A COMPARATIVE STUDY BETWEEN EFFICACY OF TOPICAL SUCRALFATE AND 5% POVIDONE IODINE IN CHRONIC LOWER LIMB ULCERS

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Dissertation submitted to

BLDE (Deemed to be University) Vijayapur, Karnataka

In partial fulfillment of the requirements for the degree of

MASTER OF SURGERY

IN

GENERAL SURGERY

Under the guidance of

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KARNATAKA

2020

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LIST OF ABBREVATIONS

ABBREVATIONS	FULL FORM
HB	Haemoglobin
Vs	Versus
PR	Pulse Rate
DM	Diabetes Mellitus
GF	Growth Factor
CBC	Complete blood Count
PVD	Peripheral vascular disease
UKB	Urine Ketone Bodies
DBP	Diastolic Blood Pressure
SBP	Systolic Blood Pressure
FBS	Fasting Blood Pressure
PDGF	Platelet derived growth factor
Rh- PDGF	Recombinant human platelet derived growth factor
US-FDA	United States Food and Drugs Administration

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1. ABSTRACT

Background:

Sucralfate [Aluminium hydroxide salt of the disaccharide sucrose octasulfate] is an oral gastrointestinal medication primarily for the treatment of active peptic ulcers. Sucralfate is used for the treatment of gastroesophageal reflux disease (GERD) and peptic ulcers.

It also shows potential utility in the healing of skin wounds. Sucralfate stimulates the proliferation of dermal fibroblasts and keratinocytes. Sucralfate enhances prostaglandin E2 synthesis in basal keratinocytes, enhances interleukin-1-stimulated interleukin-6 release from fibroblasts[2]. When applied daily to full-thickness wounds, sucralfate increased the thickness of granulation tissue.

Objectives

To compare the efficacy of Topical Sucralfate with that of a control group using 5% Povidone-iodine dressing, in the healing of chronic lower limb ulcer

Methods:

This is a prospective comparative study on chronic lower limb ulcers conducted at BLDE[DU] SHRI B.M.PATIL MEDICAL COLLEGE, HOSPITAL AND RESEARCH CENTRE, VIJAYAPURA after obtaining ethical clearance from the ethical committee with a sample size of 224

Results:

The wounds in the Sucralfate dressing-treated subjects contracted more than the wounds in the control group (71.8% Vs. 24.9%; P = 0.001 Significant) and showed early granulation tissue fill up; this suggests that Sucralfate dressing is an effective modality to FACILITATE wound contraction in patients with lower limb ulcers and can be used as an adjunct to betadine dressings for healing of Lower Limb ulcers.

2. INTRODUCTION

The problem of managing chronic wounds continues to be a challenge despite the thousands of years that have passed since mankind first succeeded in deciphering the human genetic code. One of the most frequent surgical conditions a surgeon encounters is chronic wounds, especially those that do not heal. Doctors have been experimenting with various techniques to heal these types of wounds for a long time.

During the last 20 years, many innovative dressings were introduced in wound healing, such as collagen[4], crystal violet, impregnated gauze, insulin, mercurochrome, and oxygen therapy. Recent literature says that an ulcer epithelialized more rapidly when treated with a dressing that allows moist wound healing [3].

Studies[2] have shown that topical sucralfate is a superior method for treating diabetic ulcers, as well as decubitus ulcers, venous stasis ulcers, traumatic wounds, burns, and trophic ulcers. In preclinical studies, sucralfate has been found to encourage the growth of granulation tissue, which in turn encourages the healing of cutaneous ulcers.

Sucralfate is an oral gastro-intestinal medicine used primarily to treat active peptic ulcers. It is the aluminium hydroxide salt of the disaccharide sucrose octasulfate. Peptic ulcers and gastroesophageal reflux disease (GERD) are both treated with sucralfate.

Additionally, it suggests a potential role in the recovery of skin injuries. Dermal fibroblast and keratinocyte proliferation is promoted by sucralfate. Sucralfate increases interleukin-1-stimulated fibroblasts' release of interleukin-6 and basal keratinocytes' production of prostaglandin E2. Sucralfate enhanced the thickness of granulation tissue when daily application was made to full-thickness wounds[2].

Numerous researches demonstrated the effectiveness of sucralfate[3], which resulted in the wound being completely closed and shrinking in size.

In view of new research regarding the effectiveness of sucralfate in treating lower limb ulcers, we undertook this study to ascertain if sucralfate administered topically over chronic lower limb ulcers reduces the size of the lesion more effectively than 5% Povidone-iodine treatment.

3.AIM AND OBJECTIVES OF THE STUDY

To assess Topical Sucralfate's effectiveness in treating chronic lower leg ulcers in comparison to a control group using a 5% povidone-iodine dressing.

Primary efficacy endpoint:

- Complete ulcer closure by secondary intention.

Secondary efficacy endpoint:

- Ulcer closure by secondary suturing or a split-thickness skin graft.

4. REVIEW OF LITERATURE:

ANATOMY OF LEG

The lower limb portion between the knee and the foot is referred to as the leg. Tibia and fibula are the two bones for this joint. These two bones serve to stabilize and support the remainder of the body. They also enable mobility and upright walking through their articulations with the femur, foot, and ankle, as well as the muscles that are linked to them. At the knee joint, the tibia and femur are articulated. The knee joint has three compartments.

• Lateral and medial tibiofemoral compartments

• Patellofemoral compartment

The articular surface for the talus is created at the ankle by the tibia and fibula. The ankle mortise is a unique articulation that supports the ankle joint while enhancing motion and functionality. The typical ankle joint facilitates and permits the foot's natural joint and articular motion. The lower leg is additionally divided into four compartments by the bones and fascia.

• Lateral compartment

• Anterior compartment

• Posterior compartment, superficial

• A deep posterior compartment

Bones and Joints

1. The tibia is the medial, weight-bearing bone of the leg and articulates distally with the talus and proximally with the fibula.

• Significant locations:

o Lateral and medial intercondylar tubercles divide the tibial condyles, which are horizontal proximal surfaces that engage with the femoral condyles.

o The tibial tuberosity

- The condyles' triangular superior-anterior junction
- Patellar tendon attachment point: anterior, lateral, and posterior sides of the shaft

Middle malleolus

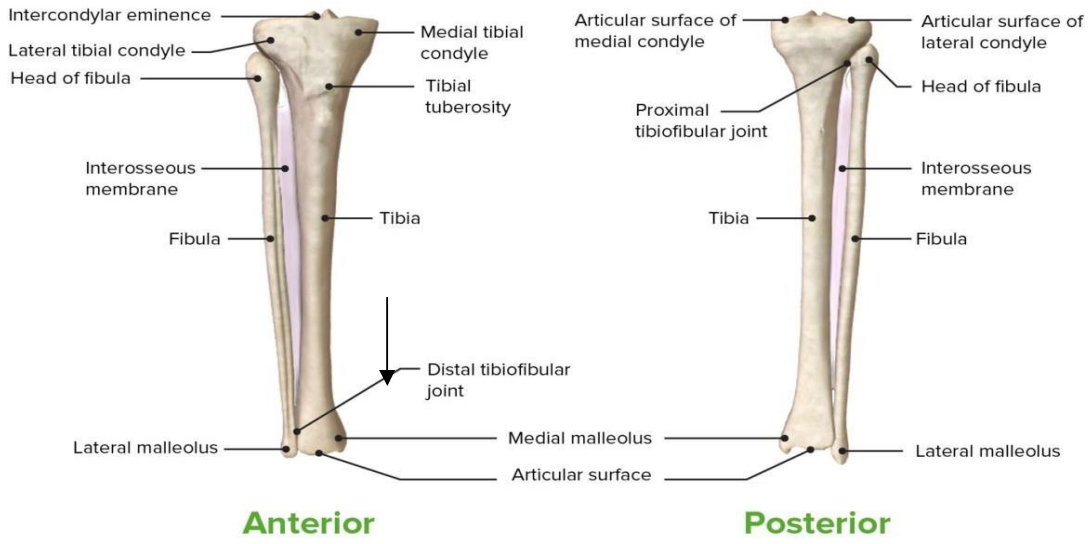
- Distal projecting
- Allows the ankle joint to articulate with the talus.

1.Fibula

- The thin, lateral bone of the leg
- Articulates with the tibia proximally and distally and with the talus distally
- Important landmarks:
    - Head:
        - Serves as the site of attachment for ligaments of the knee
        - Articulates with the tibia
    - Neck
        - Narrow
        - The common peroneal nerve wraps around it.
    - Shaft: medial, lateral, and posterior surfaces

- Lateral malleolus
  - Distal projection
  - Articulates with the talus as part of the ankle

Fig. 4.1 :BONES OF LEG



Joints

• Proximal tibiofibular joint:

o The joint in the arthrodial plane is in between lateral tibial condyle and the head of the fibula

o Supported by a strong capsule and many ligaments

• Interosseous membrane:

o Fibrous tissue directed downward and laterally

o Connects the medial border of the fibula with the lateral border of the tibia

• Distal tibiofibular Joint:

o Syndesmosis of the distal ends of the fibula and tibia

o Stabilized by multiple ligaments and the interosseous membrane

o Contains an opening on the proximal region that permits passage of the anterior tibial vessels to the anterior compartment of the leg

Facial Compartments

The anterior, posterior, and transverse intermuscular septa, along with the interosseous membrane, divide the leg into four fascial compartments, as shown below:

1. The anterior compartment

o The anterior intermuscular septum divides it from the lateral compartment.

o The tibia and the interosseous membrane divide it from the deep posterior compartment.

o Has 4 muscles:

- Tibialis anterior
- Peroneus tertius
- Extensor digitorum longus
- Extensor hallucis longus

2. Superficial posterior compartment:

o The transverse intermuscular septum divides it from the deep posterior compartment. The posterior intermuscular septum separates it from the lateral compartment.

o Comprises three muscles:

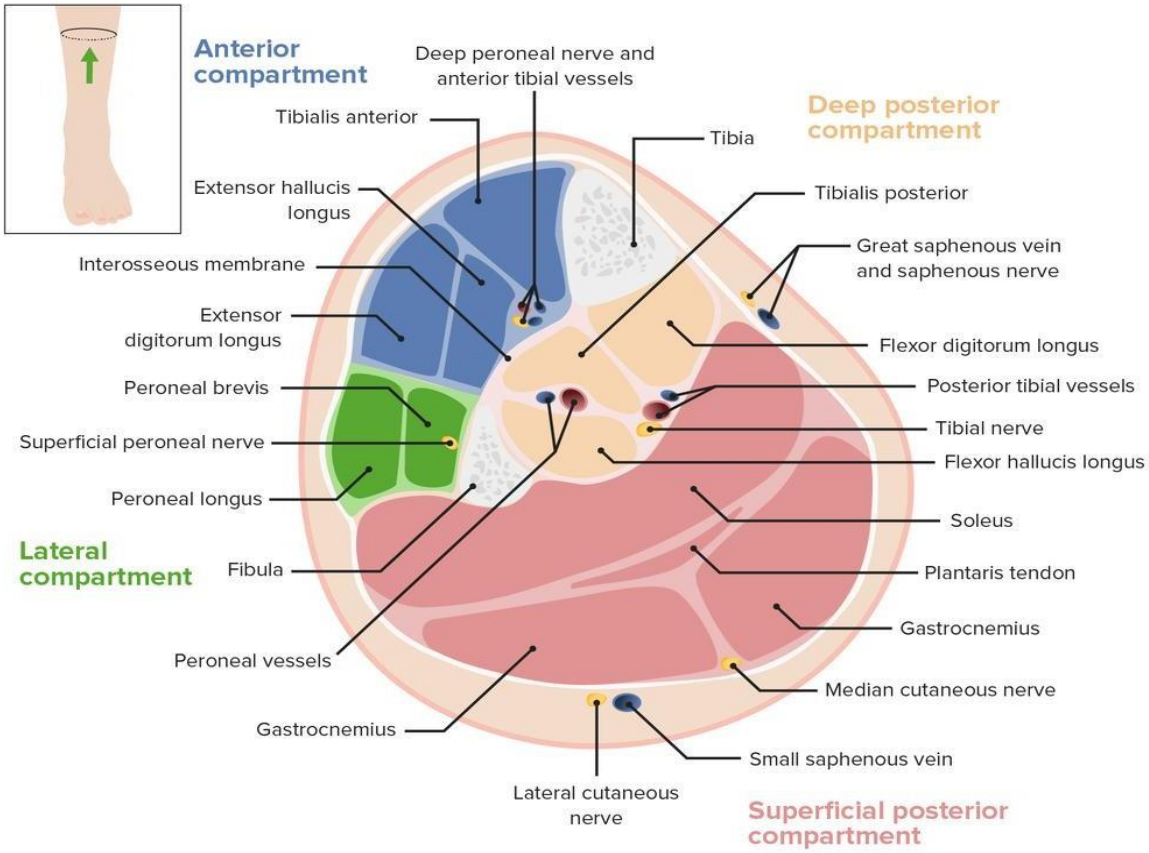
- Soleus
- Gastrocnemius
- Plantaris

3. The tibia and the interosseous membrane divide the deep posterior compartment from the anterior compartment.

The transverse intermuscular septum divides the superficial posterior compartment from the rest of the body.

- Includes 4 muscles:
  - Popliteus
  - Tibialis posterior
  - Flexor digitorum Longus
  - Flexor hallucis Longus

Fig. 4.2: FACIAL COMPARTMENTS



Anterior Compartment — Dorsiflexors

- Four muscles in the anterior compartment responsible for dorsiflexion or extension of the foot and/or toes:
    - Tibialis anterior: powerful dorsiflexor of the foot
    - Extensor digitorum longus: extends the four lateral toes and the foot
    - Extensor hallucis longus: extends the hallux and the foot
    - Peroneus Tertius: everts and dorsiflexes the foot
- Common nerve supply:

  deep fibular nerve(ventral rami of L4–S2)

- blood supply: anterior tibial artery and popliteal artery branch

Lateral Compartment

- Called as a peroneal compartment of the leg
- The muscles listed here are primarily responsible for foot eversion; they also contribute to plantar flexion and dorsiflexion.
    - Fibularis, or peroneus, longus
    - Fibularis, or peroneus, brevis
- Both muscular tendons pass posterior to lateral malleolus to enter the foot deep in relation to the peroneal retinaculum.
- Common nerve supply: primarily by the superficial fibular nerve
- Common blood supply: perforating branches from the anterior tibial artery

Posterior Compartment — Flexors

- Posterior compartment muscles are primarily responsible for plantar flexion
- Divided by transverse intermuscular septum into superficial and deep layers
    - Superficial layer muscles
        - Triceps surae which consistes of the soleus and paired gastronemii
        - Plantaris
    - Muscles of the deep layer include:
        - Popliteus
        - Tibialis posterior
        - Flexor digitorum longus
        - Flexor hallucis longus
        - Muscular tendons (except for popliteus) pass posterior to the medial malleolus(from lateral to medial flexor hallucis longus, flexor digitorum longus, tibialis posterior).
- Nerve supply: tibial nerve
- Blood supply: By fibular vessels(deep layer) and posterior tibial artery

Blood Supply

- Arteries of the lower leg

- The lower leg's blood supply is provided by the popliteal artery. At the lower edge of the popliteal fossa, the artery divides into two and sends branches to the anterior compartment, anterior tibial artery, posterior and lateral compartments, forming the tibioperoneal trunk.

➢ Leg veins in the lower part

The leg has two venous drainage networks:

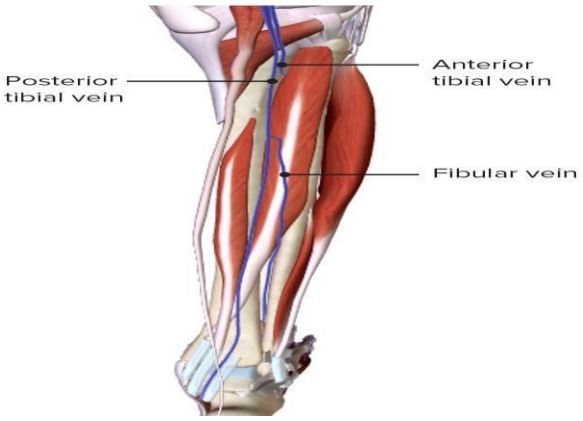
• The popliteal vein is formed by the union of the deep venous branches

- In the subcutaneous tissue are the superficial or saphenous veins.

Deep veins of the leg:

- Situated deep to the deep fascia of the leg
- Accompany the arteries of the leg of the same name:
  - Anterior tibial veins
  - Posterior tibial veins
  - Peroneal veins
- Converge at the inferior border of popliteus muscle to form the poplitealvein

Fig. 4.3: BLOOD SUPPLY OF LEG



Nerve supply

The lumbosacral plexus provides the lower limb's sensory and motor innervation (L1–S4).

• **Sciatic nerve** :divided into common peroneal nerve and tibial nerve. It is the largest and longest nerve from the lumbosacral plexus.

o The **Tibial nerve** travels inferior and posterior to the medial malleolus in the ankle through the tarsal tunnel, providing motor function to the posterior compartment of the leg and many sensory branches to the entire leg.

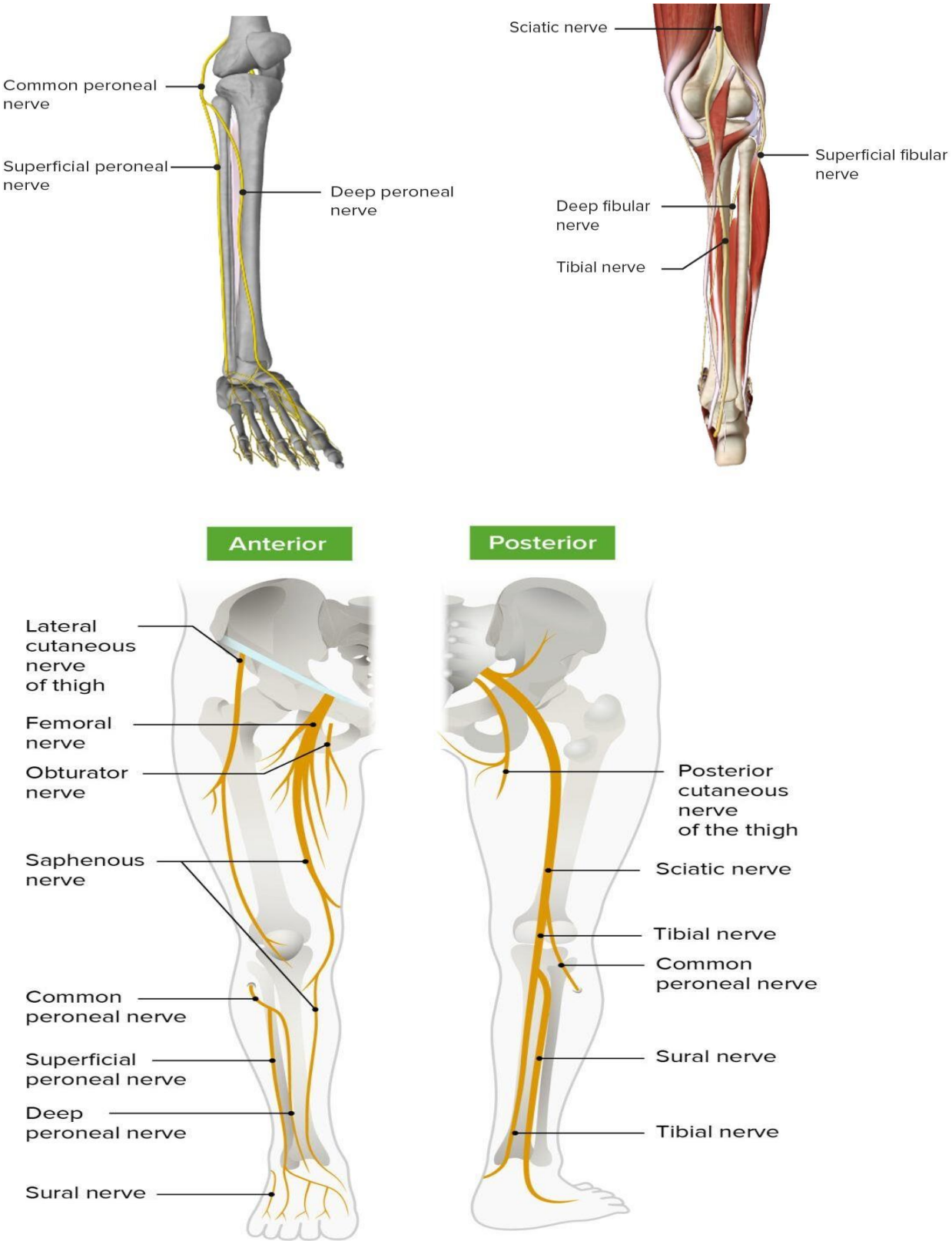
- **Sural nerve**: sensory supply to the skin across lateral edge of the foot and posterolateral part of the distal third of the leg.

o **Common peroneal nerve**, also known as the common fibular nerve, gives the short head of the biceps femoris motor function before splitting into two branches:

- **Deep peroneal (fibular) nerve** : It is terminal branch of the common peroneal nerve, supplies sensory input to the first interdigital space of the foot and motor function to the anterior compartment.
- **The superficial peroneal (fibular) nerve**, it is terminal branch of the common peroneal nerve, supplies sensory input to the dorsum of the foot and lower anterior portion of the leg as well as motor function to the lateral compartment.

✓ **Saphenous nerve**: a femoral nerve branch that emerges from the femoral triangle and provides skin on the medial half of the leg with pure sensory function.

Fig. 4.4: NERVE SUPPLY TO LEG



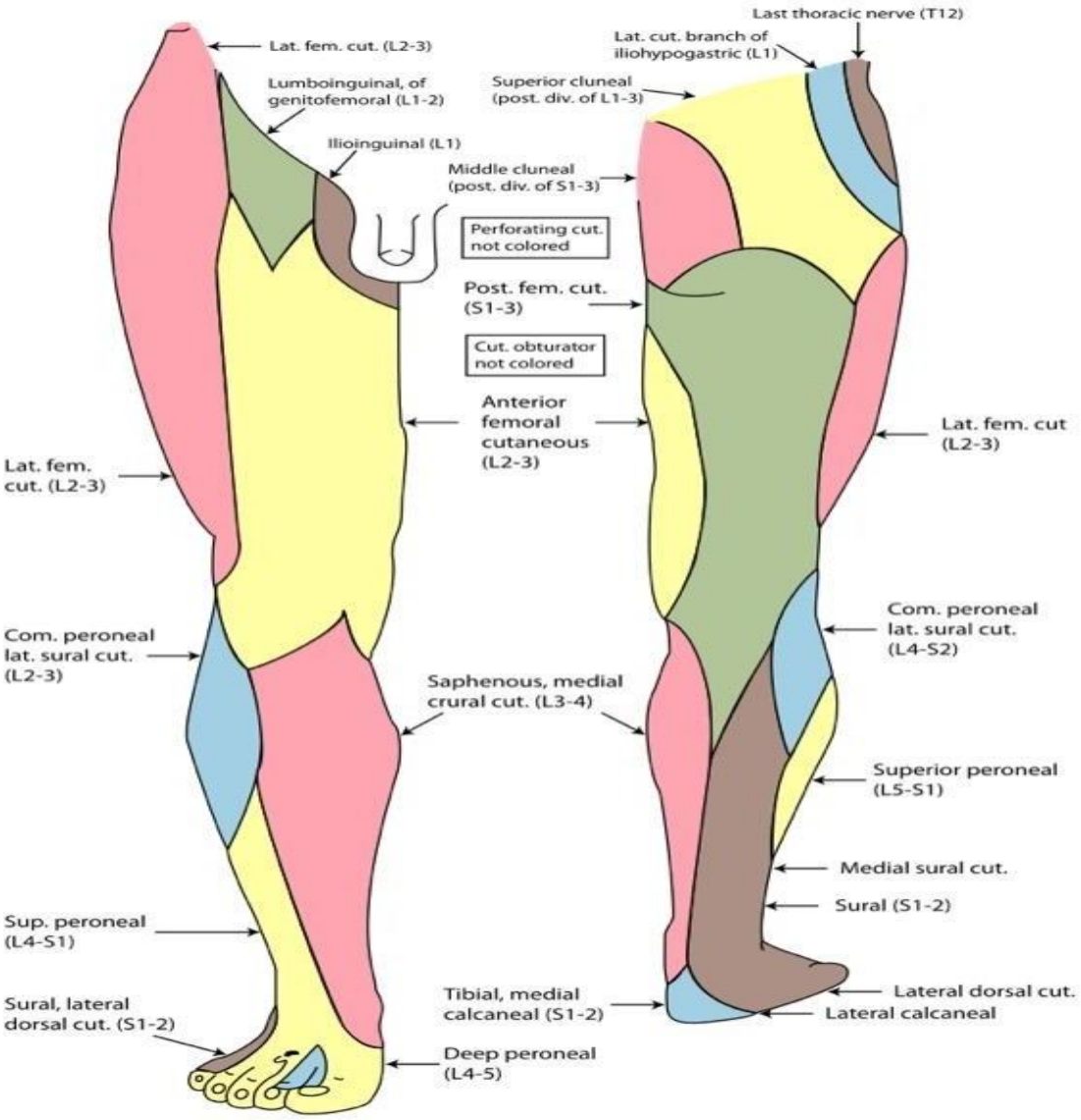


Fig. 4.5: CUTANEOUS INNERVATION OF THE LOWER LIMB

ANATOMY OF FOOT:

The anatomy of the foot and ankle is composed of numerous anatomical elements, such as bones, joints, ligaments, muscles, tendons, and nerves.

Regions of the Foot

- The hindfoot, midfoot, and forefoot are the three classical divisions of the foot. Region between the knee and the ankle, which is essential for proper operation of the foot, is also frequently referred to as the lower leg.

- The transverse tarsal joint marks the end of the hindfoot, which starts at the ankle joint which is a combination of the talonavicular and calcaneal-cuboid joints. The talus and calcaneus are the bones in the backfoot.
- The midfoot starts at the transverse tarsal joint and finishes at the tarsometatarsal (TMT) joint, which is where the metatarsals start. Compared to the hindfoot, the midfoot has a few more joints, although these joints are not as mobile. The navicular, cuboid, and the three cuneiforms make up the midfoot's five bones.
- The metatarsals, phalanges, and sesamoids make up the forefoot. When walking, the last bones to leave the ground are those that make up the forefoot. Twenty-one bones, including five metatarsals, fourteen phalanges, and two sesamoids, make up the forefoot. The four toes each have distal, middle, proximal phalanges, which are substantially smaller than those of the great toe. Only the proximal and distal phalanxes exist on the great toe.

