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Wound Healing

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Abstract

Wound represents one of the biggest surgical dilemmas with great variation in care. The reason is due to the different variants in the nature of wound & treatment, limited evidence convincing in wound care and disparate opinions among treating doctors & nurses. Tissue injury leading to a wound is a platform for multidisciplinary interventions. A wound, whether created by a scalpel, trauma or infection, undergoes a reparative process in a definite sequential manner. Hence, evidence based care should be followed thereby ensuring optimum care to the patient as well as the wound.

Keywords: Wound Healing; Evidence Based Medicine; Wound Management.

Introduction

Wound healing is a series of complex events that resurface, restore and reconstitute the tensile strength to damaged skin. A good understanding of the sequence of events, which includes molecular signals, and cells involved in wound healing, can aid in a better optimization of wound care. If the process of wound healing goes askew in any phase, it results in exuberance of fibroblastic proliferation called hypertrophic scars, keloids and contractures leading to aesthetic and functional problems. Hence the primary goal in wound care should be prevention of complications and preservation of functions.[2] any available national and international guidelines for different wounds can be followed.[1]

History

Hippocrates first defined healing by first and secondary intention.[3] Alexander Flemming discovered the first antibiotic, Penicillin.[4] The cardinal signs of clinical infection - rubor (erythema), tumor (swelling), dolor (pain) and calor (heat) was described by Celsus. Indian contribution to wound healing was done by Sushruta, the Father of ancient plastic surgery, when he described 14 different types of dressings and described ancient Indian surgical technique and wound management and noted in his book the 'Sushruta Samhita'[5] Ambroise Pare (1510-1590) proposed use of various dressings for traumatic gunshot wounds like rock alum, verdigris, vitriol, rose honey and vine.[6] Lorenz Heister from Germany wrote 'general system of surgery' and described wounds of all kinds, operations and bandages.[7] Henri Francois Le Dran (1685-1770) gave concept of debridement.[8] The routinely used Gamgee pads were described by Joseph Sampson Gamgee (1828-1886) as cotton wool covered with unbleached gauze to make dressing pads.[9] Louis Pasteur, a French Scientist, 'The Father of Microbiology' developed sterile surgical procedures and Joseph Lister, an English surgeon used gauze pieces with carbolic acid leading to significant reduction in mortality rate.[10]

The present modern era has been overwhelmed with the ever increasing number of high technology, engineered advanced wound care products like 'Living Skin equivalents', Growth factors, Cultured keratinocytes and Stem Cell Therapy.[11,12] The nervous system normally adjusts the rate of alveolar ventilation as per the demands of the body so that partial pressure of oxygen (PO_2) and partial pressure of carbon dioxide (PCO_2) in the arterial blood are hardly altered, even during heavy exercise and other respiratory stress situations.[1]

Pathophysiology

The pathophysiology of the wound healing varies according to the type of wound, if it is:

1. Acute wound (or)
2. Chronic wound

Pathophysiology of Acute Wound Healing

Acute Wound healing is characterised by three phases i.e., inflammatory phase, Proliferative phase and Maturation (remodelling) phase.

Inflammatory Phase

This phase comprises vascular and cellular events which begin immediately post injury and lasts for 2-5 days. The immediate vascular event is characterised by a brief period of vasoconstriction which can last from 3-5 seconds to 5 minutes. Followed by vasoconstriction, a persistent and progressive vasodilatation initiates within half an hour, which leads to an increased blood flow through the area, which increases the warmth at the injury site. The progressive vasodilation causes an increase in hydrostatic pressure, causing fluid leak, thereby causing local swelling.

