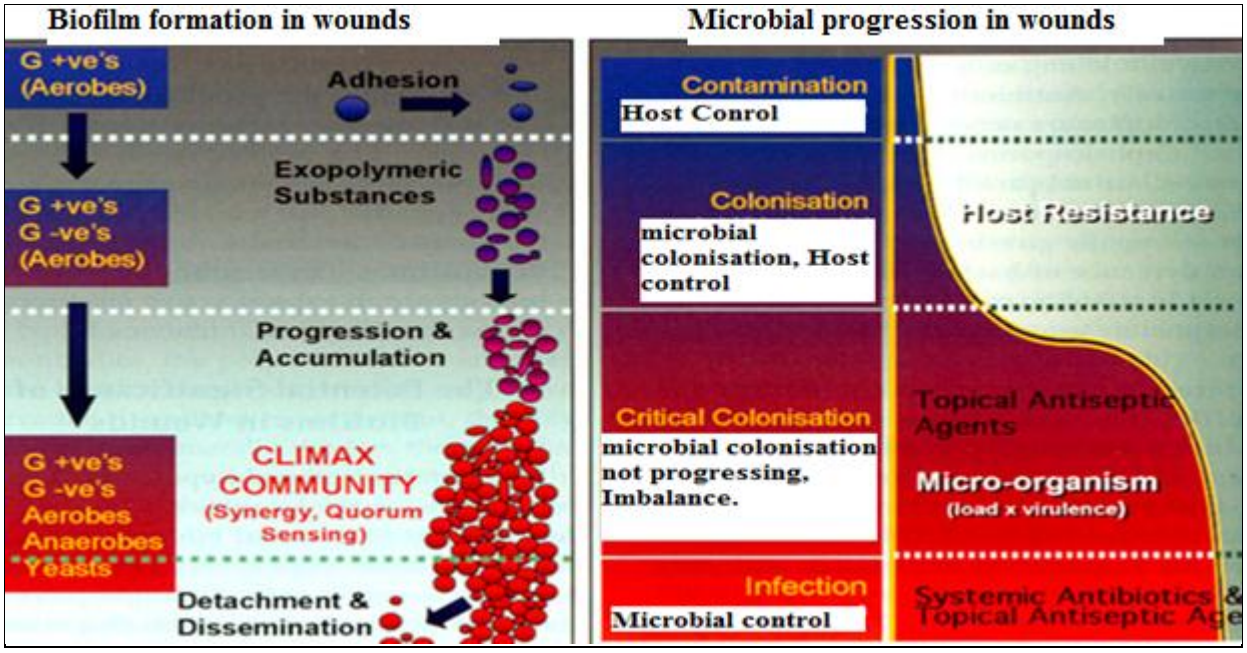


Fig 2.4: This figure above shows microbial progression and formation of biofilm inside wound (Taken from Bowler, 2003).

Recent evidence states biofilms may form inside the wound and thus help in control of infection, inflammation and in turn the healing process. Figure 2.5 explains the process with a model of biofilm. If the microbial progression not controlled during its various stages the probability of infection increases, from the first stage of wound day 1 there is change from gram positive bacteria to gram negative with anaerobes on day 6 or 8 and community formation in the human cutaneous wounds (Bowler, 2003).

3. Moisture balance:

Dressings that maintained moisture balance were tested on acute wounds and quickly the research spread to chronic wounds. The fluid present in the chronic and acute wounds have different set of moist wound healing dressing developed in the recent years is based on the fact the keeping a wound tissue moist is very helpful in the process of re-epithelialization. Properties so it is not sure if moisture retaining dressings work on the basis of the fact of maintaining a contact between wound and wound fluid is helpful. The macromolecules and growth factors can be trapped inside the tissue in reference mainly with venous ulcers but is also said to be applicable in case of chronic wounds. This interruption may is called as 'growth factor trapping'. Modulation of factors which may be at a minimal level like trapped growth factors and cytokines also material from the matrix have potential role in pathogenic abnormalities (EWMA, 2004)

4. Epithelial (edge) advancement:

Restored skin function and re-epithelialized skin helps in effective form of healing process. But if there are faults within the wound matrix or ischemia prevent in migration of keratinocytes which indirectly affects the epithelialization process. This prevents directly affects the epithelialization process because of regulatory defects, dysfunction in cellular mobility or keratinocyte adhesion (EWMA, 2004)

"Wound bed preparation should not be seen in isolation from holistic wound assessment, which encompasses the patient's psychosocial needs as well as underlying and associated aetiologies. Used in this way, if all elements of the framework are successfully addressed, many wounds should move towards healing" (EWMA, 2004)

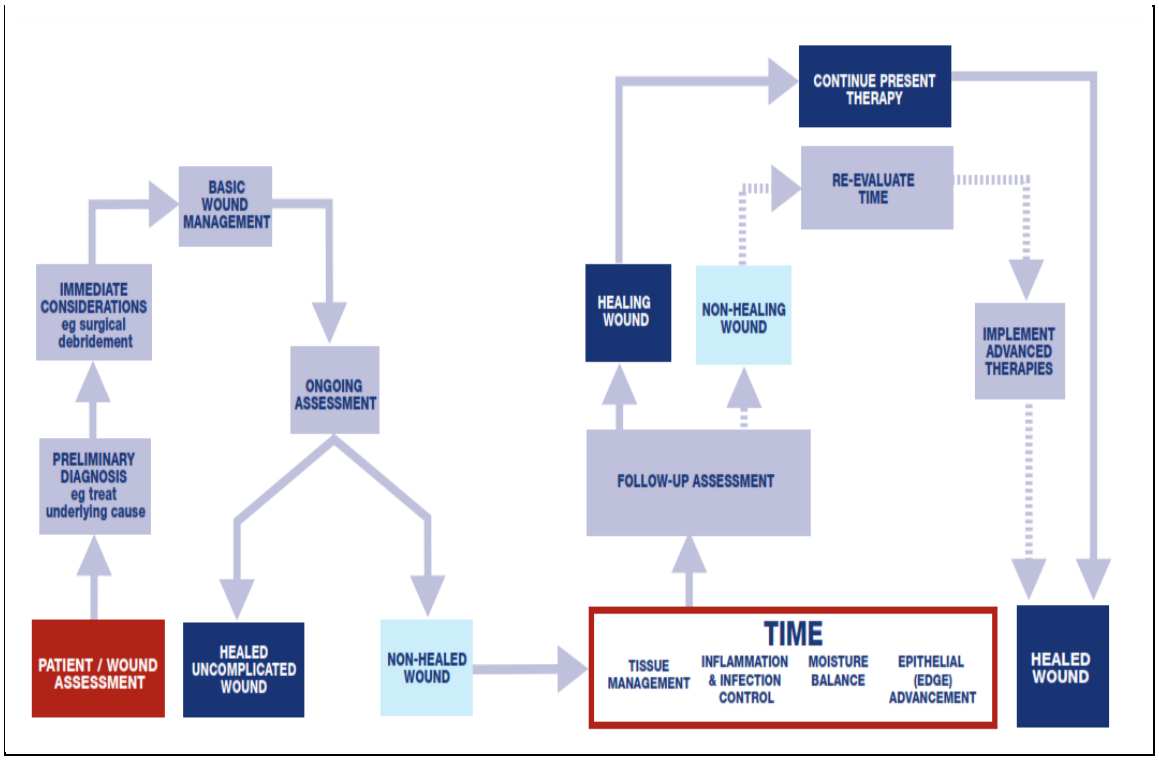


Fig 2.5: Pathway showing how wound bed preparation is applied to practice (EWMA, 2004)

2.2 Active roles of growth factors during various phases:

Inflammatory phase:

The stage lasts for 2-4 days, this starts with hemostasis and formation of platelet plug. Here neutrophils and macrophages are attracted by release of platelet derived growth factors and transforming growth factor beta (TGF-β) by the platelet plug. Microphages attract fibroblast by releasing more growth factors and neutrophils eat bacteria and other debris which are foreign.

In stages of wound healing this is considered first stage and is essential, to reduce the blood loss the blood vessels undergo automatic vasoconstriction and allow the blood to clot thus allowing blood time to clot. Inflammatory vasodilation is caused from inflammatory mediators released from damaged tissue and the mast cells, all this process happens after the vasoconstrictive phase. Hyper anemia is caused by increase in the local blood flow because of vasodilation. Raw materials are required in the repair of damaged cells and also for the

process of mitosis. The vasodilation causes flow of nutrients to injured areas. The damaged area requires to be oxygenated; this is done by the red blood cells. Oxygenation fulfills the demand of providing energy. These anabolic reactions needed to build and repair cells.

All energy production is dependent on the oxygenation of food based fuels, so if a wound is hypoxic, energy production and healing will be impeded. This explains why a good blood supply and effective tissue oxygenation is vital in the process of wound healing. The space between adjacent capillaries is enlarged due to inflammatory vasodilation so there is leaky surfaces formed allowing fibrinogen to move into tissue where they form long sticky strands and act as barrier and prevents infections to healthy tissues (Campbell, 2006).

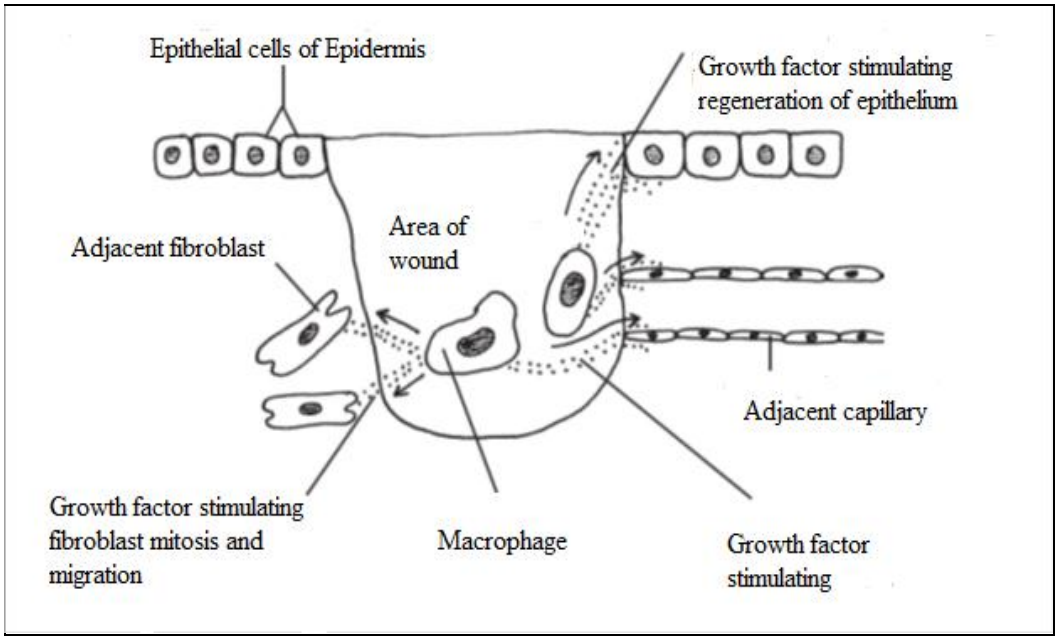


Fig 2.6: Shows the where phagocytosis occurs when monocytes ingest and digest bacteria synthesis of growth factors occur and these factors stimulate migration of healthy cells. Thus fibroblast migration and epithelialization occurs (Campbell, 2006).

Destructive phase

White blood cells like fibrinogen also move between spaces of between adjacent capillaries in endothelial cells. Neutrophils from blood migrate into within the first 24 hours. Neutrophils phagocytize foreign organisms and dead tissue which help in reducing the risk of infection. The food supply for bacteria can be gained from this dead local tissue, monocytes enter after 24 hours this helps in growing large cells called macrophages.

Amoeboid movement the process through which neutrophils and macrophages move throughout the spaces. This chemically attraction towards bacteria and debris helps in increased phagocytic activity. Macrophages also contribute in healing process by release of growth factors. Thus there is stimulation in regrowth of epithelium, fresh capillaries and fibroblast migration. A minimum of 20 various growth factors are contributors in wound healing some listed in page ahead in table 2.2. If in case suppose monocytes are not present then there will no presence of any growth factors for stimulation in process of mitosis in adjacent healthy tissues and thus no regeneration occurs in damaged tissues area (Campbell, 2006).

Proliferative phase:

There is an overlap in proliferative and inflammatory phase. The proliferative phase begins on day-3 approximately. Angiogenesis, collagen formation and epithelialization are initiated by fibroblasts. Epithelialization depends on the basement membrane, for an example during first degree wound basement membrane is intact, thus the epithelialization stage begins from the basement membrane, whereas in the case where the basement membrane is not intact then the epithelialization starts from the wound edges. During this phase a particularly important factor for wound healing is the formation of granulation tissue, Along with the fibroblasts produces the type 3 collagen (Schultz et al., 1993). When the synthesis and breakdown reaches steady state then the next phase of wound healing begins.

Collagen production of collagen is an important function of the fibroblast as it helps in increasing the strength of the wound. The fibrin-fibronectin clot is the only source holding the wound before collagen which does not help in providing much resistance against traumatic injuries. After the collagen matrix is laid by fibroblasts the cells involved in inflammation, angiogenesis and connective tissue grow, attach and multiply in this matrix.

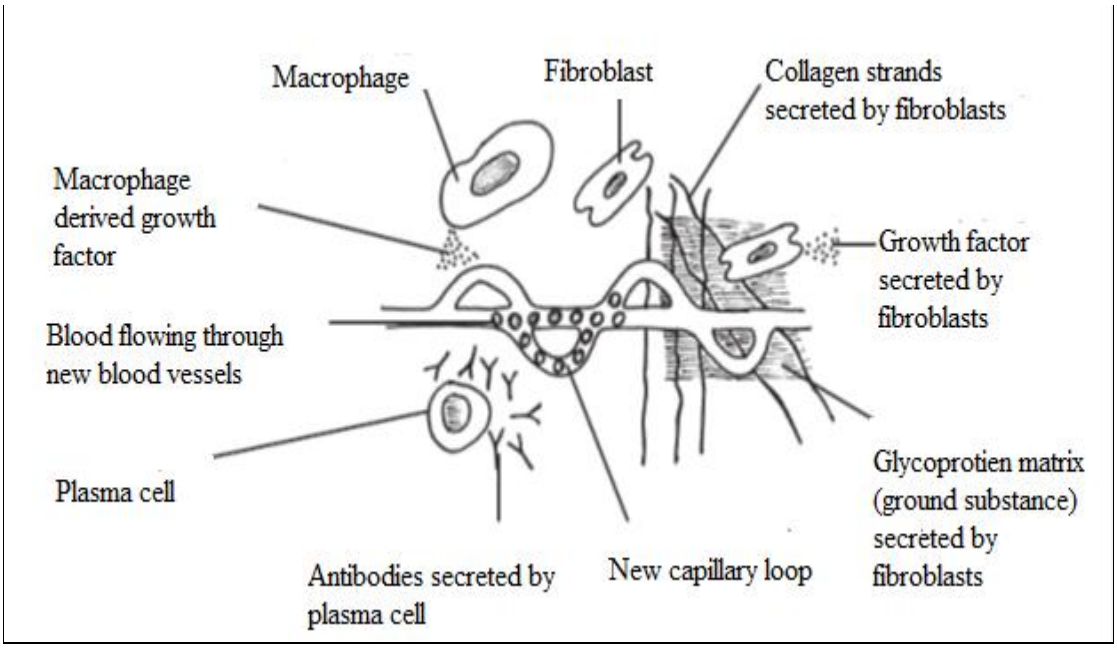


Fig 2.7: Shows the production of collagen strands, growth factors and ground substances by fibroblasts (Campbell, 2006).

After 10 hours to 3 days based on wound size the type 3 collagen and also fibronectin are manufactured in the wound site. Through the first to third week their deposition gradually increases and is at its peak. Later during phase of maturation they are replaced with a stronger form of collagen type 1.

2.3 Location of collagen and its types:

There are numerous types of collagen as list below:

Type 1: Present in all connective tissue apart from basement membrane, hyaline cartilage.

Type 2: Present in the hyaline cartilages.

Type 3: Distensible connective form of tissues like the blood vessels.

Type 4: Present in basement membrane.

Type 5: All tissues of the body.

Type 6: Same as type 5, present in all tissues.

Type 7: Dermal epidermal function.

Type 8: Descent membrane.

Type 9: Hyaline cartilage.

Type 10: Hypertrophic cartilage and also hyaline cartilage.

2.4 Remodeling Phase in wound healing:

In the normal skin the ratio between type 1 and type 2 collagen is 4:1; during this phase type 3 collagen is replaced by type 1 and the synthesis and breakdown of collagen is continuous up to a period of 1 year from 6 months after the injury. This is the continuous process till injury reaches a normal skin ratio.

When this phase is in process less hyperemic and more cosmetically appealing skin can be seen. This is because of decrease in vascularity and also strength gain is nearly as 80% of uninjured tissue as there is cross linkages formed by the collagen. This cross linkages are formed as it recognizes along the tension lines in the layer. Tissue contracts by the action of myofibroblasts which are the differentiated product of fibroblasts.

TABLE 2.2: Showing growth factor type and production site with its effects (Mitchell, 2007).

Growth factor and production site	**Effects as known till date**
1.Epidermal Growth Factor EGF: Produced by platelet, macrophages.	✓ Reduces healing time if applied topically. ✓ Stimulates fibroblast proliferation. ✓ Stimulates fibroblast to produce collagenase which happens during remodeling phase and matrix is degraded. ✓ Stimulates Keratinocytes.
2. Transforming Growth Factor. Produced by hepatocytes, lymphocytes,	✓ TGF-a: Chemotactic and mitogenic in case of fibroblasts and keratinocytes. ✓ TGF-b: Causes degradation, increases

macrophages and platelets.	collagen production, stimulates chemo attraction between inflammatory cells and helps in angiogenesis. ✓ TGF-b3: When b1 and b2 suppressed, and TGF b3 is promoted has found to heal wounds in adults without trace of scars.
3. Vascular Epithelial Growth Factor: VEGF is produced in endothelial cells.	✓ During tissue hypoxia helps in process of angiogenesis.
4. Fibroblast Growth Factor: FGF produced by T-lymphocytes, Macrophages and Mast cells.	✓ Promotes angiogenesis via endothelial cells. ✓ Granulation via fibroblasts. ✓ Epithelialization via keratinocyte migration.
5. Platelet Derived Growth Factor: PDGF is produced in platelets, endothelial cells and macrophages.	✓ Proteoglycans and collagen synthesis. ✓ Attraction of fibroblast and macrophages to site of injury.
6. Interleukins: Produced by mast cells, basophils, osteoblasts, fibroblasts, lymphocytes, endothelial cells, keratinocytes and macrophages.	✓ IL-1: Activates neutrophils and in case of keratinocytes, fibroblasts and neutrophils is chemotactic. ✓ IL-8: Is too chemotactic for neutrophils and fibroblasts. ✓ IL-4: Collagen and proteoglycans synthesis and fibroblast differentiation.

7. Keratinocyte Growth Factor: Produced in fibroblast.	✓ Keratin differentiation, migration and proliferation.
8. Colony Stimulating Factors: Produced by Lymphocytes, fibroblasts, stomal and endothelial cells	✓ G-CSF: Granulocyte- CSF, Helps in granulocyte proliferation. ✓ Granulocyte Macrophage: GM-CSF Helps in macrophage proliferation along with granulocytes.

Chapter 3: Topical therapy- A role in wound healing.

Therapy involves advantages and its own disadvantages. Differentiating on clinical stages of wound infection or microbiological is difficult with varying opinions during the treatment. Wounds that are healing may not require antimicrobials whereas infected wounds require systemic antibiotic treatment. Topical antimicrobial agents may be useful in treating non-healing wounds which are which are showing signs of infections. There is evidence suggesting use of antimicrobial agents or topical antibiotics which are available for systemic use can be useful in malodorous or burn wounds. Non-toxic antiseptics like cadexomer-iodine or silver dressings may be chosen as topical antibiotics.

Neuropathy related like diabetic foot or pressure ulcers, vasculopathy related venous stasis or arterial insufficiency ulcers, trauma related are considered in category of chronic skin wounds affecting 3% of people aged above 60 years. In these patients with chronic wounds more than 60% of patients in the United Kingdom have received antibiotic therapy for prolonged duration of 3 to 4 months (Davies et al., 2007). This chapter deals with where topical antimicrobial therapy should be considered and also deals with recently available and area they might be useful in.