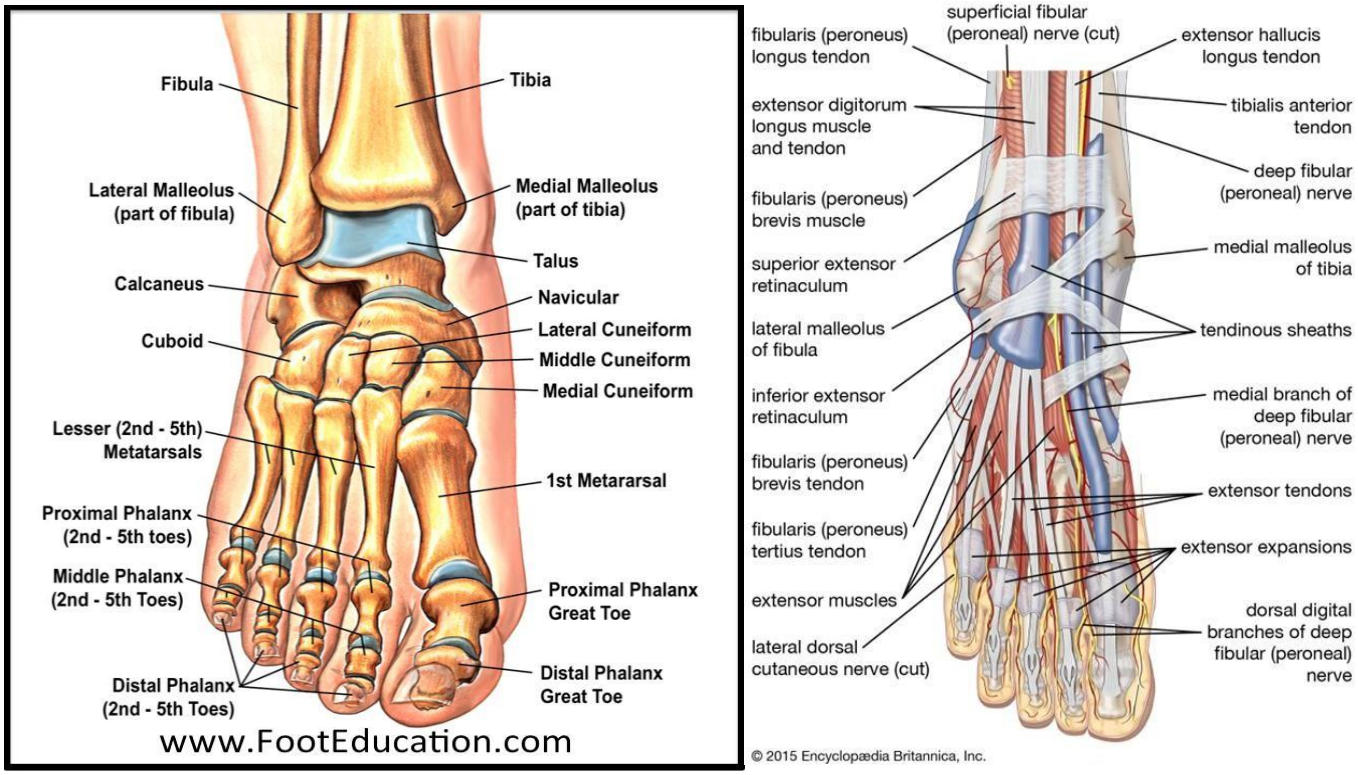


Fig. 4.6: ANATOMY OF FOOT

BACKGROUND OF WOUND HEALING

- Wound care and healing are among of the oldest topics covered in medical history and are likely among the oldest issues facing humanity.
- Early surgeons treated wounds, especially those brought on by battle, with some scientific understanding, including Ambrose, Pare, John Hunter, and Sir James Paget.
- Halsted had a strong interest in how wounds healed.
- In the early 1900s, Carrel and his colleagues conducted research on the scientific theory of wound healing. Later researchers like Carrel (1916), Harvey, and Howe (1930) examined incised wounds and added to our understanding wound healing .
- • There is a saying that goes, "There would be no life if regeneration did not take place, and there would be no death if regeneration took place everywhere."
- Treatment of wounds is a major topic oldest medical writings. Wounds and their care are discussed in seven of the 48 case reports found in Edwin Smith Papyrus (1700 BC).
- By removing foreign objects, suturing wounds, dressing them with clean materials, and shielding wounded tissues from corrosive chemicals, ancient physicians in Egypt, Greece, India, and Europe devised these delicate methods of healing wounds.
- • The "three healing gestures" notion dates back more than 4000 years, with the earliest inscription being on a clay tablet in 2200 BC.
- The three gestures are described on the tablet as:
    - o wound irrigation
    - o Making plasters

- Dressing the wound

- These gestures have endured through the ages, evolving into many variations on the same fundamental themes still present now. Hippocrates introduced the concept of dry healing to the Greeks at a period when bandages were regarded to solely protect wounds from harm.
- • During the fourteenth century, there was a greater necessity for surgeons to take an aggressive attitude, which was usually done at the expense of aseptic procedures due to the widespread use of gunpowder and the rise in the frequency of gunshot wounds. Examples include administering hot milk of magnesia, hot clay, heated bismuth, hot oil, hot wine, hot turpentine, hot feathers, hot sugar, and hot turpentine on wounds. But none of these has a proven track record of success, according to credible research.
- A renowned French army surgeon named Ambroise Pare achieved remarkable achievements treating amputation stumps with softer materials like a digestible mixture of egg yolk, rose oil, honey, and turpentine in the middle of the sixteenth century. This marked the emergence of the current phase of sensitive wound care.
- William Stewart Halsted, John Hunter, Alexis Carrel, and many other outstanding clinical biologists established the "minimum interference" theory of wound care by demonstrating that reducing tissue harm fosters speedy and successful recovery. The best outcome is achieved if the surgeon can remove all barriers to normal wound healing.
- By determining the source and creating strategies for prevention, Joseph Lister and Louis Pasteur's work established a strong foundation for the management of infection. The hospital should be kept clean, wounds should be cleaned often with soap and water, and contaminated wounds should be dressed with carbolic acid, according to Joseph Lister. Later on, bacteria were also

recognised as pathogens by Semmelweis, Ehrlich, Fleming, and Florey. A new era in wound management was ushered in by the ability of asepsis, antiseptics, and antimicrobials to control bacteria.

- The treatment of wounds was rapidly improved as a result of World War I, with comprehensive debridement being the most significant of these improvements. The idea of a moist wound environment for healing was not addressed until the 1960s.
- The moist environment would aid in debridement, minimise inflammation, ease pain, and lessen scarring in addition to defending the site from infection.
- Finally, it's critical to stress that recent developments in wound care are merely a prelude to those that will come in the decades to come.

HEALING, REGENERATION & REPAIR

Healing

"Integrated series of cellular and metabolic processes that let injured tissue recover its strength and functional integrity, or "Body replacement of destroyed tissues by the living tissue."

Regeneration

"It is a process of replacing lost tissue with a similar type of fresh tissue." Undamaged specialised cells[18] are multiplying in the vicinity. Seen in: Epidermis , Endothelium, Liver cells, and Mucous membrane.

Repair

By granulation tissue, which develops into scar tissue, missing tissues are replaced. When the surrounding specialised cells, such as those in muscle and nerve tissue, lack the ability to multiply, this is unavoidable.

Repair typically doesn't end until the harmful impact has passed. It begins during the early stages of inflammation[31]

- During repair damaged tissue is replaced by[19]:
  - Native parenchyma cell regeneration
  - By using fibroblastic tissue to fill the deficiency (scarring).
  - Using both of these methods simultaneously.

HEALING:

Definition:

"Integrated set of cellular & biochemical reactions which restore the functional integrity & regain the strength of wounded tissue" or "Body replacement of destroyed tissues by the living tissue"

Phases of HEALING:

The complex processes of wound healing and restoration entail a dynamic series of occurrences.

[1] Inflammation

[2] Coagulation

[3] Formation of Granulation tissue, Fibroplasia, Angiogenesis, and Proliferation.

[4] Epithelization

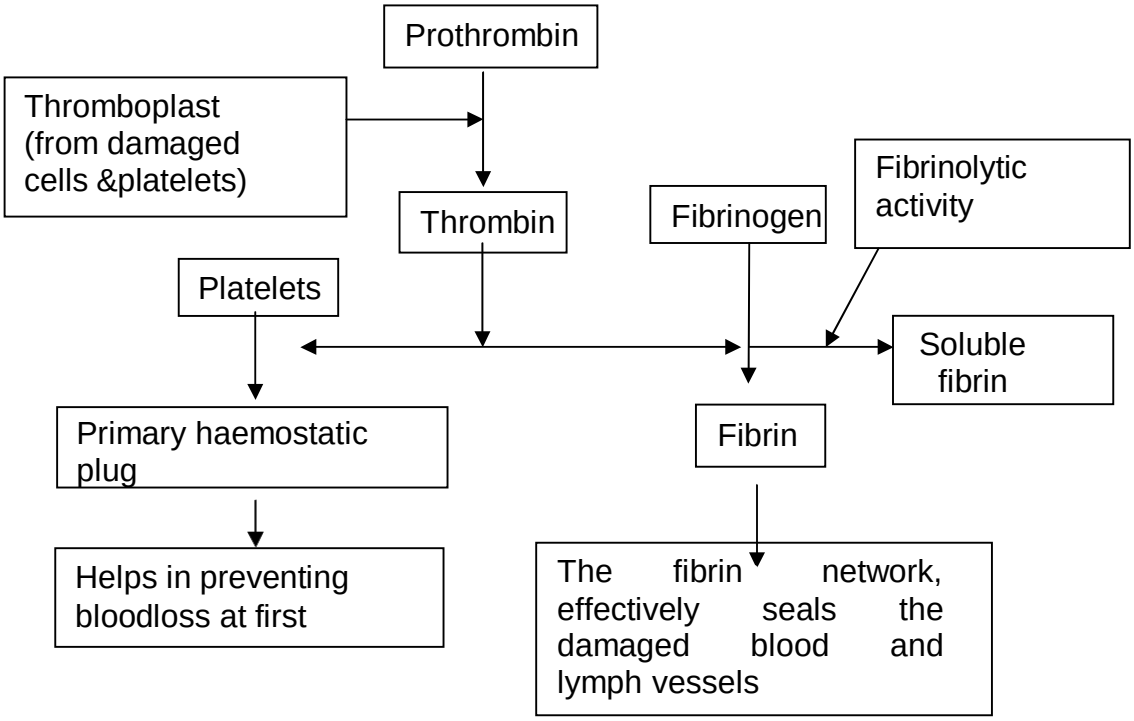
[5]Collagen Production

[6] Scar maturation, tissue remodelling, and contracture

COAGULATION:

- Contributes to the healing process by assisting in reducing blood loss, covering the wound surface, and binding the wound edges together.
- Fibrin and platelets have unmistakably been proven by Knighton et al. (1982) and Ross (1980) to be crucial in the early stages of wound healing.

Fig. 4.7: MECHANISM OF COAGULATION



GRANULATION PHASE OF WOUND HEALING :

- This phase of wound healing includes the fibroplasia, angiogenesis, and proliferation phases.

What is Granulation tissue[19]

'This is highly vascular tissue that primarily consists of

1. Fibroblasts [Proliferating Fibroblasts + Fibroblast-Derived Products]
2. The endothelial cells that line the capillaries of freshly forming blood vessels.
3. Macrophages
4. Pleuipotent cells

The following are all contained in a matrix:

1. Fibronectin

2. Proteoglycans rich in collagen and hyaluronic acid [This collagen, which was largely Type-III at first, later changed to Type-I]

Why is the term "Granulation Tissue" used?

The phrase "granulation tissue" refers to the pink, granular, and soft tissue that forms on the surface of wounds[19].

GRANULATION TISSUE FUNCTIONS:

• Seal the wound's opening

• Aids in the growth and migration of epithelial cells - Granulation tissue's connective tissue matrix serves as a nutritive substrate for regenerating epidermis, which can migrate over it and is gradually replaced by scar tissue.

Factors crucial to the production of Granulation tissue:

- Chemotactic Factors
- Growth Factors
- Structural molecules
- Proteases are enzymes that break down connective tissue matrix (Clark, 1985).

NEO-VASCULARISATION OR ANGIOGENESIS:

Proliferative phase of wound healing and restoration is crucial. It appears in[18]

• Stage of embryonic development

• During the repairs (throughout life span of an organism)

• In certain clinical circumstances

Without angiogenesis, macrophages and fibroblasts wouldn't be

able to invade the wound bed since there wouldn't be enough oxygen and nutrients[18].

These capillaries are initially weak and lack a basement membrane as well as having loose cellular junctions (Gullino, 1981). As a result, the vessels bleed abundantly at the slightest touch, which is a characteristic of freshly formed capillaries. The leaking makes it easier for cells and large molecules to enter the wound site[18].

There are four steps in angiogenesis[18,19]

Step-I: Proteolytic degradation of the parent vessel's basement membrane to enable capillary sprout development and subsequent cell migration[31]. Angiogenic stimuli operate on capillary endothelial cells to cause collagenase to be released. The basement membrane's collagen is broken down by this enzyme[18].

Step-II: The angiogenic stimulus draws endothelial cells in its direction. Because the basement membrane's basement collagen is broken down, endothelial cells can move into the peri-vascular gaps[18].

Step-III: Endothelial cell proliferation, which occurs immediately after the leading front of migrating cells. Endothelial cells migrate into the peri-vascular regions where they produce buds. Cells in and near the parent vessel proliferate to add to this process (Kalebie et al, 1983)[18].

Step-IV: Endothelial cell maturation and capillary loop organisation

- **Functional Capillary Loops:** During dermal healing, these buds quickly advance to the free surface where they branch at their terminals and come together to create functional capillary loops.
- **Superficial Capillary Plexus**: New buds grow on these loops, which causes a superficial capillary plexus to form quickly in the granulation tissue.
- **Canalization:** Endothelial cell proliferation and branching eventually get canalised to generate developing capillary buds of healed wounds.
- **Fusion:** The fusion of capillaries coming from opposite sides of the wound creates a full circulation inside it.

VASCULATURE MODIFICATION:

The vasculature is constantly being modified, which results in the obliteration of numerous capillaries (Marchesi, 1985). As each capillary loop begins to work, it supplies adjacent cells with nutrition and oxygen, allowing the fibroblasts to secrete ingredients for the matrix through which macrophages and other cells can migrate farther. This allows the matrix to function. (Zitelli, 1987)

Sequentially repeating the aforementioned proliferative and migratory processes results in the wound bed filling with granulation tissue.

MACROPHAGIA[18]

• It is a stage at which the inflammatory response's cleaning and protective functions are connected to the beginning of the reparative process

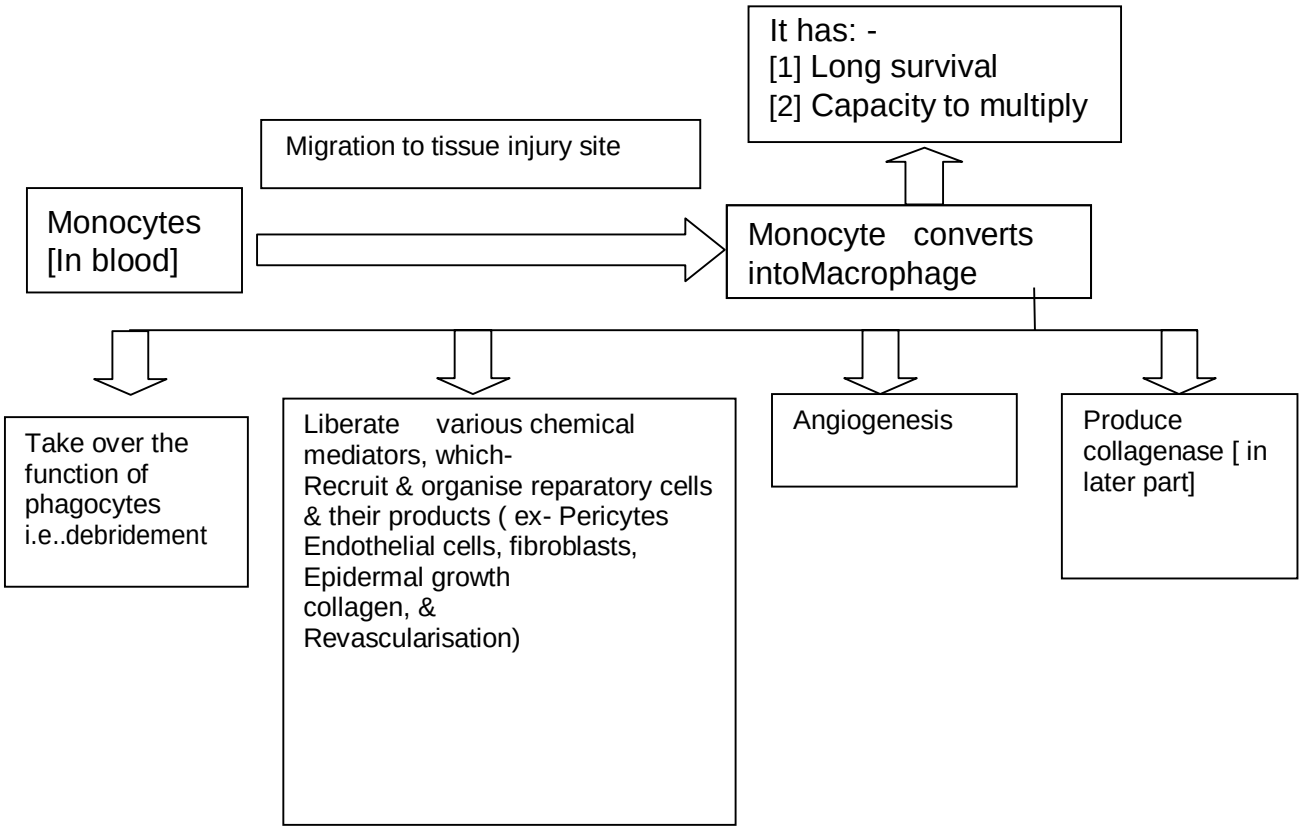
Macrophagia is the

[1] Monocyte migration [from blood] to the site of tissue damage

[2] After moving to the location of the tissue injury, monocytes transform into macrophages.

• Wound macrophages, which develop after the cells and play a crucial part in healing by releasing numerous substances, are important for dermal repair

FIG. 4.8: FUNCTIONS OF MACROPHAGES



Macrophages & angiogenesis[18]

It seems that by releasing ENDOTHELIAL GROW FACTOR, macrophages encourage

angiogenesis

Macrophages & Collagenase Enzymes :

Table 4.1: Role of Collagenase

Phases of wound healing	Sources of collagenase	Collagenase role
Initial phase of wound healing	neutrophils	They help with tissue debridement by converting the collagen of wound debris into collagen breakdown products, which are then removed by phagocytes.
In later part of wound healing	macrophages	This enzyme regulates the rate of novo collagen synthesis.

Collagen and macrophages:

Macrophages release lactate, which prompts fibroblasts to produce more collagen.

Table 4.2 : Migration of Fibroblasts – Mechanism[18]

Phase of inflammation	Chemical that causes fibroblasts to migrate by acting as a chemotactic agent:
Initial	by Fibrin-Fibronectin-Collagen Wound Base Scaffold
Later	by: [1]Macrophage -derived soluble chemical factor (Wahl, 1981) [2]Collagen -peptide (Postlethwait et al , 1978)

Fig. 4.9: FIBROBLAST'S ROLES IN THE HEALING OF WOUNDS

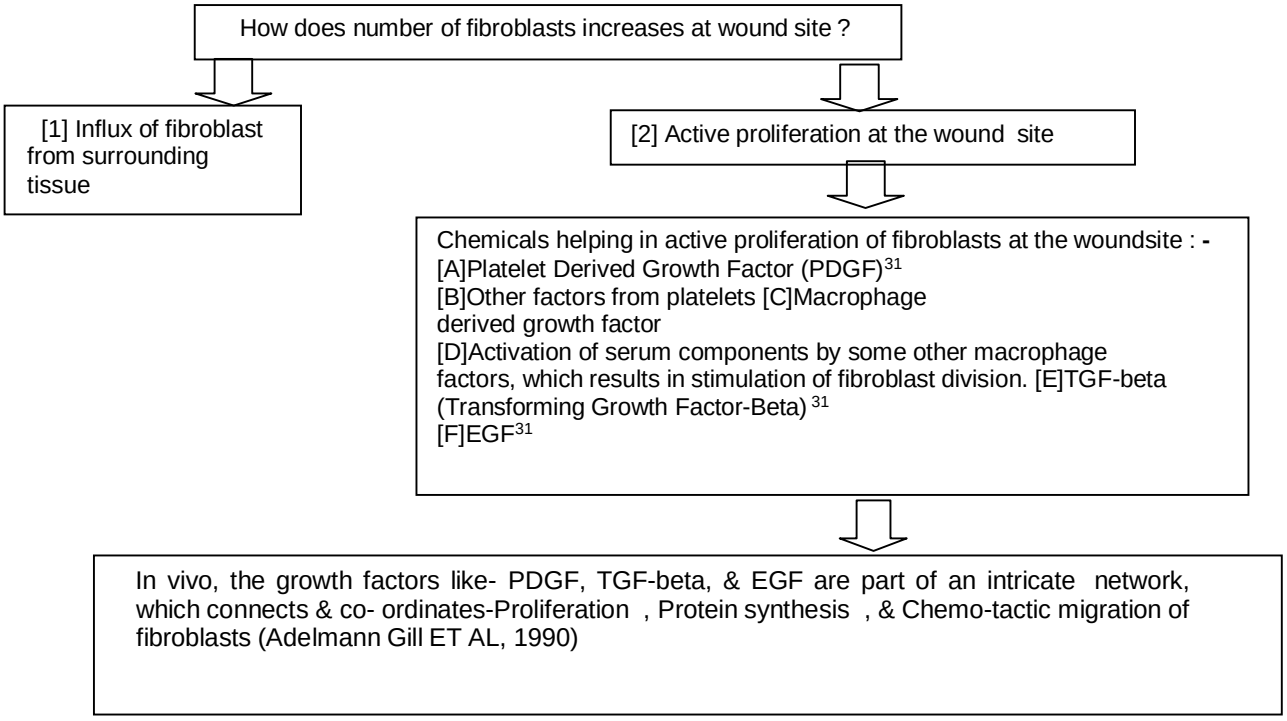
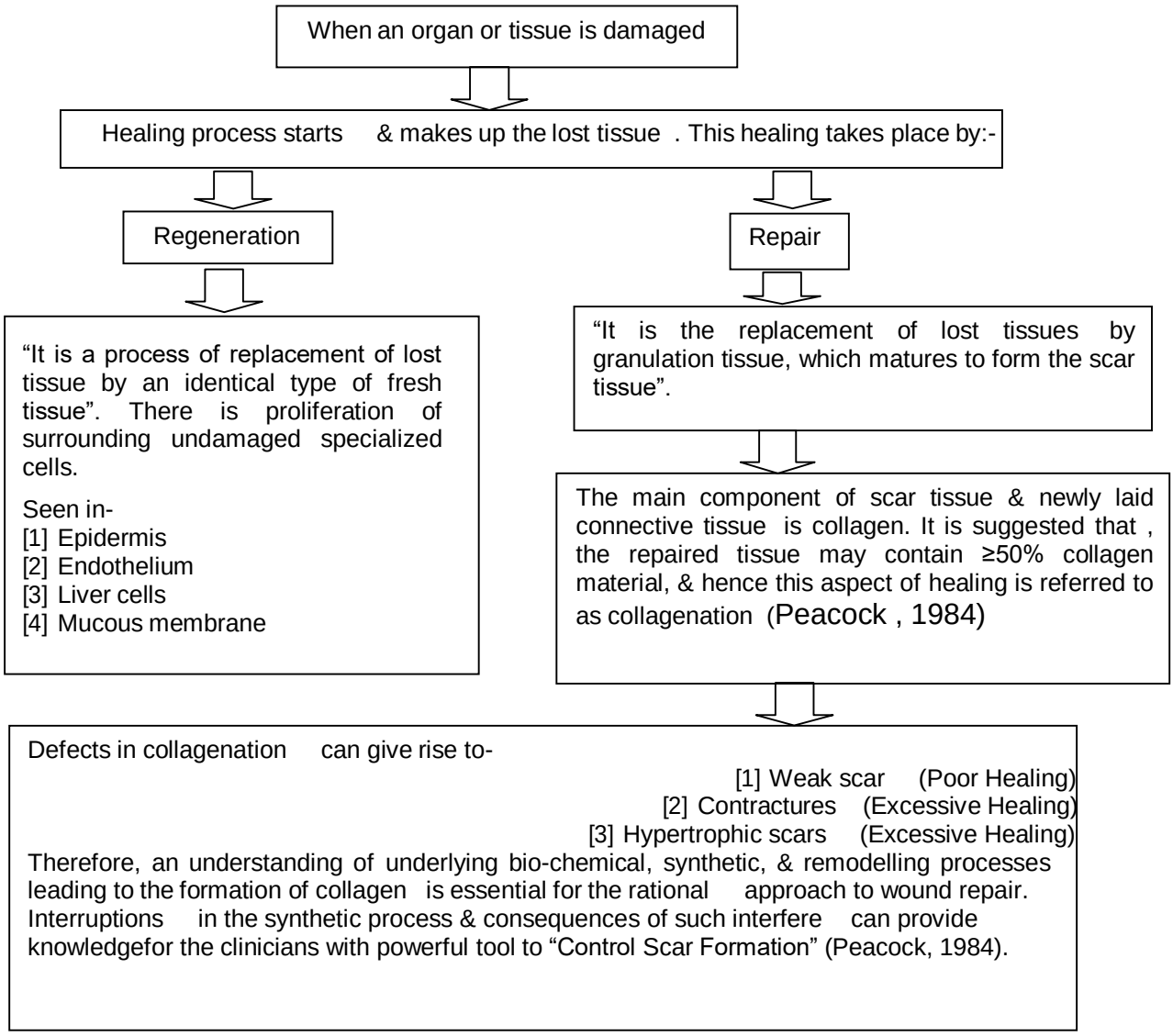


Fig 4.10: COLLAGENATION MECHANISM



Depending on the position of the wound, fibroblasts start producing collagen by day 3 or 5 of the healing process and continue to do so for several weeks[19].

COLLAGEN FIBERS :

Functions of collagen[19] :

1. Assistance for the tissues.
2. Gives other tissue types a structural framework[19].
3. Functions as a pathway for blood vessels and nerves.
4. Tensile strength is provided, bringing the wound edges together. Because of this holding power, tissue (organ) breakdown at the site of healing is prevented[19].
5. Fill the gap left by tissue loss

- The most prevalent protein in connective tissue, collagen, accounts for 25% of the body's total protein content (Peacock, 1984)[19].
- Fibroblasts are essentially the source of collagen.
- Collagen's true fibrils, which develop in the extracellular area, provide connective tissues their strength[19].
- Lysyl Hydroxy-lysyl Oxidation is a crucial extracellular alteration. It provides the basis for the structural stability of collagen and causes cross linking between alpha chains of nearby molecules. The main factor in collagen's tensile strength is cross linking[20].
- **Collagen Deposition :**Before collagen is deposited into the extracellular matrix of the healing wound, it undergoes the following four phases of synthesis:
    1. The production of tropocollagen
    2. Formation of Fibrils
    3. Maturation of Collagen
    4. Degradation of collagen.

COLLAGEN AND OTHER ECM PROTEINS DEGENERATE

- However, collagen breakdown as well as collagen production are both necessary for net collagen buildup.
- The following enzymes cause collagen and other ECM proteins to degrade[19].

Metalloproteinases[22].

- Aids in collagen and other ECM proteins' breakdown
- Zinc ions are necessary for them to function[19].

The ones that make these enzymes are.

- Fibroblasts, Macrophages , Neutrophils
- Synovial tissues
- A few cells of the epithelium

Growth factors (PDGF, FGF), cytokines (IL-1, TNF-a), and phagocytic triggers all cause their production[19].