The cells that are released during this phase are neutrophils, macrophages and monocytes. The neutrophils help in opsonisation of the bacteria. Monocytes are converted to activated macrophages, which produce growth factors and cytokines, aiding in scavenging non-viable tissue and bacteria.[13]

Proliferative Phase

The proliferative phase lasts from 2 days to 3 weeks. This phase is characterised by formation of granulation tissue. The macrophages from the infiltrative phase recruites fibroblasts, which in turn stimulate the synthesis of a network of collagen fibrils. The fibroblasts get converted into a myfibroblast (with smooth muscle) which aids in wound contraction, thereby bringing the wound edges closure and decreasing the size of the wound.[13]

Remodelling Phase

This phase begins at 3 weeks of the injuries and can last upto 2 years. The soft, gelatinous, immature collagen laid during the proliferative phase is replaced by an organized mature collagen, this provides tensile strength to the wound, which gradually increases over years, but is never as same and strong as the original tissue.[13]

Pathophysiology of Chronic Wound Healing

Chronic wound healing is characterised by an increased duration of inflammatory or proliferative phase. This impairment is due to changes in one or more of the components that aid in wound healing like growth factors, cytokines, etc., The prominent cytokines that are increased and thereby contributes to a chronic wound are Matrix metalloproteinases (MMPs) like MMP-1 (collagenase), 2 (gelatinase A) and 9 (gelatinase B), serine proteases, pro-inflammatory cytokines such as TNF-αa and interleukin-1β (IL-1β), and TGF-β. There is also a decrease in the level of Tissue Inhibitor of Metalloproteinases (TIMP).

Free radicals like Nitric Oxide (NO) can cause oxidative damage, contributing to the non-healing nature of the wounds. Non-viable tissue (slough) promotes bacterial colonisation, thereby increasing the inflammatory phase of wound healing. In addition to colonisation, with time, biofilm is produced by the bacteria, which are bacterial colonies in a polysaccharide matrix secreted by the bacteria itself. This creates a great hindrance to wound healing as it is resistant to host defence as well as extraneously applied antimicrobial agents.

Apart from external factors, various internal factors also lead to non-healing wounds. For example, diabetes is characterised by micro neuropathy; which leads to trophic changes in the skin; microangiopathy which involves thrombosis of small arteries causes ischemia and gangrene. In addition to these, the hyperglycemic state in the blood provides an excellent environment for bacterial proliferation as well as lowering resistance to infection. [14]

Types of Wound Healing

Wound healing can be of three types:

When a clean wound or a surgical incision is closed with sutures or skin adhesives it is termed as primary healing. When a wound is left open to heal on its own by means of granulation, epithelialization and wound contracture it is termed as secondary healing. When wounds are not ideal for primary closure, eg)., infected or grossly contaminated, they are left open initially for a period of 5-10 days, and then closed after the wound is clear from infection. This is termed as delayed primary closure. [14]

Anatomy

The skin acts as an inherent protective mechanism against the harshness of the external environment. It has two layers - epidermis and the dermis. The epidermis is characterised by 5 layers, from deep to superficial - stratum germinativum, stratum spinosum, stratum granulosum, stratum lucidum, stratum corneum. Stratum corneum is an accumulation of desquamated keratinocytes synthesized by the stratum germinativum, which gradually ascends up to the superficial layers and sheds. The dermis lies under the epidermis, is further divided into papillary and reticular dermis. It consists of a rich dermal vascular network, which serves the important function of thermoregulation and also supports the avascular epidermis metabolically. The other structures are fibroblasts - which synthesize structural polymers, including ground substance, collagen, and elastin. Skin appendages include sebaceous glands, hair follicles, and sweat glands (figure 1). [15]

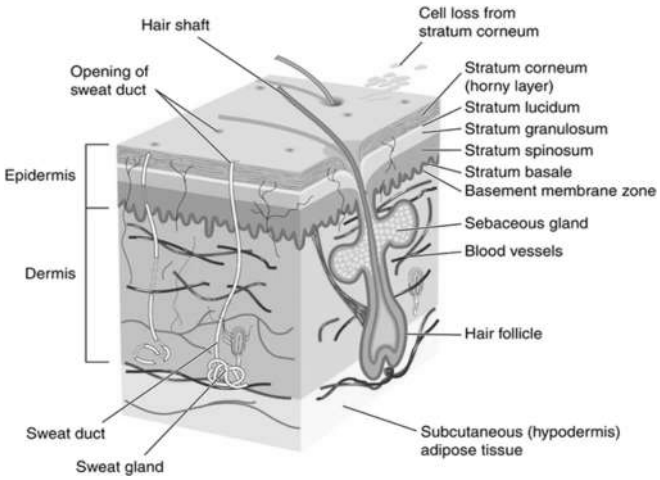

Fig. 3: Anatomy of skin.