3.1 Definition of wound infection in topical therapy:

Microorganisms colonize in all open wounds with no consequences (Scot et al., 2002). In 2002 more than 1% of population was studied to be affected by chronic wounds and estimate of 1 billion pounds spent in the treatment (Thomas & Harding, 2002). In non-damaged tissue the noticed presence of different replicating organism's adherent to wound is defined as 'colonization'. Contamination is the presence of non-replicating organisms in the wound area. An infection continuum called 'local infection' is critical colonization and is the shifting stage between colonization and invasive wound infection (Dow et al., 1999). Wound infection is decided on basis of per gram bacteria in tissue, pathogenicity of organism and capacity of host to produce immune response (Wysocki, 2002). 10^5 is the presence of micro-colonies without causing any form of clinical problems in intact skin (Freedberg et al., 'Dermatology in general medicine'). Presence of Pseudomonas species which is aerobic gram negative category shows invasion to deeper tissues areas and also shows worsening in wound area by producing tissue destroying enzymes, anti-phagocytic

and adherence mechanisms (Dow et al., 1999). Staphylococcus, Pseudomonas aeruginosa and β- hemolytic streptococcus can be cultured, also are always detected and isolated. Staphylococcus and Pseudomonas are said to be present in almost 70% of wounds with anaerobic Peptostreptococcus (Stephens et al., 2003).

Clinically as microorganisms do not display infection evidence and also sometimes heal where as category of wounds which are infected having purulent secretions and inflammation with erythema, warmth, pain and tenderness defining the host response caused by pathogenic and invasive microorganisms. For a wound to become infected the process is based on direct relationship of inoculum size and colonizing organisms and indirectly dependent on local and systemic resistance of host (White et al., 2006).

Wounds in subjects with neuropathy cause pain; ischemia may cause reduction in erythema and induration. Induration is also an effect in venous insufficiency. During secondary signs of local infection which are easily bleeding, discolored granulation tissue, wound base breakdown, foul odor etc. (White et al., 2005).

The other approach is to define infection microbiologically which may demonstrate that non-healing but apparently uninfected may have critical colonization or with certain viral species or bacteria colonization. More than 10^5 colony forming per gram of tissue is usually defined as "Bioburden". The concept of "Bioburden" remains controversial as some recent studies shifted the theory to density of organisms than on presence of particular species. Some examples are Pseudomonas aeruginosa, Peptostreptococus or Morganella merganii. Recent studies also suggest that chronic inflammation delaying in healing are more resistant to antimicrobial therapy as bacteria persist in polymeric matrix and adhesive communities to suggest clinicians in considering topical antimicrobials (Rhoads et al. 2008).

3.2 Should topical therapy be considered?

Topical therapy application has many potential advantages and also disadvantages as compared to antibiotic therapy. There are many systemic antibiotics available in the current day market, Should topical antimicrobial therapy be considered for every infected wound? Some infection may heal without antimicrobial therapy and some remains confined to superficial tissues and also cause delayed healing and exudation. Systemic infection may be

caused as many of them are immune compromised or anatomically compromised hosts thus, the inner tissue gets involved. Host response for the infection and toxins, wastes by the microorganisms are the factors (Drosou et al., 2009).

Occlusive topical antimicrobials are formulated as ointments and certain petrolatum which is good for dry lesions. Also creams which is good are for dry lesions and creams which can be washed off with water and are good for moist lesions and are less messy. Cream cover 100 square cm of skin with only a gram, but ointments cover 5% to 10% larger area. Technologies incorporate also as foams and sponges. Evaluating their efficacy with approval test is major disadvantage of these agents.

During cultures the specimen wound used usually contacts aerobic gram positive cocci and is seen with gram negative bacilli and also anaerobic. Molecular diagnosis studies have varied showing more microbial complex than before. In a study consisting of subjects with wounds under category of diabetic foot, pressure and venous stasis ulcers totally 77 chronic and 16 acute wounds showed several anaerobic organisms where detected by molecular methods but none could be isolated using culture with respect to mixed wounds category where the study was based on chronic tissues and acute biopsy study. In case of venous ulcers, 8 healing and 10 non-healing tissue specimen there were 40% of species which where detectable using molecular methods and none using isolation culture. In the last case of 19 wound specimen all could be detectable with swab and tissue PCR but 1 was not as it was of lower extremity category. This data of all detectable and non-detectable on the three cases mentioned above is shown in table 3.1 (Lipsky & Hoey, 2009).

Type of wound specimen.

Bacterial type	**Mixed Wounds**		**Venous Ulcers**		**Chronic wounds**	
	Chronic	**Acute**	**Healer**	**Non-Healer**	**SWAB**	**PCR**
Staphylococcus	65	60	100	100	28	68
Enterococcus	62	80			12	18
Pseudomonas	35	20	88	70	32	28
Proteus	24	20	25	30	126	
Citrobacter	24	20			8	28
Streptococcus	22	0	25	60		

Micrococcus			25	90		
Escherichia	14	0				
Morganella	8	0				
Serratia	3	0				
Acinetobacter	5	0				
Anaerobes			50	40	0	70
Klebsiella	5	0				

Table 3.1: Shows bacterial species isolated from various types of wounds (Lipsky & Hoey, 2009).

3.3 Advantages in the use of topical therapy:

A. At the site of infection there is high and sustaining concentration of antimicrobial.
B. Requirement of antimicrobial needed in limit total amount.
C. Systemic absorption and toxicity are potentially limited.
D. Use of novel agents not available for systemic use.
E. Reduction in development of antibiotic resistance as advantageous in avoidance of systemic usage of antibiotics.
F. Reduces institutional care as can be directly applied by the patient or caregiver.
G. Especially in children often adherence to treatment.

3.4 Disadvantages in the use of topical therapy:

A. Clinical test proves fewer agents.
B. In case of open wounds without deep soft tissue spread of infection there is minimal limit of penetration.
C. Large wounds many have systemic absorption.
D. Dermatitis or local hypersensitivity in some reactions.
E. Interference with healing process.
F. Alteration in normal flora.
G. Measurement of accurate dose varies and is difficult judgment.
H. Frequent reapplications.
I. Can be contaminated during use of multi dose (Lio et al, 'Infectious diseases of North America').
J.

3.5 Properties of an ideal topical antimicrobial:

A. Each type of infected wound with accurate targeted antimicrobial spectrum.
B. Rapid bactericidal spectrum.
C. Persistent or residual skin activity.
D. Low bacterial resistance skin activity.
E. Persistent or residual skin activity.
F. Low bacterial resistance induction.
G. Good skin penetration locally but not causing systemic absorption.
H. No allergic or toxic reaction.
I. Cosmetic and aesthetic qualities.
J. Low in cost (Patel et al., 2008).

3.6 Available types of topical antimicrobials:

3.6.1Antiseptics:

Antiseptics can be brief defined as killing solutions for inhabitant microorganisms in intact skin and some open wounds. Toxic in the case of the host tissues such as fibroblasts, keratinocytes and leukocytes but advantageous with multiple microbial targets, blood antimicrobial spectrum and anti-infective activity.

During an in vivo study the effect of prolonged acute inflammatory response or delay in collagen production is not was noted as during toxicity to host. The antiseptics are safe on intact skin application. Hydrogen peroxide has minimum bacterial and debriding activity, chlorhexidine has long term activity with gram-negative and gram–positive bacteria also may be cytotoxic in case of iodophors. Iodides have been used for more than 150 years for bacteria developing resistance. These are commonly used antiseptics (Cooper, 2007).

Now, sodium hypochloride and hexacholorphene are infrequently used in infected wounds. Cadexomer iodine is known in bacterial concentrations without tissue damage. Topical antiseptics in various wound dressing with broad spectrum are silver compounds which may be metallic. Nano crystalline and ionic. The mechanism of killing the bacteria by silver ions is damaging cell walls, membranes, respiratory enzymes and ribonucleo proteins. But silver ions get inactivated in wound environment, so there is a need to maintain sustained delivery.

Methicillin-resistant staphylococcus aureus (MRSA), vancomycin-resistant enterococci (VRE) and extended spectrum beta lactamase produces wound pathogens have proven efficacy by silver (Patel et al., 2008).

Topical formulations are appropriate for some infected wounds for an example: Mupirocin is with minimal toxicity and cross resistance although not approved. Retapamulin got its approval in 2007 with 1% semisynthetic pleuromutilin not approved in the beginning but later got its approval for treating wound with small lacerations, abrasions infected with streptococcus pyogenes (Yang et al, 2008).

3.6.2 Antibiotics:

With more susceptibility to lose effectiveness to bacterial resistance, are non-toxic with narrow spectrum and target specific cell are have antibiotics made naturally by a microorganism or synthetically produced in dilute solution to kill other microorganisms.

3.7 Topical antiseptic products for chronic wounds:

1. Product and formulation: **Acetic acid.**

Formulation: 0.25%, 0.5% and 1% solution

Bacterial spectrum: Bactericidal against most gram-positive and gram-negative organisms which also include Pseudomonas aeruginosa.

Advantages: Inexpensive with results including elimination of P. aeruginosa colonization from burn injuries.

Disadvantages: Cytotoxic in vitro but not in vivo and limited activity against biofilm.

Indications and comments: No longer as widely used as it was in the past.

2. Product and formulation: **Cadexomer iodine.**

Formulation: Gel, ointment and dressings

Bacterial spectrum: Blood spectrum of activity as some in iodine. Polysaccharide starch lattice and active agent is slowly released free iodine.

Advantages: Reduced local toxicity as compared to iodine and elemental iodine released on exposure to exudate.

Disadvantages: Causes less tissue damage compared to other iodine products but causes stinging and erythema. The effect may not persist and also the efficacy may be reduced in bodily fluids.

Indications and comments: Indicated in cleaning wet ulcers and wounds and reducing microbial load in wound environment.

3. Product and formulation: **Cetrimide.**

Formulation: solution 40%.

Bacterial spectrum: Not active against P.aeruginosa, but with fungi and bacteria.

Advantages: May be less toxic compared the other antiseptics in some cases.

Disadvantages: Potentially harmful in swallowed also may prove corrosive.

Indications and comments: Presently is not available in the U.S.

4. Product and formulation: **Chlorhexidine gluconate.**

Formulation: Solution 2% and also 4%, as liquid in 2% and 4%, hand rinse 0.5%, wipes 0.5%, sponges or brushes 4% and also foam 4%.

Bacterial spectrum: Active against gram positive and negative bacteria examples staphylococcus and P.aeruginosa respectively.

Advantages: Activity continuous up to 6 hours after the application and has few adverse effects.

Disadvantages: Hypersensitivity including anaphylaxis, bronchospasm, cough, wheezing, dyspnea. Face contact must be avoided as may cause serious injuries.

Indications and comments: 2% Chlorhexidine indicated as surgical hand scrub, hand wash and skin wound cleanser.

5. Product and formulation: **Hexachlorophene.**

Formulation: Liquid 3%, foam 0.23% with 56% alcohol.

Bacterial spectrum: Bacteriostatic against staphylococcus species and other gram positive bacteria.

Advantages: Retains residual effects on skin for several days.

Disadvantages: Rapidly absorbed and therefore may have toxic blood levels, burns application has resulted in neurotoxicity and death also causes Central Nervous System (CNS) stimulation.

Indications and comments: Not recommended routinely as causes potential toxicity.

6. Product and formulation: **Iodine compounds.**

Formulation: Solution 2% and also 2.4%, NaCl Strong iodine 5% and 10%, and Kl for iodine tincture 2% and 2.4%.

Bacterial spectrum: Microbicidal against bacteria, fungi, viruses, spores protozoa and yeasts.

Advantages: Has a broad range of spectrum.

Disadvantages: Highly toxic if ingested, do not use with occlusive dressing, cause pain, stains skin and importantly caution during use for patients with thyroid disorders.

Indications and comments: Now rarely used for wound management provided iodine products are less toxic (Cooper, 2007).

3.8 Evidence for using topical antimicrobials for treating chronic wounds:

An assessment of the efficacy of topical antimicrobials for the treatment of chronic wounds is difficult based on the available data. The suboptimal approach in use of topical antimicrobial with varying designs in vitro testing in various countries is not standardized. (Cooper, 2007). The microorganisms used, wound type induced, experimental species used may be irrelevant to chronic wounds in patients and medical conditions during studies with animal models. Therefore there is inconsistent evidence.

The case studies and reports in which humans are involved show some information. Published trials do not show patients, wound induced and have adequate samples with inappropriate control groups.

Controlled trials have been conducted using antimicrobial agents for diabetic foot ulcers, pressure ulcers, chronic leg ulcers etc. Two such are the following : 2001 Systemic review controlled trial with 30 studies and 25 randomized trials had 1436 patients, The author concluded the outcome improved with many topical substances accelerated the healing such as silver containing substances for venous ulcers and oxyquinoline ointment which was used for 1-2 stage pressure ulcers (Meara et al, 2007).

The 2008 Cochrane review supports the use of topical cadexomer-iodine. This study was based on antibiotics and antiseptic for various leg ulcers. Research is required to determine the use and effectiveness of poridone iodine, peroxide-based preparations, ethaoridine lactate and mupirocin on venous leg ulcers (Meara et al, 2008). This review also suggested use of Zinc oxide tape for its effectiveness in necrotic wounds more than hydrocolloid. Cadexomer-iodine in cavitary wounds proved no benefits.

Chapter 4: Dressings in wound management.

Understanding properties of wounds and selection of best dressing material available in market helps in management of wound healing process. The main responsibility of nurses in the clinical practice is to bring a positive outcome by using dressing that is suitable to the subject and is judged to be the best selection for maintain different wounds and their healing progress effectively. Wound assessment depends of various factors as discussed earlier, it is a difficult process of selecting an appropriate wound dressing but with suitable knowledge and understanding of the practitioner it is possible to get a positive outcome. The objective of the wound dressing is to provide optimum environment for the wound and speed up the healing and also being cost effective (Williams, 1998a).

The ideal dressing can be defined by the following:

- Dressing should be cosmetically acceptable and accelerated healing process.
- Retain or if possible remove odor also reducing pain simultaneous.
- Prevent infections for pathogenic organisms.
- Retain or store exudate.
- Minimal disturbance or uncomforting on the user or patient.

There are secondary dressings used in a combination with initial on treatment of wounds, this has become a common process but this shows lack of understanding of the wound properties and lead to extra healing time and also unnecessary expenses in healthcare with being unsafe. But some secondary dressings to secure the initial ones are bi-occlusive type of covering or Kerlex roller gauze or also a tubular net with initial hydrogel sheet. The practitioner should know the following before the use of a particular dressing on a wound:

- The action of dressing used on the wound.
- The time period it should be used.
- Limitations known in the use.
- Knowledge of correct method in application and also removal of dressing.
- Contraindications to its use (Benbow, 2004).

4.1 Hydrocolloid dressings:

Mid 1970s was the introduction of the first hydrocolloid dressing to the market, in the present day there are many forms of hydrocolloid available with features of varying thickness, various

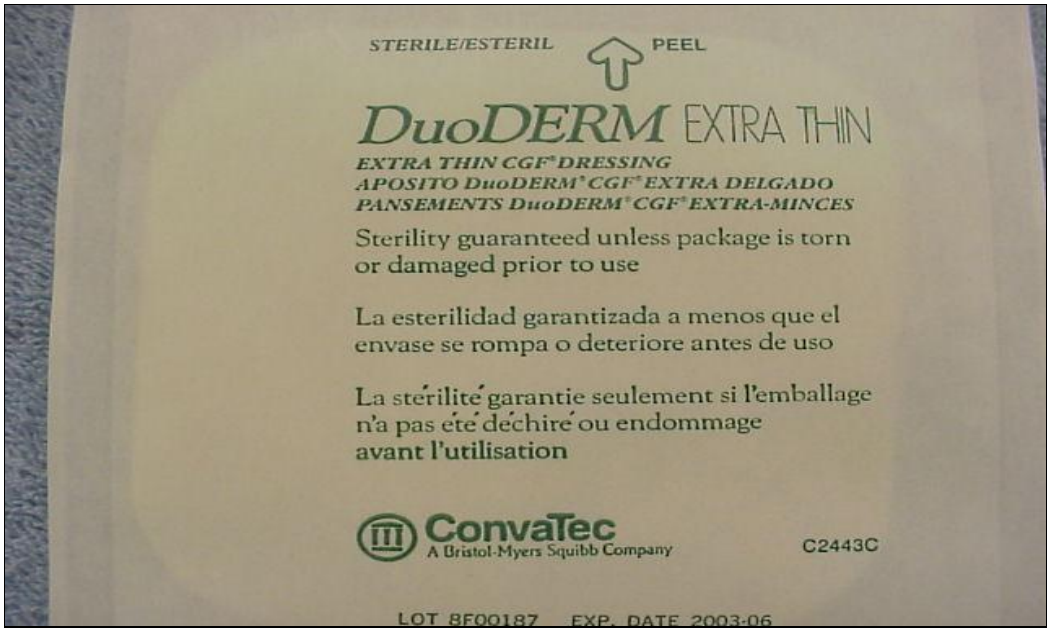


Fig 4.1: Shows Duoderm a hydrocolloid dressing (Taken from 'http://Jan.ucc.nau.edu/-daa/woundproducts.html').

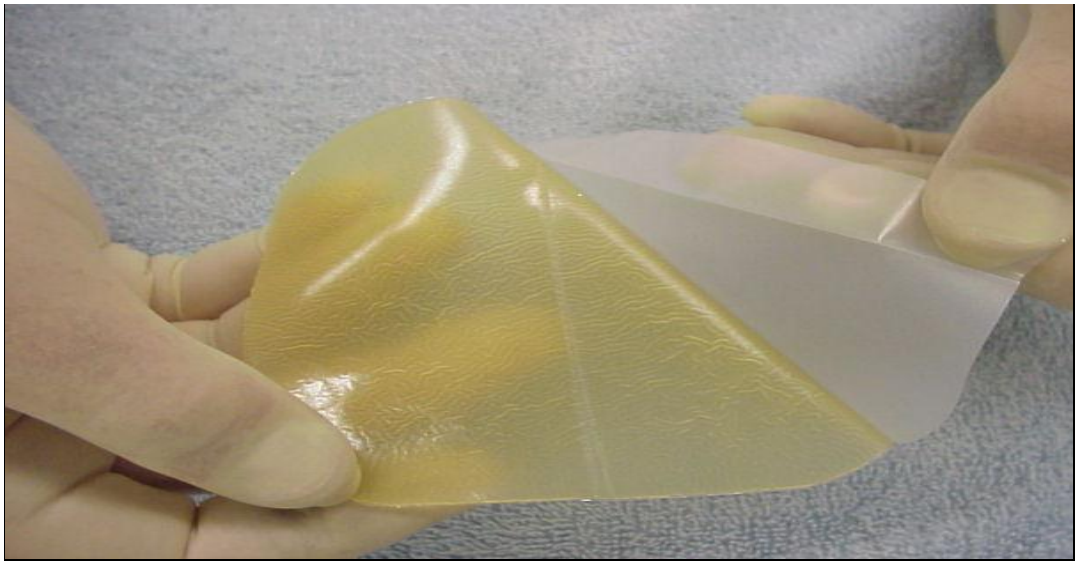


Fig 4.2: Shows Duoderm by Convatec out of the packaging also can see it is absorptive and flexible (Taken from 'http://Jan.ucc.nau.edu/-daa/woundproducts.html').

Shapes and sizes. Examples: Granuflex, Aquacel and DuoDERM extra thin/signal from ConvaTec, Ickenham, Comfeel (Coloplast, Peterborough) and Hyrdrocoll from Hartmann, Heywood. The hydrocolloid component present in the hydrocolloid dressing forms a gel when it comes in contact with moisture from the wound exudate and thus forms a protective barrier against the infection from the micro-organisms. These forms of dressing have a capacity of maintaining light to heavy range of exudate. Originally developed from the stoma products these dressing found to be helping in forming a protective barrier over the wound surface on the skin. The dressings are composed of cellulose. The dressing should be placed at a gap of 2cms from the wound border and should be left for 3-5 days so that the subject is comfortable to shower. This category of dressing can used in various wounds like pressure ulcers, leg ulcers, minimal burns, surgical and abrasion wounds. Also the use is expandable to necrotic and granulating wounds thus can be used in facilitating rehydration and debridement of dry and necrotic wounds (Williams, 1996a).The hydrofibre aqua gel is used with a secondary dressing with at its best in moderate to high exuding dry and necrotic wounds. This category has hydrocolloid fibres with very high absorbing rate. The secondary dressing used with this can be for example Duoderm Extra thin/signal for maintaining its position. The hydrocolloids can encourage the growth of anaerobic bacteria therefore proper care should be taken during their use on infected wounds (Nurse Prescriber, 2006).