- Nevertheless, collagenases are thought to degrade collagen during inflammation and wound repair[19].
- In fact, it has been shown that collagenases and their inhibitors are geographically and temporally controlled in the healing of burn wounds.
- Degradation assists in cleansing injured areas and in the connective tissue remodelling needed to fix the damage[19].

WOUND CONTRACTION[18]

- **Definition**: " Wound contraction is a process in which the surrounding skin's entire thickness moves centripetally to reduce the size of the entire thickness open wound."
- Wound contraction, which occurs in big surface wounds, is the characteristic that most clearly distinguishes primary healing from secondary healing[19].
- One of the granulation tissue's crucial functions for repair is wound contraction.
- Nearly all wounds experience the events of wound healing, from damage through fibroplasias. In excision cutaneous wounds, certain occurrences, such as wound contraction and epithelization, are typical.
- Although it is less common in humans due to the skin's stronger connection to subcutaneous tissue, wound contraction can nonetheless occur in areas like the buttocks and back of the neck. (Peacock, 1984).

• Wound contraction timing :

Depending on when the wound is sustained, wound contraction begins about the third or fourth day after the injury and lasts until the fifteenth or sixteenth day. It then ends, whether or not the wound is completely closed.

• Wound contraction rate:

- About 0.6-0.75 mm/day of wound contracture occurs (Peacock 1984).
- The size or shape of the wound does not significantly effect wound contraction, but the length of the wound perimeter might (McGrath and Simon, 1983).

- **Mechanism of wound contraction[18] :**
  - ❖ It is disputed and debatable as to how wounds contract. Numerous ideas, including Push theory, Picture Frame theory, and Pull theory has been put but not sufficient
  - ❖ According to Dollion (1987), modified fibroblasts rich in actin filaments are what cause the wound to contract, and myofibroblasts are found right beneath the wound's advancing margins[19].
  - ❖ It has been proposed that contractile epidermal cells around the borders of wounds serve as a source of force in the early stages of wound contraction (Baur et al, 1984).

Contraction of the wound can be advantageous or harmful.
Contraction from a wound can cause deformation, deformity, and functional impairment.

EPITHELIZATION[18]

- **Definition:** Epithelization is a form of wound healing that affects body surfaces.
- Lost epithelial cells in epithelialization are solely replaced by new epithelial cells, in contrast to healing by fibroplasias, when lost parenchymal cells are replaced by unrelated connective tissue. It serves as an example of regeneration-based healing.

• **Stages of epithelization** : The entire epithelization process thus consists of the following stages (Peacock,1984).

- Basal cells' dermal attachments are mobilised and loosened.

- The transfer of cells to an area where there are not enough of them.
- Cellular replacement or proliferation that results in a cell deficiency, and
- Cellular function restoration or differentiation.

- **Epithelization, which depends on a number of variables, including:**
  - ❖ Size of the wound
  - ❖ The site of the wound
  - ❖ Shape of the injury
  - ❖ Decrease in blood supply
  - ❖ Wound pathological modification.

- **Following epithelization, healing takes place in:**
  - ❖ Skin wounds,
  - ❖ Tracheobronchial surface wounds,
  - ❖ Surface wounds in the stomach, uterus, bladder, etc.

- **Epithelization timing:**
  - ❖ Within 24 hours following the development of a cutaneous wound, changes in the epidermis that lead to re-epithelization start to take place.

WOUND HEALING[19]

• WOUND HEALING MECHANISMS:

- We've seen that wound healing is a complicated (but orderly) phenomenon involving a number of processes, such as the induction of an acute inflammatory response by the wounding, the regeneration of parenchymal cells, the migration and proliferation of parenchymal and connective tissue cells, the synthesis of ECM proteins, the remodelling of connective tissue and parenchymal components, and the collagenization and acquisition of wound strength.
- Types of wound healing include:
  - **Primary union,** often referred to as healing by firsto intention, is the use of surgical sutures to close an incision after it has been cleaned and is clear of infection. Less epithelial and connective tissue cells die as a result of the incision, and the integrity of the epithelium and basement membrane is also disrupted.
  - **Secondary . Healing or second-intention healing**

- The reparative process is more difficult when there is a greater loss of cells and tissue, as in cases of inflammatory ulceration, inflammatory ulceration, abscess formation, and surface wounds that leave significant abnormalities.
- All of these cases share a significant tissue defect that needs to be filled in common. Parenchymal cell regeneration can only reconstruct a portion of the original architecture; the remaining portion of the repair is completed by abundant granulation tissue that grows in from the margin.
- Secondary union or healing by second intention are terms used to describe this type of healing.

Secondary healing is different from primary healing in a number of ways, including:

- Large tissue defects generally include more fibrin, necrotic debris, and exudates at first, which must be eliminated. Consequently, there is a stronger inflammatory response.
- Granulation tissue is created in much greater quantities. Granulation tissue, which contains a large number of scavenger white cells, is entirely responsible for the healing of major defects in deeper tissues, such as a viscus, as drainage to the surface is not possible.
- The phenomena of wound contraction, which takes place in big surface wounds, may be what most clearly distinguishes primary from secondary healing. In about 6 weeks, major flaws in a rabbit's skin shrink to 5 to 10% of their original size, mostly by contraction. At least in part, contraction has been linked to the presence of myofibroblasts, altered fibroblasts that resemble smooth muscle cells in terms of ultrastructure. The development of woundo strength and the deposition of connective tissue matrix, primarily collagen, are the outcomes of methodical wound repair.

Elements Affecting Wound Healing

- Since Lister used antisepsis, our knowledge of the mechanics of wound healing has continued to advance, and while the surgeon still has the full control necessary to totally govern healing, he now has the instruments necessary to impact it.

Cell-Cell Interactions:

In addition to the effects produced by the physical interaction between cells and the extracellular matrix, many cells also release soluble proteins known as cytokines that bind to particular cell surface receptors and function as

growth factors.

o change cellular conduct.

Programmable synthesis of many cytokines is essential for embryogenesis, the preservation of healthy tissue, inflammation, immune responses, and wound healing.

- Macrophage Derived Growth Factor (MDGF) is a protein that macrophages create when the conditions are right. MDGF promotes the proliferation of dormant fibroblasts, endothelial cells, and smooth muscle cells while causing the extracellular matrix to be deposited. The secretion of MDGF by macrophages is stimulated by fibronectin and bacterial endotoxins.
- Platelet-derived growth factor (PDGF), a polypeptide, is a potent mitogen for mesoderm-derived cells like smooth muscle cells, fibroblasts, and microglia. After platelet aggregation, PDGF, which is present in the a-granules of platelets, is released during hemostasis. Other cells produce PDGF-like substances, including macrophages, smooth muscle cells, modified fibroblasts, and endothelial cells*.

  1) The activity of PDGF at the site of a wound may affect the mobility of inflammatory cells, fibroblasts, endothelial cells, and smooth muscle cells

  2) the stimulation of neutrophils and monocytes

  3) the expansion of cells in connective tissue.

  Epidermal Growth Factor (EGF): This tiny polypeptide has a variety of physiological functions. The binding of EGF causes the cell to seem less differentiated and to start proliferating. By promoting the growth of fibroblasts and other cells, it also boosts the synthesis of collagen during the healing of wounds.

A single-chain, nonglycosylated protein called fibroblast formation factor (FGF) has the ability to induce the growth of Jj fibroblasts, endothelial cells, smooth muscle cells, and several other mesenchymal cells. Additionally, it promotes capillary development. Increased collagen, protein, and DNA levels brought on by this cytokine speed up wound healing. Two isoforms of FGF are generated by a single gene on chromosome 4.

- TGF-P, or Transforming Growth Factor-Beta

  This cytokine's name comes from the fact that altered cells in culture secrete it. High levels of TGF-p are found in platelet a-granules and activated lymphocytes. When a wound is healing, TGF-p induces fibroblasts to divide and produces more collagen and other proteins. TGF-p, when administered subcutaneously, similarly causes the development of granulation tissue.

Table 4.3 Partial list of growth factors used to accelerate the repair of chronicwounds in humans

Factor	Cell or Tissue of Origin	Selected Target Cells or Tissue	Selected Stimulatory (S) or Inhibitory (I) Actions	Clinical Trials
EGF	macrophages, monocytes	epithelium, endothelial cells	S: proliferation of keratinocytes, fibroblasts, and endothelial cells. S: keratinocyte migration.	venous ulcers
FGF	monocytes, macrophages, endothelial cells	endothelium, fibroblasts, keratinocytes	S: proliferation of endothelial cells, keratinocytes, and fibroblasts. S: chemotaxis, ECM	diabetic ulcers, venous ulcers, pressure ulcers
GMCSF	macrophages, fibroblasts, endothelial cells	hematopoietic, inflammatory cells, neutrophils, fibroblasts	S: chemotaxis of endothelial cells, inflammatory cells S: keratinocyte proliferation, activation of neutrophils	venous and arterial ulcers
HGH	pituitary gland	hepatocytes, bone, fibroblasts	S: IGF-1 production	venous ulcers
IL-1	lymphocytes, macrophages, keratinocytes	monocytes, neutrophils, fibroblasts, keratinocytes	S: monocytes, neutrophils S: macrophage chemotaxis	pressure ulcers
PDGF	platelets, macrophages, neutrophils, smooth muscle cells	fibroblasts, smooth muscle cells	S: proliferation of smooth muscle cells and fibroblasts S: chemotaxis S: ECM, contraction	diabetic ulcers, pressure ulcers
TGF-ß	platelets, bone, most cell types	fibroblasts, endothelial cells, keratinocytes, lymphocytes, monocytes	S: ECM, fibroblast activity S: chemotaxis I: proliferation of keratinocytes, endothelial cells	venous ulcers, pressure ulcers

- FGF = Fibroblast growth factor; EGF = Epidermal growth factor; GMCSF = granulocyte-macrophage colony-stimulating factor ; HGH = human growth hormone;IL-1 = interleukin-1; IGF-1 = insuling growth factor-1; PDGF = platelet-derived growth factor; TGF-ß = transforming growth factor-ß\

Wound Healing Factors:

Regional Variables

- Size, nature, and location of the wounds: An operation wound recovers more quickly. Wounds heal more quickly in locations with abundant blood flow (like the face) than in areas with insufficient blood flow (e.g., the foot). In areas where the skin adheres to bone surfaces, like wounds over the tibia, it is difficult to accomplish correct edge apposition and wound contraction.
- Vascular supply: Poor blood flow causes wounds to heal more slowly. Patients with varicose veins, for example, require more time to heal leg wounds. Bedsores are brought on by pressure-induced ischemia, which prevents them from healing. Ischemia caused by arterial obstruction, which usually affects diabetics' lower extremities, makes healing even more difficult.
- Infection: Wounds allow microorganisms to enter the body. Infection promotes the development of excessive granulation tissue, slows or prevents healing, and may result in scarring that is visibly deformed.
- Early motion, particularly prior to the formation of tensile strength, exposes a wound to continuing stressors, impeding or delaying healing.
- Ionizing radiation: Prior exposure impairs blood flow and delays wound healing. Radiation therapy inhibits the formation of granulation tissue, prevents contraction, and briefly halts cell division in a wound.
- Exposure to ultraviolet light has been shown to hasten the healing of wounds.

Systemic Factors:

- Regional vascularity:
- The vascularity of the region around the wound is significant. Systemic Factors: Poor healing is the result of impaired perfusion.
- Infections impede the healing of wounds.
- Metabolic status: Because diabetics are more likely to develop wound infections, diabetes mellitus is linked to a delayed rate of wound healing.
- Nutrition: Poor nutrition inhibits the healing of wounds. Zinc and Methionine are required for effective healing. If vitamin C levels are low, wound healing is hampered because collagen synthesis and secretion depend on it.
- Hormones: Corticosteroids hinder the healing of wounds by inhibiting the production of collagen, acting as an anti-inflammatory, and depressing protein synthesis. Growth hormone, androgens, estrogens, and thyroid hormones all have an impact on how quickly wounds heal.

Complications of Wound Healing:

- Poor Scar Formation: The major causes of poor scar generation and the problems that accompany it are inadequate granulation tissue formation or a failure to establish an appropriate extracellular matrix.
- Wound Dehiscence And Incisional Hernias: A wound dehisces or bursts due to increased internal pressure. Mortality from abdominal wound dehiscence is 30%.
- Ulceration: Leg wounds are a common example of a wound that develops an ulcer due to a lack of vascularization or blood supply.

- linked to severe atherosclerosis or varicose veins. As in the case of leprosy, tabes dorsalis, and diabetic peripheral neuropathy, persistent damage in sensory-impaired areas causes trophic or neuropathic ulcers.
- Significant Scar Formation: A hypertrophic scar or keloid is produced when extracellular matrix is deposited excessively at the site of the incision. On a histological level, both of these scar types show many, broad, and asymmetric collagen bundles.
- With more fibroblasts and capillaries than one would expect from such an ancient scar. It implies that there has been a "maturation arrest" or block in the healing process.
- When burns heal, contractures are very obvious. Joint movement may be hampered by skin and underlying connective tissue contractures. Food transit is obstructed by oesophageal or intestinal contractures[7]

DIABETES MELLITUS

Definition :

“Chronic hyperglycemia and abnormalities in protein, lipid, and carbohydrate metabolism brought on by deficiencies in insulin secretion or action, or both, are characteristics of diabetes mellitus”**.** [31-37]

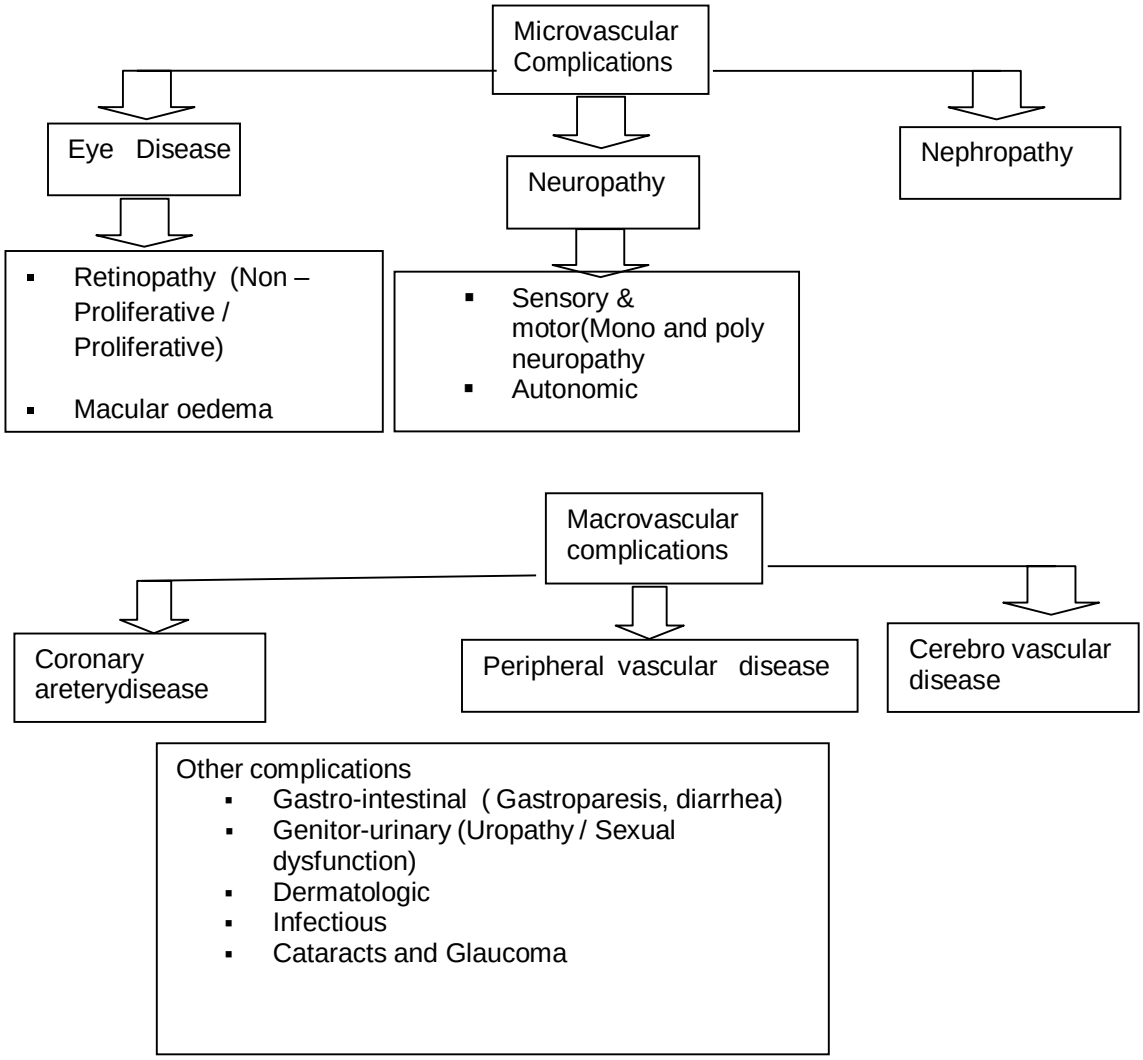
The following variables may be involved in the development of hyperglycemia, depending on the cause of the DM:

- Reduced insulin secretion
- Decreased glucose utilisation
- More glucose is produced

Chronic Complications of DM [31-37]

The majority of mortalities caused by diabetes mellitus are a result of the chronic consequences of the disease, which have an impact on multiple organ systems.

Fig. 4.11: CHRONIC COMPLICATIONS OF DIABETES MELLITUS



- The risk of developing chronic conditions increases when hyperglycemia lasts longer. They commonly appear in the second decade of diabetes.
- Many people with type 2 DM already have issues at the time of diagnosis because the disease frequently has a protracted asymptomatic stage of

hyperglycemia.

- Chronic hyperglycemia is the cause of the microvascular problems of both type 1 and type 2 DM.
- A decrease in persistent hyperglycemia protects or delays retinopathy, neuropathy, and nephropathy, according to extensive, randomised clinical trials of people with type 1 or type 2 diabetes.
- However, people with type 2 DM had two to four times more coronary heart disease events and mortality.
- These occurrences are correlated with fasting, postprandial, and Hb A 1 C plasma glucose levels.
- Dyslipidemia and hypertension are two additional variables that have a significant impact on macrovascular problems.

Mechanisms of complications

A theory explaining how hyperglycemia might result in the long-term problems of diabetes mellitus has been put forth.(Fig. 2.8).

Neuropathy And Diabetes Mellitus

- Type 2 diabetic individuals have a prevalence of 32 percent overall and above 50 percent in those over 60 years old for diabetic neuropathy.
- Diabetic neuropathy is correlated with both the duration of diabetes and glycemic management in type 1 and type 2 DM.
- Manifest as
    1. Mono-neuropathy
    2. polyneuropathy.
    3. Autonomic Neuropathy
- Both myelinated and unmyelinated nerve fibres are impacted.
- Diagnosis of diabetic neuropathy should only be made after other potential causes have been ruled out because it shares some clinical

features with those other neuropathies.

Neuropathy: Poly- and mono-neuropathy

- Distal symmetric polyneuropathy is the most prevalent type of diabetic neuropathy.
- • It seems to be:
- 1. Distal sensory loss, the most prevalent symptom at presentation
- 2. Hyperesthesia
- 3. Paresthesia
- 4. Dysesthesia

• One of the symptoms is a feeling of following that starts in the feet and progresses inward.

1. Numbness, \ Tingling
2. Sharpness
3. Burning

As neuropathy worsens, any combination of these symptoms may appear.

- Physical examination reveals
  1. Sensory loss.
  2. A decrease in ankle reflexes
  3. An abnormal sense of position.
- Lower extremities are often involved, and pain is typically noticeable while at rest and gets worse at night.
- Both chronic diabetic neuropathy and acute diabetic neuropathy, which lasts shorter than a year, have been described.
- As diabetic neuropathy progresses, the discomfort progressively fades, but the sensory loss in the lower limbs continues.
- Some of these persons may experience the onset of neuropathic pain along with an improvement in their glycemic control.

Treatment of diabetic neuropathy :

- Although better glycemic control is recommended and will speed up nerve conduction, diabetic neuropathy symptoms might not always get better.
- Avoiding neurotoxins like alcohol and supplementation of vitamins to make up for any deficiencies (BI2, B6, folate).
- Symptomatic therapy
- Since acute diabetic neuropathy pain may go away over the course of the first year, analgesics may be stopped as DM causes progressive neuronal damage.

- Chronic, painful diabetic retinopathy responds to

1. Tricyclic antidepressants, such as amitriptyline, desipramine, and nortriptyline, are effective
2. Gabapentin
3. NSAIDs (Avoid in renal dysfunctions)
4. Other (Mexilitine, Phenytoin, Carbamazepine, Capsaicin cream) It could be required to refer someone to a pain management center.

Lower Extremity Complications [31-37]

- For those with diabetes, foot infections and ulcers are a major cause of morbidity.
- These issues manifest more commonly in DM due to the interaction of several pathogenic variables.
- Peripheral artery disease, abnormal foot biomechanics, neuropathy, and slow wound healing.

Neuropathy :

More than 80% of individuals with foot ulcers have neuropathy.

Peripheral sensory neuropathy :

Interferes with the body's natural defences, allowing serious or repetitive minor injuries to occur to the foot, frequently without the patient being aware of them.

Motor and sensory neuropathy:

resulting in altered foot anatomical alterations and improper foot muscle mechanics

Autonomic neuropathy:

alters the superficial blood flow in the foot, which promotes anhidrosis and the drying of the skin, encouraging the emergence of fissures.

Peripheral arterial disease and poor wound healing:

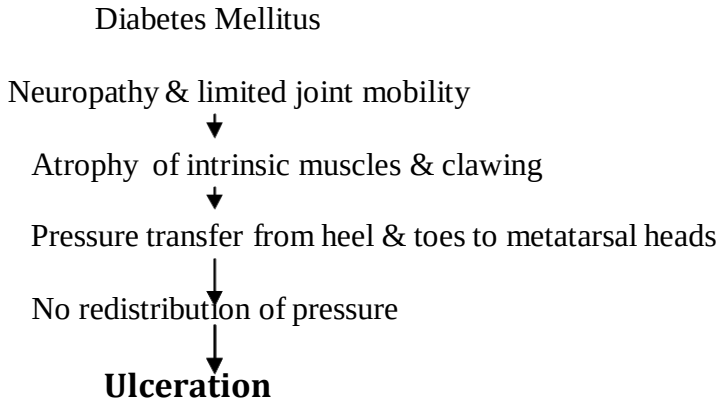
prevent minor skin fractures from healing, allowing them to grow and become infected.

Proprioception disorder:

Leads to improper weight bearing when walking and consequent callus or ulceration formation.

An estimated 15% of diabetics experience foot ulcers, and between 14% and 24% of those individuals will ultimately require foot amputation due to one or more ulcerations.

Fig 4.12 Pathogenesis of diabetic ulcers.[44-46]



1. High pressure at bony prominences

↓se plantar tissue thickness

↓

Weak intrinsic muscles of foot

↓

Imbalances of flexors & extensors causing clawing of foot

↓

Pulling away fat padding from metatarsal heads

2. Limited joint mobility [49]

Unknown etiology

↓

Collagen abnormality

↓

Thickening of skin, tendons & joint capsule Decreased tissue flexibility

↓

Increased plantar pressure

3. Trauma [50,51]

Trauma

↓

Intrinsic

↓

Repetitive stress from high pressure / Callus

Extrinsic

↓

Ill-fitting footwear

Guidelines for Diabetic Leg and Foot Examination:

History: It's critical to start by investigating the patient's history of diabetes. The "Diabetic triopathy" — a greater incidence of neuropathy, retinopathy, and nephropathy — is linked to a lengthy history of insulin-dependent diabetes.

In patients with severe triopathy, wound healing seems to take longer than usual. Severe triopathy is hypothesised to be linked to thickening of the basement membrane. Patients who have renal failure are most affected by this. When determining whether a patient is a candidate for an arteriography to further assess their arterial insufficiency, consideration of the patient's renal function is also crucial.

In addition to hypertension and tobacco use, hypercholesterolemia also contributes to the development of arterial insufficiency. Aggressive therapy of diabetic foot issues may be contraindicated in cases with severe heart disease.

Infection would appear quite likely if the patient recounts a fast expanding lesion that is accompanied by swelling or discharge, perhaps with red lines running up the leg and a fever or shaking chills.

In addition to causing lesions on its own, the common distal polyneuropathy seen in diabetics might conceal the signs of an infection and arterial insufficiency. ulcer growth over a pressure spot without any discomfort.

Patients may express discomfort, a burning sensation in their feet, a feeling of being encased in concrete or as though they are walking on glass, as well as agony. When a patient recounts a pain that runs up their legs like a knife, usually both legs are affected, and this may help to distinguish between neuropathic pain and ischemia pain. Patients with diabetic foot lesions typically have a history of ischemia, albeit again, these symptoms may be obscured by the presence of neuropathy. Peripheral vascular disease would unquestionably be more likely to exist if there was a history of

cardiac or carotid disease. The typical initial signs of peripheral vascular insufficiency include claudication or discomfort in specific muscle areas after exercise.

Sometimes, especially in smokers, inflow illness causes the ischemia, and the presenting sign may be buttock and thigh claudication. This leriche syndrome, which is brought on by aortoiliac artery occlusion, may cause male impotence.

Physical Examination:

Starting the inspection outside of the area of interest is beneficial. It is important to examine the carotids for bruits and the presence of pulses in arm. It should also be mentioned that atrial fibrillation may serve as an embolization source. An abdominal aortic aneurysm, which may also be the cause of distal emboli, should be thoroughly inspected in the abdomen.

Diabetic foot assessment includes identifying:

A. neuropathy,

B. vascular disease,

C. osteopathy.

D. Infection

Check the feet for

- o cracks, dry skin, and fissures.
- o Calluses, hyperkeratosis, infections, foot deformities, and gangrene.
- o Ulcers, sinuses, and cavities.

A. Neurologic Assessment of sensory and motor disturbances:

Testing with monofilament and tuning fork vibration

Reflexes in the tendon and pain

B. Distal pulses, the ankle brachial pressure index, transcutaneous oxygen saturation, and a duplex artery examination are used to evaluate vascularity.

C. An X-ray of the foot is used to diagnose osteomyelitis.

D. Infection is assessed whether it is superficial or deep**.**

All three stages frequently take place simultaneously. As a result, it is not rare for a patient with impaired circulation to have an infected neuropathic lesion. If the signs of ischemia are not recognized, significant neuropathy may mask them, making it difficult to administer the necessary treatments. A foot with severe neuropathy may simultaneously be warm, auto sympathetic, painless, and severely ischemic. Even a little procedure on a foot like that could result in gangrene.

✓ *Grade - 0*	*Foot at Risk*	*Prevention*
✓ *Grade-I*	*Localized, superficial ulcer*	*Antibiotics & glycemic control*
✓ *Grade-II*	*Deep Ulcer to bone, ligament, or joint Debridement,*	*Antibiotivs &glycemic control*
✓ *Grade-III*	*Deep abscess, osteomyelitis*	*Debridement, some form of amputation*
✓ *Grade-IV*	*Gangrene of toes, forefoot*	*Wide debridement and amputation*
✓ *Grade-V*	*Gangrene of entire foot*	*Below knee amputation*

THE BEST CURE IS PREVENTION:

The ultimate objectives of any contemporary team approach to the diabetic foot are to prevent ulceration and to prevent recurrence if ulceration has occurred.