Skin is a dynamic organ which undergoes various modifications and has a variable thickness. It is thickest in the soles and palm (1.5 mm thick), and thinnest behind the ears and the eyelids (0.05 mm thick). Children have thin skin which thickens as the child ages. This continues till the 4th - 5th decade of life when there is loss of epithelial appendages, elastic fibres and ground substance, which leads to thinning of the skin.

Classification

Based on the thickness of the skin involved, wounds can be classified into superficial (epidermal loss), Partial thickness wounds (epidermal and dermal loss), and full thickness wounds (epidermis, dermis, subcutaneous fat, with or without underlying muscle or bone).

Wounds can also classified based on:

Etiology
- Traumatic (Sharp/Blunt).
- Iatrogenic (Surgical).
- Burns (Thermal, Electrical, Chemical, Radiation etc.).

Duration (Length of time)
- Acute (< 6 weeks).
- Chronic (> 6 weeks) (includes diabetic ulcer, venous ulcer, pressure ulcer, malignant ulcers, traumatic ulcers etc.).

Depth
- Superficial (above sub dermis).
- Deep (traverses sub dermis).

Mode of Injury
- Abrasion: superficial skin involvement.
- Ulceration: Defect in epithelial lining (skin or mucosa).
- Incisions: By sharp objects.
- Lacerations, Contusions and Bruise: By blunt objects.
- Degloving, Traction and Avulsion Injury: shearing of skin from underlying fascia.
- Puncture Wounds: eg) needle stick injury.
- Bite Wounds (By animals, human, Snake etc.).
- Crush Injury (when body part caught between two objects).

Based on amount of contamination at the time of surgery
- Clean (Class I)
- Clean-contaminated (Class II)
- Contaminated (Class III)
- Dirty-infected (Class IV)

A wound is a breakdown in the protective function of the skin; the loss of continuity of epithelium, with or without loss of underlying connective tissue following injury to the skin or underlying tissues/organs caused by surgery, a blow, a cut, chemicals, heat/cold, friction shear force, pressure or as a result of disease, such as leg ulcers or carcinomas. [16, 17]

Epidemiology

The epidemiology of various wounds are different in different ethnicities. For example, the western population has a high prevalence of post traumatic wounds, whereas the developing Asian countries have a high prevalence of wounds due to acute and chronic conditions. [18] India being the world capital of diabetes has a high incidence of diabetic ulcers.[19]The prevalence of pressure ulcers worldwide has been reported as 6-18.5%.[20] In the USA, 80% of the lower limb ulcers are diagnosed to be venous ulcers.[21]

Etiologies

Infection: Examples Surgical site infection, leprosy, Cancrum, tuberculosis etc.,[22]

Arterial Insufficiency: Arterial insufficiency, leading to localised ischemia, hypoxia, and thereby ulceration of the area. Eg., are thromboangiitis obliterans, atherosclerosis, atheroembolisms etc.,[2]

Venous Insufficiency: Venous ulcers can occur due to faulty valves and thereby reflux of blood, like in varicose veins or due to thrombosis of the deep veins which can also case chronic venous insufficiency.[24]

Lymphedema: Ulcerated lymphangiectasia, lymphorrhea, inflammation and pustule formation, skin maceration, infection, papillomatosis and hyperkeratosis.

Neoplasms (Cutaneous): eg., Basal cell carcinoma, squamous cell carcinoma, melanoma etc.[25]

Pyoderma Gangrenosum: It starts as a small papule or collection of papules, and the central area then undergoes necrosis to form a single ulcer develops small painful papule or nodule followed by tissue necrosis and ulcerations.[26]

Calciphylaxis: It is a rare condition, most often seen in patients with chronic kidney disease mostly in the lower legs. This is due to calcification and occlusion of cutaneous and subcutaneous arteries and arterioles.[27]

Necrobiosis lipoidica: It is a rash that is most commonly seen in the shin in diabetic patients. It may harbor a squamous cell carcinoma.[28]