4.2 Hydrogel dressings:

For many years this category of dressing is being used in the treatment of dry wounds containing necrotic form of tissue. As the name suggest the hydrogel contains large amount of water about 80% and with combination of other materials like hydrocolloid materials, alginates and starch based polymers (Williams, 1998c). Hydrogels are available as an amorphous form with no definite structure with product form as gel or as sheets. Some of the examples of amorphous hydrogels are IntraSite Gel from Smith & Nephew Healthcare and Hull Purilon Gel from Coloplast, Peterborough and sheet gels include products like ActiForm Cool Activa from Healthcare, Burton-on-Trent and Geliperm from Geistlich Pharma, Chester. The hydrogels can be used in donating moisture or absorbing exudate based on the state of the wound environment. The gel facilitates autolysis or debridement of unwanted tissue from the healthy wound bed. Hydrogels can have various uses in wound types and but main use being dry and necrotic wounds and can be used for all stages of

wound healing process. Used in other areas of wound management and skin care like in dermatological conditions, inflamed skin flexures, damaged skin due to radiotherapy treatment, fistula management and rash from nappies in infants. The hydrogels give out water to dry surface secondary dressing used should be of an appropriate choice, like use of polyurethane foam is not recommended whereas instead a semi permeable film can be used as secondary dressing.

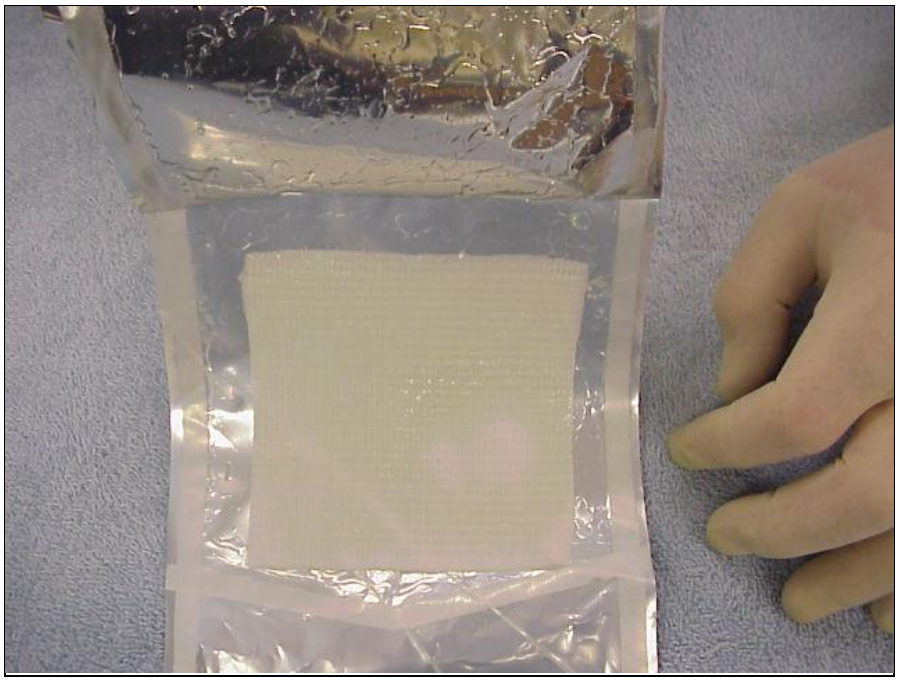


Fig 4.3: This is what a hydrogel dressing with gauze looks like, Manufactured by Curosol, notice the wet appearance (Taken from 'http://Jan.ucc.nau.edu/-daa/woundproducts.html').

4.3 Alginate dressings:

Seaweed found in 1800's found to be a good cure for sailors injured in ship battles called as 'the mariner's cure'. Formed from extract of seaweed calcium alginate, Example Sorbsan from unomedical redditch, Tegagen from 3M, Loughborough and Algosteril from Smith and Nephew healthcare, Hull. Calcium from the dressing comes in contact with the sodium from the wound exudate when alginate dressings come in contact with the wound surface and forms a gel to maintain moist environment. Cavity wounds granulation with small slough amount and moderate to high level of exudate wound these dressings are suitable but in case

of dry, hard and necrotic tissues is not suitable. The alginates are suitable in case of wounds which are bleeding as it has natural haemostats present in it and also additionally are atraumatic and free from pain when required to be removed. Additional adhesive foam dressing or semi-permeable films can be used in case of secondary dressing. (Williams, 1998d).

Fig 4.4: Shows calcium alginate dressing manufactured by Sorbsan. (Taken from 'http://Jan.ucc.nau.edu/-daa/woundproducts.html')

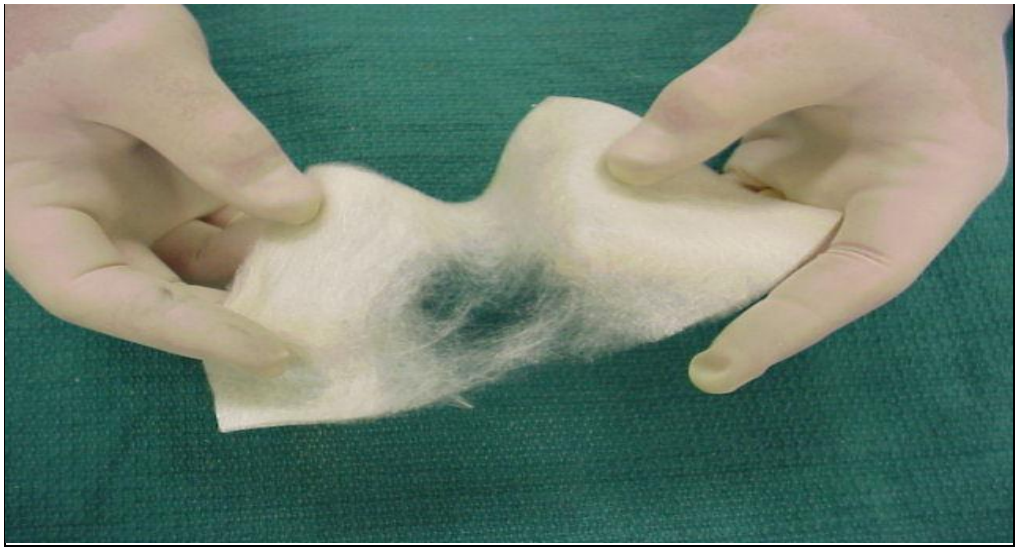


Fig 4.5: Can be easily separated and fluffed up before placing into the wound, can see cut into unwoven sheets made from seaweed (Taken from 'http://Jan.ucc.nau.edu/-daa/woundproducts.html').

4.4 Semi-permeable film dressings:

A layer of adhesive coating on a thin sheet of polyurethane; Examples include: OpSite from Smith and Nephew Healthcare, Hull, Tegaderm from 3M, Loughborough and Bioclusive from Johnson and Johnson Wound Management, Ascot.

These are permeable in case of moisture, vapor and gases, but are not permeable to liquids. The various types of film dressings vary in their Moisture Vapor Permeability (MVP), with their purpose of application, extensibility, weight and thickness (Williams, 1998a). Film dressings can be used in case of superficial and shallow wounds. Examples are those in the last stages of healing, because they are able to protect recently epithelialized wounds from trauma (Casey, 2000).They can be also used in form of secondary dressing over many primary dressings like gels, alginates and hydrofibres to support them (Williams, 1995). Proper care should be taken during the removal of film dressing. To ensure atraumatic removal many of the films have method to break free the adhesive bonding.

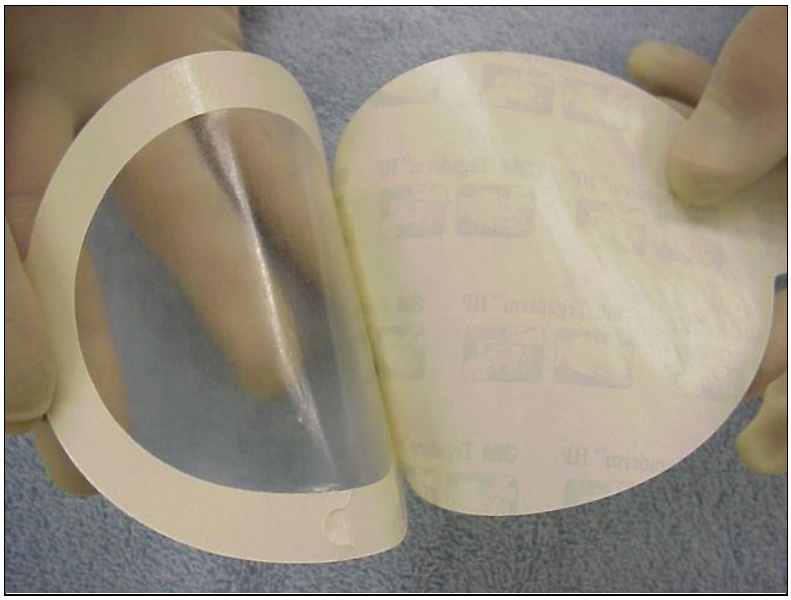


Fig 4.6: Shows a translucent Tegaderm by 3M Corporation, though translucent still gives the clinician a view of wound bed. Ref: http://Jan.ucc.nau.edu/-daa/woundproducts.html.

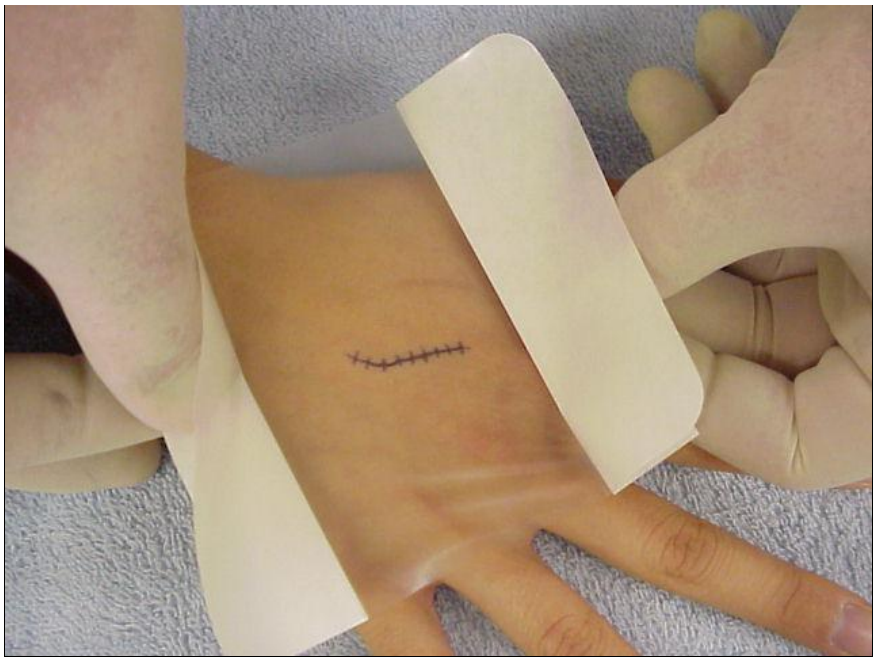


Fig 4.7: Shows a transparent dressing by Johnson and Johnson, gives the clinician a clear view of wound (Taken from 'http://Jan.ucc.nau.edu/-daa/woundproducts.html').

4.5 Foams—polyurethane, hydrocellular, soft silicone and hydro polymer dressings:

There are many forms of foams manufactured from various base materials and constructions that have same but differing level of performance characteristics. Foam dressings available in a various forms differing in shapes, sizes and thicknesses so that can be in use on moderate to heavily exuding form of wounds like pressure ulcers, leg ulcers, burns and surgical wounds. Products under this category include Allevyn hydrocellular from Smith and Nephew Healthcare, Hull, Lyofoam – polyurethane from Molnlycke, Dunstable, Tielle-hydropolymer from Johnson and Johnson Wound Management, Ascot. There are some in adhesive bordered and also non-bordered format so are useable for subjects with delicate and problematic type of skin. Example in the case patients with leg ulcer were the dressing can be retained in place with compression bandages. Foams are basically better for use in exuding granulating wounds and are not prescribed for dry superficial wounds. These are also suitable for use under the compression therapy.

Fig 4.8: Foam dressings with adhesive backings are very useful for placing over wounds smaller than the diameter of the dressing shown in A, B, C and D manufactured by Flexzan (Taken from 'http://Jan.ucc.nau.edu/-daa/woundproducts.html').

4.6 Deodorizing dressings:

Maintenance of the wounds which are fungal, bacterial and also malodorous is big challenge for many healthcare professionals (Williams, 1998e). Deodorizing dressings may be of great use in the case of managing the malodor. Examples include: CarboFlex from ConvaTec, Ickenham; Actisorb Silver 200 from Johnson and Johnson Healthcare, Ascot and CliniSorb from Clinimed. The presence of charcoal cloth within the dressings is able to absorb the gas molecules. Some can be combined with other dressing products such as the foam, silver, alginates and absorbent pads.

4.7 Iodine based dressings:

These products are antiseptics and may be useful in wide range of spectrum of micro-organisms. Some the examples are Inadine or povidone iodine from Johnson and Johnson wound management, Hull; Iodoflex or Iodosorb or cadexomer iodine from Smith and Nephew Healthcare, Hull. Inadine is used as a low-adherent also knitted and viscous form of dressing with 10% of povidone iodine. The color of the dressing changes from orange-brown to white, this show that the dressing should be changed at this point of time. The change in the color is due to usage of all povidine-iodine. On the other hand the Iodoflex and Iodosorb contain cadexomer iodine in the form of a paste, powder or as an ointment. This product is useful in wound debridement and the dosage must not exceed more than 150g a week and in case of single application is 50g. Overall even in case the treatment it should not exceed more than three months totally.

4.8 Silvers dressings:

These categories of products have antimicrobial properties. They are used in combination with other products for the benefit of multiple properties of the dressings. Examples include hydrofibre, alginate, charcoal, foam and hydrocolloid. Silver dressings can be used in various types of wound types with clinical wound infection or critical colonizing wounds or those who may have previously had a clinical wound infection. Silver therapy should only be used for short time may be 2 to 3 weeks (Lansdown, 2007).

Silver dressing such as Actisorb silver 220 can be useful in the treatment of most of the chronic wounds but in particular are recommended for the management of malodorous, infected wounds including fungating lesions, faecal fistulae, pressure sore which are infected and also in the case of exuding leg ulcers. The method used in application of this dressing is that is directly applied to the wound surface and is also covered with a secondary dressing with use of tape bandage to hold it in the same position. The choice of secondary dressing depends on the wound but normally simple absorbent pad will be enough. The dressing may be placed in between the wound contact material and that of the secondary dressing as it is not advisable to place the dressing directly with wound contact and this also reduces the activity of the dressing. The changing of the dressing in case of heavily exuding wound is

daily for the initial stage and can be retained for 7 days later when the wound is healing and cleaner compared to initial baseline period.

The following are sizes its available in:

- 9.5cm x 6.5cm
- 10.5cm x 0.5cm
- 19.0cm x 10.5cm.

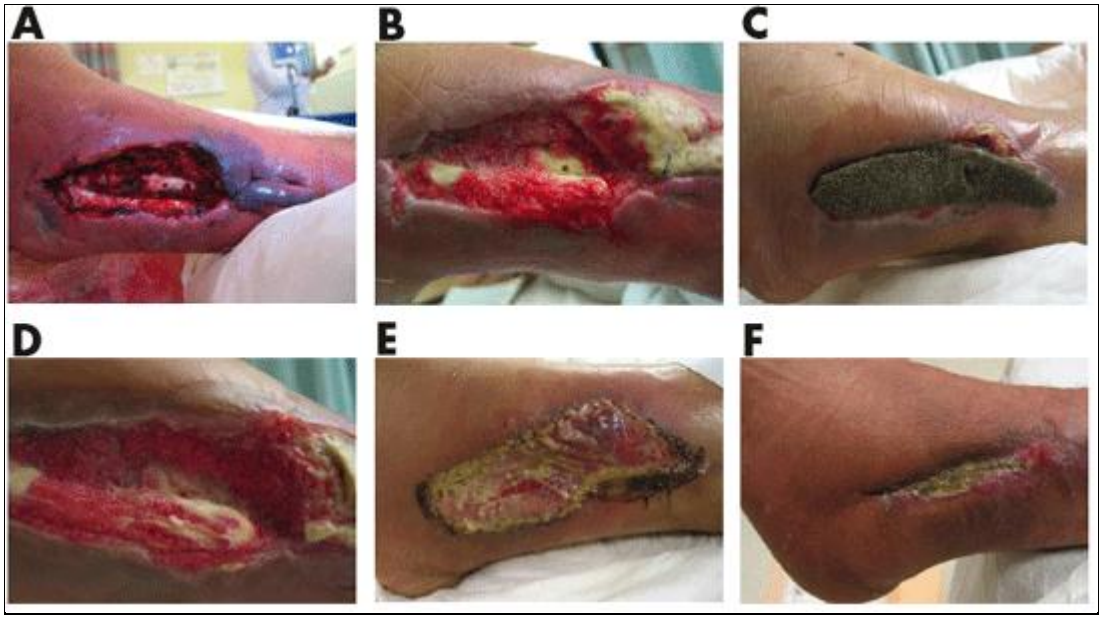
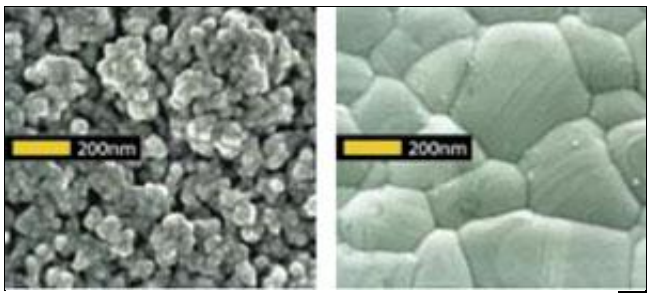


Fig 4.9: A) wound post-debridement; B) Day 22 of NPWT with standard foam dressing; C) Day 30 silver foam dressing placed in wound cavity; D) Day 35 of NPWT, after 5 days of NPWT with the silver foam dressing; E) split-thickness skin graft placed on Day 39, after 9 days of NPWT with the silver foam dressing; F) 3-month follow-up post discontinuation of NPWT (Taken from 'http://Jan.ucc.nau.edu/-daa/woundproducts.html').

4.9 Acticoat silver dressings:

Acticoat antimicrobial barrier dressing consists of mesh with double layer of high density silver coated polyethylene and covering it is a fabric of rayon and polyester. These three components are welded ultrasonically for maintenance of the integrity of this dressing. Nano-crystals of silver are formed on the mesh by vapor deposition process. Because of presence of silver the dressing exhibits antibacterial activity against wide range of gram

positive and negative which includes strains which are found to be resistant against antibiotics. Similar is the case with yeasts and fungi effectiveness.



Nano crystalline silver **Normal silver**

Fig 4.10: Shows image of normal and Nano crystalline silver (Taken from 'http://wound.smith-nephew.com/uk/node.asp?NodeId=3791').

There are chances of hypersensitivity in patients with components of the product, if found during use then the treatment should not be continued further using the same product as the safety issue with the use of Acticoat is not known till date. Before the use of the dressing Acticoat should be moistened with water instead of saline so that it provides a moist environment for healing and also enables silver to enable antimicrobial effect. The dark blue surface should be placed against the wound so the shape and size of the dressing should be changed before the application of the dressing. The surgical tape or a bandage can be used hold the secondary dressing in place. The secondary dressing is selected based on the exudate from the wound. The dressing should be placed on the wound for three days but if there are wounds with heavy flow of exudate then it is recommended to change the dressing more frequently. The Acticoat cannot be used with any oil products and antimicrobials. If the dressing is applied to wounds which are lightly exuding then there are chances that the dressing dries and adhere to wound surface. This mainly occurs in the secondary dressing if it is more absorbent and also highly permeable to water vapor. The adherence causes problem as it should be soaked to avoid any cause of pain and also trauma for the underlying tissues. Figure 4.10 shows the image of normal silver as compared to Nano silver ions. Nano crystalline silver compared to normal silver starts the process in less than 30 minutes releasing ions at 70 parts/ million (ppm) showed an in-vitro study (Yin et al., 'Journal of burn care & Smith and Nephew Inc. Hull').

Chapter 5: ULTRASOUND-THE USE IN WOUND THERAPY AND LEVEL OF SCAR TISSUE HEALING.