According to **Wagner's Grade O**: Patients with foot abnormalities and varied degrees of neuropathy may be "at risk" of developing an ulcer or an infection. They require yearly neuropathy and vascular health assessments on a regular* basis. Therefore, the importance of wearing appropriate footwear and maintaining personal cleanliness cannot be overstated.

A regular schedule for foot and shoe hygiene examination and maintenance must be established by the diabetes patient and his family. Every patient needs to learn how to shake and look at his shoes before putting them on**.** The feet should be washed

daily with a light soap, rinsed, and dried thoroughly, paying particular attention in between the toes.

The physician or other healthcare professional should always lead by example. regulating blood sugar, weight, and blood pressure; quitting smoking; and promoting daily exercise

Exercise is crucial. Regular neurological and vascular exams are crucial. Early problem detection and fast problem reporting are encouraged.

The medical management principles

- Sent pus from ulcers for sensitivity testing and culture.
- Thorough blood sugar monitoring.
- Appropriate anti-diabetic therapy, such as oral hypoglycemic medications or insulin formulations
- Depending on the results of the culture and sensitivity report, broad spectrum antibiotics should be started at the beginning and switched to other antibiotics.
- Patients with infections that pose a risk to a limb need to be hospitalised. To establish proper serum levels, it is typically advised to administer antibiotics parenterally first.

The Principles of Surgical Management:

- Prompt identification and intervention.
- Management of blood sugar
- Rest to injured area
- Complete but cautious debridement of all affected regions, followed by drainage.

- Appropriate antibiotic coverage o Dressings and wound care
- Proper rebuilding of the vascular system
- Thorough follow-up, with updated footwear and podiatric devices.
- Additional expert advice as required.

Wagner Grade 1 foot: These patients have cellulitis and superficial ulcers. Antibiotics prescribed appropriately and, if necessary, debridement are used to control infection. Pressure that is applied repeatedly causes ulcers. Complete bed rest, the use of a total contact cast, a walker, braces, etc. reduce pressure. Vascular reconstruction is required to address associated vascular insufficiency.

Wagner Grade 2 and Grade 3 patients have foot with deep ulcers, either alone or in combination with other problems such osteomyelitis and abscesses. The mainstay of the treatment entails aggressive surgical debridement, excision of the contaminated bone, and, if necessary, vascular repair. Education on proper foot care is crucial to prevent recurrence.

Grades 4 and 5 Wagner feet:These patients have gangrene, either localised or widespread. A suitable minor or major amputation is used in treatment, followed by vascular repair.

Local Treatment of Diabetic Foot:

Both uncontrolled diabetes and infection have negative effects on each other.

The fundamental guidelines for managing any foot infection are:

- Complete bed rest
- Diabetes control
- Appropriate wound care
- Adequate wound culture
- Adequate antibiotic administration

- Adequate drainage of any infection

Drainage: Opening all abscesses, carefully probing, and opening all sinus tracts are all part of the drainage process. Necrotic tissue is also removed, and the resting foot is given free dependent drainage of pus. The pus needs to exit downward. Gas in the tissues may be the first thing seen on an x-ray or may frequently be felt as crepitus. This is a dangerous discovery that requires quick i.v. antibiotic treatment as well as the open drainage of all affected regions.

Gangrene toe or toes or even an open amputation, may need to be amputated in order to drain an infected area. These amputations are primarily drainage treatments. The infected joints in the toes and feet must eventually be removed since the avascular joints cannot tolerate infection well. Plan ahead and make an effort to recover tissue for a potential final wound closure after an infectious region has been contained.

Dressings:

The majority of foot infections may not necessitate deep incisions or significant debridement, but the fundamentals must always be kept in mind. The following uses for dressings are listed.

- Include wound drainage
- Clean up a wound
- Prevent injury to a region
- Prevent contamination of a space
- Encourage appropriate wound healing

The following tools are necessary for bedside foot care:

1. A sterile debridement kit with

Sharp debriding scissors; a blunt-ended needle wound probe; and smooth forceps

2. Sterilized nail clippers
3. sterile dressings for wounds
4. Culture tubes, paper tape, and tube gauge
5. Medicines: Chlorazene 0.25% in Dakin's solution

Vaseline gauge, normal saline, and antimicrobial Bactracin ointment ,2.5% Bactericidal Povidone Iodine

Dakins solution is a chemical that releases chlorine and helps with local debridement by releasing necrotic tissue and eliminating germs at the same time. Additionally, Dakin's aids in reducing foul odours that come from deeply infected wounds.

Open wounds must be packed with an unfilled gauge that has been soaked with a healing solution. For the debridement of a necrotic wound, it is advised to change the packing two or three times per day. By giving the packing enough time between dressing changes, it might start to dry out and provide a gentle debridement when it is removed from the wound. Guaze that hasn't been filled is advised for packing wounds. It's important to avoid packing the wound too tightly because doing so prevents drainage. If the dressing is put correctly, it won't fall off the foot or leg and risk exposing or injuring the wound. The ideal technique to avoid a tourniquet effect and lower the danger of impairing the circulation in the foot is to spiral or wrap the roller gauge in a figure-eight pattern.

Regular Foot Dressings:

- Moisten gauze with the proper solution and gently pack the wound.
- By cutting, folding, and taping the abdomen pad, you can create a heel cup.
- Spread two 4-inch guaze sponges across the toes.
- Using a spiral roller gauze and winding it in a figure-eight

pattern, secure the primary dressing, including the heel cup.

- Tape the roller guaze down with paper tape.

Casts / Splints:

After a skin graft, a splint or is used to immobilise the limb, protect the incision, and lessen contractures after a below-the-knee amputation. Any neuropathic extremity placed in a rigid plaster cast or splint runs the risk of developing pressure sores.

Dressings for amputation stumps:

Any dressing used on an amputation stump is adjusted to the wound's requirements. The bandage is applied for wound protection than to collect and control blood and fluids because the majority of amputation wounds lack drains.

A large standard foot dressing is used for first transmetatarsal amputations. To restrict plantar flexion and prevent tension on the fragile suture line, a posterior splint may be used. A below knee amputation (BKA) necessitates a large initial prosthesis.dressing to stop the anticipated initial bleeding. A posterior splint that stretches from the buttock crease to past the end of the stump is used to treat below knee amputations. The preferred splint is a knee immobiliser with plenty of padding. Knee flexion is a normal motion or reflex that, if left unchecked, might result in a catastrophic contracture. On the third or fourth post-op day, a patient with a BKA is often measured for a prosthesis. A patella-bearing prosthesis may be fitted and the patient can start moving around eight to ten days after surgery, depending on how the stump is recovering.

The initial above knee amputation (AKA) dressing is substantial and resembles the BKA dressing. Despite the fact that individuals with AKA

frequently hold up and stretch their aching thigh, splints are not employed. Muscle exhaustion normally causes the stump to fall down, which lessens the likelihood of developing a hip contracture.

Dressings for skin grafts are typically used as the surgeon sees fit. The most typical split thickness skin graft is a mesh graft. Because the open mesh of the mesh graft allows for proper wound drainage, it has proven to be the most effective.

The initial step in the treatment of diabetic foot lesion is bed rest. Rest in bed must be complete and ongoing. The head end should be raised by 6 to 8 inches for a patients with painful ischemic foot lesion and inadequate circulation. This position, sometimes referred to as arterial position or Reverse Trendlenberg position, permits blood to flow to the feet by gravity.

Non-Surgical Modalities to Enhance Healing:

A growing number of patients have non-healing and problematic wounds due to the rapidly ageing population and patients with many concurrent diseases. Many of these individuals are not candidates for surgery, or their wounds have not healed after surgery.

1. Growth Factors

The usage of growth factors like becaplermin, a recombinant platelet-derived growth factor made possible by recombinant DNA technology, has increased as a result of a better knowledge of the cellular basis of healing. Debridement improves the efficacy of becaplermin in treating chronic neuropathic ulcers, according to a study by Steed et al.

2. Human Skin Equivalents

The development of human epidermal cell culture dates back to the 1960s, when advancements in tissue culture technology made it possible to

replace modern human skin. These were obtained from tissue sample taken from the patient, and the dermis and epidermis were separated using trypsin.

After that, sheets of autologous epidermal tissue were created by growing the keratinocytes in vitro. These sheets offered just a 50 to 60 percent permanent take and were sensitive to handle. The absence of a dermal component, essential in skin grafting, meant that new tissue takes two to three weeks to fully develop.

More dermis grafts result in better cosmetic outcomes, less wound contracture and scarring, and increased tensile strength. Dermagraft, a live, metabolically active, immunologically inert dermal tissue, was created as a result of matrix development improvements.

Dermagraft is made of cultured neonatal fibroblasts that have been grown on a biodegradable mesh made of polyglycolic acid, and it contains typical dermal matrix proteins and cytokines. The tissue closely resembles human skin and creates extracellular proteins as it develops. Patients with full-thickness diabetic ulcers with acceptable perfusion were enrolled in two investigations by Gentzkow et al. and one by Pollak et al. Statistics as a whole reveal that 51 percent of patients who got a weekly treatment of Dermagraft for 12 weeks had a full recovery, compared to 31.7 percent in the control group.

The Food and Drug Administration granted Apligraf, another living tissue substitute, approval in 1998 to treat venous leg ulcers. Apligraf is formed of a layer of stratified epithelium attached to a matrix of bovine collagen packed with fibroblasts. The result is a tissue sheet with dermal and epidermal layers that resembles human skin in terms of metabolism and biochemistry. The dermoepidermal junction, on the other hand, is flatter and devoid of hair follicles, Langerhans cells, melanocytes, or lymphocytes.

293 people with non-healing venous ulcers got apligraf or compression therapy in a trial by Falanga et al. In contrast to the control group, which took 181 days longer to heal than the Apligraf-treated patients, 63 percent of them had recovered by six months as opposed to 49 percent of them.

3. Miscellaneous Topical Agent:

Collagen : In the proliferative stage of wound healing, collagen is essential. Exogenous collagen supplies, primarily purified bovine extracts, are offered as gels, particles, and dressings made of alginate. Extra protein is provided for tissue healing by exogenous collagen. As a foreign substance, it may also "jump-start" the healing process by bringing the chronic wound back into an inflammatory phase.

Donaghue et al. evaluated the alginate dressing to treat diabetic foot ulcers (Fibracol, Johnson & Johnson, Arlington, Texas). 75 patients were assigned at random to either a dressing made of gauze or collagen-alginate. At the end of the research, the collagen-alginate group had a mean reduction in wound size of 80.6 percent compared to 61.1 percent for the gauze group. Full healing was experienced by 36% of the gauze group and 48% of the collagen-alginate group.

Hyaluronic Acid: which is also connected to enhanced mitotic activity, affects the structure and organisation of the extracellular matrix. The plasma membranes of fibroblasts and other cells produce this high-molecular-weight polysaccharide. The ability of injured foetal tissues to heal without scarring and their high concentration of hyaluronic acid have spurred extensive research.

Beta Glucan : It is a significant cell-wall carbohydrate that is obtained from grains like barley and oats. The ability of beta glucan to connect to and

activate macrophage beta-glucan receptors is what gives it its biological effects.

In addition to macrophages, beta glucan products also stimulate neutrophils, natural killer cells, T cells, and B cells. According to theory, beta glucan promotes higher tissue granulation, speeds up fibroplasia and fibrogenesis, and enhances reepithelialization by boosting macrophage infiltration.

Both BCG matrix and Glucan II are forms of beta glucan. Both are offered as multifilament mesh dressings, and collagen is also infused into BCG matrix.

Silver Arlaes: Silver compounds are effective antimicrobials that aid in the healing process. Arglaes is an inorganic phosphate that resembles other substances including silver nitrate, oxide, and chloride. Small amounts of silver are fused with sodium and calcium phosphates, and when this mixture is exposed to water, the silver releases free silver ions .

4. Pharmaceuticals :

Oxandrolone : Oxandrolone is an anabolic steroid with anticatabolic and protein-sparing effects. It has a strong anabolic to low androgenic ratio. Combining exogenous anabolic agents with dietary intervention can increase protein synthesis by a factor of three to four compared to nutritional intervention alone.

Demling and De Santi looked at eight patients who had wounds that weren't healing and had at least 10% of their body weight loss. Over a period of four weeks, nutrition was improved without having a major impact on weight gain or healing. Over the course of 12 weeks, adding oxandrolone led to gains of about 4 pounds each week. Five wounds healed completely throughout this period, while three others did so partially.

5. Devices

Vacuum Assisted Closure (VAC): Argenta and Morykwas claim that intermittent negative pressure at 125 mmHg reduces bacterial counts while increasing rates of granulation tissue growth, blood flow, and nutrient flow.

The VAC system was created by Kinetic Concepts (San Antonio, Texas) based on these observations. A wound dressing (a sponge-like material loaded with charcoal) coupled via tubing to a wound canister and a pump that creates negative pressure make up the VAC. The seal required to create a vacuum is created by a transparent drape or film placed over the dressing. Different degrees of intermittent or continuous pressure can be set for the pump. The cainster is where exudate is gathered. Edema is also believed to be reduced by the VAC[15].

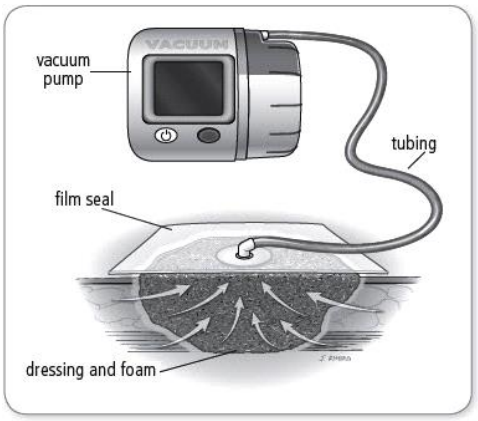


Fig. 4.13: VACUUM ASSISTED CLOSURE

Radiant Heat Bandage: Heat treatment has been utilised for a long time, particularly for musculoskeletal disorders, however it is rarely used as a wound healing technique. Heat improves the body's natural healing processes by increasing local blood flow and subcutaneous oxygen tension.

Patients with lower leg venous ulcers who used radiant heat bandages in clinical studies by Santilli and Robinson reported significant reductions in both wound size and pain over the course of two weeks with no side effects.[16]

Topical Hyperbaric Oxygen Therapy:

The goal of the therapy is to create an atmosphere with a pressure between 1.02 and 1.03 atm, which is supposed to promote neoangiogenesis, collagen synthesis, and fibroblast proliferation. Anaerobes, which are frequently an expected component of the flora on diabetic feet, can thrive in this deadly environment. In order to give topical hyperbaric oxygen, a sealed polyethylene bag is placed over the injured area, and 100 percent oxygen is delivered at a pressure between 20 and 30 mmHg. 2 to 2.5 hours are allotted for treatments.

In a Landau trial, 50 patients with diabetic ulcers received either low-energy laser treatment or topical hyperbaric therapy. Over the course of three months, 25 treatments were given on average. On average, 43 out of 50 patients had their ulcers clear up. [17]

Classification of Dressings:

Over time, wound dressings have changed to better protect the raw surface of the wound, absorb exudates, prevent infection, encourage the creation of granulation tissue, and foster the perfect environment for healing. According to its intended use, dressings can be divided into two broad categories:

1. Short-term application dressings should be reapplied
2. Long-term usage or skin substitutes:

They can further be separated into:

Use until full healing is achieved on recent "partial thickness wounds."

Used on "full thickness wounds" till autografting, semi-permanent

Depending on the chemical that was used to produce the dressing, they might be categorised as conventional, synthetic, or biological dressings.

Even further divisions of the dressings within each category include:

o Primary Dressing: An item of clothing in direct touch with the wound bed.

o Secondary Dressing: An additional layer of dressing over the primary dressing.

o A dressing with an adhesive portion and a central absorbent region is known as an "island dressing."

A. Conventional Dressings:

These dressings are made of fabric materials like gauze, but because they allow moisture to evaporate, the wound bed becomes dry and desiccated and foreign germs can enter the wound. As a result, compound dressings like Tulle grass—a wide mesh gauze saturated with medical-grade paraffin—were created. The dressing is mostly non-adherent as a result. In 1980, additional advancements included the use of antibacterial creams that combined absorbent dressings with carbolic acid, mercuric chloride, penicillin, and polymyxin. Paraffin has been replaced by silicone polymer in recent innovations. Since these dressings stick less to the wounds, changing them out is less painful.

In the middle of the 1980s, the idea of moist wound dressings began to gain popularity. According to a study by Atiyeh BS, El-Musa KA, and Dham R, complete and partial thickness cutaneous wounds healed more quickly when exposed to a moist environment. Keratinocytes can move over the surface of wounds more quickly and unhindered in a moist environment, allowing cytokines to have an impact on wound contracture and reepithelialization.[18]

The development of synthetic and biological dressings for the treatment of wounds came about as a result of study into the development of more sophisticated wound dressings due to the constraints of the standard

dressings for application on full thickness wounds.

B. Synthetic Dressings:

These are classified into

1. **Films :** They are uniform dressings made of a polymer sheet that has an adhesive coated on one side. The most widely employed Polymers include dimethyl aminoethyl methacrylate, polyurethane, polyethylene, polycaprolactone, and polytetrafluoroethylene. Film dressings are ideal for superficial wounds, but their inability to absorb fluids and their impermeability to gases and water enable fluid to build up beneath the dressing, which then allows exudate to leak out and foreign germs to enter the wound surface. They are therefore not practical for deeper wounds.

2. **Foams and sprays :** In order to maintain a moist environment at the wound's surface and provide thermal insulation, foam dressings are preferred to film dressings. They are sheets of foamed solutions of polymers such polyvinyl alcohol and polyurethane. They are also thin, supple, non-adherent, and gas permeable. For the treatment of irregular cavity wounds, two examples are lyofoam and silastic foam, both of which have the advantage of being moldable in place. However, using these dressings is difficult due to many anatomical locations. Spray dressings are completely portable and are more comfortable for the wound's surface. The majority of sprays are copolymers, such as Aeroplast, which is a copolymer of modified maleic resin ester and hydroxy vinyl chloride acetate. The development of dressings that mix spray and foam, including gelatin-based sprayable foam, is the result of further study.

3. **Composite dressings :** These are composed of at least two-layer laminates. The outside layer may function as a rate controller for water evaporation while the inner layer is designed for maximum stickiness and

elasticity. For composite dressings, the following categories apply:

a. **Hydrocolloid dressing :** These dressings are complex formulations made up of a variety of gelling and elastomeric adhesive substances. The most popular component used to absorb wound fluid is carboxymethyl cellulose.

1. **Granuflex :** This substance comprises of an inner hydrocolloid/polymer complex layer and an exterior protective layer made of polyurethane foam.

2. **Epigar** : A layer of reticulated polyurethane is bonded to an exterior sheet of microporous polytetra fluoroethylene to create this composite (PTFE) Its main benefits include adhesion, accessibility, sterility, long shelf life, and low cost.

3. **Biobrane** : This composite consists of an inner nylon mesh and a polydimethylsiloxane thin, porous membrane. Both superficial and deep donor sites were successfully employed with these by Stein and Roberts et al.

b. **Hydrogel sheets :** These sheets are 3-D networks of cross-linked hydrophilic polymers**.** They engage in exchanges with aqueous solutions. Polyethylene oxide, polyacrylamide, and polyvinylpyrrolidine are the most widely utilised polymers. They might be quite useful for usage as a first aid method for thermal burns because of their special cooling powers. Vigilon, a reinforced polyethylene oxide hydrogel enclosed in two polyethylene sheets, serves as an illustration. However, they are difficult to maintain and slippery to use when there is a large shear force.

c. **Hydrogel Amorphous :** These are identical to sheet hydrogels chemically, but the polymer has not been cross-linked to form a sheet. Alginate, collagen, and complex polysaccharides are present in traces in them. They excel in supporting autolytic debridement in wounds and supplying moisture to a dry wound eschar. It might be difficult to retain the amorphous hydrogel in the wound bed, though, because to its viscosity. Hydrogel wound dressings have

a quicker rate of closure and re-epithelialization than hydrocolloid wound dressings.

d. Gels :

There are numerous Gel-based treatments available in various forms. For instance, Wichterlie and Lim developed a hydrogel based on hydroxyethyl methacrylate that is biocompatible and non-toxic (HEMA). PHEMA PEG (Hydran) hydrogel, which is produced instantly on the wound surface, was later developed by Nathan et al. A brand-new type of wound dressing known as Geliperm was later developed by Wokalek et al. in 1977. It is formed by polymerizing agarose and acrylamide. A further alteration led to the creation of a cross linked polyethylene oxide hydrogel.

e. **Super Absorbents :** This dressing has an island design with a centre section of non-woven absorbent covering the superabsorbent particles enclosed inside, such as Combiderm, Conva Tec., etc. An exceptionally thin hydrocolloid serves as the adhesive portion of the dressing.

In cases of severe burn injuries with a dearth of skin donor sites, all of the aforementioned dressings are merely temporary coverings and are often utilised in conjunction with other techniques of alternate wound closure.

C. Biological Dressings :

These are generated from natural tissues, which often contain different formulations and mixtures of lipid, collagen, and elastin. They are significantly better than synthetic dressings because they:

1. To prevent the wound from drying out, restore the water vapour barrier.
2. Minimize heat loss from evaporation
3. Limit the exudate from wounds' loss of protein and electrolytes

4. Avoid bacterial wound infection to avoid sepsis for the patient and the wound.
5. Enable less agonising dressing changes
6. Allow painless joint movement
7. Make debridement of wounds easier
8. Make a good granulation tissue bed for deep wound autografts.
9. Can be utilised to determine whether a later autograft would succeed.
10. Shorten the recovery period for donor sites and partial thickness burns and
11. Enhance healing effectiveness, stop overactive fibroblasts, and lessen contraction.

The following are some examples of biological dressings: allograft, heterograft, embryonic membranes, embryofoetus, and newborn skins, films of reconstituted collagen from bovine and other sources, fibrin, cultured epidermal grafts, dermal matrix grafts, and cultured dermal matrix composite grafts.

Allograft :

Although it is most frequently taken from cadavers, allograft skin can typically be obtained from a family member. The most successful treatment for thermal injuries, particularly for severe full-thickness burns, is the use of fresh frozen lyophyilized allograft. Although they have been utilised as allografts, amniotic membranes are poor at preventing evaporative water loss that causes wound dehydration.

Xenograft :

Pig skin is the most often used material for these grafts because, despite

being different at the microscopic level, it mimics human skin structurally in terms of texture, adherence, and collagen content.

Allografts and xenografts have the fundamental disadvantage of developing blood vessels, which necessitates their removal unless immunosuppressive drugs are employed to prevent rejection. Overusing immunosuppressive drugs also increases the risk of wound infection.

As a result, the following are the main drawbacks of employing allografts and xenografts:

1. Non-uniform
2. difficult and expensive to achieve
3. Complicated to clean up and store aseptically
4. Possess a limited shelf life
5. Possibility of antigenic
6. Possess a chance of strange pollutants and
7. One or more complex elements may cause hypersensitivity.

Collagen Dressings :

In light of collagen's distinctive structural and functional properties, the creation of collagen dressings makes sense. The fibril or fibre is the collagen aggregate form with the most distinct characteristics. A number of structural requirements are placed on the molecules contributing to the creation of such aggregates by the packing arrangement for molecules within collagen fibrils. The collagens not only provide mechanical support for the connective tissue but also serve as a crucial substrate for cellular adhesion and migration. As a result, collagen is regarded as a crucial morphogenetic element in the development of the embryo and the process of regeneration.

Collagen has a hydrophilic character due to the high concentration of

diamino dicarboxylic amino acids and carbohydrate moieties in its molecular structure, which results in a surface shape that is optimal for cell attachment.

Engineered Skin Substitutes: Since 1980, bovine collagen has been used extensively as a culture substrate. By culturing convergent keratinocyte sheets on a simple Type I collagen contracted by the addition of cutaneous fibroblast, Bell et al. successfully transplanted the gels to cover whole thickness wounds. Since then, modifications and enhancements to the culture conditions have been made, such as the use of hydrated collagen gels for the culture of fibroblasts, which caused the collagen fibrils to be reorganised in the plane of cell spreading through the binding interaction between cell processes and collagen molecules. Additionally, cells growing on collagen lattice actively participate in the manufacture of glycosaminoglycans, which also significantly contributes to the acceleration of healing. In order to create a superior skin substitute, keratinocytes might be cultivated over these reorganised gels, which act as a dermal-like matrix.

Keratinocytes Keratinocytes developed on a substrate made of fibrous dermal collagen show the same ultrastructural alterations that are often connected to differentiation. Continuous sheets with typical desmosomal connections quickly form as a result of cell proliferation on collagen. By employing human free dermal collagen stabilised with low quantities of glutaraldehyde for the growth of human epidermal cells, more advancements in the manufacture of skin substitutes were made. Keratinocytes grown on such porous substrates are exposed to an air/liquid interface, which enhances their physiological environment and enables them to differentiate more fully and more closely resemble the parent tissue. According to the permeable substrate utilised to sustain the cells, this type of air/liquid culture systems is categorised into three groups.

1. **Synthetic Membranes :** The use of cadaveric allograft skin was

discontinued following the excision of burn wounds in favour of a temporary living skin replacement made of human neonatal fibroblasts grown in biobrane, a biosynthetic dressing material.

2. **Dermal Equivalent** : Keratinocytes may be cultured atop live fibroblasts located in constricted collagen gel in order to form a composite dermal epidermal skin substitute that enables strong adhesion of human keratinocytes to the dermal substrate for graft survival on the wound. The cultured composite dermal epidermal skin substitute has been further enhanced by the use of matrix peptides like RGD (arginine -glycine aspartic acid peptide). Since these peptides strengthen cellular adherence to the dermal substrate as well as interactions between cells and their matrix.

3. **Dead De-Epidermized dermis :** The acellular de-epidermized dermis showed to be less immunogenic and to serve as a natural foundation for the building of artificial skin, making it a useful treatment for burns with significant connective tissue loss. These human skin composites performed better as skin substitutes on wounds because they were made of healthy human keratinocytes and fibroblasts on human acellular, de-epidermalized dermis.[14,15]

Cost consideration :

The expense of treating chronic illnesses has become increasingly essential in today's globalised world, and a surgeon's ability to manage chronic wounds and its financial effects is crucial. Topical sucralfate is thought to be more affordable than traditional dressing methods because of the following reasons:

- Less time is needed for the wound to granulate or heal.
- A better response to defensive therapy techniques like flaps, grafts, etc. After topical therapy is finished

- sucralfate is less expensive than other dressing materials.