Vasculitic wounds: They can present as painful, erythematous nodules with ulcerations over lower legs in patients with autoimmune diseases.[29]

Anticoagulant (warfarin) induced skin necrosis: It commonly occur 3 to 5 days after initiating treatment due inactivation of factor 2,7,9,10 by warfarin and inactivation of proteins C and S.[30]

Mucormycosis: India contributed to approximately 71% of the global cases of mucormycosis in patients with COVID-19 based on published literature from December, 2019, to the start of April, 2021. It can initiate as a sinus infiltration which can progress to a devastating erosion of the skin and bone.[133]

Burns: Burns can be due to various etiologies like thermal, electrical, chemical, radiation, frostbite or frictional burns[31-36]

Trauma: It can be a single wound or multiple wounds. It can be as simple as a superficial dermal abrasion to a complex injury involving skin, fascia, muscle, vessels, nerves and bones.[37-43]

Pressure (decubitus) Ulcers: Pressure ulcers develop due to ischemia induced by prolonged external pressure on tissue which is commonly seen in bed ridden hospitalized, unconscious, and patients on ventilators with or without paraplegia, quadriplegia [44,45]

Neuropathy (Diabetic): Diabetic ulcer can be attributed to both autonomic and sensory neuropathy. It can also cause neuropathic osteoarthropathy (Charcot foot) leading to chronic non healing ulcers [46-49]

Idiopathic: (eg) Acne Keloidalis Nuchae (AKN) which is characterized by follicular based papule and pustules on the occipital scalp or nape of neck [50]

Investigations

Investigations are done for finding the cause of the wound, factors leading to a slow wound healing, and for assessment for fitness of the wound for reconstruction.[51-57]

This include Complete Blood count, renal function tests, Liver function tests; Coagulation studies; Tissue cultures;

Pulse volume recordings, Doppler studies, Ankle Brachial Index (ABI); plain radiography of the involved area, Computed Tomography, Magnetic Resonance Imaging for osseous abnormalities; vascular doppler studies, and Duplex studies, Edge wedge Biopsy to rule out malignancy in chronic wounds; Lymphoscintigraphy for Lymphoedema patients.

Complications

Acute complications: Bleeding from the wound, loss of tissue, colonisation by multiple drug resistant pathogens leading to antibiotic resistance, biofilm formation; Chronic complications: Sinus formation, fistula, malignant transformation in the ulcer bed (Marjolin's ulcer), osteomyelitis, Post wound healing complications: Contractures, deformity, systemic amyloidosis, heterotopic calcification, hypertrophic scars, keloids, cutaneous horn, verrucae.

Systemic complications: Anaemia, fluid and electrolyte loss, septicaemia, etc.

All the above said complications significantly impair the quality of life of the patient thereby adding to the morbidity of the condition.[58-61]

Documentation and Assessment

Wound assessment includes assessing the wound dimension, type of tissue, colour, shape, depth of the wound and nature of the edges, margins, floor, and base. These can be done by various techniques like estimation by ruler, digital planimetry, wound tracing, stereophotogrammetry, technical procedures (e.g. computer, image analysis, and colour imaging using hue saturation and intensity) and photography.

Two tools commonly used to monitor and quantify wound healing are the Bates-Jensen Wound Assessment Tool (BJWAT) and Pressure Ulcer Scale for Healing (PUSH).[62-68, 146]

Presumptive assessment for the risk of an ulcer development helps in preventing the morbidity that occurs with a formed ulcer. Braden scale is one such tool which helps in assessing risk of pressure ulcer development.[69] Risk of development of diabetic ulcers can be assessed with the help of National Diabetes Education Program (NDEP).[70]

Wound Bed Preparation (WBP)

As described by Falanga, Wound bed preparation (WBP) is defined as the process of removing barriers to facilitate healing.[71] Principles of wound bed preparation are better understood with the acronym **'T.I.M.E'**.

TIME stands for:

'T': Tissue - This is an assessment and management of the tissue in the wound, if it is non-viable or deficient. If the tissue is non-viable (necrotic) it should be debrided or removed.