Ultrasound is a very useful physical modality used in scar tissue healing and various wound healing therapies. The usage of how the ultrasound works so that the clinicians are well versed with selection of whether this therapy has possible use in healing of particular wound and also monitoring its effectiveness is explained in this chapter. Ultrasound (US) is in use since 50 years now. Up to the 1900's kHz US was not in picture and only MHz US was being used, US is a mechanical vibration that is transmitted above the upper limit of human hearing, i.e., above 20k Hz where 1 Hz= 1 cycle/ second and 1 kHz= 1000 cycles/ second. The molecule of the media through which it passes is caused to vibrate by the mechanical vibration of the US, the media can be biological tissue and thus due to this output of the US there can be therapeutic healing (Dyson, 2003).There has been use of MHz US since 50 years, till the 1990s 0.3 to 5 MHz was being used and there is latest rapid use of 30 to 50 MHz US as it has shown better therapeutic effect (Peschen et al, 1997).

5.1 Therapeutic properties

a Frequency:

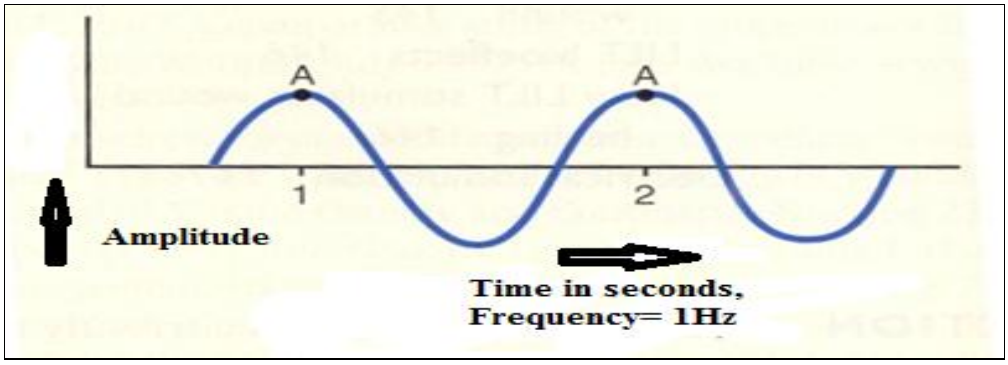


Fig 5.1: Shows frequency with time and amplitude (Taken from Morison et al, 2004).

The therapeutic properties of the US are dependent on the frequency of the US, i.e., the number of times the molecule present in the US completes a cycle and come back to its original position represented by 'f' and 'T' is the time period is the time taken by the molecule to complete a cycle. Kilo Hz US is known as long wave US as lower the frequency

the longer the wavelength therefore the frequency and the wavelength are inversely related in relation.

b. Attenuation: The power of the US is reduced as during transmission through the tissues it gets absorbed and scattered, higher frequencies have more energy whereas the lower penetrate deeper, kHz and MHz are absorbed by proteins but passed through water and fat. Kilo Hz can even pass through bone and metal. Example in stage 4 level pressure ulcers kHz can be more useful as the bone is involved, if it is a superficial wound the 3MHz can be useful and deeper wound then 1 MHz can be used. Coupling agents such as hydrocolloid dressing and films are to be used during the usage of the US as these reflect with various agents like the skin, air, collagen etc. These coupling agents help the US to passes exactly through the woun**d.**

c. Half-value thickness: When the US is transmitted through certain tissues because of absorption, scattering and reflection the intensity decreases. The intensity to be reduced to one-half to the surface intensity is called as half-value thickness. ”The intensity available at any depth within the tissue is inversely proportional to the depth of penetration” (Sussman & Dyson. 2001). Even if applied from lateral aspect of limb the kHz waveform can reach medial limb without any use of probe, even within the dressing area reducing pain caused from application of pressure , therefore US is recommended for painful and infected wounds.

5.2 Therapeutic ultrasound equipment: To produce therapeutic levels of MHz US, this consists of microcomputer controlled high frequency generator and attached to an applicator or treatment head with the use of coaxial cable. Transducer changes one form of energy to another, the head in this equipment consists of piezoelectric crystals such as Lead Zirconate Titanite (LZT). This disc when applied with electrical energy converts it to US contracting and expanding at same frequency.

The ultrasonic field: The size and shape of the transducer causes the ultrasonic field to vary accordingly, it also changes the field on how it is placed on the applicator. The pressure change in the tissue is caused also is varied on the surface and distance from the applicator. US is emitted at the output of the disc-shaped transducer, which is called as first cylindrical and also the region is known as near field or Fresnel zone. In the following zone the energy

distribution is extremely variable, but in case of region of far field the distribution of energy is regular and beam is diverged.

Formula:$d = a^2/\gamma$.

Here‘d’ represents distance from the transducer to far field region.

‘a’ represents radius of the transducer.

‘γ' Represents wavelength of US.

Fig 5.2: Shows a ultrasound device producing MHz frequency with transducer connected U.S (Taken from Morison et al, 2004).

The usage of the therapy may involve immersing the part to be treated in a water bath this is done so that the treatment region is in the far field. Along with this form of treatment, US therapy involves usage of irregular energy beam of near field region for treatment of tissue.

Measuring the non-uniformity is by Beam Non-uniformity Ratio (BNR) which is the ratio between spatial peak intensity I[SP] and spatial average intensity I[SA]. Result with

use of applicators producing low BNR is more predictable and safer in nature compared to high BNRs. In the latter case is more damaging (Ziskin & Michlovitz, 1990).

Fig 5.3: Shows a ultrasound device producing kHz frequency with transducer connected U.S (Taken from Morison et al, 2004).

Fig 5.4: Shows an ultrasound device producing both MHz and kHz frequencies with transducer connected U.S (Taken from Morison et al, 2004).

Intensity: Intensity symbolized by 'I' and unit used in measurement is Watts which is the energy per unit area. Applications have ERA (Effective Radiating Arc), I is space over the applicator surface known as Spatial Average [SA], in time know as Temporal Average [TA].

5.3 Application of US in wound healing process:

A film dressing, gel with water content are mediums which are best suitable for the transmission into tissues as US is always reflected from interfaces such as air and skin also air and soft tissues. For the treatment of tissues a wound should be always covered with a hydrocolloid dressing such as an example Granuflex by Convatec and also either warm sterile saline or film covering as a dressing such as an example Opsite by Smith and Nephew.

Using a coupling medium for an example Aquasonic 100 Gel from Parker Laboratories Inc. on the surface of US emitting face helps in smooth movement on the skin surface and also over the covering of the dressing.

Parameters used during treatment procedure: In case of typical wound are as follows.

- Frequency f=3MHz
- Duration of application =5 minutes.
- Waveform as in pulsed format and not as continuous.
- Pulse duration =2 milli seconds.
- Space duration=8 milli seconds.
- Intensity in spatial average, temporal average I[SATA]=0.2 W/cm^2 is considered and not I[SAPA] Intensity in spatial average, pulse average.

5.4 Bio effects of US:

In vascularized tissue temperature if high than prescribed causes thermal necrosis. There are some clinical benefits of thermal effects which can be achieved by 1 MHz and 3MHz continuous US. At 3MHz energy absorption is only to the level of superficial tissues which may be about 2cm beneath surface, whereas 1MHz can reach 5 cm deep. In case of pulsed wave as it reduces the temporal average intensity level it also causes reduction in thermal effects.

5.5 Non-thermal effects: There are three main non-thermal effects which are advantageous in healing process; this can only be gained by using a pulsed wave so that it produces low spatial average intensities. Thus helps in achieving the three benefits as the following.

1. Cavitation.
2. Standing wave formation.
3. Acoustic streaming.

1. Cavitation:

Changes in the calcium activities of tissues can be achieved by movement of micron-sized bubbles present in the fluids. When subjected to a US field the bubbles oscillate and cause expansion and contraction as per the cycle of the waveform.

Stable Cavitation: Is a beneficial process which is helpful in stimulation of healing process in the wound region. Cell activity can change permeability to calcium ions; stable cavitation makes diffusional changes by the bubbles close to cell membrane.

Unstable Cavitation: Hazardous in nature to tissues as the bubbles explained above explodes causing membrane damage and also forming free radical group. This happens during no movement occurring in the applicator head during the treatment forming a standing wave at high level of intensities (Sussman & Dyson, 2003).

2. Standing wave formation:

During the procedure if the applicator in not moved or is kept still at a position the waveforms emitted move and are reflected back and forward in the applicator and reflector interface; reflector surfaces being for example soft tissues and bones. There is accumulation of energy and thus increase in damage levels; an example such as blood cells flow are stopped, endothelial cells being damaged (Dyson & Pond, 1973).

3. Acoustic streaming:

Increase in the cell membrane permeability level and more protein synthesis are the outputs of an unidirectional fluid movement on acoustic boundaries such as bubbles or cell membranes due to the mechanical pressure wave of US beam (Ziskin & Michlovitz, 1990).

5.6 How US stimulates the wound healing process:

Working of US: Acoustic streaming and stable cavitation produces movement of calcium ions into the plasma membranes, thus the healing occurs as cell involved in the process of healing are now active and this achieves calcium entry (Dyson, 1995).

There is amplified response achieved when the cell is on the pathway of US beam, this causes an organized healing process to run smoothly by differentiating, dividing, migration, growth, phagocytosis and synthesis of growth factors and matrix materials based on the cell involved in the process, for some example such as the following.

- Polymorphs phagocytize debris.
- Fibroblasts synthesize collagen.
- Migration occurs in endothelial cells.
- Division occurs in producing new capillaries.

5.7 Attributions of US in acute wound healing:

When a wound begins a process of healing it enters the first phase which is known as temporary acute inflammation, with the usage of US this phase can be shortened in time period and also the next phase which is proliferative phase progresses more rapidly (Dyson, 1995).

In the first phase the growth factors are produced and secreted, there is evidence which supports the US in a feedback to the body during healing process and acute skin injuries treated in inflammatory phase produces reparative tissue better compared to control wounds (Hart, 1993).

5.8 Attributions of US in chronic wound healing:

In venous leg ulcers treatment US application first using a high intensity MHz US or usage of kHz US via water bath usage, so that they activate a least part of wound and reaches acute inflammatory phase of healing process and debrides the wound thus activating wound healing. When acute inflammation is reached by using low intensity which does not produce thermal effects as high intensity used earlier during the procedure helps in accelerated healing in venous leg ulcers (Dyson et al, 1976).

Parameters used during treatment procedure:

- Frequency f=3MHz
- Duration of application =5 minutes.
- Waveform as in pulsed format and not as continuous.
- Pulse duration =2 ms.
- Space duration=8 ms.
- Intensity in spatial average, temporal average I[SATA]=0.2 W/cm^2 and I[SAPA] Intensity in spatial average, pulse average=1.0 W/cm^2 .

These parameters when applied to periwound region there were observed initiation of acute inflammation. Application of long wave in kHz also proved effective alternative for venous leg ulcers. In this alternative form of therapy water bath is used as shown in fig 5.5. Here acoustic streaming helps in removing necrotic tissue from superficial area and causes tingling sensation (Peschen et al., 1997).

The kHz treatment parameters to control group to cause acceleration in healing are as follows:

- Frequency f=3MHz
- Duration of application =10 minutes, 3 times a week.
- Waveform as continuous.
- Intensity in spatial average, temporal average I[SATA]=0.1 W/cm^2.

The control wounds and US treated wounds were also covered with hydrocolloid dressings and compression therapy, in time of 12 weeks there was decrease in area of wound by 55.4% in comparison to 16.5% of control.

MHz parameters which were applied on pressure ulcers

- Frequency f=1 MHz
- Duration of application =5 minutes every day.
- Waveform as in pulsed format and not as continuous.
- Pulse duration =2 ms.
- Space duration=8 ms.

- Intensity in spatial average, temporal average I[SATA]=0.1 W/cm^2 and I[SAPA] Intensity in spatial average, pulse average=0.5 W/cm^2 .

5.9 Outcomes expected from US:

In acute wounds US when used reaches acute inflammatory phase, during this phase there is increased inflammation and early achievement in reaching proliferative phase of healing. In case of chronic wounds there is warmth, edema and darkening of tissues. In necrotic wound there is formation of clean wound bed. The progress of any wound should be monitored during treatment (Sussman & Dyson, 2003). The healing depends on intrinsic and extrinsic factors, suppose the healing of wound is deteriorated and size is not reduced then status should have to be reviewed, this step is taken in 2 to 4 weeks. There may be repeated initiation of acute inflammation required.

Fig 5.5: Shows a podiatry bath incorporating a rectangular kHz ultrasound transducer (Taken from Morison et al, 2004).

5.10 Monitoring healing process with high-resolution US imaging:

Fig 5.6: Shows a portable high density ultrasound scanner device produced by Longport Inc. (Taken from Morison et al, 2004).

Non-invasive, rapid and painless are the advantages of monitoring the treatment effectiveness. Thus with therapeutic roles explained earlier US adds diagnostic role in wound care and management (Dyson et al, 2003). Causing no damage to the subject this technique allows in visual inspection of tissue within, around the wound region in way of biopsy. The technique is called US bio microscopy as using 20 MHz US there can be high resolution and magnified pictures of living tissues obtained. Here telemedicine comes into picture as these digitized images can be mailed, archived for analysis from any remote site. Any nurse or clinicians treating and dressing the wound if spends few minutes with patients can scan the wound region with a friendly high resolution scanners such as one shown in fig 5.6 can save time and also record with camera and make out changes between tissue fluid, debris, granulation.

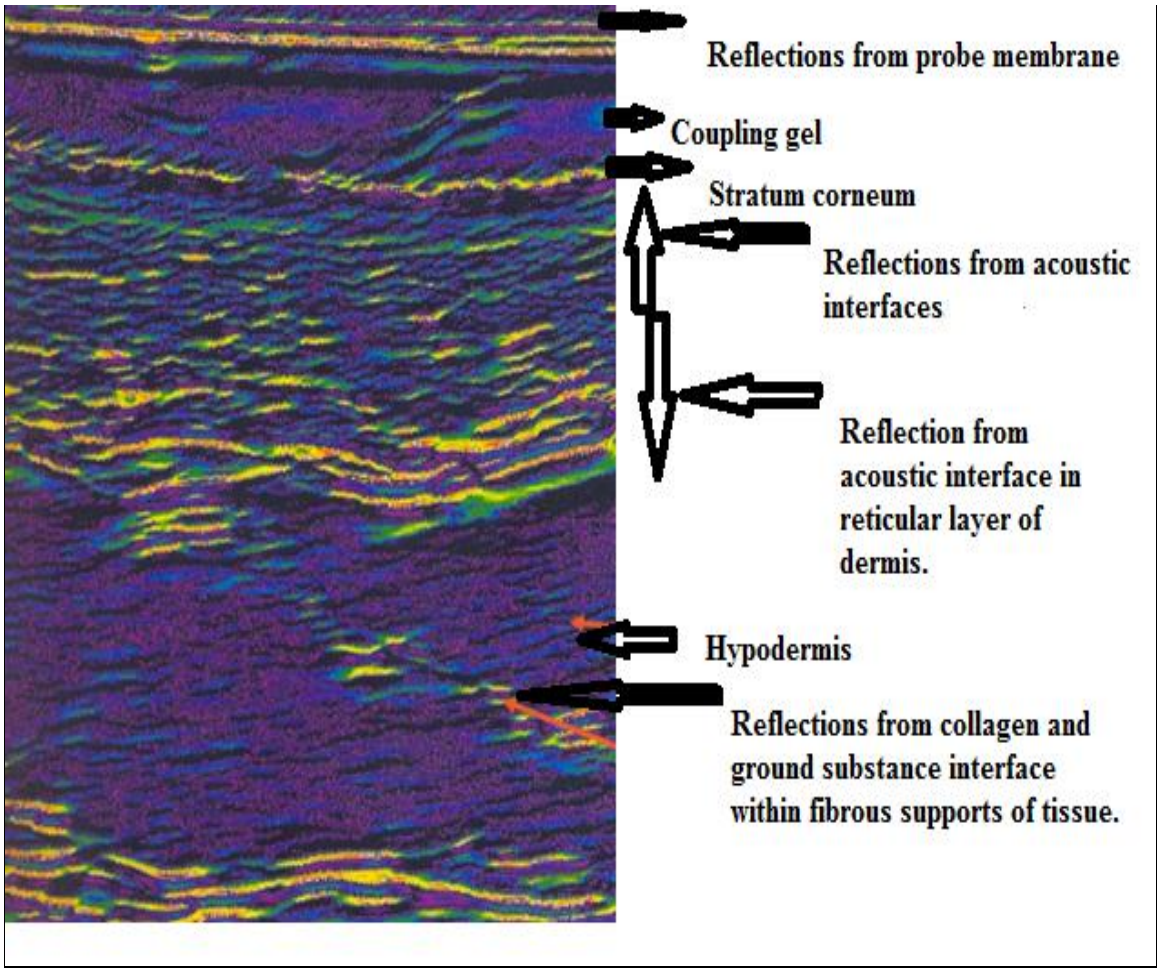


Fig 5.7: Shows high resolution ultrasounds scan of intact skin on the inner aspect of the forearm, (Taken from Morison et al, 2004).

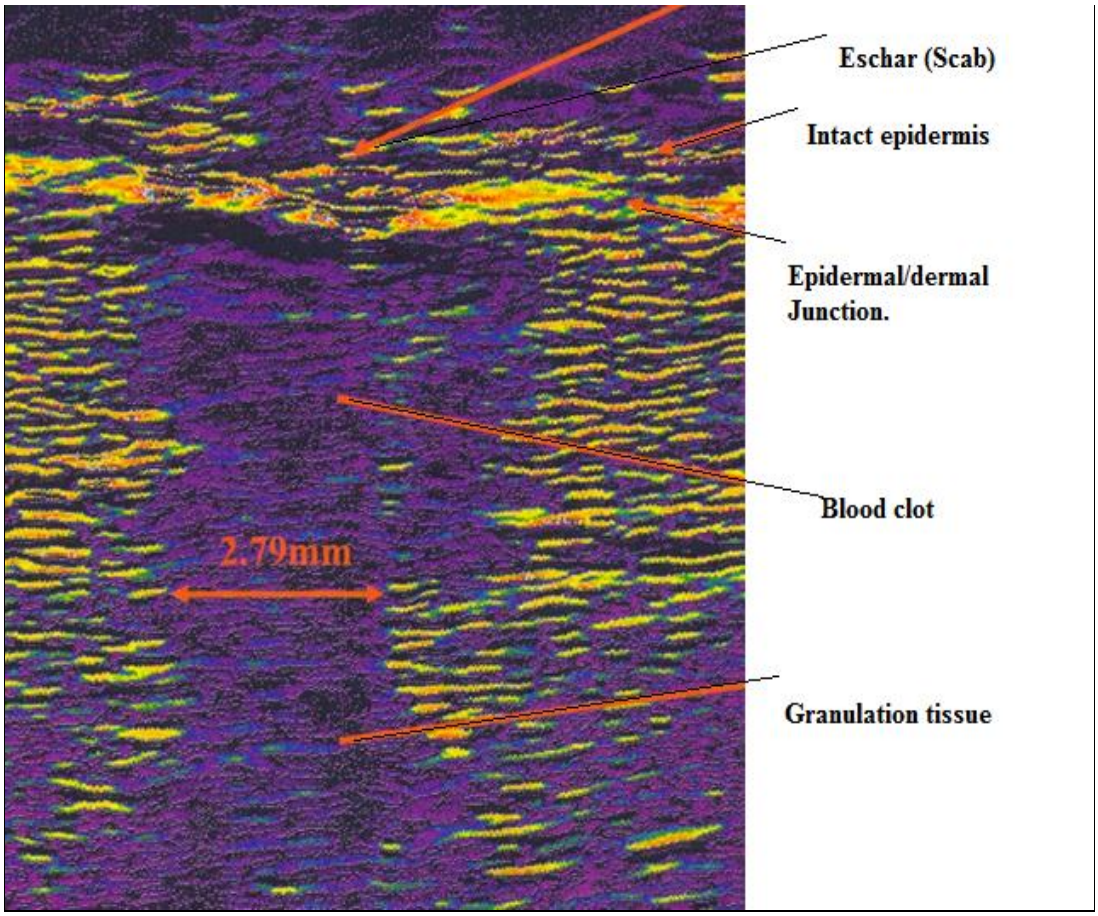


Fig 5.8: Shows high resolution ultrasounds scan of healing skin 7 days after a full thickness punch biopsy (Taken from Morison et al, 2004).