As a result, topical sucralfate moist dressing is discovered to be an effective and affordable method for treating chronic lower leg ulcers.[21]

REGARDING THE DRESSING USED IN THIS STUDY:

TOPICAL SUCRALATE DRESSING :

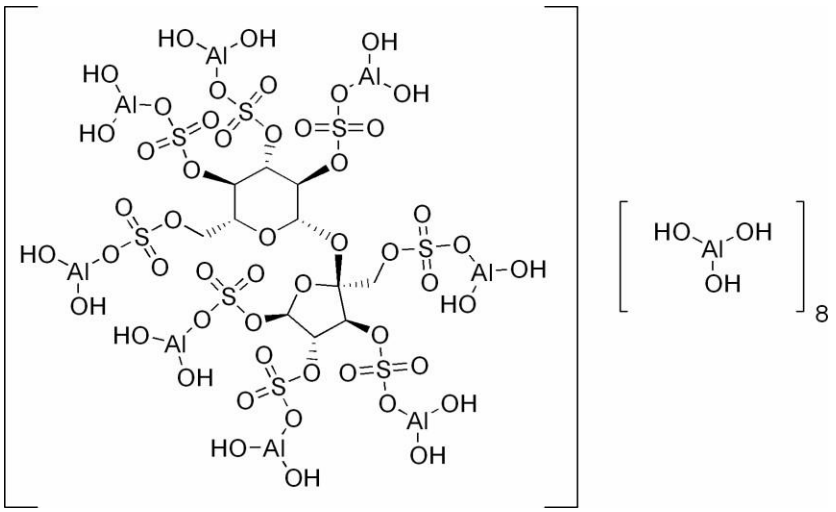
Sucralfate is oral gastrointestinal drug that is primarily used to treat active duodenal ulcers. Additionally, stress ulcers and gastroesophageal reflux disease (GERD) are both treated with sucralfate.

Sucralfate is a sucrose sulfate-aluminum complex that binds to the hydrochloric acid in the stomach and functions as an acid buffer with cytoprotective qualities, in contrast to other types of drugs used to treat peptic ulcers. Sucralfate was approved by the American Food and Drug Administrationo (FDA) in 1981.

CHEMICAL DATA :

Formula : $C_{12}H_{54}Al_{16}O_{75}S_{8}$ Mol. mass: 2086.75 g/mol

STRUCTURE OF SUCRALFATE:



SYSTEMATIC NAME: Hexadecao—hydroxytetracosahydroxy[8-[1,3,4,6-tetra-O-sulfo-β-Dfructofuranosyl-α-D-glucopyranoside tetrakis(hydrogen sulfato)8-)]] hexadecaaluminum

Leg ulcers, diabetic ulcers, decubitus ulcers, as well as the quick and effective healing of skin imperfections like burns, skin cracks, scratches, and other non-infected wounds, have all been studied in relation to sucralfate.

Sucralfate reacts with the skin damage to create a barrier of protection over the affected area.

It is well known that sucralfate has been used for many years to treat stomach and duodenal ulcers. It is given as a tablet and a suspension. Sucralfate lines the mucosas of the stomach and duodenum in these pharmacological forms by producing a covering epithelium that protects the surface of the injured tissue. Contrary to what was said earlier, traditional forms of sucralfates have a substantially greater capacity to adhere to injured skin epithelium and their effect is independent of skin pH. Clinical research have shown that several non-contaminated sources of effective skin renewal and wound healing.

Palliative, frequently futile treatments are frequently used to treat venous ulcers. It is clear that wound healing requires angiogenesis, cell proliferation, extracellular matrix remodelling, tissue inflammation, and proper re-epithelialization.

In order to effectively treat venous ulcers, a medicine should have the ability to enhance each of these basic factors.

Sucralfate is a basic sucrose sulphate aluminium compound that shares structural similarities with heparin but lacks its anticoagulant action. Despite sharing a structural resemblance with sucrose, sucralfate is not metabolised as a sugar in humans.

Honey, whose use was first documented by the Egyptians in 1600 BC, is one of the oldest substances used in wound care. In recent years, there has been

increased interest in the use of sucrose as a wound dressing. Many lesions, including bedsores and diabetic ulcers, have been successfully treated with granulated sugar or pastes consisting of caster and icing sugar.

Recent research has demonstrated that sucralfate stimulates the expression of various factors involved in tissue repair processes as well as EGF and other factors. Additionally, it has been shown that sucralfate has stimulating effects on vascular factors, including angiogenesis, which are crucial for tissue repair. Topical sucralfate has been studied successfully for second and third degree burns, dystrophic epidermolysis bullosa, peristomal and perineal dermatoses, moist radiotherapy desquamation, erosion and ulceration of the perineal area, vaginal ulceration, and non-healing, full-thickness venous stasis ulcers resistant to 8 weeks of conventional therapy.

Sucralfate may be able to bind basic fibroblast growth factor, preventing it from degrading and allowing it to function as an angiogenetic protein.

Furthermore, it has been demonstrated that sucralfate inhibits the synthesis of interleukin-2 and interferon- from damaged skin cells and promotes the proliferation of keratinocytes and dermal fibroblasts in culture.

MOA:

The "1x1x1" mechanism of action, which states that sucralfate has three main actions one for acute prevention, one for both acute and chronic protection, and one for chronic ulcer healing defines the activity of sucralfate at the moment.. The maintenance of mucosal vascular integrity and blood flow, which ensures prompt epithelial restitution to repair superficial lesions, is one of sucralfate's most important acute actions.

The enhanced binding of sucralfate to fibroblast growth factor and epidermal growth factor enhances angiogenesis, granulation tissue, and epithelization for ulcer

healing. The molecular mechanism of action for sucralfate may be explained by the 1x1x1 mechanism of action theory, which focuses on the significant effects of the drug's actions (which include more than a dozen acts).

Sucralfate wound healing methods may include the following: Stimulation of fibroblast proliferation encouraging the growth of granulation tissue; decreasing collagenase activity and inhibiting glucocorticoid activity; inhibiting microorganisms directly or indirectly through inflammatory cell action; and neovascularization.

Sucralfate (sucrose octa-sulphate) in suspension was tested for its ability to combat 128 strains of Gram-negative bacteria in vitro. Both bactericidal activity for 68 isolates and inhibitory activity for all isolates were demonstrated. Sucralfate's in vivo therapeutic success may be attributed to its inhibitory and bactericidal antibacterial action.

5.MATERIAL AND METHOD

SOURCE OF DATA :

Patients who have been hospitalised to surgery wards or who are visiting the opd with lower limb ulcers that have persisted for more than two weeks at **BLDE[DU] SHRI B.M. PATIL MEDICAL COLLEGE, HOSPITAL AND RESEARCH CENTER, VIJAYAPUR** after obtaining ethical clearance from the ethical committee

STUDY PERIOD:

OCTOBER 2020 to NOVEMBER 2022.

METHOD OF COLLECTION OF DATA:

Patients will be randomized into two groups of study and control group based on alternate numbers.

Out of 224, patients, 112 will take treatment in the form of 5%povidine iodine dressings, and 112 will take treatment with sucralfate dressing.

The nature of the study to be given will be explained to the patients, and written informed consent will be obtained from them before enrollment.

Photographs of the ulcers both before and after dressing will be taken.

The wound area will be calculated by multiplying the length by the width following a comprehensive clinical evaluation and ongoing research (ulcer should be less than 10cm x10 cm).

For both groups, the dressings will be changed every other day. Three weeks of alternate-day follow-up will be given to the patients in both groups. Plannimetry will be used to measure the result, or the area of the target ulcer, using a clear graph sheet. Results will be calculated by using the student 't' test.

DRESSING TECHNIQUE:

For 5%povidone iodine dressing:

The ulcer will be cleaned with normal saline, and a povidone iodine-soaked gauze piece will be kept over the ulcer which will be covered with a pad and roller bandage.

For topical sucralfate dressing :

The ulcer will be cleaned with Normal Saline. Sucralfate cream [brand – Sucral] will be applied over the ulcer, and it is covered with a pad and roller bandage.

The wounds in both the groups will be inspected, and the wounds will be compared in terms of:

- The amount of granulation tissue fill up.
- Reduction in mean ulcer surface area.
- The Number of days required for healing.

After 21 days, healing of the wound will be assessed by the following parameters

- The amount of granulation tissue fill up.
- Reduction in mean ulcer surface area

6. INCLUSION AND EXCLUSION CRITERIA

INCLUSION CRITERIA:

1. Patients in the age range of 12 to 75.

2. Lower limb ulcers that have been present for more than two weeks.

3. Less than 10 × 10 cm in size

4. Both Diabetic and non-diabetic patients.

EXCLUSION CRITERIA:

1 Vascular insufficiency patients

2 Immunocompromised patients

3 Osteomyelitis associated with it, ulcers with exposed bone or tendon, or the presence of a Charcot joint, diabetic toe gangrene.

4. Skin malignancy

5. Diabetic ketoacidosis and Critically ill patients

7.SAMPLING

TOTAL SAMPLE SIZE:

With the Anticipated Proportion of area reduction of the wound in Conventional dressing and Sucralfate in Diabetic ulcers 14.6 **%** and 35% resp, the study would require a sample size of 112 per group. (i.e. a total sample size of 224 assuming equal group sizes), to achieve a power of 95% for detecting a difference in proportions between two groups at a two-sided p-value of 0.05.

Formula used

- $\mathbf{n= \frac{(z_\alpha+z_\beta)^2\ 2\ p*q}{MD^2}}$

Where Z= Z statistic at a level of significance
MD= Anticipated difference between two proportions
P=Common Proportion
q= 100-p

STATISTICAL ANALYSIS:

- The data obtained will be entered in a Microsoft Excel sheet, and statistical analysis will be performed using a statistical package for the social sciences (Version 20).
- Results will be presented as Mean ±SD, counts and percentages, and diagrams.
- For normally distributed continuous variables between two groups will be compared using independent t-test for not normally distributed variables Mann Whitney U test will be used. Categorical variables between the two groups will be compared using the Chi-square test/Fisher\s Exact test.
- $p<0.05$ will be considered statistically significant.

INVESTIGATIONS / INTERVENTIONS:

Investigations required in this study are routine investigations.

Those are:

1. Complete blood count, RBS, HbA1c
2. Tests for serology (As per Universal Safety Precautions).
3. Culture sensitivity of the discharge from the ulcer
4. X-ray of the local part whenever indicated
5. Chest x-ray, ECG whenever indicated
6. LFT, Blood urea, serum creatinine whenever indicated

REVIEW OF LITERATURE:

Reddy M.V. (2019) conducted a prospective research on 50 diabetic foot ulcer patients who were admitted inside and clinically assessed. Group A (n = 25) and Group B (n = 25) of patients were separated. Sucralfate was applied topically to patients in Group A, while honey was applied topically to patients in Group B. When the wounds in both groups were examined after 7 days, 14 days, and 21 days, it was discovered that the mean ulcer size had decreased in both groups on days 7, 14, and 21 ($p>0.5$), with Group A experiencing a greater percentage of mean ulcer size reduction than Group B at the end of 21 days (p value > 0.05). 10 (or 40%) of the ulcers in Group A and 9 (or 36%) of the ulcers in Group B were fully epithelized. The primary end point of the trial, complete epithelization of the ulcer or ulcer bed ready for split skin grafting, occurred at 21.04 days in Group A and 23.20 days in Group B (P value 0.05). So they came to the conclusion that while topical sucralfate and honey were both beneficial in accelerating the healing of diabetic foot ulcers, topical sucralfate was superior to honey for local application.

Gulati S.(2014) did a study to compare the healing of chronic wounds with honey dressing vs. Povidone iodine dressing in adult subjects with chronic wounds of ≥6 weeks of duration, attending wound care clinic in Surgical Out Patient Department of All India Institute of Medical Sciences, Surgical Out Patient Department of Jai Prakash Narayan Apex Trauma center, New Delhi. Forty five subjects were taken into two groups i.e., Honey & Povidone iodine dressing group. Dressing was done on alternate day basis for 6 weeks of followup period. Main outcome measure was complete healing at 6 weeks. Wound healing status was assessed at 2 weekly intervals till 6 weeks. Seven out of 22 subjects in honey treated group achieved complete healing as compared to none

out of 20 subjects in Povidone iodine treated group. There was a significant decrease in the wound surface area, pain score & increase in comfort score in Honey dressing group in comparison to the Povidone Iodine group at 0.05 level of significance. Honey dressing is highly effective in achieving healing in chronic wounds as compared to Povidone iodine dressing.

Rani BS (2021) did a study on sucralfate in comparison with the povidine iodine in healing of diabetic foot ulcers. He selected 100 patients, of whom he treated 50 with povidone iodine dressings and another 50 with sucralfate dressings. Following therapy, each patient underwent a thorough clinical assessment. Additionally, pertinent research was conducted. After thorough debridement, the initial wound area was measured for length x width. For three weeks, patients in both groups received dressings once daily and subsequently underwent daily follow-up monitoring. They found results as statistically significant and concluded that the ulcers in subjects treated with sucralfate dressing (S group) contracted more than the ulcers in the patients treated with povidone iodine.

Nagalakshmi, et al. (2017) conducted a comparison study of the effectiveness of topical sucralfate and conventional dressing in the management of diabetic ulcer in 100 patients at the Tirunelveli Medical College Hospital, Tirunelveli, and came to the conclusion that sucralfate dressing is an effective modality to facilitate area of wound reduction in patients with diabetic foot ulcers and can be used as an adjunct to conventional mode of treatment.

Preethi SP (2019) did a comparative study of efficacy and cost effectiveness of topical sucralfate and conventional dressings in diabetic ulcers in 100 patients over a period of two years 2017-2019 in JSS hospital Mysore and concluding that Topical sucralfate considerably speeds up the healing of wounds by encouraging the growth of granulation tissue, which in turn lowers bacterial load, slough, and discharge.

Civele.et al. (2007) did a study on Effect of sucralfate , an agent for gastroprotection on the healing of split thickness skin graft donor sites in 32 patients from April 2004 to December 2005 in Diskapi Beyazit Hospital , Ankara, Turkey and concluding that the healing on the sucralfate areas was inevitably and strikingly more rapid than the regular paraffin gauze-applied areas by 3.7 days.

8. RESULTS

TABLE NO. 8.1: SEX DISTRIBUTION

		GROUP				Total	
		CONTROL GROUP		STUDY GROUP			
		Count	% in group	Count	% in group	Count	% in group
SEX	FEMALE	22	19.6%	20	17.9%	42	18.8%
	MALE	90	80.4%	92	82.1%	182	81.2%
TOTAL		112	100%	112	100%	224	100%

Incidence of chronic lower limb ulcers were more in males (81.2%) as compared to females (18.8%).

GRAPH NO. 1 : SEX DISTRIBUTION

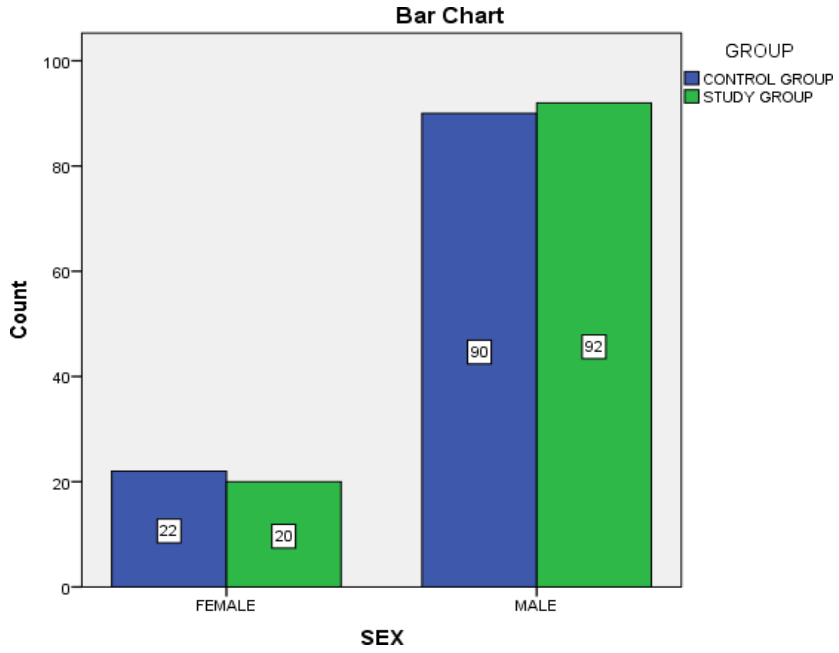


TABLE NO.8.2: MEAN AGE

Variables	Group	N	Mean	SD
AGE	CONTROL GROUP	112	52.446	13.495
	STUDY GROUP	112	52.339	15.42

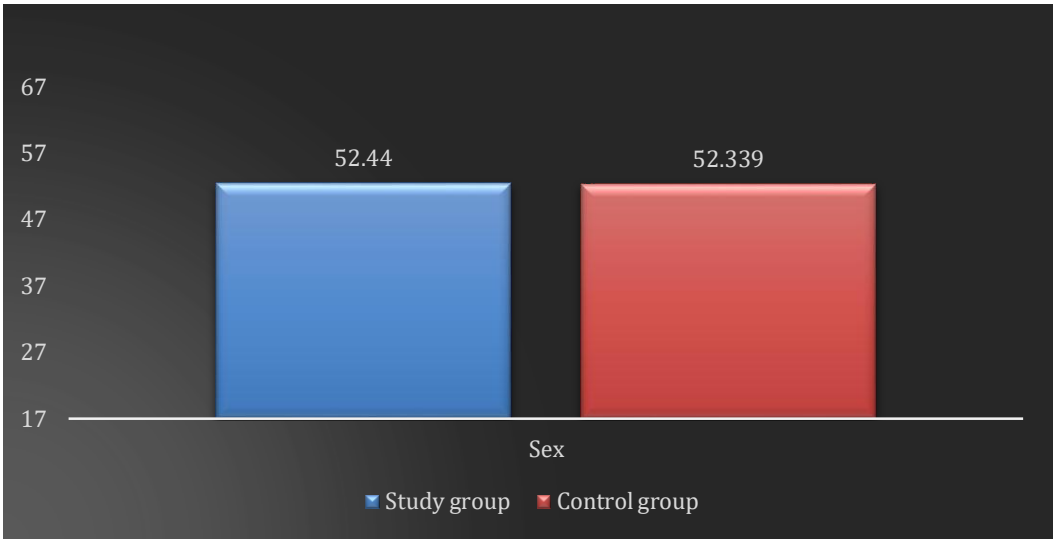
The mean age in the study group was 52.339 years and in the control group was 52.446 years

TABLE NO. 8.2.1: AGE DISTRIBUTION

Age Distribution	Count	Percentage
12-20	4	1.7%
21-30	18	8.03%
31-40	30	13.3%
41-50	47	20.9%
51-60	53	23.6%
61-75	72	32.1%

Majority of the patients in our study are in between 61-75years age group i.e about 72 patients(32.1%)

GRAPH NO.2 MEAN AGE:



GRAPH NO. 2.1: AGE DISTRIBUTION

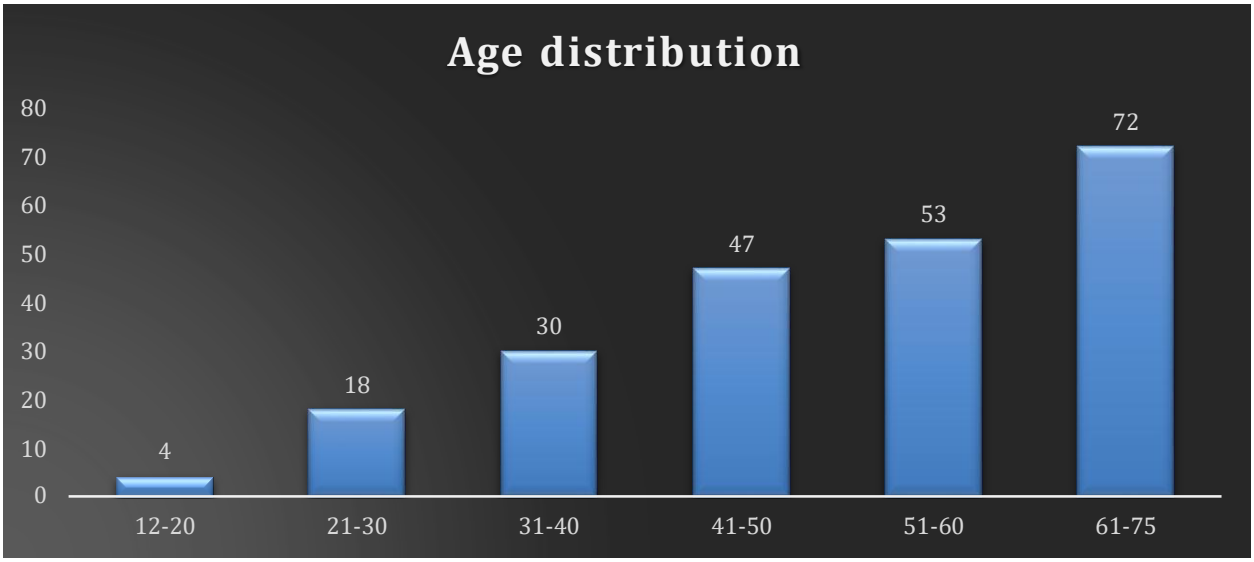


TABLE 8.3: ONSET

		GROUP			
		CONTROL GROUP		STUDY GROUP	
		Count	% in group	Count	% in group
TRAUMATIC/SPONTANEOUS	SPONTANEOUS	82	73.2%	79	70.5%
	TRAUMATIC	30	26.8%	33	29.5%
	Total	112	100%	112	100%

In this study, 71 % of the ulcers were spontaneous in origin 29 % were traumatic in origin

GRAPH NO 3: ONSET

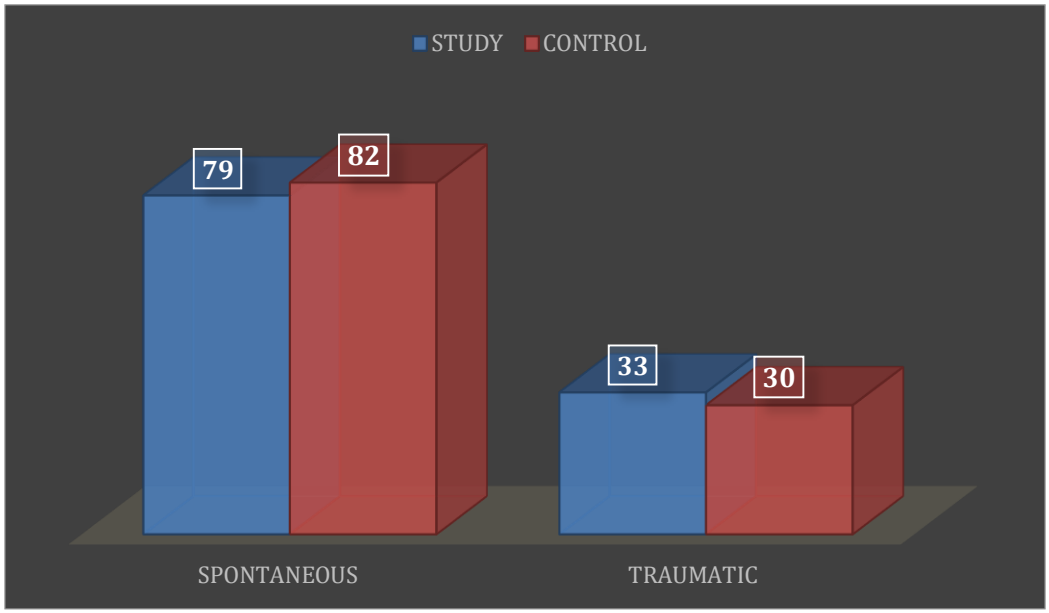


TABLE 8.4: SITE OF ULCER

		GROUP				Total	
		CONTROL GROUP		STUDY GROUP			
		Count	% in group	Count	% in group	Count	% in group
SITE	D OF FOOT	54	48.2%	71	63.3%	125	55.8%
	D OF FOOT, MS OF LEG	19	16.9%	16	14.2%	35	15.6%
	MS OF LEG	16	14.2%	8	7.1%	24	10.7%
	MM OF FOOT	6	5.3%	5	4.4%	11	4.9%
	P OF FOOT	5	4.4%	3	2.6%	8	3.5%
	LS OF LEG	5	4.4%	4	3.5%	9	4.01%
	D OF FOOT, MS OF FOOT, LS OF FOOT	4	3.5%	2	1.7%	6	2.6%
	LM OF FOOT	3	2.6%	1	0.8%	4	1.7%
	D OF FOOT, LS OF LEG	0	0%	2	1.7%	2	0.8%
TOTAL		112	100%	112	100%	224	100%

Most of the patients in our study has ulcer over dorsum of foot about 125 patients(55.8%)

*D OF FOOT – DORSUM OF FOOT, P OF FOOT- PLANTAR OF FOOT, MM OF FOOT – MEDIAL MALLEOLI OF FOOT, LM OF FOOT – LATERAL MALLEOLI OF FOOT, MS OF LEG – MEDIAL SIDE OF LEG, LS OF LEG – LATERAL SIDE OF LEG.

TABLE 8.5: DIABETES MELLITUS

		GROUP				Total	
		CONTROL GROUP		STUDY GROUP			
		Count	% in group	Count	% in group	Count	% in group
DM: PRESENT/ABSENT	ABSENT	84	75%	84	75%	168	75%
	PRESENT	28	25%	28	25%	56	25%
	TOTAL	112	100%	112	100%	224	100%

In this study total of 56 (25%) individuals were diabetic and 168(75%) individuals are non diabetic.