Different methods of debridement can be used. It can be broadly classified into:

- Medical (enzymatic e.g. papain urea[72], chemical, larva therapy, biological agents[73], hydro jet debridement[74] etc.)
- Surgical (sharp, laser, ultrasonic etc.).[75, 76]

After debridement, the Deficient tissues may be covered by either primary or secondary wound closure in the primary setting[77], or covering initially by biological skin substitute[78] or cover with skin graft or flap later.[79]

'I': Infection and Inflammation management to restore bacterial balance. Bacterial load when it exceeds 10^5 to 10^6 organisms per gram adversely affects the wound healing, whatever the organism may be. Wound cleansing by irrigation with saline, use of antimicrobials, super oxidized solution[80], silver solution, Nano crystalline dressing etc., antibiotics and anti-inflammatories, can reduce the bacterial load and thereby aid in wound healing.

'M'- Moisture helps in wound healing. But in the form of an exudate it is detrimental. Methods of exudate control includes direct methods like use of absorbent dressings, Negative Pressure Wound Therapy (NPWT)[81, 82]and oedema control.[83]

'E'- Edge of wound (Non-advancing or undermined) management. This involves stimulated the epithelium in the edge of the wound to advance with various adjunctive therapies like Growth factors, [84]Autologous Platelet Rich Plasma (APRP) therapy[85], Autologous Lipoaspirate therapy.[86]

To conclude introduction of various newer adjunct dressings and state of art technologies helps in a speedy wound bed preparation and thereby allowing a definitive cover of the wound as early as possible [87]

Management

Management of an acute or chronic wound can be either Medical or surgical and can be done separately or concomitantly.

Medical Management

General Medical Treatment

A. *Resuscitation:* The initial management of the patient always follows ABCDE protocol (Airway, Breathing, Circulation, Disability, Exposure). After stabilizing the patient hemodynamically, wound care is started. Tetanus prophylaxis should be given. In case of other associated system injuries, multidisciplinary care should be done.

   If the patient presents with a chronic wound, the systemic condition and associated problems should be looked for and have to be addressed before initiating wound management. [88]

B. *Non-Surgical Debridement:* A clean lacerated wound presenting immediately after the injury (within 6 hrs), primary closure should be done, with no tension across the suture line. But if a patient has a compromised vascularity, it is better to wait, allowing the collateral channels to open.

   In a chronic wound, if there is no necrotic tissue, then a medical debridement can be done like with pulse lavage therapy with hydro jet etc. Wet gauze is safer to use than dry gauze as it may not disrupt the healthy granulation tissue.[88]

C. *Nutrition:* Anemia due to blood loss or preexisting nutritional deficiency which requires blood and nutritional replacement in acute wounds. Hypoalbuminemia and anemia in chronic wound, can be managed by providing 1.25-1.5 g of protein per kilogram of body weight and 30-35 calories/kg gradually increased according to the size of the wound. Micronutrients have to be supplemented [89]

D. *Infection:* Certain topical antimicrobials like Hydrogen peroxide are cytotoxic to healthy cells and interfere with epithelialization. Systemic antibiotics according to tissue culture reports can be

added. The bacterial load should be reduced by debridement of dead tissue.

E. *Dressing:* Dressing can be primary dressing which covers the wound, or a secondary dressing which is used to cover the primary dressing. Dressing serves to protect the wound from the external environment. Nature of dressings can vary. Newer techniques of antibiotic incorporated dressings for infected wounds like antimicrobial coated dressing is useful.[90]

F. *Adjuvant Modalities:* Growth factor rich autologous platelet rich plasma and other topical agents, Egg membrane, autologous lipoaspirate (Fig. 3) cultured keratinocytes have been described (fig. 2 a, b, c).[91]

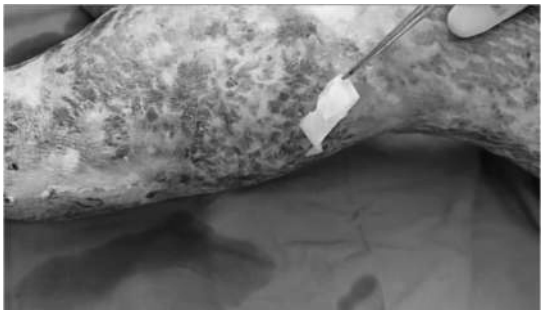

Fig. 2a. Egg membrane being applied on the wound.