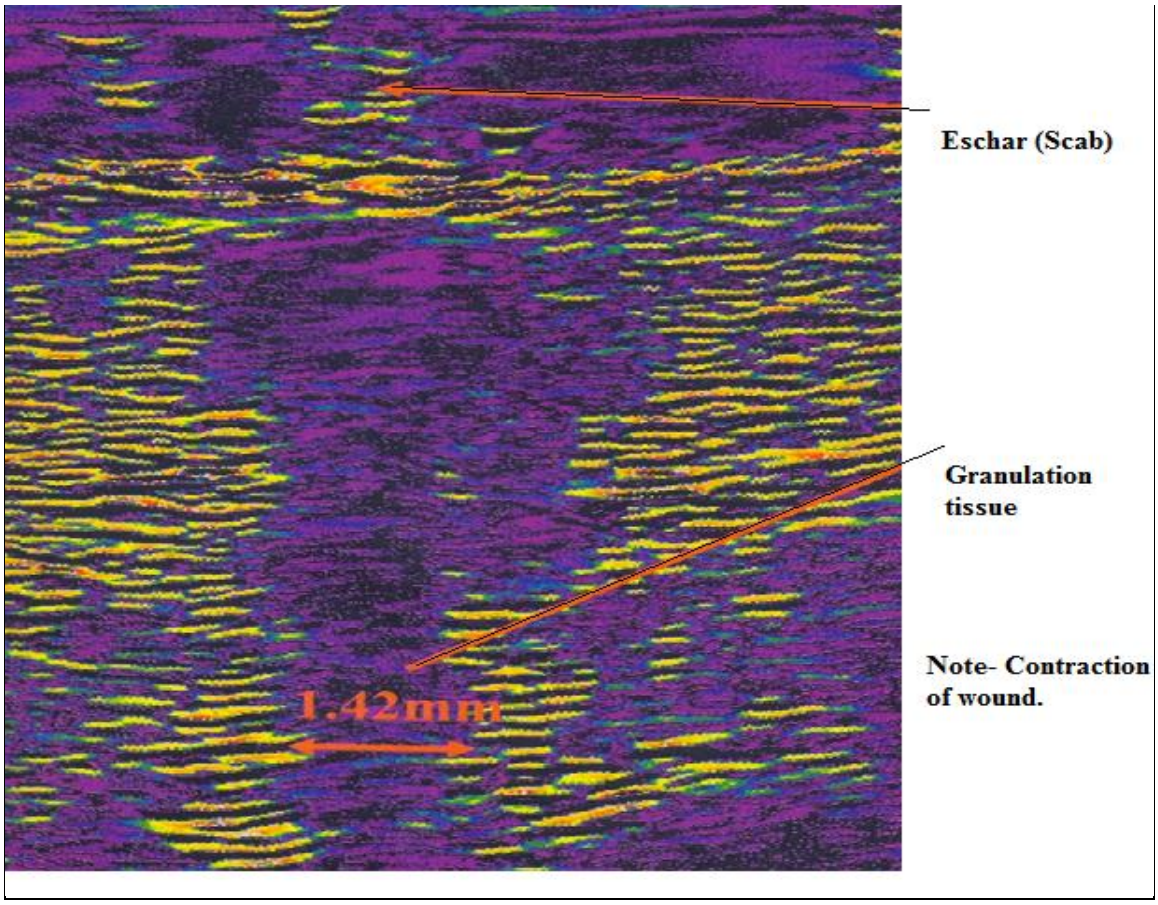


Fig 5.9: Shows high resolution ultrasounds scan of healing skin 14 days after a full thickness punch biopsy (Taken from Morison et al, 2004).

tissue, scar tissue and layers of skin. This provides vertical resolution of 65µm and software provided with scanners helps in measurement of linear and area. Information data collected can be stored, secured and retrieved with all images and patient notes. Such as images shown above with intact skin, healing skin in period of 7 to 14 days, refer to figure 5.7, 5.8 and 5.9.

Chapter 6: Hyperbaric oxygenation in process of wound healing.

6.1 Hyperbaric oxygenation:

"Is a systemic, intermittent administration of oxygen under pressure", for a hyperbaric environment to exist the atmospheric pressure should be greater than 1 atmosphere absolute (ATA) (Hammarlund et al., 1995). Clinically hyperbaric exposure occurs when the ATA increases above the level of 1.4 ATA per square inch gauge pressure (psig) (UHMS, 1996), at level of 2.0 to 2.4 ATA pressure the subject is breathing 100% oxygen and also at the same time physically being exposed to a hyperbaric environment. If oxygen is applied topically then there is no improvement in the wound healing process as there are no therapeutic effects present, in hyperbaric oxygenation when applied under pressure then has therapeutic , toxic and side effects also it interacts with other drugs and causes non compatibility issues (Heimbach et al., 1998).

Modern usage of the therapy began in 1955 in cancer treatments like reducing the radiation (UHMS, 1999). Hyperbaric oxygenation medicine and diving medicine information worldwide in produced by UHMS and there are also designed treatment protocols and practices. Listed are indication and current researches in the field of hyperbaric oxygenation are listed below in table 6.1

Table 6.1 Indications for the use of hyperbaric therapy (Bryant, 1993).

Indications for hyperbaric therapy:
➢ Air/gas embolism
➢ Decompression sickness
➢ Carbon dioxide poisoning
➢ Crash injury
➢ Exceptional blood loss
➢ Clostridial myonecrosis
➢ Necrotizing soft tissue infections
➢ Chronic refractory osteomyelitis
➢ Thermal burns
➢ Radiation tissue damage

- Compromised skin grafts/flaps
- Intracranial abscess

There are two main benefits of this therapy, 1. Mechanical effect: Boyle's law states that as there is increase in the level of barometric pressure there is decrease in size or volume. The size of embolism can be reduced due to this therapy which causes air/gas embolism.

2. Increased oxygenation of tissues: Henry's law states "gas dissolved in a liquid is directly proportional to partial pressure of dissolved gas". There is increase in oxygen tension by 10 to13 folds higher than oxygen at ambient pressure (Hammarlund et al., 1995).

Table 6.2: Different investigations in progress under hyperbaric oxygenation therapies (Bryant, 1993).

Hyperbaric therapy under investigation:
➢ Acute myocardial infection
➢ Acute cerebral vascular accident
➢ Closed head injury
➢ HIV/AIDS
➢ Cerebral palsy
➢ Radiation cystitis/proctitis
➢ Multiple/ Cluster headache
➢ Sickle cell crisis
➢ Spinal cord injury
➢ Rheumatic diseases

6.2 Hyperbaric oxygenation in the process of wound healing:

Depriving oxygen or state of hypoxia is essential for the process of wound healing. Diabetes, vascular disease, skin flaps or grafts, trauma, irradiation etc. are main cause in result of chronic wounds. Oxygen is also essential in the process to heal any wounds as it has lot of beneficial outputs such as metabolism of energy, polymorph nuclear cell function and antibacterial activity.

During the process of hyperbaric oxygenation the compound tissues are supplied with increase oxygen supply as there is increase in capacity of blood cells in carrying of oxygen, this restores perfusion and cellular functioning. Diffusion can be achieved by supplying oxygen at 2 to 3 folds more than at a non-barometric level causing it to attribute to healing and neovascularization. This process helps also in vascularization diffusion and in turn decreases circulation with vasoconstriction (Hammarlund et al., 1995).

6.3 Procedure involved in the hyperbaric oxygenation therapy:

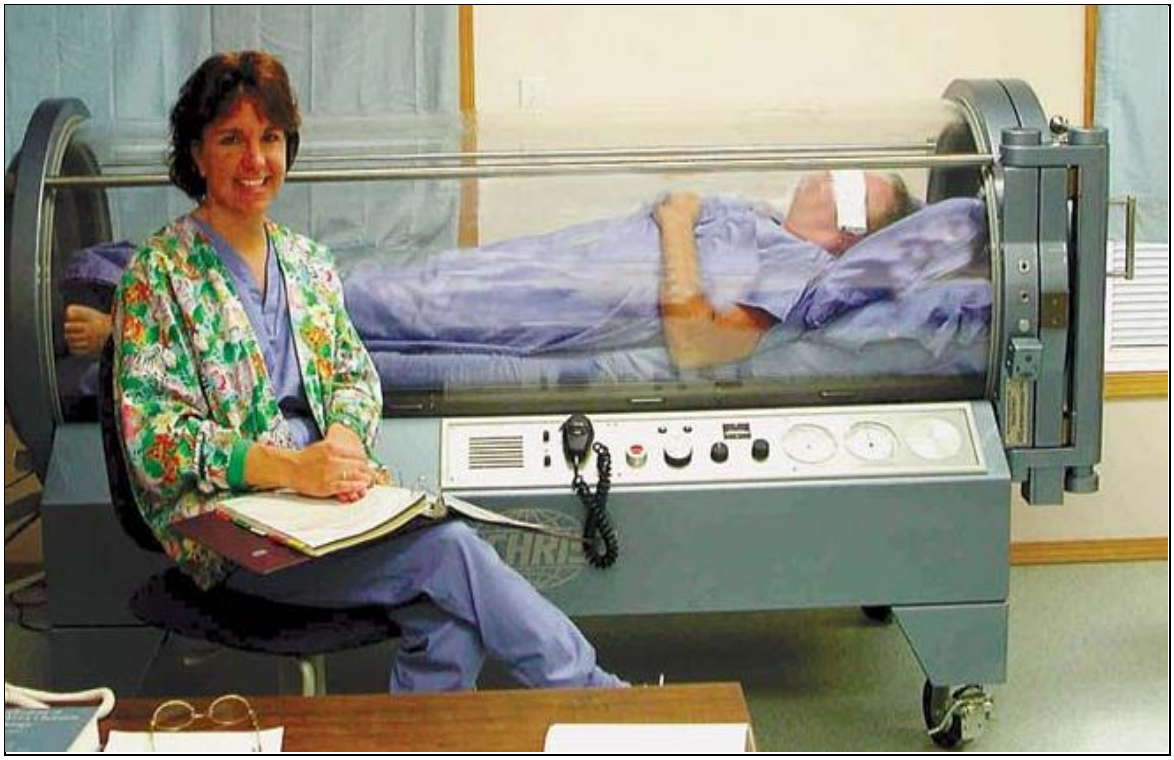


Fig 6.1: Shows a clinician with a subject in Mono-place hyperbaric oxygen chamber manufactured by Sechrist Inc. (From'http://drcranton.com/images/HBO_Chamber.jpg&imgrefurl=http://drcranton.com/hbo.htm&h=500&w=750&sz=73&tbnid=BKxa_wgjNK9j3M:&tbnh=90&tbnw=135&prev=/search%3Fq%3Dhyperbar').

There are two kinds of chambers which are involved and available called as mono-place and multi-place chambers. Mono-place mainly seen in outpatient departments, procedures up to 44 psig or 3 ATA of compressed oxygen, it is comparatively inexpensive than multi-place. This chamber also can be placed with low construction cost wherever there is adequate

supply of gas, along with all the advantageous mentioned adding to it is the main advantage being that technician or the nurse can be staffed with the chamber. The main disadvantages include no direct contact and monitoring difficulty of the subject than apart from visual inspection. ECG, blood pressure, arterial, central venous, wedge and pulmonary blood pressure and temperature are different parameters that are monitored (Hart & Strauss, 1995).

In case of multi-place chamber nurse can also enter with the subject, this can be used in case of several patients at the same time based on the size of the chamber; size depending on whether the patient is ambulatory or bed-bound. The major disadvantage of this chamber being the cost involved in setting up and number of staff required as chamber operator, tender and nurse or physician (UHMS, 1994).

Fig 6.2: Shows a multi-place hyperbaric oxygenation chamber, with different subject inside and wide space available for many to be treated at the same time. (Taken from 'http://hyox.com/wp-content/uploads/2009/11/Home__1B1.gif').

6.4 Side effects of the therapy: There is cause of ear pain resulting in hematoma of the tympanic membrane of the ear called as 'Aural barotrauma' or 'ear squeeze', pressure equalization is required in such cases. 'Sinus barotrauma' is sinus pain and hemorrhage in sinus, nasal passage should be applied nasal decongestant to avoid this (Kidder, 1995). There are changes in visual activity, Myopia is worsened or presbyopia will be corrected, changes are not known (Maki, 1996). Seizure activity can be caused by increased toxicity level of oxygen. Therefore the patient with a previous history should not be involved in this treatment (Clark, 1995).

Some of common side effects in this therapy is Claustrophobia, subjects experiencing should be assured and also a tender should be present, during mono-place a only verbal and visual contact can be maintained, whereas with multi-place physical comfort reassures the subject (Kindwall, 1997).

6.5 Patient selection for the treatment:

There are contraindications of hyperbaric oxygenation treatment, any cavity filled with air such as ears and sinus should be checked or equalization of pressure gradient. A chest x-ray examination to rule out any trapped air within the lungs can be used. Patient using bleomycins are ruled out from therapy as this increases toxicity of oxygen. Along with this patients using pneumothorax, Cis-platinum, Sulfamylon and disulfiram are too ruled out. Pregnancy, emphysema, pneumonia, bronchitis, hyperthermia, any known malignancy and seizures are ruled out for the therapy (Heimbach et al.,1998).

6.6 Protocol during treatment and safety of patient: All protocols are outlined by UHMS; a patient basically receives treatment 5 to 7 times per week and 90 minutes each at 2.0 to 2.4 ATA. This is continued till 40 to 60 treatments. Physician helping out the patient decides the duration of duration of therapy (UHMS, 1996). As far as safety is concerned there are 2 factors involved in patient preparation and safety, the first being nature of hyperbarics example atmospheric pressure changes. Preventing aural and sinus barotrauma is by assisting the patient about the air equalization techniques. Pneumothorax can be prevented when the subject does not hold the breath. Measuring levels of blood sugar before the treatment is done of the subject with diabetic condition as the therapy can lower the blood sugar level. Hypertension and hyperthermia should be checked as therapy is a vasoconstrictor. The temperature increased more than a level of 102^{o} F causes oxygen toxicity.

Chapter 7: Electrical stimulation and its contributions to wound healing.

Many chronic wounds may heal slowly, be stagnant or may worsen despite of clinicians put their best efforts to promote tissue repairs. Due to failure in body's endogenous bioelectric system there is no contribution in repair process of the wound. A use of electric current to transfer energy from an external source into the wound tissue at therapeutic levels of electric current which is at sequence of micro current electrical pulses so that they interact with the healing biological process which is dormant in non-healing chronic wound. During this therapy 2 electrodes are used in the transfer of current to the surface of the skin which is adjacent to the wound edge. Studies have reported beneficial effect in promoting of healing process by this type of therapy have been around for years. Example galvanic stimulation, the healing process does not depend on one mechanism of action as there has been data gathered on different actions. This showed there where galvanotaxic effects during which based on the relative charges of the cells got attracted to electrodes. The reason noticed on this was there was interruption in biological flow of electricity that controls transfer of molecules between cells, communication and behavior.

The current delivered via 2 electrodes adjacent to skin surface must have net effect to create a flow of ions through the wound tissue. There is acceleration in wound healing process during the ES by vasodilation of the capillaries by increasing in their size thus in density, perfusion and oxygenation which encourages in granulation and also fibroblast activity. Neutrophils, macrophages, fibroblast and also epidermal cells are the cells which help in autolysis, anti-inflammatory activities, granulation and resurfacing the epidermis. These cells involved carry either positive or negative charges. ES stimulates in galvonotaxic attraction and accelerates in healing. Galvonotaxis is phenomenon where positive and negative charged cells migrate towards electrical filed of opposite polarity.

50% increase in the rate of healing by ES has been seen in varies studies like attributing antibacterial effect inhibiting reproduction of the bacteria shown in case study and also increase in blood flow in wounds.

Invasive and non-invasive are 2 main types of techniques used with a biopsy yields quantitative results. Invasive methods may destroy tissues, but destroyed tissue help in obtaining data. On the other side the non-invasive method does not destroy the tissues but

the results are subjective where it is essential to take photographs with precise calibration so that calculation can be made using a computer. There can be errors during calculation and also this type of procedure does not explain about the wound bed and tissues surrounding it but it only gives information of the surface wound. High resolution images from a high frequency ultrasound and new increasing important form of diagnostic tools help the clinicians. Recent addition of 20MHz transducers have helped to use the tool on wounds and help to gather accurate statistical and verifiable data on healing of the lower structures without the need for a biopsy. This demonstrates changes in all 3 layers (epidermis, dermis and subcutaneous tissues) of the skin during healing. There is an early indication of improvement or deterioration by study of the wound bed before they become clinically evident (Sussman et al, 1998).

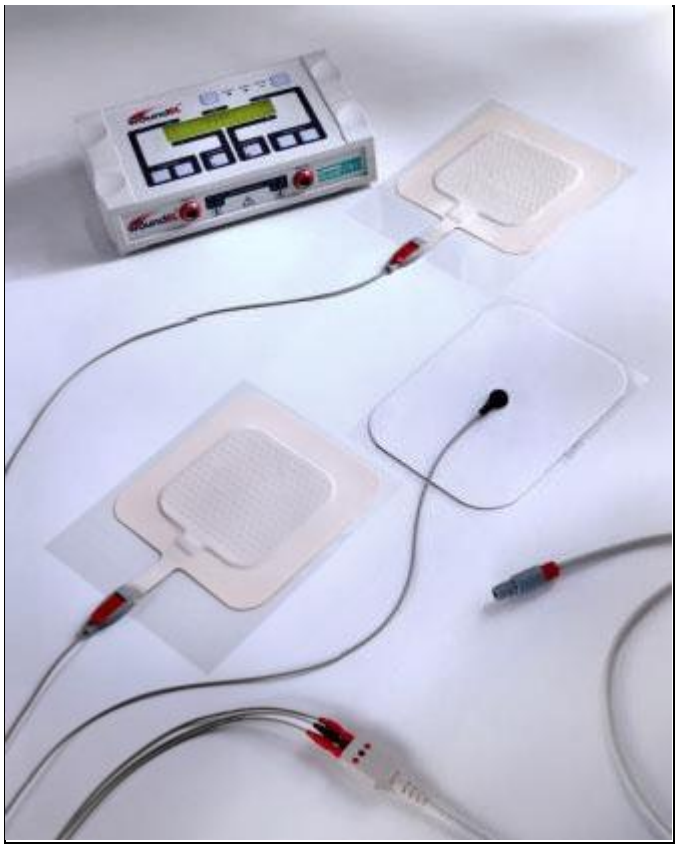


Fig 7.1: This image shows various electrodes that can be used during the process of electrical stimulation.

(Taken from 'http://www.gerromed.de/gerromed.de/en/images/woundEL.gross.jpg')

7.1 Body's endogenous bioelectric currents:

There are many equipment's electrically powered used in several disciplines in treating illness or injury or to diagnose and evaluate like electro analgesia for pain control in chronic wounds, nodal activity of heart pacing devices, hearing by cochlear stimulation, stimulation in paralyzed limbs for movement, ECG of heart, EEG of brain, EMG of skeletal muscle etc. has proved body produces electrochemical signals by endogenous bioelectric system (Sussman et al, 1998).

7.2 Cutaneous bioelectric current:

The Trans-Epithelial Potential (TEP's) in the human skin ranges from 10mV to almost 60mV. TEP may depend on the region of measurement, TEP are from electric positive voltages from dermis of superficial wounds and electronegative measured from the intact skin surface (Illingsworth et al, Clinical physiology measurement). The result of the sodium channels in skin's mucosal surface allow extra cellular sodium to diffuse inside the epidermal cells. The presence of skin battery by measuring with a reference electrode placed in the skin dermis and electrode placed in multiple positions on the intact skin demonstrated TEP. Stratum corneum has average negative potential of 23.4mV. The exocrine sweat gland produces electrical activity which is the skin battery. There is drastic reduction of TEP and in turn reduction of cutaneous bioelectric currents when the compound amiloride which blocks sodium channels in skin was applied (Wolcott, 1966).