TABLE 8.5.1: AGE DISTRIBUTION IN DIABETES MELLITUS

		GROUP		Total
		CONTROL GROUP	STUDY GROUP	
		Count	Count	Count
	21-30	1		1
	31-40		1	1
	41-50	7	6	13
	51-60	7	12	19
	61-75	13	9	22
TOTAL		28	28	56

Most of the diabetic patients are in the age group of 61-75 years

TABLE 8.5.2: SEX DISTRIBUTION IN DIABETES MELLITUS

		GROUP		Total
		CONTROL GROUP	STUDY GROUP	
		Count	Count	Count
SEX	FEMALE	2	7	9
	MALE	26	21	47
TOTAL		28	28	56

TABLE 8.5.3: DURATION OF DIABETES MELLITUS

		GROUP		Total
		CONTROL GROUP	STUDY GROUP	
		Count	Count	Count
	0-5yrs	9	12	21
	5-10yrs	7	5	12
	10-15yrs	2	2	4
	15-20yrs	6	6	12
	>20yrs	4	3	7
TOTAL		28	28	56

TABLE 8.5.4: HBA1C LEVELS IN DIABETES PATIENTS

		GROUP		Total
		CONTROL GROUP	STUDY GROUP	
		Count	Count	Count
	6-8%	5	8	13
	8-10%	9	13	22
	10-12%	11	2	13
	12-14%	2	0	2
	>14%	1	5	6
TOTAL		28	28	56

GRAPH NO 4: DIABETES MELLITUS

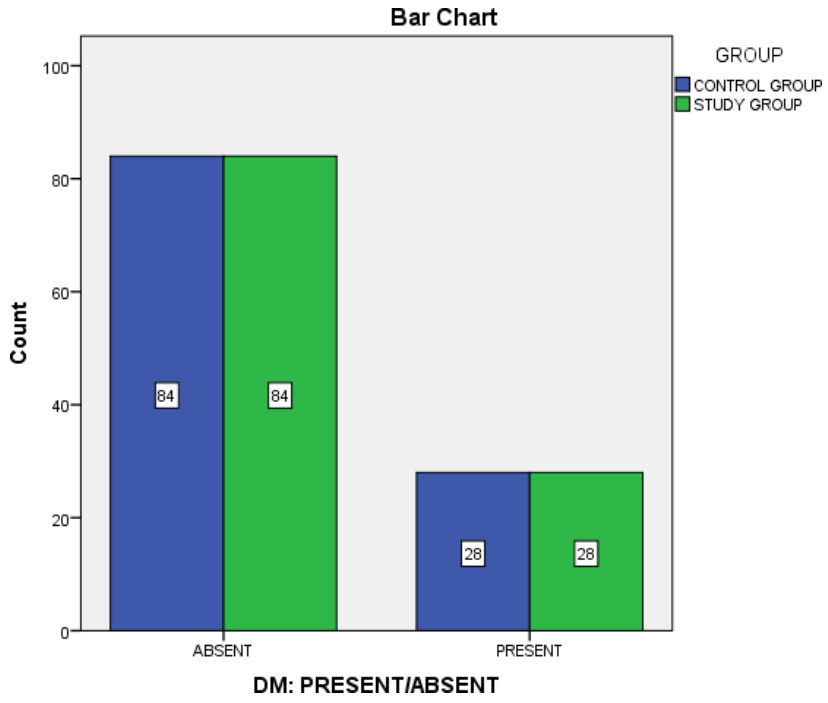


TABLE NO 8.6: CULTURE & SENSITIVITY – ON FIRST VISIT

			GROUP		Total
			Study	Control	
	KP	Count	25	34	59
		%	22.3%	30.4%	26.3%
	PA	Count	31	23	54
		%	27.6%	20.5%	24.1%
	SA	Count	23	21	44
		%	20.5%	18.8%	19.6%
	EC	Count	8	13	21
		%	7.1%	11.6%	9.4%
	PM	Count	0	3	3
		%	0%	2.7%	1.3%
	EF	Count	2	1	3
		%	1.8%	0.9%	1.3%
	AB	Count	0	1	1
		%	0%	0.9%	0.9%
	STERILE	Count	23	16	39
		%	20.5%	14.3%	17.4%
Total		Count	112	112	224
		%	100%	100%	100%

In the study group 23 were positive for SA, no patients for PM, 31 for PA, 8 patient showed EC, 25 patients showed KP ,2 patients showed EF, 23 of them did not show any growth. In the control group 21 of them were positive for SA. 3 of them for PM, 23 for PA , 34 for KP, 1 for AB, 1 for EF and 13 of them for EC. 16 of the patients did not show any growth

*KP - KLEBSIELLA PNEUMONIA, PA - PSEUDOMONAS AURAGINOSA, SA - STAPHILOCOCCUS AUREUS, EC - ESCHERICHIA COLI, PM - PROTEUS MIRABILUS, EF - ENTEROCOCCUS FAECALIS, AB - ACINETOBACTER BAUMANNII

TABLE NO 8.7: CULTURE & SENSITIVITY – AFTER 14 DAYS

		GROUP				Total	
		CONTROL GROUP		STUDY GROUP			
		Count	% in group	Count	% in group	Count	% in group
PUS CULTURE SENSITIVITY(AFTER) (POSITIVE/NEGATIVE)	NEGATIVE	51	45.5%	105	93.8%	156	69.6%
	POSITIVE	61	54.5%	7	6.2%	68	30.4%
	Total	112	100%	112	100%	224	100%

Negative culture in 105 patients in the study group, whereas 61 patients in the control group still had a positive culture.

GRAPH NO 5: PUS CULTURE AND SENSITIVITY

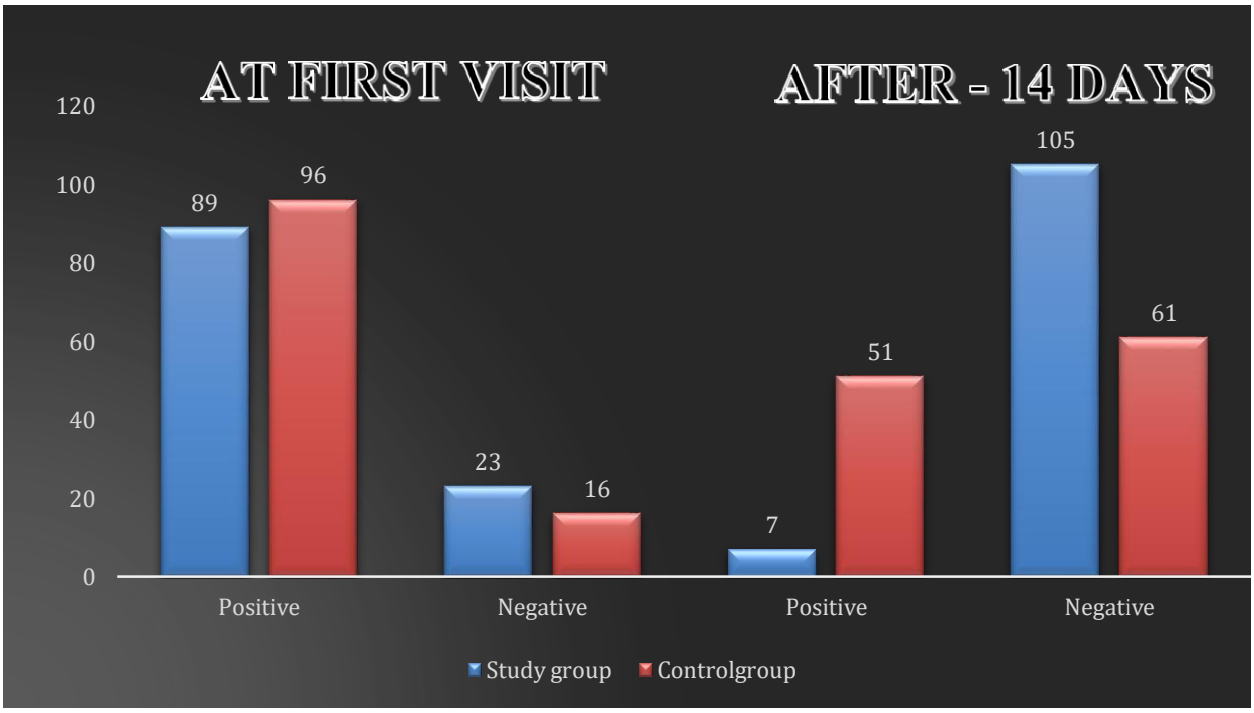


TABLE NO 8.8: AMOUNT OF GRANULATION TISSUE FILL UP

		GROUP				Total	
		CONTROL GROUP		STUDY GROUP			
		Count	% in group	Count	% in group	Count	% in group
GRANULATION TISSUE FILL UP IN 2 WEEKS (COMPLETE/PARTIAL)	COMPLETE	71	63.4%	100	89.3%	171	76.3%
	PARTIAL	41	36.6%	12	10.7%	53	23.7%
	Total	112	100%	112	100%	224	100%

In this study complete granulation tissue fill up was shown in 100(89.3%) patients in study group and 71(63.4%) patients in control group

GRAPH NO 6: AMOUNT OF GRANULATION TISSUE FILL UP

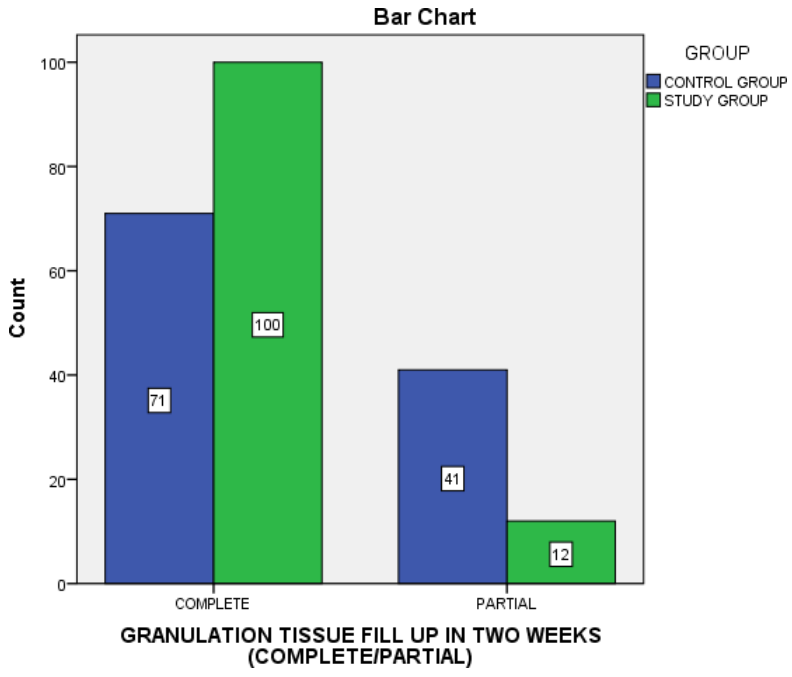


TABLE NO 8.9: WOUND CONTRACTION:

Variables	Group	N	Mean	SD	Mann-Whitney U Test value	p-value
INITIAL AREA OF ULCER IN CM^2.	CONTROL GROUP	112	36.116	19.984	6947	0.164
	STUDY GROUP	112	33.795	21.883		
FINAL AREAOF ULCER IN CM^2.	CONTROL GROUP	112	28.188	17.051	10610	< **.001**
	STUDY GROUP	112	10.696	9.63		
% AREA REDUCTION	CONTROL GROUP	112	0.249	0.16	459	< **.001**
	STUDY GROUP	112	0.718	0.129		

Study group had better wound contraction of 71.8% as compared to the control group, the mean wound contraction was 24.9% which is statistically significant with p value <0.001

GRAPH NO 7: PERCENTAGE REDUCTION:

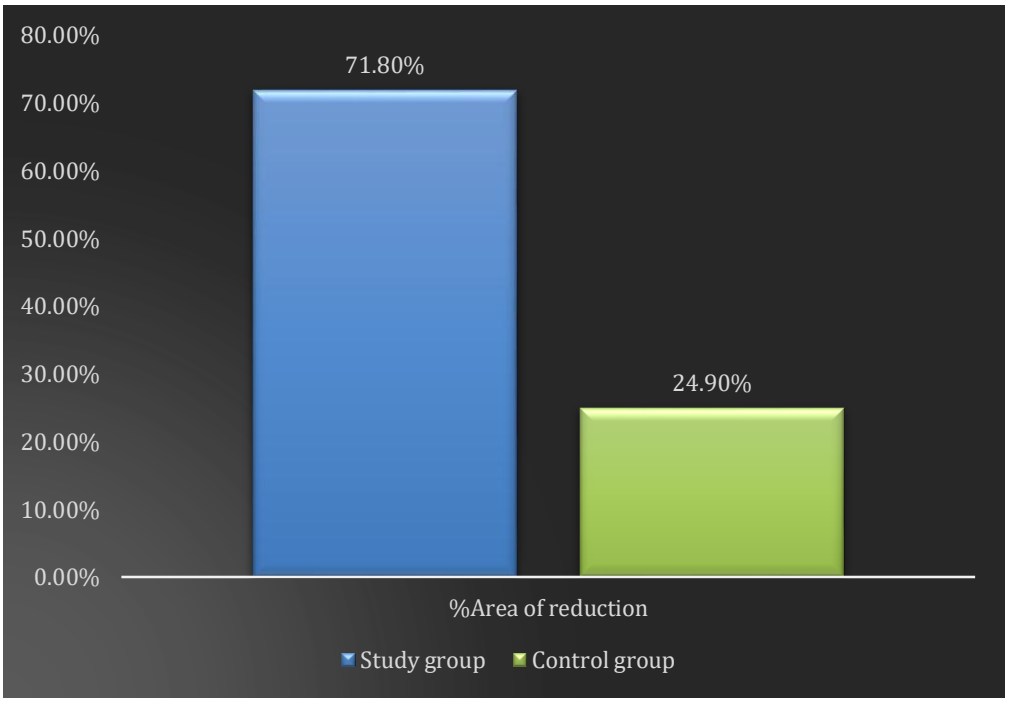


TABLE NO 8.10: MODE OF HEALING :

	BY SECONDARY INTENSION		HEALING BY				TOTAL	
	Count	% in group	SECONDARY SUTURING		SPLIT THICKNESS SKIN GRAFTING			
			Count	% in group	Count	% in group	Count	% in group
STUDY GROUP	10	8.92%	11	9.821%	91	81.25%	112	100%
CONTROL GROUP	3	2.67%	9	8.03%	100	89.2%	112	100%
TOTAL	13	5.8%	20	8.9%	191	85.2%	224	100%

In this study 10(8.9%) patients ulcer healed by secondary intension in study group where as 3(2.67%) patients ulcer healed by secondary intension in control group.

9. DISCUSSION

Every surgeon hopes to find the ultimate dressing, one that facilitates hassle-free chronic ulcer healing. Successful wound care must prevent unfavourable reactions including infection, maceration, and allergies while also keeping the wound moist. Lower leg ulcers are long-lasting lesions that have stopped growing on the surface of the skin.

Sucralfate helps in proliferation of dermal fibroblasts and keratinocytes. It also enhances prostaglandin E2 synthesis in basal keratinocytes, enhances interleukin-1-stimulated interleukin-6 release from fibroblasts[45]. When applied to full-thickness wounds daily, sucralfate increased the thickness of granulation tissue. It also promotes rapid epithelialization of 2nd degree burns

The present study was conducted at BLDE[DU] SHRI B.M.PATIL MEDICAL COLLEGE, HOSPITAL AND RESEARCH CENTRE, VIJAYAPURA to study the effect on chronic lower limb ulcer healing dynamics

In our study it was seen that the incidence of chronic lower limb ulcers were more in males (81.2%) as compared to females (18.8%).

TABLE NO – 9.1: AGE COMPARISSION WITH OTHER STUDIES

	MEAN AGE
OUR STUDY	52.33 YEARS
NARWADE P et.al.:	50.72 YEARS

Study conducted by Narwade P, Saxena on non diabetic chronic leg ulcers :etiology and management stated that chronic leg ulcer presented during sixth decade with a male to female ratio of 5:1which shows similar results in this study

The second national data source, NHDS documented higher hospital rates in males suffering from chronic lower limb ulcers.

The mean age group in the study group with chronic lower limb ulcers were 52.33 years and in the control group were 52.44 years.

In this study, 71 % of the ulcers were spontaneous in origin, 29 % were traumatic in origin.

TABLE NO – 9.2: ONSET COMPARISION WITH OTHER STUDIES

	SPONTANEOUS	TRAUMATIC
OUR STUDY	71%	29%
G NAGALAXMI et.al.:	73%	27%

In our study about 125(55.8%) patients had wounds over dorsum of foot which is seen in majority of patients.

TABLE NO–9.3: SITE OF ULCER COMPARISION WITH OTHER STUDIES

SITE OF ULCER	DORSUM OF FOOT
OUR STUDY	55.8%
G NAGALAXMI et.al.:	30%

In our study 56(25%) individuals are diabetic and 168(75%) patients were non-diabetic.

In our study the culture and sensitivity of the ulcers before the commencement of sucralfate dressings were positive for many microorganisms. In the

After sucralfate dressings were given culture obtained on the 14th day surprisingly showed –ve culture in patients in the study group, whereas patients in the control group still had a +ve culture.

This may account for the antimicrobial activity of Sucralfate. A series of experiments was conducted to determine the rate of bacterial growth in human gastric juice at various pH values in relation to the addition of sucralfate and antacid.

Whereas the addition of antacid resulted in bacterial growth in gastric juice, sucralfate showed an antibacterial effect. This may account for the decreased rate of pneumonia among intensive-care

Patients who are receiving artificial ventilation and being treated with sucralfate for the prevention of stress-induced gastrointestinal bleeding compared with the rate in patients receiving conventional prophylaxis with histamine (H2)-antagonists or antacids.

In our study it was observed that participants receiving Sucralfate dressing had better wound contraction of 71.8% as compared to the control group in whom the mean wound contraction was 24.9%.These were found to be statistically significant on Mann -Whitney U test ($p<0.001$) suggesting that Sucralfate enhances wound healing in chronic Lower Limb ulcers. Which is similar to study done by G NAGALAXMI et.al.:

TABLE NO -9.4 WOUND CONTRACTION COMPARISION WITH OTHER STUDIES

WOUND CONTRACTION	STUDY GROUP	CONTROL GROUP
OUR STUDY	71.8%	24.9%
PREETI et.al.:	70.4%	29.6%
G NAGALAXMI et.al.:	41.97%	18.37%

In a study done by Preethi SP on comparative study of efficacy and cost effectiveness of topical sucralfate and conventional dressings in diabetic ulcers in 100 patients shows about 70.4% reduction in ulcer surface area where as control

group shows only 29.6% reduction in ulcer surface area.

In our study complete granulation tissue fill up is seen in about 100(89.3%) patients in study group and 71(63.4%) patients in control group which shows significant amount of patients showing good amount of granulation tissue fill up with the use of sucralfate.

Feasibility of this study:

In the present study we have taken 224 patients suffering from chronic lower limb ulcers(>2 weeks). Patients were taken up for study based on inclusion and exclusion criteria. Out of 224 patients, 112 (92 males, 20 females) were study cases and 112 (90 males and 22 females) were control. Participants included in the study group were treatedwith Sucralfate dressing from day 01 to day 14. All 112 patients selected for Sucralfate treatment complied for the 14 days period of the study. The initial area measurement was taken on day 01 and final area measurement on day 14 was taken on transparent sheet.

All 112 patients selected as a control complied for the 14 days duration period of the study. The initial area measurement on day 01 final area measurement on day 14 was taken on transparent sheet. The area measurement was done using planimetry.

We have applied the following formula to calculate % reduction in area of wound after 14 days period in both cases and control groups.

$$\text{Rate of contraction of wound after 14 days of treatment} = \frac{(\text{Initial area} - \text{Final Area})}{\text{Initial area}} \times 100$$

We have found 24.9% contraction of wounds in the control groups as compared to 71.8% contraction of wounds in study group. Therefore, study groups have a better percentage of wound contraction as compared to the control group. On applying Mann -Whitney U test $p<0.001$ which is significant.

From our study, we can say that Sucralfate dressing therapy facilitates wound healing in patients suffering from chronic lower limb ulcers.

10. CONCLUSION

The wounds in the Sucralfate dressing-treated subjects contracted more than the wounds in the control group (71.8% Vs. 24.9%; P = 0.001 Significant) and showed early granulation tissue fill up; **this suggests that Sucralfate dressing is an effective modality to Facilitate wound contraction in patients with lower limb ulcers** and can be used as an alternative to Betadine dressings for healing of Lower Limb ulcers.

11. SUMMARY

To help lower limb ulcers heal more quickly, numerous therapeutic techniques have been developed. Patients with lower limb ulcers often experience unexpected and occasionally difficult healing.

The study included 224 patients with lower limb ulcers. They were divided into two groups, each with 112 people.

Sucralfate dressing was administered to one group, and traditional therapy was used to treat the control group. Between the two groups, a comparison study of the % area wound reduction was conducted.

In the study group with chronic lower limb ulcers, the mean age was 52.3 years old, whereas it was 52.4 years old in the control group.

In our study, it was shown that participants who received Sucralfate dressing experienced better wound contraction, with a mean wound contraction rate of 71.8%, compared to the control group who received betadine dressing, where the mean wound contraction rate was 24.9%.

According to the Mann-Whitney U Test, these were statistically significant (p 0.001), indicating that sucralfate speeds up the healing of chronic lower limb ulcers.

In the study group, 23 patients samples were positive for SA, no patients positive samples for PM, 31 patients tested positive for PA, 8 patients tested positive for EC, 25 patients tested positive for KP, 2 patients tested positive for EF, and 23 patients did not exhibit any growth. 21 of them in the control group tested positive for SA. thirteen of them for EC, three for PM, 23 for PA, 34 for KP, one for AB, one for EF, and three for 16 patients showed no growth at all.

Surprisingly, 105 patients in the experimental group had a negative culture after receiving sucralfate dressings, while 61 patients in the control group continued to have a positive culture on the 14th day.

Comparing the topical Sucralfate dressing group to the traditional dressing group, a higher rate of granulation tissue formation was observed. The group receiving topical Sucralfate dressings saw shorter hospital stays. Sucralfate dressing applied topically seems to be a cost-efficient, widely accessible therapeutic treatment for wound healing.

As a result, it might be advised for the treatment of chronic Lower Limb ulcers as an adjuvant to betadine dressings. Sucralfate dressing therapy was proven to be more effective, safe, and a wound healer.

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ANNEXURE – I

WITH USE OF SUCRALFATE

ON DAY 1 **ON DAY 7** **ON DAY 14**

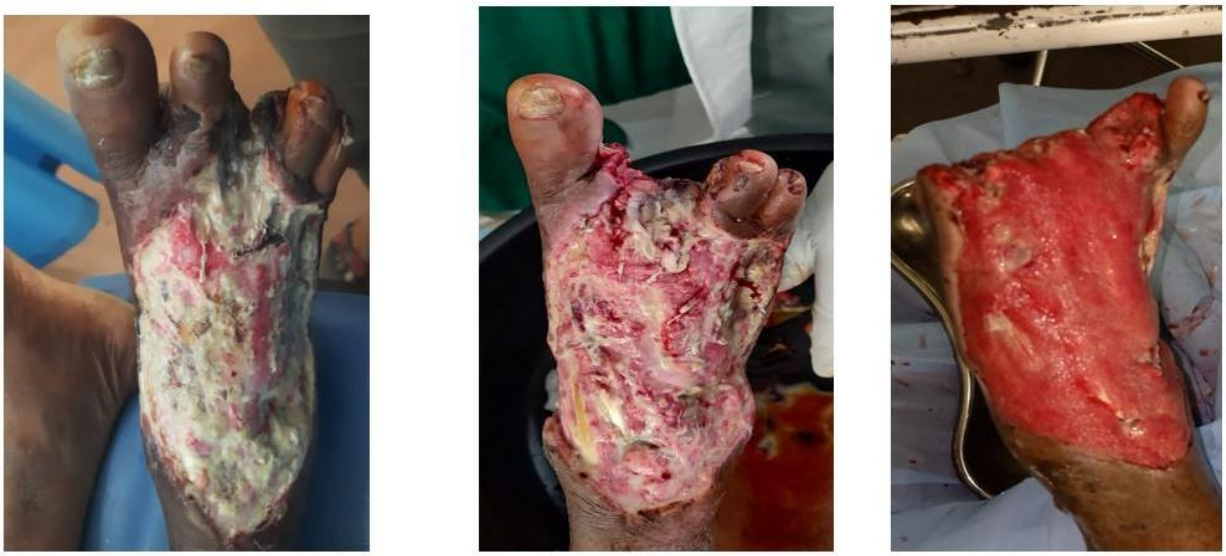

IMAGE 1

ON DAY 1 **ON DAY 7** **ON DAY 14**

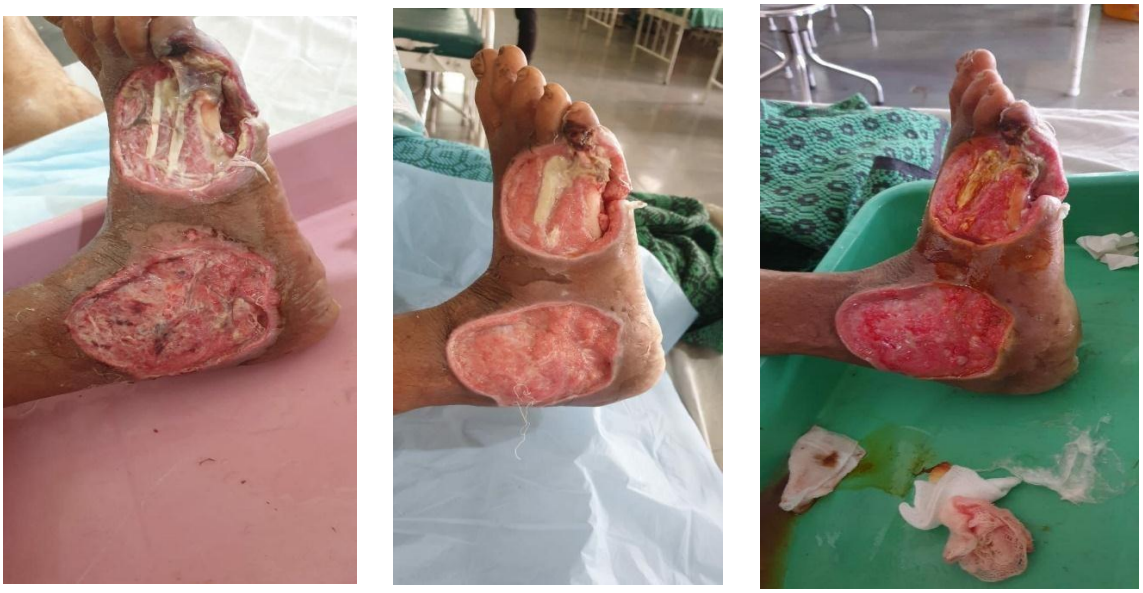

IMAGE 2

WITH USE OF BETADINE(ON DAY 1 AND DAY 14)

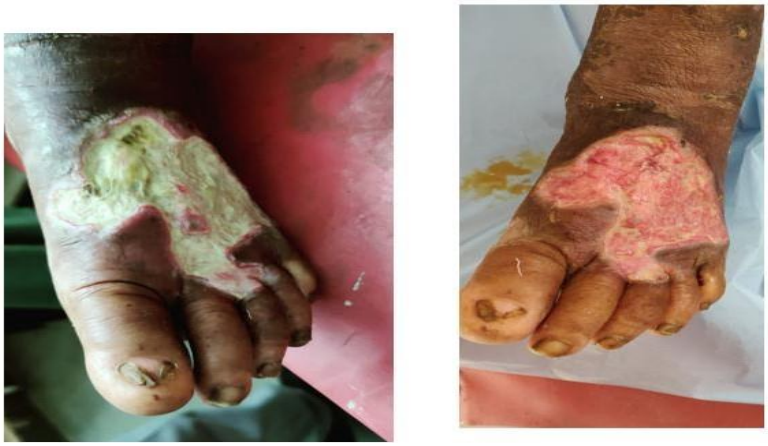

IMAGE 3

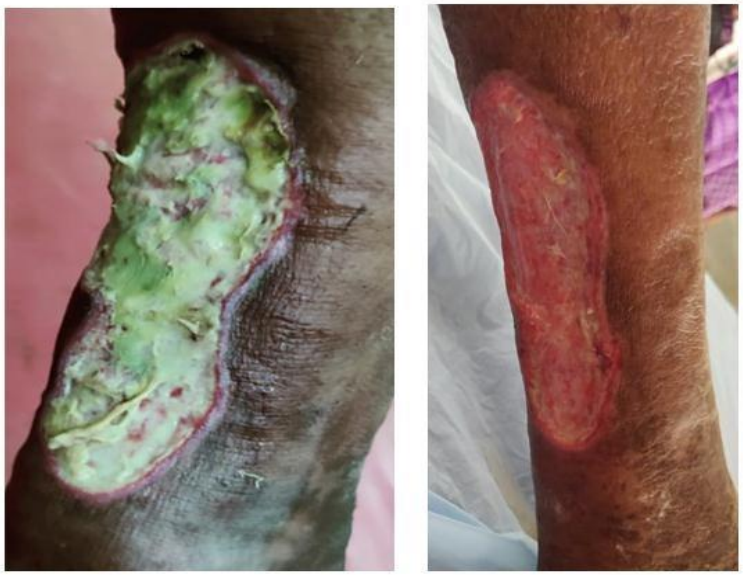

IMAGE 4

ANNEXURE – II

9. INFORMED CONSENT FORM

TITLE OF THE PROJECT:

"A COMPARATIVE STUDY BETWEEN EFFICACY OF TOPICAL SUCRALFATE AND 5%POVIDONE IODINE IN CHRONIC LOWER LIMB ULCERS."