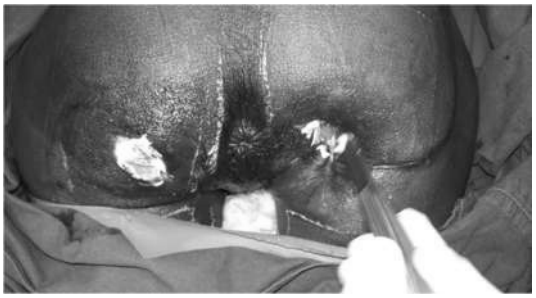

Fig. 2b: Sucralfate being applied in pressure sore.

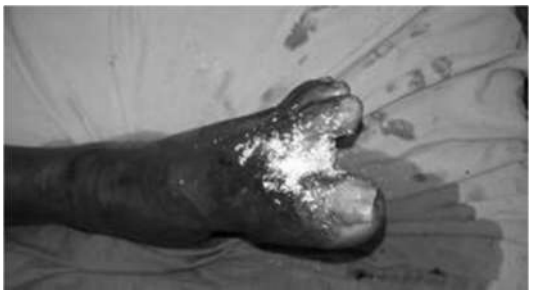

Fig. 2c: Vit D applied over the wound.

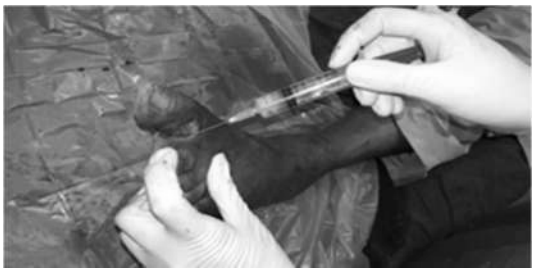

Fig 3: Autologous lipoaspirate infiltrated in the wound.

G. *Relieve Pain:* Pain can be avoided by techniques like use of topical lignocaine gel, moistening the gauze with saline before removal to avoid adherence to the wound bed, topical and systemic pain relievers.[92]

H. *Negative Pressure Wound Therapy (NPWT):* It refers to any device that tightly seals the wound creating a near airtight environment with a negative pressure of 125 mm Hg. Various modifications of NPWT combination with oxygen and irrigation, known as Regulated Oxygen Enriched-Irrigation Negative Pressure Therapy (ROI-NPT).[93] It can also be used with oxygen and irrigation, known as Limited Access Dressing (LAD) (figure 4).[94]

I. *Hyperbaric Oxygen Therapy:* HBOT is the use of 100% oxygen at pressures greater than atmospheric pressure while the pressure of the treatment chamber is increased to greater than 1 atmosphere absolute(ATA) or more. It is useful in compromised skin grafts and flaps, crush injuries, arterial insufficiencies, necrotizing fasciitis etc., [95]

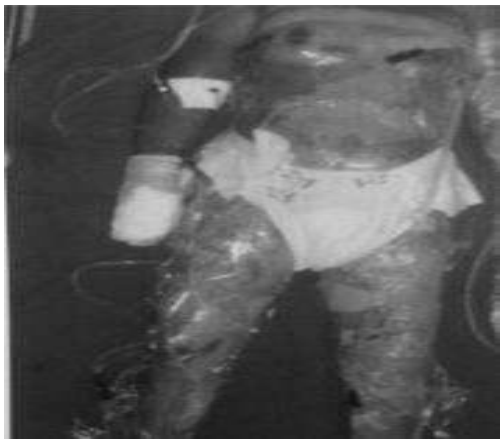

Fig. 4: Limited Access dressing.

J. *Physiotherapy:* Physiotherapy comprises of correct positioning of the limb within splints, usage of pressure garments, off-loading foot wear, air mattresses, cryotherapy, exercises which may be active or passive, electrical and ultrasonic stimulation of the muscles, laser therapy, hydrotherapy etc.,[96]

Specific Medical Treatment (according to type of wound)

A. *Pressure Ulcers:* It includes frequent position change every 2 hours,[97] adequate cushioning at the pressure points eg.,air bed[98] avoiding of maceration with urine/stool/sweat,[99] using antiperspirant.