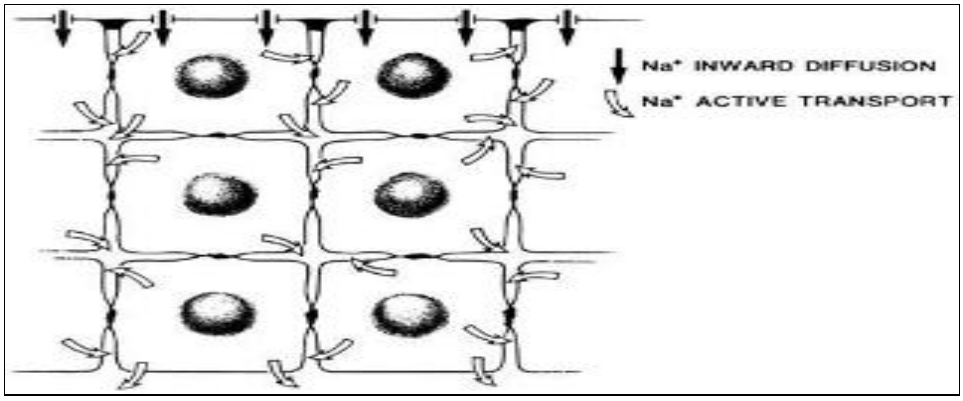


Fig 7.2: Diagram shows sodium transporting to syncytial epithelium (Vanable et al, 1989).

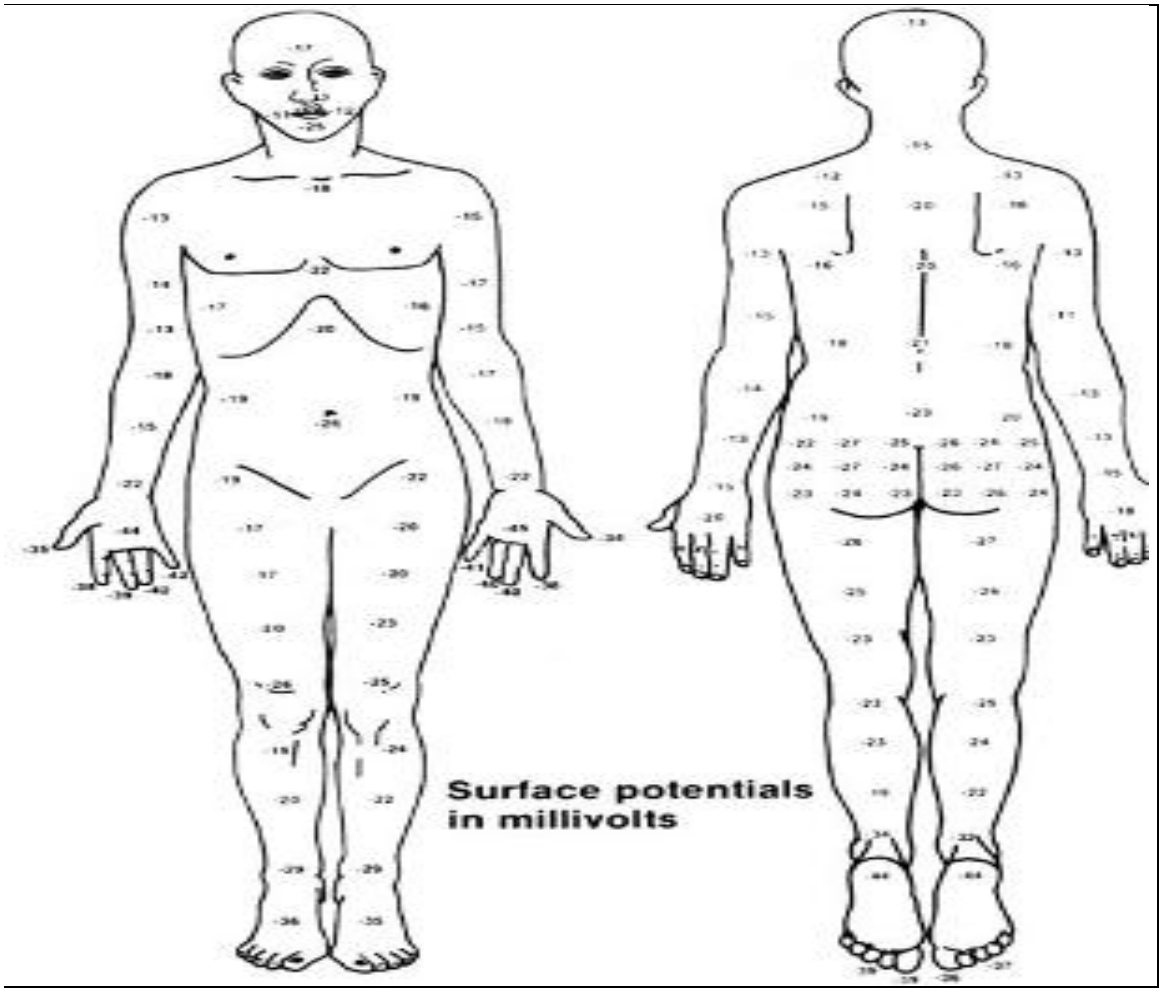


Fig 7.3: Average typical human battery potential at average person of age 29 years (Foulds & Banker, 1983).\

7.3 Injury wound current:

Electrical leak occurs in case of wound and this injury produces short circuits in the skin battery in the region of wound because of this there is an outflow of current from the moist wound area. The current of injury present in wound area in the form of an ionic current and is measurable form of data which was recorded to be 35µA/square cm in amputated fingers of children and wounds in guinea pigs showed 10 to 30 µA/square cm. This current stops when wound dries and when sustained in moist wound environment as shown in amphibian skin wounds and this data is beneficial in wound healing process (Cheng et al, 1982). Injury current at 29.6±8.6mV for 4 days was recorded in porcine model whereas at same time 5.2±12.6mV in exposed wounds proved wound current of injury sustained in occlusive, moisture dressings that enhanced healing rate. The newly regenerated epithelium creates

resistance and reduces escaping currents and fully developed epithelium it is nonexistent (Alvarez et al, 1983).

7.4 In-vitro study of exogenous currents:

There have been numerous studies which give us an insight into the activity of wound healing process at cellular and physiological level of mechanism when the wounds are exposed to electrical stimulation enhancing the wound. The studied varied from how cell responds to different frequencies and amplitude, migratory effects, cell synthesis and metabolism. By supplying 1000V/cm of electrostatic field study showed 20% increase of DNA and collagen synthesis when applied for 14days through fibroblast culture (Bourguignon et al, 1989). In other case with a healthy human fibroblast with application HVPC (High Voltage Pulsed Current) increased 160% rate of protein synthesis a DNA. Current of 50 to 75V parameters and 100 pulses per second (pps) frequency showed maximum synthesis and current of 250V above inhibited protein and DNA synthesis with cells close to proximity of the cathode (Bourguignon et al, 1989). Calcium uptake increase and thus increases in protein and DNA synthesis was reported. Exposed fibroblast to 100V and 100 pps had reported levels of Transforming Growth Factor (TGF-β) 6 times greater than control fibroblasts (Falanga et al, 1987). Applied to rat skin 0.5mm thick and at 500 µA for a period of 2hrs increased adenosine triphosphate concentration 5 times and amino acid uptake 30 to 40% even at 50 µA (Cheng et al, 1982).These in-vitro studies showed that ES mechanisms enhances soft tissues healing by opening of calcium channels, up regulating of insulin and TGF-β receptors, collagen and DNA synthesis.

7.5 Cell Migration:

Table 7.1: Cell Migration and the phenomenon of Galvanotaxis (Kloth et al, 1983).

Phase healing polarity	Effects	Cell polarity	Current
Inflammatory (+)	Phagocytosis and autolysis	Neutrophil (-)	DC
(+)		Macrophage (-)	DC

Activated neutrophil (+) DC (-)

Phase healing polarity	Effects	Cell polarity	Current
Proliferative DC (-) PC (-)	Fibroplasia		Fibroblast (+)
Remodeling PC (-)	Wound contraction		Microblast (+)
PC (-/+) PC (+)	Epithelialization		Keratinocyte (-) Epidermal (-)

Cell migration is an important process helps in wound healing, is affected by ES. During the inflammatory stage of the healing macrophages move towards the anode and leukocytes towards the cathode region where there is infection. The neutrophil moves towards the anode and the cathode, this shows electro responsiveness during chemically mediated events.

During the in-vivo study, 6 hours of ES on the human skin 69% of 500 cells where post-stimulated and 45% of the neutrophils in control wounds category. 20% greater epithelialization was found in wound stimulated for 7 days, with two 30 minutes sessions placing cathode on day'0' and anode from day 1 to 7. Galvonotaxic effect created cutaneously applied current showed a lot of difference on an average by 24% (Mertz et al, 1993). The basis of selecting anode and cathode is based on various studies that where conducted in-vivo and in-vitro.

The table 7.2 gives the data on movement of cells, Galvanotaxis theory during healing. Here DC=Direct current and PC is the pulsed current (Kloth et al, 1983).

Phases of Healing	Effects	Cell polarity	Current polarity	References
Inflammatory	Phagocytosis and autolysis	Macrophage (-). Neutrophil (-). Neutrophil (-). Activated Neutrophil (-).	DC (+). DC(+) PC(+) DC(-)	(Orida & Feldman, 1982)
Proliferative	Fibroplasia	Fibroblast (+)	PC(-) DC(-)	(Bourguignon et al,1989).
Remodeling	Wound contraction and epithelization	Microblast (+) Keratinocyte (+) Epidermal (-)	PC(-) DC(-) DC(-)	(Stromberg, 1988)

7.6 Antibacterial effects of ES:

The ES studied in-vitro and in-vivo reported bactericidal or bacteriostatic effect on colonizing wound infecting microbes. Escherichia Coli was very little or not at all effected by AC whereas during DC bacteriostatic effect occurred when <0.1 µA AC and mA cathodal DC was delivered through Pt (Platinum) electrodes. The decrease in bacterial growth was due to buffered pH levels of the cells (Rowley et al, 1974). Pseudomonas organisms were pathogen free for several days after DC supplied. Silver anode electrode had excellent growth inhibiting capacity with minimum toxic effects from corrosion, pH and gas production. 100 µA of DC with silver wire anode had a bacteriostatic and bactericidal effect due to presence silver cations deposited. HVPC and DC compared 50 to 800mA and 100pps for 30 minutes of HVPC applied found inhibitory effects on saureous whereas DC applied 4 anodes 1 to 5mA and 10mA cathode also inhibit S. aureous growth (Guffey & Asmussen, 1989). The acid pH of anode and alkaline pH of cathode during DC kills bacteria but there is no electrochemical change during HVPC. In-vitro human studies shows antibiotic

effectiveness against biofilm cells in increased in presence of a week electric field. Thus efficiency of silver dressings can be improved replacing silver ions in wounds by anode DC.

Table 7.3: This table is based on In vitro and In vivo studies on antibacterial effect of ES (Kloth et al, 1983).

Study Type	Pathogen(s)	Current	Electrode	Polarity	Growth Rate
In vitro Bacteriostatic	Escherichia coli	DC	Pt		Cathode
		AC	Pt	None	
Effect					
In vivo Bacteriostatic	Pseudomonas Aeruginosa	DC	Cu mesh gauze		Cathode
In vitro Bactericidal	S aureus	DC	Silver wire		Anode
In vitro No Bacteriostatic (Toxic end product)	S aureus, E coli	HVPC	Stainless steel		Anode
In vitro	E coli Klebsiella P Aeruginosa S aureus	HVPC	Stainless steel	Anode	All
Cathode inhibited (Gas and pH)					All
In vivo Bacteriostatic	Oral Bacteria	DC	Silver	Anode	

7.7 ES on Acute wounds:

7.7.1. ES effect on skin grafts, donor sites and musculocutaneous flaps:

Weak anodal DC 20-40µA on guinea pig model through silver nylon dressing for 5 days showed a) Healing partial thickness scald burns.

b) Split-thickness grafts.

c) Donor sites.

DC treatment showed more rapid re-epithelialization than control wounds and control grafts. When treated with DC treatment showed decreased contraction, rapid re-epithelialization, improved hair survival, decreased dermal fibrosis

In case of full thickness skin grafts in post-traumatic quality of dermis and epidermis ES of 4.5 µA of DC applied for 3 days. With three surgically implanted electrodes, anode on top of graft along with cathode as second and third inactive electrode on top showed presence of necrotic skin on the 7^{th} day on 80% to 90% of graft with control and cathodic stimulation using anodal DC 50% was necrotic with thicker dermis and intact epidermis (Politis et al, 1989).

In skin flap, necrosis was 28% in control animals, 13.2% in ES when skin flaps where stimulated with electrode with cathode because of vasoconstriction and negating reperfusion severe ischemia was prevented. This studies suggested survival of failing skin grafts and musculocutaneous flap (Im et al, 1990).

7.7.2: Augmentation of wound angiogenesis.

In patients with venous leg ulcers wound when not improved for several months in standard care showed improvements when monophasic PC device (Transcutaneous electrical nerve stimulation). A monophasic PC 140µA pulse duration delivered weak DC of 630 µA at 128 pps is used and first 7 to 14 days delivered via cathode and 3 to 10 days as anode, when the healing progresses the current is reduced to 315 µA. This study showed improvement in capillary density of venous leg ulcer patients at the rate of 43.5% as there was increase in oxygenation of capillaries**.** Improvement in post-stimulation at the rate of 11.55

capillaries/square mm from the recorded pre-stimulation base line 8.05 capillaries/square mm when seen under light microscopy. There is also increase in oxygen tension from 13.5 to 24.7 mmHg thus increasing skin perfusion seen by laser Doppler fluxmetry.

7.7.3: Improvement of tissue oxygenation with ES.

Cells require oxygen, hypoxic environment oxygen becomes inefficient and cells die and anoxic environment oxygen helps in healing process. In patients with spinal cord injuries the transcutaneous partial pressure of oxygen effect the ES seen by recording $PtCO_2$ considerably before 30 minutes ES and after 30 minutes. Post-stimulation it increased considerably when diabetic patients and normal subjects delivered current placed over gastroc-soleus muscle for 30 minutes at level adequate to elicit a contraction in diabetic patients showed no significant increase and had delayed response. But when ES was delivered through a silver mesh sock this group of diabetic patients did not have a delayed response, this study showed increase in cutaneous oxygen saturation and local perfusion with the use of silver mesh sock in improving oxygenation (Gagnier et al, 1998).

7.8: ES on lower extremity chronic wounds.

Including ES there are several therapeutic interventions to treat lower extremity chronic wounds like topical and systemic antibiotics, topical antiseptics and dressings, compression bandages, hyperbaric oxygen, negative pressure wound therapy which is discussed in following chapter, biologically engineered skin substitutes and growth factors. Wounds based on ulcers by venous insufficiency, non-ischemic and ischemic diabetic wound reviewed ES enhances lower extremity chronic wounds (Wolcott et al, 1969).

7.8.1: Venous insufficiency wounds with ES.

Microampere DC used to treat venous leg ulcers for 6 hours daily for six weeks for a group of 15 patients, there was mean healing rate of 14.4% resulted in mean reduction of volume by 85% (Wolcott et al, 1969). Previously compared the study of standard compression therapy and ES reviewed only decrease in area by 63% when treated 79 months. HVPC was delivered directly for wounds for 50 minutes 6days/ week for continuously seven weeks. Then the polarity was switched to anode after 1 to 3 weeks showed decrease in wound size than baseline wound where negative polarity of active electrode placed on saline moist

gauze for 4 weeks and not treated with ES showed size reduced on half of initial than compared to direct ES treatment (Houghton et al, 2003).

7.8.2: ES on Non-ischemic diabetic neuropathy.

Electrically stimulated closure of wounds with non-ischemic diabetic neuropathy is proved by many studies like one involving 15 subjects out of whom 12 of them were healed when HVPC was applied for mean period of 2.6 months with anodal stimulation for 1 hour, 3 day/week during the treatment (Alon et al, 1986).

In case of biphasic asymmetric PC on same wound when given 20 minutes twice a day for 12 week and polarity changed each time 42% closure of wound compared to 15% of controls. During both waveforms in symmetric or asymmetric there was 60% closure compared to control wound treated with standard care. ES was delivered to the ipsilateral lower extremity at 50V, 80 pps and pulse with duration of 100 μs with Dacron mesh silver nylon stocking and worn during night for 8 hours and compared with ES device patient group delivered 20 hours a week, 65% was reported in first group and 35% in second group. Thus concluded ES enhances healing diabetic foot ulcers adjacently with local wound care (Peters et al, 2001).

7.9: ES on lower extremity ischemic wounds:

ES in this case too was reported positive outcome. Possible amputation of the distal extremity avoided when a subject with juvenile onset diabetic mellitus was treated with HVPC with cutaneous electrodes applied adjacent to abscess and mild pulsating muscular contraction where elicited twice daily. It reviewed increase in blood flow and healed subjects with ischemic ulceration on distal legs and feet, also advanced distal gangrene where treated for period of 5 to 6 years with antiplatelet drugs pentoxifylline and included vasodilating drugs experienced progressive deterioration of lower extremities, but still continued on same drugs under ES treatment regimen they diminished, 20 minutes daily for 1 year many showed significant progress included disappearance of pain and stagnation of gangrenous progression and complete healing occurred.

One electrode applied to the peroneal nerve near the head of fibula and either between second and first metatarsals in extremity. Amplitude set to 15 to 30mA and pulse

frequency at 1 to 2 pps. This produced rhythmical painless muscle contraction between the electrodes proved pain free walking 87.5 m to 421.4 m and oxygen saturation from 73.46 % TO 95.45 % (Debreceni et al, 1995).

Table 7.4: Study of lower extremity wounds treated with ES (Kloth et al, 1983).

Dressing current dosage and polarity	**Study of design**	**Wound diagnosis**	**Current Type and group**	**Number of wounds**	**Wound healed/Time**	**Reference and books**
Switched polarity cathode anode cathode, 200-800 µA 6 H/D for 0.8 to 15. Week	Case study	Mixed	DC	75	40/9.6 Week	(Wolcott et al, South medical Journal).
Dacron silver mesh sock	RCT	Diabetic PVD and Non-PVD	HVPC	11 Electrode active	Not studied	(Peters et al, Physical medicine rehabilitation).
50-100 A/cathode	Case studies	Venous	DC	8	100/30 d	(Assimacopoulos, American Journal of Surgery)

Chapter 8: Negative pressure towards wound therapy.

Seal aspirative therapy, vacuum pack therapy, vacuum sealing, vacuum assisted closure and pressure therapy are others names for Negative Pressure Wound Therapy (NPWT). This

form of therapy is not a new concept in the process of wound healing. The therapy is helpful in accelerating healing by mechanical treatment which uses an application of negative pressure (KCI, San Antonia, Texas) VAC. Reducing bacterial colonies, evacuates wound fluid and stimulates the formation of granulation tissue all this is done by placement of foam sponge in a wound bed and sealing this with a drape also with an application of sub atmospheric pressure with an evacuation tube controlled with help of computerized pump. On the basis of wound the pump can be adjusted to level of negative pressure to be applied, during this therapy the device used can be programmed to provide varying levels of pressure and also set to be continuous and intermittent modes.

This chapter will discuss on the use of NPWT with different variables like wound fillers mainly gauze and foam, when used with wound contact layer, various pressure settings and impact of NPWT on bacterial bio burden. Evidence and recommendations are graded through Scottish Intercollegiate Guidelines Network (SIGN) classification system. NPWT have been in the picture for 15 years and have a broad range of treatment goals. The aim of this review is to give on clinical recommendations and guidance to clinicians on decision of NPWT variables and scenarios. Variable being Wound Contact Layer (WCL), wound filler and negative pressure etc. A group of expert panel was set by SIGN and records on NPWT or vacuum assisted closure and topical negative pressure without using any filters was pulled from National Library of Medicine (NLM) and study was conducted on 1026 records from October 1996 to August 2010 for investigating pressure levels, wound fillers and WCLs with their effects on NPWT in microbiology.

Gain in blood perfusion, more delivery of required nutrients to the wound area, faster formation of granulation tissues and evacuation of fluid from wound with reduction of bacteria are the advantages of NPWT (Argenta et al, 1993). The brief explanation of this procedure is that it aims to create negative pressure and thus helps to create suction. This pressure created then drains the fluids, cellular waste and the cells which are present inside blood vessels and the tissues surrounding the wound. Thus this helps in healing by changing the growth and shape of the surface tissues. Foam is placed on the wound and drain tube is placed over the foam. A large piece of transparent tape is placed over this area with the healthy part of the tissue securing the foam and draining. Fluid is drawn to a disposable canister through the tube connection with a vacuum source. The device also has an alarm to

alert the provider if the seal breaks and also when the canister is filled. In 1997 Muller and his colleagues noticed formation of granulation tissue in 14 forms of defects when NPWT was used subjects with grafts and chronic problems have developed faster recovery time with NPWT (Muller, 1998). Same in case of case of traditional topical therapy was slower (Hartnett, 1998).