NAME OF THE INVESTIGATOR: DR. GUTTA SANTHAN HARSHA

NAME OF THE GUIDE: DR. MANJUNATH. S. KOTENNAVAR

CONFIDENTIALITY OF RECORDS:

I understand that medical information produced by this study will become a part of this hospital record and will be subjected to the confidentiality and privacy regulation of this hospital. Information of a sensitive, personal nature will not be a part of only by a code number. The code key connecting the name to numbers will be kept in the medical records but will be stored in the investigator's research file and identified separate secure location.

If the data are used for publication in the medical literature or teaching purposes, no names will be used and other identifiers such as photographs and audio or videotapes will be used only with my special written permission. I understand that I may see the photograph and videotapes and hear audiotapes before giving this permission.

REQUEST FOR MORE INFORMATION:

I understand that I may ask more questions about the study at any time **Dr. GUTTA SANTHAN HARSHA** is available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during this study, which might influence my continued participation.
If during this study, or later, I wish to discuss my participation in or concerns regarding this study with a person not directly involved, I am aware that the social worker of the hospital is available to talk with me.
And that a copy of this consent form will be given to me to keep and for careful reading.

REFUSAL OR WITHDRAWAL OF PARTICIPATION:

I understand that my participation is voluntary and I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice to my present or future care at this hospital.

I also understand that **Dr. GUTTA SANTHAN HARSHA** will terminate my participation in this study at any time after he has explained the reasons for doing so and has helped arrange for my continued care by my physician or therapist if this is appropriate

INJURY STATEMENT:

I understand that in the unlikely event of injury to me/my ward, resulting directly to my participation in this study, if such injury were reported promptly, then medical treatment would be available to me, but no further compensation will be provided.

I understand that by my agreement to participate in this study, I am not waiving any of my legal rights.

I have explained to_____the purpose of this research, the procedures required and the possible risks and benefits, to the best of my ability in patient's own language

Date:

Dr. M.S. Kotennavar
(Guide)

Dr. Gutta Santhan harsha
(Investigator)

Participant's name:

Address:

TITLE OF THE PROJECT:

"A COMPARATIVE STUDY BETWEEN EFFICACY OF TOPICAL SUCRALFATE AND 5%POVIDONE IODINE IN CHRONIC LOWER LIMB ULCERS."

The details of the study have been provided to me in writing and explained to me in my language. I confirm that I have understood the above study and had the opportunity to ask questions. I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without the medical care that will normally be provided by the hospital being affected. I agree not to restrict the use of any data or results that arise from this study provided such use is only for the scientific purpose(s). I have been given an information sheet giving details of the study. I fully consent to participate in the above study.

_____ _____

(Participant) (Date)

_____ _____

(Witness to signature) (Date)

_____ _____

(Investigator to signature) (Date)

ANNEXURE III

PROFORMA

NAME: CASE NO.:

AGE: IP NO./ OP NO.:

SEX: DOA:

RELIGION: DOD:

OCCUPATION: WEIGHT: BMI:

ADDRESS:

-
-

CHIEF COMPLAINTS WITH HISTORY OF PRESENTING ILLNESS:

PAST HISTORY:

DIABETES MELLITUS:
Duration
Treatment
HYPERTENSION:

HISTORY OF ANY DRUG INTAKE:

PERSONAL HISTORY:

DIET:
APPETITE:
SLEEP:
HABITS:

FAMILY HISTORY:

GENERAL PHYSICAL EXAMINATION:

VITALS :

PULSE RATE :

BLOOD PRESSURE :

RESPIRATORY RATE :

TEMPERATURE :

LOCAL EXAMINATION:

INSPECTION OF FOOT WITH ULCER SITE:

SIZE:

SHAPE:

SURROUNDING SKIN:

FOOT DEFORMITY:

SURFACE AREA OF:

ULCER DEPTH OF:

PALPATION SENSATION:

PULSATIONS:

CLINICAL DIABETIC FOOT GRADING (WAGNER‟S):

OTHER SYSTEMIC EXAMINATION:

RESPIRATORY SYSTEM:

CARDIOVASCULAR SYSTEM:

CENTRAL NERVOUS SYSTEM:

PER ABDOMINAL EXAMINATION:

INVESTIGATIONS:

COMPLETE BLOOD COUNT
BT, CT
SEROLOGY
GLYCEMIC LEVELS
RBS: FBS: PPBS: HBA1C:
PUS CULTURE AND SENSITIVITY:
XRAY FOOT AP AND OBLIQUE VIEW (WHENEVER REQUIRED):
ECHOCARDIOGRAPHY (WHENEVER REQUIRED)

Cost of the procedure -

Duration of the procedure -

Outcomes/followup:

Comments (if any)

B.L.D.E. (DEEMED TO BE UNIVERSITY) IEC/No-09/2021 Date-22/01/2021

(Declared vide notification No. F.9.37/2007-U.3.(A) Dated 29.2.2008 of the MHRD, Government of India under Section 3 of the UGC Act, 1956)

The Constituent College

SHRI. B. M. PATIL MEDICAL COLLEGE, HOSPITAL AND RESEARCH CENTRE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Institutional ethical committee of this college met on 11-01-2021 at 11-00 am to scrutinize the synopsis of Postgraduate students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected and revised version synopsis of the Thesis has been accorded Ethical Clearance

Title: A prospective study of comparison between efficacy of topical sucralfate and 5% povidine iodine in the management of chronic lower limb ulcers.

Name of PG student: Dr Gutta Santhan Harsha, Department of Surgery

Name of Guide/Co-investigator: Dr Manjunath.S.Kotennavar, Professor
Department of Surgery

DR .S.V.PATIL
CHAIRMAN, IEC
Institutional Ethical Committee
B L D E (Deemed to be University)
Shri B.M. Patil Medical College,
VIJAYAPUR-586103 (Karnataka)

Following documents were placed before Ethical Committee for Scrutinization:

1. Copy of Synopsis / Research project
2. Copy of informed consent form
3. Any other relevant documents.

11

20BMSUR005-GUTTA-A COMPARATIVE STUDY BETWEEN EFFICACY OF TOPICAL SUCRALFATE AND 5% POVIDONE IODINE IN CHRONIC LOWER LIMB ULCERS

ORIGINALITY REPORT

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ANNEXURE – IV [MASTER SHEET]

	GROUP	AGE	SEX	TRAUMATIC/SPONTANEOUS	DM: PRESENT/ABSENT	DURATION AND TREATMENT	SITE OF ULCER	INITIAL AREA OF	FINAL ARE	% AREA REDUCTION	HBA1C	PUS CULTURE SENSITIVITY(BE	PUS CULTURE SENSI	GRANULATION	WOUND C	WOUND C	HEALED BY	PRIMARY	INTE
2	STUDY GROUP	55	MALE	SPONTANEOUS	ABSENT		D OF FOOT	60	21	65%		PSEUDOMONAS	NEGATIVE	COMPLETE	YES				
3	STUDY GROUP	25	MALE	TRAUMATIC	PRESENT	SINCE ONE YEAR ON T.METFORMIN	D OF FOOT	24	6	75%	7.60%	STERILE	NEGATIVE	COMPLETE	YES				
4	STUDY GROUP	60	MALE	SPONTANEOUS	PRESENT	SINCE 30 YEARS ON T.GLIMIPRIDE 2	D OF FOOT	28	10	64%	10.70%	KLEBSIELLA	NEGATIVE	COMPLETE	YES				
5	STUDY GROUP	46	FEMALE	SPONTANEOUS	ABSENT		MM OF FOOT	24	6	75%		STAPHYLOCCOCUS AUREUS	NEGATIVE	COMPLETE	YES				
6	STUDY GROUP	62	MALE	TRAUMATIC	ABSENT		LM OF FOOT	54	20	62%		KLEBSIELLA	NEGATIVE	COMPLETE	YES				
7	STUDY GROUP	75	MALE	SPONTANEOUS	ABSENT		D OF FOOT	90	30	67%		PSEUDOMONAS	NEGATIVE	COMPLETE	YES				
8	STUDY GROUP	72	MALE	SPONTANEOUS	ABSENT		D OF FOOT, MS OF LEG, LS OF LEG	45	10	77.80%		PSEUDOMONAS	NEGATIVE	COMPLETE	YES				
9	STUDY GROUP	25	FEMALE	TRAUMATIC	ABSENT		MM OF FOOT	24	6	75%		PSEUDOMONAS	NEGATIVE	COMPLETE	YES				
10	STUDY GROUP	74	MALE	SPONTANEOUS	PRESENT	SINCE ONE YEAR ON IRREGULAR MEDICATIONS	D OF FOOT	54	10	81.40%	6.80%	PSEUDOMONAS	POSITIVE	COMPLETE	YES				
11	STUDY GROUP	60	MALE	TRAUMATIC	PRESENT	SINCE 10 YEARS ON IRREGULAR MEDICATIONS	D OF FOOT, MS OF LEG	38	12	68%	11.20%	KLEBSIELLA	NEGATIVE	COMPLETE	YES				
12	STUDY GROUP	30	FEMALE	SPONTANEOUS	ABSENT		D OF FOOT	30	6	80%		PSEUDOMONAS	NEGATIVE	COMPLETE	YES				
13	STUDY GROUP	65	MALE	TRAUMATIC	PRESENT	SINCE 20 YEARS ON T.GLIMIPRIDE	D OF FOOT	35	10	71.40%	8.40%	PSEUDOMONAS	NEGATIVE	COMPLETE	YES				
14	STUDY GROUP	75	MALE	SPONTANEOUS	ABSENT		D OF FOOT, MS OF LEG	18	4	77.70%		STAPHYLOCCOCUS AUREUS	NEGATIVE	COMPLETE	YES				
15	STUDY GROUP	25	MALE	TRAUMATIC	ABSENT		D OF FOOT, MS OF LEG	24	10	58.30%		PSEUDOMONAS	NEGATIVE	COMPLETE	YES				
16	STUDY GROUP	43	MALE	TRAUMATIC	ABSENT		D OF FOOT	12	4	66.60%		STAPHYLOCCOCUS AUREUS	NEGATIVE	PARTIAL		YES			
17	STUDY GROUP	40	MALE	SPONTANEOUS	ABSENT		D OF FOOT	24	9	62.50%		PSEUDOMONAS	NEGATIVE	COMPLETE	YES				
18	STUDY GROUP	46	MALE	SPONTANEOUS	PRESENT	SINCE 8 YEARS ON INJ.ACTRAPID	D OF FOOT, MS OF LEG	27	6	77.70%	9.20%	KLEBSIELLA	POSITIVE	COMPLETE	YES				
19	STUDY GROUP	45	MALE	TRAUMATIC	ABSENT		D OF FOOT	80	56	30%		PSEUDOMONAS	NEGATIVE	COMPLETE	YES				
20	STUDY GROUP	40	MALE	SPONTANEOUS	ABSENT		D OF FOOT	60	18	70%		PSEUDOMONAS	NEGATIVE	COMPLETE	YES				
21	STUDY GROUP	60	FEMALE	SPONTANEOUS	PRESENT	SINCE 20 YEARS ON INJ.ACTRAPID	MS OF LEG	20	6	70%	9.90%	PSEUDOMONAS	POSITIVE	COMPLETE	YES				
22	STUDY GROUP	65	MALE	TRAUMATIC	ABSENT		D OF FOOT	48	18	62.50%		PSEUDOMONAS	NEGATIVE	COMPLETE	YES				
23	STUDY GROUP	60	MALE	SPONTANEOUS	ABSENT		D OF FOOT	60	32	46.60%		KLEBSIELLA	NEGATIVE	PARTIAL	YES				
24	STUDY GROUP	52	MALE	SPONTANEOUS	ABSENT		LS OF LEG	30	6	80%		PSEUDOMONAS	NEGATIVE	COMPLETE	YES				
25	STUDY GROUP	48	MALE	TRAUMATIC	ABSENT		D OF FOOT	40	12	70%		PSEUDOMONAS	NEGATIVE	COMPLETE	YES				
26	STUDY GROUP	57	MALE	SPONTANEOUS	ABSENT		MS OF LEG	32	4	87.50%		STAPHYLOCCOCUS AUREUS	NEGATIVE	PARTIAL		YES			
27	STUDY GROUP	55	MALE	SPONTANEOUS	PRESENT	SINCE 2 YEARS ON INJ.H ACTRAPID	D OF FOOT	80	48	40%	11.10%	KLEBSIELLA	NEGATIVE	COMPLETE	YES				
28	STUDY GROUP	74	MALE	TRAUMATIC	PRESENT	SINCE 15 YEARS ON INJ.H.ACTRAPID	MS OF LEG	20	6	70%	8.60%	KLEBSIELLA	NEGATIVE	COMPLETE	YES				
29	STUDY GROUP	65	FEMALE	SPONTANEOUS	ABSENT		D OF FOOT	15	4	73%		ESCHERICHIA COLI	NEGATIVE	COMPLETE	YES				
30	STUDY GROUP	30	MALE	TRAUMATIC	ABSENT		D OF FOOT	28	8	71.40%		PSEUDOMONAS	NEGATIVE	COMPLETE	YES				
31	STUDY GROUP	60	FEMALE	SPONTANEOUS	ABSENT		MS OF LEG	24	9	62.50%		STERILE	NEGATIVE	COMPLETE	YES				
32	STUDY GROUP	50	FEMALE	SPONTANEOUS	ABSENT		D OF FOOT, MS OF LEG	69	20	71%		STERILE	NEGATIVE	COMPLETE	YES				
33	STUDY GROUP	62	MALE	TRAUMATIC	PRESENT	SINCE 30 YEARS ON T.METFORMIN	D OF FOOT, MS OF LEG, LS OF LEG	28	8	71%	9.30%	STERILE	NEGATIVE	COMPLETE	YES				
34	STUDY GROUP	28	MALE	SPONTANEOUS	ABSENT		D OF FOOT	24	6	75%		STERILE	NEGATIVE	PARTIAL	YES				
35	STUDY GROUP	73	MALE	SPONTANEOUS	PRESENT	SINCE 20 YEARS ON T.METFORMIN	MS OF LEG	80	32	60%	8.00%	PSEUDOMONAS	NEGATIVE	COMPLETE	YES				
36	STUDY GROUP	50	FEMALE	TRAUMATIC	PRESENT	SINCE 2 YEARS ON T.GLIMIPRIDE	D OF FOOT	8	0	100%	10.50%	STERILE	NEGATIVE	COMPLETE			YES		
37	STUDY GROUP	45	MALE	TRAUMATIC	PRESENT	SINCE ONE MONTH ON T.METFORMIN	D OF FOOT	63	30	52.30%	15.20%	PSEUDOMONAS	NEGATIVE	COMPLETE	YES				
38	STUDY GROUP	75	MALE	SPONTANEOUS	ABSENT		P OF FOOT	6	0	100%		STERILE	NEGATIVE	COMPLETE			YES		
39	STUDY GROUP	61	MALE	SPONTANEOUS	PRESENT	SINCE 10 YEARS ON T.GLIMIPRIDE	D OF FOOT	15	3	80%	12.40%	STERILE	NEGATIVE	COMPLETE		YES			
40	STUDY GROUP	75	MALE	TRAUMATIC	PRESENT	SINCE 40 YEARS ON IRREGULAR MEDICATIONS	D OF FOOT	12	2	83.30%	11.40%	STERILE	NEGATIVE	PARTIAL		YES			
41	STUDY GROUP	54	MALE	SPONTANEOUS	ABSENT		MM OF FOOT	20	4	80%		STAPHYLOCCOCUS AUREUS	NEGATIVE	COMPLETE	YES				
42	STUDY GROUP	15	MALE	SPONTANEOUS	ABSENT		P OF FOOT	12	0	100%		STERILE	NEGATIVE	COMPLETE			YES		
43	STUDY GROUP	62	MALE	SPONTANEOUS	PRESENT	SINCE 6 YEARS ON INJ.H.ACTRAPID	D OF FOOT	30	12	60%	10.10%	STAPHYLOCCOCUS AUREUS	NEGATIVE	COMPLETE	YES				
44	STUDY GROUP	43	MALE	TRAUMATIC	PRESENT	SINCE 4 YEARS ON T. METFORMIN	D OF FOOT	35	20	43%	11.40%	PSEUDOMONAS	NEGATIVE	COMPLETE	YES				
45	STUDY GROUP	50	MALE	SPONTANEOUS	ABSENT		D OF FOOT	15	6	60%		STERILE	NEGATIVE	COMPLETE		YES			
46	STUDY GROUP	35	MALE	SPONTANEOUS	ABSENT		D OF FOOT , MS OF LEG	48	12	75%		STAPHYLOCCOCUS AUREUS	NEGATIVE	COMPLETE	YES				
47	STUDY GROUP	50	MALE	SPONTANEOUS	ABSENT		D OF FOOT , MS OF LEG	32	12	62.50%		ESCHERICHIA COLI	NEGATIVE	COMPLETE	YES				
48	STUDY GROUP	65	MALE	SPONTANEOUS	ABSENT		D OF FOOT , MS OF LEG	60	17	71.60%		KLEBSIELLA	NEGATIVE	COMPLETE	YES				
49	STUDY GROUP	68	MALE	SPONTANEOUS	ABSENT		D OF FOOT , MS OF LEG	64	18	71.80%		ESCHERICHIA COLI	NEGATIVE	COMPLETE	YES				
50	STUDY GROUP	65	MALE	SPONTANEOUS	ABSENT		D OF FOOT, MS OF LEG	27	10	63%		PSEUDOMONAS	NEGATIVE	COMPLETE	YES				
51	STUDY GROUP	68	MALE	TRAUMATIC	PRESENT	SINCE 20 YEARS ON T.METFORMIN	D OF FOOT, MS OF LEG	24	5	80%	7.30%	STAPHYLOCCOCUS AUREUS	NEGATIVE	COMPLETE	YES				
52	STUDY GROUP	38	FEMALE	SPONTANEOUS	ABSENT		LS OF LEG	42	12	71.40%		STERILE	NEGATIVE	PARTIAL	YES				
53	STUDY GROUP	56	MALE	SPONTANEOUS	ABSENT		MS OF LEG	32	8	75%		STERILE	NEGATIVE	COMPLETE	YES				
54	STUDY GROUP	55	MALE	SPONTANEOUS	ABSENT		D OF FOOT	50	32	36%		STERILE	NEGATIVE	COMPLETE	YES				
55	STUDY GROUP	42	MALE	SPONTANEOUS	PRESENT	SINCE 8 YEARS ON T.METFORMIN	MS OF LEG	20	6	70%	11.20%	STAPHYLOCCOCUS AUREUS	NEGATIVE	COMPLETE	YES				
56	STUDY GROUP	57	MALE	SPONTANEOUS	ABSENT		D OF FOOT, MS OF LEG, LS OF LEG	34	11	67.60%		KLEBSIELLA	NEGATIVE	COMPLETE	YES				
57	STUDY GROUP	70	MALE	SPONTANEOUS	ABSENT		D OF FOOT	48	12	75%		KLEBSIELLA	NEGATIVE	COMPLETE	YES				
58	STUDY GROUP	40	MALE	SPONTANEOUS	ABSENT		D OF FOOT	48	12	75%		KLEBSIELLA	NEGATIVE	COMPLETE	YES				
59	STUDY GROUP	73	MALE	TRAUMATIC	ABSENT		D OF FOOT	42	8	80.90%		STAPHYLOCCOCUS AUREUS	NEGATIVE	COMPLETE	YES				
60	STUDY GROUP	50	MALE	SPONTANEOUS	ABSENT		MS OF LEG	20	6	70%		STERILE	NEGATIVE	PARTIAL	YES				
61	STUDY GROUP	72	FEMALE	SPONTANEOUS	ABSENT		D OF FOOT	70	20	71.40%		PSEUDOMONAS	NEGATIVE	COMPLETE	YES				
62	STUDY GROUP	35	MALE	SPONTANEOUS	ABSENT		D OF FOOT	18	6	66.60%		STERILE	NEGATIVE	COMPLETE	YES				
63	STUDY GROUP	70	MALE	TRAUMATIC	PRESENT	SINCE 8YEARS ON T.METFORMIN	LM OF FOOT	12	2	83%	7.40%	KLEBSIELLA	NEGATIVE	COMPLETE		YES			
64	STUDY GROUP	38	MALE	SPONTANEOUS	ABSENT		D OF FOOT	28	8	71.40%		STERILE	NEGATIVE	COMPLETE	YES				
65	STUDY GROUP	50	MALE	SPONTANEOUS	PRESENT	SINCE ONE MONTH ON T.METFORMIN	D OF FOOT , MS OF LEG	62	14	77.40%	8.60%	KLEBSIELLA	NEGATIVE	COMPLETE	YES				
66	STUDY GROUP	60	MALE	SPONTANEOUS	PRESENT	SINCE 5 YEARS ON T.GLYCOMET	D OF FOOT	42	12	71.40%	11.60%	PSEUDOMONAS	NEGATIVE	COMPLETE	YES				
67	STUDY GROUP	65	MALE	TRAUMATIC	ABSENT		D OF FOOT , MS OF LEG	31	11	64.50%		KLEBSIELLA	NEGATIVE	COMPLETE	YES				
68	STUDY GROUP	40	MALE	SPONTANEOUS	ABSENT		MS OF LEG	27	10	63%		KLEBSIELLA	NEGATIVE	COMPLETE	YES				
69	STUDY GROUP	40	MALE	SPONTANEOUS	ABSENT		LS OF LEG	32	8	75%		ESCHERICHIA COLI	NEGATIVE	COMPLETE	YES				
70	STUDY GROUP	70	MALE	TRAUMATIC	ABSENT		D OF FOOT , MS OF LEG	34	9	73.50%		PSEUDOMONAS	NEGATIVE	COMPLETE	YES				
71	STUDY GROUP	62	FEMALE	SPONTANEOUS	ABSENT		D OF FOOT , MS OF LEG	70	13	81%		PSEUDOMONAS	NEGATIVE	COMPLETE	YES				
72	STUDY GROUP	70	MALE	SPONTANEOUS	PRESENT	SINCE 30 YEARS ON T.GLIMIPRIDE 2	D OF FOOT	80	24	70%	7.50%	PSEUDOMONAS	NEGATIVE	COMPLETE	YES				
73	STUDY GROUP	24	FEMALE	SPONTANEOUS	ABSENT		MS OF LEG	15	6	60%		STERILE	NEGATIVE	COMPLETE	YES				
74	STUDY GROUP	65	MALE	TRAUMATIC	PRESENT	SINCE 20 YEARS ON T.GLIMIPRIDE	D OF FOOT	24	6	75%	8.80%	STAPHYLOCCOCUS AUREUS	NEGATIVE	COMPLETE	YES				
75	STUDY GROUP	59	MALE	SPONTANEOUS	ABSENT		MS OF LEG	21	4	80.90%		KLEBSIELLA	NEGATIVE	PARTIAL		YES			
76	STUDY GROUP	35	MALE	SPONTANEOUS	ABSENT		D OF FOOT	48	12	75%		STAPHYLOCCOCUS AUREUS	NEGATIVE	COMPLETE	YES				
77	STUDY GROUP	61	MALE	SPONTANEOUS	ABSENT		D OF FOOT	48	12	75%		KLEBSIELLA	NEGATIVE	COMPLETE	YES				
78	STUDY GROUP	63	MALE	TRAUMATIC	ABSENT		MS OF LEG	28	6	78%		STAPHYLOCCOCUS AUREUS	NEGATIVE	COMPLETE	YES				
79	STUDY GROUP	35	MALE	SPONTANEOUS	ABSENT		D OF FOOT	80	24	70%		ESCHERICHIA COLI	NEGATIVE	COMPLETE	YES				
80	STUDY GROUP	66	MALE	SPONTANEOUS	PRESENT	SINCE 20 YEARS ON T.GLIMIPRIDE	D OF FOOT	42	12	71%	12.40%	PSEUDOMONAS	POSITIVE	COMPLETE	YES				
81	STUDY GROUP	75	MALE	TRAUMATIC	ABSENT		MS OF LEG	24	6	75%		STAPHYLOCCOCUS AUREUS	NEGATIVE	COMPLETE	YES				
82	STUDY GROUP	55	FEMALE	SPONTANEOUS	ABSENT		D OF FOOT	20	6	70%		ENTEROCOCUS FAECALIS	NEGATIVE	COMPLETE	YES				
83	STUDY GROUP	55	MALE	SPONTANEOUS	ABSENT		MS OF LEG	24	6	75%		STAPHYLOCCOCUS AUREUS	NEGATIVE	COMPLETE	YES				
84	STUDY GROUP	37	MALE	SPONTANEOUS	ABSENT		D OF FOOT	15	3	80%		ESCHERICHIA COLI	NEGATIVE	PARTIAL		YES			
85	STUDY GROUP	60	MALE	TRAUMATIC	ABSENT		D OF FOOT	28	12	57%		ESCHERICHIA COLI	NEGATIVE	COMPLETE	YES				
86	STUDY GROUP	50	MALE	SPONTANEOUS	ABSENT		MM OF FOOT	12	4	66.60%		PSEUDOMONAS	NEGATIVE	COMPLETE	YES				
87	STUDY GROUP	35	MALE	SPONTANEOUS	ABSENT		MS OF LEG	16	6	62.50%		KLEBSIELLA	NEGATIVE	PARTIAL		YES			
88	STUDY GROUP	55	MALE	TRAUMATIC	ABSENT		MM OF FOOT	6	0	100%		STAPHYLOCCOCUS AUREUS	NEGATIVE	COMPLETE			YES		
89	STUDY GROUP	60	FEMALE	SPONTANEOUS	ABSENT		D OF FOOT	20	6	70%		KLEBSIELLA	NEGATIVE	COMPLETE	YES				
90	STUDY GROUP	18	MALE	SPONTANEOUS	ABSENT		P OF FOOT	6	0	100%		PSEUDOMONAS	NEGATIVE	COMPLETE			YES		
91	STUDY GROUP	45	MALE	SPONTANEOUS	ABSENT		D OF FOOT	15	6	60%		STAPHYLOCCOCUS AUREUS	NEGATIVE	COMPLETE	YES				
92	STUDY GROUP	45	MALE	TRAUMATIC	PRESENT	SINCE 15 YEARS ON IRREGULAR MEDICATIONS	D OF FOOT , MS OF LEG	36	14	61%	10.90%	ENTEROCOCUS FAECALIS	POSITIVE	COMPLETE	YES				
93	STUDY GROUP	36	MALE	SPONTANEOUS	ABSENT		D OF FOOT	24	6	75%		KLEBSIELLA	NEGATIVE	COMPLETE	YES				
94	STUDY GROUP	72	MALE	SPONTANEOUS	ABSENT		D OF FOOT, MS OF LEG	47	14	70%		PSEUDOMONAS	POSITIVE	PARTIAL	YES				
95	STUDY GROUP	65	FEMALE	SPONTANEOUS	ABSENT		MS OF LEG	10	0	100%		ESCHERICHIA COLI	NEGATIVE	COMPLETE			YES		
96	STUDY GROUP	72	MALE	TRAUMATIC	ABSENT		LS OF LEG	15	6	60%		STAPHYLOCCOCUS AUREUS	NEGATIVE	COMPLETE	YES				
97	STUDY GROUP	60	MALE	SPONTANEOUS	ABSENT		D OF FOOT	4	0	100%		STERILE	NEGATIVE	COMPLETE			YES		
98	STUDY GROUP	35	FEMALE	SPONTANEOUS	ABSENT		D OF FOOT , MS OF LEG, LS OF LEG	72	18	75%		KLEBSIELLA	NEGATIVE	COMPLETE	YES				
99	STUDY GROUP	72	MALE	TRAUMATIC	ABSENT		D OF FOOT , MS OF LEG	114	36	68%		KLEBSIELLA	NEGATIVE	COMPLETE	YES				
100	STUDY GROUP	70	MALE	SPONTANEOUS	ABSENT		D OF FOOT , MS OF LEG	75	30	60%		STAPHYLOCCOCUS AUREUS	NEGATIVE	COMPLETE	YES				
101	STUDY GROUP	35	MALE	SPONTANEOUS	ABSENT		D OF FOOT	32	8	75%		STERILE	NEGATIVE	COMPLETE	YES				
102	STUDY GROUP	45	FEMALE	SPONTANEOUS	ABSENT		MM OF FOOT	12	2	83.30%		KLEBSIELLA	NEGATIVE	COMPLETE		YES			
103	STUDY GROUP	44	MALE	SPONTANEOUS	ABSENT		D OF FOOT	24	8	66%		PSEUDOMONAS	NEGATIVE	COMPLETE	YES				
104	STUDY GROUP	56	MALE	SPONTANEOUS	PRESENT	SINCE 5 YEARS ON T.GLYCOMET	D OF FOOT , MS OF LEG	26	8	69.20%	8.10%	KLEBSIELLA	NEGATIVE	PARTIAL		YES			
105	STUDY GROUP	75	FEMALE	TRAUMATIC	ABSENT		D OF FOOT	35	15	57.10%		PSEUDOMONAS	POSITIVE	COMPLETE	YES				
106	STUDY GROUP	46	FEMALE	SPONTANEOUS	ABSENT		D OF FOOT	24	6	75%		STAPHYLOCCOCUS AUREUS	NEGATIVE	COMPLETE	YES				
107	STUDY GROUP	25	MALE	SPONTANEOUS	ABSENT		D OF FOOT	4	0	100%		STERILE	NEGATIVE	COMPLETE			YES		
108	STUDY GROUP	38	MALE	SPONTANEOUS	ABSENT		LS OF LEG	21	8	62%		STAPHYLOCCOCUS AUREUS	NEGATIVE	COMPLETE	YES				
109	STUDY GROUP	54	MALE	TRAUMATIC	PRESENT	SINCE 10 YEARS ON MEDICATIONS	LM OF FOOT	15	6	60%	12.40%	KLEBSIELLA	NEGATIVE	COMPLETE	YES				
110	STUDY GROUP	18	MALE	SPONTANEOUS	ABSENT		MM OF FOOT	6	2	66.60%		STERILE	NEGATIVE	COMPLETE	YES				
111	STUDY GROUP	43	MALE	SPONTANEOUS	ABSENT		D OF FOOT	20	6	70%		STAPHYLOCCOCUS AUREUS	NEGATIVE	COMPLETE	YES				
112	STUDY GROUP	37	FEMALE	SPONTANEOUS	ABSENT		P OF FOOT	6	0	100%		STAPHYLOCCOCUS AUREUS	NEGATIVE	COMPLETE			YES		
113	STUDY GROUP	30	MALE	SPONTANEOUS	ABSENT		P OF FOOT	9	0	100%		STERILE	NEGATIVE	COMPLETE			YES		
114	CONTROL GROU	65	MALE	TRAUMATIC	PRESENT	SINCE 30 YEARS ON T.METFORMIN	D OF FOOT	36	24	33%	7.40%	PSEUDOMONAS	POSITIVE	COMPLETE	YES				
115	CONTROL GROU	45	MALE	SPONTANEOUS	ABSENT		D OF FOOT	60	48	20%		PSEUDOMONAS	POSITIVE	COMPLETE	YES				
116	CONTROL GROU	70	MALE	SPONTANEOUS	PRESENT	SINCE 15 YEARS ON IRREGULAR MEDICATIONS	D OF FOOT, MS OF LEG	104	77	25%	6.70%	STAPHYLOCCOCUS AUREUS	POSITIVE	PARTIAL	YES				
117	CONTROL GROU	60	FEMALE	SPONTANEOUS	ABSENT		D OF FOOT	80	72	10%		KLEBSIELLA	NEGATIVE	COMPLETE	YES				
118	CONTROL GROU	53	FEMALE	TRAUMATIC	PRESENT	SINCE 20 YEARS ON T.GLIMIPRIDE	D OF FOOT, MS OF LEG	42	30	28%	8.20%	KLEBSIELLA	POSITIVE	PARTIAL	YES				
119	CONTROL GROU	64	MALE	SPONTANEOUS	ABSENT		D OF FOOT	63	56	11.10%		KLEBSIELLA	NEGATIVE	COMPLETE	YES				
120	CONTROL GROU	58	MALE	SPONTANEOUS	ABSENT		D OF FOOT	72	64	11%		KLEBSIELLA	POSITIVE	COMPLETE	YES				
121	CONTROL GROU	56	MALE	SPONTANEOUS	PRESENT	SINCE 20 YEARS ON T.GLIMIPRIDE	LM OF FOOT	8	6	25%	9.80%	KLEBSIELLA	POSITIVE	COMPLETE	YES				
122	CONTROL GROU	55	FEMALE	SPONTANEOUS	PRESENT	SINCE 2 YEARS ON IRREGULAR MEDICATIONS	D OF FOOT	42	35	16.60%	8.20%	KLEBSIELLA	NEGATIVE	COMPLETE	YES				
123	CONTROL GROU	73	MALE	SPONTANEOUS	ABSENT		D OF FOOT	28	24	14.20%		PSEUDOMONAS	POSITIVE	PARTIAL	YES				
124	CONTROL GROU	42	MALE	TRAUMATIC	PRESENT	SINCE 20 YEARS ON IRREGULAR MEDICATIONS	D OF FOOT, MS OF LEG ,LS OF LEG	29	20	31%	7.30%	KLEBSIELLA	POSITIVE	COMPLETE	YES				
125	CONTROL GROU	60	MALE	SPONTANEOUS	ABSENT		D OF FOOT, MS OF LEG	24	21	12.50%		PSEUDOMONAS	POSITIVE	COMPLETE	YES				
126	CONTROL GROU	55	MALE	SPONTANEOUS	ABSENT		D OF FOOT	28	24	14%		PSEUDOMONAS	NEGATIVE	PARTIAL	YES				