B. *Venous Ulcer:* It comprises edema management with compression garments and limb elevation, surgical management of the incompetenet perforators by ligation of the same.[100]

B. *Diabetic Foot Ulcers:* Prevention is done by instructing the patient to inspect the foot everyday for wounds, the ulcer can be managed by debridement, dressings, assessment for osteomyelitis followed by antibiotic therapy. Control of blood glucose, management of

peripheral arterial insufficiency is paramount. Wound coverage can be done by Split Skin grafts, or biological dressings or application of growth factors stimulating spontaneous wound healing, negative pressure and hyperbaric wound therapy.[101,102]

D. *Lymphedema:* It includes Complex decongestive therapy, limb elevation, compression garments.

E. *Burns:* It includes fluid resuscitation, stabilising hemodynamics. This is followed by wound management, and pain control. Wounds can be managed with Silver sulfadiazine dressings, or biological (collagen) dressings. Secondary infection prevention, pressure sore prevention and avoiding of contractures with splints is mandatory.[103,104]

F *Malignant Wounds:* This includes antibacterial impregnated dressing, local antibiotics, exudate control dressings like hydrogel dressing.[105]

G. *Bleeding Wounds:* Control of bleeding can by conservative measures-compression and limb elevation, by medical management (topical 1:1000 adrenaline etc) or by surgical management (ligation or cauterization is done.[106]

H. *Chemo-Extravasation:* Once extravasation of cytotoxic drugs has been recognized the immediate management is to stop the infusion. The cannula should not be removed as it may be required to aspirate the drug and to give neutralizing drugs. This is followed marking of the area to assess progress, cold compression if the compound is non vesicant, hot compression of the compound is vinca alkaloids.[107]

Surgical Management

A. *Debridement, Incision and Drainage, Amputations:* Dead non viable tissue has to be debrided, which can be either sharp dissection with a knife, or using latest technologies like radiofrequency, ultrasonic waves etc. If an entire limb or body part is non viable beyond salvage, amputation has to be done.

B. *Primary Closure:* Initially primary closure was done with sutures. With advent of many new technologies, it can be done with steristrips, medical glue etc.

C. *Delayed Primary Closure:* If the wound is not amenable for suture closure, once it is free of bacteria and filled with healthy granulation tissue, it can be covered according to a reconstructive ladder. Newer modalities like bioengineered skin grafts can be used.[108]

D. *External Tissue Expansion Wound Closure (ETEWC):* If delayed primary closure is not feasible, then External tissue expansion aided wound closure (ETEWC) can be used. This utilizes the biomechanical properties of skin, but the drawback is that it will take time for the wound to close (figure 5).

E. *Bioengineered Skin Substitutes:* A biological skin substitute can be used as temporary cover which contains collagen from various sources and stimulates the wound bed for healing. eg. Apligraf is a bovine collagen[109] Dermagraft contains human fibroblast-derived dermal substitute.[110,111]

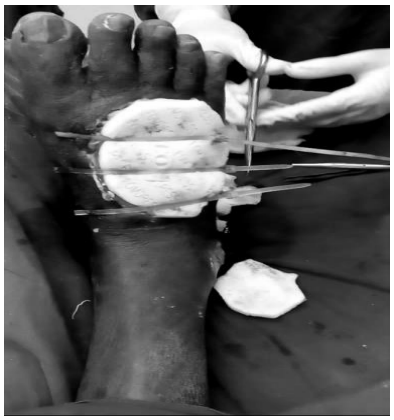

Fig. 5. Ziplock tags as a external tissue expansion device.