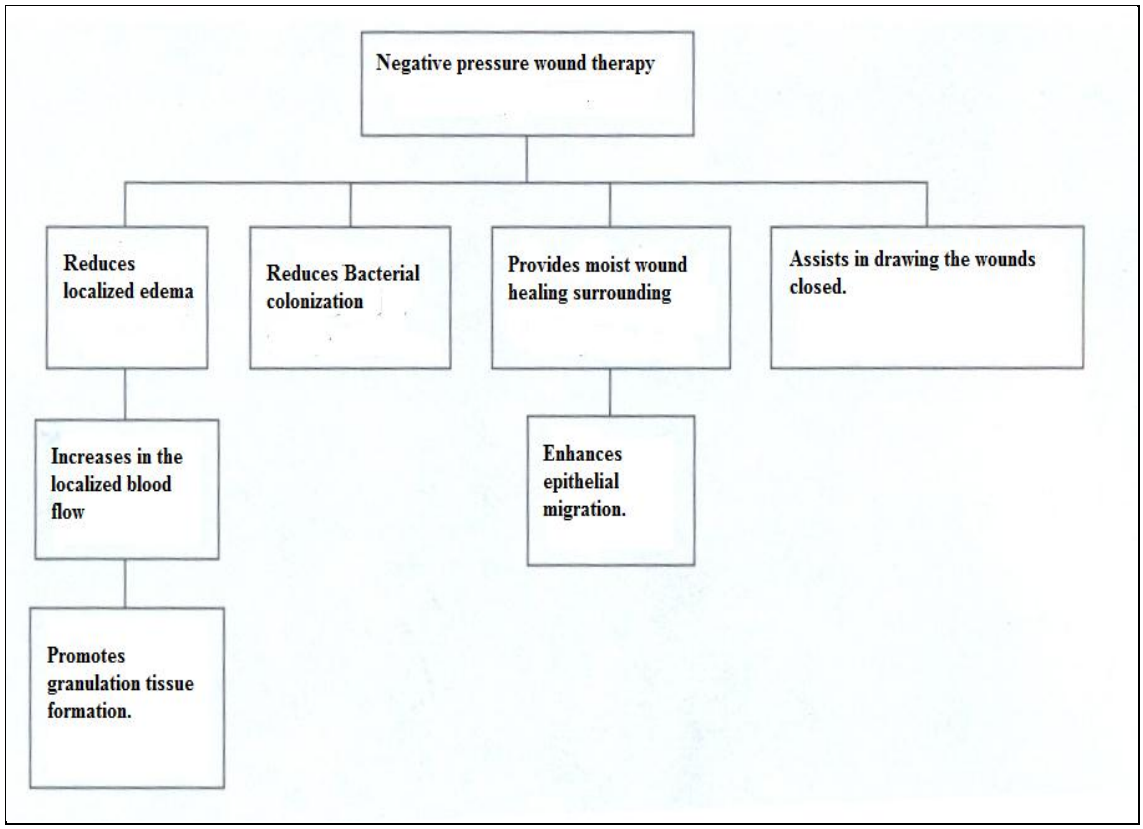


Fig 8.1: This is flowchart which shows the schematic of progress of wound healing process with the use of NPWT (Bryant, 1993).

8.1 Physiological basis of NPWT:

Accumulation of fluid and also edema in and around the wound bed are the problems which does not allow the wound in the healing process to progress positively. Edema causes the compression in the circulation system of blood, by application of NPWT there is decrease in fluid and edema (Morkywas, 1997).

When NPWT was found a negative pressure at the level 125 mmHg showed 4 times better blood flow when NPWT was used in the treatment. There is a release of biochemical

messengers helpful in wound healing process adding for the wound progress with more constant blood supply and granulation tissue production. The tissue depends on the growth of new capillaries in turn to produce collagen matrix. Due to mechanical stretch that the cells present experience in the negative pressure surrounding there is more cellular proliferation and neo-angiogenesis, reduced size of wound and epithelialization is expected (Ryan & Barhill, 1983).The main cause of infection is growth of bacteria and this is due to presence of fluid in the wound, removal causes decrease in colonization of the wound. Helps in achieving a higher oxygen value, nutrient content and circulation thus producing resistance against any kind of infections. Bacterial count shows reduction with NPWT (Argenta et al, 1993).

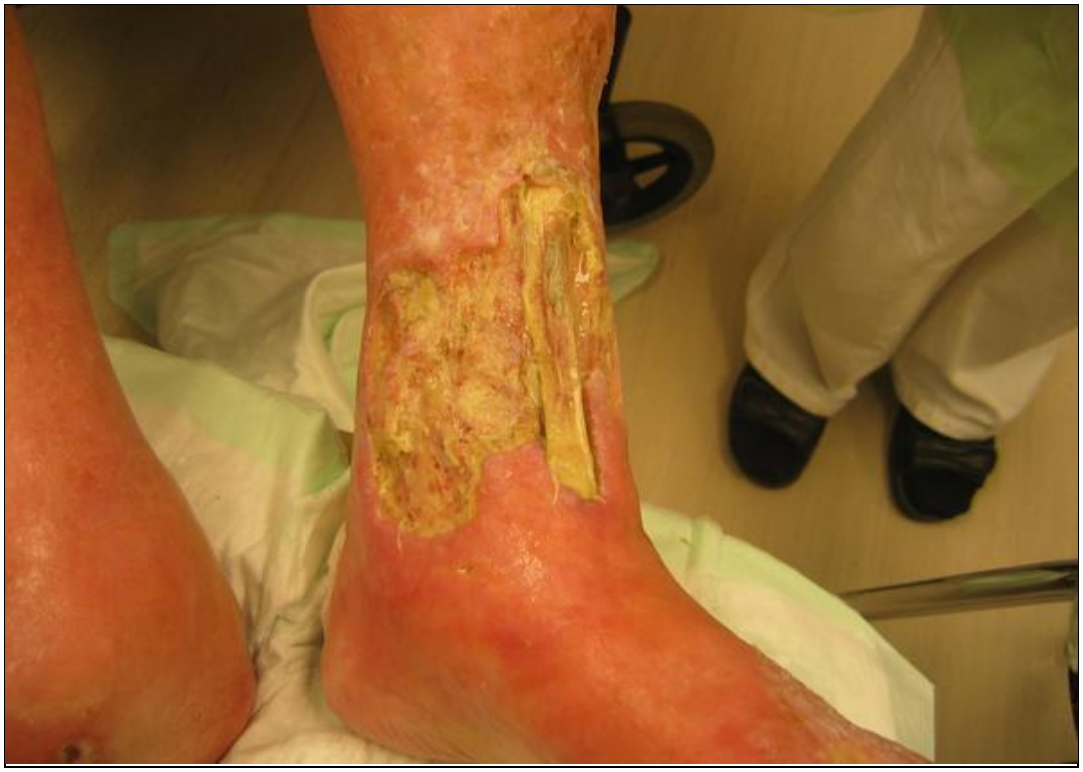


Fig 8.2: Photo showing leg before treatment with negative pressure was initiated.

Taken from http://www.worldwidewounds.com/2010/December/Oien/NPWT.html

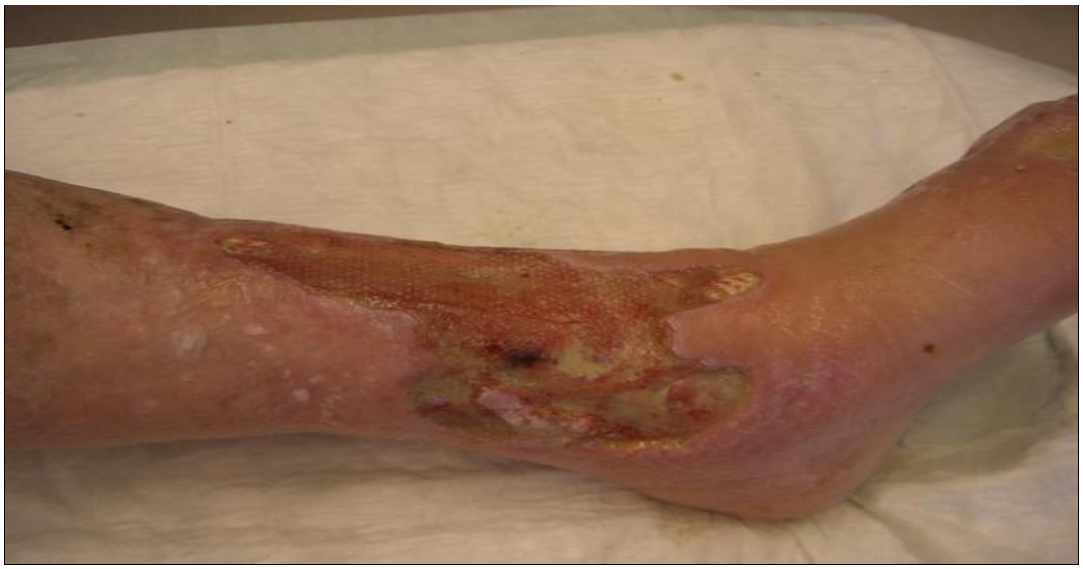


Fig 8.3: Three weeks treatment with negative pressure resulted in the formation of granulation tissue and reduction of edema. Thereafter a hydrocolloid dressings and reduced compression therapy for another 13 weeks until the ulcer was healed. Taken from http://www.worldwidewounds.com/2010/December/Oien/NPWT.html

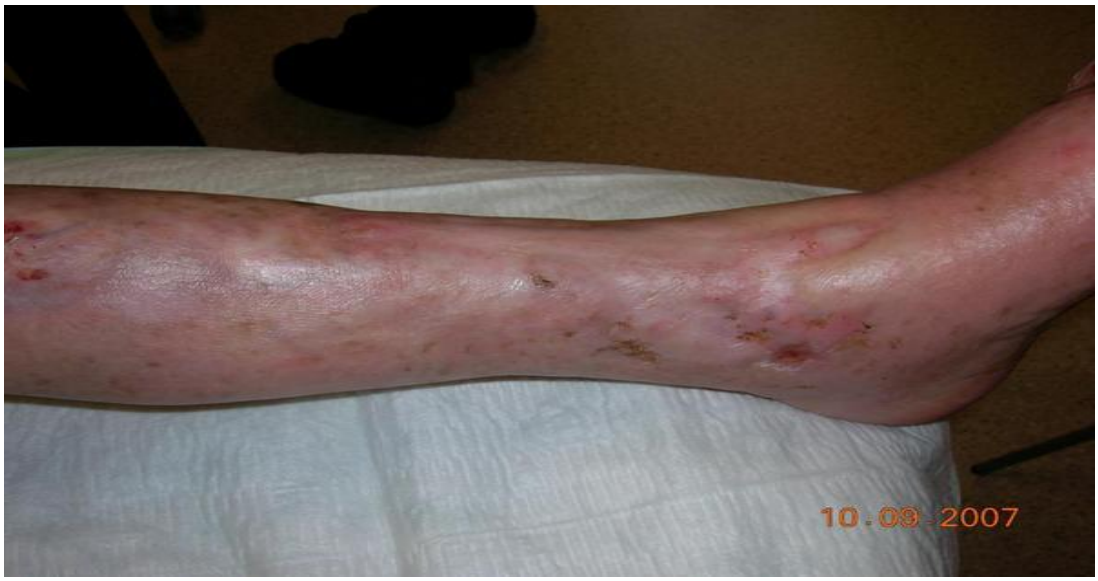


Fig 8.4: complete ulcer healing after 16 weeks of treatment with no recurrence at follow up 22 months later.

Taken from http://www.worldwidewounds.com/2010/December/Oien/NPWT.html

NPWT is designed in a way that there is moist wound bed profiting the healing also the influx of third space fluid help in maintaining moist and clean wound bed thus helps in

increasing growth factors and cytokines, epithelialization and important first step of granulation tissue formation.

8.2 Indications and contraindications to be noted during NPWT:

NPWT is helpful in solving problems with many chronic wounds, evolved from this issue used in many acute and sub-acute wounds now. Stage 3 and 4 pressure ulcers, vascular wounds and neuropathic ulcers are healed with this therapy. Problems caused from incisions, mesh grafts and muscle flaps are profited by NPWT. Also has quality of helping the subject's body to learn to heal on its own capacity as it stimulates and accelerates assisting wound healing process. Malignant wound margins, untreated osteomyelitis and nonviable tissues are contraindications of NPWT (Bryant, 1993).

The therapy should not be used for patients with:

- Wound that require hemostasis.
- Wound malignancy.
- Untreated osteomyelitis.
- Necrotic tissue not had been debrided.
- With fistulae to organs or body cavities.

The therapy can be used on various cases of wound healing including:

- Chronic or acute form of wounds.
- Sub-acute form of wounds.
- Chronic diabetic wounds.
- Pressure ulcers.
- Meshed grafts and flaps.

The procedure should be conducted only after wound cleaned necrotic and dead tissues or else there will no presence of granulation tissue formation, this is the reason why nonviable tissues are removed during initial process. In order to achieve this clean wound bed there is proper assessment of the subject conducted, in case of osteomyelitis there should be antibiotics or debridement in bone which is infected should be used as adjunct treatment. Malignant wounds are not considered because there is no difference in cell proliferation

during negative pressure mechanical force and during this time there is rapid reproduction of cell and mechanical stretch produced. Subject is checked for stable hemostasis, a subject using anticoagulants and suffers active bleeding can be considered for the process. VAC can be placed over heart, lung, liver and spleen so when organs are exposed this process can be successfully used (Morkywas, 1997).

8.3 Management and protection of the wounds and its results:

Changing the dressing is performed every 48 hours during use of device, in order to make sure that there is normal distribution of negative pressure reticulated polyurethane dressing is used which is produced by open cell ensuring communication. Shaped as required the foam is placed on complete area of the wound region. Using evacuation tube on the top of foam with presence of cut slits towards proximal end. This placement helps in remaining fluid from the wound and collecting it in a chamber called as canister. A computer programmed pump is used for the process, Pump size can be from 14 inch length, 12 inch of height and 8 inch of width with weight being about 9 pounds as shown in figure 8.5 below. Power source is an AC outlet battery.

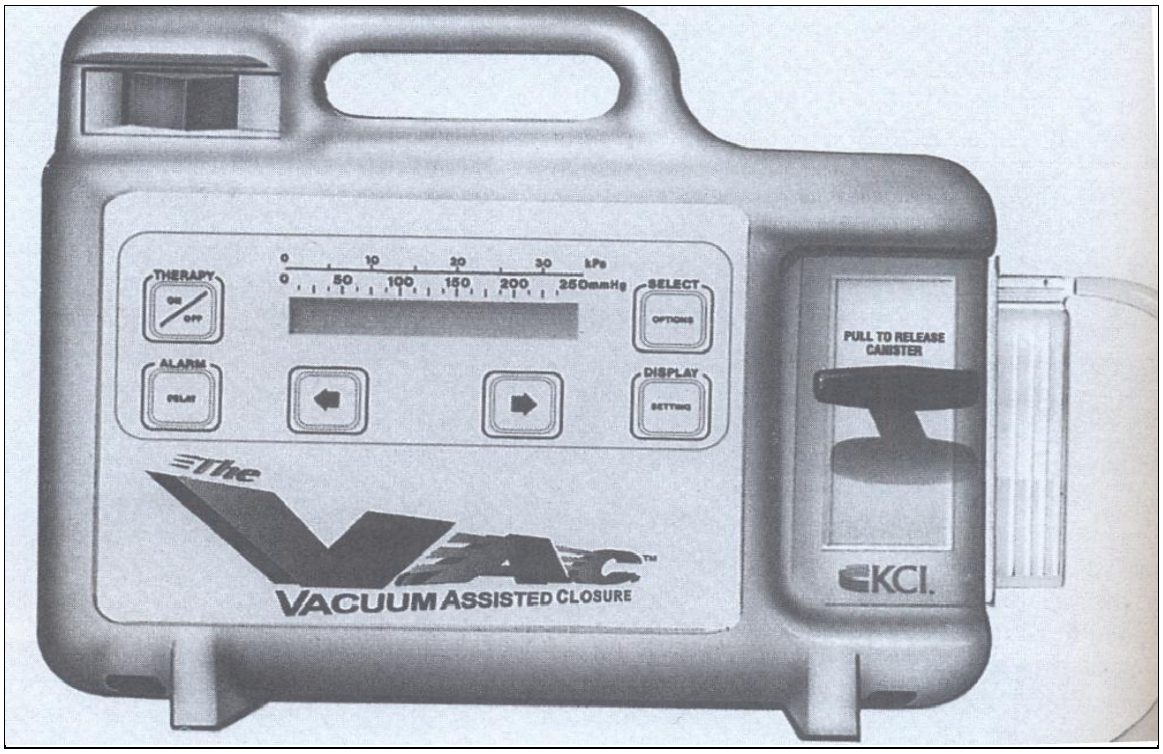


Fig 8.5: Shows a non-portable VAC, with alarm and display also connected tubing to canister (Bryant, 1993).

Smaller size portable units are available with 4 inch by 2 inch and 2 pounds weight; with this size it is helpful to position it on the subject's belt powering it by rechargeable battery source as shown in figure 8.6 below.

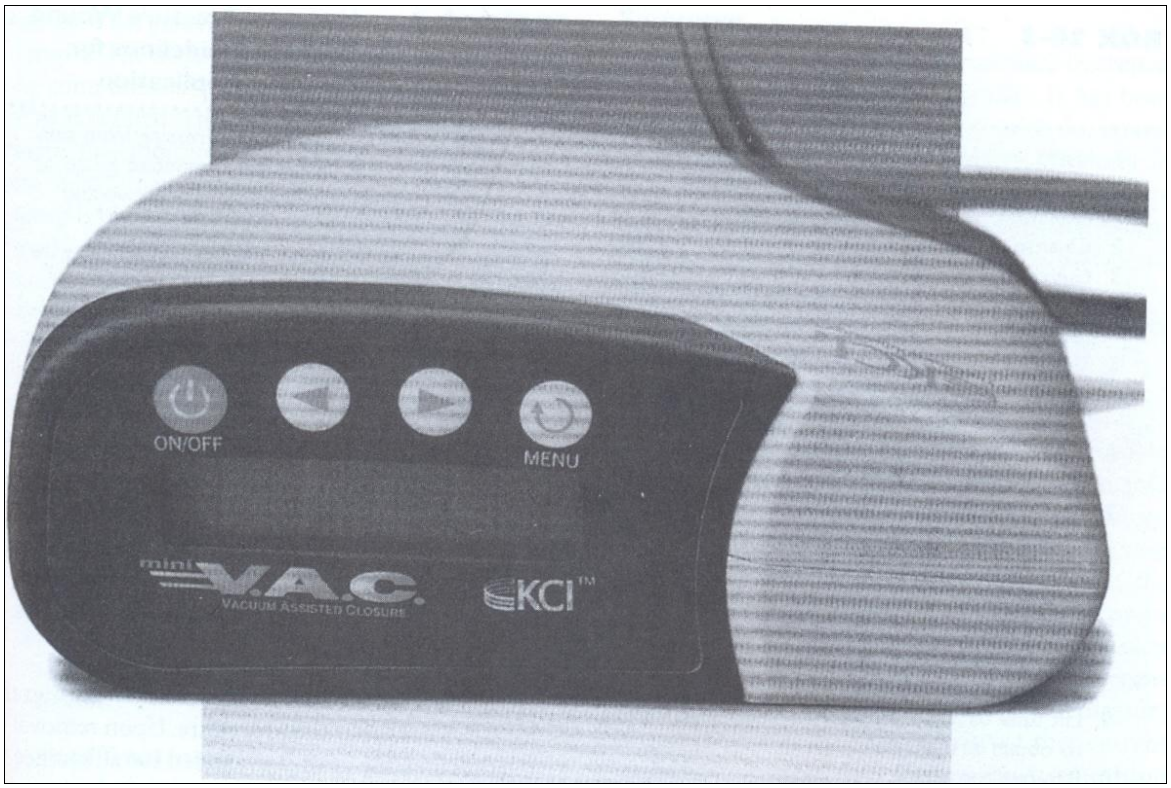


Fig 8.6: Shows a smaller portable VAC, with alarm and display also connected tubing to canister, connectable to the belt (Bryant, 1993).