127	CONTROL GROU	65	MALE	TRAUMATIC	ABSENT		D OF FOOT	50	45	10%		ACINETOBACTER BAUMANNII	POSITIVE	COMPLETE	YES			
128	CONTROL GROU	35	MALE	SPONTANEOUS	ABSENT		D OF FOOT , MS OF LEG	23	18	21.70%		PSEUDOMONAS	NEGATIVE	COMPLETE	YES			
129	CONTROL GROU	75	MALE	TRAUMATIC	PRESENT	SINCE 5 YEARS ON T.GLYCOMET	D OF FOOT , MS OF LEG	34	30	11.70%	9.70%	KLEBSIELLA	POSITIVE	PARTIAL	YES			
130	CONTROL GROU	35	MALE	SPONTANEOUS	ABSENT		D OF FOOT	48	42	12.50%		PSEUDOMONAS	POSITIVE	COMPLETE	YES			
131	CONTROL GROU	65	MALE	SPONTANEOUS	ABSENT		D OF FOOT	45	40	11.10%		PSEUDOMONAS	NEGATIVE	COMPLETE	YES			
132	CONTROL GROU	74	MALE	SPONTANEOUS	PRESENT	SINCE 6 YEARS ON METFORMIN	D OF FOOT	45	32	28.80%	7.20%	KLEBSIELLA	NEGATIVE	COMPLETE	YES			
133	CONTROL GROU	72	MALE	TRAUMATIC	PRESENT	SINCE 30 YEARS ON IRREGULAR MEDICATIONS	D OF FOOT , MS OF LEG	48	38	21%	9.80%	KLEBSIELLA	POSITIVE	COMPLETE	YES			
134	CONTROL GROU	70	MALE	TRAUMATIC	ABSENT		D OF FOOT	80	70	12.50%		STERILE	NEGATIVE	COMPLETE	YES			
135	CONTROL GROU	56	MALE	SPONTANEOUS	ABSENT		D OF FOOT	70	54	23%		PSEUDOMONAS	POSITIVE	COMPLETE	YES			
136	CONTROL GROU	57	MALE	SPONTANEOUS	ABSENT		D OF FOOT	40	36	10%		PSEUDOMONAS	NEGATIVE	PARTIAL	YES			
137	CONTROL GROU	52	MALE	SPONTANEOUS	ABSENT		MS OF LEG	24	20	16.60%		PSEUDOMONAS	POSITIVE	COMPLETE	YES			
138	CONTROL GROU	50	MALE	SPONTANEOUS	ABSENT		D OF FOOT	80	72	10%		KLEBSIELLA	NEGATIVE	COMPLETE	YES			
139	CONTROL GROU	61	MALE	TRAUMATIC	PRESENT	SINCE 4 YEARS ON T. METFORMIN	LS OF LEG	30	20	33.30%	8.00%	ESCHERICHIA COLI	POSITIVE	COMPLETE	YES			
140	CONTROL GROU	30	MALE	SPONTANEOUS	ABSENT		D OF FOOT	54	48	11.10%		STERILE	NEGATIVE	PARTIAL	YES			
141	CONTROL GROU	39	MALE	SPONTANEOUS	ABSENT		MS OF LEG	18	15	16.60%		STAPHYLOCCOCUS AUREUS	NEGATIVE	COMPLETE	YES			
142	CONTROL GROU	45	MALE	SPONTANEOUS	ABSENT		D OF FOOT	40	35	12.50%		KLEBSIELLA	NEGATIVE	COMPLETE	YES			
143	CONTROL GROU	50	MALE	SPONTANEOUS	ABSENT		D OF FOOT	32	28	12.50%		ESCHERICHIA COLI	POSITIVE	COMPLETE	YES			
144	CONTROL GROU	42	MALE	SPONTANEOUS	ABSENT		D OF FOOT	20	12	40%		KLEBSIELLA	POSITIVE	COMPLETE	YES			
145	CONTROL GROU	62	FEMALE	SPONTANEOUS	ABSENT		D OF FOOT	28	24	14.20%		STAPHYLOCCOCUS AUREUS	POSITIVE	PARTIAL	YES			
146	CONTROL GROU	60	FEMALE	TRAUMATIC	PRESENT	SINCE 15YEARS ON INJ.H ACTRAPID	D OF FOOT	15	12	20%	14.10%	PSEUDOMONAS	POSITIVE	COMPLETE	YES			
147	CONTROL GROU	52	MALE	SPONTANEOUS	ABSENT		MM OF FOOT	12	8	33%		STERILE	NEGATIVE	PARTIAL		YES		
148	CONTROL GROU	60	MALE	SPONTANEOUS	PRESENT	SINCE 6 YEARS ON T.GLIMIPRIDE	D OF FOOT	48	42	12%	18.10%	ESCHERICHIA COLI	POSITIVE	PARTIAL	YES			
149	CONTROL GROU	25	MALE	SPONTANEOUS	ABSENT		D OF FOOT	20	12	40%		STERILE	NEGATIVE	COMPLETE	YES			
150	CONTROL GROU	65	MALE	SPONTANEOUS	ABSENT		D OF FOOT ,MS OF LEG ,LS OF LEG	42	36	14.20%		ESCHERICHIA COLI	POSITIVE	PARTIAL	YES			
151	CONTROL GROU	56	MALE	TRAUMATIC	PRESENT	SINCE 20 YEARS ON IRREGULAR MEDICATIONS	MM OF FOOT	15	12	20%	9.60%	ENTEROCOCUS FAECALIS	POSITIVE	COMPLETE	YES			
152	CONTROL GROU	36	MALE	SPONTANEOUS	ABSENT		D OF FOOT	32	28	12%		STERILE	NEGATIVE	COMPLETE	YES			
153	CONTROL GROU	26	MALE	SPONTANEOUS	ABSENT		D OF FOOT	18	15	16.60%		STERILE	NEGATIVE	COMPLETE	YES			
154	CONTROL GROU	65	MALE	SPONTANEOUS	ABSENT		D OF FOOT	48	35	27%		ESCHERICHIA COLI	POSITIVE	PARTIAL	YES			
155	CONTROL GROU	55	MALE	TRAUMATIC	PRESENT	SINCE ONE YEAR ON T.METFORMIN	D OF FOOT	30	24	20%	7.80%	PSEUDOMONAS	POSITIVE	COMPLETE	YES			
156	CONTROL GROU	75	MALE	SPONTANEOUS	ABSENT		MM OF FOOT	8	6	25%		STERILE	NEGATIVE	COMPLETE		YES		
157	CONTROL GROU	40	MALE	SPONTANEOUS	ABSENT		D OF FOOT	24	18	25%		ESCHERICHIA COLI	POSITIVE	PARTIAL		YES		
158	CONTROL GROU	36	MALE	SPONTANEOUS	ABSENT		D OF FOOT	14	12	14.20%		ESCHERICHIA COLI	POSITIVE	COMPLETE	YES			
159	CONTROL GROU	55	MALE	SPONTANEOUS	ABSENT		MS OF LEG	27	24	11.10%		STERILE	NEGATIVE	COMPLETE	YES			
160	CONTROL GROU	59	MALE	TRAUMATIC	ABSENT		LS OF LEG	28	24	14.20%		STERILE	NEGATIVE	PARTIAL	YES			
161	CONTROL GROU	55	MALE	SPONTANEOUS	ABSENT		D OF FOOT	42	30	19%		KLEBSIELLA	NEGATIVE	COMPLETE	YES			
162	CONTROL GROU	55	MALE	TRAUMATIC	ABSENT		D OF FOOT	48	42	12%		ESCHERICHIA COLI	POSITIVE	COMPLETE	YES			
163	CONTROL GROU	55	MALE	SPONTANEOUS	ABSENT		D OF FOOT, MS OF LEG	48	41	14.50%		KLEBSIELLA	NEGATIVE	COMPLETE	YES			
164	CONTROL GROU	48	MALE	SPONTANEOUS	PRESENT	SINCE 5 YEARS ON T.GLYCOMET	D OF FOOT, MS OF LEG	14	12	14.20%	15%	ESCHERICHIA COLI	POSITIVE	PARTIAL	YES			
165	CONTROL GROU	65	FEMALE	SPONTANEOUS	ABSENT		D OF FOOT	28	24	14%		PSEUDOMONAS	NEGATIVE	COMPLETE	YES			
166	CONTROL GROU	58	MALE	TRAUMATIC	ABSENT		D OF FOOT	28	18	35.70%		PSEUDOMONAS	NEGATIVE	PARTIAL	YES			
167	CONTROL GROU	48	FEMALE	SPONTANEOUS	ABSENT		D OF FOOT	28	21	25%		ESCHERICHIA COLI	POSITIVE	COMPLETE	YES			
168	CONTROL GROU	40	MALE	SPONTANEOUS	ABSENT		MS OF LEG	40	35	12%		STAPHYLOCCOCUS AUREUS	NEGATIVE	PARTIAL	YES			
169	CONTROL GROU	45	MALE	SPONTANEOUS	ABSENT		D OF FOOT	80	63	21.20%		PSEUDOMONAS	POSITIVE	COMPLETE	YES			
170	CONTROL GROU	72	MALE	TRAUMATIC	ABSENT		D OF FOOT , MS OF LEG	54	41	24%		KLEBSIELLA	NEGATIVE	PARTIAL	YES			
171	CONTROL GROU	45	MALE	SPONTANEOUS	ABSENT		LS OF LEG	24	20	16.60%		STAPHYLOCCOCUS AUREUS	POSITIVE	COMPLETE	YES			
172	CONTROL GROU	41	MALE	SPONTANEOUS	ABSENT		MM OF FOOT	15	10	33.30%		ESCHERICHIA COLI	NEGATIVE	PARTIAL	YES			
173	CONTROL GROU	63	MALE	TRAUMATIC	PRESENT	SINCE 9 YEARS ON IRREGULAR MEDICATIONS	D OF FOOT , MS OF LEG	33	24	27%	8.40%	STAPHYLOCCOCUS AUREUS	POSITIVE	COMPLETE	YES			
174	CONTROL GROU	50	MALE	SPONTANEOUS	ABSENT		D OF FOOT	28	18	35.70%		PSEUDOMONAS	NEGATIVE	PARTIAL	YES			
175	CONTROL GROU	49	FEMALE	SPONTANEOUS	ABSENT		D OF FOOT , LS OF LEG	60	41	31.60%		KLEBSIELLA	POSITIVE	COMPLETE	YES			
176	CONTROL GROU	43	MALE	SPONTANEOUS	ABSENT		D OF FOOT	24	20	16%		STAPHYLOCCOCUS AUREUS	NEGATIVE	PARTIAL	YES			
177	CONTROL GROU	32	FEMALE	SPONTANEOUS	ABSENT		D OF FOOT , MS OF LEG	27	24	11.10%		STAPHYLOCCOCUS AUREUS	POSITIVE	COMPLETE	YES			
178	CONTROL GROU	60	FEMALE	TRAUMATIC	ABSENT		D OF FOOT	15	12	20%		STAPHYLOCCOCUS AUREUS	POSITIVE	COMPLETE	YES			
179	CONTROL GROU	75	MALE	TRAUMATIC	PRESENT	SINCE ONE YEAR ON MEDICATIONS	D OF FOOT, MS OF LEG	54	41	30.50%	8.50%	KLEBSIELLA	POSITIVE	PARTIAL	YES			
180	CONTROL GROU	62	MALE	SPONTANEOUS	ABSENT		D OF FOOT, LS OF LEG	72	50	30.50%		KLEBSIELLA	POSITIVE	COMPLETE	YES			
181	CONTROL GROU	55	MALE	TRAUMATIC	PRESENT	SINCE 20 YEARS ON T.GLIMIPRIDE	D OF FOOT	30	24	20%	9.40%	STAPHYLOCCOCUS AUREUS	POSITIVE	PARTIAL	YES			
182	CONTROL GROU	60	MALE	SPONTANEOUS	PRESENT	SINCE 4 YEARS ON T. METFORMIN	D OF FOOT	48	35	27%	8.50%	KLEBSIELLA	POSITIVE	COMPLETE	YES			
183	CONTROL GROU	62	MALE	SPONTANEOUS	PRESENT	SINCE ONE YEAR ON MEDICATIONS	D OF FOOT	48	32	33.30%	8.30%	KLEBSIELLA	POSITIVE	COMPLETE	YES			
184	CONTROL GROU	48	FEMALE	SPONTANEOUS	ABSENT		D OF FOOT	24	20	16%		STERILE	NEGATIVE	PARTIAL	YES			
185	CONTROL GROU	65	MALE	TRAUMATIC	ABSENT		D OF FOOT	28	24	14.20%		PSEUDOMONAS	POSITIVE	COMPLETE	YES			
186	CONTROL GROU	62	MALE	SPONTANEOUS	ABSENT		MS OF LEG	56	42	25%		KLEBSIELLA	NEGATIVE	COMPLETE	YES			
187	CONTROL GROU	45	FEMALE	SPONTANEOUS	PRESENT	SINCE ONE MONTH ON MEDICATIONS	D OF FOOT , MS OF LEG	26	18	30%	11.40%	STAPHYLOCCOCUS AUREUS	POSITIVE	PARTIAL	YES			
188	CONTROL GROU	65	MALE	TRAUMATIC	ABSENT		D OF FOOT	40	28	30%		STERILE	NEGATIVE	PARTIAL	YES			
189	CONTROL GROU	25	MALE	SPONTANEOUS	ABSENT		D OF FOOT	15	12	20%		STERILE	NEGATIVE	COMPLETE	YES			
190	CONTROL GROU	58	MALE	SPONTANEOUS	ABSENT		D OF FOOT	12	8	33.30%		STAPHYLOCCOCUS AUREUS	POSITIVE	COMPLETE		YES		
191	CONTROL GROU	30	MALE	SPONTANEOUS	ABSENT		D OF FOOT	54	40	26%		PSEUDOMONAS	NEGATIVE	PARTIAL	YES			
192	CONTROL GROU	25	FEMALE	SPONTANEOUS	ABSENT		D OF FOOT	32	28	12%		KLEBSIELLA	NEGATIVE	COMPLETE	YES			
193	CONTROL GROU	45	FEMALE	SPONTANEOUS	PRESENT	SINCE ONE YEAR ON MEDICATIONS	P OF FOOT	12	2	83%	14.30%	KLEBSIELLA	POSITIVE	PARTIAL		YES		
194	CONTROL GROU	60	FEMALE	TRAUMATIC	PRESENT	SINCE 30 YEARS ON MEDICATIONS	D OF FOOT	28	18	36%	8.40%	KLEBSIELLA	POSITIVE	COMPLETE	YES			
195	CONTROL GROU	45	MALE	SPONTANEOUS	ABSENT		D OF FOOT , MS OF LEG	29	24	17.20%		PSEUDOMONAS	NEGATIVE	COMPLETE	YES			
196	CONTROL GROU	65	MALE	SPONTANEOUS	ABSENT		MS OF LEG	30	24	20%		STAPHYLOCCOCUS AUREUS	POSITIVE	COMPLETE	YES			
197	CONTROL GROU	65	FEMALE	TRAUMATIC	ABSENT		D OF FOOT	32	21	34.30%		KLEBSIELLA	NEGATIVE	PARTIAL	YES			
198	CONTROL GROU	44	MALE	SPONTANEOUS	ABSENT		D OF FOOT	24	15	37.50%		STAPHYLOCCOCUS AUREUS	POSITIVE	COMPLETE	YES			
199	CONTROL GROU	49	FEMALE	SPONTANEOUS	ABSENT		D OF FOOT	48	35	27%		KLEBSIELLA	POSITIVE	COMPLETE	YES			
200	CONTROL GROU	50	MALE	SPONTANEOUS	ABSENT		P OF FOOT	12	8	33.30%		PSEUDOMONAS	NEGATIVE	COMPLETE		YES		
201	CONTROL GROU	57	FEMALE	SPONTANEOUS	ABSENT		D OF FOOT	30	20	33%		ESCHERICHIA COLI	POSITIVE	PARTIAL	YES			
202	CONTROL GROU	63	MALE	TRAUMATIC	ABSENT		D OF FOOT	70	54	23%		STERILE	NEGATIVE	PARTIAL	YES			
203	CONTROL GROU	18	MALE	SPONTANEOUS	ABSENT		D OF FOOT , MS OF LEG	32	18	43.70%		PSEUDOMONAS	POSITIVE	COMPLETE	YES			
204	CONTROL GROU	56	MALE	SPONTANEOUS	PRESENT	SINCE 10 YEARS ON T.GLYCOMET	D OF FOOT	90	72	20%	7.30%	KLEBSIELLA	POSITIVE	COMPLETE	YES			
205	CONTROL GROU	65	MALE	SPONTANEOUS	ABSENT		D OF FOOT	40	28	30%		STERILE	NEGATIVE	COMPLETE	YES			
206	CONTROL GROU	71	MALE	TRAUMATIC	ABSENT		D OF FOOT	28	18	35%		PSEUDOMONAS	NEGATIVE	PARTIAL	YES			
207	CONTROL GROU	65	MALE	TRAUMATIC	ABSENT		MS OF LEG	18	15	16%		STAPHYLOCCOCUS AUREUS	POSITIVE	PARTIAL	YES			
208	CONTROL GROU	31	MALE	SPONTANEOUS	ABSENT		D OF FOOT	48	42	12.50%		ESCHERICHIA COLI	POSITIVE	COMPLETE	YES			
209	CONTROL GROU	56	FEMALE	SPONTANEOUS	ABSENT		D OF FOOT	90	72	20%		STAPHYLOCCOCUS AUREUS	NEGATIVE	PARTIAL	YES			
210	CONTROL GROU	60	MALE	TRAUMATIC	PRESENT	SINCE 20 YEARS ON IRREGULAR MEDICATIONS	D OF FOOT , MS OF LEG	26	14	46.10%	16.40%	STAPHYLOCCOCUS AUREUS	POSITIVE	COMPLETE	YES			
211	CONTROL GROU	75	FEMALE	SPONTANEOUS	ABSENT		MS OF LEG	15	8	46%		STAPHYLOCCOCUS AUREUS	NEGATIVE	PARTIAL		YES		
212	CONTROL GROU	47	MALE	SPONTANEOUS	ABSENT		LS OF LEG	12	2	83%		STERILE	NEGATIVE	COMPLETE			YES	
213	CONTROL GROU	46	MALE	SPONTANEOUS	ABSENT		D OF FOOT	28	18	35.70%		PROTEUS MIRABILUS	POSITIVE	COMPLETE	YES			
214	CONTROL GROU	34	MALE	SPONTANEOUS	ABSENT		D OF FOOT	42	30	28.50%		STAPHYLOCCOCUS AUREUS	NEGATIVE	PARTIAL	YES			
215	CONTROL GROU	30	MALE	SPONTANEOUS	ABSENT		D OF FOOT	48	42	12.50%		PROTEUS MIRABILUS	POSITIVE	PARTIAL	YES			
216	CONTROL GROU	40	MALE	SPONTANEOUS	ABSENT	SINCE 5 YEARS ON T.METFORMIN	D OF FOOT	35	30	14.20%	11.40%	KLEBSIELLA	NEGATIVE	COMPLETE	YES			
217	CONTROL GROU	37	MALE	SPONTANEOUS	ABSENT		P OF FOOT	6	0	100%		STAPHYLOCCOCUS AUREUS	POSITIVE	PARTIAL			YES	
218	CONTROL GROU	47	MALE	SPONTANEOUS	PRESENT	SINCE 8 YEARS ON T.METFORMIN	D OF FOOT	24	18	25%	6.90%	KLEBSIELLA	POSITIVE	COMPLETE	YES			
219	CONTROL GROU	65	MALE	TRAUMATIC	ABSENT		D OF FOOT	48	35	27%		KLEBSIELLA	NEGATIVE	COMPLETE	YES			
220	CONTROL GROU	25	MALE	SPONTANEOUS	PRESENT		D OF FOOT	18	12	33.30%		STAPHYLOCCOCUS AUREUS	NEGATIVE	PARTIAL		YES		
221	CONTROL GROU	25	FEMALE	SPONTANEOUS	ABSENT		MM OF FOOT	6	0	100%		STERILE	NEGATIVE	COMPLETE			YES	
222	CONTROL GROU	45	FEMALE	SPONTANEOUS	PRESENT	SINCE 3 YEARS ON T.METFORMIN	D OF FOOT	35	30	14%	7.60%	KLEBSIELLA	POSITIVE	PARTIAL	YES			
223	CONTROL GROU	65	MALE	TRAUMATIC	ABSENT		D OF FOOT	24	20	16.60%		KLEBSIELLA	NEGATIVE	COMPLETE	YES			
224	CONTROL GROU	45	MALE	SPONTANEOUS	ABSENT		D OF FOOT	15	8	46.60%		KLEBSIELLA	NEGATIVE	COMPLETE		YES		
225	CONTROL GROU	66	MALE	TRAUMATIC	ABSENT		D OF FOOT	21	18	14%		PROTEUS MIRABILUS	POSITIVE	PARTIAL	YES			