F. *Fasciotomy:* Compartment syndrome is characterised by a rise in intracompartmental pressure within the limb. It has to be managed immediately. This is done when the pressure rises to 10-30mmhg from the patient's diastolic pressure.[112]

G. *Escharotomy and Escharectomy:* Eschar is a thick, tough, non-elastic burn tissue, and can contribute to burn induced compartment syndrome. This can be managed by either an escharotomy-where the eschar is surgically divided and the underlying tissues are allowed to relax or escharectomy, -where the eschar tissue if non viable and is excised.[113]

H. *Tangential Excision:* This technique, similar to a skin graft, but involves excision of unhealthy tissue with a skin graft knife, until healthy dermal bleed is noticed. Following this procedure, the wound either left for healing by secondary intention or can be covered with skin graft, or temporary substitutes.[114]

I. *Sequential Excision:* Unlike escharotomy or tangential excision, this involves staged excision of the burnt tissue, followed by cover with skin graft. This can be done in areas like face.[115]

J. *Aspiration or Deroofing of Burn Blisters:* Burn blisters can be aspirated or deroofed with a scalpel, specifically over joints and other vital structures whose function may be affected.[116]

K. *Autologous Skin Grafting:* If the wound bed is ideal it can be closed with autologous skin graft in various forms.

L. *Flaps:* The higher rung of the reconstruction ladder comprises flaps. Wounds with exposed bare bone or cartilage or tendon without paratenon are not suitable for coverage with skin grafts. In those scenarios, flap cover can be done. Flap can be either local flap, regional flap, pedicled flap, propeller flap, random flap, or axial flap, perforator flap, free microvascular flap can also be skin only flap, fasciocutaneous flap, muscle flap, or combination. [118]

M. *Tissue Expander Assisted Wound Closure:* Tissue expansion utilises the expansile property of the skin recruiting adjacent normal skin for wound coverage, expanding it with a tissue expander.

Tissue expander plays a role when there is a paucity of microvascular free tissue for transfer. But the disadvantage is that it takes time.[119]

Foetal Wound Healing

Wound healing in a fetus differs from adult wound healing in that it heals with very minimal scarring. The exact mechanisms of healing in the foetus are unclear. Minimal inflammatory response with a marked deposition of glycosaminoglycans, particularly hyaluronic acid is seen during foetal wound healing. Foetal wound healing is an organ specific response as organs other than skin and bone are unable to regenerate scarlessly. Sterile, warm amniotic fluid rich in growth factors, hyaluronic acid and fibronectin could modulate healing. The foetus has very low pO2 and foetal fibroblast achieves repair without macrophages.[137]

Recent Advances

The most eminent of all is gene therapy, where delivery of a gene into a wound would turn the specific gene on and off and thereby promoting faster wound healing and avoiding abnormal hypertrophic scars or keloids.[120]

Mesenchymal stem cell as a delivery vector to deliver the genes has been proposed.[121].The ultimate goal is to produce artificial skins that are readily implantable.[122] Various other methods described in wound dressings and treatment are quaternary ammonium compounds in wound healing[134], PolyHexaMethylguanide in wound bed preparation[137], combination therapy of negative pressure and autologous platelet rich plasma[138], filling of substances like collagen in wound cavities to promote wound healing[139], use of Microporous Polysaccharide Hemosphere Technology in wound healing[140], use of prolotherapy in wound management[158], Use of hemoglobin[141] and sucralfate[142] in wound bed preparation, Use of Non-Suction Epidermal Blister Grafting (NSEBG) for wound cover[143], Use of cholecalciferol granules[144] in diabetic ulcers, use of Technology Lipido-Colloidal (TLC) with Silver Impregnated Poly Absorbent Fibre.[145]

Indian Experience in Wound Healing

Wound healing in India has evolved to a greater extent, beginning from Sushruta to the present century. India has been privy to various techniques like homeopathy, acupuncture, herb mix pastes, yoga and music therapy.[123] Research has been done on the effectiveness of various natural herbs like propolis,[124] Grewia tiliaefolia,[125] Jatyadi Taila,[126] Curcumin,[127] Carissa spinarum Linn,[128] Pyrostegia venusta,[129] and many herbs.[130] A holistic approach to wound management has also been described.[136]

The Society for Wound Care and Research (SWCR) have come out with general clinical guidelines for wound management. Similar to ABCDE for trauma management, ABCDE approach to wound management has been described.[135, 132]

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