Transparent dressing placement on wound over the foam and placed tubing positioning it safely with drape and leaving the distal end to be connected to canister, Negative pressure from 75mm Hg to 125 mm Hg is applied depending on properties of wound. Based on the guidelines in table 8.1 and table 8.2 the mode of therapy can be continuous or intermittent. The intermittent mode is used to make efforts on release of biochemical messengers which helps the wound by mechanical stretch production. This is applied by varying from pressure to non-pressure. The tubing is kept lengthy so that there is no movement around the pump area, this tubing can be separated for time from 2 to 6 hours/ day. If more time is required the moist saline gauze replaces the sponge. Skin graft fail due to accumulation of fluid under the region of graft and also due to movement of graft as the tight fit with vascular rich bed is risked. Therefore during the use of NPWT on mesh skin graft the process involves intra-

operation, the non-adherent dressing is laid on graft before the sponge is positioned. The dressing helps in protection of graft which is fragile in nature from shear and any trauma when the removal of dressing is done. NPWT helps the graft positioning it and also removing fluid beneath so that the contact between vascularized bed and graft remain; this process is for 4 to 5 days after procedure. Graft is checked for adherence; if cleared then NPWT is discontinued. If not then additional 3 days procedure continues with also if required added with non-surgical bed side prepared baked graft.

Everyday maintenance of NPWT involves the following:

- Checking periwound site.
- Checking computerized pump and parameters.
- Checking fluid collection.
- Area around the wound dressing is checked for warmth.
- Drainage amount and properties of fluid assessed every day.
- Wound measurement.
- Fluid and tissue characterization.
- Odor.
- Each time monitoring during dressing change.

The filled canister is changed once full or everyday as required, the device has alarm and display showing and alerting once fail, if the pump is tilted and pressure changed during the process. If the dressing has presence of any leaks then the pump is not able to maintain pressure prescribed so the dressing are checked accurately, if leaks are present then extra dressing or tape can patch the punctured region. Suction and removal cause pain (Hartnett, 1998). Therefore analgesics can be used, or also lowering pressure reduces the amount of pain felt so that the subject can sustain the therapy.

Table 8.1: The guidelines which are to be followed during the dressing application process
to provide a profitable outcome desired (Hartnett, 1998).

Steps:
1. The canister to drain the wound fluid is always place besides the pump in the console; during the placement it should be precautionary step not to contaminate the distal end.
2. According to the schedule cleaning the wound should be maintained.
3. There is optional use of skin sealant to intact skin adjacent to the wound region.
4. The dressing is cut into pieces of required sizes and inserted into the undetermined space so that they can be also retrieved when there is a need for.
5. Cut open a hole for insertion of the tubing if the dressing space covering is reduced in area or use the existing gap for placement of the tubing.
6. The transparent dressing should get adjusted to body's complex structure and therefore some dressing is covered in periwound area so that it sticks with the region.
7. Use of transparent film over the dressing region positioning it in place is good option; the dressing should be wrinkle free as possible.
8. Transparent film is pinched getting hold of the tube and pushed under the tubing so that an airtight seal is obtained.
9. Reinforcing the tube is done after the plastic liner is removed and also the proliferated edges are removed and tube is then reshaped as required by body contours and additional transparent film is used.
10. The tubing's are always placed at a distance from any kind of bony structures, and thin gauze or another other form of dressing is always placed between the skin and tube interface so that any pressure damages can be avoided by doing so.
11. Distal end of the tube now can be connected to the canister and the clamps can be opened.
12. For proving that an airtight is achieved the dressing contract down once the pump is switch on with setting at required level of pressure levels.

Table 8.2: The guidelines which are to be followed during the dressing application removal process to provide a profitable outcome desired (Hartnett, 1998).

Steps:
1. The adhesive has strong bond with the skin, so water damped gauze or cloth should be used while removal of transparent film which is done towards the wound from the skin area so that this workouts as gentle procedure and helps in breaking the bond between. 2. Irrigate the wound and removal of the dressing is done using any instrument like a forceps is handy. 3. Clean the wound region. 4. Assessment of wound is done and periwound area is conditioned.

With this two above tables of guidelines always a clean gloves, goggles and gown should be worn it any anticipation of wound is expected.

Chapter 9: Role of Advanced Practice Nurses (APNs) – Additional knowledge towards wound management.

Theoretically and practically suitable healthcare professional with respect to a concerned field are unique group of highly skilled professional expert in practice with what is required by the subjects with wounds and working based on the basis of variety of requirements of the organization. An APN can carry out roles in various sectors of healthcare. Some branches that an APN can follow as their profession are as an expert in clinical practice, educator, consultant, leader or manager and also as a researcher. This chapter is based on the analyses of the roles of APNs in wound care and care delivered by specialist practitioners.

9.1 Issues affecting the capabilities of APNs in wound care:

Better way of understanding the background and historical issues in this field which causes inefficiencies in APN practice can be understood with an illustrated example in the table below.

Case study 9.1: This study gives an example explaining inefficiency in APN practice (Morison et al., 2004).

A nurse who is an American APN and has graduated from course as CNS (Clinical Nurse Specialist) which is a Master's of nursing based on adult health and illness. Education also includes wound, ostomy and continence (WOC) post bachelor specialty education. If the nurse develops an active business in consulting based on his/her gained education and experience in caring subjects with chronic wounds inside the state boundaries, then the nurse can be consulted by physicians, health specialists from any hospitals, sub-acute facilities and other extended care facilities. Now apart from the home state the nurse drives across state borders, due to the legal reasons the nurse who is a CNS cannot function as an APN as this is not his/her home state. Therefore there is a loop hole in the system and this causes suboptimal continuity to the patients because the legal rules suggest that the nurse has to depend on the busy physicians or their assistants. There is a waste of clinical experience and anachronistic structure.

The nurses provide wound care at specialist and also advanced practice level. There are also a category of individuals who would rather prefer specialty wound care than advanced practice level. (Bryant, 2004). The main reason being scope of practice as in the table explained above and the other regulatory mandates with legal responsibilities also include education. These levels of differences overlap and it might be not possible to provide advanced practice nursing without specialty wound care experience (Beitz, 2000).

9.2 Development in APNs education:

The regulation and licensure to practice as professional nurse may vary based on the emerging needs of patients, historical development and societal context in the respective nations. Earlier a 2 or 3 year hospital based course, 2 or 4 year based associate degree and WOC nursing after the course was open to all nurses at any above mentioned level of education in the US. But from the year 1983 the rules were revised and bachelor's degree was made a must for an entry to specialty practice (WOCN 1998). Supposedly expanding enormously in the current day emerging patient needs the master's degree course has provided many fields of practice to the nursing sector (WOCN, 2001).

In the U.K, similarly the nursing education has changed from hospital based diploma courses to 3 year diploma in university or a 3 or 4 year based degrees. The nurses who are older in respect to current day nurses are prepared in widely different levels and background in nursing education. The case is same in comparison on countries like Australia and New Zealand. This category of education system has also affected nurses who are older and practice in their respective countries (Lusk et al, 2002). Now generally with all the changes the current day minimal international rules with respect to many countries state that postgraduate experience is a must for practice (Faller, 1996).

9.3 The nature of Advanced Practice Nursing:

The roles of APNs existed in the U.S far before but the term 'advanced practice nursing' was not coined before 1985 (Gray et al, 2000). Clinical practice which consists of characteristics of specialization, expansion and advancement can be defined as advanced practice nursing.

- Specialization is limiting the nursing focus in only one field.

- Expansion is crossing boundaries of medical practice and thus acquiring new knowledge and skills in practice fields.
- Advancement consists of both specialization and expansion with graduate level education in nursing and integration of theoretical, research based and practice knowledge (American nurses association, 1995 and 1996).

Today APNs have extensive supervised training and knowledge during their master's degree for nursing. The care provided by these professionals is based on the advanced comprehensive nursing theory and assessment and intervention skills.

The APNs evolved from the four roles which included the following: Nurse anesthetist, nurse midwife, clinical nurse specialist (CNS) and nurse practitioner (NP). The latter two roles NP and CNS deliver chronic wound care. The nurse anesthetist provides care in acute wounds and outpatient type of settings, nurse midwives provide care for women and newborns, CNS are experts in the bedside care and acute care (National association of clinical nurse specialists, 1999). To reach the goals practice patterns and outcome management process is crucial during CNS practice. The knowledge acquired through graduate level education there has been a convergence between CNS and NPs (Secherist & Berlin, 1998).However the two roles may be different in foreseeable future (Lincoln, 2000). The CNS will provide indirect influence on healthcare as an educator, researcher, expert clinician and consultant (Doughty, 1996). Remarkable achievement by wound care CNS Lancellot in 1996 and her colleagues in the field of treatment of pressure ulcers best practices in prevention and treatment where identified. The actions of APN (CNS) developed a wound care treatment for home based care. Functioning as direct caregiver, educator, researcher and consultant helped in full fruition of wound care development programme. Named as 'pillars of care management' the leadership qualities are based on the following;

- Good clinical management.
- Outcome based measurement with a good procedural data collection.
- Stratifying the population.
- Guidelines based on the evidence.

The category of driving forces of proliferation in specialization of nursing both externally and internally around the world, some external forces are as follows:

- Increase in complexity of care.
- Introduction of new and advanced technologies.
- Changes in needs of population.
- Structural changes in the system of healthcare.
- Consumer demand.

Some of the internal forces include:

- Developments in the field of nursing science.
- Expansion in nursing care boundaries.
- Paralleling with other medical specialties.
- Crave for more financial profit and autonomy.
- Extension in more post bachelor curriculum.

The WOCN certification board does not provide advance level practice wound care even though it is required and there are possible participants available, WOC specialist nurses help in developing wound care and minimizing the expenditure in healthcare and also including avoiding of the skin breakdown litigation in case with the pressure ulcers (Kaufman, 2000).

9.4 A comparison of advanced practice nursing and that of specialty level of wound care:

As the advanced practice nursing is evolving the comparison of advanced and specialized nursing is unstructured throughout the world. The U.K and the U.S are the best examples where the wound care today is in a transition with effective use of healthcare resources and economic backup (Humphris -Professional Nurse). In the U.K this area has evolved in the past 20 years in vast range of areas. The specialist British nurses work in the field ranging from inflammatory bowel disease, diabetes, nutrition and wound care. The need for Tissue Viability Specialists (TVS) has increased as there has been an increase in demand of efficacy and due to changes in the healthcare system currently. The TVSs practice mainly focusing on the persons with chronic and non-healing wounds. The roles of TVS include in

the field of quality assurance, education and clinical as that of the WOCs. The duties for this category of professionals include audit of procedures and outcomes, implementation of standards and care, self-education and evaluating the impact of continuing education (CE).Apart from ordering treatments and prescriptive authority the roles are important in the field of leg ulcers, pressure ulcers, tropical therapy, Doppler assessment, conservative sharp debridement and compression therapy (Newton, 1999).

In the U.K, TVS roles where not standardized and data showed that for most of the candidates this was a new sector to work on which was recorded as 90%, in the selected had 6% master's degree and 28% had bachelor's degree and also 39% category had no background but agreed that the continuing education was critical. However in the field of wound care and physiology 34% had completed degree in nursing education in tissue viability and in this the main areas of focus included pressure ulcers, leg ulcers and wound care management. The roles described by professional as 'clinical nurse specialist' without proper background education and also there is a confusion between the title nurse practitioner and nurse specialist (Flanagan, 1998a).The United Kingdom Central Council has demanded in clarification of education with regards to role of CNS and NP. In the past decade the UKCC has specified certain set of rules for specialist education and practice and also advanced education and practice (UKCC, 2001). The abilities of specialist nursing practice included things such as demonstration of high level of clinical decisions, monitoring and improvements in standards of care, audit, skilled leadership qualities and mentoring the colleagues (Flanagan, 1998a).

Chapter 10: Conclusion of the thesis:

The goal of the report has been to help the clinicians with the current day understanding of the therapies and market in wound healing with available devices and products for treatment of various chronic and acute wounds. Currently field is undergoing an exciting growth and innovation driven by an increasing number of chronic wounds and new medical understanding of ways of operating both economically and clinically.

The initial chapters provided basic knowledge on skin which would help in better understanding in treatment and identification of process and solving the issue subject is facing. Restored skin function and re-epithelialized skin helps in effective form of healing process. The concept of 'TIME' should be adopted by clinicians increasing the potential of wound healing. This type wound bed preparation offers chances in healing of chronic wounds. Used directionally and if all elements of the framework are successfully addressed, many wounds should move towards healing" (EWMA, 2004)

Evidence suggested biofilms may form inside the wound and thus help in control of infection, inflammation. Recent studies also suggest that chronic inflammation delaying in healing are more resistant to antimicrobial therapy as bacteria persist in polymeric matrix and adhesive communities to suggest clinicians in considering topical antimicrobials. The concept of "Bioburden" remains controversial as some recent studies shifted the theory to density of organisms than on presence of particular species. Assessment of the efficacy of topical antimicrobials for the treatment of chronic wounds is difficult based on the available data concluded the outcome improved with many topical substances accelerated the healing such as silver containing substances for venous ulcers and oxyquinoline ointment which was used for 1-2 stage pressure ulcers. Zinc oxide tape for its effectiveness in necrotic wounds more than hydrocolloid. The microorganisms used, wound type induced, experimental species used may be irrelevant to chronic wounds in patients and medical conditions during studies with animal models and therefore there is inconsistent evidence.

There are secondary dressings used in a combination with initial on treatment of wounds, this has become a common process but this shows lack of understanding of the wound properties and lead to extra healing time and also unnecessary expenses in healthcare with being unsafe. The hydrocolloids showed to encourage the growth of anaerobic bacteria and

therefore proper care should be taken during their use on infected wounds (Nurse Prescriber, 2006). Hydrogels can have various uses in wound types and but main use being dry and necrotic wounds and can be used for all stages of wound healing process. Used in other areas of wound management and skin care like in dermatological conditions, inflamed skin flexures, damaged skin due to radiotherapy treatment, fistula management and rash from nappies in infants. The alginates are suitable in case of wounds which are bleeding as it has natural hemostats present in it and also additionally are atraumatic and free from pain when required to be removed. Film dressings can be used in case of superficial and shallow wounds like in the last stages of healing, foam dressings moderate to heavily exuding form of wounds like pressure ulcers, leg ulcers, burns and surgical wounds. Foams are basically better for use in exuding granulating wounds and are not prescribed for dry superficial wounds. Deodorizing dressings may be of great use in the case of managing the malodor. The products are antiseptics and may be useful in wide range of spectrum of micro-organisms like Iodoflex and Iodosorb useful in wound debridement

Silver dressings can be used in various types of wound types with clinical wound infection or critical colonizing wounds or those who may have previously had a clinical wound infection. Silver dressing such as Actisorb silver 220 can be useful in the treatment of most of the chronic wounds but in particular are recommended for the management of malodorous, infected wounds including fungating lesions, faecal fistulae, pressure sore which are infected and also in the case of exuding leg ulcers. Nano-crystals of silver recent development is the dressing that exhibits antibacterial activity against wide range of gram positive and negative which includes strains which are found to be resistant against antibiotics. Similar is the case with yeasts and fungi effectiveness but the drawback being the product safety of Acticoat is not known till date. .

Ultrasound is a very useful physical modality used in scar tissue healing and various wound healing therapies. The usage of how the ultrasound works so that the clinicians are well versed with selection of whether this therapy has possible use in healing of particular wound and also monitoring its effectiveness is explained in the chapter. It is not mature to abandon the ultrasound therapy at this point of time as there is lack of evidence in this field, studies must be done on ultrasound units such as coupling medium and transducer. Reliable methods in measurement of performance of ultrasound physiotherapy equipment have to be

developed so that standard dosage delivery for ultrasound therapy can be ensured. Adequate randomized controlled clinical studies are required to know the usage of ultrasound therapy. In venous leg ulcers treatment US application showed that it activates a least part of wound and reaches acute inflammatory phase of healing process and debrides the wound thus activating wound healing and when acute inflammation is reached by using low intensity which does not produce thermal effects as high intensity helps in accelerated healing in venous leg ulcers. Application of long wave in kHz also proved effective alternative for venous leg ulcers, the control wounds and US treated wounds were also covered with hydrocolloid dressings and compression therapy, in time of 12 weeks there was decrease in area of wound by 55.4% in comparison to 16.5% of control.

The technique of US bio microscopy is non-invasive, rapid and painless are the advantages of monitoring the treatment effectiveness. Thus with therapeutic roles explained earlier US adds diagnostic role in wound care and management. Causing no damage to the subject this technique allows in visual inspection of tissue within, around the wound region in way of biopsy. Here telemedicine comes into picture as these digitized images can be mailed, archived for analysis from any remote site.

In hyperbaric oxygenation when oxygen applied under pressure then has therapeutic, toxic and side effects The two main benefits of this therapy are: The size of embolism can be reduced due to this therapy which causes air/gas embolism and there is increase in oxygen tension by 10 to13 folds higher than oxygen at ambient. The hyperbaric oxygenation therapy proved " Just to test if it works" approach as all wounds are not a candidate and concentrated more on hypoxia type of wounds as it can be treated with reduction of oxygen showed the origin of the wound is to be considered before the therapy. The therapy as expensive is considered as last option after all considerations initially, however can make a difference with proper assessment of below and above knee amputation circulatory pathways and pre-amputation preparations.

Negative pressure therapy has been a treatment that has provided positive results. It has its uses in closure, reduction of size and granulation of wounds before surgical closure. The wound care nurse should be confident with indications for the applications of the therapy. There are still additional trials needed to improve the quality of the therapy. The therapy for

now can be used on various cases of wound healing including chronic or acute form of wounds, sub-acute form of wounds, chronic diabetic wounds, pressure ulcers and meshed grafts and flaps

Electrical stimulation performed on the on wounds is considered investigational till date therefore has been limited in its applications towards wound healing. The devices can be marketed for approved indications such as edema, pain etc. The manufacturer is insisted by the FDA (Food and Drug Administration) to provide details on all randomized trials conducted with regards to the therapy in the Product Market Approval application (PMA). There are rigorous trials to be conducted in the field on chronic wounds for the wide spread application of this therapy. However I would like to conclude saying that these therapies when used as a combination would be more helpful in treating most of the chronic wounds. The subject background should be considered and on the basis of treatment and its effectiveness the treatment should be decided. If the therapy proves non effective then focus should be shifted towards other therapies which can be used/.

Many factors will affect the practice in wound care as there are many levels of practitioners emerging, the nurse specialized in electronic communication and research finding in application of delivery care will prosper. The chronic wounds will require high level knowledge in prescriptive authority especially for topical medicine, computer data assessment and advanced physical assessment. The wound healing field is vast and rewarding therefore nurses placed well at cost effective wound care delivery at specialist level will be benefited. Concluding the thesis with the hope it will be useful reference for clinicians for the treatment of chronic and acute wounds and strategy management in the [process of wound healing also with a hope that new technologies and treatments emerging in following years to come will solve the issue of different wounds and be helpful to the society.

Chapter 11: Future Trends in wound healing.

In the field of electrical stimulation there has been development on wirelessly controllable implantable materials called BIONic neurons, these are well controllable electrical fields which is safe, effective, low cost and precise to the local site and controlled by miocrostimulators. Introduced into the body through 12 inch gauze needle and controlled by external RF coil providing it command and digital signals. Under clinical trials with the TES there are 2 types of BION's, BION 1 produces 0.2-30 mA at 4-512mS and BION 2 can measure the muscle length, limb acceleration of the limb for sensory feedback control for Functional Electrical Stimulation (FES). BIONs with rechargeable battery operation with platinum and carbon electrode are feasible alternative for long term use. BIONs with current or feasible forms may answer questions for solving abnormalities of tissue growth in wound healing (Loeb-Medical Engineering & Physics).

The future concept is to produce a device which would miniaturize the concept of wound area measure and being non-invasive and comfortable to the subject. This is based on mapping of wound on the basis of electrode skin potential. There is major difference between the magnitude of impedance in partially regrown skin than compared open wounds, this concept of not disturbing the healing process and externally capturing the image of the wound so that it can be stored and studied can come true with a PDA (Powered Laser Digitizer).

Fig 11.1: This Figure shows a PDA device externally collecting data from a wound (Taken from 'http://medgadget.com/2007/08/portable_digitizer_for_wound_monitoring.html').

This concept is helpful for the patients to manage the ulcers on their own with help of guidance of the clinician. There can be wireless transmitter inserted in electrode array dressing to record the data and miniaturize the device. The intelligent technology in this device takes images of the patient wound area using a high end camera and thus allowing precise quantitative data analysis from the images captured and stored. This can be used to store patient record in an electronic format, printing, electronic distribution, and archiving. Data on wound's measurements taken is available so the step wise progress of the wound status can be analyzed. This information can be sent to different hospitals and required experts for analysis from the database through use of current telemedicine. With the use of wireless technology a nurse in a field can send data to the main hospital for consultation from any site. This kind of transfers can help in instant decision making based on data and images of the wound to be treated thus proving advantageous (Sonja et al., 2010).

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